

Ethno medical uses of *Vitex trifolia* and *Vitex rotundifolia*: a review

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ABSTRACT

Vitex trifolia and *Vitex rotundifolia* are the two varieties from the *Vitex* genus (family Lamiaceae) that are especially notable for their ecological and therapeutic characteristics. *Vitex trifolia*, sometimes known as the "simple leaf chaste tree," is a tiny tree or shrub found in tropical and subtropical climates. *Vitex rotundifolia*, sometimes known as the "roundleaf chaste tree," is a creeping shrub found near coastlines, notably in Asia and the Pacific Islands. Both species are rich in bioactive compounds, including terpenoids, flavonoids, and iridoid glycosides, which have a variety of therapeutic applications. Because of powerful analgesic, anti-inflammatory, antibacterial, and antioxidant qualities, these herbs have been utilized for a very long time. These historic uses are supported by current pharmacological research, which indicates that it may be utilized to treat respiratory, cutaneous, and inflammatory conditions. *Vitex rotundifolia* is essential for stabilizing coastal dunes and reducing erosion, whereas *Vitex trifolia* encourages biodiversity in mixed forests. Despite their benefits, overharvesting and habitat destruction pose a threat to the sustainability of many species. Further studies should concentrate on sustainable manufacturing, finding new bioactive components, and creating standardized extracts for medical use.

Keywords: Vitex, antibacterial, anti-inflammatory, and antioxidant.

I. INTRODUCTION

Frequently cultivated in warm temperate and subtropical environments are approximately 250 species of vitex trees and shrubs. The species in question is *Vitex trifolia*, with a particular focus on the variant *simplicifolia*. *Vitex trifolia* is a small tree which primarily inhabits countries bordering the Pacific and Indian Oceans, and is classified as belonging to either the Lamiaceae or Verbenaceae family. This plant is also cultivated in gardens due to its vibrant blooms and application in time-honoured treatments. [1]

The alternative name "three leaflet Vitex" for this tree originates from its distinctive leaf arrangement, comprising three or sometimes five small leaflets that are attached at their bases, with the longest leaflet situated in the center. For many years, people have employed plants to alleviate or cure diseases. References to medicinal plants are frequently mentioned in the ancient Indian scriptures known as the

Vedas, which were composed between 3500 and 800 B.C. "Virikshayurveda" is an ancient text on traditional herbal medicine that pre-dates the Christian era. The ancient literature known as the "Rig Veda" was composed approximately 2000 B.C. [2]

Further pharmacological investigation has shown the substance to possess notable properties, including antioxidant, anti-inflammatory, liver protection, anticancer, anti-forgetting, antibacterial, antiviral, antimalarial, and muscle-relaxing effects. Research points to numerous health benefits linked to *V. trifolia* has been used in traditional medicine to treat a variety of ailments.[3]

In various traditional medical systems, all components of the *Vitex* species are utilized as medicinal remedies, with the leaves proving to be of particular value. The primary objective of this research was to investigate and contrast the antioxidant properties and total polyphenolic content of ethanolic extracts obtained from *V. negundo* and *V. trifolia* leaves through various antioxidant assessments.[4]

The genome sequence of *V. trifolia* is 154,444 base pairs long. The chloroplast DNA consists of a quadripartite circular structure, featuring two areas of inverted repeats spanning 25,687 base pairs, a single-copy segment of 17,922 base pairs, and a larger single-copy region of 85,148 base pairs. The genome's GC content is 38.3% due to its composition of bases, consisting of 30.5% adenine, 31.3% thymine, 18.8% guanine, and 19.4% cytosine. The plastome of *V. trifolia* has equal inverted repeat lengths, but it is 74 base pairs longer than those found in other species. The lengths of the LSC and SSC regions in *V. trifolia* are greater than those found in *V. rotundifolia*. The sequence contains information for 131 genes; specifically, 87 encode mRNA, 36 encode tRNA, and 8 encode rRNA. This group comprises 28 genes responsible for self-replication, 45 genes related to photosynthesis, seven unidentified genes that are conserved along with six additional genes, and open reading frames [5].

