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Review Article

ANACYCLUS PYRETHRUM: A BRIEF OVERVIEW OF PHYTOCHEMISTRY, TRADITIONAL USES, AND POTENTIAL THERAPEUTIC PROPERTIES

Vishal Thakur[1], Apoorva Pathania[2], Harmandeep Kour[2], Anu Radha Pathania*[2]
[1]*Research Scholar, Department of Pharmaceutics, Himachal Institute of Pharmacy, Paonta Sahib, Himachal Pradesh, India*
[2]*Department of Chemistry, University Institute of Sciences, Chandigarh University, Gharuan, Mohali Punjab, India*
**Corresponding author: anuthakur2014@gmail.com*

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ABSTRACT
Since ancient times, *Anacyclus pyrethrum* has been utilized as an aphrodisiac. In Ayurvedic medicine, the plant is used to boost libido and enhance sexual performance. Pyrethrins and anacyclins, among other plant substances, improve vaginal blood flow and sensation. It raises libido and promotes hormone synthesis. The plant is also claimed to have powerful antioxidant qualities that enhance overall well-being. In addition to being used for its intended purpose, *Anacyclus pyrethrum* is thought to provide potential health advantages. It functions as an oxygen inhibitor and has anti-inflammatory qualities that might help in the fight against chronic illnesses, including cancer and heart disease. Additionally, some research has revealed that the herb may have neuroprotective qualities, making it a viable therapy for brain diseases like Alzheimer's. The herb *Anacyclus pyrethrum* has a long history of use as a traditional medicine. It is a powerful natural medicine thanks to its aphrodisiac effects and oral health advantages. Additionally, the possible health advantages outside of its regular use make for an intriguing research topic.

Keywords: *Anacyclus Pyrethrum*, Phytochemistry, Pharmacological Activity, Antidepressant Activity.

1. INTRODUCTION
Anacyclus Pyrethrum L. (Compositae, Asteraceae), sometimes called "African pyrethrum" or "Tigenthast," is an eternal, procumbent plant that was native to Northern Africa and grown in the Mediterranean [1]. The World Health Organization (commonly known as the WHO) recognized the significance of herbal remedies in public health care in underdeveloped countries. The roots as well as the leaves of *Anacyclus pyrethrum* (AP) DC play crucial role in ancient Ayurvedic as well as in the Unani systems of integrative health & herbal remedies of the East. The root of AP has been claimed to have therapeutic benefits in traditional systems of medicine [2]. Several rheumatic and neuralgic conditions affecting the head, teeth, and face can be treated with it. A local ethnobotanical investigation revealed that it might have anti-diabetic properties [3]. According to earlier chemical research at Bendjeddou, 2003, Ching, 2007, the plant has immunomodulatory capabilities [4-5]. Its root is used as a sternutatory, sialagogue, and dizzy all over Algeria. The herb is extensively recognized in Indian medicine as a tonic and rejuvenator [6]. The AP root has antibacterial and anti-inflammatory characteristics, as well as insecticide qualities [1]. Infections of the respiratory tract and liver disorders are also treated with it [1, 4]. In Unani and Ayurveda, Anacyclus Pyrethrum (Linn) De Candolle was known as "Spanish pyrethrum root," "Aaqarqarhaa," and "Aaqarqarhaa," respectively. Its roots are strong, compact, and fussy-form, the size of a little finger, having leaf stub at the top most and very lesser or no hair-like radicles; outwardly brownish, enormously fissured endlong [7]. There are about 1,700 native species and subspecies in North Africa, half of which are found only in Morocco [8]. It belongs to the genus Anacyclus among 13 year lies and is an eternal's specie found mainly in North-Western Africa and other Mediterranean countries [9]. Numerous Anacyclus plants are used in conventional medicine, including *A. pyrethrum, A. radiatus, A. valentinus, A. cyrtolepodioid* & *A. clavato*. Its pharmaceutical applications are because of flavonoids and terpenoids in it [9-10]. The AP L. (Asteraceae), also known as "African Pelitre" or

"Tigenthast" by Moroccans [11], was selected from the ecology of the entire Mediterranean basin. It is an indigenous herbaceous and eternal genus [8] existing in a sunlit environment. In North Africa, the genus occurs in the feral, loamy, well-depleted soils [11]. All types of liver damage caused by chemotherapeutic drugs & numerous toxicant leads to damage to hepatocytes and, thus, their malfunction [12]. Drug-induced hepatitis is indeed a significant concern in the treatment of TB. Hepatitis refers to inflammation of the liver, and it can be caused by various factors, including certain medications used to treat TB, which causes a mortality rate of about 5% [13]. Isoniazid (INH) & rifampicin (RIF), the Ist-lines drugs for tuberculosis chemotherapy, are well known & associated with hepatotoxicity [14-15]. Understanding the pharmacokinetics and pharmacodynamics of AP will help refine dosing regimens and evaluate possible drug interactions. In addition, studying its long-term effects and exploring possible synergistic effects with other medicinal plants or conventional treatments could expand its therapeutic applications. To fill the knowledge gaps, comprehensive studies to determine the efficacy and safety of AP are added. These investigations include standardized extraction methods, identification, and quantification of active substances, pharmacological mechanisms, and clinical studies.

