

Phytochemical And Pharmacological Activities Of Wood Apple: A Systemic Review



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ABSTRACT

Background: Wood apple, botanically known as *Feronia elephantum* syn. *Limonia acidissima*, is a member of the Rutaceae family and has been valued in Ayurveda for its multifaceted medicinal properties. Traditionally used in managing various ailments, the plant is reported to be rich in significant pharmacological activities that include hypoglycaemic, hepatoprotective, antitumor, antimicrobial, and larvicidal effects, among others. The observed therapeutic benefits of this plant are attributed to bioactive phytochemicals, including alkaloids, flavonoids, polyphenols, lignans, and terpenoids. Despite its extensive use in traditional medicine, its phytochemical and pharmacological profile needs consolidation through a systematic review.

Objectives: The present review aims at compiling and analysing the existing scientific literature on the phytochemical composition and pharmacological activities of Wood apple, providing full insight into its medicinal potential.

Methods: This study presents a critical review of the literature about Wood apple, conducted in major databases like PubMed, ScienceDirect, Web of Science, Scopus, and Google Scholar for articles published between 2010 and 2024. The search was conducted by using keywords such as Wood apple, *Feronia elephantum*, *Limonia acidissima*, phytochemistry, and pharmacological activities associated with Boolean operators (AND/OR). Based on a structured selection process, only studies that described the phytochemical constituents and pharmacological activities of Wood apple were included.

Results: A review of literature revealed the presence of bioactive principles, which are responsible for its therapeutic use. Experimental studies indicated that Wood apple possesses antidiabetic, hepatoprotective, antimicrobial, Anti-hyperlipidaemic and anti-inflammatory activities. Besides, preclinical studies have pointed out its potential role in fighting against oxidative stress and metabolic disorders.

Conclusion: Wood apple (syn. *F. elephantum*, *L. acidissima*) is a rich source of bioactive phytochemicals like flavonoids, coumarins, alkaloids, essential oils, phenolic compounds, tannins, steroids, triterpenoids, carbohydrates, and amino acids. These are the constituents responsible for the wide pharmacological activities of this plant and, therefore, represent an important plant within traditional and modern medicine. Further research is needed to explore the full potential of *F. limonia* in drug development and nutritional applications.

Keywords: Wood apple, *Feronia elephantum*, *Limonia acidissima*, phytochemistry, pharmacological activities, traditional medicine, bioactive compounds.

1. INTRODUCTION

Human has been very close to the nature with its evolution and through thousands of years of observation process, it has come to know the medicinal properties of various plants and they are being used by human as traditional medicine to treat diseases. These medicinal plants having therapeutic activities as anthelmintic, antibacterial, antiviral, antifungal, antidiabetic, anticancer, anti-inflammatory, diuretic, antihyperlipidemic, antipyretic etc., due to presence of various phytochemicals such as alkaloids, flavonoids, polyphenols, lignin's, terpenoids etc. Numerous

herbal plants and their formulations to treat the diseases are reported in Ayurveda.

Feronia elephantum, member of the family Rutaceae, is described in Ayurveda as *Kappitha*, has been used medicinally for thousands of years to treat the various diseases or clinical conditions by traditional healers. It is a religious plant which is native to Indian subcontinents.¹ Almost all part of the plant is used for various medical conditions. It has hypoglycaemic, hepato-protective, antitumor, antimicrobial and larvicidal activity.²

2. METHODOLOGY

Information regarding phytochemicals and pharmacological activities of *F. elephantum* was collected from different online databases such as PubMed, Science direct, Web of science, Scopus, Google scholar, Science direct, etc., and literatures published from 2010 to 2024 were searched thoroughly for relevant articles. The keywords *Feronia elephantum*, *F. limonia*, *Limonia acidissima*,

Anisifolium limonia, *Crateva balangas*, *Crateva vallanga*, *Feronia balanghas*, phytochemistry, pharmacological activities, combined with “AND” and “OR” Boolean operators were used. Relevant appropriate research article containing phytochemical analysis and pharmacological potentials were retrieved. Article retrieval and screening process is presented in **Figure 1**.

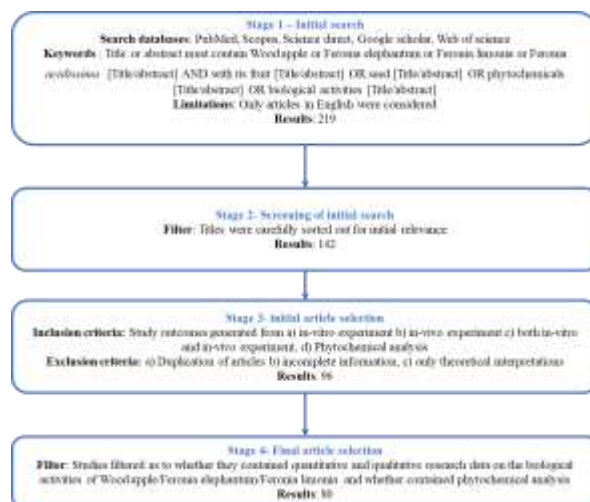


Figure 1 Showing steps for selection of articles

3. PLANT DESCRIPTION

3.1 Taxonomic classification and common name

Kingdom: Plantae

Phylum: Tracheophyta

Class: Magnoliopsida

Order: Sapindales

Family: Rutaceae

Genus: *Feronia*

Species: *elephantum*³

3.2 Synonyms

L. acidissima L., *F. limonia* (L.) *Anisifolium limonia* Kuntze, *Crateva balangas* K.D.Koenig, *Crateva vallanga* K.D.Koenig, *Feronia balanghas* K.D.Koenig.⁴

