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REVIEW ARTICLE

Chemical constituents and pharmacological potential of *Gmelina arborea* Roxb. (Lamiaceae): A review

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Abstract

Gmelina arborea Roxb. has been widely used in traditional medicine and is considered a vital component of Brihatpanchamoolya. It is also commonly used in modern medicine due to its rich content of phytochemicals. The primary constituents include lignans, flavonoids, tannins, glycosides and other bioactive compounds. Notably, the roots of *Gmelina arborea* contain glycosides, particularly flavone glycosides such as apigenin-7-rutinoside, luteolin-7-glucuronide, sitosterol, quercetin and apigenin. The leaves are rich in iridoid glycosides, flavonoids and sterols. The stem contains several lignans, including gmelanone, iso-arboreal, paulownin and gmelinol. Additionally, the flower contains verbascoside, a compound belonging to the class of iridoid glycosides. This species has diverse pharmaceutical applications, including anti-inflammatory properties. It also exhibits a wide range of beneficial effects, such as antioxidant, hepatoprotective, anticancer, neuroprotective, anti-tumour, cardioprotective, anticonvulsant and antihyperlipidemic activities. This study aims to bridge the gap between traditional knowledge and modern research by examining the pharmacological and phytochemical properties of *G. arborea*. A comprehensive review was conducted using well-known academic databases, including PubMed, Google Scholar and Science Direct. The findings were summarized and documented using bibliographic information, which may pay the way for future researcher in this area.

Keywords

Gmelina arborea; brihatpanchamoolya; phytoconstituents; molecular mechanism; pharmacology

Introduction

Gmelina arborea Roxb. also known as the Kandahar tree, white teak, Gamhar (in Hindi) and Kashmiri tree, belongs to the Verbenaceae family (1, 2). This species is native to India, Bangladesh, Southern China, Thailand, Sri Lanka, Cambodia, Myanmar, Laos and the Indonesian island of Sumatra. *G. arborea* can grow to a height of approximately 40 m with a diameter of 140 cm (3). The tree is characterized by a crooked, branchless trunk that typically measures 6-9 m in length and has a large crown with low branches (4). The bark is generally gray and has a somewhat thin texture. The leaves are simple, oppositely arranged, 10 -25 cm in length and 5-18 cm in width (5). The flowers are arranged in panicle-like cymes of 15-30 cm and usually appear after the leaves have fallen. The fruit is a drupe, about 2.25 cm in length, containing 1-4 seeds (6) (Fig. 1).

Fig. 1. Figure of *G. arborea* plant.

Researchers have identified several chemical components derived from this tree. The heartwood contains lignans such as (+)-arboreol, (+)-paulownin, (+)-gmelinol and (+)-epieudesmin as well as iridoid glycosides, coumarins, flavonoids, furanoresorcinol and an isoxazole alkaloid (7), all of which possess significant health benefits and diverse application (8-10). A coumarin glycoside-containing apiose was extracted from the root (10, 11). The leaves of the plant were found to contain luteolin, a type of flavone as well as alkaloids and gmelinoside, an acetylated iridoid glycoside (12, 13).

The objectives of this review are to provide a summary of the most recent developments and techniques in the chemical analysis of bioactive substances present in *G. arborea* extract and to discuss specific analytical methods that can be utilised for the identification of these chemical constituents.

Methodology

This investigation involved an in-depth analysis of prominent academic databases, including PubMed, Google Scholar and ScienceDirect, with a focus on articles published whithin the last 5 years. The search utilized specific keywords such as "*Gmelina arborea*", "Gambhari", "chemical constituents" and "pharmacological efficacy". This approach yielded substantial information on the pharmacological characteristics, chemical constitutions, traditional uses and therapeutic potential of *G. arborea*. The methodological framework provided a systematic approach to identifying relevant scholarly publications, research articles and reviews that align with the study's objectives. The collected resources were meticulously examined to extract key information on the chemical components, historical application and analytical methods associated with *G. arborea*.

Traditional therapeutic use of *G. arborea* in different Ayurvedic formulations

The traditional medical practice of Ayurveda in India dates back 3000 years (14, 15). Today, scientists world wise emphasise the use of herbal remedies for the prevention and treatment of various diseases due to their unique therapeutic properties and minimal side effects compared to conventional drug delivery systems (16, 17). Several formulations containing *G. arborea* are catalogued in databases of medicinal plants used in Ayurveda for treating a range of ailments (17). The various formulations of *G. arborea* are detailed in Table 1.

Phytoconstituents

Phytochemical screening has revealed the presence of bioactive components in various parts of *G. arborea*, including the leaves, roots, fruits and stem barks. Numerous phytochemicals have been extracted and isolated from the entire plant, as elaborated discussed in this section (23).

