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A Comprehensive Review Of Anacyclus Pyrethrum (Akarkara)

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Abstract : Anacyclus pyrethrum, commonly known as Akarkara or Pellitory root, is a medicinally important plant belonging to the Asteraceae family. Traditionally employed in Ayurveda, Unani, and North African folk medicine, it has been utilized for neurological, reproductive, and oral health-related disorders. This review provides a detailed account of its taxonomy, morphology, ethnobotanical uses, phytochemical composition, and pharmacological activities including nootropic, aphrodisiac, anti-inflammatory, immunomodulatory, and antimicrobial properties. Special emphasis is placed on correlating traditional knowledge with modern scientific validation. The review also highlights toxicological considerations, conservation challenges, and future prospects for drug discovery. Despite promising pharmacological evidence, further clinical studies are necessary to establish safety and efficacy. This comprehensive overview underscores the therapeutic significance of Anacyclus pyrethrum and its potential for modern medicine.

Keywords : Anacyclus pyrethrum; Akarkara; Ethnobotany; Phytochemistry; Pharmacology; Traditional medicine.

INTRODUCTION

Medicinal plants have historically served as the cornerstone of healthcare systems worldwide, providing the foundation for traditional therapies and modern drug discovery [1]. Among these, Anacyclus pyrethrum DC commonly known as Akarkara or Pellitory root, is a perennial herb belonging to the Asteraceae family [2]. Its ethnomedicinal significance spans across regions including India, North Africa, and the Mediterranean basin [3]. Traditionally, the plant has been employed for managing neurological, reproductive, oral, and gastrointestinal disorders [4].

In the Ayurvedic system of medicine, Akarkara is recognized as a potent nervine tonic, aphrodisiac, and remedy for speech impediments [5]. Similarly, the Unani system prescribes its root powder for ailments such as epilepsy, paralysis, and dental pain [6]. North African folk traditions report its utility in treating fever, digestive complaints, and cold-related conditions [7]. Such widespread applications underscore the plant's importance across diverse medical systems.

Modern phytochemical investigations have validated the presence of several bioactive constituents including alkylamides (pellitorine, anacycline), flavonoids, sterols, and essential oils [8,9]. These compounds are believed to contribute to its broad pharmacological actions such as nootropic, immunomodulatory, and antimicrobial effects [10]. Despite these findings, comprehensive pharmacological validation and clinical studies remain limited, necessitating further research [11].

Figure 1 : Anacyclus pyrethrum

Given its wide-ranging therapeutic claims, Anacyclus pyrethrum has emerged as a promising candidate for drug discovery and pharmacological exploration. However, issues such as overharvesting in its native habitats, lack of standardized extracts, and insufficient toxicological profiling pose significant challenges [12,13]. This review aims to provide an updated and comprehensive synthesis of the plant's ethnobotany, phytochemistry, pharmacological activities, and future prospects.

Medicinal plants continue to play a central role in global healthcare, particularly in developing countries where up to 80% of the population depends on traditional remedies [14]. According to the World Health Organization, over 21,000 plant species are used for medicinal purposes, highlighting the vast diversity of bioresources that contribute to ethnomedicine [15]. Within this spectrum, Anacyclus pyrethrum holds a unique place as a herb with both cultural and pharmacological significance.

Historical Background

The use of A. pyrethrum can be traced back to ancient civilizations, where it was documented in classical Ayurvedic texts such as the Charaka Samhita and Sushruta Samhita [16]. In Unani medicine, described by scholars like Avicenna (Ibn Sina), Akarkara was classified as a powerful stimulant and remedy for nervous system disorders [17]. In Europe, the plant was introduced through Arabic pharmacopoeias during the Middle Ages and was later included in traditional European herbal manuals [18]. Its reputation as a sialogogue and aphrodisiac cemented its importance across cultures.

Distribution and Cultivation

Anacyclus pyrethrum is native to the Atlas Mountains of Morocco and Algeria, where it is still primarily harvested [12]. It has been naturalized in parts of Spain, France, and India due to its medicinal demand [19]. In India, cultivation occurs in Rajasthan and Himachal Pradesh, supported by the herbal drug industry [20]. The plant thrives in dry, rocky, and sandy soils, reflecting its adaptability to arid climates. The high market demand, however, has led to overharvesting, making conservation strategies critical [21].

Economic and Commercial Importance

Akarkara roots are widely traded in herbal markets across South Asia and North Africa. They are incorporated into formulations like tooth powders, herbal tonics, and aphrodisiac preparations [2]. In India, the crude drug is listed in the Ayurvedic Pharmacopoeia and forms part of several proprietary medicines [22]. The increasing global interest in natural products has also led to its export to Europe and the Middle East, where it is marketed as a natural stimulant [23].

Taxonomy

Anacyclus pyrethrum belongs to the family Asteraceae, which is one of the largest families of flowering plants. The genus Anacyclus consists of about 12 species, primarily distributed in the Mediterranean region and North Africa [27].