2. PHYTOCHEMISTRY OF *ANACYCLUS PYRETHRUM*

2.1. Essential Oil Containing Chemical Compounds

In essential oil investigations of AP, that was arranged from Ben Slimane area, there is 32 components existing constituted roughly 92.67% of the entire organic make-up. The bulk of compounds identified are oxidative sesquiterpenes (58.96 %) obeyedhydrocarbons' sesquiterpene's (24.19 %). Spathulenol (20.47%), Germacrene D (16.48%), Caryophyllene oxide (13.20%), 4-(14)-salvial-1-one (8.27%), Caryophyllene-4 (14), and 8-(15)-diene5-ol (7.30%) are the most likely major components [16]. According to the study on AP from Timahdit, Morocco, the sample obtained just before blooming had 42 compounds, whereas the sample taken shortly after flowering included 36 compounds. These components contribute 91.32% and 91.82% of the total essential oil content, respectively. The most abundant class of compounds identified is oxygenated sesquiterpenes. It varies from 89.17 % (before blooming) to 90.58 % (after blooming) during the maturity period [17]. Similitude, as demonstrated in, this category comprises greatest number of Algerian species. In this investigation, the percentage of sesquiterpenes changed between 37.1% and 58.6% before and after blooming [18].

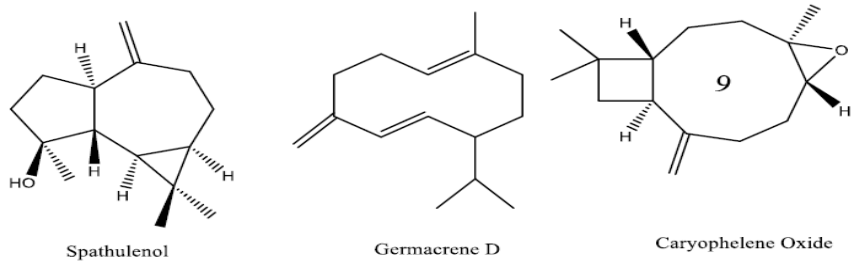


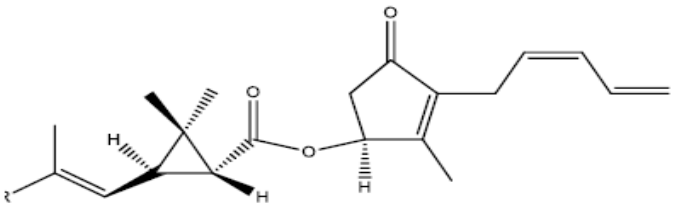
Fig. 1: The chemical structures of AP's volatile components

According to one study [16], the proportion of the major ingredient Spathulenol increase's significantly after blooming (16.9 %) over before blooming (13.31 %). Hence, a fraction as to germacrene 4-(15),5,10-(14)-tren-1-α-ol inside the specimen obtained post blooming increased (12.89 %) compared to the sample collected pre-blooming (2.07 %) [18]. Moreover, Selina-3, 11-dien-6-ol had a larger proportion pre-blooming (9.24%), while the cedryl acetate molecule had a higher percentage after post-blooming (8.10 %). After blooming, caryophyllene oxide levels drop (9.65 to 7.11%). Similarly, the first culture period gradually increased the amounts of -biotol and salvial-4(14)-en-1-one (5.16% and 4.66%, subsequently). Despite this, the rate of eudesma - 4 - (15), 7-dien-1-ol, & hemachalol rose during the second session. (5.85 % and 5.67 %, subsequently) [17]. Likely, previous Moroccan investigations reported spathulenol to be the most prevalent component in AP EOs [19, 20]. The EOs from AP in Morocco conceivably classed as a Spathulenol Chemotype based on these findings, regardless of harvest season. Furthermore, In Algeria,

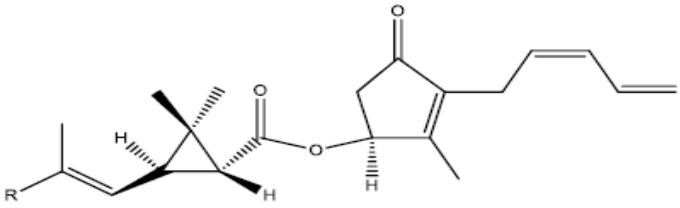
this EOs isolated out of AP pre and continued to blooming had a germacrene-D chemotype (13.4 % & 5.1 %, subsequently). Spathulenol levels are consistent pre and throughout blooming (4.7 % and 4.2 %, subsequently) [21]. Actually, the acitinic study of the indispensable oils altered quantitatively as well as qualitatively, which can be attributed to a variety of factors including harvesting period, anabolismreactions of these valuable ingredient, plant germination, geographical & genetics origin [22].

