Decoding *Vitex altissima* L.: A review of its ethnobotanical heritage, phytochemical composition and therapeutic potential

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Review

Abstract

Background: Vitex altissima L. known as the "Peacock Chaste Tree" belongs to the Verbenaceae (Lamiaceae) family. Traditionally it is used for furniture making, relieve rheumatic swellings and body pain. The plant has gained attention for its significant pharmaceutical potential in traditional Chinese medicine as its bark and roots are used to treat rheumatism and pain. The plant's rich content of alkaloids, saponins, flavonoids and phenolic compounds contribute to its antioxidant, anti-inflammatory and antimicrobial properties.

Methods: This review aims to gain a comprehensive understanding of *Vitex altissima* L. by conducting an extensive literature search using platforms such as PubMed, ScienceDirect, Google Scholar, Ayush, e-Charaka, SpringerLink and relevant books.

Results: Vitex altissima L. is traditionally utilized by ethnic and tribal groups in South India to treat various ailments, including urinary disorders, stomatitis, ulcers and jaundice. The plant is rich in phytochemicals such as flavonol glycosides, flavonoids, steroidal saponins, alkaloids etc. includes compounds like agnuside, negundoside, corosolic acid, vitexin, altissinone, quercetin, tetradecanoic acid, viridiflorol etc. These compounds underpin the plant's broad pharmacological activities, comprising antimicrobial, anthelmintic, antiviral, wound healing, anti-inflammatory, antioxidant, anticancer, hepatoprotective, nephroprotective, insecticidal and larvicidal effects.

Conclusion: This review highlights *Vitex altissima* L. as a potent source of phytochemicals with substantial pharmacological value, contributing to our understanding of its biological activities and offering potential for advancements in medicinal and industrial fields in future.

Keywords: Vitex altissima L., Review, Ethnobotany, Pharmacology.

Background

Ethnobotany is increasingly recognized as a vital approach for identifying new medicinal plants or revisiting previously studied species for the extraction of beneficial bioactive compounds. Preserving ethnobotanical knowledge is vital for discovering and documenting essential medicinal plants (Thirumalai *et al.* 2009). Present review is crucial for advancing our understanding of plant-based therapies and to ensure the conservation of valuable medicinal resources for future use

(Wintola & Afolayan 2010). The use of traditional and complementary medicine is on the rise in both developed and developing countries. Traditional remedies are especially significant, serving as the primary and sometimes the only form of treatment for nearly 80% of the global population (Hamilton 2003), which is frequently encountered in proximity to riverbanks, scrub jungles and deciduous forests, thriving particularly on laterite and alluvial substrates (Manjunatha *et al*. 2007). *Vitex altissima* L. stands as a majestic deciduous giant, reaching towering heights of up to 35-40 meters. Its expansive presence graces the landscapes of Indo-Malaysia, Indo-China and Sri Lanka (Sekar *et al.* 2019). Primarily found in the Western Ghats and spanning the entirety of South India, this tree thrives not only in evergreen and semi-evergreen forests but also in deciduous forests and sacred groves (Sundaresan *et al.* 2020). The species is characterized by its grey, fibrous with scaly bark, trifoliate leaves and angular or winged petioles. The flowers of *Vitex altissima* L. appear bluish-white with terminal paniculate cymes. Wood, characterized by its robust and dense nature, exhibits a brownish-grey hue and a fine, compact grain. It is resistant to splitting and warping, it possesses excellent polishing qualities. This versatile material finds application in construction, furniture making and cart manufacturing due to its durability and reliability (Sedai *et al.* 2016). Due to low germination rates *V. altissima* L. is considered threatened tree in Western Ghats, Sudhakara and Veenadevi (2013) stated that treatments like soaking seeds in 200–300 ppm gibberellic acid, alternate wetting/drying, and straw fire treatment help improve germination. The plant also has a notable background of traditional medicinal utilization. A comprehensive biodiversity assessment is vital for understanding the species coexisting with *Vitex altissima* L. Liyanage (1997) noted its scarcity due to over-exploitation, though it remains abundant in disturbed forests in Sri Lanka. Parthasarathy (1999) highlighted its prominence in disturbed sites in southern Western Ghats contributing and supporting ecological dynamics, hosting up to 13 epiphyte species (Annaselvam & Parthasarathy 2001), serving as a vital food resource for the Great Pied Hornbill (Balasubramanian *et al*. 2011; Kannan and James, 1999) and supporting pest larvae such as *Hyblaea puera* (Kumar *et al.* 2002). It thrives in diverse habitats, including moist deciduous and riparian zones (Thomas *et al.* 2012) and shows high growth performance in the Eastern Ghats (Tamilselvan *et al*. 2021). Studies by Raju *et al.* (2014) documented its importance to butterfly pollinators, further emphasizing its ecological role. The phytochemical analysis of *Vitex altissima* L. reveals the presence of various secondary metabolites, including alkaloids, flavonoids, terpenoids and phenolic compounds. These constituents contribute to the antioxidant, anti-inflammatory and antimicrobial properties, suggesting a potential role in the management of oxidative stress-related disorders and infectious diseases (Dayana *et al*. 2015; Sekar *et al.* 2019). Britto *et al.* (2011) studied drought stress effects in *Vitex altissima* L., identifying proteins of 178.825 kD and 149.105 kD in stressed plants. This overview underscores of *V. altissima* L. multi-faceted pharmacological profile, encouraging further research to unravel its therapeutic utility. Bridging traditional wisdom with modern science, *Vitex altissima* L. beckons as a promising source for novel pharmaceutical discoveries. The exploration of *Vitex altissima* L. pharmacological potential opens avenues for the development of novel therapeutic agents and emphasizes the importance of integrating traditional knowledge with modern scientific approaches for the discovery of new medicines. The present study aims to provide updated insights into the ethnobotanical uses of *Vitex altissima* L. by examining its bioactive components as reported in the literature.

Materials and Methods

To achieve the study's objectives, an extensive search was conducted across databases including ScienceDirect, PubMed, Google Scholar, regional ethnobotanical texts, and AYUSH. The search focused on the morphology, ethnomedicinal uses, geographical distribution, phytochemistry, pharmacology, Ayurvedic potential and biomedical applications of *Vitex altissima* L. Keywords such as "*Vitex altissima* L." "Review" "Ethnobotany" "Pharmacology" were employed, utilizing OR/AND operators to refine the search. English was selected as the primary language for the study.

