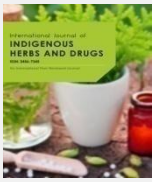
Review Article

International Journal of Indigenous Herbs and Drugs
Content Available at www.saap.org.in ISSN: 2456-7345



REVIEW ON TANACETUM PARTHENIUM

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Article Info

Article History
Received on: 15-01-2025
Revised on: 22-02-2025
Accepted on: 11-03-2025

Abstract

Tanacetum parthenium (feverfew) is a traditional medicinal herb widely used for its therapeutic properties, particularly in the prevention and management of migraines. This review explores the botanical characteristics, phytochemical composition, pharmacological activities, and therapeutic applications of T. parthenium. Its bioactive compounds, parthenolide, exhibit potent anti-inflammatory, antioxidant, and antimicrobial properties, making it a promising agent for managing a variety of chronic conditions, including arthritis, neurodegenerative diseases, and cancer. The mechanisms of action involve modulation of inflammatory pathways, inhibition of prostaglandin synthesis, and reduction of oxidative stress. Despite its potential, challenges such as variability in chemical composition, safety concerns, and limited clinical trials hinder its integration into mainstream medicine. Future research should focus on standardizing formulations, conducting clinical trials, and exploring novel therapeutic applications. This review underscores the importance of T. parthenium as a versatile herbal remedy with significant potential in modern healthcare, provided its limitations are addressed.

Keywords: Tanacetum parthenium, Anti-inflammatory, Migraine, antioxidant, Microbial Degradation.

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DOI: https://doi.org/10.46956/ijihd.v10i1.674

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Introduction

Feverfew (Tanacetum parth enium*L.*) belonging to the family Asteraceae (daisies) is a daisy- like perennial plant found commonly in gardens and along roadsides. The name stems from the Latin word febrifugia, "fever reducer." The first-century Greek physician. Dioscorides prescribed feverfew for "all hot inflammations." Also known as "featherfew," because of its feathery leaves. It is a short, bushy, aromatic perennial that grows 0.3–1 m in height. Its yellow-green leaves are usually less than 8 cm in length, almost hairless, and pinnate-bipinnate (chrysanthemum-like). Its yellow flowers bloom from July to October, are about 2 cm in diameter. They resemble those of chamomile (Matricaria chamomilla*)*, for which they are sometimes confused, and have a single layer of white outer-ray florets. This aromatic plant gives off a strong and bitter odor. Its yellow-green leaves are alternate (in other words the leaves grow on both sides of the stem at alternating levels), and turn downward with short hairs. The small, daisy-like yellow flowers are arranged in a dense flat- topped cluster fig-1[1].

Figure 1. Feverfew (Tanacetum parthenium): Whole plant (a), flower (b), and feathery leaves(c) [1]

Increasing the number of antibiotic resistance bacteria has led to a demand for new agents that could be used to decrease the prevalence of bacterial diseases (Lis-Balchin & Deans, 1997). Available evidences show that essential oils extracted from plants could be employed as antimicrobial agents in food systems (Sefidkon & Ahmadi, 2000). Recently, screening for new plants with antibacterial activity has been the subject of many investigations since their essential oils with antibacterial activity could be the promising agents for this purpose (Dorman & Deans, 2000; Imelouane et al., 2009). Feverfew (Tanacetum parthenium L.) is a perennial herbaceous essential oil-bearing plant belongs to Asteraceae family. The species of genus Tanacetum have been used as medicinal plants for over 2000 years (Omidbeigi, 2007). Interest in the genus has been stimulated by its biological activities, particularly as insect antifeedants, antitumor and antimicrobial activities due to its sesquiterpenoid constituents (Burt, 2004). This genus has been found in different regions of many countries including Iran, Anatolia, Jordan, Iraq, Turkey, Afghanistan and Pakistan (Awang, 2000).