3.3 Vernacular name:

Sanskrit: *Kapittha*, *Kapipriya*, *Dadhiphala*, *Surabhicchada*, *Puspa phala*, *Dadhittha*, *Dantasatha*.⁵

Hindi: *Kaith*

Bengali: *Kathabel*

Tamil: *Velaga*

Malayalam: *Vilavu*

English: Elephant Apple, Wood Apple

4. MORPHOLOGICAL STUDIES

Size: A small deciduous glabrous tree, with slender branches having rough and spiny bark, approximately 9 meter in height. It is habituated for monsoon climate but can survive in drought area light soils. Leaves having thick imparipinnate and are alternatively arranged. 5-7 leaflets about 25-30 millimetres in length and 10-20 millimetres in width are present in leaves (**Figure 2**). Citrus scent is evaporated on crushing the leaves. Its flowering season is between February to March month.

Its fruiting period is during cold season i.e. about October to November months. Fruits are globose round, grey-white in colour, rough and woody hard and 2-3 inch in diameter. Inside the hard rind it contains a pulpy core which is brownish and aromatic resinous in nature. The pulp is sour or sweet in taste and a number of small whitish seeds are embedded in it.^{1,6}



Figure 2 Wood apple tree in a natural habitat and A. Leaf, B. Fruit

Representation images of Wood apple tree, leaves and fruit are showing in Figure 2.

5. NATURAL DISTRIBUTION

Kapittha is indigenous to India, Pakistan, Myanmar, Malaysia and Java, China and other part of Southeast Asia.² It is widely distributed in almost all part of India.⁷ The *Feronia elephantum* Correa (F.E.), *F.*

limonia swingle (F.L.), *L. acidissima* (L.), and *Schinus limonia* (s.c) are the species of *Feronia* which is mainly found in India.^{5,3} Figure 3 is showing worldwide distribution of Wood apple.

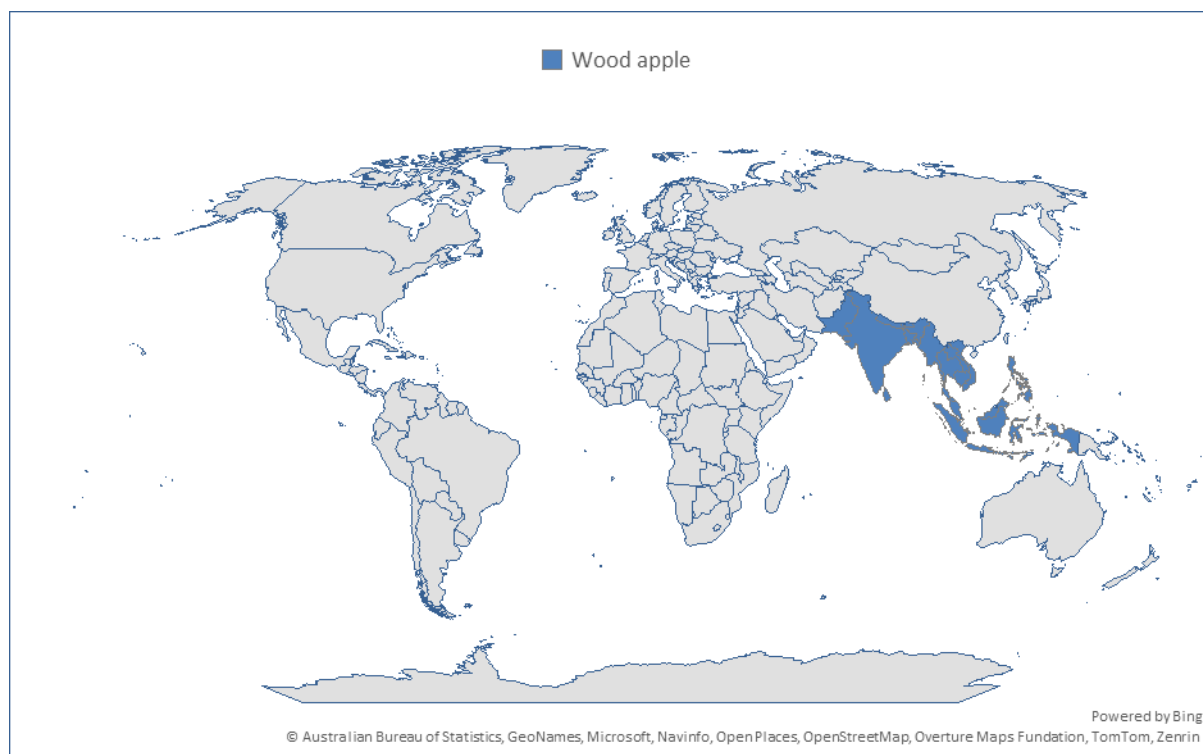


Figure 3 Natural distribution of Wood apple

6. ETHNOMEDICINAL USES

Ethnomedicinally its various parts have been utilized by folklore to treat various medical conditions.