Table 1: The taxonomical classification of Anacyclus pyrethrum *[27]*

Taxonomic Rank	**Classification**
Kingdom	Plantae
Subkingdom	Tracheobionta (Vascular plants)
Superdivision	Spermatophyta (Seed plants)
Division	Magnoliophyta (Angiosperms)
Class	Magnoliopsida (Dicotyledons)
Order	Asterales
Family	Asteraceae
Genus	Anacyclus
Species	Anacyclus pyrethrum DC.

Pharmacognostic Characteristics

The dried root of A. pyrethrum is the main part used medicinally. Macroscopically, the root is cylindrical, light brown, and produces a tingling sensation on the tongue due to its alkylamide content [24]. Microscopically, diagnostic features include thick-walled xylem fibers and starch granules in parenchyma [25]. Pharmacognostic characterization has been used to authenticate genuine drug samples and prevent adulteration with other species, a significant concern in the herbal industry [26].

This study was done by gathering all the available information and creating a database about the species through a detailed review of existing literature. As a result, we were able to assess how much we know about A. pyrethrum and whether that knowledge is sustainable. While preparing this review, we made sure to provide a thorough description of the species, especially focusing on the current research, the chemical makeup of the plant, the chemical composition of its essential oils, and how these vary. This helped us understand the importance of this species in traditional herbal medicine as well as in modern medical practices.

The focus was on the most recent biological effects that have been proven by scientific research. Also, reports were shared about the safety of using it. So, more research is needed to check how well it works and if it's harmful, using evidence from studies. Since plant-based treatments might be cheaper and safer, it's important to support schools and universities to do more studies on different animals. This will help prepare for future tests and make sure the herbal parts are used safely in the body.

Botanical Description

Anacyclus pyrethrum DC., a perennial herb of the family Asteraceae, is widely known for its medicinally valuable roots and distinctive morphological features. It is native to North Africa, especially Morocco and Algeria, but has also adapted to other regions with similar climatic conditions, including parts of southern Europe and India [19]. The plant is well recognized for its robust growth habit, characteristic inflorescence, and pungent roots that yield tingling sensations when chewed — an identifying feature of the authentic species [22].

1. Habit and Habitat

The plant grows naturally in dry, rocky, and sandy soils at altitudes between 400–1,500 meters above sea level [20]. It thrives in regions with a Mediterranean-type climate, preferring full sunlight and well-drained soils [19]. In India, A. pyrethrum is cultivated mainly in the states of Rajasthan and Himachal Pradesh, often as a winter crop under irrigated conditions [34]. The species demonstrates high tolerance to drought stress, which contributes to its persistence in arid zones.

2. Root Morphology

The root is the principal medicinally used part of A. pyrethrum. It is cylindrical, tapering, and measures between 5–15 cm in length and 1–2 cm in diameter [8]. The external surface is light brown, longitudinally wrinkled, and shows concentric markings. The inner surface is whitish, and when cut, exudes a slightly aromatic odor. The taste is intensely acrid and tingling, primarily due to the presence of N-alkylamides such as pellitorine and anacycline [28].

The secondary xylem shows lignified fibers and vessels arranged in radial patterns, which serve as diagnostic features for identification and standardization of crude drug samples [26].

Figure 2 : Anacyclus pyrethrum

Macroscopically, the roots possess a hard, woody texture and are characterized by a distinct aroma when powdered. Microscopically, transverse sections reveal cork composed of several layers of tangentially elongated cells, followed by parenchymatous cortex containing starch grains and oil globules [25].

3. Stem Characteristics

The stem of A. pyrethrum is erect or ascending, 20–60 cm tall, and much branched at the upper portions [18]. It is slightly hairy, angular, and greenish-grey in appearance. The young stems are herbaceous, but as they mature, they become partially woody at the base. The internal structure consists of epidermis covered with trichomes, collenchymatous hypodermis, and a vascular bundle arranged in a ring-like pattern — typical of dicotyledonous herbs [29].

4. Leaves

The leaves are alternate, sessile or shortly petiolate, and pinnatisect with narrow linear lobes. The lamina is 3–6 cm long, greyish-green, and covered with fine hairs on both surfaces, giving the plant a somewhat silvery appearance [30]. The leaves exhibit reticulate venation and contain essential oil glands that impart the characteristic fragrance to the aerial parts. Leaf anatomy shows palisade and spongy mesophyll cells, chloroplast-rich tissues, and numerous secretory canals [31].

The leaves play a major role in photosynthetic efficiency and adaptation to drought conditions, with the trichome covering helping to minimize water loss through transpiration [32].

5. Inflorescence and Flowers

The inflorescence is a solitary capitulum (flower head), typical of the family Asteraceae, borne singly on long peduncles arising from axils of upper leaves [33]. Each capitulum measures 2–3 cm in diameter and comprises two types of florets — ray florets (white) and disc florets (yellow). The involucre is hemispherical, consisting of 2–3 series of overlapping bracts covered with short hairs [34].

The ray florets are female, uniseriate, and exhibit ligulate corollas that are white on the upper surface and purplish underneath. The disc florets are bisexual, tubular, and yellow, contributing to the plant's characteristic flower appearance [35]. The androecium consists of five syngenesious stamens forming a tubular structure around the style, and the gynoecium is bicarpellary, syncarpous, with an inferior ovary — typical of the composite family [36].