Feverfew is an aromatic plant with about 65 cm height, white inflorescence and achene fruit that grows in stony slopes and river beds (Mozaffarian, 1996; Rechinger, 2002). Tanacetum species contain sesquiterpenoids and flavonoids mainly, whereas the other terpenoids and phenolic compounds are rarely found in these plants (Bernath, 2000). Sesquiterpenoids as the main constituents of the genus, supposed to be the bioactive principles of plants. Flavonoid and essential oils are also pointed out as active substances in some species. Oil composition of T. parthenium, T. argyrophyllum, T. aucheranum and T. chiliophyllum has previously been reported. However, to the best of our knowledge no biological assays of feverfew have so far been performed [2].

History

Historically, the plant has been placed into 5 different genera, thus some controversy exists as to which genus the plant belongs. Former botanical names include: Chrysanthemum parthenium (L.) Bernh., Leucanthemum parthenium (L.) Gren and Gordon, Pyrethrum parthenium (L.) Bernh, and *Matricaria parthenium* (L.). It has been alternately described as a member of the genus *Matricaria*.

The ancient Greeks called the herb "Parthenium," supposedly because it was used medicinally to save the life of someone who had fallen from the Parthenon during its construction in the 5th century BC. The first-century Greek physician Dioscorides used feverfew as an antipyretic. Feverfew also was known as "medieval aspirin" or the "aspirin" of the 18th century [3-10].

The plant has been used to treat arthritis, asthma, constipation, dermatitis, earache, fever, headache, inflammatory conditions, insect bites, labor, menstrual disorders, potential miscarriage, psoriasis, spasms, stomach ache, swelling, tinnitus, toothache, vertigo, and worms. Feverfew also has been used as an abortifacient, as an insecticide, and for treating coughs and colds. Traditionally, the herb has been used as an antipyretic, from which its common name is derived [11].

In Central and South America, the plant has been used to treat a variety of disorders. The Kallaway Indians of the Andes Mountains value its use for treating colic, kidney pain, morning sickness, and stomach ache. Costa Ricans use a decoction of the herb to aid digestion, as a cardiotonic, an emmenagogue, and as an enema for worms. In Mexico, it is used as an antispasmodic and as a tonic to regulate menstruation. In Venezuela, it is used for treating earaches.

The leaves are ingested fresh or dried, with a typical daily dose of 2–3 leaves. The bitterness is often sweetened before ingestion. Feverfew also has been planted around houses to purify the air because of its strong, lasting odor, and a tincture of its blossoms is used as an insect repellant and balm for bites. It has been used as an antidote for overindulgence in opium [12].

Ancient uses

The ancient medical applications of feverfew have been characterised broadly improve three main groups: Treatment for fever and headache use in cases of difficulties in labor, threatened miscarriage, and regulation of menstruation; and relief of stomach ache, tooth ache and insect bites. Recording too Thach, Charles Estienne declares. Stampt and applied on to teeth or ear and site that aketh. It wholly swassaaegth the pain on the teeth [13].

Modern uses

Feverfew is currently widly used to mitigate migraine attacks as a palliative in ardhritis and for the treatment of psoriasis however hhile is a climate that since the 16th century, feverfew has been used by more people in the u.k. for arthrites then for migraine most for the reached attention has been for caused on the later condition (see later).the beamitic upsurge of interest in feverfew from migraine occurred following newspaper accountants of for able responses in sufferes those conditions was restrictions to conventional medicinal. In the stimulations for this burgeoning attention was experiments of anngenkins, a doctor wife who id 1973 at age 68. Upon the suggestion on elder father of a friend of her friend had experimenting with feverfew. The world gentleman integestngly enough had found feverfew helpful

in treating is arthrtise. After increasing those from one small three. After five months. The vomiting associated with the migraine attacks supported [14].

Botanical Description

- Kingdom: *Plantae* (Plants)
- Subkingdom: *Trachiobionta* (Vascular plants)
- Super division: *Spermatophyta* (Seed plants)
- Division: *Mangliophyta* (Flowering plants)
- Class: *Magnoliopsida* (Dicotyledons)
- Subclass: *Asteridae*
- Order: *Asterales*
- Family: *Asteraceae* (Aster family)
- Genus: *Tanacetum* (tansy)
- Species: *Tanacetum parthenium* (feverfew)

Morphological Characteristics

- **Size**: A small bush that can grow up to 70 cm (28 in) high.
- **Leaves**: Light yellowish green, fern-like, and have a strong scent.
- **Flowers**: Daisy-like to rounded balls, with white to creamy outer petal rays and a button-like yellow centre.
- **Stem**: Straight with longitudinal grooves in brown-red colour.
- **Root**: Short and direct.
- **Fruit**: Achene fruit.
- **Habitat**: Grows in stony slopes and river beds.
- **Spread**: Spreads rapidly by seed and can cover a wide area after a few years.

