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Journal home page: <http://www.pharmasm.com>CHEMICAL COMPOSITION AND MEDICINAL USES OF *ANACYCLUS PYRETHRUM*

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ABSTRACT

Anacyclus pyrethrum (Akarkara), a vulnerable herb commercially producing pyrethrum drug extracted from the roots of the plant is an important Ayurvedic medicine. The flower another significant part possesses insecticidal property. The plant mainly contains alkaloids, tannins, triterpenes, flavonoids, sterols, some trace metals and phenols. The roots mainly contain an ester pyrethrine and *N*-alkylamides (pellitorine) that enhances its medicinal value. The plant is used as sex stimulant, antidiabetic, antioxidant, treating asthma, cardiac diseases, and throat problems, remove laziness, nerves weakness, carminative, stomach, arthritis, sciatica, diuretic, tooth and gum problems, aphrodisiacs, hiccoughs, epilepsy, headache, pains, muscle relaxant, worm infestation, anti-rheumatism, anticonvulsant, brain tonic, common cold and other human related disorders. The plant is a natural pesticide and also shows antimicrobial properties. This study is based on phytochemistry and medicinal properties of the plant with main concern on employing new scientific tools for its mass production and protection.

KEYWORDS: *Anacyclus pyrethrum*, phytochemical, medicinal.

INTRODUCTION

Anacyclus pyrethrum, Indian trade name 'Akarkara' is a small hairy herbaceous perennial belonging to Asteraceae family. The plant native of Arabia, mainly distributed in North Africa, Mediterranean region, Himalayas^[1] Spain and in India it is found along the Himalaya, Jammu and Kashmir, Bengal ^[2] and in Northern parts. Akarkara described an aphrodisiac drug has multiple uses in Ayurveda and Unani medicine ^[3]. Kenya is the leading producer of pyrethrum extract along with Rwanda, Tanzania and Australia ^[4].



Fig: Flower and roots of *Anacyclus pyrethrum*

The plant root commonly known as 'pellitory root' possess medicinal property. Pyrethrins are registered as botanical insecticide products by United States Environmental Protection Agency (EPA) [5].

Pyrethrum is cultivated in tropics at an attitude of 1500 to 3500 meters, requiring dry to soft sandy soil, 800-1300 mm rainfall, 15-25°C temperature and sunny periods interrupting rainfall for its cultivation. The leaves are smooth, pinnate and alternate, with cutted segments. Stems lie on the ground and bear one large terminal flower, with yellow disk and white rays. Fruit is a obovate achene [6]. Roots are brown in colour, 7-15 cm in length with cylindrical shape having aromatic odour and pungent taste with hairy rootlets [1]. Bark contain 1-2 circles of resin ducts, having distinct odour; sweet taste, pungent, tingling, acrid showing sialagogue effect. The flower is picked up when it is about 70% open. Plant produces 300 to 400 kg drugs/hectare [6].

The continuous exploitation of the drug as a natural stimulant and insecticidal property lead to decline in the population categorizing it under vulnerable species according to latest IUCN Red list [7]. Various studies have concerned on detailed phytochemical and therapeutic study on valuable medicinal plant in the surrounding for a proper pharmacological application [8, 9, 10] with special concern on their conservation status [11, 12, 13]. This research is designed to study the chemical composition and medicinal potential of *A. pyrethrum* (Akarkara) for exploring it as a safer and natural drug along with safeguarding this nature wonder with sustainable use.

