ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info/jasr

ISSN
0976-9595
Review Article

A COMPREHENSIVE REVIEW ON ETHNOBOTANICAL, PHYTOCHEMISTRY, BIOACTIVITIES AND MEDICINAL MYSTERIES OF *VITEX TRIFOLIA* LINN (THREE-LEAVED CHASTE TREE)

Geeta Parkhe[1, 2]*, Prabhat Kumar Jain[1]

[1]*Department of Biotechnology, SRK University, Bhopal, MP, India*

[2]*Scan Research Laboratories, Bhopal, India*

**Corresponding author: parkhegeeta227@gmail.com*

ABSTRACT

Since the beginning of the cosmos, nature has been enriched with plentiful resources are being given away for the betterment of humankind. Nature has the plethora of biologically lively compounds those are potential to prevent ailments. By virtue of usual support, India has been a province with abundance of natural plants possessing immense therapeutic consequence. Above time countless medicinal plants have been recognized and used in India to treat diverse types of diseases. The World Health Organization has listed 21,000 plants, which are used for medicinal purposes approximately the world. Amongst these 2500 species are in India, out of which 150 species are used commercially on a moderately huge level. India is the major maker of medicinal herbs and is called as botanical backyard of the world. The purpose of present review is to make available up-to-date information on botany, ecological biodiversity, morphology, medicinal uses, phytochemistry and pharmacological activities on diverse parts of *Vitex trifolia* Linn (*V. trifolia*). This review was assembled using technical literature from electronic explore engine such as Springerlink, BioMed Central, PubMed, Scopus, ScienceDirect, Scielo, Medline and Science domain. Supplementary texts were obtained from books, book chapters, dissertations, websites and other technical publications. *V. trifolia* (Verbenaceae) have ethno-pharmacological significance and have been conventionally utilized by local people in remedies for a variety of illness. A huge number of the species of the Genus *Vitex* are extensively employed in Indian conventional systems of medicine. An entirety of 270 plant species of genus *Vitex* have been recognized universal. *V. trifolia* is used in Ayurveda and Unani. These species are wealthy source of secondary metabolites such as polyphenolic compounds, terpenoids, phytosterols, protein and amino acids, tannins, and saponins. *V. trifolia* has hepatoprotective, anti-inflammatory, analgesic, trypanocidal, antimicrobial, anti-quorum sensing, mosquito larvicidal and repelling, antimalarial, trachea-spasmolytic, wound healing, estrogenic, vascular relaxation, antinociceptive, anthelmintic, molluscidal, anti-tubercular and mice repelling properties. It is notable that casticin or vitexicarpin isolated from *V. trifolia* exhibits effective cytotoxicity against an extensive range of cancer cell lines via diverse modes of molecular action. This review highlights the ethnobotanical, phytochemical, traditional, pharmacological information available on *V. trifolia*, which might be helpful for scientists and researchers to find out new chemical entities accountable for its claimed conventional uses.

Keywords: *V. trifolia* Linn, Verbenaceae, Three-Leaved Chaste Tree, Phytochemistry, Pharmacological activity, Ayurveda, Medicinal uses

1. INTRODUCTION

Nature is considered as eternal sources for various medicinal agents and drug development. There are about 250000 species of plants in the universe among them 6% have been found to be biologically active and 15% have undergone phytochemical testing [1]. It is expected that about 80% out of more than 4000 million people of the world depend on the traditional medicines to meet the demand for primary health care needs [2].

Whereas 70-80% people of developing Asian countries rely on the traditional medicine despite the availability of allopathic medicines in many areas of the community [3]. The utilization of plant-based medicines is known as ethnomedicine. The aim of ethnopharmacology is to facilitate the discovery of the bioactive compounds from natural sources [4]. Plants remain an excellent basis of novel drugs and novel chemical entities. Medicinal plants serve for the development of both natural products and their derivatives. For example anti-malarial drug