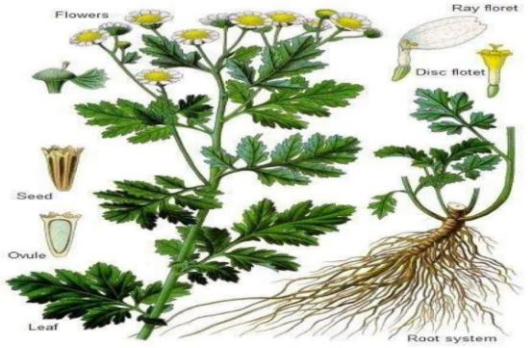

Figure 2: Morphological characteristics of Tanacetum Parthenium [1]

Chemical Composition

The essential oils isolated from Tanacetum species have variable chemical constituents. Chemo variation is a well-known fact in Tanacetum species which is encountered on species level, and on subspecies level. The main chemical constituents reported in the essential oils of Tanacetum were camphor, bornyl acetate, α–phellandrene, chrysanthenyl acetate, α – terpinene, p-cymene, terpinene-4-ol, α–terpineol, verbenone, α-phellandrene, α-terpinene, tetradecane, caryophyllene oxide. α thujene, α-pinene, camphene, β-pinene, p-cymene, limonene, γ-terpinene, benzaldehyde, sabinene, pinocarvone, borneol myrtenal, β-caryophyllene, humulene epoxide-i, (e)-lavandulyl acetate, spathulenol, (e) sesquilavandulol, thymol, carvacrol, α-cadinol, cis- α-trans-bergamotene acetate, decanoic acid, caryophylla-2(12),6(13)-dien-5-ol (caryophylladienol-ii), pentacosaneheptacosane, hexadecanoic acid, monoterpene hydrocarbons, sesquiterpene hydrocarbons, oxygenated monoterpenes, and oxygenated sesquiterpenes in the essential oil of T. argentums [15].

Phytochemical Properties

A variety of metabolites have been identified from different parts of the feverfew plant. The most extensively studied classes of phytochemicals found in feverfew include sesquiterpene lactones and flavonoids. Additionally, other compounds present in the plant belong to phytosterols, triterpenoids, fatty acids, phenolic acids, and essential oils.

Sesquiterpene Lactones

Sesquiterpene lactones are a class of sesquiterpenoids that contain a lactone ring. Sesquiterpene lactones are the most important secondary metabolites of feverfew. Based on the chemical ring structures, these compounds are classified mainly into eudesmanolides, germacranolides, and guaianolides. Parthenolide, a germacranolide, is the major sesquiterepene lactone of this plant, composed of up to 85% of the total sesquiterpene. Several sesquiterpene lactones fig 3have been identified and reported, including artecanin, artemorin, balchanin, canin, costunolide, 11,13-dehydrocompressanolide, estafiatin, epoxysantamarin, 3,4-β-epoxy-8-deoxycumambrin B, 1-β-hydroxyarbusculin, 3-β-hydroxycostunolide, 3-β-hydroxyparthenolide, 3-β-hydroxy-anhydroverlotorin, hydroxypelenolide, parthenolide, peroxyparthenolide, reynosin, ridentin, secotanapartholide A, secotanapartholide B, santamarine, tanaphartolide A, tanacetin, manolialide, and tanaparthin-α-peroxide [16].

