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Pharmacognostic and phytopharmacology study of *Anacyclus pyrethrum*: An insight

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ABSTRACT

Anacyclus pyrethrum an amazing medicinal plant is one of the most widely growing species of the family Asteraceae. The present review endow with significant information about its phytochemical investigations, pharmacological activities and medicinal properties as a folk medicine to treat several disease like anti-rheumatic, analgesic, antibacterial, antiviral, *carminat*ive, anti-catarrh, improve digestion, emmenagogue, febrifuge, nervine, vermifuge, and sialagogue. The plant has been reported several pharmacological actions such as antidiabetic, immunostimulating effect, inhibitory effects, antidepressant activity, anticonvulsant activity, memory-enhancing activity, aphrodisiacs, antimicrobial activity, antioxidant, local anesthetic effect, insecticidal effect, action on COX and LOX, interactions with testosterone, interaction with libido, and it interaction with testicles. Mainly the root portion has beneficial properties that can serve the mankind. The entire plant can be extensively studied for further future prospective.

INTRODUCTION

World Health Organization (WHO) appreciated the importance of medicinal plants for public health care in developing nations. *Anacyclus pyrethrum* DC roots and leaf have important role in the traditional Ayurvedic and Unani system of holistic health and herbal medicine of the East. Especially the root of *Anacyclus pyrethrum* is reported to have good medicinal values in traditional system of medicine (Kishor and Lalitha, 2012). *Anacyclus pyrethrum* from Asteraceae family and Anacyclus genus is a native plant of India and Arabic countries and its root has therapeutic effects (Naderi *et al.*, 2012). *Anacyclus pyrethrum* (Linn) De Candolle, commonly known as 'Spanish pyrethrum root' in English, 'Aaqarqarhaa' in Unani, and 'Aaqarqarhaa' in Ayurveda. It is widely recognized in Ayurvedic system of Indian medicine as tonic and rejuvenator. Its root is hard, compact, fusi-form about the size of the little finger, with sometimes leaf - remnants at the top, and beset with few or no hair-like rootlets; externally brownish, deeply fissured longitudinally (Puri *et al.*,2003). It contains essential oils and an alkaloid pellitorine that is intensely pungent constituent with a mixture of isobutyl amide. Traditionally, plant is used as antibacterial, anti-inflammatory and tonic to the nervous system (Tyagi *et al.*, 2011). *Anacyclus pyrethrum* commonly known as pellitory and Akarkara in Hindi local language is perfectly recognized in traditional and herbal medicine and has a positive effect on regulating the immune system (Sharma *et al.*, 2010). North Africa possesses almost 1700 endemic species and subspecies and half of them are specific to Morocco (Oualid *et al.*, 2012). To *Anacyclus* genus, belong 13 annual and perennial species mostly encountered in North -West Africa and also in other Mediterranean countries (Harald, 1978). Many *Anacyclus* species such as *A. pyrethrum, A. radiatus, A. valentinus, A. cyrtolepodioide* and A. *Clavatus* are used in traditional medicine. Their medicinal properties are due to the presence of flavonoids and terpenoids (Harald, 1978; Efraim *et al.*, 2008; Benitez *et al.* 2010). In the Mediterranean wide flora, *Anacyclus pyrethrum* L. (Asteraceae), commonly named "African pyrethrum" or "Tigenthast" by Moroccan people (Batanouny, 2005) was chosen. It is an endemic herbaceous and perennial species (Oualid *et al.*, 2012) present in sunny medium. In North Africa, the species is encountered in wild on slimy and well-drained soils (Batanouny, 2005).

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Vernacular names

English	:	Pellitory
Hindi	:	Akarakara
Marathi	:	Akkirakaram
Arabi	:	Aquargarha
Sanskrit	:	Agragrahi, Akarakarabha

Taxonomy

Kingdom	:	Plantae
Division	:	Spermatophyta,
Sub–division	:	Angiosperms,
Class	:	Dicotyledons,
Sub class	:	Metachlamydae,
Order	:	Companulatae,
Family	:	Compositae or Asteraceae,
Genus	:	*Anacyclus,*
Species	:	*Pyrethrum.*

Fig. 1: *Anacyclus pyrethrum* Plant.

