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

Afreen Usmani, Mohd Khushtar, Muhammad Arif, Mohd. Aftab Siddiqui, Satya Prakash Sing, Md Mujahid

Faculty of Pharmacy, Integral University, Lucknow, UP-226026, India.

**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 diseases like anti-rheumatic, analgesic, antibacterial, antiviral, *carminative*, anti-catarrh, improve digestion, emmenagogue, febrifuge, nervine, vermifuge, and sialogogue. The plant has been reported several pharmacological actions such as anti-diabetic, 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. cyrtolepidoide* 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 "Tigenthash" 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).
Vernacular names

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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 places 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 antihistaminic 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 qualitative and quantitative changes. The percentage of the major constituent spathulenol increases significantly from April (13,31%) to June (16,9%). Germacrane -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 germacrane-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%) / Caryophyllene 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%)/ germacrane -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).

**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, Flavonoids, 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 galanga* markedly increased 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 phentoin, valproate and lamotrigine or by drugs that block glutamatergic excitation mediated by the N-Methyl – D aspartate (NMDA) receptor such as felbamate (Fielding et al., 1995). The ethanolic extract from roots of AP can inhibit voltage dependent sodium ion channels as phentoin 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 magnocellular 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 Streptococcus 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.

Immuo-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 anaclyus 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 anti diabetic, 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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