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Review Article

Phytochemical Diversity and Pharmacological Perspectives of *Vitex leucoxylon* L.f.: A Comprehensive Review

Sachin Patil[1], Suraj Devkar[2], Priyanka Patil[2], Akash Lashkare[3], and Sagar Deshmukh[2*]

[1]Department of Botany, Anandibai Raorane Arts, Commerce and Science College, Vaibhavwadi – 416 810, Affiliated to University of Mumbai, MH, India

[2]Department of Botany, The New College, Kolhapur-416 012, Affiliated to Shivaji University, Kolhapur, MH, India

[3]Department of Botany, Shri. Vijaysinha Yadav Arts and Science College, Peth Vadgaon- 416 112, Affiliated to Shivaji University, Kolhapur, MH, India

Abstract: *Vitex leucoxylon* L.f. (family Lamiaceae) is a large deciduous tree with a spreading crown and trunk, distributed in peninsular India and Sri Lanka. Traditionally, the plant has been used in medicine for the treatment of fever, joint pain, jaundice, anaemia, asthma, cancer, wounds, headache and catarrh, with specific mention in Ayurveda for managing bone disorders. Pharmacological studies have revealed hepatoprotective, antioxidant, anti-inflammatory, antidepressant, antimicrobial and analgesic activities. Phytochemical investigations have identified bioactive compounds including β-sitosterol, dimethyl terephthalate, isovitexin, vitexin, agnuside and aucubin, particularly concentrated in leaves and bark. In the present review, a systematic search was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure transparency and reproducibility. A total of 152 records were identified through database searches such as PubMed, Scopus, Elsevier, Springer and Google Scholar using the keywords as "*Vitex leucoxylon* L.f.," "ethnobotany" ands "pharmacology" from the period of 1994 to 2025. After removing duplicates (5 records), 147 studies were screened based on titles and abstracts. Following eligibility assessment of full texts, 107 articles met the inclusion criteria and were synthesized in this review. The identification, screening, eligibility and inclusion of pertinent research are all summarized in the PRISMA flow diagram. Future pharmacological and phytochemical research on *V. leucoxylon* L.f. is highly promising due to its wide therapeutic potential and phytoconstituent profile. This PRISMA-based systematic review reveals despite its enormous pharmacological potential, rigorous standardized, analytical, and clinical studies are needed to translate *Vitex leucoxylon* L.f. into an evidence-based therapeutic resource.

Keywords: Iridoids, *Vitex leucoxylon* L.f., Phytochemistry, Pharmacology, Ethnopharmacology, Systematic Review.

1. INTRODUCTION

The genus *Vitex* (family Lamiaceae) comprises approximately 270 species, characterized by their diverse bioactive constituents and wide range of medicinal properties [1]. These species are traditionally used to treat conditions such as disorders related to inflammation, infections and female reproductive health [2, 3]. *Vitex leucoxylon* L.f. is a deciduous tree with a thick trunk and spreading crown, commonly distributed throughout the Deccan Peninsula of India [4]. It is a riparian species native to peninsular India and Sri Lanka, predominantly growing in alluvial soil types. Ecologically, the plant occurs in mid-storey habitats, is light-dependent and is typically found along river floodplains that undergo periodic inundation. It acts as a natural sand binder and plays an important role in preventing riverbank erosion [5]. The leaves of *V. leucoxylon* L.f. are used in traditional medicine to cure fever, catarrh, headaches, and possess anti-depressant, analgesic, anti-parkinsonian, and anti-

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* Corresponding Author: Sagar Deshmukh <sageraea@newcollege.ac.in>

microbial activities [6]. In Ayurveda, the plant is reported to be beneficial in the treatment of bone disorders, jaundice, asthma, anaemia and malarial fever, with leaf decoctions commonly prescribed for therapeutic purposes [7, 8]. In addition to being applied to wounds, burns, and cuts, leaf paste is said to have antidiabetic qualities [9, 10]. Additionally, the plant is used for medicinal baths in malarial fever [11], as well as for managing joint pain [12], and cancer [13, 14]. It is further documented to promote wound healing, reduce cholesterol levels and exhibit anti-inflammatory, hepatoprotective and insecticidal properties. The root and bark are considered astringent, while the root has also been employed as a febrifuge [15-18]. Phytochemical investigations have identified several compounds from its leaves and bark, such as β-sitosterol, vitexin, dimethyl terephthalate, isovitexin, agnuside and aucubin [19]. HPTLC profiling of *Vitex leucoxylon* L.f. leaves provides a reliable tool for identification and standardization [20]. AgNPs synthesized from *Vitex leucoxylon L.f.* leaf extract are rich in flavonoids, terpenoids, phenols, tannins and saponins, showed stronger antioxidant, anti-inflammatory, cytotoxic and wound-healing activities than the extract alone, with maximal effects against oral cancer and significant *in vitro* wound closure and anti-inflammatory responses [21]. Despite its traditional importance and emerging pharmacological evidence, the available scientific information on *Vitex leucoxylon* L.f. remains fragmented and scattered across different studies. To date, a comprehensive synthesis of its phytochemical constituents, ethnomedicinal applications and experimentally validated pharmacological activities is lacking. This review aims to integrate traditional medicinal knowledge with modern pharmacological findings, thereby establishing a scientific rationale for the therapeutic applications of *Vitex leucoxylon* L.f.. The documentation of its diverse bioactive constituents and experimentally validated biological activities highlights its potential as a valuable source for novel drug leads. Furthermore, the need for thorough research to examine its pharmacological and phytochemical potential is further reinforced by its ecological role and ethnomedicinal significance. *Vitex leucoxylon* L.f. was selected for this review due to its emerging yet limited pharmacological evidence, diverse phytochemical composition, and documented bioactivities, particularly in light of the substantial therapeutic potential demonstrated by related species such as *Vitex negundo* L. and *Vitex trifolia* L. The aim of this systematic review is to comprehensively summarize phytochemical diversity, and pharmacological properties of *Vitex leucoxylon* L.f., identify research gaps and propose directions for future investigation.

2. METHODOLOGY

2.1. Data Sources and Retrieval

A comprehensive literature search was conducted in May 2025 in accordance with PRISMA guidelines, using PubMed, Scopus, Web of Science, and Google Scholar (Figure 1). Grey literature sources, such as books, theses, patents, and regional journals, were also considered. The search strategy used combinations of keywords such as "*Vitex leucoxylon"*, "Phytochemistry", "Pharmacology", "Taxonomy" and "Phytoconstituents". To ensure inclusivity, no date restrictions were applied, and both experimental and clinical studies were considered. Records were restricted to the English language, with duplicates removed through systematic screening. Additionally, backward and forward citation tracking enhanced coverage of relevant literature. The search yielded 152 records, of which 147 remained after duplicate removal. Following the eligibility assessment, 107 studies were included in the qualitative synthesis, comprising 74 original articles, 20 review articles, 6 books, 4 theses, 1 book chapter, 1 patent, and 1 conference paper. These studies formed the basis of the qualitative synthesis. PubMed, Scopus, Web of Science, and Google Scholar and Chemical structures and diagrams were prepared using ChemDraw software, while conceptual illustrations were designed in a mind-map format.