Vitex rotundifolia is a traditional folk medicine plant with an extensive history of usage..The fruits, leaves, roots, blossoms, and stems of *Vitex rotundifolia* have all been shown to have therapeutic effects, but the fruit has received the most attention in research and use.The leaves and berries of *Vitex rotundifolia* are widely employed as medicinal components throughout Asia. Conventional remedies often employ them to

alleviate a range of health issues, such as cold fever, headaches, eye pain, diarrhea, dysentery, postpartum recovery, bruising, and other problems. The names are Fructus Viticis and Folium Viticis. In modern therapeutic settings, this treatment is often employed to address a range of health issues, such as senile cataract, middle ear infections, nasal inflammation, headaches, and facial nerve pain, resulting in successful clinical outcomes. [6]

Medicinal plants, which are rich in bioactive substances like terpenoids, flavonoids, and alkaloids, have been of great interest in medication research for a long time. The presence of therapeutic bioactive chemicals among flora and fauna is not exclusive to terrestrial plants; numerous marine species also possess these compounds. *Vitex rotundifolia* is very commonly regarded as Beach Vitex. Long-standing ethnopharmacological uses have been observed in European and Asian nations, namely China, Korea, and Japan, for the coastal shrub *Vitex rotundifolia*. Although the precise origin of the usage of the Vitex species in natural remedies is unknown, famous botanist and herbalist Christopher Hobbs claims that it has been used medicinally for almost 2,000 years. [7]

This paper highlights the significance of *Vitex trifolia* and *Vitex rotundifolia* in traditional medicine, pharmaceutical applications, and their ecological roles, also underscoring the need for conservation efforts and further study.

II. PHOTOCHEMICAL CONSTITUENTS

Vitex rotundifolia, *Vitex trifolia* contain a variety of bioactive compounds with medicinal properties, such as halimane-type diterpenes, vitetrifolins, flavonoids, alkaloids, saponins, Casticin, Siridoids including eucommiol, iridolactone, pedicularis-lactone, 1-oxo-eucommiol, agnuside, and VR-I (10-o-vanilloyl aucubins), 16, viteoidi, viteoid ii, and trans- and cis-eurostoside. Frequent reports indicate that numerous bioactive compounds isolated including flavonoids, phenolic acids, and terpenes, exhibit diverse biological and pharmacological activities in both laboratory settings and living organisms^[7].

III. PHARMACOLOGICAL ACTIONS of *Vitex trifolia*

A. Bronchodilator Activity

Huang et al. studied how casticin reduced airway inflammation, oxidative stress, and hypersensitivity in an asthma mouse model's respiratory tract, along with the tracheal epithelial cells' inflammatory and oxidative responses. BALB/c mice were randomly assigned to five separate groups: a normal control group, a group with OVA-induced asthma, and a group with OVA-induced asthma that received intraperitoneal injections of either 5 or 10 mg/kg of casticin or prednisolone. Studies on asthmatic mice have shown that casticin reduces hypersensitivity, goblet cell overgrowth, and oxidative damage in their airways. Physiological investigations have shown that Casticin reduces Th2 cytokine levels in pulmonary fluids and regulates the production of Th2 cytokine and chemokine genes in the lung. Treatment with Casticin also safely reduced inflammation and oxidative stress in the airways of asthmatic mice. In consequence, BEAS-2B cells treated with casticin exhibited significantly decreased levels of pro-inflammatory cytokines and exotoxins, and there was a reduction in THP-1 monocyte cell adhesion to BEAS-2B cells resulting from decreased ICAM-1 expression. Consequently, casticin acts as a potent immunomodulator, which effectively minimizes pathogenic changes in asthmatic mice through its ability to suppress the production of Th2 cytokines.^[8]