Morphological characteristics

Vitex altissima L. is a large tree, woody, 10 - 15 m tall. Wood is grey with an olive-brown tinge, hard, dense, and heavy. Branchlets slender, subterete or obtusely 4-angular in young. Branches thick, sturdy, that are beginning to drop slightly. The bark is thick, weathered grey, dark brown, lenticelled, pubescent in young branches. Nodes annulate with a band of hairs; internodes long. Leaves 3-foliolate, occasionally 5-foliolate, decussate, rarely unifoliate, opposite; convex or keeled on the underside, and flattened on the top. Petiole flattened, winged for the entire length in older leaves, densely pubescent. Leaflets lanceolate, ovate, oblanceolate or elliptic, acute at base, undulate, entire, rarely obcordate, acute to acuminate at apex. Middle leaflets subequal, central one is larger, lateral leaflets, obscure margined. both sessile or sub sessile, thick, dark green glabrous above, lower surface also glabrous except ribs, ribs silky white hairy, sharp; lateral nerves distinct beneath. Panicles terminal and supraciliary, hoary tomentose, clustered densely along the branches. bract slightly falcate, lanceolate or oblong, caducous, pubescent or hoary outside and sparsely hairy at inside, hoary tomentose in upper half inside, slightly broader at the middle, blunt at apex. Flowers sessile, two to four together, bluish white or pinkish in color. Calyx cupular, 5-toothed, subequal, teeth acute with purplish stripes inside, tomentose. Corolla infundibular, 2-lipped, 5-lobed, white tinged

with blue or violet; upper lip 2-lobed; lobes ovate, suborbicular, crenulate, obtuse, silky white glandular hair outside, lower lip 3-lobed, middle lobe twice in size than lateral lobe. Lateral lobes oblong, obtuse, entire. Stamens 4, didynamous, densely villous at throat, pubescent outside. subglobose, filaments slender, white hairy or feathery at base; anther lobe brown to black, sub globose, villous at apex; divaricate, basifixed, Style stout, recurved. Stigma 2-lobed; lobes short, subulate, subequal. Ovary globose, superior, 4-locular, stout, silky hairy at apex. Drupes globose, fleshy, purple, white-dotted, white silky at top, turning black at ripening; 1 – 2 seeded. Seed white, ovate at base, acute at apex. Flowering and fruiting occur during March and July (Cooke 1958; Sunilkumar & Antony 2013). Morphological characteristics are shown in (Figure 1).

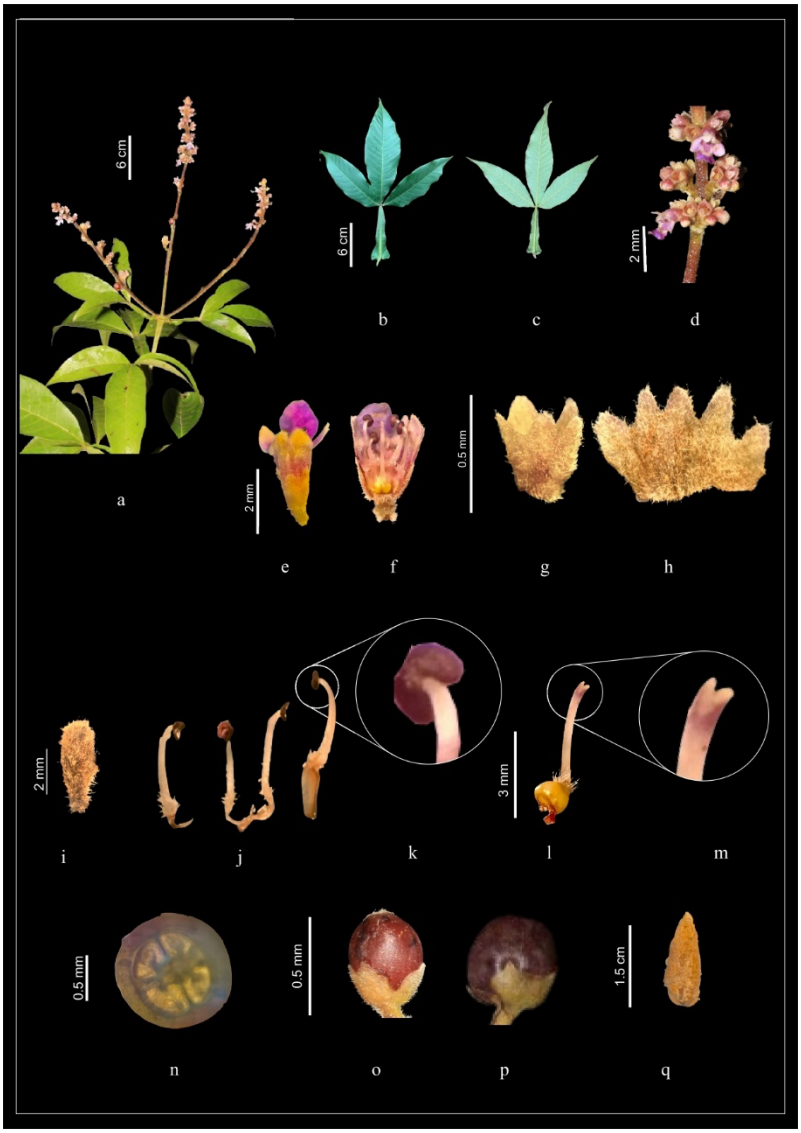

Figure 1**.** Morphological features of *V. altissima* L. **a.** Habit **b & c**. Leaf adaxial and abaxial **d.** Panicle **e.** Entire flower **f.** L.S of flower **g & h.** Non-dissected and dissected calyx **i.** Bract **j.** Stamens **k.** Anther lobes enlarged **l.** Style **& m.** Stigma **n.** T.S. of ovary **o.** Unripe drupe **p.** Ripened drupe **q.** Seed

Ethnobotanical Heritage

Ethnobotanical uses of *Vitex altissima* L. vary across communities, some traditional applications include the utilization of various parts of the plant for medicinal purposes. The plant has some important direct uses for humans and also exhibit superior fuelwood qualities (Sedai *et al.* 2016). Mishra *et al.* (2023) reported *Vitex altissima* L. as the primary timber species at sawmills in Sirsi taluk, Uttara Kannada district of the Western Ghats region, Karnataka. In traditional Chinese medicine, the bark and roots of *Vitex altissima* L. have been employed to address conditions such as rheumatism and pain. Additionally, extracts from the plant have been studied for their potential anti-inflammatory and antioxidant properties, suggesting a range of potential health benefits derived from its ethnomedicinal uses that are listed and shown in (Table 1 and Figure 2).

Table. 1 Ethnobotanical uses of *V. altissima* L.

