REVIEW ARTICLE

The Genus *Tanacetum*: A Comprehensive Review

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ABSTRACT

The genus *Tanacetum* belongs to the family compositae or asteraceae. The literature review sheds light on medicinal, herbicidal and disinfectant properties of *Tanacetum* species of flowering plants through effective isolation of ecologically significant essential oils. Species of *Tanacetum* have been used as therapies in traditional medicine since early times throughout the world. Hydro distillation and the microwave-assisted process have been utilized to isolate volatile oils, ethyl esters and other derivatives from herbaceous plants of *Tanacetum*. The literature review of phytochemical studies on different *Tanacetum* species revealed many chemical constituents. *Tanacetum* species have traditionally been used to manufacture cosmetics, dyes, preservatives, insecticides, medicines, and herbal remedies. Attention is increasing in species of *Tanacetum* due to its essential oils, bioactive compounds like the presence of sesquiterpene lactones, and bitter substances, which have been exhibited in biological activities like growth-regulating, cytotoxicity, anti-microbial activity, anti-viral activity, and anti-cancer activity etc. This also discusses the impact of fluctuating environmental conditions, especially greenhouse conditions, on concentrations of potent secondary metabolites like parthenolide and flavonoid derivate. The genus is grown extensively in many parts of the globe. Its importance as a medicinal plant is expanding rapidly, with more robust findings confirming its wide range of medicinal applications.

Keywords: Anti-cancer, Flavonoids, Hybridisation, *Tanacetum*, Tansy.

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INTRODUCTION

Therapeutic advantages of plant extracts have been known since ancient times; however, lack of proper scientific technologies prevented optimal utilization of medicinal plant extracts. In the current era, scientific and technical advancements have made proficient sequestration of medicinal plant components.[1] This review focuses on the medicinal properties of flowering plants belonging to *Tanacetum,* predominant in the northern hemispheres. *Tanacetum parthenium,* commonly known as feverfew, a species under the specified genus, has been identified as a potent anti-inflammatory agent due to the significant component parthenolide (PRT), a sesquiterpene lactone. Leaves of feverfew have been proven to significantly alleviate migraines and act as a natural pain-killer to help painful periods. Scientific research shows that fluctuating environmental conditions influence the concentration of this secondary metabolite in *T. parthenium*. The increased concentration of PRT has been observed in plants with a reduced water supply and immediately exposed to sunlight before harvest. Hence, greenhouse conditions of plant cultivation aid in regulating the phytochemical composition of plants belonging to the Asteraceae family. Another crucial secondary metabolite influencing cell-cycle progression is phenol components of *T. parthenium*.[2] Manipulating environmental conditions observed elevated levels of phenol contents on administering ultraviolet light. Hence, both parthenolide and phenol components are regulated by changing ecological conditions. Essential oils sequestered from this family of flowering plants have been proven to have been tested for medicinal values. Hence, this review article focuses on varied isolation techniques, namely distillation by water which allows effective isolation of volatile oils. Post isolation, spectroscopic techniques, namely nuclear magnetic resonance (NMR) and mass spectroscopy, are implemented to chemically analyze the composition of these bio-essential oils derived from flowering plants of *Tanacetum*. Chromatography techniques to separate these essential oils' biochemicals will be discussed.[3] Ether extracts of *T. santalinoides* and its integral oil derivatives subjected to both gas chromatography and mass spectroscopy led to the practical chemical analysis of constituent bio-chemicals. Thymol, the main component of the plant, as mentioned earlier, and its anti-microbial property

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will be discussed in this review article. Non-steroidal drugs for treating inflammation have been reported to cause side effects such as stomach ulcers and increased risk of high blood pressure.[4] Hence, the advantages of plant-based anti-inflammatory components will be discussed in this review paper. Furthermore, the therapeutic benefit of plant-derived medicinal components over synthetic drugs is illustrated in this study. This research review presents specific experiments with bacterial strains that highlight th e anti-fungal properties of these secondary metabolites.