arteetheris derived from artemisinin which is isolated from the traditional plant, Artemisia annua L. (Asteraceae). There are few more derivatives of artemisinin under clinical trials in Europe to be used as anti-malarial drugs [5]. Evidence shows that there was an involvement of the use of various traditional medicines in the early health care systems of developing countries [3]. The rapid increase of the knowledge regarding the optimistic effects of the plant-derived compounds accelerates using these agents to cure diseases [6]. The genus *Vitex* belonging to the family Verbenaceae is comprised by 250 species of little trees and shrubs, occurring in tropical to moderate regions [7]. Traditionally several of its species are being used for sprains, inflammation, as anti-tubercular, anticancer, diuretic, rheumatic pains, respiratory infections, premenstrual problems, anti-fungal, in migraine and insecticidal. There are regarding 12 species accessible in India with medicinal value [8, 9]. Regarding 28 species of this genus have been examined phytochemically and were reported to contain terpenoids, ecdysteroids, flavonoids, iridoid glucosides etc. *V. trifolia* Linn is frequently known as chaste tree (English) and jalanirgundi (Sanskrit) (Fig.1). *V. trifolia* is a large coastal shrub or small tree growing from 1 to 4 meters high, for a while prostate or ascending in habit with the stems covered by soft hairs (tomentose). Flowers are appearing in summer or late summer and 6-12 inch long. *V. trifolia* has been used as sedative, anti-inflammatory, rheumatism and the common cold in Asian countries [10]. In this article we have gathered a briefly and targeted pack of information about *V. trifolia* which hope to be useful in near future for scientist society. Varied medicinal uses of the plant stand in corroboration to its pharmacological activity profile discovered in the current past. Consolidation of its pharmacological activities and its relationship with its conventional uses would open new areas of research for discovery of new drugs and a variety of formulations. The Taxonomic account of *V. trifolia* consists of kingdom: Plantae-plants, division: Angiosperms, class: Eudicots, Unranked: Asterids, Order: lamiales, Family: lamiaceae, verbeniaceae, Genus: Vitex, Species *trifolia,* Binomial name *Vitex trifolia* [11]. The vernacular names of the plant is Three-Leaved Chaste Tree, Simple leaf chastetree (English), Pani-samalu (Bengali), Nichinda, Pani-ki-Sanbhalum, Sufed-Sanbhalu (Hindi), Karinochi, Lakki (Kannada), Chara-nosi, Karinochi (Malayalam), Urikshibi (Manipuri), Indrani, Lingur, Nirgundi (Marathi) Svetasurasa (Oriya), Indranika, Indrasurasa, Jalanirgundi (Sanskrit), Karunochi, Nirnocci (Tamil), Vaavilli, Chiruvavil (Telugu) [12]. In this article we have gathered a briefly and targeted pack of information about *V. trifolia* which hope to be useful in near future for scientist society.

2. BOTANICAL DESCRIPTION

Three-Leaved Chaste Tree is a shrub or small tree, less that 5 m in height with the stems covered by soft hairs (tomentose). The green leaves of *V. trifolia* have resinous glands tomentose beneath and 7-12 pairs of lateral nerves, terminal and supraaxillary, 5-26 cm long panicles [13]. Three-foliolate leaflets are elliptic or oblong-obovate, slender, canaliculate, 0.5-3.5 cm long and grey-appressed petioles. Usually obtuse or acute to cuneate at base, entire along margins, acuminate at apex lengthy leaflet, middle leaflets 2.5-6.5×1-3.5 cm, petiolules 0.5 cm long, lateral leaflets are 2.5-4.5×1-1.5 cm the terminal leaflet sessile, 5-6.3 by 2.5-3.8 cm the lateral smaller, sessile, all glabrous above, very densely white-tomentose beneath, base tapering; common petioles 1.3-1.6 cm long [14]. The flowers are born in panicles or clusters up to 18 cm in length. Individual flowers have purple to violet two-lipped corollas that are approximately 5 mm long. The stamens are in 2 pairs and the ovary is superior, or develops above the corolla. The fleshy fruits are about 6 mm in diameter and contain 4 small black seeds. The stems are usually procumbent often rooting at the nodes and annulate nodes and 2.5-5 cm long internodes forming mats several meters in diameter and with soft hair called tomentose, fragrant flowers with pedicels of 0.5-1 cm long [15]. Corolla is hairy, lavender to blue. Tube is about 8 mm long, the larger central love of the lower lip has a white blotch at the base; limb is 12 mm in the greatest diameter. Fruit is rounded, 4 to 5 mm in diameter.

Fig. 1: Photograph of leaves of *Vitex trifola* Linn

3. GEOGRAPHICAL DISTRIBUTION

V. trifolia (*syn. V. rotundifolia L. f, V. ovata thumb*) is extensively dispersed throughout sandy beaches of the tropics and sub-tropics. Occurring in South, Southeast and East Asia, it is found from the foot of Himalayas southwards throughout greater part of India, western ghat and in Andamans. It is distributed in Bangladesh, Srilanka, America Afghanistan China, Malaya, Indonesia, Philippines, New Caledonia, New Guinea, Philippines, Japan and Madagascar [16-19].