Sr. No.	Plant part used	Formulation	Application/uses	References
1	Root	Decoction	Used to treat malaria and blackwater fever	Chopra *et al.* 1956, Manjunatha *et al.* 2007.
2	Stem	NA	Orally taken to remove wound scar	Vasugi, 2014
3	Bark	Juice	Applied externally to relieve phlegm from chest	Sunilkumar, 2013
4	Bark/ Leaf	Extract	Applied on body to relief pain	Sunilkumar, 2013
5	Bark/ Leaf	Juice/Decoction	Externally applied against rheumatic swellings and chest pains	Vasugi, 2014; Manjunatha *et al.* 2007
6	Leaf	Paste	Consume with coconut water to treat stone in Gallbladder	Sunilkumar, 2013
		Paste	Applied externally on infected part of skin infections	Rajakumar and Shivanna, 2010
		Juice	Used to treat wounds alone or mixed with turmeric for better result	Sunilkumar, 2013
		Extract	Inflammation, wound, ulcer, allergy, eczema	Vasugi, 2014
		Decoction	Orally taken to remove wound scar	Vasugi, 2014; Ayyanar and Ignacimuthu, 2009
		NA	Remedy for thoracic discomfort	Chopra *et al.* 1956

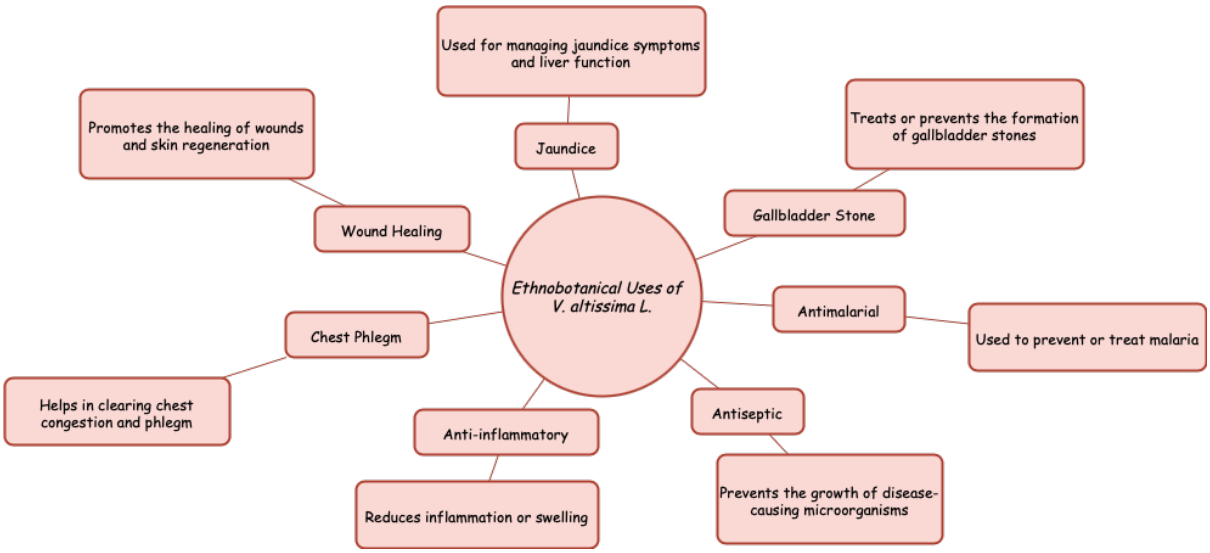

Figure 2. Outline of ethnobotanical Uses of *V. altissima* L.

Phytochemical composition

Many researchers have studied the phytochemical composition of *Vitex altissima* L. by quantitative method. The leaf extracts have been subjected to preliminary phytochemical screening, revealing the presence of various bioactive compounds such as alkaloids, carbohydrates, flavonoids, phenolic acids and saponins. High-Performance Thin-Layer Chromatography (HPTLC) fingerprinting has also been employed for the identification and standardization of phytochemical components, aiding in the precise quantification of active compounds in *Vitex altissima* L. (Sekar *et al.* 2019). Notably, the leaves of *Vitex altissima* L. are rich in biologically active compounds, particularly anti-inflammatory agents. The agnuside and negundoside, two additional iridoids, were also isolated from the leaf extract, further emphasizing the pharmacological potential of *Vitex altissima* L. (Sridhar *et al.* 2004). Investigators have documented an array of distinct chemical compounds, precisely catalogued in the table No. 2, revealing the diverse and multifaceted nature of chemical constituents in plants shown in (Figure 3).

Therapeutic Potential

Vitex altissima L., a prominent medicinal plant in traditional systems of medicine, is valued for its diverse pharmacological properties. Rich in bioactive compounds, it has been traditionally used to treat a variety of ailments. The therapeutic potential of *Vitex altissima* L. is multifaceted and can be enumerated as follows.

Antimicrobial activity

Ganapaty *et al.* (2005) revealed that leaf extracts of *Vitex altissima* L. exhibited moderate antibacterial activity against a range of tested bacteria. Notably, these extracts demonstrated no antifungal activity against *Aspergillus niger* van Tieghem at a concentration of 50 mg/mL, indicating a selective antimicrobial effect. Subsequent research conducted by Kannathasan *et al.* (2011) utilized the disc diffusion method to examine the antibacterial properties of methanol extracts against various strains, including *Bacillus subtilis* (Ehrenberg) Cohn*, Escherichia coli* (Migula) Castellani and *Staphylococcus aureus* Rosenbach. The results displayed mean zones of inhibition ranging from 14.800 ± 0.793 mm to 8.130 ± 0.814 mm, with minimum inhibitory concentrations (MIC) noted between 125.0 µg/mL and 2000.00 µg/mL. Dayana *et al.* (2015) expanded these findings by investigating hydro-alcoholic extracts derived from *Vitex altissima* L. The study demonstrated pronounced antibacterial efficacy against microorganisms such as *Klebsiella pneumoniae* (Schroeter) Trevisan and *Vibrio cholerae* Pacini, with significant inhibition zones noted, particularly against *K. pneumoniae* (Schroeter) Trevisan. Interestingly, the extract displayed inhibitory effects even at low concentrations against *Escherichia coli* (Migula) Castellani and *Staphylococcus mutans* Rosenbach. However, it exhibited limited antifungal activity, showing no inhibition against *Candida albicans* (C.P. Robin) Berkhout and *Candida tropicalis* (Castellani) Berkhout. Further investigations by Thomas *et al.* (2013) assessed the antifungal potential of *Vitex altissima* L. against various fungal strains, including *Aspergillus flavus* Link and *Penicillium* sp. Link, the comprehensive analysis indicated a noteworthy sensitivity pattern, revealing effectiveness against all tested fungi. Sathish *et al.* (2015) examined various extracts, including acetone, chloroform, ethanol and petroleum ether, against several bacterial strains, including *E. coli* (Migula) Castellani*, Pseudomonas mirabilis* Hauser and *Bacillus cereus* Frankland & Frankland. The study found MIC values ranging from 8.7 to 19.5 µg/mL, demonstrating that *Vitex altissima* L. extracts could rival standard antibiotics such as streptomycin. Irulandi *et al.* (2017) noted that ethyl acetate extracts displayed significant antagonistic effects on *Bacillus subtilis* (Ehrenberg) Cohn, achieving a zone of inhibition of 19.67 ± 1.53 mm, which surpassed the impact on other tested bacteria. Bhavana *et al.* (2019) utilised *Vitex altissima* L. leaves, for the green synthesis of SnO_2 NPs, exploring antibacterial and anticancer activities. The SnO_2NPs showed noteworthy antibacterial effects towards *E. coli* (Migula) Castellani & Chalmers*, Pseudomonas desmolyticum* (Imshenetsky) Gupta & Meyer and *Staphylococcus aureus* Rosenbach. Preethi-naidu *et al*. (2020) further contributed to this body of research by examining the antibacterial activity of various extracts, noting that the ethyl acetate extract showed noteworthy activity against *K. pneumoniae* (Schroeter) Trevisan and *Agrobacterium tumefaciens* (Smith & Townsend) Conn, with inhibition zones of 15 mm and 14 mm, respectively, in comparison to the reference drug chloramphenicol (17 mm). Natekar *et al.* (2022) made a significant contribution to mycological research by documenting novel occurrences of meliolaceous fungi on *Vitex altissima* L., identifying *Moullava spicata* (Dalzell) Nicolson and *Moullava altissima* (Lamarck) Gagnon & G.P. Lewis as previously unreported species, thereby enhancing knowledge of the fungal diversity associated with this plant.