6.1 Unripe fruits:

Its unripe fruit is *amla* (sour), *ushana*, *ruksha*, *laghu*, and astringent in nature. They are alexipharmic and balancing the vitiated *Kapha dosha*. It is used in chronic diarrhoea, dysentery, hiccup, itching, pharyngodynia, constipation and dyspepsia. It is also used to treat the whooping cough.⁸

6.2 Ripe fruits:

The ripe fruit of *F. elephantum* is sour-sweet in taste, *kashaya* (astringent), *grahi* (absorbent), *ruchijanaka* (taste-producing), *śītavīrya* (as of cooling virtues or properties), *veery vardhak* (semen enhancer), *Duṣpācyā* (hard to digest) and pacifying the vitiated *tridosha* but specifically *vata* and *pitta dosha*. It is used to treat the *Śvāsa roga* (~asthma), *kṣayarōga* (~tuberculosis), diseases due to aggravation of *rakta dosha*, *vaman* (vomiting), hiccup, cough, and poisoning. They are carminative and used as appetizer.⁸

6.3 Seed and seed oil:

Its seeds are used to treat the heart disease, headache, erysipelas and poisoning. Oil of the seeds is *kashaya*, *grahi*, *ruchikara* (palatable), and balancing the vitiated *pitta* and *kapha dosha*. It is used to cure the hiccup, cough, and vomiting.

6.4 Pulp:

Its pulp is used to manage the diabetes mellitus, amoebiasis and locally for venous bug bites.^{8,9}

6.5 Leaves and flowers:

Its leaves are used in anorexia, vomiting, hiccup, pneumonia, diarrhoea and cough. The juice of the

leaves is useful in ear colic. Its flowers are useful to reduce the effects of toxin.^{8,9}

6.6 Gum:

It is useful in diarrhoea, dysentery, gastritis, haemorrhoids, and diabetes.^{8,9}

7. PHYSICO-CHEMICAL PARAMETERS

Physicochemical parameters such as ash values, moisture content, extractive values, and fluorescence analysis are essential for evaluating the purity and quality of medicinal plants. The key physicochemical findings for Wood apple leaves, bark, and stem are presented in **Table 1**.

Table 1. Physico-chemical parameters of various part of Wood apple.

Parameter	Volume % w/w (Leaves)	Volume % w/w (Bark)	Volume % w/w (Stem)	Volume % w/w (Fruit pulp)	Reference
Total Ash Value	10.16% ± 0.33	8.56%	10.00%	1.55%	10, 11, 12, 13,14
Acid Insoluble Ash	4.13% ± 0.08	0.90%	5.50%	17.6%	10, 11, 12, 13,14
Water Soluble Ash	0.46% ± 0.03	4.8%	2.16%	41.2%	10, 11, 12, 13, 14
Moisture Content	-	4.9%	7.55%	78.62%	11, 12, 13, 14, 15
Loss on Drying	-	11.46%	-	-	11, 13
Water Soluble Extractive	9.06% ± 0.34	3.32%	5.7%	-	10, 12, 13, 15
Alcohol Soluble Extractive	5.43% ± 0.23	3.12%	2.7%	-	10, 12, 13, 15
Petroleum Ether Extractive	1.90% ± 0.05	0.72%	-	-	10
Sulphated Ash	-	-	16.30%	-	12
Crude Protein	-	-	-	3.76%	14
Crude Fibre	-	-	-	2.95%	14
Crude Fat	-	-	-	2.50%	14
Carbohydrate Content	-	-	-	10.62%	14
Energy Value (Kcal/100g)	-	-	-	80.00	14

8. PHYTOCHEMISTRY

F. elephantum possesses a diverse phytochemical composition including flavonoids, coumarins, alkaloids, essential oils, phenolic compounds, tannins, steroids, triterpenoids, carbohydrates, and amino acids. Some flavonoids include 5,7-dihydroxy-6,8-dimethoxyflavone-7-O-β-D-glucopyranoside¹⁶ and luteolin from the fruit pulp were identified.^{17, 18} Coumarins, such as marmesin, have been isolated from the fruit pericarp and stem bark.^{19,20,21} In addition, a novel alkaloid named as feronine and several alkaloid precursors have been reported by Pitchai et. al..²² Terpenes and phenolics compounds

such as limonene, α-pinene, β-caryophyllene, linalool, and geraniol are the major constituents of the essential oils obtained from leaves and fruit pulp.^{23, 24} Phenolic compounds and tannins were obtained by using solvent concentration methods.²⁵ Some steroids and triterpenoids, such as β-sitosterol and lupeol, have been identified in the stem bark.¹² Its fruit has a rich source of carbohydrates and amino acids, including leucine, isoleucine, and valine.^{26, 27} These compounds are responsible for the plant's medicinal and nutritional properties. Major compounds of *F. elephantum* are presented in **Table 2**.

Table 2 Showing major phytochemicals in different parts of Wood apple

S.N.	USED PART	EXTRACT	METHOD	PHYTOCHEMISTRY SUMMARY	REFERENCES
1	Flowers	Acetone Extract	Column Chromatography	p-coumaric acid, Bergapten, N-phenylpropanamide, N-(2-methylphenyl) acetamide, N-(4-methoxyphenyl) acetamide, A novel compound 5-hydroxy-3-(1,2 dihydroxyprop-1-enyl)-1-methylquinolin-4-on. 1-[4-aminomethyl] (phenyl).	22

