MINISTRY OF PUBLIC HEALTH OF UKRAINE
THE NATIONAL UNIVERSITY OF PHARMACY

ACTUAL QUESTIONS OF DEVELOPMENT OF NEW DRUGS

BOOK OF ABSTRACTS OF XX INTERNATIONAL SCIENTIFIC AND PRACTICAL CONFERENCE OF YOUNG SCIENTISTS AND STUDENTS, DEVOTED TO THE 90TH ANNIVERSARY OF DOCTOR OF SCIENCE IN PHARMACY, PROFESSOR DMITRI PAVLOVYCH SALO

April 25-26, 2013
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А43 **Актуальні питання створення нових лікарських засобів:** тези доповідей всеукраїнської науково-практичної конференції молодих вчених та студентів (25-26 квітня 2013 р.). – Х.: Вид-во, 2013. – 316 С.

Збірка містить матеріали науково-практичної конференції молодих вчених та студентів «Актуальні питання створення нових лікарських засобів».

Матеріали згруповано за провідними напрямками науково-дослідної та навчальної роботи Національного фармацевтичного університету. Розглянуто теоретичні та практичні аспекти синтезу біологічно-активних сполук і створення на їх основі лікарських субстанцій; стандартизації ліків, фармацевтичного та хіміко-технологічного аналізу; вивчення рослинної сировини та створення фітопрепаратів; сучасної технології ліків та екстемпоральної рецептури; біотехнології у фармації; досягнень сучасної фармацевтичної мікробіології та імунології; доклінічних досліджень нових лікарських засобів; фармацевтичної опіки рецептурних та безрецептурних лікарських препаратів; доказової медицини; сучасної фармакотерапії, соціально-економічних досліджень у фармації, маркетингового менеджменту та фармакоекономіки на етапах створення, реалізації та використання лікарських засобів; управління якістю у галузі створення, виробництва і обігу лікарських засобів; інформаційниих технологій у фармації та медицині; основ педагогіки та психології; суспільствознавства; філології.

Для широкого кола наукових і практичних працівників фармації та медицини.

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Editorial board: *corresponding member of NAS of Ukraine Chernykh V.P, prof. Kovalenko S.N., Zatylnikova O.O., Andriyanenkov O.V.*
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A43 **Actual Questions Of Development of New Drugs:** Abstracts of XX International Scientific And Practical Conference Of Young Scientists And Student (April 25-26, 2013). – Kh.: Publishing Office, 2013. – 316 P.

Book of Abstracts includes materials of Scientific and Practical Conference of Young Scientists and Students «Actual questions of development of new drugs».

Materials are groupped according to the main directions of scientific, research and educational work of the National University of Pharmacy. Teoretical and practical aspects of the synthesis of biologically active compounds and development of medicinal substances on their basis; standardization of drugs, pharmaceutical and chemical-technological analysis, the study of raw materials and herbal remedies development, modern drug technology and extemporal recipe; biotechnology in pharmacy, modern advances in pharmaceutical microbiology and immunology, clinical trials of new drugs, pharmaceutical care for prescription and OTC-drugs, evidence-based medicine, modern pharmacotherapy, socio-economic studies in pharmacy, marketing management and pharmacoeconomics during the development, implementation and use of drugs, quality management in development, production and trafficking of drugs; information technologies in pharmacy and medicine; basics of pedagogy and psychology; social science; philology are presented.

For a wide audience of scientists and pharmaceutaical and medicinal employees.

UDC 615.1

Шановні колеги!

Прийміть найщиріші вітання від Організаційного комітету XX Міжнародної науково-практичної конференції молодих вчених та студентів «Актуальні питання створення нових лікарських засобів», яка в цьому році присвячена 90-річчю від дня народження доктора фармацевтичних наук, професора Дмитра Павловича Сало.

Метою роботи конференції є знайомство з новими розробками видатних вчених, можливість обміну досвідом, науковими задумами та ідеями, представлення та обговорення результатів роботи, можливість почути оцінку своєї роботи з боку відомих фахівців. Крім того, Конференція надає нові враження, натхнення студентам та молодим вченим для нових відкриттів.

Беручи до уваги важливість інтеграції потенціалу вітчизняних вчених у світову наукову спільноту, а також у зв'язку з великою зацікавленістю іноземних колег нашими здобутками та планами, цьогорічну збірку тез доповідей було вирішено видати англійською мовою – мовою міжнародного спілкування.

У збірці тез Міжнародної науково-практичної конференції студентів та молодих вчених «Актуальні питання створення нових лікарських засобів» представлено матеріали досліджень молодих науковців та студентів вищих навчальних закладів України, Росії, Казахстану та Іспанії.

Щиро бажаємо делегатам та учасникам наукового молодіжного форуму творчих звершень, плідних контактів, міцного здоров'я, успіхів у реалізації життєвих планів і наукових ідей!

З повагою, Організаційний комітет.

Dear colleagues!

Please accept sincere congratulations from the Organizing Committee of the XX International Scientific and Practical Conference of Young Scientists and Students «Actual questions of development of new drugs», devoted to the 90th anniversary of Doctor of Science in Pharmacy, Professor Dmitri Pavlovych Salo.

The aim of the Conference is to familiarize scientific authority with new developments of prominent scientists, to exchange experience, research conceptions and ideas, to represent and discuss the research results, also the Conference provides an opportunity to hear the assessment of work by renowned experts. Moreover, the Conference gives new experiences and inspiration to students and young scientists for new discoveries.

Given the importance of integration of Ukrainian scientists' potential to the international scientific community, but also due to the high interest of foreign colleagues in our achievements and plans, this year's Book of Abstracts was decided to be published in English - the language of international communication.

In the Book of Abstracts of the International Scientific and Practical Conference of Young Scientists and Students «Actual questions of development of new drugs» research materials of young scientists and students of higher educational establishments of Ukraine, Russia, Kazakhstan and Spain are presented.

We wish the delegates and participants of the Youth Forum creative achievements, productive contacts, good health, successful life plans realization and scientific ideas implementation!

Sincerely, Organizing Committee.

SECTION 1

SYNTHESIS OF PHYSIOLOGICALLY ACTIVE SUBSTANCES

MICROWAVE SYNTHESIS AND QUANTITATIVE DETERMINATION OF PHARMACOLOGICALLY ACTIVE OF 3,5-DIBROMO-N-PHENYLANTHRANILIC ACIDS BY TWO-PHASE TITRATION

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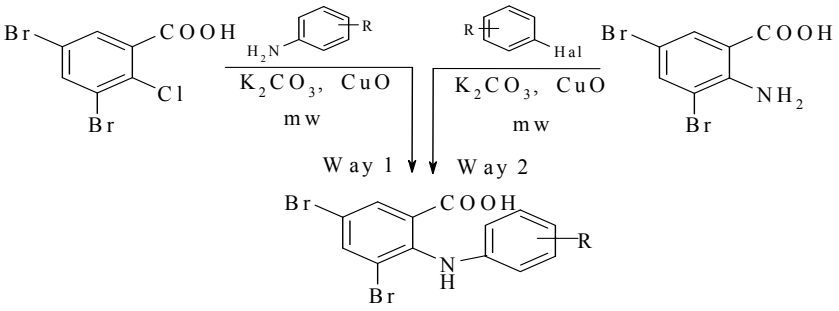
According to the literature derivatives of anthranilic acids are the parent compound for the synthesis of many drugs with different pharmacological actions, and the method of their quality control has significant drawbacks, including significant time.

The aim of our work was to develop a method for the synthesis of 3,5-dibromo-N-phenylanthranilic acids under microwave irradiation and also to develop an express method of their quantitative determination.

The synthesis of 3,5-dibromo-N-phenylanthranilic acids was carried out by reacting of 3,5-dibromo-2-chlorobenzoic acid with arylamines (way 1) and arylation of 3,5-dibromoanthranilic acid by substituted of halogen benzene (way 2) among the n-amyl alcohol, in the presence of copper oxide, and potassium carbonate, in the microwave reactor at 180 °C:



For the quantitative determination of synthesizing acids was developed the method by the two-phase titration. The method consists in the direct titration with 0.1 M solution of NaOH of the two-phase system, consisting of the organic phase, which contains the analyzed substance (not soluble in water) and the aqueous phase, where the indicator - phenolphthalein. This extraction equilibrium is disturbed and the sodium salt of 3,5-dibromo-N-phenylanthranilic acid passes into the aqueous phase. The experimentally selected n-octanol, as organic phase, which had the highest solubility of the test compounds. These data of quantify of the new compounds by two-phase titration, characterized by a high accuracy and representativeness. The relative error of this method is less than 0.5%. Given technique an express, reliable, and favorably differs from the method of potentiometric titration.

The synthesized 3,5- dibromo-N-phenylanthranilic acid have been subjected to pharmacological screening for anti-inflammatory, analgesic, diuretic, antibacterial and antifungal activity, and exceeded the activity of reference drugs.

NOVEL TETRAZOLO[1,5-C]QUINAZOLINE-(6H)-5-ONES(THIONES) DERIVARIVES AS PROSPECTIVE ACTOPROTECTORS

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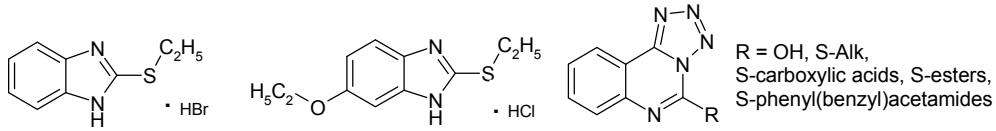
Introduction. Professional activity of the modern man often carried out under conditions of prolonged influence of unfavorable physical and chemical factors, continuous emotional stress, that can cause disadaptation of the body with subsequent illness, decrease of immunity system. In extreme situations, it is necessary to prevent or quickly remove the physical fatigue that occurs during the work. Chemicals, that are dealing with such problems, are known as actoprotectors: drugs for the stimulation of efficiency, which increase resistance to the acute oxygen deficiency and high ambient temperatures. The common representatives of actoprotectors are benzimidazole derivatives - Bemithylum and Etomerzolum, which exhibit sufficient actoprotective activity (Fig.).



Bemithylum Etomerzolum Tetrazolo[1,5-*c*]quinazoline

In spite of the high necessity in the pharmaceutical market, the range of such drugs is quite limited. So, the purpose of the study was to explore the actoprotective activity among new biologically active condensed heterocyclic tetrazolo[1,5-c]quinazoline-(6H)-5-ones(thiones) derivatives.

Materials and methods. The novel tetrazolo[1,5-c]quinazoline-(6H)-5-ones(thiones) derivatives were obtained and further studied for actoprotective activity at the Pharmacology Department of Vinnitsa National Medical University named after M.I. Pirogov at the 327 linear white rats of both sexes weighing 180-230 g. Control groups were formed with 13 rats, and the remaining animals were divided into the groups of six ones. Actoprotective activity was assessed by swimming test with additional weight in normotermia, hyperthermia and hypothermia.

Results. It was determined that derivatives of tetrazolo[1,5-c]quinazoline as well as Bemithylum show actoprotective activity, manifested by longer swimming test in normo-, hyper-and hypothermia. Leader compounds in normothermia appeared to be namely 5-S-derivatives of tetrazolo[1,5-c]quinazoline.

Conclusions. 5-Substituted tetrazolo[1,5-c]quinazoline-(6H)-5-ones(thiones) turned to reveal actoprotective effect besides already proven fungicide, bactericidal, and anticancer activities.

SYNTHESIS OF SUBSTITUTED 2-HETERYL-[1,2,4]TRIAZOLO [1,5-C]QUINAZOLIN-5(6*H*)-ONES AS POTENTIAL ANTICANCER DRUGS

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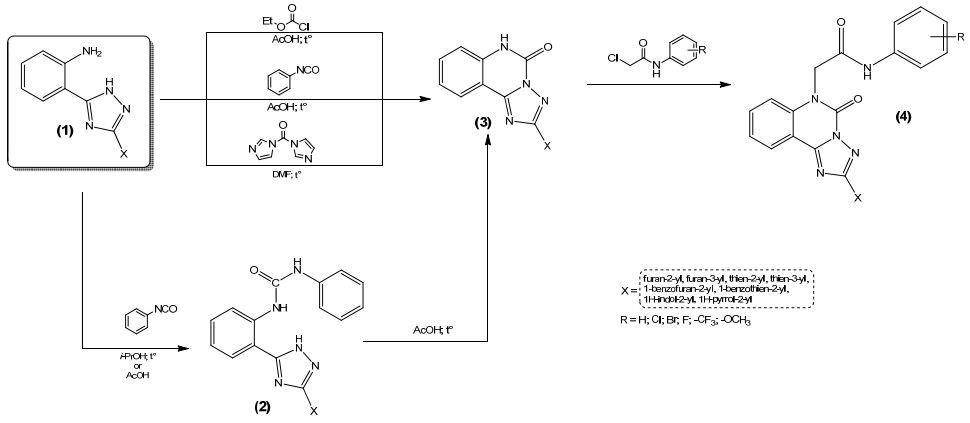
There is a significant amount of works which devoted to annulation of triazole cycle to quinazoline fragment with forming of 1,2,4-tryazoloquinazolines, and the synthesis of [1,2,4]triazolo[c]quinazolines systems are widely known and understood. It is known that derivatives of [1,2,4]triazolo[1,5-*c*]quinazolines have diversified pharmacological activity. Among these was found compounds with high anticancer, antimicrobial, antiviral, antifungal, nootropic action etc.

Following our work on the research of heterocyclizations of [2-(3-heteryl-[1,2,4]triazolo-5-yl)phenyl]amines (1) as classically 1,5-NCCCN-binucleophiles with electrophilic reagents, we have investigated the interaction of compounds (1) with isocyanates, N,N'-carbonyldiimidazole and ethyl chloridocarbonate. The results showed that 5-oxo substituted was formed, and in the case of two-stage synthesis with isocyanates initially formed corresponding ureas (2), which was cycled in compound (3). Further, compounds (3) were modified by reaction with 2-chloro-N-phenylacetamides to form the corresponding derivatives (4).



The structure of the synthesized compounds and the direction of the reaction [5+1] cyclocondensation was definitely proved with the LC-MS, ^{1}H, ^{13}C, NMR and mass spectra. It was conducted initial screening of all of obtained compounds on anticancer activity.

SYNTHESIS AND ACID BASE PROPERTIES OF 4,5-DIMETHOXY–N-PHENYLANTHRANILIC ACIDS IN BINARY SOLVENT DIOXANE – WATER

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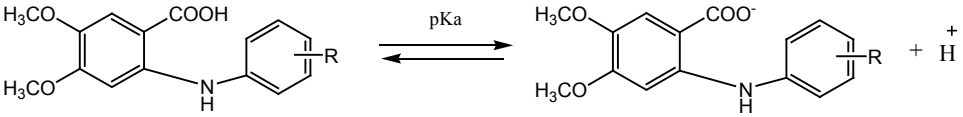
The derivatives of N-phenylanthranilic acids make up a promising group for the search of new biologically active compounds. The substances with high anti-inflammatory, analgesic and diuretic activity were found among these compounds. 4,5-Dimethoxy- N-phenylanthranilic acids were prepared according to the Ulman's reaction by reacting of 4,5-dimethoxy-2-chlorobenzoic acid with aromatic amines in the solid phase without a solvent in the presence of a copper catalyst and potassium carbonate.

Ionization constants of the acids were determined by potentiometric titration in the binary dioxane – water solutions (60 vol/% of dioxan) at 25 °C:



Isonization pKa of the derivatives of 4,5-dimethoxy-N-phenylanthranilic acids in binary solutions of dioxane and water at 25 °C

N	R	Output,%	pKa
1	H	92	7,44±0,03
2	2'-CH_3	94	7,56±0,02
3	4'-CH_3	95	7,58±0,03
4	3',4'-$(CH_3)_2$	95	7,61±0,04
5	4'-OCH_3	90	7,63±0,02
6	4'-OC_2H_5	94	7,65±0,02
7	4'-OC_3H_7	92	7,67±0,02
8	4'-Cl	93	7,27±0,02
9	4'-Br	96	7,28±0,03

The influence of the substituent's nature and position in the non-anthranilic fragments of N-phenylanthranilic acids on their pKa has been analyzed.

BIOSYNTHETIC ABILITY EDIBLE MUSHROOMS FAMILY PLEUROTUS UNDER ELECTROMAGNETIC RADIATION

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Basidiomycetes are source of complete protein and biologically active substances. In many countries (Japan, Germany, France, the USA, etc.) they are using as producers of commercially important substances with pharmacological properties.

In scientific sources there are many evidences of a pronounced anti-inflammatory activity of extracts from fungi P. ostreatus, availability in it of lovastatin, antioxidant Ergothioneine. But important value is the ability of fungi Pleurotus in formation of antibiotic substances.

Support of original biosynthetic activity of production strains and in some cases of exceeded - is a complex task that requires searching of new alternative methods.

The purpose of the work is to study the influence of electromagnetic fields (EMF) on the linear growth rate of higher Basidiomycetes FAMILY Pleurotus.

The object of the study was higher Basidiomycetes cultures from collection of the Department of Mycology Institute of Botany. MG Kholodny NAS of Ukraine: Pleurotus ostreatus (Jacg.: Fr.) Kumm 1684 and Pleurotus sajor-caju (Fr.) Sing 1,661. These cultures are characterized by a high rate of fruiting and the ability to grow on various substrates. Growth of higher fungi pure cultures was studied on glucose-potato agar after 10 -, 20 - and 40-min influence of EMF on 8 - and 14-day culture. In parallel was made a control experiment. EMF was created by the linear induction machine (LIA).

Maximum. magnification of linear growth in fungi is achieved within 20 min of field influence with control for both 8 – and 14-day old cultures and according is: for Pl. ostreatus - 10.25 and 14% for Pl. sajor-caju - 23.67 i 25.75%. Experiments showed that the 40-min processing by EMF inhibits the growth of studied fungi, and 10-minute action is not enough to stimulate their biosynthetic ability. The reason of the increasing biosynthetic ability of biologically active substances is an active action of EMF with induction 0.1 Tl and frequency 50 Hz on the enzyme systems of cells that accelerates the transport of nutrients and metabolic products formation. To verify in reliably validity of this hypothesis need to conduct some researches on the molecular level.

Conclusions: 1) the effect of stimulation of biosynthetic ability by EMF depends on the duration of the field action and of the inoculum, 2) it was found that a sign of increased biosynthetic ability after electromagnetic treatment of cultures Pleurotus is not fixed genetically and has the ability to reversion.

DESIGNING NEW TYROSINE KINASE INHIBITORS AS ONE OF THE STAGES OF DEVELOPING A NEW ANTITUMOR DRUG

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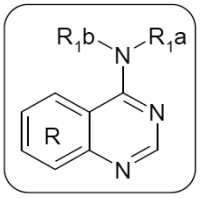
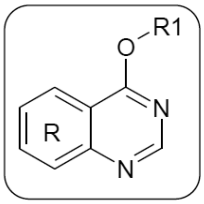
The increase in varieties of oncological disease requires the development of new drugs with more selective actions. We have analyzed modern medicines that belong to the so-called “targeted” drugs, which have been recently identified as the most promising in the field of oncology. Angiogenesis inhibitor drugs, are identified as one of the main drugs in the “targeted” group. Tyrosine kinase inhibitors, based on the number of substances of synthetic origin, are actively being investigated as antiangiogenic drugs for the treatment of malignancies.

In the construction of organic molecules - promising tyrosine kinase inhibitors, we have chosen two basic structures: 4-N-alkyl substituted quinazolin and 4-O-aryl substituted quinazolin.



4-N-alkyl substituted quinazolin



4-O-aryl substituted quinazolin

The basis of modifying the basic structures of these molecules is based on the principle of optimization of these formations by the input of these new chemical groups and fragments.

We undertook an analysis of various approaches to the synthesis of libraries of 4-N-alkyl and 4-O-aryl substituted quinazolin. Discovered were optimal methods for obtaining new compounds based on selected basic structures.

Synthesized were 40 new compounds, and their physicochemical properties (solubility, hydrophobicity, melting point) were studied. The structure of the synthesized compounds was proven by IR- and NMR-spectroscopy, and purity - by thin-layer chromatography.

Research in this area continues. There are plans to conduct biological screening of derived substances to identify compounds that exhibit the greatest antiangiogenic activity.

ANTIOXIDANTS IN SEARCH OF ORIGINAL SERIES FUNCTIONAL DERIVATIVES OF 7-R-8-THIOTHEOPHYLLINE

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In the arsenal of modern medicine, there are many effective medicines containing in the structure of molecules the active pharmaceutical ingredient free or substituted mercapto, and provide multi-directional pharmacological actions: antihypertensive (captopril), mucolytic (acetylcysteine), antioxidant (thioctic acid), antiviral (arbidol). However, the potential of this class of compounds is far from exhausted.

The results of the study of the biological activity of 7,8-disubstituted theophylline sustained earlier, indicate the effectiveness of newly synthesized compounds expressed as antioxidant agents. Therefore, we thought it appropriate to introduce the thio group in 8 position in xanthine bicycle and get a number of relevant functional derivatives.

As a starting compound used 8-bromotheophylline that the interaction with a number of alkylating agents ((2-bromoethyl)benzene, (3-chloropropyl)benzene, (3-chloroprop-1-enyl)benzene and 1-(3-chloroprop-1-ynyl)-4-fluorobenzene) forms 7-arylalkyl-8-bromotheophylline. The latest, using an excess of sodium sulfide nonahydrate, were transformed in necessary for us 7-R-8-thyotheophyllines.

Further research has focused on the synthesis and pharmacological potentials of the above substances. For this purpose, 7-R-8-thyotheophyllines disposed of S-alkylation reactions with a variety of halogenalkyles and their functional substituted. Obtained a number of derivatives of the original 7-R-8-S-theophylline, which structure and personality is proved by the use of modern physical and chemical methods of analysis. Some earlier undescribed substances were subjected to further chemical reactions, both to the chemical modification of the molecule, and produce structures with pharmacophoric groups and improve the pharmaco-technological characteristics of substances. In particular, the synthesized a number of salts and hydrazides of relevant thyoethanoic acids to 8 positions of the molecule theophylline and formed amino derivatives of 2-thioxothiazolidin-4-one.

Computer prediction was conducted biological activity of the compounds, which showed their promise in this regard, which was confirmed in further pharmacological research methods *in vitro* and *in vivo*.

A number of promising substances, the effectiveness of which is significantly higher than the reference drugs. Research in this area continues.

ALKYLATION OF 7-PHENYLSULFONYL-6,7-DIHYDRO-1*H*-CYCLOPENTA[*D*]PYRIMIDINE-2,4(3*H*,5*H*)-DIONE

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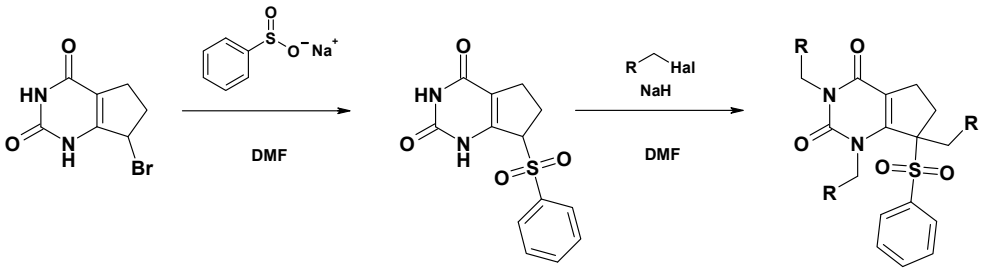
It is well known that derivatives of the 6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione have a wide range of biological activity and low toxicity. Previously, it was found that derivatives of the 6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione are able to effectively remove spasms of smooth muscles and also possess the expressed analgesic activity.

In continuation of the study of derivatives of 6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione as potential biologically active compounds we investigated the behavior of 7-phenylsulfonyl derivative of 6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione in the alkylation reactions with various alkyl halides.

7-Phenylsulfonyl-6,7-dihydro-1*H*-cyclopenta[d]pyrimidine-2,4(3*H*,5*H*)-dione was obtained by the reaction of 7-bromo-6,7-dihydro-1*H*-cyclopenta[d]pyrimidine-2,4(3*H*,5*H*)-dione with sodium sulfinate in DMF at 80 °C. The alkylation reaction of 7-phenylsulfonyl-6,7-dihydro-1*H*-cyclopenta[d]pyrimidine-2,4(3*H*,5*H*)-dione was carried out using alkyl halide, sodium hydride as a base and DMF as a solvent.

It was found that alkylation reaction carries out not only by amide group but also by a CH-fragment, which was activated by phenylsulfonyl group.



These results make it possible to obtain a wide range of new derivatives of 6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione for studies of their biological activity.

The structure of the synthesized compounds was confirmed by NMR, IR and mass-spectra methods.

SYNTHESIS OF THE OF 6-(1*H*-BENZIMIDZOL-2-YL)-5-METHYL-THIENO[2,3-*D*]PYRIMIDIN-4(3*H*)-ONE DERIVATIVES AND THEIR ALKYLATION STUDY

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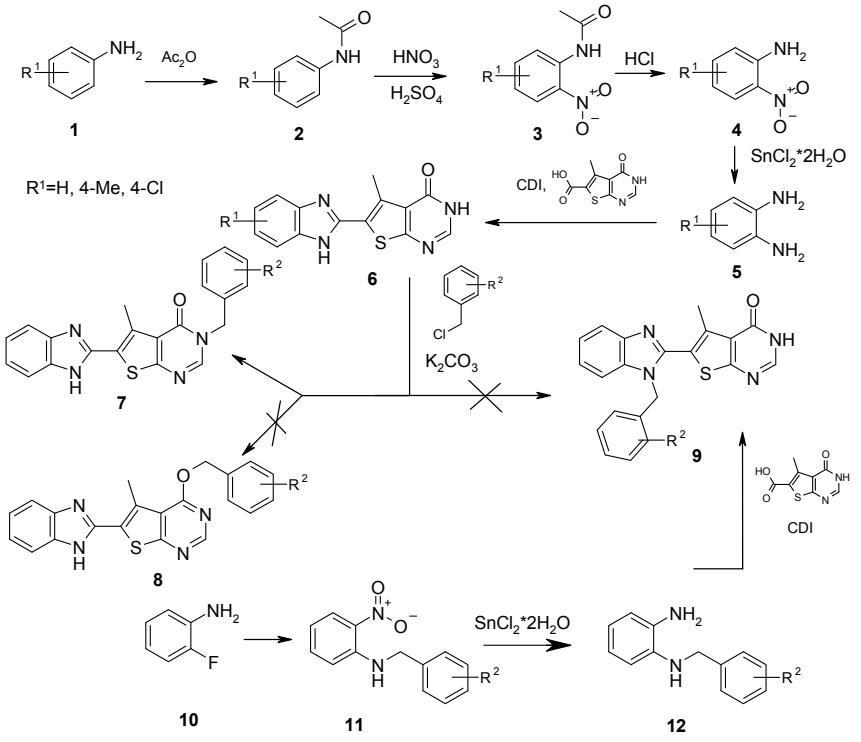
The derivatives of thieno[2,3-d]pyrimidine-4(3H)-ones are well known due to their pharmacological properties, which are extensively studied last years. Among the derivatives of benzimidazole there are many biologically active compounds together with the substances, which are already well known for the pharmaceutical market. Thus we combined these two pharmacophores into a novel heterocyclic system and studied the ways of its alkylation.



R²=H, 4-Me, 4-Cl

The synthesis has been performed according to the scheme; the compounds **6** have been obtained by interaction of *ortho*-phenylenediamines **5** with 5-methyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxylic acid imidazolide. The regioselectivity of alkylation reaction for compound **6** has been assigned by NOESY spectra. For isomeric alternative product **9**, which in the NOESY-experimental conditions may behave similarly to O-alkylated product **8**, the alternative synthesis has been performed. It was established that product **9** and compound **8** are different.

SYNTHESIS OF N^1-SUBSTITUTED 2*H*,7*H*-[1,2,4]TRIAZOLO [4,3-*A*]PYRAZINE-3,8-DIONES

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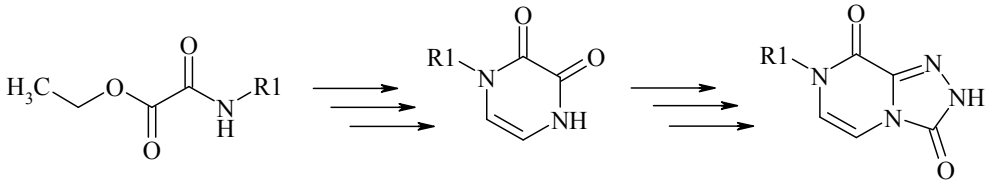
Current research in the field of cancer therapy suggests an important role of derivatives of glutamic acid in the pathogenesis of cancer. Substances that competitively inhibit interaction with glutamate AMPA and NMDA-receptors are likely to be useful in the treatment of oncological diseases. Therefore, further study of [1,2,4]triazolo[4,3-a]pyrazines that exhibit the above mentioned pharmacological effects, and creation of drugs based on them, is a perspective area of medical chemistry.

Scheme of synthesis [1,2,4]triazolo[4,3-a]pyrazines, which is frequently used in organic synthesis, starts with 2,3-dihlorpirazynes and is based on the cyclization of obtained 2-chloro-3-hidrazynopirazynes under halides of carboxylic acids followed by N-alkylation of the resulting intermediate. The disadvantage of this method is that only a limited set of substituents can be introduced to the position 7 of cyclization product.

Previously, we reported that we developed circuit of synthesis [1,2,4]triazolo [4,3-a]pyrazine-8-ones, which comes from monoamides oksalamic acid monoesters and is based on a sequential formation of 1-substituted pyrazine-2,3-diones, 3-hloropirazyn-2-ones and 3-hidrazynopirazyn-2-ones, which further in anhydrous dimethylformamide medium in the presence of 1-(1*H*-imidazol-1-ilcarbonyl)-1*H*-imidazole (CDI) is cyclized to N^1-substituted 2H,7H-[1,2,4]triazolo[4,3-a] pyrazine-3,8-diones.



The structure and purity of the obtained compounds were confirmed by elemental analysis and ^1H-NMR spectroscopy.

SYNTHESIS AND KINETICS OF ALKALINE HYDROLYSIS REACTIONS OF METHYL ESTERS OF 3,5-DINITRO AND 3,5-DICHLORO-N-PHENYLANTHRANILIC ACIDS IN BINARY DIOXANE-WATER SOLVENT

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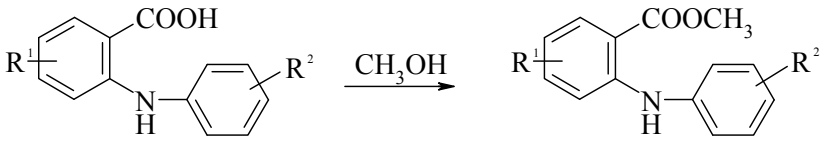
The synthesis of new methyl esters of 3,5-dinitro- and 3,5-dichloro-N-phenylanthranilic acids was carried out (scheme 1):

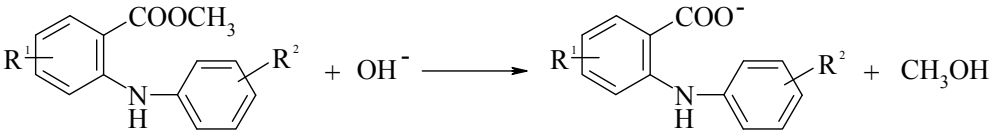
Scheme 1



The structure and purity of synthesizing compounds was confirmed by elemental, IR-, ^{1}H-NMR-spectral, chromatographic analysis and qualitative tests.

Kinetic of alkaline hydrolysis reactions of 18 derivatives of 3,5-dinitro- and 3,5-dichloro-N-phenylanthranilic acids methyl esters was studied in the mixed dioxane-water solvent in the temperature range of 45-85 °C. The reaction fits following equation:

Scheme 2



R^1 = 3,5-NO_2, 3,5-Cl; R^2 = H, 2'-CH_3, 4'-CH_3, 3',4'-$(CH_3)_2$, 4'-OCH_3, 4'-OC_2H_5, 4'-OC_3H_7, 4'-Cl, 4'-Br

Bimolecular reactions rate constants, energy, enthalpy, entropy and free activation energy have been calculated. Effects of electronic nature and position of substituents in non-anthranilic molecule fragment of substrate on above-mentioned parameters have been analyzed. Validity of isokinetic correlation with enthalpic control has been shown and isokinetic temperature was determined.

It was established, that the synthesized substances have anti-inflammatory, analgetic, diuretic and bacteriostatic activity (DL_{50}=1530-2000 mg/kg). These investigations testify to prospects of search of biologically active substances among the given chemical compounds.

SYNTHESIS OF 2-N-R-AMINOMETHYL-3-BENZYLQUINOLIN-4-ONES AS POTENTIAL NEUROTROPIC AGENTS

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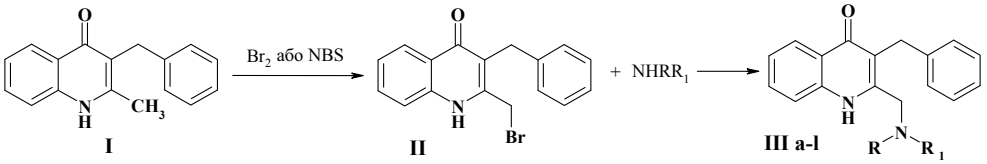
Halogenation of heterocycles is a powerful tool for their further modification. In order to expand the chemical diversity of derivatives based on quinolin-4-one scaffold we have investigated 3-alkyl-2-methylquinoline-4-ones bromination.

Bromination of 3-substituted 2-methylquinoline-4-ones was performed with molecular bromine and N-bromosuccinimide in such solvents as glacial acetic acid and chloroform respectively, in the presence of catalytic amounts of benzoyl peroxide or without it.

According to the obtained results it has been shown that in the case of 3-benzyl-2-methylquinoline-4-one **I** halogenation takes place with the methyl group in C-2 position of quinolone ring, and 3-benzyl-2-brommetylquinolin-4-one **II** was isolated as the main product with yields 63% (Br_2) and 73% (NBS) respectively.



III a R=C_6H_{13}, R'=H; **b** R=*cyclo*-C_6H_{11}, R'=H; **c** R=C_6H_5, R'=H; **d** R=*o*-$CH_3C_6H_4$, R'=H; **e** R=*m*-$CH_3C_6H_4$, R'=H; **f** R=*p*-$CH_3C_6H_4$, R'=H; **g** R=*o*-$CH_3OC_6H_4$, R'=H; **h** R=*p*-$CH_3OC_6H_4$, R'=H; **i** R=*m*-ClC_6H_4, R'=H; **j** R=C_2H_5, R'=C_2H_5; **k** R+R'=piperidine; **l** R+R'=morpholine.

Also it has been shown that bromination of 2-methylquinoline-4-ones with other alkyl substituents (methyl, propyl, butyl) at C-3 position occurs with low regioselectivity, which does not allow to use this reaction as a preparative method for the synthesis of corresponding 2-brommetylderivatives.

Synthesized 3-benzyl-2-brommetylquinolin-4-one **II** was used in reactions with various amines. Alkylation of corresponding amines by 3-benzyl-2-brommetylquinolin-4-one **II** via heating in DMSO/K_2CO_3 leads to formation of target 2-N-R-aminomethyl-3-benzylquinolin-4-ones **III a-l** rapidly and with high yields.

This direction is a logical continuation of the research of quinoline-4-one derivatives with aminoalkyl substituents, because these structural determinants should impart a neurotropic orientation of pharmacological action to these molecules through structural similarity to known ligands of 5-HT receptors.

SYNTHESIS OF N-[(1Z)-2-(ALKYLAMINO)-2-OXO-1-(2-OXO-1,2-DIHYDRO-3N-INDOLE-3-ILYDEN)ETHYL]BENZAMIDES

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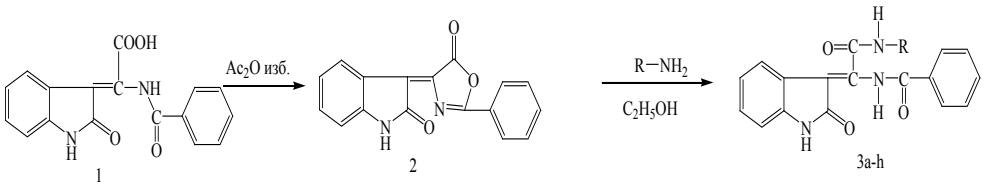
With the purpose of base encroachment of biologically active compounds as nootropic medicines we have synthesized the range of alkylamides of (2-oxo-1,2-dihydro-3*H*-indol-3-ylidene)-2-hydroxy-acetic acid.

The synthesis of the target products has been carried out using of 2-phenyl-4-(2-oxoindoliniliden-3)-5-oxazolone (2) obtained by reacting acid (1) with an excess of acetic anhydride as a precursor. N-[(1Z)-2-(alkylamino)-2-oxo-1-(2-oxo-1,2-dihydro-3H-indole-3-ylidene)ethyl]benzamides 3a-h have been obtained by heating (2) water bath with equimolar amount of respective alkylamines for 20 minutes using ethanol as a solvent.

Synthesis has been carried out according to the following scheme:



where: R= CH_3; C_2H_5; C_3H_7; iso-C_3H_7; C_4H_9; C_6H_{13}; $CH_2C_6H_5$; $(CH_2)_2C_6H_5$

N-[(1Z)-2-(alkylamino)-2-oxo-1-(2-oxo-1,2-dihydro-3H-indole-3-ylidene) ethyl]benzamides are yellow crystalline substances with high melting points. The substances are insoluble in water, but soluble in such organic solvents as dimethylformamide, 1,4-dioxane.

The structure of the compounds synthesized have been confirmed by the data of the elemental analysis, spectral data, X-ray diffraction analysis (compound 3b) and their individuality has been proved by thin-layer chromatography.

SEARCH FOR NEW SCAFFOLD OF THIAZIDES-LIKE DIURETICS

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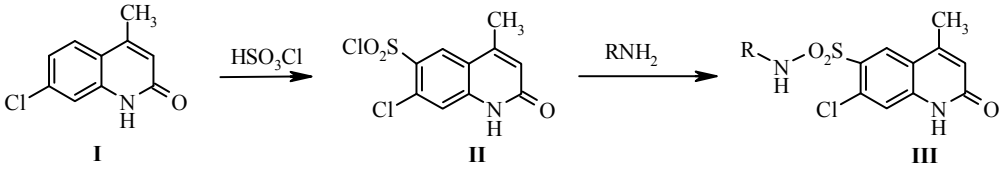
Thiazide and thiazide-like diuretics have formed the cornerstone of the management of hypertension for several decades. They are optional first-line antihypertensive agents for people aged 55 years or older, their effects are seen at low doses but still have metabolic side-effects. Therefore, the discovery of new effective and safe thiazide-like diuretic drugs represents a challenging goal for a research area.

We have supposed that sulfonamides III that have similar structure with hydrochlorothiazide would also have diuretic activity. And it has been successfully confirmed in our previous work for derivatives with aliphatic substituents (III, R=Alk). So the purpose of this work was to synthesize a series of new quinoline-2-ones with sulfonamide moiety bearing different aromatic substituents (I, R=Ar) and study their diuretic activity.

Synthesis of target sulfonamides is shown on scheme:



I **II** **III**

According to the obtained pharmacological data these compounds acted similar to hydrochlorothiazide in the experiment in rats. Among tested compounds 7-chloro-4-methyl-2-oxo-1,2-dihydroquinoline-6-sulfonic acid anilide (III, R=Ph) has shown the most significant diuretic activity. From the structure–activity point of view, it was found that any substitution, especially in case of *o*-position, in the benzoic ring of sulfonarylamides reduces diuretic activity of synthesized compounds.

Aso sodium, potassium, chlorides and creatinine content in urine and serum of rats also has been measured for synthesized compounds. In all cases increased diuresis was provided mostly due to Na^+ excretion and Na^+/K^+ ratio was more favourable for new compounds then that of hydrochlorothiazide. Determination of acute toxicity of the most active compound (III, R=Ph) in mice (per os) has shown that LD_{50} is more than 10000 mg/kg. That looks promising because LD_{50} of hydrochlorothiazide is about 3000 mg/kg (per os).

Thus, 7-chloro-4-methyl-2-oxo-1,2-dihydroquinoline-6-sulfonic acid anilide could be considered as a lead compound from this series of new sulfonamides that deserves further investigation, in particular as hypotensive agent.

COMBINATORIAL LIBRARY OF 2-((2-OXO-3-ARYL-2H-[1,2,4]TRIAZINO[2,3-C]QUINAZOLIN-6-YL)THIO)ACETAMIDES WITH HETEROCYCLYL FRAGMENT: DESIGN AND SYNTHESIS

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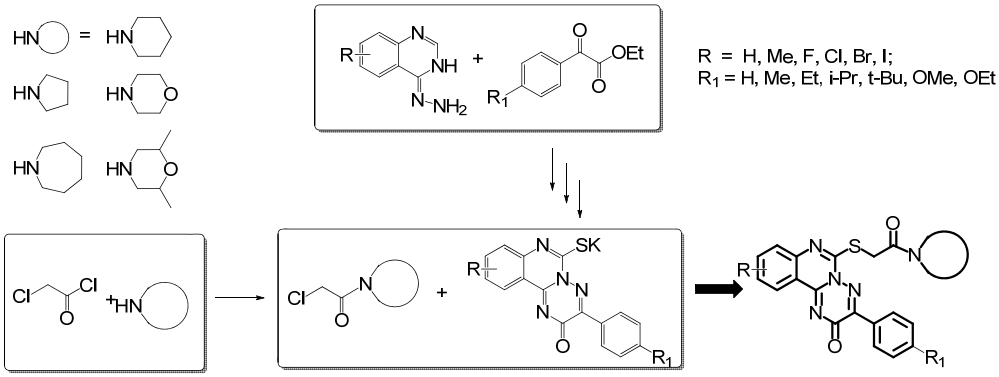
6-Thiosubstituted triazino[2,3-c]quinazolines were described as perspective anticancer, antimicrobial and antiviral agents, however some aspects of mentioned compounds still insufficient known. As we consider creation of valid QSAR models is one of the perspective research directions that can simplify the following drug design investigations for presented class of compounds. So we aimed to provide design and synthesis of the required combinatorial library. As starting components for target compounds synthesis we used corresponding substituted potassium 2-oxo-3-aryl-2H-[1,2,4]triazino[2,3-c]quinazoline-6-thiolates and 2-chloracetamides.



The first ones were obtained as result of series of reactions starting from the substituted 4-hydrazinoquinazolines and ethyl 2-oxo-2-arylacetates. Mentioned synthetic pathways allow directed introducing of the required fragments in the structure of the final compounds. Structure of synthesized compounds was proved by complex of physicochemical methods. As result of virtual screening some of the substances were selected by National Cancer Institute for in vitro testing on anticancer activity.

SYNTHESIS OF NEW POLYCYCLIC SYSTEMS CONTAINING FLUOROQUINOLONE FRAGMENTS ASSOCIATED WITH THE 1,3-THIAZOLE OR 1,2,4-OXADIAZOLE CYCLE

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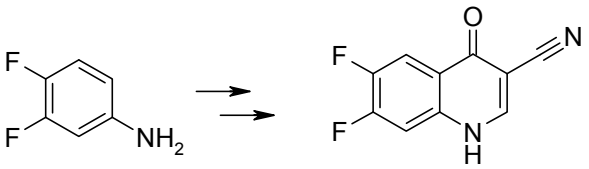
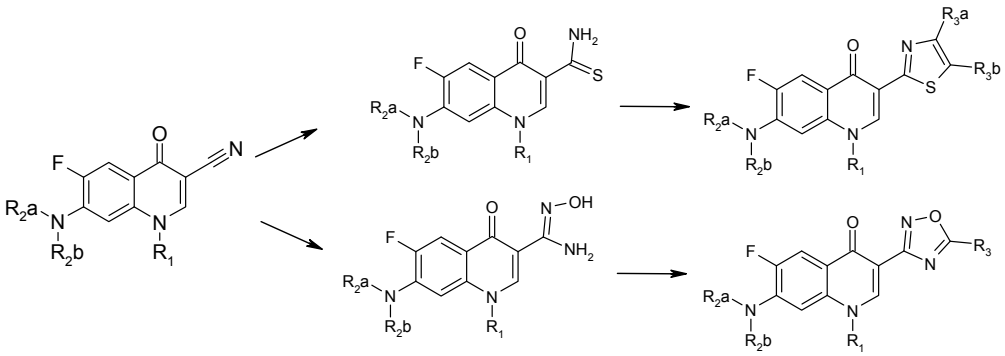
The work is focused on the development of new and effective antimicrobial substances quinolone series. The use of heterocyclic bioisosteres carboxyl group or its derivatives in the 3rd position of the fluoroquinolone core is of interest to improve the pharmacological properties of perspective drugs.

We have synthesized two new classes of heterocyclic systems containing the 3 rd position fluoroquinolone 1,3-thiazol-2-yl or 1,2,4-oxadiazol-3-yl fragments. The work is based on the use of the synthetic potential of the 3-cyano-6,7-diftorhinolin-4, obtained by the reaction of the Gold Jacobs:



Has been designed and optimized for the path leading to the target poliheterocyclic classes as follows:



The structure of the synthesized compounds was confirmed by NMR, IR and UV spectroscopy and mass spectroscopy.

SYNTHESIS AND PHARMACOLOGICAL ACTIVITY OF DERIVATIVES OF 7-OXAMOYLSUBSTITUTED 3-OXO-1, 2,-DIHYDROINDAZOLE

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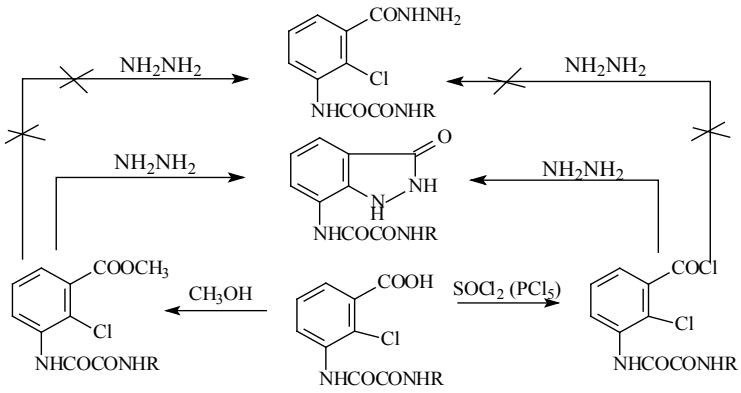
The synthesis of new biologically active substances is a search for alternative medicines that are used to treat various diseases. Especially useful the search for new synthetic compounds which have combined antibacterial, antifungal and anti-inflammatory effects is especially actual. In view of the above scientific interest is presented by newly synthesized 7-oxamoylsubstituted 3-oxo-1, 2,-dihydroindazoles.

7-oxamoylsubstituted 3-oxo-1, 2,-dihydroindazoles are obtained in two ways: by holding the reaction of hydrazinolysis of methyl esters of amides of 3-carboxy-2-chloroxanyl acid when heated for 30-40 minutes and due to hydrazinolysis of chloranhydrides of these derivatives:



де R - CH_2CH_2OH, C_3H_7-i, C_4H_9-н, $CH_2C_6H_5$

The structure of the synthesized compounds is confirmed by a set of modern physical and chemical methods: data of elemental analysis, IR-, and NMR spectra.

According to the results of pharmacological screening there have been found substances among 7-oxamoylsubstituted 3-oxo-1, 2,-dihydroindazoles which exhibit moderate anti-inflammatory, fungistatic and bacteriostatic activity. Bacteriostatic effect of the synthesized compounds was studied with regard to Staphylococcus aureus, bacillus subtilis, colibacillus, pseudomonas aeruginosa. Bacteriostatic MIC regarding intestinal microbial groups is within 31,2-250 mcg / ml. Fungistatic activity was studied with regard to Candida fungus (Candida albicans, Microsporum canis). Acute toxicity of obtained dihydroindazoles does not exceed the acute toxicity of outcoming compounds. According to the classification of K.K. Sidorov 7-oxamoylsubstituted 3-oxo-1, 2,-dihydroindazoles belong to the class of low-toxic substances (DL_{50} > 2500 mg/kg).

SYNTHESIS, PHYSICOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF 9-(R-BENZILIDEN)HYDRAZINOACRIDINES

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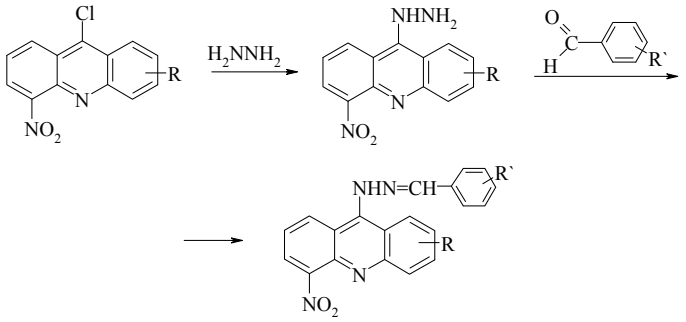
The synthesis of 5-nitro-9-(R-benziliden)hydrazinoacridines (scheme):

Scheme



R=H, 1-CH_3, 2- CH_3, 3- CH_3, 2.3-$(CH_3)_2$, 4-OCH_3, 2-Cl;
R`=H, OCH_3, OH, F, NO_2, $N(CH_3)_2$

The structure and individuality of the synthesized substances confirmed by the ultimate analysis, IR-, UV-, NMR-spectroscopy, chromato-mass spectrometry, counter synthesis, data qualitative reactions and thin-layer chromatography.

The computer prognosis of possible types of pharmacological activity is conducted on program of 18 first synthesized connections of 5-nitro-9-(R-benzi-liden)hydrazino acridines. It was established that the synthesized substances have antimicrobial, antifungal, anti-inflammatory, diuretic, antidiuretic and analgesic activities. According to classification by K.K. Sydorov synthesized compound at intra stomashentering belong to low toxicity compounds. A number of regularities of the «structure-activity-toxicity» relationship have been determined.

9-(4`-Metoxybenziliden)hydrazine-5-nitroacridine reveals the high antimicrobial, antifungal, anti-inflammatory, chloplogic activities with a low toxicity (DL_{50}>5500 mg/kg). A project of the analytical and normative documentation has been elaborated for this substance.

SYNTHESIS AND STUDY OF THE ANTI-CANDIDA ACTIVITY OF DERIVATIVES OF IMIDAZO[1,2-A]PYRIMIDINE

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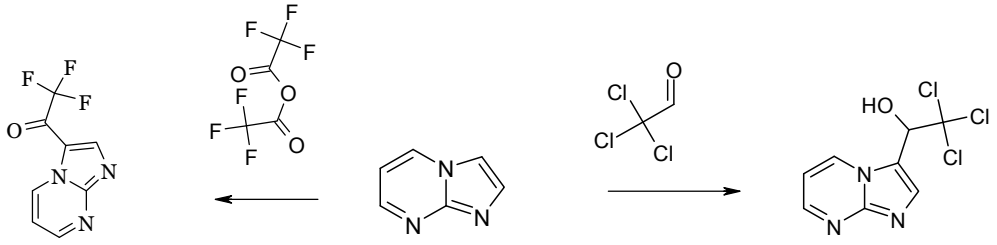
Antifungal agents occupy an important segment of the pharmaceutical market, but because of the rapid spread of resistant strains of microorganisms, the improvement of existing and finding of new antimycotic medicines becomes a very important issue. The derivatives of imidazo[1,2-*a*]pyrimidine are promising for searching for new synthetic antifungal drugs.

The aim of our work was the development of methods for synthesis of new derivatives of imidazo[1,2-a]pyrimidine and study of the anti-candida activity of compounds produced.

We performed the synthesis of imidazo[1,2-*a*]pyrimidine **1** and conducted the modification of the molecule by entering of highly lipophilic fragments into its structure. So, the 3-(trifluoroacetyl)imidazo[1,2-*a*]pyrimidine **2** was obtained at the reaction of the initial **1** with trifluoroacetic anhydride under argon atmosphere. In the reaction with chloral in glacial acetic acid, the 3-(2,2,2-trichloro-1-hydroxyethyl) imidazo[1,2-*a*]pyrimidine **3** was produced:



2 **1** **3**

The structure of the synthesized compounds was proved by the elemental analysis data, and by 1H-NMR spectroscopy.

The study of the anti-candida activity of the samples produced was performed by two-fold serial dilutions. As a result, a significant activeness of the substance **2** with respect to the strains of C. albicans at a concentration of 31.25 mg/mL (reference drug - fluconazole - 15.6 mg/ml) was identified. The compound **3** showed a high level of activity to other causative agents of mycoses.

The results of studies conducted indicate the reasonability of a further modification of the basic structure of imidazo[1,2-*a*]pyrimidine with the aim to search and develop antifungal agents.

IDENTIFICATION OF DERIVATIVES OF IONIZATION CONSTANTS 5-METHYLTHIENO[2,3-*D*]PYRIMIDINE-4(3*H*)-OH-6-CARBOXILIC ACID

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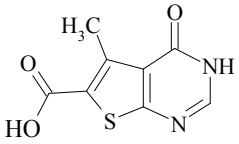
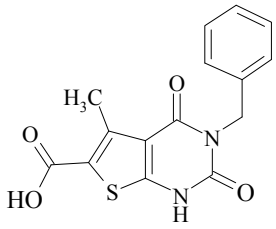
Derivatives of 5-methylthieno[2,3-*d*]pyrimidine-4(3*H*)-on-6-carboxylic acid are biologically active compounds. However, these compounds in the un-ionized form are soluble in water, making it difficult to introduce them into dosage forms. For further selection of salt formation cation we have determined the ionization constants of compounds **1-5** by alkalimetryc non-aqueous titration. The media for determining was the mixture of dioxane-water (1:1), equivalence point had been determined potentiometrically. Results were processed statistically.



1



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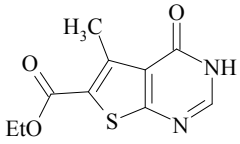

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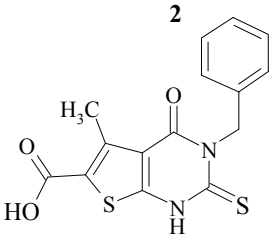

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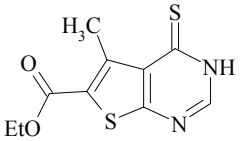

5

As a result, it was found that acids **1-3** are strong enough dibasic acids. We found, that acid **3** is the strongest acid, which contains a Sulfur atom in position 2.

Ionization constants for the 5-methylthieno-[2,3-*d*]pyrimidine-4(3*H*)-(thi)on-6-carboxylic acids esters **4** and **5** have been determined additionally, it was shown that compound **5** reveals more acidic properties.

Thus it was found that the most suitable for salt formation with the basics, including weak ones are compounds containing sulfur atom in the pyrimidine nucleus.

NEW BIOLOGICALLY ACTIVE HETEROCYCLIC DERIVATIVES OF 2-ACYLISOTHIOCYANATE-9,10-ANTHRAQUINONE

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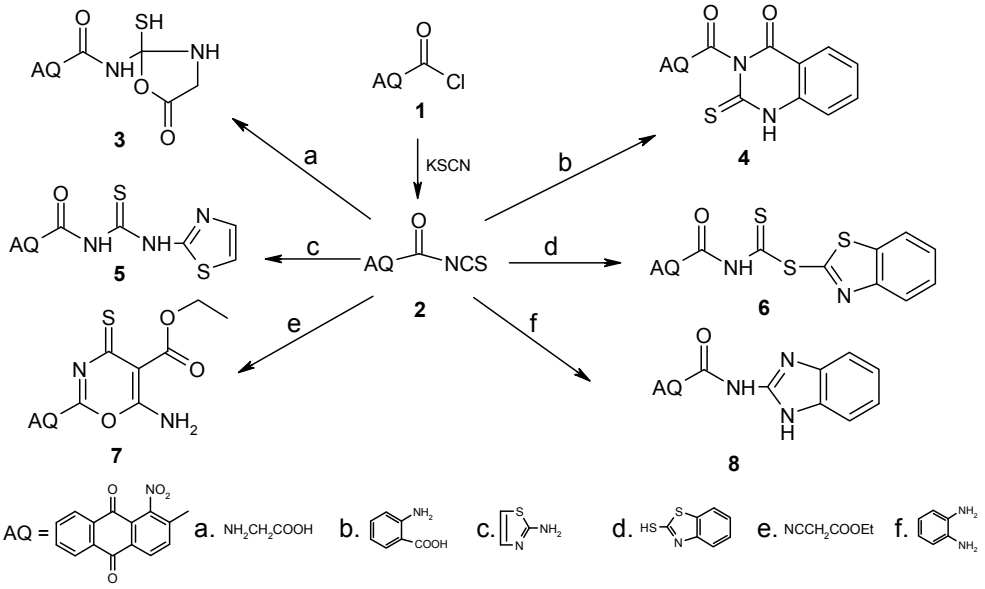
Derivatives of 9,10-anthraquinone is one of the most important classes of organic compounds. Chemistry of anthraquinone and its derivatives have long stood out into an independent and large area of organic chemistry. Interest of anthraquinone and its derivatives due to ample opportunities for getting them as substances needed modern technology and medicine.

The aim of the research was the synthesis and investigation of new promising heterocyclic derivatives of 2-acylisothiocyanate of 1-nitro-9,10-anthraquinone (AQ-CONCS, 2). For derivatives (3-8) was carried out a one-step interaction of 1-nitro-9,10-anthraquinone-2-carbonylchloride (1) with potassium thiocyanate in acetone at heating the reaction mixture for 2 h. followed by addition of the appropriate reagent - glycine (a), 2-aminobenzoic acid (b), 2-aminothiazole (c), 2-mercaptobenzothiazole (d), ethyl cyanoacetate (e) and o-phenylenediamine (f).



Experimental biological screening by difussion method revealed compounds with antimicrobial action against strains Staphylococcus aureus, Mycobacterium luteum and Candida tenuis. Serial dilutions technique was defined minimum inhibition concentrations of new heterocyclic derivatives of 2-acylsothiocyanate-9,10-anthraquinone.

SECTION 2

THE STUDY OF MEDICAL PLANTS AND HERBAL REMEDIES

PHYTOCHEMICAL RESEARCH OF GALIUM *SEMIAMICTUM KLOK*. HERB

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Galium semiamictum Klok. (*Galium* L. genus, Madder family – *Rubiaceae* Juss.) is spread in the Kharkiv region.

It is a perennial herbaceous plant with ascending or rectangular stems 50-170 cm high, leaves are obovate, small, flowers of white color, gathered in paniculate oblong inflorescence. The plant grows on the fringes of gullies groves or forest-steppe oak forests.

It is known that biologically active substances (BAS) of *Galium semiamictum* Klok. herb are presented by flavonoids – quercetin and luteolin derivatives, roots and rhizomes accumulate anthraquinones of alizarin type.

The aim of our study was a preliminary photochemical research of major BASs' of *Galium semiamictum* Klok. herb. The object of the study was air-dried herb harvested in the phase of full flowering in the Kharkiv region in summer 2012.

By general qualitative chemical reactions in aqueous extract tannins (condensed tannins dominate) have been identified; in aqueous and alcohol (50% ethanol) extracts saponins (steroid saponins predominated) have been identified; in alcohol (70% ethanol) extract after reaction with the Trimm-Hill reagent iridoids have been identified; the presence of flavonoids was confirmed by reactions with alkali, iron (III) chloride, aluminum chloride, cyanidin *reaction*, the result of *Bryant's* cyanidin *reaction* shows that flavonols glycosides dominate in the raw material, by reaction with diazotized sulfanilic acid coumarins have been identified in alcohol (96% ethanol) extract.

Chromatographic study of main BAS has been carried out by one- and two-dimensional paper chromatography and one-dimensional thin layer chromatography on *Silufol* and *Sorbfil plates. According to the* R_f values, staining after interaction with specific chromogenic reagents chlorogenic acid, coumarin, rutin and asperuloside have been identified.

Obtained results provide the basis for further phytochemical research of *Galium semiamictum* Klok. herb.

MORPHOLOGICAL AND ANATOMICAL STUDIES OF LEAVES OF SCORZONERA HISPANICA

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The aim of our research was to study the morphological and anatomical features of leaves of Scorzonera hispanica L. Plants were grown in *Botanical garden of* National University of Pharmacy and harvested in the first year life. For anatomical study were used leaves fixed in a mixture of glycerol:alcohol:water (3:2:1), specimens were prepared by commonly accepted techniques, exam under microscope MBI-G, magnification x400 or x600 and camera "Canon PowerShot A720 IS". Leaves formed in compact erect or slightly spreading root rosette. Leaves stalked, egg-shaped or prolate-lanceolate, acuminate, with many veins, entire or wavy edges, light green color, up to 35 cm in the lower and middle part of the stem, stalk-wrapped at the base, prolate-lanceolate, upper leaves are spicular.

Leaves have dorsiventral type of structure. The upper and lower epidermises are single-layered. The upper epidermis has densely located almost rectangular or oval cells. Cells of the lower epidermis are parenchymatic with wavy, irregularly thickened cell walls. Stomata are located regularly on the upper epidermis and are abundant on the lower epidermis. Actinocytic stomata cells are round or slightly elongated in shape and have 4 or 5 guard cells. On the upper and lower epidermis are located large simple unicellular trichomes. Trichomes branched into 4-6 long rays with thin cell walls, often twisted and deformed. On the lower and upper epidermis there are small round regular-shaped glandules of essential oil, that are typical for Asteraceae family. Assimilation system consists of palisade parenchyma and harvesting cells. Palisade parenchyma is located perpendicularly to the cells of the upper epidermis and is composed of one or two layers of cells where photosynthesis takes place. Below are loosely located round shaped harvesting cells. Besides the function of photosynthesis, harvesting cells accumulate products of photosynthesis, which formed in palisade parenchyma cells. Further to the lower epidermis the entire space occupied by loosely placed oval-rounded or slightly elongated cells of spongy parenchyma. Good visible latex tubes - multicellular segmented without anastomoses, located along the leaf veins, their lateral branching sprouts are pierced all mesophyll. Latex tubes are filled with latex, which becomes brown-orange color being treated with alkali.

Central vein represented by open bicollateral vascular bundles with two areas of phloem, that are oriented outward and toward the center of the xylem. Between the external phloem and xylem areas is cambium. Other vascular bundles are collateral, open, with well-defined xylem as well. In the veins, phloem is oriented to the underside of the leaf blade, xylem - to the top. There are all the histological elements of these tissues in the phloem and xylem of leaves. Near the veins located the surrounding parenchyma cells. Established morphological and anatomical features of leaves of S. hispanica will be used for QCM (Quality Control Methods) developing.

ORGANIC ACIDS IN THE BARK OF BERLIN AND BALSAMIC POPLARS

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Organic acids are found in all living beings and play an important role in maintenance of acid-base balance in organisms, because after their full oxidization they give many of valuable alkaline components. In our present-day conditions of sedentary life style, stress situations and polluted environment that lead to the accumulation of acid products inside us, the alkalizing influence of organic acids has a great value in the rehabilitation of human organism.

The aim of our work is investigation of composition and amount of organic acids in the bark of Berlin poplar (Populus berolinensis Dipp.) and balsam poplar (Populus balsamifera L.).

Materials and methods. The bark was harvested in October, 2012 from trees growing in the Karazin KNU botanic garden. The research was made using Agilent Technology HP 6890 GC-chromatograph with mass-spectrometer detector 5973N. Identification of volatile components was made by comparing mass-spectra that we got with the data of NIST 02 library.

Results. In both samples 16 organic acids were identified: 10 aliphatic and 6 aromatic. General amount of acids in the bark of Berlin poplar was 18348.2 mg/%, and 10508.2 in the balsam poplar's bark. Oxalic (6036,5 mg/% and 2624,9 mg/%), citric (2624.9 mg/% and 2094.3 mg/%) and hepta-2,4-dienic (1103.3 mg/% and 969.7 mg/%) acids dominate among aliphatic acids. These acids are used in pharmaceutical and food industries as acidifiers and preservatives. Citric acid is part of the drug "Blemaren", that is used for dissolving and preventing generation of urine acid's and mixed concretions in kidneys. Aromatic acids are represented by anisic (6068.7 mg/% and 2986.0 mg/%), salycilic (1139.3 mg/% and 624.4 mg/%) and benzoic (796.8 mg/% and 401.7 mg/%) acids, that are strong antiseptics and anti-inflammatory agents.

Conclusion. Gathered data show that bark of Berlin and balsamic poplars contain a sufficient amount of carboxylic acids, what allows us to prognoses antiseptic, anti-inflammatory, litolitic influence of the drugs made from them.

INVESTIGATION OF RAW MATERIAL REPRESENTATIVES OF *BETULACEAE* FAMILY

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Leaves of many plants on earth are the accessible type of digister which is used in various aims. Many different types of plants suffice for the receipt of a few ten of kinds is productive leaves as pharmaceutical plants raw materials.

Plants of Betulaceae's family are common in our country. But these plants are not source of pharmaceutical raw materials. In Folk Medicine of many countries Betulaceae's representatives extensively were used. For example, leaves of species birch Betula verrucosa Ehrh. have litolitic, diuretic, hypoazothemic effect, leaves of black alder Alnus glutinosa (L.) Gaertn. have astringent, antitumor action, leaves of fibert Corilus avellana L. are antioxidant.

The goal of our investigation isdetermination options of standartisation leaves available and widely in-use domestic plant Alnus glutinosa (L.) Gaertn. For this process we collected 5 series of leaves of this type of plant of different districts of sprouting. We studied such parametres as macroscopic, microscopic diagnostic signs, loss in-bulk at drying, and also quantitative maintenance of sum of oxidable phenols and sum of flavonoids.

To the macroscopic diagnostic signs taken by us form of basesare widely cuneate, the form of edge of leaf plate is heteromerous doubl-serate, the apex isbilobular. Central and lateral veins are deep of upside of leaf plate and protuberant is on downside. An upside saves a characteristic tack. Smell fragrant is specific. Taste is expressed bitter.

Microscopic signs which have a diagnostic value are a type of leaf plate is dorsiventral, type of stomatos apparats isanomocitic. Type, localization of trikhom is simple and ferrous hairsprings. A presence of druz is in the parenchima of leaf plate, central vein and petiole.

A loss in-bulk at drying makes in the analysable series of raw material is not more 10.0%. Maintenance of sum of oxidable phenols is not below 12%, a sum of flavonoids in a count on a hyperoside is not below 3.5%.

Findings in basis of project MCQ "Alder leaves" "Alni folia" will used.

ACTUAL ASPECTS OF HERBA ORIGANI STANDARDIZATION

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Introduction: Medicinal plant material (MPM) 'Herba Origani' consists of the whole or cut dried aerial parts of *Origanum vulgare* L. (*Lamiaceae*), harvested during the flowering phase. According to the European pharmacopoeia, Origani herba is defined as dried leaves and flowers separated from the stems of *Origanum onites* L. or *Origanum vulgare* L. *subsp. hirtum* (Link) Ietsw., or a mixture of both species. Herba Origani has various pharmacotherapeutic properties: antiseptic, diuretic, cholagogue, antispasmodic, emmenagogue, carminative, diaphoretic, tonic, stomachic and many others. It is used in treating colds, cough and bronchial catarrh, and is used as a diaphoretic and an expectorant. Other uses include the treatment of bloating, stimulation of appetite and as a antispasmodic and sedative agent.

Aim: To study chemical composition of phenolic compounds of MPM Herba Origani, make quantitative analysis of determined chemical compounds, define the diagnostic features that facilitate identification of the plant.

Materials and Methods: *O. onites* samples were collected during the flowering season from Turkey, in July 2012; *O. vulgare* from All-Russian Institute of Medicinal and Aromatic Plants (VILAR), in June 2012. The essential oil was obtained by hydrodistillation; composition of the volatile constituents was established by Carlo Erba Instruments gas-liquid chromatograph equipped with a flame ionization detector. The chemical study of herb alcoholic extracts was made by qualitative reactions, thin-layer chromatography and the differential UV-visible spectropho-tometry (Varian Cary 50 UV-Vis Spectrophotometer) determination of total flavonoids with using of state standard sample of luteolin-7-glucoside. The quantitative determination of tannic substances in tannin equivalent was carried out by titration with 0.1 N potassium permanganate in water extraction.

Results: Herba Origani onites contains 2.60% of volatile oil in anhydrous drug and herba Origani vulgaris 0.08% respectively. The major component of the essential oil is thymol (*O. onites* – 56.21%; *O. vulgare* – 45.73%). The percentage of flavonoids in luteolin-7-glucoside equivalent was 1,25±0,01% in *O. onites* and 0,98±0,02% in *O. vulgare.* The amount of tannic substances in tannin equivalent in *O. vulgare* equals 9.5%, in *O. onites* 18.6%.

Conclusion: The methodological approaches to the standardization of MPM Herba Origani were developed.

NEW UPGRADED MEDICAL FORMS HYDRO-ALCOHOLIC EXTRACTS FROM HERBAL RAW MATERIAL

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Introduction. In today's time challenges Pharmacy is not only the synthesis and the search for new biologically active substances including synthetic or natural substances, but also continuous improvement of existing substances that create more effective formulations based on them, which would allow them to reduce side effects, improve bioavailability or prolong duration of action and make them more comfortable for patients to use.

The aim of abstract - to improve formulations based on aqueous-alcoholic extracts of herbal raw materials for external or internal use for example tinctures.

Materials and Methods: Studies were selected object tinctures: Sophora Japanese, Calendula, Eucalyptus, Propolis, some excipients (glycerol, dimethylsulfoxide, and some polymers enabled in medicine).

Studies. As a result of the addition some of excipients (polymers, glycerol, dimethylsulfoxide) in different proportions were obtained new formulations tinctures. Their viscosity depended on the amount of polymer and the amount of alcohol in tinctures that we use. With increasing mass fraction of polymer in the composition and decreasing concentration of alcohol the viscosity of the samples increased. Organoleptic properties of new forms did not change, except that the samples acquired sweetish taste of the presence of glycerol.

Conclusions. As a result of purposeful addition of some excipients to the already well known water-alcohol forms a tincture for external or internal use: Sophora Japanese, Calendula, Eucalyptus and Propolis can change their important biopharmaceutical properties. So with the addition of some polymers that allowed for external and internal use, you can achieve prolonged duration of action and a protective film. To improve the bioavailability of bioactive substances can be added dimethylsulfoxide. It should be noted that the alcohol that remains in the sample does cautery effect on tissue and can cause pain, but these effects can be reduced by reducing the proportion of tincture and mixed them with the dilution of other suitable solvents. While on the other hand alcohol acts as a preservative that prevents microorganisms multiply in the dosage form. So open up new perspectives in the development of the old formulations - tinctures. For example in the application of advanced dosage forms for external application on the affected skin or gums in the mouth or in their internal administration. And using appropriate containers such as tubes with the appropriate form of the tip or dosing device drugs can be easily and accurately applied dose.

INVESTIGATION OF RAW MATERIAL XANTHIUM STRUMARIUM OF ASTERACEAE FAMILY

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Xanthium strumarium, zobnik; turitsa (Asteraceae) is a one-year herbaceous plant, woolly, gray-green in color, with an unpleasant odor.

In Romania this plant is officinal and on its basis herbal drug "Adenostop" for the treatment of enuresis and BPH is created. High content of iodine plant helps reduce the thyroid. This plant has antibacterial, antifungal, anti-inflammatory, diaphoretic, antipyretic and diuretic effects.

The chemical composition is studied insufficiently. The leaves contain a lot of iodine, alkaloids, vitamins C (almost 31.8 mg). Seeds contain fatty oil, resins, glycosides ksantostrumarin and iodine.

One of the stages of research the Xanthium strumarium grass is to identify the dynamics of the recovery of extractives. As extractants were used purified water and water-ethanol mixture. Looking at the exit of extractives, we can say that the largest number of substances was extracted when we used as an extractant 30% alcohol aqueous, 20% alcohol aqueous and water.

Also, for this series of extractants studied the dynamics of extraction the amount of phenol oxidation. For this group of substances optimum extractants were 50% aqueous alcohol (5.20±0.01%) and 40% aqueous alcohol (5.04±0.01%). In view of these two factors, for further technological research we selected 50% alcohol like the optimal extractant.

We the qualitative and quantitative composition of fatty acids studied. A result of research we identified and quantified, in lipophilic complex of leaves and stem, 7 fatty acids: lauric, myristic, palmitic, stearic, oleic, linoleic and linolenic acids. In lipophilic complex of leaves and stems prevailed the content of unsaturated fatty acids. Of saturated fatty acids prevailed content of palmitic acid, it was 24.13% (for leaves) and 17.20% (for stem) of the amount of fatty acids. Of unsaturated fatty acids dominated content of linolenic acid, it was 43.99% (for leaves) and 44.28% (for stem) of the amount of fatty acids. Among of identified fatty acids the minimal content had the lauric acid, it was less than 1% of the amount of fatty acids.

The obtained results will be used in future research and in development of new drugs based on lipophilic complexes of Xanthium strumarium leaves and stem.

INVESTIGATION OF RAW MATERIAL REPRESENTATIVES OF *RUBIACEAE* FAMILY

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Motherland of madder dyeing Rubia tinctorum L. (Rubiaceae) is Mediterranean, widespread on the south of Russia, Ukraine, in Byelorussia. Marena dyeing is a heat-loving and moisture-loving plant with a long vegetation period. Plant with a powerful mainroot which thick rhizomes walk away from. Roots and rhizomes are covered a red-brounish slabby bark. In the rhizomes of madder dyeing are carbohydrates, pectins, squirrel, organic acids (apple, wine, lemon), triterpenoids, antrakhinons (purpurin, pseudopurpurin, ibericin, rubiadin, alisarin), iridoids, ascorbic acid. In above-ground part found out carbohydrates, iridoids, phenolcarbonic acids and their derivatives, coumarins, flavonoids (quercetin, kaempferol, apigenin, luteolin and rutin).