Anthelmintic activity

Preethi-Naidu *et al*. (2020) evaluated the anthelmintic activity of petroleum ether, ethyl acetate, and ethanol extracts of *Vitex altissima* leaves against *Pheretima posthuman* Vaillant. Tween-80 (1%) in normal saline was used as the control, while albendazole was used as the standard reference. They recorded paralysis when the worms exhibited no movement except upon vigorous shaking and death was confirmed by the loss of motility in hot water along with fading of body color. Among the tested extracts, the ethanolic extract at a concentration of 60 mg/ml demonstrated the most significant anthelmintic activity, inducing paralysis within 43 minutes and causing death within 70 minutes, outperforming albendazole. Future research can explore the isolation and characterization of active compounds from *Vitex altissima* leaves to enhance anthelmintic efficacy and mechanisms of action.

Antiviral activity

Maria-john *et al.* (2015) unveiled diverse medicinal properties of ethnic plants against H_1N_1, accompanied by metabolic variations. The concentrations of *Vitex altissima* L. extracts employed in the anti-viral assay and their impact on the toxicity against the H_1N_1 virus was reported as IC_{50} 1145.86 ± 78, CC_{50} 42.41, with a therapeutic index of 0.037. Furthermore, the reported total phenolic content was 62.39 mg/g and the total flavonoids content was 46.33 mg/g. The investigators also reported that there was a high phenolic content and high cytotoxicity to Malin Darby canine kidney cells. Masi *et al.* (2020) analysed bioactive compounds from *Vitex altissima* L. species and tested binding affinity against HIV's reverse transcriptase.

That results, compared with commercial drugs, showed greater efficacy of *Vitex altissima* L. compounds, suggesting potential for AIDS treatment. This study promotes the development of safer therapeutic lead molecules from traditional plants.

Wound healing activity

Manjunatha *et al.* (2007) utilized incision, excision and dead space wound models for evaluating the wound healing activity. Through topical application, the ethanol leaf extract of *Vitex altissima* L. exhibited an impressive 96.22 % recovery within eighteen days of injury in rats. This discovery offers scientific validation for the traditional medicinal use of *Vitex altissima* L. in facilitating wound healing.

Antioxidant activity

Sridhar *et al.* (2004) isolated iridoid glucosides from *Vitex altissima* L. leaves, identifying compounds like Agnuside and Negundoside, which did not show 5-lipoxygenase inhibitory activity at concentrations up to 1000 µM. However, notable antioxidant activity was observed, with IC_{50} values for superoxide free radical scavenging of 24.3 µM, 32.0 µM, and 31.9 µM for 6'-O-trans-Caffeoylnegundoside, 2'-O-p-Hydroxybenzoyl-6'-O-trans-caffeoylgardoside and 2'-O-p-Hydroxybenzoyl-6'-O-trans-caffeoyl-8-epiloganic acid, respectively. In DPPH radical scavenging assays, IC_{50} values were 15.2 µM, 10.9 µM and 11.4 µM, while a paw edema assay showed 200 mg/kg doses of 6'-O-trans-Feruloylnegundoside resulted in a 20% inhibition, indicating potential anti-inflammatory effects. In a subsequent study, Sridhar and Subbaraju (2005b) reported presence of triterpene acids, such as corosolic acid (80%) and epicorosolic acid (79%), which exhibited potent 5-lipoxygenase inhibitory activity (500 µM), surpassing nordihydroguaiaretic acid. Additionally, flavonoids vitexin and luteolin 7-O-glucoside displayed significant antioxidant activity with IC_{50} values of 62 µg/mL and 8 µg/mL for superoxide scavenging; 43 µg/mL and 7.4 µg/mL for DPPH assays, respectively, outperforming vitamin C and BHA. Vasugi and Raju (2014) noted the highest total phenolic content (260.26 ± 5.20 mg TAE/g) in the acetone extract of stem bark, followed by the methanol extract of leaves (242.37 ± 18.81 mg TAE/g), while water extracts exhibited the highest tannin content (22.73 ± 1.46 mg TAE/g). The acetone extract of leaves demonstrated highest flavonoid concentration (17.43 ± 2.87 mg RE/g) and the water extract of leaves showed the highest DPPH radical scavenging activity (IC_{50} 23.37 ± 0.37 µg/mL). The methanol extract of fruit exhibited strong hydroxyl radical scavenging (IC_{50} 23.57 ± 0.10 µg/mL). Sundaresan *et al.* (2020) demonstrated that the methanol extract of *Vitex altissima* L. leaves exhibited significant antioxidant activity (IC_{50} 45.752 µg/mL) and 91.92% DPPH radical scavenging at 200 µg/mL, with antimicrobial assessments revealing activity against *Pseudomonas aeruginosa* Schroeter for hexane and chloroform extracts. Sunitha *et al.* (2023) identified thirty-seven compounds in the essential oil of *Vitex altissima* L., with antioxidant activity assessed *via* nitric oxide and DPPH assays yielding an IC_{50} of 834.07 µg/mL, slightly higher than gallic acid, while the DPPH assay showed potent activity (92.12 ± 2.19 µg/mL), surpassing ascorbic acid (49.72 ± 0.360 µg/mL). Vedula *et al.* (2022) utilized barks from mature *Vitex altissima* L. plants, which were shade-dried, powdered and extracted using methanol in a Soxhlet apparatus. Adult Wistar albino rats of both sexes served as the animal model. The study measured total flavonoid content at 10.11 ± 1.11 mg/g (rutin) and phenolic content at 112.2 ± 5.12 mg/g (gallic acid). *Vitex altissima* L. exhibited robust DPPH radical scavenging activity, surpassing ascorbic acid with an IC_{50} value of 29.37 ± 2.11 µg/mL, while showing a reducing power that was three times lower than ascorbic acid (IC_{50} 93.33 ± 3.14 µg/mL vs. 35.47 ± 2.12 µg/mL).