2.2. Non-Volatile Ingredients

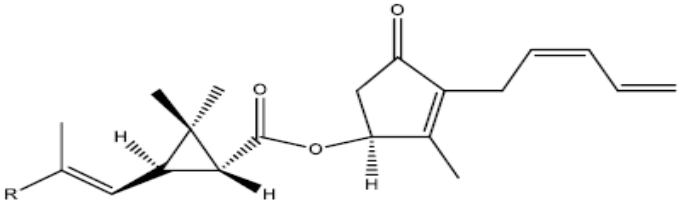
Numerous investigations have been conducted on the chemical component of AP. The existence of atropines (alkaloids), lowering chemicals, & catechins tannins was discovered during a phytochemical investigation of the plant's leaves, petals, roots, and flower heads. This plant also includes 3,4,5-tri hydroxybenzoic acid, phytosterols, isoprenoids, seaweed, warfarin, waterfowls, & homicides [17, 23] as vestiges such as Chromium, Iron, Zinc, Cd, Cu, Pb, and Ni [24]. Flowers contain an important flavone and cresolase compared to the leafy canopy and radicle. The aerial portions contain a lot of tannins, whereas the roots include a lot of alkaloids. The most prevalent bioactive chemicals, n-alkyl amides [25] & keen brown amber, discovered Gallotannic acid, oligosaccharides, gingiva's, different chemicals, C18H25NO, PEA; phetamine, polyacetylenic amides I-IV, sesame seeds, and pectin [23, 26] are the most prevalent in the roots. The literature detected each combination pertaining to isobutyl amides of monosaturated acids with decalin as a major chemical in a detailed investigation against the lucid element of the radicle [27]. Similarly, radical hydrogenation and acid hydrolysis generate each amalgamation as regards decanoic, dodecanoic, and tetradecanoic acids that are feasibly isolated with hydrophobic chromatography [28].



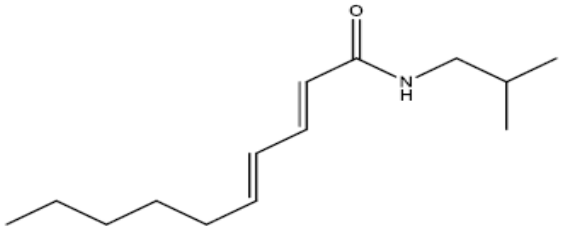
Pyrethrin I (R=CH_3)
Pyrethrin II (R=$COOCH_3$)



Jasmolin I (R=CH_3)
Jasmolin II (R=$COOCH_3$)



Cinerin I (R=CH_3)
Cinerin II (R=$COOCH_3$)



Pillitorin

Furthermore, Pyrethrins detected in the plant's root is a six naturally grouped esters that are: three are chrysanthemum acid esters (pyrethrin I, cinerin I, and jasmolin I), & three are Pyrethrins (pyrethrin II, cinerin II, and jasmolin II). In a study, the alcohol fractions found were pyrethrelone, cinerolone, & jasmolone in pyrethrins 1 & 2, cinerins 1 & 2, and jasmolins 1 & 2 [29]. Several investigations [17, 23] revealed the existence as to pyrethrins and pellitorin in the radicle of AP. The isolation as to pellitorin yields a novel crystalline compound with a melting temperature of 121°C that crystallizes in white needles from Chloroform-benzene & is partially dissolved in benzene [28]. The existence of alkaloids, bioflavonoids, tannic acid, corticosteroids, isoprenoids, reducing sugars, lube, steroidal glycoalkaloids', anthraquinones, & amino acids has been reported in Ethan extractor from the radicles, leaflet, and trunk [24], aqueous and methanolic extractions [23], methanolic and aqueous extraction [17], and aqueous and ethanoic's out of the manifested radicle [30]. While the investigation as to the ethanol extractor of the wilted radicles suppress n-alkyl amides

using High-Pressure liquid chromatography alongside UV detection adjoining's electrification spray ionization tandem mass spectrometry (HPLC/UV/ESI-MS) confirmed the discovery as an aspect of 13 chemicals [27, 31]. Among these, six are considered new compounds: undeca-2E,4E-diene-8,10-dinoic acid n-methyl isobutyl amide, Undeca-2E,4E-diene-8,10-diene-8,10- diyn-oic acid isobutyl amide, tetradeca-2E,4E-diene-8,10-diynoic acid tyramide, tetradeca-2E,4E, XE/Z-trienoic acid tyramide, tetradeca-2E,4E, XE/Z, YE/Z-tetraenoic iso-butyl amide and deca-2E,4E-dienoic acid-n-methyl isobutyl amide [31].