2	Fruit	Methanol Extract	FTIR, Analysis,	GC-MS	Alkaloid and saponins, Flavonoids, Phenols, Alkanes, Amino acids, α , β -unsaturated esters, Nitro compounds, Aromatics, Aliphatic amines, Carboxylic acid, and Alkyl halides functional groups, Linoleic acid, Octadecanoic acid, Hexadecanoic acid, Maltol, Vinly guaiacol, Furanone, Ascorbic acid, Luteolins, fixed oil.	3,, 2, 16, 28, 29, 30
			FTIR, H-NMR, and LC-MS studies.		Luteolin - 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-chromen-4-one, (C15H10O7).	31
			GC-MS Analysis		2,5- Furandione, dihydro-3-methylene (44.78%), n-Hexadecanoic acid (6.62%), 5-Eicosene, (E)- (4.04%), cis-13-Octadecenoic acid (6.08%) and γ -Sitosterol (2.99%), cis-Aconitic anhydride (5.19%), Ethanol, 2,2'-[(1-methylethyl) imino]bis- (6.27%) and Propanedioic acid, ethyl-, diethyl ester, and Dodecanoic acid (4.48%).	32
			Column Chromatography		5,4-dihydroxy-3-(3-methyl-but-2-enyl) trimethoxy-flavone-7-O-b-D glucopyranoside.	16
		Soxhlet Sequential Extraction	Reverse Phase-High Pressure Liquid Chromatography.		Essential amino acids- Highest -Isoleucine, Phenylalanine and Tryptophan, Moderate- Valine, Histidine and Leucine, Lowest- Methionine, Tyrosine, Lysine and Threonine. Non-essential amino acids- Proline, Glycine, Aspartic acid, and Alanine.	26
			Column Chromatography, TLC		Alkaloids, Carbohydrates, Glycosides, Saponins, Flavonoids, Tannins, Phenolic Compounds, Vitamin-C, Proteins, Phytosterol, Triterpenoids and Amino acids.	33, 34
			Gas Chromatography - Mass Spectroscopy (GCMS).		Oleic acid, n-hexadecanoic acid, Palmitoleic acid, and Octadecanoic acid. Sterols - Sitosterol, Stigmasterol, Ergost5-en-3-ol, (3beta.).	28
3	Rind	Methanolic Extract	GC-MS chemical analysis		Alkaloids, Saponins, Gum and Mucilage.	2
		Aqueous Extract	GC-MS Analysis		Alkaloid, Tannin, Phenol, Flavonoid, Glycosides, Saponins, Triterpenoids, Gum and Mucilage.	35
		Methanolic Extract	GC-MS chemical analysis		Alkaloids, Saponins, Gum, Mucilage, Flavonoids, Steroids, Glycosides, Carbohydrates, and Phenolic Compounds.	3, 35
		Methanol Extract	Vacuum Liquid Chromatography, Flash Chromatography, Radial Chromatography		3 Coumarins -Auraptene, Osthol, And Xhantotoxin.	20
		Ethanol Extract	GC-MS Analysis		2-Propenenitrile, 3-(3,4-dimethoxyphenyl)-(60.72%), Phenol, 4-(3-hydroxy-1-propenyl)-2-methoxy-(9.35%), 3-(2-NAcetyl-N-methylaminoethyl)indol (1.15%), cholesta-8,24-diene-3-ol, 4-methyl-(3a'-4a')- (0.86%).	36
5	Seed	Methanol Extract	GC-MS chemical analysis		Alkaloids, Flavonoids, Saponins, Gum and mucilage, and Fixed oil.	35
6	Root	Soxhlet Sequential Extraction	UV, IR, NMR and mass spectral studies.		Flavonoid - 5-hydroxy-2- (4-hydroxyphenyl)-7-methoxy-6-(3-methylbut-2-enyl) chroman-4-one (First isolation)* along with Imperatorin, Bergapten And Xanthotoxin.	37
7	Leaves	Methanolic extract	Column Chromatography, TLC		Alkaloids, Carbohydrates, Glycosides, Saponins, Proteins and amino acids, Phytosterols, Phenolic compounds, Flavonoids and Resins.	10, 38, 39, 40
		Soxhlet Sequential Extraction	UV, IR, NMR and mass spectral studies.		Flavonoid - 5-hydroxy-2- (4-hydroxyphenyl)-7-methoxy-6-(3-methylbut-2-enyl) chroman-4-one (First isolation) along with Imperatorin, Bergapten and Xanthotoxin.	37

	Hexane and Ethyl acetate Extract	Column Chromatography Followed by GC-MS Analysis,	Estragole (50.82%), Trans-anethole (p-propenylanisole, anise camphor) (14.98% and Caryophyllene (9.22%).	41
	Aqueous extract	Preliminary Phytochemical screening by standard method of Kokate and Harborne	Saponins, Tannins, Proteins, Carbohydrates and Flavonoids.	9
	Ethanol Extract	GC-MS ANALYSIS	7- Norbornadienyl t-butyl ether (17.26%), 2-isopropyl-5-methyl-1-heptanol (11.40%), 1-Octanol, 2-butyl (8.47%), Phenol, 4-[2-(dimethylamino)-ethyl]- (4.56%), 2,3-Dimethylquinolin-4(1H)-one (3.58%), Ethyl iso-allocholate (1.63%).	36
		Column Chromatography and Standard methods	Carbohydrates, Steroids/ Terpenoids, Flavonoids, Tannins, Phenols, Glycoside, Flavonoids, and Flavonol.	42, 43, 44, 45
8	Essential Oil of Leaf	GC-MS ANALYSIS	Estragole, Cis-dihydro- β -terpineol and P-cymene β -pinene (28.4%), Z-anethole (22.1%), methyl chavicol (12.0%) and E-anethole (8.1%). Eudesma-4 (14)11-diene (46.3%), Carvacrol (29.6%) and 1,5-cyclodecandine (13.4%).	23, 46, 47
9.	Essential Oil from Fruit Pulp	GC-MS ANALYSIS	Thymol (52.22%), Dodecanoic acid (19.34%), α -pinene (4.02%), Carvacrol (3.86%), Camphoric acid (3.25%) and Caryophyllene oxide (3.06%).	24

*(Fourier transformation – infra – red (FT – IR) spectrum)

9. PHARMACOLOGICAL ACTIVITIES OF F. LIMONIA

The phytochemical constituents of *F. limonia* contribute to its diverse pharmacological activities, including antioxidant, antimicrobial, hepatoprotective, cytotoxic, and anti-inflammatory properties.

