HEMP AS A MEDICAMENT

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The cycle of lectures and discussions "Hemp as a Medicine" was originally created for a scientific conference of universities held in Olomouc on December 10, 1954. One section was dedicated to medicinal and especially to the antibiotic effects of hemp.

Other section comprises experiences with matters contained in the hempseed. These matters were extracted by water or salt solutions and hot milk – they principally include edestin, cholin and trigonelin. The first one is a perfect protein providing all the important amino acids necessary for treatment of tuberculosis and for growth, while the others are important for liver.

INTRODUCTION

Within the scope of a systematic study of antibacterially effective substances present in the flora growing in the temperate climate of Czechoslovakia, the researchers have undertaken to investigate more than 3,000 different plant species. In this way they came upon the Indian hemp plant - *Cannabis sativa* var. *indica* - which has been investigated in detail. The subsequent finding of the antibacterial effect of the extract from *Cannabis indica* - direct evidence was provided some years ago at our Institute

of Hygiene - stimulated much interest in cannabis from the medical point of view, and resulted in numerous reports published from different institutes and departments. Independently from the Kabelik's team, the antibacterial effect of the extracts from *Cannabis sativa* was described and studied some years later, particularly by Ferenczy and Drobotko. The interest of Czech clinicians was aroused in this respect by the very good results achieved with the antibacterially effective substances from various plants referred to in the literature.

The preliminary results obtained were published in 1952 in the Czechoslovakian medical journal *Lekarske listy* and in a compilation of communications submitted at the scientific conference held by the university in Olomouc in 1955. A survey of their work was published in the journal, *Die Pharmazie*, 1957-1959.

The Study is divided into the following sections:

1. **History of the medicinal use of hemp.** Treatment with cannabis in ancient, folk and official medicine up to the beginning of the twentieth century.
2. **Properties of isolated substances.** A brief survey of the methods of isolation and the physical and chemical properties and structures of the isolated antibacterial substances. Preparation of extracts, bacteriological technology, spectrum of bacteria sensitive to Cannabis indica.
3. **Methods and results of the bacteriological experiments.** On the basis of the mentioned dependence, conclusions should be drawn as to the practical utilization of the preparations with antibacterial substances from cannabis at varying pH of some pathological processes as, for example, in suppurant wounds, furuncles, otitis, sinusitis and the like.
4. **Survey of clinical experiences.** A systematic investigation of the mid-European flora has been carried out in order to establish the presence of antibacterially effective substances. A high content of remarkably active substances has been found present in *Cannabis sativa var. indica* and in *Cannabis sativa*, a plant cultivated for the industrial utilization of the hemp fibre. It has been investigated in detail from the bacteriological and the chemical viewpoint and

from the standpoint of the eventual applicability of the effective substances in clinical practice.

Experimentally we could evidence the bactericide effect of the substances from cannabis *in vitro* upon a number of micro-organisms. Finally, the experiments made in clinical practice, particularly in stomatology, otorhinolaryngology, gynecology, dermatology, phthisiology, with some pharmaceutical preparations containing antibacterial substances from cannabis have been reported.

Attention has been drawn to the advantageous utilization of the active substances from cannabis in veterinary medicine, and particularly in preventive medicine for anthropozoonoses.

5. **Therapeutic results in stomatology.** Application of substances obtained from hemp in teeth treatment and preservation stomatology.
6. **Cannabis indica in oto-rhino-laryngology.** A positive response due to antibiotics obtained from hemp could be observed in patients with otitis, sinusitis, ulcers of the anterior narines, furuncular otitis and chronical otitis.
7. **Importance of hemp seeds in the tuberculosis therapy.** The application of the hempseed in the tuberculosis therapy is based on a thirty years' experience acquired with regard to diet at the sanatorium in Jince. The right function of the liver has always been considered by the authors as the necessary supposition for complete assimilation: that is why those commands and limitations, nowadays known as the fundamental rules of a liver diet, have been stressed.
8. **References of the study.**

Sources:

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History of the medicinal use of hemp

Treatment with cannabis in ancient, folk and official medicine up to the beginning of the twentieth century

By J. Kabelik

The knowledge of narcotics and stimulants extends far back to ancient and medieval times but since then, as far as is known, no new discoveries have been made. In Europe, of course, some of them appear not to have been known until later, as was the case with the narcotics of the Old World - for example, with hashish. Europeans learned of it for the first time through the Crusaders, but its deliberate use as well as abuse - according to Perrot - came from Napoleon's soldiers, who introduced it after their return from the Egyptian campaign.

Cannabis is, however, a very old cultivated plant apparently indigenous to central Asia. Cannabis was found by our archaeologists to have existed in central Europe in the Bylony Culture (7,000 years ago). The Chinese knew of it perhaps 4,000 years ago, certainly in the 9th century B.C., primarily as a medicinal herb and a century later as a textile plant. According to Herodot, the Scythians knew it as a plant which can be spun and as an oil-producing plant and, apparently, even as a narcotic which they made use of in their steam baths - the sauna. Perhaps the earliest accounts of the medicinal utilization of cannabis may be found in Indian medical literature. Ancient Indian surgery, according to Susrat (Samhita), used hyoscyamus and cannabis as anaesthetics. From the Egyptian medical papyruses, information has been gained about a plant from which cordage could be made, and it was probably cannabis which was referred to. But no records could be found on its narcotic action. The preparations made from it (in all probability from the cannabis shoots) were applied externally-namely, exclusively as antiseptics - and then perhaps even as analgetics, in the same way as in Hellenic medicine. Cannabis extracts have been employed for

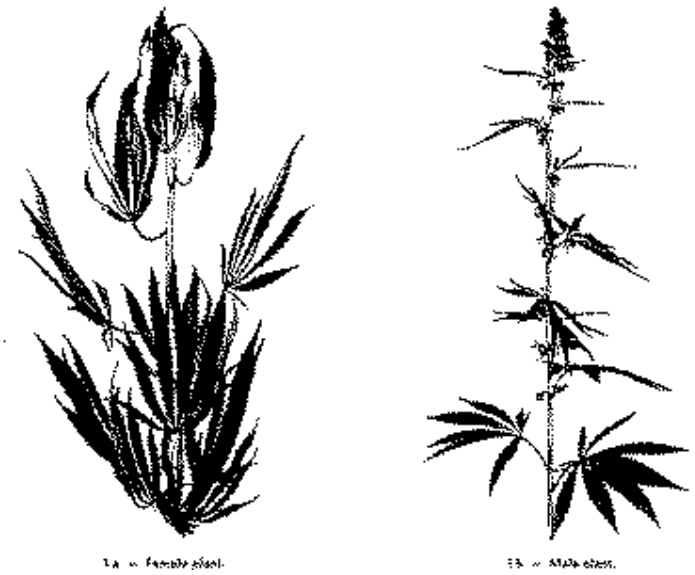
irrigation in diseases of the anus, and in form of compresses the drug has been applied to sore toenails. In Rhamses' papyrus, washing sore eyes with extracts from cannabis and also from some other plant is recommended. The papyrus of Berlin recommends fumigation with cannabis in some undefined disease. Cannabis has been prescribed in feverish diseases of the bladder and, even at present, in homoeopathic medicine it ranks first when cystitis is treated. Furthermore, extracts combined with honey were injected into the body of the uterus to achieve constriction of the uterus and, externally, an ointment combined with fat was applied antiseptically in the same way as was done in medieval medicine up to the present time. Cannabis shoots were well known to Galen and to Dioscorid. Homer's nepenthes - potion of oblivion - has been identified by some authors as a cannabis drug, but generally it is believed to be a preparation made from *Hyoscyamus muticus* - a plant familiar to the Egyptians. Both these authors make greater use of the seeds and of the oil extracted from them than of the cannabis shoots. It is the same in old popular and even in modem medicine. The seed pulp was a favourite dish, and from the seeds an edible, industrial and medicinal oil was obtained. In Czechoslovakia, a preparation from seed pulp was recently introduced by Sirek to act as a roborant diet in treatment of tuberculosis.

Comprises an extensive survey of reports by authors from the USSR. The botanical-historical and technical aspects of cannabis are not dealt with in this report.
But hemp seed does not form the subject matter of this paper; it is only treatment with cannabis shoots which is discussed, and only with regard to the healing of wounds, and not to the hashish effect.

The uses mentioned in the Egyptian papyruses point fundamentally to antiseptic use. Analogous uses were known, in varying degrees, to African natives and were recorded in medical herbals. There is no information on the narcotic action. It is of interest that in Egypt they are supposed to have learned of the hashish effect only during the Middle Ages, from the Arabs. This could be explained by the fact that the Arabs were the first to import the variety producing the physiologically active resin, for at present *Cannabis indica* Lam. is not considered to he a species but a variety of

Cannabis sativa L. and not even a particular variety, Cannabis is a very variable and plastic plant of variable height and variously membered and formed leaves; there exists a monoecious variety, too. Any cannabis plant can produce hashish under favourable climatic conditions. Vice versa, according to Pulewka the Indian variety does not always produce the narcotic substance, not even in warm countries. Plants cultivated in 369 places in Anatolia did not produce hashish substances throughout; the occurrence was conditioned by the climate and the habitat. Likewise, the hashish effect has not been found present in *Cannabis indica* cultivated in north Moravia, though this variety grows exceedingly well. The stem attains a height of about 4 m, bears rich seeds, and the tops produce resins which have a very pronounced antibiotic and analgesic effect. It is possible, however, that there was no hashish-producing Variety grown in ancient Egypt, for the climate was, at that time, in all probability rather damp and subsequently much cooler than it is at present. This may be concluded from the fact that in antiquity in Italy and the Balkans snow was a more frequent phenomenon than it is nowadays, and north Africa was the granary of Rome, and not a desert.

FIGURE 1, Cannabis sativa var. indica



All the information obtained from European folk medicine with regard to treatment with cannabis shows clearly that there do not appear to be any narcotic substances in it, or if there are then only in a negligible amount. Instead of that, emphasis has been laid on the antiseptic effect, hence on the antibiotic and to a small extent even on the analgetic effect, which has been upheld in official medicine up to the beginning of this century. In Austria, up to World War I, a salicylate collodion combined with *Extractum Cannabis* was prescribed for application to corns. Unna's green salve, which was used as a remedy for lupus, contained: *Acid salicyl.*, *Liq. Stib. chlorati* aa 2.0, Extr. *Cannabis ind.*, *Creosoti* aa 4.0 , *Adeps lanae* 8.0. It may be noticed that the substances contained in cannabis have a powerful antibiotic effect upon Myc. tuberculosis, as will be discussed later. On the basis of the results obtained from our investigations, it is suggested that in many analogous cases it would be advantageous to return to cannabis preparations again.

The ancient herbals and those of the Middle Ages mentioned medical use of the seed, the roots (emoelients) and of the tops containing resinous substances. As previously stated, only the latter will be discussed here in detail. The leaves and the juice extracted from them or the macerated leaves were used as a vermifuge for horses, and fisherman soaked the ground with a liquid prepared from them to force up the dew-worms, which they used as bait. Tabernaemontanus and Kramerarius recommended kneading the dried leaves with butter and application of them in form of an ointment to burns. We have obtained positive results with extracts from cannabis in treatment of burns. Ruellius cit. advised the use of cannabis extract as ear-drops in the treatment of ear ache, and also for treatment of wounds and ulcers. Women stooping due to a disease of the uterus were said to stand up straight again after having inhaled the smoke of burning cannabis. In cystitis and in urinary diseases, a decoction of hemp shoots with wine and water was recommended; the steam was allowed to rise as hot as could be endured against the perineum, after which the patient was advised to urinate. This use has more to do with the analgetic than the antiseptic effect. As previously mentioned, homoeopaths value highly both the teep cannabis D_2 - 0.25 g (teep is the fresh drug ground with lactose) and the *tinctura Cannabis indicae* D_3 up to D_4 which are employed in cases of cycstitis and

of urethritis. The homoeopathic utilization of cannabis is fundamentally based on its effect on the central nervous system - i.e., in migraine as discussed in Schoeler's *Kompendium* and by Auster & Schaefer. The homoeopaths do not otherwise utilize the antiseptic effect when they employ it internally; it is only the centrally sedative action they make use of in the same way as the allopathists did formerly - i.e., in gastralgias and the like. In these cases of internal application the antiseptic effect is, however, doubtful save in the case when the intestinal flora is concerned.

So far the cannabis preparations - hashish preparations - have been frequently investigated therapeutically, particularly in neurology and in psychiatry, but they were abandoned because the results achieved were not uniform. Nevertheless it would be advantageous to utilize the analgetically sedative effect without the narcotic action of the hashish. Burroughs Wellcome & Co. manufacture a special product: Cannabine Tannate - cannabis combined with tan, *Hydrastis canadensis* and *Secale cornutum* - which has a sedative effect in metrorrhagias and in dysmenorrhagias. From earlier times, otorhinolaryngologists have preserved a prescription against *tinnitus aurium:* ZnO, Extr. *Valerianae*, Extr. *Hyoscyami,* Extr. *Cannabis* aa 1.6 M.f. pill No. 60, D.S. 3-5 pills daily per os. Finally, some years ago, in the *American Journal of Pharmacy*, vol. II (cit. Dinand), the following treatment was recommended in migraine: before meals take for a fortnight conscientiously and daily 0.015 g Extr. *Cannabis indicae*, the third week 0.02 g, the fourth week 0.03 g, to be continued for some months. In all these cases it is the action on the central nervous system which makes its influence felt. Of rather particular interest is the frequent combination of cannabis with tan both for internal and external application. We have obtained very good results in stomatitis aphtosa, gingivitis, and in paradentoses with a mouth wash of the following composition: *Tinct. Cannabis* 20.0, *Tinct. Salviae*, *Tinct. Chamomillae, Tinct. Gemmarum populi* (or another tan - for example, *Tinct. Gallarum*) aa 10.0, to be applied in the form of sprays or liniments to the inside of the mouth. The use of cannabis as an analgetic but not as an antibiotic in stomatology has been also briefly mentioned by Hegi.

FIGURE 2, Cannabis sativa - engraving from the Czech edition of Mathioli's herbal from the year 1596

In folk medicine particular use is made of the seed. But we also come across the utilization of the shoots for antibiotic and repellent purposes. Around cabbage plants, cannabis plants are grown to repel pieris (caterpillars), and twigs of cannabis are hung in bedrooms to repel gnats and flies.