Anti-inflammatory activities:

Mehalingam *et al.* (2014) investigated the analgesic, anti-inflammatory and antipyretic properties of *Vitex altissima* L. leaf extracts following oral administration to rats, it exhibited substantial dose-dependent suppression of pain and inflammation, coupled with noteworthy antipyretic effects. No toxicity was observed at a dose of 5g/kg body weight. These findings substantiate the traditional usage of *Vitex altissima* L. in managing pain and related ailments, highlighting its therapeutic potential. Ganapathy *et al.* (2018) assessed the anti-inflammatory and analgesic potential of the ethanolic extract derived from the stem bark of *Vitex altissima* L. Two dose levels 150 and 450 mg/kg body weight were administered orally and the results were compared to reference drugs (indomethacin) for anti-inflammatory and acetylsalicylic acid for analgesic activity. Prior to the studies, an acute toxicity assessment was conducted, indicating the non-toxic nature of the plant at levels below 5g/kg. The ethanolic extract from the stem bark of *Vitex altissima* L. demonstrated significant dose-dependent anti-inflammatory and analgesic effects. These findings suggested that the extract holds promise as a potent option for managing inflammatory diseases and pain.

Table 2. Phytoconstituents in *V. altissima* L.

Class	Compounds	Plant part	Solvent	Quantification	Biological activity	Reference
Terpenes and Terpenoids						
1	1,3-Cyclohexadiene, 5-(1,5-dimethyl-4-hexenyl)-2-methyl	Leaf	Ethanol	GC-MS	Anti-tumor, Analgesic Anti-bacterial, Anti-inflammatory, Sedative, Fungicide	Sathish *et al.* 2015
2	1,6,10-Dodecatriene, 7,11-dimethyl-3-methylene-, (Z)-	Leaf	Ethanol	GC-MS	Anti-tumor, Analgesic Anti-bacterial, Anti-inflammatory, Sedative, Fungicide	Sathish *et al.* 2015
3	2a,3a,24-trihydroxyurs-12,20 (30)-dien-28-oic acid	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
4	α-Caryophyllene	Leaf	Ethanol	GC-MS	Anti-tumor, Analgesic Anti-bacterial, Anti-inflammatory, Sedative, Fungicide	Sathish *et al.* 2015
		Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
5	Caryophyllene	Leaf	Ethanol	GC-MS	Anti-tumor, Analgesic Anti-bacterial, Anti-inflammatory, Sedative, Fungicide	Sathish *et al.* 2015
		Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
6	Corosolic acid	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
7	Epicorosolic acid	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
8	Epimaslinic acid	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
9	Euscaphic acid	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
10	Euscaphic acid glucoside ester	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
11	Germacrene D	Leaf	Ethanol	GC-MS	Anti-tumor, Analgesic Antibacterial, Anti-inflammatory, Sedative, Fungicide	Sathish *et al.* 2015
		Leaf	Ethanol	FTIR	Anticancer	Naganathan *et al.* 2016
12	Maslinic acid	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
13	Phytol	Leaf	Ethanol	GC-MS	Anti-microbial, Anticancer, Anti-inflammatory, Hypocholesterolemic, Nematicide, Anti-coronary, Anti-arthritic, Hepatoprotective, Anti - androgenic	Sathish *et al.* 2015
		Leaf	Ethanol	FTIR	Anticancer; Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020

14	Squalene	Leaf	Ethanol	FTIR	Anticancer	Naganathan *et al.* 2016
		Leaf	Ethanol	GC-MS	Anti-bacterial, Anti-oxidant, Anti-tumor, Cancer preventive, Immunostimulant, Chemo preventive, Lipoxygenase-inhibitor, Pesticide	Sathish *et al.* 2015
15	Ursolic acid	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
Esters						
1	1, 2-benzene dicarboxylic acid, butyl octyl ester	Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
				GC-MS	Anti-microbial, Anti-fouling	Sathish *et al.* 2015
2	Hexadecanoic acid ethyl ester	Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
3	Lauric acid	Leaf	Methanol+ Benzene+ Sulphuric acid	GC-MS	Larvicidal	Kannathasan *et al.* 2008
4	Linoleic acid	Leaf	Methanol+ Benzene+ Sulphuric acid	GC-MS	Larvicidal	Kannathasan *et al.* 2008
5	Linolenic acid	Leaf	Methanol+ Benzene+ Sulphuric acid	GC-MS	Larvicidal	Kannathasan *et al.* 2008
6	Myristic acid	Leaf	Methanol+ Benzene+ Sulphuric acid	GC-MS	Larvicidal	Kannathasan *et al.* 2008
7	Oleic acid	Leaf	Methanol+ Benzene+ Sulphuric acid	GC-MS	Larvicidal	Kannathasan *et al.* 2008
8	Palmitic acid	Leaf	Methanol+ Benzene+ Sulphuric acid	GC-MS	Larvicidal	Kannathasan *et al.* 2008
9	Stearic acid	Leaf	Methanol+ Benzene+ Sulphuric acid	GC-MS	Larvicidal	Kannathasan *et al.* 2008
Essential oils						
1	α-Santalol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
2	5-epi-7-epi-α-Eduesmol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
3	allo-Aromadendrene	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
4	allo Himachalol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
5	Aromadendrene	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023