Medicinal forms possess a spasmolytic, diuretic, bile-expelling action. Due to the chemical composition a madder is instrumental in softening influence of stone of gall-bladder and buds, destroys salts from an organism, strengthening reductions of musculature of urinoexcretory ways. Enters in the complement of preparation "Cistenal", possessing all transferred dignities. The rhizome of madder in folk medicine is widely used as extracts, decoctions, powders, extracts for a hepatotherapy, gall-bladder, buds, organs of breathing and urinoexcretory ways. Effective at an osteochondrosis, gout and poliartrits. Pigmental spots, ulcers, dermatomikozy retreat, if to process the staggered areas of skin. From stems madders prepare ointment for treatment of injuries, and also at breaks.

A purpose of researches is an analysis of raw material of rhizomes with the roots of madder dyeing, presented at the pharmaceutical market of Ukraine. Purchased by us in the pharmacy retail network of next firms. A commodity expert analysis is produced. Thus, there is considerable divergence in the numerical values of parameters of raw material of madder dyeing different firms of producers.

I did the commodity expert analysis of raw material of roots and rhizomes of madder dyeing from the different manufacturers, such as the Company "Belovody", Moscow, PP "Naturalis-Ukraine", village Trojans Zhytomyr region, Pharmacy Ltd. "Medicinal Plants" Kharkov, "FitoBioTehnologii" Kiev.

TERPENOIDS COMPOSITION OF *LAVANDULA ANGUSTIFOLIA* AERIAL PARTS

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Abroad, lavender is widely used as drugs that have antiseptic, antispasmodic and sedative action (Nervofluks, Altaleks, Lalabi etc...). While in Ukraine, lavender is just used as a source of essential oil to produce the drug "Livian" with wound healing action. Essential oil is obtained from the flowers and inflorescence.

In the literature there are data on the biological activity and chemical composition of flowers that have about 20% of the total mass of herb, but the most part of the plants, stem (63%) and leave (17%), was not used in pharmaceutical and medical practices, while the whole plant contains essential oil.

The purpose of the study was to examine the qualitative and quantitative composition of terpenoids in aerial parts of lavender (*Lavandula angustifolia*) to determine its use in pharmaceutical practice.

The objects of study were the flowers, leaves and stems of lavender.

The study of the qualitative composition of the terpenoids was performed by thin layer chromatography on silica gel plates (0.25 mm) using as a mobile phase of toluene - ethyl acetate (85:15) with double running start. To visualize zones of terpenoids, plates were treated by anisaldehyde reagent and heated for 15 min at 105°C. A more detailed study of terpenoids of lavender aerial parts was performed by gas chromatography using a gas chromatograph Agilent Technology 6890 with mass spectrometric detector 5973. Quantitative content of terpenoids was determined by method of normalization.

As a result, it was found that the content of terpenoids in lavender flowers was 0.14%. The dominant components among terpenoids were linalool, linalooloxid and herniarin. Content of terpenoids in the stems was 0,025%, the dominant components were borneol, krypton, para-cymen-8-ol. Content of terpenoids in leaves was 0.05%, the dominant components were 8-acetoxylinalool, 1-acetoxylinalool.

The obtained results indicate the prospects of using aerial parts of *Lavandula angustifolia* as a source for essential oils and medicines.

PHARMACOGNOSTIC RESEARCH OF POPULUS NIGRA L.

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Populus is a genus of 25–35 species of deciduous flowering plants in the family Salicaceae, native to most of the Northern Hemisphere. English names variously applied to different species include poplar, aspen, and cottonwood.

Populus section Aigeiros – black poplars, some of the cottonwoods. North America, Europe, western Asia temperate:

Populus deltoides – Eastern Cottonwood (Eastern North America),
Populus fremontii – Fremont Cottonwood (Western North America),
Populus nigra – Black Poplar (Europe) Including Populus afghanica,
Populus Ч canadensis (P. nigra Ч P. deltoides) – Hybrid Black Poplar,
Populus Ч inopina (P. nigra Ч P. fremontii) – Hybrid Black Poplar.

It is a medium-sized to large deciduous tree, reaching 20–30 m (rarely 40 m) tall, with a trunk up to 1.5 m diameter. The leaves are diamond-shaped to triangular, 5–8 cm long and 6–8 cm broad, green on both surfaces. The buds are tarry. The species is dioecious (male and female flowers on different plants), with flowers in catkins and pollination by wind. The growth of tree is very quickly.

Their bark, buds and the leaves of Populus which contain various classes of biologically active substances phenolic glycosides, flavonoids, tannin, organic acids, vitamins, terpenoids. However the Populus nigra L. isn't studied enough.

Our goal is the research dynamic of accumulations of biologically active substances in leaves of Populus nigra L. Was studied and optimal terms on their harvest have been determined. These leaves were gathered for the research in Kharkiv, Chernigiv, Donetsk, Rivno regions in 2011-2012. There were pointed the presence of compounds (of tannins, amino, organic and hydroxycinnamomic acids, phenolic glycosides, flavonoids, terpenoids) when the primary studying of the Populus nigra L. leaves was. By the method of gas chromatograpy/mass spectrometry was investigated composition of essential oil of leaves of of the Populus nigra L., which grows on Ukraine. The research was made using Agilent Technology HP 6890 GC-chromatograph with mass-spectrometer detector 5973N. Identification of attar components was made by comparing mass-spectra that we got with the data of NIST 02 library. 45 components are identified. Major of them were salicylic aldehyde (57,5mg/kg), eugenol (85,9mg/kg), squalene (69,9mg/kg).

The main morpho-anatomical diagnostic characteristics of the leaves of Populus nigra L.

PHYTOCHEMICAL RESEARCH OF POPULUS ALBA L.

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There are about 30 kinds of Populus in Ukraine. Their bark, buds and the leaves of Populus which contain phenolic glycosides, flavonoids, tannin, organic acids, vitamins, terpenoids. However the Poplar genus plants aren't studied enough.

Populus alba, commonly called abele, silver poplar, silverleaf poplar, or white poplar, is a species of poplar, most closely related to the aspens (Populus sect. Populus). It is native from Spain and Morocco through central Europe (north to Germany and Poland) to central Asia. It grows in moist sites, often by watersides, in regions with hot summers and cold to mild winters.

Populus alba L. is a huge tree. Its height is up to 30m (rarely more), with a trunk up to 2 m diameter and a broad rounded crown. The bark is smooth and greenish-white to greyish-white with characteristic diamond-shaped dark marks on young trees, becoming blackish and fissured at the base of old trees. The young shoots are covered with whitish-grey down, including the small buds. The leaves are 4-15 cm long, five-lobed, with a thick covering of white scurfy down on both sides but thicker underneath; this layer wears off the upper side but not the lower, which stays white until autumn leaf fall. Larger, deeply lobed leaves are produced on fast-growing young trees, and smaller, less deeply lobed leaves on older, slow-growing trees.The buds are tarry. The growth of tree is very quickly.

Our goal is the research of qualitative composition and quantitative composition of flavonoids in the leaves of Populus alba L. These leaves were gathered for the research in Kharkov, Donetsk regions and in the Crimea in 2011-2012. There were pointed the presence of phenolic compounds (phenolic glycosides , flavonoids, tannin) when the primary studying of the Populus alba L. leaves was. The presence of flavonoids was defined in the ethanol extracts with cyanidin test, ferric(III) chloride. In results of reaction show the presence of flavonoid aglycones and glycosides. Besides the substances of flavonoids were discovered due to chromatographic method. For this method the paper "Filtrak"(FN №№ 1,4,12) and silica gel TLC plats were used. In accordance with the reference pattern rutin, quercetin, ferulic, chlorogenic, salicylic asides were identified. The method of spectrophotometry(410 nm on the spectrophotometr СФ-46) was applied for the analysis of flavonoids. The contain of flavonoids is turned out not less 1,2%. The Populus alba L. has the practical interest as a source for getting plant drugs of many-sided pharmacological action due to considerable quantity of phenolic compounds.

STUDY OF ANATOMIC STRUCTURE OF ROOT BIDENS TRIPARTITA

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Bidens tripartita is an herbaceous annual plant, that is widespread in Ukraine as a weed. The herbs of Bidens tripartita are included to the XI edition of USSR pharmacopoeia; this plant is not in official in Ukraine. In folk medicine decoctions of the herbs are used at in case of metabolic and digestion disturbances and diseases of urino-genital organs as diuretic, cholagogic, metabolic, anti-inflammatory, vitamin drug. Infusions and decoctions of the herbs are used externally for treatment of different diseases of skin. There is information about the study of anatomic structure of herbs Bidens tripartita in literary sources. However, we have not found out any data concerning study of anatomic structure of root.

The aim of the work is studying of anatomic structure of Bidens tripartita root and determination of microscopic diagnostic characters of the raw material.

Materials and methods. Raw material was prepared in the Vinnitsa and Kharkiv areas in 2012. Microslides for the studying of anatomic structure were made from fresh-collected, fixed, dried and soaked raw material. The light microscope "BIOLAM LOMO" (Russia) with 200x, 400x and 800x zoom was used for work. The obtained data was registered by the digital photocamera OLYMPUS FE - 140 and processed by Adobe Photoshop CS3.

Results. Anatomic structure of the root of Bidens tripartita is secondary non-bundle type. The covering tissue is periderm, which is formed with the parenchymatous thin-walled cells. The cortex parenchyma is presented by parenchymatous cells with thin insignificantly winding shells. There are small-diametered (in cross-sectional view) rounded secretory channels closer to a phloem. They are organised in a circle. The phloem is thin-walled and a cambium is well-expressed. A xylem is presented by spiral and stair vessels. The remnant of primary xylem is tetracrepid, which testifies tetracrepid radial bundle in the primary structure of root.

Conclusions. The diagnostic characters of anatomic structure of root are the secretory channels in cortex parenchyma and the tetracrepid remnant in the primary xylem.

RESEARCH OF VOLATILES OILS OF COWBERRY LEAVES

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In the world there is a trend growing interest in herbal medicine. Microorganisms are resistant to many existing antibacterial agents and the use of medicinal plant raw material for making antimicrobial drugs is a promising direction of pharmaceutical science. Cowberry (*Vaccinium vitis idaea L.*) is a promising plant for creation a new uroseptic phyto medicine. Stocks of this plant in Ukraine are sufficient. In traditional medicine biologically active compounds of cowberry leaves are used to treat kidneys and urinary tract diseases. Cowberry leaves herbal tea, phyto medicine and dietary supplements (complex infusion Pankov, "Phytoren", "Milona14", "Burdok-C", "Glucosyl", "Cystophyt- forte") are available at the market.

There is description of the phenolic compounds of cowberry leaves in the literature only, while plant has a noticeable smell. The purpose of our study was to investigate the chemical composition of cowberry volatile substances.

Research was carried out by chromatography-mass spectrometry on gas chromatograph Agilent Technology 6890 with mass spectrometric detector 5973. Indexes retention of components were calculated on the results of analyzes of substances with the addition of a mixture of normal alkanes (C_{10}-C_{18}). Identification of compounds was achieved by comparison of obtained mass spectra with the mass spectra of reference compounds with high probability identified by program recognition of spectra databases.

Quantitative content of compounds was calculated from the ratio of components peak area to the sum of all peaks area in the chromatogram (method of normalization). The content of volatile matter is 0.25%.

It was found 29 substances, among which such compounds as benzoquinone, etylkapronat, *trans*-linalooloxide, *cis*-linalooloxide, hydroquinone, loliolid, *cis*-neofitadiene, hexahydrofarnezylacetone, nonacosane were identified. Dominant agents are hydroquinone, benzoquinone, *cis*-neofitadiene. Presence of identified volatiles component enhances uroseptic effect of medicinal plant materials.

The results are the foundation for the development of new drugs based on isoprenoids.

PROSPECTS OF HORSE CHESTNUT TINCTURES IN WOUND TREATMENT

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One of the basic principles of wound treatment is the prevention and treatment of wound infections. General treatment of wounds include: antibacterial, anti-inflammatory, immune correcting, symptomatic therapy. The priority in this area is phytomedications, since they have pronounced therapeutic activity and thus a much smaller range of side effects, a wide range of therapeutic effects and little toxicity. Their pharmacodynamics allows them to influence several pathological circuits (antiseptic, anti-inflammatory, analgesic, and others); significantly greater range of herbal remedies enables to individualize therapy and to find an adequate replacement.

Chestnut horse or Horse Chestnut ordinary, - Aesculus hyppocastanum L – have a long-term usage in scientific and folk medicine mainly as a vasotonic, vasoconstrictive and analgesic active remedy, as a plant with a high phytoncide degree, however, the antimicrobial action of chestnut horse remains poorly investigated, especially when applied topically.

The aim of the work was to study the antimicrobial properties of chestnut horse tinctures.

As a feedstock the flower buds of horse chestnut (Aesculus hyppocastanum L) was selected. Antimicrobial activity of tinctures (obtained by maceration at 40° and 96° ethanol) were determined by standard strains Candida albicans (ATCC 668853), Baccilus subtilis (ATCC 6633), Staphylococcus aureus (ATCC 25923 (F-49)), Pseudomonas aeruginosa (ATCC 27853 (F-51), Staphylococcus epidermidis (191), Proteus vulgaris (152), Corynebacterium xerosis (NCTC 12078) and Escherichia coli (ATCC 25922). Common convenient methods such as the agar diffusion method and the method of serial dilutions using standard culture media (BCH, MPA, Saburo) were used. Evaluation of antimicrobial activity of infusions was estimated taking into account the bactericidal action of ethanol.

The antimicrobial action of chestnut flower tincture (40 є) with respect to S. aureus, B. subtilis, S. epidermidis, P. vulgaris and bloom chestnut tincture (96 є) with respect to S. aureus, C. xerosis, P. aeruginosa, S. epidermidis were iscovered; buds chestnut tincture (40 є, 96 є) did not show any antimicrobial activity. Bactericidal concentration chestnut flower infusions (96 є) concerning Candida albicans was 1:8.

The research of antifungal and bactericide activity of chestnut horse tinctures on clinical isolates of bacteria and fungi from wound field, including their strains, multiresistant to antibiotics is planned.

LEAVES AND STEMS OF *LAURUS NOBILIS L. (LAURACEAE)* – PERSECTIVE SOURCE OF MEDICINAL RAW MATERIAL

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Laurus nobilis - is an eternal-green tree or bush, sprouting in subtropical climate. It is widely used as decorative, food spicy, source of essential oil, cineola and camphor.

All parts of plant contain essential (laurel) oil, tannic matters, resins, bitter tastes which give them a typical fragrant smell and pleasant-bitter taste. The level of contents of essential oil in leaves arrives at 3 to 5.5%, in fruits is up to 1%. In addition, in fruits found out of 25- 45% fat oil, starch, phytosterol, hydrocarbon of lauran, mucus and sugar. In the complement of essential oil of Laurus nobilis pinen, cineol, myrcene, limonen, camphor. Fat oil consists of glycerids of laurinic and palmitinic acids. From a bark and wood of laurel, which is cultivated in Japan were selected the alkaloids of aktinodarfnin and launobin, linalool, different organic acids and other compounds. Decoctions and extracts of raw material are applied for treatment saccharine diabetes, otitis, cold, bronchitis, antritis, migraine, arthritis, osteochondrosis, osteoartroze, alcoholism, eczema, psoriasis, hypergidrosis, hyperpiesis.A purpose of this work is a research of morphological and anatomic features of leaves and stems of Laurus nobilis. Raw material was collected in November-December, 2012 on a peninsula Crimea. A macroscopic analysis was conducted by stereomicroscope and magnifying glasses. A microscopic analysis was conducted by preparations from a surface, transversal, longitudinal cuts with a subsequent analysis by microscope “Micros” (Austria) and jigging a digital photocamera “Canon”. Leaves are next, have short petiole, smooth edged, naked, simple, their length is from 6 to 20 centimeters and breadthways are from 2 to 4 centimeters, with an original spicy smell; the leaf plate is oblong, lancet or elliptic, to bases is narrowed, from above rifle-green, from a lower side more light.The personal touch of anatomic structure was a presence of the ductings of skhizogenic type.

We have established morphological and anatomical features. These structural components can be used to identify materials in future research and became the basis of individual sections of the scientific work.

PHENOLIC COMPOUNDS OF *GALIUM APARINE* L. HERB

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Catchweed bedstraw (*Galium aparine* L.) is a perennial herb belonging to the genus *Galium* L., Madder family (*Rubiaceae* Juss.). The main species' distinctive morphological features are weak central stem with whorls of 6-8 leaves that are rather widely separated from each other. Both the central stem and leaves have stiff hairs that point downward. The central stem is 4-angled and furrowed. Leaves are linear-oblong, smooth along the margins (except for stiff hairs), and sessile. Above the upper whorls of leaves, single flowers and/or small cymes of 2-3 flowers are produced. Flowers consist of 4 white petals with pointed tips, 4 stamens, 2 styles and a pair of green carpels that are joined together at the base of the flower. The blooming period occurs from late spring to mid-summer and lasts about 1-2 months.

Previous studies revealed that *Galium aparine* L. herb accumulates iridoids and flavonoids, in roots iridoids and anthracene derivatives of alizarin type have been identified. The plant is included in the British Pharmacopoeia, is a part of homeopathic medicines, is used in folk medicine in treatment of genitourinary system's diseases, fever, bleeding.

The aim of our work was to study phenolic compounds of *Galium aparine* L. herb. The object of the study was air-dried herb harvested in the phase of plant's full flowering in Artemivs'k, Donetsk region in summer 2012. By means of conventional qualitative chemical reactions in aqueous extract tannins have been identified (with a prevalence of condensed group), in 70% alcoholic extract flavonoids have been identified, in 96% alcoholic extract coumarins have been identified.

By means of one- and two-dimensional paper chromatography and one-dimensional thin layer chromatography on *Silufol* and *Sorbfil plates* by chromatographic characteristics chlorogenic acid, coumarin, scopoletin and rutin have been identified. Quantification of hydroxycinnamic acids was carried out in 70% alcoholic extract by direct spectrophotometry. Hydroxycinnamic acids' content in terms of chlorogenic acid was 2.14%. Quantification of flavonoids was carried out in 70% alcoholic extract by differential spectrophotometry using standard sample of rutin. The content of flavonoids was 0.95%.

These results provide the basis for further in-depth phytochemical research of *Galium aparine* L. herb as a new source of phenolic compounds.

RESEARCH OF THE CHEMICAL COMPOSITION OF BIOLOGICALLY ACTIVE SUBSTANCES OF IRIS SIBIRICA L.

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Siberian Iris (Iris sibirica L.) – species of Iris, family Iridaceae. The healing properties of this plant have been long known, in folk medicine rhizomes used as an expectorant, anti-inflammatory, antacydy agent in diseases of the digestive system, from the powder made flour and dust. According to the literature leaves of Siberian Iris contains of the organic acids (myristic, undetsylic, tridecylic, benzoic acid), glycoside iridin, starch, tannins, essential oil, the main component is a monoterpene ketone irony.

The aim of work was the study of qualitative and quantitative composition of active substances Siberian iris, harvested in M.M. Gryshko National botanic garden.

Leaves and rhizomes of Siberian iris used as raw materials. For the analysis received 70% alcohol and water extraction by exhaustive extraction with a water bath. For preliminary phytochemical analysis of the biologically active substances of the rhizomes and leaves of Siberian iris using the well-known reaction of identification and paper chromatography. Established the existence of such classes of biologically active substances: triterpenoid saponins (barite precipitation reactions with water, 10% solution of basic lead acetate, the reaction Fountain-Candel), hydrolysable tannins (reaction with iron ammonium alum), flavonoids (tsianidine reaction), coumarins (lactone test).

Also for the study of the chemical composition of leaves and rhizomes of Siberian iris chromatographic analysis was performed on paper (Filtrak FN – 4) with the solvent system: butanol – acetic acid – water (4:1:2) and 15% acetic acid. Phenolic compounds identified in daylight and UV light before and after treatment with ammonia vapors. The chromatograms revealed several compounds of the dark brown, yellow, blue, purple, which was referred previously to the phenolic compounds. The quantitative content of some classes of phenolic compounds. By spectrometry to determine the content of phenolic compounds in the leaves – 1.98%, rhizomes – 2.6% in terms of gallic acid. Flavonoids content was in the leaves – 1.34%, rhizomes – 1.29%. By the permanganatometrii method the content of tannin was (SF XI): rhizomes – 13.95% in the leaves – 2.6%.

The leaves and roots of Siberian iris are perspective material for creating medicines.

PERSPECTIVE OF THE USE OF MEDICINAL PLANTS IN THERAPY OF ALLERGIC SKIN DISEASES

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A requirement in medicinal drugs from a plant material remains very high. It is connected with a number of their advantages, namely: possibility of the long-term use, soft therapeutic action, availability and non-toxicity. As a result of reduction of natural supplies of medical plants, perspective is an alternative biotechnological method of production of biologically active substances (BAS) from the in vitro culture. The use of the experience of ethnomedicine for treatment of allergic skin diseases (ASD) shows in practice, that phytotherapy allows to diminish considerably the amount of medicamental therapy. Drugs from plants, drying the skin and intensificating its acidic reaction, possess expressed bactericidal action. The wide range of biological action of the phytodrugs is explained by the multicomponent composition of BAS.

We have conducted the analysis of scientific original sources with the aim of screening of medical plants that are used in treatment and prevention of ASD. Logical- structural analysis allowed to define a typical BAS of which are contained medical plants and have a wide range of pharmacological activity: antipruritic, antiinflammatory, bactericidal, astringent, restorative (tonic), sedative actions.

We have set a correspondence between phytochemicals composition of medical plants and its antiallergic properties. The following classes of BAS are perspective in complex antiallergic therapy: flavonoids (rutin, quercetinum (Inula helenium, Potentilla erecta)), polysaccharidess (glucoribine (Ribes nigrum), pectin compounds (Bupleurum falcatum), inulin (Inula helenium)), coumarins (xantotoxine, izobergaptene (Inula helenium, Potentilla erecta, Angelica archangelica, Pastinaca sativa)), sesquiterpene lactones (alantolactone, izoalantolactone, dihydro-alantolactone (Humulus lupulus, Betulla pendula, Matricaria chamomilla, Inula helenium)), tannic substances (Inula helenium, Potentilla erecta, Gladiolus imbricatus, Veronica officinalis, Juglans regia, Viola tricolor), saponins (Saponaria officinalis, Betula alba, Calendula officinalis).

As a result of the conducted analysis it is possible to recommend the following medical plants as material for development and research of the new plant-based preparations: Gladiolus imbricatus, Inula helenium, Potentilla erecta, Saponaria officinalis, Betula pendula, Calendula officinalis, Veronica officinalis. Complex BAS of these medical plants will allow the provision of the basic directions of antiallergic therapy.

MORPHOLOGICAL AND CHEMICAL STUDIES OF HERB OF PORTULACA OLERACEA L.

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Garden purslane Portulaca oleracea L., genus Portulaca L., family Portulacaceae Juss., order Caryophyllales. Annual herbaceous succulent plant.

The stem is 10-35 cm high, glabrous, fleshy, reddish, stretched, often pinned to the ground or ascending, branched from the base. The leaves are alternate, upper nearly opposite, sessile, cuneate-oval or oblong-cuneate, obtuse on the top, narrowed to the base, fleshy, 1-2 cm long and 0.5-1 cm wide. Stipules scarious, often reduced to small setae. Flowers solitary or 2-3, sitting in the stem-branching or in the leaf axils, 8-12 mm in diameter. Ovary is semi-inferior. Sepals 2, falling at fruiting. Obovate petals 4-6, yellow, caducous, the column with linear stigmas deeply divided into 3-6 branches, 6-15 stamens. Fruit - ovoid capsule up to 8 mm long, unilocular, open by cap. The seeds are very small, numerous, kidney-shaped, lumpy and shiny, from brown to black color.

Purslane drugs have contributed to increasing the heart rate, constrict blood vessels and increase blood pressure, show hemostatic effect at internal bleeding. Purslane reduces blood sugar levels and can be recommended to the diet of patients with a mild form of diabetes.

The analysis of the volatile compounds of purslane herb using chromatography-mass spectrometric method on Agilent Technologies 6890 chromatograph with a mass spectrometer detector 5973 was carried out. Chromatography column - DB-5 capillary with an inner diameter of 0.25 mm and 30 m long. Speed of injection of the sample - 1.2 ml / min for 0.2 min. Flow rate gas (helium) - 1.2 ml / min. The temperature of sample heater - 250 °C. Oven temperature from 50 °C to 320 °C, the heating rate of 4 °C / min.

It were identified and determined the content of 42 compounds. Identified dominant volatile components: hexahydrofarnesylacetone, squalene, linalool and phenylacetaldehyde. Fig.1.

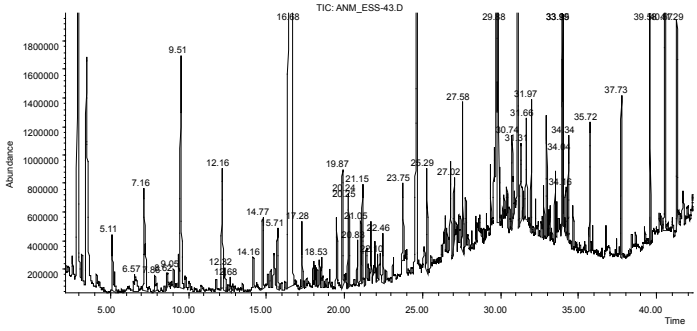

Fig.1. Chromatogramm of the volatile compounds of Portulaca oleracea herb.

Rich chemical composition is the base for further research of Portulaca oleracea L.

THE BIOLOGICAL INVESTIGATION OF ARALIA GUIFOYLEI LEAF

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An actively researched area of plant use is treat of medicinal plants. Currently, about fifty percent of all pharmaceutical drugs have their origin from plants. Plants that once were considered of no value are now evaluated and developed into drugs with little or no side effects.

Aralia guilfoyei is often locally used as a form of folk medicine in Nigeria in the management and treatment of diabetes. Hence, this scientific work was carried out to confirm this folkloric medical claim and practice.

The purpose of biological investigation to carry out an experimental find on Aralia guilfoyei leaves about its possible possession of antidiabetic biological active substances and properties. The research was carried out in Medicinal University of Pot Harcourt, Nigeria on albino wistar rats (30 males and 6 females) and run through a period of 21 days.

The effect of distilled water extract of Aralia guilfoyei leaf on the histology of the liver on alloxan induced diabetic albino wistar rats was evaluated. The fast's blood glucose was measured uses one touch life scan glucometer, body weight was monitored and the slides of the liver tissue were carefully prepared uses haematoxylin and eosin dye method.

The extract at the treated dose (0,5 ml twice daily) significantly fast's blood glucose level in the treated rats compared with the diabetic but untreated rats (test control). At 0,5 ml twice daily administration of the extract, a significant increase in body weight was observed compared with the diabetic untreated group. The liver histology indicated significant recovery with the improve body weight and rejuvenate the damaged of the alloxan induced diabetic albino wistar rats been confirmed.

The purpose of our following investigation the phytochemical study of Aralia guilfoyei leaf, collected in Nigeria in the summer 2012.

The leaves were dried at the normal temperature and tested for the main groups of biologically active substances. Identification teste and chromatographic analysis of herbal drug have been carried out. By our tests and chromatography we found out the presence of polysaccharides, different classes of phenolic compounds, saponines. The herbal drug studying is going on.

ELEMENTAL COMPOSITION OF *GALIUM SALICIFOLIUM* HERB

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Galium salicifolium Klok. is a widespread representative of Plathygalia DC section of *Galium* L. genus, Madder family (*Rubiaceae* Juss.) in Ukrainian flora.

Earlier, we studied phenolic compounds and *components* of the *essential oil* of *Galium salicifolium* herb.

The aim of this work was to study whether elemental composition of *Galium salicifolium* herb *complies* to the requirements for *heavy metals content* as stated in State Pharmacopoeia of Ukraine. Raw material was harvested in the phase of plant's full flowering in Lisopark, Kharkiv, in summer 2012.

Study of elemental composition was carried out using atomic emission spectrophotometry on the base of DNU "STC" Institute for Single Crystals" of NAS of Ukraine. Samples were evaporated from the craters of graphite electrodes in the discharge arc AC power 16 A at 60 seconds exposure. As a source of excitation spectra IMS-28 was used. Spectra were recorded on film using the spectrograph DFS-8 with 600 lines / mm diffraction grating and three-lens lighting slit. Spectral lines in the samples were registered at wavelengths from 270 to 347 nm comparing with a mixture of mineral elements standard samples using microphotometer MF-4.

15 elements in *Galium salicifolium* herb have been identified and quantified. Of these, 6 were macroelements (K, Na, Ca, P, Mg, Si) and 9 were microelements (Fe, Mn, Al, Pb, Sr, Ni, Mo, Cu, Zn).

The elemental content in *Galium salicifolium* herb was 3434.84 g μg/100g. Macroelements (μg/100g) potassium (1500), calcium (430) and silicon (400) were dominant. Among microelements (μg/100g) phosphorus (90), iron and aluminum (ana 80) predominated.

There were no or were beyond the device's determinative capabilities next microelements: cobalt and lead (<0.03), cadmium (<0.01), arsenic (<0.01) and mercury (<0.01).

As a result it was found that *Galium salicifolium* herb meets the requirements for *heavy metals content* as stated in State Pharmacopoeia of Ukraine.

THE INVESTIGATION OF PHENOLIC COMPUNDS OF VEGETATIVE AND GENERATIVE BUDS OF POPULUS SIMONII CARR.

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One of the type of raw material that is used in phytotherapeutic practice are buds. In folk medicine in different countries black poplar buds are known as herbal drugs, which have anti-inflammatory and antibacterial activities. Harvesting buds is very hard work because they are very small (3-7 mm) also entering of other parts of plants such as buds, which began to blossom (2%) twigs and generative buds (8%) is limited in raw materials.

Our attention was attracted by the one type of balsam poplar that is widely cultivated in Ukraine - Chinese poplar (Populus simonii Carr.). Chinese poplar buds are much larger (13-20 mm) than black poplar buds and have the same chemical composition, but it is difficult to distinguish the vegetative buds from generative buds.

The aim of our work was a comparative study of the content of phenolic compounds in the vegetative and generative buds of Chinese poplar. The buds were harvested in March, 2012 from trees, growing on the territory of botanic garden of National Pharmaceutical University. All existing buds were removed from the branches. It was found that 60% from the harvested material are generative buds, which are almost twice larger than vegetative buds. The generative buds composed 30% embryonic male inflorescences, the other part is covering scales, which contain the principal amount of phenolic compounds and essential oils.

The amount of phenolic compounds was determined by spectrophotometric method. Quantitative content of phenilpropanoids are calculated to chrisine by the methods developed for the determination of phenolic compounds in propolis. Quantitative content of hydroxycinnamic acids was calculated in terms to chlorogenic acid by the method described in the article «Nettle leaves» from the State Pharmacopoeia of Ukraine. Results of determination are given in the table.

Example	Content, %	
	Phenilpropanoids	Hydroxycinnamic acids
Embryonic male inflorescences	-	0,28 ± 0,05
Covering scales of generative buds	11,84 ± 0,08	0,38 ± 0,06
Vegetative buds	25,64 ± 0,11	0,60 ± 0,06

The obtained data suggest the possibility of using as medicinal plant the mixture of vegetative and generative buds of Chinese poplar.

THE PHARMACOGNOSTIC STUDY OF VERNONIA AMYGDALINA

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Bitter leaf (Vernonia amygdalina L., Family Asteraceae.) is originated from Nigeria in West Africa. Common names: Bitter Leaf , Mujonso, Ewuro, Etidot etc. It is a shrub or small tree of 2 – 5 m with petiolate leaf of about 6 mm diameter and elliptic shape. The leaves are green with a characteristic odour and a bitter taste. Bitter leaf has a gray or brown colored bark; the bark has a rough texture and is flaked. The branches of the shrub are brittle and break off easily. The green leaves are oblong to lance like in shape, they are veined, and bear pale soft hairs on the underside. Bitter leaf bears small white flowers, these flowers bloom in clusters during the spring. The plant bears small fruits, which have slightly hairy small nuts inside.

The herb is found growing wild along the edges of agricultural fields. An indigenous African species, it grows in most parts of Sub-Saharan Africa. In Nigeria, and in many parts of East Africa, bitter leaf is eaten as vegetables. Soups and stews are made from the leafy greens of this plant, while the herb is prepared the same way the spinach is used in the West. Many animals eat this plant when they are sick. It was also discovered by zoologists that animals use the plant to cure themselves. They also revealed that chimpanzees, inhabiting the Mahale Mountains of Tanzania, have been observed chewing the pith of the bitter leaf possibly due to its ability to ward off parasites.

According to the literature bitter leaf contain the Steroid glycosides. These class of substances possess a potent anti-parasitic, anti-tumor, and bactericidal effects. The bitter leaf is mainly employed as an agent in treating Schistosomiasis, a disease caused by parasitic worms. Some studies that validate the traditional use of Bitter leaf in the treatment of malaria in Africa, a new study has found that the best mode of preparing local recipe using the leaves was to soak it in water-alcohol mixtures. Some of the medicinal uses of the herb by the literature data: Diabetes, Pain relief, general weakness, stroke, pneumonia, insomia, Arthritis.

The purpose of our investigation the phytochemical study of Vernonia amygdalina leaf, collected in Nigeria. The leaves were dried at the normal temperature and tested for the main groups of biologically active substances. By our tests and chromatography we found out the presence of polysaccharides, different classes of phenolic compounds. The herbal drug studying is continues.

DETERMINATION OF NITROGEN CONTENT IN ARTEMISIA L. SPECIES HERBS

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Nitrogen is one of the main macronutrients required for plant life. It is part of amino acids and proteins (nitrogen's share in these compounds is about 15-19%), nucleic acids, chlorophylls, enzymes, many of vitamins, phosphatides, ATP, alkaloids etc. The total nitrogen content in plants is within the limits of 0.5-5% and more depending on the species, age, stage of vegetation, organ, soil type, mineral nutrition conditions and so on. Nitrogen content is an important indicator of food and fodder value of plants and indirectly allows to evaluate the quantitative content of nitrogen-containing biologically active substances (BAS).

The aim of our study was to determine the content of nitrogen in the herbs of 10 species of the genus Artemisia L. The objects of study were the following species (according to subgenera): subgenus Artemisia Less. - A. absinthium L., A. vulgaris L., A. austriaca Jacq., A. abrotanum L., A. annua L.; subgenus Dracunculus Bess. - A. dracunculus L., A. arenaria DC., A. campestris L., A. marschalliana Spreng.; subgenus Seriphidium Rouy - A. nutans Willd. Herbs for research were harvested in Kharkiv, Lugansk, Kiev oblasts and Crimea in 2010-2012 years during the phases of budding and flowering.

Determination of nitrogen content was performed by CHNS-O elemental microanalysis method. For investigation we used CHNS-O elemental analyzer EuroVector series EuroEA3000 working in principle based on the dynamic combustion sample weight of 0.5 mg in an oxygen atmosphere, with next divide by chromatographic separation of gases formed. This method is characterized by high accuracy and the ability to use for the analysis of trace materials.

According the results of research was established that nitrogen content in herbs of studying species was from 2.2% to 5.1%. The highest nitrogen content was founded in A. annua L. (5.1%) and A. abrotanum L. (4.3%) herbs; the lowest - in A. marschalliana Spreng. (2.2%), A. vulgaris L. (2.5%) and A. austriaca Jacq. (2.6%) herbs.

AMINO ACIDS COMPOSITION OF ARTEMISIA NUTANS WILLD. HERB

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Artemisia nutans Willd. (A. cretacea Kotov, Seriphidium nutans (Willd.) Sojõk) - perennial herb belong to the subgenus Seriphidium Rouy of the genus Artemisia L. of the family Asteraceae (Compositae). The stem is straight, 30-50 cm in height, lignified at the bottom. The plant is grayish by reason of the dense felt pubescence. Leaves are alternate, two or three times pinnatisected, terminal leaf lobes are ovate-lanceolate, flowers are reddish, baskets are about 3-3.5 mm in length and 2 mm in width, on the pedicles up to 3 mm, drooping, collected in a spreading paniculate inflorescence. In Ukraine founds in the left-bank steppes and the Donbas, grows mainly on chalky slopes.

Data on the chemical composition of A. nutans Willd. herb in the literature are scarce. We have previously investigated the composition of the essential oils of this herb material, and the purpose of this work is to study its amino acid composition.

The object for study was A. nutans Willd. herb, harvested in the budding stage in the Bilovodsk region of the Lugansk oblast in summer 2011.

The amino acids composition determination was carried out by the chromatograph of the Agilent Technologies firm (model 1100). The chromatographic column size 4.6Ч50 mm filled with oktadecilsilyl sorbent corning 1.8 micron ZORBAX-XDB-C18 has been used for the analysis. Preparation of samples for determination of free amino acids was carried out in the vials, adding 0.1 N hydrochloric acid containing 0.2% β-mercaptoethanol in the ultrasonic bath for 2 h. To determine the total content of amino acid hydrolysis was performed by 6 N hydrochloric acid containing 0.4% β-mercaptoethanol for 24 h. Identification was performed by the retention time of amino acids standards.

According to results of the research the quantitative content of 20 amino acids has been determined. The free amino acids content was 797.0 mg/100 g (0.8%), the total amino acids content – 6040.3 mg/100 g (6.0%). Dominant among free amino acids was proline, dominating the overall content – proline, glutamic acid (with glutamine), aspartic acid (with asparagine), arginine and alanine.

RESEARCH OF THE VOLATILE COMPOUNDS CONTAINED IN LIPOPHILIC EXTRACT FROM ARTEMISIA MARSCHALLIANA SPRENG. HERB

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Artemisia marschalliana Spreng. - perennial semishrub belonging to the subgenus Dracunculus Bess. of the genus Artemisia L. of the family Asteraceae (Compositae). Flowering shoots are straight, strong, 40-100 cm in height, ribbed, brownish or reddish color, lignified at the bottom. Leaves are twice pinnatisected, with narrow linear segments. The whole plant is more or less densely pubescent. Baskets are about 2-3 mm in length, almost sessile, ovate, collected in one-sided inflorescences. Spread in the steppe and forest-steppe zones from Western Europe to Western Siberia, and in North America. In Ukraine - everywhere except the Carpathians. Grows in dry open places prefers sandy soils.

According literature, the A. marschalliana Spreng. herb contain essential oil, flavonoids, hydroxycinnamic acids. We have carried out the phytochemical study of the herb and extracts from it. The aim of this work was chromatography-mass -spectrometry study of the volatile compounds contained in the lipophilic extract of the A. marschalliana Spreng. herb.

The object of research was the chloroform extract, obtained by circulation extraction method in Soxhlet extractor. The herb was harvested in the Kharkiv oblast in summer 2011.

For investigation we used chromatography-mass-spectroscopy method. Conditions of research: chromatograph Agilent Technology 6890N, equipped with mass-spectrometric detector 5973N, capillary chromatographic column INNOWAX with inner diameter 0.25 mm and in length of 30 m. In order to identify the individual components the data of mass spectra libraries NIST 05 and WILEY 2007 had been used.

According to the results of the research the quantitative content of 40 compounds has been established. Among them are monocyclic monoterpenoids (1,8-cineole, β-thujone), bicyclic sesquiterpenoids (β-eudesmol), aromatic compounds (eugenol, methyl chavicol, benzaldehyde, benzyl alcohol), triterpene sapogenins (α-and β-amyrins) steroids (β-sitosterol, β-stigmasterol acetate), fatty acids and their esters, hydrocarbons.

MORPHOLOGICAL, ANATOMICAL AND PHYTOCHEMICAL RESEARCH OF VERONICA LONGIFOLIA L. HERB

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Veronica longifolia L. - perennial herb of the family Scrophulariaceae, is widespread in Europe, the Caucasus, Central Asia, Siberia and the Far East. Plants of the genus Veronica L. is not sufficiently fully researched in morphological and anatomical, so their morphological differentiation is difficult. The chemical composition of the plant was not completely studied. It is known that the herb contains saponins, flavonoids (luteolin, cynaroside), iridoids (aukubin, catalpol), choline, tannins, fatty and essential oil, coumarins, hydroxycinnamic acids.

The aim of investigation was to study the morphological and anatomical definition and diagnostic signs of V. longifolia L., and preliminary phytochemical studies of the grass of this species. The object of research was the herb of V. longifolia, harvested in the summer 2012 in Ukraine. The research was conducted by used thin-layer and paper chromatography, as well as with the use of qualitative reactions.

This plant can be identified by macroscopic signs: stems are strong, straight, glabrous or shortly feathery, 30-150 cm in height, sessile leaves, opposite leaf aestivation or placed 2-4 in verticil, long-lanceolate, with almost cordate or flat base, or linear-lanceolate with wedge base, glabrous or little feathery below. Apical raceme up to 25 cm in length, single or multi-lateral racemes.

The study shown that for V. longifolia L. diagnostic signs are: celled and bicellular curved warty trichomes located on the edge of the leaves, stems densely covered with long, slightly warty, curved trichomes; flower with densely feathery calyx, with straight celled, curved and warty multicellular trichomes and glandular trichomes with celled or bicellular peduncle and celled or bicellular head.

Previous studies revealed the presence of such groups of biologically active substances (BAS): saponins, flavonoids, tannins of condensed group, iridoids. Chromatographic methods revealed the presence of at least 3 iridoids, 6 flavonoids, 4 hydroxycinnamic acids.

In results of our investigation was established series micro- and macroscopic signs that allows reliably differentiate the studied type of V. longifolia L. herb. The results of the phytochemical screening create preconditions for further in-depth study of V. longifolia L. herb as a promising source of BAS.

COMPOUNDS OF ESSENTIAL OILS IN ROOTS OF HAMERION ANGUSTIFOLIUM (L.)

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Essential oils are important group of biological active substances. They have wide spectrum of therapeutic action and that gives the opportunity take the important place among medical and prophylactic medicines. The most specific pharmacological effects of essential oils are anti-inflamatory, analgetic, antiseptic, antiviral, antitoxic, antioxidative activities, and also influence on motility of gastrointestinal tract, liver, brain, blood circulation functions, take part in functioning of cell membranes, possess vasodilator and anticoagulative activities.

There are no information in scientific publications about the contents of essential oils in roots of Hamerion angustifolim. That's why the purpose of our research was to study the components of essential oils in roots of Hamerion angustifolium collected in the Ternopil region.

The essential oils from Hamerion angustifolim were isolated by steam distillation using vial. Components of essential oils were studied by chromatography Agilent Technology 6890N with mass spectrometric detector 5973N.

Results of studying compounds of essential oils in roots of Hamerion angustifolium showed that it contains 24 components which are identified 23. The dominant compound of essential oils is squalen. Part of squalen is 175,7 mg/kg. It's known that squalen has the immunomodulatory and anti-tumor activities, normalize cholesterol metabolism, activates the regenerative processes in the human body. Essential oil in roots of Hamerion angustifolium contain nonacosane (30,8 mg/kg), pentacosane (30,3 mg/kg), alpha-bisabolol (25,9 mg/kg), heptacosane (23,4 mg/kg), nonane acid (20,0 mg/kg) too.

Accept previous compounds, essential oils in a small amounts contain nonanal, decanal, methyleugenol, hexahydrofarnesylacetone, heneicosane, docosane, hexacosane, tetracosane, eicosane.

We consider that the drugs of Hamerion angustifolim will display pharmacological activities due to the presence of essential oils in the contents of investigated plant.

STUDY OF LIPOPHILIC FRACTION OF SUGAR MAIZE COLUMNS AND STIGMAS

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Subtype conventional sugar maize is becoming increasingly common in the economy of Ukraine. A variety of chemical composition and a wide range of applications in medicine of maize columns and stigmas indicates the rationality of study of herbal drug harvested from genetically enhanced form of maize – sugar content gene carrier sugary-1.

In the experiment, grinded raw material exhaustively extracted with chloroform in the Soxhlet apparatus, then concentrate and determined the content of lipophilic substances as calculated to the absolutely dry raw materials. The composition of lipophilic extracts include lipids, chlorophylls, carotenoids and other substances. Qualitative determination of chlorophylls and carotenoids was performed on TLC plates «Silufol» and «Sorbfil" in the solvent system: hexane - acetone (6:2) - the first direction; hexane - acetone (6:4) - the second direction. Localization of chlorophylls on chromatograms indicated by the green coloring, and in filtered UV light (λ = 366nm) – by the bright red fluorescence. Carotenoids identified in visible light as yellow and orange spots, and in filtered ultraviolet light - as brown spots. Chromatograms were treated with 10% solution of phosphoric-molybdenum acid and kept in the oven for 5-7 minutes at 80-90 ° C. Spots corresponding carotenoids become blue-violet. Analysis of content of pigments, which included in the group of chlorophylls was determined by spectral method at photocolorimeter. Analysis of content of carotenoids was determined by spectrophotometric method (λ=450nm).

Lipophilic extract of maize columns and stigmas had yellow-garnet color, a faint characteristic odor and thick homogeneous consistency. The lipophilic fraction output, so as chlorophyll and carotenoids content are given in the table 1.

Table 1

Content of lipophilic substances, chlorophylls and carotenoids in columns and stigmas of maize sugary-1

Herbal drug	Content of lipophi-lic substances, %	Amount of chlorophyll content, %	Amount of carotenoids content, %
columns and stigmas	3.54±0.10	0.50±0.01	186.23±1.42

Analysis of the chromatogram showed the presence of 4 substances referred to the chlorophyll and 7 substances of carotenoid structure in maize columns and stigmas. For the first time studied the lipophilic fraction of columns and stigmas of sugary maize - perspective herbal drug for the pharmaceutical industry.

PHYTOCHEMICAL RESEARCH OF PRUNELLA SPECIES

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Prunella (self-heal) is genus of perennial herbaceous plants of the family Lamiaceae. Genus includes about 15 species, in Ukraine are growing 3 species: P. laciniata, P.vulgaris and P. grandiflora. These species are also known as decorative and ornamental. Selfheal attracts the researcher's attention because for its wide range of applications in folk medicine as an antiviral, antibacterial, anti-inflammatory agents.

Herbal drugs of Prunella species were collected during the 2011-2012 years in blossom time in Dergachevsky region and Botanical Garden of NPhU. Study of phenolic compounds was carried out using paper chromatography and TLC compared with reference compounds in following solvent systems: butanol-acetic acid – water 4:1:2, 4:1:5, 2, 15 and 30% solution of acetic acid, chloroform-methanol-water 24:14:3, toluene- ethylacetate - formic acid 50:40:10. After developing the chromatograms were dried and analyzed in UV-light before and after spraying by specific reagents. Phenolic compounds were identified by a specific fluorescence in UV light (365 nm, blue, yellow, brown color) using the specific reagents. We succeed to identify about 18 phenolic compounds in herb of P.vulgaris, 21phenolic derivatives in herb of P. grandiflora and 17 compounds in herb of P. laciniata.

We noted the presence in herbs of three species of Prunella hydroxycinnamic acid derivatives, especially rosemarinic, caffeic, chlorogenic and ferulic acids. Among the identified flavonoids there are quercetin, kaempferol, their glycosides and derivatives.

Analysis of total hydroxycinnamic acids was performed by the method of the European Pharmacopoeia, which is given for herbal drug of rosemary and lemon balm leaves. By spectrophotometric method using Folin-Chokolte reagent was determined total hydroxycinnamic derivatives at wavelength λ= 505 nm expressed as rosmarinic acid (Spectrophotometer "Evolution 60S"), with the reference into anhydrous herbal drug. Found that in the Prunella vulgaris herb total hydroxycinnamic acids is 4,8±0,08%, and in the Prunella grandiflora herb 4,5± 0,09%, in the Prunella lanceolata herb 3,5%±0,06.

The data meets the requirement with the content of active substances of the European Pharmacopoeia monographs for leaves of lemon balm and rosemary. Therefore it is possible to assume that the species of the genus Prunella is a perspective source of therapeutic and preventive agents.

DETERMINATION OF FATTY ACIDS IN THE LEAVES, RHIZOMES AND ROOTS OF ANGELICA SILVESTRIS L.

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ANGELICA SILVESTRIS L. is perennial plant of Celery family with short thick rhizome, straight fistular stem with height of 1.5 m, two-three feathery leaves and white or cream flowers gathered into large umbrellas. In Ukraine, ANGELICA SILVESTRIS L. grows all over the country except Crimea among the bushes on the banks of rivers and ponds, on wet meadows. The plant is used in folk medicine as a diuretic and anti-flatulent agent.

The aim of our study was a quantitative and qualitative determination of fatty acids in the leaves, rhizomes and roots of ANGELICA SILVESTRIS L., which were prepared in Husyatyn District, Ternopil Region in August 2012. Qualitative and quantitative analysis of fatty acids in raw materials was determined by method of gas chromatography at the National Institute of Vinegrowing and Wine "Magarach" under the supervision of B.O. Vynohradov using chromatography Agilent 6890.

The results showed the presence of 15 fatty acids, including 4 unsaturated in the studied objects. In lipophilic extract of rhizomes and roots were found 14 fatty acids, unsaturated fatty acids dominate – oleic - 12.72% and linoleic - 32.63%. In lipophilic extract of ANGELICA SILVESTRIS L.'s leaves were found 11 fatty acids; the largest share have: linoleic - 22.41% and linolenoic - 18.23% acids. From the saturated fatty acids the highest content in the extract of rhizomes and roots has hexadecylic acid - 32.35%, in the extract leaves - hexadecylic - 26.63% and tetradecanoic - 14.27% acids.

In the rhizomes and roots of ANGELICA SILVESTRIS L. was found lauric acid, which is present in leaves, and its content is 2.09%.; palmitooleic acid, content of which in leaves is 2.33% arachic acid 0.87% and 7,10,13-*hexadecatrienoic* acid 7.39%. Pentadecanoic acid was not found in the leaves of ANGELICA SILVESTRIS L., but it is present in rhizomes and roots, and the content of which is 3.37%.

Thus, received results of our research indicate promising outlook of the research of this wild plant and ascertainment of possible pharmacological properties.

FEATURES OF STANDARDIZATION AND QUALITY CONTROL OF HERBAL DRUG - HERB CENTAURY

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Centaury normal or umbrella - Centaurium erythraea Rafn. (-C. Umbellatum Gilib.) Belongs to the family of Gentiana (Gentianaceae). This is one-or two-year herb 10-40 cm tall. Grows in dry areas between shrubs on the hills, meadows, plains and forest edges, especially on clay soil.

Centaury herb widely used in traditional medicine - with reduced appetite, indigestion, especially with increased gastric acidity, heartburn, flatulence, gastrointestinal bleeding, liver disease, biliary tract and kidneys. It is part of the delicious teas, gastric fees and bitters.

Herb of centaury is also part of such drugs as Canephron H (used in the treatment of chronic infections of the bladder (cystitis) and kidney (pyelonephritis), noninfectious chronic inflammation of the kidneys (glomerulonephritis, interstitial nephritis), alcoholism, to prevent the formation of urinary stones in including after removing them), Depurafluks (used in acute and chronic constipation), Bittner and Maurer balms.

Over the last decade, an interest to herbal medicines (drugs) has grown significantly due to the softer effect, less addictive and side effects compared to synthetic drugs. Introduction to the domestic medical practice of a new herbal drug (HD), products of its processing, expanding the range of herbal remedies for improved system of standardization and quality control.

Purpose of work is standardization and control of quality herbal drugs herb of centaury accordance with the requirements of the European Pharmacopoeia (EP).

Detailed botanical description of this HD conducted microscopic and macroscopic methods. Qualitative analysis of materials identified by thin-layer chromatography (TLC) with identification markers - flavonoids: rutin and swertiamarin. Tests for purity HD conducted in terms: “Foreign matter”, “Bitterness value”, “Loss on drying” and “Total ash”.

The research has allowed to determine the parameters of standardization of centaury herb that can be used to develop relevant Pharmacopoeia articles and production standards for input control.

The results of testing methods of monographs EP and researches for standardization of centaury herb can be used in the development of monographs State Pharmacopoeia of Ukraine for this kind of HD.

DETERMINAIN OF BIOLOGICALLY ACTIVE SUBSTANCE IN ANTIDIABETIC PLANTS GATHERING

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Diabetes is difficult medical and social problem not only national, but also international scale. Number of patients with diabetes in the world increases every year. Prevalence of this disease needs further search for additional methods of traditional and nontraditional treatments. Appointment of drugs from medicinal plants can be a good alternative for the treatment of diabetes type II.

One of the basic principles of herbal medicine in diabetes type II is the using of plants that are rich in vitamins, organic acids and other biologically active substances which increase the body's defenses. That is why it is important to determine the qualitative and quantitative composition of biologically active substances in antidiabetic plants gathering.

The aim of our study was phytochemical analysis of antidiabetic plants gathering, which includes Equiseti arvensis herba, Sambuci flores, Inulae rhizomata et radices, Hyperici herba, Tiliae flores, Polygoni avicularis herba, Myrtilli folium, Urticae folia.

The results showed that the antidiabetic plants gathering contains tannins, which is confirmed by qualitative reactions with bromine water (sediment), 1% solution of gelatin (turbidity). The reaction with solution of iron (III) ammonium sulphate showed black-green color, indicating the presence of condensed tannins. Quantitative analysis showed that the content of tannins in antidiabetic plants gathering is 6.86% in terms of absolutely dry raw materials.

Quantitative determination of organic acids was performed using pharmacopoeial alkalimetry method. The results showed that the content of organic acids in antidiabetic plants gathering is 2.579% in terms of absolutely dry raw materials. The results of the qualitative and quantitative composition of organic acids were determined by gas chromatography Agilent Technologies (model 1100), showed that antidiabetic plants gathering contains 18 organic acids. In large amounts found citric (1341.1mh/kh), akonitic (781.7mh/kh), oxalic (732.4mh/kh), malic (722.8mh/kh), malonic (322.1mh/kh) acids.

These results showed that this antidiabetic plants gathering is a rich source of biologically active substances and therefore can be an effective tool to improve metabolic processes in patients with diabetes.

QUANTITATIVE DETERMINATION OF UNSATURATION DEGREE OF ANISE OIL BY PEROXY ACID OXIDATION REACTION

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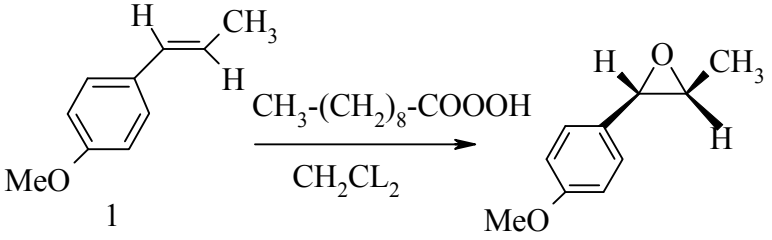
Anise oil (Latin Anisi salami) is an essential oil, which is extracted from pounded dried Pimpinella anisum L. riped by distillation with steam, included into State Pharmacopoeia of Ukraine (SPU 1.2, P. 360-362). It is widely used in medical practice, the food industry and the national economy (aromatic substance, flavorant (Heyfyts LA Dashunyn VM, 1994). Terpenoid trans-Anetole (n-metoksipropenilbenzen, izoestrahol) (the main component of the oil) is leaked from oil by vacuum rectification with subsequent freeze and is used for flavoring of chewing gum, to impart anise smell and taste to alcohol, confectionery, honey, nuts, it is also a component of various spices. It is also used in the manufacture of perfumes, deodorants for soaps and detergents industrial flavoring. Methods of gas (GC) and liquid chromatography to quantify are recommended.

The reaction kinetics of epoxidation anethole were studied by iodometric titration method using peroxycaprinic acid. It was found that for 40 min in methylene chloride medium peroxycaprinic acid reacts with unsaturated group quantitatively and stoichiometrically: 1 mole anethole (see Figure, 1) consumed 1 mole of oxidant. These results were obtained by the new iodometric method of quantitative determination of anethole for the remainder of oxidant and the total content of ingredients of anise oil containing unsaturated ligament (anethole, metylkhavykol, limonene, linalool, α-pinene and other monoterpenoids). The results were compared with those obtained by GC. RSD ≤ 1% (n = 5; P = 0.95%).



1

$$CH_3(CH_2)_8C(O)OOH + H_2SO_4 + 2KI = CH_3(CH_2)_8C(O)OH + K_2SO_4 + I_2 + H_2O$$
$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6.$$

DETERMINATION OF TOTAL POLYSACCHARIDES AND TANNINS IN SOME SPECIES OF SALVIA

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The genus Salvia (commonly known as sage) is a broad genus belonging to the family Lamiaceae, which is consisted approximately 900 species. The most of Salvia species are a rich source of phenolic acids, terpenoids, phenolic compounds, flavonoids, polysaccharides and other. Polysaccharides are known to be useful in the treatment of inflammatory conditions and bacterial or viral infections. The aim of our study was to establish the quantity of total polysaccharides and tannins in some species of Sage herbs.

The objects of our study were of herbs of Salvia verticillata L., Salvia patens L. and Salvia officinalis L., collected in the phase of mass flowering in June 2012 at the National Botanical Garden of M.M. Grishko, Kyiv.

Determination of quantity of total polysaccharides and tannins conducted in aqueous extracts.

To determine the content of total polysaccharides to aqueous extracts of researched herbs of Sage was added 96% alcohol, centrifuged, filtered and obtained precipitate washed with a mixture of water - 96% alcohol (1:3) and successively washed with 96% alcohol, acetone, ethyl acetate. Filter with sediment was dried in air, then to constant weight at temperature of 105 °C.

The content of total polysaccharides was calculated by gravimetric method, on the dry raw materials, in %, using the difference between the mass of empty filter and mass of filter with precipitate. To determine total tannins to aqueous extracts of researched herbs of Sage was added indigo sulphonic acids and titrated with 0.02 M solution of potassium permanganate to appear the golden yellow color.

As a result, the research found that most content of total polysaccharides have been found in the herb of Salvia verticillata L. – 9.23%, slightly lower in the herb of Salvia officinalis L. – 7.32% and the lowest in the herb of Salvia patens L. – 5.80%.

The largest content of total tannins was investigated in the herb of Salvia verticillata L. – 13.94%, slightly lower in the herb of Salvia patens L. – 8.58% and the lowest in the herb of Salvia officinalis L. – 7.66%.

As seen from the obtained results the herb of Salvia verticillata L. is the most promising raw materials on the total content of the two groups of biologically active compounds - polysaccharides and tannins.

DEVELOPMENT OF METHODICS OF THE QUALITATIVE AND QUANTITATIVE ANALYSIS OF THE COMBINED PHYTOPREPARATION "DENTOS" FOR STOMATOLOGY

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The creation of effective and safe medicines for stomatologic practice is represented the actual direction because as according to WHO data, infectious and inflammatory diseases of the periodontal has to 95% of adult population of the globe and to 80% of children. On the basis of department of pharmacognosy with botany and bases of phytotherapy of Samara State Medical University the combined remedy «Dentos» was developed. It is representing alcohol-water extraction from five species of medicinal plants, namely: leaves of *Eucaliptus viminalis* Labill., bark of *Quercus robur* L., flowers of *Calendula officinalis* L., herbs of *Echinacea purpurea* (L.) Moench., essential oil of *Caryophyllus aromaticus* L.

Purpose: it is substantiated of approaches to standardization of the phytopreparation "Dentos" and development of techniques of the qualitative and quantitative analysis.

Materials and methods: phytopreparation "Dentos", State standard samples rutin and eucalimin, caffeic acid; spectrometry, TLC, HPLC.

The received results: The phytochemical and analytical researches of studying of parameters of quality of "Dentos" were carried out. There were proposed chemical reactions on the phenolic compounds and characteristics of electronic spectrum of absorption ("maximum" at 275 nm and "shoulder" at 330 nm) for the qualitative analysis. For the quantitative analysis there were proposed to use the permanganatometric method of definition of the total oxidized substances (not less than 0,7 %); direct spectrophotometric method of determination of total phenylpropanoids (calculated on caffeic acid: not less than 0,3 %) and the phenolaldehydes (calculated on eucalimin: not less than 0,1 %); differential spectrophotometric method for definition of total flavonoids (calculated on rutin: not less than 0,2 %).

Conclusions: The created approaches for standardization and the offered methods of the analysis allow to estimate objectively the authenticity and quality of new medicine "Dentos" and, therefore, to create the conditions for the manifestation of a target spectrum of its pharmacological activity.

PHYTOCEMICAL RESEARCH OF JERUSALEM ARTICHOKE

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The Jerusalem artichoke (Helianthus tuberosus L.) is used in folk medicine since ancient times. The tubers of this plant contain to 22% inulin, that is insulin substance of plant origin. Inulin is the unique natural polisakharid, it consists 95% of fructose. In a stomach inulin is not assimilated, the part of it dissociates to short fructose chainlets and separate molecules of fructose, which get to the bloodstream. It is very important for people, who are ill with the diabetes mellitus, because fructose is being assimilated without insulin participation (unlike glucose). That's why such people are recommended to use the Jerusalem artichoke tubers.

The purpose of research is a phytochemical study of Jerusalem artichoke herb and tubers,which are cultivated in Ukraine.

The previous study of chemical composition of herb and tubers by high-quality reactions was fulfilled. Monosugars, aminoacids, polysaccharides, phenolic substances were found out. A chromatographic study was carried out on the «Filtrak» paper in the following solvent systems: acetone – butanol – water (7:2:1) – for a study monosaccharide composition of water-soluble polysaccharides; n-butyl alcohol – acetic acid – water (4:1:2) and 15% acetic acid – for the detection of phenolic substances – flavonoids and hydroxycinnamatic acids, aminoacids; ethyl acetate – acetic acid (8:2) – for identification of ascorbic acid. For determination of quantitative content of a number of biologically active substances such methods as gravimetry, alkalimetry, permanhanatometry, spectrophotometry were used.

Rhamnose, arabinose, glucose, lactoglucose, xylose, fructose from monosugars were identified. Not less than 12 substances from aminoacids were found out, among them aspartic and glutaminic acids, methionine, arginine, phenylalanine were identified. Chlorogenic and neochlorogenic acids from hydroxycinnamatic acids in both types of raw material were identified. Polysaccharides content was not less than 10% in a herb, in tubers – 38%. Ascorbic acid content was 0,012% for tubers and 0,015% – for a herb, organic acids content was 1,866% for tubers, 1,194% – for a herb, phenols oxidation sum was not less than 6% for tubers, not less than 25 % – for a herb, hydroxycinnamatic acids sum was about 1,17% for tubers, 7,7% – for a herb, flavonoids sum was 1,7% for a herb.

Conclusion: the jerusalem artichoke herb and tubers phytochemical study is a perspective way for development in medicine.

STUDY OF QUALITY COMPOSITION OF LEAVES OF BURDOCK LARGE

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The aim of the work is a previous study of qualitative composition of leaves of burdock large.

Materials and methods. The leaves of burdock large were prepared in the Vinnitsa and Kharkiv areas. We used test-tube reactions and chromatography on the paper and thin layer of sorbent for preliminary research of qualitative composition of the raw material.

Test-tube reactions were carrying out with the Feling's reagent of at heating (sugars), with 0.2% spirit solution ningidrin at heating (amino acids).

The chromatography on the paper was carried out in the systems of solvents: on the presence of sugars, phenolic acids and phlavonoids cleared n-butanol- acetic acid icy-water (4:1:2); was used on sugars – cleared n-butanol-piridin-water (6:4:3); on organic acids – cleared n-butanol-formic acid-water (4:1:5), cleared ethylacetate-formic acid-water (3:1:1); on phenolic acids and phlavonoids – 2%, 5% and 15% acetic acid. The chromatography in thin layer of sorbent was carried out in the system of solvents by a chloroform-alcohol methyl (9:1).

Results. The presence of sugars was confirmed by the results of positive reaction with the Feling's reagent (orange copper (II) oxide sediment was formed) and chromatography on the paper (where not less than three sugars, two of which were identified as D-glucose and D-fructose, were seen observed). Positive reaction from 0.2% spirit solution ningidrin before and after hydrolysis showed that raw material contained free and fixed amino acids. We identified organic acids (apple and lemon), phenolic acids (chlorogenic and ferulic), phlavonoids (kempherol and quercetinum) by chromatography on the paper.

Conclusions. At result of the research it was determined that the leaves of burdock large contain carbohydrates (D-glucose and D-fructose were identified), free and fixed amino acids, organic acids (apple and lemon), phenolic acids (chlorogenic and ferulic) and phlavonoids (kempherol and quercetinum). The obtained data will be used in further researches while determinating quantitative content biologically active substances in the leaves of burdock large.

RESEARCH OF ESSENTIAL OILS OF LABRADOR-TEA SHOOTS

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Comprehensive study of underinvestigated species today is the urgent task of modern pharmaceutical science in the world.

Promising plant for research is Labrador-tea (*Ledum palustre*). This plant has a large area of distribution and significant resource base in the forest area of Ukraine. The essential oil is a major component of all parts of the plant except the roots. Also plant is rich in tannins and flavonoids. In folk medicine Labrador-tea is usually used as antitussive, anti-inflammatory, antispasmodic, diuretic, diaphoretic, disinfectant and sedative. In official medicine it is used only as antitussive herb due to content of ledol in essential oil on the base of which the drug "Ledin" was created and registered in Ukraine but not represented in the pharmacies. This indicates that the potential of plant raw material was used insufficiently.

The purpose of our study was to examine the composition of the essential oil of Labrador-tea shoots to determine the prospects for a new drug creation on the base on it.

Essential oil from Labrador-tea shoots was obtained by method of steam distillation. The time of distillation was 2 hours. It was determined that the plant raw material contains 0.7% essential oil.

Qualitative and quantitative composition of components of Labrador-tea shoots essential oils were defined by paper chromatography and Chromato-Mass-Spectrometry using a gas chromatograph Agilent Technology 6890 with mass spectrometric detector 5973. Identification of compounds was performed by comparison of obtained mass spectra with library data NIST05-WILEY (about 500,000 mass spectra). Indexes retention of components were calculated on the base of results of analyzes of substances with the addition of a mixture of normal alkanes (C_{10}-C_{18}).

In general, 23 substances were detected in the essential oil, 15 of which were identified. It was also found that the dominant components were ledol, neofitadiene and α-terpinylacetate.

The results of investigation will be used to create a new medicine and its standardization.

INVESTIGATION OF ANTIOXIDANT PROPERTIES OF EXTRACTS FROM SELECTED MEDICINAL PLANTS

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Plants are potent source of flavours, pigments and biologically active substances that commonly used in pharmaceutical and food technologies.

The aim of the work was investigation of antioxidant compounds content in extracts from plant materials, evaluation of their antiradical activity to determine the possibility of their using in different brunches of food industry as a functional ingredients or dietary supplements.

The herbs of oregano (*Oгнganum vulgбre L.*), roots of burdock (*Arctium lappa L.*), shoots of blueberries (*Vaccнnium myrtнllus L.*) and licorice roots (*Glycyrrhнza glabra L.*) were chosen for investigation. These plants have a lot of bioactive water soluble components with antioxidant activity. Selected species have a wide area of distribution in Ukraine, original organoleptic properties and not expensive.

The water was used for extraction. The optimal extraction conditions were experimentally determined. Under these conditions the yields of the extractions were 2.0-3.2 %.

The total phenolic content of the extracts was determined using a Folin-Ciocalteu assay. It was expressed as mg Gallic Acid equivalents (GAE) per 100 ml of the plant extract. Ascorbic acid content was determined by colorimetric assay with *Tillman's reagent.* All samples were analysed in triplicate and averaged.

The free radical scavenging activity of the extracts, based on the activity of the stable 1,1-diphenyl-2-2-picrylhydrazyl (DPPH, Sigma-Aldrich, USA) free radical, was determined by a method described by Brand-Williams et al., 1995 with our modification. The synthetic antioxidant ascorbic acid was used as positive control. The antioxidant activity was expressed as mM of the ascorbic acid equivalent (AAE) antioxidant capacity per 100 ml of the extract.

The total phenolic content was ranged from 43.2±2.09 to 69.8±3.76 mg GAE per 100 ml of extract, maximum amount of the vitamin C was 5.7±0.323 mg ascorbic acid in shoots of blueberries extract. Free radical scavenging capacity of the extracts ranged from 0.60±0.0178 to 7.91±0.248 mM of AAE antioxidant capacity per 100 ml of the extract. The highest activity was determined for the extract of oregano herbs.

The results were showed that tested extracts possess potent antioxidant activity and may be considered as natural source of antioxidants.

STUDY OF LIPOPHILIC FRACTION OF SPREADING WOODRUFF HERB

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Continuing studies of biologicaly active compounds (BAC) of spreading woodruff – *Asperula humifusa* (M.B.) Bess. which belongs to madder family (*Rubiaceae)* we obtained different fractions by extracting the raw material sequentially with different solvents in order of their polarities increase. The aim of our work was to study lipophilic compounds of spreading woodruff herb collected in the flowering phase in summer 2011 near the city of Eupatoria the AR of Crimea.

The chloroform fraction was obtained by exhaustively circulating extraction with chloroform of powdered air-dried herb in the Soxhlet apparatus. Yield made up 3.23%.

Preliminary studies were carried out using thin layer chromatography (TLC). By the magnitude of *Rf* and colour of spots in visible light and UV-light before and after treatment of chromatogram with corresponding chromogenic reagents chlorophylls, isoprenoids – irydoids, carotenoids have been found. Composition of the lipophilic fraction was studied by the method of three-dimensional scanning spectrofluorimetry in visible light and UV-light using spectrofluorometer Hitachi F4010, reprogrammed for 3DF-measurement. Scanning parameters: excitation wave length range – 220-800 nm, fluorescence wave length range – 220-800 nm, scan step – 10 nm, gap of excitation / fluorescence – 5/5 nm.

The results of the current study showed that the chloroform fraction of spreading woodruff herb contains chlorophylls – 554.57 mg/g (λexc 250-310 nm, λexc 360-440 nm, λemi 610-690 nm) and carotenoids – 313.58 mg/g (λexc 340 - 360 nm, λemi 670-750 nm). The presented results could serve as a foundation for further phytochemical studies of BAC of spreading woodruff herb.

SECTION 3

STANDARTIZATION OF DRUGS. PHARMACEUTICAL AND CHEMICAL-TOXICOLOGICAL ANALYSIS

COMPARATIVE CHARACTERISTICS OF METHODICS FOR THE QUANTITATIVE DETERMINATION OF SMALL CONCENTRATIONS OF CITRIC ACID

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The proposed work continues to research conducted at the Department of Analytical Chemistry for the development of methodics of quantitative determination of low concentrations of drug substances and intermediates for their synthesis. The purpose of this study was a comparative evaluation of the previously proposed methodics of a quantitative determination of low concentrations of citric acid photometric method of analysis.

Field of use of citric acid (CA) in medical practice in low concentrations (0.2%) is varied: CA is part of the drug as the correlation of taste, as a mandatory supplement along with the enzymes (0.5 to 20%) is introduced into composition of oral, parenteral, rectal dosage form for the treatment of diseases of the circulatory system and digestive system - diabetes, nephritis, hepatitis, pancreatitis, hypertension and others. CA and sodium citrate is used as anticoagulant for preservation of blood, and is a part of beauty.

CA is one well-studied compounds. In high concentrations State Pharmacopoeia of Ukraine regulates Alkalimetric determination of citric acid monohydrate (titrant - a solution of sodium hydroxide, phenolphthalein indicator). We will be of interest to reproduce the proposed methodics of the direct and indirect determination of low concentrations of CA photometric method of analysis, statistical process of the results, check for meaningful bias (by Student), to compare the reproducibility of two photometric methodics by Fisher.

For comparative evaluation techniques it was selected direct photometric determination with CA Ferum(III)-ions at a wavelength $\lambda max = 420 \pm 10$ nm, and the indirect determination CA, based on the interaction of excess ions Ferum(III), not reacted with citrate ions from solution ammonium thiocyanate at $\lambda max = 490 \pm 10$ nm (calibration curve method, the correlation coefficients $r = - 0,9850$, $r = 0,9931$, respectively). According to the results of the calculation of the Student both techniques are burdened by systematic error, and methodic of direct photometric determination by Fischer is more reproducible.

THE DEVELOPMENT AND RESEARCH OF THE ION-SELECTIVE ELECTRODE FOR KANAMYCIN

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Kanamycin sulfate refers to the aminoglycoside antibiotics series and has a broad spectrum of antimicrobial activity. Therefore, there is a need for the development of express methods of analysis of the kanamycin sulfate in dosage forms and in the biological fluids (blood, urine, saliva). The literature describes the ISE on kanamycin with the plasticized membranes based on ion associates kanamycin with tetrafenilborat and acid chrome black. However, the proposed electrodes are characterized by a narrow range of detectable concentrations ($1 \cdot 10^{-3}$-$4 \cdot 10^{-5}$ M), and low specificity of membrane $K^{ïîò}_{A/B} \approx 1$ in the presence of organic ions, which complicates analysis of kanamycin in the complex dosage forms. Probably, this is the influence of the properties of membrane of active electorodes. However, in the literature there is a description of the usage of substance with active electorodes with the heteropolianions of Keggin's structure ($XMe_{12}O_{40}^{n-}$, where X(P,Si), Me(Mo(V); W(VI); V(V))). They are insoluble compounds in water, but readily soluble in organic solvents, allowing their use in plasticized ISE membranes. Therefore, we proposed ISE for kanamycin sulfate with the use of associate kanamycin sulfate with phosphomolybdic acid as active electrode substance. The reaction with this reagent is characterized by high sensitivity. Maximum concentration C_{lim} is $(3,6 \pm 0,1) \cdot 10^{-5}$ g/sm^3, and limiting dilution V_{lim} is $(1,7 \pm 0,1) \cdot 10^4$ g/sm^3.