Figure 3 : Anacyclus pyrethrum Flower

The flowering season extends from April to June, depending on climatic conditions. Pollination is mainly entomophilous, facilitated by bees and other insects attracted by the bright flowers [37].

6. Fruit and Seed

The fruit is a ribbed achene, oblong, and measures approximately 1.5–2 mm in length [12]. Each achene contains a single seed, without a pappus (unlike many other members of Asteraceae), which restricts long-distance dispersal but favors local propagation. The seeds are small, brownish, and rich in carbohydrates and fatty acids. Germination occurs readily under moderate moisture conditions, though dormancy may occur under extremely dry environments [38].

7. Anatomical and Cytological Features

Anatomical investigations reveal that the cortex of the root is rich in parenchymatous cells containing oil globules, while the xylem contains lignified fibers responsible for the mechanical strength of the roots [39]. Stomata on the leaf surface are of the anomocytic type, and trichomes are multicellular and uniseriate [40]. Cytological studies report a diploid chromosome number of 2n = 18, consistent with other members of the genus Anacyclus [41].

8. Ecological and Adaptive Traits

The plant exhibits strong ecological plasticity, tolerating poor soils, low rainfall, and extreme temperatures. Adaptations such as deep root systems, hairy leaves, and reduced transpiration rates enable its survival in arid environments. These physiological and morphological adaptations make A. pyrethrum an important model for studying drought-resistant medicinal herbs [42]

Phytochemistry of Anacyclus pyrethrum :

Phytochemical analysis of Anacyclus pyrethrum has revealed the presence of a wide array of secondary metabolites that contribute to its pharmacological potential [43]. The major chemical classes include alkylamides, alkaloids, flavonoids, saponins, tannins, steroids, and essential oils. These compounds are primarily localized in the root portion, which is the most used part of the plant for therapeutic purposes.

1. Alkylamides (Major Active Constituents)

Alkylamides are considered the bioactive signature compounds of A. pyrethrum. The most dominant are , anacycline, inhuline, and pyrethrine. These lipophilic amides are responsible for the plant's characteristic pungent, tingling sensation on the tongue when tasted.

- Pellitorine (C14H25NO) is the principal amide, known for its insecticidal, antimicrobial, and neurostimulatory properties.
- Anacycline has shown aphrodisiac and nootropic activity in preclinical studies.
- These compounds act on sensory neurons and may stimulate salivation and neural activation through TRPV1 receptor modulation [44].
- Extraction of alkylamides is typically done through ethanol, methanol, or supercritical CO_2 extraction, followed by analysis using GC–MS or HPLC methods [45].

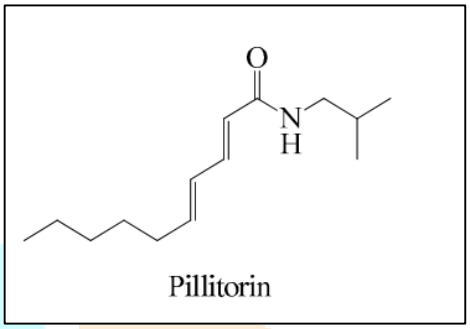

Figure 4. Structure of Pillitorn

2. Essential Oils and Volatile Compounds

The essential oils derived from A. pyrethrum roots and flowers contain monoterpenes, sesquiterpenes, and aliphatic hydrocarbons.The major constituents include β-farnesene, spathulenol, caryophyllene oxide,and 1,8-cineole.These volatiles contribute to the aromatic and therapeutic properties of the plant, such as anti-inflammatory and antimicrobial activities [46].

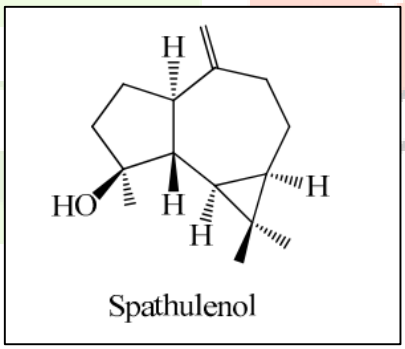

Figure 5. Structure of Spathulenol

The chemical profile of essential oils can vary depending on the geographical origin, climatic conditions, and stage of plant growth, which may affect its pharmacological potency [47].

3. Flavonoids and Phenolic Compounds

Flavonoids represent another significant class of bioactive molecules in A. pyrethrum. Quercetin, kaempferol, and apigenin derivatives have been isolated from the ethanolic extract of aerial parts.These polyphenolic compounds exhibit strong antioxidant, anti-inflammatory, and neuroprotective effects, which may contribute to the plant's traditional use in memory enhancement and stress management [48].

Phenolic acids such as gallic acid and caffeic acid further enhance the free radical scavenging capacity of the extract, providing protection against oxidative stress–induced cellular damage [49].

4. Steroids, Saponins, and Tannins

Minor but pharmacologically important components include stigmasterol, β-sitosterol, and campesterol, which are known to regulate lipid metabolism and inflammatory pathways [50].

