

# A Comprehensive Review on Plant *Anacyclus Pyrethrum* and Analytical Methods for its Active Constituents

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**Abstract:** *Anacyclus pyrethrum* (*A. pyrethrum*) is a wild species belonging to the family Asteraceae, which is used in traditional medicines. The herb known as "akarkara" (*Anacyclus pyrethrum*) is used in conventional medicine and has a wealth of phytochemicals, such as phenols and flavonoids. Its extracts contain an ester pyrethrine and N-alkylamides (pellitorine) which are said to have aphrodisiac, analgesic (painkilling), anti-inflammatory, and anticonvulsant properties. Akarkara is a common brand name for supplements made from *Anacyclus pyrethrum*, but other names like pellitory root are also used. *Anacyclus pyrethrum* extracts have been shown to have antimicrobial and antioxidant activity in cell culture experiments. The antioxidant activity, analgesic properties, neuroprotective properties against epileptic seizures, and memory-enhancing properties are also being studied on it. Different analytical methods for the estimation and separation of the chemical constituents are listed comprehensively in the review.

**Keywords:** *Anacyclus pyrethrum*; phytochemical; medicinal, analgesic; anti-inflammatory; analytical methods.

## I. Introduction:

A perennial herbaceous plant, *Anacyclus pyrethrum* resembles chamomile in appearance and habitat. It is a member of the Asteraceae family, generally known as the Compositae [1,2], the majority of species are herbaceous plants, which also include shrubs, vines, and trees. It should be found in North India, Himalayas other Mediterranean states, North Africa, and Arab countries. The leading producer of pyrethrum extract is Kenya, which produces approximately 70% of the world's consumption. Rwanda, Tanzania, and Tasmania are also large producers of pyrethrum.

It's popular as a spice. It causes heat, tingling, and redness when applied to the skin [3,4]. The chemical constituents of *A. Pyrethrum* has been investigated extensively in the past, showing the presence of an extensive spectrum of phytochemicals, with over 100 compounds thus far being characterized. The roots of *A. pyrethrum* have been recommended for the treatment of toothaches, secretions from the mouth, digestive problems, angina, male infertility, lethargy & paralysis of the limbs & tongue [5]. Gout and sciatica are treated with them in the form of cream-based animal fats, which are also used to prevent disease. [6].

## II. Botanical Aspects:

**2.1 Morphology:** Perennial plant in the Asteraceae family named *A. pyrethrum* has height range of 40 to 60 cm [4,9,10], it is distinguished by a profusion of simple or small branching stems that emerge from the ground and bear delicate, finely cut, pubescent leaves. Its yellow-hearted blooms have purple petals on the exterior and white ray florets inside. The roots are long, thick, and fibrous, with a brown exterior and a white interior [11,12].

**2.2 Taxonomy and the Geographical Distribution:** *A. pyrethrum* is an endemic species of the Asteraceae family native to Morocco and Algeria. According to some writers, it is indigenous to India, Morocco, and Algeria [13,14,15]. The Mediterranean area, India, and North Africa are where *A. pyrethrum* is most commonly found [13,16,17]. It has been reported that the species can be found throughout Central Asia, North Africa, , and the Chinese province of Xinjiang according to another study[18,19].

**2.3 Traditional Use:** *A. pyrethrum* to treat several diseases such as rheumatic diseases, gastrointestinal diseases, oral diseases, respiratory diseases, genitourinary diseases and skin diseases [20,21].