3. TAXONOMIC STATUS

Vitex leucoxylon L.f. was first described by Carl Linnaeus the Younger in *Supplementum Plantarum Systematis Vegetabilium* (1781) from the forests of Ceylon (Sri Lanka) [22]. In the protologue, Linnaeus noted that the leaves resemble five fingers and that the plant bears a monospermic berry (containing a single seed). He further described its oblong, petiolate leaves and dichotomous panicles, remarking that the species closely resembles *Vitex trifolia* L., but differs by possessing glabrous leaves and dichotomous panicles from the first branching

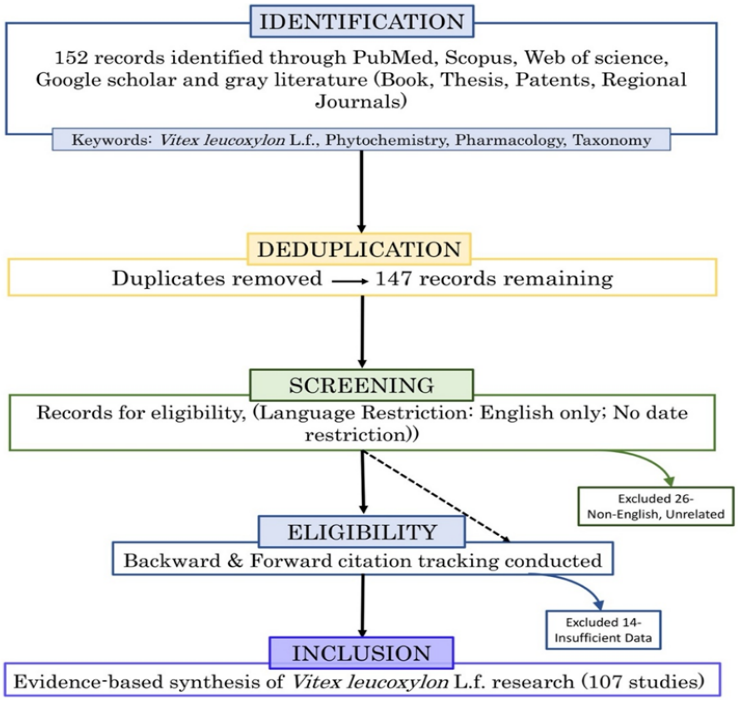

Fig. 1. PRISMA flow diagram of 107 studies on *Vitex leucoxylon* L.f. during May, 2025.

[22]. In 1971, Harold Moldenke described a new variety, *Vitex leucoxylon* L.f. var. *zeylanica* Moldenke, based on smaller leaflets measuring 2.5 - 9 cm in length and 1.3 - 5 cm in width, with margins more or less serrate and surfaces dull grey-green above [23]. Later, in 1977, Moldenke reassigned this taxon to the rank of forma, as *V. leucoxylon* f. *zeylanica* (Moldenke) Moldenke, possibly due to its morphological variation within the species [24]. Earlier, Roxburgh (1832) had described *Vitex saligna* [25]; however, in 1977, Moldenke reduced this taxon to a new status, *V. leucoxylon* L.f. *saligna* (Roxb.) Moldenke, based on leaf morphology. The mature leaflets were described as uniformly narrow, elliptic and thinly chartaceous, being 3 - 4 times longer than wide, with an acute to acuminate apex. Subsequent observations confirmed that these were merely morphological variations within *V. leucoxylon* L.f. Hence, all formae and varieties proposed by Moldenke, are now considered synonyms of *V. leucoxylon* L.f. [24].

3.1. Morphology of *V. leucoxylon* L.f.

Vitex leucoxylon L.f. is a medium-sized deciduous tree, native to India and Sri Lanka, attaining a height of up to 12 m. The stem and branches are obtusely quadrangular. The leaves are compound, with obovate to oblanceolate leaflets that are thin-coriaceous, glabrous, with apices rounded to acute and bases attenuate to cuneate. The margins vary from entire to toothed. Petiolules and petioles are well developed. The inflorescences are axillary or terminal, consisting of loose, spreading panicles or corymbose dichasial cymes. Flowers are bisexual, zygomorphic and hypogynous. The calyx is cupular to campanulate, appressed-pubescent and without teeth. The corolla is cream to purplish in color, with a 5 mm long tube and five lobes, arranged into an obtuse upper lip and lower lip. Stamens are four, didynamous, with paired filaments. The ovary is superior and hairy at the apex, with a long style. The fruit is a drupe, ellipsoid to oblong in shape. Each fruit generally contains four seeds. Flowering occurs from February to April, while fruits and seeds are present throughout the year [25]. The detailed morphological characters are given in Figure 2.

3.2. Geographical Distribution

Vitex leucoxylon L.f. is distributed at altitudes up to 900 m and extending northward to Jhansi and parts of Bihar. The species commonly grows along riverbanks, streams, and ponds, and is well represented in evergreen and semi-evergreen forests. Across Asia, the species occurs in India, Pakistan, Sri Lanka, Myanmar, Indonesia and Malaysia. Within India, it is recorded from several

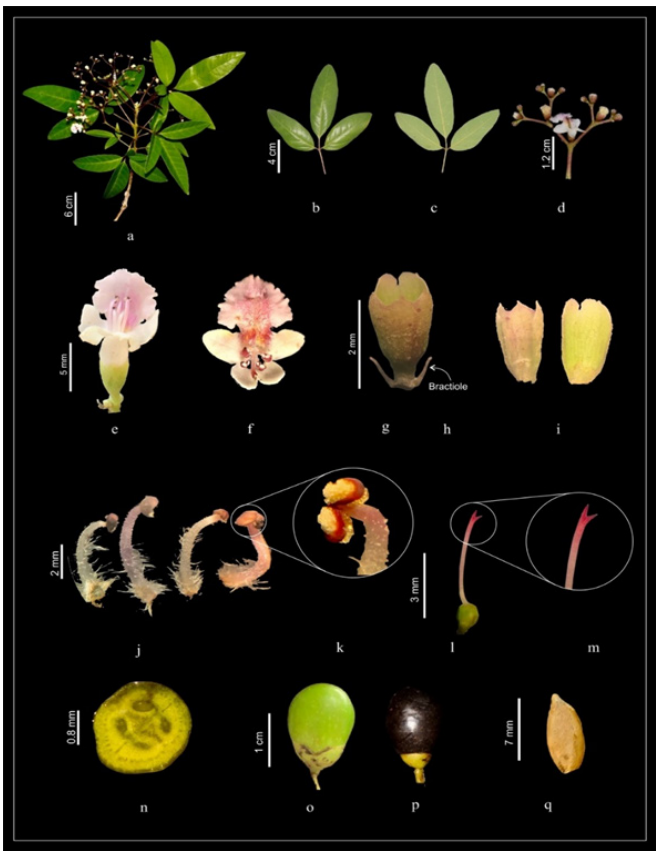

Fig. 2. Morphological features of V. leucoxylon L.f. (a) Habit, (b & c) adaxial and abaxial leaf surfaces, (d) panicle, (e) entire flower, (f) longitudinal section of flower, (g) non-dissected calyx, (h) Bracteole, (i) Dissected calyx, (j) Stamens, (k) Anther lobes enlarged, (l) Style, (m) Stigma, (n) Transverse Section of ovary, (o) Unripe drupe, (p) Ripened drupe, and (q) seed.

states, including Andhra Pradesh, Karnataka, Goa, Kerala, Maharashtra, Madhya Pradesh, Odisha, Uttar Pradesh and Tamil Nadu. In deciduous forests, it is often found scattered along streams, from the Western Ghats to the plains [26].