Picric acid, HNO_3, CH_3COOH, H_2SO_4, Hydrochloric acid, $FeCl_3$, aqu. & alc. KOH, NH_3 tinctures, and iodine tinctures were discovered using HPTLC in the alcoholic extraction of the radicle [32]. Another chemical identified by GC-MS in an ethanol extractor was palmitic acid, 9,12-octadecadienoic acid (Z, Z)-, white tar, decahydro-1,1-dimethyl-, 7-tetradeca-2,4-dynamite, benzofuran 2-carboxaldehyde, and gamma-sitosterol [33]. AP radicle contains 7- pure alkamides that have been detected by MS and NMR. These compounds are deca-2E,4E-dienoic acid 2-phenylethylamide, deca-2E,4E-dienoic acid isobutyl amide (pellitorin), tetradeca-2E, 4E-diene-8,10-dienoic acid,deca-2E,4E,9-trienoic acid isobutyl amide, isobutyl amide (anacycline), dodeca-2E,4E-diene-4-hydroxy-2-phenylethyl amide acid, undeca-2E,4E-diene-8,10-diynoic acid isopentyl amine & tetradeca-2E,4E,12Z-triene-8,10-dienoic acid isobutyl amide [34-35]. In addition, column chromatography followed by HPLC discovered mixes of two additional alkamides that is undeca-2E,4E-dien-8,10-dienoic acid, 2-phenylethylamide and deca-2E,4E-dienoicacid,4-hydroxy-2-phenylethylamide [35]. Work-up on the ethanolic aqueous extracts of the bloom heads, leaflets and seeds of *AP* validate the existence of 20 composites disclosed by GC-MS, tyramide, and isovaleric acid are among the ingredients. These amalgamations were Ist investigated in addition to the specific amalgamation likewise alkylamides ((2,4)-n-isobutyl-2,4-undecadien-8,10-diynamide, n-isobutyl-dodeca-2,4,8,10-tetraena-mide, n-isobutyl-2,4-octadiene-6-monoynamide, n-isobutyl-2,4-heptadiene-6-monoynamide and n-isobutyl-2,6,8-datrieneamide) [36]. Furthermore, quantitative and qualitative research on AP methanolic extract concerned with n-alkyl amides is being conducted since they exhibit various fractionation routes that may be used to identify components here contained in the plant. Using this method, 21 compounds were discovered, together with 20 n-alkyl amides and one citric or gluconic acid. In this plant, two new ingredients were discovered for the Ist time: (2E, 6Z,8E)-n-isobutyl-2,6,8-diatrinamide and (2E,7Z)-n-isobutyl-2,7-tridecadiene-10,12-diynamide [37]. Furthermore, using UPLC-Q-TOF-MS chromate-graphy, novel substances were discovered including, dodeca-2E,4E, E-trienoic acid-4-hydroxy phenylethyl amide 4-oh-phenylethylamide, undeca-2E,4E-diene-8,10-diynoic acid, tetradeca-2E,4E-ne-trienoic-8,10-diynoicacid, and tetradeca-2E,4E-ne-trienoic acid are all examples of phenols [37].

3. THERAPEUTIC APPLICATIONS OF *ANACYCLUS PYRETHRUM*

3.1. Diabetes prevention

Diagnosing and prognosing diabetes mellitus depends on sugar concentration in our blood. For the region that excessive endogenous dextrose, insulin deficiency leads to a drastic increase in blood glucose and a far-reaching change in body weight. Insufficiency of insulin may cause a tempered malfunction of tissue lipids and proteins [38]. Although many anti-diabetic plants and herbs have been used in traditional medicine for ages, they must first undergo current research methods testing before being employed in modern medicine. As a result of oral treatment with AP root extracts, insulin levels were improved, and blood sugar concertation in STZ-induced diabetic rats was significantly lowered. Mahadeva and Subramanian (2009) theorized that aqueous extracts might suppress hyperglycaemia through their stimulation of remnant beta-cells to secrete more insulin or through their regeneration of beta-cells [39]. The root also possesses some biological principles that are insulin-protective or insulin-like. Based on phytochemical screening, the root contains alkaloids, amino acids, tannins, alkaloids, saponins, terpenoids & steroids, which can act against diabetes [40]. The lack of insulin results in a defective amino acid/protein metabolism, leading amino acids to act as antihyperglycemic envoys [41]. Antihyperglycemic effects are found in phenolic compounds. Alkaloids, as well as tannins have been reported as to possess hypoglycemic properties. In opposition to indirect envoy like sulphonylureas, which function by encouraging the pancreatic beta cells to release more insulin., saponin is familiar to reduce serum cholesterol levels & might be categorized as a straightforward hypoglycaemic envoy [42-43].

3.2. Anti-inflammatory, anti-nociceptive, and anti-oxidant activities

The research on natural oxygen inhibitors has focused on several studies on AP [30-47]. In an earlier discussion, the litterateur and his fellow workers debated the anti-oxidant effectiveness of MeOH extract, the aqueous extract & the Chl. Extract out of the trunk & leaflets of *A Dalmatian* reaped in Algeria, with the help of the DPPH· and FRAP techniques [47]. Via DPPH· methodology, it was observed that Methanol extract has a high anti-oxidant power (IC50 of 0.056 mg/mL), followed by Aqu. ext. with an IC_{50} of 0.114 mg/mL and Chl. ext. with an IC_{50} of 0.154 mg/mL. FRAP procedures revealed that the MeOH extract had an unbreakable bring-down power in comparison to the other extracts brought out [34]. Manouze et al. [30] evaluated the efficacy of oxygen inhibitors such as MeOH ext. and aqu. ext. of the A. pyrethrum tuber in the Marrakesh-Morocco region in 2017. Litterateur, therefore, used three techniques: DPPH, FRAP, and BCB. Using these three approaches, the MeOH extract had a significant oxygen inhibitory action with IC50 values of 12.38, 50.89, and 107.07 g/mL, subsequently. the aqu. extract displayed an anti-oxidant action with IC50 values of 13.41, 60.17, and 120.66 g/mL, respectively. Furthermore, Elazzouzi et al. [47] investigated the anti-oxidant activity of the A. pyrethrum root in the Timatidite area of Morocco. We discovered this because MeOH ext., BuOH fra., AcEth fra., and Res pha. from the AP radicle showed IC50 values of 0.152 mg/mL, 0.155 mg/mL, and 0.144 mg/mL, subsequently [47]. In 2020, a comparable litterateur studied the anti-oxidant properties of the A. pyrethrum radicle using DPPH methods. The litteraturer observed that the IC50 of this element is 30.50 milligrams per millilitre [46].