Saponins and tannins contribute to the plant's antimicrobial and immunostimulant properties. The presence of these compounds has been confirmed through standard qualitative tests such as Froth, Ferric chloride, and Liebermann–Burchard reactions [51].

5. Distribution of Phytochemicals in Different Parts

Plant Part	Major Compounds	Reported Activities
Root	Pellitorine, Anacycline, Alkylamides	Neurostimulant, Aphrodisiac, Analgesic
Leaves	Flavonoids, Phenolic acids	Antioxidant, Anti-inflammatory
Flowers	Essential oils, Terpenes	Antimicrobial, Aromatic
Seed		

Table 2. Distribution of phytoconstituents in different parts of Anacyclus pyrethrum *[52]*

6. Modern Analytical Techniques

Recent advancements in chromatographic and spectroscopic analysis have enabled accurate quantification and standardization of A. pyrethrum extracts.

- HPLC and LC–MS/MS are widely used to determine alkylamide concentration.
- GC–MS is preferred for volatile compounds and essential oils.
- NMR spectroscopy assists in elucidating molecular structures of newly identified metabolites [53].

Standardization using these techniques ensures quality control and batch consistency, which are vital for developing herbal formulations [54].

Extraction and Isolation Techniques :

Extraction and isolation are critical steps in phytochemical studies, as they allow the separation of bioactive compounds from the plant matrix for further characterization and pharmacological evaluation. In Anacyclus pyrethrum, various techniques have been employed depending on the polarity of the compounds of interest.

1. Extraction Techniques

a) Maceration

- Maceration is the simplest extraction method, where powdered plant material is soaked in a suitable solvent (ethanol, methanol, water, or petroleum ether) at room temperature.
- The solvent penetrates the plant cells, dissolving the bioactive compounds.
- After a certain period (usually 24–72 hours), the mixture is filtered, and the solvent is evaporated under reduced pressure to obtain crude extracts.
- Advantage: Simple and requires minimal equipment.
- Limitation: Time-consuming and less efficient for compounds present in low concentrations.

b) Soxhlet Extraction

- Soxhlet extraction is widely used for A. pyrethrum roots. Powdered plant material is placed in a thimble and repeatedly washed with hot solvent.
- This method ensures exhaustive extraction of both polar and non-polar constituents.

- Solvents commonly used include ethanol, methanol, chloroform, and petroleum ether.
- Advantage: Efficient and can extract large amounts of compounds.
- Limitation: Heat-sensitive compounds may degrade.

c) Ultrasonic-Assisted Extraction (UAE)

- Uses ultrasonic waves to disrupt plant cell walls, enhancing solvent penetration.
- Reduces extraction time and increases yield.
- Particularly effective for alkylamides and flavonoids from A. pyrethrum.

d) Supercritical Fluid Extraction (SFE)

- Uses supercritical CO_2 as the solvent under controlled temperature and pressure.
- Selective extraction of non-polar compounds (e.g., essential oils) is possible.
- Advantage: No solvent residues and environmentally friendly.
- Limitation: Expensive equipment.

2. **Isolation Techniques**

After extraction, the crude extract contains a mixture of compounds. Isolation separates individual bioactive constituents.

a) Column Chromatography

- Silica gel or Sephadex is used as the stationary phase.
- The crude extract is loaded onto the column, and elution is performed with solvents of increasing polarity.
- Compounds are separated based on differences in polarity, molecular size, and affinity to the stationary phase.

b) Thin Layer Chromatography (TLC)

- Used as a preliminary step to monitor fractions from column chromatography.
- Helps in detecting the presence of flavonoids, alkylamides, and other secondary metabolites.

c) High-Performance Liquid Chromatography (HPLC)

- Allows high-resolution separation and purification of compounds.
- Coupled with UV, MS, or PDA detectors, it provides qualitative and quantitative analysis.
- HPLC is extensively used for standardization of A. pyrethrum extracts.

d) Preparative HPLC and Crystallization

- For isolating pure compounds in sufficient quantity for structural elucidation and bioactivity studies.
- Often followed by spectroscopic techniques (NMR, MS, IR) to confirm structure.

Biological Studies :

1. Antibacterial Activity and Antifungal Activity

The bacterial activity and antifungal activity are important for preventing periodontal diseases. In the oral cavity, the number of bacterial species is extensive. Streptococcus mutans appears from the start of life, while streptococcus sanguinis appears after tooth eruption. Streptococcus sanguinis and staphylococcus aureus are responsible for gingivitis and peri-implantitis, respectively. Streptococcus mutans is considered as the main factor of tooth decay. These bacteria are particularly important for periodontal diseases.

The antibacterial activity of Anacyclus pyrethrum was tested in vitro. A versatile microplate bioassay allows for screening medicinal plants and identifying bioactive principles in a quick and effective manner. The isolation of the extracted Ayurvedic root enabled to determine the antibacterial activity. Lind. The diameter of the inhibition zone was 20mm, 17mm, 18mm, and 17mm for staphylococcus aureus. To analyze the activity, the inhibition zones were calculated by subtracting the observed diameter by 5mm. The use of Anacylus pyrethrum via its alcoholic extract was tested. The antifungal activity was estimated using the disc diffusion method. The microbial agar plates were inoculated and incubated for 72 h at 28°C. The inhibition zone was determined by the diameter in millimeters.