Chemical composition

Various studies reported a number of chemical constituents in *A. pyrethrum*. The phytochemical screening of roots, leaves and flowers revealed presence of alkaloids, reducing compounds and cathechic tannins. Further, plant contains other chemicals such as gallic tannins, triterpenes, sterols, mucilage, coumarins, saccharids and holosids [14] along with some trace metals like Zn, Fe, Cu, Cd, Cr, Ni and Pb [15]. The flavonoid, total phenol and polyphenols contents are highest in flowers compared to leaves and root. The roots are rich in alkaloids while the aerial parts are rich in tannins and flavonoids. Root contains a brown acrid resin, a trace of tannic acid, inulin, gum, various salts, and lignin [16]. The roots of the plant is aphrodisiac due to presence of bio-active compound *N*-alkylamides [17]. Seven pure alkamides were identified by mass- and NMR-spectroscopic methods as deca-2*E*,4*E*,9-trienoic acid isobutylamide, deca-2*E*,4*E*-dienoic acid isobutylamide (pellitorine), deca-2*E*,4*E*-dienoic acid 2-phenylethylamide, tetradeca-2*E*,4*E*-dien-8,10-diynoic acid isobutylamide (anacycline), undeca-2*E*,4*E*-dien-8,10-diynoic acid isopentylamide, dodeca-2*E*,4*E*-dien acid 4-hydroxy-2-phenylethylamide and tetradeca-2*E*,4*E*,12*Z*-trien-8,10-diynoic acid isobutylamide. Further a mixture of two other alkamides were

detected by column chromatography followed by preparative HPLC as deca-2*E*, 4 *E*-dienoic acid 4-hydroxy-2-phenylethylamide and undeca-2*E*,4*E*-dien-8,10-diynoic acid 2-phenylethylamide^[18].

Detailed study of the crystalline constituents of the roots exhibited a mixture of isobutyl amides of unsaturated acids with decadiene as an important constituent ^[19]. Hydrogenation and acidic hydrolysis of the roots yield a mixture of decanoic, dodecanoic and tetradecanoic acids which can be separated by reversed-phase partition chromatography ^[20]. Root also contain an alkaloid, pyrethrine, which is an ether- extract, composed of acid fat and resin and volatile oil and pellitorin^[16]. The pyrethrins obtained from the roots are a naturally-occurring group of six chemically-related esters, each of which is insecticidally active. Three (pyrethrins I- Cinerin I, Jasmolin I) are esters of chrysanthemic acid, and three (pyrethrins II, Cinerin II and Jasmolin II) of pyrethric acid. The alcohol moieties detected in the study are pyrethrelone, cinerolone and jasmolone in pyrethrin 1 and 2, cinerin 1 and 2, and jasmolin 1 and 2 respectively ^[6]. Pellitorine, is a mixture of isobutylamides and its isolation yield a new crystalline substance which crystallizes from chloroform-petrol in white needles and sparingly soluble in petrol with melting point 121° ^[20].

The study of the ethanolic root, leaf and stem extracts of the plant revealed presence of steroids, triterpenes, reducing sugar, sugar, alkaloids, flavonoids, saponin, tannins, anthraquinones and amino acids (Subasri and John,2016). HPLC/UV/ESI-MS of ethanolic extract of dry roots containing N-Alkylamides detected 13 compounds ^[19, 21]. Out of these thirteen, six viz undeca-2*E*,4*E*-diene-8,10-diynoic acid N-methyl isobutylamide, undeca-2*E*,4*E*-diene-8,10-diynoic acid isobutylamide, tetradeca-2*E*,4*E*-diene-8,10-diynoic acid tyramide, tetradeca-2*E*,4*E*,*XE/Z*-trienoic acid tyramide, tetradeca-2*E*,4*E*,*XE/Z*,*YE/Z*-tetraenoic isobutylamide and deca-2*E*,4*E*-dienoic acid N-methyl isobutylamide, are identified as novel compounds ^[21]. Chromatographic HPTLC of the alcoholic extract of root shows presence of picric acid, HNO₃, CH₃COOH, H₂SO₄, HCl, Ferric chloride, Aqueous KOH, Alcoholic KOH, Ammonia solution and Iodine solution^[1]. Gas Chromatography-Mass Spectroscopy analysis of ethanol extract of the root shows presence of Palmitic acid, 9,12-Octadecadienoic acid (*Z,Z*)-, Naphthalene, decahydro-1,1-dimethyl-, 7-Tetradecenal, (*Z*)-, N-Isobutyl-tetradeca-2,4-dienamide, Benzofuran2-carboxaldehyde and gamma.-Sitosterol^[22]. The hydro-methanol root extracts of the plant shows an effective antioxidative activity depending on the concentration of polyphenols, inhibiting the formation of free radicals with negative impact on oxidation of macromolecules ^[16].