Studies have shown that ISE electrode's function is linear in the range $(1,0 \pm 0,2) \cdot 10^{-2}$ – $(3,0 \pm 0,2) \cdot 10^{-4}$ M with the slope 26 ± 1 mV, that corresponds to the characteristics of ISE for two charge ion. The response time of electrodes at the minimum concentration of kanamycin sulfate is 20-30 sec. Drift potential of our electrodes per week does not exceed 3-4 mV, and their working life is not less than 4-5 months.

Thus, the proposed ISE for kanamycin sulfate can be used to analyze kanamycin sulfate by the method of ionometry for liquid and solid dosage forms.

QUANTITATIVE DETERMINATION OF PENICILLINS BY IODOMETRIC METHOD USING POTASSIUM HYDROGENPEROXOMONOSULPHATE

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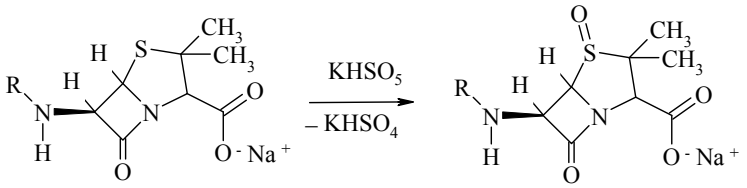
A new simple, accurate and precise titrimetric micro-procedure is developed for the analysis of semisynthetic penicillins (amoxicillin trihydrate, ampicillin trihydrate, sodium oxacillin and disodium ticarcillin) in pure sample (substance), tablets, lyophilized powder in vials for injection solution and capsules using potassium hydrogenperoxomonosulphate (PMS) as the oxidant. The method is based on the oxidation of penicillins with PMS in acid medium and the unreacted (excess) PMS is determined iodometrically under basic conditions.



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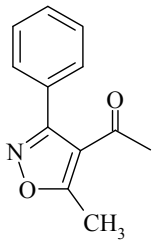

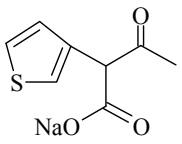

Oxacillin Ticarcillin

$$KHSO_5 + 2\,KI + 2\,KHSO_4 = I_2 + KHSO_4 + H_2O + 2\,K_2SO_4$$
$$I_2 + 2Na_2S_2O_3 = 2\,NaI + Na_2S_4O_6$$

The reaction conditions have been optimised and the stoichiometry of the reaction has been evaluated. 1 mol of penicllin is per 1 mol of KHSO5, quantitative interaction proceeds in 1 minute. A linear relationship exists between the amount of the drug and the titration end-point as shown by the values of correlation coefficient, r (0.9991–0.9999). The methods were applied to the analysis of dosage forms with results comparable to those given by the official methods. A propose method are indirect visual titration methods, and are simpler than, and superior to, many existing methods for the assay of penicillins. RSD ≤ 2.35 % (for substance ≤ 1.7%) (δ = –0.1…+1.0%).

ASPIRIN KINETIC-SPECTROPHOTOMETRIC ASSAY WITH PEROXYMONOSULFATE

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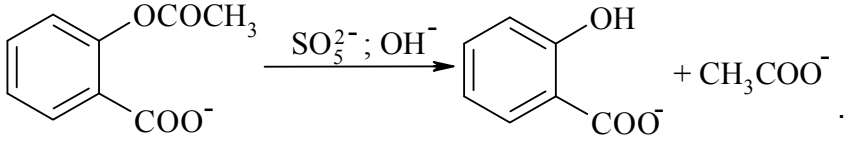
Aspirin, also known as acetylsalicylic acid (ASA), is a salicylate drug, often used as an analgesic, antipyretic and an anti-inflammatory medication. It also has an antiplatelet effect. Today, aspirin is one of the most widely used medications in the world, with an estimated 40.000 tonnes of it being consumed each year. The SPhU and PhEur recommend to quantitate aspirin titrimetrically. The scientific literature describes kinetic, spectrophotometric, fluorescent, potentiometric, chromatographic and other methods for aspirin assay. We propose a new catalytic indicator reaction of ASA hydrolysis (perhydrolysis) with potassium hydrogen peroxymonosulfate (HPMS) for aspirin quantitation. Tangent method of differential kinetic method analysis was used. The optimum reaction conditions has been evaluated: c(HPMS)3.8×10^{-3}mol L^{-1}, 10.5-11.0 pH range. In this case the maximum difference between the rate of catalytic (perhydrolysis) and non-catalytic (alkaline hydrolysis) decomposition of ASA was observed and therefore to measure the indicator reaction rate with sufficient accuracy under the first-order reaction kinetics. The hydrolysis product of ASA (salicylate) is monitored at 295 nm during 15 min.



Calibration graph for aspirin was obtained: tgα=(96.9±8.3)×*c*-(0.003±0.001), (r=0.999). It has linear dependence up to 200μmol L^{-1}. The limit of quantitation (LOQ) is 20μmol dm^{-3}. For five determinations of aspirin 8, 12 and 16μmol L^{-1} concentrations RSD was 2.4%, 1.6% and 1.0% (n=5;P=0.95) respectively. Method has satisfactory reproducibility and accuracy (RSD≤2.4, δ≤-0.1%). Aspirin substance contains 99.97±0.01% of ASA.

Thus a highly selective and sensitive spectrophotometric method has been developed for the determination of aspirin based on hydrogen peroxide catalytic effect on the alkali hydrolysis of ASA. The proposed method is simpler and expresses in comparance with well-known one. Statistical comparison of the results with those of an official method shows excellent agreement and indicates no significant difference in precision. The proposed method does not require the use of toxic solvents or reagents and sophisticated equipment.

KINETIC SPECTROPHOTOMETRIC DETERMINATION OF CEFADROXIL BY COUPLE CONJUGATED PEROXOACIDIC OXYDATION AND PERHYDROLYSIS REACTIONS PRODUCT

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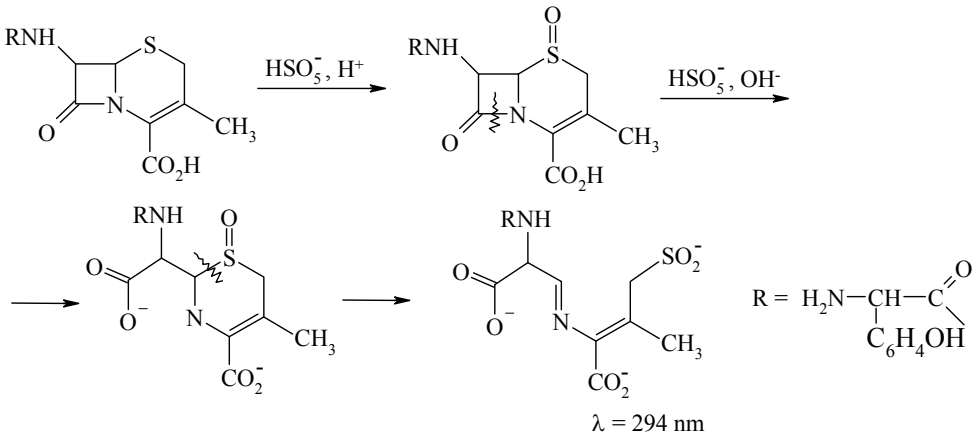
Cefadroxil is chemically designated as 7-[[2-amino-2-(4-hydroxyphenyl)acetyl] amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid is a derivate of 7-aminodezacetoxy cephalosporin acid (7-ADCA). It is an antibiotic remedy – semisynthetic first-generation cephalosporin β-lactam antibiotic of a wide range of application. Like all β -lactam antibiotics, cefadroxil binds to specific penicillin-binding proteins located inside the bacterial cell wall, disrupting the last stage of bacterial cell wall synthesis. It is produced in the form of capsules, 0.5 and powder for suspension preparation.

The aim of investigation is to observe new procedure of cefadroxil pure substance and capsules quantitative determination by kinetic spectrophotometric method by the product of two conjugated reactions of peroxoacidic oxidation and perhydrolysis in alkali medium using potassium hydrogenperoxomonosulphate as analytical reagent ($KHSO_5$). Chemical transformation is given on the scheme:



Advantages of the given procedure are high sensitiveness, precision and reliability of the results, the absence of expensive device, toxic solvents and special facilities as in HPLC method, simple and rapid in application. Linear concentration ranges varied from 0.9-7.3 μm mL^{-1}. Limit of detection is 0.91 μm mL^{-1}. For cefadroxil pure substance *RSD*=2.03% (accuracy δ=–0.23%), for capsules *RSD*=2.98% (δ=–0.42%).

QUANTITATIVE DETERMINATION OF POTASSIUM HYDROGENPEROXOMONOSULFATE BY VOLTAMMETRY AT CARBOSITALL ELECTRODE

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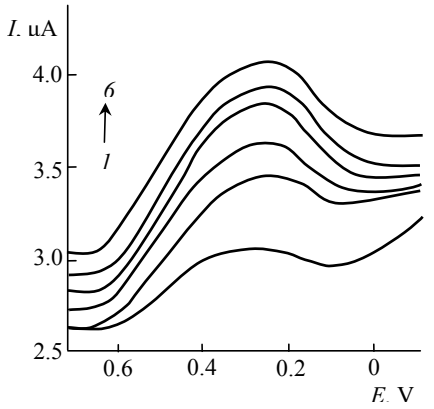
Potassium hydrogenperoxomonosulfate ($KHSO_5$, PMS) in the form of stable potassium salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, known as Oxone™, is widely used in agriculture and medicine as a disinfectant, antiseptic and sterilizing agent.

The aim of the research was to determine the feasibility of the method of quantitative determination of PMS by cathodic voltammetry using carbositall electrode (CE) (Russia) as indicating (working) electrode. Electrochemical measurements were carried out in the analyzer ABC-1.1 (Volta, St. Petersburg) with a three-electrode scheme by alternating current mode with square wave modulation in potential range +1.0…–1.2V, W=1000rpm, amplitude 40mV, ν=65Hz. CE was used as a working and an auxiliary electrode, and Ag,AgCl/KCl(sat) electrode type EVL-1M4 as a reference electrode.

The peak was obtained at E_p=+0.25V on the background of 0.2mol L^{-1} $KHSO_4$ (pH≈0.8), whose height was rising proportionally to PMS concentrations increasing.

Equation of PMS reduction on working electrode is $HSO_5^- + 2e + 2H^+ = HSO_4^- + H_2O$.



c ($KHSO_5$), 10^{-5}, mol L^{-1}: *1* – 0.9; *2* – 1.8; *33* – 2.7; *4* – 3.6; *5* – 4.5; *6* – 5.4; pH≈0.8(background – $KHSO_4$, *c*=0.2mol L^{-1}); E_p=+0.25V(Ag,AgCl/KCl sat)

Linear concentration ranges of PMS varied from $(0.9–5.4)\times10^{-5}$mol L^{-1} is $I_p=(8.4\pm2.0)\times10^3\times c+(0.2\pm0.1)$(r=0.992); limit of detection is 8×10^{-6}mol L^{-1}. For $(3.6–5.4)\times10^{-5}$mol L^{-1} PMS *RSD*=(2.9-2.65%)(*n*=5;P=0.95%). Thus, new voltammetric method of PMS determination in aqueous solutions using CE (glassy carbon) electrode as indicating (working) electrode was developed and the possibility of its quantitative determination was shown.

DEVELOPMENT OF THE ISOLATION PROCEDURE FOR CLOPIDOGREL USING OXALIC ACID

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Clopidogrel belongs to the antiplatelet medicines and is the world standard in the correction of changes of blood rheological properties. This medicine belongs to the low-toxic drugs, however in the case of the lethal poisoning by unknown substance the forensic medical expert-toxicologist must establish the total list of medicines taken by the patient, but not only the medicine, which is the direct reason of poisoning. At the same time the attempts of suicides using clopidogrel as a monomedicine are fixed.

Research purpose. In this paper we set ourselves as an object to develop the optimal conditions of clopidogrel isolation from biological matrices.

Materials and methods. 10 g of the model mixture of biological material with clopidogrel were placed into the beaker and coated with 20 ml of water, following which the mixture was acidified with 10% oxalic acid solution to pH = 2 and kept for 2 hours while continuously shaking. The mixture was centrifuged (during 30 min. under 3000 revolutions per minute) and the centrifugate was collected into the clean beaker. Infusion of biological material with new portions of acidified water was carried out twice for 1 hour more. The «acid» water extracts were joined, placed into the separating funnel and extracted with chloroform by portions of 10 ml three times. The obtained extracts («acid» chloroform extract) were joined, filtrated through the paper filter («red strip») with 1 g of sodium sulphate anhydrous into the measuring flask with the capacity of 25.0 ml and the solution was diluted to the volume by chloroform (extract 1). The «acid» water extract were alkalified by ammonia solution to pH = 11 and extracted with chloroform by portions of 10 ml three times. The obtained extracts («alkaline» chloroform extract) were joined, filtrated through the paper filter («red strip») with 1 g of sodium sulphate anhydrous into the measuring flask with the capacity of 25.0 ml and the solution was diluted to the volume by chloroform (extract 2).

The extract 1 was used for identification of clopidogrel carboxylic acid and the extract 2 was used for identification of clopidogrel by the methods of thin layer chromatography (TLC) and high-performance liquid chromatography (HPLC). For their quantitative determination we used the methods of HPLC, UV-spectrophotometry and extraction photometry.

Results and conclusion. The developed procedure allowed to isolate about 50% of clopidogrel carboxylic acid and 55% of clopidogrel from the biological matrices.

DEVELOPMENT OF THE ISOLATION PROCEDURE FOR PHENYTOIN USING SODIUM HYDROXYDE

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Anticonvulsant and antiepileptic drugs become the objects of investigations in practical work of chemists-toxicologists often enough – the medicines are drastic, and the cases of poisonings by them are widespread. In literary sources there is the information about the cases of acute and lethal phenytoin poisonings.

Research purpose. In this paper we set ourselves as an object to develop the optimal conditions of phenytoin isolation from biological matrices.

Materials and methods. 10 g of the model mixture of biological material with phenytoin were placed into the mortar, 10 g of clean sand were added to it and the mixture were ground carefully. The homogenized mass was placed into the beaker, the mortar was washed by 20 ml of water and washing liquid was placed into the beaker. 2 ml of 10% sodium hydroxide solution were added into the beaker with the homogenized biological material. The beaker content was kept for 30 min. while continuously shaking, following which the mixture was centrifuged (during 30 min. under 3000 revolutions per minute) and the centrifugate was collected into the clean beaker. Infusion of biological material with new portions of alkalescent water was carried out twice for 30 min more. 0.05 mole/dm^3 sulphuric acid solution was added to the joint alkaline water extracts to pH = 2. The liquid was heated on the water-bath for 20 min., and then centrifuged (during 30 min. under 3000 revolutions per minute). The centrifugate was collected into the separating funnel and extracted by equal volume of diethyl ether three times. The obtained extracts («acid» ether extract) were joint and extracted by 10% sodium hydroxide solution by portions of 20 ml twice. 25% sulphuric acid solution was added to the joint alkaline water extracts to pH = 2 and the liquid was extracted by equal volume of diethyl ether twice. The obtained extracts («acid» ether extract) were joint, filtrated through the paper filter («red strip») with 1 g of sodium sulphate anhydrous into the measuring flask with the capacity of 50.0 ml and the solution was diluted to the volume by diethyl ether.

The obtained extract was used for identification of phenytoin by the methods of thin layer chromatography (TLC), gas-liquid chromatography (GLC), high-performance liquid chromatography (HPLC) and for its quantitative determination by the methods of GLC, HPLC, UV-spectrophotometry and extraction photometry.

Results and conclusion. The developed procedure allowed to isolate about 80% of medicine from the solid biological matrices.

THE DETERMINATION OF TRAMAL IN DROP OF SOLUTION BY TRAMAL SELECTIVE ELECTODEM (TSE)

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In chemical-toxicological studies we often have to deal with small amounts of samples with small amounts of certain substances, that analyze, the measurement electrode potential coefficient (EPC) in tramal solution were carried out on digital ionomer I-130. To reduce the rate of leakage of solution salt of bridge electrode, we used a capillary nozzle with length 1-1.5 cm and a diameter of capillary 0.5 mm. The attachment secured by capillary electrode. Electrode impedance electrode with a nozzle is in the range 17-20 ohms.

The initial solution of tramal hydrochloride wit a concentration $1.0 \cdot 10^{-1}$ M were prepared with substance tramal hydrochloride pharmacopoeial purity. Other solutions were prepared by consecutive 10-fold dilution to a concentration of $1.0 \cdot 10^{-6}$ M. The temperature of all solutions was equal. On the ion selective electrode (ISE) membrane for tramal and butt cap electrode were applied 1 drop of tramal solution and immediately gently were dried using filter paper. Then we applied on the ISE membrane 1drop of solution that investigates and summarized in a drop side butt cap electrode. The measurements of each tramal selective electrode (TSE) element were carried out every minute for 10 minutes. Most stable value system capacity observed for 3-7 minutes of measurements. For the small concentrations of the drug ($1 \cdot 10^{-6}$ - $1 \cdot 10^{-5}$ M) the stability of potential is reduced, that is likely due to the surface-active phenomena. The interval of linearity of electrode function is $(1.0 \pm 0.2) \cdot 10^{-1}$–$(1 \pm 0.4) \cdot \cdot 10^{-5}$ M with slope 56±1 mV for fifth minute of measurement. The minimum concentration is $3.2 \cdot 10^{-5}$ M that can be defined in these conditions. So, in 1 liter of tramal solution contains $9.6 \cdot 10^{-3}$ g, and detection limit in drop of solution (≈ 0.05 ml) will be about 0.48 mg. The proposed method of determination of tramal in drops by the TSE for the drug can be used for pharmaceutical and chemical-toxicological analysis.

SEARCH OPTIMIZATION OF BIOLOGICALLY ACTIVE SUBSTANCES AMONG DERIVATIVES ORTOHALOHENBENZOIC ACIDS

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Among the aromatic acids important are substituted benzoic acids and their derivatives, interest which is due to high chemical activity, allowing their use for the synthesis of a number of structures. Accumulated a wealth of information about the biological properties of the molecular mechanism of action, metabolism and pharmacokinetics derivatives orto-halohenobenzoic acids.

Based on nitro-, bromo-, chloro-, 3-oxamoyl (succinoyl)- and 3- or 5-sulfamoyl substituted ortho-halohenobenzoic acids synthesized and studied biological activity of these compounds: D-(+)-glucosylicammonium salts; D-(+)-glucosamine, methyl esters, alkyl-, aryl- and heterylamides, hydrazides and their derivatives – R-idenhydrazydes, arensulfohydrazides, β-N-acylhydrazides, β-N-(o-tolylsuccinamido) hydrazides, hydrazides, R-idenhydrazides 3-carboxy-2-chloroxanilic and 3-carboxy-2-chlorsuccynanilic acids and their derivatives, benzoic peroxide and perbenzoic acid with chlorine, bromine, sulfamoylic and nitro- substituents in the benzene ring, potassium, sodium, copper and aluminum salts, ortho-substituted halogenbenzoates 9 aminoacridin; ortho-substituted halogenbenzoates 8-oxyquinoline.

During the pharmacological screening of derivatives of ortho-halogenbenzoic acids for 22 tests found substances that exhibit high choleretic (18), inflammatory (17), analgesic (12), antioxidant (10), diuretic (14), local anesthetic (5), antiarrhythmic (7), funhistatic (10), bacteriostatic (22), antiviral (3) and other biological effects. At 27 substances as BAS (biologically active substances) obtained 18 patents of Ukraine and certificates.

A structural and pharmacological analysis of pharmacological studies 356 agents and offered a number of ways to optimize the search of biologically active substances among derivatives of ortho-halogenbenzoic acids.

Thus, the established patterns of connection “structure - pharmacological activity - toxicity” in a series of derivatives of ortho-halogenbenzoic acids can be used for further synthesis of biologically purposeful and recommended for the development of drugs with a wide spectrum of pharmacological action.

THE TEST SAMPLES ATTESTATION FOR THE IDENTIFICATION OF ACTIVE SUBSTANCE BY THIN-LAYER CHROMATOGRAPHY IN THE 9TH ROUND OF PROFICIENCY TESTING SCHEME

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The purpose of the work was to perform the attestation procedure for the tablets samples in order to use them as test samples for the active substance identification assignment by thin-layer chromatography (TLC) in the 9th round of Proficiency Testing Scheme for the laboratories of medicines quality control (PTS).

As test samples some kinds of fluoroquinolone antibiotics were selected: tablets of ofloxacin, norfloxacin, ciprofloxacin and pefloxacin. Identification is carried out by comparison with ciprofloxacin hydrochloride – the reference substance (RS) of the State Pharmacopoeia of Ukraine (SPU).

Although that positive result for the ciprofloxacine tablets is obvious, the attestation was intended to show the possibility to uniquely identify the active ingredient in the test samples as well as verify their stability and uniformity for the testing purposes.

Since for the test assignment the Identification procedure from "Ciprofloxacin Tablets" monograph of the SPU has been proposed, it also has been used for the attestation procedure. During the attestation process some improvements were made to the procedure - preparation of the test solution (sample weight, dilution), and the fixed distance of 15 cm for the front of mobile phase was established.

In order to verify the possibility of using these test samples in laboratories with various instrumentation levels and to confirm the results objectivity, the spots have been applied on the chromatographic plates either manually or using the automatic sampler Linomat (Camag, Switzerland).

As a result the tablets samples have been approved as test samples for using in the test assignment of active substance identification by TLC for the 9th round PTS. Also the critical parameters of the test samples and SPU RS of Ciprofloxacin hydrochloride spots conformity evaluation have been determined. They are an R_f value, a size of spot, an intensity of absorption at 254 nm, and a color of fluorescence at 365 nm.

APPROACHES TO DEFINITION OF «SPECIFICITY» TERM IN FORENSIC AND TOXICOLOGICAL ANALYSIS

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The objects of analysis in forensic toxicology are biological samples, that allow to attribute the procedures of forensic and toxicological analysis to the category of bioanalytical methods, which also should be validated according to the advices of International Conference on Harmonisation (ICH).

The purpose of this work is review of approaches to the definition of validation parameter «specificity» according to the requirements of Food and Drug Administration (FDA), European Medicines Agency (EMA), United Nations Office on Drugs and Crime (UNODC) and Scientific Working Group for Forensic Toxicology (SWGTOX) guidances and analysis of their positive and negative sides in relation to forensic toxicology.

The method of the work carrying out is comparative analysis.

The term «specificity» is used without differences from the term «selectivity» in the discussed papers.

The FDA guidance gives us the following definition: «selectivity is the ability of an analytical method to differentiate and quantify the analyte in the presence of other components in the sample».

The EMA guidance said: «selectivity is the ability of the bioanalytical method to measure and differentiate the analyte(s) of interest and internal standard in the presence of components, which may be expected to be present in the sample».

The UNODC guidance: «specificity/selectivity is 1) the parameter concerned with the extent to which other substances interfere with the identification and, where appropriate, quantification, of the analyte(s) of interest; 2) the measure of the ability of the method to identify/quantify the analytes in the presence of other substances, either endogenous or exogenous, in a sample matrix under the stated conditions of the method».

The SWGTOX guidance: «interference studies – interfering substances from common sources must be evaluated in all screening (except immunoassays), qualitative identification, and quantitative methods».

The «integrated» parameter «specificity/selectivity», which describes satisfactorily both screening methods and methods of identification and quantitative determination, should be introduced in forensic and medical toxicology for validation of the methods of discovery and determination of toxic substances in human body.

THE DEPENDENCE OF THE OXIDATION-REDUCTION POTENTIAL OF THE SYSTEM PEROXOMONOSULFATE / SULFATE ON pH

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Oxidized HSO_5^- and reduced HSO_4^- forms of the system are weak and strong acids respectively, so along with the reactions of oxidation-reduction reactions of deprotonation proceed:

$$H_2SO_5 \rightleftarrows H^+ + HSO_5^- \quad pK^a_{H_2SO_5} = 0.4; \quad HSO_5^- \rightleftarrows H^+ + SO_5^{2-} \quad pK^a_{HSO_4^-} = 9.3$$

$$H_2SO_4 \rightleftarrows H^+ + HSO_4^- \quad pK^a_{H_2SO_4} = -2.8; \quad HSO_4^- \rightleftarrows H^+ + SO_4^{2-} \quad pK^a_{HSO_4^-} = 1.95.$$

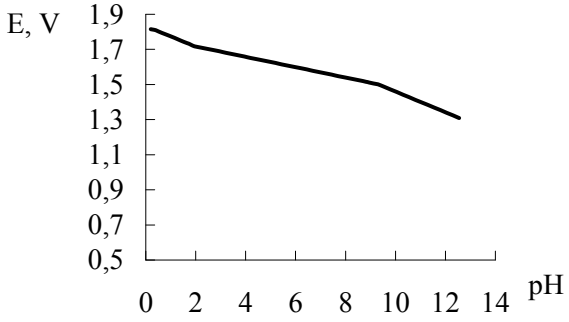
The generalized equation of electrochemical interaction of peroxomonosulfate /sulfate system is (charges of the particles here and subsequently are omitted):

$$\sum_{i=0}^{2} \alpha_{H_iSO_5} \cdot H_iSO_5 + (2 + \sum_{i=1}^{2} i \cdot \alpha_{H_iSO_4} - \sum_{i=1}^{2} i \cdot \alpha_{H_iSO_5}) \cdot H^+ + 2\bar{e} = \sum_{i=0}^{2} \alpha_{H_iSO_4} \cdot H_iSO_4 + H_2O.$$

The dependence of the oxidation-reduction potential on the pH of the system relative to the standard hydrogen electrode ($c_{H_iSO_5} = c_{H_iSO_4} = 1$ mol L^{-1}) can be expressed as:

$$E = E^0_{H_2SO_5, 2H^+/H_2SO_4, H_20} - \frac{\vartheta}{2}(pK^a_{H_2SO_5} + pK^a_{HSO_5^-} - pK^a_{H_2SO_4} - pK^a_{HSO_4^-}) - \frac{\vartheta}{2}(2 - p + q) \cdot pH + \frac{\vartheta}{2} \lg \frac{c_s(H_2SO_5)}{c_s(H_2SO_4)},$$

were: $p = \sum_{i=1}^{2} i \cdot \alpha_{H_jSO_5}$, $q = \sum_{i=1}^{2} i \cdot \alpha_{H_jSO_4}$; $\alpha_{H_{\omega}SO_5}$ and α_{HSO_4} are mole fraction of protonized of oxidized and reduced forms.



Thus, when the solution pH changes the protolitic form of the particles changes, and, therefore, the form of the generalized equation of electrochemical interaction changes, which leads to the dependence of E on pH as shown on Fig.

VALIDATION OF SPECTROPHOTOMETRIC TECHNIQUES FOR QUANTITATIVE DETERMINATION OF PREDNISOLONE

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Prednisolone is a medical drug of corticosteroids group marked by a relatively active pharmacological effect, and so requires meticulous quality controlling. The Quantitative determination of prednisolone may be done by spectrophotometric technique based on Standard Method (SM), as recommended by the International Pharmacopeia; or, by the Absorption Index Method (AIM) as recommended by the European Pharmacopoeia and the State Pharmacopoeia of Ukraine (SPU). Since the named methods are relatively suitable for application in laboratory conditions, we decided to validate those methods and used the validation results for subsequent development of a technique for quantitative determination of prednisolone in officinal medical drugs.

Validation was performed by use of the spectrophotometers Specord-200 and Specol-1500. The equipment, chemical reagents and volumetric glassware were compliant with SPU requirements. Statistic processing of data was done on the basis of standardized procedures for the minimal range 80-120% of technique application, for 9 precise concentration values within the entire range. When assessing linear dependence we determined that at 120% concentration the spectrum properties undergo changing, where by linearity is not observed; therefore, having completed the assessment of sample homogeneity we decided to conduct all further estimations for 8 concentration values in the range of 80-115%.

As part of determining the precision of technique, we calculated a one-sided confidence interval for the probability of 95%, which totaled in 1.78 and 1.35 for the MS (Specord-200 and S pecol-1500 respectively), and in 1.86 and 1.49 respectively for the SPU; the above values exceed the value of maximum acceptable uncertainty for analysis. However, the values of systematic error in MS are relatively low (δ=0.02 and δ=0.20), contrasted by those of SPU (δ=4.50 and δ=9.78). The above clearly proves that the MS for prednisolone was prone for in correct results, which prevents the MS from being used in routine analysis. Therefore, all further measurements (robustness and interlaboratory accuracy) were only done for the MS. Adding 2 drops of 0.01 M solution of NaOH or HCl gave the value $\Delta_{pH,}$%=0.31, which did not exceed the value of maximum systematic error (δmax=0.31). The value of technique reproducibility was also appropriate for applying the technique in various laboratories and on various types of equipment, which is compliant with the SPU requirements.

CREATE TEST SIMULATOR TRAINING CHEMIST (PHARMACIST) - ANALYST

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Currently, the control of knowledge of students in educational institution is not possible without the use of test technologys, in particular computering. It is known that the test has three main closely related functions: control, training and educational. This is important in the training of general specialists of chemical and pharmaceutical profile – future chemists and pharmacists -analysts.

The object of our work was to create test simulators for knowledge control of students of the National University of Pharmacy on subjects "Analytical Chemistry", "Analytical chemistry and instrumental methods of analysis". Previously we studied the experience of several leading domestic and leading the CIS educational institutions: Russian Chemical-Technological University D. I. Mendeleev, St. Petersburg Chemical-Pharmaceutical Academy and others.

Materials and methods. On the first stage was chosen about 20 objects to create test simulators – mostly pharmaceutical preparations of inorganic nature described in State Pharmacopoeia of Ukraine and other pharmacopoeias. Number of them are used in the food industry, agriculture, and as reagents in pharmaceutical analysis, etc… In the future, this list will significantly expand. Each of the test simulators consists of a package of 20 tests, in which a particular object is analyzed (for example, pharmaceuticals, etc…). Students answer questions of the qualitative analysis (identification of cations and anions) and the quantitative analysis (classical and instrumental methods). For computer implementation of these tasks, we used «MyTestX». It is a system of programs, including the program of testing of students, test editor and results log. «MyTestX» allows you to work with 10 types of tasks: single choice, multiple choice, establishing the order of the sequence, establishing conformance and others. In these tasks (single choice, multiple choice, an indication of the order), you can use one to ten (inclusive) of the options answer. Program «MyTestX» is perfected over 10 years and has two versions one of which is nonprofit. Any educational institution, student or teacher can use it for free on the basis of the license agreement.

Conclusions. Generated test simulators can be used for knowledge control for second-year students of the National University of Pharmacy of different departments before the final module control, and for third-year student and up in the study of special subjects (pharmaceutical chemistry, etc…), for the fourth-year students before writing the license examination "KROK 1" at the context of preparation of students for the subject "Methods of Pharmacopoeial analysis," which is taught at the Department of Analytical Chemistry, National University of Pharmacy.

DETERMINATION OF METHIONINE BY REACTION WITH POTASSIUM HYDROGENPEROXOMONOSULPHATE

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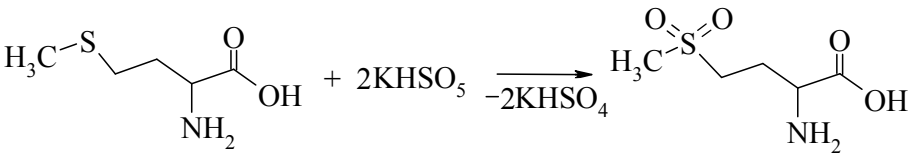
Methionine - (2RS)-2-amino-4-(methylthio)butyric acid, (Met) which is necessary for growth maintenance and nitrogen equilibrium of a living organism, is among essential amino acids in compliance with chemical structure and is widely used in medical practice.

The SPU recommends using acidimetric method for determination of content ground substance of Met. According to this method determination demands relatively large sample weight of Met and using toxic solvents. Procedures of iodometric method for determination of agent are described in literature. The disadvantage of this method is duration (0.5-4 hours). The new oxidation-reduction reaction, named S-oxidation of Met by potassium hydrogenperoxomonosulphate (PMS) in the medium of the phosphate buffer solution (pH 7.8-8.2) was suggested by us as analytical for Met. It is determined by kinetic method that oxidation reaction of atom sulfur of Met to sexivalent state (formation of the conformable sulfonic derivation, $MetSO_2$) by potassium hydrogenperoxomonosulphate is passed comparatively quickly (4 min) and quantitatively (presented on the scheme). This oxidant is characterized by higher stability in water solution unlike iodine solution and oxidation process of sulfide group is passed more selectively.



The thin layer chromatography was used for identification of the formed reaction product (Silufol®, n-butanol-CH_3COOH-H_2O (60:25:15), R_f=0.25±0.05; Sorbfil, n-butanol-CH_3COOH-H_2O (60:25:15), R_f=0.42±0.05). According to the researches the new method for the semi-microdetermination of content ground substance of Met was worked out. This method is based on measurement by the iodometric titration method of the reagent ($KHSO_5$) quantity, which is used on interaction with Met. The RSD for the determination of content ground substance of Met was 0.72%. The accuracy for analysis results of Met was tested by „introduced - found" (δ=+0.5%). Advantages of the suggested method are higher sensitivity (0.05 mg) and expressivity (to 7 min).

USAGE OF THIN LAYER CHROMATOGRAPHY METOD FOR CHEMICAL-TOXICOLOGICAL ANALYSIS OF PIOGLITAZONE

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Pioglitazone is an oral thiazolidinedione antidiabetic agent, which use in type 2 diabetes mellitus treatment and acts primarily by decreasing insulin resistance. Antidiabetic action mechanism of drug is also realized by inhibition hepatic gluconeogenesis and improving glycemic control. Monograph of pioglitazone hydrochloride is absent in leading pharmacopoeias yet. Determination of pioglitazone by various analytical methods such as spectrophotometric, HPLC and LC MS in tablet formulations and human plasma has been reported in literature sources. Thin layer chromatography (TLC) is one of the most widely applied method in chemical-toxicological analysis, which use in the stages of preliminary and confirmatory researches. Proceeding tasks of chemical-toxicological searches, TLC can be used as an analytical and preparative method. The aim of the work was developing the TLC-procedures of pioglitazone determination acceptable for chemical and toxicological researches of drug. As investigated objects substance of pioglitazone hydrochloride and tablets Glutazone (Ukraine, Kusum Pharm) and Pioglar (India, Ranbaxy) were used. According to physical-chemical properties of pioglitazone methanol was selected as solvent. Behaviour of pioglitazone was investigated in different chromatographic conditions. Chromatographic plate Sorbfil, Armsorb and Merck were used as stationary phase. Solvents systems of general TLC-screening recommended by the International Committee of systematic toxicological analysis of the International Association of Toxicologists court (TIAFT), general systems of TLC-screening of acid and neutral agents and others were used as mobile phase. When using the mobile phase chloroform-methanol (90:10) Rf value pioglitazone was 0.82, 0.7, 0.79; chloroform-acetone (80:20) – 0.55, 0.42, 0.42; toluene-acetone-methanol-25% solution of ammonia (50:20:10:0.02) – 0.57, 0.57, 0.57; chloroform-toluene-acetate acid conc-ethanol (4.5:4.5:1:1) – 0.45, 0.45, 0.51 respectively. The most acceptable defined system chloroform-toluene-acetic acid conc.-ethanol (4.5:4.5:1:1). Detection of spots (areas of absorbance) of substances on the chromatogram was carried out in different ways: irradiation by UV light, action by general and specific detecting reagents. The most optimal reagent was Dragendorff spray modified on Munje (limit of detection 0.01 mg). Proposed procedure of chromatographic determination of pioglitazone can be used in the researches of extracts of biological material in a chemical-toxicological analysis on this drug.

DEFINITION OF LIMIT CONTENT ACCOMPANYING IMPURITIES MULTICOMPONENT MEDICINES

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In the world pharmaceutical market well represented drugs for combination therapy. These drugs contain two or more active substances which potentiate the therapeutic effect or directed to treatment of diseases with different, usually concomitant symptoms while using only one drug.

Stability studies of each active substance are needed in the presence of other active substances and excipients in the production and storage of combined drugs. The main criterion for the stability of the finished product is a dynamics of growth contents accompanying impurities degradation, which can significantly to influence on the effectiveness and safety of the drug.

Analytical method for determining the content limit accompanying impurities creates in the process of the stability studies of pharmaceutical substances and finished products. This method is based on the profile of impurities formed as a result the influence of negative environmental factors: light, oxidation, moisture, temperature, etc. Medicinal product exposes the relevant stress conditions and determines which additives are formed by chemical degradation of the drug. The analytical data allow to determine dynamics of accumulation impurities accompanying drug and concluded about its stability during production and storage.

Purpose of research is detection the least stable among the other active ingredient, degradation of which will be the first in the same conditions for all substances and identify predominant impurity of this substance for the implementation of its control in the actual product.

For the purpose the research was conducted degradation of components of the drug with 1 M solution of hydrochloric acid and sodium hydroxide and 3% solution of hydrogen peroxide.

A specific method was developed for determining the content limit of active substances by HPLC with UV method of detection based on these data. Method of determining allows minimal time, material and human resources to control product quality at the same time by two parameters as “Related substances” and “Assay”.

According to various conditions degradation of drugs were found less stable active substance and the overwhelming impurity of this substance. For confirmation of correctness the proposed method was conducted validation in accordance with the requirements of State Pharmacopoeia of Ukraine.

PHARMACEUTICAL PREPARATION AND IRON SALTS INTERACTION RESEARCH

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Pharmaceutical preparations market is constantly changing and evolving. Nowadays the WHO Essential Medicines List numbers almost 8,000 registered substances. Safety requirements for medications are constantly raising, that's why particular attention should be paid to drug-drug, food-drug and drink-drug interactions research. Wrong combination can reduce bioavailability, pharmacological activity, as well as increase toxicity and side effects appearance.

Considering mentioned above, the purpose of the research was to study metronidazole, ciprofloxacin, tetracycline and iron salts interactions. As far as iron salts are a part of some types of mineral water, Coca Cola and Baikal drinks, they are also included in iron deficiency drugs composition. It should be noted that the iron salts are on the food coloring list (E-172), which means that it may be used in the EU, the USA and Ukraine.

The research was carried out using UV spectrophotometry methods where the absorbance of metronidazole, ciprofloxacin, tetracycline and their ferrous sulfate, ferric chloride complexes was measured. Solutions were prepared using the same method: the exact weight of a substance dissolved in the purified water with a few drops of phenolphthalein and were used 0.1 M sodium hydroxide solution adding until the color of the solution changes to a slightly pink, then samples of metal salts were added to the drugs solution in the ratio of (2:1 ($FeSO_4$) and 3:1 ($FeCl_3$)), diluted to 100.0 ml with the same solvent and 5.0 ml of this solution diluted with a purified water to a volume of 100.0 ml.

There was no significant difference in the absorption maxima between the correspondent pharmaceutical substances given alone and given with various iron salts. The absorption maxima were registered at the same wavelength, namely, metronidazole showed λ_{max} at 320 nm, ciprofloxacin – at 276 nm, tetracycline – at 358 nm. However, the absorbance intensity difference could be observed between the complexes studied and the water solution of drug substance.

In terms of the results obtained in experimental conditions, we may conjecture that formation of complexes, which can influence pharmacotherapeutic activity can be possible as a result of the interaction between specified drug substances and iron salts.

DEVELOPMENT OF THE ISOLATION PROCEDURE FOR KETOTIFEN USING SULPHURIC ACID

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Ketotifen fumarate is the medicine with antihistamine action, however, it should be noted that the medicine can show expressed sedative action, strengthen the action of hypnotic and antipsychotic agents, and alcohol. The cases of poisonings by the medicine are known, however the methods of its chemical and toxicological analysis are developed not enough.

To develop the ketotifen isolation procedure from biomatrices.

10 g of the model mixture of biological material with ketotifen were placed into the beaker and coated with 20 ml of 0.01 mole/dm^3 sulphuric acid solution, following which the mixture was acidified with 20% sulphuric acid solution to pH = 2 and kept for 2 hours while continuously shaking. The mixture was centrifuged (during 10 min. under 5000 revolutions per minute) and the centrifugate was collected into the clean beaker. Infusion of biological material with new portions of water acidified with sulphuric acid was carried out twice for 1 hour more. The «acid» water extracts were joined, placed into the separating funnel and extracted with chloroform by portions of 10 ml three times. The obtained extracts («acid» chloroform extract) were joined, filtrated through the paper filter («red strip») with 1 g of sodium sulphate anhydrous into the measuring flask with the capacity of 25.0 ml and the solution was diluted to the volume by chloroform (extract 1). The «acid» water extract were alkalified by ammonia solution to pH = 11 and extracted with chloroform by portions of 10 ml three times. The obtained extracts («alkaline» chloroform extract) were joined, filtrated through the paper filter («red strip») with 1 g of sodium sulphate anhydrous into the measuring flask with the capacity of 25.0 ml and the solution was diluted to the volume by chloroform (extract 2).

The extracts 1 and 2 were used for identification of ketotifen by the methods of thin layer chromatography (TLC) and high-performance liquid chromatography (HPLC). Their quantitative determination we carried out by the methods of HPLC, ionometry, UV-spectrophotometry and extraction photometry.

We could not find ketotifen in the extract 1 and identified it in the extract 2. The developed procedure allowed to isolate about 60% of ketotifen from the biological matrices – all medicine was present in the extract from the alkaline medium, that correspond to the theoretical information about ketotifen ionisation constant.

APPROACHES TO DETERMINATION OF SPECIFICITY IN FORENSIC AND TOXICOLOGICAL ANALYSIS

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There are two points of view on when a method should be regarded to be selective. One way to establish method selectivity is to prove the lack of response in blank matrix. However, this approach has been subject to criticism in some review, which stated from statistical considerations, that relatively rare interferences will remain undetected with a rather high probability. The second approach is based on the assumption that small interferences can be accepted as long as precision and bias remain within certain acceptance limits.

The purpose of this work is review of approaches to the determination procedure of validation parameter «specificity» according to the requirements of Food and Drug Administration (FDA), European Medicines Agency (EMA), United Nations Office on Drugs and Crime (UNODC) and Scientific Working Group for Forensic Toxicology (SWGTOX) guidances and analysis of their positive and negative sides in relation to forensic toxicology.

The method of the work carrying out is comparative analysis.

All considered documents foresee the carrying out of the blank-matrix samples analysis – both spiked with analyte and without it, and standardize their quantity – from five to ten. Thus the UNODC guidance has the differences in requirements to the quantity of such samples depending on the type of analysis, and the EMA guidance allows to use less quantity of sources in the case of rare biological matrices.

The true absence at the level of lower limit of quantification (FDA, UNODC) or a little higher (UNODC), or the response, not exceeding 20% from the lower limit of quantification for analyte and 5% for an internal standard (EMA) is accepted as an absence of response in blank-matrix. The SWGTOX guidance does not standardize this parameter.

The question about the number of blank-matrix sources used for parameter «specificity/selectivity» determination is in need of further discussion. From our point of view, this number should depend on the method of analysis used (for example, chromatography or spectrophotometry, thin layer chromatography or high-performance liquid chromatography at al.), and also should be different in the methods of qualitative and quantitative analysis.

THE DEVELOPMENT AND SUBSTANTIATION OF THE OPTIMAL TECHNIQUE FOR QUANTITATIVE DETERMINATION OF RESORCINOL IN THE DOSAGE FORM

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Resorcinol – 1,3 – dihydroxybenzene – antiseptic, disinfectant which is used in the treatment of skin diseases (itching, eczema, sycosis, seborrhea, fungal infections of the skin). Resorcinol is used in low concentrations (0.25–2.0%), being a keratoplastyc (necrotic, healing) medicine, as a component of lotions and ointments. Higher concentrations of resorcinol (5.10% ointment) have specific keratolytic (promotes rejection of the horny layer) and cauterizing properties. In cases of higher concentration of resorcinol (30-50%) the cauterizing effect is more pronounced.

In accordance with the pharmacopoeial requirements it is recommended to use the bromatometry method for the quantitative determination of resorcinol in the substance. Quite often, resorcinol is used in combination with salicylic acid, and in this case by the bromatometry method both components are titrated simultaneously. For the purpose of economical expenditure of the dosage form and reduce the time to analyze the task of our research has become the development of spectrophotometric technique, allowing to quantify both components in the same sample, as well as its validation.

For the development of technique the investigation of UV – absorption of resorcinol, salicylic acid and in their joint presence at the concentration 2.0 Ч 10^{-5} g / ml in the solution of 70% alcohol has been carried out. The acidity or basicity of the solution significantly affects on the absorbance at the wavelength of 300 nm (salicylic acid). Therefore, it has been proposed to carry out the quantitative definition with the help of addition of aluminum chloride1% solution to the analytical solution. The aluminum cation together with salicylic acid forms the stable complex compound, which has the maximum absorption at the wavelength of 314 nm. According to the developed method for the quantitative determination of resorcinol it is necessary to measure the optical density of the analytical solution at the maximum at the wavelength of 282 nm, for the quantitative determination of salicylic acid - 314 nm, relative to the solvent - 70% alcohol.

For the developed technique for the quantitative determination of resorcinol in the presence of salicylic acid the process of validation has been conducted. The following parameters have been taken into consideration: robustness, linearity, accuracy, precision and reproducibility. These results meet the criteria of acceptance.

DEVELOPMENT OF STATE PHARMACOPOEIA OF UKRAINE MONOGRAPH "DIACAMPH"

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Antidiabetic agent Diacamph tablets 0.250 g, designed in NPhU, according to the decisions made by the scientific advisory council of State Pharmacological Center of Ministry of Healthcare of Ukraine from 26.02.2004 r. allowed for medical use.

For the introduction into manufacture it was appropriate to develop of SPU monograph "Diacamph" for the active pharmaceutical ingredient. In order to fulfill this task five series of diacamph were synthesized by the way of receipt, regularized of relevant technological documentation. Diacamph by formula – $C_{16}H_{20}N_2O_2$, by molecular weight – 272.35, by chemical name – (±)-cys-3-(2'-benzimidazolyl)-1,2,2-trimethylcyclopenthancarboxilic acid, contains basic substance – from 98.5 % to 101.0 %, which is a crystalline powder, white or nearly white, practically insoluble in water R, soluble in 96 % alcohol R, little soluble in methylene chloride R, $T_{m.p.}$ about 255 °C. Identification. 1. UV absorption spectrum of 0.001% diacamph solution in 96% alcohol R in the range from 220 nm to 300 nm has three absorption maxima at wavelengths of 247 nm±2, 276±2 nm and 283±2 nm. 2. IR spectrum of diacamph in disks with KBr (1 mg of substance in 300 mg KBr) has the characteristic bands of valence and deformation vibrations at 750, 1470, 3430, 2980, 1295, 1690 cm^{-1}. 3. TLC: stationary phase – plate Merck (silica gel GF_{254}), mobile phase – ether R – formic acid anhydrous R – 96% alcohol R – water R (90:7:10:3), developer – potassium iodobismuthate R2 solution (solution for spraying). In the chromatogram of test solution the main spot is manifested at WSS of diacamph spots (Rf ~ 0,31), corresponding in size and color. 4. Reaction of formation of ammonium salt with copper (II) sulfate R (reaction for carboxyl group, blue precipitate). Impurities (TLC in the above conditions). In the chromatogram of test solution (100 μg of diacamph), any spot other than the principal (Rf~0,31) is not intense than spot on the chromatogram of reference solution (100 μg of diacamph WSS) by size and color. The content of heavy metals in the synthesized samples did not exceed 0.001% (10 ppm). Loss in weight on drying not more than 1.0%. The content of sulfated ash – less than 0.1%. Assay. Potentiometric titration in glacial acetic acid medium by 0.1 M solution of perchloric acid R and titration by 0.1 M sodium hydroxide solution R. The powder of diacamph stored in a dark place. The technological impurities of diacamph: α-2'-aminophenylamid of (±)-cys-1,2,2-trimethylcyclopenthancarboxilic acid and lactam of (±)-cys-3-(2'-benzimidazolyl)-1,2,2-trimethylcyclopenthancarboxilic acid.

REACTIVITY OF N-[(2-OXOINDOLIN-3-YLIDENE)-2-OXIACETYL] AMINOACIDS METHYL ESTERS

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In the study of the pharmacological activity of N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl]aminoacids and their esters, synthesized at the Department of Analytical Chemistry, National University of Pharmacy it was found that a wide spectrum of biological effects is characteristic for them.

The aim of this work was to study the reactivity of methyl esters of N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl]aminoacids to optimize the conditions of their synthesis and develop mathematical models of interrelation "structure-biological activity" enabling targeted searches of compounds with desired high level of biological effects.

Acid-base balance was studied by potentiometric titration. The titrant used was a standard 0.05 M aqueous solution of potassium hydroxide, free from carbon dioxide. Concentration of solutions titrated - 0,005 M at the point of half neutralization. Potentiometric titration was performed on ionomer EV - 74 using a glass (ЭСП 43-074) indicator electrode. The reference electrode was a silver chloride electrode (ЭПВ-1). The experiment was carried out at 25^{o}C with a threefold repetition. The accuracy of the results was assessed by means of mathematical statistics of small samples (confidential probability 0.95). Mixed solvent was received from bidistillate free from carbon dioxide and 1, 4 - dioxane.

CONCLUSIONS:

1. By studying acid-base balance the reactivity of methyl esters of N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl]aminoacids was investigated. It was were found that they have the function of weak monobasic acids. An equation of ionization by enol hydroxyl was worked out.

2. Measuring of 9 methyl esters N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl]aminoacids' ionization constants has shown that the extend of polymethylene chain weakens ionization.

3. By Hammett equation a quantitative assessment of the impact of methylene units on the aminoacid fragment of molecule was carried out and a low sensitivity of the reaction center to extend of polymethylene chain was identified.

DEVELOPMENT OF TLC-METHOD FOR AUTHENTIFICATION OF ROSMARINIC ACID IN EXTRACT OF SALVIAE OFFICINALIS

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Above-ground part of different types of clary, in particular preparations of Salviae officinalis, which are widespread at the pharmaceutical market, is widely used in medicine.

It is scientifically well-proven that antioxydant and antiseptic properties of extracts of clary are predefined by rosmarinic acid which is the marker of sort of Salvia.

In spite of popularity of application of this plant in modern medicine, the analysis of literature showed that authentication and quantitative determination of rosmarinic acid in extractions of clary are not enough.

Therefore next researches were directed on determination of optimum terms of authentication of rosmarinic acid by the TLC (thin-layer chromatography)-method.

Materials: 70% alcoholic extract leaves of clary medical, aluminium plate 60 F254 (Merck) 20*10 sm.

Methods: laboratory, instrumental – TLC, analytical.

Results. A mobile phase is a toluene: ethylformiat : formic acid in correlation (50:40:10). A division on the plate was during 45 min. System of developers: solution of difenilboriloxyethylamine 1% and solution of macrogoal 5% at the temperature of 110°C . A plate is looked over in UF-light at a wave-length 366 nm.

It is discovered a basic spot with blue fluorescence which is the same as a standart of rosmarinic acid in color, form and the value of Rf (coefficient of division), that confirms the presence of rosmarinic acid in the probed object.

Summary. This method can be used for authentification of rosmarinic acid in extract of Salviae officinalis.

SPECTROPHOTOMETRIC ASSAYS OF LORATADINE IN TABLETS

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Loratadine (Claritin) is the second-generation of antihistamine. In terms of chemical structure loratadine is ethyl 4-(8-chlorine-5,6-dihydro-11H-benzo[5,6]-tsyklohepta[1,2-b]pyridine-11-ylidene) piperidine-1-carboxylate. In pharmaceutical market of Ukraine we have many drugs which contain loratadine.

Frequent use of loratadine drugs, the necessity of working out MCQ for each manufacturer of drugs needs improvement of existing, developing and introducing of new methods of quantitative determination of active ingredient in pharmaceutical dosage forms.

In quantitative analysis, the absorption spectrophotometry is often used, in the ultraviolet and in the visible region of spectrum. This method is characterized by high accuracy, specificity and reproducibility, faster performance and economy of reagents and test substances.

The aim of our work is the development and validation of methods of spectrophotometric determination of loratadine in tablets.

While studying the literature, it has been found that quantitative determination of loratadine in drugs by absorption spectrophotometry in the UV spectral region practically was not described. However, the ability of loratadine to absorb light in the UV region spectrum is used for identification of its substance and tablets. Therefore, we chose this method for the quantitative determination of loratadine in tablets.

We carried out quantitative determination of loratadine in tablets using the method of absorption spectrophotometry in the ultraviolet region, the calculation of quantitative content was performed by the method of standard and that of rate absorption. Methods of quantitative determination of loratadine in tablets were validated according to the SPU under the standardized procedure of validation, the methods of quantitative analysis of drugs. Following the basic validation characteristics were determined: specificity, linearity, accuracy, precision, repeatability, internal laboratory precision, limit of detection, limit of quantification and range of application. These characteristics did not exceed the eligibility criteria according to the SPU. Therefore the technique can be included to SPU monograph on the pills of loratadine.

In the future we will do spectrofotometric determination of lorsatadine with hydroxamic reaction in substance and tablets.

QUANTITATIVE DETERMINATION OF ANTIDEPRESSANT TRAZODONE BY UV-SPECTROPHOTOMETRIC AND EXTRACTION-SPECTROPHOTOMETRIC METHODS

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Antidepressant poisonings occupy a leading position among the psychotropic drug intoxications in the world. Trazodone (2-[3-[4-(3-Chlorophenyl)-1–piperazinyl]propyl]-1,2,4–triazolo[4,3-*a*]-pyridin–3(2*H*)-one) is a bicyclic antidepressant which is widely used in the modern treatment of the depression disoders. However, the medicine is associated with neurological side effects including depressed mood, sleep disterbances and autonomic dysregulations. Trazodone was the primary cause of acute and lethal poisonings. The lethal dose of trazodone was 2–4 g by *per os* administration, postmortem concentrations were reported: blood 15 mg/L, bile 45 mg/L, liver 57 μg/g, urine 2.5 mg/L. The aim of this study was to develop simple and sensitive methods of trazodone quantitative determination by the UV-spectrophotometric and the extraction spectrophotometric methods. Preliminary the light absorption of trazodone in UV-region of spectrum was studied, the wavelengths of maximum absorption of the medicine in methanol solutions were detected at 251 (E^1_1=251, ε=10250) and 310 (E^1_1=45, ε=1850) nm and shoulder at 275 nm. For the UV-spectrophotometric determination the light absorption of trazodone at the wavelength of 251 nm was used. The linearity of the calibration curve was within the range of concentrations from 5 to 50 μg/mL. The equation of the regression line was the following: $Y=(0.0227\pm3\cdot10^{-4})\cdot X+(0.011\pm9\cdot10^{-3})$;·(r=0.999), where Y is absorbance and X is the concentration (μg/mL); LOQ=6 mg/mL (RSD=15.8%); at the medium and high concentration level RSD did not exceed 3.0%. The extraction spectrophotometric method in visible region was developed on the base of the reaction of ionic associate formation with methyl orange, the acidic azodye. The linearity of the calibration curve was within the range of concentrations from 10 to 150 μg of trazodone introduced into a sample. The equation of the regression line was the following: $Y=(0.007\pm10^{-3})\cdot X+(0.019\pm0.009)$; (r=0.999), where Y is absorbance and X is concentration (μg per a sample); LOQ=13 μg (RSD=13.3%); at the medium and high concentration level RSD did not exceed 2.1%.

Thus, the methods developed satisfy the requirements of the chemical and toxicological analysis by the sensitivity and precision and can be used in toxicological study of biological samples on trazodone.

OPTIMIZATION OF THE DETECTION OF BACTERIAL ENDOTOXIN IN THE PARENTERAL DRUGS

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Detection and quantification of bacterial endotoxin in parenteral drugs by the gel-clot and turbidimetric kinetic techniques is hindered by the presence of inhibitors or activators. The purpose of the present study is to overcome interfering factors that might cause inhibition or enhancement of the Bacterial endotoxin test in parenteral drugs.

Materials and Methods. Interference factors were examined in samples of 4 parenteral drugs: Sodium chloride solution for injection 0.9%, Dextrose solution for injection 5%, Gentamicin sulfate solution for injection 4%, Dextran 40 solution for infusion 10%. Lyophilized Limulus Amoebocyte Lysate, Control standard endotoxin Escherichia coli and LAL reagent water of "Associates of Cape Cod Inc." (USA) was used in this study. Inhibition is defined as a significant difference between the end points of positive water control and positive product control using standard endotoxin.

Results. The present study indicated that tested samples interfere with the Limulus Amoebocyte Lysate to different degrees. Sodium chloride, dextrose and gentamicin sulfate inhibit the gelation reaction, dextran 40, however, in turbidimetric kinetic method shows enhancement. Initially, conditions were optimized for treatment of these samples by dilution. It was possible to overcome interference by dilution the samples of sodium chloride and dextrose. This procedure was simple, rapid, and did not involve addition of any reagents to sample that could potentially add contaminating endotoxin. Inhibition due to pH is recognized in gentamicin sulfate, but no inhibition is observed after pH adjustment by Tris-HCl buffer. Adjustment of the pH is needed to avoid inhibition of the gelation reaction because in gentamicin sulfate the pH is below optimal range. Dextran 40 gave a "false positive" test result in gel-clot assay and showed intense enhancement of gel formation both before and after dilution in photometric assay. The gelation reaction of Limulus lysate by dextran 40 may depended on (1-3)-β-D-glucan to a great extent. The optimized glucan neutralization procedure resulted in the most sensitive detection of endotoxin.

Conclusions. Treatment of sample to overcome interference is required before parenteral drug can be successfully assayed for endotoxin.

SECTION 4

PHARMACEUTICAL TECHNOLOGY

MICROSCOPIC ANALYSIS OF LORATADINE AND CINNARISINE

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Kinetosis is complex of disorders of vegetative nervous system which arise in motion or acceleration time. Rate and clinical course depend of individual characteristic of vestibular apparatus and nervous system in tote.

Take into account two different mechanisms of kinetogenesis there are two different methods of treatment. In the first place it is development through over stimulation of vestibular apparatus's receptors. In this case therapy consist in drugs which lower excitability of vegetative nervous system, for example, H1-histamine blocker, anticholinergic drug. In the second place symptom complex develop because of imbalance of information which comes to central nervous system from visual analyzer, otolithic and viscus receptors. For treatment it is reasonable to use drugs for improvement adaptive properties of brain. For achieving this goal it can be used nootropic drugs. But diagnosis is very difficult almost impossible by which mechanism kinetosis develop.

Having regard to the state of the market of drugs which are used for treatment of kinetosis we can make conclusion that assortment is limited and the drugs take effect on one of two mechanisms.

Research target was study of form and size of action drugs for creation composition of complex drug for treatment kinetosis.

Methods and materials. On the grounds of literature data for designing composition of drug there was used third generation of H1-histamine blocker loratadine and potassium channel blocker nootropic agent cinnarizine.

For analysis there was used laboratory microscope "Konus Academy" with built-in camera-ocular ScopeTek series DEM. Pictures was worked up by program MiniSee/ ScopePhoto which gives possibility to see sizes of powder.

Results. Substance of loratadine has white crystal system. Crystals have rod-shaped form. Form factor amount 0.25. Size averages 0.5-1.5 mkm.

Cinnarizine is white or ivory crystal powder. It ascribe to monoclinic system. Form factor account 0.28. Size averages 0.5-3 mkm.

Conclusion. Form and size of this two substance are alike. The results give possibility to assume good porosity. Small dispersion indicates good compressibility, but bad friability.

Research shows possibility of using direct pressing after rational choice of accessory substances.

STANDARDIZATION OF CAPSULES WITH FLAMIN AND ORNIDAZOLE

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There is currently a trend towards the creation of combined drugs. When in a single tablet or capsule “all purpose”, the patient is much more likely that it will be treated successfully.

This method of administration of the drug called “compliance” (from the English. - Compliance), and the role of this combination of drugs can not be overstated.

For the treatment of bacterial infections of it was developed a pharmaceutical composition in the form of capsules with Flamin and Ornidazole, having high antimicrobial activity.

Flamin is dried herbal extract which made from immortelle flowers. It contains mainly flavonoids and the most important among them is chalcon isosalipurposide.

The aim of our research is to create methods of analysis of total flavonoids (chalcones) in capsules with flamin and ornidazale.

The analysis of the UV-spectra of Flamin (λ_{max}= 290 and 370 nm), its main component izosalipurpozide (λ_{max} =370 nm), and ornidazole (λ= 319nm) can make the right choice of the wavelength for the analysis of the amount of flavonoids.

We have proposed to determine the flavonoids at 370 nm and not at 315 nm, as previously recommended drugs by pharmacopoeia’s monograph.

Analysis was performed using a spectrophotometer «Evolution 60S». In developing the method used officinal standard sample (FSO) izosalipurpozide.

We analyzed a number of series of capsules with Flamin. The possibility for a direct spectrophotometria total of flavonoids in capsules at a wavelength 370 nm. We determined content of total flavonoids in the capsules should be not less than 0.01 g (not less than 1.6%) with the reference into isosalipurpozide. We propose a project for the pharmacopoeia’s monograph for Flamin, which provides the use of standard isosalipurpozide at new wavelength (370nm) to determine the total of flavonoids in capsules with ornidazole and Flamin.

SUBSTANTIATION OF DOSAGE FORM FOR ANTITUSSIVE MEDICINE WITH IMMUNOMODULATING ACTION

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Recent years, Ukraine shows a rapid growth in respiratory diseases in the population. In this category children are the most vulnerable, which is associated primarily with weakened or underdeveloped immune systems. Therefore the problem of prevention and treatment of childhood diseases is relevant.

The aim of research was to choose the optimal dosage form and to develop a technology for antitussive medicine with immunomodulating effect, with the possibility of use in pediatric practice.

To achieve this goal we have analyzed the market of drugs for the treatment of upper respiratory tract, in which result we conclude that the leading group is antitussive drugs of plant origin. However, we have found that today in the pharmaceutical market of Ukraine there are no drugs of combined action that would combine an antitussive and immunomodulating effects.

When choosing the optimal dosage form (DF), we have, on the basis of literature, stopped at the syrup, which is the most common medicinal form for children. To the composition of syrup as the main active ingredients we've included polyextract with plantain leaves, sage grass and ivy leaves and immunomodulator of plant origin, which is a glycoprotein oligopeptide composite preparation. As auxiliary substances we used xanthan gum and sorbitol.

Polyextract has been received by reperkolation using percolator Timatic Micro (Italy). As extractant used purified water, the ratio of raw material and extractant 1:10. The ratio of herbal drug in the extract is 5:1:1. Assessment of the extract quality was carried out according to SPU.

The syrup obtained by the addition of sorbitol to polyextract with stirring until dissolved. In the resulting syrup immunomodulator was added in required quantity. In order to keep microbiological purity of the syrup a preservative should be added to the composition. The syrup quality indices studied by the methods according to SPU, vol.1.

Thus, the results allowed to substantiate the structure and technology of complex product in the form of syrup, possessing anti-cough and immunostimulating action.

HISTORY AND PROSPECTS OF ANTI-DIABETIC DRUGS SCREATING

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Diabetes Mellitus is the most common metabolic disorder, its prevalence varying widely worldwide. The purpose of our work was consideration of basic types of antidiabetic medications, histories of their creation and prognosis of development and issue in Ukraine.

The pharmacotherapy of diabetes began in the 1920s with the isolation of insulin from animal pancreas. For years, insulin was the only pharmaceutical option for treating either type 1or type 2 diabetes. Then, in the 1950s, the introduction of tolbutamide (a sulfonylurea) and phenformin (a biguanide) offered options for oral treatment of type 2 diabetes. By antidiabetic agents include drugs and synthetic hormone insulin, orals glucose-lowering medications. Appointment of certain antidiabetic agents depends on the type of diabetes and the disease severity. In the face of ongoing scientific progress, it is important not to lose sight of the proven treatments of the past. There is a disquieting tendency to simply add new agents to current therapy without maximizing the benefits of the options already available. The prospect of patients receiving 3 or more oral hypoglycemic agents in an effort to suppress hyperglycemia is troublesome, particularly when little effort has been made to address obesity, which is the main cause of type 2 diabetes in so many patients. Furthermore, the ever-expanding armamentarium of new pharmaceutical agents increases the cost of treatment and the likelihood of drug-related side effects.

The preferred oral agent of the treatment of type 2 diabetes is still metformin, which is available in generic form everywhere in the world, costs little, and does not promote weight gain. It favor maximizing the tolerated dose of metformin before adding additional agents. The sulfonylureas are now all available as generics and are appropriate add-on therapy when metformin alone at maximum dosage is insufficient.

Insulin is very effective at controlling hyperglycemia but has been underutilized in patients with type 2 diabetes because of the unpopularity of injections. As a result, many patients have received multiple oral hypoglycemic agents without achieving acceptable glucose levels. The types of insulin, their composition, producers, popularity at the market were considered in our work. Short description of companies on the production of insulin was given.

The conclusion is in-process given in relation to the prognoses of creation and issue competitiveness of antidiabetic drugs in Ukraine on domestic industry enterprises especially of insulin.

DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF METFORMIN HYDROCHLORIDE EXTENDED RELEASE TABLETS

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Presently distribution of pancreatic diabetes accepted epidemiology character and it is one of main reasons of population death rate in majority of the world countries. Metformin hydrochloride is an orally administered medicine, which is widely used in the management of type-2 diabetes, a common disease that combines defects of both insulin secretion and insulin action. It is of large interest creation of antidiabetic medicines of metformin hydrochloride in the form of extended release tablets.

The aim of the current study was to design an oral sustained release matrix tablet of metformin hydrochloride and to optimize the drug release profile.

Metformin hydrochloride (N, N-dimethylimidodicarbonimidic diamide hydrochloride) is a member of the biguanide class of oral antihyperglycemics and is not chemically or pharmacologically related to any other class of oral antihyperglycemic agents. Metformin hydrochloride is a white to off-white crystalline powder that is freely soluble in water and is practically insoluble in acetone, ether, and chloroform. Metformin hydrochloride extended-release tablet is designed for once-a-day oral administration using the swellable matrix coated with a permeable membrane technology. The tablet is similar in appearance to other film-coated oral administered tablets but it consists of a swellable active core formulation that is coated by a permeable membrane. The core formulation is composed primarily of drug with swellable matrix excipients. Upon ingestion, water is taken up through the membrane, which in turn causes swelling of the polymer in an active core which control the drug release from the membrane. The rate of drug delivery is totally depending on the degree of swelling of the control release polymer and membrane thickness.

The pharmacotechnological properties analysis of the test substance has shown that the substance has insufficient value of flowability, about what the angle of repose and highly dispersed particles of powder testifies also. Compressibility of substance is also not satisfactory. The wet granulation technology has utillized for tablets production taking into account the overdose of test substance in one tablet. Both the binder and film polymer plays major role for the sustained release of metformin. The developed tablets correspond to Ph. Eur., 7th edition, on all of indexes.

SEMI-SOLID DOSAGE FORMS: OINTMENTS OF MULTIPLE EMULSIONS AND THEIR STABILITY

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Over the past decades ointments have been the center of attention of research for treatment of dermatological, ophthalmic, and even nasal pathologies. Ointment may also have a transdermal function where the skin is not the target organ, and systemic absorption is considered. Ointments serve three functions including: protectorant, emollient, and a vehicle (carrier) of medicaments.

There are four types of ointments: oleaginous (hydrocarbon) bases, adsorption bases, water removable (emulsion) ointments, and water soluble ointments each having different capabilities of withholding water. Selection of an appropriate base for an ointment or cream formulation depends on the type of activity desired (e.g., topical or percutaneous absorption), compatibility with other components, physicochemical and microbial stability of the product, ease of manufacture, pourability and spreadability of the formulation, duration of contact, chances of hypersensitivity reactions, and ease of washing from the site of application.

Of particular interest are microheterogenous dispersed systems composed of two immiscible phases, oil and water. Our research will mainly focus on emulsions which have the ability to carry medicinal active substances, specifically multiple emulsions. Multiple emulsions are complex polydispersed systems where both oil in water and water in oil emulsion exists simultaneously that are stabilized by lipophillic and hydrophilic surfactants respectively. There are two types of multiple emulsions, water/oil/water, or oil/water/oil. These systems are also known as liquid membrane systems.

The main problem with multiple emulsions is its instability, which is represented by transformation of the complex emulsion to a simple oil/water or water/oil emulsion. The most important physical instability phenomena for multiple emulsions are: creaming, sedimentation, aggregation and coalescences of the dispersed droplets, and inversion and separation of the phases.

In our research, we will be experimenting using various techniques and materials to obtain stable multiple emulsions in accordance to the calculations and the proper methods of preparation of such medicinal dosage forms.

STUDY OF PHYSICAL AND MECHANICAL PROPERTIES OF HYDROPHILIC POLYMER MATERIALS

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Stomatological diseases as periodontosis, stomatitis and gingivitis are very common today. According to the WHO data about 80% of adult population suffers from periodontal diseases. It makes development of topical semi-solid stomatological anti-inflammatory and antibacterial drugs actual. For these medicinal forms prolonged action and other biopharmaceutical aspects caused by base properties are very important. The purpose of this study was comparing of hydrophylic gelling polymers properties and forming of the base composition for semi-solid drugs (films and gel).

Properties of polymers of five groups (gums, alginates, carbomers, chitosan and cellulose derivatives) were analyzed according to the literature data. For the polymers with best signs of compatibility with active ingredients physical and mechanical properties (for film bases), rheological parameters (for gel bases) and necessity of few components combination for the base forming were studied.

The results of study showed that anion gelling matters (sodium alginate, sodium methylcellulose) and colloidal solutions of gums are not suitable for using as a bases for drugs containing chlorhexidine because of its inactivation. Carbomer gels lose its viscosity in acid medium so can't be used as a base for medicinal matters with solution's pH less than 7. Alginic acid and chitosane have reparative effects, neutral pH, no irritative action and were found rational components of anti-inflammatory films. While studying of chitosane and alginate films they have shown both positive and negative physical and mechanical properties. Besides, the combination of these matters can give the optimal properties to the film base. Gums were found good components for the gels containing plant (CO_2) extracts. But studying of gums structure and mechanical properties have shown that hydrocolloidal gel of guar and xanthan gum does not fit the rheological optimum and can't be used as a gel base. The combination of gums with carbomer 940 P gives optimal rheological parameters to the gel base used for CO_2 plant extracts gel.

The conclusion of the study is that combinations of alginic acid and chitosane (for films containing chlorhexidine, glucosamine and metronidazole) and carbomer 940 P with gums (for gel with CO_2 extracts of chamomile and salvia) can have optimal properties as a polymer bases for these medicines.

STUDY OF OAK BARK'S TECHNOLOGICAL PROPERTIES AND THEIR INFLUENCE ON EXTRACTION

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Introduction. The bases of many medicinal herbal remedies are extracts of medicinal herbs. Given these considerations, the aim of our study was to conduct search and create thick oak bark extract - a new, standardized national substance of natural origin. Raw oak was largely seen as the source of tannins. Oak bark contains about 20% tannins, which include both condensed and hydrolysable tannins. Oak bark also contains organic acids, polysaccharides, proteins, flavonoids, micro-and macronutrients. Drugs from oak bark have astringent, anti-inflammatory, haemostatic and antiseptic effects. Oak bark decoction is used to treat inflammatory conditions of the mucous membranes of the mouth and upper respiratory tract. Also, it takes for internal application for treating diseases of the gastrointestinal tract, and inflammatory diseases of the genitourinary system. In the production of extracts basic technological operations are extracting the plant material. Improvement and intensification of production in order to increase the yield of the target product requires a detailed analysis of various factors that affect the extraction. Therefore, a process of extraction is necessary to consider the technological properties of herbal drug. The main technological properties of herbal drug include: moisture, content of extractives share, volume and bulk supply of raw materials, porosity, intercellular environment and free volume of layer materials, particle size and other plant material. The effectiveness of extraction of active substances is largely dependent on the nature of the plant material, the degree and method of grinding. We had been placed next task - to examine how the impact of grinding oak bark on its technological properties and efficiency of extraction of raw materials.

Materials and methods. To solve this problem oak bark crushed by different ways: cutting and machining of additional rolling. Prepared from these methods raw materials were evaluated by a number of process parameters.

Results and discussion. The present research has been indicate the basic technological properties of oak bark, which is composed of specific surface - 184,60 ± 1,60%, bulk weight - 0,60 ± 0,003%, porosity - 0,51 ± 0,01%, intercellular environment - 0 34 ± 0,01%, humidity - 8,47 ± 0,12%. Determined that additional grinding bark oak rolling way possible to intensify the process of extracting and increase the quantity of extractives substances and tannins. All further shredded raw observed intensification of the extraction process and increases the quantity of extractive substances (from 10,23 ± 0,20% to 17,10 ± 0,34%), tannins in recalculate from pirogalol (from 2,92 ± 0,04% to 4,49 ± 0,06%).

Conclusion. As a result, studies proved the feasibility of using additional rolling at the stage of raw mill and studied technological parameters of oak bark, which we will take into account when choosing a method of extraction, extraction equipment, technical specifications and additional equipment.