During the Middle Ages cannabis decoctions were given to cattle for diarrhoea. In Argentina cannabis is considered a real panacea for tetanus, melancholia, colic, gastralgia, swelling of the liver, gonorrhoea, sterility, impotency, abortion, tuberculosis of the lungs and asthma. In Argentina even the root-bark has been collected in spring, and employed as a febrifuge, tonic, for treatment of dysentery and gastralgia, either pulverized or in form of decoctions. The root when ground and applied to burns is said to relieve pain. Oil from the seeds has been frequently used even in treatment of cancer; we have also come across this application in European folk medicine. Also in Argentina, in folk medicine, hemp shoots extracted with butter (*Extr. Cannabis ind. pingue*) are supposed to have a powerful hashish effect, it is believed already, in an amount of 0.1 g; it is employed as a remedy in the Basedow disease. The ethereal extract is less active, and in Argentina it is administered for headache, neuralgia, gout, rheumatism, chorea, melancholia, hysteria, delirium, gastralgia and anorexia. The aqueous macerated product has no narcotic effect at

all, and is employed for treatment of tuberculosis of the lungs and as a hypnotic for children and to relieve spastic constipation. An infusion of the leaves is considered to possess a diuretic and a diaphoretic effect. In Europe we also come across many of these uses. Thus Graemer (cit. Dinand) recommends the following for treatment of gastralgia: 0.75 g Extr. *Cannabis ind.*, 10 g ether; 10 drops daily on sugar. For rheumatism a decoction of leaves (15-20 g/0.5 1) is taken internally, and externally poultices prepared of seeds and packings of shreds or tow are used. In Brazil hemp is considered to be a sedative, hypnotic and antiasthmatic remedy. A pronounced antibiotic effect has been observed in South America, where fresh leaves after being ground are used as a poultice for furuncles, and in folk medicine in Europe for treatment of erysipelas (Dinand). Even seed pulp is applied in such cases, but as there are no antibiotics in the seeds we must assume that there is another therapeutic factor involved. In the popular treatment of headache, the plant is preserved in vinegar together with juniper, and the extract is used in form of compresses. Githens and also Watt & Breyer-Brandwijk report on the utilization of cannabis (dagga) in South Africa. There it is smoked because of its narcotic action, but it is also used medicinally. Next to the effect upon the central nervous system we find a considerable use as an antibiotic. For example, the Xosa tribe employs it for treatment of inflammation of the feet. In Southern Rhodesia it is a remedy for anthrax, sepsis, dysentery, malaria and for tropical quinine-malarial haemoglobinuria. The Suto tribe fumigates the parturient woman to relieve pain. These analgetic, sedative and antibiotic properties of cannabis in internal and external application are well known to African tribes.

It may be concluded that ancient and folk medicine have utilized cannabis as an antibiotic and analgesic externally and later as a sedative internally. Narcotic effect has been observed in hot climates only.

Properties of isolated substances

A brief survey of the methods of isolation and the physical and chemical properties and structures of the isolated antibacterial substances

By F. Santavy & Z. Krejci

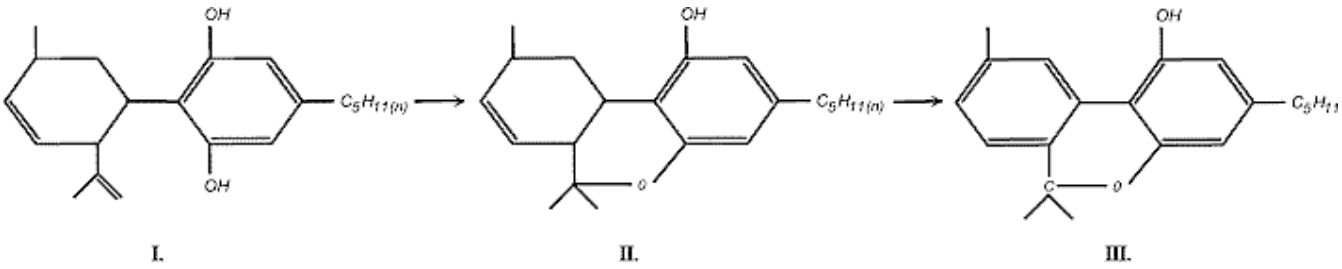
During the last two decades, attention has been drawn to the isolation and toxicology of the substances contained in the plant, *Cannabis sativa*. The following substances have been isolated: cannabinol, cannabidiol, tetrahydrocannabinol, quebrachitol (*l*-inositolmonomethylether), 1-methyl-4-isopro-pylbenzen, the so-called cannabol of phenolic character which yields a readily crystallizing ester with the chloride of the azobenzencarbonic acid and an optically active and volatile material which was not studied in more detail. In addition, from the individual parts of the plant a series of less important substances has been isolated and listed in detail in Wehmer's compendium. The quantitative changes of carotene found present in *Cannabis sativa* have been investigated by Lebedev.

It is perhaps also of interest that cannabis greatly increases the hypnotic effect of barbiturates.

Moreover there exists a series of communications concerned with the isolation and study of substances contained in cannabis which can be extracted from the petrol extract due to its solubility in alkaline lye or in sodium carbonate. The most detailed work in this line was carried out by Todd *et al*. But none of the authors succeeded in isolating from that portion any acid in crystalline form,-i.e., either an acid itself or its derivative - designating it or determining its constitution. Probably it was the amorphous substance isolated by us and the cannabidiolic acid which was studied further that Todd *et al*. had in hand (see below) but they conclude: "... it is concluded that the alkali-soluble portion of the resin contains esters of cannabidiol and cannabinol with a phenolic acid ".

Among the isolated and identified substances mentioned above, cannabinol, cannabidiol and tetrahydrocannabinol proved to be pharmacologically interesting with

regard to the hashish effect; a specific hashish-effect is produced only by tetrahydrocannabinol. The formulas of these three substances are:



I. II. III.

All these compounds have already been prepared synthetically and, in addition, a series of homologous derivatives has been prepared for the purpose of establishing the relationships between the constitution and the biological effectiveness.

At this stage of the development of the investigation of substances contained in *Cannabis sativa* we began a new line of investigation when one of us found that there are substances contained in it which show an antibiotic effect upon some micro-organisms.

1. Starting material

Fresh or dried pistillate flowers of the cannabis plant (*Cannabis sativa var. indica* - fig. 3) were used in order to extract the active substances. A plant was used which was not cultivated in a tropical climate, but in the temperate climate of Czechoslovakia for more than five years. We know perfectly well that this factor had undoubtedly a considerable influence both upon the quantitative production of the effective substances or, respectively, upon the composition of the substances contained in the cannabis, and this has been also confirmed by Pulewka. Consequently, it may be assumed that this inconstant "variety indica" has become closely similar to *Cannabis sativa*, a plant grown for industrial purposes. Positive results have also been obtained when investigating effective substances contained in *Cannabis sativa* L., a plant commonly cultivated particularly in Slovakia for the industrial utilization of the hemp fibre. We succeeded in showing that the drug from

this plant contains antibacterially effective substances. Unfortunately, the drug from the warmer, tropical or subtropical regions was not available for comparison. The drug obtained from Romania and Yugoslavia did not vary fundamentally in comparison with the raw material available in Slovakia. It must be born in mind that the various cannabis species cultivated in the same climate differ considerably with regard to the quantity of the biologically active substances present; the quantity of the substance amounted from about 0.2 g to 25 g/kg. Likewise, the varying quality of the period of vegetation (dry, rainy, warm and cool weather and also the manure) produces a considerable effect upon the production of the resin and, subsequently, of the biologically active substances. The best, and most valuable raw material yielding antibacterial substances and containing on the average 1-1.5% effective resin substances has been found at the stage when the seed is mature.

FIGURE 3, Cannabis sativa var. indica - plant shoots. A - Flowering shoots of the pistillate plant (rich in resins). B - Flowering shoots of the staminate plant.

2. Method of isolation

The preliminary experiments showed that the biologically effective substances (46-50) of the resin from *Cannabis sativa* may be easily extracted with ether; the paper chromatography revealed that highly polar substances were being dealt with. After

having carried out a series of preliminary experiments, our method of isolation was as follows.

Fresh and rapidly dried tops and leaves of *Cannabis sativa* were extracted in the cold in a percolator with benzene or, preferably, with petrol ether. After partial distillation of the solvents under reduced pressure at 30°C, the residue was carefully extracted with 4% natrium hydroxide, into which both the acids and the substances of phenolic character could be taken up. They were extracted with chloroform after acidification.

First of all the oily residue was shaken in a nitrogen atmosphere with an aqueous $NaHCO_3$ solution with which the acids, particularly the cannabidiolic acid, were extracted to yield a slightly yellow product. By shaking with $NaHCO_3$ an oily residue was obtained which was shown to consist in the main of substances of phenolic character. Both the acid and the phenolic fractions produced an antibacterial effect upon some micro-organisms.

TABLE 1

Output and biological activity of the single fractions isolated from cannabis

	Output (grammes*)	Biological activity
Petrolether fraction	59.0	+++
Ether fraction	0.6	+
Chloroform fraction	0.2	-
Ethanol-chloroform fraction	0.05	-
Aqueous residue	6.3	-
Phenolic constituent		+++
Acetylated phenolic constituent		++
Acid constituent (cannabidiolic acid)		++++
Acetylated cannabidiolic acid		+++
Acetylated and hydrogenated cannabidiolic acid		++++
Cannabidiol		+++
Trans-cinnamic acid		-

* Values referred to 1 kg of dried material.

After three reprecipitations the acid fraction was allowed to dry over a long period under water pump vacuum at 20°C to yield a colourless glassy substance, the empirical formula of which is $C_{22}H_{30}O_4$ '[&alpha]$_D^{24}$ -95° ± 8° (c = 1.00 in chloroform); [&alpha]$_D^{24}$ -115° ± 4° (c = 1.05 in ethanol). The substance crystallized readily after acetylation, m.p. 80-100°/127-128°, [&alpha]$_D$ -114° ± 4° (c = 1 in ethanol).

Repeated isolations showed that the antibiotically effective cannabidiolic acid from *Cannabis sativa* is very sensitive to atmospheric oxygen (particularly in a warm atmosphere) and, furthermore, that the acid undergoes changes due to higher temperature and a simultaneously reduced pressure.

Modification according to Schultz & Haffner.

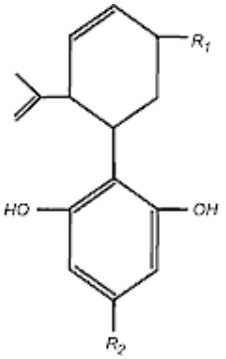
From some of the crops the acetylester of the acid, m.p. 95-100/ 110-15° was obtained. According to our assumption, there are either two isomers present whose occurrence is conditioned by the climate, or these substances are interconvertible.

FIGURE 4, Rate of inhibition of the acid and phenolic fraction of the extract from cannabis upon the inoculated staphylococcus (meat peptone broth) 1 - Acetylated fraction from which the cannabidiol acid crystallized. 2 - The acetylated phenolic residue.

3. Determination of the structure

As previously mentioned, the biologically active acid isolated from *Cannabis sativa* has the empirical formula $C_{22}H_{30}O_4$, and yields, when acetylated, a diacetyl derivative $C_{26}H_{34}O_6$ whose extinction curve in the UV-range closely resembles that of the

cannabidiol derivatives. At the beginning of our experimental work, therefore, the acid obtained by us was already called cannabidiolic acid:



$R_1 = CH_3$, $R_2 = C_4H_{10}COOH$ nebo $R_1 = COOH$, $R_2 = C_5H_{11}$ (n) nebo $R_1 = CH_3$, $R_2 = C_5H_{11}$ (n) -COOH

By boiling with alkali, the acetylated cannabidiolic acid is saponified and partially decarboxylated, which results in precipitation of a substance of phenolic character from the solution, particularly after its saturation with carbon dioxide. That the substance undergoes decarboxylation was best seen when we tried to purify the proper acid isolated by us or the acid liberated from its acetylester by the help of sublimation. The process gives rise to cannabidiol, a substance characterized by the positive Beam-reaction and as 3,5-dinitrobenzoate. This supports our former view that, regarding the structure, the antibacterially effective acid, isolated from *Cannabis sativa*, is closely related to cannabidiol.

The position of the carboxy1 group in the molecule of the cannabidiolic acid was studied along the physical-chemical pathway.

On comparing the optical rotation of the cannabidiolic acid, its acetyl derivative and its tetrahydro derivative with the cannabidiol, derivatives we found a remarkable correspondence. An analogous agreement exists between the derivatives of the tetrahydrocannabinol and hexahydrocannabinol; acetylation and methylation do not bring about a significant change in the degree of the optical rotation. The percentage rate of the molecular optical rotation of the hydrogenated and the unhydrogenated derivatives is, as far as these three groups are concerned, practically the same. The optical rotation changes only with the varying position of the double bond of the B-

ring and because of the formation of an ethereal bridge due to conversion of cannabidiol into tetrahydrocannabinol. From the above it may be concluded that the carboxyl group of the cannabidiolic acid does not seem to be attached to some carbon of the isocyclic nucleus where it could lead to the formation of a further optically active centre, but that it is attached either to the aromatic nucleus or to some other carbon where an optically active centre cannot be formed. The ready decarboxylation excludes its position on the carbons 7, 9 and 15.

TABLE 2

Values of the optical rotation of the single substances (in ethanol) (Degrees)

Substance	[L]D	D
Cannabidiolic acid and its derivatives		
Cannabidiolic acid	-115	-412
Diacetyl derivative	-114	-504
Tetrahydrodiacetyl derivative	-22	-98
Cannabidiol and its derivatives		
Cannabidiol (2)	-125	-393
3,5-dinitrobenzoate (2)	-76 *	-513
Dimethylether (2)	-133	-455
Monomethylether (2)	-118	-373
Tetrahydrodimethylether (3)	-28	89
Tetrahydrodiacetyl derivative (3)	-30	-104
Tetrahydrocannabinol and its derivatives (l b, 4)		
Isomer I	-267	-834
Isomer II	-130	-406

Hexahydrocannabinol	-70	-220

* Acetone

In addition, we have tried to determine the position of the carboxyl spectroscopically. The acetyl derivative of the cannabidiolic acid shows an inflexion in the UV-range, or a maximum at the same wavelength as cannabidiol, or its derivatives (fig. 5). Analogously, the same maxima are produced by the diacetylester of the hydrogenated cannabidiolic acid.

Evidently, therefore, the carboxyl group, of the cannabidiolic acid is not conjugated with the double bond of the nucleus B.

Still more striking is the behaviour of the carboxyl group in IR-spectroscopy (fig. 6). We attribute the frequency at 1770 cm $^{-1}$ to both phenoacetoxy groups. The frequency at 1698 cm $_{-1}$ to the free carboxy group, or to its carbonyl, respectively. This frequency does not vary, either with the acetylester of the cannabidiolic acid or with its hydrogenated product (cf. table 3).

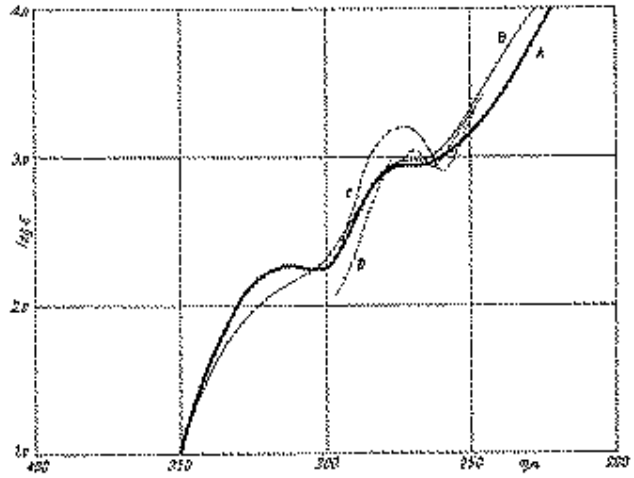
Our thanks are due to Dr. Horak, Institute of Chemistry, Academy of Sciences, Prague, for the measuring of the infra-red spectra and their evaluation.