Botanical Classification of *Tanacetum*

Tanacetum refers to a genus of 160 flowering plant species belonging to the aster family. These plants have been proven to have medicinal significance and might act as better alternatives to synthetic drugs that often cause detrimental health effects.
Kingdom: Plantae (Plants)
Subkingdom: Trachiobionta (Vascular plants)
Superdivision: Spermatophyta (Seed plants)
Division: Magnoliophyta (Flowering plants)
Class: Magnoliopsida (Dicotyledons)
Subclass: Asteridae (Sympetalous)
Order: Asterales (Flowers made up of florets)
Family: Asteraceae (Aster family)
Genus: Tanacetum (Tansy)

HABITAT

These perennial herbaceous plants are native to north temperate zones. However, common tansy with the scientific abbreviation of *T. vulgare* is considered an exotic species as it may thrive in regions outside its native habitat. *T. camphoratum* is a species belonging to aster family and is native to the Pacific Ocean of North America, extending from British Columbia to California. *T. vulgare* occurs predominantly in Canada and the United States. *T. parthenium* occurs in mountain shrubs and slopes and might grow as weeds of gardens and waste places. *T. balsamita* is native to the eastern regions of North America. Blue tansy or *T. annuum* thrives in the Mediterranean region and is majorly cultivated in Morocco.[5]

History

Flowering plants belonging to the Tanacetum genus contain certain biochemical constituents in the volatile oils derived mainly from aerial parts traditionally used to treat migraines, fever, infertility, and aid relief to women during childbirth.[6]

ESSENTIAL OILS

These are concentrated non-polar, water repellent liquids mainly composed of volatile chemical compounds obtained from plants. These plant-derived hydrophobic liquids are primarily composed of terpenes.[7]

Method of Isolation

Hydro-distillation

Hydro-distillation is a conventional method of extracting bioactive compounds and other secondary metabolites in plants. Three primary physiochemical processes involved are hydro-diffusion, followed by hydrolysis, in which bonds between molecules are broken with the liberation of the water molecule (Figure 1). The final step is decomposition by heat supply; the solvents used are inorganic. This isolation process is conducted before the dehydration of plant components.[8]

Direct Steam Distillation

This isolation technique introduces crude plant extracts in distillation flasks, and the stem is passed through the plant extract. Volatile oil content is passed through a water condenser and steam and sequestered into collection flasks.[1]

Microwave-assisted Process (MAP)

This extraction process involves utilizing microwave energy for heating solvents in contact with affluent plant parts. Thus, the aid of the heated solvent to separate measurable components from crude extracts isolates volatile oils from other constituents of plants. This isolation method of plant extracts and essential oils aids to effectively sequestering bioactive compounds and determining their penitential in treating inflammation and curing bacterial and fungal infections.[1]

Pharmacological Investigation

Anti-oxidant Activity

Hydro distillation techniques were adopted to isolate volatile oils from aerial parts of *T. cilicicum*. The anti-oxidant property of essential oils was determined by ferric reducing antioxidant power (FRAP) and radical scavenging assays that increase immune responses and alleviates the risk of degenerative diseases. The ability of essential oils to reduce ferrous to ferric ions at low pH levels aids in evaluating the potential radical scavenging capability of anti-oxidants. Furthermore, the skills of essential oils to act as potent hydrogen donors are tested through the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method. The ability of plant derivatives to donate hydrogen to diphenyl picrylhydrazyl gives a measure of its anti-oxidant property.[9]

The anti-oxidants are the type of compounds that inhibit oxidation. It has been identified that oxidation mainly occurs when the chemical reaction produces free radicals by leading

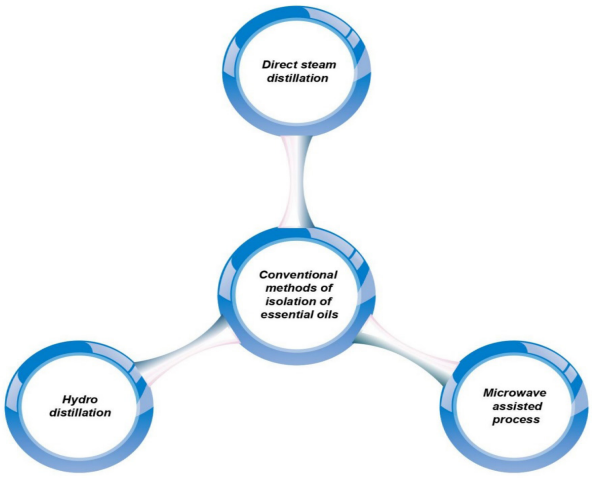

Figure 1: Conventional methods of isolation of essential oils from the genus *Tanacetum*

the chain reactions that can damage the cells of organisms. Moreover, anti-oxidants like thiols or ascorbic acid can eliminate the chain reactions for producing more oxides.[10]