4. CULTIVATION

V. trifolia cultivate well on exposed coastal sand dunes. It likes fertile, moist, well-drained soils. Water well in the summer and shun the extremes of soil moisture, neither drought nor water logging. If propagating seeds, sow freshly collected seed in a mix of sand and coir. If propagating by cuttings, take them when the plants are not in flower or fruit (apical cuttings with at least two nodes). Cuttings should be rooted in a well-drained rooting medium such as perlite and coir under mist [20].

5. MICROSCOPIC EVALUATION

The leaflet has flat adaxial surface 140 µm broad along the ridged part of the leaflet and 120 µm thick in between the ridges. Thick and prominent adaxial epidermis with rectangular cell and fairly thick walled subepidermal layer with 10 µm thin cuticle. The hypodermal layer is 15 µm thick. The midrib is thick. The epidermal layer is a thin with small cells. The ground tissue of the midrib consists of circular thin-walled dense parenchyma cells [21]. The vascular system of the midrib has vascular strand consists of numerous parallel rows of xylem which are about six cells angular and thick walled with narrow parenchymatous space in between the xylem rows. The adaxial is circular and collateral the abaxial epidermis is narrow with dense non-glandular trichomes. The mesophyll consists of four layers cylindrical cells. The height of these palisade and spongy parenchyma cells reduced gradually toward the lower part.

6. PHYTOCHEMICAL CONSTITUENTS

The plant contains polyphenolic compounds, flavonoids, proteins, tannins, phytosterols, and saponins. Fruits of *V. trifolia* consist [22-24] of essential oil, dihydrosolidagenone, *Vitex trifolia* A-G, monoterpenes along with diterpenes, terpineol, beta-sitosterol-3-O-glucoside, alpha-pinene, 3,6,7-trimethylquercetagetin [25], hexanic and dichloromethanic were extracted from stem [26]. The methyl-*p*-hydroxy benzoate was reported [27]. 6 flavonoids have been isolated [28]. 15 compounds were isolated from *V. trifolia*. Leaves and bark contain a flavones, artemetin, essential oil, 7-dimethyl artemetin [29], friedelin and some alkaloids and non-flavonoids. Caryophyllene is the main sesquiterpene. Vitricin, a new alkaloid, has been isolated from the plant [30] *V. trifolia* contains palmitic acid, ethyl-p-hydroxybenzoate, 3,4-dihydroxybenzoic acid, 4-hydroxy-3-methoxybenzoic acid, caffeic acid, hydroxyl ethyl cinnamate, luteolin, quercetin, apigenin, casticin, and 3,6,7-trimethylquercetagetin. Phytochemical examination of the ethyl acetate portion afforded stigmasterol [31], caffeic acid [32], 7-*O*-glucopyranoside [33], 3, 6, 4'-trimethoxy quercetin 7-*O*-glucopyuranoside [34] and quercetin 7-*O*-neohespridoside [35].

7. TRADITIONAL USES

Application of leaves 3 to 4 times daily provides relief for localized burning in the soles of the feet. The leaves are fiery in a clay pot without the addition of water, then applied when adequately hot and held in place by a bandage. Decoction of leaves used for perfumed baths and used in amenorrhea. In India, leaves used as diuretic, anodyne and emmenagogue. Leaves in fomentations and baths used for cure of beri-beri and burning of the feet. Dry fomentation of leaves used for contusions, sprains and rheumatism. Infusions used for intermittent fevers with scanty urine, rheumatism and as febrifuge. Crushed leaves mixed with ghee applied to ringworm infection. Juice collected from crushed plant is mixed with equal amount of honey, boiled and the collected oil is filtered and a teaspoon is taken twice daily for tuberculosis. Juice from crushed leaves applied to skin rashes. In Malaya, decoction of roots is drunk for fever and after childbirth. Leaves are ground with garlic, pepper, turmeric and boiled rice and made into pills and given for consumption. Powdered leaves used as febrifuge, antiseptic, catarrh, for headache, watery eyes and to promote growth of the beard and treatment of breast cancer. Powdered fruit, sweetened or mixed with honey, or in decoction, used as cephalic, nervine and emmenagogue. Leaves used internally or externally in baths to cure itching associated with Ciguatera fish poisoning. In Chinese medicine, dried fruit has been used for headache, migraine, colds, eye pain and cure certain cancers. Roots used as tonic, expectorant and febrifuge. Flowers and seeds used in making leis. Leaves are burned

as insect or mosquito repellent. Wood used for fuel and for light construction [36].