**Table 1: Several traditional uses of the *A. pyrethrum***

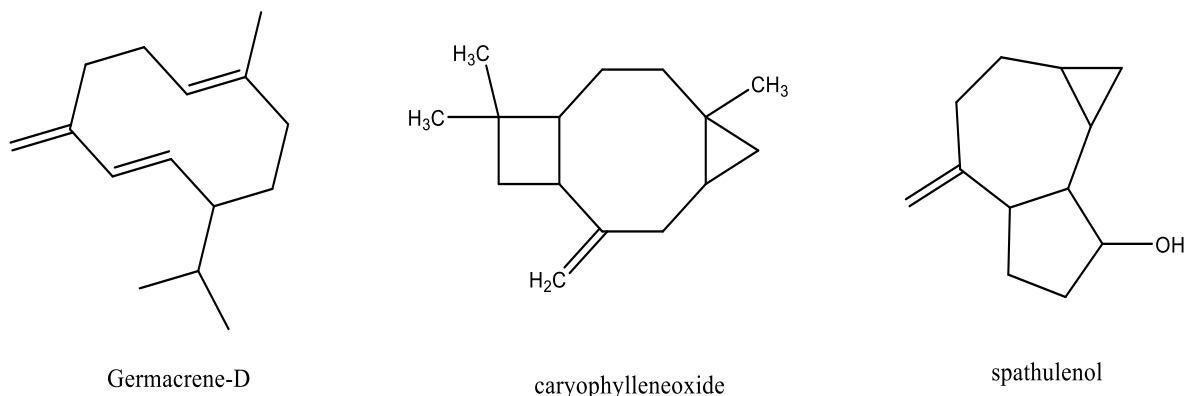
Part used	Preparation mode	Medicinal use
Stem	Powder	Reproductive system tumours [21]
Root	Decoction	Stomach diseases [20]
Root	Powder	Rheumatic, gastrointestinal, oral diseases, respiratory, genitourinary, skin and dermatitis diseases [23,24]
Root	Decoction/ Powder	Articular rheumatism, dental pain, intestinal pain and colic [24,25]
Root	Decoction/infusion	sore throats, toothache and skin revitalization [26]
Root	Decoction/ Powder	Osteoarthritis disorders, stomatitis, inflammation of the urinary and genital organs, and respiratory diseases [1,24]

## III. Phytochemistry Of *Anacyclus Pyrethrum*:

*Volatile components in Anacyclus pyrethrum:* The essential oils (EOs) of *Anacyclus pyrethrum* have been extracted for a very long time using hydro distillation. [27,28]. This species doesn't produce much EOs, and its yield isn't much more than 1%. A chemical analysis of pyrethrum collected from Ben Slimane revealed 32 compounds, or 92.67% of its chemical composition - . [29]. Among all discovered chemicals, oxidative sesquiterpenes are the most prevalent category (58.96%). hydrocarbon sesquiterpenes (24.19%). In terms of composition, it consists

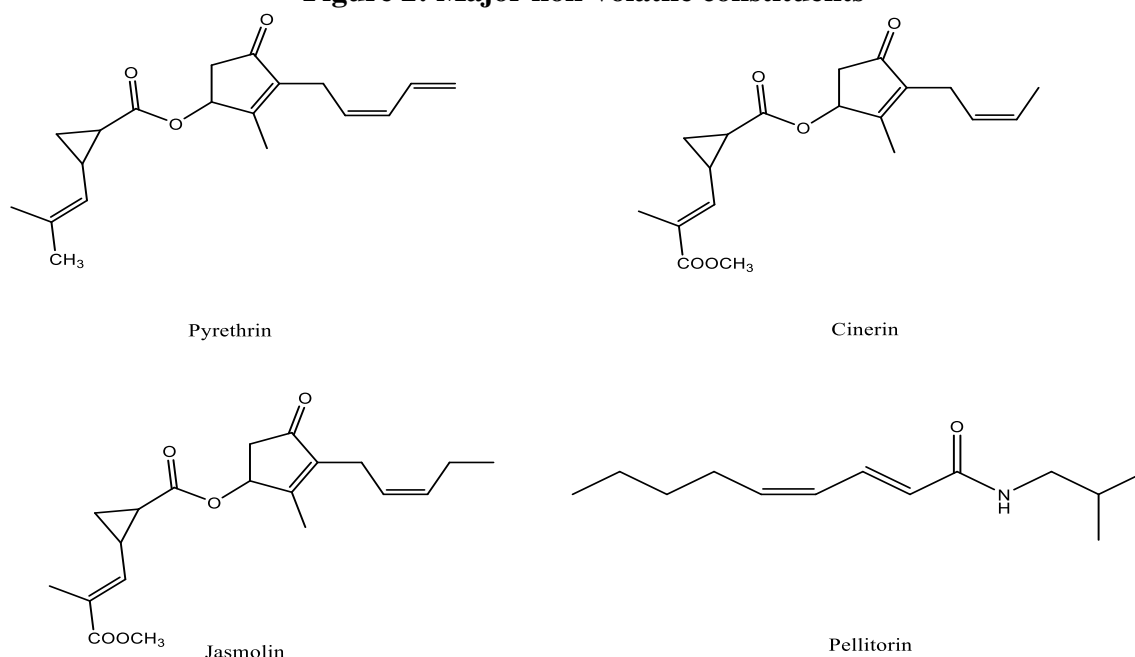
mainly of spathulenol (20.47%), germacrene-D (16.48%), caryophyllene oxide (13.20%), 4-(14)-salvial-1-one (8.27%), caryophyllene-4(14), and 8(15)-diene5ol (7.30%) [30,31].