In addition, cell reinforcements are the sort of mixes that repress oxidation. The cell reinforcements like thiols or ascorbic corrosive can also dispense with the chain responses for creating more oxides.[11] In nutrition science, it is seen as a substance, when present at low obsessions appeared differently about those of an oxidizable substrate decreases or prevented the adverse effects of responsive species, for instance, free oxygen and nitrogen species or average physiological limits in humans (Figure 2).[12]

Anti-bacterial Activity

Essential oils were sequestered from aerial parts of *T. santolinoides and* were analyzed to contain Thymol as a major biochemical component by gas–liquid chromatography (GLC) and mass spectrometry (MS) techniques. *In-vitro* assays were conducted to confirm the anti-microbial properties of plant extracts. They could inhibit the growth of bacterial cultures, namely *Escherichia coli* and *Bacillus subtilis,* thus acting as a potent germicide. Extracts of *T. aucheranum* and *T. chiliophyllum* have been proved to work against thirty-three strains of bacteria by inhibiting their essential metabolic pathways that prevent bacterial reproduction and growth. Cell cycle inhibition is another powerful method of destroying pathogenic bacteria and alleviating various pathological diseases. Extracts of *T. balsamita*, when analyzed by a combination of spectroscopy and chromatographic techniques, have proven to be majorly composed of β-thujone, which on conducting in-vitro assays have shown potent anti-bacterial properties by cell cycle inhibition of eight strains of gram-positive and gram-negative bacteria, including *B. subtilis* and *Escherichia coli,* respectively (Table 1 and Figure 2).[13]

Anti-Leishmann Activity

Plant extracts of *T. parthenium* have been proven to inhibit the growth of *Leishmann's amazorensis*. Proton nuclear magnetic resonance imaging analyzed the presence of PRT as a significant component of plant extracts. *In-vitro* assays showed PRT to act against the promastigote form of *L. amazonensis* by 50% reduction of survival index of the parasite through inhibition of cell growth.[14]

Figure 2: Pharmacological activity shown by the genus '*Tanacetum*'

Anti-microbial Activity

Plant extracts isolated from *T. santolinoides* have been confirmed to act as potent anti-microbial agents by conducting in vitro experiments to test the effect of these metabolites on the growth phase of pathogenic yeast *C. albicans* on the administration of these bioactive compounds inhibition of cell cycle of pathogenic yeasts were observed. The cell fortresses are the sort of mixes that smother oxidation. It has been seen that oxidation by and significant happens when the mixed response passes on free radicals by driving the chain responses, which can hurt creatures' cells. Moreover, the cell strongholds like thiols or ascorbic damaging can renounce the chain responses for making more oxides.[15]

Anti-viral Activity

Essential oils isolated by chromatic and spectroscopic techniques have been proven to inhibit metabolic pathways of viruses that might cause serious health problems in mammals and other warm-blooded animals. Inhibiting potent viral growth without causing any side effects makes these plants derivate to act as better alternatives to synthetic anti-viral agents and may help provide effective treatment to humans affected by viral diseases.[16]

Anti-cancer Property

Chronic inflammation is a hallmark of cancer as the prolonged action of immune cells may target the body's healthy cells, thereby elevating autoimmune disorders. Plant extracts and metabolites are obtained from perennial herbaceous plants of the *Asteraceae* family. *T. parthenium* constitutes a secondary metabolite, namely PRT, that aids to effectively treating migraines and provides relief from painful periods.[16] Ethyl acetate esters of *T. cilicium* act as anti-inflammatory agents that are a commercial alternative to non-steroidal synthetic drugs as these synthetic drugs increase the chances of severe health complications like stomach ulcers and severe chronic heart disease. Such effective anti-inflammatory substances help alleviate heart diseases and mitigate the risk of cancer.[17]

DISCUSSION

Crude extracts and essential oil derivatives of *Tanacetum* flower plants were isolated through processes like MAP (microwave-assisted function), distillation in water, or direct steam distillation methods. Chemical analysis through TLC (Thin layer chromatography) and a combination of gas chromatography and mass spectroscopy techniques led to determining major therapeutic constituents of plant derivatives (Table 2).

T. santolinoides (DC.) has been proven to act as a medicinal plant due to the anti-microbial property of its hexane ether

Table 1: Compounds isolated from different species of the genus *Tanacetum*.