8. REPORTED PHARMACOLOGICAL ACTIVITIES OF *VITEX TRIFOLIA* LINN

8.1. Antioxidant and free radical scavenging activity

Sreedhar et al., evaluated *in-vitro* antioxidant activity and free radical scavenging potential of roots of *Vitex trifoliate*. The selected plant extracts and known antioxidant ascorbic acid at various concentrations produced dose dependent inhibition of superoxide radicals, hydroxyl radicals, lipid peroxidation and DPPH radical activities [37].

Aweng et al., reported antioxidant, antibacterial activity and phenolic compounds of *Vitex trifolia* Var, *Simplicifolia* linked with anticancer. The extracted of *V. trifolia* was analyzed and found to be high in antioxidant activity of phenolic compound. Phytochemical screening exposed the presence of alkaloids, saponins, phenolics, flavonoids, tannins and terpenoids [38].

Yahaya et al., determined antimicrobial and antioxidant activities of extracted essential oils in some aromatic plants. The antioxidant activities of the essential oils of different plants under investigation showed a dissimilarity which may be as a result of the difference in their chemical compositions. Antimicrobial activities showed that all the essential oils were inhibited on the entire five microorganisms being used [39].

8.2. Antimicrobial activity

Geetha et al., evaluated antibacterial potential of *V. trifolia* against certain pathogenic bacterial strains [40].

Natheer er al., evaluated various extracts of *Morinda citrifolia*, *V. trifolia* (leaf) and *Chromolaena odorata* for antibacterial activity. The extracts showed comparable antibacterial activity towards bacterial isolates, supporting its traditional use and suggesting a potential use for the treatment of infectious disease and development of chemotherapeutic agents [41].

Murugan and Mohan., evaluated two medicinal plants, *V. trifolia* and *Aristolochia indica* for potential bacterial activity against *S. aureus, K. pneumonia, B. subtilis, E. coli, S. typhi* and *P. aeruginosa*. A benzene extract of leaves of *V. trifolia* exhibited highest inhibition against *B. subtilis* [42].

Phani and Kumar., Studied crude powdered extracts of leaves of *V. trifolia*, *V. negundo* and *V. leucoxylon* showed antibacterial activity against both gram positive and gram negative organisms viz., *B. subtilis* and *E. coli* [43].

8.3. Analgesic, Anti-inflammatory and anti-arthritic activity

Kulkarni., evaluated the anti inflammatory activity of plant extracts at different dose intervals by using two models Carrageenan induced rat paw edema and Xylene induced ear edema in Mice. Significant reduction in paw volume ($P<0.01$) and ear edema were observed in all treated groups. Alcoholic extract showed more activity than aqueous extract and also in dose dependent manner [44].

Matsui et al., showed aqueous extract of *V. trifolia* significant dose- and time-dependent inhibitory activity on interleukin (IL)-1B, IL-6 and iNOS mRNA synthesis [45].

Goverdhan and Bobbala., studied the effect of *V. trifolia* leaf extract for the anti-nociceptive and anti-inflammatory activity in experimental animals. This study demonstrates that leaf extract of *V. trifolia*has significant anti-nociceptive and anti-inflammatory activity [46].

Pfuzia et al., studied the anti-inflammatory property of the aqueous extract of the leaves of *V. trifolia* by carrageenan induced paw oedema, granuloma pouch and formaldehyde induced arthritis method. The extract shows noteworthy anti-inflammatory activity when compared with the control and comparable efficacy with the standard [47].

Matsui et al., evaluated in vitro regulatory effects on the expression profile of lipo polysaccharide(LPS)-induced inflammatory genes focusing on regulation of chemo kinesC-X-C motif 10(CXCL-10)and C–C motif ligand 3(CCL-3) and cyclo-oxygenase (COX)-2 [48].

Kulkarni., studied analgesic potential of *V. trifolia* on acetic acid induced writhing test in mice and Tail immersion method in rats. The data concluded that the *V. trifolia* possess the both central and peripheral analgesic potential [49].

Ankalikar and Viswanathswamy., evaluated effect of hydroalcoholic extract of *V. trifolia* for anti-inflammatory activity. The extract at both the doses has effectively suppressed carrageenan induced inflammation. Similarly less wet exudate formation is seen at higher dose suggesting inhibitory effect of the compounds on vascular permeability and controlled formation of dry exudate indicative of the effect on proliferative phase. Hematological parameters, lymphocyte count at both the doses and histological studies of the granuloma tissue were also performed revealing decrease in levels of macrophages, mast cells and other inflammatory

mediators in groups treated with the extract as compared to animals treated in control group [50].