TABLE 3

IR-frequency values within the carbonyl range

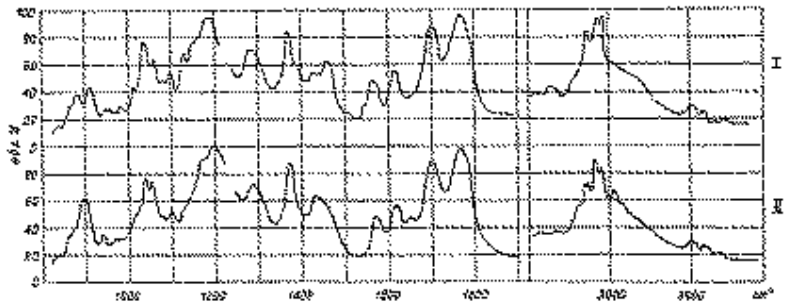
	Concentrated Solution	**Diluted solution**	**Dioxan**
	In chloroform		
Acetylester of the cannabidiolic acid	1698 cm-1	1700 cm-1	1728 cm-1
Hydrogenated acetylester of the cannabidiolic acid	1698 cm-1	1700 cm-1	1728 cm-1

FIGURE 5, UV-spectra of the cannabidiol derivatives (in ethanol). A - Acetylester of the cannabidiolic acid. B - Hydrogenated acetylester of the cannabidiolic acid. For comparison the curves of the dimethylether of the cannabidiol (C) and of the dimethylether of the dihydrocannabidiol (D) have been taken from the literature.



With regard to the fact that the frequencies of the carbonyl of both acetoxy compounds (i.e., of the saturated and of the unsaturated) are found to be the same, it may be assumed that it is not a carboxyl situated in position 4, 5 and 9 which is being dealt with, for the disrupture of the conjugation due to reduction would be followed by a shift of the frequency to higher values. On the contrary, the frequencies observed in chloroform (1698 cm-1) and in dioxane (1728 cm-1) evidence again that it is not the alicyclic acid (i.e., in position 1,2,3,6) - namely, one whose carbonyl is not conjugated - for the frequencies of such acids have been found to appear in the higher frequency region (in chloroform at about 1715, in dioxane at about 1740 cm-1). But there was a very good agreement to be seen with regard to the frequency of benzoic acid (in chloroform 1694, in dioxane 1724 cm-1).

FIGURE 6 IR-spectra I - Acetylester of the hydrogenated cannabidiolic acid. II - Acetylester of the cannabidiolic acid. Both compounds have been solved in chloroform.



If we take it for granted that there is a carboxyl attached to the aromatic nucleus, it is only conceivable in position 3 (or 5, respectively).

The frequency at 1615 cm-1 belongs to the aromatic vibrations and the frequencies at 900 and 1650 cm-1 which disappear during hydrogenation must be attributed to methylene in isopropylene.

On the basis of the organically preparatory experiments carried out so far, comparison of the optical rotation and of the UV- and the IR-spectra, the formula for cannabidiolic acid suggested by us is as follows:

(3-methyl-6-isopropenyl-4'-n-pentyl-2',6'- dihydroxy-l,2,3,6-tetrahydrodiphenyl-3'-carboxylic acid)

The arrangement of the substituents of the nucleus A of the cannabidiolic acid, as formulated by us, does not appear to be exceptional among the natural substances obtained from plants. If, in the case of the cannabidiolic acid, we do not take into consideration the partially aromatic nucleus B, we obtain the olivetolic acid which has been found present in numerous plants. This substance is also readily decarboxylized and thus converted into olivetol which forms the aromatic moiety of

cannabidiol. There are also some deeply related reactions ($FeC1_3$,$CHC1_3$+ 10% KOH, Vanillin + HCl) to be found in both groups of these substances.

Independently from us (1955) Schulz & Haffner (1958) isolated and described the above-mentioned cannabidiolic acic. The determination of the constitution was carried out (1959) by means of the organic-preparative methods which led them to the same results as those obtained by us (1958). In their communication the authors conclude that the cannabinols occur in the plant due to decarboxylation of the aforementioned cannabidiolic acid.

In addition to the cannabidiolic acid a further acid, m.p. 131-133°, has been isolated from *Cannabis sativa*, and identified by us as *trans*-cinnamic acid.

SUMMARY

Our study of the Mideuropean flora with regard to its contents of substances producing antibacterial effects comprehends 3,000 species from which the Indian hemp - Cannabis indica - grown in Czechoslovakia has been selected for elaborate investigation. A preliminary method of isolation accomplished by paper chromatography with the disclosure of an effective zone in the biological way has been described.

The most advantageous methods of extraction were determined, and the bactericide effect of the hemp substances experimentally proved in vitro on Gram-positive microorganisms: Staphylococcus pyogenes autreus haemolyticus, Staphylococcus aureus - resistant to penicillin, Streptococcus beta haemolyticus, Streptococcus viridans, Pneumococcus Cornyebacterium diphteriae, and Bacillus anthracis.

Gram-negative microorganisms of the typhus-coli group remain resistent, as well as Pseudomonas aeruginosa and Proteus vulgaris. An excellent antibacterial effect on Mycobacterium in vitro even in a dilution 1:150,000 could be ascertained.

A parallel between the bactericide effect of isolated, amorphous, and crystal substances, and a comparison of the sensibility of the two applied bacterial methods, both the modified Oxford method and the tests in a liquid medium was made in detail. The limit of efficacy in the maximal dilution of biologically active substance (1:100,000) and the velocity of their effect in various dilutions were determined. The influence of inactivating factors has been studied in detail. Blood, plasma, and serum partly inactivate them and reduce their antibacterial effect.

As a conclusion, a comparison of the efficacy of these active substance[s] with penicillin and streptomycin at various pH was worked out, and a summary of hemp preparations manufactured for the purpose of clinical application in stomatology, oto-rhino-laryngology, dermatology and phthisiology has been given.

Methods and results of the bacteriological experiments

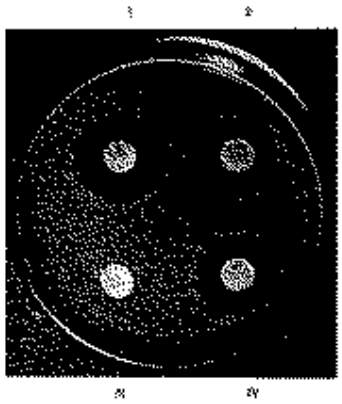
By Z. Krejci

I. - PRELIMINARY BACTERIOLOGICAL EXPERIMENTS WITH EXTRACTS FROM Cannabis sat. var. indica

1. Preparation of extract for the preliminary microbiological evaluation

It was clear from the beginning of our experimental work that the antibiotic effect of the drug must stand in close relationship with the content of the resin substances contained in the leaves and, particularly, in the shoots of the pistillate plant (fig. 3). The ground drug was extracted by the method devised by Carlson. The different parts of the plant (roots, stems, leaves, shoots and seeds) were extracted at higher temperature, normal room temperature, and even at 1°C, at the ratio of 1:5, with ethylalcohol, ethylether, a physiological solution, 1.5% sulphuric acid, and 1% sodium hydrocarbonate. The extraction was carried out to advantage with organic solutions, particularly with petrolether, benzene and ethylalcohol.

FIGURE 7, Rate of the inhibitory effect of the raw extract from cannabis upon Staphylococcus aureus (modified Oxford method). One drop of the extract has been used for carrying out the test. I - Extract in 70 per cent ethyl alcohol . II - Extract in 96 per cent ethyl alcohol. III - Diethyl ether extract. IV - Control test with 96 per cent ethyl alcohol.

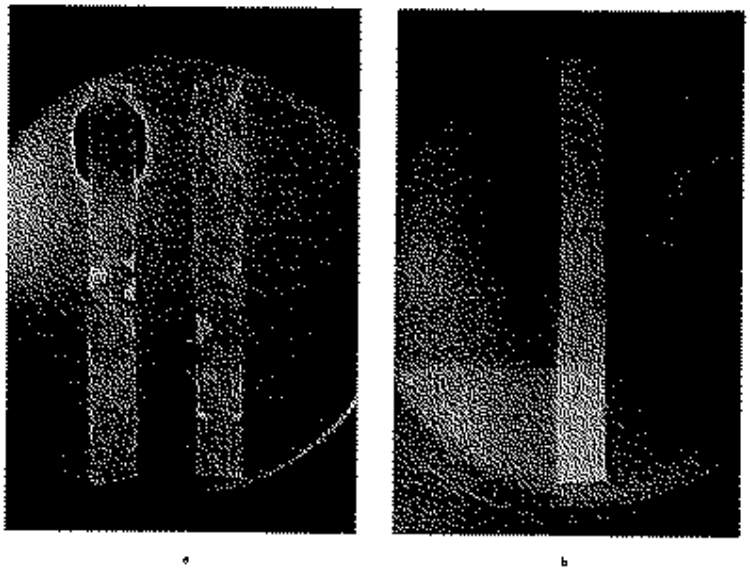


2. The bacteriologic technique

The extracts prepared in various ways and by using various kinds of solvents were tested for the presence of antibacterially effective substances by the help of the modified Oxford method. On an Agar culture medium contaminated with the examined microbe, a filter paper 10 mm in diameter, saturated with the antibiotic, was applied. The inhibition zone around the butts found present after 24 hours of incubation was used for the evaluation of the effectiveness of the substance. In order to ascertain the maintenance of a given set of conditions, particularly the same amount of microbes, most of the tests were carried out in bacteriological culture mediums with inoculated microbes (fig. 7).

The other and more detailed investigations (the rapidity of the effect, the inhibition factors and so on) were carried out routinely in the fluid medium of peptone water or, with the aid of Sauton culture mediums (BK), respectively.

FIGURE 8 Chromatography illustrating the inhibitory effect upon the growth of the staphylococcus around the antibiotically active zone; undimensional ascending paper chromatography. b shows two zones running into each other (cf. details in the text).



The preliminary experiments concerning the isolation of biologically active substances were performed by the help of the ascending chromatography or the capillary analysis. The antibacterially effective fractions were detected by placing the chromatograms into inoculated culture mediums. The zone which inhibited the growth of the microbes was considered to be biologically active (fig. 8a, b).

An analogous method based on the capillary analysis and used for the isolation of effective substances is illustrated in fig. 9. The terminally situated zone in the ring chromatogram when placed into an Agar medium inoculated by staphylococcus produces a considerable inhibitory effect upon the growth of the above-mentioned micro-organisms. Further work showed that the chlorophyll contained in the plant extract does not produce any direct antibiotic effect.

3. Spectrum of bacteria sensitive to active substances obtained from cannabis

The investigations were carried out with specimens of gram-positive micro-organisms - i.e. *Staphylococcus pyogenes aureus* - and from the gram-negative series the *Escheria coli* were used. The extracts produced a remarkable bactericide effect upon *Staphylococcus aureus*, whilst *E. coli* showed to be resistant. On the basis of these preliminary findings we have aimed our work in this direction. Proof could be furnished that the cannabis extracts produce a very satisfactory antibacterial effect upon the following microbes: *Staphylococcus pyogenes aureus, Streptococcus alpha haemolyticus, Streptococcus beta haemolyticus, Enterococcus, Diplococcus pneumoniae, B. subtilis, B. anthracis, Corynebacterium diphtheriae and Corynebacterium cutis* - i.e., all of them gram-positive micro-organism. Note-worthy is the effect upon *Staphylococcus aureus* strains, which are resistant to penicillin and to other antibiotics (fig. 10).

That was one of the peculiar properties of cannabis which was found to be most attractive. We saw the possibility of utilizing the antibiotic locally without any danger of producing resistant strains to other antibiotics administered at the same time throughout treatment. We must also remember the very good effect of substances

from cannabis upon *Staphylococcus aureus*, particularly nowadays, when a high percentage of staphylococcus diseases offers resistance to penicillin. It is interesting that staphylococci manifesting various degrees of resistance to one or more antibiotics (erythromycin included) are sensitive to the antibiotics from cannabis in the same degree throughout. So far, we have not observed that any resistance of the staphylococcus strains to these substances would arise. The degree of the artificially produced resistance to these substances, as shown by Martinec, corresponds with the origin and the degree of resistance to substances of the phenolic type and to other disinfectants.

FIGURE 9 Inhibitory effect upon staphylococcus when placing the circular paper chromatotogram - capillary analysis - into inoculated Agar. The light centre and the spots around the periphery of the Agar plate indicate the boundary of the inhibitory zone produced by the active substance. It appears that there are two biologically active substances present whose partition factors show to be different; evidence in this respect could be brought forward chemically.

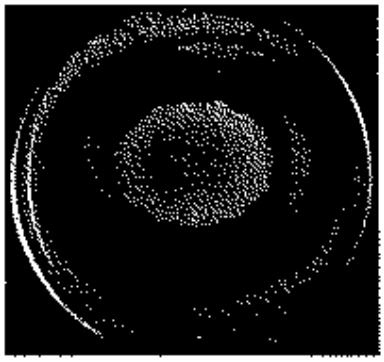


FIGURE 10 A parallel drawn between the rate of the inhibitory effect of the extract from Cannabis indica and of penicillin upon penicillin resistant strains of Staphylococcus aureus. I - 2% acidum carbolicum liq. II - 1,000 OU of penicillin. III - Hemp extract in 70% ethyl alcohol. IV - Hemp extract in 96% ethyl alcohol.

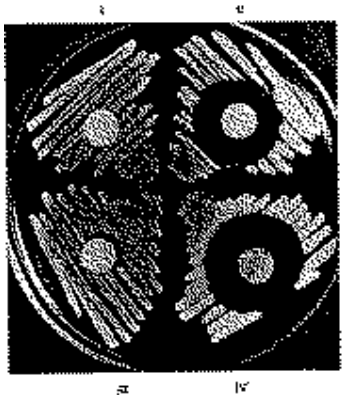
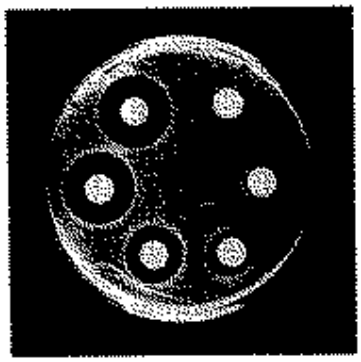


FIGURE 11 Preliminary titration of the IRC-effect upon Staphylococcus aureus (Oxford method). Concentrations: 2%, 1%, ?%, 1:1,000, 1:10,000, 1:100,000



The tests carried out with other micro-organisms, particularly with gram-negative strains, just as well as with fungi and yeast, gave negative results (table 4). On the contrary our work evidenced the positive effect of the isolated substances upon *Mycobacterium tuberculosis*.

TABLE 4

Effect of the Cannabis indica resin upon some common pathogene micro-organisms

Investigated strain	**Effect**
1. Micrococcus albus	Positive
2. Staphylococcus pyogen. aureus haemolyt. sensitive to penicillin	Positive
3. Staphylococcus pyogen. aureus haemolyt. resistant to penicillin	Positive
4. Streptococcus alpha haemolyt.	Positive
5. Streptococcus beta haemolyt.	Positive
6. Enterococcus	Positive
7. Diplococcus pneumoniae	Positive
8. Erysipelothrix rhusiopath	Positive
9. Sarcina lutea	Positive

10. Corynebact. diphtheriae	Positive
11. Corynebact. Cutis	Positive
12. Bac. anthracis	Positive
13. Bac. Subtilis	Positive
14. Bac. mesentericus	Positive
15. Clostridium perfringens	Positive
16. Escherichia coli	Negative
17. Salmonella typhi	Negative
18. S. paratyphi B	Negative
19. Sh. Shigae (Sh. Flexneri, Sh. Kruse Sonnei)	Negative
20. Pseudomonas aeruginosa	Negative
21. Proteus vulgaris	Negative
22. Mycobacterium tuberculosis	Positive

II. - BACTERIOLOGICAL EXPERIMENTS CARRIED OUT WITH ISOLATED AND PURIFIED RESIN FROM CANNABIS

As previously mentioned in the section on chemistry, both the perfect extraction of the effective substance and the method of isolation of the resins have been elaborated and patented. Whilst the preliminary investigations were carried out with hemp extracts obtained by the help of some organic solvents (ethylalcohol, ethylether, petrolether, benzene), the proper work and study of the antibacterial effect were accomplished throughout by the help of the purified substance of resin nature, further on designated as the IRC (Isolated Resin from Cannabis), from the viewpoint of chemistry a mixture of acid and phenolic fractions; hence, we have used not the crystalline forms which have been shown to be less effective but the mixture mentioned above - the resin. The crystalline forms have been found particularly useful for the evaluation of the chemical structure, the determination of the chemical and physical properties and the constitution of the effective substances.