Name of Plant	*Part of Plant*	*Isolated compound*	*Significance*
T. parthenium	Aerial leaves	Apigenin and luteolin	Inhibition of arachidonate metabolic pathways in immune cells[5].
T. santolinoides	Aerial stalks, leaves and stems	Thymol (18%), Trans-thujone (17.5%)	Anti-microbial activity against *Bacillus subtilis*, *E. coli* and *Candida albicans*[18].
Sexual hybrids of *T. parthenium and T. vulgare*	Aerial leaves	Parthenolide (PRT)	Inhibition of polymorph nuclear leucocyts in humans[1].
T. vulgare	Aerial stalks, leaves and stems	Methyl esters	Anthelminthic activity against trematode adult flatworms[10].
T. balsamita	Aerial stalks, leaves and stems	B-Thujone, 1,8-cineole and α-thujone	Anti-microbial action against both gram-positive and gram-negative bacteria and fungi[12].
T. cinerariifolium	Flower heads	Pyrethrin	Insecticides that are non-toxic to mammals and other warm blooded animals[21].
T. microphyllum	Aerial stalks, leaves and stems	Carbomethoxy flavonol, centaureiden	Anti-inflammatory activity by specifically exhibiting anti-edema activity[2].
T. parthenium	Aerial leaves, stalks and stems	Parthenolide	Anti-leishmann and anti-microbial activity[21].

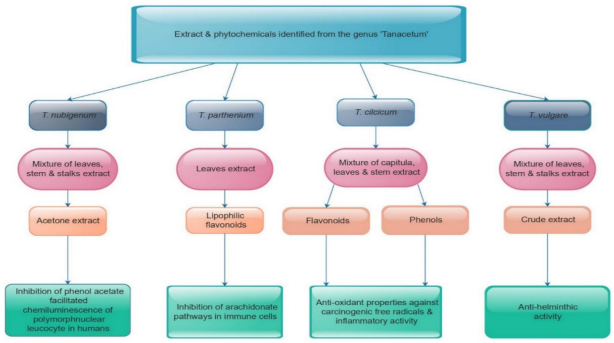

Figure 3: Extract and phytochemical identified from the genus '*Tanacetum*'[1,5,10,20]

extracts and essential oils derived from aerial parts of the plant. Capillary GLC techniques and MS were utilized to analyze its chemical components. Thirty components were identified as the biochemical constituents of volatile oils. The significant component placed was thymol, followed by trans-thujone. Chemical analysis of the ether extracts identified similar components as that of volatile oils in addition to palmitic acid and its esters. *In-vitro* studies conducted with essential oils showed anti-microbial activity of specified plant derivatives against gram-negative bacteria *E. coli* along with anti-microbial action against gram-positive bacteria *Bacillus subtilis* and pathogenic yeast, *Candida albicans* (Figure 4 and Table 1).[18]

Parthenolide is present in the highest concentration in *T. parthenium* and *T. vulgare* as per data obtained through NMR studies. Studies have shown that *T. parthenium* can significantly alleviate migraines and provide relief from painful periods, highlighting its anti-inflammatory property. As per chemical, analysis, feverfew contains 38% of specified bio-active compounds in its flower tips and 0.98% in its leaves.[16]

Recent scientific studies reviewed in this study have identified increased concentration of Parthenolide in *T. larvatum*, making it a new commercial source of this specified germacranolide.

Plant metabolites, flavonoids constituting T. parthenium and T. vulgare, are pharmacologically tested to inhibit crucial metabolic pathways of arachidonic acid in leukocytes. NMR studies confirm the biochemical structure of methyl esters of *T. parthenium*. The biophysical technique determines two significant components: apigenin and luteolin, common in vascular flavonoids of the two species of *Tanacetum* plants.[4]

T. argyrophyllum has been observed as having both anti-inflammatory and anti-microbial activity due to the therapeutic potentials of its volatile oil extracts α-Thujone is a significant component of *T. argyrophyllum* var. *argyrophyllum*. *T. cilicicum* has been subjected to *in-vitro* analysis by isolating its various extracts that have shown anti-oxidant activity by conducting specific assays like 'radical scavenging potential' assays. Lipoxygenase inhibiting quantitative and qualitative assays lead to analyzing the anti-inflammation properties of mentioned flowering plants. Furthermore, 'ferric-reducing power' assays highlighted maximum anti-oxidant potentials of ethyl acetate extracts isolated for capitula of plants. Thus both radical scavenging and ferric reduction power assays led to identifying ethyl esters of the plant capitula to act as a significant source of anti-inflammatory and anti-oxidant compounds.