**Figure 1: Major volatile constituents**



*Non-volatile components of Anacyclus pyrethrum*: Alkaloids, reducing chemicals, and catechins tannins were discovered during the phytochemical analysis of the plant's leaves, flowers, roots, and flower heads [32,33,36,37]. This plant also includes other substances such as geese, holocides, coumarins, gallic tannins, sterols, triterpenes, and mucilage. Compared to the leaves and roots, the flowers have the largest concentration of flavonoids and polyphenols [34,38,41]. Tannins are plentiful in the aerial portions whereas alkaloids are found in great quantities in the roots. The bioactive substances n-alkylamides are the most significant chemicals found in the roots. There are three chrysanthemum acid esters (jasmolin I, pyrethrin I, and cinerin I) and three pyrethrins (jasmolin II, pyrethrin II, & cinerin II) [35]. Pyrethrins, which are present in roots, are chemically related esters made up of six compounds. Research found that pyrethrins 1, 2, cinerins 1, 2, and jasmolins 1 and 2 contain pyrethrelone, cinerolone, and jasmolone alcohol fractions. Several investigations have verified the presence of pyrethrins and pellitorin in the roots of *A. pyrethrum* [32,39,40].

**Figure 2: Major non-volatile constituents**



#### IV. Analytical Methods For Anacyclus Pyrethrum:

- **LC-MS N-alkyl-amide Profiling of an Ethanolic A. pyrethrum Root Extract:** Using an embedded polar column in gradient reversed-phase liquid chromatography/UV/electrospray-ionization ion trap mass spectrometry, an N-alkyl amide profiling from ethanolic Anacyclus pyrethrum DC was performed. Root extract was carried out. The quantification was carried out using UV whereas the identification was carried out using MS1 & MS2 fragmentation data. One 2-phenylethylamide, three N-methyl isobutyl amides, five N-isobutyl amides, & four tyramides were found among 13 N-alkyl amides [42].
- **Validated separation NP-HPLC method:** There are six insecticidal components of pyrethrum extract: pyrethrin I, cinerin I, jasmolin I, pyrethrin II, jasmolin II, cinerin II, and that can be quantitatively determined using a robust analytical methodology. In addition to demonstrating selectivity, accuracy, precision, linearity, range, ruggedness, and robustness, this method has the advantage of ease of use and efficiency. Using an HP1100 HPLC system with a diode-array detector, HPLC assays were carried out in accordance with our developed normal-phase method (Hewlett-Packard, Wilmington, DE). The column was a Spherex Cyano (25 cm 4.6 mm i.d., 5 μm particle). 1.5 mL/min of 97.75:2.25 hexane-THF used as the mobile phase. The detector wavelength was set at 240 nm, and the column oven was set to 25 °C [43].
- **Estimation of pyrethrins by liquid chromatography–tandem mass spectrometry:** Selective Reaction Monitoring (SRM) mode was used to track two distinct transitions for each pyrethrin component in order to individually quantify and confirm the presence of pyrethrins in A. pyrethrum. Depending on the kind of material, extracts were made with acetone/water or acetone, and raw extracts were immediately injected into the LC-MS/MS equipment. A. pyrethrum samples were tested at 0.05 mg/kg and 0.5 mg/kg for linearity, accuracy, precision, specificity, limit of quantification (LOQ), and limit of detection (LOD) (referred to the sum of all pyrethrins). For all of the pyrethrin components, the acetone/water (70:30) extraction method produced satisfactory recoveries (70–110%) and good precision (below 14%) recovering between 71 and 107%, with RSDs under 15% [44].
- **Identification and analysis of Essential oil throughout vegetative cycle from Algerian Anacyclus pyrethrum by GC-MS:** Three developmental phases of the essential oils from the aerial portions of Anacyclus pyrethrum L. were examined (vegetative, floral budding and flowering). Oil output was discovered to vary according on the stage of growth, with blooming producing the maximum oil concentration (0.019% w/w). GC and GC-MS analysis of the chemical makeup of essential oils revealed a total of 91 components. The most prevalent category of sesquiterpenes was oxygenated, regardless of the stage being studied. Their level grew noticeably as the fruit ripened and ranged from 37.1% to 58.6%. Staphylococcus aureus and Candida albicans bacterium strains were both responsive to the oil. They therefore constitute a low-cost source of naturally occurring antibacterial compounds that may be utilised in pathogenic systems [45].