Consequently, all the results mentioned below will refer to the IRC, tested upon *Staphylococcus aureus haemolyticus*.

TABLE 5

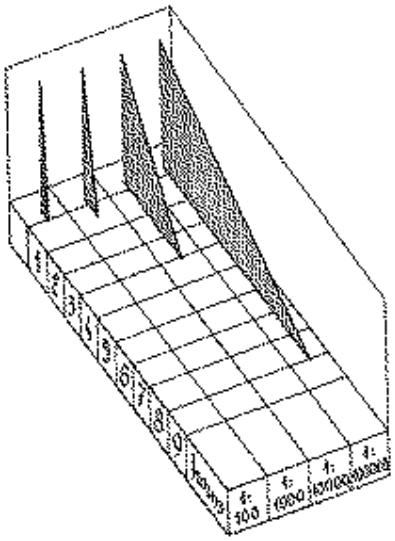
Velocity of the bactericide effect of various IRC-concentrations upon the investigated micro-organisms

IRC-concentration	Velocity of the effect when adding antibiotics
1 : 100	Immediately sterile
1 : 1,000	Sterile after 15 to 30 minutes
1 : 10,000	Sterile after 3 hours
1 : 100,000	Sterile after 8 hours
1 : 1,000,000	After 24 hours remarkably inhibited growth
Control without IRC	Massive growth and opacity

4. Determination of the magnitude of the bactericide effect

It could be demonstrated by us that the IRS produces a pronounced bactericide effect *in vitro*; in lower concentrations the growth and reproduction, of sensitive bacteria are but slowed down. The rate of the effect in vitro has been tested both by the help of the modified Oxford method on solid culture mediums and in fluid mediums of peptone water. The Oxford method was shown to be by far the least sensitive. There were shown to be many factors involved which have no connexion with the antibiosis as, for example, diffusion, the number of inoculated microbes and so forth. It can be utilized with advantage only for purposes of orientation (fig. 11). Whilst the maximum of the effect of the IRC-dilution was found to be with a concentration of about 1:10,000 when the Oxford method was used, the tests carried out in the fluid medium of peptone water evidenced a bactericide effect still in a dilution of 1:100,000 after inoculation within 24 hours, and a significant inhibition of the growth in a dilution of 1:1,000,000.

FIGURE 12 A tridimensional graphic representation of the velocity of the bactericide effect of various IRC-concentrations upon staphylococcus aureus in fluid media in vitro



The antibacterial magnitude of the IRC-effect in ethylenglycol upon the BK H/37 RV strain in a Sauton fluid medium was found by titration up to a dilution of 1:100,000. In detailed work carried out in the Laboratory for Bacteriology of the Sanatorium at Vysne Hagy (High Tatra) where independent tests for control were carried out, the limit of the effect upon the same strain of *Mycobacterium tuberculosis* was determined to be present up to a dilution of 1:150,000.

FIGURE 13 Graphic representation of the decrease of the number of micro-organisms after various time-intervals and in different IRC-concentrations

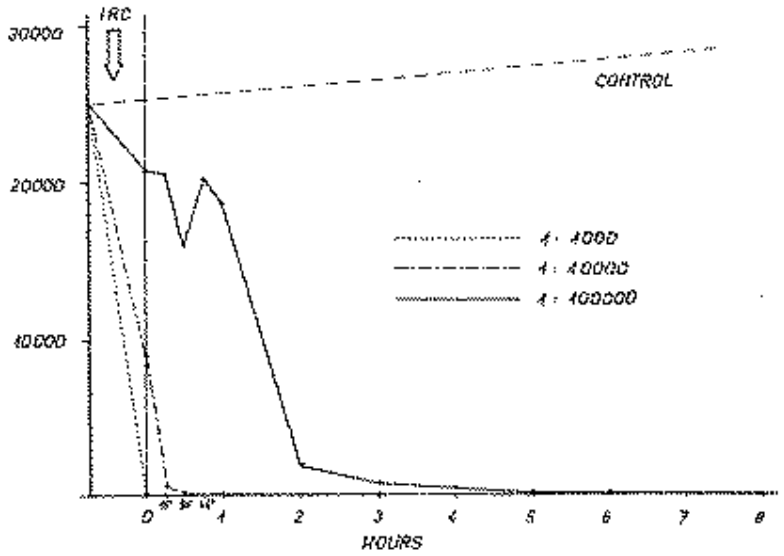


TABLE 6

Velocity of the bactericide IRC-effect upon Staphylococcus aureus

Number of colonies

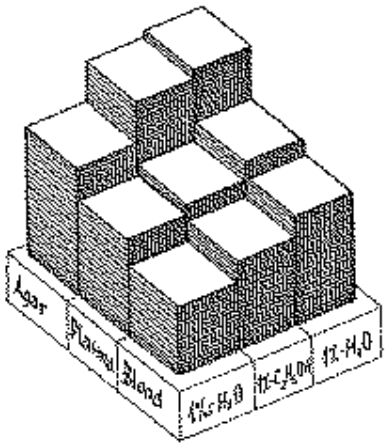
Time control	IRC 1:100	IRC 1:1,000	IRC 1:10,000	IRC 1:100,000	Control
Immediately after application of antibiotics	-	5	8,640	20,600	25,000
After 15 minutes	- -	3	560	20,500	
After 30 minutes	-	-	37	16,000	
After 45 minutes	- -	-	-	20,300	Proportional increase of the number of the microorganisms
After 1 hour	-	-	29	18,800	
After 2 hours	-	-	12	1,760	
After 3 hours	-	-	14	278	

After 4 hours	-	-	-	240	
After 5 hours	-	-	-	32	
After 6 hours	-	-	-	21	
After 8 hours	-	-	-	4	
After 12 hours	-	-	-	-	
After 24 hours	-	-	-	-	Massive growth

5. Determination of the velocity of the bactericide effect of the various IRC-concentrations upon test

The velocity of the bactericide effect was determined with the aid of the routinely used method in the medium of pep-tone water infected with staphylococcus (100,000,000 bacteria in 5 ml). We recorded the time within which the infected peptone water became sterile due to the appropriate IRC concentration. The results obtained were shown to be uniform (table 5, and diagram in fig. 12).

FIGURE 14 Graphic representation of the influence of the inactivating substances in vitro upon the decrease of the IRC-effect in solid culture media



Resin isolated from	Agar	Agar plasma	Blood-Agar
Cannabis indica			
10/ $_{00}$ aqueous solution	20	15	11
1% alcohol solution	26	16	14
1% aqueous solution	27	19	17

FIGURE 15 Effect of the inactivating substances in vitro upon the decrease of the antibacterial IRC-effect in: 1 - Meat-peptone Agar. 2 - Agar with 10% plasma.

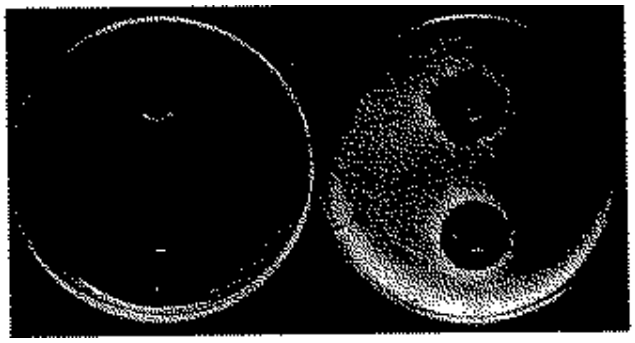


FIGURE 16 Graphic representation of the influence of the inactivating substances in vitro upon the decrease of the IRC-effect in fluid media; evaluated after a period of 24 hours

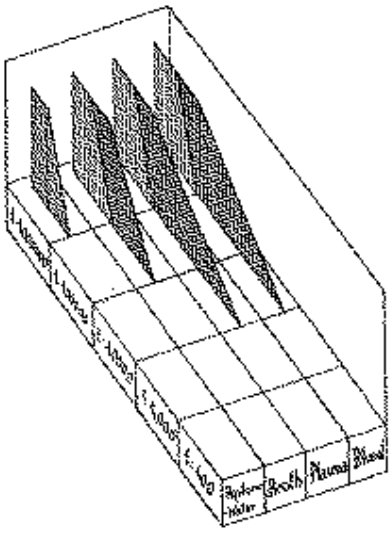
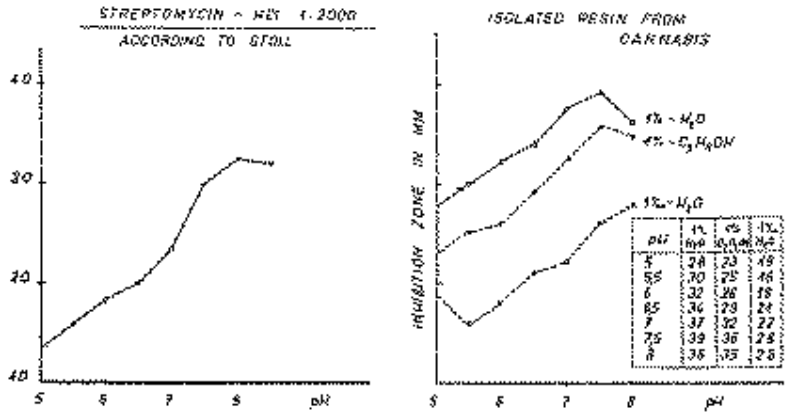
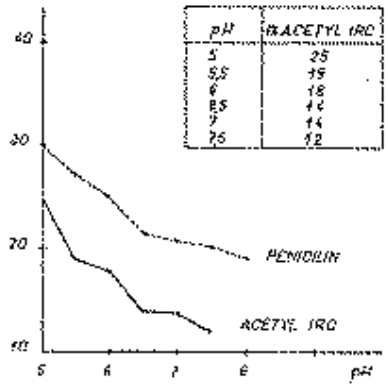


FIGURE 17 Graphic representation of the pH-effect upon the activity of streptomycin (Stoll) and of the IRC when staphylococcus species are concerned



Analogously we followed the decreasing number of bacteria. Fifty cc of sterile peptone water were infected with a diluted 18-hour-old *Staphylococcus aureus* culture which, according to the control, contained 30,000 micro-organisms in 1 cc. Into each of the individual flasks the IRC was added, progressively diluted from 1:100 up to 1:100,000 and, with the aid of the usual method of cultivation, and after definite time intervals, the decreasing number of bacteria in 1 cc was recorded (table 6, and diagram in fig. 13).

FIGURE 18 Graphic representation of the pH-effect upon the activity of penicillin (Stoll) and upon the acetyl derivative of the acid from cannabis



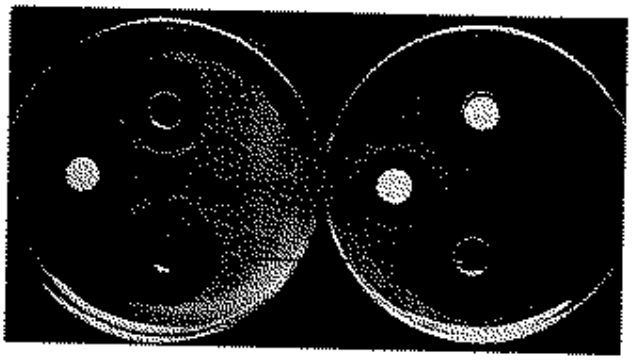
Substances inactivating the antibacterial effect of the IRC

A detailed study has been carried out in vitro on solid and in fluid culture mediums with regard to the effect of blood, serum, cysteine, thiosulfate, meat peptone broth and Sauton medium upon the bactericide magnitude of the IRC. All the substances mentioned above, save for cysteine and thiosulfate, showed a decrease in the biological effect to a larger or smaller extent (fig. 14, 15). Whilst in the standard peptone water there could be observed a bactericide effect upon the staphylococcus up to a concentration of 1:100,000, under the same conditions after addition of an amount of 10 per cent blood or plasma the concentration showed itself active only up to a dilution of 1:1,000. It is interesting to notice that bloods of various origin, and even of different groups, do not produce the same inactivating effect. In the same way, in comparison with the medium of peptone water, the peptone broth showed a decrease in the bactericide effect by one degree (fig. 16).

6. Effect of the pH-value upon the antibacterial effect of the IRC

Stoll et al published a report dealing with the problem of the dependence of the magnitude of the antibacterial effect upon the pH-value with regard to penicillin and streptomycin. They found that at lower pH-values the anti-biotics of acid character produce a more pronounced effect than at the pH-value within the alkaline range (penicillin). On the contrary, the effectiveness of streptomycin rises steeply with the rising pH. In our experiments the same results were obtained. We followed on solid culture mediums, and at pH-values that varied between 5 and 8, the rate of the inhibiting effect upon *Staphylococcus aureus*. The various concentrations tested were as follows: (*a*) natrium salts of the IRC in alkaline aqueous solutions, (*b*) the crystalline acetyl derivative of the isolated cannabidiolic acid.

FIGURE 19 pH-effect upon the IRC-action upon Staphylococcus aureus in meat-peptone Agar a - 1 per cent IRC (sodium-salt) in alcohol (5 drops placed into a depression in the Agar-surface). b - 1 per cent IRC (sodium-salt) in water (5 drops placed into a depression in the Agar-surface). (one drop on filter paper applied to the Agar-surface). c - 1 per cent IRC (sodium-salt).



In the first case the increasing effectiveness of the solution along with the rising pH-values bore analogy to the one of streptomycin (fig. 17).

On the contrary, in the second case, the effectiveness of the acid tested showed an increase on the acid side, which was analogous with the effect of the pH-value upon the antibiotic effect of penicillin (fig. 18).

As may be seen from both diagrams, there is a noticeable difference to be found with regard to the size of the inhibition zones under standard conditions and varying pH. The maximum of sodium salts in water lies at about pH 7.5, subsequently approximately at the pH of the plasma. Less advantageous is the considerable decrease of the effect in an acid medium - for example, of a suppurant wound. The photograph of fig. 19 portrays the considerable disparity as to the effectiveness of the isolated substances at varying pH under conditions which are otherwise maintained. The same concentrations of active substances have been tested in parallel line in an Agar culture medium once at pH 5.5, and the second time at pH 7.5.

SUMMARY

On the basis of the dependence mentioned above, conclusions should be drawn as to the practical utilization of the preparations with antibacterial substances from

cannabis at varying pH of some pathological processes as, for example, in suppurant wounds, furuncles, otitis, sinusitis and the like.

Survey of clinical experiences

I. Some chemical and physical properties of the isolated effective substances (IRC) particularly with regard to their stability

By Z. Krejci

The antibiotically active and effective substance (IRC) of resinous appearance and nature, utilized at present for the preparation of the antibacterial preparations, does not appear to be a chemical entity, but a mixture of two substances. It is of acid nature conditioned by the presence of phenolic and carboxyl substances. These acid substances retain their antibacterial properties even after acetylation and following division in the neutral portion (acetylated phenols) and the acid one (acetylated-phenol-acid).