2. Antioxidant Activity

Flavonoids and phenolic acids such as quercetin, kaempferol, and caffeic acid contribute to the free-radical scavenging ability of the plant. DPPH and FRAP assays reveal strong antioxidant capacity, supporting its traditional use in managing oxidative stress–related disorders.

The ethanolic extract of Anacyclus pyrethrum was able to remove hydroxyl radicals and hydrogen peroxide, and this ability grew stronger as the amount of the extract used increased. During the screening process, phenol was identified as the active compound in Anacyclus pyrethrum. Because the extract contains phenolic compounds, it can help neutralize nitric oxide, and the ability to do so increases with higher doses. The test also showed that the reducing power of the extract increases as the concentration of the compound goes up [27].

3. Antidiabetic Activity

For a long time, people with diabetes have used traditional herbal medicines in different forms as extra help to manage diabetes complications [47]. In a list of plants previously published, Pyrethrum was mentioned as a remedy used in traditional diabetes treatment, and this has been written about in scientific papers [42]. In this review, a study by Shahraki et al. [51] showed that giving diabetic rats an alcoholic extract from the root of A. pyrethrum (made with 96% ethyl alcohol) helped improve damaged tissues in diabetic rats (using doses of 100 and 150 mg/kg).

Other studies on diabetic rats [52,53], which were made sick with alloxan or streptozotocin, found that an aqueous extract from the root of A. pyrethrum at doses of 300 mg/kg and 250 mg/kg helped lower blood sugar levels.

After treatment, the high blood sugar levels in these rats came back close to normal. The plant A. pyrethrum was tested for its ability to block alpha-amylase. The ethanolic extract from its root strongly reduced alpha-amylase activity in a dose-dependent way (IC50 = 29.25 µg/mL) [42]. This study also shows that A. pyrethrum might be helpful in managing diabetes. Earlier research found that A. pyrethrum contains certain compounds like alkylamides, alkaloids, and phenolics in its extracts [53]. Before using these extracts in people, it is important to test their effectiveness in living animals [54].

4. Antioxidant Activity

Antioxidant activity refers to the capacity of bioactive compounds to counteract oxidative stress by neutralizing reactive oxygen species (ROS) and free radicals that damage lipids, proteins, and DNA. Excessive oxidative stress is implicated in the pathogenesis of several chronic disorders such as neurodegenerative diseases, cardiovascular dysfunction, infertility, diabetes, and aging. Natural antioxidants derived from medicinal plants have gained increasing importance due to their safety and multifaceted therapeutic effects. Anacyclus pyrethrum (Akarkara), a well-known traditional medicinal herb, has demonstrated potent antioxidant potential in various biological studies, supporting its ethnomedicinal claims as a rejuvenating and brain-tonic plant[40].

Phytochemical screening of A. pyrethrum root and aerial extracts has confirmed the presence of flavonoids (quercetin, kaempferol, apigenin), phenolic acids (gallic acid, caffeic acid), and alkylamides (pellitorine, anacycline)—all of which are recognized contributors to antioxidant defense. These secondary metabolites act through multiple mechanisms, including hydrogen atom donation, electron transfer, metal ion chelation, and inhibition of lipid peroxidation. The synergistic interplay between phenolic and amide compounds is believed to enhance the overall antioxidant efficacy of the plant.

5. Antidepressant and Anxiolytic Activity

Depression and anxiety are among the most prevalent neuropsychiatric disorders worldwide and are often closely linked with other systemic illnesses, particularly cardiovascular diseases[46]. A growing body of evidence suggests a bidirectional relationship between depression and cardiac dysfunction. Patients suffering from cardiovascular diseases frequently develop depressive symptoms due to physiological stress and inflammatory imbalance, while chronic depression itself can exacerbate cardiovascular risk by altering neuroendocrine and autonomic regulation. This interplay underscores the importance of managing depression not only for mental health but also for maintaining cardiovascular stability.

Modern research has increasingly focused on identifying plant-based compounds with neuroprotective and mood-stabilizing properties as safer alternatives to synthetic antidepressants, which often produce adverse side effects. In this context, Anacyclus pyrethrum (Akarkara), traditionally used as a nervine tonic and rejuvenating herb in Ayurvedic and Unani medicine, has gained scientific interest for its potential antidepressant and anxiolytic effect[16].

The antidepressant and anxiolytic activities of A. pyrethrum have been evaluated using several standard animal behavioral models. Among these, the Forced Swim Test (FST) and the Tail Suspension Test (TST) are the most widely employed to assess depressive behavior[39]. In these models, animals are placed in an inescapable environment (water cylinder or suspended by the tail), and the duration of immobility—an indicator of behavioral despair—is measured. Administration of A. pyrethrum root extract produced a significant reduction in immobility time in both FST and TST compared to control groups, indicating prominent antidepressant-like activity. The findings suggest that bioactive compounds in the extract may act through monoaminergic pathways, possibly increasing levels of neurotransmitters such as serotonin, dopamine, and noradrenaline in the brain.