6	Bicyclogermacrene	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
7	Caryophylla-4 (12),8 (13) diene-5α-ol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
8	Caryophylla-4(12),8(13) diene-5β-ol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
9	Caryophyllene Oxide	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
10	Drimenone	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
11	E-Phytol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
12	Globulol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
13	Humulene epoxide II	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
14	Linalool	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
15	Palustrol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
16	Spathulenol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
17	trans-Caryophyllene	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
18	trans-Isoeugenyl phenyl acetate	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
19	trans-Isolongifolanone	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
20	Viridiflorol	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
21	α-Gurjunene	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
22	α-Humulene	Leaf	—	GC-MS / GC-FID	Antioxidant, Anticancer	Sunitha *et al.* 2023
Fatty acids						
1	Octadecanoic Acid	Leaf	Ethanol	GC-MS	—	Sathish *et al.* 2015
		Leaf	Ethanol	FTIR	Anticancer; Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
2	9,12-Octadecadienoic acid	Leaf	Ethanol	GC-MS	Hypocholesterolemic, 5-α-reductase inhibitor, Antihistaminic, Anti-eczemic, Anti-acne	Sathish *et al.* 2015
3	Dodecanoic acid	Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
		Leaf	Ethanol	GC-MS	Anti-oxidant, Anti-bacterial, COX-1 & COX-2 inhibitor, Anti-viral, Hypocholesterolemic, Candidacidal	Sathish *et al.* 2015
4	Hexadecanoic acid, ethyl ester	Leaf	Ethanol	GC-MS	Anti-oxidant, Hypocholesterolemic nematicide, Pesticide, Lubricant, Anti-androgenic, Flavor, Haemolytic 5-α reductase inhibitor	Sathish *et al.* 2015
5	n-Hexadecanoic acid	Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020

		Leaf	Ethanol	GC-MS	Anti-oxidant, Hypocholesterolemic nematicide, Pesticide, Lubricant, Anti-androgenic, Haemolytic	Sathish *et al.* 2015
6	Tetradecanoic acid	Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
Flavone and Flavonoids						
1	2″-O-p-hydroxy benzoyl orientin	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
2	luteolin 7-O-glucoside	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
3	Vitexin	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
Iridoids						
1	2′-O-p-hydroxybenzoyl gardoside	Leaf	Ethyl acetate	HPLC	Antioxidant, Anti-inflammatory	Sridhar *et al.* 2004
2	2'-O-p-hydroxybenzoyl-6'-O-trans-caffeoyl-8-epiloganic acid	Leaf	Ethyl acetate	HPLC	Antioxidant, Anti-inflammatory	Sridhar *et al.* 2004
3	2'-O-p-hydroxybenzoyl-6'-O-trans-caffeoylgardoside	Leaf	Ethyl acetate	HPLC	Antioxidant, Anti-inflammatory	Sridhar *et al.* 2004
4	2'-O-p-hydroxybenzoyl-8-epiloganic acid	Leaf	Ethyl acetate	HPLC	Antioxidant, Anti-inflammatory	Sridhar *et al.* 2004
5	6′-O-trans-caffeoylnegundoside	Leaf	Ethyl acetate	HPLC	Antioxidant, Anti-inflammatory	Sridhar *et al.* 2004
6	6′-O-trans-feruloylnegundoside	Leaf	Ethyl acetate	HPLC	Antioxidant, Anti-inflammatory	Sridhar *et al.* 2004
7	Agnuside	Leaf	Ethyl acetate	HPLC	Antioxidant, Anti-inflammatory	Sridhar *et al.* 2004
8	Negundoside	Leaf	Ethyl acetate	HPLC	Antioxidant, Anti-inflammatory	Sridhar *et al.* 2004
Phenolics						
1	Eugenol	Leaf	Ethanol	GC-MS	Analgesic, Anesthetic, Allergenic, Anti-bacterial, Anti-convulsant, Anti-inflammatory, Anti-oxidant, Anti-pyretic, Anti-salmonella, Anti-staphylococcus, Anti-septic	Sathish *et al.* 2015
		Leaf	Ethanol	FTIR	Anticancer; Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
Sugar compounds						
1	3-Pyridinecarboxylic acid, 6-amino-d-Mannose	Leaf	Ethanol	GC-MS	Anti-microbial, Anti-inflammatory	Sathish *et al.* 2015
2	D-Mannose	Leaf	Ethanol	FTIR	Anticancer; Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
Other compounds						
1	4, 6-Octadienoic Acid	Leaf	Ethanol	FTIR	Anticancer; Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
2	1, 3-Cyclohexadiene, 5-(1, 5-dimethyl-4-hexenyl)-2-methyl	Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020

3	1,6,10-Dodecatriene, 7,11-dimethyl-3-methylene	Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
4	3,7,11,15- tetramethyl-2- hexadecen-1-ol	Leaf	Ethanol	GC-MS	Antimicrobial, Anti-inflammatory	Sathish *et al.* 2015
				FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
5	3-Pyridine Carboxylic Acid,6-Amino	Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016;
6	9, 12-Octadecadienoic acid	Leaf	Ethanol	FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
7	Altissinone	Leaf	Ethyl acetate	HPLC	Antioxidant	Sridhar *et al.* 2005a
8	Benzene, 1-(1,5-dimethyl-4-hexenyl)-4-methyl- [Aromatic-Curcumene]	Leaf	Ethanol	GC-MS	Anti-oxidant, Anti-inflammatory, Anti-cancer	Sathish *et al.* 2015
				FTIR	Anticancer, Anti-HIV	Naganathan *et al.* 2016; Masi *et al.* 2020
9	Benzene, 1, 4-dichloro 4, 6-Octadienoic Acid	Leaf	Ethanol	GC-MS	—	Sathish *et al.* 2015
				FTIR	Anti-HIV	Masi *et al.* 2020
10	1, 4-Dichloro Benzene	Leaf	Ethanol	FTIR	Anticancer	Naganathan *et al.* 2016