Mustarichie et al., reported the formulation of tablets of ethanol extract Legundi as an adjuvant to anti-inflammatory drugs on breast cancer. Tablet formulations prepared by wet granulation method in five variations of concentrations of Na-starch glycolate as a disintegrator. The results of this study indicate that the variation in concentrations of Na-starch glycolate as a disintegrator in the formula III is the most optimal concentration, i.e by 25 mg at the time were destroyed during the 12 minutes 36 seconds [51].

8.4. Anticarcinogenic activity

Mathankumar et al., studied the synergistic anticarcinogenic potential of *V. trifolia* and *Triticum aestivum* ethanolic extracts [52].

Garbi et al., investigated the cytotoxic activities of *V. trifolia* leaf extracts against MCF-7 and Vero cell line. Meanwhile the same extract showed a moderate inhibition against Vero cell lines [53].

Wang et al., investigated the inhibitory effect of vitexicarpin on the proliferation of human cancer cells and its mechanism of action. Vitexicarpin significantly inhibited the proliferation of human cancer cells; the cells treated with vitexicarpin showed characteristic morphology typical for apoptosis and gave dose-dependent sub-G0/G1 peak in the flow cytometric analysis and DNA ladder on agarose gel electrophoresis. In Western blotting analysis, the cleavage of PARP and caspase-3, the release of cytochrome from mitochondria into the cytosol, the decrease of Bcl-2 expression level, and the down-regulation of the ratio of Bcl-2/Bax expression level were examined in the K562 cells treated with vitexicarpin [54].

Jose et al., evaluated the effect of ethanolic extract of *V. trifolia* against trypan blue dye exclusion assay against Daltons ascites lymphoma cell lines. The dose of ethanolic extract of *V. trifolia* decreased average increase in body weight, reduced the packed cell volume (PCV) viable tumor cell count and increased the life span of DAL treated mice and brought back the hematological parameters near to normal values. All the values were found to be statistically significant with control group at $p<0.01$. These observations are suggestive of the protective effect of extracts in Dalton's Ascitic Lymphoma (DAL) [55].

Liou et al., isolated Casticin from *V. trifolia* and found to have anti-inflammatory and anti-tumor properties and casticin reduced airway hyper responsiveness (AHR), airway inflammation, and oxidative stress in the lungs of a murine asthma model and alleviated inflammatory and oxidative responses in tracheal epithelial cells [56].

Chan et al., reported that anticancer and anti-inflammatory properties of casticin from Vitex species [57].

Hernandez et al., Hexane and dichloromethane extracts showed toxicity against several cancer lines in culture. The hexanic extract from the leaves completely inhibited the growth of the fungal plant pathogen Fusarium species [58].

Vasanthi et al., evaluated the cytotoxicity of n-hexane fractions of *V. trifolia* in two cancer lines: HepG2 and HeLa. Results showed VT to be highly effective against both HepG2 and HeLa cancer lines at concentration of 80 μg/ml. Findings suggest a potential for use in liver and cervical cancers [59].

Zheng et al., Study of fruits isolated seven new labdane-type diterpenoids, vitextrifoline A-G (1-7), along with eight previously reported analogues. The Isolates were tested against four human cancer cell lines: All were found inactive with IC50 <5μg/ml [60].

8.5. Hepatoprotective activity

Manjunatha and Vidya., showed *V. trifolia* could provide significant protection against CCl4-induced hepatocellular injury. The hepatoprotective activity is supported by histological studies of liver tissue [61].

Anandan et al., showed ethanolic extract of flowers of *V. trifolia* possess hepatoprotective activity on CCl4-induced hepatic injury in rats. The activity was comparable to standard drug, silymarin [62].

8.6. Larvicidal activity

Kannathasan et al., studied of four species of Vitex against Culex quinquefasciatus larvae, the highest larvicidal activity was found with the extract of *V. trifolia* [63].

Kannathasan et al., studied larvicidal activity of fatty acid methyl ester extracts of *V. altissima, V. negundo* and *V. trifolia* against early fourth-instar larvae of Culex quinquefasciatus, the extract of V. trifolia showed the highest Larvicidal activity [64].