9.1 Antioxidant Activity

The antioxidant activity of *F. limonia* has been extensively studied. Srivastava et al. (2021) demonstrated that the phenolic compounds and flavonoids present in the plant exhibit strong free radical scavenging activity.²⁵ The study found that the antioxidant activity of *F. limonia* is comparable to that of ascorbic acid, a well-known antioxidant. Similarly, Senthilkumar and Venkatesalu (2013) reported that the essential oil from the fruit pulp of *F. limonia* possesses significant antioxidant activity, as measured by the DPPH radical scavenging assay.²⁴ In a study by Vikhe et al. (2021), the aqueous extract of *F. limonia* gum demonstrated significant antioxidant activity by scavenging free radicals and reducing lipid peroxidation. The extract also increased the levels of antioxidant enzymes such as SOD, CAT, and GPx, which protect cells from oxidative damage.⁴⁸

Daphedar et al. reported that silver nanoparticles synthesized from *L. acidissima* fruit extract exhibit

strong antioxidant activity due to their high phenolic and flavonoid content, neutralizing free radicals and reducing oxidative stress.⁴⁹ Similarly, Nyoe et al. found that extracts of *L. acidissima* fruit possess significant antioxidant properties and antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli*.¹⁴

The antioxidant potential of *L. acidissima* stem bark was evaluated using the DPPH free radical scavenging assay. The chloroform soluble fraction exhibited strong antioxidant activity with an IC₅₀ value of 18.8 ± 1.24 μ g/ml, comparable to the standard antioxidant Butylated hydroxytoluene (BHT) with an IC₅₀ of 17.69 ± 2.36 μ g/ml. The petroleum ether fraction showed moderate activity with an IC₅₀ value of 37.64 ± 3.87 μ g/ml. These results suggest that the chloroform fraction is rich in phenolic compounds contributing to its potent free radical scavenging capacity.⁵⁰

The methanolic extract of *F. limonia* fruit pulp (MEFL) demonstrated potent radical scavenging capacity against DPPH and ABTS radicals and showed high total antioxidant activity via the phosphomolybdate method. This antioxidant potential was positively correlated with its total phenolic content, suggesting that the phenolic compounds contribute to its free radical scavenging effects, highlighting its potential as a natural dietary antioxidant source.⁵¹ Similarly, the crude methanol

extract (CME) of *F. limonia* bark and its chloroform fraction (CLF) displayed strong antioxidant activities in DPPH and hydroxyl radical scavenging assays, with the CLF showing the highest phenolic and flavonoid content (18.16 µg GAE/g and 160.20 µg GAE/g, respectively). The study identified Umbelliferone (7-hydroxycoumarin) as a key antioxidant compound isolated from the chloroform fraction, which also demonstrated notable lipid peroxidation inhibition capacity.⁵² Furthermore, essential oil extracted from *F. elephantum* (syn. *F. limonia*) leaves exhibited substantial antioxidant activities, including DPPH and hydroxyl radical scavenging and metal chelating activities, which could be beneficial for food preservation and therapeutic applications.⁵³ Additionally, an aqueous extract of *L. acidissima* (syn. *F. limonia*) fruit pulp and rind showed a dose-dependent increase in antioxidant activity, validated by the phosphomolybdenum assay, underscoring the fruit's potential in mitigating oxidative stress.⁵⁴

9.2 Antimicrobial Activity

The antimicrobial activity of *F. limonia* has been attributed to its essential oils and alkaloids. Senthilkumar et al. (2010) reported that the leaf essential oil of *F. limonia* exhibits strong antibacterial activity against Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus* and *Escherichia coli*.²³ The study found that the antibacterial activity of the essential oil is due to the presence of terpenes and phenolic compounds. Similarly, Pitchai et al. (2012) demonstrated that the alkaloids present in *F. limonia* exhibit significant antimicrobial activity.²² In a study by Islam et al. (2018), the ethanolic extract of *F. limonia* fruit pulp demonstrated significant antibacterial activity against both gram-positive and gram-negative bacteria, including *Staphylococcus aureus*, *Escherichia coli*, and *Shigella shiga*. The extract also exhibited antifungal activity against *Candida albicans*.⁵⁵ The antimicrobial activity of *F. limonia* is attributed to its ability to disrupt microbial cell membranes and inhibit the synthesis of essential microbial enzymes. Patil and Taranath also demonstrated that zinc oxide nanoparticles derived from *L. acidissima* leaves have potent antibacterial effects, particularly against *Mycobacterium tuberculosis*.⁵⁶