DIFFERENT BASES OF PHARMACEUTICAL CREAMS AND THEIR DISPERSED SYSTEM

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Once widely used, ointments have been largely substituted by creams and gels

Oil-in-water creams are more comfortable and cosmetically acceptable as they are less greasy and more easily washed off using water.

Water-in-oil creams are more difficult to handle but many drugs which are incorporated into creams are hydrophobic and will be released more readily from a water-in-oil cream than an oil-in-water cream.

Water-in-oil creams are also more moisturizing as they provide an oily barrier which reduces water loss from the stratum corneum, the outermost layer of the skin.

The main advantage of creams over other semisolid systems is their ability to easily dissolve both hydrophobic and hydrophilic drugs. Creams are softer than ointments and are preferred because of their easy removal from containers and good spreadability over the absorption site.

The most important consideration with respect to creams is the stability of the finished product. The stability of a pharmaceutical emulsion is characterized by the absence of coalescence of the internal phase, absence of creaming, and maintenance of elegance with respect to appearance, odor, color and other physical properties.

The instability of a drug may lead to the loss of its concentration through a chemical reaction under normal or stress conditions. This results in a reduction of the potency and is a well-recognized cause of poor product quality. The degradation of the drug may make the product esthetically unacceptableif significant changes in color or odor have occurred. The degradation product may also be a toxic substance.

Cream formulations may contain fats and oils with high percentage of unsaturated linkages that are susceptible to oxidation degradation and development of rancidity. The addition of antioxidants retards oxidation of fats and oils, minimizes changes in color and texture and prevents rancidity in the formulation.

We are planning a complex research the effect of different physical, chemical and technological parameters on the stability of cream preparations.

STUDYING THE KINETICS OF DRYING EMULSIONS IN THE OINTMENT "GLITATSYD"

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Currently, the medicine used for a variety of nature and prescribing. However, the need for new, effective and affordable medicines, including possessing painkillers, anti-inflammatory, reparative action and used to treat wounds, inflammation of various etiologies and dermatological diseases, not being fully met.

The department of industrial technology of drugs developed combined ointment with anestezin, nitazol and dry extract of licorice root to treat dermatological diseases and wounds of various etiologies. As hydrophilic non-aqueous solvents (HNS) ointment composition includes propylene glycol and polyethylene oxide – 400. Previous studies have found that these substances are optimal for dissolution of active substances and must be introduced into the ointment in the form of an emulsion.

In order to determine the kinetics of drying emulsion with hydrophilic non-aqueous solvents were produced samples of corn oil, emulsifiers OS – 20 and MGS and HNS (propylene glycol and polyethylene oxide – 400) in different concentrations. The control sample was a warehouse, which is injected hydrophilic non-aqueous solvents. Drying emulsions was determined by the difference of the initial weight of the test sample and the change in mass, which was determined during the day every hour. The study was conducted at 25 ± 2 0C.

During the investigations it was found that the presence of hydrophilic non-aqueous solvents can reduce the degree of drying bases. Increasing the concentration of HNS increases water sorbtion and time osmotic action. Introduction to the basics propylene glycol provides osmotic activity, which increases proportionally with increasing concentration of the solvent.

These results suggest that a decrease in the concentration of hydrophilic non-aqueous solvents is impractical, will decrease to the solubility of substances.

Based on the investigations for moderate osmotic activity, reducing drying, increase the solubility of the active ingredients of the drug, developed, introduced propylene glycol and polyethylene oxide – 400 total of 20%.

ROYAL JELLY

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French agronomist Kayas was the first who received the evidence of the therapeutic action of the royal jelly. In 1953 he published the book named “Bees - the fountain of youth and life,” in which one can read that “the use of royal jelly creates a sense of youth and vigor.” A great number and variety of vitamins and other vital elements confirms the high biological activity of the royal jelly and the possibility of its use as a power or a remedy. The most effective way to use the royal jelly is the sublingual method.

When it is taken perorally, being in the stomach the royal jelly is completely exposed to destruction by gastric juices. It is known that in the mouth there is no hostile environment, so the royal jelly is rapidly and almost completely absorbed through the skin, bypassing the liver barrier that creates the optimum concentration of the components in the blood. The external application of royal jelly is found in the form of alcoholic emulsion of the aqueous solutions, creams, and the ointments. Royal jelly is produced in the pharmacy in the form of the “soft” tablets, which include 20 mg of royal Jelly 0,5 g of glucose and 1-2 drops of honey for the conservation and band components. The alcoholic solution of royal jelly is a convenient and easily accessible form of preparation and application.

The potential administration of royal jelly can be also assumed. Especially, this method was practiced in 50-60’s of the last century. The preparation of such drugs is a complex process, and the benefits are minor. The potential administration of the drug is shown in tuberculosis in the recovery period, asthma, poor circulation, liver disease, pancreatitis, anemia, gout, kidney disease, peptic ulcer disease. There are many drugs that contain the jelly such as: Apilaktoza, Apimin - B Apitok, Apifor, Vitadon, Vitas, KolGel. The biological basis of the production technology of royal jelly is the quality of the bee colony to grow new queens of the young larvae of worker bees according to the selection or exclusion of the uterus. The most favorable season for royal jelly is late spring and early summer - the period of intensive development of families.

Royal jelly has biostimulating, antiviral, and toning properties and it is used in premature senile weakness, diffuse cerebral sclerosis and vascular spasm in the brain, heart, angina, and viral diseases.

The lack of information on the benefits of the royal jelly and its application are the main reasons hindering the increase of its production in Ukraine apiaries.

IMPROVING OF THE COMPOSITION AND TECHNOLOGY OF EXTEMPORANEOUS VAGINAL SUPPOSITORIES WITH DOXYCYCLINE

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Vaginal infections are a source of significant morbidity among women. The main causes of infectious vaginal infections are vaginal candidiasis, trichomoniasis and bacterial vaginosis. Thus, the need for further study of the problem of treating vaginal infections is relevant.

The aim is improving the composition and technology of extemporaneous vaginal suppositories with doxycycline for treatment vaginal infections.

A study of the pharmaceutical market of industrial produced medicines for the treatment vaginal infections was conducted. Found that the most medicines are of foreign origin – 81 % and the Ukrainian market represented only 20 % of medicines.

Today in Ukraine in the pharmacies, there is a lack of extemporaneous produced medicines for the treatment vaginal infections. Extemporaneous production of medicines allows individual approach to patients, which consider the characteristics of an organism, disease, symptoms of it and its stage. This is the main principle and advantage of preparation medicines «ex tempore». Analysis of extemporaneous compounding of the pharmacies in Kyiv and Kharkiv showed that most doctors prescribe vaginal suppositories, which incorporate the following ingredients: doxycycline, dimeksid, synthomycine liniment, menthol (in different ratios) on the base of hard fat. Based on our own research was chosen as active substance doxycycline and base of natural origin: cocoa butter and beeswax (developed at the Department of Drug's Technology led by prof. Yarnykh T.G. and assoc. prof. Chushenko V.M. and on which patent was obtained), which identified a number of advantages over synthetic bases. The base mixes well with a variety of medicines, has a distinct melting point and high ductility, and expresses reparative and lubricating effect, on this base vaginal suppositories are prepared by the casting method that significantly reduces process.

The research allowed improving the composition and developing technology of extemporaneous vaginal suppositories with doxycycline on the base of cocoa butter by the casting method for treatment vaginal infections.

USING OF MODERN EXCIPIENTS FOR DEVELOPING OF SOFT MEDICINES.

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Developing of effective drugs involves use of a wide range of excipients with various pharmaceutical properties. Excipients influence the pharmacological activity of the drugs, increase the efficiency, stability and shelf-life and affect the manufacturing processes. Excipients help to develop and produce pharmaceutical systems with suitable physical, chemical and therapeutic properties.

Today, the actual task of pharmaceutical science is to develop effective soft drugs for external use - ointments, creams, gels, pastes and liniments. For the manufacturing of modern pharmaceutical dosage forms technogists use different excipients, each of those plays different roles in composition: bases (lanolin, petrolatum, silicone), solvents (mineral and vegetable oils, ethyl and isopropyl alcohol, propylene glycol, glycerin, dimethyl sulfoxide, collagen), enhancer of penentation ,antimicrobial preservatives (benzalkonium chloride, chlorhexidine, miramistin, benzyl alcohol), osmotically active agents, lubricants, emulsifiers (sodium lauryl sulfate, Twins, Sola higher fatty acids, ethoxylated oil, cholesterol, Spencer), thickeners, antioxidants (tocopherol, ascorbic acid, citric acid) etc.

Excipients are the active components of the ointment which promote bioavailability of active ingredients. Excipients must meet medical prescription of drugs and geused in biologically harmless and compatible with body tissues they should not have allergic or toxic effects and interact with drugs. Also they should be cheap.

Emulsifiers (surfactants synthetic and semi-synthetic origin) play the important role in the production of ointments. Today, the modern market offers a wide range of emulsifiers to create ointments of emulsion type: Eumulgin B1, B2, B3, HRE-60, Cutina E 24 (nonionic surfactants for creams and emulsion oil / water), Generol R (emulsifier for emulsion water / oil), Dehymuls SML (lipophilic emulsifier for pharmaceutical emulsions).

Based on the above mentioned, we should noticed that using of modern exipients is very actual for regulation and improving of pharmacological, technological and consumer properties of new effective drugs for topical application at stage of its developing.

STUDY OF COMPOSITION AND TECHNOLOGY OF HEPATOPROTECTIVE AND IMMUNOSTIMULATIVE ACTION DRUG

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At present, most of the population suffers from diseases due to weak or weakened immunity. However, modern clinical medicine has proved that at liver diseases violation of one of its functions is observed, including protein generating (including immunoglobulin synthesis), which leads to disruption of humoral immunity circuit.

Therefore, the problem of creating a combined action drug of immunomodulating and hepatoprotective action is relevant for practical pharmacy.

The aim of research was to choose optimal dosage form and to develop a technology for hepatoprotective and immunostimulative action drug.

As ingredients used natural substances: vegetable sunflower protein and MX-factor substance which is a glycoprotein olygopeptide composite preparation.

During the experiment used the following technologies and research methods according SPU: for granulate - fractional composition, determination of the flowability parameters, angle of repose, bulk volume and bulk density; for capsules - average weight, disintegration time.

As the optimal dosage form we have chosen hard capsules because they are more attractive from a technological point of view than other dosage forms.

At reception of granules used vegetable Sunflower protein powder as a component of immunostimulating action and MX-factor as a moisturizer and components with immunomodulative and hepatoprotective effects. The resulting granules were tested for residual moisture that was 5.35%, and fractional composition (about 95% takes the fraction with particle size 100 microns). For further research used granules fraction with particle size 100 microns. Granular had sufficient fluidity - 9 s / 100 g, which has allowed to avoid the use of extra excipients.

Filling of number 4 size capsules with obtained granulate was performed using capsule machine.

Capsules after filling were weighted - average weight of filled capsule is 0.15 g, and the mass of the empty shell - 0.05 g. Thus, a capsule contains 0.1 g of active ingredient. Capsule disintegration time was, on average, 7 minutes, which meets the requirements of regulatory documents. Thus, in the course of research, proposed the composition and technology of immunomodulating and hepatoprotective action preparation in the form of hard capsules.

THE MODERN AUXILIARY SUBSTANCES USED IN THE TABLET MANUFACTURING TO PROLONG THE THERAPEUTIC EFFECT

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The cardiovascular diseases are the urgent problem of our time. It's one of the main reasons of population mortality.

In order to achieve therapeutic effect, a drug needs to reach the right place in the body at the right time. For some drugs, this may be achieved by simple solutions or solid dosage forms with an instant drug release while, for others, one has to modify the drug release. The clinical effect of low - molecular - weight substances is often related to the concentration of the drug in the blood plasma.

The stability of a drug in the solid state or in aqueous solution is a critical parameter when selecting an appropriate manufacturing process. A drug in an oral extended-release (ER) formulation reaches aqueous environments with, for example, variations in pH (1 –8), ionic strength, and bile salt concentration, which requires high chemical stability of the drug. Furthermore, the substance should be stable not only against chemical degradation such as hydrolysis but also against enzymatic degradation (metabolism) during the passage from the lumen to the systemic blood circulation.

The main principles related to ER systems are as follows: insoluble matrix formulations; membrane - coated solid dosage forms including osmotic pump systems; soluble hydrophilic matrix formulations.

The term *insoluble matrix tablet* refers to tablets in which the drug is embedded in an inert carrier that does not dissolve in the gastrointestinal fl uids. The carrier material in insoluble matrix tablets can be based on insoluble lipids or polymers, both matrix builders whose function it is to keep the matrix together during the passage through the gastrointestinal tract and thus prolong the diffusion path of the drug before it is released from the formulation.

One way to protect the drug from being directly released is to coat the system with an insoluble film. This can be achieved, for example, by enteric coatings, where the film - forming materials are insoluble in aqueous solutions at low pH but soluble at high pH values. As film - forming material, water - insoluble substituted cellulose derivatives such as ethylcellulose have been suggested as well as synthetic polymers such as methylacrylates.

Hydrophilic matrix tablets are composed of an active substance,a hydrophilic polymer, release modifiers, lubricants, and glidants. So the rational choice of the excipients promotes the modifed release of the drugs.

STUDYING OF TECHNOLOGICAL PROPERTIES OF ACTIVE PHARMACEUTICAL INGREDIENT MALONIC ACID DERIVATIVE INTENDED FOR DEVELOPMENT OF TABLETS

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Compound from a number malonic acid derivatives was synthesized in Saint-Petersburg chemical-pharmaceutical academy. This compound has antiischemic and antioxidant properties. During the development of composition and technology of tablets with active pharmaceutical ingredient (API) of malonic acid derivative (MAD), physical-mechanical and technological properties of this compound were studied.

Researches of properties of API (fractional composition, bulk density, relative and true density, porosity, compressibility, loss on drying) were carried out with 6 standard laboratory batches. Investigated API is polydisperse powder with isodiametric particles. Researching of API fractional composition showed that the most part of these particles contains small fraction (less than 0.25 mm) that is why API has poor flowability. The particles of API have the following size rating: less than 0.25 mm – 75.2 $\pm$3.7%, 0.25-0.50 mm – 14.8$\pm$3.7%, 0.50-2.00 mm – 10.0$\pm$3.7%. Bulk density of API was determined by the method of free sprinkling with conditional compaction. The bulk density of API is 0.331$\pm$0.022 g/cm^3. True (absolute) density was determined as follow: tablets were pressed with the powder of API (mass - 0.40 g) with using a laboratory hydraulic press that provided pressure 680 MN/m^2 to make tablets with almost zero porosity. The true density of API is 1.271$\pm$0.023 g/cm^3. Porosity and relative density of API were calculated by using true and bulk density. The relative density of API is 26.1$\pm$1.9%, the porosity of API is 72.7$\pm$2.3%.

Model tablets with diameter 9 mm and mass 0.30 g were pressed with the hydraulic press. Pressure 120 MN/m^2 were used to determine compressibility of API. Compressibility of API was determined by compressive strength needed for destruction of model tablets. The strength was determined by the Erweka instrument type TB-2. The compressibility of API is 5.0$\pm$0.2 kg. The loss of drying was determined by the method of drying in vacuum drying box at 60$\pm$2 ^{0}C and residual pressure 1.3 kPa to constant mass. The loss of drying of API is 0.60$\pm$0.08%. It is estimate that API MAD has poor wetting with water, low bulk density, tolerable compressibility and very low flowability. After drying API is easily electrized. Addition hydrophilic fillers, surfactants and disintegrants in composition tablet and procedure of wet granulation were used for producing tablets with API MAD.

THE ETIOLOGY AND DRUG TREATMENT OF THE MASTITIS

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Mastitis is a benign disease diagnosed in almost one-quarter of women aged under 30.

According to the WHO, "Mastopathy is a fibrocystic disease (FCD), characterized by the impaired ratio of epithelial and connective tissue components, a wide spectrum of proliferative and regressive changes of the breast tissue." According to the statistics this disease occurs in 60-90% of women predominantly in the age of 30-50.

Hormones, the complex compounds of plant origin, which are similar to the sex hormones in structure and action, are often used in the treatment of mastitis.

The effect of the phytoestrogens in the treatment of mastitis is related to their weak estrogenic activity, as well as the ability to block the activity of the enzyme aromatase adipose tissue (this enzyme is the most effective for patients who suffer from obesity), which is involved in the conversion of androgens to estrogens.

Linking to the estrogen receptors, the phytoestrogens displace estradiol because of the binding to the receptors, which may partly explain their anti-proliferative effects, they are the inhibitors of the enzymes involved in the functioning of receptors that control the growth factors, and have an antioxidant effect. Food which is rich in phytoestrogens, also contain the coarse vegetable fibers that promote the binding of steroids in the gut and excretion.

Breast is considered to be a precancerous condition, therefore, a long-term use of antioxidants - vitamins E and C, beta-carotene, phospholipids, selenium and zinc is needed. It is also important to use drugs containing potassium iodide, which helps normalize the hormone ovaries. Seafood contains iodine as well.

Mastopathy most often affects women who deal with intellectual labor and psychological overloads, stress.

Often it is the women of childbearing age with healthy lifestyles and some terminated pregnancies, latch of breastfeeding. It can be concluded that the state of breast reflects the social, psychological and physical health of women.

Taking into account the severity and frequency of breast cancer, the number of deaths and the limited arsenal of drugs for the prevention and timely treatment of the disease, the technology and methods for the quantitative analysis of the extreme medicine were developed at the department of ATL headed by D.P.Sala.

PERSPECTIVES OF USING OPHTHALMIC INSERTS FOR TREATING GLAUCOMA PATIENTS

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Glaucoma as a cause of blindness ranks second position among the eye diseases. According to the literature, about 3% of the world's population suffer from glaucoma, about 7 million patients with this disease suffer from blindness in both eyes, and this number is steadily increasing. The prevalence of glaucoma has increased by 36,7 % in Ukraine for the last 6 years, morbidity – by 29,8 %, while the dispensary group increased by 40,3 %. This growth indicates a significant disabling impact of glaucoma, and, no doubt, make it an important social problem.

The aim of research was to analyze of the medicinal forms variety for the glaucoma treatment, which are represented in the pharmaceutical market of Ukraine.

The analysis was performed by using secondary sources, including information from the Rx-index, which enables us to track changes in the structure of the proposal within the overall range of antiglaucoma drugs. Statistical data processing was carried out using Microsoft Excel 2007.

An informative array of 60 drugs, which has 43 retail and 12 international non-proprietary names was generated at the first stage – the analysis of official information sources on registered and approved for medical use in Ukraine medicines.

Marketing analysis in the plane of drugs offers by medicinal form indicates the maximum share of eye drops (93.33%). The part of pills is 5%, eye gels – 1.67%. These medicinal forms have disadvantages comparing to eye inserts. Eye inserts allow to make controlled dosage of medicinal matters, to ensure prolongation, to decrease quantity of medicinal matters, increase therapeutical concentration of medicinal matter in eyes tissues, to short treatment course, to provide treatment in the conditions of inability of using other eye medicinal forms.

At composition market segmentation it was found that group S 01 E – «Antiglaucoma drugs and miotics" is represented mostly by one-component medicines (83,33%), while the combined medicines share is only 16, 67%.

So, there are new prospects for expanding the range of polyvalent combined eye inserts of domestic production in group S 01 E – «Antiglaucoma medicines and miotics" to achieve the therapeutic effect.

CRITERIA FOR EXCIPIENTS SELECTION IN THE PHARMACEUTICAL DEVELOPMENT OF LIQUID PLASTER FOR TREATMENT OF FOOT MYCOSES

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Introduction. One of the pharmaceutical factors affecting the effectiveness of drug preparations is nature and quantity of excipients. Since excipients are critical and essential components of all drug products, the selection of excipients in the development of new preparations must be theoretically and experimentally substantiated.

The aim of the work was to summarize requirements for excipients used in the pharmaceutical development of liquid plasters for treatment of foot mycoses.

Materials and methods. Pharmaceutical and medical data sources. Methods: search and systematization of information, logical analysis.

Results. Liquid plaster (skin glue) is a liquid which after drying creates a thin film on the skin. Development of plaster composition depends on its pharmacological purpose, but the manufacture of such preparations is complicated by the absence of general pharmacopoeia article on liquid plasters. Basic pharmaco-technological requirements for excipients used in liquid plasters production are: to provide the uniformity of solution, and to provide the forming of uniform, transparent, elastic film with good adhesive properties after solvent evaporation. Lots of excipients are used in liquid plaster production, but film-forming agents, solvents and plasticizers are included in all formulations. Film-forming agents must be capable of forming a continuous film. Solvents must have a high solubility coefficient regarding the plaster components and rapidly evaporate without remaining the odour. Plasticizers must be low-molecular compounds which are included into the formulation to provide the elasticity to formed film.

The rate at which an active ingredient migrates through the skin is determined by the molecular weight and lipophilicity of the compound, but it can also be affected by different absorption or penetration enhancers. Therefore, it is necessary to include the penetration enhancer in the composition of antifungal plaster.

Conclusions. Substantiated selection of excipients is an important stage in pharmaceutical development. To develop the composition of liquid plaster for treatment of foot mycoses, it is rational to use the following groups of excipients: film-forming agents, solvents, plasticizers, and penetration enhancers.

CREATION OF SUPPOSITORIES FOR CHILDREN BASED ON THE PLANT COMPONENTS

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Over the past few years, there has been a tendency to constant increase of the number of children with various pathologies, including viral origin. In modern pediatric practice among various medicinal forms the greatest interest have suppositories and, accordingly, rectal route of administration of medicines, which has a number of advantages.

Medicines in suppository form quickly show the main pharmacological effect, eliminate irritation of stomach and duodenal ulcers, and prevent inactivation of the medicine in the liver and gastrointestinal tract. In addition, this medicinal form is one of the safest in pediatric practice.

A right combination of medicinal substances, primarily of natural origin can effectively achieve the desired antiviral activity. From this point of view, the most promising is the following plant raw material: licorice roots, essential oils of chamomile and tea tree.

For preparation suppositories, we used thick licorice extract, essential oils of chamomile and tea tree, which can inhibit the development of a variety of microorganisms, effectively restoring the natural immunity. As a suppository base for children's rectal suppositories, we used hard fat (type A).

Suppositories were prepared using replacement coefficient of thick licorice extract, physical and chemical properties of the main components and excipients by the method of pouring.

In order to establish the optimal concentration of thick licorice extract in the suppositories researches on the antiviral activity of glycyrrhizin acid in the State Institution "Institute of Microbiology and Immunology named by Mechnikov of National Academy of Sciences of Ukraine" were conducted.

The concentration of essential oils of chamomile and tea tree in suppositories justified based on microbiological studies. Study of antibacterial activity of model samples was carried out in experiments in vitro using agar diffusion.

Thus, based on the studies we have justified the concentration of active ingredients in suppositories for children based on the plant components: thick licorice extract - 21.7 %, essential oil of chamomile - 0.875 % and essential oils of tea tree - 0.875 %.

STUDY THE EFFECT OF EXCIPIENTS ON PHARMACO-TECHNOLOGICAL PROPERTIES OF TABLETS WITH COMPOSITE CHICORY AND CORN EXTRACT

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Rational and integrated use of famous medicinal plants, as well as search for new sources of biologically active compounds with the purpose of extension the nomenclature of drug preparations are essential and topical questions.

The aim of the work was to study different groups of excipients for manufacturing the tablets with composite extract of chicory and corn.

Materials and methods. Excipients which are most commonly used in manufacturing the tablets with phytoextracts were included in a plan of experiment. Excipients were selected from the following groups: glidants, samples of microcrystalline cellulose (MCC), binders and fillers. In order to find the relationship between the composition and basic quality parameters of tablet, method of mathematical experiment planning was used.

The results of investigations show that the uniformity of tablet mass with chicory and corn extract depends on each factor under investigation. Among studied brands of MCC, the least deviation in the tablet mass occurs when MCC 102 and MCC 101 are used.

An important parameter that characterizes the mechanical strength of tablets is friability. Obtained tablets of all series have a required friability. It was determined that fillers, glidants and binders affect this parameter more than MCC.

It was also studied the resistance to crushing of tablets with composite chicory and corn extract. MCC and glidents have the most effect on this parameter.

The other important quality parameter of tablets is disintegration time. Variance analysis of experimental data revealed that excipients significantly affect the disintegration time of tablets.

Conclusions. Formulations that include neusilin or aerosyl, microcrystalline cellulose 101 or 102 (as glidants), croscarmellose sodium or potato starch (as fillers), starch paste or hydroxypropylmethylcellulose solution (as binders) are selected for further investigations.

DEVELOPMENT OF METHODS FOR ESTIMATION OF DEGREE SUBEXTRACTION BY COUNTERFLOW EXTRACTION PROCESS OF HERBAL RAW MATERIAL

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Introduction. As a way to organize the counterflow extraction process - is the most effective in terms of economic consume of extragent. We can receive more concentrated extracts with such process organization that reduces the cost of the subsequent evaporation.

The aim of abstract - to obtain a suitable model for calculating of degree subextraction for forecasting parameters of the extraction process.

It is known that the degree subextraction (φ), equal to the amount of biologically active substances (BAS) in expeller to their original amount into raw materials and depends on:

• nature of raw material, extragent, BAS and express in the distribution coefficient BAS between phases (m);

• coefficient retention of extract by skeleton of raw material (Ku);

• coefficient of excess extragent ratio (β).

Materials and methods: The object of study was chosen herb of Leonurus; material - ethyl alcohol 70% v/v. Analysis conducted by gravimetry of dry residue in extracts.

Studies. As a result of the joint solution of equations describing the laws of conservation of mass, equilibrium and kinetics of the extraction process, we determine the degree of dependence of subextraction as:

$$\varphi = \frac{1}{1 + A \cdot (A_0 - \varphi_2)} \cdot \prod_{i=2}^{n-1} \left(\frac{1}{1 + A \cdot (1 - \varphi_{i+1})} \right) \cdot \frac{1}{1 + A}$$

where $A = \dfrac{\beta \cdot (Ku + 1)}{\dfrac{1}{m} + Ku}$;

$$A_0 = \frac{\beta - \dfrac{Ku}{Ku + 1}}{\beta}$$

To confirm the adequacy of the mathematical model, we examined five steps maceration of Leonurus herb by 70% v/v ethanol solution. Accuracy between the data and the mathematical model and the experiment represented less than 5%.

Conclusions: the results of the calculation show that the mathematical model is sufficient to adequately describe the process of extraction. What makes it possible to carry out calculations at different conditions of the extraction process with subsequent analysis of the results.

THE ELEBORATION OF THE DOSAGE FORMS WITH CHONDROPROTECTIVE EFFECT

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Diseases of the musculoskeletal system are one of the most pressing health and social problems of the world because of their high prevalence, significant disability and invalidity, the difficulty of early diagnosis and treatment of patients. Among the diseases of the musculoskeletal system the most frequently diagnosed one is osteoarthritis that affects up to 20 % of the population of our planet. The degradation occurs in osteoarthritis cartilage tissue, which is manifested above all the destruction of proteoglycan complexes with subsequent dehydration of the cartilage. It significantly modifies the metabolism, reducing synthesis of the main molecules - proteoglycans and collagen type II. Therefore, based on the pathogenetic prerequisites for effective pharmacotherapies the inflammatory reaction and pain to normalize the metabolism of the cartilage are suppressed.

Nowadays we use the symptomatic medicine of fast action, which include analgesics, non-steroidal anti-inflammatory drugs, corticosteroids. As well as symptomatic there are slow-acting drugs - chondroprotective funds, which include glucosamine, chondroitin, diacerein, piaskledin, alflutol, hyaluronic acid. Glucosamine is a monosaccharide, which is the precursor of many glycosaminoglycans such as chondroitin sulfate, kerotan sulfate, hyaluronan. In the development of pharmaceutical dosage the forms with transdermal effect gave special attention to not only active, but also auxiliary substances. It is known that there is a complex interaction between them that induces considered auxiliary substances as an inert carrier of drugs, as well as an important means to maximize the therapeutic effect. The properties of the base must be confirmed with the purpose of destination ointment. The basis for the surface action of the chondroprotective ointments, on the contrary, should not be able to be absorbed without disturbing the local action of the cure ointment at the same time.

Some special requirements, which have a significant impact on the stability and kinetics of the drug, have been established, such as: the pharmacological indifference, the lack of effects of chemical and physical incompatibility, the stability of physical and chemical properties in the manufacture of ointments and storage, the ability to set limits to release the active ingredients, the ability to be easily removed from the skin.

The object of our work is to study the interaction of support and the active ingredients in pharmaceutical dosage forms of chondroprotective drugs, and the design and composition of the search and technological methods that can provide the high quality of the resulting product with the optimal therapeutic efficacy.

SECTION 5

MODERN BIOTECHNOLOGY

ANTIADHESIVE ACTIVITY OF *RHODOCOCCUS ERYTHROPOLIS* IMV AC-5017 EXTRACELLULAR METABOLITES

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Bacterial adhesion on different surfaces is a key problem in infections that allows subsequent colonization, invasion and internalization of pathogens, particularly in dentistry. A lot of efforts have been directed to avoid bacterial attachment, such as studies of changing the superficial properties of contact surfaces by conditioning surface-active substances (SAS). Surface-active substances are surface active products of microbial origin. They have several advantages over synthetic surfactants, because of their biodegradability, reduced toxicity, availability from cheap raw materials, biocompatibility, the effectiveness at extreme temperature, pH, salinity, emulsifying ability, antimicrobial and antiadhesive properties.

In previous studies the oil-oxidizing bacteria identified as *Rhodococcus erythropolis* EK-1was isolated from oil-contaminated soil samples. The strain EK-1 was deposited in the Depositary of microorganisms of the Institute of Microbiology and Virology of National Academy of Sciences of Ukraine at the number of IMV Ac-5017.

It was also shown the antimicrobial activity of *Acinetobacter calcoaceticus* IMV B-7241 and *Rhodococcus erythropolis* IMV Ac-5017 cell-free supernatant against bacteria and yeast and antiadhesive properties of *Acinetobacter calcoaceticus* IMB B-7241 cell-free supernatant on linoleum, ceramic, steel and plastic.

The aim of this work is to study the antiadhesive activity of *R. erythropolis* IMV Ac-5017 extracellular metabolites on dentures.

It was determined that *R. erythropolis* IMV Ac-5017 extracellular metabolites possessed the antiadhesive activity against all tested microorganisms (*Candida albicans* D-6, *Bacillus subtilis* BT-2 and *Escherichia coli* IEM-1) on denture basis and the antiadhesive effect depended on the dilution factor. The highest reduction of adhesion (60–80%) of tested microorganisms was observed for the cell-free supernatant. The pretreatment of silicon surfaces with cell-free supernatant in low SAS concentration (0.125 mg/ml) significantly decreased the adhesion of all bacteria and yeast: the highest reduction of adhesion for *C. albicans* D-6, *E. coli* IEM-1 and *B. subtilis* BT-2 was 70, 55 and 46% respectively, while D-6, IEM-1 and BT-2 strains adhesion on acrilic surfaces was reduced on 77, 50 and 57%.

Thus, as a result of the work it was stated that *R. erythropolis* IMV Ac-5017 extracellular metabolites are promising for use as anti-adhesive agents in dentistry.

STUDYING OF BREAD BAKERY YEAST

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Since time immemorial bread is basic food for man, which contains the row of useful and necessary for the vital functions of organism albumens, albuminous connections, high molecular fats, starch, and stuff. In addition, there is an enough body of vitamins of group B, cooperant the balanced functioning of the nervous system for man in the bread. The components of his preparation are a wheat and rye flour of different sorts, salt, water and yeasts.

The useful physiological properties of yeast have led to their use in the field of biotechnology. Fermentation of sugars by yeast is the oldest and largest application of this technology. Many types of yeasts are used for making many foods: baker's yeast in bread production; brewer's yeast in beer fermentation; yeast in wine fermentation and for xylitol production. While history of baking of bread is calculated a not alone millennium, concept "yeasts" appeared relatively recently, only near 150 years back. It happened since in 1854 Lewie Paster engaged in research of a spirit fermentation and opened, that microorganisms are need for this process which they lift a liquid "lift" a liquid are needed. Here for these isolated and constantly increased microorganisms and began to use a deep-rooted in baking of bread word "yeasts". Today bakery production as the most developed industry of food industry uses yeasts of new generation —thermophilic yeasts – Saccharomyces cerevisiae. They are biological debonders influencing substantially on the volume of the prepared product. Consequently, a leading role belongs to them in forming of quality of bread and bake goods. Distinguished yeasts are of up-river and basilar fermentation. There are a few separate races in each of these groups. Bakery yeasts are valued proliferous races, possessing a good carrying capacity and firmness at storage. A carrying capacity is determined both the features of races of yeasts and method of conduct of production. A reaction of environment where yeasts are in must be a little sour. An alkaline environment oppresses zymic cages. Knowledge of biochemical nature of thermophilic yeasts –Saccharomyces cerevisiae and application of their useful properties in a bakery production, in the end, allow deciding main tasks, standings before industry on the whole: decline of production inputs, improvement of quality and expansion of assortment in accordance with the requirements of consumer demand unit of bakery products. On chair of biotechnology pass various experiences and researches that help students with the doctrine.

THE POSSIBILITY OF CO-CULTURE OF WINE YEAST SACCHAROMYCES CEREVISIAE AND LACTIC ACID BACTERIA LACTOBACILLUS PLANTARUM

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Wine contains a rich set of useful nutrients, minerals and other biologically active substances and has curative properties, which are the results of complex biochemical changes that occur with various microorganisms. Grape wine is called the product obtained by alcoholic fermentation of the juice or pulp of fresh or dried grapes. It is believed that the main role in the formation of flavor and aroma of wine play wine yeast, responsible, primarily, for the intensity of the flow of alcoholic fermentation, during which two main products are produced from glucose - ethyl alcohol and carbon dioxide, as well as intermediate by-products: glycerol, acetic acid, acetaldehyde, acetone, citric acid, pyruvic acid, malic acid, fusel alcohols, etc. The result is a so-called "green wine" with a distinctive spicy flavor, astringency and bitter aftertaste, which is caused by the large amount of malic acid. To date, the domestic wine require additional time to "maturation." At the same time, it is not typical for young wines of France and Spain due to the fact that, along with activation of wine yeast a range of lactic acid bacteria contained initially on the surface of grapes is involved in the formation of the bouquet. Lactic acid bacteria involved in the malolactic fermentation, providing soft flavor and a decrease in pH due to the formation of lactic acid. Malolactic fermentation in wine starts when the alcohol fermentation has not been finished yet and there is a sugar. The temperature of the alcoholic fermentation of 15 - 25 ° C is favorable for the malolactic fermentation. If the destruction of malic acid occurs at low temperature - the process is slow and can take several months, and at high temperature - foaming of young wine, it is important to keep the temperature conditions. Spontaneity microflora and variability of its composition may lead to unauthorized fermentation products that can change the organoleptic characteristics of the final product. On the one hand, there is evidence of the existence of races dairy cultures, capable of simultaneous development with alcohol yeast, on the other - some sources said that they have antagonism under anaerobic culture conditions. Therefore, the study of possibility of co-culture Saccharomyces cerevisiae W748 (Saccharomyces cerevisiae WET 136) and Lactobacillus plantarum is interested for the intensification of biotechnological processes for production of wine is interested and we can use the results in the development of wine production technology, eliminating the stage of "maturing".

STUDY OF BIOLOGICAL FEED ADDITIVES "BATSELL" PRODUCTION COMPANY "BIONA"

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For us, as future professionals in biotechnology, it is important to know about our future job. It is therefore I chose the object of research producer feed additive, dynamic international company that leads the market biotechnology - company «Biona» (Evpatoria).

The company is looking for, the development and implementation of natural solutions Agro Industry using biotechnology. The company specializes in developing and manufacturing biological products for crop, livestock, including poultry feed under the brand «Biona» and "subsistence farming".

The current trend to reduce the cost of lives to ckand feed safety of the replacement of animal protein to vegetable found several problems: low digestibility of proteins presence anty nutrient factors – no starch polysaccharides and improve my cotoxins in feed.

In addition, in the digestive tract of birds, pigs and young ruminants missing enzymes that break down complex polysaccharides such as celluloseno starch, hemicellulose, pentazany, β-glucans, pectins.

Introduction enzyme-probiotic preparation "Batsell" in animal feed to stimulate development cellulolytic Rumin ococcusal bus, byisolating a strain of Bacillus subtilis 8130 endohlyukanaz enzyme that depolarize cellulose for the initial stages of digestion of fiber, destroying the walls of plantcells, with the release of the evaluable energy-dense carbohydrates, proteins, and fats.

Also, the drug stimulates the digestion of nutrients, when the production of enzymes in the body of animals and birds is limited. Probiotic properties of the drug can prevent many diseases caused by pathogenic microflora to form normal, utility in testinal microflora, primarily due to Lactobacillus sp., Accelerates twice the growth rate cellulosic Ruminococcus albus, which provides fiber hydrolys is also increases the immune status.

This increases the productivity of animals and birds are reduced by 10-15% and costs by 20% the cost of feed per unit of output, improved performance playback, enhanced preservation of livestock, reduced costs of medicines and improved economic performance.

The department of biotechnology of National University of Pharmacy conducted research on biological feed additives manufacturing company «Biona».

ANALYSIS OF DRY WHITE WINE "CHARDONNAY" ON ORGANOLEPTIC AND PHYSICOCHEMICAL QUALITY FACTORS

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Benefits of dry wine have been proved a lot of times. Considering the components of red or dry white wine, one can say that it contains a large amount of protein, calcium, sodium, magnesium, selenium, iron, zinc, copper and many other nutrients which are utterly necessary for the normal functioning of human being. All dry wines contain biologically active substances, flavonoids, quercetin, wildlife reserve, polyphenols and tannines.

Since ancient times, dry wine has been an excellent antiseptic, diuretic, and also a sedative of natural origin. Dry wine is widely used for medicinal purposes. In small doses, this drink supports heart muscle; it is a prevents atherosclerosis; it effectively reduces blood cholesterol level and dilates blood vessels. Doctors strongly recommend to use dry wine with anemia, two glasses of wine before meals or directly during meals significantly improve the health of the sick person. It has long been treated with vitamin deficiency is the use of dry wine. With regular and moderate consumption of high-quality dry wines are largely clear blood vessels.

In Ukraine, there is a tendency to reduce processing grapes into wine materials by enterprises, as compared with 2009 production in 2012 fell by 26% and it is 23 million dal of wine per year.

There wasn't a culture of wine consumption in our country, and still it is not observed. Poverty of most part of the population causes drinking inexpensive ordinary mass commercial fortified wine or vodka, and here unscrupulous manufacturers earn much money, while the wine consumers and society are the ones who loose in this situation. Lack of legislative control has led to an increase of "shadowy" wine production, unpunished increasing of counterfeit items production and poisoning of consumers. According to scientists of National Institute of Wine and Grapes "Magarach" the share of counterfeit products is 30-41%. The main types of counterfeit products are the following: the adding of water – 43%, lack of correspondence to varietal composition – 9%, lack of correspondence to organic acids – 23%, lack of correspondence to the authentic over the content of glycerol – 12%, the adding of dye – 2% and flavorings – 3%, the other indicators – 8%.

Having analyzed the market of wine production in Ukraine at the Department of Biotechnology of National University of Pharmacy we began to research the complex analysis, including the organoleptic and physicochemical characteristics, quality of dry white wine of "Chardonnay" by Ukrainian producers.

MICROBIAL BACTERIOLYSINS AS THE BASE OF SUPERFICIAL MEDICAL MEANS

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Antimicrobial preparations are widely presented in the range of modern medicines. Considering a problem of expansion of the microbial pathogens resistance, actual there is a studying of new active ingredients and creation of effective antiseptic means.

One of such substances is the bacteriolytical enzyme preparation Cytorecifen of a microbial origin. Its preparations in the form of powder are developed for medical application and as a part of detergents. However considering tha advantage of soft medicinal forms of antiseptic preparations it seems to be expedient to creation the ointment or gel form on the base of an offered preparation.

Establishment the possibility of soft forms on the base of Cytorecifen development for medical and cosmetic use was the purpose of represented research. The most used excipients as a part of soft forms (fillers, stabilizers, preservatives, etc.) were for this purpose analysed and chosen and their influence on antimicrobial activity of an enzyme preparation in relation of Staphylococcus aureus and Bacillus cereus is studied.

As excipients of various functionality were used polyoxyethylene (400 and 1500), polyethyleneglycol, silicon dioxide, vaseline, glycerin, dimexidum, lidocaine, myramistim. Considering ranges of concentration of these substances as a part of ready forms, prepared their individual and combined mixes with an enzyme preparation. Cytorecifen′s residual antimicrobial activity in mixes determined by a turbidimetric method and expressed in absolute units and as a percentage in relation to activity of the preparation.

At interaction with polyoxyethylene, polyethyleneglycol and silicon dioxide activity of enzyme decreased for 15-25% that is obviously connected with its partial adsorption on these carriers. In concentration used in ointments (10-20%) glycerin and vaseline reduced activity of a preparation for 5-7%. The same falling of activity was noted at effect of lidocaine, dimexidum and myramistim. For the last various influence in a narrow range of concentration – from enzyme activation (in concentration of 0.2%) to 50% of inhibition (is established at 0.5-1%).

The received results allow the absence of critical influence of the studied excipients on Cytorecifen′s activity and take possibility to use the determined regularities for development of soft medicinal forms compositions on it base.

PROSPECTS OF USING GOAT MILK FOR MAKING FERMENTED BEVERAGES “BIFIFORM” AND “SIMBILAKT”

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One of the current trends in pediatric therapy for the treatment of upper respiratory tract infections, such as viral respiratory infections, whooping cough, measles, flu, bronchitis, is antibiotictherapy. Despite their relative safety, the use of drugs aimed at the destruction of pathogens leads to dysbiosis of the gastrointestinal tract of children. Changes in the microflora in dysbiosis, usually develop gradually. In the initial stage of development of dysbiosis reduced functional activity of the representatives of the normal flora, especially antagonistic their activity and the ability to adhere. When effects of etiologic factors appear is saved the dysbiosis quantitative changes are appeared in the normal flora. The conditions for the change of intestinal homeostasis, changes occur in the pH, which contributes unbeatable growth of pathogenic microorganisms. Growing share of the blowing flora, and as a result, there is intestinal bloating. Reduction of the normal flora in the gut leads to disruption of digestive processes, reduces the absorption of nutrients, vitamins and minerals. In the result, the activity of pathogenic flora increases formation of toxins in the intestines, brakes detoxification processes in the gut lumen of the protective bacteria, increases the toxic load on the liver cells, disrupted its function. Pathological process in the intestine is accompanied by reduction of local immunity and general immunological resistance.

The children can have superinfection and they can be allergic to a lot of products, including cow’s milk and its products. Simultaneously with antibiotic pediatricians recommend the use of probiotic preparations, such as “Bifiform”, “Linex”, or, more preferably, for children - dairy products containing live bacteria. Data analysis of the literature showed the promise of goat milk for making milk beverages containing live lactobacillus and bifidobacteria, as less allergenic and more favorable to the normal flora.

Goat milk contains 2 times less αS1 - casein, which is a strong allergen for people. A β-casein is 2.3 times higher in goat, and thus there is formed a soft clot easily digested in the human stomach. The size of the protein molecules of goat milk is less than cow’s, which leads to a rapid and complete disintegration of the action of digestive enzymes of man. Fat globules of goat milk are - 2 microns, and the cow - 4 5mkm. Goat’s milk still characterized by a high content of calcium, magnesium, chlorine, phosphorus, and selenium. The presented data show the perspectives of the goat’s milk as a raw material for production of dairy products based on sourdough “Bifiform” and “Simbilakt”.

The comparative analysis of starters in the fermentation of cow and goat milk is planned to carry out at the Department of Biotechnology of the National University of Pharmacy.

RESEARCH BLUE-GREEN ALGAE SPIRULINA PLATENSIS

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It is well known that the quality of food depends largely on our health and longevity. Its importance to human overestimated. Balanced, balanced diet, including protein, fat, carbohydrates, fiber, vitamins and minerals, you can move to the 20-30 years old age and thus extend their life, to cure many chronic diseases.

In the current situation in Ukraine, the most effective, economically feasible and scientifically sound way to optimize the structure of supply and the shortfall of natural components is widely used dietary supplements. In the biological concept of human development fit well with the blue-green algae - Spirulina platensis.

It is known that spirulina - the most valuable and useful product in the world. It is a living organism, keeping intact millions of years due to its unique biochemical composition.

Balanced by the nature of vitamins, minerals and amino acids are amazing - 1 gram of dry spirulina powder contains not less nutrients than 1 kilo of fresh vegetables and fruits.

Biomass is spirulina contains all the substances that are necessary for human life, and they are absorbed by the body much easier than similar materials in other products.

Dried Spirulina contains about 60% (51–71%) protein. The protein content in high concentrations does spirulina unique product for vegetarians, which is so important for plant protein.

In modern civilization, the ability of spirulina effectively rid the body of toxins, toxins, radionuclides is particularly relevant. For people living in big cities Spirulina should become a regular feature of the daily diet.

One of the most pressing challenges of biotechnology is driven biosynthesis of microalgal pigments such as chlorophyll, carotenoids, xanthophylls, phycobiliproteins.

It is important that the pigments derived from herbal ingredients, not toxic. We also know that in the incoming spirulina plant pigments phycocyanin, chlorophyll A, carotenoids, which are powerful antioxidants, showing bactericidal effect.

At the department of biotechnology research pharmacy are blue-green alga Spirulina platensis, namely its antimicrobial properties.

THE INDUCTION OF CALLUSOGENESIS OF HYPERICUM PERFORATUM L. AND HYPERICUM MACULATUM CRANTZ. IN CULTURES IN VITRO

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Among medicinal plants widely used in medicines there are the representatives of the genus of Hypericum L.: H. perforatum L. and H. maculatum Crantz. Naphtodianthrones, flavonoids and hyperforin derivatives are the main carriers of the biological activity of these plants. Biotechnological as well as traditional methods are used to control and regulate secondary metabolite synthesis.

The aim of our investigation was the induction of callusogenesis from leaf, stem and root explants of H. perforatum and H. maculatum.

Aseptic plants H. perforatum and H. maculatum received by sprouting seeds in vitro condition have been used in the experiment. For the induction and callus initiation from leaf (0.16-0.25 sm^2), stem and root (5-6 mm) explants of aseptic plants have been planted into Murashige and Skoog nutrient medium with twice decreased macro- and microsalts concentrations, supplemented with (0.1-2.0 mg/l) 6-benzylaminopurine (BAP), (0.1-1.0 mg/l) 2.4-dichlorophenoxyacetic acid (2.4-D) and (0.5-1.0 mg/l), 1-naphtaleneacetic acid (NAA). The callus induction (CI) frequency has been carried out 3 weeks after the beginning of the experiment.

It has been found out that the basal medium with 0.75 mg/l NAA and 0.75 mg/l 2.4- D was the most effective among tested variants. Independently of the type of the basal medium and the species of plant stem explants (CI=95-100%) had the greatest callusogenetic activity. In the same time, leaf and root explants showed a greater ability to form callus in the case of H. perforatum.(82 and 77% appropriately). These indices were twice less for the leaf and a little less (CI=71%) for the root explants. Exogenous growth regulators influenced on the qualitative characteristics of callus – their colour and consistency. Thus, the callus received from the nutrient medium with 0.75 mg/l NAA and 0.75 mg/l 2.4-D was greenish and had friable consistency, and on the nutrient medium with 0.1 mg/l BAP and 1.0 mg/l 2.4-D – was yellowish and had a solider strcture.

Thus, we have demonstrated the ability to callus formation of H. perforatum and H. maculatum, and received proliferatively active leaf, stem and root origin callus cultures from the plant of these species.

MODERN ASPECTS OF MICROBIAL RESISTANCE TO ANTIBIOTIC THERAPY

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With the discovery of antibiotics, which have selectively actions on microorganisms, it seemed that an era of final victory over infectious diseases has begun for humanity. And soon the phenomenon of resistance was discovered.

Translated from the Latin «resistentia»— means "resistance, stability". Resistance — is the ability of a microorganism to carry much higher concentration of the drug rather than the other microorganisms (bacterias) of the same strain. According to the study of American Group, only for the period 2009-2011, the number of metillin-resistent Staphylococcus aureus in the nasopharynx of children increased from 1% to 10%. One of the reasons for the increase of resistance in the world is the use of antibiotics for feed-staff of farm animals.

Resistance of microorganisms to antibiotics is caused by several factors. Acquired resistance - under the influence of the antibiotic on the bulk of these microorganisms die and resistant cells continue to multiply. Resistance of these organisms is inherited, giving rise to a new antibiotic resistance. That is why doctors strongly warn patients to keep on the started antibiotics course to the end, otherwise, survived microorganisms can become stirpes of the resistant strain. Also very important factor is that, that the microorganisms which are resistant to one antibiotic simultaneously can be resistant to the other antibiotics too, because of the similarity of action mechanism. It is called «cross-resistance». For instance, bacterias that are resistant to tetracycline simultaneously acquire resistance to chlortetracycline, oxytetracycline.

If we talk about the genetic basis of resistance, then it is based on the presence of outer factors of chromosome, resistant to drugs like - plasmids and transposable elements. The rate of development of resistance and the restraint are linked with the species and even strain's agent (or pathogen). Frequently, Staphylococcus, Escherichia, Salmonella, and Pseudomonas aeruginosa show resistance. Nowadays, when antibiotics are widely used, resistant microorganisms to the antibiotic drugs are encountered very often. We may conclude that the precipitously introduction of new antibiotics requires us quick regulation and improvement of knowledge about antibiotics and antibiotic resistance.

Knowledge on this important issue will help us to save many lives and prevent the spread of resistant organisms.

ALGAE AS PRODUCERS OF FEED PROTEIN

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Algae is the large heterogeneous group of organisms, defined in contemporary literature as a complex of lower photoautotrophic eukaryotes. Traditionally, the algae also include Cyanobacteria (so called "blue-green algae") – a group of oxyphototrophic prokaryotes, which have a significant convergent similarity with true algae.

Algae are widely used in biotechnology. Methods of biological treatment of wastewaters, based on the green-algae cultivation in open water reservoirs, received a worldwide recognition. Algae are used as a source of organic manure, biologically-active substances, vitamins and amino-acids.

Many species of algae are considered as promising producers of food and feed proteins. Phototrophic way of eating relieves these organisms from the need to consume an organic matter. This, correspondingly, allows to cultivate them on extremely poor nutrient media, which do not contain an organic substances, like a sugars and amino acids. At the same time, eukaryotic (true) algae are unable to fix a nitrogen, so the media for their cultivation must contain a nitrogen sources.

Rate of rise of algal biomass is 7–10 times bigger than in higher plants, and their nutritional qualities are in some cases even better, than in plant protein (which is usually poor in essential amino acids). E. g., the concentration of essential amino acids in the culture of alga *Chlorella* sp. is 1.5–2 times higher than in soybean seed – the most protein-rich plant material. The Food and Agriculture Organization of the UN assigned the algal protein with the score of 2.2-2.6 points.

The cultivation of algae should be considered as an energetically advantageous technology, which surpasses even the yeast cultivation in the level of recourses economy. The case is that fungi are heterotrophs, and thus require the addition of some organic substances to the culture medium. In addition, the algae are the only microorganisms for which the cultivation in open systems, such as the surface layer of the ponds, is well developed.

However, the use of algae as producers of the protein is limited to a large extent by the insufficient knowledge of their physiological and biochemical properties. The fact is that, in addition to a desired product, algae may produce some toxic and allergenic compounds. In this connection, deep studies with the experimental evaluation of total impact, caused by algal protein, are needed to avoid an adverse effects of its usage.

BEER QUALITY CONTROL

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Beer has been a valuable biotech products for a long time, the third most popular in the world and the most popular alcoholic drinks. The main objective is to get beer manufacturers of quality products. Beer can be brewed for the wrong technology, with the addition of stale components, dirty water and does not even meet the standards of quality. Quality of the beer, which took control of the laboratory, is generally defined organoleptic characteristics at the time of tasting. Organoleptic properties include: color, flavor, foam, head retention, clarity and taste. All components that are used in brewing, directly or indirectly affect the organoleptic properties. Transparency, color, flavor, hop bitterness, flavor and foaming determine tasting to 25 point scale. The color of each kind of beer must be constant. It depends on the chemical composition of malt, hops and water, as well as the mode of preparation of wort and beer. Microorganisms in beer can cause abnormal smell. Beer made from malt with low aromatic content, has inferior flavor and color. The taste and aroma of beer affect the quality of malt, the amount and method of problem hops, water hardness, the race of the yeast fermentation conditions, the duration of exposure in the basement of the camp, and other factors. Important for the taste of beer is good saturation with carbon dioxide. This gives it a refreshing taste.

Microbiological monitoring is an essential area of work to evaluate the quality of raw materials, semi-finished and finished products in breweries. It is performed at all stages of the process and includes objects are most important and sensitive in biological terms. The most important microbiological indicators are common bacterial contamination and the presence of coliform bacteria. Finished beer is tested for biological stability, as well as determine the overall bacterial contamination and the presence of coliform bacteria. Biological resistance of each beer characterized by a time during which there is no development in it microflora. After the determination of the resistance microscopy performed by defining major groups of microorganisms that cause changes in the wort. In must also determine the total bacterial contamination of the contents of acid-forming microorganisms. The aim of our work was to study the domestic and foreign methods of determination of each indicator, and a comparison of the organoleptic and microbiological parameters of different beers, both domestic and foreign production. Studies have shown compliance with the majority of beers, both domestic and foreign production indicators of quality control of the product.

PREVENTIVE TREATMENT DRUGS OF PROBIOTICS

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The theme of our research is to improve probiotics by creating effective combinations of probiotic cultures and combined dosage forms of probiotic cultures with an antimicrobial agent for the prevention and treatment of dysbacteriosis different etiologies.

Despite advances in modern medical science, dysbacterioses continue pressing problem of medicine, although many doctors do not consider it as a separate disease, but as a symptom that accompanies any disturbances in the body. For the prevention and treatment of dysbiosis probiotic preparations are using.

The general idea of probiotics reduced to artificial intestinal colonization alive missing representatives of the microflora that can displace pathogenic strains of microorganisms and to restore normal intestinal microbiocenosis.

Probiotic preparations are divided into the official record of drugs and to have the status of biologically active additives (BAA), which are recorded separately. BAA are not drugs. If the issue of registered medicines is monitored each production series, the nutritional supplements tested as food products.

Among probiotics are dietary supplements that have been going on for many years with good results. For example, Narine, Primadofilyus, Acipol in capsules, liquid Bifidumbacterin, Biovestin and Biovestin-lacto (liquid), Normoflorin, Eufloriny B and L, Polibakterin, Primadofilyus, Multidofilyus etc.

Officially registered drugs probiotics – Bifidumbacterin, Bifidumbacterin forte, Pobifor, Lactobacterin, Biobakton, Gastrofarm, Colibacterin, Linex, Omniflora, Bifilong, Bifatsid, Bifikol, Baktisporin, Biosporin, Sporobacterin, Bactisubtil, Enterol, Bifiform, Hilak forte, etc.

Conventional dosage form release agents probiotics is freeze-dried biomass in bottles manufactured for over 50 years. And now we can meet these probiotics in pharmacies because of technology is well-proven. But in recent years there is a tendency to create formulations that would maintain the viability and activity of microorganisms belonging to the probiotic, and combine them with other active ingredients, often with antibacterial against pathogenic bacteria, but has no effect on the microorganisms of the probiotic.

Now you can find probiotics in capsule form, in suppositories, liquid, actively put into practice sorbed probiotics. At the department of biotechnology of the National University of Pharmacy research on the development of new dosage forms with probiotics are conducted. The opportunity of the use of probiotics with lavender oil, which has some antibacterial and antifungal activity, is showed. We plan to carry out a more comprehensive screening of different types of essential oils and choose the most effective combination of probiotics with essential oil.

Furthermore, the development of effective national dietary supplements with probiotics, which every year are popular with consumers, is relevant and promising line of therapy.

THE STUDY OF THE ENZYMATIC PROPERTIES OF YEAST USED IN THE PRODUCTION OF ALCOHOL

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For today there is a fairly intense competition in the alcoholic beverage market in Ukraine. Therefore, obtaining a high yield of alcohol is one of the most important challenges facing the future engineers of biotechnology. It should also be borne in mind that the alcohol industry's manufacturing base has hundreds of plants with sufficient capacity to meet the needs of alcohol in food quality. Active equipment distilleries stable volume of alcohol production can be increased to 2,000 million liters or more per year without introducing any additional capacity. However, in recent years due to the increasing challenges of production of alcoholic beverages, low profitability significantly decreased the level of technical equipment of the enterprises. Wear of main equipment of most distilleries reaches 50%, the technology is somewhat outdated and meet modern requirements. In addition, the German race yeast offered for fermentation are expensive and do not address the needs of producers of alcohol production in volume. A primary industrial alcohol is ethanol, or ethyl alcohol. Alcoholic fermentation is one of the oldest, best known and most important of industrial fermentations. In this process, ethyl alcohol is produced from carbohydrate materials (such as sugars) by yeasts.

The aim of this work is research new sugar-containing raw materials that can be used as an additional component for the growth media to get more alcohol yeast.

According to the literature, as a component of the practical and scientific interest is the Jerusalem artichoke (Helianthus tuberosus L.), characterized by a high content of macro and micro nutrients, especially phosphorus, potassium, etc., water-soluble B vitamins, biotin, and endogenous enzyme activity, and most importantly, a valuable polysaccharide inulin (16-24% by weight of tubers). Moreover, the advantage of using different types of raw materials from Jerusalem artichoke (juice, pomace, homogenates, extracts) also lies in the fact that they are traditionally used in the different branches of economy. Consequently, the use of tubers in the production of alcohol yeast does not require health changes in the process of preparation. It would therefore be appropriate to look for new opportunities to increase the productivity of existing strains of Saccharomyces cerevisiae. For it is necessary to study their enzymatic properties when cultured in media containing various quantitative carbohydrate. In particular, further as an additional component for growth media will be selected the aqueous artichoke extract which will be obtained with boiling the chopped tubers in the ground water treated with acidified to pH 4 - 5. These data will be used for the development of new media for culturing yeast to produce alcohol at Department of Biotechnology of the National University of Pharmacy.

SECTION 6

PHYSIOLOGICAL AND BIOCHEMICAL BASIS OF ACTION OF BIOLOGICALLY ACTIVE COMPOUNDS

ASPARTAME IS THE MOST DANGEROUS SUBSTANCE IN THE MARKET

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The world we live in plagued by people suffering from diabetes and other diseases such hyperglycemia, hypoglycemia and these are caused by increase or decrease of sugar in the body and if not managed or good health care the outcome are very fatal and very expensive to manage. As a result of these researchers came out with substances that is alternative to sugar known as sugar substitute.

Aspartame is made up of 40% aspartic acid, 50% phenylalanine and 10% methanol. Aspartate acts as neurotransmitter in the brain by facilitating the transmission of information from neuron to neuron. Too much aspartate in the brain kills certain neurons by allowing influx of too much calcium in to the cell, this influx triggers excessive amount of free radicals which kills the cells. Aspartate is an amino acid taken in its free form significantly raises the blood plasma level of aspartate, the excess aspartate in the blood plasma shortly after ingesting aspartame leads to high level of neurotransmitters in certain areas of the body. The excess aspartate slowly begins to destroy neurons. A few of the many chronic illness that have been shown to be contributed to by long term exposure to excitatory amino acid damage include: multiple sclerosis, memory loss, hormonal problems, hearing loss, epilepsy, Alzheimer's disease, Parkinson disease, brain lesions.

Phenylalanine is an amino acid found in the brain and it is also known as molecule of love. Persons with the genetic disorder phenyl ketonuria cannot metabolize phenylalanine. This leads to dangerous high levels of phenylalanine in the brain sometimes lethal. Excessive levels of phenylalanine in the brain can cause the levels of serotonin to decrease leading to emotional disorders such as depression.

Methanol is a deadly poison that caused some skid row with alcoholics to go blind or dead. Methanol is generally released in the small intestine when the methyl group of aspartame encounters the enzyme chymotrypsin. The most well-known problems from methanol poisoning are vision problems including misty vision, contraction of vision fields, blurring of vision, obscuration of vision, retinal damage and blindness, formaldehyde known as carcinogen causes retinal damage, interferes with DNA replication and cause birth defects.

Finally, from the symptoms we can now conclude that aspartame the most dominant artificial sweetener in the food market is very dangerous.

STUDY OF ANTIOXIDANT POLYPHENOLS GRAPES

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The most important metabolic liver disease is nonalcoholic steatosis and nonalcoholic steatohepatitis. A leading role in the accumulation of lipids in hepatocytes and in the pathogenesis this disease is the process of generation of free radical oxidation and reactive oxygen species. Generation of reactive oxygen species leads to stimulatio of lipid peroxidation and so that to the development of necrosis of liver cells. At the same time there is change in the metabolism of plasma lipids and lipoproteins. A lot of hepatoprotective substances are used for the treatment of fatty liver. A group of natural (plant and animal) and synthetic preparations which increase resistance of hepatocytes to pathological effects, rendering harmless enhance the function of hepatocytes, contribute to the restoration of disturbed functions of liver cells. A wide range of pharmacological effects demonstrated plant polyphenols. A source of plant polyphenols is *Vitis vinifera*. A wide range of properties, for example antioxidant, immunomodulating, antiinflammatory activities, were shown for grape polyphenols. The purpose of this research is the study of antioxidant action of grape seeds polyphenol complexes.

The study was conducted on models of rats weighing 150-200 g, are kept in a vivarium of National University of Pharmacy. During the experiment, rats were divided into five groups. Animals from 2nd and 3rd group were kept on the high carbohydrate content diet. Animals 4th and 5th group were kept on the high fat content diet. Rats from 3rd and 5th groups received in doses 9 mg/100 g weight (in terms of polyphenols) within 21 days. Levels of lipid peroxidation products as malondialdehyde (MDA) and antioxidant vitamins as vitamin E and vitamin C were estimated in the liver and serum of experimental rats.

It was found that lipid peroxidation is higher and plasma antioxidant vitamins like vitamin E and vitamin C were lower in serum of rats were kept on a high carbohydrates and high lipids diet. Grape seeds polyphenols complex introduction decreased MDA level in rat serum and liver and increased endogenous antioxidant level in blood and liver of experimental rats.

The findings suggest that the grape seed polyphenols complex introduction exert a beneficial effect by inhibition of lipid peroxidation in rat serum and liver.

CORRECTIVE EFFECT OF COMPLEX ANTIOXIDANTS ON THE EXAMPLE OF PHYTOCOMPOSITION ON BEHAVIORAL REACTIONS OF OLD RATS

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The purpose of research is to study of changing of old rats' behavioral reactions with phytocomposition. **Objectives of the study.** Mitochondrial reactive oxygen species are important determinants of aging rate parameters, but the use of individual antioxidants are widely used in geriatrics. Herbal products that contain complex of antioxidants may be useful for the correction of aging. It is interesting to study the influence of phytocomposition (oily balsam herbal: pumpkins, wheat germ, nettle, sea buckthorn in a certain ratio), containing vitamin E, ascorbic acid, bioflavonoid, etc., on the aging process.

Materials and methods. Experiments were carried out (in accordance with all ethical standards for the treatment of animals) on 30 white rats, which were divided into three series: 1 - bw mature rats 242±6,7 g, 2 - old animals bw 365±13,9 g, 3 - old animals bw 350±19,1 was treated for 10 days with phytocomposition, daily, oral, dose of 0.25 ml/kg. The study of behavioral reactions was performed at baseline and after cessation of phytocomposition in the test "open field". It served as the control of young and old rats treated with an equivalent volume of saline solution, exposure time - 300 s.

Results and conclusions. In the test "open field" in old rats lengthens of freezing 1,2 - and 3-experienced sessions of 1.7, 1.9 and 4.7 times respectively. It is a sign of emotion, worry, anxiety and uncertainty. In this case, to the 3rd session duration of freezing in the young animals decreased 2.3-times from baseline (young ones quickly get used to and adapt to the new environment). In old rats, these abilities were impaired. Under the influence of phytocomposition figure was slightly different from those of young animals in both of observation period. In old rats had reduced the number of squares crossed outside in all terms of research, but most expressed in the 3rd session to 2.8 times . Thus, motor activity and research were reduced in these animals. Under the influence of phytocomposition the number of crossed outer squares reached the control level, which allows us to assume that introduction of phytocomposition reduces anxiety and improves motor-exploratory activity in old rats. Also in old rats with phytocomposition substantially corrected the number of stands on their hind legs and the length of stands without reliance in all periods of observation. Thus, the introduction of phytocomposition weakens anxiety and increases motor and orienting-exploratory activity in old rats in the test. The problem of old age is the extinction of research and cognitive activity. Adequate correction could lead to a substantial improvement in the quality of life of older people.

STRESS – FRIEND OR FOE?

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Modern man always lives on the edge of stress. The reason for that become a lot of factors, such as bad ecology, hard pace of city life, aggressive social environment, political instability, financial crises, etc.

The term itself – "stress" – became commonplace for people already in short, which is embedded in the idea of the changes in behavior, and a whole range of feelings and emotions that arise in complex situations or high risk, which have become an integral part of modern life.

The study of adaptive processes is closely linked with the concept of emotional tension and stress. This was the basis for the determination of stress as a nonspecific reaction to the requirements imposed on it, and considers it as the general adaptation syndrome.

Known foreign psychologist Hans Selye, the founder of the Western theory of stress and nervous disorders, identified the following stages of stress as a process:

- A direct reaction to the impact (stage alarm);
- The most effective adaptation (stage of resistance);
- Infringement of the adaptation process (stage of exhaustion).

Stress is part of everyone's life, it cannot be avoided. Important and stimulating, creative, formative influence of stress in the complex processes of education and upbringing. But stress factors should not exceed the adaptive abilities of a person, as in these cases may be deterioration of health and illness – somatic and neurotic.

Unfortunately, not all the time we can get out of the pressure stress factor, few people know how to keep defenses from exhaustion. Do not always remember that the costs of failure in dealing with stress – the disease. When an illness jammed the mechanism of regulation of blood pressure, the doctor calls her hypertensive disease. The growing number of patients with hypertension, in which a constant level of blood pressure is abnormally high, shows that more people are trying to cope with stress at any cost, even at the expense of health.

Without stress life is impossible, and even harmful. However, the stressors are different: stressor – one that brings great benefits to our health, stimulating creativity, stressor - from which you can easily dismiss, and an hour or two just to forget or to remember with a smile and a sense of dissatisfaction. But occurs (and much more often than we would like) stressor – the enemy that hardly strikes most vital organs.

HEPATOPROTECTIVE EFFECTS OF GRAPE SEEDS POLYPHENOLCOMPLEX

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Under constant stress, environmental degradation, and poor nutrition, the liver is one of the most deprived organs in our body and it needs a serious protection. A lot of synthetic and natural compounds and preparations can provide an adequate protection which normalize different liver functions and contribute to the restoration of hepatocytes. Plant polyphenols demonstrate a wide range of pharmacological effects. A rich source of polyphenols is *Vitis vinifera*. Grape seeds are waste products of the winery and grape juice industry. These seeds contain lipids, proteins, carbohydrates, and 5-8% polyphenols depending on the variety. Polyphenols in grape seeds are mainly flavonoids, including gallic acid, the monomeric flavan-3-ols catechin, epicatechin, gallocatechin, epigallocatechin, and epicatechin 3-O-gallate, and procyanidin dimers, trimers, and more highly polymerized procyanidins. The purpose of this research was to study lipotropic action of complex polyphenolic compounds extracted from grape seeds.

The study was conducted on models of rats weighing 150-200 g, are kept in a vivarium of National University of Pharmacy. During the experiment, rats were divided into five groups. Animals from 2nd and 3rd group were kept on the high carbohydrate content diet. Animals 4th and 5th group were kept on the high fat content diet. Rats from 3rd and 5th groups received grape seeds polyphenols complex in doses 9 mg/100 g weight (in terms of polyphenols) within 21 days. After the experiment, the animals were decapitated under chlorasole-urethane anesthesia. Liver enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyltransferase (HHTP) and alkaline phosphatase (ALP) were routinely tested in the serum using standard sets.

It was found that the activity of ALT, AST, HHTP, ALP was significantly increased in rats kept on a high-calorie diet. Prolonged administration of grape seeds polyphenol complex significantly reduced activity of liver enzymes in the serum, indicating that the improvement of the liver in experimental animals

These data shown a general hepatoprotective activity of grape seeds polyphenol complex.

GROWTH HORMONE DEFICIENCY

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The somatotroph cells of the anterior pituitary gland produce growth hormone. releasing hormone and is inhibited by somatostatin, both of which are produced by the hypothalamus. This problem may happen if the person does not produce enough growth hormone. Most of the time, the cause of growth hormone deficiency is unknown. It may be present at birth (congenital) or develop as the result of an injury or medical condition. Severe brain injury may also cause growth hormone deficiency.

Children with physical defects of the face and skull, such as cleft lip or cleft palate, may have poorly developed pituitary glands and decreased growth hormone level. The child's growth may range from flat (no growth) to very shallow (minimal growth). Although it is uncommon, growth hormone deficiency may also be diagnosed in adults. Possible causes include: tumors involving the pituitary gland or hypothalamus in the brain, severe head injury.

Children with growth hormone deficiency have a slow or flat rate of growth, usually less than 2 inches per year. The slow growth may not appear until a child is 2 or 3 years old. The child will be much shorter than most or all children of the same age.

Children with growth hormone deficiency still have normal body proportions, as well as normal intelligence. A physical examination - including weight, height, and body proportions -- will show signs of slowed growth rate. The child will not follow the normal growth curves. Hand x-ray (usually the left hand) can determine bone age. Normally, the size and shape of bones change as a person grows. These changes can be seen on an x-ray and usually follow a pattern as a child grows older.

Testing for growth deficiency requires more than a simple blood test. Testing is usually done after your child's pediatrician has explored other causes of poor growth.

Growth hormone causes the body to make insulin-like growth factor and insulin-like growth factor binding protein 3 Tests can measure these growth factors.

Magnetic resonance imaging (MRI) of the head can show the hypothalamus and pituitary glands.

Tests to measure other hormones levels (lack of growth hormone may not be the only problem) may be done. Treatment involves growth hormone injections given at home. Patients often receive a growth hormone injection once a day. Side effect: headache, fluid retention, muscle and joint aches.

MORPHOLOGICAL STUDY OF QUINOCARB INFLUENCE ON DEVELOPMENT OF HEMODYNAMIC PULMONARY EDEMA IN RATS

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During the study results of research on morphological study of quinocarb influence on development of hemodynamic pulmonary edema were represented.

Materials and Methods. Respiratory part of rat lung tissue was studied and also state of small bronchus epithelium. The tissue fragments taken operatively were examined for histology. A single solution of 0,1% of adrenalin was injected intramuscularly to rats and 20 hours before injection of adrenalin the quinocarb and hydrochlorothiazide were given by injection. Lung tissue sample was drawn up 2 hours after adrenalin injection. All tissue material was fixed up in 10% solution of formaline. Tissue sections were stained with hematoxyline and eosine. On microslides a conventional grade of alveolar edema intensity, congestion, and failure of alveolar pattern according to the standard fifth-grade system were defined. In order to obtain statistical outputs the non-parametric analog of univariate dispersive analysis – Kruskal-Wallis was used during the comparing samples of relative variances, after that the criteria of Mann-Whitney was used.

Results and discussion. Data resulting from the study have shown that the respiratory part of lung tissue of intact group of rats was in normal and had a preserved alveolar pattern of parenchyma, while in group with the control pathology the respiratory part of rat lung tissue had a significant edematous nature, liquid was present inside alveolar cavities after adrenalin injection, interalviolar septums were demolished, occurrence of hemorrhages was observed, thrombosis, expanded emphysematosa alveoli, tissue pattern was deformed. Preventive and curative injection of quinocarb substances improved significantly the state of rats' lung tissue up nearly the norm. Any characteristics of pulmonary edema were found, typical histoarchitecture was preserved, perivazal tissue was normal. Respiratory part of parenchyma of pulmonary section of the rat injected with hypotiaside was characterized by nested-structured pulmonary edema with, alveolar parenchyma, closed to normal.

Outputs. Quinocarb in a dosage of 10 mg/kg improves state of rats' lung tissue that confirms its high anti-edema action.

LIPOTROPIC ACTION OF GRAPE SEEDS POLYPHENOL COMPLEX

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Currently, the most significant metabolic liver disease is fatty liver (or steatosis). This basic metabolic underlying hepatic steatosis is insulin resistance, which leads to slower processes of lipolysis and exogenous deposition of fats and carbohydrates. Lipotropic factors are important factors that contribute to the normalization of lipids and cholesterol metabolism in the body, leading to a decrease in the degree of fatty infiltration of the liver. One of the representatives of substances that exhibit lipotropic action are plant polyphenols. A rich source of polyphenols is *Vitis vinifera*. Grape seeds are waste products of the winery and grape juice industry. These seeds contain lipid, protein, carbohydrates, and 5-8% polyphenols depending on the variety. Polyphenols in grape seeds are mainly flavonoids, including gallic acid, the monomeric flavan-3-ols catechin, epicatechin, gallocatechin, epigallocatechin, and epicatechin 3-O-gallate, and procyanidin dimers, trimers, and more highly polymerized procyanidins. The purpose of this research was to study white lipotropic action of complex polyphenolic compounds extracted from grape seeds.