6. Anticonvulsant Activity

Epilepsy is a chronic neurological disorder characterized by recurrent seizures caused by abnormal electrical activity in the brain. Despite the availability of modern antiepileptic drugs, their use is often limited by adverse side effects, tolerance, and incomplete seizure control[24]. This has led researchers to explore medicinal plants as alternative sources of anticonvulsant agents. Anacyclus pyrethrum (Akarkara), known for its traditional use as a nervine stimulant and brain tonic, has shown promising results in experimental models of epilepsy.

The acute toxicity of the ethanolic root extract of A. pyrethrum was first evaluated in female albino mice to ensure safety before pharmacological testing. Doses of 300, 2000, and 5000 mg/kg body weight were administered orally according to OECD guidelines. The extract produced no mortality or significant behavioral abnormalities, indicating a high margin of safety and suitability for further biological evaluation[12].

The anticonvulsant activity of the extract was assessed using two standard experimental models: the Maximal Electroshock (MES)-induced seizure test and the Pentylenetetrazole (PTZ)-induced seizure test[37]. In the MES model, seizures were produced by delivering a controlled electric stimulus through corneal electrodes using a stimulator apparatus. The extract significantly reduced the duration of tonic flexion, tonic extension, and clonic phases, as well as lowered mortality rates, when compared with control animals. These effects suggest protection against the spread of electrical impulses in the brain, similar to that of standard antiepileptic drugs such as phenytoin.

7. Aphrodisiac Activity

Since ancient times, humans have used medicinal and aromatic plants to enhance sexual performance, stimulate libido, and improve reproductive health. Among such plants, Anacyclus pyrethrum (Akarkara) holds a prominent place in traditional Ayurvedic and Unani medicine for its strong aphrodisiac and rejuvenating properties. Scientific studies have validated these traditional claims through experimental investigations on animal models[36].

The aqueous root extract of A. pyrethrum has been shown to significantly increase body weight, testicular size, and reproductive organ weight in male rats. It also enhanced epididymal sperm count while reducing the percentage of abnormal spermatozoa, suggesting improved spermatogenic function. These effects indicate stimulation of the hypothalamic–pituitary–gonadal axis, leading to elevated androgen (testosterone) secretion[7].

Further research by Sharma et al. reported that the methanolic extract of A. pyrethrum roots exhibits strong androgenic potential, improving male fertility by promoting spermatogenesis and increasing serum testosterone levels. Additionally, the extract raised seminal fructose concentration and enhanced copulatory behavior such as mounting frequency and latency, in a dose-dependent manner[23].

Collectively, these findings confirm that Anacyclus pyrethrum possesses potent aphrodisiac activity, supporting its traditional use as a natural sexual stimulant and fertility enhancer with promising therapeutic value for male reproductive disorders.

8. Anesthetic Activity

Local anesthetics are pharmacological agents that cause a temporary and reversible loss of sensation when applied to a specific area of the body, without affecting consciousness. They function by blocking nerve impulse transmission, thereby preventing the perception of pain. Over the years, various plant-derived compounds have been investigated for their anesthetic potential due to their natural safety profile and minimal side effects[52]. Among these, Anacyclus pyrethrum (Akarkara) has gained attention for its remarkable local anesthetic properties, which support its traditional use in relieving toothache and oral discomfort.

The local anesthetic activity of A. pyrethrum was evaluated using ethanolic, petroleum ether, and aqueous extracts prepared through Soxhlet extraction. The study was conducted on guinea pigs, which are considered reliable models for local anesthetic testing. Results demonstrated that the ethanolic extract at 1% and 2% concentrations produced a significant loss of sensation, comparable to that of standard anesthetic drugs. Similarly, the 2% petroleum ether extract showed marked anesthetic efficacy, followed by the 1% petroleum ether and 2% aqueous extracts, while the 1% aqueous extract produced minimal response.

Histopathological examination of the treated skin tissues revealed no inflammatory or degenerative changes, indicating that the plant extracts were well-tolerated and safe for topical application[43]. Moreover, both the aqueous and alcoholic extracts (2%) showed a longer duration of anesthetic effect in experimental animals such as frogs, guinea pigs, and rabbits when compared to xylocaine (lidocaine), suggesting a sustained action on sensory nerves.

A clinical trial conducted on dental patients undergoing minor oral surgeries further validated these findings. The 2% alcoholic root extract of A. pyrethrum provided effective local anesthesia with prolonged duration and minimal side effects when compared to xylocaine. This pioneering study establishes A. pyrethrum as a promising natural local anesthetic agent, combining efficacy, safety, and extended action, making it a potential candidate for pharmaceutical development in pain management and dental care.

9. Anti-Inflammatory Activity of A. pyrethrum

Inflammation is a physiological response that plays a central role in the pathogenesis of many diseases, including chronic and acute conditions. Research has demonstrated that Anacyclus pyrethrum (A. pyrethrum) exhibits significant anti-inflammatory properties across various experimental models. Several studies have focused on assessing the efficacy of different extracts from the roots, leaves, seeds, and flower heads of A. pyrethrum in both in vivo and in vitro models of inflammation[27].