Going deeper into the matter showed that the biological effectiveness of the active amorphous substances is not so stable as was previously assumed. On the contrary, their effectiveness decreases due to the oxidizing action of atmospheric oxygen, particularly in a warm atmosphere. In an oxygen-free medium, even at higher temperatures (in the autoclave) they are comparatively stable.

The effective substances are all readily soluble in common organic solvents - namely, in ethylalcohol, ethylether, chloroform, benzene, petrolether and so on. At pH 7 they are slightly soluble in water and in physiological solutions. This property is a certain drawback in these substances both for clinical utilization and precise pharmacological evaluation. Because of their acid nature they are readily soluble in aqueous solutions of alkalis - i.e. in sodium and potassium hydroxide, sodium carbonate, sodium hydrocarbonate and so on. They can be easily emulsified, and as emulsions they are comparatively stable.

1. *The pharmacodynamic effect of the antibacterial substances from* Cannabis sativa var. indica

The pharmacological evaluation was carried out at the Institute for Pharmacology of the Medical Faculty of the Palacky University. Klabusay & Lenfeld succeeded in showing some well-defined effects of the isolated amorphous substances (IRC): analgetic, anticonvulsant, and, when locally applied, the initially irritative and later on anaesthetic effects.

The *hashish effect* due to tetrahydrocannabinol could not be found in substances obtained from plants cultivated in the moderate climate of Czechoslovakia - i.e. it could be evidenced neither in animal experiments nor in experiments carried out on man (*per os*).

The *analgetic action* was studied in white rats by the help of the method of mechanical irritation according to Levy and Buchel in the modification according to Votava and in guinea pigs by the method according to Regnier. The IRC was administered perorally in emulsions with gum arabic in doses from 100 to 50 mg/kg; and also subcutaneously and intraperitoneally in ethylenglycol up to 500 mg/kg weight. From these experiments it could be seen that the IRC produces an analgetic action when administered perorally in doses of 100 mg, subcutaneously and intraperitoneally - i.e., from 50 mg/kg onward. Higher doses (500 mg/kg) of the IRC result in intensified analgesia lasting for some hours and complete inhibition of the activity of the central nervous system or sleep.

The *anticonvulsive effect* was evaluated in white mice and in frogs. The convulsions were produced in mice by pentamethylentetramine (0.1 g/kg intraperitoneally), in frogs by strychnine by administering doses of 40 mg/kg subcutaneously. The effective dose of the IRC preventing convulsions due to pentazole in 50% of mice was established as 0.61 g/kg *per os*; for strychnine an effective dose of 0.83 g/kg when applied subcutaneously.

The determination of the *local anaesthetic effect* was carried out by evaluation of the surface anaesthesia according to the method of Lebduska & Vrba using the cornea of rabbits and guinea pigs, and by the evaluation of the anaesthesia according to the method of infiltration of Bulbringe & Wayda, using the skin of guinea pigs. The IRC was applied in ethylenglycol. The IRC was effective from the concentration of 5% and up, whereas a total local an?esthetic effect could be observed only by using a 10% concentration; it lasted for about 45 to 90 minutes.

The *toxicity* was determined in mice by administering an emulsion with gum arabic, and the death rate recorded within 48 hours. By the Burn method, LD_{50} was established as 1.83 g/kg *per os*. Smaller doses did not produce any remarkable changes in mice; doses of 1 g/kg (IRC) were followed, after some hours, by a slight inhibition of the motor function with apathy and immobility. Larger doses resulted in a total inhibition of the activity of the central nervous system, sleep and exitus within 24 hours.

The *local compatibility* was evaluated on the cornea of rabbits by administering a solution in drops and by application of the solutions of the tested substances into the subcutaneous area of the auricle of the rabbit. The effect of the IRC upon the mucous membranes was locally irritating. On local application to the skin no clinical evidence of acute irritation was found. The intramuscular application resulted in an inflammatory reaction with the exudation of the liquid.

2. Clinical experiences

In recent years a series of pharmaceutical preparations have been prepared and clinically examined particularly with regard to the needs of stomatology, otorhinolaryngology, gynaecology, dermatology and the like. The preparations have been locally applied throughout but parenteral administration has not been made use of, particularly because of the poor solubility of the examined substances in physiological solutions. Besides, some of the properties such as the pharmacological one (irritation) and the bacteriological one (inactivation with blood and serum) of the

active substances which have been isolated do not allow a suitable utilization of these preparations by means of injections.

For the needs of stomatology, an aseptic dentin powder was prepared, impregnated with 2 to 5% of biologically active substances (IRC) from cannabis. This dentin powder containing IRC was successfully used for the indirect covering (in about 300 patients) and for the direct covering of the pulp (70 cases), in beginning pulpitis and irritation of the pulp. Even in cases like that we notice the obvious advantage of the antibacterial effect of the locally anaesthetic action. Save in cases of massively infected pulps (Soldan) did not record any failures.

Somewhat less uniform results were obtained with this preparation by Simek, who applied dentin combined with IRC or a special salve containing IRC. In uncomplicated *Caries profunda*, a remarkable and spontaneous effect could be achieved in 64% of the patients; in *Caries profunda*, with an incidental opening of the vital pulp, in 38.4% of the patients. In *Pulpitis partialis*, the results of this therapy were positive in 41% of the investigated cases. The authors have, on the whole, acknowledged the anaesthetic effect of these preparations.

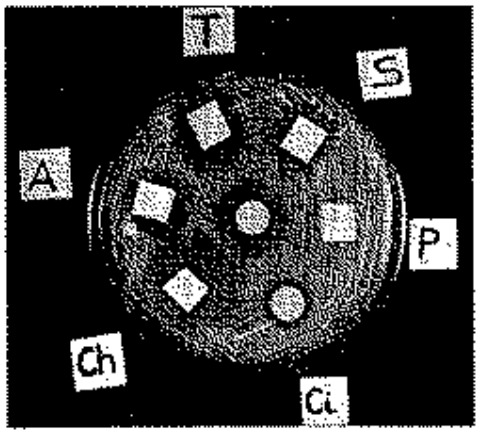
Very advantageous is the application of the effective substances from cannabis in *otorhinolaryngology*. Hubacek reports on the very good results obtained particularly after application of 1% of an alcoholic solution of the IRC and of a dusting powder (boric acid with 2 to 5% of the IRC) in acute and chronic otitis, furunculosis of the outer part of the nostrils and of the external auditory meatus, and even in some cases of bilateral sinusitis, the latter having been treated without success with a series of punctions and penicillin irrigations. He describes an interesting case of bilateral chronic *Sinusitis maxillaris*, lasting for about three years and treated without success with a total of about 30 punctions. After application of our IRC preparations, one side was treated as a control with penicillin, but with negative result, and the other side with three IRC punctions and irrigations. The side treated with negative effect with penicillin was easily and successfully treated with cannabis preparations. In the same way Navratil illustrates in his small table of chronic otitis a considerable improvement

in 13 of a total of 18 cases. All the cases under investigation were also controlled bacteriologically. In clinical practice the very good results achieved with the preparations mentioned above - i.e. with the alcoholic solution and the dusting powder-stand in support of the good results obtained *in vitro* and justify the suggestion to have both these preparations made available for pharmaceutical production.

The manifold utilization of these substances particularly in the form of alcoholic solutions with glycerine has been confirmed by the results obtained after application of this preparation in *obstetrics* in order to prevent staphylococcic mastitis in the treatment of rhagades and fissures on the nipples of nursing women. Of great importance is the locally anaesthetic component together with the antibacterial effect, particularly upon *Staphylococcus aureus*, which is considered to be the causing agent of the postpartum inflammation of the mamma. Heczko & Krejci evidenced staphylococcus in 84% of the total of 160 parturient women. It is significant that in 89% of cases the staphylococcus was resistant to penicillin, in 18% to streptomycin, and in some cases resistant to penicillin, streptomycin, aureomycin and terramycin and sensitive only to chloromycetin and to the IRC.

The publication of the results obtained from these investigations evoked a lively interest among obstetricians who up to the present have tried to find means of substitution both for the inadequate and still used gentian violet, and the local inefficacious application of some antibiotics as, for example, aureomycin, which has been recommended by some authors.

FIGURE 20 Comparison of the inhibitory effect of some antibiotics in combination with active substances from cannabis upon Staphylococcus aureus P - penicillin 100 OU; S - streptomycin 1 mg; T - terramycin 5 mg; A - aureomycin 5 mg; CH - chloramphenicol 5 mg; Ci - tincture cannabis Zone in the centre of the plate - 2 per cent of IRC.



For the purpose of *dermatology*, a salve containing 2% of effective substances has been prepared and found very useful in pyodermia of staphylococcic etiology, infected burns, and particularly in decubitus of immobile patients in rehabilitation centres. Of great interest was the follow-up of a physician and pathologist, who was treated with the IRC for a severe infection of the thumb of the right hand, an injury he suffered in the dissecting room. The severe condition, threatening amputation, and the absolute resistance of the microflora to available antibiotics were overcome by substances from cannabis.

The results obtained in treatment of specific *tuberculous fistulas* and published by Procek as well as the up to now unpublished results of the investigations carried out must be considered as preliminary ones even though the antituberculosis effect *in vitro* is very satisfactory.

In the cases mentioned above, no extraordinary allergy of the organism to effective substances from cannabis or any particular ability of the IRC to sensitize were observed.

In conclusion we may still consider the interesting results Sirek achieved. He mentions his experiences for some years past with hemp seeds in the therapy of

tuberculosis. The hemp seed was ground and extracted with milk at a temperature of 60-80 degrees of C. It represented a protein-rich moiety of the curing diet for tuberculous children, in whom a remarkable improvement due to this diet was observed by the author. But the assumed antituberculotic action of cannabis seeds could not be evidenced in experiments on guinea pigs. Therefore, in the cases reported by Sirek, the therapeutic effect can be only explained by the healing nutritious diet in which the specially prepared seed is of great importance.

In human therapy the best results have been obtained with the following medicaments combined with substances derived from cannabis: dusting powder together with boric acid (otitis), ointment (staphylococcus infected wounds, staphylodermia and so on), ear drops (otitis chron.), alcohol solutions with glycerine (treatment of rhagades on the nipples of nursing women - prevention of staphylococcic mastitis), aqueous emulsions (sinusitis), dentin powder with the IRC (caries). The preparations mentioned above have been already tested clinically, and will eventually be made available for production.

The high yield of effective substances (average 1.5% of the IRC in the dried drug), the considerable amount of raw material available (1.5 million hectares of cannabis plant culture in the world), and the subsequent low price both of the raw material and of the effective substances allow us to utilize the antibacterially effective substances from cannabis in *veterinary medicine*. Such use, which is analogical to human medicine, is comparatively wide: infected wounds (dusting powder), panaris of sheep and cattle (dusting powder), otitis in dogs (ear drops, dusting powder), mastitis in cattle, postpartum trauma, lacerated wounds and so on. Especially veterinary workers, workers concerned with cattle breeding, employees in slaughter houses, cutters and so on consider the preparations containing biologically active substances to be an important contribution to the prevenion of tuberculosis, anthrax, swine erysipelas and brucellosis in various streptococcic and staphylococcic infections of the hands and the like. The results achieved in this field, but unpublished as yet, justify the greatest optimism.

A considerably higher resistance against virus pneumonia has been observed in mice fed with hemp seeds.

In view of the results obtained with antibacterially effective substances isolated from cannabis, it may be concluded that they are superior and have numerous advantages as antibiotics.

The results obtained in clinical practice must receive, for the most part, a positive evaluation. In many cases satisfactory and in some cases even surprisingly good results have been obtained, particularly where a microflora resistant to a series of other antibiotics was concerned. Naturally drawbacks had to be recorded. Further clinical experiences and practice will be necessary for a definite evaluation of this antibacterially effective substance.

SUMMARY

A systematic investigation of the mid-European flora has been carried out in order to establish the presence of antibacterially effective substances. A high content of remarkably active substances has been found present in *Cannabis sativa var. indica* and in *Cannabis sativa*, a plant cultivated for the industrial utilization of the hemp fibre. It has been investigated in detail from the bacteriological and the chemical viewpoint and from the standpoint of the eventual applicability of the effective substances in clinical practice.

In old herbals and in folk medicine in Europe, Africa and America, mention has been made of the utilization of cannabis as an antibiotic and analgetic medicament particularly for external use. The hashish effect has been known only to nations with a warm climate. In Europe, hashish made its appearance as a narcotic at the time of Napoleon's campaign in Egypt, but contrary to morphine and cocaine, its use was not widespread. In spite of this, from the pharmacological viewpoint, official medicine has investigated the hashish effect on the central nervous system whilst the analgetical and antiseptic effects have been unjustifiably forgotten.

In the chemical section of this work, the most suitable methods of extraction have been described and the technique for the isolation of effective substances developed. At the beginning of the procedure two antibacterially effective fractions were obtained: the acid and the phenolic. Then from the acid fraction a biologically active crystalline acid could be isolated. On the basis of the elementary analysis, the optical rotation, the UV- and the IR-spectroscopy, the following constitution has been established:

3-methyl-6-isopropenyl-4-n-pentyl-2-6-dihydroxy-1,2,3,6-tetrahydrodiphenyl-3-carboxylic acid.

Because of its close relationship to cannabidiol, it has been named cannabidiolic acid. The second-antibacterially ineffective acid has been identified as *trans*-cinnamic acid. In addition, the following unsaponified constituents have been isolated: paraffin (n-nonacosane) and higher alcohols.

Experimentally we could evidence the bactericide effect of the substances from cannabis *in vitro* upon the following gram-positive micro-organisms: *Staphylococcus aureus haemolyt, Staphylococcus aureus*-resistant to penicillin, *Streptococcus alpha, Streptococcus beta haemolyticus, Pneumococcus, Enterococcus, Corynebacterium diphtheriae, Bacillus anthracis, Erysipelothrix rhusiopath*. A significant antibacterial effect upon the *Mycobacterium tuberculosis in vitro* could be observed up to a dilution of 1:150,000.

The gram-negative micro-organisms of the coli-typhus group, as well as the *Pseudomonas aeruginosa, Proteus vulg*. and, in addition, the yeast and the fungi, proved to be resistant.

The limit of the effectiveness of the maximal dilution of the biologically active substances (1:100,000) and the velocity of the effect of various concentrations could be established.

The effect of the inactivating factor has been studied in detail. Blood, plasma and serum partially inactivate and decrease the antibacterial effect.

A comparison between the effectiveness of the active substances from cannabis and that of penicillin and streptomycin has been carried out at various pH.

Finally, the experiments made in clinical practice, particularly in stomatology, otorhinolaryngology, gynecology, dermatology, phthisiology, with some pharmaceutical preparations containing antibacterial substances from cannabis have been reported. Attention has been drawn to the advantageous utilization of the active substances from cannabis in veterinary medicine, and particularly in preventive medicine for anthropozoonoses.

A preliminary pharmacologic investigation of the hemp substances was carried out. It was ascertained that the isolated hemp extract possesses analgetic, anticonvulsive and locally anaesthetic properties. Administered to white mice per os its toxicity was determined with 1.83 g/kg as LD-50.* (*Ed. note...LD-50 ratio of 18,300:1 for a concentrated extract.) Acid II and the acetylderivative of the canabidiol-acid - pure substances obtained from hemp do not possess these pharmacologic properties.