Kannathasan et al., studied, a crystalline compound methyl-phydroxybenzoate was isolated from the methanol extract of *V. trifolia* leaves and it was identified by 1H and 13C NMR and single crystal X-ray diffractometer. The larvicidal potential of the isolated compound was evaluated against early 4th instar larvae of Culex quinquefasciatus and Aedes aegypti. The

compound exhibited 100% larval mortality of both the mosquitoes at 20 ppm with LC50 values of 5.77 and 4.74 ppm against C. quinquefasciatus and A. aegypti, respectively [65].

8.7. Other activities

Devi and Singh et al., determined the contents of total phenol as well as antioxidant activity, the chemical composition and anti-dermatophytic activity of the *V. trifolia* essential oil of the leaves [66].

Garbi et al., evaluated antigiardial, antiamoebic activity and explore the cytotoxicity of petroleum ether and methanolic extracts of *V. trifolia* (leaves) *in vitro* [67].

Tiwari et al., isolated a new halimane diterpenoid, 13-hydroxy-5(10),14-halimadien-6-one (**1**) and two new labdane diterpenoids, 6α, 7α-diacetoxy-13-hydroxy-8(9),14-labdadien (**2**) and 9-hydroxy-13(14)-labden-15,16-olide (**3**), for the first time, along with fifteen known compounds, from the hexane soluble fraction of methanolic extract of *V. trifolia* leaves and evaluated for antitubercular activity against Mycobacterium tuberculosis H37Rv in BACTEC-460 assay [68].

Manaf et al., evaluated the effect of a dietary herbal mix comprised of petroleum ether and methanolic extracts, *Strobilanthes crispus* and *Aloe vera* on the growth performance, disease resistance and histology of *Oreochromis* sp. for 60 days [69].

Jangwan et al., isolated β-sitosterol and two triterpenoids: ursolic acid acetate and platanic acid from ethanolic extract of *V. trifolia* leaves. β-sitosterol was previously isolated from the leaves, stem and seeds of *V. trifolia*. Ursolic acid acetate has been isolated for the first time in this plant species. Platanic acid has been reported for the first time in *V. trifolia* and even in the family of this plant: *Verbenaceae*. A preliminary molluscicidal test for ethanol, chloroform and n-hexane extracts of leaves of *V. trifolia* against *Biomphalaria alexandrina* adult snails showed that ethanol extract of leaves was more effective than n-hexane extract and chloroform extract after 24 h exposure [70].

Arifin et al., determined the chemical compounds in the leaves *V. trifolia* and its repellent activity to male mice. The study began by isolating the hexane extract, ethyl acetate extract, and methanol extracts of the leaves of *V. trifolia* [71].

Kiuchi et al., investigated trypanocidal constituents of the fruits of *V. trifolia*. Activity-guided isolation of the acetone extract resulted in the isolation of two new norditerpene aldehydes, 1 and 2, together with five known diterpenes: vitexifolin E (3), vitexifolin F (4), vitexilactone (5), 6-acetoxy-9-hydroxy-13(14)-labden-16,15-olide (6), and previtexilactone (7) [72].

Mamjunatha and Vidya., Studied on the wound healing potency of ethanol leaf extracts of *V. trifolia* and *V. altissima* showed both extracts to possess significant would healing potency. Of the two, *V. trifolia* showed maximum healing activity compared to *V altissima* [73].

9. CONCLUSIONS

V. trifolia plant has been discovered comprehensively for their phytochemical and pharmacological activities. From the previous accounts, it is evident that *V. trifolia* plant has been used ethno-medicinally as a precious therapeutic agent for a variety of diseases, as we have illustrated in this article. Moreover, many research works have proven its uses beyond the ethno-medicinal ones in experimental animals. A variety of compounds which were separated from this plant may be accountable for its pharmacological activities.

10. REFERENCES

1. Verpoorte R. *J Pharm pharmacol*, 2000; **52(3)**:253-262.
2. Farnsworth NR, Akerele O, Bingel AS, Soejarto DD, et al. *Bull World Health Organ*, 1985; **63(6)**:965.
3. Sheng-Ji P. *Pharma Biol,* 2001; **39(sup1)**:74-79.
4. Fabricant DS, Farnsworth NR. *Environ Health Perspect,* 200; **109(Suppl 1)**:69.
5. Balunas MJ, Kinghorn AD. Life Sci, 2005; **78(5)**:431-41.
6. Abbasi AM, Khan MA, Ahmad M, Zafar M, et al. *African J Biotech*, 2009; **8(8)**:120-123.
7. Mabberley DJ. The plant-book: A Portable Dictionary of the Vascular Plants, 2nd ed, Cambridge University Press: Cambridge, U.K; 1997.p.749.
8. Kirtikar JD, Basu BD. Indian Medicinal Plants Vol-III, 2nd ed; (1981) NISCOM: New Delhi 1937.
9. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants, NISCOM: New Delhi; 1956. p.56.
10. Nadkarni KM. Indian materia medica. Bombay Popular Prakashan: Bombay; 1976.p. 1281.
11. Meena A, Singh U, Yadav A, Singh B, et al. *Int J Pharm Clin Res,* 2010; **2**:1-9.
12. BinoySM, Cheriyan V. *Asian J Pharm Clin Res*, 2018; **11(4)**:12-14.
13. Jose BE, Jebaseelan S, Meera R. *J Pharm Sci Res,* 2017; **9**:1056-1062.