4. PHYTOCHEMISTRY

Chemical compounds: *Vitex leucoxylon* L.f. serves as a rich reservoir of diverse phytoconstituents represented across different plant parts, as shown in Figure 3 and phytoconstituents diversity displayed in Figure 4. To date, at least 117 compounds have been reported from different parts of the plant, representing a wide spectrum of primary and secondary metabolites. These include 38 miscellaneous compounds, 14 terpenoids, 12 esters, 12 fatty acids, 9 sugars, 8 volatile organic compounds, 7 flavonoids, 7 phenolics, 4 iridoids, 3 flavones and 3 terpenes. For systematic understanding, the identified compounds can be classified into: Basic metabolites (sugars, fatty acids, esters); Derived groups (phenolics, flavones, flavonoids, iridoids); Complex secondary metabolites (terpenes, terpenoids, volatile organic compounds) and Miscellaneous compounds (unique or unclassified phytochemicals). A detailed summary of these phytoconstituents is presented in Supplementary Table 1 (arranged according to their biosynthetic categories, from basic metabolites to complex secondary metabolites), and their structural illustration, given in Figures 5-8 synopsize the chemical makeup of *Vitex leucoxylon* L.f., elucidating a wide range of primary and secondary metabolites that conjointly contribute to its nutritional and pharmacological importance. These chemical structures were redrawn by us using ChemDraw software based on the structures reported in the literature and structural information obtained from PubMed sources. Figure 5 represents sugars and fatty acids/esters representing primary metabolites. The presence of mono- and oligosaccharides such as glucose, mannose, lactose, maltotriose, dextrins and cyclodextrins indicates

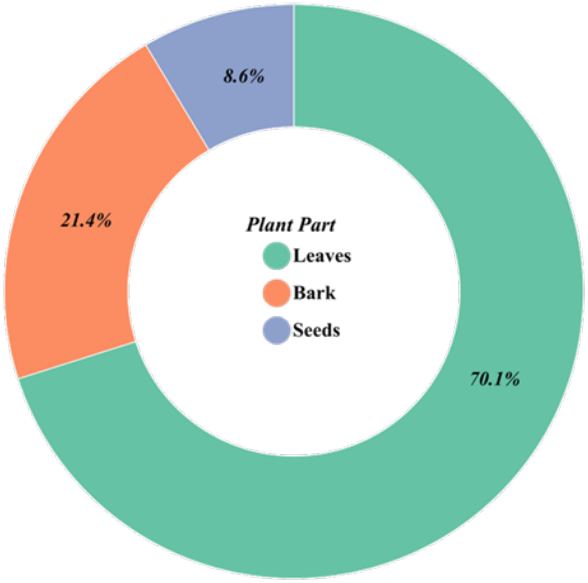

Fig. 3. Distribution pattern of chemical constituents in *Vitex leucoxylon* L.f. plant part.

Fig. 4. Rose plot of phytoconstituent distribution in *Vitex leucoxylon* L.f.

active carbohydrate metabolism and energy storage functions. Saturated and unsaturated fatty acids, including hexadecanoic, octadecadienoic and octadecatrienoic acids and their esters, highlight their role in membrane structure, metabolic regulation and nutritional value. Figure 6 illustrates terpenes, terpenoids, triterpenoids and iridoids, which form a major bioactive group in *V. leucoxylon* L.f.. Compounds such as caryophyllene, phytol, betulinic acid, corosolic acid, β-sitosterol, aucubin and agnuside are widely reported for anti-inflammatory, antioxidant, hepatoprotective and anticancer activities, supporting the medicinal relevance of the species. Figure 7 presents phenolics, flavones and flavonoids associated with antioxidant and protective functions. Phenolic acids, coumarin, cinnamaldehyde and flavonoids such as vitexin, isovitexin and kaempferol glycosides contribute to free radical scavenging and cytoprotective effects. Figure 8 summarizes miscellaneous compounds, including hydrocarbons, long-chain alcohols, aldehydes, amides and sulfur- and nitrogen-containing compounds, reflecting the chemical diversity and potential ecological and biological roles of the plant. Overall, the metabolite profile shown in Figures 5-8 demonstrates that *Vitex leucoxylon* L.f. is chemically rich, containing essential primary metabolites and diverse bioactive secondary compounds, providing a strong basis for its traditional use and pharmacological potential that mentioned in Supplementary Table 1.

5. PHARMACOLOGICAL ACTIVITIES

The pharmacological activities of *Vitex leucoxylon* L.f. have been systematically categorized to provide a clear understanding of its therapeutic potential. These activities are arranged in a streamlined sequence, beginning with general protective effects, followed by metabolic regulation, organ-specific actions, nervous system effects and finally phytotoxicity. The detailed pharmacological activities are presented in Figure 9 and Supplementary Table 2 summarises the pharmacological potential of *Vitex leucoxylon* L.f., providing detailed information on the plant part investigated, type of pharmacological activity, nature of the extract, dose and route of administration, standard drug used, control or assay conditions, experimental method, inducing chemical (if any), biological model or microbial strain tested and the detailed results, thereby offering a comprehensive framework for interpretation and guiding further pharmacological investigations.

5.1. Antimicrobial Activity

In ethnomedicine, several folklore plants used by tribal communities in the Western Ghats of India have been screened for antimicrobial activity. Furthermore, *V. leucoxylon* L.f.-derived biosynthesized silver nanoparticles (AgNPs) demonstrated broad-spectrum antibacterial