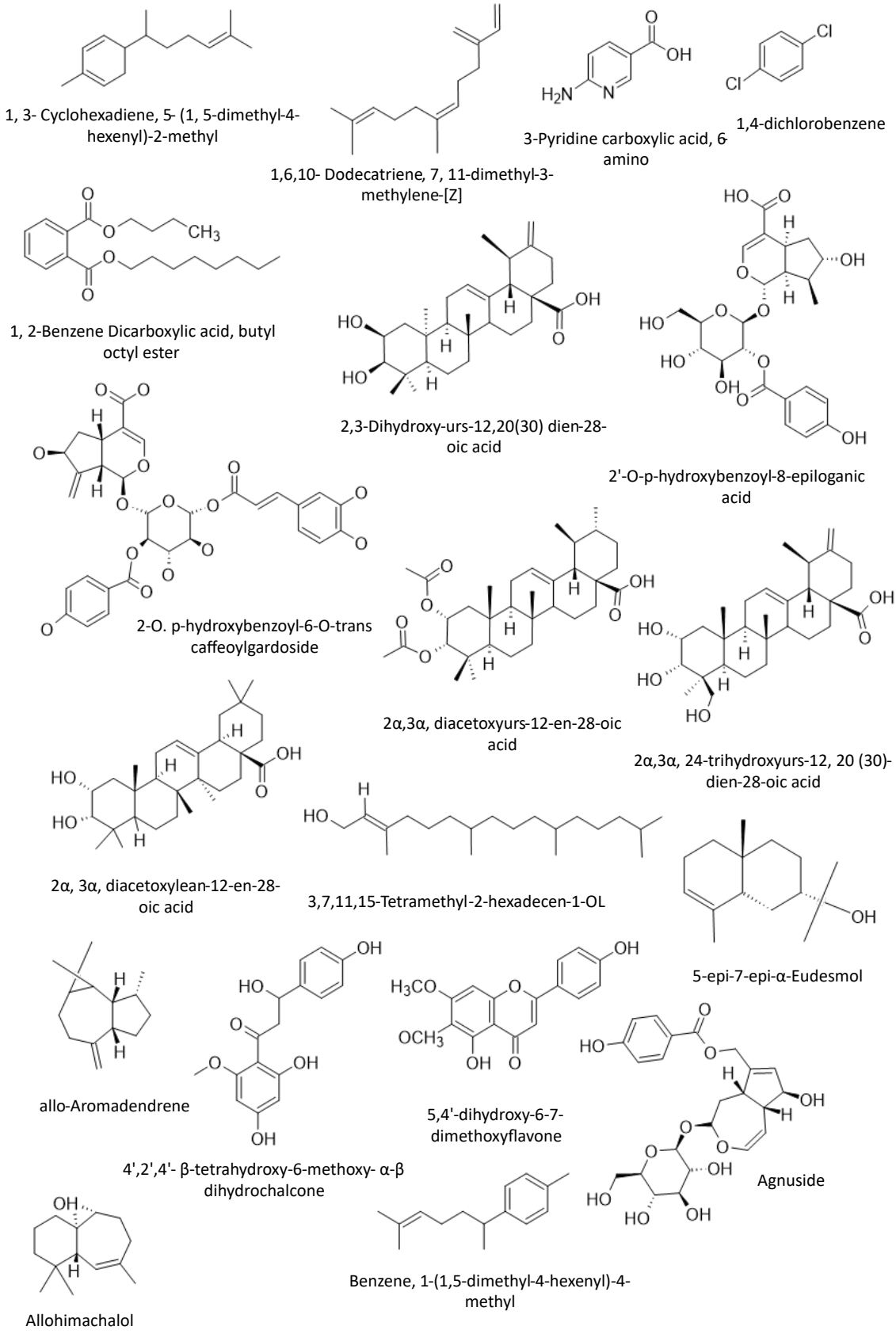

Figure 3. Chemical structure of some phytoconstituents.

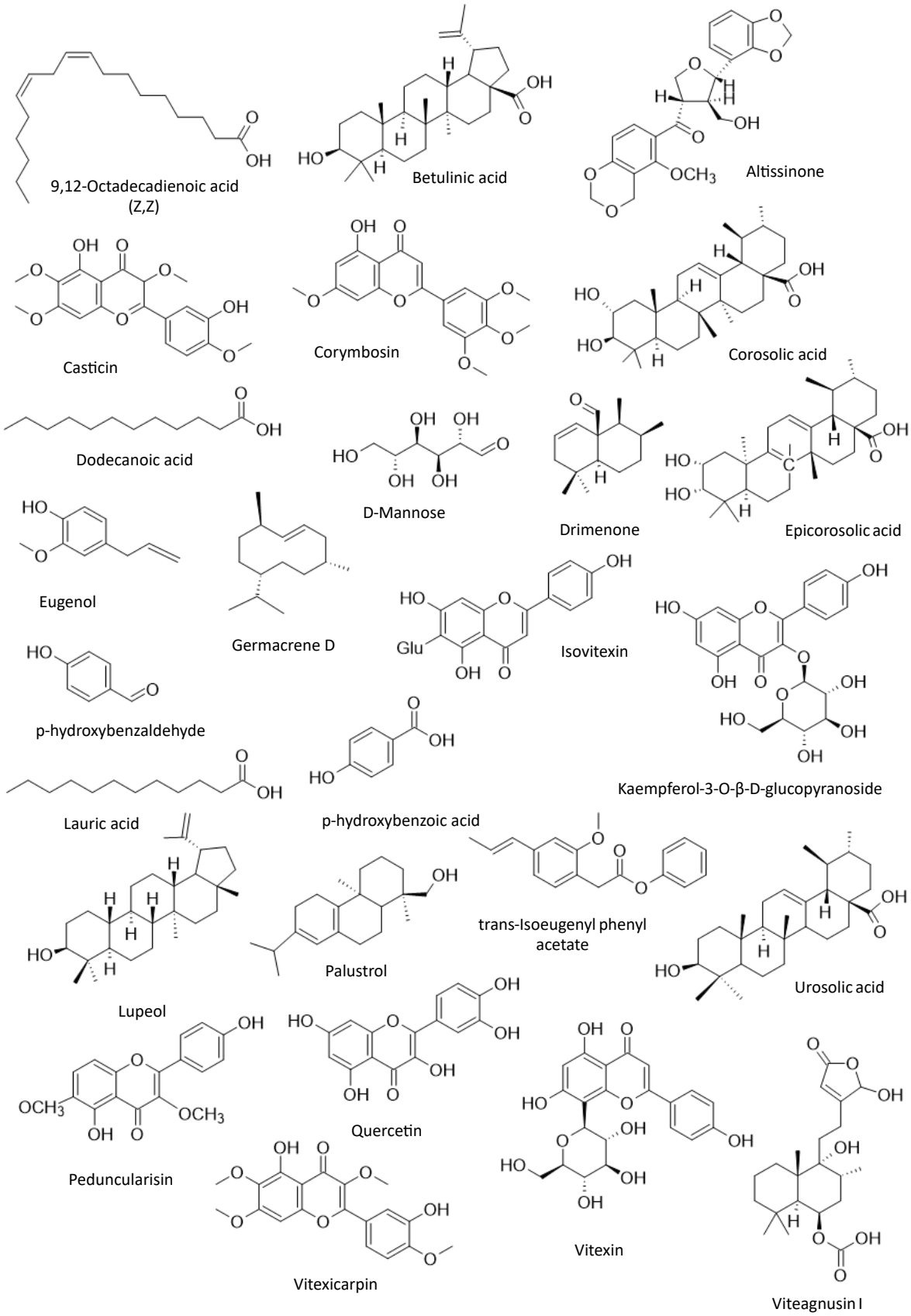

Figure 3. Chemical structure of some phytoconstituents.