The *in-vitro* assay has determined that the leaf extracts of sexual hybrids inhibit human immune cells called polymorph nuclear leukocytes despite constituting only trace amounts of parthenolide. This pharmacological analysis defines that parthenolide is not the sole metabolite responsible for all vital pharmacological activities of plants belonging to the genus *Tanacetum*.[19]

Essential oils isolated from aerial parts of *T. santolinoides* by hydro-distillation were subjected to capillary gas-liquid chromatographic separations and mass spectroscopy to separate and analyze the concentration of different biochemical constituents present in this species that are crucial to its medicinal properties. The chemical analysis led to identifying thirty biochemical components. Major constituents include Thymol (18%), trans-thujone (17.5%), 1, 8-cineole, and other

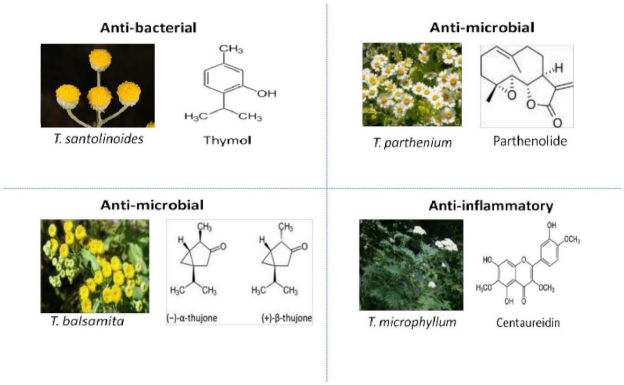

Figure 4: Pharmacological properties shown by the compounds isolated from the genus *Tanacetum* **(A)** Thymol, an anti-bacterial compound isolated from *T. santolinoides*[18]. **(B)** Parthenolide, an anti-microbial compound isolated from *T. parthenium*[21]. **(C)** Thujone, an anti-microbial compound isolated from *T. balsamita*[12]. **(D)** Centaureidin, an anti-inflammatory compound isolated from *T. microphyllum*[2].

constituents. When analyzed for their components, hexane-ether extracts produced a similar pattern of biochemical constituents. Ether extracts were analyzed to additionally constitute palmitic acid, its esters, sitosterol, and flavonoids. Volatile oils of feverfew have been proven to act as potent anti-microbial agents by inhibiting cultures' growth containing *E. coli, B. subtilis,* and *C. albicans*. Liquid chromatography was conducted under medium pressure conditions, and silica gel column chromatography was performed to yield two sesquiterpene lactones, one being parthenolide (principal component) and the other being douglanine.[18]

Quantitative analysis was conducted by performing Proton NMR spectroscopic experiments with internal standards as butylated hydroxytoluene (BHT).

Aerial parts of plants whose extracts were isolated include capitula, leaf, and steams. Comparing the concentration of essential metabolites in distinct aerial parts proved capitula to have the highest parthenolide and total phenolic content reserves. Hence, ethyl acetate extracts derived from capitula can be an effective commercial alternative to synthetic anti-inflammatory drugs and synthetic anti-oxidants.[20]

Research studies conducted on crude extracts and volatile oils derived from *T. vulgare* prove this plant to have a potent anthelmintic activity that provides effective treatment against schistosomiasis. Crude extracts are also isolated with similar distillation methods and are then subjected to chemical analysis through combined gas chromatography-mass spectrometry (GC-MS) techniques. β-Thujone has been identified as a significant biochemical constituent of *tansy*. This plant extracts act as potent vermifuges by decreasing the motor activity of adult worms. Optimal concentrations of 200 µg/mL of crude extracts have been proven to decrease the production of developed worm eggs and reduce reproductive rates of trematode flatworms. Confocal microscopic scanning techniques have been used to confirm the action of specified plant extracts on trematode worms.

T. microphyllum has been proven to be of medicinal value due to the anti-inflammatory function of two flavonoids that have been yielded from CH_2Cl_2 extract centaureidin and carbomethoxy flavonol are the two flavonoids that have anti-edema properties and thus aid to the mitigated risk of cancer by alleviating inflammation which is a 'hallmark of cancer' (Figure 4).

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