Lignans

Lignans were among the first compounds isolated from *G. arborea*. Reserach indicates that the heartwood of the plant contains 14 lignans, with arboreol being the first lignan isolated, characterized by the molecular formula 2a, 6e-dipiperonyl-1e-2e-dihydroxy-3,7-deoxy-bicyclo-[3,3,0]-octane (24). The lignan compounds **[**compound **1-14]** are derived from the heartwood and their structures and molecular descriptions are detailed in Table 2.

Iridoid glycosides

In their research, Hosny and Rosazza successfully isolated a total of 15 iridoid glycosides from the leaves of *G. arborea* (31). The primary compound identified is structured as 6-O-α-L-rhamno-pyranosyl-catalpol (RPC) **[1]**, known for its remarkable stability. As esters, these iridoid glycosides exhibit significant reactivity, easily undergoing isomerization or reacting with other functional groups to form a variety of molecules. Subsequent substitutions at the "α" positions have led to the discovery of new compounds, designated as Gmelinoside A through L **[2-13]**. Additionally, 2 more compounds, 6-O-(3”-O-trans feruloyl)-α-L-RPC **[14]** and 6-O-(2”-O-acetyl3”,4”-O-di-trans-cinnamoyl)-α-L RPC **[15],** have been identified (34). The arrangement of iridoid glycosides in compounds 1 to 15, with substitutions at positions R1-R5 by various functional groups, is depicted in Fig. 3.

Another study documented the discovery of 6 previously reported iridoid glycosides derived from the leaves of *Gmelina arborea* (34). Variations in the chemical structure were observed at the 6-O-position, where the main chain included possibly (benzoyl) **[16]**, (trans-cinnamoyl) **[17]** or (cis-cinnamoyl) **[18]** groups. Similar combinations were also detected at the R1 sites [19-21] in the presence of hepta-acetate. The structure of these glycosides is illustrated in Fig. 4.

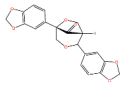
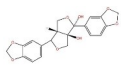
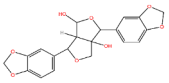
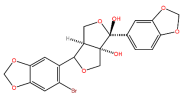
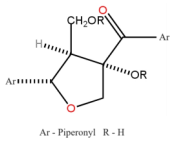
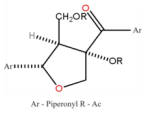
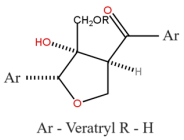
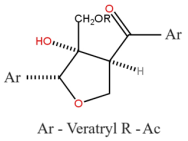
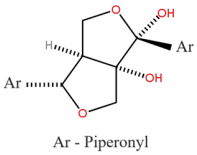
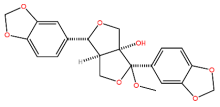
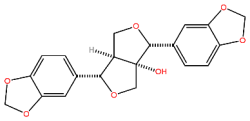
The presence of iridoid glycosides in the flowers of *G. arborea*, which exhibited notable hepatoprotective properties, has also been reported (35). Fig. 5 and 6 display the structure of these glycosides. Additionally, verbascoside (36), isolated from the hairy roots of *G. arborea* (Fig. 7), has demonstrated cytotoxic and hepatoprotective activity.

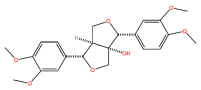
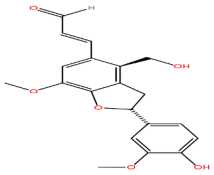
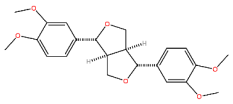
Table 1. Different Ayurvedic formulations of *G. arborea.*