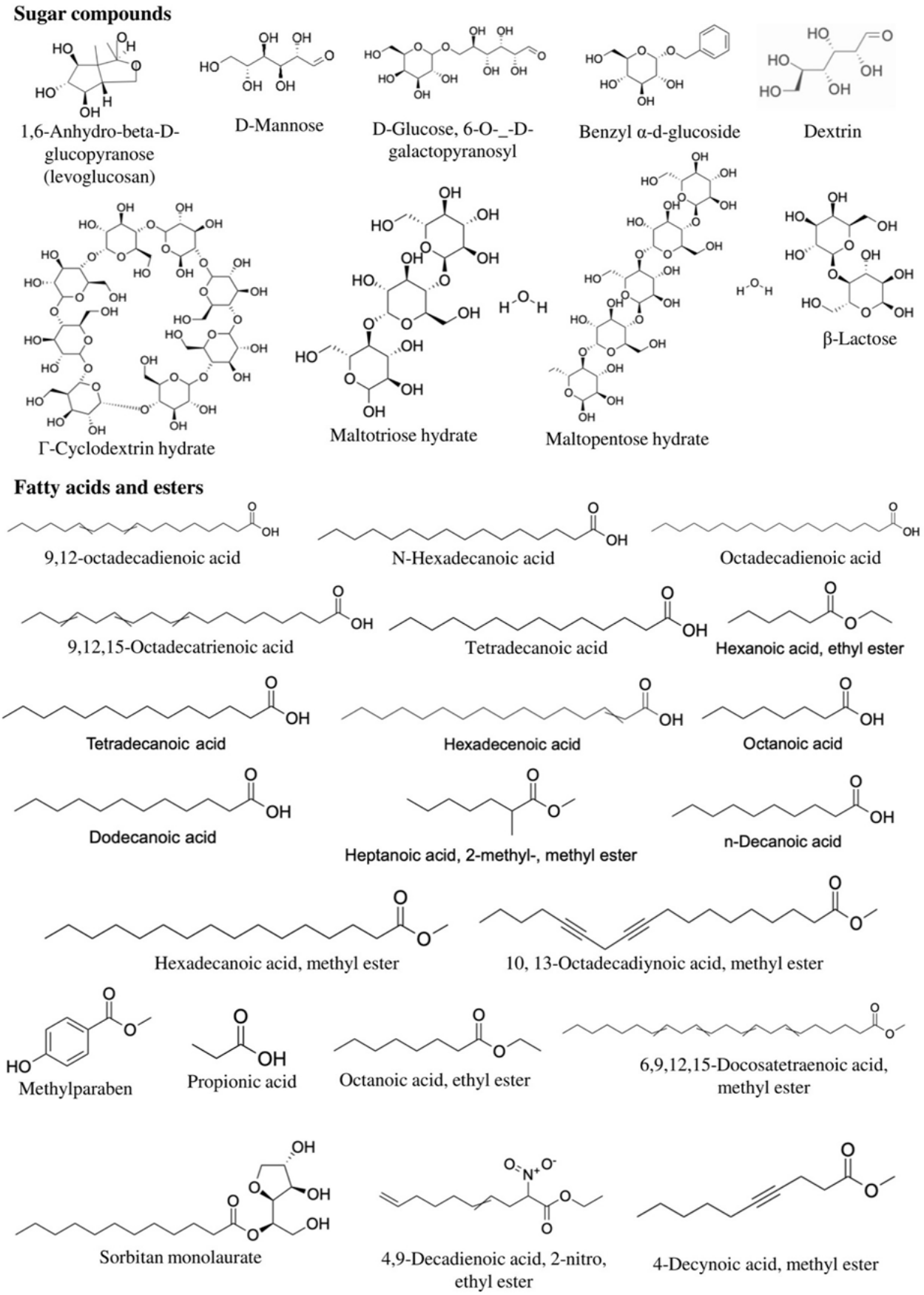

Fig. 5. Structure of phytochemicals characterized from *Vitex leucoxylon* L.f.

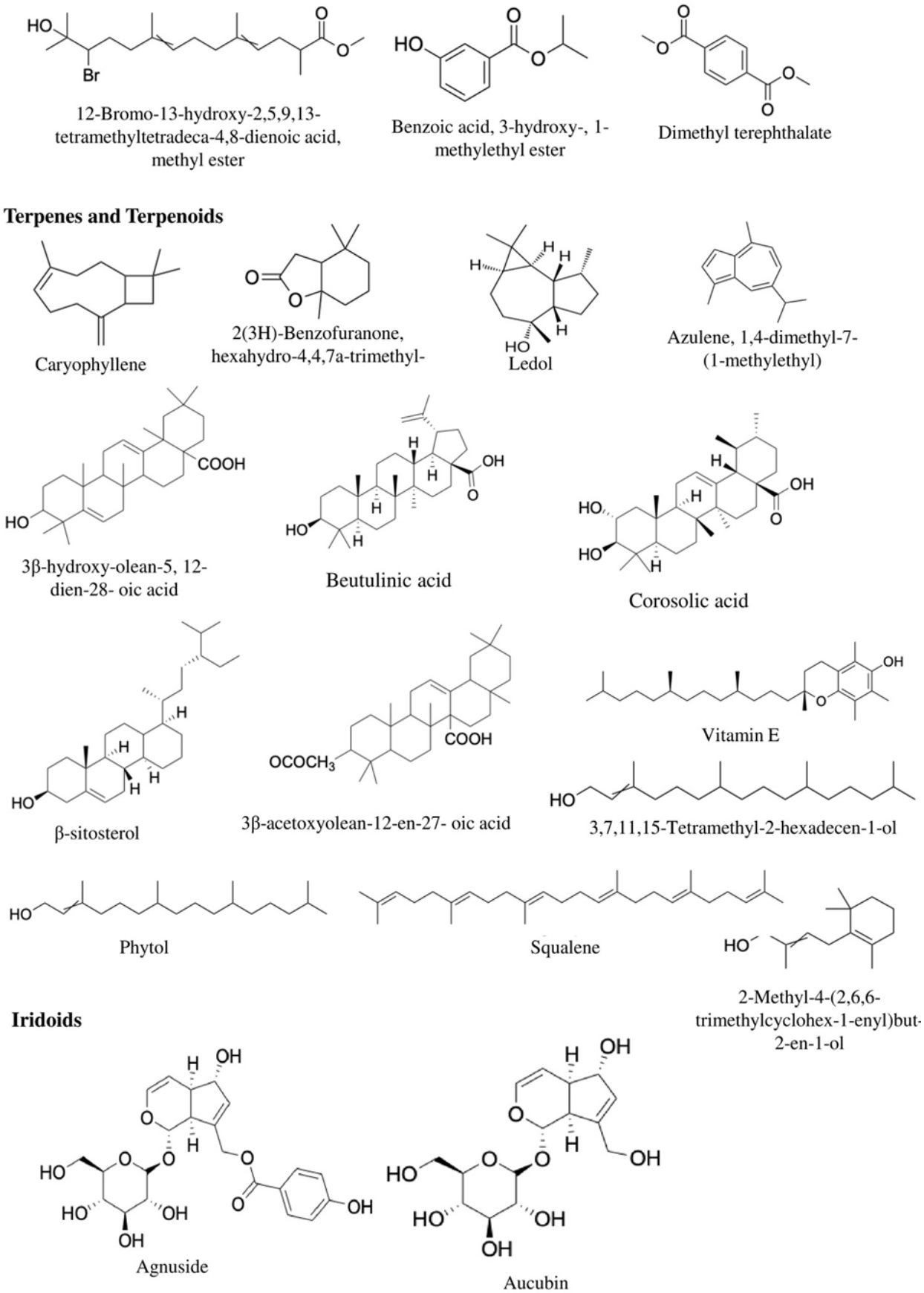

Fig. 6. Structure of phytochemicals characterized from *Vitex leucoxylon* L.f.