Pharmacological Properties

Anti-inflammatory Activity

Anti-inflammatory activity has also been reported in some species of Tanacetum. T. microphyllum was useful in treating various inflammatory disorders. T. vulgare extracts have been shown to inhibit carrageenan -induced rat paw edema. The inflammatory activity has also been reported for T. vulgare and T. larvatum. In a human polymorphonuclear leukocytes based bioassay, it was observed that some species of Tanacetum such as T. vulgare, T. ptarmiciflorum, T. parthenium, and T. niveum, inhibited phorbol myristate induced chemiluminescence of human polymorphonuclear leukocyte. Anti-inflammatory activity of Tanacetum is attributed to its parthenolide contents that impair platelet activation in human blood. However, some other compounds such as flavonoids present in the plant may cause anti-inflammatory effect [17-19].

Antioxidant Activity

Tanacetum products are widely used in health food as food preservatives, while tansy extracts can be effectively used as antioxidant in rapeseed oil [20].

Antimicrobial Activity

The results exhibited that the total oils of Tanacetum balsamita possess moderate antimicrobial activities against all the tested microorganisms. T. parthenium has been reported for anti bacterial and anti-fungal activities. Antimicrobial activity has been reported of the essential oilsisolated from T. parthenium, T. vulgare, T. corymbosum, T. macrophyllum, and T. cilicium [21].

Antibacterial Activity

The parthenolide present in the T. parthenium plant leaves and seeds has been found active against gram positive bacteria, yeast and filamentous fungi. The sesquiterpene lactones, tanargyrolide, tabulin, iso special form, 8-α-hydroxy anhydroverlotorin, tanacchin, a germacranolide with 1,5- ether linkage and dentatin A, isolated from T. var. argyrophyllum exhibited bactericidal effects against Staphylococcus aureus, and Escherichia coli [22].

Anticancer Activity

Tanacetum species such as feverfew (T. parthenium) and its major constituents, parthenolide, sesquiterpene lactones have exhibited anticancer activity against cells derived from human carcinoma of the nasopharynx (KB). Furthermore, parthenolide was shown to inhibited DNA synthesis in HeLa cell lines and it was suggested that the anti-tumour activity occurs at the DNA replication level, probably by interfering with the DNA template. The cytotoxic effect of parthenolide occurs due to its action, such as serotonin release inhibition, protein tyrosine kinase, and protein kinase C inhibition, these enzymes have very important role in various aspects of cell cycling. Other species such as T. densum ssp. Sivasicum, T. argentums Sp. Argenteum, and T. praeterium Sp. Praeterium also possess cytotoxic activity. The cytotoxic effect of Tanacetum is believed to occur due to its sesquiterpene lactones contents that showed cytotoxic activity against human cell lung carcinoma and the human colorectal cell lines [23].

Feverfew's Medicinal and Therapeutic Properties

Migraine

Several clinical trials have been conducted on the migraine prophylactic effect of feverfew and its bioactive components, especially parthenolide. Based on a randomized double-blind placebo-controlled clinical trial, the frequency and severity of migraine attacks were reduced in patients who took a capsule of dried feverfew leaves (2.19µmol parthenolide/dose) once a day. In another double-blind, randomized, placebo-controlled clinical study, patients who consumed capsules containing 6.25 mg of MIG-99, a CO2 extract of feverfew, experienced the highest level of benefit compared to those in the groups taking capsules with 2.08 mg and 18.75 mg. Moreover, the headache intensity and pain frequency were reduced in children who suffered from migraine and tension-type headaches after taking a nutraceutical formulation containing feverfew, *Andrographis paniculata*, CoQ10, riboflavin, and magnesium [24].

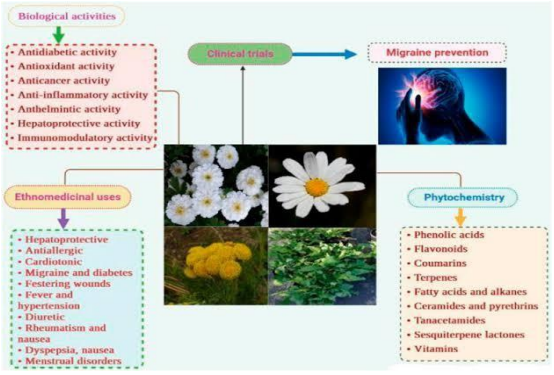

Figure 3: Properties of Tanacetum Parthenium.