Fig: 2 Root of *Anacyclus pyrethrum.*

Distribution

It is found in North Africa, Arabia, Syria, Algeria, elsewhere in the mediterranean region and varieties of this drug are seen in some place of India such as Jammu and Kashmir, Bengal. It is imported to India from Algeria. They have slight aromatic smell and persistent pungent taste (The Wealth of India).

TRADITIONAL USES

The extraordinary properties of Akarkara are listed as under:

Aphrodisiac: The extracts of plant roots increase libido or sexual urges and delays ejaculation.

Analgesic: It reduces or ends pain by causing numbness.

Anti-rheumatic & Anti-arthritic: It gives relief in rheumatic arthritis by increasing circulation.

Anti-Bacterial & Anti-viral: Akarkara has also shown antibacterial and anti-viral properties and thus it keeps you safe from a large number of air-borne & water-borne infectious diseases caused by bacteria and virus.

Antibiotic: It also inhibits microbial or biotic growth in the body.

Anti-catarrhal: Akarkara root also exhibits anticatarrhal properties, i.e. it expels old catarrh.

Carminative: It expels gases from intestines.

Digestion: Akarkara roots aid in digestion by stimulating secretion of saliva and other digestive juices as it goes down the digestive system.

Diuretic: The diuretic property of Akarkara root increases frequency and quantity of urination, thereby helping detoxify the body.

Emmenagogue: It gives relief from irregular, delayed and obstructed menstruation.

Febrifuge: The alkaloids present in Akarkara makes it a good febrifuge by virtue of its anti-microbial antiviral and anti-bacterial properties.

Nervine: Akarkara is famous for treating nervous or neurotic disorders.

Vermifuge: The anti-biotic and anti-microbial properties of the alkaloids present in Akarkara roots makes it a good vermifuge too and help in destroying the worms in our intestine.

Sialagogue: It increases production & secretion of saliva. This can aid in digesting food & give relief from dry mouth and is frequently used for toothache. (Annalakshmi *et al.,* 2012, Selles *et al.,* 2013; Doudach *et al.,* 2012).

PHYTOCHEMISTRY

Phytochemical screening has identified various secondary metabolites such as alkaloids, reducing compounds, tannins, flavonoids and coumarins (Hanane *et al.,* 2014). Chemical analysis of roots shows the presence of three fatty acids, a sterol and ten unsaturated amides. The most important compounds discovered in roots are pellitorin, anacyclin, phenylethylamine, inulin, polyacetylenic amides I-IV, and sesamin. The species contains also tannins, gum and essential oil traces (Selles *et al.,* 2012; Zaidi *et al.,* 2013, Sujith, 2012).

The yields of *A. Pyrethrum*'s essential oils obtained during the two harvest periods are:

The yield during June (0.07%) is higher than the one during April (0.05%). These rates are relatively high compared to those obtained in Algeria by Selles *et al.* (2013) (0.019%). Intraspecific variations of the yields can be attributed to the harvesting period. Several authors confirmed that the best yield occurs at the flowering stage (Selles *et al.,* 2013; Ghanmi *et al.,* 2010; Simonnet *et al.,* 2006; Bourkhiss *et al.,* 2011).

Analyses of *A. Pyrethrum* from Timahdite area (Morocco) revealed the presence of 42 compounds for April sample and 36 compounds for June sample. These compounds represent about 91,32 % and 91,82 % of the total of these Essential oils (Hanane *et al.*,2014).