All the investigated substances were observed to bring forth local irritations. Further studies will have to explain this irritative effect with regard to the fact that the extract from the drogue, (sic) when being deprived of a part of its ballast substances only, does not show to be an irritative factor in clinical use but, on the contrary, does relieve pain entirely, a fact having been known to ancient physicians, and nowadays newly confirmed both by stomatologists and oto-laryngologists.

Therapeutic results in stomatology

THERAPEUTIC RESULTS IN STOMATOLOGY AFTER APPLICATION OF SUBSTANCES OBTAINED FROM CANNABIS INDICA

Cannabis substances were applied either in the form of a 5% hempsalve with lanolin, or they were used in the form of alcohol extracts for mouth sprayes. (sic) The application of these substances shows significant positive results in the treatment of herpes labialis, paradental painful gum pockets, gum capuches over the wisdom teeth, dry sockets, aphthae and ulcerous gingivostomatitis. More than five hundred patients were subjected to this treatment.

Cannabis substances found their application to practical advantage mixed with sterile tooth-powder for the treatment and maintenance of a vital tooth pulp. This was done in cases of indirect covering of the tooth pulp (about 300 patients - 80 of whom were reexamined), and in those of direct covering (about 70 cases - with 15 patients reexamined). Even here quick analgesia was considered to be the positive effect. In two patients, direct covering was experienced with teeth destined for extraction beforehand, and the extraction performed a certain time thereafter and the teeth studied histologically. For general therapeutic use, it is suggested to verify these methods in further cases or, eventually, to find methods of a more suitable application of cannabis substances in direct or indirect covering of the tooth pulp.

APPLICATION OF THE CANNABIS INDICA EXTRACT IN PRESERVING STOMATOLOGY

In 64% of patients with deep dental caries incidence, and in more than 30% cases of casually opened or irritated tooth-pulp, and finally in 41% of persons suffering from pulpitis partialis positive response could be observed when treated with cannabis paste. This result corresponds to the analogous number obtained on application of the Lezovic-paste. (Paste containing a high ratio of streptomycin, penicillin, tricresol

or benzocaine respectively.) The anaesthetic effect of cannabis has been attested: in numerous cases with negative response to therapy painlessness lasting for several days could be attained, in many patients painless necrosis could be achieved. In a number of cases the failure was due to an unsuitable vehicle that did not liberate the antibiotic in the right proportion. (The same vehicle as with the Lezovic-paste was made use of.) Future research work will have to include further clinical control, histological investigations and the search for a more proper vehicle.)

Cannabis indica in oto-rhino-laryngology

STUDY ON THE EFFECT OF CANNABIS INDICA IN OTO-RHINO-LARYNGOLOGY

A positive response due to antibiotics obtained from hemp could be observed in patients with otitis, ulcers of the anterior narines, and furuncular otitis. With chronical otitis positive results could be obtained in most cases -- failure, however, in patients with pyocyaneum and proteus infections. The most striking effect could be observed with sinusitis, particularly with both-sided sinusitis maxillaris when one side had been treated with penicillin on control with negative result, whilst the other side had been healed by three punctures of hemp extract. The sinus resultlessly treated wit penicillin showed an immediate positive response to hemp thereafter.

EFFECTIVENESS OF CANNABIS INDICA ON CHRONIC OTITIS MEDIA

Local application of cannabis indica was experienced in 18 patients suffering from chronic otitis media, and in 4 patients after mastoidectomy. A significant improvement was noticed in 13 cases of chronic otitis. Up to the present, our experiences are of a rather short time, i.e. of three weeks only. It will be necessary to test cannabis with other more proper vehicles that would gradually liberate antibiotica on a satisfactory scale.

Importance of hemp seeds in the tuberculosis therapy

INTRODUCTION

During the thirties and forties, in the absence of antibiotics, chemotherapeutics and surgical methods, tuberculosis was rather effectively treated with a therapeutic diet, developed by a team of medical doctors in a sanitarium for patients suffering with tuberculosis at Jince.

The concept was based on two assumptions:

1. In order to fight tuberculosis effectively, nutrition must supply building material for renewal of tissues destroyed by the disease, be it lungs, other organs, or muscles.
2. The whole diet must support effective function of the liver, thus assuring proper assimilation and utilization of nutrients.

In addition to the selection of nutritious and well-balanced dietary components, attention was paid to the preparation of the food; namely assuring that the nutrients would not be denaturalized. coagulated or rancid due to improper storage or cooking methods.

Two components were considered most important and irreplaceable in the whole diet: oat flakes and a specially processed extract of hemp seed.

It was hemp seed, which attracted the author's attention. It is high in protein (33.0%) and its main protein type, edestine, is well known for its wealth of enzymes and unusual amino acid composition. Most valuable is the amino acid arginin, which is considered essential for formation and growth of new tissue. While other sources of plant protein, for instance soybean protein, contain 6.8% of arginin, edestin contains approximately 3 times as much arginin - 19.0%. This property is of great importance in balancing of diets, requiring high level of arginin.

Before nationalization of the Czechoslovakian Pharmaceutical Industry in 1948, an extract of hemp seed, EDEZYME. was available on the market. Today it is produced as a "home remedv" according to a following recipe:

Ground hemp seed is mixed with warm milk (60 to 80 degrees C) and maintained at this temperature for at least half an hour. Keeping the product in a water bath, while constantly mixing, prevents coagulation of edestin on the bottom of the container. Finished product must be pressed and filtered to separate the indigestible and irritating outer layer of seeds from the colloid solution. One dose prepared from 3/8 of a liter of milk and 50 to 80 grams of hemp seed should be consumed by the patient every second day.

Inclusion of **EDEZYM**, oat flakes and other, more common dietary components, was tested on two groups of children suffering from tuberculosis in both prewar and war periods. Though no other medication was used and food was rather scarce, all children were considered successfully treated or improved at the end of treatment period. Dietary and/or medical properties of hemp seed deserve our full attention.

PLEASE NOTE: The enclosed study from Czechoslovakia in 1954 bears the limitations of what knowledge was available at the time. In the year 2000, The HempNut Health and Cookbook by Richard Rose and Bridgette Mars (www.TheHempNut.com) added this information to the findings of the Czech Study: "Essential Fatty Acids (found in hemp seeds) help restore wasting bodies by improving the damaged immune systems. They also make it easier for the patient to liquify and expel the mucus built up in the lungs."

IMPORTANCE OF HEMP SEEDS IN THE THERAPY OF TUBERCULOSIS BY JOSEF SIREK

Tuberculosis Hospital at Jince: Chairman: MUDr. Josef Sirek

Chair of the working group: Prof. Dr. Jan Kabelik

I.

If we are discussing the use of hemp seed in the therapy of tuberculosis, we don't think about chemotherapy in today's sense of the word, not even the treatment specifically directed against the Koch bacillus and not a treatment oriented towards diseases that cause changes in the lungs. We think of a total conservative treatment with the emphases on its dietetic or therapeutic nutrition. Therapeutic nutrition becomes then a branch of therapy, namely as a part of the overall effort to "treat the whole human being". For this reason we, according to the Soviet example, begin to understand the importance of the treatment through nutrition in therapy, not excluding physiotherapy. These are, however, the beginnings, lacking direction and therefore up to this point, not too fruitful. One should not be, however, surprised. Even in the Soviet Union the whole question of treatment through nutrition is still controversial, and even the most important nutritional work of the Pevzner school has been subjected to a very critical assessment. Although it was primarily M.I. Pevzner and out of other Soviet authors namely L. M. Model who also in conjunction with tuberculosis rightfully stressed the most important elements of the treatment through nutrition. Another Soviet author, O. L. Gordon, in his presumation entitled "Justification of treatment through nutrition in the clinic and prospects for its expansion" said the following: "Treatment through nutrition is a therapeutic method. As a part of complex therapy it has two goals: To satisfy the physiological needs of the sick organism and to actively influence the pathological process. In this aspect the treatment through nutrition differs from the ordinary nutrition of a sick person". F.K. Mensikov coworker of the Clinic for treatment through nutrition, added that during complex therapy of all diseases proper nutrition is a primary need, while a nutrition which does not take into account the status of the patient could have a negative effect. "Particularly, the treatment through nutrition has an important effect in situations where we need to support regeneration of the tissues, namely when we

don't have a medication which could actively support such process". (Presented on December 10, 1954, at the occasion of a scientific conference at Palacky University at Olomouc, as a part of the topic "Hemp seed as a treatment").

It would not be correct to talk about "treatment through nutrition" and not expect from it more than just mere nutrition or doubt that it may actively contribute in the sense of treatment. Even today's physiotherapy, though it has at its disposal rather effective means, can't ignore that such means can be used only for particular patients, and even here one can't put all one's eggs into one basket. In this connection we should remember the words of V.L. Ejnis, used in conclusion of his article 'The work of I. P. Pavlov and clinics of tuberculosis':

"Despite the significant successes of chemotherapy, antibiotics and surgical treatment which substantially improved the prospects of physiotherapy, the fundamental basis of the treatment is still systematic care leading to an increase in the overall resistance of the body. It is now also an important task to improve hygenic-dietetic therapy, incorporating the nutrition of the patient, suffering from tuberculosis".

II.

Towards the end of the first world war physiotherapy freed itself from it helpless position and began a successful attack against tuberculosis. Artificial pneumothorax, exairesa frenicu thoracocaustics, thorakoplatics, extrapleural pneumothorax, Streptomycin, chemotherapy, lobotomy, those are some of the stops on this victorious journey. They are also unquestionable, partial successes, each of which went through a period of excessive hopes and to a point, each of them contributed to the fact that we have forgotten at least partly, the concept of the "Whole human". It leads to a certain indifference to the physiological points of view, hygienic-dietetic treatment, which was critiqued by V.L. Ejnis. The hygienic-dietetic treatment was, by some quiet agreement, reserved for cases, where, for various reasons it was impossible or was not indicated to use "active" means of therapy.

In the mutual competition for the development of new means of 'active" therapy, our small and in every way, poorly equipped sanitarium at Jince, had only minimum opportunity to participate. The role of Cinderella, however, had some advantages. The less we have been in a position to keep pace with the modern physiotherapy, the more we have concentrated on areas, which were ignored by others. In our small sanitarium we have been in a better position than in other, bigger institutes, to concentrate on hygienic-dietetic treatment, formats the medical nutrition. We have done it correctly. And today, with thirty years of experience behind us, we ieel gratified that the Soviet science gradually confirms nearly everything that we have found, be it empirically, by induction or by a series of trials. In perfect function of the liver we have seen a key to the perfect assimilation of nutrients; the first order of the day in our medical nutrition was the following: Exclude or limit to the maximum, food which will burden the liver or in some cases, cause damage to the liver. In nutrition of the patients with tuberculosis put emphasis on components which will protect the liver and enable their smooth function. This way, we actually developed a "liver diet" sooner, more or less coincidentally. We laid the foundation, which became a logical pre-condition of every dietetic effort. The role of the liver for the nutrition of a human, and a sick one in particular, is in its variability so immensely important, that it must be recognized by everyone who would like to maintain the "whole human" in good health, or enable him to recover from whatever sickness.

In keeping with this principle, we have concentrated on excluding or reducing from the nutrition of our patients, less valuable fats, namely rancid or burned, all fried, roasted foods, pork drippings or boiled butter, all meats preserved by salt and canning, all smoked sausages, beef and duck meat, duck eggs and spicy foods. On the other hand, we have emphasized the diet of our patients, a relative surplus of proteins, in the form of light types of meat, dietetically processed, cottage cheese, which was specifically processed to avoid coagulation and denaturalization. sour milk. yogurt, raw egg yolks or only partially boiled to avoid coagulation. Out of fats we recommended only natural fresh butter, fresh cream, olive oil without signs of rancidity, fresh or preserved fruit without any artificial preservatives, imported fruits from the south in fresh or dry form, nuts and almonds. Out of vitamins we

recommend plentiful levels of vitamins B1, A and C. We will use potatoes as a side dish but fewer flour based side dishes. boiled vegetables or vegetables steamed with butter, or if possible, raw (carrots). Use few desserts, but of good quality.

With this diet, we have incorporated into the nutrition of our patients, important substances, contained in non-denaturalized fresh fats and proteins and known as liver protecting components (methionine, choline, insitol, unsaturated short chain fatty acids) and amino acids, which are considered metabolically most valuable (methionine, tryptophan. tyrosine. fenylalanine and others). Lastly, we are adding substances, without which the liver can't properly function (thiamin, carotine, ascorbic acid, vitamin F).

This regimen, aimed at liver protection, was combined with a reduction of the daily meals to three, at most four, with 4-5 hours intervals without any food or drink. This also lead to the elimination of over burdening the liver, sometimes blamed on the frequent presentation of food.

These dietetic provisions were practiced in Jince a quarter century ago, and represented at that time, and even now, a courageous deviation from common practice. Similarly, a suggestion of Prof. Arnerling, from Olomouc, requesting that the nutrition of patients, suffering with tuberculosis. must fully respect the function of the liver, was an expiring voice in the desert. Only long-term effort and undying persistence enabled us to keep such reforms alive and viable until the time, when the Soviet science on "medical nutrition' demonstrated their competency.

III.

The value of the tree can be judged by the fruit. The value of the medical nutrition by the nutritional and medical results. If we value individual nutritive components during the systematic nutritional and medical trials using such criteria, we would soon find out the importance of the correct selection of particular proteins as well as their state and preparation. Though meat is the most common source of protein and its importance in nutrition is beyond an argument, in medical nutrition, it's importance is

far behind the proteins in milk and eggs. Eggs represent exclusive building material of the bird's embryo, while milk is a primary source of nutrients in quickly growing and well prospering young mammals. I think that we rightfully call these proteins "plastic", as they are the true material from which the body tissues are built. A daily intake of 100-150 grams of specially prepared loose cottage cheese in the state of hydrogel, and two egg yolks mixed together with other components of the diet, will have much more positive effect on the health status of a sick person than their weight or caloric equivalent in the form of meat. We can't however, expect such effects in a cottage cheese which is coagulated, denaturalized, or prepared by quick coagulation of milk which was too acidic and brought to too high temperature. Similarly, the egg yolk must not be coagulated by boiling to a "hard" state or by frying or other inappropriate preparation methods.

With diseases, such as tuberculosis, which in its active stage is characterized by its tendency for destruction of not only the affected organ (lungs), but as well of the whole body (loss of weight, autolysis of muscles and other tissues, we can't value enough such food, which can serve the living organism as building material. As well, we must present this rare material to the patient's organism in a natural colloid state in which the specific dynamic effect will be best preserved.

The importance of this premise will be more obvious if we, in addition to proteins of animal origin, include proteins of vegetable origin.

The main sources of vegetable proteins, suitable for the nutrition of human are seeds, grains and other fruits. Some can be eaten in a raw state, fresh or professionally dried (nuts or figs); in this later case we should not worry about denaturalization. Unfortunately. the majority of people depend for their nutrition on cooked and baked foods, made out of meal. The aleurone layer of the cereal grains, containing dietetically important proteins and rich in vitamin B1 will remain in the mill. The rest is denatualized by baking or boiling in water. It is hard to believe that professionally prepared oat flakes, in a dose of 15-20 grams will affect the distinct restitution of nutritional status and stimulate healing processes. On the other hand, a

ten to twenty times higher dose of cereal proteins in denaturalized and coagulated state, will have no effect in this area. There are, however, certain differences between oats and other cereal grains.