The above figures are the mean of three ascertainment ± SEM, ***p <0.001 distinction from the BHT group and ***p <0.001 noteworthy distinctout of the quercetin group,2,2-diphenyl-1-picrylhydrazyl; ferric reducing-oxygen inhibitor power; β- carotene, BCB, chemical removal;dibutylhydroxtoluene.

Recently, Jawhari and his colleagues conducted a comprehensive investigation into the anti-oxidant and anti-microbial potential by DPPH & FRAP of the Methanol ext. of the radicle, leaflets, petals, & germs of 2 genus of *A. pyrethrum* (*A. pyrethrum* versus pyrethrum (L.) & An AP versus *depress us* (Ball) Maire) find out Morocco's timidities region. The report shows the remarkable anti-oxidant & anti-microbial efficacy seen by the leaflets of AP var. *depressus* (Ball) Maire (IC50 = 0.03 mg per milliliters), which give attribute to phenols, flavones, and alkyl-amides of *AP* [44]. Rather the germs having similar properties have an excessive reduction potential (0.25 mg/mL). Radicle of AP var. *P* (L.) displayed the topmost overall oxygen inhibitors activities, with 708.74 mg equivalent ascorbic acid per gram.

Table 1: Anti-oxidant capabilities of AEAPR, MEAPR, BHT, and quercetin as measured by DPPH, BCB, and, FRAP tests [48]

Specimencollected	Test		
	FRAP (µg/ml)	BCB(µg/ml)	DPPH (µg/ml)
BHT	7.09 ± 0.10***####	4.30 ± 0.33***####	4.21±0.08***####
MEAPR	50.89 ± 1.25***####	107.07 ± 4.14***####	12.38±0.25***####
Quercetin	2.29 ± 0.10	0.95 ± 0.02	1.07 ±0.01
AEAPR	60.17 ± 4.48	120.66 ±3.61	13.41±0.67

3.3. Antibacterial activity and antifungal activity

All pathogenic bacteria were inhibited by aqueous and methanolic extracts of AP, AP with methanolic extract showing the best results. Using methanolic extracts of *Klebsiella pneumoniae* and aqueous extracts of *Pseudomonas aeruginosa*, *Staphylococcus aureus, Escherichia coli, Bacillus subtilis,* and *Micrococcus luteus* were shown to have the strongest antibacterial activity followed by MIC 6.25mg/ml. In general, the depletion in bacterial feasibility was dependent on dose and was greater than the depletion in cell viability ($p<0.05$) (table 2) [38].

This antibacterial action may be due to supplementary metabolites such as terpenoids, phenolics, and alkaloids found in this plant (North African Medicinal Plants Guide), Gram-negative bacteria, which cause many infectious illnesses, which stand out for having a lipopolysaccharide-rich outer membrane that renders them immune to several antibiotic drugs.All extracts

(AP methanolic & aqueous extractors) were bactericidal against Gram- +ve& -ve bacteria [49].

3.4. Anticonvulsant, anxiolytic and neuro-toxicity profile

Currently, a variety of synthetic anticonvulsant drugs are available for use in the management, control, and/or treatment of epilepsy patients. Due to their scarcity, higher cost, and increased toxicity, anticonvulsant medicines produced from plants and other natural sources are in desperate need of research. Although AP root is frequently utilized by Unani doctors to treat epilepsy, there is little research on the plant's therapeutic effectiveness in the biomedical literature. Female albino mice were used to test the acute toxicity of an ethanolic root extract of AP. The ethanolic extract was administered in dosages of 300, 2000, and 5000 mg/kg. Maximum electroshock-induced seizures were used to assess the anticonvulsant activity. Implementing a stimulator device, electric stimulation was administered. Tonic flexion, extension, clonus, and mortality from convulsions were among the convulsion phases that we timed. The impact on seizure is also studied using the pentylenetetrazole (PTZ) technique [50].

Table 2: The minimum inhibitory concentration (MIC) of the extracts of the plant tested against different bacteria. Data represent the MICs (mg/mL) [48]

	Standard Reference Bacterial Strains					
	Gram- '-'-ive Organisms			Gram- '+'-ive Organisms		
Extracts	EC	KB	PA	SA	ML	BS
AE, AP	3.125	3.125	6.25	3.125	3.125	3.125
ME, AP	3.125	6.25	3.125	3.125	3.125	3.125

EC: Escherichia coli ATCC 54127, SA: Staphylococcus aureus ATCC 6538, ML: Micrococcus Luteus ATCC 9341, BS: Bacillus subtilis ATCC 6633, PA: Pseudomonas Aeruginosa ATCC 15442 and KB: Klebsiella Pneumoniae CIP 53153, AE: aqueous extract; ME: Methanolic Extract; AP: Anacyclus Perythrum.

3.5. Anabolic, aphrodisiac and reproductive activity

The *Vajeekarana* is the most significant use of AP in Ayurveda [7]. It falls under *Shukrastambhaka* drug [51]. It prolongs ejaculation and improves the quality of the semen. Everywhere AP has been utilized mostly in *Shukrastambhaka* Formulations, from *Gada Nigraha* to *Siddha Prayoga Sangraha* [52]. It is utilized in a variety of aphrodisiac compositions in the Unani System of Medicine, both for internal use and topically. Recent studies have also demonstrated this drug's *Vajeekarana* impact [53]. Similar to the rise in penile erection index seen with testosterone treatment, male rats' penile erections were also enhanced by analyzing *A. pyrethrum's* aqueous extract. The presence of nitrous oxide (NO)-based intervention was indicated by a rise in PEI in the treated groups [54]. In comparison with testosterone treatment, the impact is significantly more prominent in the group treated with *A. pyrethrum* aqueous extract (100 mg.kg-1). The control on the extracts (50 and 100 mg.kg-1 b. w.) altered both sexual orientation and behaviour, definitely indicating improved sexual performance. The histopathological analyses of testis sections from distinct groups served as further validation for this activity. The findings support the idea that medication extracts might improve male rats' overall sexual performance.