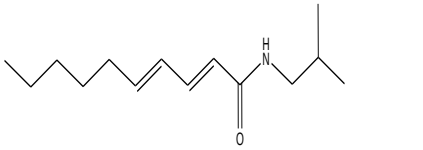
Oxygenated sesquiterpenes are the most abundant group among the identified compounds. Their level rises from 89,17 % (April) to 90,58 % (June) during maturation step. Similarly, this group is the most abundant in the Algerian species as showed by Selles *et al*. (2013). In his study percentage of sesquiterpenes rises from 37,1% to 58,6 % respectively before and after flowering stage. Comparison of essential oils' chemical composition showed quantitative and qualitative changes. The percentage of the major constituent spathulenol increases significantly from April (13, 31%) to June (16, 9%). Germacra -4 (15),5, 10 (14) - trien -1-a –ol percentage also increases from April (2,07%) to June (12,89%). We also note that selina -3 ,11- dien- 6-a -ol has its highest proportion in the first period (9,24%) while acetate cedryl highest percentage is obtained during the second period (8,10%). The percentage of caryophyllene oxide falls from April to June (9,65 to 7,11%).

Finally, it is important to note the high rates of β-biotol and salvial -4 (14) -en-1-one during the first period of harvest (5,16% and 4,66% respectively). Eudesma -4 (15),7- diene-1- ol and β – himachalol have their high rates during the second period (5,85% and 5,67% respectively).

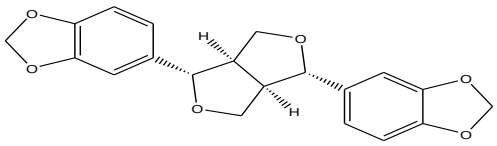
In *Anacyclus pyrethrum* roots essential oils, spathulenol is the most important compound at both stages (April and June). So whatever the time of harvest, the plant EO can be classified as spathulenol chemotype. However, in other studies the results are quite different. *Anacyclus pyrethrum* EO from Algeria is dominated by germacrene-D and defined by the germacrene-D chemotype (Selles, 2012; Selles *et al.*, 2013).

Since in both harvest periods, essential oils have other major constituents like germacra-4 (15), 5, 10 (14)- trien -1-a-ol, caryophyllene oxide , etc. Then, we can define intermediate chemotypes such as chemotype of April with spathulenol (13,31%) / caryphylene oxide (9,65 %) /cedryl acetate (8,10%)/ and eudesma -4 (15) ,7- diene-1-β-ol (5,85%). And the chemotype of June with spathulenol (16,9%)/ germacra -4(15) , 5, 10(14)- trien-1-a-ol (12,89 %)/ and selina -3, 11-dien-6-a-ol (9,24%). Indeed, the difference observed in compounds content between these two collection dates can be explained by the biosynthesis process of these main constituents (Ghanmi *et al.*, 2010).

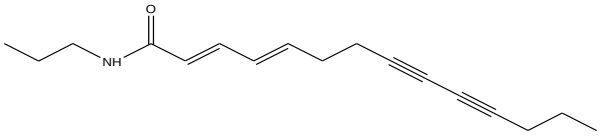
Therefore, Asteraceae family is particularly characterized by the chemical polymorphism. This chemical variation can depend on the harvest period of the plant. This period constitute a parameter which influences both chemical yield and quality of the essential oil (Garneau, 2001).