A. pyrethrum plant also yields essential oils with maximum production in June month during flowering stage [23, 24, 25]. A study conducted in Morocco reveals presence of 42 compounds in April and 36 in June month in essential oil with oxygenated sesquiterpenes as the most abundant group including spathulenol, Germacra -4 (15), 5, 10 (14) - trien -1-a -ol, selina -3 ,11- dien- 6-a -ol, acetate cedryl, β -biotol, salvia -4 (14) -en-1-one, Eudesma -4 (15), 7- diene-1- ol, β - himachalol^[14]. Similar study in Algeria shows dominance of germacrene-D and essential oils have other major constituents like germacra-4 (15), 5, 10 (14)- trien -1-a-ol, caryophyllene oxide, spathulenol/ caryophyllene oxide /cedryl acetate/ and eudesma -4 (15), 7- diene-1- β -ol^[14]. Spathulenol is the most important constituent of essential oil of plant root therefore the plant EO can be classified as spathulenol chemotype [25].

Medicinal uses

In North Africa the roots of the plant have been used in medicine since the time of Dioscorides, and mention of the drug is made in the B.P.C. 1934 (*Pyrethri radix*) [20]. Roots are used as traditional medicine in East [1]. They possess rejuvenative properties and were considered as aphrodisiac and sexual stimulant in male [19,26,27], Pyrethrum root containing isobutylamide, anacycline, inulin and a trace of essential oil have potentiality in reducing the dose of insulin in diabetes mellitus patient and also decreases the plasma glucose and serum cholesterol levels^[6]. Plant root also exhibit mollusidal and anti-inflammatory activity^[19], analgesic, anti-rheumatic, carminative, antiviral, anti-catarrh, improve digestion, emmenagogue, febrifuge, vermifuge and nervine activity^[25]. They are exclusively used as a sialagogue in headache, neuralgic and rheumatic affections of the face, toothache, etc., or as a local stimulant in epalsy of the tongue or throat, or relaxation of the uvula [6, 25]. Root induces copious salivation when chewed and gives rise to an intense burning taste^[20], present inhibitory effects, immunostimulating effect, memory-enhancing activity, anticonvulsant activity, antioxidant, antidepressant activity, aphrodisiacs, antimicrobial activity, insecticidal effect, local anesthetic effect, and stimulate testosterone, libido and testicles^[25]. The powdered root forms a good snuff to cure chronic catarrh of the head and nostrils and to clear the brain, by exciting a free flow of nasal mucous and tears^[6]. Herb has also been found effective in erectile dysfunction [28]. A mixture of Akarkara root powder, honey and Acorus Calamus (Vacha) helps improving Delayed Speech Development or Childhood apraxia of speech (CAS) in children.

The flowers have long been exploited commercially for their natural insecticides collectively known as pyrethrins [6,19]. Pyrethrum flower produces Pyrethrins that kill insect by disrupting their nervous systems. They are toxic to the “sodium channel,” the cellular structure that allows

sodium ions to enter a cell as part of the process of transmitting a nerve impulse. This leads to repetitive discharges by the nerve cell which causes paralysis and death and is a safest insecticide which is "nontoxic to humans and pets [29].