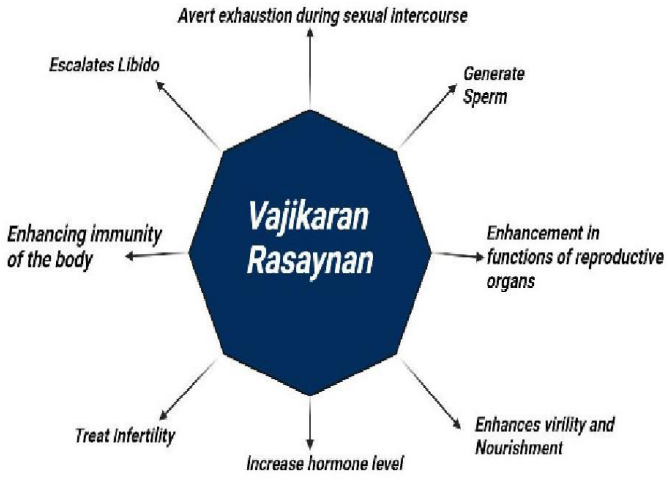


Fig. 3: Action of Vajikaran Rasayana

Additionally, the drug has a persistent and long-lasting effect on the total sexual performance measured throughout this trial. Direct effects on sexual desire might result from elevated blood testosterone levels or from experiencing a testosterone-like effect. This may

be brought on by a shift in neurotransmitter levels, or their effects within cells might potentially alter sexual behaviour [55]. The systemic component of the endocrine system and the testis interrelate intricately during spermatogenesis [56].

3.6. Anti-inflammatory activity

Inflammation is a symptom of a variety of diseases. Several *A. pyrethrum* preparations have been shown to have anti-inflammatory action in a rat model of inflammatory edoema. Manouze and colleagues studied the in vivo effects of a methanolic and aqueous extract of *A. pyrethrum* radicle on xylene-induced rat ear edoema and Freund-induced whole rat claw edoema. These researchers observed that the extracts investigated significantly reduced the ear and foot edoema produced by xylene and CFA, respectively. These extracts were given orally in doses of 500 &250 mg/kg, which reduced the mechanical hypersensitivity responses brought on by CFA. This decrease began one hour and thirty minutes after the therapy and persisted for seven hours. Both extracts were treated chronically, which decreased the mechanical hypersensitivity in the chronic pain states brought on by the CFA [28]. Additionally, someone's findings have demonstrated that *A. pyrethrum's* leaflet, grains, radicle, and florets heads have extremely significant anti-inflammatory effects on rat edoema. Inhibition in the oral therapy groups after an hour of treatment varied from 61% to 71% [36]. However, the proportion of resistance ranged from 60% to 82% and was higher in the groups that had percutaneous treatment Alkaloids (pellitorin), particularly alkylamides, may operate by decreasing neurogenic inflammation, whilst flavones have a diaphragm-stabilizing effect by lowering vasodilation, which increases the solidity and integrity of blood vessel walls [36, 44]. Additionally, in a different study, several A. pyrethrum extractions (Aqueous as well as methanoic extraction and Chloroform extract) were found to have substantial anti-inflammatory activity [45].

3.7. Antidepressant activity

Haloperidol causes catalepsy by obstructing dopamine neurotransmission, which was prevented by AP root extract. In the tail suspension test (TST) and forced swim test (FST), a normal animal exposed to a non-soluble unpleasant situation alternates between immobility and agitation. While seeking is the cause of anxiety and uses a lot of energy, being immobile saves energy. Following antidepressant therapy, animals struggle harder, even in dire circumstances, and they are less immobile for longer periods. The immobility duration was decreased in both the FST and TST, which indicates that AP root extract has a substantial antidepressant-like effect. Alpha2 adrenoreceptor agonist is clonidine. It is selective for the CNS's vasomotor center's presynaptic alpha2 receptors. This binding prevents NE from being produced, which reduces sympathetic outflow and causes a drop in body temperature. The hypothermia caused by clonidine and reserpine could both be reversed by AP root extract, whereas reserpine causes hypothermia owing to peripheral neuronal catecholamine depletion. According to the debate, AP root extract may have an antidepressant effect by either reducing inflammatory biomarkers or by interacting with the adrenergic or dopamine receptors, which would increase the levels of noradrenaline and dopamine in mouse brains [57].

It has been established that those with significant depression have greater amounts of innate immune cytokines, adhesion molecules, chemokines, acute-phase proteins, and chemokines, indicating an active innate immune response [58]. On Swiss male albino mice, an experiment involving haloperidol-induced catalepsy, locomotor activity, forced swimming test (FST), tail suspension test (TST), clonidine-induced hypothermia, and Reserpine-induced hypothermia was designed. An increase in ambulatory behavior was seen when *Anacyclus pyrethrum* root extract was administered, showing that the photoactometer had a stimulating effect. Since AP radicle extraction reduces immobility, the Forced Swim Test and Tail Suspension Test both demonstrate a significant antidepressant effect. The effects of clonidine and reserpine-induced hypothermia in mice were successfully reversed with 100 as well as 200 mg/kg doses of AP root extract [59].