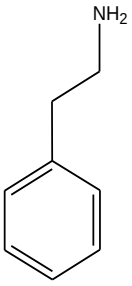
Pellitorine



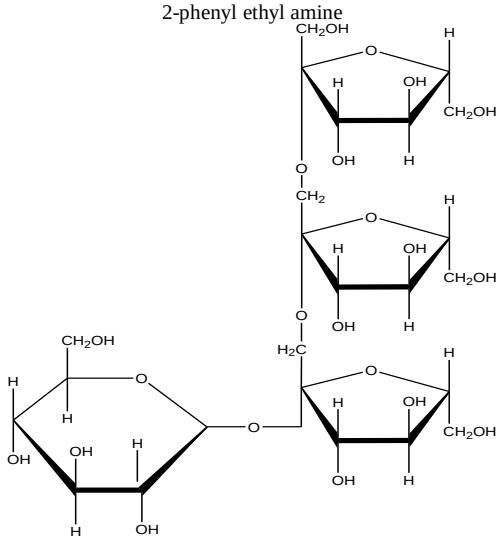
Sesamine



Anacylin



2-phenyl ethyl amine



Inulin

TOXICITY STUDIES

Acute (oral) toxicity studies of *Anacyclus pyrethrum* root in albino rats, No mortality and significant changes were showed in body weight and wellness parameters at 175, 550 and 2000 mg/kg body wt. doses, which reveal the safety of these extracts in the doses up to 2000 mg/kg body weight (Kishor and Lalitha, 2013).

PHARMACOLOGICAL STUDIES

Antioxidant effect

The ethanolic extract of *Anacyclus pyrethrum* was evaluated for in vivo and ex-vivo Antioxidant activities by using different experimental model at different concentration 25, 50, 100, 200, 400 microgram/ml. Antioxidant potential of *A. pyrethrum* root may be due to their photochemical constituents such as Phenol, Flavinoids, Alkaloids, Tannins (Sujith *et al.*, 2011).

Antidiabetic

The antidiabetic activity of aqueous root extract of *Anacyclus pyrethrum* was evaluated in alloxan induced diabetic rats. The aqueous root extract of *Anacyclus pyrethrum* at a conc. of 150 and 300 mg/kg was orally administered to Alloxan induced diabetic rats. The prominent levels of blood glucose in the diabetic rats reverted back to near normal after treatment with the aqueous root extract of *Anacyclus pyrethrum* (Tyagi *et al.*, 2011).

Immunostimulating effect

Hot water polysaccharide extracts of *Anacyclus pyrethrum* was tested for their immune stimulating activity in mice. The fractions from *Anacyclus pyrethrum* and *Alpinia galanga* showed a marked stimulating activity on the reticulo-endothelial system (RES) and increased the number of peritoneal exudates cells (PEC), and spleen cells of mice. In this case, the optimum doses were 50 and 25 mg/kg for the 2 fractions, respectively. On the other hand, the polysaccharide extracts of both *Anacyclus pyrethrum* and *Alpinia galangal* markedly incerased the production of the murine spleen cells in vitro using two tests (in vitro and in vivo effect). The results of the in vivo effect at a doses of 50 and 25 mg/kg, showed a encouragement index better than obtained with the in vitro effect at 50 and 25 mg/ml for *Anacyclus pyrethrum* and *Alpinia galanga*, respectively. While the extract of *Citrullus colocynthis* showed much weaker and changeable immunostimulating activity (Bendjeddou *et al.*, 2003).

Antidepressant activity

Patients with major depression has been found to exhibit evidence of an activated innate immune response as reflected by augmented biomarkers of inflammation, including innate immune cytokines, acute-phase proteins, chemokines & adhesion molecules (Dantzer *et al.*, 2008).

An experiment was planned by different method such as locomotor activity, haloperidol induced catalepsy, forced swimming test (FST), tail suspension test (TST), clonidine induced hypothermia & Reserpine-induced hypothermia on Swiss male albino mice. Root extract of *Anacyclus pyrethrum* showed an increase in ambulatory behavior indicating a stimulant effect of the photoactometer. AP root extract produces a significant antidepressant effect in both Forced Swim Test and Tail Suspension Test as they reduced the immobility. AP root extract was found to be effective in reversing hypothermia produced by clonidine and reserpine in mice at doses of 100 and 200 mg/kg (Badhe *et al.*, 2010).

Anticonvulsant activity

Electro-convulsive shock, inducing Hind limb tonic Extension (HLTE) in 99% of the animals, was previously determined (Kamalinejad *et al.*, 2000) corneal electrode were used for bilateral delivery of electrical motivation Electro-convulsive alarm (50mA for 0.2 sec) was delivered through corneal electrode to induce HLTE phase in mice. The electrical stimulus was functionalized by using a stimulator apparatus for five groups of six each (Gautam, 2011).