A study by Buvanaratchagan and Dhandapani evaluated the antifungal properties of an ethanolic extract from *L. acidissima* leaves against common dermatophytic fungi. Utilizing the disc diffusion method, the extract was tested against *Trichophyton mentagrophytes*, *Microsporum canis*, and *Epidermophyton floccosum*, with Ketoconazole serving as the reference control. The results demonstrated that the ethanolic leaf extract

exhibited significant antifungal activity against all three dermatophytes, with zones of inhibition measuring 32.42±1.43 mm for *T. mentagrophytes*, 27.56±0.95 mm for *M. canis*, and 28.62±1.37 mm for *E. floccosum*. These effects were comparable to those of Ketoconazole, which showed inhibition zones of 45.62±2.24 mm, 39.86±1.43 mm, and 32.61±1.88 mm, respectively. These findings suggest that *L. acidissima* leaves possess potent antifungal properties, supporting their traditional use in treating fungal infections.⁵⁷

9.3 Hepatoprotective Activity

The hepatoprotective activity of *F. limonia* has been attributed to its flavonoids and triterpenoids. Dar et al. (2013) demonstrated that the flavone glycoside isolated from *F. limonia* exhibits significant hepatoprotective activity against paracetamol-induced hepatotoxicity in albino rats.¹⁶ The study found that the flavone glycoside reduces the levels of liver enzymes, including ALT, AST, and ALP, in the serum of rats, indicating its hepatoprotective effect. Similarly, Kumar et al. (2012) reported that the triterpenoids present in the stem bark of *F. limonia* exhibit hepatoprotective activity.¹²

In a study by Dar et al. (2012), the ethanolic extract of *F. limonia* fruit pulp demonstrated significant hepatoprotective activity by reducing serum levels of liver enzymes (ALT, AST, ALP) and improving histopathological changes in the liver. The extract also exhibited antioxidant activity by increasing the levels of glutathione (GSH) and superoxide dismutase (SOD), which play a crucial role in mitigating oxidative stress-induced liver damage.⁵⁸ Similarly, Mishra et al. (2017) assessed the aqueous (ASFE) and ethanol (ESFE) extracts of *F. elephantum* (syn. *F. limonia*) stem bark and root. The extracts (50 and 100 mg/kg) significantly restored liver function biomarkers (SGOT, SGPT, ALP, TB, TC, TP) to near-normal levels. Histopathological analysis revealed reduced hepatic necrosis and improved architecture, suggesting membrane stabilization and parenchymal cell regeneration.⁵⁹

Syed et al. (2008) investigated the methanolic extract (ME) of *F. limonia* leaves (200, 400, 600 mg/kg). The extract effectively normalized liver biomarkers and improved histological features by reducing fatty degeneration and maintaining liver architecture. The hepatoprotective effect was attributed to antioxidant phenolic and flavonoid compounds.^{60, 61}

Sharma et al. and Jain et al. confirmed the hepatoprotective efficacy of *F. elephantum* leaf and fruit extracts, demonstrating their ability to prevent chemically induced liver damage in diabetic and non-diabetic rats.^{62, 63, 64} Additionally, Meshack and Gupta reviewed its hepatoprotective potential, emphasizing its role in reducing liver enzyme levels and lipid peroxidation.⁶⁵ The hepatoprotective

mechanism of *F. limonia* is attributed to its ability to scavenge free radicals, inhibit lipid peroxidation, and enhance the activity of antioxidant enzymes.

In a study by Upadhyay et al. ferolactone, a novel compound isolated from the fruit of *F. limonia* was administered in albino Wistar rats to assessing the compound's efficacy against carbon tetrachloride (CCl₄)-induced hepatotoxicity and its effects were compared to those of the standard hepatoprotective drug, silymarin. The results demonstrated that ferolactone significantly reduced elevated levels of serum enzymes associated with liver damage, including serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), and alkaline phosphatase (ALP). Additionally, there was a notable increase in total protein (TP) levels, indicating improved liver function. Histopathological examinations further confirmed the hepatoprotective effect, revealing substantial recovery of liver tissue architecture in ferolactone-treated animals. These findings suggest that ferolactone from Wood apple exhibits potent antihepatotoxic activity, comparable to that of silymarin, supporting its potential therapeutic application in managing liver disorders.⁶⁶

9.4 Gastroprotective and Antiulcer Activity

Mishra et al. found that *F. elephantum* fruit pulp extract alleviates gastric ulcers in albino rats by inhibiting oxidative stress and inflammatory mediators.⁶⁷ The ability of *F. limonia* to mitigate liver and gastric damage suggests that it may be useful in treating liver disorders and peptic ulcers.

A study evaluating *F. elephantum* leaf and bark extracts on indomethacin-induced ulceration in albino rats demonstrated significant ulcer-protective effects. The extract (500 mg/kg) administered thrice at 12-hour intervals before NSAID exposure effectively reduced ulceration. Parameters such as gastric juice volume and acidity were significantly lowered, comparable to the standard antiulcer drug ranitidine (20 mg/kg).⁶⁸ The leaf extract showed superior antiulcer potential compared to the bark extract, suggesting a stronger protective effect. Mechanistically, the protective effect is attributed to the inhibition of NSAID-induced cyclooxygenase (COX) inhibition, reduction in gastric acid secretion, and enhancement of mucosal defence mechanisms, particularly via flavonoids and tannins, which have astringent properties aiding in ulcer healing.