The study was conducted on models of rats weighing 150-200 g, are kept in a vivarium of National University of Pharmacy. During the experiment, rats were divided into five groups. Animals from 2nd and 3rd group were kept on the high carbohydrate content diet. Animals 4th and 5th group were kept on the high fat content diet. Rats from 3rd and 5th groups received grape seeds polyphenols complex in doses 9 mg/100 g weight (in terms of polyphenols) within 21 days. After the experiment, the animals were decapitated under chlorasole-urethane anesthesia. Triacylglycerols (TG), phospholipids (PL), cholesterol (LDL) levels were defined in the liver and in the blood serum.

We have found that in rats were kept on high carbohydrate diet and high fat diet, triglycerides and cholesterol levels were increased in the liver and serum. A significant decrease of PL level was shown in the liver tissue. These data indicate about a reduction in the functional state of the liver. Grape seeds polyphenol extract supplementation reduced serum levels of TG and TG level in liver. This fact was accompanied by increasing of PL levels in serum and liver.

The findings suggested that the grape seeds polyphenols have strong pronounced lipotropic effect and may be beneficial in preventing of nonalcoholic steatohepatitis progression.

SECTION 7

PRE-CLINICAL PHARMACOLOGICAL STUDY OF NEW DRUGS

ANTIINFLAMMATORY ACTIVITY OF TABLETS FROM BARK ASPEN EXTRACT ON THE FORMALIN INFLAMMATION MODEL

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Actual problem of modern medicine and pharmacy is the development of effective anti-inflammatory agents plant based raw materials. Previously, we studied the pharmacological activity of the extract from the bark aspen and the expediency of a dosage form, especially as the global pharmaceutical market of more than 40 different drugs dosage forms of aspen. The chemical composition of the extract from the bark aspen defined by Professor V.N. Kovalev, dosage form - pill developed by Professor T.A. Groshovij.

The aim of the study was to determine the specific anti-inflammatory activity of tablets from the bark aspen extract (TBAE) in an experimental model of inflammation in the rat formalin versus Altan and diclofenac sodium.

Acute inflammatory edema was modeled by subcutaneous injection in the rat hind paw 0.1 ml of 2% formalin solution, which causes destruction of the protein membranes. Experiments were performed on four groups of rats for five animals in each: Group 1 - untreated animals, group 2 - TBAE treated at a dose of 50 mg/kg, group 3 - treatment comparator Diclofenac Sodium 8 mg/kg, and Altan group received 15 mg/kg. The study drug injected one hour before the injection of the inflammatory agent. After 3 hours of formalin injection amount of edema and the inhibition percentage of edema determined by onkometr.

Analysis of the results shows that the strong anti-inflammatory effect on the formalin model of edema, TBAE have a dose of 50 mg/kg. Their effect is not inferior to the effect of diclofenac sodium (64% and 62%, respectively), and exceeds the activity of comparator plant Altan (64% and 58%, respectively).

Such action of studied TBAE may be due to the inhibition of lipid peroxidation and the structural integrity of the membrane preserving, thus reducing vascular permeability.

PROGESTERONE ROLE IN THE PATHOGENESIS OF THE UTERINE BENIGN TUMORS

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A uterine myoma is the most widespread benign tumour of the genital system among the reproductive age women, its frequency varies from 15 to 30%. In spite of numerous research, nowadays there is no definite answer to the question about progesterone role in the development of this disease. Purpose of the research: to study the progesterone role in pathogenesis of uterine myoma.

Materials and methods: analytical informations analysis of scientific research.

Research results. According to modern concept uterine myoma develops on background hyperestrogenism, progesteronedeficiency states, hypergonadotropism, and its growth depends on the concentration of cytosolic receptors and the complex mechanisms of their interaction with endogenous or exogenous by injected hormones. It is known that after the menopause the myoma nodi reduce, but is not discovered whether it is a consequence receptors or the result reduction of low levels of estrogen, progesterone and androgen.

Progesterone is involved in the changes in the endometrium, associated with the menstrual cycle: his influence in the second half of the menstrual cycle there is overgrowth of the mucous membrane of the uterus, changes the functional state of the fallopian tubes, vagina and breasts. Progesterone influences on a tissue-target through specific cytosolic proteins (receptors) that are induced by hormone-receptor complex activating. Then it is translocated to, where it connects with the acceptor sites of chromosomes and initiates genes transcription and specific proteins synthesis that provide biological effect. At the beginning of development of tumor in myometrium tissues concentration of receptors is not changed and accompanied by normal content of estrogens and progesterone in blood. With time passing amount and activity of total progesterone receptors decrease and estrogenic increase, that results in absolute or relative hyperestrogenism on the background the progesterone deficiency (below 7 ng/ml). Hormonal violations stimulate hyperplastic processes in the endometrium. Thus estrogen renders stimulate growth of myoma, and progesterone realizes it, that explains inadmissibility of prescription for treatment of uterine myoma of medicines, which are complete analogues of progesterone, in spite of its deficiency.

Conclusion. Decline of progesterone receptors concentration in a myometrium cell, accompanied by hypoprogesteronemiya, is the obligatory link of uterine myoma pathogenesis.

THE STUDY OF THE 2-BENZAMIDE-2-(2-OXOINDOLIN-3-ILIDEN) ACETIC ACID DERIVATIVES ON THE ANTIHYPOXIC ACTIVITY

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Hypoxia is the universal pathological process, which accompanies and determines the development of the different pathologies. Therefore, the pharmacological preparations with the purposive action on the metabolic processes in hypoxia - antihypoxants are of special interest. These agents improve the oxygen uptake by the organism, decrease the oxygen demand of the organs and tissues and thus promote the increase of the resistance to the oxygen deficiency. The objective of the research: To carry out the screening of the antihypoxic activity of the 24 compounds of 2-benzamide-2-(2-oxoindolin-3-iliden) acetic acid under the conditions of the acute hypobaric hypoxia.

Methods of the study: The study was conducted in 200 white nonlinear sexually mature male rats of 180-200 g bodyweight under the conditions of the acute hypobaric hypoxia. The acute hypobaric hypoxia was simulated in the modified flow pressure chamber by means of imitation of the lifting of rats at a height of 12000 meters. The "ascent" and the "descent" of the animals were carried out at a rate of 50 km/h. The animals were kept on the "high-altitude plateau" up to the moment of the second agonal breath, following which the "descend" on the previous zero height has been done. The investigated substances were administered intraperitoneally in a dose 15 mg/kg 35 minutes before the modeling of hypoxia. The following life time parameters of the animals - loss of posture, time until the appearance of the second agonal breath, time of the posture renewal were fixed.

Results: The analysis of the research results has showed, that the most statistically probable action among the derivatives of the 2-benzamide-2-(2-oxoindolin-3-iliden) acetic acid have substances under numbers 14 ((Z)-N-(2-(naphthalen-1-ilamino)-2-oxo-1-(2-oxo-1-propylindolin-3-iliden)ethyl)benzamide) and 15 ((Z)-N-(1-(1-methyl-2-oxoindolin-3-iliden)-2-oxo-2-(phenylethylamino)ethyl) benzamide), which increased the lifetime in hypoxia by 59.4% and 67% ($p<0.05$) respectively as compared with control. The emergence of seizures and other visual signs of the adverse effects after the administration of these drugs and the modeling of hypoxia were not fixed.

Summary: The findings are the experimental grounds of the availability of the new antihypoxants synthesis on the basis of the 2-benzamide-2-(2-oxoindolin-3-iliden) acetic acid derivatives.

EXPERIMENTAL STUDY OF ANTIHYPOXIC ACTIVITY OF RONKOLEUKIN

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Purpose of study was determination of recombinant IL-2 (Ronkoleukin) influence on dynamics of afterhypoxic changes in tissues of rats' brain with experimental focal stroke, mainly functional activity of mitochondria ant thiol-disulfide system. Antihypoxic activity of Ronkoleukin (0,01 mg/kg) comparing to Tiotriazoline (50 mg/kg) was studied on the model of experimental photoinduced trombose of brain in rats. In homogenate of brain in rats with experimental focal stroke in early and distant afterischemic periods after initiation with cyclosporine-A by spectrophotometry was determined opening of mitochondrial pore and activity of thiol-disulfide system (levels of reduced forms of glutations and thiols, activity of glutationperoxidase and glutationreductase).

On a background of administration of Ronkoleukin was noted significant stabilization of mitochondria functional activity (by blocking mitochondrial pore opening) and state of thiol-disulfide system – normalization of activity of glutationperoxidase and glutationreductase, increase of levels of reduced forms of glutations and thiols on the background of reduction of their oxidized forms. By mitochondrial activity on the model of focal stroke Ronkoluekin can be compared to Tiotriazoline and on some indexes even better.

Ronkoleukin has solid antihypoxic effect in afterischemic damages that can be used as perspective therapy in complex therapy in afterischemic stroke and for effective protection of brain tissue.

THE INFLUENCE OF "MOMETASONE WITH CERAMIDES" CREAM IN THE COURSE OF ALLERGIC CONTACT DERMATITIS

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The main drugs for treating inflammatory skin diseases are local medical forms for glucocorticosteroids (GCS). Despite of the high is efficiency using drugs with GCS is significantly limited by the spread of local and systemic side effects. When prolonged applied GCS on the skin is the development of atrophic skin changes observed (the skin loses tone, becomes dry, thin, etc.). Therefore, in order to reduce the possibility of manifestation of atrophic skin changes and more effective local action in the treatment of dermatitis, led by Professor Lyapunov N.A., cream with mometasone furoate on the hydrophilic-lipophilic base, which contains ceramides (natural phospholipids – components of extracellular matrix of skin, regulating regeneration and apoptosis epidermal cells) was developed.

The aim of this work was to study the influence of "Mometasone with ceramides" cream in the course of allergic contact dermatitis (ACD) in rats. The object of the study was "Mometasone with ceramides" cream and the drug for comparison, was "Elokom" cream, manufactured by "Schering-Plough", Belgium.

In the experiment 18 rats females were divided into 3 groups: group 1 – control pathology, groups 2, 3 – rats treated with "Elokom" and "Mometasone with ceramides" creams were used. For the development of AKD the animals were coated with solution of 2,4-denitrochlorbenzene by P.M Zalkan's method. The intensity of the pathological changes in the skin was expressed in scores (0-5 points).

The analysis of the got results rotined, that on the 7-th day of treatment the animals of the controlled pathology group led pathology had group increased lesion (3.67 points), which was characterized by erythema, dryness, itching, the appearance of necrosis areas, formation of erosions and crusts, there was flaking epidermis. In groups of animals treated with "Elokom" and "Mometasone with ceramides" creams the reduce of visual manifestations was observed on the 7th -day of the treatment times in 1.8 times and 1.7 times, respectively, compared with the peak of pathology, respectively. The skin of the animals which was less hyperemic, erosion disappeared, peeling of damaged layers of the epidermis and its regeneration were observed.

Thus, in the course of experimental studies found, that the studied creams have shown the high anti-inflammatory effect on the model of ACD. the promising is the further pharmacological study of "Mometasone with ceramides" cream in order to increase the effectiveness and safety of inflammatory skin diseases treatment.

ACUTE TOXICITY STUDIES OF SUPPOSITORIES, CONTAINING QUERCETIN, COENZYME AND TIOCTIC ACID AND THEIR COMBINATIONS

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The metabolic syndrome – also called the insulin resistance syndrome – is a multifaceted syndrome characterised by five major abnormalities: insulin resistance, glucose intolerance (impaired glucose tolerance/non-insulin-dependent diabetes mellitus (NIDDM)), hypertension, obesity, and dyslipidaemia (hypertriglyceridaemia and low HDL-cholesterol). Oxidative stress in all aerobic organisms including herbivorous insects is caused by reactive oxygen species (ROS), such as superoxide-anion radical ($^{\bullet}O_2^-$), hydrogen peroxide (H_2O_2) and hydroxyl radical ($OH^{\bullet}$). The formation of $^{\bullet}O_2^-$ may evoke the cascade of other reactive oxygen species and results in alterations within structures of macromolecules such as DNA, protein and lipids. The oxidative stress was assessed with generation of the hydrogen peroxide, total content of the thiols and the lipid peroxidation products (TBARS).

The purpose of research. The aim of this study was to investigate the acute toxicity of suppositories. containing quercetin, coenzyme and tioctic acid. This comprehensive plan to use the drug in treatment of metabolic disorders and metabolic syndrome, diabetes, and other vascular lesions.

Materials and methods. Acute toxicity of suppositories containing quercetin, coenzyme and tioctic acid and their combinations was studied in 50 mature white mongrel rats weighing 180-200 males g and females weighing 160-180 g under a single rectal introduction to the wide range of doses, as recommended DETS Health of Ukraine.

The results of research. As a result, the study found that the introduction of suppositories containing active inhradiyinty and their combination at doses 5000 mg / kg did not result in death of the animals does not affect the mass ratios of the internal organs, indicating the absence of significant toxicity study drug at this dose and characterizes it as a relatively harmless (V class toxicity, LD50> 5000 mg / kg) according to conventional toxicological classification of substances.

According to recommendations of the State Pharmacological Center MoH Ukraine installation medium lethal dose suppository containing quercetin, coenzyme and tioctic acid and combinations thereof in this case is impossible. In the study of specific pharmacological activity suppository installed pronounced therapeutic and prophylactic properties of the drug on the model of the metabolic syndrome.

Findings. The results indicate the feasibility of further preclinical danyh substances to create on their basis a new effective and safe drug for the pharmacological correction of metabolic disturbances in diabetology and cardiology.

NEW POTENTIAL OF RHEUMATIC DISEASES IMMUNOBIOLOGICAL THERAPY

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Chronic inflammation in rheumatoid arthritis (RA) and many other systemic diseases of connective tissue extend beyond the joints. Patients with RA have an increased risk of disease development in cardio-vascular system, lungs, eyes, musculoskeletal system. Effective control of inflammation becomes important and is the key to improving outcomes for patients with rapidly progressive RA. Traditional treatments are often ineffective for patients with RA, as they do not completely suppress the inflammation that causes its progression.

Thanks to the appearance of biological agents, especially inhibitors of tumor necrosis UPE-a, there were alternative effective means obtained, which are characterized by high efficiency and ensure rapid and sustained improvement.

The purpose of the research. To study the state of rheumatic diseases immunobiological treatment.

Materials and methods. We have researched the effectiveness of the drug "Rituximab" – Mab-Thera for patients with an inadequate response to the ongoing complex treatment in serum department 27 GKB Kharkov.

Obtained results. Mab-Thera application for 22 patients with RA is accompanied with clinical improvement of state of the disease with a marked reduction in the immune-inflammatory activity. Mab-Thera prescription for patients with systemic lupus erythematous with active lupus nephritis resistant to basic drugs leads to reduction of the nephritic syndrome and stabilization of the nephritis course. Mab-Thera prescription for patients with Sjogren's syndrome, accompanied by high activity, leads to improved clinical and laboratory parameters of the disease.

Summary. Thus, the use of new biological agents for the treatment of systemic connective tissue diseases can slow the progression of the disease, and also to achieve stable, long-term remission of it in most cases.

CHRONOPHARMACOLOGICAL ASPECTS OF BLOOD DISEASE THERAPY

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High frequency and risk of diseases of the blood determines the interest in a review and optimization of the existing schemes of treating diseases of the blood system and the development of drug chronoschemes considering people organisms' sensitivity to its action.

Found that in the morning preparations of iron are poorly absorbed and the amplitude of its content in the blood increases. Iron is better absorbed and assimilated in the evening hours: 21-24 h. At this time it's concentration in the blood by 16-30% lower than at 8-12 h. Iron, which is absorbed in the first half of the day, poorly utilized and promotes side effects. Therefore the preparations of iron used to treat iron deficiency anemia should be prescribed only in the second half of the day.

The chronotherapy of patients with rheumatic heart disease should be performed with heparin at 20 h (5000 units) and at 24 h (10,000 units), with curantylum once at 20 h (150 mg), and with fraxiparin - once at 16 h. This chronostrategy allows to achieve reliable clinical effect and the positive blood coagulation dynamics earlier than the traditionally therapy. Using of smaller daily and course doses halved the risk of side effects.

The chronotherapy with acetylsalicylic acid (ASA) of patients with diabetes should be held once a day at 22 h in a dose of 125 mg. This chronoscheme improves anticoagulative and inhibits coagulative activity of the blood. Also, taking aspirin during the second half of the day decrease the risk of gastric bleeding on 40%. Thus ASA should be administered as a preventive measure once in the second half of the day. This chronoscheme of ASA used at patients with diabetes decreases the incidence of myocardial infarction for 40% and also decreases the risk of myocardial infarction at the morning for 55%. The chronotherapy of patients with diabetic nephropathy with signs of disseminated intravascular coagulation with trental should be performed at 22-23 h in a dose of 150 mg, which helps to normalize chronostructure of circadian rhythm of hemostasis.

Based on the foregoing information it is worth paying attention to the necessity of developing new chronoschemes of blood diseases treatment in order to improve its effectiveness and safety.

INFLUENCE OF EXTRACTIONS OF RUTA, ARTICHOKE, BUPLEURUM AND SALSOLA COLLINA UPON THE INDEXES OF PEROXIDATION OF RATS' LIPIDS ON THE BACKGROUND OF CCL_4 ACTION

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Issue of a medicinal liver injury becomes more actual recently. First of all, it connects with the fact that most of medicinal preparations widely used by people are dispensing without receipt in Pharmacies network. 1000 preparations approximately can cause an acute medicinal liver injuries, above 200 from them are potentially toxic. According to the pharmacoepidemiological study the average of acute medicinal liver injuries equals 4,2-5,3% of all side effects. Sulphanilamids are such medicines. Thereby pharmacological science pays a deep attention to the search for new effective and harmless preparations with a hepatoprotective action.

The aim of this research was an experimental study of antioxidative and hepatoprotective characteristics of herbal extractions of Ruta, Artichoke, Bupleurum and Salsola Collina on the model of tetrachlormethane hepatitis for rats.

Materials and methods. The experimental studies were carried out according to the bioethical requirements on mature white rats with the weight 180-200 gr.. The model of an oxidative stress was run by intraperitonial injection of the 25% oily solution of CCL_4 to the experimental animals. The herbal extractions were given by preventive mode into stomack in the range of dosage 0,2-0,5 ml/100 gr. of body weight of animals.

Results and discussions. The hepatoprotective action of the studied original herbal extracts was revealed. While an acute toxic hepatitis caused by tetrachlormethane, they are detecting an antioxidative and membranoprotective effects. These effects are confirmed by reducing of ALT and AST activities, content of crude bilirubine in blood serum, final and intermediate products of the lipid peroxidation, decreasing of risk of glutathione-dependent enzymes' activity. The phytoextracts usage allows to reduce an impaired homeostasis, structure and integrity of the membranes of hepatocytes, to inhibit lipids peroxidation as one of the links of hepatitis pathogenesis, to stimulate and antioxidative protection, biligenesis and biliary excretion, to activate reparative processes of the liver tissue.

Outputs. The profilactic injection of herbal extractions of Ruta, Artichoke, Bupleurum and Salsola Collina to white rats on the backgrounds of an antioxidative stress goes with a hepatoprotective effect which was more obvious while application of the extracts of Bupleurum and Artichoke.

WAYS OF INCREASE OF EFFICIENCY OF TREATMENT OF WOUND PROCESS

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Dynamic development of surgery and dermatology constantly makes new demands to treatment of wounds. Main of modern requirements to treatment of wound process in a phase of regeneration and reorganization of a hem is normalization of processes of microcirculation and restoration of barrier functions of the injured skin. That's why the problem of development and improvement of wound healing preparations for treatment of wounds is actual.

Today one of perspective wound healing preparations dexpanthenol is. However, the majority of preparations with the dexpanthenol don't conform to modern requirements since they are prepared on a fatty basis which creates "steam effect" and disturbs an expectoration of an exudate from a wound.

In this regard, under the leadership of Professor Lyapunov N.A. three monocomponent creams on hydrophilic basis with dexpanthenol, ceramides (as substances that restore the barrier function of the skin) and troxerutin (improves microcirculation) for the topical treatment of wounds in the phases of recovery and reorganization of the scar were developed and improved.

Studying of influence of creams on process of healing and formation of a strong hem on model of a linear wound at rats was a purpose of this research.

In the experiment 24 rats weighing 210-240 g were used. For creation of a linear wound to rats under a thiopental anesthesia on a site of skin of a back an incision was made, at once seams were imposed and leather was processed by 5% iodine solution. Animals were divided into groups: the 1st – animals that weren't treated, the 2nd, 3rd, 4th groups – animals that were treated with cream contained troxerutin, cream with ceramides and cream with dexpantenol for 5 days. Further skin sites with wounds were cut out and research on scar durability was conducted.

The results showed that according to tensiometry indicators all studied creams authentically increase durability of neogenic scar tissue and expressiveness of their reparative activity was: cream Troxeruthin - 37.2%, cream with ceramides - 76.2% and cream with Panthenol - 76.5% .

Therefore, further research of these creams or their combinations for the purpose of studying of mechanisms of their influence on reparation processes is perspective.

THE EXPERIMENTAL INVESTIGATION OF THE NEW OIUTMENT WITH AETHONIUM FOR TREATMENT OF THE PURULENT WOUNDS

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Rational treatment of purulent wounds is one of the difficult problems of modern clinical surgery. One of the effective methods of wounds treatment is a local drug treatment using ointments. According to the basic medical and biological requirements for ointments used to treat wounds, they must affect most stages of wound healing process.

The aim of our study was to investigate the antimicrobial, anti-inflammatory and wound healing activity of a new ointment of with aethonium and to compare it with the activity of combination ointments Inflarax and Laevomekol.

The investigation of antimicrobial activity of new ointment with aethonium was conducsed in vivo on the model of purulent necrosis process in rats with wound infection coused by (Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Candida albicans). According to the results of experiment it has been established that the ointment with aethonium has an expressed antimicrobial effect, shows the absentce of microbial contamination and decrease of the term of healing to 7 days when the reference drugs promots healing to 5 days as compared with the control pathology group.

The study of anti-inflammatory activity on the model carrageenin-induced edema of rat pow of ointment with aethonium has showed the highest anti-inflammatory effect (33,3 %), exceeding the effect of the ointment Laevomecol (25,1%).

The study of wound healing effect on the model of a linear cut wounds in rats has shown that the ointment with aethonium promotes rapid wound healing and scar formation, its therapeutic effect exceedes effects (172,7 %) of ointments Laevomecol (151,8 %) and Inflarax (54,8 %).

So, according to the results it has been established that the new ointment with aethonium possesses an expressed antimicrobial, anti-inflammatory and wound healing effects and is a perspective subject for further pharmacological investigations in the field of treatment of purulent wounds.

CHRONOPHATOLOGY OF HEPATOPROTECTIVE AND CHOLERETIC MEDICINES

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The liver and biliary tract pathology takes the leading place among the gastro intestinal tract (GIT) diseases. For the last 20 years there is an increase in the incidence of hepatobiliary system disease, and the cases of death from this disease are doubled. According to the World Health Organization statistics the number of patients suffering from various disorders of the GIT is over 2 billion people. In Ukraine, the prevalence of chronic hepatitis and liver cirrhosis increased at least 2.5 times over the past 20 years.

The pharmaceutical market counts 91 brand name medicines for the liver and biliary tract diseases treatment. There is a huge amount of medicines, but the problem of increasing incidence of hepatobiliary system disorder is not solved.

A very important component of effective therapy for any disease is to mention individual chronophysiological and chronopathological characteristics of the organism. The liver activity depends on many factors including chronotype of the patient, his chronosensitivity to medicines, foods and hormonal status.

Back in 1928, Forhenom discovered dependence between the rhythm of bile secretion and accumulation of glucose in the liver relied on the circadian rhythms during a day. The experimental study of mass liver changes, glutathione, glycogen and nucleotides accumulation in hepatocytes, the activity of some microsomal enzymes in animals depending on their day-night life style was shown in the literature. The dependence between the volume of bile and cholesterol-bilirubin content in it at different times of day and seasons was carried out. The maximal filling of the gall bladder is between 6 and 9 o'clock in the morning, and then gradually decreases and reaches its minimum in 21.00. After 9 p.m. the cycle recovers and undergoes a gradual increase in the volume of bile.

The data about the liver and gall bladder cycle activity are very important for rational selection of chronohepatoprotective schemes as the activity of enzyme systems of hepatocytes influences the metabolic rate of drugs in a certain period of time, and accordingly increase their efficiency by 30-50 % and to decrease their toxicity.

Thus, in order to ensure effective and safe treatment of liver and biliary tract diseases should be considered chrohobiologic rhythms of each patient, including their chronsensitivity to hepatoprotectors and choleretic medicines.

THE STUDY OF TOXICITY EFFECT OF NEW DRUG FOR TREATMENT OF DISEASES OF PROSTATE

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Diseases of prostate gland like benign prostatic hyperplasia and chronic prostatitis are among the most important problems in modern urology and andrology. That's why one of the priorities of medicine and pharmacy is improving therapy of these diseases through the creation of new drugs. Considering it was generated combined prostatoprotector in the form of suppositories and at this time complex of preclinical studies is holding. Complex of preclinical studies of the new drugs necessarily containes study of chronic toxicity: prolongated exposure of the new drug on functional status of organs and organ systems that allows to evaluate its degree of safety for clinical use and prevent the possible side effects.

So, the aim of this work is studying of prolongated exposure of the new prostatoprotector suppositories (NPS) on functional status of organs and organ systems of male rats with its introduction in therapeutic dose 168mg per kg and in dose 1680 mg per kg which is in 10 times bigger than the therapeutic dose during one month. Study was held according to the guidelines by Ministry of Health of Ukraine (Ed. O.V. Stefanov, 2001).

It was found that prolongated rectal introduction of NPS in therapeutic dose 168mg per kg and in dose 1680 mg per kg which is in 10 times bigger than the therapeutic dose during one month doesn't cause negative changes from general trophic processes, peripheral blood, functioning of central nervous system, liver, kidneys and cardiovascular system. But it was significantly relative to control group determined that NPS in both dosages causes increasing of the relative weight of the heart in male rats, decreasing in serum ceruloplasmin's activity, level of total lipids and increasing excretion of urea. Changes of some indicators due to specific pharmacological activity of components of the NPS and in disease could have only positive outcome.

So, the results show that NPS in therapeutic dose is save and promising for further application in industrial production and broad medical practice.

PHARMACOLOGICAL STUDY OF SORBUS AUCUPARIA LEAVES EXTRACT

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Due to the fact that recently, according to pharmacologists, many modern drugs do not conform to the requirements of safety, that's why attention of professionals attracted to drugs based on herbal substances. Phytomedication in opposite to synthetic one cause fewer complications, almost non allergic, so they can be use for a long time, especially for rehabilitation patients. Biologically active compounds that are presence in plants give a different pharmacological action make it possible to used phytomedication in treatment of many diseases. An example is a drug based on leaves of Sorbus aucuparia.

The aim of the work was experimentally proved the feasibility of using Sorbus aucuparia leaves extract (SALE), developed at the Department of Pharmacognosy NUPh under O. Kryvoruchko for the treatment of inflammatory joint disease.

Was found (on models of karahenin and zymozan edemas) that the anti-exudative activity of SALE is equal to comparison drug quercetin. Also was defined conventionally-effective dose of SALE, which was 100 mg/kg and used in further studies.

On the model of necrotic ulcers in rats SALE showed distinct anti-alterative effect (delay formation of wounds and reducing their size). By reparative action SALE exceeded activity of diclofenac sodium and quercetin. By antiproliferative effect SALE inferior to indomethacin and diclofenac sodium.

SALE had mild analgesic (23.3%) and antipyretic (29.4%) activity that is in 2 times inferior to diclofenac sodium and analgesic activity at the same level as quercetin.

On the model of adjuvant arthritis SALE slightly (by 8.7%) yielded to diclofenac sodium action in their ability to reduce the edema of the rats' limbs. However, SALE prevailed comparison drug to the effect on WBC on 36% and had made a positive impact on biochemical parameters which exceeded diclofenac sodium ALT activity (10%), content of TP (22%), the level of TBA (37%) and the level of GR (54%).

These results suggest that SALE is a perspective substances to create drugs with anti-inflammatory and anti-arthritic action.

MECHANISM OF IMMUNE RESPONSE ON INJECTION OF DIPHTHERIA-TETANUS MODIFIED ANATOXIN

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Vaccines prophylaxis belongs to the guiding factors of reduction morbidity, heaviness of clinical trial and lowering of death-rate and the number of complication among the sick on infection diseases. The important achievements in medicine with the questions of liquidation smallpox in the world, important reduction morbidity on poliomyelitis, diphtheria and measles became possible only due to effective vaccine preparations against exciters of these infections. Not only children but also adults need carrying out vaccination because of the need to be defended from diseases, which threaten difficult complications. To such methods of prophylaxis might be taken antigen inoculation diphtheria-tetanus modified anatoxin.

Purpose of studies is to explore the mechanism of immune response on injection of diphtheria-tetanus modified anatoxin.

Stuff and technique: information-bibliographic analysis of scientific studies.

Results of studies. The component parts of diphtheria-tetanus modified anatoxin include the mixture of tetanus and diphtheria antitoxins, which relate to high-cleaned toxins, which do not have a generally toxic influence on human organism but cause an immunology reaction. In the mechanism of immune response on injection of diphtheria-tetanus modified anatoxin there are a few stages: induction, immune regulation, effector stage, stage of immunology mind. In the induction stage antigens are captured by macrophageins, the procession and presentation to T-lymphocytes takes place. The immune regulation stage is characterized by proliferation and differentiation of immune competent cells, activation of bone marrow, ripening in plasma cells, formation of mind cells. Effector stage is the stage of activation of effector cells and formation of circulatory antibodies. In general, the process of immune response injection of diphtheria-tetanus modified antigen lasts about three weeks. The main antibodies appearing due to injection antigens are IgG whose functions are neutralization of viruses and toxins, opsonization and lysis of bacteria.

Conclusions. Diphtheria-tetanus modified anatoxin belongs to injections which cause the beginning of specific immunity, which remains in the organism for a long time and by a new contact with microorganisms stimulates a powerful immune response.

PERSPECTIVES OF THE DEVELOPMENT OF DRUGS BASED ON GOUTWEED (AEGOPODIUM PODAGRARIA L.)

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Introduction. The goutweed (GW) is a widely-spread perennial herb that has been used in empirical medicine for a long time. Our research work is focused on the study of GW preparations including the determination of certain groups of biologically active substances contribution to pharmacological properties.

Objects. The models of the ethylenglycole-induced kidney as well as carbon tetrachloride-induced liver injury in mice were used for screening. Ischemia/reperfusion (I/R) injury of liver as well as kidney in rats were used for in-depth investigation of the nephroprotective and hepatoprotective activity. Besides the potassium oxonate-induced hyperuricemia and the carrageenin-induced paw oedema models were applied (all models were in accordance with the bioethics requirements).

Results. It has been proven that the most significant nephroprotective activity on the model of the ethylenglycole-induced kidney injury is inherent to the GW rhizomes extract (1 g/kg), the GW leaves extract (1 g/kg), the GW leaves protein-polysaccharide complex (200 mg/kg), flavonoid trifolin (50 mg/kg). The most effective on the ischemic acute renal failure model in rats are the GW leaves extract and trifolin that increase the survival rate, prevent anuria, normalize renal functions, reduce proteinuria and hyperazotemia. GW rhizomes extract and leaves protein-polysaccharide complex are somewhat inferior to the aforesaid preparations. All investigated preparations surpasse chophytol (5 ml/kg) by efficacy.

The tincture (5 ml/kg), the extract (1 g/kg), protein-polysaccharide complex (200 mg/kg) of the GW leaves and trifolin (50 mg/kg) are the most effective in carbon-tetrachloride induced acute liver injury. On the model of the liver I/R, they not only prevent lethality, but suppress cytolysis and normalize AST/ALT ratio. Trifolin and the extract counteract cytolysis, reduce oxidative stress, and normalize plasma levels of TNF-α, IL-1α, IL-4, soluble Fas ligand. The effect is comparable with that of standard drug silibor (200 mg/kg). The tincture and the extract of the GW leaves reduce the intensity of hyperuricemia and have anti-inflammatory action.

Conclusion. The preparations obtained from GW exert wide range of metabolic effects, have a beneficial influence on the course of liver and kidney I/R injury, possessing nephro- and hepatoprotective, anti-inflammatory, hypouricemic effects. The results substantiate the expediency of development of drug based on GW.

COMMUNICATION ALCOHOLIC LIVER DAMAGE LEADS TO DISTURBANCE PORPHYRIN METABOLISM

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Purpose: Investigate the porphyrin metabolism caused by alcohol intoxication in rats.

Materials and methods used for the experiment, two groups of 20 rats each. First group every day for 90 days were injected intraperitoneally 40% ethanol, the second group control - healthy animals. Porphyrin exchange characterized by the level of coproporphyrin and uroporphyrin in urine; porphyrins in hepatocytes was determined by fluorescent microscopy. Prolonged administration of ethanol to rats results in the development of liver cirrhosis and disturbance of porphyrin metabolism in animals. After long-term administration of ethanol one group was divided into two subgroups: 1a - the rats that had disturbed porphyrin metabolism and 1b - animals that have found no such changes. Porphyrin exchange characterized by the level of p-aminolevulinic acid, porphobilinogen (Method Mauzerall and Granick), uroporphyrin (using Hoffman), coproporphyrin and uroporphyrin in urine (using Koskelo), the accumulation of porphyrins in the hepatocytes was determined by fluorescent microscopy. Urine collection, animals were placed in a special place - urinals. The daily amount of urine ranged from 2.5 to 18.5 ml. Porphyrins in the urine by a 1 every 3 days using a spectrophotometer SF-4F, pretreated urine by the method of Brugsch and Berman. Statistical processing of the results was performed by analysis of variance, t-Student test. Liver damage in various stages of intoxication studied morphological, morphometric and biochemical methods of investigation.

Results.The study showed that animals 1a group showed increases in protoporphyrins (21,6 ± 2,9 nmol per 1 g of creatinine, $P < 0.05$ versus control) and coproporphyrin (289,2 ± 29,9 nmol 1 g of creatinine, $p < 0.05$ versus control) in urine. Biochemical studies of the functional state of the liver showed a significant increase in total bilirubin in the group with abnormal porphyrin metabolism in comparison not only to control, but with the group without affecting porphyrin metabolism. Significantly increased rates of total lipids, cholesterol, and transaminases compared to intact animals. The results show that chronic administration of alcohol to animals not only leads to liver toxicity and the development of acute hepatitis, but also to disturbance of porphyrin metabolism. Such disturbances were observed only in some animals (4%, $p < 0.05$), which obviously had a genetic predisposition to gemoporhyria. Alcohol intoxication has identified this pathology.

THE NERVOUS SYSTEM DESINCHRONOSIS AND THEIR CHRONOPHARMACOLOGICAL CORRECTION

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Disorganization of biological rhythms of the nervous system is associated with the emergence of pathogenesis of anxiety and neurotic disorders. Chronobiological initial defect can be a source of disturbances in emotional and autonomic areas and an increase in stress sensitivity. Between the development of anxiety and disruption of biological rhythms are closely interrelated: chronobiological similarity of neurosis and mental depression, suggests a pathogenetic identity in their rhythmic nature of the disease process. Spotted an annual periodicity in the number of suicides, which are directly linked to the development of mental depression. With the rhythm of the nervous system due to the advance of vascular accidents. Chronobiological defect may be due to the initial organic or functional pathology of the brain or nervous system disorders may be secondary - the result of a primary disruption of biorhythms.

The rhythmic nature of the nervous system and its relation to circadian dysrhythmia violations allow us to consider the prospect of treatment of nervous system disorders with chronopharmacological position, that helps to correct the nerve disorders caused by unfavorable, rhythm destabilizing effects. For example, administration of antidepressants once at midnight gives faster results, unlike to take them at a different times of the day or fractionally within a day. In case of administration of phytoadaptogens at afternoon, they normalize the rhythms of cellular components of the hemostatic system: increaseing the value of the mezor and amplitude of circadian rhythms, shifting the acrophase of ACTH on 2-3 hours and cortisol on 6-12 hours that satisfies the chronoregime of healthy people. Adaptogens (Siberian ginseng, ginseng, glycyram) are most effective in the first half of the day, immunostimulants, membrane stabilizers and biologicals medicines (bifidum and laktobakterin) are the best in the evening. Therefore, to increase the secretion of glucocorticoids by the adrenal cortex adaptogens should be administered in the first half of the day (especially in the morning), vitamin B6 (only in the morning). Thus, neurotropic drugs normalizing the disorganized rhythms of nervous system, promotes the effective and rapid restoration of its functions.

CRONOPHARMACOLOGICAL ASPECTS THERAPY HYPERTENSION

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The latest research in the field of chronobiology, chronopatology and chronopharmacology pharmacists and doctors are pushing to revise the already established treatments of various diseases. One of these diseases is hypertension.

Hypertension is considered as the result of adaptation to stressful situations. The signs of pathological desynchronosis include a high percentage of false rhythm (50%), a significant increase in the area walk acrophase study parameters (more than 6 hours) of synchronization of biorhythms, up to antiphase, the discrepancy biorhythms chronotype patients, rapid changes in the amplitude of the rhythms, complaints permanent headaches, poor sleep, appetite, increased irritability, and sometimes aggressiveness (in hypertensive patients stage II).Studies have shown that the severity of violations of the circadian rhythm of blood pressure (BP) increases with the severity of hypertension.

Research in the last 20 years have shown convincingly that chronotherapy hypertension calcium channel blockers, angiotensin-converting enzyme (ACE), β-blockers, central hypotensive effect of drugs, diuretics and other means allows stable clinical effect at an earlier date, the lower doses of drugs and better portability than their traditional purpose without the circadian rhythm of blood pressure. Thus the study of verapamil, scientists discovered that a single evening reception provides high concentrations in the morning, including reducing rapid increase in blood pressure in the morning, without inducing nocturnal hypotension. In addition, the drug is effective for ischemic heart disease, especially in the morning, when the risk of ischemia is greatest. Verapamil is a well-studied drug in terms chronopharmacology: optimal drug concentration in the blood should be made between 04.12 hours, when there is a maximum increase in blood pressure and heart rate associated with awakening. Under the influence of verapamil is a beneficial effect on the structure of ultradian blood pressure. In the treatment of verapamil hronoskheme comes significant reduction in systolic and diastolic blood pressure at all time periods. Based on the above information, you should pay attention to the need for new regimens of antihypertensive drugs already known to improve its effectiveness and safety.

HEPATOPROTECTIVE ACTIVITY LIPOPHILIC AND HYDROPHILIC LIME LEAVES EXTRACT RESEARCH

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Paracetamol is the one of the most used non-prescription drugs in Ukraine. As one of the most effective analgesics and antipyretics, paracetamol is nevertheless a potential hepatotoxic agent.

Not only overdose of paracetamol, but even its long-term use contributes to the development of drug hepatitis, especially for people with hepatitis of various etiologies or patients with diabetes mellitus.

Paracetamol hepatotoxicity caused not only by the result of covalent binding of its highly reactive metabolite N-acetyl-4-benzohinonimin with macromolecules of hepatocytes, but also by activation processes of free-radical oxidation (FRO) with enzymatic and non-enzymatic dysfunction of antioxidant systems.

The purpose of the research. Hepatoprotective activity lipophilic and hydrophilic lime leaves extract research.

Materials and methods. This work is devoted to the experimental research of the hepatoprotective properties of hydrophilic (PL-1) and lipophilic (PL-2) lime leaves extracts. Investigations have been carried out on the paracetamol hepatitis model of rats. White mongrel male rats with weight 180-220 g have been used in this research.

Obtained results. As a result of these experiments revealed that the use of PL-1 and PL-2 in drug-induced hepatitis caused by paracetamol reduces the intensity of cytolytic and free radical processes in the liver, increases the activity of the antioxidant system of hepatocytes and contributes to the normalization of carbohydrate, protein and lipid metabolism, and recovery processes bile production and secretion.

Efficiency of researched extracts is 20% higher on average than the efficiency of the reference drug silibor in the intensity of the hepatoprotective action.

Summary. Conducted research testifies the advisability of further preclinical lime leaves extracts studies to create new domestic plant hepatoprotector on their basis.

EFFECTS OF INDOLINOREN ON RENAL EXCRETORY FUNCTION IN RATS WITH ACUTE RENAL FAILURE

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Research objectives – to investigate the influence of indolinoren on the state of renal excretory function in experimental acute renal failure (ARF).

Materials and methods. Studies were carried out on 40 nonlinear white female rats weighing 180-220 g. ARF was induced in experimental rats by single injection of 50% glycerol solution in dosage 10 ml/kg. Experimental animals were divided into 4 groups: 1 – intact control; 2 – control with pathology; 3 – ARF + indolinoren (29,5 mg/kg); 4 – ARF + furosemide (6 mg/kg). Indolinoren and furosemide were administered intragastrically in therapeutic-preventive regiment during 3 days before inducing ARF and 2 days in the setting of ARF. Efficacy of indolinoren was evaluated by the rate of excretory renal function on the first and second day of ARF.

Obtained results. In glycerol-induced acute toxic kidney injury in rats the significant violation in renal excretory function took place. Oligoanuretic stage of ARF occurred, anuria appeared in 20% of cases on the 2-nd day of experiment and in 60% of cases – on the 3-rd day. Thereof, diuresis in rats of control group in relation to intact group of animals on the 2-nd day of experiment was 0,55±0,10 ml/100g (for rats without anuria), on the 3-rd day – 0,26±0,05 ml/100g (for rats without anuria).

Indolinoren has shown an accurate increase of diuresis in ARF: on the 2-nd day diuresis was – 1,74±0,14 ml/100 g that is approximately 4 times higher in relation to control group of animals. On the 3-rd day of experiment diuresis slightly decreased and was – 1,23±0,27 ml/100 g for the total group of animals and 1,53±0,22 ml/100 g – for animals without anuria. Anuria appeared in 20% of animals. It was established that in experiment indolinoren was inferior to comparative drug on the 2-nd day and there was no significant difference on the 3-rd day.

Conclusions. Indolinoren in acute renal failure exerts nephroprotective properties, promotes the increase of diuresis, prevents development of anuria.

RESEARCH OF ANTIHYPOXIC ACTIVITY OF 7-CHLORBENZYL-8-SUBSTITUTED THEOPHYLLINUM

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One of the most important tasks of modern experimental and clinical pharmacology is the search for new chemical compounds and the development of new medicines, improve the survival rate of the body in situations of acute hypoxia.

The aim of this research was a study of antihypoxic activity first synthesized **7**-chlorbenzyl-8-substituted theophyllinum.

Materials and methods: the objects of the study were 11 substances selected among **7**-chlorbenzyl-8-substituted theophyllinum.

The investigated substances entered intragastrically experience rats, in a dose 0,05 LD50 as a 3-5%. In 30 minutes of rats placed in the isolated chambers by volume of 3000 mls and measured time to the offensive of the agonic state. By preparation of comparison was chosen mexidol. Mexidol entered intragastrically in a dose 5 mgs/of kg as a 3-5% water suspension. An equivalent amount of 3-5% suspension of water was entered in rats of control group.

Among **7**-chlorbenzyl-8-substituted theophyllinum the most antihypoxic activity was shown by compound 5 - 7-p-chlorbenzyl-8-p-phtorobenzylidenhydrazino theophyllinum, which in a dose 16,3 mg/of kg increased life-span of rats in the conditions of acute normobaric hypoxia on 72,7%. Replacement in 8th position of molecule **7**-chlorbenzyl-8-substituted theophyllinum of п- phthorobenzylidenhydrazinum (comp.5) on п-bromobenzylidenhydrazinum (comp. 4), cause to reduction of antihypoxic activity from 72,7% to 7,3%. Reference drug mexidol also showed antihypoxic activity and increased life-span in rats on 66,9% in the conditions of acute normobaric hypoxia with a hypercapnia.

Thus, the results of this stage of screening researches, shows that the antihypoxic activity of compound 5 exceeds of reference drug mexidol.

Conclusions: **7**-chlorbenzyl-8-substituted theophyllinum the most antihypoxic activity was shown by compound 5 - 7-p- chlorbenzyl-8-p-phtorobenzylidenhydrazino theophyllinum, which in a dose 16,3 mgs/of kg increased life-span of rats in the conditions of acute normobaric hypoxia on 72,7%. Derivates 7-п-methylbenzil-8-substituted theophyllinum are the perspective group of organic matters for the subsequent leadthrough of purposeful synthesis and pharmacological screening with the purpose of creation on their basis of effective of effective antihypoxic preparations.

THE STUDY OF THE DENSE VIOLET EXTRACT REPARATIVE EFFECT ON THE LINE SLICED WOUNDS MODEL IN RATS

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The problem of an effective and safe drug therapy of inflammatory diseases is still not solved, so always the search for the new treatment regimens and drugs with unconventional mechanisms of action and minimal side effects are conducted. One of promising direction for safe and effective medicines creation is phytotherapy. The information about the use of violet tricolor in folk medicine and phytochemical analysis of its row material show its anti-inflammatory effect. The previous studies have shown anti-inflammatory effect of the dense violet extract, obtained at the department of botany (National University of Pharmacy) under the supervision of Gontovaya T.N., so it made sense to determine the presence of reparative effect of the studied agent. The study of reparative effect of dense violet extract on a model of line sliced wounds in rats was carried out. As a reference medicine quercetin – a herbal medicine with anti-inflammatory effects was chosen.

A model pathology was reproduced under the manual of preclinical study of the medicines. To obtain the wounds on the shaven back skin area (5x3 cm^2) of rats under the barbamyl anesthesia (0.8 ml of 1 % barbamyl solution per 100 g of animal weight) the 5 cm cut was done. Then immediately 1 cm apart of each other 5 sutures were applied and the skin was treated with 5 % alcoholic solution of iodine. The medicine under the research was administered intragastrically in health-care regime 5 days before and 5 days after the model pathology: the dense violet extract in a dose of 25 mg/kg, quercetin in a dose of 5 mg/kg.

According to the results obtained in the control pathology group the strength of formed scar tissue indicated tensiometry index that was 322.4 g. Administration of studied drugs sowed the significant increase in strengthening of scar tissue formation, but in different degree. Thus, in the group of animals treated with the dense violet extract, this index was 508.7 g, which is 1.6 times more active comparing to the control pathology group. Quercetin has strengthened the scar tissue formation in 1.4 times, tensiometry index corresponded 446.1 g.

Thus, the results of the study showed that the dense violet extract has strong reparative effect (57.8%), which is slightly higher than the activity of the reference medicine (38.4%) that was carried out on the line sliced wounds model in rats.

ANTI-CYTOKINE THERAPY FOR PSORIASIS

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Currently, psoriasis is one of the most common and severe chronic dermatoses of multifactorial nature, characterized by hyperproliferation of epidermal cells, keratinization disorders, inflammatory reaction in derma, as well as changes in various organs and systems.

Many recent studies have shown that psoriasis occurs on a ground of the imbalance of immune system, which changes the composition of T-lymphocytes subpopulation, reduces suppressor function of T-lymphocytes and subsequent overproduction of serum immunoglobulins, circulating immune complexes of physiologically active substances.

A cascade of immune reactions runs population of basal keratinocytes, which, under the influence of trigger factors acquire the ability to transform into a population of proliferating cells that form easily separated scales and have immunogenicity. As a result growing imbalance in the system Th1/Th2 - cytokines accompanied with increased level of cytokines IL-1, 2, 6, 7, 8, γ- interferon which act as mediators in processes of keratinocytes hyperproliferation and inflammatory mediators. Also an important role in the pathogenesis of immune inflammation belongs to TNF-alpha, which is a cytokine with a wide action spectrum and which is a mediator of inflammatory response and participate in reactions of immune system and development of autoimmune processes.

Thus, given the characteristics of the pathogenesis of psoriasis, application of anticytokine medicines in complex treatment for disease as biological immune response modifiers that block T-cells or prevent their migration into tissue, increase the level of Th2-cytokines in order tonormilize imbalance of Th1/Th2, is sound. The greatest experience of anticytokines application in patients with psoriasis was accumulated using rimekeyd chimeric compound based on hybrid mouse and human IgG1 monoclonal antibodies to TNF-alpha. Rimekeyd forms stable complexes with the TNF-alpha, inhibits its biological activity and lyses (or induces apoptosis) TNF- producing cells. Remikeyd treatment reduces inflammation in the epidermis and normalizes the process of keratinocyte differentiation. Compared with traditional basics medicines for systemic treatment of psoriasis anticytokines have selective effect on pathogenesis and much safer.

STUDY DECREASES OF THYROID PEROXIDASE ANTIBODIES CONCENTRATIONS IN PATIENTS WITH AUTOIMMUNE THYROIDITIS

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In areas with severe selenium deficiency there is a higher incidence of thyroiditis due to a decreased activity of selenium-dependent glutathione peroxidase activity within thyroid cells. Selenium-dependent enzymes also have several modifying effects on the immune system. Therefore, even mild selenium deficiency may contribute to the development and maintenance of autoimmune thyroid diseases.

Purpose. Study decreases thyroid peroxidase antibodies concentrations.

Materials and methods. We performed a blinded, placebo-controlled, prospective study in female patients (n = 70; mean age, 47.5 + 0.7 yr) with autoimmune thyroiditis and thyroid peroxidase antibodies (TPOAb) and/or Tg antibodies (TgAb) above 350 IU/ml. The primary end point of the study was the change in TPOAb concentrations. Secondary end points were changes in TgAb, TSH, and free thyroid hormone levels as well as ultrasound pattern of the thyroid and quality of life estimation. Patients were randomized into 2 age-and antibody (TPOAb)-matched groups; 36 patients received 200 μg (2.53 μmol) sodium selenite/d, orally, for 3 months, and 34 patients received placebo. All patients were substituted with L-T4 to maintain TSH within the normal range. TPOAb, TgAb, TSH, and free thyroid hormones were determined by commercial assays. The echogenicity of the thyroid was monitored with high resolution ultrasound. The mean TPOXb concentration decreased significantly to 63.6 % (P = 0.013) in the selenium group vs. 88 % (P = 0.95) in the placebo group. A subgroup analysis of those patients with TPOAb greater than 1200 IU/ml revealed a mean 40% reduction in the selenium-treated patients compared with a 10% increase in TPOAb in the placebo group.

The results obtained. TgAb concentrations were lower in the placebo group at the beginning of the study and significantly further decreased (P = 0.018), but were unchanged in the selenium group. Nine patients in the selenium-treated group had completely normalized antibody concentrations, in contrast to two patients in the placebo group (by χ^2 test, P = 0.01). Ultrasound of the thyroid showed normalized echogenicity in these patients. The mean TSH, free T_4, and free T_3 levels were unchanged in both groups.

Conclusions of the findings. We conclude that selenium substitution may improve the inflammatory activity in patients with autoimmune thyroiditis, especially in those with high activity. Whether this effect is specific for autoimmune thyroiditis or may also be effective in other endocrine autoimmune diseases has yet to be investigated.

THE MEXIDOL AND EMOXIPIN INFLUENCE ON THE PEROXIDATION PRODUCTS GENERATION IN THE CHRONIC HYPOXIA

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The irreversible changes and the cell death in hypoxia are caused by the disturbances of the metabolic pathways in the cytoplasm and mitochondria, emergence of the acidosis, activation of the free radical reactions, damage of the biological membranes. Taking into account the importance of the correction of the prooxidant-antioxidant balance under the conditions of the chronic hypoxia, the use of the 3-oxypiridine derivatives emoxipin and mexidol as potent antihypoxants with antioxidant properties is appropriate. Objective of the research – to study the influence of emoxipin and mexidol on the peroxidation products generation in the blood plasma of the sexually mature male rats under the conditions of the chronic hypobaric hypoxia. The research study was carried out in white laboratory male rats of 120-180 g bodyweight. The animals were divided into 4 groups: the 1st group was formed of intact animals; the animals of the 2nd group were influenced by the hypobaric hypoxia in the modified flow pressure chamber by means of imitation of the lifting of rats at a height of 4000 meters above sea level with the rate 24 km/h for 2 hours daily during two weeks. The animals of the 3rd and 4th groups were injected intraperitoneally with emoxipin and mexidol in a dose 100 mg/kg of the bodyweight after the modeling of the chronic hypoxia. Then the animals were euthanized and blood samples were collected. The content of the malondialdehyde (MDA) and oxidation-modified proteins (OMP) in a blood plasma were determined. The use of the emoxipin under the conditions of the chronic hypoxia promoted the reduction in the MDA content in 1.6 times ($p \leq 0.05$) compared to animals of the 2nd group influenced by the hypoxia. This parameter was reduced in 1.8 times ($p \leq 0.05$) with the administration of mexidol. The use of mexidol and emoxipin in the chronic hypoxia resulted in reduction of the OMP content in the blood plasma of rats. What is more, OMP rate of the treated animals was in 1.3 times less than in animals with hypoxia. Thereby, mexidol and in a less degree emoxipin, are able to substantially adjust the deep imbalance in the prooxidant-antioxidant system by the active interaction with primary and hydroxyl radicals of the peptides and by inhibition of the lipid peroxidation in a blood plasma by the free radical scavenging action. It should be noted, that mexidol shows more significant effect on the prooxidant content in the blood plasma of rats due to the opportunity of the direct interaction with lipophilic and hydrophilic radicals in the phospholipid membranes in the chronic hypoxia.

NON-DRUG ARTERIAL HYPERTENSION TREATMENT FOR YOUNG PEOPLE WITH OVERWEIGHT

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Arterial hypertension (AH) treatment is an activation of organism internal reserves. The majority of patients with AH and overweight need lifestyle modification first.

The basic treatment for these patients is unloading dietary therapy. Dosed fasting has its complex effects on the patients suffering from AH. It restores self-regulation, compliance with the pumping function of the heart and level of peripheral vascular resistance, reduces cardiac output and blood pressure on the myocardium.

The purpose of the research. To study non-drug arterial hypertension treatment for young people with overweight.

Materials and methods. Patients with early stage of AH combined with overweight were prescribed a short absolute "dry fasting" for 1-3 days with subsequent limitation of taking water at 10-12 ml / kg per day, throughout the whole discharge period. Starting from the first day of fasting drug therapy was revoked.

Obtained results. At the beginning of the third day of blood pressure (BP) was reduced by 10%, and to 10.9 days in 53% of patients blood pressure was close to the norm for this age group already. After the course carried out, if it is necessary to prescribe drugs, the dose of antihypertensive drugs is decreased by 39.5%. It is prescribed infusions and decoctions of herbs (valerian root, motherwort herb, fruit Aronia) as maintenance therapy. It is recommended to follow a vegetarian days, hypocalorie and hyposodium diet, reducing excess weight, avoiding harmful habits, sufficient physical activity of cyclic type (walking, jogging, skiing), that in the presence of contraindications in combination with diet, 58% of patients with early stage hypertension lead to normalization of ABP level.

Summary. Non-drug treatment for patients with AH combined with a healthy lifestyle have a positive effect, since more than half of the patients had a normalization of ABP level.

INVESTIGATION CARDIOPROTECTION PROPERTY PREPARATION "LATIRON" IN MODEL ADRENALINI MYOCARDITIS

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Cardiovascular disorders are on the second place by their frequency in the world. Some drugs which promote rhythm, permeability of blood vessels normalization, edema of tissues diminishing, microcirculation improvement, as well as metabolic processes in heart muscle and blood vessels improvement are widely used as cardioprotectors.

Cardioprotektor the action of "Latiron" conducted at one is the main model of ischemic blow myocard-adrenalini myocarditis of heart muscle.

In the experiment rats were used, which were separated into four groups by six rats in each: 1-st group – intact control, 2-nd group – control pathology, 3-rd group animals with pathology treated with "Latiron", 4-th group – animals with pathology treated with preparation "Korvitin".

As a result of the experiment was found, that single intramuscular injection of 0.1% - 1.0 adrenalini hydrochloride solution lead to substational changes in myocardium and serum of blood.

In the group of animals with control pathology changes peculiar for acute ischemic-necrotic processes was of serious in myocardium. Number of heart contraction were increased by 35% systolic index was decreased by 30%, shift segment S-T from isolinea.

Adrenalinas damage was combined with peroxide oxidation: TBA level – reagents in homogenate and serum increased by 2.9 times glutathione decreased by 1.7 times ASAT increased by 2 times. Pathology of myocardium was characterized by development of proliferation and exudation processes in myocardium that promoted increases of heart mass coefficient by 1.2 times in group animals with control pathology in comparison with intact control.

Application of "Latirona" and "Korvitina" lead to decrease cardiotoxic effects of large doses of adrenaline: decreasing of number of heart contraction by 20%, increasing of systolic index by 65%, decreasing of phenomena ischemia (segment ST in normal).

Result. Aplication of "Latiron" notice increases level glutathione in serum blood by 30% in homogenate of myocardium by 60% in comparison with not treatment animals.

INFLUENCE OF EXTRACTS FROM ARONIA MELANOCARPA LEAVES ON URIC ACID METABOLISM IN RATS

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Introduction. Taking into account the growing interest in traditional medicine there is a great demand for planned research of herbal drugs phyto-pharmacological properties. For the many plants the broadening of types of plant raw material that are used for development of drugs is reasonable. One of such plants is aronia or chokeberry (Aronia melanocarpa (Michaux.) Elliot) which fruits are widely used in atherosclerosis, arterial hypertension, blood coagulation disorders etc. The leaves of aronia are believed to be the perspective raw materials, as their extract, according to the experimental data available in literature, counteracts the disturbances of glucose metabolism and peroxidative oxidation balance. It is rational to investigate the influence of the aronia leaves extract on uric acid metabolism that is closely associated with carbohydrate metabolism, oxidation as well as arterial hypertension pathogenesis.

Objects. Water and ethanol extracts of the aronia leaves were obtained at the department of pharmacognosy (NUPh) by post-graduate V.A. Samojlova. The model of potassium oxonate-induced hyperuricemia in rats was used (all studies were in accordance with the bioethics requirements). The doses of the extracts have been chosen according to the data of previous experiments on the intact rats that elucidated the influence of aronia leaves extracts on the uric acid renal excretion under the conditions of water load induced diuresis. The contribution of renal mechanism to the possible effectiveness of aronia preparations on the beforementioned model of hyperuricemia was estimated. Urochol was chosen as the reference drug of herbal origin with the proven influence on the renal excretion of uric acid.

Results. It has been established that the investigated preparations differ in their influence on the excretory renal function under the conditions of hyperuricemia in rats. One of aronia extracts shows a tendency to the increment of uric acid excretion coupled with the favourable increase in diuresis and reduction of uric acid concentration in urine that to some extent reminds the effect of Urochol.

Conclusion. The results substantiate the expediency of further investigation of the preparations obtained from aronia leaves in order to ascertain their mechanisms of action and phytopharmacological patterns.

PHARMACOLOGICAL ACTIVITY OF BURDOCK THICK EXTRACTS ON THE MODEL OF BENIGN PROSTATIC HYPERPLASIA OF RATS

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Benign prostatic hyperplasia (BPH) is one of the most common diseases of middle-aged and old men. According to the literature, symptoms of BPH are shown in more than 40% of men 50 years aged and over 90% of cases in men over 80 years. In connection with this searching and creating efficient and secure prostate protective drugs, capable of simultaneously affecting on different pathogenetic chains of BPH, is important and urgent. Promising in the treatment of BPH is a herbal complex of biologically active substances which provide distinct therapeutic efficacy and safety.One promising plants with potential prostate protective properties is burdock.

The aim of the work was to study the influence of the thick root extract (TREB) and leaves (TELB) of burdock received at the Department of Botany of National pharmaceutical university, led by prof. Khvorost O.P., on the course of sulpiride-induced benign prostatic hyperplasia of rats.A model BPH reproduced by intraperitoneal introduction of sulpirid (eglonil, Sanofi-Aventis, France) at a dose of 40 mg / kg for 30 days. TREB and TELB at a dose of 75 mg / kg and the reference drug prostaplant forte at a dose of 35 mg / kg was administered intraperitoneally in clinical mode from 30 to 52 day experiment.At the 53 day euthanasia was made in animals and levels of estradiol, testosterone and dehydrotestosterone in the serum were assessed.In the serum of animals of the pathology control group was observed a reliable decrease in testosterone (2.8 times) and increase of dehydrotestosterone content (1.9 times) and of estradiol (1.7 times) compared with the relevant indicators in animals of the intact control group, that testimonies about the development of BPH.

The use of studied drugs contributed to the normalization of all biochemical markers of BPH.Thus, under the influence of TREB testosterone in blood serum increased by 2 times, under TELB - by 2.3 times compared with the rate in the control group pathology.Level of dehydrotestosterone in TREB group decreased by 1.7 times, the group TELB – by 1.9 times, levels of estradiol decreased by 1.7 times in both groups of animals. All figures were not significantly differerent from that of intact control and product comparison.

Thus, on the model of sulpiride-induced BPH in rats TREB and TELB enhance androgen production, the level of androgenic saturation and of value-estradiol and testosterone are promising prostate protectors.

THE EFFECTIVENES OF QUERCETIN DRUGS IN EXPERIMENTAL DIABETES TYPE II WITH OBESITY

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It's quite determined an obvious correlation between the levels of morbidity and mortality from cardiac-vascular complications in diabetes and the disorders of lipid metabolism.

The aim of the research is to conduct a comparative study of the impact of quercetin preparations – corvitin and lipoflavon on diabetic dyslipoproteinemia. Experiments were made on nonlinear albino rats, which were divided on 4 groups: 1 – intact animals (control), 2 – rats with diabetes (single intraperitoneal injection of streptozotocin – STZ, "Sigma", 30 mg/kg body weight) and obesity (previous feeding with high-fat diet during 1 month), animals of 3d and 4th groups with diabetes and obesity were injected intraperitoneally corvitin and lipoflavon (10 mg/kg during 2 weeks).

It was found that experimental diabetes type II with obesity is accompanied with a significant lipid metabolism dysregulation. Total cholesterol (CH) level increased by 104%, low density lipoproteins (LDL) – 163%, triglycerides (TG) – 155%, phospholipids (PhL) – 139%, while high density lipoproteins (HDL) level decreased by 52% versus control. Corvitin caused decrease the levels of CH, LDL, TG, PhL – 40%, 52%, 42%, 38% with concomitant increase HDL level by 71%, while the lipoflavon – dicreased these indicators by 50%, 43%, 55%, 42% respectively and increased HDL level by 98%.

Conclusion. In the experimental diabetes type II with obesity corvitin more so lipoflavon (combination of quercetin with phosphatidilcholine) attenuates the disorders of lipid metabolism.

PECULIARITY OF CYTOKINE CEREBROPROTECTION IN EXPERIMENTAL HEMORRHAGIC STROKE

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The search for new drugs for correction of hemorrhagic stroke is still actual. Ischemic damage of brain tissue leads to the formation of energetic deficit, development of glutamate-calcium and cytokine cascade. Increases production of local inflammatory reaction, genes of early reaction are induced and mechanisms of cell death are activated. In response on expression of IL–1 its receptor antagonist is secreted (IL-1Ra) and then IL–2. The purpose of work was studying of effect of cytokine drugs – IL-1Ra and IL-2 (ronkoleukin) on the dynamics of index of carbohydrate-energetic balance, oxidant stress, expression of genes of the early reaction and the intensity of postinsult neurological and cognitive disorder in experimental hemorrhagic stroke (administration of autoblood in internal capsule of brain in rats) in administration in dose of IL-1Ra 7,5 mg/kg and of ronkoleukin 0,01 mg/kg during 18 days. In homogenate of brain using the biochemical methods the ATP, ADP, AMP, the content of products of oxidative modification of protein (AFG and KFG), peroxidation of lipids (DK, TK, MDA). Antioxidant protection was evaluated by the activity in brain tissue SOD, catalase, glutathionperoxidase. Expression of c-Fos protein in sensor-motor zone of cortex was founded by the indirect immunofluorescence. Using the standard methods oriental-studying habits, neurological deficit (by scale of Stroke – index McGrow), the conditioned reflex of passive avoidance. We set that administration of IL-1Ra (mostly) and ronkoleukin optimizes all indexes – decreases degree of oppression of oxidative processes in Krebs cycle, increases the intracellular stock of ATP, stabilizes the activity of pro- and antioxidant results when the synthesis of c-Fos protein was inducted, activation of apoptosis, improves the index of movement activity, psychoneurological status using the McGrow's Stroke-index and the procreation of reflex of passive avoidance. Effects more expressed in recovery period that testifies the necessity of application of cytokine drugs as cerebroprotective in hemorrhagic stroke.

ANTICONVULSANT ACTIVITY AND RELATED NEUROTROPIC EFFECTS OF DRY EXTRACTS FROM SOME REPRESENTATIVES OF FUMARIACEAE, LAMIACEAE, SOLANACEAE AND POLEMONIACEAE FAMILIES

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Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences. Despite the availability of a wide range of antiepileptic medicines a problem of the search for new drugs with anticonvulsant properties among the herbal medicinal products remains acute. It is well known that a high level of safety is inherent in herbal remedies, even in long-term use. In addition, herbal medicines usually have a complex influence on the disease pathogenesis.

The purpose of the research was the evaluation of anticonvulsant activity and related neurotropic properties of such herbal substances as aqueous and 50 % ethanolic dry extracts of *Leonurus cardiaca L.*, aqueous and 50 % ethanolic dry extracts of *Origanum vulgare L.*, aqueous dry extracts of *Ocimum basilicum L., Hyssopus officinalis L., Stachys annua L., Salvia officinalis L., Thymus serpyllum L., Fumaria officinalis L., Fumaria schleicheri Soy.-Willem., Hyoscyamus niger L., Datura stramonium L., Polemonium caeruleum L.* Aqueous and 50 % ethanolic dry extracts of *Leonurus cardiaca L.*, aqueous dry extract of *Ocimum basilicum L.* and aqueous dry extract of *Fumaria schleicheri Soy.-Willem.* in the dose of 100 mg/kg showed an expressed anticonvulsant activity on the models of seizures with different pathogenesis in mice (namely corazole-induced, tiosemicarbaside-induced and strychnine-induced seizures). These substances have been selected for further research in the combined open field test, a rotating rod test, an elevated plus maze, a conditional reaction of passive avoidance test, Porsolt behavioural despair test (tail suspension test in mice) and on the model of traumatic brain injury in rats.

According to the results of the aforesaid tests it has been established that aqueous and 50 % ethanolic dry extracts of *Leonurus cardiaca* render potent anxiolytic properties. Aqueous dry extract of *Fumaria schleicheri* also shows anxiolytic properties without negative influence on muscle tone, coordination of movements, cognitive processes and memory. Aqueous dry extract of *Ocimum basilicum* also renders significant cerebroprotective effect on the model of traumatic brain injury.

INFLUENCE DIURETICS AND CENTRIFUGAL ACCELERATION ON THE RENAL EXCRETORY FUNCTION

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The purpose of the study - an analysis of the combined effect of the centrifugal acceleration and diuretics on renal excretory function.

Materials and methods. Studies were carried out using ultra centrifuge radius with the attached straight and curved cells canisters for animals. The experiments investigated the effects of alternate diuretics (furosemide in the threshold dose of 1 mg/kg subcutaneously, hypothiazide and dry extract of Hyperici herba 20 mg/kg orally) on renal excretion of water, electrolytes and creatinine against the effects of optimal radial acceleration 3g. Animal control and experimental groups were given the study drug experienced group is further subjected to gravitational effects. Determined hourly (1st hour, 2nd hour, 3rd h, 21 hour) diuresis, natriyuresis and kaliyuresis by flame photometry, creatininuresis by photoelectrocolorimeter.

Results. Against the effects of furosemide radial acceleration 3g in 1 h causes a decrease in urine output by 30% ($p > 0.05$), kaliyuresis by 50% ($p > 0.05$) creatininuresis by 30% ($p > 0.05$) and natriyuresis it increases by 110% ($p < 0.05$); in the 2 h study diuresis and creatininuresis increased by 20% ($p > 0.05$) and natriyuresis and kaliyuresis - by 120% and 110%, respectively ($p < 0.05$); for 3 h values of all indices down - on diuresis 90% ($p > 0.05$) and natriyuresis by 30% ($p > 0.05$), kaliyuresis by 10% ($p > 0.05$) and creatininuresis by 90% ($p > 0.05$); after 21 h only change rates of diuresis and creatininuresis - reduced by 90% and 180%, respectively ($p < 0.05$). The hypothiazide gravitational effects at similar results in 1 hour trial to reduce urine output by 20% ($p > 0.05$) and natriyuresis by 10% ($p > 0.05$), kaliyuresis by 70% ($p < 0.05$), while creatininuresis increase 40% ($p > 0.05$); for 2 h and 3 h were observed inaccurate changing all the studied parameters in the test group; after 21 h urine output increased research by 60% ($p < 0.05$) and natriyuresis by 100% ($p < 0.05$), 50% kaliyuresis ($p > 0.05$), creatininuresis by 100% ($p < 0.05$) compared with the effect of the diuretic without gravity. The dry extract of Hyperici herba against the background of gravity in 1 hour experiment stimulated diuresis by 110% ($p < 0.05$), natriyuresis by 160% ($p < 0.05$), kaliyuresis by 220% ($p < 0.05$), creatininuresis by 50% ($p > 0.05$); in 2 h, 3 h, 21 h a reliable growth indicators have been noted.

Conclusions. Therefore, the gravitational effect on the kidney is an important factor regulating renal excretion. Additional effect of gravity can significantly increase the pharmacological effect of diuretics.

HEPATOPROTECTIVE ACTIVITY OF SPIROCYCLIC DERIVATIVE OXINDOLE UNDER ACUTE HEPATIC ISCHEMIA

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Statistical data of the World Health Organization indicate that over 30% of adult population of the World suffers from hepatic disorders. One of severe hepatic pathologies is hypoxic hepatitis (HH). 61.5% of hospital mortality cases result from hypoxic hepatitis. There is a lack of drugs for optimal treatment of this disease.

The goal of the research is: to study the influence of spirocyclic derivative oxindole on animal survival under acute hepatic ischemia.

Materials and methods. The research was made on white nonlinear rats. The weight of rats was 180-240 g. Acute hepatic ischemia was modeled through clamping the vascular pedicle of the liver and bile passage. Animals were divided into groups as follows: - pseudo-operated animals; - controlled abnormality; - animals receiving "77" compound at a dose of 5 mg / kg; - animals receiving "vita-melatonin" drug for comparison at a dose of 5 mg / kg; - animals receiving "thiotriazolin" drug for comparison (synthetic hepatoprotector) at a dose of 48 mg / kg in the same mode.

Results and discussion. Hepatoprotective activity of spirocyclic derivative oxindole products and of "vita melatonin" and "thiotriazolin" drugs for comparison was evaluated on such integral indicator as reduction of mortality. 25-minute hepatic ischemia without pharmacological protection in animals of controlled abnormality group showed a high level of mortality (64.3%). This indicated the severe state and exceeded the indicator of pseudo operated group (0%, $p < 0.001$).

Medical and preventive injection of "77" compound and "vita-melatonin" and "thiotriazolin" drugs for comparison reduced the mortality level in every treatment groups. However, the protective effect of "77" compound was mostly pronounced and reduced the mortality rate to 0%, and it significantly exceeded the index of "vita-melatonin" drug (40%, $p < 0.001$) and "thiotriazolin" hepatoprotector (25%, $p < 0.01$).

Conclusions. On the background of acute 25-minute hepatic ischemia succeeded by reperfusion, "77" compound - a new substance 4,3 '- spiro [(2-amino-3-nitril-4,5-dihydropyran [3,2-c]chromene-5-on)-5-methyl-2´-oxindole] shows evident hepatoprotective effect. It is verified with integral index of mortality decline of animals with acute distress.

Hepatoprotective activity of the studied compound is much more effective than activity of "vita-melatonin" and "hiotriazolin" drugs for comparison.

INVESTIGATION OF PHARMACOLOGICAL PROPERTIES OF DERIVATIVES OF D-(+)-GLUCOSYL AMMONIUM SALT OF N-PHENYLANTHRANILIC ACID

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Experience in the development of new safe anti-inflammatory drugs shows that great progress can be achieved if the research of NSAIDs goes in the way of combining low-toxic chemical compounds. As an example of these compounds is to create products based on derivatives of N-phenylanthranilic acids, which have anti-inflammatory, analgesic, diuretic, cholagogue, antimicrobial and antifungal activity, low toxicity compared to other NSAIDs.

The aim of our study was to investigate the anti-inflammatory activity of 6 compounds of D-(+)-glucosyl ammonium salt of 3-oxamoil substituted N-phenylanthranilic acid.

In the research we used 60 white non-linear mice with weight of 18-22 g, which were divided into 10 experimental, 1 control group and 2 groups of comparison drug.

In the group of derivatives of D-(+)-glucosyl ammonium salt of 3-oxamoil substituted N-phenylanthranilic acid, the most promising substance is the compound under the designation 1353- CGC, as it showed anti-inflammatory activity at the level of 33.73%, which exceeds the mefenamic acid. It should be noted that the introduction of glucosamine in the structure of N-phenylanthranilic acid increases the anti-inflammatory effect, which adjusts with the previous studies.

All other substances in their anti-exudative activity were less active and did not exceed the activity of sodium diclofenac.

As a result, analysis of the research results of 6 newly synthesized compounds showed that derivatives of D-(+)-glucosyl ammonium salt of N-phenylanthranilic acid have anti-inflammatory activity and they are a promising group to find safe substances with anti-inflammatory activity by means of their more detailed study and modification. Also, using the results of the study of anti-exudative properties, we observe the phenomenon of pharmacodynamic synergism, which is related to reciprocal potentiation of the pharmacological effects of glucosamine and N-phenylanthranilic acid.