Group I served as control (vehicle treated) (i.p.); Group II served as standard (received phenytoin sodium 25 mg/kg body weight, i.p.)Group III, IV, V were treated with ethanolic extract as 200, 400, and 600mg/kg body weight, i.p. respectively. The current was delivered after 30 min of intraperitonial insertion of control and standard. The incidence and duration of HLTE was noted. It shows that the extract significantly decreased the duration of HLTE phase in maximum electroshock induced seizures.the MES test is considered to be a predictor of likely therapeutic efficacy generalized tonic-clonic seizures (Loscher & Schmidt, 1998). MES induced tonic seizures can be prevented either by drugs that inhibit voltage dependent Na ion channels, such as phenytoin, valproate and lamotrigine or by drugs that block glutamatergic excitation mediated by the N-Methyl – D asparatate (NMDA) receptor such as felbamate (Fielding *et al.*, 1995). The ethanolic extract from roots of AP can inhibit voltage dependent sodium ion channels as phenytoin in MES induced tonic seizures. The effect on motor co-ordination was evaluated using rota rod apparatus.

Pre selected mice were placed on the horizontal rotating bar.The test was conducted on five groups of 6 mice each , 30 min after the administration of ethanolic extract (200, 400, 600 mg/kg i.p) and diazepam (1 mg/kg i.p) and normal saline (Mandgary and Sayyah, 2003). A significant dose dependent muscle relaxant activity of AP was observed in rota rod apparatus compared to that produced by diazepam.

Memory-enhancing activity

Memory enhancing effects of *Anacyclus pyrethrum* at three doses 50, 100, 200 mg/kg in Albino wistar rats (Ronald *et al.*, 2012). Central cholinergic system is considered as the most important neurotransmitter involved in regulation of cognitive functions (Levander *et al.*, 2009). Impaired cognitive functions are the major characters of Alzheimer diseases (AD) (Iriti *et al.*, 2010). Loss of cholinergic neurons in nucleus *Basalis magno* cellular is of cortex is one of the most important features of AD, primarily accounting for memory loss (Patel *et al.*, 2011). Scopolamine is a centrally acting cholinergic agent, which causes destruction in teach (Chilakwad *et al.*, 2010). The treatment with drugs, which augment cholinergic neurotransmission, causes an improvement in cognitive deficits in AD (Pattewar *et al.*, 2011).

Aphrodisiacs

The investigation was undertaken to estimate their effects on sexual behavior in male rats at a doses of 50 and 100 mg/kg. Male (32) wistar rats were divided into control group, testosterone group, low dose (50mg/kg) petroleum ether extract (PEE) group and high dose (100mg/kg) PEE group, petroleum ether extract (PEE) obtained from the roots of *Anacyclus pyrethrum* was incorporated orally to albino rats once daily & 0.5 mg/kg (body weight) of testosterone was given intramuscularly twice weekly and served as positive control. The course of treatment was 28 days. The effects of PEE and testosterone modify in body and accessory sexual organ weights, sexual behavior, penile erection and sexual performance were studied before treatment after 15 and 28 days of treatment and 7 and 15 days after treatment. Unlike testosterone, the PEE of *Anacyclus pyrethrum* shows efficacy in rats tested after the lapse of 7 and 15 days of discontinuation of treatment. This suggests that the drug has prolonged effect and capacitate the treated rats for improved sexual potential (Sharma *et al.,* 2009).

Antibacterial

Anacyclus pyrethrum extract produced little antibacterial effect against *Staphylococcus aureus* and *Streptococcus sanguis*. The plant did not have any antibacterial effect against *Sreptococcus mutans* and *Pseudomonas aeruginosa* (Naderi *et al.,* 2012).

Local anesthetic effect (Clinical study)

A local anesthetic consequence of *Anacyclus pyrethrum* is investigated in vivo. In a double blind study in 200 dentistry patients, the local anesthetic effect of an alcoholic extract of the roots (2%, freshly dissolved in sterile distilled water) was compared with that of 2% Xylocaine hydrochloride solution (Devasankariah *et al.,* 1992).