3.8. Memory-enhancing activity

Anacyclus pyrethrum shows memory-improving effects in Albino wistar rats at dosages of 50, 100, and 200 mg/kg [60]. The most crucial neurotransmitter for controlling cognitive functioning is thought to be the central cholinergic system. [61]. Alzheimer diseases (AD) are primarily characterized by impaired cognitive abilities. A centrally acting cholinergic drug called scopolamine. The loss of cholinergic neurons in the cortex's nucleus

basalis magno cellular is one of the most significant features of AD, which mostly causes memory loss. e damages the brain in teaching. Cognitive problems in AD are improved by medication that increases cholinergic neurotransmission. [62].

3.9. AP in rheumatoid arthritis treatment

Anacyclus pyrethrum possesses anti-inflammatory properties, which can help alleviate the symptoms associated with rheumatoid arthritis, such as joint pain, swelling, and stiffness. It is believed that the plant's bioactive compounds, including alkamides and flavonoids, contribute to its anti-inflammatory effects by modulating inflammatory pathways and reducing the production of pro-inflammatory substances in the body. Furthermore, Anacyclus pyrethrum has been shown to possess analgesic properties, which can help manage pain associated with rheumatoid arthritis. By acting on pain receptors and inhibiting pain signaling, the plant may provide relief from joint discomfort. Additionally, *Anacyclus pyrethrum* exhibits immunomodulatory effects, which may be beneficial in rheumatoid arthritis. The plant's constituents have the potential to regulate the immune response, including the suppression of immune cells and cytokines that contribute to the inflammatory process in rheumatoid arthritis. While Anacyclus pyrethrum shows promise as a natural treatment for rheumatoid arthritis, it is important to note that it should not replace standard medical treatments. It may be used as a complementary approach to conventional therapies under the guidance of a healthcare professional. Further research, including well-designed clinical trials, is necessary to validate the efficacy, safety, and optimal dosage of *Anacyclus pyrethrum* in the management of rheumatoid arthritis [63].

3.10. Antipyretic effect

AP's ethanol extractor was produced as well as tested over 100 mg/kg of yeast-induced pyrexia in rats for antipyretic efficacy. It showed considerable antipyretic activity. The action was comparable to that of the conventional medication acetaminophen 150mg/kg i.p. The highest innocuous dose, which was found to be 2g/kg. As a result, it may function as a complementary therapy to synthetic antipyretics [63-64].

3.11. Aphrodisiacs

The study was carried out to determine their impact on male rat sexual behaviors at doses of 50 and 100 mg/kg. The male Wistar (32) rats were separated into four groups: control, testosterone, low dosage (50 mg/kg), and high dose (100 mg/kg) petroleum ether extract (PEE). Albino rats were given PEE derived from AP roots orally once a day, whereas a positive control dose of 0.5 mg/kg (body weight) of testosterone was administered intramuscularly twice a week. The whole process lasted for 28 days. Before and following therapy, at 15 and 28 days and 7 and 15 days, respectively. The effects of testosterone and PEE on penile erection time, sexual behavior, body weights of accessory sexual organs, and sexual performance were evaluated. Contrary to testosterone, rats evaluated after 7 and 15 days of drug withdrawal showed that Anacyclus pyrethrum's PEE was still efficacious. This demonstrates that the drug has a longer half-life and primes the treated rats for higher sexual potential [65].

3.12. Miscellaneous Activities

Other investigations have shown that AP extracts have hepatoprotective [66], anticancer [67], neuropharmacology [68], immunostimulants, and immune-modulators [69-70]. An aqueous-ethanol extractor of the AP root was reported to have a hepato-protective effect in rats against isonicotine hydrazide and rifampicin-induced hepatotoxicity [66]. Furthermore, AP has the potential to be a new preventative product for the treatment of Bowel cancer. Another study found that the AP extract suppressed the proliferation of cancer cells (human colon or rectal cancer (HCT)) and efficiently induced apoptosis in HCT cells [67]. The ethanol extractor of AP was shown to have considerable neuropharmacological activities in 2011 [68]. Studying AP's ability to stimulate the immune system in vivo, it was discovered that at a dosage of 50 g/mL, as opposed to 50 mg/mL, it had a greater stimulation index [69]. As a matter of fact, AP root extract demonstrated superior immunomodulatory action. The aqueous extract demonstrated greater efficacy when provided orally to rats at a dose of about 10 mg/kg [69]. Similarly, at 200 mg/kg, the methanol extractor exhibits an immunomodulatory effect in rats [70]. In contrast, the AP petroleum ether extractor was evaluated at to dosage of 50 as well as 100 mg.kg-1 and was able so as to near prevent cyclophosphamide-induced immune suppression [71].