B. Hepatoprotective Activity

The effectiveness of hepatoprotection against carbon tetrachloride-induced liver damage has been studied by Manjunatha B.K. et al. To determine the extracts' ability to safeguard the liver, a number of biochemical markers were evaluated, including total bilirubin, total protein, alanine transaminase, aspartate transaminase, and alkaline phosphatase activities. Biochemical serum tests revealed that mice exposed to ethanol and aqueous extracts experienced a substantial rise in total protein levels and a notable drop in total bilirubin and serum marker enzyme levels. The group that received CCl₄ treatment experienced a substantial increase in serum enzyme levels and a reduction in total protein amounts, which indicates liver damage. Biochemical assays showed that mice receiving ethyl alcohol and aqueous extracts had a significant increase in total protein but a significant decrease in total bilirubin and blood marker

enzymes. The group treated with CCl₄ exhibited a notable increase in serum enzymes and a reduction in total protein levels, indicating liver harm. Further evidence of the liver-protecting effect is provided by histologic examinations of liver tissue. Liver tissue histology revealed that tissues treated with ethanol and aqueous extracts contained only a small number of fatty lobules and displayed a normal hepatic structure. The current research has shown that *Vitex trifolia* offers adequate protection against liver cell damage resulting from CCl₄ exposure [9].

C. Trypanocidal Activity

Kiuchi et al. conducted a search for anti-trypanosomal compounds in Vietnamese herbal remedies. An acetone extract of the plant's fruits effectively inhibited *Trypanosoma cruzi* epimastigotes, the cause of American trypanosomiasis, also known as Chaga's disease. The trypanocidal qualities of this plant's fruits are discussed in the article, with particular attention paid to the identification and analysis of five previously identified compounds—previtexilactone, 6-acetoxy-9-hydroxy-labden-16,15-olide, vitexifolin E, vitexifolin F, and vitex lactone—as well as two recently discovered nor diterpene aldehydes. Using acetone under increasing temperatures, the dried-out fruit of *V. trifolia* was extracted. The resulting extract, which has strong trypanocidal properties in vitro, was purified using multiple column chromatography to separate various compounds called diterpenoids. These compounds' chemical structures were determined by utilising vitexifolin E and vitexifolin F. Previtexilactone and vitexilactone-6-acetoxy-9-hydroxy-13-labden-16,15-olide spectra were contrasted with spectrum data that had already been published.^[10]

D. Anti-Bacterial Activity

Krishnan Kannathasan and colleagues investigated the bactericidal activities of methanol extracts from *Vitex trifolia* leaves. Using the disc diffusion method, experiments were carried out to determine the lowest inhibitory and bactericidal concentrations against five Gram-positive and seven Gram-negative bacterial species known to cause human disease. The broad spectrum of antibacterial action exhibited by the extracts was shown to exist in the *Vitex* species due to their antibacterial activity. Among the microorganisms examined, the vitex exhibited the highest level of activity. Preliminary data indicates that the isolates had a wide spectrum of antimicrobial qualities. The use of *Vitex trifolia* is recommended for the current research

to identify the antibacterial compound that demonstrates efficacy against the human pathogenic bacterial strains being evaluated[11].

E. Anti Diabetic Activity

Researchers led by Atsuyoshi Nishina demonstrated that extracts from the Myanmar medicinal plant *Vitex trifolia* have an effect similar to rosiglitazone in stimulating the process of adipogenesis. The researchers aimed to identify compounds in *Vitex trifolia* that possessed ROS-like characteristics in this investigation. The compounds vitexlactone, vitexcarpin, and oleanolic acid were isolated through purification of the ethyl acetate's extract displayed the highest ROS-like characteristics, obtained from *Vitex trifolia*, among hexane, ethyl acetate, and methanol extracts, using various chromatographic methods. One of the isolated compounds showed the strongest ROS-like activity. The impact of ROS on 3T3-L1 cells were studied during fat formation. In 3T3-L1 cells, ROS led to a decrease in adipocyte size as well as the activation of IRS-1, ERK1/2, and JNK, but it enhanced lipid accumulation, adiponectin, and GLUT4 expression on the cell membrane. In contrast to ROS, lipogenesis-related proteins were only marginally activated. The findings of this research suggest that vitex may act as an insulin sensitizer[12].