In another study, *L. acidissima* leaf extract was tested in an ethanol-induced ulcer model. Ethanol exposure leads to severe gastric mucosal injury through oxidative stress, microvascular damage, and increased gastric acid secretion. The ethanolic leaf extract (200 mg/kg and 400 mg/kg) significantly reduced ulcer index, increased gastric pH, and

exhibited protective effects comparable to ranitidine.⁶⁹

At 400 mg/kg, the extract provided optimal gastroprotection, likely due to its antioxidant and anti-inflammatory properties. Histopathological analysis revealed reduced epithelial disruption, leukocyte infiltration, and submucosal oedema in extract-treated groups, indicating a protective role against ethanol-induced oxidative damage.

9.5 Cytotoxic Activity

The cytotoxic activity of *F. limonia* has been attributed to its flavonoids, particularly luteolin. Hanchinalmath et al. (2021) demonstrated that luteolin isolated from the fruit pulp of *F. limonia* induces apoptosis in HepG2 cells.^{17, 18} The study found that luteolin activates caspase-3 and caspase-9, which are key enzymes in the apoptotic pathway. Similarly, Nattudurai et al. (2014) reported that the fractions isolated from *F. limonia* exhibit cytotoxic activity against cancer cells.⁴¹

Thirugnanasampandan and David investigated the cytotoxic activity of essential oil from *F. elephantum* and found that it inhibits the proliferation of MCF-7 breast cancer cells, inducing apoptosis through mitochondrial pathways.⁵³ El Sayed et al. conducted a comparative metabolomics analysis and reported the antiviral potential of *L. acidissima* fruit and leaf extracts, suggesting possible anticancer applications due to their ability to modulate cellular signalling pathways.⁷⁰

The cytotoxic effects of *L. acidissima* were assessed using the brine shrimp lethality bioassay. The petroleum ether fraction demonstrated significant cytotoxicity with an LC₅₀ value of 0.2779 µg/ml, surpassing the standard cytotoxic agent Vincristine sulfate (LC₅₀ = 0.445 µg/ml). The chloroform fraction showed lower cytotoxic potential with an LC₅₀ value of 6.89 µg/ml. The pronounced cytotoxicity of the petroleum ether fraction indicates the presence of bioactive compounds with potential anticancer properties, warranting further investigation.⁵⁰

9.6 Anti-inflammatory and Anti-nociceptive Activity

The anti-inflammatory activity of *F. limonia* has been attributed to its coumarins and steroids. Purwar (2023) reviewed the anti-inflammatory properties of marmesin, a coumarin isolated from the fruit pericarp of *F. limonia*.¹⁹ The study found that marmesin reduces the levels of pro-inflammatory cytokines, including TNF-α and IL-6, in vitro. Similarly, Kumar et al. (2012) reported that the steroids present in the stem bark of *F. limonia* exhibit anti-inflammatory activity.¹² In a study by Saha et al. (2010), the methanolic extract of *F. limonia* leaves demonstrated significant analgesic activity in both

acetic acid-induced writhing and tail-flick tests in mice suggesting opioid receptor involvement. The extract also exhibited anti-inflammatory activity by inhibiting the production of prostaglandins and other inflammatory mediators.⁷¹ Samal et al. found similar analgesic activity in experimental animal models, reinforcing its potential as a natural pain reliever.⁷² Sujitha and Venkatalakshmi demonstrated that *L. acidissima* fruit extract exhibits anti-inflammatory effects through inhibition of cyclooxygenase enzymes, comparable to conventional NSAIDs.⁵⁴ In another study by Momin et al. the analgesic potential of the ethanolic extract was assessed utilizing the acetic acid-induced writhing model in mice. The extract exhibited marked analgesic activity, demonstrating 23.74% and 45.32% inhibition of acetic acid-induced writhing at oral doses of 250 mg/kg and 500 mg/kg, respectively, in comparison to the 50.36% inhibition achieved by the reference standard Diclofenac sodium at a dose of 25 mg/kg. These results substantiate the traditional therapeutic application of *F. limonia* leaves in pain management and underscore the need for further investigations to isolate and characterize the bioactive constituents responsible for the observed analgesic effects.⁴² A study by Khare et al. involved the intragastric administration of the ethanolic extract to mice at graded doses of 100, 200, and 400 mg/kg. The analgesic efficacy of the extract was evaluated through both thermal and chemical pain models. The results demonstrated a dose-dependent antinociceptive effect following a single dose of the extract, thereby corroborating the traditional use of *F. limonia* leaves in pain management.⁷³

9.7 Anti-diabetic Activity

F. limonia has been traditionally used to manage diabetes, and recent studies have validated its antidiabetic potential. The plant's gum, in particular, has been shown to exhibit significant hypoglycaemic and antihyperlipidemic effects.

In a study by Vikhe et al. (2021), the aqueous extract of *F. limonia* gum was evaluated for its antidiabetic activity in streptozotocin (STZ)-induced diabetic rats. The extract significantly reduced blood glucose levels, improved insulin sensitivity, and restored the activity of hepatic glucose metabolic enzymes such as glucokinase and glucose-6-phosphate dehydrogenase. The extract also exhibited antioxidant activity by increasing the levels of catalase (CAT) and glutathione peroxidase (GPx), which protect pancreatic β -cells from oxidative damage.⁴⁸

The antidiabetic activity of *F. limonia* is likely mediated through its ability to enhance insulin secretion, improve glucose uptake, and reduce oxidative stress. These findings suggest that *F.*

limonia gum could be a promising candidate for the development of antidiabetic drugs.