Anxiety and Depression

Based on an in vivo study conducted by Cárdenas et al., the aqueous extract of *T. parthenium* demonstrated significant anxiolytic and antidepressant effects. Anxiolytic effects were observed in the Burying Behavior Test (BBT), where *T. parthenium* at doses of 5, 10, and 20 mg/kg reduced burying behavior and increased latency, akin to the results produced by Diazepam at 0.5 mg/kg. In the Elevated plus Maze Test (PMT), *T. parthenium* showed anxiolytic effects by increasing the time spent in open arms at doses of 0.5, 1, 5, and 10 mg/kg, similar to standard drugs such as Diazepam and Alprazolam. These findings suggest that *T. parthenium* has potential therapeutic benefits in anxiety and depression, possibly mediated through the GABAergic system. The study supports the traditional use of *T. parthenium* and highlights its promise in addressing anxiety and depression disorders, providing valuable insights for its further exploration in therapeutic applications [25, 26].

Skin Disorders

There is a general belief that feverfew could protect skin against various environmental factors, such as ultraviolet irradiation. The skin protection of parthenolide-depleted extract of feverfew against UV was confirmed by both in vitro and in vivo tests. This study also showed that this extract holds radical scavenging activity against free radicals. An in vitro study suggested that feverfew can be a part of cosmetic products. This study showed that feverfew's sesquiterpene lactones inhibit melanin biosynthesis through the down regulation of tyrosinase expression in mouse B16 melanoma cells [27].

Mechanisms of Action

A proposed mechanism of action involves parthenolide specifically binding to and inhibiting IκB kinase complex (IKK) β. IKKβ plays an important role in pro-inflammatory cytokine- mediated signaling.

Inhibition of prostaglandin and serotonin release

Inhibition was irreversible and the effect was not caused by cytotoxicity. Studies have shown that lipophilic compounds other than parthenolide may be associated with anti-inflammatory activity, particularly with reducing human neutrophil oxidative burst activity [28]. Tanetin, a lipophilic flavonoid found in the leaf, flower, and seed of feverfew, blocks prostaglandin synthesis. Aqueous extracts do not contribute to feverfew's anti-inflammatory activity, but do prevent the release of arachidonic acid and inhibit in vitro aggregation of platelets stimulated by adenosine 5″-diphosphate (ADP) or thrombin. Whether or not these extracts block the synthesis of thromboxane, a prostaglandin involved in platelet aggregation, is controversial. Results suggest that feverfew's inhibition of prostaglandin synthesis differs in mechanism from that of the salicylates [29].

Methods of Extraction

Extraction methods to obtain plants' secondary metabolites have attracted much interest during the last decades. Special consideration has been given in finding innovative techniques of extraction which are green, that minimize organic solvent volume, as well as time of the process. From these specifications, extraction techniques which involves a

microwave system (to decrease extraction time), ultrasound (to decrease the use of organic solvent), and a pressurized liquid system (to decrease both extraction time and amount of organic solvent used) have been developed. Five extraction approaches (ultrasound-UAE, microwave-MAE and accelerated-ASE extractions, maceration and Soxhlet) have been used to prepare extracts from *T. parthenium*. The obtained extracts were compared in order to highlight any difference in their chemical profiles and bioactivities [30, 31].

Common Method of Preparation

Feverfew plants grown on an irrigated field near Outlook, Saskatchewan were harvested at full-bloom. The manually cut plants were kept in black polyethylene bags and transferred to a cooler before transport to the laboratory in Saskatoon, Saskatchewan where the plants were kept in a 4°C refrigerator. To conduct an experiment, a random sample of plants was removed from a bag. Leaves were separated from the plants wide and approximately 20 mm deep to form a thin layer [32].

Figure 1 shows a schematic diagram of the thin-layer drying equipment. The dryer consisted of a fan that blew atmospheric air through ducts fitted with valves, an air conditioning unit, heaters, and a drying chamber with a sample holder resting on a digital electronic balance. The air relative humidity was not controlled. A grid of five thermocouples (one at each of the four corners and one in the middle) placed upstream, immediately after the air flow atraighteners, and downstream, immediately after the sample, measured drying-air temperature. An infrared temperature sensor was used to measure the surface temperature of the samples during each drying experiment, while a pitot tube was used to measure air velocity before flowing through the sample. The logged data were stored in a personal computer [33].