4. TOXICOLOGICAL EVIDENCE

Presently, numerous plants with medical characteristics cause poisoning in Morocco and abroad, posing a severe public health hazard [72]. Furthermore, a plant is

termed poisonous if it includes one or more compounds that are carcinogenic to individuals as well as livestock and if using it results in numerous serious issues. This intensity is determined by a variety of parameters, including the portion consumed, dose, and whether the user is fasting, as well as the user's age and the conditions under which the plant is consumed [72-73]. The Asteraceae family is one of the most utilized in herbal medicine in most Mediterranean nations since it is the richest in epiphytes [46, 73] and a reservoir of poisonous plants. Furthermore, according to various surveys [74], all respondents said that all the portions of AP were harmful; therefore, its uses should be methodical, commandeered as well as have a safe use established. Additionally, pharmacologic research, as well as analysis of toxicology must be carried out in order to convert traditional plant knowledge into scientific information [2, 73-75]. Based on this knowledge, we concluded to examine the toxicity of the AP species. While studies of phytochemical analysis of AP indicate the existence of intriguing substances, they have also revealed that it is not without toxicity, and several mishaps are documented following therapeutic use. As a result, it causes toxic symptoms such as skin irritation, mucous membrane irritation, queasiness, dizziness, and breathing issues. Dosage taken orally might cause gastroenteritis, colic, diarrhea, cramps, and very bad migraines [76]. Furthermore, it may result in a headache, tinnitus, and even dizziness through its fumes [77]. The poisonous manifestation of AP is caused by a high level of toxic substances, particularly pyrethrins, as well as unsaturated amides like pyrethrin and anacycline. In excessive quantities, the latter causes pain, queasiness, and colic. Isobutyl amides act as nerve poisons by inhibiting the sodium channel. In reality, isobutyl amides damage the nerves by blocking the sodium channel. There are currently just a few toxicity studies on the AP species available in the literature. A recent investigation found that hydroethanolic extracts of different portions of AP L. types were not hazardous at low doses. In mice administered with 2000 mg/kg, certain toxic effects were observed. At this dosage, the mice experienced liver failure, inflammatory invasions, localized tubular injury, vascular bottleneck, & follicular bronchiolitis in on liver, kidneys, and spleen [78]. The radicles ethanolic extraction (1000 mg/kg) viva voce fed to wretch was assessed for sub-chronic toxicity. There were no fatalities or harmful effects found in this trial. Furthermore, there is no treatment for simultaneous harmful abnormalities in this extract. As a result, this investigation suggests that the ethanol extractor is safe for long-term use [79]. The aqueous methanol and ethanol root extracts were administered at doses of 5000 mg/kg each, and no toxicity-related symptoms, deaths, or swaps in body weight or organ weights. This suggests that administering crude extracts to developing animals has low toxicity [80]. Other AP extracts have also been tested for toxicity on animals using light ligroin's, chloroform, ethyl ethanoate, dimethyl ketone, water as well as ethanol extraction, with similar outcomes [26, 74, 81]. As a consequence, AP is very efficient in demonstrating against many species of insects; however, it has very low toxicity for warm-blooded mammal species, as well as no blatant negative impact has been discovered because of extremely fast bio-transformation, even if toxicological tests in humans have not been carried out. A thorough investigation of AP reveals that pyrethrin components have low to moderate acute toxicity when exposed to humans orally, topically, or by inhalation and that chronic exposure can have impacts on their neurobehavioral, thyroid, and hepatic systems. As a result, another investigation found that the lowest toxicity of this vertebrate neurotoxic was around 1500 mg/kg. As a result, mechanisms like metabolic detoxification that stop it from accessing the brain system are largely responsible for the low toxicity to mammals. In those who are sensitive, prolonged exposure to certain pyrethroids may irritate their skin. According to a recent study, the ethyl acetate extract used to test the toxicity of the granulated roots showed LC50 = 249.3 gram per milliliters. Four alkamides, including pellitorine, are extracted during the fractionation test of this active extract; this impact may be attributed to their existence as this number is regarded as "toxic"[82].

5. CONCLUSION

A variety of bioactive compounds can be found in AP's phytochemical profile. Many therapeutic properties of the plant have made it a popular traditional medicine ingredient. Various ailments have been treated with it, including rheumatoid arthritis, digestive disorders, respiratory problems, and dental problems. Several scientific studies have demonstrated that AP's pharmacological properties include anti-inflammatory, analgesic, antimicrobial, antioxidant, immunomodulatory, and anticancer properties. Pyrethrins, alkamides,

sesquiterpenes, flavones, and phenoplast compounds have all found inside AP phytochemical analyses. Several of these bioactive constituents contribute to the plant's therapeutic properties and have shown potential for treating a variety of conditions. In addition to affecting bacteria like *Helicobacter pylori*, AP has antimicrobial properties. Aside from its anti-inflammatory properties, it may also be an effective treatment for oxidative stress-related diseases and inflammatory conditions. AP's anticancer potential has also been investigated, with research revealing its ability to induce apoptosis, limit metastasis, and modify genes implicated in cancer growth. These data imply that AP could be a useful addition to cancer therapy techniques. While AP has promising therapeutic characteristics, more research is required to completely understand its mechanisms of action, optimise dose regimens, and evaluate its safety and efficacy in clinical settings. Nonetheless, available evidence supports its traditional use and implies that it has the potential to be a source of innovative therapeutic compounds for a variety of disorders. AP has a number of medicinal uses that can be explored in modern medicine, which could open new opportunities for medication development and enhance patient care options.

Conflict of interest

None declared

Source of funding

None declared

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