14. Thenmozhi S, Sundaram RS, Kumar JP, Bihari CG. *J Pharm Res,* 2011; **4**:1259-62.
15. Van der Valk JM, Christiene L, Mark N. *J Herb Med,* 2017; **8**:40-51.
16. Giesen W, Wulfraat S, Zieren M, Scholten L. Vitex ovata. In: Mangrove guidebook for Southeast Asia, FAO and Wetland International: 2007. P.768-769.
17. CSIR, New Delhi. The Wealth of India - A Dictionary of Indian Raw Materials and Industrial Products - Raw Materials, Publications and Information Directorate: 1985. (Reprint); Vol.-IA, p.85-91.
18. Agrawal VS. Drug plants of India. Vol-2: Cuttak: Kalyani Publisher; 1997. p.721.
19. Nesom GL. *Phytoneuron,* 2010; **11**:1-15.
20. www.kew.org/plants-fungi/Vitex-trifolia.htm.
21. Thenmozhi S, Sundaram RS, Kumar JP, Bihari CG. *J Pharm Res,* 2011; **4**:1259-1262.
22. Cousins MM, Briggs J, Chuck G, Whitwell T, et al. *Weed Sci Soc Am,* 1991; **6**:101-103.
23. Zeng X, Fang Z, Wu Y, Zhang H. *Zhongguo Zhong Yao Za Zhi,* 1996; **21**:167-168.
24. Ono M, Sawamura H, Ito Y, Mizuki K, et al. *Phytochem,* 2000; **55**:873-877.
25. Hernández MM, Heraso C, Villarreal ML, Vargas-Arispuro I, et al. *J Ethnopharmacol,* 1999; **67**:37-44.
26. Kannathasan K, Senthilkumar A, Venkatesalu V. *Acta Trop,* 2011; **120**:115-118.
27. Li WX, Cui CB, Cai B, Wang HY, et al. *J Asian Nat Prod Res,* 2005; **7**:615-26.
28. Arifin B, Nasution R, Saidi N, Marianne, et al. *Int J Chem Tech Res,* 2014; **6**:4595-4600.
29. Chan EW. *Indian J Nat Prod Resour,* 2016; **7**:107-115.
30. Roqaiya M, Begum W, Majeedi SF. *Int J Pharm Sci Res,* 2017; **7**:31-41.
31. Mustariche R, Windhu WY, Ryan W. *Int J Res Ayurveda Pharm,* 2016; **7**:114-117.
32. Ahmad FB, Holdsworth DK. *Int J Pharmacogn,* 1995; **33**:262-264.
33. Bajpai A, Ojha JK, Sant HR. *Int J Pharmacogn,* 1995; **33**:172-176.
34. Aranda E, Hernandez MM, Heraso C, Villarreal ML, et al. *J Ethnopharmacol,* 1999; **67**:37-44.
35. Kannathasan K, Senthilkumar A, Chandrasekaran M, Venkatesalu V. *Parasitol Res*, 2007;**101**:1721-1723.
36. Venkateshwarlu G, Ragyanaik E, Swapna K, Santhosh A, et al. *Asian J Pharm Res,* 2014; **4(2)**:70-71.
37. Sreedhar V, Ravindra Nath LK, Madana Gopal N, Sanjith Nath M. *Res J Pharm Biol Chem Sci*, 2010; **1(4)**:1036-1044.
38. Aweng ER, Hanisah N, Mohd Nawi MA, Nurhanan Murni Y, et al. *J Biol Sci*, 2010; **1(3)**:65- 68.
39. Yahaya MF, Kubmarawa D, Yelwa JM, Runde M. *World Sci News,* 2018; **111**:13-25.
40. Geetha V, Doss A, Pichai A, Doss A. *Ancient Sci life,* 2004; **XXIII (4)**:30-32.
41. Esath Natheer S, Sekar C, Amutharaj P, Syed Abdul Rahman M et al. *African J Pharm Pharmacol,* 2012; **6(11)**:783-788.
42. Murugan M, Mohan V R. *Sci Res Repor,* 2012; **2(1)**: 110-114.
43. Phani K, Ravi Kumar A. *Indian J Res Pharm Biotech*, 2014; **2(2)**:1104-1105.
44. Kulkarni L A. *Int J Pharm Sci Res*, 2011; **2(8)**:2037-2040.
45. Mariko Matsui et al. *J Ethnopharmacol*, 2009; **126(3)**:427-433.
46. Goverdhan P, Bobbala D. *Ethnobotanical Leaflets,* 2009; **13**:65-72.
47. Pfuzi A, Bharati devi RK, Sharatchandra KH, Debashree BN, et al. *Int J Pharm Bio Sci*, 2013; **4(2)**:588-593.
48. Matsui M, Adib-Conquy M, Coste A, Kumar-Roine S, et al. *J Ethnopharmacol,* 2012; 143: 24-32.
49. Kulkarni LA. *Asian J Pharm Clin Res*, 2014; **7(1)**:157-159.
50. Ankalikar A, Viswanathswamy AH. *Indian J Pharm Edu Res,* 2017; **51(3)**:461-471
51. Mustarichie R, Wardhana YW, Wahyudi R. *Int J Res Ayurveda Pharm*, 2016; **7(Suppl 1)**:114-117.
52. Mathan Kumar M, Tamizhselvi R, Manickam V, Purohit G. *Toxicol Int*, 2015; **22(1)**:114-118.
53. Garbi MI, Osman EE, Kabbashi AS, Saleh MS, et al. *Int Res J Natural Sci,* 2017; **5(2):**12-21.
54. Wang HY, Cai B, Cui CB, Zhang DY, et al. *Yao Xue Xue Bao*, 2005; **40(1)**:27-31.
55. Jose BE, Jebaseelan S, Meera R. *J Pharm Sci Res*, 2017; **9(7)**:1056-1062
56. Liou CJ, Cheng CY, Yeh KW, Wu YH et al. *Front Pharmacol,* 2018; **9**:635.
57. Chiang Chan EW, Wong SK, Tuck Chan H. *J Integr Med,* (2018); doi: https://doi.org/10.1016/j.joim.2018.03.001.
58. Hernandez MM, Heraso C, et al. *J Ethnopharmacol,* 1999; **67(1)**:37-44.