#### V. Activity Of Anacyclus Pyrethrum:

- **Aphrodisiac:** Throughout cultures, several herbal remedies have the potential to improve men's sexual performance; nevertheless, further research is required to determine the precise advantages and health concerns of their usage [73,74]. Rats' body weight and reproductive organs are increased by the aqueous extract of A. pyrethrum roots, which also

results in an increase in epididymal spermatozoa. The aberrant sperm count in rats was also decreased by the aqueous extract [75]. To evaluate the efficacy and safety of plant aphrodisiacs, we highly advise the creation and implementation of well-controlled clinical research.

- **Anti-Inflammatory:** A number of disorders manifest as inflammation. Experiments using a rat model of inflammatory edema have demonstrated an anti-inflammatory activity of several *A. pyrethrum* extracts. The anti-inflammatory effects of the aqueous and methanolic extract of the *A. pyrethrum* roots on xylene-induced rat ear edema and Freund-induced entire rat paw edema have been investigated in vivo by Manouze and associates [72].
- **Anti-oxidant Activity:** The MeOH extracted, Aqu extracted, and Ch extracted from *A. pyrethrum* stems and leaves collected in Algeria, using the DPPH and FRAP procedures. They discovered using the DPPH technique that the MeOH extract in the species exhibits the greatest antioxidant efficacy (IC<sub>50</sub> of 0.056 mg/mL), followed by the Aqu. ext. with an IC<sub>50</sub> of 0.114 mg/mL and the Chl. ext. with an IC<sub>50</sub> of 0.154 mg/mL. The MeOH extract has a greater reducing ability than the other extracts, according to the results of the FRAP technique [49,50].
- **Antidiabetic Activity:** Many diabetic patients have employed conventional herbal treatments in a variety of formulations as supplemental therapy to manage diabetes problems since antiquity [51,52,53]. Aqueous root extracts of *A. pyrethrum* at concentrations of 300 mg/kg and 250 mg/kg, respectively, have been shown to exhibit antihyperglycemic effects in several in vivo tests on diabetic rats caused by alloxan or streptozotocin. After therapy, the diabetic rats' increased blood glucose levels virtually reached normal levels [56,57,58].
- **Anaesthetic Activity:** Using guinea pigs chosen for an earlier investigation, the anaesthetic activity of ethanolic, petroleum ether, and aqueous extract from *A. pyrethrum* was investigated [59,60]. The findings imply that the ethanol extract exhibits strong local anaesthetic action at 1% and 2% concentrations. Similarly, 2% petroleum ether extract was superior than 1% petroleum ether and 2% aqueous extract in terms of effectiveness [61].
- **Insecticidal Activity:** Since many years ago, *A. pyrethrum*'s ability to kill insects has been shown. Numerous insects, including beetles, whiteflies, thrips, aphids, Mediterranean flour mites, leafhoppers, ants (aside from fire ants), aphids, crickets, fungal mosquitoes, pink slugs, cabbage worms, cocoon worms, Indian mealworms, mealybugs, pink beetles, spiders, troglodytes, etc. can be wiped out by this plant [38,62]. The effectiveness of natural synergistic pyrethrins was established in a research on the hair of patients with head lice (presented in the form of an aerosol foam). In comparison to another formulation based on permethrin, this one is more effective (in cream form). Likewise, a single application of pyrethrin synergistic foam doubles as an oviduct [64].
- **Anti-depressant Activity:** Swiss male albino rats were used to study the antidepressant activity of *A. pyrethrum* using a variety of techniques, including locomotor activity, haloperidol-induced stimulation, forced swim test (FST), tail suspension test (TST), clonidine-induced hypothermia, hypothermia induced by hypothermia, clonidine-induced hypothermia, and reserpine-induced hypothermia [66,66]. They discovered that the aqueous-alcoholic root extract of *A. Pyrethrum* increased ambulatory behaviour, pointing to the photometer's stimulating effects. In the forced swim test and the tail suspension test, the *A. pyrethrum* root extract has an antidepressant effect via reducing immobility. At dosages of 100 and 200 mg/kg, the *A. pyrethrum* root extract proved successful in reversing the hypothermia that clonidine and reserpine caused in rats [67].
- **Anticonvulsant Activity:** *A. pyrethrum*'s anticonvulsant properties have been thoroughly investigated and supported by multiple investigations [37]. According to a recent study, the

first experimental group's seizure latency time was longer after receiving the ethanolic aqueous extract of *A. pyrethrum* at a dosage of 500 mg/kg as opposed to the first positive control. It has been demonstrated that the petroleum ether extract of *A. pyrethrum* can significantly reduce the risk of seizures brought on by pentylenetetrazole (PTZ). Moreover, this dose-dependent extract shortened epilepsy duration and lengthened the latency of produced seizures. Remarkably, compared to the negative control, the extracts demonstrated a decrease in neurological symptoms and seizure intensity [68,69].