Manouze and colleagues investigated the anti-inflammatory effects of aqueous and methanolic extracts of A. pyrethrum roots using rat models of xylene-induced ear edema and Freund's complete adjuvant (CFA)-induced paw edema. Their findings revealed that oral administration of these extracts at doses of 250 and 500 mg/kg significantly attenuated CFA-induced mechanical hypersensitivity and reduced inflammatory edema[42]. The reduction in hypersensitivity was observed as early as 1 hour and 30 minutes post-treatment and persisted for up to 7 hours. Chronic administration of these extracts further demonstrated a pronounced effect in mitigating persistent pain associated with CFA-induced inflammation, highlighting the potential of A. pyrethrum in managing both acute and chronic inflammatory conditions.

Additional studies have evaluated aqueous-alcoholic extracts from various plant parts, including leaves, seeds, roots, and flower heads, and reported potent anti-inflammatory effects[42]. Oral administration resulted in an inhibition of edema ranging from 61% to 71% after one hour, while topical application produced even higher inhibition rates, from 60% to 82%. By the fifth hour, the anti-inflammatory effects of all extracts increased further, suggesting sustained activity.

Clinical and Therapeutic Relevance :

1. In-vivo / (very limited) human evidence

A. Animal & pre-clinical studies [57]

One study found that an ethanol-solution extract of A. pyrethrum root (alkyl-amide rich) administered to male Wistar rats (50, 100, 150 mg/kg for 28 days) increased sperm count, motility, viability, serum testosterone, LH and FSH, and improved testicular histology (spermatogenesis) vs controls[32].

A recent study in male rats exposed to cadmium (which impairs fertility) found that A. pyrethrum extract (100 mg/kg) for 56 days improved antioxidant enzyme-levels in semen, reduced lipid peroxidation, improved sperm motility/viability, hormone levels and gene-expression of sex-hormone receptors.

Another earlier study (aqueous extract, 50 & 100 mg/kg in albino rats) recorded improved sexual behaviour (increased mount/intromission frequency, reduced latency) and greater sperm count/fructose levels in seminal vesicles.

B. Human/clinical evidence

Akarkara extract has shown promising results as a fertility enhancer in animal trials, but these activities are yet to be confirmed in humans."

There is a lack of data regarding the interaction of Akarkara with other drugs… there are no safety studies about its usage in pregnant and breastfeeding women."

C. Implications

The animal data are promising for male reproductive health (spermatogenesis, hormone stimulation) and antioxidant/anti-toxicity effects[54].

The lack of human trials means one must be cautious about extrapolating to people.

Because of this gap, any therapeutic use in humans should consider the evidence as preliminary, and safety/monitoring are advisable.

2. Current herbal formulations containing Akarkara

There are a number of Ayurvedic/herbal products and formulations that include Akarkara (root of A. pyrethrum) as an ingredient or as the main herb. For example:

Table 3. Ayurvedic/herbal products and formulations

Akarkara Churna: A powder formulation of the root. (Example: "Nidco Akarkara Churna" lists root of Anacyclus pyrethrum as the ingredient.)
Akarkara Powder: As a standalone product — e.g., "Akarkara Powder" by various Ayurvedic suppliers in India.
Products for oral/ dental health: Some Ayurvedic articles list Akarkara as one of the "6 Ayurvedic ingredients that promise brighter teeth and healthier gums" because of its effect on salivation and gum health.
Traditional formulations (textual references): Ayurvedic pharmacopeia lists Akarkara in various formulations (capsules, tablets, etc) with mention of "25 to 125 mg" as posology (though this is traditional data) in The Ayurvedic Pharmacopoeia.

3. Therapeutic applications

I'll organise this by three key areas you mentioned: oral care; male infertility/sexual health; neural stimulation (and related uses).

A. Oral care

- Traditional usage: The root of A. pyrethrum has been used as a masticatory (chewed) or in lozenges, to stimulate salivary flow, relieve toothache, soothe sore throat and gum disorders.
- Modern article: The Times of India article mentions Akarkara as an Ayurvedic ingredient beneficial for teeth and gums – increases blood-flow in gums, supports natural cleaning process via increased salivation[56].

- Mechanism: The root contains alkylamides (e.g., pellitorine) and essential oils which may provide analgesic, antimicrobial and rubefacient (warming, stimulating) effects in the oral cavity. Take-away: For oral/dental health, Akarkara has a long traditional use and some mechanistic plausibility; while rigorous human trials are missing, its use in lozenges/chew for gums/teeth is relatively well-documented in Ayurvedic literature.