SECTION 8

MODERN ASPECTS OF PHARMACEUTICAL MICROBIOLOGY AND IMMUNOLOGY

BIO-COMMUNICATION OF MICROORGANISMS: CHANGING PARADIGMS IN MICROBIOLOGY

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The modern concepts in the biology demonstrate the integrity and coherence of microbial populations as peculiar "superorganisms". The first studies in this field date from the 1950s belong to Jerusalemskiy I.D. He considered the colony of microorganisms as a "space-time continuum," in which the constituent cells has several advantages: increased resistance to antibiotics, more effective use of nutrient substrates. Further research has laid the foundation for the evolution of scientific understanding of the microorganisms: from the image of independent single-cell organisms to the complex interaction of a single system of organized functionally and morphologically different types of cells. The closest analogue of a biological system can be an organization of "social insects" - bees, ants, termites.

Special attention is given to such relevant phenomena as apoptosis, bacterial altruism, quorum-effects, collective differentiation of microbial cells, and formation of population-level structures such as extracellular matrix. Emphasis is placed on the channels and agents of intercellular communication in a microbial population. Much attention is also given to the role of colony organization and intercellular communication in "parasite/commensale/symbiont-multicellular host organism systems. The row of survey thoughtful pieces of work is the last years published on microbial colonial organization and bio-communication, however enough it is developed in literature there is a question about a role evolutional-conservative (chemically identical or homological at the different forms of living) alarm molecules, salient as factors of intercellular communication and social conduct, and for multicellular animals and plants also and in more specialized roles (hormones, neyromediators). In the last decade steadily broadens list of the studied microbial processes, realized only at presence of sufficient closeness of populations (quorum). Mechanisms are exposed many of the processes a quorum and communication for microorganisms; the chemical factors of intercellular communication, responsible for closeness-dependent processes, are certain. Bio-communications are the article of new biological science under the name a biosemiotica. Three channels of communication are most evolutional-conservative: direct (physical) contact between organisms; making chemical agents, which penetrable in an environment; generation of one or another physical field. All three channels of communication are present in a population of organisms.

ANTIADHESIVE ACTIVITY OF *ACINETOBACTER CALCOACETICUS* IMV B-7241 PREPERATIONS WITH VARIOUS DEGREES OF PURIFICATION

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The formation of microbial biofilms on a medical material is a dangerous fact because of the insensitiveness of microorganisms in conglomarates to antibiotics and their resistance to environmental factors. As is known from the literature surface-active substances (surfactants) can specifically inhibit bacterial adhesion whereas they are ecologically safe for humans. Possessing such properties surfactants can be used in medicine and dentistry as new antiadhesive agents.

Previously the strain of *Acinetobacter calcoaceticus* K-4 was isolated from oil-contaminated soil samples. Nowadays it is deposited in the Depository of microorganisms of Institute of Microbiology and Virology, National Academy of Sciences of Ukraine at the number IMV B-7241. It was stated the ability of the strain to synthesize surfactants that have antimicrobial and antiadhesive properties. The preparation of crude surfactants (supernatant of culture broth) was used in previous studies. The aim of the work was to study the ability of *A. calcoaceticus* IMV B-7241 surfactants with various degrees of purification to prevent the adhesion of bacteria and yeast on the surface of the medical material: dental prostheses, urethral catheters and steel. The following preparations were used: preparation 1 – supernatant; preparation 2 – surfactants solution; preparation 3 – aqueous phase. *Escherichia coli* IEM-1, *Bacillus subtilis* BT-2 and *Candida albicans* D-6 were chosen as test cultures.

The most effective agent was preparation 2 (surfactants solution). It was shown that the decrease of the surfactant concentration from 0.36 to 0.018 mg/ml the adhesion of *C. albicans* D-6 and *E. coli* IEM-1 on steel plates and urethral catheters increased. Thus, at the concentration 0.018 mg/ml the adhesion of *C. albicans* D-6 on catheters reduced by 93.6, *E. coli* IEM-1 – 74; steel *C. albicans* D-6 – 84, *E. coli* IEM-1 – 85.4%. The lowest degree of *C. albicans* D-6 and *B. subtilis* BT-2 (15 or 8.8%) adhesion on the silicone basis was observed at the surfactant concentration 0.36 mg/ml in preparation 2. At the same concentration the adhesion of *C. albicans* D-6 on acrylic material was only 3.2%. It is worth mentioning that even the reduction of the surfactant concentration in preparations 1 and 2 to 0.018 mg/ml the high antiadhesive effect was observed in the case of silicone base processing with the suspension of *B. subtilis* BT-2. At the surfactant concentration 0.36 mg/ml in preparation 1 and 2 the degree of *E. coli* IEM-1 adhesion on the silicon basis was 41 and 64, and on the acrylic material 56 and 11.4%, respectively. It was found that even the reduction of the surfactant concentration in the preparation 2 to 0.0072 and 0.0036 mg/ml, the degree of *E. coli* IEM-1 adhesion on the silicone basis decreased by 27 and 6.4%, respectively, and on the acrylic material remained unchanged in the range of concentrations 0,036–0,0072 mg/ml, and was 31% in the concentration of surfactant 0.0036 mg/ml in preperation 2.

The results showed high efficiency of low concentrations of *A. calcoaceticus* IMV B-7241 preparations with various degrees of purification as antiadhesive agents.

PROGRAMMED CELL DEATH IN MICROORGANISMS: THE BIOLOGICAL SENSE AND EVOLUTIONARY SIGNIFICANCE

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Apoptosis, or programmed cell death, is a controlled process of self-destruction at the cellular level. In multicellular organisms, it plays an important role in personal development and maintenance of tissue homeostasis, and the violation of its regulation lead to the development of tumors and neurodegenerative processes.

A recent study shows that apoptosis can occur in unicellular organisms. *What is the purpose of microbes* in the process? What are the phylogenetic roots of apoptosis?

It's known that horizontal gene transfer is common *among* different types of bacteria. This fact makes the microbial biocenosis similar to populations of multicellular organisms. In such community, first appeared the number of integrating mechanisms: the system of chemical signals exchanged between prokaryotes to coordinate the behavior of elements of community, as well as the mechanism of programmed cell death.

It is suggested that in prokaryotes apoptosis has emerged as a mechanism of antiviral protection of populations and eukaryotes - after a long period of bacterial endosymbiosis in the host cell and the subsequent horizontal gene transfer between the symbionts.

In apoptotic pathway the leading role plays active forms of oxygen and Ca^{2+}, such as protein - inhibitors of apoptosis, possibly a viral origin.

Evolutionarily the first appeared caspases and apoptosis-inducing factor, and then gradually appeared other proteins, among them - the so-called death receptors. In bacteria, apoptosis plays an important role: in the lysis of vegetative cells during sporulation, the formation of fruiting bodies of slime molds, spontaneous autolysis of cells at high density colonies natural transformation in the process of genetic recombination, as well as the destruction of virus-infected cells.

Some genes of autolytic proteins that involved in apoptotic pathway in prokaryotes were recently described. It was observed that the specific substance – "implementors" in the form of fatty acids and glucosamine play an important role in apoptosis of prokaryotes. In prokaryotes, all proteins that initiate this process are encoded by plasmids and prophages.

EFFECT OF EXTRACT CELANDINE ON THE BIOLOGICAL PROPERTIES OF MICROORGANISMS

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Bacteria are extremely labile microorganisms. Any changes in the environmental conditions, the effect of biologically active substances lead to the inclusion of adaptation mechanisms, resulting in altered protein biosynthesis and metabolism in general. Changes and the enzymes. In this paper, as a source of biological active substances acts herb celandine (Herba Helidonii majus), which contains alkaloids: chelidonine, gomoheledonin, sangivinarin, heletrinin, berberine. For selected alkaloids gomoheledonin, heletrenin, sangivirin installed pronounced bacteriostatic activity against Staphylococcus aureus and other Gram-positive bacteria.

Study of the effect of different concentrations of extracts of celandine herbs on the biochemical activity of microorganisms was the aim of this work. Of special interest this work is in terms of development of drug resistance in microorganisms, which may be associated with the development of mutations (various morphological changes, changes in the enzyme composition) without stopping the process of cell division in the studied test cultures. These changes can be caused by the action of celandine alkaloids on the genetic apparatus of microorganisms, as well as the inclusion of protective (enzymatic) mechanisms. Sangivinarin alkaloids, chelerythrine and berberine, can form complexes with DNA intercalation by type. Also learned that the natural DNA intercalators alkaloids sangivirin heletrinin and causing disruption of ATP synthesis in mitochondria and can modify the thiol groups of SH-dependent enzymes.

As the test organisms used in the test culture: Staphyloccocus aureus and Escherihia coli as representatives of gram-negative and gram-positive bacteria. The study was conducted by the passage.

The results showed the biological properties of bacteria during prolonged cultivation in a medium containing an extract of celandine. The results are a justification for further research.

COMPARATIVE RESEARCH OF MICROBIOLOGICAL COMPOSITION OF YOGURT UKRAINIAN AND FOREIGN PRODUCTION

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Dairy products are important in human nutrition through medical and nutritional properties, pleasant taste, easy digestion. Among dairy products occupy prominent position yogurts. In modern manufacturing yoghurt are widely used ¬ flavoring and aromatic substances that increase their nutritional value and shelf life, but at the same time can significantly influence the microbiological composition of the product and fundamentally alter its useful properties due to changes in physical and chemical conditions and additional contribution transient, "random" bacteria that do not belong to the group of lactic-acid bacteria-producers.

The aim of the work was to conduct a comparative evaluation of microbiological flora additional yogurt, which does not apply to dairy yogurt cultures, and accompanies them for technological ¬ stages of their manufacture and use. Results of experimental study concomitant microflora yoghurt samples of domestic and foreign production. Microscopic, bacteriological and mycological studies in vitro yogurt samples showed many gram-positive and gram-negative secondary microflora, which has no relation to the "basic" producers that are the basis for this group of dairy products. The data showed the presence of morphologically different forms of bacteria: cocci, small and large rod-shaped bacteria, yeast cells and fungi, which created the universal nutrient media different in color, size, texture and other features of the colony. Grown on liquid nutrient media pure cultures of these organisms were also differentiated by the nature of growth.

The results demonstrated the presence in all samples of yogurt "optional" concomitant additional microflora, which does not require special conditions for culturing and growing the universal nutrient media in the presence of oxygen, indicating facultative anaerobic type of respiration characteristic of both saprophytic, so and potentially opportunistic pathogens. This provides justification for further experimental studies in this direction. The research results total mesophilic aerobic and facultative anaerobic bacteria and micromycetes in samples of yogurt are particularly important given the fact that the production of yogurt in accordance with the established manufacturers of various specifications and according to modern standards in the field of sanitary supervision of a microbiological relatively foods that contain specific microflora (these include and yogurt) is performed.

Clearly, studies are fragmented and are not intended to summarize the conclusions as to the suitability and investigated yogurt as still more serious findings require further work in the direction of systematic research facility, and to continue to identify pure cultures were obtained during our experiments. However, consideration of these issues, in our view, has attracted the attention of the public and professionals in this area to solve actual problems of increasing food quality.

PROBLEMS OVERCOME ANTIBIOTIKO-RESISTANCE

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Antibiotic resistance has always existed. The problem of antibiotic resistance among clinically important microorganisms is rooted in complex ecological and evolutionary relationships between organisms themselves, formed long before the human species. Resistant strains occur when the genome of a bacterial cell as a result of spontaneous mutation, with the participation of the plasmids. Resistance genes may fall into the bacteria by bacteriophages or captured by microbes in the environment.

Selection of antibiotic-resistant strains has been accelerated unwise prescribing - mistakes in the choice of antibacterial drug, the dosage, the duration of antibiotic therapy ill, the massive spread of self-medication. Played a large role in the total implementation of antibiotics ecosphere. This led to a sharp change in the phenotype, and in many cases - and the genotype of pathogens that cause the most widespread human infection. There has been a quantum leap in the evolution of a microcosm, this has led to the emergence of new, unknown pathogens present. Has not yet established an antibiotic effective against all pathogenic bacteria.

Ways to overcome antibiotic resistance among microorganisms:

1. World Organization of Health Care strategy to contain antimicrobial resistance (control, education).

2. Combined treatment with antibiotics. It is necessary to consider the nature of their interaction - is unacceptable to apply a combination of antibiotics, which mutually destroy each other's activity (antagonism of antibiotics). This improves the effectiveness of antibiotic therapy, to avoid complications and reduce the appearance of the adaptive properties of microorganisms.

3. Rotation of antibiotics. Alternation and change of antibiotics according to their chemical and pharmaceutical properties and mode of action reduces the selective pressure on microorganisms and prevents the formation of antibiotic resistance.

4. The development of antibiotics, specifically acting on pathogens or tropic to various organs and systems of the human body.

Antibiotic resistance - a global problem. Only simultaneous action to curb the growth of antibiotic-resistance in each country will be able to produce positive results in the world.

MICROBIAL CONTAMINATION OF COSMETICS

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Microbial contamination of cosmetic products can cause spoiling of the product, and in some cases it cause a health risk. Modern cosmetic products composed of multiple components, in aqueous media can be an ideal substrate for microorganisms, including pathogens.

So, in the production of cosmetics necessary delay or prevent the growth of foreign microflora. That's why cosmetics include antimicrobial agents, preservatives, which should keep the safety of the product for the consumer. The safety of traditional / chemical preservatives raises many questions. Parabens (the most widely used preservatives in the world) can cause a negative health effects.

The aim of this is substantiation of development cosmetics without preservatives, so-called "selfpreserving" cosmetics. In such cosmetics the traditional preservatives substituted by other cosmetic ingredients with antimicrobial properties. Selfpreserving cosmetics production carried out according to the principles of "barrier technology". This term means that the production is used the promptness of various preserving factors or barriers that prevent access of microorganisms in the final product or creating in the product bacteriostatic medium. So the aim of this technology is blocking microorganisms growth through various factors. Every factor should decrease survival potential, that would progress through the barriers the number of surviving bacteria will continue to decrease and eventually reach zero.

We studied the main methods used for the manufacture of cosmetic products with non-traditional preservatives within the concept of barrier technology.

THE CHARACTERISTICS OF MICROBIOCENOSIS IN LARGE BOWEL BY PATIENTS WITH THE DELIRIUM ALCOHOLICUM

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Alcoholism (AH) is acknowledged a serious socioeconomic problem, as the use of alcohol-containing drinks and charges on them remain high, and a drunkenness in future spreads among a population. AH results in the row of complications which show up psychical violations, accordingly by a delirium alcoholicum (AD), and many somatic and infectious diseases, in particular, community-acquired pneumonia (NAP). Together with that, the analysis of literature testifies that to the problems of change of mikroekology of organism on the whole and separate ecological niches (EN) for these patients spared not enough attention.

Materials and methods: Researches conducted on the base of Center of emergency psychiatry of the Kharkiv regional out-patient psychiatric facility № 13, it is inspected 123 patients on AD, 29 from which complication of clinical course – NAP, – in comparing to the indexes of control group (KG). The taking of material and research was conducted after standard methods (backterioscopy and cultivation of koprokulture). The statistical processing of experimental data was conducted in accordance with the rules of variation statistics.

Results and their discussions: At research of microbiocenosis of biotop of large bowel, depending on the stage and weight of clinical course of AD in comparison from KG, the decline of general amount of anaerobic microbes is marked in experimental – on 13 % for patients on AD, uncomplicated NAP, and on 19,5 % at development of NAP. There was growth of amount of aerobic and optionally anaerobic microbes (in 3 and 4 times accordingly), and also substantial decline of levels of *Bifidobacterium* spp., *Lactobacillus* spp., *Propionibacterium* spp. but subbacteria. Growth of levels of *Enterococcus* spp is fixed. but *Proteus* spp., the amount of *Streptococcus* spp was more substantial increased. but *C. albicans*, thus found out most indexes at the disease of NAP. Influence of alcohol and him metabolitiv on the level of *Clostridium* spp. but *Staphylococcus* spp. it was minimum. It follows also to mark growth almost twice of number of atypical *Escherichia* spp., while the amount of laktozopositive of collibacillus diminished for persons from AD on 6–7 % by comparison to Kg. Thus, look after disbyotive changes in epitope large bowel as a adaptive mechanism, caused intoxication by an alcohol and products of his breaking up, and also by the presence of somatopathies of gastroenteric highway, which show up as changes of biological properties and correlations of microorganisms, and also appearance of not typical amount of bacteria, for this EN, as a result is worsening of clinical course of complications of AD. Direction of correction of disbiosis is opened, where consider a waiver the first step of the use of alcohol, and also use of probiotics, with content of *Bifidobacterium* spp., *Lactobacillus* spp., what are presented at our market a few point-of-sale names.

ANTIMICROBIAL EFFECT OF COMBINED DISINFECTANTS ON THE BASIS OF THE POLYHEXAMETHYLENEGUANIDINE

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Disinfection plays a special role among the sanitary-epidemic measures in the health care facilities and pharmaceutical production technologies. Polyguanidines are perspective disinfectants with low toxicity and high efficiency, which are represented by polyhexamethyleneguanidine chloride (PHMG-Ch) and phosphate (PHMG-Ph). An important issue is to prevent the development of microorganisms resistance, what can be avoided by the creation of combined solutions.

Purpose. To determine the antimicrobial activity of combined preparations based on PHMG- Ch and PHMG-Ph in relation to test cultures of microorganisms.

Materials and methods. Solutions (%):PHMG (1); PHMG (0,8) and $(NH_4)_2S_2O_8$ (0,2); PHMG (0,8) and H_2O_2(0,2); PHMG (0,8) and $(NH_4)_2S_2O_8$ (0,1) with H_2O_2(0,1); $(NH_4)_2S_2O_8$ (0,2); H_2O_2(0,2) were used in investigations. As test cultures microorganisms: Echerichia coli, Bacillus subtilis, Staphylococcus aureus, Pseudomonas sp., Candida albicans, Aspergillus niger was used. The antimicrobial action of solutions was determined by the method of diffusion in agar. Measurement of growth delay zones was carried out at 24 and 48 h for bacteria and C. albicans, and after 24–72 h for A. niger.

Results. It is noted that in the relation to E. coli, Pseudomonas sp., B. subtilis the most effective was the solution of the PHMG with hydrogen peroxide. The relatively S. aureus and C. albicans was effective The combination PHMG with peroxide and ammonium persulphate. The combination of PHMG with peroxide and ammonium persulphate was effective against S. aureus and C. albicans. Solutions of peroxide and persulfate didn't have high antimicrobial activity against most microorganisms, but these substances increased the effect of PHMG in combined mixtures. All studied solutions, except solutions of peroxide and persulfate revealed high antimicrobial effect against A. niger on the first day, but on the third day for all solutions, growth delay zone of the fungus decreased by 5-6 mm, which indicates their fungistatic action.

Conclusions. It was found that combined working solutions were the most effective for test cultures of microorganisms as: PHMG with hydrogen peroxide; PHMG with peroxide and ammonium persulphate. Peroxide provides instant and PHMG - prolonged action, which leads to higher antimicrobial activity of combined solutions than the use of these substances separately.

PRODUCTION CAPABILITY OF ANTIBIOTICS MICROMYCETES GENUS TRICHOPHYTON

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Different types micromycetes genus Trichophyton are fungal pathogens of humans and animals with lesions of the skin, hair and nails. According to the medical classification Trichophyton distinguishes of zoonotic and anthroponotic form with contact and contact-household mechanisms of infection. According to the frequency of registration in human and veterinary medicine, these fungal infections are second after Microsporum.

An ecological approach to the analysis of the epidemiology of tinea indicates the possibility of soil as a source of pathogens. According to some researchers, in soils of varying degrees of cultivation found Trichophyton gypseum, Trichophyton rubrum, Microsporum canis and other dermatophytes, which play a significant role in infectious diseases of humans and animals. However, the ecological criteria, these species belong to soil micromycetes group geophylic dermatomycetes. Their natural reservoir in nature is the soil in which they are saprophytic stage.

It is known that for soil micromycetes characterized by powerful enzymatic systems and the ability to survive in extreme conditions of existence, including through the development of secondary metabolites and antibiotic substances. It can be assumed that these properties are inherent and dermatophytes Trichophyton genus.

In this respect, it is of interest the results of comparative studies of the morphology, growth characteristics and pathogenicity of representatives of soil geophylic micromycetes kind Trichophyton and clinical strains of Trichophyton. Their morphological and cultural were identical, and the differences in the degree of pathogenicity leveled long-term cultivation of soil micromycetes on special media.

In the analysis of the ability of pathogenic strains of Trichophyton to production of antibiotics and the assumption of the chemical nature of antibiotic substances deserves interest data of the scientific literature on cases of anaphylactic shock during the initial introduction of penicillin in patients with chronic forms of Trichophyton. The presence of an infectious-allergic component in the pathogenesis of ringworm, which is due to microbial allergens, and aggravates the clinical course of infection is known.

However, in the classical description of the pathogenesis of various forms of Trichophyton no information about the possibility of production of antibiotics pathogenic forms of Trichophyton. New information about this, of course, will allow for adequate correction of anti-infective therapy of this disease. In our opinion, the study of this question is of considerable scientific theoretical and practical interest.

SOCIAL LIFE OF BACTERIA: A FORM OF COLLECTIVE BEHAVIOR AND COMMUNICATION

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Manifestation of social behavior is characteristic not only for animals but also for many organisms - both prokaryotes (bacteria) and eukaryotes (protozoa). The goal was to compile and analyze the results of scientific research, the object of which is the collective behavior of bacteria.

Bacteria can exhibit different forms of social behavior: from affiliation ("mutual attraction") - a desire to be together, and cooperation (association of individuals to share a specific task), to collective aggression. However, many bacteria are able to actively share information with each other using a variety of communication channels: cytoplasmic bridges (contact and communication), the exchange with the help of signal chemicals (Distant chemical communication, involving furanones, pheromones, etc.), by means of electromagnetic and acoustic waves (Distant physical communication).

Like other biosocial systems bacterial groups can both homo- (consisting of the same species) and heterotypic (consisting of individuals of different species).

At present, despite the results of scientific research, supporting the possibility of exchanging information between bacteria by means of electromagnetic and sound waves, it is the physical factors of distant communication of bacteria and their role in the exchange of information are still in the stage of "primitive accumulation" of empirical data.

Noteworthy phenomenon discovered a group of scientists, led by Nobel Peace Prize L. Montagnier. The experiment proved the ability of the DNA fragments, especially bacteria and creates weak electromagnetic fields to "restore" themselves in previously uninfected cells.

Undoubtedly, the results of studies require further study and scientific evidence, but if it turns so that the bacteria do share information and are able to "teleport" DNA, these findings may lead to the development of entirely new ways to combat viral and bacterial infections, and other insights into biology.

IMMUNOMODULATORY AND ANTI-INFLAMMATORY PROPERTIES OF ANTIBIOTICS: A REVIEW

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Traditionally, the value of antibiotics is discussed in the context of their direct antimicrobial action. However, we must not forget that antibiotics are physiologically active substances with a wide spectrum of biological activities. These show scientific publications on nonantibacterial effects of antibiotics. They can further amplify or attenuate the clinical efficacy of antibiotics, especially when it comes to immunomodulatory, anti-inflammatory properties of antibiotics. A number of studies have confirmed the importance of such effects macrolide antibiotics to improve survival in patients with severe respiratory tract infections in the world is increasing research evidence to suggest that the addition of macrolides in the scheme of the treatment of severe infections even in small amounts has a positive effect on survival. pathogens. Nonantibacterial properties of macrolides - an extensive and interesting field of study. Separately, it should be said about the immunomodulatory effects of this class of antibiotics.

Proved directional dependence immunomodulatory activity of macrolides on the dose and / or duration of antibiotic administration. With azithromycin in vitro in a dose of 4 mg / ml, an increase in IL-8 production by alveolar macrophages, and the use of dose 400 mcg / ml caused reduced production of interleukin. In this study, roxithromycin showed similar immunomodulating effects. Dirithromycin in small doses has a prooxidant effect, whereas at high concentrations is a powerful antioxidant. Interestingly, the case of peritonitis in mice was accompanied by a distinct use of macrolide anti-inflammatory effect, while the use of other antibiotics did not give the same effect. The initial effect was to Sumamed to stimulate neutrophil degranulation, and the corresponding increase in the enzymatic activity of serum, while there were stimulated and increased oxidative response of neutrophils. These effects combined with the achievement of high antibiotic concentration in plasma and neutrophils.

Tetracyclines are expressed immunomodulators as inhibit matrix metalloproteases. Due to the fact that matrix metalloproteinases play an important role in angiogenesis, metastasis of malignant tumors and other pathological processes, the effects of tetracyclines nonantibacterial now also focused considerable attention in oncology. β-Lactams sometimes cause inhibition of platelet function (while maintaining their normal content in the blood), and, as a consequence, increased bleeding. The effect of β-lactams of more characteristic penicillins.

It is now known, most well-known and widely used in clinical practice, antibiotics are able to provide and nonantibacterial effects of one kind or another. Need to be aware of these effects by avoiding or minimizing the negative and improving outcomes favorable.

SECTION 9

CLINICAL PHARMACY

SOCIAL AND PSYCHOLOGICAL ASPECTS OF PROSTATITIS DISEASE

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Prostatitis (N41 at ICD-10) is one of the most common diseases that cause male sterility. In U.S. it takes 8% of all urological diseases among men aged 18-50 years and older. Morbid affection, such as urethritis, vesiculitis, benign prostatic hyperplasia, are concomitant diseases for prostatitis.

In addition to known symptoms, for instance pain during palpation of prostate, in perineum, under pubis, in *regio inguinalis*, in anus area, in small of the back, in inner thighs, in penis, in urethra, in testicles, during erection and ejaculation (painful symptom complex), weakening of erection, premature ejaculation, orgasm blunting (sexual symptom complex), frequent urination, colics, burning and discomfort during urination, imperative feelings (dysuric symptom complex), prostatorrhea, discharges from urethra, chronic pelvic pain syndrome etc., there are other symptoms specifically psychological factors.

Among the latter, it may be noted decrease of sexual desire and ability to work, neurasthenia, depression, waiting for aftereffect of illness, hypochondria, alarm condition, psychosocial deadaptation and other indicators quality of life, psychological disorders. Myocardial infarction, stenocardia, crohn's disease, prostate cancers are compared with chronic prostatitis according their influence on patients QoL. During inflammatory diseases of genital system apparatus mental disorders are formed by the psychosomatic mechanism.

Among other obtrusive doubts, fears, inclination and activity on sexual sphere (unfounded fear to fail during coitus, fear of inevitable consequences from masturbation, incurable genital disorders, venereal diseases etc.) are observed in clinical presentation of phobic option. "Soft" depressions with alarm and attention focusing for ordinary activity are the basis for psychosomatic disorders by copulative cycle and psychogenic disorders by expectation neurosis.

Antidepressants, tranquilizers, other methods of medicamental correction and psychotherapy are prescribed as treatment for patients with prostatitis after ascertained pronounced changes in their psychophysical status. One does it for increment of libido and vitality, positive mood during cure and prevention of iatrogenic fixation on disease separate symptoms.

Combined influence for symptomatology or addition pharmacological measures to psychological factors are perspective in this case. E.g. a whole number of developed in National University of Pharmacy new dosage forms (apiculture, aminoacid- and microelement-based suppositories with androgenic activity for treatment of proctitis, prostatitis, male sterility) are contributed to spermatogenesis, good feeling, improved erectile function, regulated count of sex hormones, supported high sexual activity and fecundation ability. Availability of pollen use for new prostate-protector drug (capsules "Fepolen" with expressed anti-inflammatory and analgetic action) creation was established.

PHARMACOLOGICAL TREATMENT OF OSTEOARTHRITIS IN MOROCCO

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Osteoarthritis (OA) is one of the leading causes of disability and dysfunction in the elderly population, it has been estimated that the total cost for arthritis. The risk factors of osteoarthritis include the age, major joint trauma, overload of the joint; obesity, female gender; genetic factors, congenital developmental defects, inflammatory joint disease and several metabolic endocrine disorders. Nevertheless, the complaint that leads the person with OA to seek medical attention is join pain. A big amount of pharmacologic medicine that are used to treat the symptoms of OA (e.g., simple analgesics, NSAIDs, including selective COX-2 inhibitors; opioids and intraarticular injection of glucocorticoids and hyaluronan. Nowadays, a lot of researchers report about the role of basic treatment of OA, that include chondroitin sulfate and glucose amine glycan usage.

Problem of OA in Morocco has a great importance in the public health care system due to the high morbidity, early disability, and large treatment costs. According to our research in Morocco, the most prescribed medication for the treatment of OA were Artiflex or Piascledine they have the same effect and booth of theme are dietary supplement. The second place takes drugs which contain Celecoxib (Celebrex), and Andol and Doliprane as a paracetamol. At some list of prescriptions we saw Duoxol (Paracetamol with Thiocolchicine). The prices of this treatment still very expensive; the majority of patients used only anti-inflammatory drugs as a symptomatic treatment, which leads to earlier complication of OA.

Taking into account the current situation in Morocco, we concluded that it is necessary to find out special national programs to help patients with OA to get available treatment from the state.

METHODS OF TREATMENT OF THE POSTPARTUM COAGULOPATHIC HEMORRHAGES

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Obstetric hemorrhages are one of the leading reasons of maternal deaths composing 20-25% in its structure. According to the data of WHO (2012) from 125 to 140 thousand women in a year are dying because of the hemorrhages. The treatment of the obstetric hemorrhages is performed within the following main directions: the bleeding control; the resolution of the circulatory dynamics; correction of the hemostasis disorder.

The aim of the work is to conduct the analysis of the methods' effectiveness applied to control the obstetric postpartum hemorrhages.

In Kharkov regional perinatal centre postpartum hemorrhages are pointed in 15 cases (1,4%) starting from March, 2012. 4 maternity patients had the blood loss of more than 1000ml, among them there were 3 cases of the postpartum hemorrhages and the postsurgical one (cesarean operation). The reasons of the bleeding came from the alvus hypotonia (one case) and the disseminated intravascular coagulation in three other cases.

To fight with the coagulopathic disorders of the gravids and maternity patients there was used the whole complex of surgery hemostasis and drugs methods which influence the different chains of hemostasis (negative catalysts of the fibrinolysis, cryoprecipitate, tranxenamic acid etc). In 5 cases the conservative control methods turned to be effective. The metrectomy was done for 4 maternity patients. However, all traditional methods applied to fight with the coagulopathic hemorrhage can't guarantee the unmistakable stop of the bleeding. "The new chance" appeared when the new qualitative hemostatic drug – recombinant activated factor VII (NovoSeven) - had been introduced to the clinical experience.

The drug NovoSeven was used to control the profuse obstetric bleedings for 6 maternity patients. In all cases of the hemorrhages the full stop of bleeding was reached within 15-20 minutes after the single drug injection. In all cases the drug injection gave an option of avoiding the metrectomy.

Generally, the present supervisions tell us that the introduction of NovoSeven is one of the highly efficient methods to treat the final obstetric hemorrhages and in fact it is the preserving technology for the patients with the terminal bleeding in the act of childbearing.

THE INVESTIGATION OF APPLICATION OF COMBINED TOPICAL CHONDROPROTECTORS FOR TREATMENT OF OSTEOARTHRITIS

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Osteoarthritis is the most common disease of the musculoskeletal system. According to WHO 80% of back pain is exactly caused by osteoarthritis. The 90% of population of the world aged 65 years and over are suffering from osteoarthritis.

The development of osteoarthritis wastes a lot of costs in the economic, social and psychological areas that are associated with the prevalence of this disease, a common disability of patients and the high economic costs, which include treatment of the underlying disease as well as prevention and treatment of possible complications of pharmacotherapy. Losses associated with this disease have increased in recent years and up to 3% of the total national income in developed countries such as USA, Canada, UK, France and Australia. Osteoarthritis is a chronic, progressive inflammatory joint disease which develops as a result of impaired metabolism of articular cartilage. The symptoms of disease are pain, stiffness and functional disorders of motor activity. For the osteoarthritis treatment the drugs which restore the metabolism of cartilage, as well as anti-inflammatory and analgesic agents are used.

The goal of our study was to establish the possibility of developing of new drug combination in a topical form for osteoarthritis treatment. The topical dosage form has the following advantages: for its administration the hospitalization is not required, it doesn't damage the skin, has no systemic action and commits pharmacological effects directly in the area of application.

When we are going to develop a new drug, it is important to know the opinion of the end customer — the patient. We questioned the patients which were receiving conservative treatment of osteoarthritis in the Institute of Pathology of the spine and joints. The 22 patients with arthrosis of the IInd stage and 8 patients with gonarthrosis of the IInd stage, accompanied by pain, were included in investigation. Patients were divided into three groups. The first group was consisted of patients who were treated with ketoprofen, a second group — patients were treated with chondroitin and a third group — patients were treated with course of combined therapy. The term of the treatment lasted up to 4 weeks. The option of estimation was the questionnaire of life quality. Our questionnaire was developed on the base of English questionnaire EuroQol-5D. The questionnaire included the five factors which patients have met in real life. These factors were mobility, self-care, usual activities, pain, anxienty. All of the factors were estimated from 0 to 100 points.

The assessment of life quality of patients has established that at the beginning of treatment it was marked as 72-75,5 points and was increased to 87 points only in the case of combined therapy. Based on our results, we can conclude that the usage of combined topical chondroprotectors is reasonable sense for therapy optimization. The search for new drugs in this area is appropriate.

PROSPECTS OF ALISKIREN USAGE IN DIABETIC PATIENTS TYPE 2 AS ANTIHYPERTENSIVE THERAPY

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Direct renin inhibitor (DRI) is new class of antihypertensive drugs, that has not only powerful effect on blood pressure, but also it has renal protection properties. It is especially important for patients with diabetes mellitus (DM) type 2. The first drug that is represented in this class is aliskiren.

Based on the review of the literature we have discovered the efficacy and safety of aliskiren, and a dose-dependent decrease in systolic and diastolic blood pressure. It had been confirmed in some researchers in patients with arterial hypertension the I and the II degree in placebo-controlled clinical trial. The literature sources prove antihypertensive effect of aliskiren was been staying during 2 weeks after finishing of its taking. It was also discovered the good tolerability of the drug in therapeutic dose.

Aliskiren is able to inhibit the development of kidney damage, which can be explained firstly by antihypertensive action, and secondly due to the effect of preventing tissue profibrinogennic effect of prorenin and renin. Another study reports of aliskiren ability to decrease urinary albumin excretion.

According to some researchers metabolic effect of aliskiren as blockers of the renin-angiotensin system is neutral or positive. This suggests aliskiren can be used as metabolically neutral drug in hypertensive patients DM type 2.

We have analyzed of doctoral prescriptions in 25 case histories of patients with DM type 2 and hypertension in regional hospital in Kharkiv, Ukraine. We have discovered doctors mostly prescribe the drugs from ACE inhibitor and selective β-blockers groups as antihypertensive treatment in this clinical group, and never use DRI.

Thus, the practical medicine has not follow all scientific innovation in using of new drugs, which had been appeared on the pharmaceutical market. So, introduction of clinical pharmacist help in regional hospital became necessary to improve health care in hypertensive patient with DM type 2. Clinical pharmacist could to indicate the benefits DRI for this group of the patients and accelerate the aliskiren introduction into clinical practice.

VALUE OF THE HORMONAL STATUS ON THE PREPARATION TO THE EXTRACORPOREAL FERTILIZATION OF WOMEN WITH CHRONIC SALPINGO-OOPHORITIS

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Aim and objectives of the investigation: to determine the hormonal status of women with chronic salpingo-oophoritis (CSO) in the preparation to the extracorporeal fertilization (ECF).

Materials and methods of the investigation: 24 women of fertile age with CSO were examined whose period of infecundity was 6 years in average. The patients were divided into groups according to the duration of the CSO: group 1 – duration of CSO was less than 10 years (n=10) and group 2 – more than 10 years (n=14). The control group was constituted by 20 healthy women of the corresponding age. The correlation of the hypophisis hormone prolactin (Prl) and the ovarian hormones – estradiol (E2), progesterone (Pg) was determined.

Results of the investigation: the content of E2 during the follicular phase was decreased in both groups, Pg was decreased only in the patients from group 2 in lutein phase and was 6,8±1,3 against 10,0 nM/l of the lower standard of the normal level. The content of prolactin exceeded the control amount and was in patients from group 1 – c and from group 2 612,5±7,4.

Conclusions: A mild depression of gonadotrophic action on the ovaries in hyperprolactinemia was observed which is confirmed by the decreased production of E2 and Pg is the investigated patients. Thus, taking into account the clinico-laboratorial data it is reasonable to improve the differential ECF preparation depending on the duration of the inflammatory process in the epoophoron.

FEATURES OF HIGH-TECHNOLOGY NEUROMETABOLIC MEDICATIONS

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Cerebroprotectors, or neurometabolic stimulators positively affect the highest integrative brainfunctions. They improve mental processes, increase resistance of brain to various damaging factors, including extreme loads and hypoxia.

Besides, neurometabolic stimulators can reduce neurologic deficiency and improve kortikaland subkortikalinteractions, restore energy metabolism, reduce processes of excessive peroxidation.

Modern therapy of cerebrovascular diseases introduces neurometabolicmedicationsofexpressed antihypoxicand cerebroprotective actionto treatmentschedule.

Work purpose: to analyze this class of medications.

Results. There have been pointed outsome innovative medications with mode of actiondiffering from widely applied neuroprotectors.

Metaprot ("Farmproekt", Russia). The medication mode of action activates synthesis of RNA, and proteins after that. Resulting inducible gluconeogenesisenzyme synthesis and resynthesis leads to increase of physical efficiency,and improvement of synthesis of mitochondrial enzymes and mitochondriastructural proteins.

Cytoflavinum (NTFF PolisanLtd., Russia) normalizes oxidation-reduction reactions, eliminates metabolic imbalance, increases formation of ATP in neurons, reduces production of free radicals, oppresses peroxide oxidation of lipids, restores activity of enzymatic antioxidant protection, effect positively neuromediaresulting from hypoxia, prevents ATPreduction in ischemic nervous cells, normalizes functional cellular insufficiency.

Citocoline (Ceraxon, FerrerInternacional, Spain, Neuroxon, Arterium, Ukraine) is a predecessor of key ultrastructural components of cellular membranes (mainly phospholipids), it promotes restoration of damaged cell membranes, inhibits phospholipaseaction, preventing excessive formation of free radicals, prevents death of cells, effectingapoptosis mechanism, improves cholinergic transmission.

Conclusions. The carried-out analysis of modern neurometabolic medicationsproves their high pharmacological effect and low toxicity. One should note that almost all the analyzedmedications are of foreign production. Topical problem of modern medicine and pharmacy is creation and development of a domestic medicationof expressed neurometabolic activity and low toxicity.

EFFICACY OF QUERCETIN COMBINED WITH DICLOFENAC SODIUM IN MODEL OF ALTERATIVE MYOCARDIAL LESION IN RATS

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Purpose. To determine the pharmacologic efficacy of quercetin combined with diclofenac sodium by evaluating morphofunctional changes in myocardium with alterative lesion after oral administration in rats. ***Methods.*** Alterative lesion in rat`s myocardium provided by intraperitoneal injection of furazolidon in dose 200 mg / kg and after go an hour intramuscular injection of isoproterenol in dose 40 mg / kg. (O.V.Stefanov, 2001). Alterative myocardial inflammation caused by specific cardiotoxic furazolidon activity on the ground cardiac muscle depletion under action of isoproterenol. This model permit thoroughly evaluate the pharmacologic efficacy of research object. ECG, activity of enzymes markers of cardiomyocytes damage (AST, LDH), level in the blood serum of TBA-reactive substances (TBARS) and conjugated dienes (CD), the value / mass ratio of the heart also were assessed during this research. Standard methods of light microscopy were conducted research of myocardium structure. ***Results.*** The level of enzymes markers cardiomyocytes damage has been significantly reduced at background of quercetin combined with diclofenac sodium in dose 18.2 mg / kg. The level of lipid peroxidation has been normalized: the level of TBA-reactive substances and conjugated dienes decreased in 1.3 times relative to untreated animals. In applying of quercetin combined with diclofenac sodium to treat rats with alterative myocardial inflammation caused by specific cardiotoxic furazolidon activity on the ground cardiac muscle depletion under action of isoproterenol was observed following morphological picture. Cellular infiltrates, scattered deep in the myocardium or localized papillary muscles, has been isolated. The degree of maturity of the cells is higher than in the control group. Average score for the treated group is 1.0, which is significantly lower than in the untreated group animals. Individual muscle fibers or their fragments basophilic cross-striated myofibrils has been shaded in such areas. Condition of nucleus of cardiomyocytes changed around lesioned tissue cells: they increased in size and became rounded; chromatin was located near the membrane of this cells. Venous hyperemia was same as at untreated control group. That is indicating to a high level of protective properties of research object to the rats myocardium.

Conclusions. Myocarditis due to the alterative lesion in rat`s myocardium provided by intraperitoneal injection of furazolidon and isoproterenol has been formed and morphologically confirmed on day 5 this pharmacological research. Efficacy of study composition in dose 18.2 mg / kg has been most pronounced cardioprotective effect on model alterative lesion in rats myocardium after oral administration. Research object onset reduce the expressed alteration and prevent the development of degenerative lesions of cardiomyocytes. Mechanism of cardioprotective action has been determined primarily due to antialterative, antioxidant, membrane stabilization and anabolic activity of quercetin and diclofenac sodium combination.

BRONCHIPRET® – OPPORTUNITIES OF USE

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The modern pharmaceutical industry, due to a number of factors,prefers creating drugs from chemical-synthetic sources. But despite this, the production of herbal medicines also has a market niche. Moreover, even nowadays , studies of new ways for getting herbal medicine goes on. Thanks to the efforts of Bionorica company specialists, a new level of phytoterapy was reached and it is called phytoniering.

Phytoniring is researching and further development of plant compounds (phyto) using innovative production processes and modern methods (engineering). Especially active for symptomatic treatment of colds herbs are used. Drug Bronchipret is well established in this sphere of application. The main components of Bronchipret are - extract of the thyme herb (Herba Thymi), ivy leaf extract (Hederae helicis) and primrose root extract (Radix Primulae). This combination allows to deal effectively with cough, sputum is liquefied to facilitate coughing, inflammation is docked eliminates bronchospasm and facilitates breathing. Plant components that Bronchipret consists of have sekretolitic (mucolitic), antibronhospazmolitic antiviral and antimibacterial effects. Standardized manufacturing process ensures stable chemical, physical and organoleptic properties in composition of every component. Low temperature vacuum extraction technology and appropriate plant material ensure receipt of active substances. Using these drugs in ENT practice not only improves the flow of the disease but also contributes to a more rapid recovery of the patient as in monotherapy as in complex therapy. Moreover, the use of the drug in antibiotic therapy can reduce the side effects of this group of drugs. The drug easily eliminated from the body, and during injection of thymol (which is part of the essential oil of thyme) it is created a unique effect of inhalation inside.

Bronchipret® drug was first produced only in tablet form, later - due to improved technology procurement and production is part of the extract of plant material, two dosage forms were created: syrup and drops. Buscopan with standartised composition to optimizes usage of the drug, depending on the patient. We conduct an experimental study of the major types of pharmacological activity Bronchipret in various dosage forms, suggests the appropriateness of dosage forms of the drug in the treatment of diseases of the respiratory system at different stages of development and the nature of the disease. Prediction of the pharmacological activity types in the composition of the active ingredients of the drug by dint of correlation analysis showed the presence of additional types of actions, which expands the range of applications.

THE PROBLEM OF TOXICITY OF ANTICANCER DRUGS AND THE METHODS OF IT REDUCTION

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The problem of cancer today is one of the most global and important. More than a half of the deaths in cancer patients is not due to illness, but because anticancer drugs which have the plenty of side effects with high toxicity and very low selectivity of action. All this leads to the necessity of searching and creating of compounds which could to reduce the side effects of anticancer drugs and improve the quality of life of patients with cancer. The one of compounds which could to reduce the side effects of anticancer drugs is aminosugar glucosamine and its derivatives. The anti-inflammatory and analgesic activities, hepatoprotection, cardioprotection, nephroprotection, immunomodulatory and regenerative activities are the main pharmacological properties of glucosamine. Glucosamine protects membrane structures of those organs that suffer due to anticancer drugs.

Purpose of the study is evaluation the effectiveness of derivatives of glucosamine as potential correctors of toxicity of anticancer drug cyclophosphamide, which is often used in medical practice. Protective properties of derivatives of glucosamine were studied under experiment with course administration of cyclophosphamide in mice. Animals were divided into 5 group. The first group received only cyclophosphamide, animals of other groups received derivatives of glucosamine in therapeutic doses: group 2 – glucosamine hydrochloride, group 3 – glucosamine sulfate, group 4 – N-acetylglucosamine, 5 group – composition of derivatives of glucosamine with quercetin. The estimated indicators were mortality (%) and life expectancy (days). Animals were inspected in the middle and at the end of the experiment. In the groups of animals which received only cyclophosphamide, the maximum of mortality was observed on 11th day of the experiment and at the end of the experiment it amounted up to 80% (8 mice). In groups of animals treated with derivatives of glucosamine the sharp peaks of mortality was observed on 11th day experiment. At the end of the experiment the mortality rates were as follow: group 2 – 50% (5 mice), 3 and 4 groups -– 90% (9 mice) and group 5 – 5 mice (50%).

During the experiment two promising compounds were identified – glucosamine hydrochloride and composition of derivatives of glucosamine with quercetin. These objects will be investigated as a possible correctors of toxic effects of cyclophosphamide.

SECTION 10

PHARMACOECONOMIC STUDIES OF DRUGS

EVALUATION OF ECONOMIC AFFORDABILITY OF ANTITHROMBOTICS OF HEPARIN GROUP, WHICH ARE PRESENTED AT THE PHARMACEUTICAL MARKET IN UKRAINE

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The aim. Antithrombotic agents have a special place in the treatment of patients with ischemic stroke (IS), effect of which is aimed to improve cerebral perfusion. Their effect is connecting with the improvement of the rheological properties of blood and the prevention of recurrent thrombosis. As drugs anticoagulant therapy for IS the direct-acting anticoagulants have used traditionally. The aim is to assess the affordability of antitrombotic drugs of heparin.

Materials and methods. For studding the data of informatics research system "Morion" were used. To assess the economic affordability ratio of anticoagulant therapy used solvency adequacy ratio (Ar) that characterizes the dynamics of the ratio value of therapy and solvency of a consumer. The proposed rate - the ratio of the cost of the course antithrombotic therapy of IS in accordance with the standards of treatment to the average monthly wage in Ukraine, expressed as a percentage. The higher ratio (Ar) is the less affordability of a drug for a consumer. Affordability ratio of anticoagulant therapy was calculated in several ways: Ar_1 = (average drug price / average wage) x 100; Ar_2 = (average drug price / minimum cost for living) x 100.

Results. Analysis of wholesale prices showed that the cost of antithrombotic drugs of heparin varies widely (from 53 UAH to 900 UAH per packing). Clexane (solution for injection 8000 anti-Xa IU / 0,8 ml syringe dose № 10; 902,21 UAH) and Fragmin (10,000 IU / ml amp. 1 ml № 10; 807,52 UAH) had the highest cost of packing. The lowest cost per packing was found for drugs Fraxiparine (2850 IU anti-Xa 0,3 ml syringe № 2; 58,37 UAH) and Gizende (5000 IU / ml vial. 5 ml № 10; 80,71 UAH.). Affordability ratio of antitrombotic drugs of heparin are: for enoxaparin sodium (Ar_1 = 0,20; Ar_2 = 0,03); heparin sodium (Ar_1 = 0,05; Ar_2= 0,01); nadroparin calcium (Ar_1 = 0,13; Ar_2 = 0,02); dalteparin sodium (Ar_1 = 0,30; Ar_2 = 0,05); pentosan polysulfate sodium (Ar_1 = 0,08; Ar_2 = 0,01); sulodexide (Ar_1 = 0,20; Ar_2 = 0,03); bemiparin sodium (Ar_1 = 0,17; Ar_2 = 0,03).

Conclusion. Heparin sodium and pentosan polysulfate sodium are the most affordable drugs of antithrombotic therapy. These data can be used to optimize the possible costs for treatment of ischemic stroke.

COST ANALYSIS OF ACUTE PERITONITIS ANTIBIOTIC THERAPY

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The aim: Acute peritonitis is the main reason for urgent hospitalization in surgical hospitals in Ukraine. The results of treatment are largely dependent on choice of starting antibiotic therapy. The aim - pharmacoeconomic analysis of schemes of antibacterial therapy of acute peritonitis, the recommended clinical protocol approved by the MH.

Materials and methods. The cost analysis of ten schemes antibiotic therapy (AT) in patients with acute peritonitis was conducted. These schemes are recommended by the Clinical Protocol of acute peritonitis treatment (MHO of Ukraine, order № 297, 02.04.2010) for use in practice.

Results. The schemes of antibacterial therapy are: I – ertapenem (1,0 gr intravenously (iv.) 1 time/day); II – cefotaxim (1,0 gr im. 3 times/day and metronidazol 100 ml (sol. 0,5%) iv. 2 times/day); III – amoxicillin clavulanate (1,2 gr 3 times/day); IV – moxifloxacin (400 mg 1 time/day); V – levofloxacin (500 mg iv. 1 time/day and metronidazol 100 ml (sol.0,5%) iv. 2 times/day); VI – cefepim (2,0 gr iv. 2 times/day and metronidazol 100 ml (sol.0,5%) iv. 2 times/day; VII – cefoperazone + sulbactam (2,0 gr 3 times/day); VIII – meropenem (500 mg iv. 4 times/day); IX – imipenem + cilastatin (500 mg/500 mg iv. 4 times/day); X – ciprofloxacin 400 mg iv. and metronidazol 100 ml (sol.0,5%) iv. 2 times/day. Three variants for each scheme were calculated: the schemes with original drugs, the schemes with generics and the schemes with Ukrainian generics. Doses and duration of AT were calculated in accordance with the Clinical Protocol of acute peritonitis treatment (MHO of Ukraine, order № 297, 02.04.2010). The costs of second-line antibiotic treatment (in the absence of the first line antibiotic effect), hospitalization, for additional expert advice and additional surgical intervention (if it is necessary as a result of antibiotic therapy failure) were calculated too. The prices were taken from the price-lists of surgical clinics in Ukraine. The costs range of treating one patient with acute peritonitis with original drugs are 3891 UAN (scheme I) - 7994 UAN (scheme VI). The costs range with generics of ukrainian production are 1924 UAN (scheme V) - 5413 UAN (scheme VIII) (1 EUR = 11,65 UAN).

Conclusions: The costs of treatment schemes for patients with acute peritonitis with use of less expensive generic drugs are not always cheaper than the costs of original drugs using. The optimal schemes for treatment of patients with acute peritonitis were selected. Higher direct costs offset due savings in indirect costs (rehabilitation).

PHARMACOECONOMICAL ANALYSIS OF PHARMACEUTICAL DRUGS FOR TREATMENT OF CHILDREN AFFECTED WITH GASTRITIS AND DUODENITIS IN THE SPECIALIZED HOSPITAL

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Improvement of the organization and advance of medical and pharmaceutical quality of care for children affected with gastritis and duodenitis is the main issue of the day. Therefore, the aim of this research was to carry out retrospective analysis of medical histories of children affected with gastritis and duodenitis, receiving in-patient treatment in the treatment-and-prophylactic establishment in Odessa in 2010-2011.

Materials and research methods: appointment sheets; systemic and survey, frequency, and pharmacoeconomical (ABC and VEN) analyses.

Research findings. ABC frequency analysis was conducted in the first phase of the study. For this purpose all recorded drugs were divided in three groups based on the descending order of administrations: 18 INN drugs were classified into group A providing 69,23% of administrations, in groups B and C - 30 (26,22% of appointments) and 13 (4,55% of appointments) respectively. Drugs classified into group A were the ones that were prescribed most often and almost all of them are included into the list of drugs recommended by Treatment Protocols for chronic gastritis and chronic gastroduodenitis in children (2010). As a result of ABC / VEN-analysis, the AV group (essential) and AE group (required) included 12 drugs from 10 pharmaceutical groups, which provided 167 appointments (56.3%) to help children affected with gastritis and duodenitis in a hospital. In the second phase of the study, ABC analysis was carried out taking into account expenses and drug distribution was presented based on their specific weight in the index of total consumption from most to least expensive. Drugs were classified into groups A, B, C if their costs were 73.23% (8799.47 UAH.), 19.92% (2393.42 UAH.) and 6.85% (823.30 UAH.) from the total cost respectively. I.e. the most expensive is the group A, which accounts for over 89% of prescriptions in the form of 34 drugs. This analysis allowed us to determine the optimal range of the studied drugs for health facilities, which includes drugs that have more than 5 appointments and A/V or A/E status. Their costs were 38.1% of the total.

Conclusions. Application of ABC/VEN-analysis methods was used to identify the main group of medicines for rational pharmacotherapy of children with gastritis and duodenitis, with the aim of introducing the drugs to official drug lists.

ABC- ANALYSIS OF PHARMACOTHERAPY OF COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN

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The aim of this study: ABC-analysis of pharmacotherapy community-acquired pneumonia (CAP) in the pulmonology department of children's clinic in Sumi.

Materials and methods. The analysis of 100 histories of patients with CAP at the age of 10 to 12 years was conducted. Study duration - 6 months (May - October 2012). Pharmacoeconomic methods: ABC-analysis were used.

Results. According to the analysis of histories of patients with CAP 92 trade names (TN) of drugs, which are consistened to 66 international nonproprietary name from different pharmacological groups (drugs, that affect the respiratory system, drugs that affect the digestive tract and metabolism; antimicrobial agents for systemic) were identified. Among them 49% of drugs are used for treatment CAP, 51% of drugs - for the treatment of associated diseases (acute laryngitis, acute sinusitis, chronic tonsillitis, acute suppurative otitis media, acute conjunctivitis, acute bilateral sinusitis).

The results of the ABC-analysis showed that the group A consisted of 15 TN, which spent 79.75% of the total expenditure for all investigated TN, in group B - 31 TN with moderate cost (15.09%) in groups C - 46 TN with low cost (5.16%).

The drugs, which included in the most costly group A, used to treatment both CAP and associated diseases. They were representatives of the following pharmacological groups: antibiotics cephalosporins, macrolides, aminoglycosides, probiotics, mucolytic agents; expectorants, antiseptics, homeopathic drugs, blockers of H_1 histamine receptors, drugs that stimulate the processes of immunity. Among them cephalosporin antibiotic "Lorakson» («Exir Pharmaceutical», powder for solution for injection 1000 mg bottle, № 12) has largest costs (30.80%). This drug has the high cost of packing (299.26 UAN), the high cost of a course of treatment of the CAP in one patient (534.39 UAH) and administered half of patients with CAP in this department.

Conclusion. The results of the ABC-analysis of pharmacotherapy of pediatric patients with CAP identified the structure of the cost of drugs and the most expensive among them. These results can serve as a basis for further study of the question of rational pharmacotherapy of pediatric patients with CAP at this department.

SECTION 11

MANAGEMENT AND MARKETING IN PHARMACY

MANAGEMENT OF MARKETING ACTIVITY OF THE DRUGSTORE

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The high level of the market saturation by medicines, degree of knowledge of consumers, high requirements of consumers to medicines, increase in quantity of drugstores are the reasons of an competition aggravation at the pharmaceutical market. It is quite clear that in the fight for consumer in modern conditions of competition environment, firms which as much as possible satisfy needs of the clients, providing them economy of money, convenience of acquisition of goods and effective communications, will win.

Vigorous marketing activity is a guarantee of financial success. Thus effective realization of a marketing complex provides commercial success of a drugstore, its steady position at the pharmaceutical market.

The purpose of our research is studying and the analysis of use of marketing complex components in a drugstore, development the directions of improvement in marketing activity.

As an object for research a drugstore working in Kharkov is chosen. It is engaged in retail trade of medicines, products of medical consumption, means of the hygiene, special foodstuff.

The SWOT-analysis method is used for establishment strong and weaknesses of the organization, and also opportunities and threats from environment. The SWOT analysis of the drugstore and also its two competitors has been carried out for comparing of conditions of internal and external environment.

Marketing activity of a drugstore at the market has been analyzed, an assortment of the drugstore has been studied, competitive advantages of the drugstore have been estimated.

A poll of a drugstore's visitors and inhabitants of the area using specially developed questionnaire for definition of their opinion about the key parameters defining formation of loyalty to a drugstore has been carried out.

Evaluation of the work of pharmacists according to "converting indicator" has been used. The motivating actions of sales promotion increasing indicators of purchases have been offered. Recommendations about improvement of estimation of level and quality of marketing activity of the drugstore have been developed.

STATUS AND PROSPECTS OF NATIVE PRODUCTION OF DRUGS IN KAZAKHSTAN

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Creation of national pharmaceutical industry, increase profitability and competitiveness of existing plants, the earliest increase in the share of native production of drugs to 50% by 2017, identified as top priorities for economic development.

The purpose of this research is to analyze the current state of the native production of medicines.

Assessment of the real level of development of the pharmaceutical industry was carried out on the basis of data from the State register of medicines in Kazakhstan as of February 19, 2013.The list of registered drugs of Kazakh production, was noted accounting for 12% of the total number of positions of the nomenclature in the specified register.

Currently there are about 79 domestic manufacturers of medicines. The main production is concentrated in eight major Kazakh refineries, which account for 74%. The largest portion of the plant is «Santo.Member of Polpharma Group» -29%, while the share of other "Kyzylmay", "Shansharov-farm", "Nobel", "Romat", "Global Pharm", "Zerde-phyto", "Dosfarm" is in band reception 3-10%. Besides investigating the manufacturers, we have analyzed the range of medicines and dosage forms revealed that the highest percentage of the production comes from such dosage forms such as tablets and solutions (31.2% and 18.1%, respectively), and the minimum - syrups and sprays (2.4% and 2.8%, respectively).

Thus, in the pharmaceutical market in Kazakhstan slow growth of domestic production is being observed. Performance of the raised task on increasing native produced medicines to 50% by 2017, while maintaining a similar rate of growth is problematic.

Necessary to implement a set of measures to enhance the system of national pharmaceutical industry as due to the significant expansion of the above eight leading enterprises and the creation of new businesses that meet modern requirements and drug manufacturers.

PROCUREMENT PERFORMANCE MEASUREMENT IN THE LEBANON PHARMACEUTICAL COMPANY

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Lebanon pharmaceutical companies are starting to understand the importance of procurement as a strategic function of the organization. As the competition is increasing, different ways of creating competitive advantages are being researched, evaluated and implemented. In the case of supply chain and particularly procurement, the benefits of optimization are mostly clear - Kerkhoff (2005) notices that the financial situation of the company can be improved through the procurement function by locating and exploiting the potential for increased profit and reduced procurement expenditures. So, the purpose of our research to define purchasing position in corporate business plan in Lebanon pharmaceutical companies. Procurement department, like all other departments in a company, is an element of the overall organization, which must contribute to the achievement of the corporate goals. Thus a clear link between the corporate strategy and procurement strategy is crucial to understand, follow and implement in each function and action. The position of the procurement department in the overall strategic map of a company can be exemplified as in the Fig. 1.

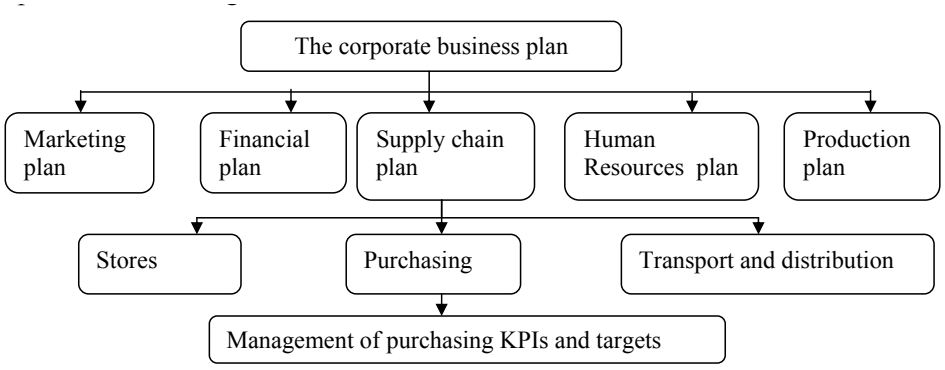

Fig.1 Purchasing position in corporate business plan of Lebanon pharmaceutical company

It is clear, that although each department has its own strategy, goals and KPIs, all these factors must feed upwards to the corporate business plan. Moreover, the strategy and targets of the procurement function should not only reflect the company's vision and development directions, but as well should represent the perception of the top strategic managers to the procurement function.

RESOLUTION OF CONFLICT SITUATIONS IN ACTIVITY OF THE FIRST TABLE PHARMACIST

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Research objective: Level of rendering of the pharmaceutical help to the population depends on many factors: economic, social, psychological and other character. In professional activity of pharmacists it is necessary to reveal, analyze and consider their influence, and, respectively to correct actions of workers of a drugstore, first of all in the sphere of communication with visitors of the chemist's organizations.

Materials and methods: The conflicts are one of the main reasons for decrease in overall performance of a drugstore. For the purpose of their identification we carried out questioning of visitors of a number of drugstores of the city of Almaty.

Questions reflected psychological characteristics of communication, the possible reasons of emergence of conflict situations. Criteria of efficiency performance of drugstores were defined.

Results: The main reasons for emergence of conflict situations are as a result established:

- return of the bought goods – 84 %;
- lack of a demanded preparation – 26 %;
- mistake in professional activity of the personnel – 37 %;
- queue existence – 24 %;
- violation of ethical principles – 54 %;
- inexperience of the personnel – 4 %;

The main directions for optimization of work of a drugstore are established, namely: improvement of appearance of a drugstore and interior of a drugstore, skill level of the personnel, range of a drugstore, appearance of the pharmacist.

Conclusions: Methods on increase of level of rendering of the pharmaceutical help are offered the population, competitiveness of a drugstore and a role of vocational training of pharmacists, and also a method of check of efficiency of correcting actions. Ways of the prevention and permission of conflict situations are offered.

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON THE PHARMACEUTICAL MARKET IN THE REPUBLIC OF KAZAKHSTAN

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Non-steroidal anti-inflammatory drugs (NSAID) are widely used in modern clinical practice. More than 30 million people use NSAIDs annually worldwide. The reasons behind high usage of NSAIDs are the following: the wide range of their pharmacotherapeutic applications; heir anti-inflammatory, analgesic and antipyretic effects; their effectiveness in treatment of various diseases.

Our goal is the general estimation of assortment and quality of NSAIDs on the pharmaceutical market of the Republic of Kazakhstan (RK).

We conducted quantitative and qualitative market studies of the size, share and segmentation of the NSAIDs market.

The studies show that NSAIDs are represented by 85 trade names at the pharmaceutical market of the RK, most of them are foreign products. The share of locally produced is only 1.16% of all registered in the RK drugs. The main exporters of NSAIDs are: India (which exports 18 trade names to the RK market and its share is 21%); Germany and The Russian Federation - 9 trade names (11%); the RK - 8 trade names (9%); Japan - 6 trade names (7%); Belarus - 5 trade names (6%). Other producers come from Great Britain, Italy, Turkey, Estonia, Bulgaria, Ireland, Spain, Poland, Romania, France, Armenia, Egypt, USA, Thailand, Switzerland, Hungary; and they export 4 or less trade names, with a market share of approximately 1-4% each. The analysis of available NSAID dosage types shows that gels occupy the leading position - 38%; the share of capsules, ointments, pills and plasters is around 7-11% total. The share of injections, eye drops, granules, trans-dermal systems and other drug forms makes 1-4% of the market.

Thus, the small market share of local NSAIDs (1.16%) in the assortment of drugs of this group and their high usage in treating the most common diseases in the RK indicates the necessity for local pharmaceutical companies to produce them.

MARKETING RESEARCH OF PHARMACEUTICAL MARKET OF THE ANTIHISTAMINES FOR SYSTEMIC USE

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Today an allergy is a global medical and social problem of civilization. Its prevalence is increasing worldwide every year, and approximately doubled every 10 years.

According to the data of World Health Organization an allergy is the third highest rate of morbidity among other nosology. If this trend continues, then by 2015, a half of the residents of the European continent will feel the impact of this disease. According to data of world statistics, allergic diseases reached on average 10% of the globe.

The purpose of our study is the marketing research of the Ukrainian market of antihistamines for systemic use.

We analyzed the assortment of group medicines R06A «Antihistamines for systemic use" presented at the pharmaceutical market of Ukraine. The total number of antihistamin medicines for system use at the Ukrainian pharmaceutical market is 15 international non-proprietary names (81 trademarks, including 20 domestic, 61 medicines of foreign production), which indicates the saturation of the market of import drugs.

At the market among foreign manufacturers are products of companies of the USA, United Kingdom, India, Hungary, Switzerland, and Canada. Medicines of test group are mostly in the form of tablets (34%).

The next step of our study is expert evaluation of antihistamines among doctors and pharmacists of Kharkov. The experts evaluated the medicine's effectiveness and the level of demand, the level of provision of the pharmacies with medicines of the group.

Experts consider the most effective are medicines of III and II generations. The biggest demand medicines are Loratadin, Fexofenadin, Levocetirizin, Cetirizin. The analysis shows a high level of provision of pharmacies in Kharkov with antihistamines: Loratadin "Farmak", Fenistil «Novartis» (Switzerland), Cetirizin Sandoz "Salyutas Pharma GmbH, Sandoz" (Germany).

The preferences of medical specialists during the appointment of antihistamines to patients have been analyzed. The factors that guide consumers in selecting the study medicines have been defined.

THE ASSORTMENT ANALYSIS OF MEDICAL PREPARATIONS FOR TOBACCO ADDICTION TREATMENT

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During last years WHO and International Bank conducted global investigations of harm, which smoking causes, and as it was detected that tobacco is more serious reason of death and disability than other diseases themselves. According to statistic site, every second man and every fifth woman smoke in Ukraine.

Totally there are nearly 9 million of active smokers, which make up the third part of employable population of Ukraine. Ukraine occupies the 17-th place in the list of country – leaders in number of smokers. For the last 20 years the number of women smoking increased in 4 times.

Sociological investigations show that the most part of smokers (60-70%) try to give up this bad habit, but tobacco addiction can be as strong as heroin addiction.

The aim of the work is to analyze the home market of preparations for tobacco addiction treatment.

The methods of investigation. The field investigations were carried out by visitors' questionnaire in Kharkiv, Kupyansk and Kirovograd chemist's shops.

The results of investigations. At present 50 visitors of chemist's shops were questionnaired. 52% of men and 48% of women took part in a questionnaire. It was stated that 46% of people questionnared smoke. 26% - don't smoke, but used to smoke earlier.

Additional method of treatment in case of tobacco addiction is medicametous therapy. For the last years the assortment of medical preparations of this group has expanded and it has been presented by such medical preparations as: Nicoretto, Nicotinell in the form of chewing gums and transdermal plasters; Tabex, Tabacum plus, Champix – in the form of tablets. The preparations in the form of chewing gums and tablets are in great demand among the consumers for tobacco addiction treatment. Everyone, who wants to give up smoking, has an opportunity to choose price optimal and suitable preparation according to its medical form.

Conclusion. The obtained results attested about necessity of this problem investigation and medical preparation popularization for tobacco addiction.

MARKETING FEATURES OF CUSTOMERS SERVICES IN PHARMACIES

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Quality customer service is the basis for keeping a competitive market position. Pharmacy should consider the wishes of clients and satisfy them by the best way in order to succeed. In order to develop recommendations aimed at improving the quality of service in pharmacies, we have carried out research of consumer preferences regarding choosing pharmacy. As an object of study were chosen pharmacy #233 (Kharkov). The results obtained from questionnaires of 87 pharmacies' visitors during November-December 2012.

Successful activity of pharmacy and its competitiveness depends on the ability to satisfy customer needs. Established that 85.0% of respondents rated the work of staff as good, 92.0% satisfied with the work schedule of pharmacy, 78.2% satisfied with the assortment of medicines in the pharmacy. The criteria that led to the choice of pharmacy include: high quality of service (93.1%), convenient schedule of pharmacy (92.0%), speed of customer service (92.0%), wide assortment (88.5%) and highly qualified staff (86.2%). Customers pharmacies are not satisfied with the location of pharmacies (47.0% think the location is not convenient). Customers are not satisfied with the location of pharmacy (47.0% think that the location is not convenient). First of all visitors of the pharmacy are paying attention on convenient planning of salesroom (noted 94.3%), spacious of premises (95.4%), orderly placing of medicines on the shelves (92.0%), availability of information to consumers (87.4%). Clients of pharmacy #233 can quickly find the right medication because showcases decorated neatly and signed. Buyers at the pharmacy needed more information about medicines. Respondents noted that as additional services they are interested in consultation with pharmacists on common questions like how to use medicines, their side effects, compatibility, time of reception, the ability to order medications by phone etc.

The results indicate that the quality visitor services in pharmacy based on a combination of factors such as culture of service (including mood pharmacist during communicating with customers), improvement of information and advisory services, training of staff, the quality and speed of service, expansion of assortment. Consequently, the results allowed determining the factors that led to the selection of pharmacy by consumers and take them into account in developing recommendations of client-oriented strategy. To the pharmacy staff was recommended to take part in training on the formation of loyalty programs for customers.

THE INVESTIGATION SERVICE LEVEL IN CHEMIST'S SHOPS BY «MYSTERY CUSTOMER» METHOD

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The aim of our work was to get the reliable data on service level in Kharkiv chemist's shops, shortcomings detection of service process.

The main task of retail pharmaceutical business is client involvement and loyalty maintenance during the service process. Nowadays one of the methods of problem detection in service technology is observation by «Mystery Customer» method. The «Mystery Customer» is a specially trained person, unknown to sellers, who under the guise of a customer comes to the shops and registers his observations and impressions in special report. Such checkups give the executives clear conceptions about real service level, which their company provides and detect the shortcomings.

The methods of investigation. During the investigation, telephone monitoring by «Mystery Customer» method was used. In order to detect the staff professional level of chemist's shops, the group of medical remedies for dry cough treatment was chosen. Telephoning, the interviewer introduced herself as a woman, who was interested in cough remedies for children. She asked to give her some recommendations.

The result of investigation. We conducted the telephone monitoring among 31 chemist's shops from 6 networks of pharmacies in Kharkiv. In 80% of calling cases, pharmacists remained polite and were interested in client's consulting. Testing staff on irritability at condition of «poor audibility», it was stated that pharmacists patiently answered the questions in half of investigated chemist's shops. In 40% of chemist's shops pharmacists attentively explained all the details of the questions, asked counter-questions about health status, character and causes of illness. Rather more number of chemist's shops tried to clarify the request, so as to remain polite, but not going into details to solve the person's problem: she was provided several alternative variants and advised to consult a doctor. 9% of respondents provided the problem solving, not asking about health status. In 79% of chemist's shops pharmacists gave clear understandable explanations. The monitoring has shown high service level. But in order to improve the process of service, it is necessary to conduct regularly trainings and develop motivation programs for personnel.

RESEARCH OF FACTORS INFLUENCING ON THE POTENTIAL OF THE PHLEBOTROPIC DRUGS MARKET IN UKRAINE

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Phlebotropic drugs are the basis of pharmacotherapy of chronic venous disease (CVD) of the lower limbs. Pharmaceutical market of Ukraine has 51 drugs with phlebotropic action for system and local usage produced by 33 manufacturers from 14 countries. The market volume of phlebotropic drugs in the first half year of 2012 exceeded 958 mln grn.

The purpose of the research is study the factors influencing the formation of potential of phlebotropic drugs market in Ukraine. Data of scientific sources, reports of epidemiological studies, and doctors', pharmacists' and final consumers' questionnaires have been analyzed.

Phlebotropic drugs market potential in Ukraine is formed under the influence of many factors of general and specific character. General factors include volume and structure of product proposal, living standard and population needs, its social, and sex and age composition; the level of market saturation with drugs, cosmetics and special food supplements and etc. Specific factors include common disease incidence of the population; the level and availability of medical and pharmaceutical care; the attitude to CVD problem of medical and pharmaceutical community and patients; the treatment methods; the compliance of patients; the appearance of new effective drugs. Among the factors favoring the development of phlebotropic drugs market in Ukraine can be named high number of CVD cases; the majority of female in demographic structure; considerable number of middle-aged and elderly people; the increase of conservative treatment tendencies of CVD etc. Level of usage of phlebotropic drugs is growing due to educational programs for general practitioners and pharmacists; advertisement and information materials about CVD and methods of their treatment in medical and pharmaceutical journals and popular sites and information given by medical representatives, and other ways of promotion. Factors restraining the development of phlebotropic drugs market in Ukraine include low income level of the population; low level of CVD diagnostic; underestimation of CVD problems by general practitioners, pharmacists and patients; low level of the patients' compliance. Tendency of population to self-treatment and patients' perception clinical symptoms of CVD as aesthetic problems results in uncontrolled use mainly of topical drugs, cosmetics and special food supplements.

RESEARCH OF COMMODITY POLICY OF PRODUCTION PHARMACEUTICAL ENTERPRISE

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The modern terms of pharmaceutical market development are characterized by the uncertainty of external environment, strengthening of competition, at the market, growth of requirements of users to quality of medications and terms of service. It is especially important for the pharmaceutical enterprises to adapt the commodity policy to the terms of market, simultaneously taking into account the necessities of society, as medications are the products of high social meaningfulness.