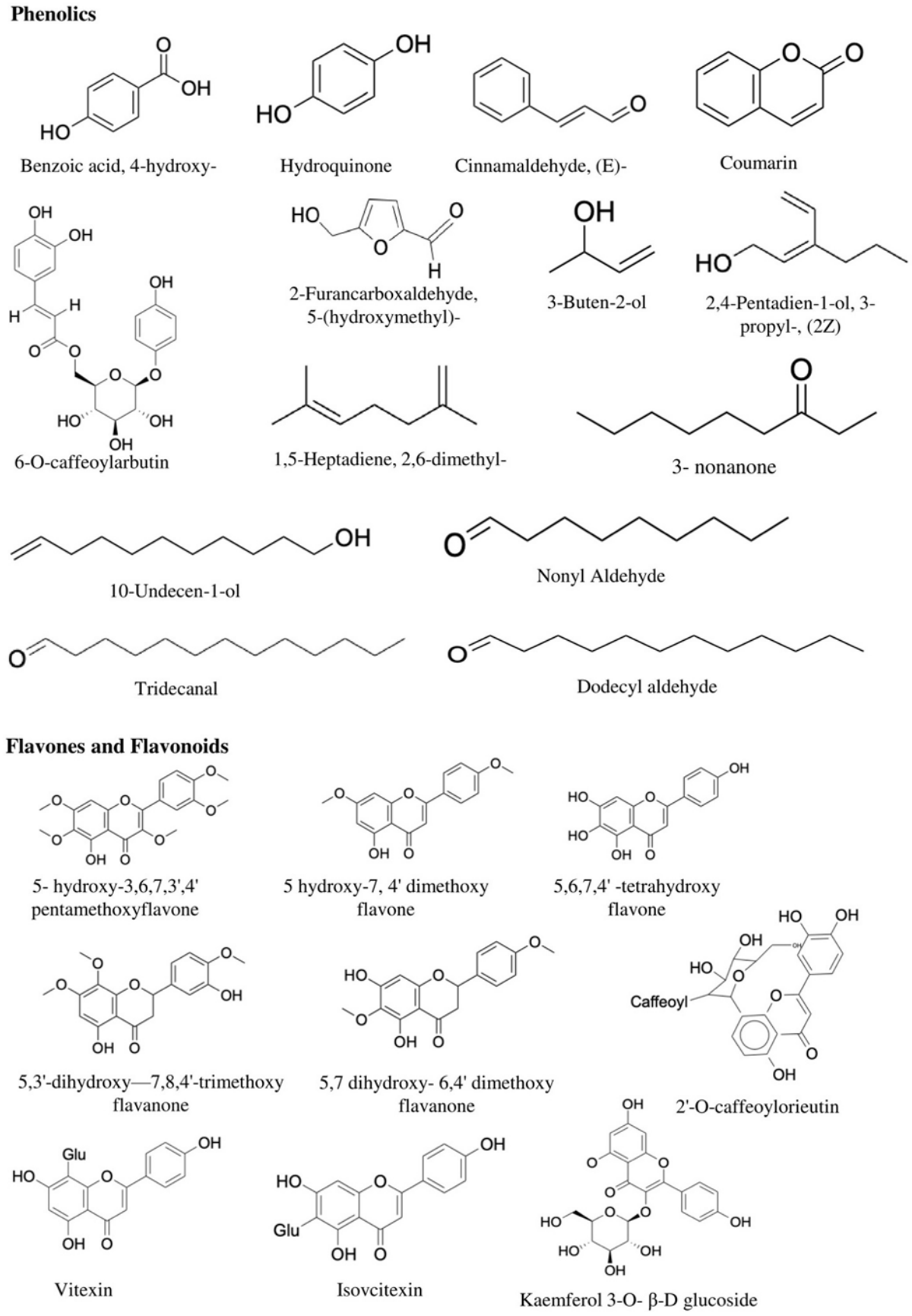

Fig. 7. Structure of phytochemicals characterized from *Vitex leucoxylon* L.f.

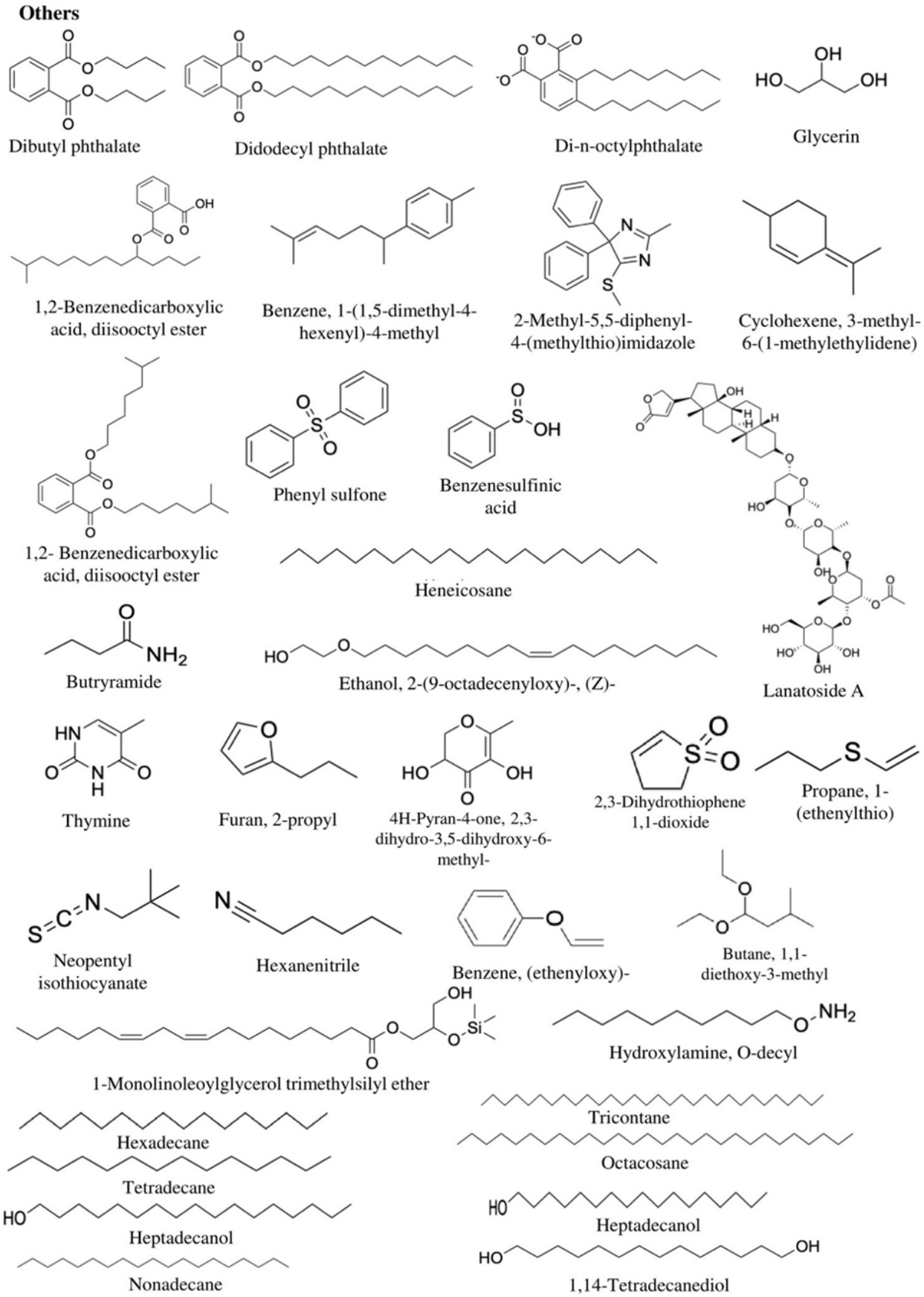

Fig. 8. Structure of phytochemicals characterized from *Vitex leucoxylon* L.f..