B. Male infertility / sexual health

- Traditional use: In Ayurveda and Unani, Akarkara is listed as a "Vajikaran Rasayana" (aphrodisiac tonic) used for sexual dysfunction, seminal weakness, etc.
- Animal evidence: As noted above, studies in rats showed improved sperm parameters, hormones, testicular histology. e.g.: 50–150 mg/kg for 28 days improved sperm count, motility, testosterone[57].
- A combination study: One study comparing A. pyrethrum + Tribulus terrestris in rats improved fertility parameters more than either alone.
- Limitations: No well-controlled human trial identified. Efficacy in humans remains to be confirmed. And long-term safety for this use is not fully established[50]. Take-away: There is moderate pre-clinical evidence supporting Akarkara in male fertility/sexual health, but human evidence is lacking; therefore it should be used cautiously and perhaps as an adjunct rather than standalone proven therapy.

C. Neural stimulation / nervous system tonic

- Traditional indication: Some sources list Akarkara as "nerve tonic", "nervine stimulant", used in disorders like hemiplegia, paralysis, neuralgia.
- Mechanistic hints: The alkylamides may interact with sensory neurons, and root chewing causes tingling/-numbing in mouth, indicating neural activity.
- Modern research: While in-vitro and animal studies show anti-inflammatory, analgesic, antioxidant and neuro-protective potential of A. pyrethrum (e.g., as noted in a review).

Future Prospects :

1. Standardized Phytopharmaceuticals

- Develop extracts with consistent levels of key bioactive compounds (like alkylamides).
- Standardization ensures reproducible quality, safety, and effectiveness.
- Can be made into capsules, tablets, or powders for specific uses like male fertility or oral care.
- Select and authenticate raw plant material to avoid adulteration and ensure uniformity.
- Optimize extraction methods to maximize yield of active compounds while maintaining stability.

2. Nanotechnology-Based Formulations

- Encapsulating Akarkara extract in nanoparticles or nanoemulsions can improve absorption, stability, and targeted delivery.
- Useful for oral care (gum absorption) or neural stimulation (better delivery to nerves or brain).
- Still experimental, but promising for better herbal medicines.
- Controlled-release nanocarriers can maintain steady levels of bioactives for better therapeutic effect.
- Combine with other synergistic herbs in nanoformulations to create more potent herbal products.

3. Clinical Validation and Safety Testing

- Human studies are very limited, most evidence is from animal experiments.
- Future research should include:
  - Safety studies (toxicity, safe dose)
  - Clinical trials to prove effectiveness in humans
  - Herb-drug interaction studies to ensure safety.
- Determine safe dosage ranges for long-term use in different populations.
- Monitor clinical outcomes such as sperm parameters, oral health indices, or cognitive/neural function.

4. Molecular Docking and Mechanistic Studies

- Computer-based studies (in-silico docking) can predict how Akarkara compounds interact with targets (like enzymes or receptors).
- Helps identify active compounds and design better drugs.
- Needs follow-up with lab experiments and animal testing.
- Screen multiple bioactive compounds to find the most promising candidates for therapy.

SUMMARY

Anacyclus pyrethrum (Akarkara) is a perennial medicinal plant with significant therapeutic and pharmacological potential, widely recognized in traditional systems of medicine such as Ayurveda and Unani. The plant's roots are the most valued part and are rich in diverse bioactive compounds including alkylamides, alkaloids, flavonoids, saponins, tannins, steroids, and essential oils. These secondary metabolites are responsible for its multifaceted biological activities and form the basis for its traditional applications in oral care, male fertility, neural stimulation, and as a general tonic. Phytochemical analyses and modern extraction techniques such as Soxhlet extraction, maceration, ultrasonic-assisted extraction, and chromatography have enabled the isolation and characterization of these active constituents, providing a foundation for further pharmacological evaluation.

Preclinical studies in animal models have demonstrated the efficacy of Akarkara in multiple therapeutic domains. For male reproductive health, ethanol and aqueous root extracts have been shown to improve sperm count, motility, viability, and serum testosterone, along with favorable effects on luteinizing hormone and follicle-stimulating hormone levels. In neural applications, the alkylamide-rich extracts exhibit nerve stimulation effects and potential neuroprotective activities. Additionally, Akarkara has demonstrated antioxidant, anti-inflammatory, antimicrobial, and local anesthetic properties, supporting its traditional use in oral care and wound healing. These findings underscore the plant's potential as a multipurpose therapeutic agent; however, robust human clinical trials are currently lacking, limiting definitive conclusions regarding safety and efficacy in humans.

Several Ayurvedic and herbal formulations containing Akarkara are commercially available, including powders, churna, lozenges, and standardized extracts. These preparations are primarily used for oral hygiene, aphrodisiac effects, and as neural tonics. Despite the widespread traditional use and commercial availability, variability in raw material quality, extraction procedures, and bioactive content highlights the necessity for standardization of extracts**.** Standardized phytopharmaceuticals with reproducible bioactive profiles are essential for ensuring consistent therapeutic outcomes, safety, and regulatory compliance.

CONCLUSION

Akarkara is a promising medicinal plant with diverse therapeutic potentials, particularly in male reproductive health, neural stimulation, and oral care. While preclinical studies support its efficacy, clinical validation and standardization are essential to develop safe and effective herbal medicines. Integrating traditional knowledge with modern research approaches could unlock its full pharmacological potential and pave the way for novel phytopharmaceuticals.

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