Aqueous macerate extract of the plant shows active inhibition against susceptible *Staphylococcus aureus* and *Escherichia coli* germs collected from the hospital [14]. Plant extract also exhibit free radical scavenging or antioxidant activity against the stable radical DPPH as tested by using a UV-visible spectrophotometer [30]. 5-diphenyltetrazolium bromide (MTT) and flow cytometry assay of plant extract induce apoptosis in colorectal cancer cells by increasing the caspase 3 mRNA expressions, decreasing Bcl-2, Vimentin and MMP1, along with arresting cell cycle in G1 stage[31]. The essential oil of the plant is a natural antibacterial agent against *Staphylococcus aureus* and *Candida albicans* strains [24]. Crude hexane extract of *Akarkara* species has potentiality in causing lethality of malaria and filaria mosquito larvae [32]. Aqueous root extracts of *A. pyrethrum* increases serum testosterone and gonadotropins (LH, FSH) levels due to presence of pyrethrin or pellitorin which is an alkyl amide showing positive impact on reproduction in rats[33].

The ethanolic extract of roots of *Anacyclus pyrethrum* shows antimicrobial activity[19,15], neuropharmacological activity[34], aqueous and alcoholic extracts of roots exhibited anaesthetic activity[19,35,36], natural pyrethrins mouse in head lice eradication[37], pyrethrum marc are used against sheep gastrointestinal Nematodes[38], root extract exhibit antidepressant effect by interaction with adrenergic and dopamine receptor in Swiss male albino mice [39], ethanolic extract shows myorelaxation and anticonvulsant activity on albino mice [40], hot water polysaccharide extracts exhibited immunostimulating activity in mice[41], oral administration of dried powdered root with petroleum ether extracted with water which are suspended in 1% sodium CMC shows aphrodisiac and reproductive activity in Wister albino rats[42], eugenol and the extracts of *Anacyclus pyrethrum* and *Spilanthes calva* are traditionally used during the preparation of chewable tobacco for tobacco-induced mutagenicity[43], sulfuric acid extract of the leaves and stems are used as corrosion inhibitor for mild steel[44], acetylcholinesterase enzyme inhibition, a neurotransmitter present in RBC membrane catalyzing the breakdown of acetylcholine, as confirmed by spectrophotometric and TLC bioassay[45]. Alkylamide-rich ethanol solution extract increases body weight, sperm count, motility, and viability, serum testosterone, luteinizing hormone, follicle-stimulating hormone concentrations, spermatogenic activities and seminal fructose content in rats[46].

Gas chromatography-mass spectrometry analysis of methanol extract for anesthetic activity against *Cyprinus carpio* fish reported 1-4 minute recovery time depending on dosage without showing any lingering adverse effects on the animal [29]. The methanolic extract of plant at 800 mg/ml shows antibacterial effect on *Escherichia coli* [47]. The undiluted 2% methanol extract showed minimal antibacterial action against *B. Subtilis*, *S. aureus*, *E. coli*, *S. typhi* and *K.Pneumonia* [29]. Dichloromethane root extract of *Anacyclus pyrethrum* L. shows a moderate antiprotozoal activity against the NF54 strain of *Plasmodium falciparum* and against *Leishmania donovani* (amastigotes, MHOM/ET/67/L82 strain) [18]. Hydroalcoholic extract of *A. pyrethrum* (HEAP) root significantly prevented seizures; seizure induced oxidative stress and cognitive impairment by normalizing cholinesterase activity in Male Wistar rats [48]. In another study HEAP exhibited anticonvulsant activity when tested in Male albino mice and reduces malondialdehyde (MDA), glutathione (GSH) and ROCK II expression in whole brain of the animal [49].

CONCLUSION

Anacyclus pyrethrum yielding pyrethrum drug is an important Ayurvedic herb with immense medicinal value. The plant as a natural pesticide and aphrodisiac and impotency stimulant is a popular medicine recognized by global pharmaceutical agencies and requires an efficient technology for its preservation and safer use. The use of modern scientific methods for mass production and conservation of the species is highly recommended.

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