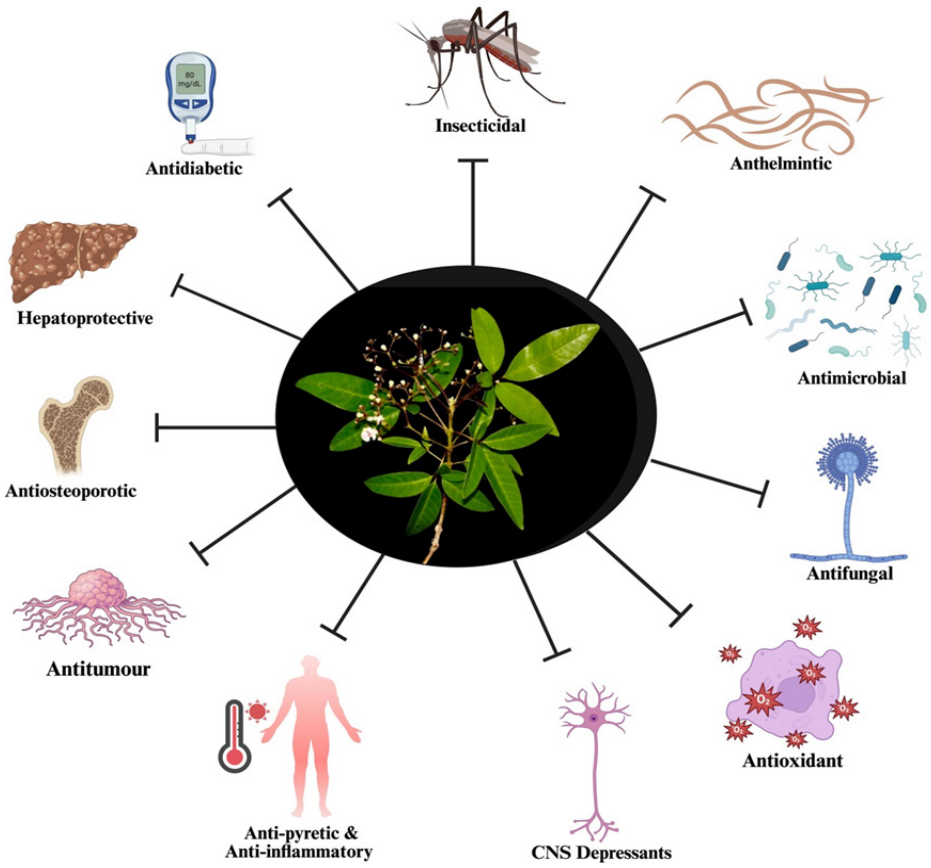

Fig. 9. Pharmacological activities of *Vitex leucoxylon* L.f.

action with potent suppression of Gram-negative bacteria and antifungal activity similar to positive controls. Activity against *Escherichia coli, Bacillus subtilis, Proteus mirabilis, Enterococcus species* and *Klebsiella pneumoniae* was shown by Ananthi. Notably, all five examined pathogens were successfully suppressed by zinc oxide and Mo-doped zinc oxide nanoparticles, which demonstrated the greatest suppression against *Enterococcus*. Additionally, antifungal activity against *Candida albicans, Aspergillus fumigatus* and *Aspergillus niger* was demonstrated using silver and copper nanoparticles produced from *V. leucoxylon* L.f. [21]. Methanolic leaf extracts of *V. leucoxylon* L.f. demonstrated strong antibacterial activity against most tested bacteria except *B. subtilis*. At 50 µg/cup, compounds such as lupeol, betulinic acid, vitexicarpin, vitexin, heptadecanol, *p*-hydroxybenzaldehyde and *p*-hydroxybenzoic acid exhibited antibacterial efficacy comparable to chloramphenicol. For antifungal activity, heneicosanoic acid and *p*-hydroxybenzoic acid showed effects similar to nystatin, while vitexicarpin, betulinic acid, vitexin and *p*-hydroxybenzaldehyde produced moderate antifungal activity [27]. Seasonal variation was also observed: ethanol extracts of summer leaves showed the highest inhibition against *Salmonella paratyphi*, *Enterococcus faecalis*, *Vibrio cholerae* and *Staphylococcus aureus*, whereas winter leaf extracts were most effective against *E. coli* and *S. paratyphi* [28]. Leaf extracts of *Vitex leucoxylon* L.f. exhibited notable antibacterial activity against both gram-positive and gram-negative bacteria [29].

5.2. Antioxidant Activity

The antioxidant capacity of *Vitex leucoxylon* L.f. has not been extensively studied, but what little is known about it shows that it is highly active. Ethanolic leaf extracts have demonstrated the highest antioxidant potential, effectively scavenging superoxide, hydroxyl and DPPH radicals in a concentration-dependent manner. Additionally, bark extracts exhibited inhibition of *in vitro* tissue lipid peroxidation [28]. Among solvent fractions, ethyl acetate leaf extracts showed the strongest antioxidant activity across multiple *in vitro* assays

while hexane and methanol extracts displayed no significant effects compared to the standard antioxidant butylated hydroxytoluene (BHT) [30].

5.3. Anti-Inflammatory Activity

Several studies have demonstrated the anti-inflammatory potential of *Vitex leucoxylon* L.f. using experimental models. In carrageenan-induced rat paw oedema, both ethanolic and aqueous bark extracts (500 mg/kg) significantly inhibited paw swelling in albino Wistar rats. Phytochemical screening and acute toxicity assays confirmed safety and the extracts showed comparable efficacy to the reference drug indomethacin [15]. Similarly, ethanolic leaf extract (ETE) and cold aqueous infusion (CAI) suppressed carrageenan-induced oedema and granulation tissue formation in rats, while also reducing acetic acid-induced writhing. Both extracts exhibited analgesic and anti-inflammatory properties, with CAI additionally lowering serum total cholesterol levels and modulating behavioural despair tests in mice [16]. Further evidence supports the anti-arthritic activity of the ethanolic bark extract, which significantly reduced paw oedema in Freund's complete adjuvant (FCA)-induced arthritis. The extract downregulated pro-inflammatory cytokines TNF-α and IL-1β, indicating immunomodulatory action. Based on preclinical safety and efficacy studies, the 5-lipoxygenase (5-LOX) inhibitory fraction of *V. leucoxylon* L.f. bark extract is considered a promising candidate for arthritis management [18]. Leaf and stem bark extracts (chloroform and methanol fractions) were also tested in carrageenan-induced paw oedema models, confirming traditional claims of anti-inflammatory efficacy. Among bioactive constituents, vitexin showed remarkable potency, being ~12.5 times more effective than ibuprofen in suppressing inflammation [27]. Hydroalcoholic and ethanolic extracts further indicated that the anti-inflammatory and analgesic effects are mediated via suppression of prostaglandin biosynthesis [31]. Aqueous stem bark extracts demonstrated benefits in acute inflammation but were associated with reduced wound-breaking strength, reflecting complex effects on tissue repair [32]. Additional *in vivo* studies reported that leaf extracts and cold aqueous infusions significantly reduced carrageenan-induced oedema, granulation tissue formation and serum cholesterol levels [33]. Leaf extracts was evaluated by the HRBC membrane stabilization method using 0.36% NaOH-induced hypotonic haemolysis in vitro. Both hydroalcoholic and ethanolic extracts showed significant membrane stabilization activity. The hydroalcoholic extract showed 96.63%, 90.97%, and 84.16% inhibition at 50, 100, and 1000 µg/mL, respectively, while the ethanolic extract showed 99.03%, 90.02%, and 84.43% inhibition at the same concentrations. The standard drug prednisolone exhibited 99.03%, 97.23% and 98.85% inhibition. The results indicate strong anti-inflammatory potential of the *V. leucoxylon* L.f. leaf extracts, especially the ethanolic extract, which showed activity comparable to prednisolone. [34]

5.4. Anti-Pyretic Activity

The ethyl acetate bark extract of *Vitex leucoxylon* L.f. demonstrated significant antipyretic activity by inhibiting inflammation and reducing fever [35]. No significant variation in baseline temperature was observed at 0 h between treatment groups. However, both the ethyl acetate extract and aspirin markedly reduced the rectal temperature of pyretic rats at the second, third-, and fourth-hours post-treatment. These findings suggest that the ethyl acetate bark extract of *V. leucoxylon* L.f. possesses potent antipyretic properties.

5.5. Analgesic Activity

Cold aqueous infusion and *Vitex leucoxylon* L.f. leaf extract were found to reduce spontaneous motor activity in mice [16]. They also potentiated d-amphetamine-induced stereotypy, enhanced oxotremorine-induced tremors and shortened immobility duration in the behavioural despair test. Furthermore, both the ethanolic extract and the cold aqueous infusion of *V. leucoxylon* L.f. significantly inhibited acetic acid-induced writhing, confirming their analgesic and neuropharmacological activities. *Vitex leucoxylon* L.f. shows promise as a source of novel analgesic and neuroactive agents, warranting further in detail study.