Reddy et al. demonstrated that methanol fractions of *F. elephantum* fruit enhance glucose metabolism in type 2 diabetic rats via α -amylase inhibition and PPAR- γ activation, leading to improved insulin sensitivity.^{74,75}

9.8 Anti-hyperlipidaemic effect

Vikhe et al. reported that *F. elephantum* gum significantly reduces hyperlipidaemia in diabetic rats by lowering serum cholesterol and triglyceride levels.⁴⁸ Pandit et al. observed lipid-lowering activity of *F. limonia* leaf extract in hyperlipidaemic rats, supporting its potential as a cardiovascular protective agent.⁷⁶ These findings suggest that *F. limonia* could be developed into a natural therapeutic agent for managing metabolic disorders, particularly diabetes and dyslipidaemia.

9.9 Neuroprotective and Antidepressant Effects

Rakhunde et al. demonstrated that *F. limonia* fruit extract mitigates ischemia-reperfusion-induced brain injury in rats by reducing oxidative damage and inflammation, protecting neuronal integrity.⁷⁷ Jatav et al. investigated its antidepressant activity, showing that ethanolic extracts of *F. limonia* leaves improved behavioural markers of depression in Swiss albino mice, possibly through serotonin modulation.⁷⁸ The neuroprotective effects of *F. limonia* highlight its potential as a natural remedy for neurodegenerative diseases and mental health disorders.

9.10 Reproductive and Endocrine Effects

Dhanapal et al. reported that *F. limonia* fruit pulp exerts reversible antispermatic and antisteroidogenic effects in male rats, indicating its potential use in male contraception.⁷⁹ Verma documented the ethnobotanical use of *F. limonia* in livestock, highlighting its role in treating reproductive disorders.⁸⁰ The hormonal modulation effects of *F. limonia* suggest its potential for therapeutic applications in reproductive health.

9.11 Diuretic and Nephroprotective Activity

The diuretic potential of *F. limonia* was assessed in a study utilizing methanolic extracts obtained via Microwave-Assisted Extraction (MAE) and Bath Sonication Extraction (BSE). In an experimental model using male albino rats, extracts administered at 200 mg/kg exhibited significant diuretic activity, as evidenced by increased urine output and electrolyte excretion. The urine volume increased significantly ($p < 0.001$) with the BSE extract, with notable enhancements in sodium, potassium, and chloride excretion.⁸¹ The sodium-to-potassium ratio remained within physiological limits, suggesting a

natriuretic mechanism of action similar to low-ceiling diuretics.

Oxidative stress plays a critical role in nephrotoxicity, particularly in conditions such as fluorosis. An experimental study assessed the impact of *F. limonia* fruit powder on fluoride-induced renal damage in rats. Animals exposed to 100 ppm sodium fluoride (NaF) exhibited increased lipid peroxidation (TBARS) and decreased levels of antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Administration of *F. limonia* fruit powder at doses of 2.5, 5.0, and 10.0 g% in the diet significantly restored antioxidant enzyme activity and reduced renal lipid peroxidation.⁸² This nephroprotective effect is attributed to the plant's rich polyphenol, flavonoid, and ascorbic acid content, which counteract oxidative damage.

9.12 Antihyperuricemic Activity

A study by Yusnaini et al. investigated the antihyperuricemic potential of the ethanolic extract of *L. acidissima* fruit in potassium oxonate-induced hyperuricemic rats. The extract significantly reduced serum uric acid levels and downregulated urate transporter 1 (URAT1) expression, demonstrating a potential mechanism for its action. The extract also exhibited strong antioxidant properties. However, higher doses (400 mg/kg) were associated with increased blood urea nitrogen (BUN) levels, indicating potential renal toxicity. These findings suggest that *L. acidissima* fruit extract may be a promising candidate for hyperuricemia management.^{83, 28, 84}

9.13 Antidiarrhoeal activity

The ethanolic leaf extract of *F. limonia* demonstrated significant antidiarrhoeal activity in some studies using the castor oil-induced diarrhoea model in mice. Bellah et al. (2014) reported a dose-dependent reduction in diarrhoeal frequency and severity at doses of 250 mg/kg and 500 mg/kg, showing statistically significant results ($p < 0.02$ and $p < 0.001$) compared to the standard drug loperamide.⁸⁵ Similarly, Momin et al. found that the extract exhibited moderate antidiarrhoeal effects, effectively reducing diarrhoeal episodes in a comparable model. Both studies suggest that the extract's antidiarrhoeal mechanism may involve antisecretory action, highlighting *F. limonia*'s potential as a natural therapeutic agent for managing diarrhoeal disorders.⁸⁶

Conclusion

Wood apple is a promising natural resource with significant pharmacological potential due to its bioactive phytochemicals, including flavonoids, coumarins, alkaloids, phenolic compounds, and

terpenoids, which drive its extensive pharmacological activities. The plant's traditional use in Ayurveda for treating conditions such as diabetes, liver disorders, microbial infections, and inflammation is substantiated by contemporary scientific studies, which demonstrate its antioxidant, antimicrobial, hepatoprotective, cytotoxic, anti-inflammatory, antidiabetic, antihyperlipidemic, neuroprotective, and diuretic effects. These activities are mediated through mechanisms such as free radical scavenging, enzyme inhibition, and modulation of cellular pathways, as evidenced by robust in vitro and in vivo data and highlight its potential as a natural therapeutic agent for managing metabolic, infectious, and inflammatory disorders. However, further research is imperative to validate its efficacy and safety through well-designed clinical studies, explore underlying molecular mechanisms, and develop standardized formulations and nutritional applications.

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