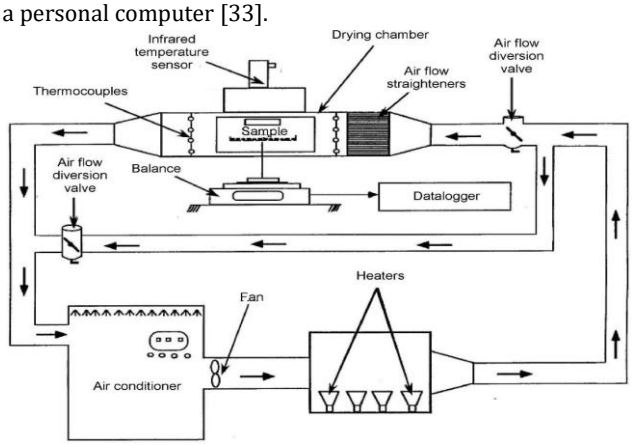

Figure 4: Schematic diagram of thin-layer drying equipment.

Dosage

Pediatric

Feverfew should not be used in children younger than 2 years. In older children, adjust the recommended adult dose to account for the child's weight. Most herbal dosages for adults are calculated on the basis of an average of 150 lb (70 kg) adult. Therefore, if the child weighs 50 lb (20–25 kg), the appropriate dose of feverfew for this child would be 1/3 of the adult dosage.

Adult

For migraine headaches: Take 100–300 mg, up to 4 times daily, standardized to contain 0.2– 0.4% parthenolides. Feverfew may be used to prevent or to stop a migraine headache. Feverfew supplements may also be CO_2 extracted. For these, take 6.25 mg, 3 times daily, for up to 16 weeks. For inflammatory conditions (such as arthritis): 60-120 drops, 2 times daily of a 1:1 w/v fluid extract, or 60-120 drops twice a day of 1:5 w/v tincture [34].

Safety, Toxicity, and Adverse Effects of Feverfew

Drug interactions with feverfew are not well documented, but there is a potential for interactions when it is coadministered with substances such as anticoagulants, antiplatelet agents, nonsteroidal anti-inflammatory drugs (NSAIDs), salicylates, or thrombolytic agents [35]. Feverfew should not be used in individuals who have allergies to other plants in the Asteraceae family, including aster, chamomile, chrysanthemum, ragweed, sunflower, tansy, and yarrow. Given its potential antiplatelet effects, it is advised against using it in patients who are undergoing surgery [36].

Conclusion

Tanacetum parthenium (feverfew) is a valuable medicinal herb with a rich history of use in traditional medicine and significant potential for modern therapeutic applications. Its diverse pharmacological properties, particularly its anti-inflammatory, antioxidant, and antimicrobial effects, make it a promising candidate for managing chronic conditions such as migraines, arthritis, and neurodegenerative diseases. There are several sesquiterpene lactones in T. parthenium (L.), with a larger concentration of parthenolide polar and lipophilic. In the flower heads and leaves are flavonoids. In addition, the roots of the plant have high concentrations of triterpenes and sterols. Feverfew is also used as a vermifuge and laxative, as well as a spasmolytic for colic, colitis, and griping. Feverfew has been evaluated for numerous therapeutic applications, notably for managing neurological disorders and cancers. Moreover, it has a positive impact on the management of inflammatory diseases, such as asthma, ulcerative colitis, and endometriosis. Future studies should delve into the synergistic effects of *T. parthenium*'s bioactive components on specific signaling pathways. More exploration of additional signaling pathways beyond NF-κB, MAPK, and Akt could unveil novel molecular targets for drug development. With due consideration further plant's beneficial properties, it can be recommended as a secure, crucial medicinal herb for all of humanity.

Funding

Nil

Acknowledgement

Authors are thankful to the management of Ratnam Institute of Pharmacy.

Conflict of Interest

No Conflict of interest

Informed Consent and Ethical Statement

Not Applicable.

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