In oats, the aleurone layer is preserved. In addition to vitamin B1, oats contain vitamin B2 in larger quantities than other cereal grains. In its protein structure, the gliadin form dominates over glutenin; the fat content is much higher, giving the oat flake a hazelnut flavor and contributing to the elimination of hunger. The content of gluconins, components which lower the blood sugar, has the same effect "per se" as insulin has when applied parenterally. The majority of the strong points of oats are wasted if oat flakes are boiled in water or in soup, or denaturalized by other improper method. What will be left is just a food, rich in calories but without the medical-nutritional effects. Only the milk and careful preparation will keep the proteins of oat grains in colloid and dietetically active state.

IV.

From the oat grain there was a direct route to the hemp seed or "semenec". Not perhaps because our forefathers considered hemp seed porridge and soup as "not bad food", but because by its content of edestin and a wealth of enzymes, hemp seed ranks among the best seeds overall.

Chemically, edestin differs substantially from gliadin and other cereal proteins. It is closer to the proteins of nuts and oil seeds and contains a high amount of arginin (up to 19%), which is the amino acid that encourages growth and formation of new tissues. Similarly, as in casein it contains methionine, which is known for its protective function of the liver. As casein, it contains tryptophan (important pro-vitamin pp-niacine), which is missing in cereals and without which it is impossible to achieve a nitrogen balance. It contains nearly all known amino acids, namely the essential ones, without which the growth and well being of the organism is impossible. Without it, food could never be complete and hvpoproteminaemy occurs - an event, singled out the by Soviet author L.M. Model as the root of the disease of tuberculosis. It is impossible in this short presentation to go into greater detail. Let's,

however, bear in mind that the amino acids, which are the most important in the medical nutrition - tryptophan, tyrosinc, phenylalaninc - are separated during the digestion of edestin first. Furthermore, the arginin, cystein and alaninc content in edestin is much higher than in other proteins of plant or animal origin. Finally, amino acids, which are in edestin in smaller quantity than in proteins of animal origin, can be easily replaced in medical nutrition by cottage cheese. There are plenty of reasons why hemp seed edestin should be, in addition to cottage cheese, egg yolk and oat gluten, included among the most important components of medical nutrition for patients with tuberculosis.

As we have witnessed in conjunction with the other proteins, it is of great importance, particularly in the case of edestin, to maintain it in colloid state. From this point of view, our product **EDEZYM** (the name originated from two words: edestin and enzyme), was very suitable. It has been available on the market for a number of years, though was discontinued after the nationalization of the pharmaceutical industry, in 1948. We may use, however, a simple home preparation, assuming that we have a high quality hemp seed, no older than two years, in which all the proteins and enzymes are still fully active (in order to find out we may conduct a germination test). Old recipes, in which our forefathers prepared the hemp seed soup or porridge, are not useful anymore. In the majority of cases, they lead to coagulation and denaturalization of edestin. In the preparatory stage we have to remove the outside layer of the seed, which in contrast to oats, is indigestible, discourages the intake and is irritating during the digestion. The only remaining solution is to transfer the content of the seed into a colloid solution and remove the indigestible residue by pressing and sifting.

The best method is based on the extraction of ground hemp seeds by hot milk (60-80 degrees C). The content is constantly mixed while it is kept in a water bath (double boiler), which prevents the excessive heating of the bottom of the container. If this is not done properly, edestin starts to coagulate from the bottom. Sometimes it fully coagulates. Milk could be skimmed, but must be fully fresh and without preservatives. Sweet whey may be used as well. We can obtain it by the coagulation

of casein with chymosine. Maceration of the hemp seed, at the above mentioned temperature. should last at least half an hour, preferably more. The finished colloid must be aggressively pressed, filtrated, in some cases mildly sweetened and offered to the patient either immediately or kept at a temperature of 60 degrees C in a water bath, until used. This will prevent hydrolics or fermentative breakdown of the active components. One dose, prepared from 3/8 litre of milk and 50-80 grams of hemp seed, should be consumed by the patient every second day on an empty stomach.

V.

The human organism is capable of dealing, under favourable conditions and to a certain level, with the tuberculosis illness without particular treatment. During times, when calmetisation was unknown and modern antibiotics and tuberculostatics were not available, the majority of primary effect cases were healed spontaneously, at least as far as children beyond the baby stage are concerned. Certainly, the modern organization of the fight against tuberculosis (calmetization, the introduction of child preventative medicine, regular Rig check-ups) lead to a significant reduction in small children morality and proving that we can't rely too much, or exclusively, on the spontaneous healing and protective properties of the child's organism.

This is more true in cases of post primary (secondary) child tuberculosis of lungs and lymphatic glands. Here, as well, we can see a significant tendency for spontaneous healing, but the assumption of favorable conditions plays a decisive role. It was for this reason, that during the not so distant past, the cases of "secondary" lung tuberculosis, prevalent in children of school age, the mortality level was rather high, namely among poor people.

This fact underlies again the importance of living conditions. In mature individuals (therial lung pthisis), though the spontaneous healing of lung damage is much rarer than in children, it is much more probable where the living conditions are more favourable. It is for this reason, that a higher percentage of mature people were saved from the upper layers of the society.

It is true, however, that wealth and poverty must not necessarily synonymous with good and bad living conditions. But, in contrast to the present days when living conditions in our countrv are more or less uniformly provided, wealthy people were able to assure for themselves favourable living conditions, assuming they understood what represents "true favourable living conditions". Money without knowledge is not enough. The knowledge, which is required, is defined in every time period by the scientific content of the term "hygienic-dietetic healing".

The substance of this "term" developed historically, is changing constantly and will, in conjunction with the general scientific development, continue to change always. It was not a long time ago, when overfeeding a patient suffering from tuberculosis, without taking into consideration the effect on the liver function, was considered purposeful and desirable. Today we have corrected many things, however, many more cry for change. The fast and successful development of "active" treatment methods seems to absorb excessively the attention of ftisoclogs and this leads to insufficient interest in systematic improvements and scientific involvement in hygienic-dietetic methods. This is happening at times when nobody denies that even the most effective "active methods" must be supported by hygienic-dietetic methods, the necessary foundation of all anti-tuberculosis treatments.

Why, then, despite all the progress in "active" therapy, do the hygienic- dietetic methods (foremost the medical nutrition) remain the necessary foundation of all treatments? Why from those methods (and specifically from them) do we expect the fulfillment of the favourable conditions, which make the treatment much easier, and which in some cases, make spontaneous healing possible?

To generate or restore such conditions, during which the human organism is capable of dealing successfully with the disease, is the main mission of hygienic-dietetic treatment and specifically the medical nutrition. If we are successful and wish to call the resulting healing process "spontaneous" it is only a question of suitable terminology.

If; by using the certain system of medical nutrition, we achieve, in the treatment of tuberculosis, spontaneous healing with considerable probability or regularity, and if we, at the same time. achieve a restitution of the overall nutritional state, during which the tuberculosis slowed down and decreased, then we have solved our problem. This means that we have found the favourable conditions, under which the human organism can better resist the tuberculosis, or deal with it successfully.

VI.

As a testing stone of such systems of medical nutrition, we can best use the cases of post primary (secondary) child tuberculosis of lymphatic glands and lungs, accompanied by substantial degradation of total nutritional status of body development. Such cases tend to show a substantial tendency towards "spontaneous healing', assuming that the living conditions are favorable. If we can achieve, in such cases, dramatically favourable turns for the better as far as the healing of the lung damage and as far as the nutritional status and body development is concerned, then we have, with the highest probability, presented a proof that the system we have used represents the "favorable conditions".

In the following part, I present two groups of children which will offer the necessary documentation for this case.

The first group of 16 children (8 boys and 8 girls) was treated in Jince sanitarium in 1938. In this difficult period, when the sanitarium - at that time a private enterprise - was, because of the world's economic crises, basically idling. Faced with the threat of Hitler's occupation, I have offered the Red Cross in Prague an expense free stay and treatment for 20 children with tuberculosis. In a few days we filled the first floor of the building by these, exceptionally welcomed guests, sick members of Prague's poor from the following districts: Nusle, Pankrac, Michle, Kosire and Kobylisy. After a few days we excluded four of the 20 children and returned them back to Prague. Two were excluded because we did not diagnose any active tuberculosis changes and two others for other reasons. The remaining 16 children remained under treatment for various lengths of time, as is discussed later.

The children came to us in a state of more or less depressed nutrition. The tuberculosis (primary and secondary) was confirmed and checked by the Prague doctors, from whom we received the children.

While with us, the children (as well as the mature patients) were offered meals three times a day. They drank only during the meal. There could be no doubt that they were not overfed. Once a day, they had the main meal, based on meat. once a day they received 100 g of cottage cheese, 25 g of cream (in Czech: "rozhuda"). Once a day they were offered oat porridge made from 15 g of oat flakes. At noon, always after they consumed soup, they received 75 g of shredded carrots with few drops of lemon juice and a soup-spoon of cream. Twice a day they received 100 grams of fruit, twice a day 20 g of fresh butter from a farm. Otherwise they received mixed home meals with one limitation. All foods, which would have excessively burdened the liver, were excluded.

The children did not use any other medication, with the exception of colloidal extract of hemp seed. **EDEZYM**, which was described in part IV. Three times a day the children received soup spoon of Edezym, always a quarter hour before the meal (without a drink), then vitamin B1 and vitamin C. They received two tablets daily, though the food was rather vitamin rich.

The lack of appetite and fussiness toward food, characteristic in children suffering with tuberculosis, was gone in all children, without exception, during the first days of treatment. We also noticed in all children from the first days, a distinct and pervasive change in the total health status.

The boys gained on average 1 kg. within 14 days; girls within 20 days. Boys increased their height by 1 cm in 35 days, girls in 38 days. The diameter of the rib cage was increasing in boys by 1 cm in 18 days, while in girls in 20 days. This improvement in the total physical state and body development in all 16 children is

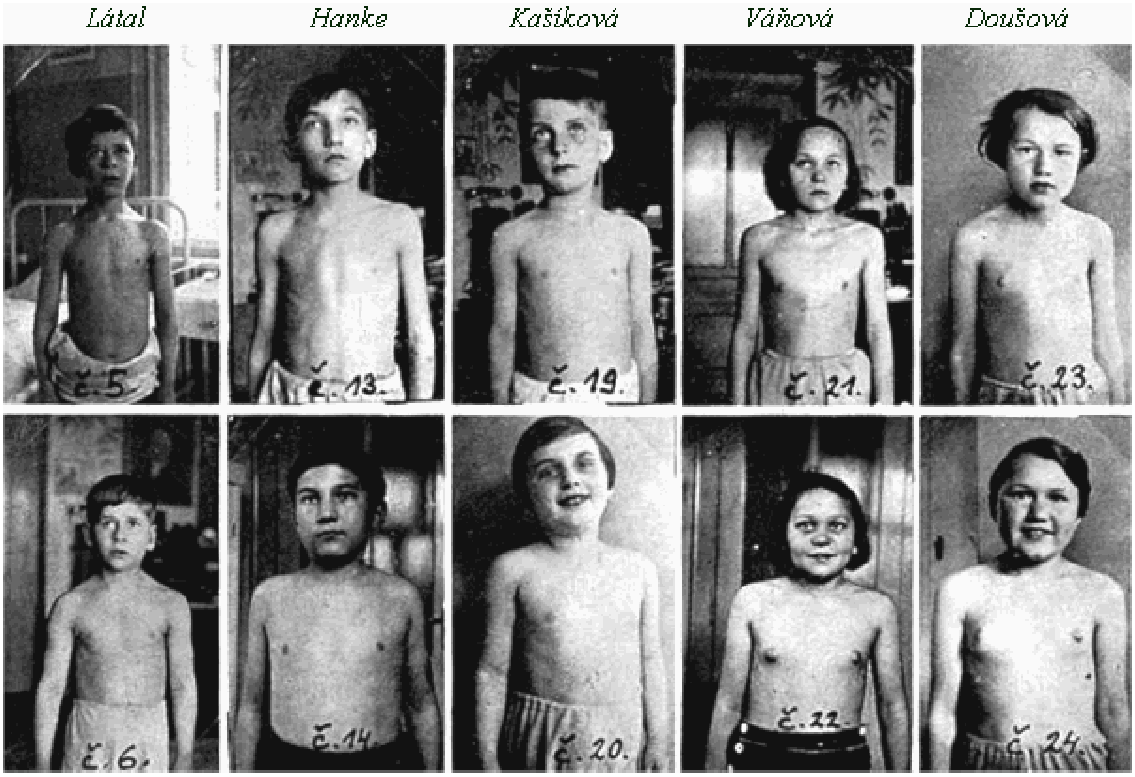
obvious from the pictures, made at the beginning of the treatment. Together with the data, collected from individual children, they are presented in the following overview:

Picture No.	Age (years)	Child's name	Treatment duration	Weight gain (+kg)	Growth in cm	Ribcage diameter	
						(Insp.) In cm	(Exp.) In cm
1-2	6	Jartym Otakar	99	1.6	1.5	1	0
3-4	6	Beck Jindrich	49	1.3	1.5	2	1
5-6	8	Látal Ladislav	52	4.3	1.5	3	3
7-8	8	Skrivánek Mir.	82	3.-	2.-	5	2
9-10	8	Dittrich Karel	52	2.5	1.5	2	0
11-12	8	Machcinyk Jar.	73	3.1	2.-	2	1
13-14	12	Hanke Bohumil	126	13.-	3.5	9	9
15-16	16	Kocman Mirosl.	153	20.-	6.-	14	12
17-18	3	Fádrhonsová Olga	222	3.-	4.5	4	2
19-20	7	Kasíková Helena	159	8.6	4.5	10	8
21-22	11	Vánová Marie	174	10.-	5.-	6	5
23-24	11	Dousová Marie	238	7.5	7.5	8	6
25-26	12	Pulkrábková Hel.	61	3.5	1.-	7	4
27-28	12	Záhlavová Marie	52	6.2	1.-	7	5
29-30	12	Srutová Ružena	159	13.1	5.-	11	10
31-32	12	Prosková Miluse	126	7.2	3.-	5	5

Since the whole group of 16 children were treated at the same time and by the same method, with results indisputably positive there is no doubt. that the treatment was effective. The food, offered three times a day, was neither more abundant or calorically richer than the one which was offered in other institutions and in a majority of families where a child was identified as sick and in need of substantial nutrition. On the contrary, at those institutions we could talk about overfeeding, where meals are presented five or six times a day and the caloric value is higher.

The calories on the plate are not helping if we can't formulate the diet in such a way that the nutrients are utilized and assimilated. Our approach can be summarized in three parts:

1. Preventing overburdening of the liver and other digestive and metabolic organs with harmful foods, offered too frequently. We are trying to encourage their proper functioning by offering some ingredient with specific properties (vitamins and others).
2. We are offering, if possible at every meal, some of the "plastic" proteins, which we have recognized as being natural building material, essential for the formation of animal and plant organisms (cottage cheese, egg yolk, reserve proteins from various plant products, cereal and specifically oat gluten, edestin from hemp seed).
3. Such "plastic" proteins are offered in seemingly small daily doses (for instance 100 g of cottage cheese, I yolk, a few nuts, barely 15 to 20 grams of oats and same amount of hemp seed) but in colloid form, not denaturalized and not coagulated.



Pictures of some children at the beginning and the end of treatment.