59. Vasanthi VJ, Radhjeyalakshmi R, Nasrin F. *Int J Pharmacog Phytochem Res,* 2014; **6(3)**:449-453.
60. Zheng CJ, Zzhu JY, Yu W, Ma XQ, et al. *J Nat Prod*, 2013; **76(2)**:287-291.
61. Manjunatha BK, Vidya SM. *Indian J Pharm Sci,* 2008; **70(2)**:241-245.
62. Anandan R, Jayakar B, et al. *Pak J Pharm Sci*, 2009; **22(4)**:391-394.
63. Kannathasan K, et al. *Parasitology Res,* 2007; **101**:6.
64. Kannathasan K, Senthilkumar A, Venkatesalu V, Handrasekaran M. *Parasitology Res*, 2008; **103(4)**:999-1001.
65. Kannathasan K, Senthilkumar A, Venkatesalu V. *Acta Tropica,* 2011; **120**:115-118.
66. Devi WR, Singh CB. *Int J Phytocosmetics Natural Ingredients,* 2014; **1**:5.
67. Garbi MI, Osman EE, Dahab MM, Koko WS, et al. *Adv Med Plant Res,* 2015; **3(1)**: 1-7.
68. Tiwaria N, Thakur J, Saikia D, Gupta MM. *Phytomedicine,* 2013; **20**:605-610.
69. Manaf SR, Daud HM, Alimon AR, Mustapha NM, et al. *J Aquac Res Development,* 2016; **7**:4
70. Jangwan JS, Aquino RP, Mencherini T, Picerno P, et al. *Karba polonica,* 2013; **59**:4.
71. Arifin B, Nasution R, Saidi N, Aprilia S. *Int J ChemTech Res,* 2013; **6(11)**:4595-4600.
72. Kiuchi F, Matsuo K, Ito M, Qui TK, et al. *Chem Pharm Bull*, 2004; **52(12)**: 1492-1494.
73. Mamjunatha BK, Vidya SM, et al. *Phytotherapy Res,* 2014; **21(5)**:457- 461.