5.6. Anticancer Activity

The antitumour activity of *Vitex leucoxylon* L.f. has been investigated using Dalton's ascitic lymphoma (DAL) in mice [36]. Tumours were induced by intraperitoneal injection of DAL cells and animals were subsequently treated with

ethanol and chloroform extracts of *V. leucoxylon* L.f. (250 and 500 mg/kg) for 14 consecutive days. Oral administration of both extracts prolonged the survival of DAL-bearing mice and restored altered haematological parameters in a dose-dependent manner. The effects were comparable to those of the standard drug 5-fluorouracil (20 mg/kg), with the ethanolic extract demonstrating superior antitumour efficacy relative to the chloroform extract. In another study, *V. leucoxylon* L.f. extract conjugated carboxymethyl cellulose (CMC) membrane is used for bone regeneration, wound healing, and anticancer treatments [37]. The treatment also induced chromatin condensation, nuclear damage and tumour cell death, thereby slowing tumour progression. Additionally, the steroidal fraction improved antioxidant status in treated animals, suggesting a dual role in tumour suppression and oxidative stress reduction.

5.7. Anti-Diabetic Activity

Studies on *Vitex leucoxylon* L.f. suggest that the plant has promising antidiabetic potential [38]. When tested using *in vitro* methods, the aqueous extract stood out by showing notable α-amylase inhibition (54.61 ± 0.46%) and a strong ability to enhance glucose uptake (57.13 ± 0.44%). Compared to extracts prepared with other solvents, the water-based extract performed better, indicating that it contains compounds that are particularly effective in controlling carbohydrate digestion and improving glucose utilization.

5.8. Anti-Helminthic Activity

The anthelmintic potential of *Vitex leucoxylon* L.f. was assessed through *in vitro* studies using *Pheretima posthuma* (Indian earthworm) as the test organism [39]. A distinct dose-dependent response was observed in extracts tested at doses ranging from 50 to 250 mg/20 ml with activity increasing as the concentration increased, among all the solvent extracts tested, the methanolic extract was the most effective for anthelmintic activity. Further studies are required to isolate active compounds and confirm its anthelmintic efficacy *in vivo*.

5.9. Hepato-Protective Activity

Various experimental models have been used to assessed hepatoprotective potential of *Vitex leucoxylon* L.f.. Initially they induce liver damage in albino mice by using carbon tetrachloride (CCl_4), which was ameliorated by alcoholic leaf extracts, as noticed by improvements in key biochemical parameters, including alkaline phosphatase, bilirubin, serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) [12]. These outcome corroborated the protective effect of *Vitex leucoxylon* leaf extracts against hepatotoxic compounds. Pre-treatment with silymarin (standard), methanolic and chloroform leaf extracts, and chloroform bark extract produced significant hepatoprotective effects, whereas the methanolic bark extract showed no protective activity [27]. Additionally, ethanolic leaf extract (EVL) was tested in male Wistar rats for antioxidant and anti-hepatocarcinogenic properties against diethylnitrosamine (DEN) and phenobarbital sodium (PB). EVL treatment exhibited a clear dose-response relationship in hepatoprotection, with the high dose gives stronger antioxidant and protective effects [31]. These Results emphasize *Vitex leucoxylon* L.f. as a credible source of hepatoprotective phytochemicals, justifying further investigation.

5.10. Anti-Osteoporosis Activity

Chronic alcohol abuse (CAA) represents a significant risk factor for osteoporosis, associated with impaired bone metabolism and structural deterioration. The ethanolic leaf extract of *Vitex leucoxylon* L.f. (EEVL) has been evaluated in a CAA-induced osteoporosis model using male albino rats [8]. Animals were divided into four groups, six in each group, after grouping the biochemical parameters such as serum calcium, phosphorus, alkaline phosphatase and urinary levels of calcium, phosphorus and creatinine were quantified. Rats treated with EEVL, vitamin D_3 and calcium supplements exhibited a favourable outcome that higher serum calcium and phosphorus levels, along with markedly reduced alkaline phosphatase activity compared to the disease control group. Further, the administration of EEVL resulted in an important reduction in the excretion of calcium, phosphorus, and creatinine in the urine. These biochemical benefits have been proven by radiographic study, which revealed the prevention of bone loss. Each of these results show that EEVL has strong anti-osteoporotic properties, indicating

that it may be used as a phytotherapeutic remedy for osteoporosis brought on by alcohol. Plants rich in flavonoids and saponins are known to support bone formation and reduce bone loss. Similar compounds, including flavonoids, saponins, and iridoid glycosides are reported in *Vitex* species and may help improve calcium metabolism and bone mineralization. However, research on *Vitex leucoxylon* L.f. is still limited compared with *Vitex negundo* and *Vitex trifolia*. Therefore, further studies are needed to identify the active compounds responsible for its anti-osteoporotic effect.

5.11. CNS Depressant Properties

The central nervous system–depressant properties of *Vitex leucoxylon* L.f. have been experimentally studied by Nair [40]. When compared to the control group, animal models' spontaneous and forced locomotor activity were significantly reduced when ethanolic extracts of the plant were taken orally at doses of 250 mg/kg and 500 mg/kg, respectively. The maximum effect was observed at 1hour post-administration. Although the magnitude of the depressant effect was lower than that of the standard reference drug, *Vitex leucoxylon* L.f. extract exhibits a noticeable reduction in aggressive behaviour, with responses closely resembling those of the standard.

5.12. Insecticidal Activity

The insecticidal efficacy of *Vitex* species has been evaluated by Sahayaraj *et al.* [41] against *Corcyra cephalonica* Stainton. Pulverized leaf material of *Vitex leucoxylon* L.f., *V. negundo* Linn., and *V. trifolia* Linn. at concentrations of 0.5, 1.0, 1.5, 2.0 and 2.5 g/100 g tested on groundnut seeds. Treatments substantially decreased kernel damage, dry mass loss, larval weight, fertility and survival of the pest. This extract reduced development time, larval weight and fecundity, indicating its potential as an eco-friendly botanical pesticide. Further studies on active compounds and field evaluation are needed to confirm its potential as a sustainable biopesticide.

5.13. Phyto-toxicity

Toxicity studies are important for understanding whether medicinal plants are safe for use. In this study, a combined extract of *Vitex leucoxylon* L.f., *Vitex negundo* L., and *Vitex trifolia* L. was tested for both short-term and repeated-dose toxicity in mice. During the acute toxicity study, animals received a single oral dose of up to 2000 mg/kg and were observed for seven days. No deaths or noticeable changes in behaviour or physical condition were recorded, suggesting good safety at high doses. In the sub-acute study, mice were given the extract orally at doses of 200 and 400 mg/kg for 28 days. Throughout the treatment period, no harmful effects on body weight, behaviour, or survival were seen. Blood and biochemical tests also remained within normal ranges, indicating no systemic toxicity [42]. Overall, these results support the traditional use of *Vitex* species and show that *V. leucoxylon* L.f. extracts are well tolerated at therapeutic levels, but further detailed investigations such as long-term toxicity, chronic toxicity and clinical studies are required to confirm their safety profile.