F. Anti-Oxidant Activity

Vitex trifolia species from the Lamiaceae family have been evaluated by Sarla Saklani et al for their antioxidant potential through an assay of ethanolic extracts. Strategies were adopted to test the antioxidant capabilities of several *Vitex trifolia* extracts. Chelation strategies using β -carotene and linoleic acid with ferrous ions, as well as DPPH and nitric oxide scavenging, were used. In comparison to renowned antioxidants like ascorbic acid, butylated hydroxytoluene, and ethylene diamine tetraacetic acid (EDTA), the *Vitex* genus demonstrated high antioxidant activity across all evaluated methodologies. *Vitex trifolia* includes an expanded quantity of phenolic chemicals and flavonoids, and it has strong antioxidant qualities. Significant connections were found involving the antioxidant activity and the total quantities of phenolic components and flavonoids in *Vitex trifolia* within this research. [13]

G. Anti cervical cancer activity

Peng et al. studied the anti-cervical malignancy properties and probable mechanisms of Rotundifuran, a natural substance derived from *Vitex trifolia*. Researchers discovered that Rotundifuran might prevent the proliferation of cervical cancer cell lines, including HeLa and SiHa cells ($IC_{50} < 10$ micromoles) by triggering cell death in a lab setting. Further studies confirmed the antitumor properties of Rotundifuran in a HeLa cell-inoculated xenograft model. The study also discovered that Rotundifuran's cytotoxic activities are related to a kind of cell death caused by reactive oxygen species and mediated by the MAPK and PI3K/Akt signalling pathways. Furthermore, Cyr61 was identified as a possible target for Rotundifuran in cervical cancer cells using proteomics analysis and a drug affinity responsive target stability coupled mass spectrometry technique known as DARTS-MS.[14]

H. Anti hepatic cancer activity

Studies have confirmed that *Vitex trifolia* ethanolic extracts possess anti-cancer properties. This study quantified RNA/protein ratios in microsomal membranes with and without *Vitex trifolia* extracts, the intent is to assess the extent to which these extracts attenuate disruption of ribosomal membranes produced by 3, 8 Di amino 5 ethyl 6 phenyl phenanthridinium bromide (EB), a recognised degranulator. The extract's cytotoxicity was then assessed in HCT 116 and A549 cell lines. *Vitex trifolia* protects liver microsomes against the carcinogen's capacity to trigger degranulation. EB greatly impeded the development of the cancer cell lines HCT 116 and A549. *Vitex trifolia* ethanolic extracts have been proven to have strong anti-carcinogenic and anti-degranulatory capabilities, owing to their capacity to inhibit EB-induced liver microsomal degranulation. Furthermore, these extracts inhibit the growth of cancer cells in cell lines. [15]

I. Inhibitory Effect on Inflammation

New directions for the creation of safer anti-inflammatory medications have been made possible by Ghafari et al.'s investigation of the molecular mechanisms of vitex plants and their biological targets. Using a variety of techniques, several researchers have investigated *Vitex trifolia*'s anti-inflammatory properties. In order to assess the anti-inflammatory qualities of methanol, aqueous, and hydro-alcoholic

extracts from the leaves of the *Vitex trifolia* plant, Laxmikant, Ankalikar, and Viswanathswamy conducted in vivo tests. The anti-inflammatory effects of the plant's leaf aqueous extract and fruit methanol extract were assessed in different tests using RAW 264.7 cells; both extracts demonstrated anti-inflammatory capabilities.[16]

J.Spasmolytic Activity

Alam et al. acknowledged the activity, and the only compound found active in the trachea spasmolytic bioassay was vitexcarpin, as per an in vivo study assessing The primary active metabolites found in the n-hexane extract of *Vitex trifolia* are viteosin and vitexcarpin. A comparable effect was seen using guinea pig trachea sensitised to ovalbumin, which was stimulated for 30 minutes at a minimum concentration of 1.3×10^{-5} M. The research indicates that preserving the membrane function of mast cells may enable Vitexcarpin to counteract the effects of histamine released by sensitized mast cells. [17]