Anticancer activity

Some plant compounds showed potential activity against cancer, but their effectiveness as standalone treatments is unclear. Bhavana *et al.* (2022) assessed cytotoxic impact of CuO NPs, synthesized using *Vitex altissima* L. on human lung carcinoma cell line (A549). The cells were treated at 37°C for 24 hours with different concentrations of CuO NPs, with cisplatin used for standardization and as a control. The determined IC_{50} value of CuO NPs against the A549 cell line was 147.48 µg/mL, indicating a significant cytotoxic effect. Additionally, the cytotoxicity of CuO NPs against normal mouse fibroblast cell lines (L929) was observed at the same concentrations, resulting in an IC_{50} value of 193.76 µg/mL. The results suggested that the IC_{50} value of CuO NPs was higher for L929 cell lines compared to A549 cell lines, suggesting lower toxicity for normal cells. Naganathan *et al.* (2016) exhibited a broad range of binding energies, ranging from -4.67 kcal/mol to -18.47 kcal/mol, aligning well with standard and ideal binding energy criteria. The compound 3, 7, 11, 15-Tetramethyl-2-hexadecen-1-ol demonstrated maximum effectiveness against BCL-2, while 1, 6, 10-Dodecatriene, 7, 11-dimethyl-3-methylene-[Z] exhibited the highest effectiveness against HER2. Both of these compounds were identified in *Vitex altissima* L. *In vitro* cytotoxicity on MCF-7 cell lines revealed a substantial impact, with an IC_{50} value of 269.51 µg/ml. Sunitha *et al.* (2023) utilised MTT assay against DLD-1 and L929 cell lines findings indicated significant anticancer activity, with an LC_{50} of 19.45 µg/mL for DLD-1 and 100.93 µg/mL for L929. From these findings *Vitex altissima* L. showed strong anticancer and antioxidant properties, suggesting its potential for future research and therapeutic use.

Hepatoprotective activity

Krishna *et al.* (2005) studied the effect of methanol extract of plant leaves on male Wistar albino ats with weights ranging from 150 to 200 grams to assess hepatoprotective potential. Acute toxicity studies revealed LD_{50} values of 200 mg/kg for aqueous and methanol leaf extracts, with a 20 mg/kg dose selected for further investigation. In the study involving CCl_4-induced rats, the methanol extract from *Vitex altissima* L. demonstrated significant changes in various parameters. The treated group showed considerable alterations in total bilirubin 0.62 mg/dl, alanine transaminase 144.99 IU/L, aspartate transaminase 231.76 IU/L, alkaline phosphatase 204.48 IU/L and total protein 8.24 gm %, compared to the CCl_4 induced group shows 2.33 mg/dl, 1392 IU/L, 2227 IU/L, 423.28 IU/L and 5.82 gm % respectively.

Nephroprotective activity

Vedula *et al.* (2022) utilized barks from mature *Vitex altissima* L. and administrated as dose of 100 and 200 mg/kg to rats for study of reno-protective activity. The toxic control significantly increased serum creatinine (4.42 ± 0.45 mg/dL) and urea (337.33 ± 30.42 mg/dL) levels compared to the control. The higher dose of *Vitex altissima* L. provided superior renoprotection, reducing serum creatinine and urea levels to 1.75 ± 0.96 mg/dL and 124.5 ± 17.96 mg/dL, respectively, compared to the lower dose 3.68 ± 0.77 mg/dL and 171.33 ± 19.66 mg/dL, respectively.

Insecticidal and larvicidal activities

Srinivasa and Nandini (2018) evaluated insecticidal properties of *Vitex altissima* L. leaf extracts against the red spider mite *Tetranychus macfarlanei* Baker & Pritchard a major threat to okra crops in India. The methanol extract showed the highest effectiveness, causing 71% mortality and 49% repellence, outperforming other solvents. Kannathasan *et al.* (2007) found that *Vitex altissima* L. leaf extract was effective against *Culex quinquefasciatus* Say larvae, with an LC_{50} of 128.04 ppm. Later, Kannathasan *et al.* (2008) reported that its Fatty Acid Methyl Ester extract showed stronger larvicidal activity, with an LC_{50} of 14.82 ppm and an LC_{90} of 41.25 ppm. These results suggested its potential for mosquito control.

Toxicological studies

Vasugi and Raju (2014) assessed toxicity, that indicated the ethanolic extract of *Vitex altissima* L. stem bark had no lethality up to 4000 mg/kg, it inhibited edema formation by 57.74%, similar to indomethacin (10 mg/kg), while showing 50.50% granuloma inhibition in chronic inflammation models.

Conclusion

The extensive review on *Vitex altissima* L. underscores its considerable pharmacological potential across diverse therapeutic domains. This plant demonstrates notable acaricidal, antibacterial, anticancer, anti-inflammatory, antioxidant, hepatoprotective, larvicidal and wound healing activities. Such findings provide a robust foundation for further exploration and validation of its therapeutic applications. Additionally, identification of active compounds and the elucidation of their mechanisms of action position *Vitex altissima* L. as a promising candidate for drug development. It is essential the cumulative insights garnered from these studies significantly enhance our understanding of the biological activities of *Vitex altissima* L. and pave the way for potential breakthroughs in various medical fields.

Declarations

List of abbreviations: AYUSH (Ayurveda, Yoga, Naturopathy, Unani, Siddha and Homeopathy), **BCL-2** (β-cell lymphoma 2), **BHA** (butylated hydroxyanisole), **BW** (Body weight), **CCl_4** (Carbon tetrachloride), **cm** (centimetre), **CuONP's** (copper oxide nanoparticles), **DLD-1** (colorectal adenocarcinoma cell line), **DPPH** (2,2-diphenyl-1-picrylhydrazyl), ***E. coli*** (Escherichia coli), **FAME** (Fatty Acid Methyl Ester), **GA** (Gibberellic acid), **HER-2** (human epidermal growth factor receptor 2), **IC_{50}** (Half-maximal inhibitory concentration), **IU/L** (International Units Per Litter), **ITS** (Internal Transcribed Spacer), **kD** (kilodalton), **Kcal/mol** (kilocalorie per mole), **kg** (Kilogram), **L929** (normal fibroblast cell line), **LC_{50}** (Lethal concentration 50)**LD_{50}** (lethal dose 50), **MCF-7** (human breast cancer cell line), **mg** (milligram), **mg/dl** (Milligrams per decilitre), **ml** (millilitre), **mm** (millimetre), **MTT** (3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide), **µg** (microgram), **µM** (micrometre), **PPM** (Parts Per Million), **RE** (rutin equivalent), **ROS** (Reactive Oxygen Species)**, SnO2NP's** (tin(IV) oxide nanoparticles), **TAE** (Tris acetate Ethylenediamine tetraacetic acid), ***V. altissima* L.** (*Vitex altissima* L.).

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