Research of commodity policy of pharmaceutical production enterprise includes such stages: the comprehensive study of assortment of produced medicines according to pharmacotherapeutical groups and medical forms, analysis of dynamics of sale, SWOT-analysis of enterprise, ABC-analysis of sales, forecasting of sale volumes of produced medicines, formulation of recommendations about the improvement of commodity policy of the enterprise.

A research object is a pharmaceutical enterprise LTD «Pharmaceutical Company «Здоров'я». As a result of SWOT–analysis the strong sides of enterprise are the reliable monitoring of market, flexible policy of prices, introduction of GMP, high qualification of personnel, adjusted sale network. Among threats are: strengthening of competition, unstable currencies course, decline of living standard of population, appearance of analogical medicines. Possibilities include introduction of new publicity technologies, development of informative industry, appearance of new suppliers, and improvement of management.

The next stage of our researches was the analysis of dynamics of products sale in the last few years, which shows that relatively considerable slump of sales volumes is connected with period of economic crisis.

The ABC-analysis of medicines was conducted on the basis of index of profit from a sale. The group A includes 4 medicines which provide 50% of the profit. This group is perspective and it deserves a maximum of marketing efforts. The group B includes 15 drugs of company profit (profit share is 30%). The group C includes 115 medicines with total profit share 20%.

XYZ-analysis was conducted on the degree of predictability of selling drugs. Forecasting of sales was conducted by the example of drugs for cardiovascular system and showed a positive trend of sales in future periods.

PSYCHOLOGICAL FEATURES OF INTERACTION OF THE PHARMACIST AND PATIENT

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Research objective: to study various aspects of professional activity of the pharmacist - "first table worker"; to find out psychological "risk factors" of work of the pharmacist: (intensive emotional communication, syndrome of emotional burning out (SEB), dropping of level of an efficiency of communication, incomplete understanding of the maintenance of the functions); to investigate methods of communication of the pharmacist and the patient; to tap the most optimum strategy of behavior and communication of the pharmacist with the patient

Materials and methods: psychological methods of communication were analyzed. The psychological negative factors connected with daily activity of the pharmacist are investigated. The most acceptable were allocated for daily use in practice of communication of the pharmacist - "first table worker" with patients methods.

The received results: with use of the questioning which has been carried out in 25 drugstores of the city of Almaty, it is established that the greatest number of claims is expressed on the incorrect relation to the visitor of a drugstore depends on type of temperament of the pharmacist. Also with questioning were defined the main demands to personal qualities of the pharmacist:

- steadiness – 38 %;
- concentration – 44 %;
- good memory of-52 %;
- attentiveness – 64 %;
- possession of speech – 48 %;
- politeness – 74 %;
- goodwill, keenness – 82 % of respondents.

Conclusions: professional principles and styles of interaction of the pharmacist with the patient are presented, his structure is offered. Ways of optimization of interaction of the pharmacist - "first table worker" and visitors of a drugstore are shown.

EVALUATION OF CONSUMER PREFERENCES OF CALCIUM CHANNEL BLOCKERS

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Medicines of different pharmacological groups, including calcium channel blockers are used for the treatment of heart disease. They reduce the need of heart in oxygen (due to the weakening strength of heart contractions) and increase its delivery (due to expansion of blood vessels). They prevent spasm of the coronary vessels, reduce the heart rate.

The purpose of our study is definition of consumer preferences at the market in the segment of the medicines of group of calcium channel blockers.

The studies were conducted on the basis of historical, documentary, logical, economic and statistical, marketing analysis, and field studies. A field studies are based on primary data collection using the methods of observation and a poll.

A results of the the poll showed that consumers prefer a calcium channel blockers by foreign producers (53.3%). At the same time, half of respondents (46.7%) preferes the domestic medicines, due to their quality and price affordability.

The analysis revealed that the main criteria for the consumer affecting the decision to buy medicines of this group are the efficiency of implementation - 10 points, safety - 8.7 points; price - 8 points, number of intakes - 7.2 points; drug form - 6.5 points.

Due to the fact that calcium channel blockers are a prescription drugs, a crucial factor influencing their purchase are a prescription by the doctor (84% of respondents).

According to the results of consumers questioning and professionals it was found that the most preferred dosage form is a sustained-release tablets (more than 31%). Studies have shown that at the market of calcium channel blockers the sales volume (in a cost and volume terms) leading positions has medicines on base of Amlodipin.

Thus, results of our studies have shown that in the process of the choice of calcium channel blockers customers prefer a highly effective and safe medicines with affordable prices. The determining factor influencing the purchase of calcium channel blockers are doctor prescription. The medicine of choice for consumers is Amlodipin.

MONITORING OF PHARMACEUTICAL MARKET OF LEBANON

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The purpose of our researches is the study of situation at modern pharmaceutical market of Lebanon. The size of Lebanon's pharmaceuticals market is $1.28 billion in 2012, an increase of 6.4 percent from $1.2 billion in 2011. Spending on pharmaceuticals was equivalent to 2.94 percent of gross domestic product last year, which ranks Lebanon in seventh place globally behind a number of small African states where international aid is distorting pharmaceutical purchasing patterns. Forecast spending on pharmaceuticals is 2.91 percent of GDP in 2012, 2.87 percent of GDP in 2013 and 2.8 percent of GDP in 2014.

70 percent of the Lebanese market consists of imported pharmaceuticals, and expected the market to remain almost entirely reliant on imports.

There are about 6,000 types of drugs on the local market, with 80 percent of them imported by about 50 firms from more than 508 factories in 25 countries. Domestic production represents 10 percent of the market in volume terms but less than 4 percent of the market in value terms.

The prescription medicines represented around 73 percent of total market value last year. It attributed the high share of prescription medicines to the widespread use of patented drugs, which account for 66 percent of total spending on prescription drugs, and to the relatively high prices of generic drugs.

The nation's consumers are faced with the task of choosing medicines for themselves and their families in a marketplace where foreign imported medicaments and locally manufactured medicaments compete but not over the same grounds. Consumers in Lebanon are of three types: high-income consumers, middle-income consumers, and low-income or poor consumers. Lebanese consumers are remarkably self-reliant when faced with treating most common health problems, choosing to call a doctor only for the most serious or specialized health care needs. In treating themselves, they rely heavily on a variety of OTC products, viewing these medications as generally safe but not entirely risk free. Many recognize the possibility that their use of OTCs may mask a more serious health problem, and many also admit using more than the recommended amount of an OTC because they felt it necessary to effectively relieve their symptoms. Consequently, consumers rely heavily on their pharmacists' recommendations and on labeling information when selecting and using these medicines.

THE ROLE OF STAFF IN INTRODUCING GMP REQUIREMENTS FOR THE PHARMACEUTICAL INDUSTRY

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Companies producing pharmaceutical products must produce it in such a way as not to jeopardize the consumers because of failure to follow safety, quality and efficiency. The responsibility for achieving this level of quality lies with the company and the guarantee of its security is a quality system. All of its components must be adequately secured by competent personnel, the actions of which largely depends on the observance of all the elements of Good Manufacturing Practice (GMP).

Today's problems in Republic of Kazakhstan is the shortage of qualified personnel in the pharmaceutical industry and needs for relatively high wages of experienced professionals.

The strategy of the pharmaceutical industry in Kazakhstan is defined in the Program for the Development of the Pharmaceutical Industry of Kazakhstan for 2010-2014, developed in the under the State Program of Forced Industrial-Innovative Development of Kazakhstan for 2010-2014, pursuant to orders of the president of the Republic of Kazakhstan. Main objective of the program - the modernization of existing facilities and construction of new pharmaceutical enterprises in line with requirements of GMP.

Implementation of GMP - an important step to significant increase the quality of products that can compete in the international pharmaceutical market.

One of the main stages of the implementation of GMP standards in a GMP pharmaceutical manufacturing is to prepare highly qualified professionals that meet international standards and requirements of the system of GMP.

We have the basic requirements for the personnel of pharmaceutical production in accordance with the basic rules of GMP and ways to implement them in the domestic pharmaceutical companies.

Identifies need gradual training personnel to work in the new conditions for close cooperation between management personnel and employees of business units. The role of managers of enterprises is to create the right conditions to ensure product quality, and production staff - in unmistakable compliance with requirements GMP.

SECTION 12

SOCIO-ECONOMIC RESEARCH IN PHARMACY

REGIONS MODERN DEVELOPMENT TRENDS STUDY

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The significance of the study is determined by the fact that state management modern development trends allow redistributing duties and authorities between the state and its regions. Nowadays, regions are becoming economically more independent.

The region is a complex social and economic system featuring a great deal of industrial, agricultural, demographic and labour power factors, as well as those of financial and social spheres. The financial sphere reflects general welfare level, investment potential, and financial safety of a region.

The goal of this work was to analyse of the existing approaches to financial safety management of a region.

The analysis showed that the changes taking place in regional financial and economic policy form two of its directions. The first direction provides for changing the structure of an economic region; the second direction consists in improving the regional development. Such an approach allows for increasing the role and responsibility of regional authorities in providing financial safety of a region.

In forecasting financial safety performances, trend models were used in the work.

According to the existing approaches to management, financial safety is mainly based on the analysis and generalization of financial and economic performances. In evaluating the effectiveness of the North-Eastern Region financial safety management, the following performances should be considered:

- volume of export and import delivery;
- gross regional product;
- unemployment rate;
- volume of foreign investment;
- region's balance of payment;
- local budget deficit.

THE ROLE OF INTELLECTUAL CAPITAL IN THE ENTERPRISE

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Relevance. At the present stage of development of Ukrainian cost is largely created by the use of not only physical assets, but also intangible - technology, relations with customers and suppliers, employees' knowledge and culture in the organization - intellectual capital.

The purpose of the study analysis of the structure of intellectual capital and the effect of its individual elements on the performance of the company.

Methods and materials research. In the study used the methods of structural analysis, content - analysis and others.

Studies have shown that the elements of intellectual capital is human capital and intellectual property. Intellectual property - are products of creative activity in the organization. In accordance with Article 41 of the Law of Ukraine "On property" intellectual property rights are the works of science, literature and art, discoveries, inventions, utility models, industrial designs, innovations, trademarks for goods and services, the results of research and other results of intellectual work. In turn, human capital includes - knowledge, expertise (skills) and professional quality of the organization.

Human capital is an integral part of enterprise management system. As the role of the human factor is increasing. And come to the fore the qualities of staff, professionalism, creativity, intellect, with abilities and skills in their respective fields, communication skills, physiological characteristics, socio-demographic characteristics.

To take their rightful place among the other countries of the world and take the path of innovative development of the economy, Ukraine should recognize national priority is the development of its intellectual capital.High level of intellectual capital of the company guarantees high performance. Without implementation of effective intellectual capital management company is not able to get the maximum profit and maintain high competitiveness of the market in modern post-industrial economy.

PROBLEMS OF UNEMPLOYMENT ARE IN UKRAINE

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One of native socio-economic problems of the modern stage of development of home economy and important description of competitiveness of labour-market is unemployment. Excessive unemployment is negatively represented on all economy of country, for this reason a study of this question for today is actual.

An aim is research of principal reasons, consequences of unemployment, and also development of suggestions in relation to the decline of this phenomenon in Ukraine. Such socio-economic phenomenon understands under unemployment, when part economically an active population application to the labour force can not find. Main reasons of high unemployment rate are such: slump of economy and corresponding reduction of the combined demand on labour force; structural changes (inter-branch, внутрішньогалузеві, regional); motion of labour force(professional, social, regional). Next to it passive politics at the market of labour is directed in support the profits of population in case of loss of work and financed from the special funds. The degree of negative influence of unemployment on the state in a country depends on the concrete parameters of economic situation. For this reason, it is a problem, that needs to be decided and that needs a deep scientific analysis and making on this basis of practical recommendations, that can be used for development and realization of effective socio-economic politics, productive employment sent to providing economically active population of country, reduction of unemployment rate to the minimum socialpossible level. Thus, it is possible to offer such measures, in relation to reduction of unemployment rate in Ukraine:

it is a decline of taxes for enterprises, on condition of maintenance of workplaces(for the compensation of charges on the reception of new workers);

it is a grant of favourable credits the state for salary payment additionally busy on a production, that in size will equal a salary;

it is creation of new workplaces, due to taking of credits for a technical reequipment and expansion of enterprises;

it is creation of centers of studies of young people to those professions, chances on employment in that most high;

it is providing of employment of перенавчання or in-plant training of shots the special services, in accordance with the necessities of industries that develop;

it is realization of the special fairs of labour for educational establishments, with the aim of employment of graduating students.

Unemployment, became a research object and by the article of research is a labour-market in Ukraine. For introduction in an action of these measures to the state necessary money, that is why I suggest to compensate these charges due to introduction of the differentiated rates of taxes, id est the greater rate of tax, accumulation of money will answer greater profits by means of state deposits with top rates, and also jumboizing of fines for violation of current legislation. Thus, inculcating the offered measures, we can attain reduction of unemployment, increase of amount of the employed population and, as a result, general improvement of economic and social situation rate in a country.

OPTIMIZATION OF PHARMACEUTICAL PATIENTS WITH LIVER DISORDERS IN TERMS OF COST REIMRURSEMENT DRUGS

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The purpose of our work is a study of assortment of medicinal preparations, which are used for treatment of illnesses in gastroenterologies, and also ways of exposure and treatment of patients, on condition of reimbursatsii cost of medical preparations.

One of the most widespread problems of modern gastroenterology is a chronic disease of liver. With this problem, in most cases, the people of capable age clash. Principal reasons is a wrong way of life, abuse of alcohol, groundless application of medical preparations majority from what metabolized in a liver and causes it`s functional overload, and also different pathologies. The leadthrough of effective drug therapy requires certain efforts and money, that not always in a sufficient measure possibly.

Basic principle of pharmaceutical help is providing of economic and physical (presence at the market of country) availability of medicinal preparations for all layers of population which is provided by functioning of mechanism of government control of pricing.

The system of reimbursatsii is the socio-economic system the purpose of which is providing of availability of medical preparations and pharmaceutical help on the whole, the subject of which are the authorized authorities which carry out compensative payments from certain sources, and the object are certain categories of diseases and patients.

Researches rotined that for today indemnification of charges on treatment of the probed category of patients is not foreseen a domestic legislation, although practice confirms such necessity.

Thus, the conducted researches rotined social exposure of domestic patients with disorders of functioning of liver and absence of mechanism of reimbursatsii cost of ambulatory consumption of medicinal preparations type patients.

PSORIASIS AND ITS PROBABLE CAUSES

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Psoriasis is a skin disease characterized by the formation of reddish spots and patches covered with silvery scales: tends to run in families.

Psoriasis comes to the front in the practical dermatology. The considerable prevalence, chronic disease with short periods of a remission, absence of a common scientifically based etiopathogenetic therapy determines extremely urgency and importance of the psoriasis problem.

Unfortunately, today psoriasis is not just a complex disease; it's a life-long condition that has its causes and initiating agents (procatarxis) that affect the severity of the psoriatic disease. Today in Ukraine among the major problems that lead to a lack of medical and social care for the patients with psoriasis, we can select the absence of a representative statistics of the dermatosis causes.

The aim of our study was the investigation and analysis the causes of the psoriasis disease among outpatients with using of the social survey method.

80 respondents have been interviewed. There were 60 percents of women and 40 percents of men among them. During the research it has been determined that psoriasis began for the majority of patients (57%) at the age of 18 years (58% of girls and 51% of young men); 98% of the respondents "got acquainted" with the dermatosis at the age of 40, notably in the most active age. It confirms the social significance of the diseases.

We have analyzed the causes of the disease. It was found that for the majority of the patients the cause of the psoriasis had became nervous and mental stress – for 41.67% of the respondents. Among the other reasons they indicated heredity – 22.06%, provoking diseases (pseudoinfluenza, flu, measles) – 12.26%, the damage of the skin – 5.88%, bad habits (alcohol, smoking) – 4.41%, the birth of a child – 6.3% of women, drugs (antibiotics, hormones, NSAIDs) – 2.94%. About 7% of the patients could not specify the cause.

Thus it was established that, using only pathogenetically-symptomatic treatment without etiological factors wasn't possible to cure psoriasis. That is why we consider the regular monitoring of the psoriasis' causes and establishment of a representative statistic as an important aspect of the problem solving.

CARDIOVASCULAR DRUGS IN THE TREATMENT SOCIALLY SIGNIFICANT DISEASES IN KAZAKHSTAN

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Within the framework of the State Programme for Development of public health of the Republic of Kazakhstan "Salamatty Kazakhstan" for 2011 - 2015 years, an improvement of diagnostic methods, treatment and rehabilitation of basic social diseases, first of all cardiovascular ones are scheduled. According to the World Health Ranking (2012), coronary (ischemic) heart disease was the cause of 48,332 deaths, or took 31.27% among 50 leading causes of the death in Kazakhstan in 2011, and together with data on mortality from coronary heart disease, stroke and hypertension, pointed percentage rises up to 50.11%.

The aim of our study was to investigate the pharmaceutical market in the Republic of Kazakhstan in the group of drugs used in the treatment of cardiovascular diseases, that has a leading position in the structure of morbidity in the country.

The study was conducted using data on the volume of retail sales and procurement of finished medicines in the pharmaceutical market of Kazakhstan for the year 2012, received from «Vi-ORTiS» consulting agency.

We determined the proportion of cardiovascular drugs, which was 8.9% in the amount of $ 140.8 million. The total range of the studied group of drugs includes 809 specimens for the treatment of cardiovascular disease (with C code within ATC classification). The main supplier countries of these drugs: Germany (105 specimens), India (80) Russia (79) Ukraine (74), Hungary (54). Producers from 35 different countries deliver 340 kinds of cardiovascular drugs on the pharmaceutical market of Kazakhstan. Domestic manufacturers (12 companies) deliver only 77 kinds of medicines. It is found that 101 ATC-C codes of the 128 ones do not contain cardiovascular drugs of Kazakh producers.

Thus, we have determined the perspective directions for development of domestic production in the field of cardiovascular drugs.

SCIENTIFIC AND PRACTICAL APPROACHES TO DETERMINING ENVIRONMENTAL RISK FOR ENTERPRISES IN PHARMACEUTICAL INDUSTRY

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Relevance of the topic due to the increase of allergic diseases, abnormalities in neuro-psychological and physical development, the deterioration of the immune, endocrine and central nervous and cardiovascular systems of the body and its reproductive function. The main reasons for the growth of environmental pollution are production processes in industry, where are ignored facts of regulatory inconsistencies jobs, low level of environmental consciousness of society, a high proportion of technology-intensive, low effectiveness of treatment facilities, inadequate legal and economic mechanisms of environmental protection. The share of the impact of these factors on health is 40%.

The aim of the study is to highlight the theoretical aspects and analyze problems in management of environmental risk in pharmaceutical companies.

Materials and methods. In study were used system analysis, clustering method and method of determination.

Results. Environmental risk conditions pharmaceutical companies – a possibility of an adverse impact on the environment or emergency situations at pharmaceutical companies, leading to the deterioration of the ecological situation in the region and public health.

Components of environmental risk for conditions pharmaceutical companies are: environmental, social, ecological, economic, natural, environmental and man-made risks, the last one in turn are divided into risk of obsolete equipment, obsolete technology and the risk of harmful substances.

On the basis of these studies determined that the appropriate method of calculating the integral indicator of environmental risk is a taxonomic method.

Conclusions. Implementation of the proposed methodology for determining the magnitude of environmental risk for pharmaceutical companies will significantly increase the degree of their competitiveness, because pharmaceutical companies that produce products necessary to maintain public health, should not cause more damage to their health.

THE SYSTEM OF REMUNERATION OF LABOUR IS AFTER GRADES

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Organization of remuneration of labour - one of key problems in the modern economy of Ukraine. On all stages of development of economy a salary was one of main factors that provide the effective system of material stimulation of workers and that form the motivational mechanism of labour activity. Stability, development and efficiency of personnel, directly depends on his motivation - as material, so not material. Exactly motivation is the primary purpose of the system of grades. Systems the remunerations of labour, that is used in our time on most domestic enterprises, morally became antiquated. It appears in that they take into account neither the specific of work of enterprise in a market economy nor different responsibility and results of labour of workers that hold identical positions. Therefore introduction of remuneration of labour after grades is actual enough.

A research object is a process of motivation, thus, as a system of grades (position positions) is the family the corporate "table of ranks", in that every cluster(grades) of positions is answered by the wage level, it will influence on the desire of workers, improve the labour. Grades is the method of creation of universal hierarchy of positions for all personnel of company; system of estimation, that allows to define the even indemnifications accepted for all workers on the basis of comparison of relative value for the company of different areas of work. On the basis of the system of grades social politics of company, motivational programs and programs of quarry development, is also developed. Mainly - a company gets possibility to pick up on the key trends of activity of necessary people and reasonably to pay a powerful lot of money to the best employees. It was educed after realization of theoretical analyses, that introduction of the system of grades on domestic enterprises envisages next advantages: optimizes placing of labour resources; will help to manage the fund of remuneration of labour and do the system of extra charge of salary flexible; will facilitate the process of codeindexing of salaries; will put in order the disbalance of salary on an enterprise; will allow to define, position of any level treats in what sum to the enterprise; will allow to remove substantial unefficiency of work; will decide the problem of extra charge of additional charges for the work, executed on standards that are below or higher post; will allow, if necessary, quickly to conduct the analysis of structure of both post salaries and permanent part of salaries, and also from to watch their dynamics.

Thus, as a conclusion can be said, that exactly the system of grades allows to "link" the remuneration of labour and business logic, and also untie the knot of the problems related to motivation of personnel.

RESEARCH OF DYNAMICS OF MORTALITY IN STRUCTURE OF CEREBROVASCULAR DISEASES

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Stroke is a major health and social problem, as it is the second leading cause of death and the first - among the disability population in all countries. Stroke has a devastating impact on lives of patients and those who provide care of them, and it is a huge financial burden on health care systems in different countries.

The aim of our study is to analyze mortality from cerebrovascular diseases in Ukraine. The main emphasis is placed on the mortality from vascular cerebral pathology in a general population during five years, according to the State Statistics Committee and the Center for Health Statistics of the Ministry of Health of Ukraine.

Mortality is one of the most important demographic indicators of public health, which characterizes the state of health of the population in terms of spreading the most severe pathology.

It should be noted that the positive typical feature of recent years is a reduction in the absolute number of deaths by 98 289 persons and overall death rates - by 11.4%. The similar trends demonstrate the mortality of the population of Ukraine due to cerebrovascular diseases for the study period. Thus, the number of deaths from cerebrovascular diseases decreased by 6,893 persons, particularly from stroke - by 2,783 persons, including ischemic stroke - 678 persons. This trend is also similar to the mortality due to vascular brain diseases (table 1).

Table 1.

The structure and dynamics of mortality from cerebrovascular diseases of the population of Ukraine

Diseases	Years	Mortality		Diseases	Years	Mortality	
		Absolute number	Per 100 000 population			Absolute number	Per 100 000 population
All cases	2007	762 877	1641,8	All strokes	2007	42 405	91,3
	2011	- 664 588	1454		2011	39 622	86,7
	Δ, %	98 289	- 11.4		Δ, %	- 2 783	- 5.0
Cerebro-vascular diseases	2007	102 503	220,6	Ischemic stroke	2007	21 006	45,3
	2011	95 610	209,2		2011	20 328	44,6
	Δ, %	- 6 893	- 5.2		Δ, %	- 678	- 1.5

Thereby the results of the analysis presented here indicate that a favorable trend in mortality in the structure of cerebrovascular diseases has been observed in Ukraine during last five years.

ANALYSIS OF THE COST OF IN PHARMACEUTICAL OF WOMEN AND CHILDBIRTH

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Childbirth - is a complex multistep physiological process that terminates pregnancy and is accompanied by birth. The correctness of delivery of birthchild largely reflects on the outcomes for both the mother and the fetus.

It has been proven long ago that the majority of complications developing during pregnancy can be prevented by correct preparing, namely by the minimazation of shortfall of vitamins, examination, diagnosis of possible disease states and their correction.

Analysis of the literature, statistical data from the Ministry of Health of Ukraine showed that timely diagnosis, correct preparation and management of pregnancy allows to birth the baby, while not sacrificing baby's or mother's own health.

The goal of our research is to determine the cost of pharmaceutical providing of the women during pregnancy and childbirth for the rational use of medicines.

To implement this goal the following tasks delivery were defined:

- to analyze and summarize the literature on the costs of pregnancy and childbirth as abroad and in Ukraine;
- to conduct the survey women heve been registered in counseling maternity centers of the Kiev in order to determine the actual cost items;
- to calculate solvency of adequacy ratio of average labor cost for the citizens of Ukraine, Germany and the USA.

Following research conclusions were drawn:

1. Data analysis and literature survey on the total cost of women during pregnancy and childbirth in Ukraine and abroad show that Ukraine accounted for a larger percentage of other costs are almost 70% of the total cost, and abroad in average direct and indirect costs are almost identical for under normal childbirth as they related as 45% to 55%, and cesarean section 52% to 48% (respectively);

2. The calculation of the solvency adequacy ratio average cost of childbirth showed that more affordable value for German citizens (average ratio - 3), then the U.S. (3.7) and slightly worse than the citizens of Ukraine (almost 4). But the quality of services have been provided differentiated significantly .

3. Conducted studies have shown that complex of training programs for childbirth and the use of drugs in pregnancy and childbirth are not rational and do not fully meet the actual requirements of women.

FORMING OF THE PROCESS MODEL OF CRO LOGISTIC ACTIVITY IN CLINICAL TRIALS AREA

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According to the research, efficiency of contract research organizations (CRO) activities in clinical trials (CT) mostly depend on reasonable logistic strategy and logistics-based management. Logistic approach in management allows increasing both profit and quality of logistic service, guarantying effectiveness of CRO flow processes management in order to get more competitive advantages in world CT market. So far as effectiveness of logistic services in CT influences the CT quality, it becomes necessary to develop the process model of CRO logistic activity. The necessity of process technologies implementation inclinical trials management in order to ensure their quality is stated in ISO standards as well.

While forming the process model of CRO logistic activity each business-process should be considered as a unit of the whole logistic mechanism of organization functioning. In this connection the compatibility and interaction of particular processes within CRO process system should be investigated. Based on the analysis it had been justified that effective logistic activity of CRO requires the integration of main business-processes in through supply chain management in order to facilitate compliance with ISO and GxP.

The most important rule to be followed while forming the supply chain logistic business-processes is concentration of all CRO logistic management functions in one subunit. This allows to ensure the optimal resources flow taking into account the dynamics of both external and internal medium, and also changes in inner through processes. Only in this case CRO enables handling of logistic in order to ensure provision of clinical center with essential medicines and biological samples in certain quantity and assortment at certain time guaranteeing the quality of all processes.

PHARMACEUTICAL MARKET RESEARCH ANTIBACTERIAL MEDICATIONS FOR ACUTE BRONCHITIS

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Respiratory diseases are among the most common infant diseases and remain social and medical issue of Pediatrics. One of the most common infectious diseases of the respiratory tract is acute bronchitis. The aim of the study was to analyze the pharmaceutical market of antibiotics used for the treatment of acute bronchitis in pediatrics.

For the treatment of acute bronchitis in childhood according to clinical protocols doctors are using 3 groups of antibacterial remedies. According to anatomical- therapeutic-chemical classification (ATC-classification) there are a group of antibiotics: J01D - other beta-lactam antibiotics, what includes cephalosporins, J01C - penicillins and macrolides J01F-(J-antimicrobial agents for systemic use, J01-antibacterials for systemic use).

According to the State Expert Center of the Ministry of Health of Ukraine as of March 2013, Ukraine has 341 registered trade names of antibacterial remeiess including registration forms. In the analysis of registered medications for the treatment of acute bronchitis for brand name was found, that the largest part are cephalosporins III generation (36% of the total number of registered medications), followed by macrolides (29%). Further housed combined penicillins (26%) and cephalosporins, I generation (9%).

Market analysis has shown that the vast majority of Indian occupied remeies (137 trade names), followed by Ukraine (108 trade names of medications). Value of tradename remeies for treating acute bronchitis in childhood of domestic and foreign production is 32% and 68% respectively.

Found that the market for these medicines is dynamically developed structure, in which the main directions of the strategy and tactics of forming mainly are making foreign companies. It should be noted that Ukraine has a wide range of antibacterial remeies, which is quite sufficient for pharmaceutical providing for children with acute bronchitis.

SOCIAL EPIDEMIOLOGICAL ASPECTS OF PHARMACEUTICAL PROVISION OF PATIENTS WITH INFECTIOUS DISEASES IN UKRAINE

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Despite the significant advances in the struggle against infectious diseases in the world, the epidemic situation in Ukraine in recent years is quite complicated. Most acutely it applies to infections, which can be warned by the prophylaxis of immunity medicines, as one of the most effective preventive measures.

The purpose of our study was the effectuation of the analysis of infectious diseases in Ukraine in the framework of the National programme of immunization and protection against infectious diseases. Statistical methods were used during the research.

According to the survey results, infectious diseases in Ukraine is undulating in nature and does not tend to decrease (tabl. 1).

Table 1

Dynamics of the registered infectious diseases in Ukraine

	$K_{2001/2000}$	$K_{2002/2001}$	$K_{2003/2002}$	$K_{2004/2003}$	$K_{2005/2004}$	$K_{2006/2005}$	$K_{2007/2006}$	$K_{2008/2007}$	$K_{2009/2008}$	$K_{2010/2009}$	$K_{av.}$
Coefficient of augmentation of the outbreaks number	0,605	1,077	1,429	0,875	1,257	1,023	1,044	0,915	1,186	0,882	1,005
Coefficient of augmentation of the victims number	4,480	0,260	1,919	0,881	0,630	0,838	1,000	0,882	1,591	0,574	0,982

According to the data of the Table 1, the maximum growth rates of outbreaks were recorded in 2003 compared to 2002 (1,429), in 2005 compared to 2004 (1,257), in 2009 compared to 2008 (1,186). On average for the studied years this index was 1,005. Maximum growth rates of the number of victims were observed in 2001 compared to 2000 (4,480), in 2003 compared to 2002 (1,919), in 2009 compared to 2008 (1,591). The average index of the number of victims for 2001-2010 was 0.982. The negative factor is that the children dominated in the structure of the affected (on average 56.3% of the total number of affected). Raises concerns that in some years number of affected children reached almost 70 – 80%.

Therefore, it can be argued, that the situation of infectious diseases among the population of Ukraine is quite unfavorable. Solving this problem, in our opinion, is to improve activities by strengthening control using of public funds for the procurement of immunobiological products, optimization of the national legislation on the quality control of immunobiological preparations, stimulation of the child vaccination.

THE ANALYSIS OF STATE OF PHARMACEUTICAL CARE OF CHILDREN UNDER 3 YEARS OLD IN THE REIMBURSEMENT SYSTEM OF MEDICINES

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Today, due to the predicament of economic situation and insufficient budget financing of health care system, the level of providing of pharmaceutical care of privileged categories population, which primarily includes of social-vulnerable people and children remains unsatisfactory. The problem is becoming stronger due to increased incidence of population in particular its children's contingent. Given the aforementioned, the objective of our work was to investigate the current state of pharmaceutical care of children under 3 years old on preferential terms. During the research we used interrogatories methods of analysis in particular questionnaires, and statistical and mathematical methods of data processing. In a questionnaire survey were involved consumers of medicines who had children under 3 years old.

According to the results of a questionnaire survey of consumers of medicines to assess the current state providing pharmaceutical care of children under 3 years old, who are eligible to receive medicines by free prescription at the legislative level, it has been found that the only 10,4 % of children under 3 years old enjoy the right to acquire medicines by free prescriptions. At the same time it has been found that the 54,2 % of respondents weren't informed about the reimbursement system of medicines to privileged categories and groups of population. Also it has been found that in case of appointment of treatment of children under 3 years old only 2,3 % of physicians proposed to use the medicines from the "Budget list" which are dispensed by free prescription.

On average their right to free and privileged medicines respondents have assessed by 5 %. In addition 59,3 % of respondents say the existing reimbursement system of medicines needs improvement. According to the opinion of the respondents, promising areas are improving the system of budget financing and introduction of compulsory health insurance, it can act as a guarantor an additional source of money for reimbursement system of medicines to the population in conditions of limited financing of national health care system. Thus, we can argue that today the pharmaceutical care of children under 3 years old on preferential terms is low enough. Such a state, in our opinion, due to the lack of compulsory health insurance and effective mechanisms of reimbursement system of medicines, and as a result, limited funding of privileged categories of population and low awareness of citizens about their privileged status.

STUDY OF THE SYSTEM OF FREE DRUGS SUPPLY IN KAZAKHSTAN

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The purpose of this study is to analyze the state of free drug supply in the Republic of Kazakhstan, as well as the results of the state program "Salamatty Kazakhstan 2011-2015" at the beginning of 2013. We used the statistics of the program, government regulations, reference literature, proceedings of the conference, professional news publications, etc.

Found that during the period 2010 - 2013 years number of items of drugs dispensed for the guaranteed volume of free medical care (GVFMA) increased from 179 to 276 positions i.e. by 44%. To the list of drugs in a free vacation were additionally included drugs in the following pharmacotherapeutic groups: antihypertensive drugs (22preparata), anticancer drugs (20), antidepressants (16), antidiabetic agents (11), antimicrobial agents (3), and the remaining seven pharmaceutical groups are a total of 25 agents.

The range of diseases that are subject to free drugs, are expanded from 46 to 49 diseases, with help of including systemic lupus erythematosus, Gaucher disease and rickets. The amount allocated for the purchase of drugs for free drugs, has increased during the study period from 77 to 85 billion tenge (10%). By increasing the funding of free drug coverage from 2012 grace holiday discount of 50% was replaced by free of charge one.

Conclusion: The increase in budgetary allocations, expanding range of diseases and increase of positions of drugs in the system of free medicine provision shows its dynamic development and meet the following state program "Salamatty Kazakhstan 2011-2015."

MODERN APPROACHES TO FORMING OF COMPETITION STRATEGY ON PHARMACEUTICAL ENTERPRISES

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The most important problem of any pharmaceutical enterprise that works in modern terms, is the problem of its survival and providing of continual development. The decision of this problem consists in creation realization of competitive edges that largely can be attained on base of the worked out and effective strategy of development of enterprise. Without regard to that research of strategy of competition and competitiveness enough works, analysis of mechanisms of providing of competitiveness of enterprises, are sanctified to in a complete measure not studied. Id est, the process of providing of competitiveness of enterprises, that includes for itself dividing into the concrete stages and requires the use of certain instruments, is investigational not enough; the clearly formed mechanism of providing of competitiveness during realization of that there are possible support and updating of competitive edges and competitiveness of enterprise is absent; investigational not enough dependence, in force of absence of objective logical and reliable models, between the criteria of competitiveness of enterprises - competitive edges and resources, sources of competitive edges .

Aim of competition strategies of pharmaceutical enterprise - to provide it competitive edges of enterprise at the market in relation to active competitors.

The key aims of competition strategy of enterprise consist in the following: to expose the theoretical and methodological aspects of determination of the optimal stages and procedures of complex development and realization of competition strategy process; to outline factors and terms of choice of effective strategic alternative and her successful realization.

The scientific novelty of research consists in a ground development of methodical and practical recommendations on creation of organizationally-economic mechanism of forming of competition strategy of pharmaceutical enterprise in new market conditions, forming of marketing of enterprises of pharmaceutical industry, that is based on the use of marketing principles of research of necessities of target groups of consumers, environment and taking into account of dezyderativ of the social ethic marketing, strategies.

SOCIAL PARTNERSHIP IS IN SYSTEM LABOUR RELATIONS ON PHARMACEUTICAL ENTERPRISES

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In becoming and functioning of labour relations of new type important role called to play social partnership - system of mutual relations between the workers of pharmaceutical enterprises, employers, by public authorities, organs of local self-government concordance of interests of workers and employers sent to providing on questions adjusting of labour relations, what is especially actual in the conditions of introduction on the pharmaceutical enterprises of the system of management of quality.

The aim of scientific research consists in opening of socio-economic relations that is folded between workers and employers, by public concerning determination of terms of will hire, payment and labour protection on pharmaceutical enterprises, providing of favourable terms of vital functions authorities.

The scientific novelty of research are consists of:

- development of hierarchy of economic interests of subjects of social partnership in the conditions of pharmaceutical production;
- ground of factors that determine economic interests of pharmaceutical enterprises;
- development of criteria of remuneration of labour of managerial staff of industrial pharmaceutical enterprises.

Task of scientific research are:

1. Define institutional bases of social partnership in the system of social labour relations on pharmaceutical enterprises.
2. Estimate the value of social partnership in perfection of remuneration of administrative labour on industrial pharmaceutical enterprises.
3. Educe tendencies and prospects of development of partnership in the system socially - labour relations and to work out suggestions on perfection of his mechanism in the conditions of introduction on the pharmaceutical enterprises of the system of management of quality.

The practical value of scientific research consists in creation of mechanism of management sociallabour relations on pharmaceutical enterprises, that will assist the increase of them financially - economic results of activity.

THE RESEARCH OF MORBIDITY AND MORTALITY FROM AIDS IN UKRAINE

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Nowadays the problem of pharmaceutical provision for patients with HIV infection and AIDS is recognized as a priority public health in Ukraine. According to international experts in Ukraine registered 440,000 people with HIV and AIDS (1.63% of the population aged 15-49 years). The rate of spread of AIDS shows that Ukraine takes one of the first places among European countries. Every day about 52 Ukrainian diagnosed with HIV infection, 12 - AIDS and 7 die.

Objects: To analyze the incidence and mortality of HIV and AIDS in Ukraine. According to the Ukrainian Center for Prevention and Control of AIDS Health of Ukraine, 01.07.2012, officially registered 10,051 new cases (incidence rate of HIV 21.9 per 100 thousand population). Incidence of HIV infection has increased in 4 regions. The largest increase was registered in Nykolaev, Dnipropetrovsk, Odessa, Donetsk and Sevastopol (from 50.6 to 28.4 per 100 thousand population). It should be noted that these regions also lead and prevalence of HIV infection among injecting drug users. Diagnosis of AIDS established in 5168 HIV-infected individuals (AIDS incidence rate is 11.3 per 100 thousand population), including 42 children under the age of 14 years. The mortality rate from AIDS-related diseases, is 4.5 per 100 thousand population. The greatest mortality from AIDS-related diseases are observed in the Dnipropetrovsk region is 14.1 per 100 thousand population; in Donetsk - 10.8; Odessa - 7.5; Nikolaev - 5.9; in Sevastopol - 8.1 on 100 thousand people. The lowest incidence of AIDS observed in Ternopol region - 1.3 per 100 thousand population, Zacarpatskiy rigion - 1.4 and Chernovtsi - 1.4 per 100 thousand population.

Analysis of morbidity and mortality from AIDS indicates substantial rate of growth. Revealed that the number of cases of AIDS every year in Ukraine is increasing, in addition, marked a significant regional difference.

RESULTS OF ANALYSIS OF HEALTH EXPENDITURE ALL OVER THE WORD

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Health expenditures are defined on the basis of their primary or predominant purpose of improving health, regardless of the primary function or activity of the entity providing or paying for the associated health services; including both the health of individuals as well as population. It covers the provision of health services (preventive and curative), family planning activities, nutrition activities, and emergency aid designated for health but does not include provision of water and sanitation.

The main goal of our investigation was comparative analyses of health expenditure in different country. According to the WHO data the world is divided into six regions. The countries with the highest and lowest health expenditures in each region have been selected (table).

Table

Countries with highest/lowest health expenditure by world regions*

Region	Highest of health expenditure		Lowest of health expenditure	
	Country	Amount per capita, $	Country	Amount per capita, $
Africa	Guinea	804	Eritrea	11
American R.	USA	7960	Haiti	40
European R.	Luxemburg	8262	Tajikistan	44
East Meditraninan R.	United Arab Emirates	1704	Pakistan	20
West Pacific R.	Australia	3945	Lao People's Democratic Republic	39
South East Asia	Maldives	355	Myanmar	14

*"Report of WHO 2012 statistics", part II

While in Lebanon there are 617 USD health expenditure per capita, that is less 40% then UAE (country with highest expenditure in the region). And Ukraine has 200 USD health expenditure per capita, that is just 2% of country with highest expenditure in the region (Luxemburg).

In conclusion our findings may be used in future investigation of improving of health system of developing countries.

RESULTS OF ONCOLOGIST'S QUESTIONNAIRE ON QUALITY OF ANTICANCER DRUGS TO ABDOMINAL CANCER

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Today there are a large number of anticancer drugs which are used for treatment of malignant tumors of various origins, development stages, localization. Simultaneously, there is a growing incidence of and mortality from malignant neoplasm. The most common form of cancers was breast cancer (429 900 cases, 13.5% of all cancer cases), followed by colorectal cancers (412 900, 12.9%) and lung cancer (386 300, 12.1%). Lung cancer, with an estimated 334 800 deaths (19.7% of total), was the most common cause of death from cancer, followed by colorectal (207 400 deaths), breast (131 900) and stomach (118 200) cancers. So in time are improving of existing approaches of the pharmacotherapy of the most socially significant malignant pathologies that include stomach and rectum cancers.

Purpose: analysis of expert evaluation of medicines used for the treatment of patients with stomach and rectum cancer by calculating the average of multidimensional expert opinion in the following parameters - "Efficiency", "Side Effects", "Frequency assignment", "Prospects" and "Availability". Materials and methods: the task was performed by the method of questionnaire survey of experts in the field of oncology. The questionnaire included 48 medicines for the treatment of cancer of the stomach and rectum. It was questioned 35 specialists (oncologists) hospitals of different cities of Ukraine. Results processed using MS Excel.

Results of calculations according to all medicines were ranked into three groups (h): a high level h_1 - from 1.46 to 1.05, consist of 28 medicines, accounting for 58.33% of the sample, the medium level h_2 - from 4.1 to 0.64, which have included 13 medicines, which totaled 27.08% of the sample; h_3 - conventionally below 0.63, which included 7 medicines, which share 14.58% is. Maximum value - 1.46, the minimum - 0.22. Number of medicines with the assessment of medium and high levels - 41, which were 85.41% of the total number of medicines. According to the results of ranking the values of the medicine's index multidimensional medium for further studies recommended the use of the medicines from the groups h_{1-2} - with high and medium multidimensional expert opinion (value).

Conclusions: in order to improve the efficiency of treatment of patients with stomach cancer and rectal cancer the regimens of the pathologies treatment should include anticancer medicines with high and medium levels of multidimensional expertise (expert opinion).

INTESTINAL INFECTIONS IN CHILDHOOD: APPROACHES TO PHARMACOTHERAPY OF VIRAL DIARRHEA

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Rotavirus infection is a form of acute intestinal infection, which is determined by the rotavirus (genus Rotavirus, family Reoviridae). Come down with rotavirus infection is possible at any age, but most common this disease is among children. The virus is transmitted by the fecal-oral route. It infects and damages the cells that line the small intestine and causes gastroenteritis (which is often called "stomach flu" despite having no relation to influenza). Consequence of diarrhea is dehydration, which is linked with the main risk of the disease. Disease with adequate therapy usually ends after 4-7 days with full recovery.

To investigate current approaches to the treatment of viral diarrhea in childhood 257 hospitals sheet charts of patients aged from birth to 9 years of Vinnytsia, Chernihiv, Mykolaiv and Zhytomyr regions were estimated. Analysis by gender had howed that nearly 60% of patients are boys, so morbidity of viral diarrhea is slightly higher among boys. Exploring the age structure of patients led to the conclusion, that the highest level of disease is among children from 7 to 24 months - more than 50% of the sample (132 persons).

Analysis of prescriptions to patients with viral diarrhea (enteritis) had showed that the most widespread medications in regimens are antimicrobial remedies used for the treatment of intestinal infections (proportion of prescriptions 11.7%) and antimicrobial agents for systemic use, which largely consists of cephalosporin antibiotics (proportion of prescriptions 5,1%) and aminoglycosides (0,80%) (ATC groups A07AX, J01DD, J01GB). Mostly, illness is accompanied by fever, so significant part in therapy take antipyretics (ATC groups M01AE, N02BE) – 3,91%. Major role in improvement of condition of the patient plays restoring water and salt balance, that's why in every case of the disease leading method to combat dehydration is rehydration. In some cases, instead of infusional therapy which is less physiological for children, comparing with oral agents, are used saline solutions for oral rehydration (ATC group A07CA), proportion of prescriptions is 4,70%.

The real structure of children with viral diarrhea by gender and age has been investigated. Also prescriptions for treatment of the disease by pharmacotherapeutical groups have been analyzed.

The obtained results may be used in further studies to optimize pharmaceutical providing children with a diagnosis of "viral diarrhea."

ORGANIZATIONAL AND LEGAL REFORM OF HEALTH CARE SYSTEM IN TURKMENISTAN

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To increase the efficiency of the health care policy reform is conducted and is an important part of social policy. Therefore, in July 1995, Turkmenistan has developed and implemented the State program "Saglyk" (Health), which became the political foundation of health reform. In 2011, the State Programme of the pharmaceutical industry in 2011-2015 was approved by the President of Turkmenistan. The purpose of the program is to reduce the dependence on imported Turkmenistan medicines (drugs) and the use of its own production capacity, raw materials, science and technology. The implementation of the "State program of development of pharmaceutical industry of Turkmenistan for 2011-2015" would modernize production capacity of the domestic pharmaceutical industry, set up production of strategically important new drugs that provide the population with high-quality drugs, develop science and technology and innovation, to achieve its refocusing on import substitution and growth export opportunities.

In 2010 it was created Turkmen State Scientific and Production Association "Turkmendermansenagat." It includes agribusiness "Desperado," pharmaceutical company «Saglyk», joint venture "Turkmenderman - Ajanta Pharma Limited" and the plant "Tenekar." Today, Turkmenistan pharmaceutical companies produced more than 200 drugs that meet international standards for quality and efficiency. They include such medicine form as solutions for injection, capsules, tablets, ointments, extracts, syrups. It should be noted that the domestic drugs dispensed by prescription insurance with payment of 90% of their value.

As part of the "State Program of Medical Industry, 2011-2015" in order to improveof satisfaction the needs of the population in the domestic production of medicines, expanding the range of pharmaceutical products, improve its quality and affordability by Turkmen State Scientific and Production Association "Turkmendermansenagat".

Today, Turkmenistan's policy aims to improve the pharmaceutical supply of the population through the establishment of effective, safe and quality medicines produced domestically.

FORMING OF ORGANIZATIONALLY-MOTIVATIONAL MECHANISM OF COMMERCIALIZATION OF INTELLECTUAL PROPERTY IN PHARMACY

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Currently efficiency of intellectual property system determines a competitiveness, strategic positions and prospects of development of modern pharmaceutical enterprise. The balanced and effective control system of intellectual property allows to the enterprise in good time to react at a current market situation and global processes in the world pharmaceutical market.

Purpose of work is analysis and systematization of methodical approaches of forming of organizationally-motivational mechanism of commercialization of intellectual property in pharmacy.

Activation of scientific and innovative activity in pharmacyis carried out with the use of one of two basic approaches. First from them, at the level of company, includes: cut down tax on innovative companies, development and introduction of the scientific government program, creation of centers of informative support of inventors, noncommercial distribution of results of fundamental researches as scientific and technical information, Internet-resources, conferences, symposiums, exhibitions. It is necessary organization of the patent-licensed services in companies. Thus the primary purpose of patent policy of organization supposes forming of strategic aims of innovative company in the field of intellectual property and also rights and duties in area of the patent-licensed activity both companies and its employees, providing of balance of their interests.

The second approach, at the level of inventors, is based on strengthening of their innovative activity in organizations. Following principles are necessary adhered: material and moral encouragement of authors of suggestions, inventions and developments; maintenance of effective communications with colleagues both into a firm and after its limits; promotion. The special policy for inventors, which including the large circle of legal, financial, organizational and other directions must be developed, and the wide spectrum of stimulants actions must be used.

It was established that forming of organizationally-motivational mechanism of commercialization of intellectual property in pharmacyallows to the pharmaceutical companies to support and extend quality and efficiency of the activity, to increase at the pharmaceutical market of Ukraine part of domestic preparations accessible for the wide layers of population.

RESEARCH OF ROLE OF ELASTICITY OF DEMAND AND SUPPLY IS IN ACTIVITY OF FIRM

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Elasticity - one of the most important categories of economic science. The concept of elasticity allows to find out how adaptation of market is to the changes of his factors. It is usually assumed that at a price increase on a wound businessmen are advantageous to promote suggestion of commodity, promote the volumes of realization. However so is not always: a situation is possible, when the increase of price will result not in a height, and vice versa, to the decline of profit yield by virtue of reduction of demand and corresponding reduction of sale.

Purpose: the impact of the elasticity of demand and supply in the activities of the company.

Research object - the elasticity of supply and demand.

Article of research -depending on the factors and determining the effect of elasticity on the activities of the enterprise.

Methods: content-analysis of concept “Elasticity”.

Researchers showed that on elasticity the amount of accessible commodities-substitutes, place of product, influence in the budget of customer, his belonging to the articles of necessity or luxury, and also duration of analyzable period of time is all the factors influencing on elasticity of demand. Really, at a price increase we can give up the additional pair of shoe, valuables, but hardly we will shorten purchase of bread, meat and milk. The practical value of coefficient of elasticity consists in the facilitation of prognostication that, which one industries have chances on prosperity, and what in the future, more credible than all, stagnation expects. For example, high positive elasticity of demand on cars portends prosperity in a motor-car sphere on a long-term prospect, while subzero elasticity on the profit of demand on an agricultural produce supposes chronic difficulties. The different types of elasticity differently characterize a market condition: elasticity of demand at price shows on how many percents one variable economic quantity will change at a change other on one percent, and can be used by an enterprise for planning of production and realization of products volumes. Thus, elasticity of demand is the necessary factor of prognostication of behavior of enterprise at the market, as in a long-term prospect as well as in short-term.

RESEARCH OF INFLUENCE OF SOCIAL STRESS ON THE DEVELOPMENT OF CARDIOVASCULAR DISEASES

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It is well known that a human is a social being and his health is closely linked to the social welfare of the atmosphere around it. Most stresses have a social origin, their beginning is due to many factors, among which the most important are the social, sociopsychological and personality factors. People, who are constantly experiencing stress, are prone to a variety of diseases, including depression, allergic reactions, peptic ulcer disease, cardiovascular disorders and some types of cancer. The aim of our study was to determine the effects of social stress on the development of cardiovascular diseases. The study used systematic and comparative methods.

The current economic and political situation in Ukraine creates for human increased mental stress – at work, on the street, at home. The high degree of mental trauma and strain of higher nervous activity may cause the transition to chronic emotional stress, which underlies the development of coronary heart disease. It should be noted that a large number of stressful situations and negative emotional effects of inhibiting the activity of the cerebral cortex. The weakening of control by the cerebral cortex leads to disruption of vascular tone.

According to research by the American Wake Forest University Baptist Medical Center, social stress stimulates the release of hormones that leads to the postponement of fat on the internal organs, which in turn provokes the development of coronary atherosclerosis, the clogging of blood vessels. It has been found that natural protection from the negative effects of stress is the hormone estrogen, which causes the existence of gender differences, including susceptibility men to cardiovascular diseases in a younger age than women. Also it has been found that hormonal imbalance leads to rapid development of hypertension, coronary heart disease and other cardiovascular diseases.

Thereby social stress is one of the leading factors of cardiovascular diseases, which should be considered when developing treatment programs and prevention this pathologies.

FEATURES MANAGEMENT OF THE INTELLECTUAL CAPITAL AT THE PHARMACEUTICAL ENTERPRISES

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Actuality. In the modern world there are important economic transformations associated with the intensification of accumulation and use of intellectual capital. Unlike the previous period, when the determinatives of development were material substance and financial capitals, intellectual capital has become increasingly important today. As follows from works of many scientists-economists, an intellectual capital is the strategic factor of economic development.

A research aim consist in determination of intellectual capital structure that is based on his consideration in three aspects: as a factor of production, as an object of right of ownership and as an intangible asset (object of possession, authentication and estimation).

Research materials. Because the conception of intellectual capital began to emerge comparatively recently - at the end of 90th of XX of century, important scientific problem of effective management of intellectual capital at the enterprise level, the separate aspects of that were investigated by such known specialists, as T. Styuart, L. Edvinson and M. Meloun, E. Bruking, F. Yevdokimov, M. Lepa, V. Neyenburg, A. Kozyryev, M. Bendikov, A. Voronkova, A. Stupnitskiy and other, it remains unexploited: formation mechanism of intellectual capital, the definition of criteria and develop methods to assess the effectiveness of the management of this resource. In addition, conception of intellectual capital, his determination needs further research as an economic category, analysis of his structure.

Got results. The conducted analysis showed that, on domestic pharmaceutical enterprises generally no defined approach to the use of non-material assets due to the complexity of their identification, existing imperfect legislation and insufficient development of methodical recommendations for their assessment.

Conclusion. Using the proposed approach to determine the structure of the intellectual capital of pharmaceutical companies will make it more objective valuation, which significantly affects the market value of the pharmaceutical companies.

PROBLEMS AND PERSPECTIVES OF INNOVATION ACTIVITY IN UKRAINE PHARMACY

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The success of pharmaceutical production depends on the use of modern technology and competitiveness of drugs - from matching their recent achievements of scientific and technological progress. Practical use of innovative ideas in pharmacy leading to the creation of original drugs, the use of innovative technologies for production, application of new ideas organizational and economic nature.

As a result of studying the works of the leading scientists in the field of pharmacy found that the most relevant innovations in pharmacy are: production of new medicines; improve technologies; new methods of promotion; innovation in logistics and marketing pharmaceutical companies; innovative methods of personnel management.

The aim of the study is to create socio-economic and organizational conditions for effective reproduction, development and use of scientific and technological potential of the company, ensuring the implementation of modern clean safe, energy-saving technologies, production and marketing of new competitive drugs.

The objective of research are: provide financing resources priorities of scientific developments; expanding sources of funding on specific targets, venture funds; creating mechanisms to encourage and efficient use of private and foreign investment in priority research and development; initiation create parks, techno, business incubators and scientific centers.

Scientific novelty of the work is to develop a methodology for assessing the effectiveness of Implementation of innovation in the pharmaceutical company using economic and mathematical modeling.

Thus, the importance of innovation for sustainable economic development of the pharmaceutical companies is recognized in most countries of the world. However, implementation of Ukraine features innovative advances in pharmaceutical science greatly complicated by the lack of stable funding innovation and support from the state.

FEATURES OF GROUND OF PROJECTS DECISIONS IN THE CONDITIONS OF RISK

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Relevance of research. Expansion pharmaceutical companies associated with the implementation of relevant projects, the analysis of which should justify taking better option.

The purpose of the study is to determine the criteria by which a decision on the most appropriate options for implementing the project.

Materials and methods. The starting materials for the study served as the theoretical framework of project analysis, literary sources of investment management, practical advice on evaluating the effectiveness and risk of projects. Methods: Analysis, matrix method. Determining risk of design solutions was carried out according to the criteria: variation, standard deviation, coefficient of variation, criteria Bayes, Wald, Laplace, Savage and Hurwicz.

Results. To identify features selected application in the analysis of the literature of design criteria decision making under risk was investigated alternative investment project. Description of options: 1) the acquisition of new equipment, 2) reconstruction of the workshop and purchase new equipment. For each of the options considered two conditions of financing the project: 1) at their own expense; 2) the own funds (50%) and loans (50%).

To determine the effectiveness of the design decisions were calculated metrics such as net present value, profitability index, discounted payback period, internal rate of return. Considering two alternatives for the above parameters, it was concluded that both options are effective, but all indicators are more effective is the second option.

The analysis of criteria Bayes, Laplace, Wald, Savage and Hurwicz, one could argue that the less risky is the second version of the project.

Conclusions. With all of the estimated parameters, we can conclude that the most appropriate criteria to introduce a second version of the project - reconstruction workshop and purchase new equipment. All performance evaluation of investment projects are each in close relationship and provide an opportunity to assess the effectiveness of various parties. Also in the study and selection of the projects should also performance indicators and criteria considered comprehensive risk investment projects.

PHARMACEUTICAL MARKET RESEARCH OF MEDICINES AGAINST TUBERCULOSIS IN UKRAINE

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With the global financial crisis were performed many social protection programs of chronic deseases. In Ukraine, the fight against the epidemic of tuberculosis is recognized as one of the main priorities of the state policy in the field of health. According to statistics in 2011, 30 659 people contracted tuberculosis, including 937 - children under 18 years, and died about 6500. It should be noted that the structure of morbidity according to age groups leading position occupied by citizens of working age - 81%. In terms of the prevalence of tuberculosis, Ukraine is in seventh place in Europe and fourth in the world - for its multi-form. Therefore, the problem of using modern and more effective methods of early diagnosis, treatment and prevention of desease appears as actual medical and pharmaceutical issues and socio-economic lines. One of the steps to solve this problem is to study multi modern pharmaceutical market of medicines against tuberculosis to determine the main trends of its development.

Objects. The main purpose is to study the current problems of pharmaceutical care of patients and Ukrainian market of medicines against tuberculosis.

The analysis of the State Register of drugs Ukraine as of 01.11.2011 was found that in Ukraine 269 protyvotuberkuloznyh trade names of drugs (including registration forms) at 31 INN (including combined) from 76 manufacturers 15 countries. In the analysis of registered drugs to treat tuberculosis brand name has been found that the largest share are medicines against tuberculosis II series, 69.88%, of which the bulk of ciprofloxacin - 22.3% of all drugs, ofloxacin and gatifloxacin 14.13% and 7 and 8%, respectively. Drugs and several second place, namely rifampicin (5.95%), ethambutol (4.09%), pyrazinamide (3.72%), isoniazid (3.72%), rifabutin (2.23%). Analysis of the range showed that the vast majority take drugs Indian - 133 and Ukrainian - 93 medicines. It should be noted that the share of foreign drugs is quite significant is up to 62.43%. Among the dosage forms 54.28% occupied tablets, 14.5% - capsules, 17.10% - solutions for infusion / etc 'injections, 6.69% - powder for solution for infusion / etc' injections, 3.72% - granules.

After analyzing all the data presented it can be concluded that Ukraine medicines against tuberculosis range is quite wide, which allows for effective treatment.

RESEARCH OF SOCIAL INTELLECT AS LEADING PSYCHOLOGICAL FACTOR WHICH PROMOTES EFFICIENCY OF WORK OF PHARMACISTS

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For today the Social intellect (SI) appears one of leading psychological factors, on which efficiency of co-operation between a pharmacist and patients depends. Diagnosticating of level of SI allows to examine him not only as basis of socialization and adaptation of pharmaceutical worker in modern society but also as a necessary condition of successful capture by professional skills and adaptations in a professional environment.

Social reality of contemporaneity pulled out on front-rank positions the basic requirements to the pharmaceutical workers which require the presence of such criteria from specialists, as a persistence, initiativeness and social competence.

In connection with it, the more actual is become by the competence approach to a selection, to the studies and placing of pharmaceutical workforce. It allows to examine SI not only as basis of socialization and adaptation in modern society but also as a necessary condition of successful acquisition by professional skills of specialist and adaptation in a professional environment.

SI - ability to understanding of the intentions, senses and emotional states of a human after verbal and unverbal displays and assists to development of foresight in interpersonality relations. A SI is examined as a system of intellectual capabilities, constrained, above all things, with cognition of behavior information. The psychological factor is professionally important quality for the pharmacy workers of and allows to forecast progress of their activity. A SI is the difficult, integral system of interdependent cognitive capabilities, effective development of which is related to the certain stages of forming of psycho-social and cognitive spheres of personality.

It is necessary to notice that the modern specialists of pharmaceutical branch often appear not ready to social co-operation and acceptance of the proper structural decisions in professional activity.

Thus, presence well the developed skills of SI is not only a social category but also appears a necessary professionally important factor which must be enforced to the workers of pharmaceutical industry and is a near-term criterion which allows to forecast progress of their activity.

IMPROVEMENT OF LOGISTIC SERVICING PROCESS AT THE PHARMACEUTICAL COMPANY

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Object of research is to define the ways of increasing the efficiency of the logistics process of customer service at the pharmaceutical company in quality management.

Results of work were based on use of approach process development of advanced process model of logistic servicing at the pharmaceutical enterprise.

It is proved that logistic servicing of the pharmaceutical companies should be considered as a way of consecutive performance of functions and operations on ensuring supply of medicines of the corresponding quality to the client taking into account their individual needs for conditions of optimal expenses for a performance of the mission of participants logistic pharmaceutical chains on timely providing the population with necessary and qualitative medicines and commercial interests realization of participants of a logistic chain.

By results of research process model of logistic servicing at the pharmaceutical company was improved and adapted for requirements of the international quality standards and proper practices (GDP, GSP).

It is proved that results of researches will allow to increase quality of logistic servicing of the pharmaceutical company and also to increase efficiency of providing population with medicines.

ESTIMATION OF INNOVATIVE POTENTIAL OF KHARKOV REGION

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Relevance of the study determined the expansion of innovative sphere, the intensification of innovation, which is an important priority for the region's development. Combining scientific potential with other elements of local economic complex is a necessary prerequisite for successful socio-economic and cultural development.

The purpose of research is to evaluate the innovative capacity of the region.

The object of this work is the innovative potential of the Kharkov region. Item – analysis of individual components of innovation potential, namely the latest technical equipment companies, highly trained, state support.

The study identified the main problems and prospects of increasing innovation potential Kharkiv region using tiered SWOT-analysis. Evaluation showed a high level of innovation infrastructure in the region. It includes a dozen independent organizations and dozens of units of scientific and industrial organizations and enterprises ("Kharkov Technologies," Industrial Park "Rohan", Kharkiv Centre for Scientific Technical and Economic Information), patent information departments, laboratories and departments' of commercialization developments marketing departments, technical schools etc.

To go on an innovative way of development is important to ensure an adequate system of support and funding technological development, reorientation and upgrading of enterprises, restructuring, introduction of innovative motivation to maximize the innovation potential. Despite the difficulties and obstacles innovation developed in the Kharkiv region, which increases its attractiveness.

THE BASIC ASPECTS OF THE NATIONAL PHARMACEUTICAL INDUSTRY IN THE REPUBLIC OF KAZAKHSTAN

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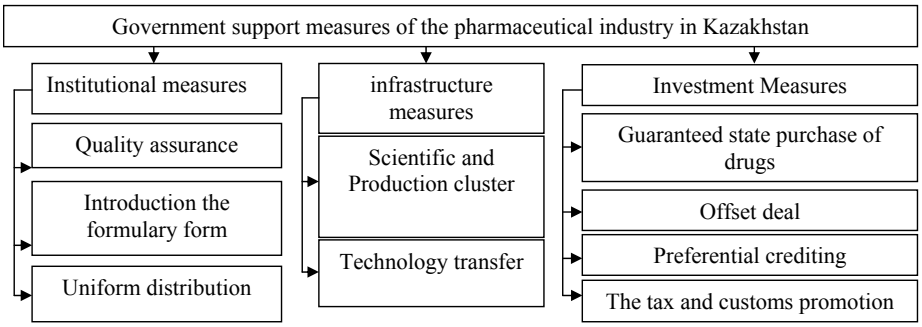
The Program for the development of the pharmaceutical industry in 2010-2014 was approved in August 2010 by the government of the Republic of Kazakhstan. The basic objective of the program is the modernization of existing pharmaceutical production and construction of new pharmaceutical companies, introduction of GMP. By decision of Kazakhstan Public health ministry the domestic manufacturers should move to the present standard by the end of 2014.

The national policy of the pharmaceutical industry supposes implementation of appropriate institutional, infrastructural and investment measures in combination with wide government support of the pharmaceutical industry in Kazakhstan. We analyzed the specified complex of measures necessary for the successful realization of the state reform program of industrial pharmaceutical sector of economy in Kazakhstan (Fig. 1), improvement of investment climate, increase of product quality, development of domestic enterprises competitiveness.

Fig.1



The basic measures of domestic pharmaceutical industry government support

Phased implementation of these measures in the activity of pharmaceutical companies of Kazakhstan will require joint fruitful efforts of the government, sector of the national economy and effective scientific developing national pharmaceutical science.

SECTION 13

QUALITY MANAGEMENT IN THE PHARMACEUTICAL AND MEDICAL INDUSTRY OF UKRAINE

ON THE RELEVANCE OF SEARCH FOR THE RATIONAL ASSESSMENT METHODS OF THE PHARMACEUTICAL QUALITY SYSTEM'S EFFECTIVENESS

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The dynamic development of the pharmaceutical market and increasing competition are placing new demands on the organization of pharmaceutical companies' management. In these circumstances, the implementation of quality management systems (QMS) in accordance with the international standards ISO 9000 is a strategically-based solution. In pharmaceutical enterprises, such systems are called pharmaceutical quality systems (PhQS). One of the important aspects of the PhQS is to constantly assess and monitor its effectiveness in order to analyze the causes of discrepancy and reduce risks to quality.

Our research is aimed at studying the approaches, methods and tools used in assessing the PhQS effectiveness. The methodological basis of the study is the statistical and other methods of QMS effectiveness assessment employed at the leading domestic and foreign enterprises. Information base: industry regulatory requirements, published and enterprise data. The study uses comparative, documentation, operational, factor and logical analysis methods. The subject of this study is the PhQS, and the object is the procedures for monitoring and assessment of the PhQS processes.

We have investigated and analyzed the approaches and methods of performance assessment of different management systems' processes. Among modern methods, the following are most commonly used: the method of comparison of the planned and achieved processes output values and characteristics, the calculation of QMS effectiveness based on the expert scores, model of index normalization of effectiveness assessment, enterprise effectiveness and QMS maturity level self-assessment methodology, integrated approaches to quality management self-assessment that include audit, QMS analysis, self-assessment according to the defined criteria, self-assessment according to the criteria of international models of excellence, additional methods – instrumental, registration, computational, sociological. In our view, the calculation of QMS effectiveness based on the expert scores is the most rational method to assess the PhQS effectiveness, which is the subject of our further research.

METHODOLOGICAL ASPECTS OF EDUCATIONAL STANDARDS OF TRAINING SPECIALISTS QUALITY MANAGEMENT IN PHARMACY

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Effective pharmaceutical quality system (PQS) is the most important element of achieving competitive domestic pharmaceutical products through unquestioning quality. However, today the acting PQS is ineffective mostly due to the lack of specialized knowledge of quality management (QM) in the heads and specialists of pharmaceutical companies (PC).

In this survey we have analyzed the situation in Ukraine and the world concerning training of QM in general and pharmacy in particular. As a result from the analysis we found that in Ukraine specialty "QM" is not included in the classifier according to Resolution № 787 of the Cabinet of Ministers of Ukraine on August 27, 2010. In Europe at the moment in "QM" trains specialists in 28 countries and more than 90 universities and business schools. In the European Union there is a single coherent system as the European Organization for the preparation, registration and certification of specialists in QM. Therefore, the need for specialized knowledge in professional quality department of the PC is no doubt. This problem can be solved by developing and implementing educational standards of training of QM in pharmacy-based competency approach.

The aim of our work was the detailed study of the functional responsibilities of professionals QM of the PC in the design, implementation and operation PQS based on the experience and mistakes in creating PQS national experts and achievements of foreign scientists. With this experience we have identified and proposed core competencies for future QM specialists. Among them, identified the following: the ability to formulate goals and objectives within PQS processes, develop process model PQS; apply methods and tools for analysis and optimization of processes PQS, to determine appropriate resources to implement and support PQS and others. Also for the effective application of management and skills training programs to professionals QM proposed that such vocational and practical subjects as means and methods of quality management, basic system approach qualimetry, document management, QM processes, TQM, statistical methods in QM, certification and standardization of pharmaceutical products, metrology and measuring equipment and other subjects.

Thus, the formation of the specialty "QM" will allow specialists with the best way to implement quality standard ISO 9000, make PQS useful for PC and workers by embedding it in a system of PC.

VALIDATION OF THE CHOICE OF NEUTRALIZATION METHOD FOR THE ANTIBACTERIAL FUNCTION OF A DRUG DURING THE CONTROL METHODS OF MICROBIOLOGICAL CLEANLINESS

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In the drug control phase according to the characteristic of microbiological cleanliness at the stage of the methods development it is worse to take into account all the factors, that can influence its producibility under a routine control. One of the neutralization methods is the dilution method. The expediency of the choice of such method should be proved.

The aim of this work was to check, if it is worse take into account the stage of the pre-amplification, using the method of control of microbilogical cleanliness, at the sample of plant extracts. Acceptance criteria was chosen according to The State Pharmacopoeia of Ukraine (SPhU) 1.4. Reducing the amount of the test-microorganisms cells in compare with control was counted as a coefficient of the methods applicability, which meaning shouldn't be higher then 50 %:

$$C_{\text{of applicability}} = \frac{(CFU_{\text{gotten with the sample}} - CFU_{\text{ogotten during the positive control}})}{CFU_{\text{ogotten during the positive control}}} \times 100\ \%,$$

At the first stage of the development taking into account the known antibacterial activity of the drugs there was chosen the dilution method for the neutralization. The first method didn't include the stage of the pre-amplification, that means that the inoculum of the test-microorganisms was put directly into 1 ml of the drug and was planted at the double-dish. By the second method whole the volume of the prepared sample was inoculated and it was held for different time: 5, 15, 30 minutes.

As investigation result were gotten dates of the meaning diapason of C of applicability % under different conditions of the experiment was: 2-15 % without pre-amplification, 30-60 % with pre-amplification and exposition of 5 minutes, 40-80 % with pre-amplification and exposition of 15 minutes, 60-100 % with pre-amplification and exposition of 30 minutes.

As we can see from the experiment, the first neutralization method using the dilutions without the pre-amplification stage gave us false positive result of the applicability of the method.

As a result, there were chosen other methods for the neutralization of the antibacterial action: method of the membrane filtering and dilution method, using in activators.

SECTION 14

INFORMATION TECHNOLOGY IN PHARMACY AND MEDICINE

CREATION OF THE APPLIED SOFTWARE FOR MULTICRITERIA OPTIMIZATION MODELS FOR OPERATION WITH WORKING CAPITAL FUNDS OF PHARMACEUTICAL ENTERPRISES

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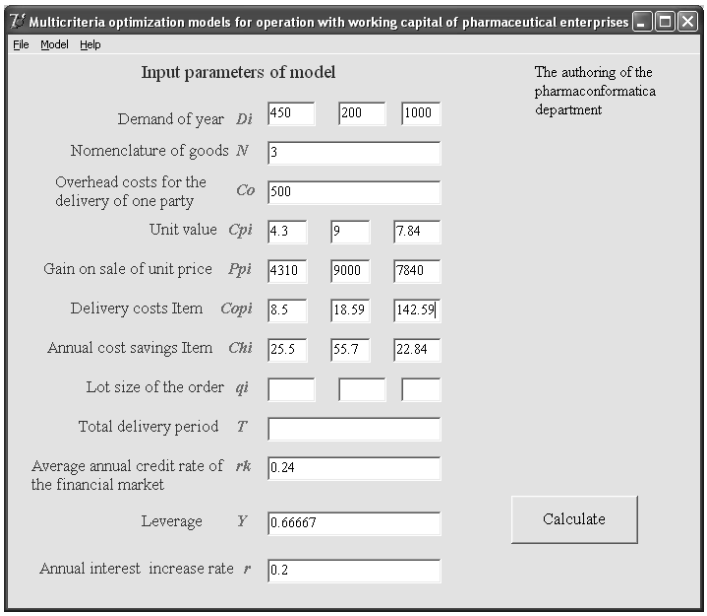
The modern phase of economic development in the pharmaceutical market of Ukraine is characterized by scarcity of funds and temporary insolvency of some members. It requires improvement of the existing optimization models of management with working capital funds of the pharmaceutical enterprise. One-criteria or multi-criteria optimization models for management tasks of funds of the enterprise, considering the cost money over time can be used as such models. The goal of creating software is automatization of calculation of optimal (while ensuring the maximization of the intensity of the enterprises incomes flows) period of product supply and batch size of drugs by the pharmaceutical enterprise. These parameters objectively reflect the capabilities of the pharmaceutical enterprise. The input parameters for the calculation are representing in the picture 1.



The results of the modeling with established programs, graphically demonstrate that the use of multi-criteria models of working capital management leads to the significant changes in the optimal values of the periods of supply and size of drugs batches. In this case the defined parameters are adequately mapped with the real characteristics of practical activities of the pharmaceutical enterprise. This, in turn, can be used in the recommendation development to improve the management of working capital of the pharmaceutical enterprises.

DIGITAL PROCESSING OF LIGHT SCATTERING PATTERN WHEN MEASURING THE SIZE OF MICRO-PARTICLES

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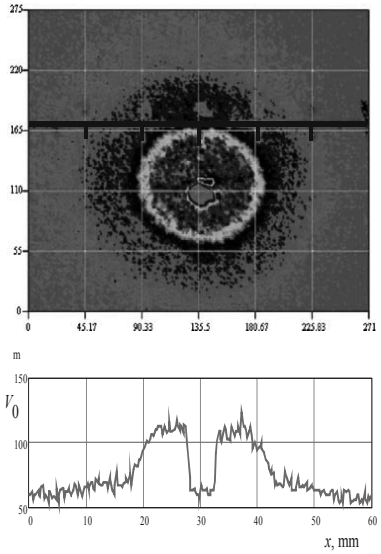
The paper deals with the method of measuring the size of micro-particles. The method is based on the computer processing of digital image of scattering pattern. Optical methods are often used for measuring the size of micro-particles and based on the fact, that the shape of scattering pattern by particles depends on the relation d/λ (d is particle size, λ is radiation wave-length).

Pollen of a plant was chosen as an object of the experiment. As it turned out its particles have the shape near to spherical.