K.Anti-Viral Activity

In an in vitro test, Vimlanathan et al. found that *Vitex trifolia* exhibited substantial antiviral activity against Molluscum contagiosum and Herpes simplex viruses, with notable effectiveness observed at concentrations of approximately 0.25 µg/mL and 0.5 µg/mL for both viruses, and at 0.4 µg/mL. Importantly, this antiviral effect was achieved without inducing significant harm. The discovery suggests that *Vitex trifolia* could be a reliable and effective natural source for creating potent and secure antiviral medications. Investigating the specific bioactive compounds of *Vitex trifolia* involved in antiviral treatments and expanding its clinical applications could potentially increase the research into the therapeutic potential of this plant. [18]

L.Anti-HIV Activity

A group of researchers led by Woradulayapinij examined the impact of 80% ethanol and water-based extracts from 20 different plants on multiple characteristics. Research into Thai medicinal plants and their impact on HIV type 1 reverse transcriptase activity. The findings revealed that at a concentration of 200 micrograms per milliliter following one hour of incubation, the water-based extracts of *V. trifolia* (aerial part) demonstrated an exceptionally high inhibition ratio (% IR) of over 90%. A control experiment

utilised Doxorubicin hydrochloride, leading to a 98.3% reduction in HIV-1 reverse transcriptase activity when used at a concentration of 1 mM. The research indicates that due to their substantial inhibitory effect on HIV-1 reverse transcriptase activity, *V. trifolia* extracts have considerable potential as candidates for further investigation into the development of anti-HIV medications^[19].

M. Anti-Malarial Activity

Shah and Rahim et al. employed semi-structured questionnaires and interviewing informants to acquire further information regarding plants associated with malaria and its symptoms. Studies on the anti-malarial properties were carried out on compounds derived from 70 various plant species, which encompassed 62 unique genera and 34 diverse families. The research revealed that the Solanaceae family was most frequently referenced, with seven plants displaying promising antimalarial properties. The Lamiaceae family showed notable results, especially with *Vitex trifolia*, which was discovered to have antimalarial properties and was used in Pakistan's Soon Valley region to treat malaria. The significance of specific plant species in traditional contexts is reinforced by their possible antimalarial characteristics. These findings underscore the importance of certain plant species in traditional settings due to their potential antimalarial properties [20].

N. Wound Healing Activity

In *Vitex trifolia* ethanol leaf extract, the concentration of hydroxyproline, a compound associated with collagen synthesis, was 2,567 µg/100 mg, significantly higher than the 1943 µg/100 mg found in the negative control. The tensile strength of the positive control's incision wound tissue was 600.00, compared to 578.20 in the *Vitex trifolia*. The ethanol leaf extract of *Vitex trifolia* showed higher concentrations of hydroxyproline, an indicator of collagen synthesis, at 2,567 µg/100 mg, than the negative control, which had levels of 1943 µg/100 mg. *Vitex trifolia* produced notably heavier granuloma dry weights (157.30 mg/100 g) than the control group (33 mg/100 g), indicating a more extensive process of tissue repair. *Vitex trifolia* demonstrated enhanced outcomes compared to the positive control (181 g), yielding a higher dead space wound tissue tensile strength of 491.20 g; this exceeded the tensile strength of the positive control

(181 g). Studies indicate that *Vitex trifolia* has a considerable influence on improving the quality of wound healing, including its effects on scar formation and multiple other wound healing parameters. [21]

O.Larvicidal Activity

Research conducted by Tandon et al. discovered that *Vitex trifolia* was effective in deterring mosquitoes when given at a low concentration. Research led by Tandon et al. in 2008 examined the essential oils of *Vitex trifolia* and found that while they offered some advantages, they also negatively impacted adult emergence, reproductive capacity, and egg viability, as well as increasing the duration of larval stages, larval mortality, pupal duration, and adult physical abnormalities. [22]