Action on cox & lox

Bauer *et al.,* (1994); studied that polyunsaturated alkamides isolated from, *Anacyclus pyrethrum* (L.) were shown to possess inhibitory activity in *in-vitro* cyclooxygenase (sheep seminal microsomes) and 5 lipoxygenase (porcine leukocytes) assays. Activity showed to depend on the particular structure of the alkamides.

Immunomodulatory activity of petroleum ether extract of *Anacyclus pyrethrum*

Sharma *et al*. (2010) investigated that the PEE-treated rats were able to overcome cyclophosphamide - induced myelo suppression as evidenced by the normalization of blood parameters. Survival rate of albino rats was improved in *Candida albicans*-infected animals by treatment with the extract ($p < 0.05$). An increase in delayed type hypersensitivity response (DTH), percentage neutrophil adhesion, and in vivo phagocytosis by carbon clearance method was observed after treatment. Extract administration also increased the HA titer value and IgG antibodies.

Immuno-stimulant activity increased two-fold upon doubling the dosage of extract administered. While a significant ($p < 0.05$) improvement was observed in the humoral component, a highly significant ($p < 0.01$) effect was observed in the cellular components of the immunity evaluated. The results thus provide a basis for the use of *A. pyrethrum* as an adaptogen and immunomodulator in the Ayurvedic system of medicine

Interactions with Hormones

Testosterone

Sharma *et al.,* (2010) investigated that supplementation of *A. pyrethrum* ethanolic root extract (50-150mg/kg) over 28 days in rats distinguished dose-dependent increases in testosterone and luteinizing hormone to approximately two-fold of baseline (exact values not given). Sharma *et al.,* (2011) analysed that it is though anacyclus works via stimulating the hypothalamus, as the alkylaimde class of molecules (also seen in *Spilanthes acmella*) have been known to work in this manner. It may increase testosterone in otherwise normal rats alongside its fertility enhancing effects.

Interactions with Sexuality

Libido

Sharma V *et al.,* (2013) analysed that a water extract of *A. pyrethrum* at 50-100mg/kg over 28 days appears to possess libido enhancing properties due to enhancing the penile erection index (202%), mounting and intromission frequency (increases of 196-266% and 173-384%, respectively), and latency instance for mounting and intromission (82-90% and 63-76% of baseline, respectively). All parameters chase dose and time dependence (100mg/kg outperforming 50mg/kg and 28 days outperforming 15 days) and persisted for up to 15 days after supplementation. Results appear to have relatively potent libido enhancing properties which persist for a few weeks after supplement cessation.

Interactions with Organ System

Testicles

Sharma *et al.,* (2012) investigated that oral ingestion of 50-150mg/kg of an ethanolic root extract of *Anacyclus pyrethrum* over 28 days to male rats appears to causes increases in the weight of the testicles (2.6-12.3%) and in particular both the epididymis (8.6-26.1%) and seminal vesicles (4.3-9.8%). The higher doses were comparable to 0.5mg/kg injections of testosterone and were not associated with any abnormal histological signs. In regards to semen the above doses have been noted to increase sperm motility, viability, fructose content, and count. There appear to be increases in testicular weight and seminal parameters suggest increased fertility in male rats.

CONCLUSION

From this review that *Anacyclus pyrethrum* contains a number of Phytoconstituents, which reveals its uses for different therapeutic purposes. The roots can be used for the treatment of various disorders in human being such as antidiabetic, immunostimulating effect, inhibitory effects, antidepressant activity and anticonvulsant activity memory-enhancing activity, aphrodisiacs, antimicrobial activity, antioxidant, local anaesthetic effect, insecticidal effect, action on COX and LOX, interactions with testosterone, interaction with libido, and it interaction with testicles. Still more work is required with the *Anacyclus pyrethrum* to investigate the mechanism of actions with other therapeutic activity

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