6. SUMMARY

The phytochemical constitution of *Vitex leucoxylon* L.f. exhibits a rich and diverse spectrum of bioactive compounds present across various plant parts, including leaves, bark and seeds. These main compounds Contain sugars, fatty acids, esters, terpenes, terpenoids, iridoid glycosides, flavonoids, phenolic compounds, volatile components and other secondary metabolites. Notably, leaves has relative higher phytoconstituents than bark and seeds, representing leaves as the main metabolite site. This deviation may elucidate the higher antioxidant and pharmacological activity of leaf extracts reported earlier [1, 3] .

Flavonoids and flavones including vitexin, isovitexin, kaempferol glycosides and methoxylated flavones are strongly associated with antioxidant and anti-inflammatory activities. These compounds scavenge ROS and inhibit lipid peroxidation. earlier studies shown that flavonoid-rich extracts of *Vitex* species possess significant wound healing, anti-inflammatory and hepatoprotective effects [18, 19, 32]. This correlates well with the high total phenolic and flavonoid content observed in antioxidant assays.

Among sugars, the presence of D-mannose is predominately important because it has been noted for anticancer, anti-inflammatory and antiviral activities [43], although maltooligosaccharides

such as maltotriose and maltopentose show immunoregulatory and prebiotic capability [44, 45]. Levoglucosan, D-mannose, maltotriose, maltopentose, gamma-cyclodextrin hydrate, dextrin and lactose indicates an crucial role in energy storage, osmotic equilibrium and precursor functions for secondary metabolism [46]. These compounds may circuitously support plant defence mechanisms and pharmaceutical applications.

Fatty acids stand for a dominant class in leaves and bark. Major compounds such as n-hexadecanoic acid, octanoic acid, linolenic acid (9,12,15-octadecatrienoic acid), oleic acid, dodecanoic acid and octadecanoic acid are well known for antioxidant, antimicrobial, anti-inflammatory and anticancer properties. n-Hexadecanoic acid demonstrate anti-inflammatory activity through enzyme inhibition [47], whereas octanoic acid shows strong antibacterial and biofilm-eradicating properties against *Staphylococcus aureus* [48, 49]. Unsaturated fatty acids such as linolenic and linoleic acid derivatives potent free radical scavengers and membrane stabilizers that supports hepatoprotective and anti-inflammatory activities.

Terpenes and terpenoids has one of the most pharmacologically significant groups in *V. leucoxylon* L.f.. Caryophyllene, phytol, squalene, β-sitosterol, betulinic acid, corosolic acid and vitamin E are major compounds detected. β-Caryophyllene is a well-established sesquiterpene with anticancer, analgesic, anti-inflammatory and antibacterial properties [50]. Squalene is well-known for immunostimulatory and anticancer potential [51, 52]. β-sitosterol has strong antidiabetic and apoptosis-mediated anticancer effects [53 - 55].

Corosolic acid, a pentacyclic triterpenoid (ursane-type) among a carboxylic acid functional group, validates convincing antidiabetic effects by reducing blood glucose levels as well as noticeable anti-inflammatory activity through modulation of inflammatory pathways [56]. The ester component, including hexadecanoic acid methyl ester, methylparaben, benzoic acid esters and various fatty acid esters, indicates preservative, antimicrobial and pesticidal capacity. Hexadecanoic acid methyl ester is prominent source for the antioxidant and hepatoprotective properties [57], while methylparaben and benzoic acid derivatives shows preservative and antimicrobial effects. These esters support infection control and shelf life improvement. Whereas, phytol shows antimicrobial, cytotoxic, antioxidant and anti-inflammatory potential [58].

Iridoid glycosides such as agnuside and aucubin are important chemotaxonomic markers enhancing its medicinal value . Agnuside has been reported for antioxidant, angiogenic and anticancer effects [59, 60], whereas aucubin unveils antioxidant, neuroprotective, hepatoprotective, anti-fibrotic and anticancer potential [61, 62].

Phenolic compounds such as cinnamaldehyde, hydroquinone, coumarin, caffeoylarbutin derivatives and hydroxybenzoic acids further support the antimicrobial, hypoglycemic, anti-inflammatory and anticancer potential of the plant. hydroxybenzoic acid derivatives show strong antibacterial and antioxidant effects [63]. Whereas Coumarin is exceptionally important because of its multi-target anti-inflammatory and anticancer potential [64, 65]. These phenolics are principal contributors to oxidative stress reduction via hydrogen donation and free radical stabilization.

Volatile compounds such as tridecanal, nonyl aldehyde, undecenol derivatives and pentadienol derivatives enhance primarily to antibacterial and antifungal activity. Tridecanal reported for antibacterial, antifungal and antioxidant properties [66, 67], whereas nonanal shows antifungal and antidiarrheal effects [68, 69]. These compounds function as natural defences against pathogens and stress.

Additional compounds such as di-n-octyl phthalate, ethyl iso-allocholate, glycerin, heptacosane, lanatoside A and thymine indicate broader cardioprotective, antidiabetic, antimicrobial and anticancer potential. Heptacosane reported to overcome multidrug resistance and antimalarial activity [70], although ethyl iso-allocholate shows potential antidiabetic and antioxidant activities by insulin signaling pathways [71].

7. CONCLUSIONS

This PRISMA-based systematic review highlights current knowledge on the taxonomy, phytochemistry and pharmacological potential of *Vitex leucoxylon* L.f., emphasizing its rich phytochemical and wide range of experimentally demonstrated bioactivities.

The integrated evidence validates the presence of diverse metabolite classes, including terpenoids, flavonoids, iridoid glycosides, phenolics and fatty acids, which are associated with pharmacological activities such as antimicrobial, antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, anticancer and CNS-related effects. However, the review also reveals that the pre-existing literature is largely preclinical, methodologically heterogeneous and analytically fragmented, with considerable variability in plant part selection, extraction procedures, analytical platforms, experimental models and evaluative metrics. Many phytochemical reports rely predominantly on GC–MS-based characterization without complementary structural validation, while pharmacological studies frequently employ crude extracts with limited mechanistic insight, standardized dosing and toxicity analysis.

Future research should therefore emphasis standardized extraction and analytical methods, consolidation of multi-analytical metabolomic approaches like LC–MS/MS and NMR and quantitative standardization of bioactive markers to facilitate reproducibility and cross-study uniformity. Identifying compound-specific activity correlations, molecular mechanisms of action and structure–activity correlations will be essential for translating ethnomedicinal claims into experimentally validated therapeutic leads. concurrently, systematic toxicological assessments, pharmacokinetic evaluations and well-designed clinical studies are required to evaluate safety, efficacy and bioavailability. Addressing these critical gaps will reinforce integrative synthesis of evidence and improve alignment graphical representations and the synthesized narrative, thereby supporting the systematic progression of *V. leucoxylon* L.f. as a substantiated source of bioactive compounds for pharmaceutical and therapeutic uses. These efforts will not only strengthen its pharmacological relevance but also support its inclusion in evidence-based drug discovery and bioprospecting. Overall, *Vitex leucoxylon* L.f. represents a pharmacologically promising yet under-validated medicinal species that warrants systematic translational research.

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9. AUTHOR CONTRIBUTIONS

SBP: Gathered the data and prepared the manuscript. SPD: Handled formatting. PVP & AVL: contributed as co-authors. SAD: carried out the review and corrected. The final version of the manuscript has been read and approved by all authors..

10. ETHICAL STATEMENT

This work does not include any studies involving human or animal subjects.

11. CONSENT FOR PUBLICATION

All authors have provided their consent for publication of this manuscript.

12. CONFLICT OF INTEREST

The authors declare no conflict of interest.

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