P.Anti Amnesic Activity

Mohanbabu and colleagues. Aqueous extract from *Vitex trifolia* leaves at 20 mg/kg per body weight showed significant anti-amnesic effects in both the passive avoidance and T-maze models ($p < 0.01$). The extract had a maximum proportion of time spent in the probe quadrant of 60.75%, resulting in a much lower escape delay time (12s) than the control group (29s). The results showed a nearly twofold increase in memory retention compared to the control and other treatment groups.[23]

IV.PHARMACOLOGICAL ACTIVITY of *Vitex rotundifolia*

I.Anti Breast Cancer Activity

Jan Rehmat and co-authors investigated the cytotoxic effects and cell death pathways triggered by the extract and fractions of *Vitex rotundifolia* leaves in breast cancer cell cultures. The cytotoxicity activity was assessed using the MTS test. Cell death mechanisms were studied using externalization of phosphatidylserine and late-stage DNA fragmentation. After 72 hours, a 50% decrease in the growth of T-47D cells was observed at a concentration of 79.43 μ g/ml when using the methanol extract. Testing the T-47D cell line revealed cytotoxic effects in response to fractions F1, F2, and F3, out of the seven fractions examined, with an IC₅₀ value of less than 30 μ g/ml after a 72-hour period. Findings from the TUNEL assay and the Annexin V/PI apoptosis detection assay indicated that active fractions of *Vitex rotundifolia* prompted both early and late apoptosis (DNA fragmentation) in the T-47D cell line. Chemical profiling of *Vitex rotundifolia* revealed the presence of potential metabolites (Vitexcarpin) via Caspase GloTM

luminous testing and western blot analysis in its fractions. The findings of his research point to the significant potential of active metabolites found in fractions of *Vitex rotundifolia* as a potential treatment option for breast cancer. [24]

2. Anti-Oxidant Activity

A study published by Deniz GY and colleagues demonstrated the significant antioxidant properties of *Vitex rotundifolia*. The study of the radical scavenging effect on 1,1-diphenyl-2-picrylhydrazyl revealed that his research demonstrated the strong antioxidant capabilities of the methanolic extract from *Vitex rotundifolia* twigs. The flavonoids 7-orientin and 3,4-di-O-caffeoylquinic acid, a compound derived from quinic acid, exhibited significant antioxidant capabilities. Research has demonstrated that vitexilactone, a compound isolated from *Vitex rotundifolia*, displays pronounced antioxidant properties, and it has been identified as a reliable and effective substitute treatment for kidney damage resulting from cisplatin-induced nephrotoxicity in rats. Ferric thiocyanate testing revealed that ferruginol, a diterpenoid abietane compound found in *Vitex rotundifolia*, displayed greater antioxidant capabilities than 3-tert-butyl-4-hydroxyanisole. To evaluate *Vitex rotundifolia*'s antioxidant properties in animal tissues or blood samples, conducting an in vivo study is required. The most widely used in vivo techniques for evaluating the antioxidant properties of a given extract are lipid peroxidation assays. [25]

3. Anti bacterial Activity

Kawazoe K. et al. evaluated the antibacterial properties of *Vitex rotundifolia* by examining either an extract of the plant or compounds isolated from it. The extracts show the lowest minimum inhibitory concentrations against *Pseudomonas aeruginosa* and *Staphylococcus aureus*, with their capacity to inhibit bacterial growth having been proven. Research has found that isolated compounds from the underground portion of *Vitex rotundifolia*, encompassing vitrofolal C, vitrofolal D, and detetrahydroconidendrin, display efficacy against methicillin-resistant *Staphylococcus aureus*, achieving a minimum inhibitory concentration of less than 64 µg/mL against eight out of eighteen strains. In addition, extracts of *Vitex rotundifolia* have been discovered to contain the most potent antibacterial compounds in the chloroformic

and ethyl acetate fractions, with MIC values between 4 and 8 mg/mL effective against both gram-positive and gram-negative bacteria. [26]