- **Other Activities:** According to additional investigations, *A. pyrethrum* extracts also have hepatoprotective, anticancer, neuropharmacological, immunostimulant, and immunomodulatory properties [70,71,72]. The immunomodulatory activity of the *A. pyrethrum* root extracts was superior. Rats given the aqueous extract orally demonstrated increased activity at a level of 10 mg/kg [78,81]. The methanolic extract, which was tested on rats, also shows an immunostimulatory effect at a dose of 200 mg/kg. While the 50 and 100 mg/kg dosages of the petroleum ether extract of *A. pyrethrum* were unable to reverse the immunosuppression brought on by cyclophosphamide [81,82]. Moreover, *A. pyrethrum* has potential as a novel therapy for the treatment of colorectal cancer. Another study shown that the *A. pyrethrum* extract efficiently induced apoptosis in human colorectal carcinoma (HCT) cells and dramatically suppressed the development of cancer cells [83].

## VI. Precautions:

- Care should be taken if one is suffering from problems of gastric ulceration, acidity and intestinal inflammation in any form.
- It is not safe during pregnancy and breastfeeding higher doses and long-term use should be highly managed under the supervision of an Ayurvedic physician.
- By taking the Akarkara plant there is increase in the secretion of saliva and the blood pressure become low.
- Akarkara increases menstrual flow and Uterine contractions.
- Higher Doses may cause: Acidity, Heartburn, Burning sensation, Excessive Saliva Production [4,7,9,81].

## VII. Toxicological Evidence:

The existence of intriguing chemicals in *A. pyrethrum* has been established by phytochemical investigation; nonetheless, it is not without toxicity, and several mishaps have been documented following therapeutic usage [84,85]. As a result, it produces toxic symptoms such nausea, dizziness, and respiratory problems in addition to possible skin and mucous membrane irritation. Comparable side effects from oral treatment include gastroenteritis, colic, diarrhoea, cramps, and excruciating headaches. Lastly, it can cause headaches, ringing in the ears, and even fainting through its vapours. *A. pyrethrum*'s poisonous manifestation is caused by the presence of toxic substances, specifically pyrethrins and unsaturated amides like pyrethrin and anacycline. At low doses, the hydroethanolic extracts of the various *A. pyrethrum* (L.) variety components were not poisonous [86,87].

However, mice given 2000 mg/kg of the substance showed certain harmful side effects. The liver, kidneys, and spleen of the animals showed histological alterations at this dosage, including hepatic distress, inflammatory infiltration, localised tubular necrosis, vascular congestion, and lymphoid hyperplasia [90,91,97]. Oral administration of the root ethanolic extract (1000 mg/kg) to rats was tested for sub chronic toxicity. According to this study, there

were no fatalities or negative impacts. Moreover, there is no remedy for concurrent toxic abnormalities in this extract [92,95,99].

A. pyrethrum extracts reveals that the pyrethrins' constituents have low to moderate acute toxicity when consumed orally, applied topically, or breathed by people, and that prolonged exposure can have negative effects on the nervous system, the thyroid, and the liver [93,94,102,104].

### VIII. Conclusions:

A fascinating member of the Asteraceae family and an indigenous to Morocco and Algeria, *Anacyclus pyrethrum* is used in traditional medicine to cure a wide range of ailments. We have discussed the botany, traditional usage, phytochemistry, pharmacological application, and toxicity of *A. pyrethrum* in this review. The results gathered attest to this species' potential. In fact, pharmacological actions like antioxidant, anti-inflammatory, hepatoprotective, anticancer, neuroprotective, antidepressant, and aphrodisiac effects have been researched in experimental investigations. Many studies have also demonstrated the abundance of secondary metabolites, such as terpenoids, polyphenols, alkaloids, etc., in this species. They support its widespread usage in conventional therapy. Various analytical methods are also discussed in this short comprehensive review. Nonetheless, it is important to note that there aren't many studies on isolating and fractionating its components.

### IX. Acknowledgment:

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