The particles are placed between two glass plates. The laser radiation (λ = 0.65 μm) goes through the plates and falls on white screen, which is placed at the distance of L = 307 mm from plates with particles. The scattering pattern looks like a system of concentric light and dark rings, because all the particles are of approximately identical size and shape. The angular dimensions of rings can be found from the analysis of diffraction problem about plane electromagnetic wave on a sphere:

$$F(\varphi) = \rho^4 \left(\frac{J_1(\rho\varphi)}{\rho\varphi} \right)^2,$$



The scattering pattern and intensity distribution along its axis

where $\rho = \pi d/\lambda$, φ is scattering angle, $J_1(z)$ is Bessel's function. Sizes of diffractions rings (positions of minima and maxima of intensity) are determined by the values of zeros of Bessel's function

In our experiment we have found the parameter of diffraction problem: ρ = 68.8. Diameter of particles can be calculated by the formula $d = \frac{\rho \cdot \lambda}{\pi}$. At the wave-length of laser irradiation λ = 0.65 μm the diameter of pollen particles equals to d = 14.2 μm. The obtained number coincides well with the value of particle size obtained by means of a microscope.

METRIC APPROACH BASED CLASSIFIER

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The main objective of supervised classification problems is to construct the rules (classification algorithms, or classifiers) to assign objects to one or several prescribed groups. In medical applications such kind of tasks appears when one needs to predict lethality of a disease, or to estimate patient's grade of severity, in differential diagnostics of sicknesses, gene structures analysis, image recognition, etc. There exists the category of classification methods, which use information about objects' similarity or diversity computed as based on distances between them (metric approach). As a rule these methods are in use for unsupervised classification, i.e. to solve so-called clustering or taxonomy problems. When solving a problem of metric classifier construction, classes are always treated as some subsets of the space (set) of objects. Values of feature variables serve as an object's coordinates in the space; and a classifier can be constructed as a separating surface in this space. Another grounding to build a classifier is to use distances between the object and centers of classes, or nearest neighbors in each class (and the like), to evaluate estimated probabilities of object's belonging to each class.

In contrast to the standard method described above we do not treat classes as subsets of the space of objects, but as additional qualitative feature variable which describes the object. This gives us ability to build the mathematical model for dependent variable ("class") prediction by the rest of feature variables values. The model's construction results from sequential answers for the series of questions: 1) how strong is the influence on the classification of each of the predictor variables; 2) how the weights (contributions, loadings) of predictors change in different classes; 3) how the weight of each predictor changes depending on its values.

As a result we get the classification algorithm model, based on evaluation of estimators of object's belonging to classes, which allows to comply with the influence of both quantitative and qualitative feature variables; as well as to take into account non-linearity and non-monotonicity of estimator's change depending on the change of predictor variables.

Appliance of the model developed to the number of real medical experiment originated data sets has resulted in obtaining classifiers, which have form 80 up to 95% trueness of recognition. This fact gives reasons to recommend the model suggested for further practical use and theoretical study.

THERMAL PROCESSES WITHIN IMITATION LEATHER WHEN HEATING AND COOLING

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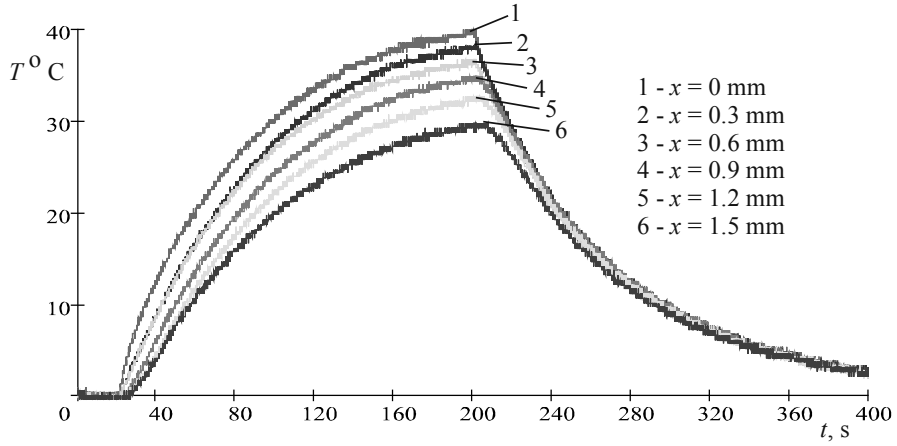
Skin covers all external surface of human body and serves as a protective barrier from traumas, radiations, overheating and infections. The skin can be easily damaged by traumas and burns. Skin transplantation is an optimum solution in such cases and imitation leather can be used as a transplantat.

The thermoregulation of organism is the important function of human skin. The purpose of our work is to define the thermal parameters of imitation leather.

The sample contains six layers of imitation leather of size 50 x 50 mm and thickness 0.3 mm each. The thermocouples are located both between the layers and on the external surfaces of the sample. Signals of thermocouples were transferred through the of analog-digital transformer to the computer.

Figure shows changes of temperature at the different depths of skin sample when heating the sample by light irradiation.



Thermal processes when heating the sample by the light irradiation

On the basis of obtained experimental data we have managed to evaluate thermal conductivity coefficient (***k*** = 0.068 W/(m*K)) and thermodiffusion coefficient (***a*** = $5.92 \cdot 10^{-8}$ m^2/s) of imitation leather.

SECTION 15

SOCIAL SCIENCE

MILITARY SETTLEMENTS IN CHUGUYEV

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The ordinary clichй : «Chuguyev is a place of birth of Repin» does not disclose all historical richness of this small city. Chuguyen is more ten years older than Kharkov and in that epoch it had been the military capital. From that time it remained the marks of military shine in its planning and appearance of the buildings. The military settlements, located in Chuguyev according to the projects of General Arakcheyev, – is one of more disputable and few investigated pages in the history of XIX century.

The object of our work: to study the experience of military settlements, the results of this governmental initiative, negative and positive aspects as well as the importance for the economic development of the country.

The military settlement is the system of military organization in Russia at the period from 1810 to 1857 which combines military service with a production work, first of all – the agrarian works.

The organization of military settlements contributed to an active development of new lands of Slobozhanshchina and South of Ukraine, to introduction of new lands in the economic relations. But sever regulation, drilling, military system made the life insufferable for settlers.

The solders had been dissatisfied of agricultural works; tensions were growing. In summer 1819 the armed revolt took place which had been suppressed with a personal participation of Arakcheyev.

This armed revolt in Chuguyev forced the government to take notice to the transformations made. Is was clear that the idea to joint two estates was the utopia. We don't know exactly the duration of the period of this socio-economic experience but the beginning of economic decline in the country stopped it. In the second half of years 1850 the emperor Alexandr II liquidated the military settlements at all the country.

Chuguyev maintained many buildings – mutes of its glorious past which had its prosperity at the period of military settlement. We hope that the architectural pearls of this city will have not the destiny of some mansion houses moribund now.

ART – THERAPY: FORM OF MANIFESTATION AND CHARACTERISTIC FEATURES

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The aim of this research is the specific features of art therapy facilitateing of it is widespread and effective impact on patients. Art-therapy – is a form of treatment, which uses art and different forms of art in order to normalize damaged the processes of life, as well as eliminating symptoms and signs of a disease, pathological condition. Nowadays for therapeutic reasonsusing different forms of art: all kinds of drawing, mosaic, collage, working with plaster, body art, sculpture and photography. Synthesis of art and medicine appeared in such specific directions as music therapy, dance therapy, etnoterapiya, dramaterapiya, vokaloterapiya etc. Methods of art therapy use teachers, social workers, and business.

The specific features of art therapy are:

- absence serious limitations in using this type of treatment. Even if a person has any pathology, then it can not be a hindrance occupation art therapy - for example, a person who can not hear, can draw, but the one who does not see, can calmly deal with stucco or sculpting;
- focus on the process, not the outcome. Absence of a certain talent is not an obstacle to art therapy classes. This therapy is not intended to create valuable works of art. What is important is what happens to the psychological state of a person in the course of treatment, rather than the aesthetic quality of the product was created;
- the desire to treat not only the illness but also to improve psychological state of the patient (in many cases determines the nature and course of the disease). In the process of artistic creation patient is a decrease of psychological stress, which allows the body to mobilize resources to fight the disease.

The possibilities of art therapy is so wide that doctors use it to treat infections and even cancer. Art Therapy is a success in the major countries of the world, such as the U.S., China and Japan. In India (Madras) opened a special center for training doctors musicoterapevtov. They have already found pieces of music for the treatment of hypertension and some mental illnesses, to whom traditional medicine is often powerless.

On condition that the pace of life, the rapid development of technology, and as a result, increasing pressure on the psyche of a modern man, art therapy will become more widespread. Moreover it is more actual if to take into account the fact that many physical (somatic) diseases are a consequence of the adverse of psychological and mental state of the individual.

ETHICAL AND AESTHETIC VIEVS OF G.S.SKOVORODA

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Ethics G.S. Skovoroda covered a wide range of issues, such as good, evil, justice, honor, conscience. But in the center of all ethical speculations was concept of "inner-propensity" (predisposition to a particular form of socially significant labor, the skill) and theory of happiness. The basic ideas of the concept of "innerpropencial labor" were formulated in dialogs "Narcissus", "Askhan" and "Alphabet, Bukvar of the world."

Philosopher was convinced that there is a universal law of "innerpropensity" thatintegrates the principle of existential balance of things, objects and creatures and that serves as the guarantor of the harmonic balance of nature. The Path is self-consciousness, comprehension and execution of your "inner yourself", "innerpropensity" (predisposition to a particular form of socially significant labor, the skill). The result is happiness which is understood as self-sufficiency (Autarky), peace of mind and dispassion.Particularities of "innerpropenciallabor" of the philosopherare free flow of thoughts about Principles, an allegorical interpretation of symbols, fulfillment of the commandmentsand the pedagogical function of educating people in virtue. Same as "innerpropensity", for Skovoroda Happiness is a natural and universal law. Pursuit of happiness is in fact pursuit of "innerpropensity". The question of human happiness was associated, and gradually developed into the question of self-consciousness, the inner essence of the person.

Intriguing is a study of a Hart as the center of spiritual and physical been of a person. "Oh, my Father! It is hard to tear the heart out of the adhesiveness of impulsive world!" - Exclaims Skovoroda at the end of his life. By Skovoroda, ethical task of a man is to understand and to find the beginning of a mystic-yourself, and in this sense, to finally become the self. But from becoming a "true man" one's impedes the Will, which urges a man to the world of struggle and suffering. "Everybody whodeifyhis will, is the enemy ofGod's willand cannotenterthe kingdom of God", - wrote Skovoroda. The motif of "weak will" in a variety of alternatives istypical for mystical traditions of both Western and Eastern worlds. It also present in works of Skovoroda, partly as a result of certain ideological influences, but much more as a reflection of personal spiritual experience, experience of constant and painful struggle with " the adhesiveness of impulsive world" and with "empirical person" in himself.

Skovoroda's ethics was not regulatory, but internally autonomous and was purely personal. The man inside while searching for his "innerpropensity" acquired a specific to him Potentiality and Actuality, which metaphysically was incorporated in God, and in the concrete historical perspective - in personal happiness. Truth, by Skovoroda,has a full value only when it promotes virtue and improves moral standings, moreover, knowledge should promote the welfare of man. Human happiness, that is the main interest of Skovoroda, is considered by him to be closely related to "innerpropensity", in other words, line of work that pertains to natural predispositions of the person.

ETHICAL ARGUMENTS «FOR» AND «AGAINST» OF CAPITAL PUNISHMENT

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Today, the most relevant are the questions about the practice of the capital punishment. Supporters and opponents of it to actively continue to advance their arguments around the world, and the purpose of my discussion will be the ethical arguments "for" and "against" of capital punishment.

Capital punishments, first of all – it's a murder, which is carried out by the state as a part of its rights to legitimate violence.

Despite the fact that European countries since the middle of the XIX century began to give up this penalty, a capital punishment is not fully eradicated.

The trend of development of this problem lies in the fact that over time changes the subjective attitude to a capital punishment. First, society unanimously recognized the need as well as the moral justification of the capital punishment.

But philosophers, scientists and public figures started to publicly express and defend opposing opinions approximately from the XVIII century.

Negative attitude to the capital punishment, arguing, first of all, ethical motives, was rapidly gaining strength.

The key of the ethical and moral arguments given that the capital punishment can be considered to be justified are the following.

1. Capital punishment – it's a fair price paid as chastisement for the murder.
2. The capital punishment is justified because its deterrent effect which helps to prevent the commission of crimes by others.
3. The capital punishment rid society from dangerous criminals.

Ethical arguments «against» the capital punishment.

1. The capital punishment renders morally corrupting effect on human society.
2. The capital punishment is unfair and deceitful because it clearly violates the human limits of competence.
3. The capital punishment is impingement on fundamental moral principle of self-worth of the human person, its holiness.

In conclusion, it should be noted that, although the adduced ethical arguments in favor of the capital punishment and do not have a logical compulsion, but nevertheless they are seem to be quite convincing for a large number of people.

REPRESENTATION OF MODERN MAN PROBLEMS IN THE ANIME SUBCULTURE

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Subculture is a standalone holistic community in mainstream culture which can be characterized with the specific system of values and life outlook of its representatives. Anime, which emerged as a trend in animation, nowadays exists as a popular youth subculture.

The word "anime" (from "animation") is a name of modern animation style. This word has another meaning. "Anima" is the Latin for "soul" or "spirit." In this sense, the anime can be understood as the art of animation of a man endowed with its vivid emotion, sensitivity and receptivity. A specific feature of anime is its addressing to an adult audience. That's why anime creators are focusing on the social, philosophical and existential problems.

Anime culture has ancient roots. Predecessors of anime are Japanese theater Kabuki and Japanese manga comics known since the 12th century. In these kinds of art images of characters output by the concise set of means, that teaches viewers to "decode" the color, form, gesture and intonation as the symbols of more complex phenomena and relationships.

Anime shows such problems of modern man, as the search of his "Self", the definition of the sense of life, mutual understanding, loneliness, love and hate, life and death, friendship, self-improvement, solidarity, war and the struggle between good and evil, ecology and ideals of healthy life.

The series of negative events that occur in life of anime-fan make our understanding of this phenomenon complicated. However, the culture of anime offers a number of instruments that can eliminate the negativity from life of contemporary person. They are creativity, tolerance, communication skills. A look at the anime as at a cultural phenomenon, and not as at the surrounding reality, allows us to use its constructive experience in overcoming of social and emotional discomfort.

PHILOSOPHY OF ABU ALI IBN SINA

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Avicenna (Abu Ali Husain Ibn Abdallah Ibn Sina) is a prominent scientist, philosopher, physician, musician and poet. Among the works of Ibn Sina his "Canon of Medicine", "The Book of Knowledge", "The Book of Healing", "The Book of Guidance and Instruction" are the best known. Great influence on the philosopher Aristotle had. In the spirit of Aristotle, Avicenna interprets the philosophical problem of the relationship between possibility and necessity, form and matter, the nature and attributes of things, soul and body and different forms of cognition. Like Aristotle, Avicenna criticizes Plato's philosophy. He considers the matter not to be a cause of imperfect things, but a necessary element of any existing thing. Important role in the formation of Ibn Sina as a thinker played Oriental spiritual tradition (works of Muhammad Khorazmiy, Al-Farabi, Abu Bakr Razi, etc.). Synthesis of different forms of knowledge has led to the formulation of the central problem of Ibn Sina's works - the relationship between God, the world and a man.

Philosopher developed the idea of co-eternity of God and the world, the ideal and the material essences. Ibn Sina believed that God, as the world's cause does not need to precede it in time. And in fact, this is a question of substance: God comes first as the cause precedes the effect. Ibn Sina's understanding of matter as eternal substrate and the root causes of the world also leads thinker to the conclusion that the world is primordial.

Metaphysics and theology of Ibn Sina led to his philosophical views on the man who was considered to be a carrier of the unique unity of the material and the spiritual substances. Therefore, the life of man, his morals, values, mind and body health are equally due to the influence of external (divine and natural) and internal (intellectual, spiritual, volitional) factors. Today we can say that Ibn Sina as a thinker has created a deep and efficient synthesis of theology, philosophy and natural sciences. A main conclusion of the works of the thinker is the recognition of human dignity as carrying both the stamp of its Creator and harmonious natural origin.

THE PROBLEM OF HAPPINESS IN THE WORK OF G.S.SKOVORODY

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Happiness is one of the most consistent and, at the same time, dynamic systems of moral consciousness. Attempts to resolve this issue accompany the history of mankind. The question of Happiness has neither time nor space limits. To the study of this problem devoted much attention philosophers of the past and the present. Indeed, there are many treatises on Happiness. Most of them are not devoted to the problem of Happiness, but ways to achieve it. In practical terms, this is the most important aspect, but in theory, it is only one of many aspects of Happiness. Question of Happiness is closely related to question of Meaning of Life. Can happiness be the meaning of life or just a means for achieving the latter? Gregory Savich Skovoroda, great Ukrainian philosopher, was among those that addressed problem of Happiness in their work. He proposed his "Formula of Happiness ": "Be happy - it is to know yourself, and your nature, to take care of your own destiny and to do what you are good at." This is a fundamental formula. Any "Formula of happiness" offered to us today by various other philosophers fits in itself trio offered by Skovoroda: Self-consciousness (to know yourself or your nature), self-improvement (to take care of your own destiny) and self-fulfillment (to do what you are good at). All three of these processes must be continuity of one another and must be in the mutual influence. Skovoroda's "Formula of Happiness" is universal. And its main element is the freedom of choice. However, the question is, is it indeed that man has a free will? In man there is always internal confrontation of opposites: love and hate, truth and lie, good and evil, beauty and viciousness. And on which of those will prevail depends one's Happiness.

Society, according Skovoroda should elevate the human spirit. It is crucial to create a cult of love, as a fundamental principle of spirituality, the primary source of the sublime in man. There is no other way to build a happy society. In the words of Skovoroda: "Isn't it Love binds everything together, creates, just as hatred destroys… What provides basis?Love. What creates? Love. What protects? Love, love! What gives pleasure? Love. Love - the beginning, the center and the end, Alpha and Omega." What is Love then? Skovoroda answers this question: "Love is the eternal bond between God and man. Love is the invisible fire that inflames the heart to God's words and will, and therefore, Love herself is God. "

Thus happiness is love and love is God. God is the fullness of love. Is not this, that essential part of the word Happiness? And does not word Happiness mean that man is One with God? That man is involved with God?

After all, God did not create us in order to establish its own strength, but to let man live, work and be happy. To achieve ultimate happiness God had armed man with suitable means, in particular, has engaged in his nature strong uncontrollable desire for Him and unconquerable desire to live in union with Him. Those that act in accordance with this requirement and get closer to the Lord, become truly happy.

THE PROBLEM OF SOURCES OF COSSACKS AS A SOCIOCULTURAL PHENOMENON

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Aim: to consider the problems of sources of Cossacks as a sociocultural phenomenon. Cossacks are unique phenomenon in world history and culture, about which much has been written and said. However, for several centuries, there has been discussion about its origins. The oldest records in the world written sources word Cossack (concerning Ukraine) is a note in the Greek "Synaxarion" of XII century. (found in Sudak) about the death of young man named Almalchu who was "killed with the sword of Cossacks." This is one of the oldest documents in which attested created troops of free soldiers, Cossacks "guard" in the southern plains, which consisted of entire families (parents, children, women) who fought for independence rather bravely and ferociously against all others that bore captivity. In ancient handwritten source "Secret History of the Mongols" (1240) mentions "Cossack" as the name of a lightly armed guard warrior. Originally Cossacks served truly guards in the southern plains, where any moment could be Mongolian or Tartar hordes. The military tradition, peculiar chivalry, which was to protect people and their faith, was born in the days of Kievan Rus. In XII-XIII centuries. Between rivers the Southern Bug and Teterev was a small Ukrainian principality (Bolohivske), customs, public order of which are very similar to cossack, zaporizhian life. Researcher M. Dashkevich believes that the customs of chivalry that it developed, created Cossacks and Cossack Host liberties. M. Kostomarov, M. Maksimovich also call the time point of Cossacks XII-XIII centuries. However, it should be emphasized that knightage of prince's army most influenced the formation of Cossack, especially after the fall of Kyiv (1240r.). This is seen in the customs, in the organization of the social system, maintenance of similar appearance, clothes, means of warfare. Byzantine historian L.Diakon in its history of wars described the portrait of Prince Svyatoslav of Kiev during the conversation with the Byzantine emperor in 900, the "beard shaved on the upper lip thick and long hair (mustache), head completely shaved, on one side hanging forelock" , i.e. "herring." With prince's warriors this habit to wear herring moved to the Cossacks and became a feature of their appearance, like a natural "uniform." Time and place of birth of the Ukrainian Cossacks various authors call differently and differently motivate this: the roots of this phenomenon sometimes look back in Scythian times of Ovid, who during his exile on the Black Sea coast (early AD) in his poem about the Scythians described Cossacks, soldiers who were in the days of Rome; and some Cossack chroniclers believed their ancestors' "Ratens'kiy" tribe of the IV century BC. The spirit of chivalry and content of aspirations were associated with the aspirations of medieval chivalry of Europe, drew roots of the Cossacks from brodnykiv, "berladnykiv" – population of Bolohivskoho principality. Most realistic, in our view, are attempts to link the emergence of Cossacks with anti-mongol movement of the Ukrainian people after the fall of Kyiv in 1240, who defended not only Ukrainian, but also the culture of all the peoples of Europe.

SECTION 16

PHILOLOGY

THE IMPACT OF BISPHENOL-A ON NEURONES

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The aim of the article is to present analyses concerning Bisphenol-A. A chemical commonly found in plastics may interfere with neurones in developing embryos. Some scientists question whether or not the new findings are relevant to humans. Quantitative and quantitative methods have been used in the article.

The results of the investigation have shown that in the past, Bisphenol-A was shown to epigenetically affect the developing nervous system, but how this happens is not clear. The new study, led by Dr Michele Yeo from Duke University, found it affected gene expression and disrupted the chemical balance of neurones. Bisphenol-A can disrupt gene expression through epigenetic mechanisms.

For example, the researchers directly exposed cultured rat, mouse and human cells to Bisphenol A. They then examined extracted cells from female mice fed on a diet of the chemical. They have relevance for identifying unique neurodevelopmental toxicity of Bisphenol-A, which could possibly play a role in the pathogenisis of human neurodevelopmental disorders.

As the result of the investigation it can be surely said that many scientists such as Dr Ian Musgrave, Phd Andrew Bartholomaeus from the University of Adelaide, the University of Canberra have proved that while the study throws light on aspects of gene regulation, it is not relevant to human exposure of the chemical. The concentrations in this study are hundreds to thousands of times higher than humans would be exposed to through the maximal permissible level of Bisphenol-A in food.

For, example, the actual brain cells were treated in culture in a very non-physiological environment - so “they were actually taken out of the animal and bathed in a solution which actually had the Bisphenol-A in it,” says Bartholomaeus who has worked in risk assessment for Food Standards Australia New Zealand, which monitors levels of Bisphenol-A in food containers.

So, the results of the investigation have proved that Bisphenol-A consumed in food or drink is metabolised before it enters the bloodstream. In terms of human risk assessment it has fairly low relevance.

LATIN LANGUAGE IN THE LIFE OF MODERN YOUTH

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The work was aimed to identify areas of Latin language use in modern youth culture. The material of the research is the expressions in Latin that are present in the name brands that are popular with young people, in electronic and online resources, and in the symbolic system of subcultures. Objective of the study is to identify the areas of the Latin language in the life of today's youth.

Latin is among the most ancient Indo-European languages. In modern life, people actively use Latin. This ancient language is often used in naming (a design of company, brands, and services names). For example, in Kharkiv there are the following stores with Latin names: «Porta» (doors), «In vino» (in wine), «Littera Nova» (a new letter), «Amnesia» (unconsciousness), etc. Latin is also used in the names of brands. Name of the company «Sony» comes from the word «sonus» (sound), «Volvo» (I drive), «Audi» (listen). In the Internet there are many sites dedicated to the Latin language and ancient culture and history. There are websites both in modern European languages and in Latin, for example, www.la.wikipedia.org, www.latinpro.info, etc.

Latin also entered the Internet sector. Classical language is widely used for creating names of computer games and so-called nicknames. Among the youth such games as «Lost: Via Domus» (the way back), «Deus Ex» (god from), «Sublustrum» (twilight), «Arx fatalis» (last stronghold) etc. are popular. There is a competition for the accelerated development of PC games called «Ludum dare» (to play). Team competition for online games took on the Latin name «Natus vincere» (born to win).

Winged Latin expressions in the original language are actively used as status on social networks. Statuses are used in programs like ICQ QIP, VKontakte, Facebook. For example, «Carpe Diem!» (seize the day!), «Fuga Temporum» (running time), «Surge et age!» (get up and do it!), «Fruere vita, dum vivis» (Enjoy while living). Latin aphorisms are often used as inscriptions in tattoos: «Veni vidi vici» (I came, I saw, I conquered), «Memento mori» (remember of death), «Carpe diem» (Seize the day), etc.

Besides, there are musical groups (often rock bands) who name themselves in Latin: «Dimicandum» (we have to fight), "Omnium Gatherum» (hash, all sorts and everything).

Thus, our analysis suggests that the Latin language, which is called a dead language, is alive and is widely used by the younger generation because the true values are eternal.

FLORISTIC LANGUAGE AND SYMBOLS

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Object of the work: to study the using of the flowers for expression of the sympathy for peoples and their importance in ancient Persia, at the period of fall of Roman empire and in aristocratic families in France. To observe an etymology of Latin botanic names. Materials: in our work we used : "Myths of peoples in the world", «Etymologic Dictionary of Latin botanic names of medical plants». Methods: in our work we used the comparative method for analysis of Latin names in etymologic dictionaries and we visited the greenhouse at the Pedagogic University.

We can find some data about the importance of the flowers in ancient myths, biblical stories and legends. Flowers play and an important role in the life of all peoples, they are the symbols of fidelity and sadness, happiness and distress, the relation with the future life and self-admiration. The etymology of Latin botanic names is very interesting. The important events are marked with the flowers; people express the fillings with the help of flowers. The flowers are used to express the sympathy for people. The language of flowers was used at the Turkish harems and later it is known in England.

So, in all epochs the flowers are considered as a souvenir for any holiday and grand occasion. A bunch of flowers, composed with a good style, is always to the point and for soul. It's very important to choose the flowers for the purpose to make happy by their beauty and freshness and to confide your secret wish and dream. In general, we forgot the nuances of the language but now we know that a red rose means a romantic and ardent love, a white rose means the modesty.The language of flowers may be realized in creation of flowers compositions, bunches of flowers and garlands.

Conclusion: you can tell about your filling with a great choice of flowers. The flowers can tell more and better than e-mail message ; moreover, they are so nice on your table.

NEW DRUG TARGETS FLU'S ACHILLES HEEL

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The aim of this article is to present a new class of influenza drug that tricks the virus by using its own mechanism of infection. So far, the drug has been used to successfully treat mice infected with lethal strains of influenza - including resistant strains of the virus. Quantitative and qualitative methods have been used in the research of the article.

The results of the investigation have shown that the flu virus has two "spikes" or proteins that it uses in the infection process. McKimm-Breschkin explains that hemagglutinin, binds the virus to a healthy cell through sugars on the cell surface. The virus is then "swallowed" by the cell where it multiplies. The virus then uses a second "spike", neuraminidase, to sever its connection to the sugar - and therefore the cell - "allowing the virus progeny to spread to uninfected cells", the research shows. The new drug stops this latter process by blocking the "mouth" of the neuraminidase so the virus remains attached to the cell and cannot spread.

As the investigation has proved, many scientists as well as the World Health Organization estimate influenza affects three to five million people globally each year, causing 250,000 to 500,000 deaths. It is important to "stay a step ahead" of the virus by developing new drugs to combat its spread.

For example, McKimm-Breschkin says it is important to "stay a step ahead" of the virus by developing new drugs to combat its spread. "With millions of poultry currently infected with 'bird flu' globally, there are still concerns about its adaptation and potential to spread among humans, causing the next pandemic," she says. She says a seasonal flu developed a random mutation in Norway making it resistant to Tamiflu. Understanding exactly how flu viruses become resistant to drugs has helped the researchers to design a better flu drug, says McKimm-Breschkin.

As the site where the drug binds is found in all flu strains, the new drug is expected to be effective even against future flu strain, she says

So, the results of the investigation have proved that the virus may not be able to develop resistance to this new type of drug because it stops a process that is common to all strains of flu.

THE HISTORY AND DEVELOPMENT OF CHECHEN LANGUAGE WITH RUSSIAN LANGUAGE

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In the history of Chechen language there were many changes because of a very difficult political situation in Chechnya and its nation's migration to other countries. In 1926 the Arabic alphabet was used in the phonetics of Chechen language. In Chechen language of that period many Arabic words appeared, such as жайна-книга (a book), до1а-молитва (a prayer). At the end of the 19th century the influence of Russian language increased and new words also appeared: картол–картошка (potato), ведар–ведро (a pail).

In 1923 Latin graphics started to be used in Chechen language, which became very popular all over the Caucasus. Up to 1927 Russian, Arabic, Latin graphic was used in all printed articles. Education was improving and developing and some technical, pedagogical, medical and military terminology was borrowed from Russian at that time. In 1944 Chechen language was forbidden, all books were destroyed and only in 1956 Chechen language was officially allowed to use in a written form.

In 1990 orthographic norms of Russian language in borrowings started to be followed: all words started to be pronounced and written as in Russian language without any phonetic changes. There are ten cases in Chechen language unlike Russian. Apart from the main six of them which have the same meaning as Russian ones, Chechen language has 4 more cases: ergative, material, locative case, relative case. Nouns in ergative case play the role of a subject with transitive verbs; in material case nouns play the role of an indirect object and in locative case as an adverbial modifier of place.

Noun in nominative case in Chechen language works as a subject with intransitive verbs (nominative case in Russian) or a direct object with transitive verbs (Russian genitive case). For example: leaves are falling - ГІАШ ОХЬАОЬГУ. A boy is reading his book - КІАНТА КНИГА ЙОЬШУ.

The forms of indirect cases are made with corresponded case endings added to the word stem. The forms of indirect cases in plural are made with case endings added to the plural suffix, the exception is genitive case, material and relative cases which in plural have other endings: - ИЙН – in genitive, - ЕХ – in material, - ЕХ in relative case.

GESCHICHTE DER HEILPFLANZEN

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Experience in the use of medicinal plants has been known since ancient times. The most famous illustration of this is the ancient Egyptian papyrus from 1600 Ebusa BC Avicenna first mentioned that the daily food can be medicine. In the Middle Ages monks described and used medicinal herbs. In 1543 Leonhard Fuchs published a book on medicinal plants in German.

Der Erfahrungsschatz über den Umgang mit Drogenpflanzen dürfte mit zu den frühesten Erkenntnissen oraler Tradition (mündliche Überlieferung) gehören. Alle in den letzten 200 Jahren aufgefundenen und erforschten oder wenigstens beschriebenen Stämme von Jägern und Sammlern wenden bei medizinischen Problemen auch Pflanzen zur Heilung an. Der *Mann vom Hauslabjoch*, allgemein bekannt als Ötzi, eine etwa 5300 Jahre alte Gletschermumie aus der ausgehenden Jungsteinzeit (Neolithikum) bzw. der Kupferzeit (Eneolithikum, Chalkolithikum), führte Birkenporlinge vermutlich als Heilmittel mit sich. Die Nutzung von Pflanzen mit der Absicht der Heilung lässt sich bereits in frühesten Schichten babylonischer, altägyptischer, indischer (Hymnen des Rig Veda) oder chinesischer Texte nachweisen, aber auch der ausdrückliche Anbau von Heilkräutern. Das bekannteste Zeugnis dieser ältesten Aufzeichnungen medizinischer Bemühungen mit zahlreichen Beispielen für Heilpflanzen und deren Anwendung ist das Papyrus Ebers das im letzten Viertel des sechzehnten Jahrhunderts vor Christus des alten Ägypten verfasst wurde. Der Grieche Dioskurides beschrieb im 1. Jahrhundert zahlreiche Heilpflanzen und deren Anwendungen. Der Zusammenhang zwischen Nahrung und Arznei wurde insbesondere in der orientalischen Heilkunst schon früh erkannt, und dementsprechend finden sich zahlreiche Hinweise in den Medizinbüchern des Orients, etwa bei Ibn Sina (Avicenna) um 1000n.Chr. Während des Mittelalters erfolgte der Anbau, die Beschreibung und Anwendung von Heilpflanzen vor allem durch Klostermönche. Der spanisch-arabische Arzt und Botaniker Abu Muhammad Ibn al-Baitar beschrieb um 1230 im *Kitab al-gami* über 1400 pflanzliche Heilmittel und ihre Rezepturen. Leonhard Fuchs veröffentlichte 1543 mit dem *New Kreüterbuch* eines der wichtigsten Kräuterbücher in deutscher Sprache, das zahlreiche Arzneipflanzen abbildet und ihre Wirkung beschreibt. Zu den Wegbereitern der modernen Phytotherapie gehören auch die Bücher des Schweizer Kräuterpfarrers Johann Künzle (1857-1945). Heute werden Heilpflanzen im Rahmen der Phytotherapie verwendet, in manchen europäischen Ländern sowie den USA spielen sie durch das Aufkommen von chemisch synthetisierten und definierten Wirkstoffen nur eine geringe Rolle.

LATINA VIVA

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The purpose of our work is research of using Latin vocabulary in modern conversational Russian. We deleted scientific, political, juristical terminology purposefully where vocabulary of Latin origin is a basic. We tried to trace use intensity of words Latin origin and an ancient Greek origin by contemporary in everyday life. We choose linguistic context which is linked with one life situation, if concretize it is linked with a choice of car and a choice of a tourist trip. Irregularity of the object is defined in the presentation of the work that we have provisionally identified as an essay.

We analyzed 1700 words in reference to the above context during our work and found 240 words of Latin origin and ancient Greek origin, it is 14 percents. In this study we investigated the etymology of each of the selected words and analyzed the frequency of their use. Most often to describe the situation we had to use such words as "tour" – 17 times, "firm" – 13 times. 35 words were met from two to six times. 82 words were used one time, such as school, chemistry, relevant, holidays, exam, republic, result, nation, official, freeway, highway, district January, a service, region, volcano, culture, ruins, popular, practical, comfortable, line, oil, civilization, passive, formality, tradition, minimum, province, antique, silk, doctor, vet, bath, active, scuba gear, hotel, rent, statement, universal, real, comment, contact, forum, compensation, director, place, person, information, novel, passenger, course, champion, motor, engineer, the plot, route, triumph, elegant, prestigious, talent, cylinder, competitor, unit, neat, commerce, priority, customer, recommendation, regulate, recommendation, mode, geometry, turbine, minute, elastic, mass, ton, basis, student, subject. The list of selected words of Latin and Greek origin, indicating the frequency of use is at the end.

APPLICATION OF METHODS OF MNEMONICS TO STUDY THE UKRAINIAN ORPHOGRAPHY AND GRAMMAR (USING THE MATERIALS OF COURSE "UKRAINIAN LANGUAGE (IN PROFESSIONAL FIELD)"

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The study of the discipline "Ukrainian Language (in professional field)" provides to refresher and study a lot of rules of Ukrainian orthography and grammar and requires some volume of time and efforts. To facilitate the process of the rules learning and to work out the skills of their practical application is the main task of our work. The object of our investigation is the using of mnemonics in study of the discipline "Ukrainian Language (in professional field)". The task of our work is the study of technologies of keeping in mind and elaboration and systematization of mnemonic exercises to master the rules of Ukrainian orthography and grammar in compliance with the materials of above mentioned course.

In our work we learn on investigation of I.D. Ladanov "Memory training" and I.Yu. Matyugin "Alchemy of memory".

As of channel of information perception we can divide all individuals into following ways: persons with visual perception, persons with audio perception and kinesthetic persons. Persons with visual perception apprehend better the visual image; persons with audio perception learn the rules by audition and persons with kinesthetic perception learn the world "by touch". They need to create the personal visual image and to note for memory. The acronyms are suitable for persons with audio perception; the schematic illustrations, named also as mental cards, are suitable for persons with visual and kinesthetic perception. But the illustration, proposed by us, are not classic mental cards. In our work we have a complex of exercises for persons with different type of information perception. Some of them are known at the secondary school and the others are elaborated individually by us and are presented for the first time.

So, in compliance with the type of channel which prevails over information perception (visual audio, kinesthetic) in learning of the rules of Ukrainian orthography and grammar one must choose the different versions of mnemonic exercises to help to retain a great volume of information in the memory and to facilitate the life of a modern student.

SECTION 17

PEDAGOGY AND PSYCHOLOGY

CONFLICTS IN THE EDUCATIONAL ENVIRONMENT THROUGH THE EXAMPLE OF STUDENTS IN STUDENT'S GROUPS

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The conflict being a social-psychological phenomenon is an obligate and integral quality of the social relations. Neither community nor a personality can be developing conflict-free, conflicts occurrence is a factor of normal development. Conflicts can appear in any field of human relations and the system of higher education isn't an exception.

Many scientists both from our country and abroad worked on the problem of conflicts, they are Kozer L., Weber M., Darendorf R., Mayo E., Grishin N. V., Antsupov A.Ya., Shipilov A.I., Dmitriev A.V., Yemelyanov S. M., Kibanov A.Ya., Druzhinin V. V., Linchevsky E.E. etc. The general thing is that the majority of authors consider the conflict to be a certain counteraction, a contradiction that can turn out as disagreements, if it is a question of interaction of people in community, society.

In the student's environment the conflicts of a various type and level can take place, the most widespread among which are: the intrapersonal conflict and the interpersonal conflict, as well as the conflict inside the group (subgroup) and between members of group; the conflict between subgroups in separate group; the conflict between formal and informal systems of the relations; intergroup conflicts.

There is quite a big number of methods and techniques of research and definition of level and degree of proneness to conflict, predisposition of the student to conflict situations. On a counterbalance to conflict situations and their prevention, a number of scientists in this field are in a process of development of the programs of prevention and elimination of conflict situations, which for sure have a great influence and help teachers in educational process.

The majority of researchers agree that the conflict is a necessary condition of community's development and along with negative functions it carries out also positive functions, development of group, community, organization, society is impossible without the conflict. Applicability of the given subject in educational society allows to talk about a necessity and importance of prevention of the conflicts in student's group.

MULTIMEDIA TEACHING TECHNOLOGIES

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XXI century is the age of high computer and information technologies. And it is impossible to imagine modern teaching without their application.

With high technologies development such things as chalk, blackboard and papers become a thing of the past in university lecturing. Instead of them screen forms of data representation such as multimedia lectures are being used.

Multimedia lecture is an interactive combination of text, graphics, sound, video and animation with lecturer's communication with the audience; it has great didactic opportunities and educational potential.

Specific differences between multimedia and traditional lectures refer to: the structured content, the block scheme of the training material, the extra-modes of presentation (sound, video, animation, and graphics), hypertext, graphic marking of main statements, definitions, formulas.

Multimedia technologies integrate potent educational resources in order to provide the environment for key-competencies forming and demonstration, and informative and communicative in the first place.

Multimedia technologies' use gives students an opportunity to take active part in educational process. Students can take chance in self-study, determination of learning sequence, using the interactive options, organizing the cooperation within a study group.

However, multimedia lectures used should be perfectly considered and well-grounded. Even the best presentation might not be a good lecture. Material will be easily forgotten when only demonstrated, not written down. Illustrating the lecture material with slides is not enough. It is important to ensure the interactive interaction during the study.

University teacher should consider multimedia as a supporting technology. No matter how attractive the innovation technologies are and how many unique options they have, the blackboard and chalk still are priorities.

ACTUALITY OF INTERACTIVE STUDY METHODS' IMPLEMENTATION IN FUTURE ECONOMISTS' TRAINING

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Involving of education sphere into market relations system requires renewing of educational content and upgrading of training methodologies. Main directions of economic higher education transformations presuppose, first of all, education and practical activity integration, individual approach amplification, development of the creative personality in the team. These directions represent objective development trends and advanced pedagogical experience, which mean the use of unconventional training and education forms and methods, such as combination of training and work. Such approaches take into account the analysis of psychological, age, professional characteristics of future economists, and the necessity of development of their skills to transform and adapt studying material content, combine working methods depending on the specific situation. These approaches also facilitate students' communicative and managerial abilities.

Economist's work is of continuous production problems solving. Therefore, implementing of concrete economic situation analyzing into the study system is necessary in order to linking training and entrepreneurship practice. In such study process new economic thinking foundations are laid, which will be helpful for future economist in decision-making and consequences reviewing.

Future specialist's professional skill modeling is a component of pedagogic process in high school. Main stages of such modeling are:

1st stage – development of initial undifferentiated interest in certain activity, which is the main in professional motivation.

2nd stage – formation of positive professional value orientations to create perfect model of future professional activity in student's conscious.

3rd stage – active formation of professional skills required in practical activity.

Implementation of this approach puts forward new requirements to organization of students' studying activity. It is facilitated by application of new interactive training methods, which are scientific-grounded complex programs of interaction between teacher and students during the studying process. The basis of interactive methods is activation training modes, which ensure the formation of personal, professional and social characteristics at students by special-created studying conditions.

THE ESSENCE OF PERSONALITY ORIENTED TEACHING

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Modern pedagogics orient on the necessity of forming a personality having its own views on events and processes, who is capable of critical thinking and perceiving different opinions, that actualizes the necessity of implementation of the personality oriented teaching in the educational field of Ukraine.

The use of the term "personality oriented teaching" was established in science by the famous pedagogue and psychologist C. Rodgers. Nowadays this term is defined as the embodiment of humanist philosophy, psychology and pedagogics. I. S. Yakymanska who lightened the ideas and principles of the personality-oriented teaching in her exhaustive studies, came up to the conclusion that each kind of teaching may be suggested to be developing, but not each one may be personality oriented.

According to the conception of the personality oriented teaching each student is a personality with its own values, attitude to the environment, subjective experience. The personality oriented teaching is a continuum of teaching, education, self-education, socialization, the unity of all these processes which develop, adapt, form, "make up" the personality.

The aim of the personality oriented teaching is the process of psychological pedagogical aid in the establishment of its subjectivity, cultural identification, socialization; searching, support, the development of a personality in person. Subjective experience of a student is defined as vital, past, private, personal, obtained from certain conditions in family, social cultural surrounding.

The study of psychological pedagogical literature allows to state that personality oriented teaching suggests the acceptance of the personality being the main subject of the teaching process. In our opinion, a teacher should direct the students to self-reliant actions, making decisions, abilities to adapt to new life conditions creative thinking, ability to react sufficiently to life's challenges.

EVALUATION OF THE PSYCHOEMOTIONAL STATUS OF PREGNANT WOMEN WITH MISCARRIAGE PREGNANCY

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Among the most important problems of practical obstetrics, one of the first places is occupied by a problem of miscarriage. Modern strategy of care patients with threatened abortion consists in an intensive drug therapy. The specified approach doesn't provide an assessment of a psychological condition of the woman and carrying out psychotherapeutic actions.

The purpose of our research was the identification of the psychoemotional changes that are happening in an organism of pregnant women with threat of miscarriage. The study involved 50 pregnant women with threat of miscarriage, aged from 19 till 37 years, with gestation terms from 12 to 28 weeks. Pregnant women whose cause of miscarriage were infectious factors, chromosomal abnormalities and extragenital pathology were excluded from the study. All women have routine screening, according to the order of the Ukraine Ministry of Health No. 624. To determine the level of women's anxiety was used the test of Spielberg-Chanina. Spielberg's scale of reactive and personal anxiety is the only technique that allows to measure anxiety and differentiated as personal property, and as a condition.

Due to the fact that in most cases pregnant women had the increased level of personal anxiety (46 and above points), it was decided to take as a criterion the level of the reduced anxiety value 35 and below points. In this case the number of pregnant women with high level of anxiety was 15 (31%), with the lowered level of anxiety – 10 (20%), and with an average – 25 (49%). In the group with high level of personal anxiety its average values are equal 52.7±6.24, and situational – 43±7.63 points. For the group with low anxiety – 31.5±2.58 and 33.3±4.36, and for group of pregnant women with average anxiety – 40.8±2.69 and 37.6±6.43 points, respectively. Considering distribution of pregnant women in the specified groups in connection with diagnosis existence "threat of interruption of pregnancy" it is possible to note that with the increasing of level of anxiety also clinical manifestations of this condition significantly increased.

The results demonstrated the relationship of emotional status of pregnant women with clinical manifestations of the threat of miscarriage. Found that pregnant women with the threat of interruption characterized by great sensitivity to stress situations, more emotional instability and a lower level of psychological health. Research has shown that the correction of psychoemotional status of women with miscarriage is needed to improve perinatal indicators and for saving pregnancy.

MISSION OF MODERN TEACHER

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Relevance. The transition from traditional education to developing led to new demands on educational activities. In this regard, requirements to modern personality of the teacher acquire their significance, which today are concentrated in the sense of his mission.

The purpose of publishing - through the prism of the new requirements to disclose the modern understanding of the mission of the teacher as his responsible role and high purpose in implementing social demand.

Since the theme is multidimensional, for her study were used complex research **methods** - historical, systematic and analytical.

The main results. Nowadays, the problem of the teacher's personality is the subject of scientific research by many researchers (V. A. Kazakov, V. N. Kuzmin, L. M. Mitin, G. Romanova, L. Savinkov and others). However, the current mission of the teacher as a separate scientific problem investigated is still quite enough.

The subject of modern teacher's mission is reflected in the State program "Teacher" which focuses on the need to develop professional-teacher's personality according to modern changes and demands of life.

In addition, the concept of education teacher noted that the mission of the modern educator is to ensure the educational process on the principles of humanism, democracy, free competition and high technology.

In history there are many examples that show what students through their teachers have achieved significant results and have become known throughout the world. Specifically Antonio Stradivari gained worldwide fame as a student of such a teacher and mentor as Nicola Amati, for the famous Greek philosopher Aristotle's science was the meaning of life through the efforts of Plato. In turn Vasari taught and trained a genius like Leonardo da Vinci, and V. Zhukovsky revealed invaluable talent of famous Russian poet Alexander Pushkin.

Conclusion. The feature of modern teacher's mission is that he is called to provide the conditions for the successful development of their students, who will be able to complete fulfillment in their future life.

SECTION 18

MODERN PHARMACOTHERAPY

PHARMACOTHERAPY HELICOBACTER INFECTIONS

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Helicobacter pylori is the most important etiological factor in peptic ulcer (92% of cases) and duodenal ulcers (70%). Epidemiological studies conducted in various countries have shown greater prevalence Helicobacter pylori and a clear dependence on the socio-economic development. Thus, in the developed countries of Europe the number of infected is 15-20%, while in some countries in Africa and Asia – 70-76%. For Ukraine, this figure is about 80-85%, and for children (depending on age) – 40-70%.

11-13 September 2011 year in Dublin (Ireland), a regular meeting of the XXIV International Working Group on Helicobacter pylori and similar bacteria in chronic inflammatory conditions of the digestive tract and stomach cancer, which was approved key provisions on the treatment of diseases of the gastrointestinal tract associated with Helicobacter pylori.

In accordance with the provisions of treatment should be carried out as follows. Should stop triple therapy with proton pump inhibitors and clarithromycin without previous study of sensitivity to clarithromycin at the level of resistance to clarithromycin in the region more than 15-20%. Clarithromycin schemes are recommended as first-line empiric therapy in regions with low resistance to clarithromycin. An alternative is to appoint quadrotherapy with bismuth. Appointment of high-dose proton pump inhibitors I (twice a day) increases the effectiveness of triple therapy. Increasing the length of triple therapy with a proton pump inhibitors and clarithromycin from 7 to 10-14 days increases the success rate of eradication by 5%. Efficiency schemes "proton pump inhibitors + clarithromycin + metronidazole" and "proton pump inhibitors + clarithromycin + amoxicillin" is equal. Some probiotics and prebiotics show good results as a complementary therapy that can reduce side effects. Proton pump inhibitors-clarithromycin-containing schemes should be adapted to the patient, in addition to the dose.

Thus, today Helicobacter pylori is important and at the same time, still little known microbiological agent of the upper gastrointestinal tract of man. Ways of improving the treatment of Helicobacter pylori infections are using of antibiotics without resistance, simplified treatment regimens (reducing multiplicity of drugs and reducing the length of the course), the choice of the most powerful and safe antisecretory drug.

NEW DIRECTIONS PHARMACOTHERAPY VERTEBROGENIC PAIN SYNDROME

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The pathology of the lumbosacral part of the vertebra in about 20-30% of all diseases of the nervous system and more than 80% of the diseases of the peripheral nervous system. Often under the influence of treatment the pain stopped by in a period of a few weeks to a month, and in 20% of cases become chronic. Of particular significance is the problem of out-patient treatment. Modern arsenal of knowledge includes recent studies that allow us to understand how undertreated acute pain leads to its perpetuation, the development of new therapeutic agents and approaches to pain management. Despite the level of achievements of modern medicine and the diversity of analgesic drugs, not all patients in the pharmacotherapy vertebrogenic syndrome adequately anesthetized. This leads to a significant deterioration, as the immediate results of treatment, and adverse remote consequences. Studies of the mechanisms of pain, giving a better understanding of the nature of acute and chronic pain. Found that acute pain as a result of inflammation of the tissues, the generation of nociceptive impulses lead to sensitization of the paths in the central and peripheral levels. This results in the increase in the excitability of spinal neurons and facilitate the process of nociceptive pain impulses along paths that lead to the formation of hyperalgesia - an abnormally high sensitivity to pain stimulus. Inadequate analgesia in these patients according to the literature in 11-65% of cases leads to chronic pain, significant disability, disability and reduced quality of life.

The aim is study a new schemes in the treatment dorsalgia with centrally acting narcotic analgesic – nefopam ("Acupan") in combination with NSAIDs – ketoprofen.

Material and methods. The study included men and woman between 19 and 47 years with the syndrome vertebralgy. For the clinical evaluation of pain was used visual analogue scale (VAS). Assessment is carried out in points or percentage, with 0 means no pain and 10 points - very severe pain to the point of tolerance. Patients were asked to make a mark corresponding to the intensity of the pain he has at the moment. To assess the overall scale SAN-being used.

Conclusions: 1. Based on the analysis of the data it can be concluded that monotherapy NSAIDs decrease pain by VAS in the first 7 days of treatment, 46,6% lower than the combined use "Acupan" and ketoprofen.

2. Application "Acupan" combined with ketoprofen in the complex pharmacotherapy acute pain vertebrogenic genesis seems appropriate, because the drug has excellent analgesic activity, especially in combination with NSAIDs.

PROPHYLAXIS OF CERVICAL CANCER

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Every two minutes a woman in the world dies from cervical cancer. In Ukraine, each year, about 16,000 cases of cancer of the female reproductive organs. One third of them – cervical cancer, from which kills nearly 2,000 women, mostly of reproductive age. Most cases of cervical cancer provokes human papilloma virus (HPV). Science knows more than a hundred varieties of it, although some cancer causing strains: 16-18, 45, 31 and 33. The most dangerous are the first three.

Ukraine has registered two vaccines for the prevention of precancerous lesions and cervical cancer caused by HPV, "Gardasil" and "Cervarix". These vaccines do not infect infection because they are based - virus-like particles "shell." Immune system produces antibodies to them, and when he finds similar elements in the body, begins to actively fight them. The studies of HPV vaccines have shown high efficiency in terms of protection against the types of viruses against which they were created ("Gardasil" prevents infection with HPV types 6, 11, 16 and 18, and "Cervarix" prevents infection with HPV types 16 and 18), but do not protect against infection by other HPV types

If at the time of vaccination woman has been infected with HPV types 16 or 18, the likelihood of vaccination precancerous lesions and cervical cancer caused by viruses of this type, is reduced to zero. Unfortunately, cervical cancer associated with HPV 16 and 18, only 70% of cases. The remaining 30% of cases triggers by the HPV types against which the vaccine has been developed yet. Therefore vaccination "Gardasil" or "Cervarix" cervical cancer or the risk of dysplasia is significantly reduced, but not completely disappear.

According to the U.S. Center for Disease Control, in the country of HPV vaccinated more than 7.7 million women. Marked not heavy side effects – 1:680 patients: fainting, pain and swelling at the injection site, headache, nausea, and rise in temperature.

Vaccination is carried out in the offices of vaccination in hospitals, three times in six months, at of 9 to the age 55 years. Maximum efficiency is observed if vaccinated before sexual debut. Then the girls formed immunity, so that even when in contact with an infected person, it will be protected. However, the effectiveness of the protection of the rest of the women decreased by only 2%.

MONTELUCAST IN TREATING OF ASTHMA

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Accordingly to World Health Organization (WHO) data, more than 300 millions of people all over the world are suffering from asthma (A) at present time. Annually kills more than 250 thousand people from this disease.

In international recommendations of GINA (Global Initiative for Asthma, 2011) for background therapy such drugs as inhalant glucocorticosteroids (iGCS), long-acting b2-agonists and antileucotrien drugs are recommended. Today the usage of antileucotrien drugs is seen as an alternative method of asthma therapy, which helps to reduce the hormonotherapy because of influencing on the leukotrien inflammation development path, which can't be influenced by iGCS. Also it helps to ensure high patients' compliance and to achieve stabile and long-lasting remission.

Leukotriens role in asthma pathogenesis is the reinforcement of mucus secretion, its clearance depression, production increase of cationic proteins that damage epithelial cells. Cysteinyl leukotrienes (CysLT) (LTC4, LTD4, LTE4) has powerful bronchoconstriction effect, they are powerful chemoattractive agents for eosinophiles, that's why one of the key-effects of leukotrien receptors antagonists of asthma is connected with suppression of eosinophile inflammation.

Montelucast is one of the first representations of antileukotrien drugs; it blocks selectively leukotrien receptors and specifically inhibits $CysLT_1$ receptors. Montelucast ability to reduce eosinophile in respiratory tract were demonstrated while experimental and clinical researches. After four weeks therapy of asthma patients by Montelucast, it reduced eosinophile number in expectoration by 48%. Montelucast triggers bronchodilatation in two hours after ingestion and also may complete bronchodilatation, triggered by b2-agonists. Obstruction duration of LTD4-specific receptors is about 24 hours, which allows prescribing the drug once per 24 hours. Montelucast effects indirectly interleukine-5 expression, and also indirectly controls processes of respiratory tract remodeling.

Montelucast is registered under the trade name (Singular®), administered in a dose of 0.5 mg and 10 mg. Montelucast is prescribed by 10 mg before bedtime per os as the first line drug for treating adults with light long-lasting asthma. Montelucast helps to reduce the dose of iGCS while combined treatment from moderately severe asthma. Montelucast is not recommended as monotherapy.

So, the new direction in treating asthma by using drugs, that are leukotrien receptors inhibitors, demonstrated high therapeutic effectiveness.

THE PHARMACOTHERAPY OF ACUTE INFECTION DIARRHEA (LITERATURE REVIEW)

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Diarrhea disease is the second leading cause of death in children under five years old, and is responsible for killing 1.5 million children every year. In the develop countries, diarrhea diseases cause an estimated 167 000 hospitalizations and 300 deaths each year among children younger than 5 years of age , who are malnourished or have impaired immunity are most at risk of life-threatening diarrhea. Diarrhea can last several days, and can leave the body without the water and salts that are necessary for survival. Most people who die from severe dehydration and fluid loss.

Diarrhea is defined as the passage of three or more loose or liquid stools per day (or more frequent passage than is normal for the individual). Frequent passing of formed stools is not diarrhea, nor is the passing of loose, "pasty" stools by breastfed babies. Diarrhea is usually a symptom of an infection in the intestinal tract, which can be caused by a variety of bacterial, viral and parasitic organisms. Infection is spread through contaminated food or drinking-water, or from person-to-person as a result of poor hygiene. Pharmacotherapy is largely symptomatic and involves fluid and electrolyte replacement, and maintenance of nutrition

During an episode of gastroenteritis, there is a decrease of protective commensal microflora, followed by an overgrowth of urease-producing pathogenic bacteria. A biotherapeutic agent or probiotic is a live microbial food supplement which beneficially affects the host by improving the intestinal microbial balance. The theoretical concept of probiotics or biotherapy was first described by the Russian scientist Metchnikov, who was awarded the Nobel Prize for medicine in 1908.

Probiotic agents offer a large number of therapeutic benefits in the prevention or treatment of several gastrointestinal disorders, including the management of acute infectious diarrhea and antibiotic-associated diarrhea. Some studies using Lactobacillus ramnosus GG have produced promising data, although other studies provide contradictory results. Saccharomyces boulardii is a non-bacterial biotherapeutic agent, and is the only biotherapeutic agent with systematic convincing data from double-blind studies. Results show significant efficacy in the prevention and treatment of acute diarrhea. The WHO, NICE, ESPGHAN, and other clinical guidelines considers Saccharomyces boulardii don't only treatment of acute diarrhea, but to be a possible treatment antibiotic-associated diarrhea or recurrent Clostridium difficile colitis.

INVESTIGATION OF THE PHARMACOTHERAPY WITH ETIFOXINE AUTONOMIC DISORDERS IN YOUNG PEOPLE

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Over the past decades, the main treatments for anxiety disorders and correction of emotional stress states were, benzodiazepine tranquilizers. Along with the main anxiolytic effect in the spectrum of pharmacological activity of benzodiazepines presented sedative, hypnotic, miorelaxant and amnesic action significantly limit their practical use in anxiety disorders. At the same time, many patients show cognitive decline, and in some cases, withdrawal and addiction, which adversely affect the quality of life for patients. The above features of the typical tranquilizers initiated research and development of drugs with selective anxiolytic effect and deprived hypnotic sedative, muscle relaxant and amnesic effects over a wide dose range. For these drugs refers anksiolitikstrezam (Strezam). The efficacy and safety Strezam associated with its specific dual mechanism of action aimed at GABA receptors and stimulation of neyrosteroidov. Among anxiolytics only Strezam having evidence "autonomic dysfunction."

The aim of the work is the presentation of clinical and pharmacological analysis of the basic laws of anxiolytic action Strezam and certain forward its application in clinical practice.

Materials and methods. The study included patients aged 17 to 30 years old, male and female with the symptoms of anxiety disorders, autonomic disorders. Anxiety level was registered in accordance with the scales «PEN», Taylor - Nemchina (MAS), Spielberg, Beck Depression Scale, Holmes, Wasserman, Wayne, San at baseline, on the 7th and 14th days. studies. With clinical and functional methods were evaluated as psychic and somatic symptoms of anxiety.

The discussion of the results. The results suggest that Stresam effective in treating anxiety disorders. The therapy performance anxiety on scales decreased by day 7 and subsequently declined steadily.

Conclusions: In clinical settings received confirmation on the availability of experimental data that Strezam has anxiolytic action. Combined therapy with the use of the drug Stresam improves treatment of autonomic dysfunction Strezam clinical efficacy is associated with reduced levels of anxiety and the normalization of the non-specific systems of the brain. Stresam drug can be recommended for neurological and somatic practice in the treatment of autonomic disorders as pathogenetically proved clinically effective and not cause addiction and withdrawal symptom.

PHARMATHERAPEUTIC CORRECTION OF DEVIANT BEHAVIOR

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A dramatic increase in deviant behavior occurres during radical reforms in all spheres of human life. Over the last decade some types of deviations have been replaced by others. Some of them that previously had latent nature were legalized and acquired the new forms. The significant changes occurred within certain types of deviations i.e. their structure, nature and quantitative indicators were changed the age limit of "deviant" was increased.

The deviant behavior is a way of an individual behavior that deviates from social norms, causing real damage to the society or the personality and accompanied by social exclusion. Thus, the individual must be examined as an external display of deviation in the form of actions that deviate from social norms. It is important to point out that public norms (rules, prohibitions, expectations) violation is an obligatory, but insufficient condition for establishment of deviant behavior.

The problem of deviant behavior is interdisciplinary. It is studied by a number of sciences. Deviant behavior is behavior which does not adhere to widely-accepted social or cultural norms. For example, murder is a form of extreme deviant behavior which violates the cultural norm which states that it is unacceptable to kill another human being. In speaking of deviance one must specify the system of reference. The same behavior may be both deviant and nondeviant, relative to different systems in which the individual is implicated.

The term "behavior" has age-old limitations and can be used when speaking about children not younger than 7-9. Only at this age (and in a number of cases and later) it is possible to talk about of the ability to understand and control one's behavior. If behavior of a child under nine substantially deviates from age norms, then behavior is expedient to examine as one of displays of immaturity, neurotic reactions or violations of psychical development.

For correction of conduct disorder in the personality disorders (in the old terminology - psychopathy) and a variety of maidens, the following groups of psychotropic drugs: neuroleptics (antipsychotics), tranquilizers (anxiolytics), antidepressants, psychostimulants, nootropics (cerebroprotect), mood stabilizers (mood stabilizers). The basic principles for the use of psychotropic drugs - symptoms and nozotsentrizm. Each drug has its indications and contraindications, depending on the identified mental disorders related to different groups.

MODERN TRENDS IN PHARMACOTHERAPY OF DISEASES CAUSED BY INFLUENZA A.

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Frequency of occurrence of influenza pandemics in the human population is associated with changes in its shifts pathogen. In the twentieth century, mankind has suffered from three influenza pandemics, the last of which took place in 1968. So there was nothing unusual in the fact that an influenza pandemic to happen again 2009-2010 years. Most deaths currently associated with influenza in industrialized countries occur in people over 65. The annual cost of the economy of the United States in connection with epidemics of influenza, according to the latest estimates, reach 71-167 billion.

Recommendations for the antiviral therapy:

1. In cases of severe or progressive disease anti-viral therapy should be administered as soon as possible.

2. Antiviral therapy is also appointed as soon as possible for patients with mild symptoms, who are at high risk for severe disease (pregnant women, infants and young children, people with chronic lung disease).

3. Antiviral therapy is not necessary for patients with uncomplicated or mild disease, non-high-risk groups.

Administration of the antiviral drugs prior to the development of the disease or in its early stages (in the first two days) helps to prevent infection. In the case of the disease, their early administration may reduce the duration of symptoms by 1-2 days.

For several years, there were only two antiviral drugs amantadine and rimantadine. At relatively low cost, these drugs are only effective against endemic influenza A.

Recently, a new class of antiviral drugs has appears: neuraminidase inhibitors. Drugs of this group oseltamivir and zanamivir have fewer side effects and less often lead to the development of resistance of the virus. Zanamivir has inhalation forms, using a special device “Relenza Diskhaler.” Pharmacotherapy is done during 5 days to 2 inhalations 2 times a day. The drug is used for the prevention and treatment of influenza A and B in adults and children older than 5 years and is relatively safe for pregnant and lactating women. Thus, the application of modern antiviral drugs can begin promptly effective pharmacotherapy, which can reduce the mortality and improve social rehabilitation of patients.

MODERN TREATING AND PREVENTING OF INFLUENZA A H1N1

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Influenza is a highly contagious acute viral disease of the respiratory tract, characterized by a short incubation period (1-2 days) and rapid cycling course (3-5 days). It affects all age groups living in different geographical conditions. High risk of complications from influenza have children < 4 year, adults > 65 year, people with chronic medical disorders, women in the 2nd or 3rd trimester of pregnancy, patients with disorders that impair handling of respiratory secretions, patients ≤ 18 year taking aspirin.

There are three variants of the virus antigen: serotypes A, B and C. One of the most active type A virus is a virus strain AH1N1 California, which today is a global pandemic with severe clinical course.

Early diagnosis of influenza AH1N1 California using rapid methods (immunofluorescence and immunochromatography analysis) improves the efficiency of pharmacotherapy aimed to reduce morbidity and to prevent complications. Treatment of influenza A H1N1 California start with general activities for the treatment of influenza (prescription of bed rest, excessive drinking, holding hygiene measures, wet cleaning), as well as the appointment of medication (anti-viral drugs: Amizon, Arbidol, Aflubin, Oseltamivir, Zanamivir; vitamin C; antipyretics: mefenamic acid, ibuprofen, paracetamol, anti-allergics: cetirizine, desloratadine, loratadine, fexofenadine, etc.)

One of the best anti-influenza drugs recommended WHO, are Oseltamivir (Tamiflu) and Zanamivir (Relenza). These drugs directly reduce the activity of neuraminidase of the viral envelope, thereby reducing the ability of the virus to penetrate into the cells and out of the infected cells. The advantages of Oseltamivir believe that it can be used to treat and prevent pregnant women and children from 1 year, and Zanamivir – an inhaled route of administration, high bioavailability, rapid onset of effect and low systemic concentrations.

For prevention of influenza AH1N1 and its severe consequences the most effective way is to carry out the vaccination. There are 2 types of vaccine: trivalent inactivated influenza vaccine (is given by intramuscular injection), live-attenuated influenza vaccine (is given intranasally). In Ukraine are allowed to use these vaccines as Influvac, Fluarix, Intasa, Vaxigrip. Thus, successful practices for preventing influenza A H1N1 is vaccination, and treatment – drug therapy.

INSULIN PUMP IS A MODERN WAY OF INSULIN THERAPY IN PATIENTS WITH TYPES 1 DIABETES MELLITUS

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Insulin pumps (IP) are having recently become the treatment of choice for the most favorable course of the types 1 diabetes mellitus. Today in the world, over 70,000 people use IP. IP a new medical device has a very small volume, intended for insulin to the patient exposed to the program in advance, with the catheter and replacement capacity are attached to insulin in the human body and are removed only when necessary, such as taking a shower, so as not to disrupt the program. Administration of the hormone is by using the remote control. Catheter after entering the needle under the skin attached patch on the belly skin, and the unit with the capacity (connected to a catheter tube) on the belt. An IP allows the replacement of slow-acting insulin for basal needs with a continuous infusion of rapid-acting insulin.

The insulin pump delivers a single type of rapid-acting insulin in two ways: a bolus dose that is pumped to cover food eaten or to correct a high blood glucose level; a basal dose that is pumped continuously at an adjustable basal rate to deliver insulin needed between meals and at night.

Indications for transfer to a pump-action insulin therapy: for labile diabetes;| tendency to hypoglycemia or hyperglycemia; increased glucose levels in the early morning hours; impairment (delay) of mental development; personal motivation.

Benefits of IP therapy: more flexibility for your lifestyle by not having to follow a strict schedule for eating, activity, and insulin injections; fewer injections; improved A1; fewer hypoglycemic episodes (low blood sugars); reduced long-term complications related to diabetes; better predictability for insulin absorption; IP deliver insulin more accurately than injections; makes diabetes management easier – if your glucose level is high or you feel like eating, figure out how much insulin you need and push the little button on the pump; using an IP eliminates unpredictable effects of intermediate- or long-acting insulin.

Although there are many good reasons as to why using an IP can be an advantage, there are some disadvantages. IP can cause weight gain; can cause diabetic ketoacidosis if your catheter comes out and you don't get insulin for hours; can be expensive; can be bothersome since you are attached to the pump most of the time, can require a hospital stay or maybe a full day in the outpatient center to be trained. Even though using an IP has disadvantages, most pump users agree the advantages outweigh the disadvantages.

CONTEMPORARY ASPECTS OF DIABETIC FOOT SYNDROME PHARMACOTHERAPY

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Diabetic foot syndrome is a late-stage complication of diabetes mellitus characterized by prolonged healing, high probability of amputation of one or both extremities and, thus, handicapped status and substantial economic losses. Having regard to the large expenses caused by diabetic foot syndrome the priority line in treatment of foot ulcerous lesions is organ-preserving strategy.

The purpose of study was review of national and international recommendations for contemporary methods of diabetic foot syndrome pharmacotherapy.

The materials of study were: recommendation of International Working Group on Diabetic Foot (IWGDF), showing the principles of lower extremities chronic ulcerous lesions treatment of the persons suffering from diabetic foot syndrome, national standards of treatment of persons suffering from diabetes mellitus and "Algorithm of Specialized Medical Aid to Persons Suffering from Diabetes Mellitus in Russian Federation" including recommendations of International Diabetic Federation (IDF 2005), American Diabetic Association (ADA 2011) as well as the data based on the results of completed international studies (ADVANCE, ACCORD, VADT, UKPDS, etc.)

Results of study: On the data of analyzed sources, irrespective of the degree of diabetic foot syndrome patient extremity ulcerous lesion the following components of conservative treatment may be marked out: unloading of affected extremity, compensation of carbohydrate metabolism, antimicrobial therapy of secondary infection and application of up-to-date means for local wound treatment (choice of dressing, application of the most efficient surgical aid and adjuvant treatment methods). In selection of ulcerous lesion local treatment means some peculiarities of wound healing process in diabetes mellitus patients must be considered (lower epithelization rate, propensity to infection process generalization and some other factors). The selection of dressing must correspond to the stage of wound healing process, support the humid condition in wound, control the level of effluent and prevent maceration lips of the wound (1st proof level). In case a traumatic defect is not reduced by 40% within 4 weeks of treatment therapeutic practice must be changed. Adjuvant treatment methods (donor skin transplantation, vacuum therapy, local growth factor treatment) may be applied only when traditional therapy turns to be ineffective (1st proof level).

Conclusion: Contemporary lines of diabetic foot syndrome, pharmacotherapy were analyzed on the materials of national and international recommendations.

ROFLUMILAST IN CHRONIC OBSTRUCTIVE LUNG DISEASE (COLD) TREATMENT

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Nowadays COLD is a significant social-economic and medical problem. World Health Organization (WHO) forecasts that by 2030 COLD would take the third place among world death reasons.

International experts' opinion, which is reflected on the pages of Global Initiative for Chronic Obstructive Lung Disease (GOLD), claims that one of the main goals of treating the disease is the decrease the number of disease occurrences and its severity.

Present-day ideas show that the key-part in COLD pathogenic mechanism has the inflammatory process that is realized also by phosphodiesterase of 4^{th} type (PDE-4) – enzyme that regulates adenosine-monophosphate periodic metabolism (pAMP). The reduction of pro-inflammatory cells activity, while suppressing PDE-4, designated this special interest for opportunities of pharmacological enzyme inhibition as the way of influence on COLD chronic inflammation intensity.

The Roflumilast is the first representation of the new class of anti-inflammatory drugs – selective PDE-4 inhibitors, that purposefully affects treatment of constitutional and lung inflammatory processes that are connected with COLD. It is recommended by GOLD since 2010.

The Roflumilast effectiveness confirmations in treating patients who have COLD, were obtained while multiple placebo-controlled clinical studies. The drug has significant anti-inflammatory effect, which lowers the COLD relapses and elongates remission periods. The Roflumilast is well combined with background therapy of COLD: with prolonged β_2-agonists and with cholinergic antagonists, also with inhaled glucocorticosteroids, which effect is enhanced. The drug is prescribed to patients who have severe COLD forms. The Roflumilast helps to increase forced expiratory volume per second significantly.

The Roflumilast is registered under the trade name (Dacsas ®) in Ukraine, European Union countries, Canada. The drug is to be taken per os one time in 24 hours by 500 mcg.

Appearance of the Roflumilast in the arsenal of drugs that are used to treat COLD, boosts COLD drug therapy opportunities and allows to influence its pathogenetic mechanisms. In accordance with already existing recommendations on treating COLD (GOLD 2011), the drug may be used as an add-on therapy to the group of patients in the most difficult state, especially with frequent disease relapses.

DETAILED PHARMACOLOGICAL STUDYING OF PHOTOPROTECTIVE CREAM WITH THE NANOPARTICLES OF DIOXIDE OF CERIUM

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Today the main problems in ecology such as global warming and damage of theozone layer can invoke risk for health because of the increased solar activity. First of all threat for health is posed by a cancer of skin, and its most malignant manifestation – the melanoma. 95% of the patients in Ukraine with a melanoma perish that is connected with late diagnostics and untimely prevention. Protection of skin against sunshine by means of UV-filters is the most effective prophylactic of the photodermatosis, aging and a cancer of skin. For today as a part of modern photoprotectors are used physical light filters on the basis of oxide of zinc and dioxide of the titan which according to literature are ineffective in the conditions of hypersensibility of skin for the sun. The huge number of factors can lead to high photosensitization of skin: certain food (a melon, a tuna, grapefruit, etc.), drugs (doxycycline, methoxalen, etc.), photoallergic reactions, genetic predisposition (a fair hair and blue eyes by phenotype).This factors indicate the need of searching to the photoprotector, which can work in the conditions of a photosensitization.

We have made detailed pharmacological studying of cream on the basis of nanoparticles of dioxide of cerium (NDC – cream) on model of a photodynamic trauma in the conditions of a photosensitization with the «Ammifurinum». The technology of this cream has been developed by the professor S.O.Tihonova. This cream had already proved us its efficiency early on the same model in normal conditions and exceed efficiency of existing photoprotectors presented in the market of Ukraine for 15% that is connected not only with a high shielding rate, but also with high antioxidant activity. Experiment is made on 30 same-gender guinea pigs divided into 5 groups on 6 animals. We did radiation by an ultra-violet lamp at distance of 10 cm within 10 minutes on shaven sites of skin about 2x2 cm in size on three on each animal. The photosensitization was done by the solution for external application “Ammifurinum” (0,3%).

Control of results carried out by Suvorov’s calorimetric ruler, level of the histamine in tissues and blood, and quantity of leukocytes. In groups where we had protected skin by the way of NDC-cream the indicators were at the level of intact animals while at animals from groups which we radiated without photoprotectorit was observed expressed erythema, the raised level of a histamine and quantity of leukocytes. It testifies to further prospects of research of cream on the basis of nanoparticles of cerium as unique, universal and powerful photoprotector.

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