4. Anti Inflammatory Activity

Le et al. isolated and differentiated one previously unknown phenolic compound, in conjunction with nineteen identified compounds, from *Vitex rotundifolia*. The anti-inflammatory properties of these isolates were assessed by examining their capacity to neutralise 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radicals and inhibit the production of nitric oxide (NO) and interleukin-8 (IL-8) in lipopolysaccharide (LPS)-stimulated cells, specifically RAW264.7 and HT-29. Compounds 12 to 14 showed significant inhibition in the nitric oxide assay, in contrast, compounds 10 and 15 demonstrated considerable inhibition. Drugs 8, 9, 13, 14, 19, and 20 were found to have the capacity to significantly reduce the production of IL-8 in the IL-8 assay, in contrast to other medications which showed only a moderate level of inhibition. Researchers found that using a virtual screening method, the binding strength was significant for protein-ligand interactions involving these active compounds, especially in relation to their ability to suppress IL-8 production. The experimental data from the IL-8 assay were found to match the docking results. Therefore, these active substances should be considered as potential subjects for additional in vivo research. This study suggests the possibility of developing new and effective compounds extracted from *Vitex rotundifolia*, and offers proof to back the progression of active fractions and components into useful products designed to treat inflammatory conditions.[27]

5. Anti Microbial Activity

A study by Islam Z et al highlighted the traditional uses of *Vitex* genus plants as anti-infective remedies in several traditional healthcare systems, demonstrating their in vitro antimicrobial properties against a diverse assortment of bacterial, fungal, and protozoal pathogens. Studies have demonstrated that vitamin extracts often exhibit antibacterial effects against a range of bacterial, fungal, and protozoal species in laboratory experiments. The biological action in question may be triggered by certain primary natural molecules present in these extracts. The analysis results support the historical use of *Vitex rotundifolia* in traditional medical practices. Furthering understanding of the medicinal properties of *Vitex rotundifolia*

and its native compounds can facilitate the creation of antimicrobial medications and contribute to the prevention and management of infectious diseases. Gaining more knowledge about the medicinal plant *Vitex rotundifolia* and its natural ingredients can assist develop antimicrobial medications and aid in the prevention and treatment of infectious disorders.[28]

6. Inhibitory Effect on Cell Proliferation

Song et al. (Hun Min Song et al.) reported that traditional medicine has been used to treat a range of conditions, including gastrointestinal infections, chronic bronchitis, inflammation, headaches, migraines, and eye pain. Research has also demonstrated that it possesses anti-proliferative properties against a range of cancer cells, encompassing those found in colorectal, lung, and breast cancer. Researchers studied the molecular processes involved in *Vitex rotundifolia*'s effect on the reduction of CDK4 and cyclin D1 levels linked to cancer cell proliferation. *Vitex rotundifolia* was shown to inhibit the growth of human colorectal cancer cell lines, including SW480 and HCT116. Concurrent with this was a decrease in Cyclin D1 and CDK4 levels, achieved through reductions in both protein and mRNA levels. *Vitex rotundifolia* led to a decrease in Cyclin D1 and CDK4 levels via proteasomal degradation., resulting in lower protein levels prior to any changes in mRNA levels. Phosphorylation of Thr286 on cyclin D1 is necessary for the degradation of cyclin D1, which is triggered by *Vitex rotundifolia*, specifically in the context of CDK4 degradation. Research employing a range of kinase inhibitors has shown that the degradation of CDK4 by *Vitex rotundifolia* is reliant on ERK1/2, p38, and GSK3, whereas the degradation of cyclin D1 by *Vitex rotundifolia* may be dependent on GSK3. This study found that *Vitex rotundifolia* prevented the activation associated with down-regulation of TCF4, specifically by inhibiting the transcriptional regulation of CDK4 and cyclin D1 mRNA levels linked to cyclin D1 transcriptional regulation. *Vitex rotundifolia* treatment also reduced the transcriptional control of CDK4 and c-myc genes. According to his research, *Vitex rotundifolia* may be a suitable candidate for developing therapeutic medicines or chemoprevention strategies for human colorectal cancer. According to his research, *Vitex rotundifolia* may be a suitable candidate for developing therapeutic medicines or chemoprevention strategies for human colo-rectal cancer.[29]