The importance of such modified and with hemp seed edestin supplemented medical nutrition will be even more obvious, when we realize, that it was the only substantive base of the whole treatment. During this medical nutrition, we have supplemented the diet with **EDEZYM**, and not used other medication or medical treatment. In 1932, other effective medications against tuberculosis were not even available.

The other 10 cases represent a looser group of children and teenagers who were treated during the second world war - during the occupation. Only one case took place earlier, in 1933, and this girl (11 year old Maria Plecita) was included to this group as, with exception of the time the treatment took place, all the other factors (pathology, therapy) were the same as for the remaining 9 children in the group.

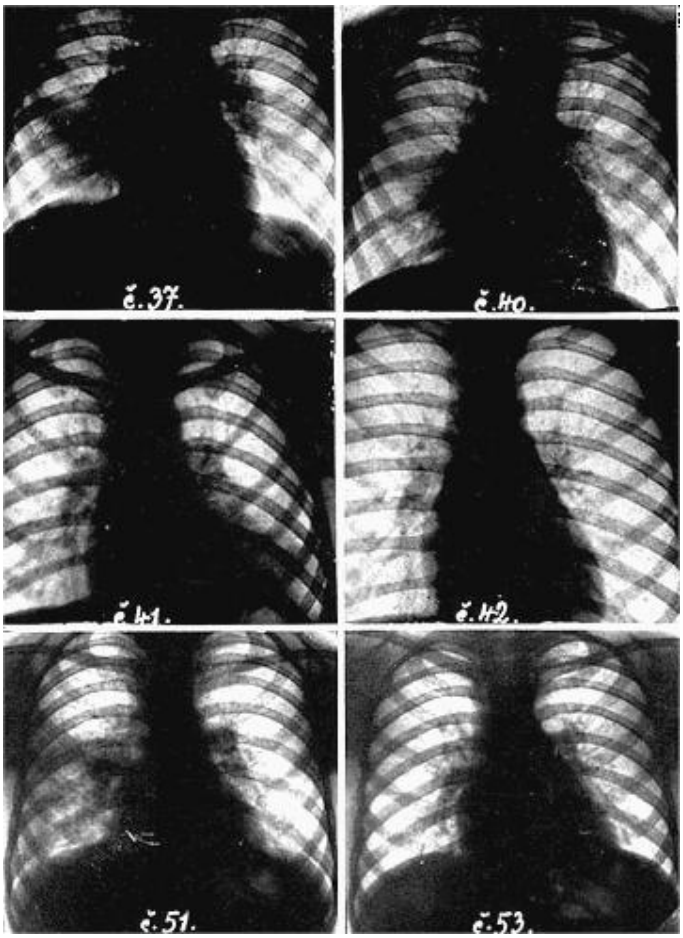
During this period the sanitarium was fully occupied by mature patients, only five years old Ludek Ledecky undertook the treatment together with his father, suffering

with tuberculosis as well. Others were treated at home, under our ambulant supervision. Even this group does not represent specific selection, it included all children we have ambulantly treated. They were considered altogether exceptional.

The level of the nation's nutrition during this period was not good and the children under the home regimen were missing many things, which the sanitarium had in abundance for the children in the first group, in 1938. There was no cream. The cottage cheese was also in short supply and when the parents of the small patients were able to acquire it, the quality was low, as it was hard and coagulated. There was a shortage of butter and high quality fats in general. Similarly, quality meat and sometimes even eggs, sugar and other important food ingredients were not available. Such nutrition was inadequate even for healthy people but even more so for the sick ones. This hard time, however, left our patient two things, which, in addition to cottage cheese, were perhaps the most important: oat flakes and EDEZYM. Consequently, we have been able, during this difficult period and with half way correct home diet, to achieve with this second group of children convincing nutritional and treatment results, equal to the ones achieved in 1938.

These cases. which were part of the second group, took place when the children were not even protected by "calmetisation" or could have been saved by chemotherapy, or by antibiotics. It is obvious as well, that at that time, we didn't have at our disposal detailed diagnostic analysis of individual cases, which would satisfy today's requirements of phthisiology. In particular, we did not have the tomographic data and so we have only estimated, using X-ray pictures, where the atelectasc ends and the inflammation changes begin, when and to what extent we can demonstrate break up and where the dissemination took place. Nevertheless, even this norrnal skiagram brings sufficiently convincing evidence, that to all children in this group, the treatment brought about a significant turn over in the disease, which was, up to this point, considered "progressive". This means that it brought about a regression of the pathological changes in glands and lungs and, in the majority, also a distinct "restitution and integrum". If we add to it that paralicly with the positive development of the lung finding. We have seen in all children, right from the beginning, a similarly

positive change in the total health status, which had, before the treatment started, deteriorated progressively. It was clear that to bring about full curative and nutritional effects, even the little which remained available from our medical nutrition during this war period (oat meal, hemp seed, a little cheese, a few yolks, and protection ofthe liver) was sufficient and that in this "little" is the substance of the effective factor.



X-rays of certain children at the beginning and the end of treatment.
Emil Langer, Ružena Hurková, Blanka Cistá

In the following table, we have summarized the curative effects. which were achieved by the treatment of the second group of ten ambulantly treated children. The summary deals with the effects of lung findings and the total nutritional state and development:

X-ray No.	Age (years)	Name	Characteristics of the disease at the beginning of the treatment	Duration in weeks	Final results of the treatment	Weight changes in kg
33, 34	14	Skopová Libuse - first treatment	10.VII.1944: Lymphadenitis hilosa, right-sided Sluk triangle. Reduction of weight -6 kg, subfebr. febr., menopause	18	17.XI.1944: Normalisation of the lung finding as well as the overall status. Menses is regular again.	+9 kg
35, 36		The same - second treatment	26.XII.1944: Pleuritis exsudat. dx., reduction in weight - 6 kg, febr. temp.	5	30.I.1945: Normalisation of the Sluk triangle, of the lung finding and of the overall status.	+8 kg
37, 38	5	Langer Emil - first treatment	24.VI.1941: Two-sided tumor of the glands, right-sided Sluk triangle	4	24.VII.1941: Disappearance of the Sluk triangle, partial regression of the glands	+2 kg
39, 40		The same - second treatment	18.I.1942: Two-sided Sluk triangle, weight loss -2 kg	38	10.X.1942: Disappearance of the Sluk triangle, regression of the glands	+4,5 kg
41, 42	8	Hurková Ružena	23.IV.1946: Physically retarded since early age, dislike for food, Pirquet ++. Soft deposit on the left lower lobe of the lungs.	28	11.XI.1946: Elimination of the lung finding, she grew and achieved normal development.	+6 kg
43, 44	11	Polácek Vítezslav	11.VI.1944: The same lung finding as in the previous case	21	9.XI.1944: Elimination of the lung finding.	+5 kg
45, 46	5	Ledecký Ludek	6.VI.1946: The same lung finding, but on the right side. Large hard lymphomas on the neck, under the jaw. Pirq. ++	21	The only case from this group treated in the Sanatorium. Liquidation of the lung finding and glands.	+4 kg
47, 48	20	Balej Antonín	1.III.1943: Lack of apetite, night sweating, weight loss-	27	3.IX.1943: Healing of the lung findings,	+7 kg

			3 kg FW 44-72. Soft deposits on the left side, changes with suspected dispers.		disappearance of the signs, restitution of the overall status.	
49, 50	19	Dupáková Jarmila	18.VII.1943: Finding as in previous case ,with distinct parahiles dispersion, FW: 52-90, BK directly positive.	22	18.XII.1943: Healing of lung findings, disappearance of the signs, restitution of the overall status.	+4 kg
51, 52, 53	6	Cistá Blanka	6.V.1944: Coughing for a few weeks, poor food intake, temperature. tumor of hil. glands. A soft deposition of the right hil is spreading to the central and lower fields.	18	6.IX.1944: Involution and calcification of the glands, resorption of the deposition changes, restitution of the overall status.	+5,5 kg
54, 55, 56, 57, 58	10	Vospálek Václav	Since early age sickly, just returned from the hospital. Cachexia. 15.VII.1940: Pleuritis exsud. sin. After reabsorption of exsud. a dispersion in size of a walnut appeared above the diaphragm. BK dir. ++	59	30.VIII.1941: Healing of lung findings, considerable improvement of the overall status. After few years of misery he managed to finish school and received trade.	+5 kg
59, 60, 61, 62, 63	11	Plecitá Marie	30.III.1933: Dispositional changes in both lower lobes of lungs. Pleuritis diaphr., parietal cachexy, Pirquet ++	12	22.VI.1933: Liquidation of lung findings, restitution of the overall status.	+6 kg

VII.

On a group of twenty-six tuberculosis stricken children and teenagers, presented in two groups in "as the herd is running" fashion (this means without any selection), we have been able to achieve positive results. From the point of treatment, nutrition, or physical development, medical nutrition, supplemented with the hemp seed edestin, had an unambiguously favorable effect.

The attached documentation, generated ten to twenty years of age, will not meet today's requirements of the phthisiology. It leaves in some cases doubts if the described type of pathological change or group of changes was or was not of the specific type. There is, however. not a slightest doubt about the following:

1. All children were included into our treatment program in the state of progressive worsening of total health status and also in the majority of cases with documented lung disease;
2. In all participants this treatment immediately caused a turn over in the sense of regression of changes caused by the disease and improvement of the overall health status;
3. In all cases, without any other medication or treatment procedures, within a usually short time, a healing of the lung or glands disease was accomplished. And, during the same short period of time, with only three meals a day, not excessively rich, a far-reaching restitution of the nutritional status and physical development was noticed.

Out of these facts it is obvious that this treatment of medical nutrition proved to be good and very effective. It was happening in a time period when similarly effective means of treatment were not available. In this sense, the treatment was saving the lives of children threatened by tuberculosis (as well as mature people) and was in a position to save many more if it only received the deserved attention.

In the first group of 16 children belonging to the poor people of the Prague suburb, somebody may have commented,that the turn over in their health status was influenced by removing these children from unhealthy living conditions and housing them in a hygienic and rather "affluent environment". It could not be denied that this was an important factor, which had a positive influence, it has an effect during each transfer of a sick child into a hospital, however, we don't see in every case such a change. We do not see such a straight forward means. As well, this objection loses it merit when we compare the first group of children with the second group which, with only one exception, did not changed their environment, but were treated at home.

Moreover, this relatively "affluent environment" was often restricted by the miserable economic condition during the war. Despite that, in such unfavorable conditions, we witness the same convincing and unambiguous results, the same overall improvement.

It is exactly this comparison of the two groups of children which leads us to the discovery of the factors which were effective in the treatment of both groups. For certainly, it was not the effect of the changed environment and "comparative affluence" which we provided for the children in the first group, but which was not available for the children in the second group. It must have been the parts of the treatment which were available to both groups. From the effective substances we should name: porridge from the oat flakes, EDEZYM from the hemp seeds, and cottage cheese. Further, we should add the protection of the liver, which means the exclusion of meals which are overburdening the liver and the exclusion of frequent presentations of meals and drinks.

If we take the preservation of liver as a logical part of the patient's hygiene, we can condense the whole topic to three factors: oatmeal porridge, EDEZYM and cottage cheese. It is not to say that raw or "soft" egg yolk, nuts, raw vegetables and fruits and other, previously discussed things are not important. But the most important, as we can conclude from our analysis, are the three: oats, hemp seed and cottage cheese. And, we repeat, that all three must be prepared in such a way that the proteins will be colloid, under-naturalized and in a non-coagulated state. All other effective substances of the medical nutrition could be, more or less, missed by the patient, as they were missed by the children in the second group, without endangering the results of the medical nutrition. If, however, one of the three basic pillars of the treatment is missing, or is damaged (denaturalized) by the improper processing, the results of the treatment are half as effective or less effective.

Today, when we don't have EDEZYM and the cottage cheese is sometimes of poor quality, we have Streptomycin, PAS, and INH, in addition to surgical methods. Let's be careful, however! A conscientious doctor always considers the strong points and

weaknesses of such medications and while treating the mature patients, or even more, while treating the children, he uses them only in cases where they are needed and in doses which are tolerable. If he understands the importance of liver protection, he is twice as careful, particularly when dealing with para-aminosalicylic acid. And makes sure "that he will not use all his ammunition before the main battle starts". This means he avoids the frivolous use of full doses of antibiotics and bacteriostatical drugs, so that in case of exacerbation or recidivity, he will not be without an effective weapon. All such unavoidable considerations must reinforce our conviction, that a means which is relatively effective and at the same time absolutely harmless when used for an extended and unlimited period, as is our medical nutrition, should not be overlooked even today, in a time of antibiotics.

We, in Jince, even today subject our patients, who are mature and chronic, to the appropriate preparation before we will use antibiotics or tuberculostatics. Those who need it, will be educated in the proper order in eating and drinking. Smokers are retrained into non-smokers and all are included into a regimen of liver protection. Usually, we achieve, particularly in disciplined patients, a nice improvement, without medication. Only in cases when the treatment progress is slow, do we, after careful consideration, use antibiotics and bacteriostatics. Patients will, however, always be supported by medical nutrition. This medical nutrition is an essential part of our patient's education while they are being treated at home.

SUMMARY

The use of hemp seed in the therapy of tuberculosis is based on our experience of the last thirty years, gained at Jince in the area of medical nutrition. In the proper function of the liver we have always seen a precondition for perfect assimilation of nutrients. For this reason we have emphasized the rules and limitations which we know today as the foundation of liver diet. We consider them to a certain point as a universal base of every medical diet. Medical nutrition during tuberculosis must stress, in addition to vitamins B1, C and A, primarily proteins and among them namely those which nature destined to serve as building material for the formation of

organisms. Such protein sources, for instance, include cottage cheese, egg yolk. reserve proteins in cereals, nuts and other fruits. It is of great importance. that such proteins are processed without denaturalization. Professionally prepared cottage cheese is a precious dietetic component, but hard and coagulated is dietetically worthless. Similarly, raw egg yolk is a good, but boiled to hard state is not. A daily does of only 10 to 20 grams of oats, in the form of professionally prepared porridge will soon prove its medicinal properties, while twenty times higher doses of cereals denaturalized by baking or cooking in water have a dietetically rather indifferent affect. The ground hemp seed, extracted with milk, heated to a temperature between 60 to 80 degrees C will have, even in such small doses, an important healing effect. We are convinced that a child with tuberculosis is the best testing ground for medical nutrition based on hemp seed.

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Only those works referred to in our paper are listed, for at that time the Bulletin on Narcotics was not available to us. In the Bulletin there are two reports to be found (Chopra, J. C.: vol. 9, No. 1, 5-32 (1957), and Ahmed Benabud: vol. 9, No. 4, 1-17 (1957)) which, in discussing the history of the utilization of cannabis in popular medicine in India and Morocco, refer to the analgesic and antibacterial effects of

cannabis (erysipelas, dysentery, gonorrheoa, cholera, etc.). Some other papers are particularly concerned with the analysis, the chemistry, and the narcotic effect of cannabis - viz., Duquenois, P.: vol. 2, No. 3, 30 (1950); Bouquet, J.: vol. 2, No. 4, 14-31 and vol. 3, No. 1, 22-46 (1951); Cordeiro de Farias, R.: vol. 7, No. 2, 6 (1955); Asahina, H.: vol 9, No. 4, 18 (1957); Joachimoglu, G.: vol. 11, No. 3, 5 (1959).

In vol. 3, No. 1, 62-81 and No. 2, 47-54 (1951) of the above-mentioned journal a comprehensive literature on cannabis and its utilization is given. In the bibliography of Bullettin, there have also been listed the periodical publications on cannabis up to 1958.