7. Menstrual Suppression Activity

According to Zhang et al., iridoid glycoside has been found to alleviate premenstrual issues and has been demonstrated to affect menopause symptoms. This study found that *Vitex rotundifolia* has a dose-dependent effect on estrogen receptors, while also interacting with progesterone receptors. The study also revealed that diterpenes found in vitex act as dopamine agonists to suppress the release of prolactin in both laboratory and in vivo settings. This study sought to offset the estrogen's stimulating impact in women with severe premenstrual syndrome, who exhibit elevated mid-cycle estrogen levels, with the goal of decreasing prolactin production. [30].

8. Anti Tumor and Leukemic Activity

Research has shown that Vitex exhibits anti-tumor effects in both human cancer cells and corresponding xenograft models in mice, largely attributed to the substantial presence of flavonoids including casticin, luteolin, apigenin, isoorientin, hesperidin, and isovitexin. Luteolin inhibits the proliferation of human myeloid leukemia HL-60 cells by inducing apoptosis. Luteolin can suppress the growth of human myeloid leukemia HL-60 cells through the induction of apoptosis. [31,32]

9. Anti Artherosclerotic Activity

According to Kim JY et al., Casticin and luteolin were identified as preventing the oxidation of both low-density lipoprotein and high-density lipoprotein via pathways involving lipid peroxidation inhibition, reductions in lipoprotein negativity, diminished hyperchromicity, decreased carbonyl content, and obstruction of apoA-I aggregation. Studies indicate that eating this fruit could have a protective effect against atherosclerosis due to its capacity to halt the oxidation of LDL and HDL, which has been shown through the substantial inhibitory effect observed. [33]

V. DISCUSSION

Modern changes in lifestyles have resulted in significant alterations to human dietary habits, thereby causing diverse disruptions in individuals' daily lives. The presence of bioactive compounds in these herbs resulted in improved well-being for the people concerned. *Vitex trifolia* and *Vitex rotundifolia* are two distinctive Chinese plants with significant cultural value, exhibiting a diverse array of biological features. The vegetal parts of these plants are rich in various bioactive compoundshalimane-type diterpenes,

vitetrifolins, flavonoids, alkaloids, saponins, Casticin, Siridoids including eucommiol, iridolactone, pedicularis-lactone, 1-oxo-eucommiol, agnuside, and VR-I (10-o-vanilloyl aucubins), 16, viteoidi, viteoid ii, and trans- and cis-eurostoside. Frequent reports indicate that numerous bioactive compounds isolated including flavonoids, phenolic acids, and terpenes which are responsible for exhibiting various pharmacological activities.

For centuries, a broad spectrum of health problems has been treated with these extraordinary herbs, such as parasitic infections, inflammation, joint pain caused by osteoarthritis and rheumatoid arthritis, wound healing, cyto toxic activities. As a result of their traditional uses, these herbs have had a profound impact on the practice of Ayurveda, Siddha, and Unani.

VI. CONCLUSION

Vitex trifolia and *Vitex rotundifolia* are notable for their multifaceted applications in medicine, ecology, and cultural practices. These compounds possess a multitude of pharmacological properties, encompassing anti-inflammatory, antibacterial effects, antioxidant, and pain-relieving effects, are substantiated by their complex phytochemical composition, which encompasses flavonoids, terpenoids, and iridoid glycosides. These traits are consistent with their long-established history of use in traditional medicine to treat inflammatory, skin-related, and respiratory disorders. Standardized pharmaceuticals, rigorous pharmacological research, and environmentally friendly agricultural practices should be the primary objectives of future projects. There is significant potential for these plants to enhance healthcare and boost ecological resilience through the combination of established knowledge and modern scientific research. This review reveals numerous unknown benefits of these plants, which future generations can utilise for their ecological and therapeutic value, making preservation and sustainable use crucial.

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