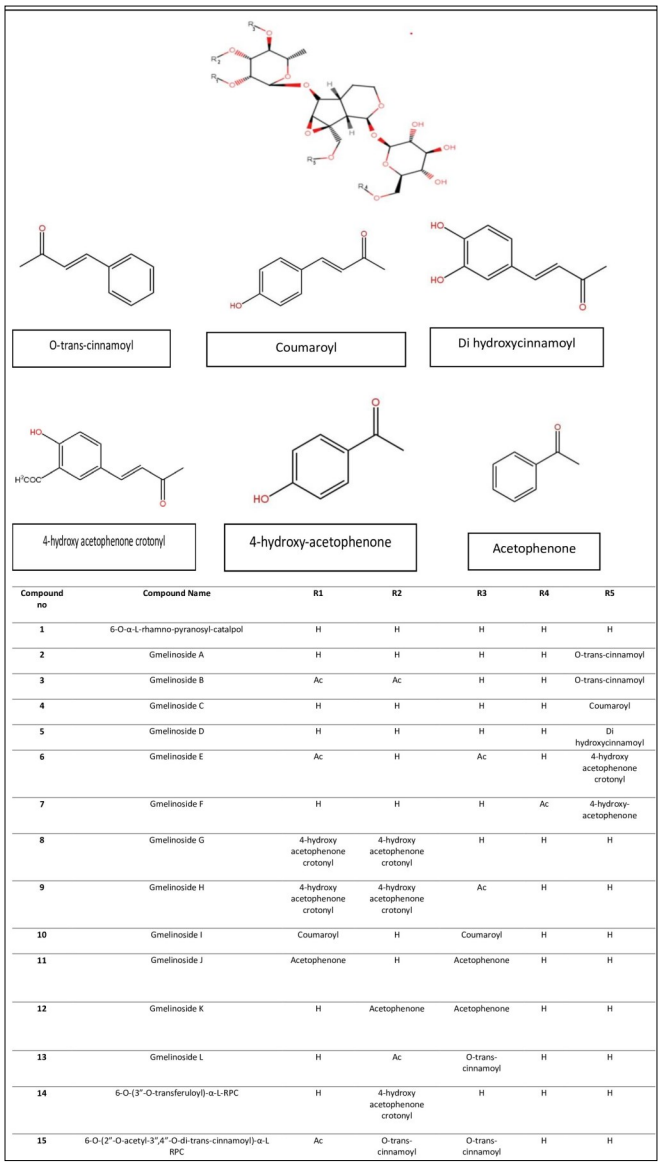
Sl. No.	Name of the formulation	% of *Gmelina* present in the formulation	Pharmacological actions	Reference
1	Dashamoolarishtam	0.52 g in 100 mL of mixture	i.Increases haemoglobin level ii.Stimulates formation of RBC Properties i.Anti-inflammatory ii.Anti-arthritic iii.Digestive-stimulant iv.Antibacterial v.Antioxidant vi.Anti-stress vii.Antidepressant	(18, 19)
2	Dashamoolaghrita and Dashamoolashatapalakaghrita	307.6 g in 768 mL ghee and 12.8 L water	Management of i. Asthma ii. Bronchitis with sputum iii. Dry and painful cough iv. Anaemia v. Spleen disorders	(19, 20)
3	Drakshadi kwacha churn	1 part in churn	Effective in treating jaundice and other related diseases Properties i.Antipyretic ii.Anti-toxic iii.Anti-emetic	(21, 22)
4	Dashamoolakvatha churna	10 % in 100 g of churn	iEffective treatment for i.Rheumatic symptoms, ii.Asthma, iii.Cough Indigestion, iv. Bodily weakness	(20, 22)
5	Arvindasava	40 g in 20 L water	Helps in gaining body weight and muscular endurance during the treatment of children's psychological issues	(19, 22)

Fig. 2. Geographical distribution of *G. arborea* (13).

Table 2. Structures of lignans isolated from *G. arborea* along with the molecular description, chemical structures, isolated part and isolation process.

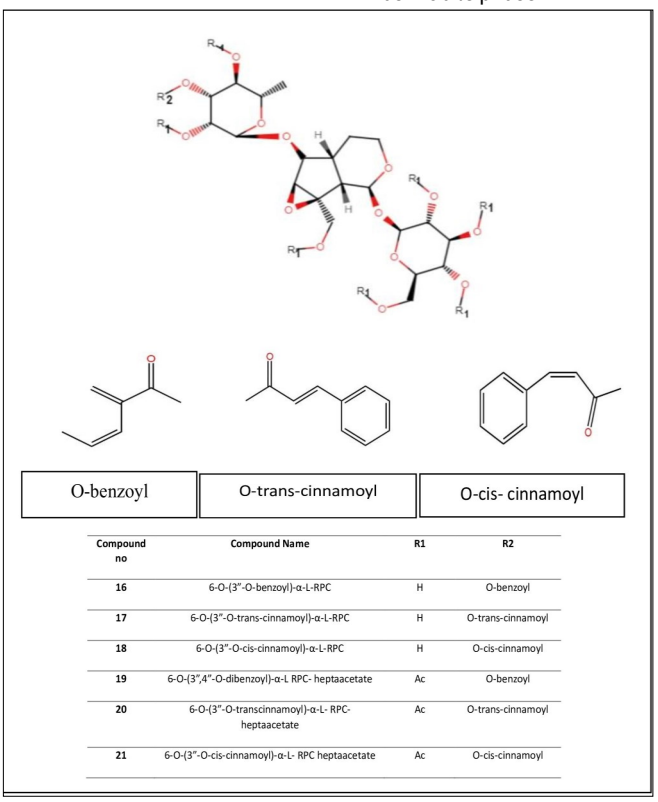
Sl. No.	Trivial name of the compound	Empirical formula	Molecular formula	Molecular weight	Chemical structure	Plant part from which isolated	Process of isolation elaboration	Reference
1.	Gmelanone	C_3H_2O	$C_{20}H_{16}O_7$	368.3 g/mol		Heartwood	TLC, silica gel as stationary phase and benzene-ethyl acetate as eluent	(25)
2.	Isoarboreol	C_2H_2O	$C_{20}H_{18}O_8$	386.4 g/mol			TLC, silica gel as stationary phase and benzene-ethyl acetate as eluent	
3.	Gummadiol	C_2H_2O	$C_{20}H_{18}O_8$	386.4 g/mol			TLC, silica gel as stationary phase and benzene-ethyl acetate as eluent	
4.	6-Bromo-isoarboreol	C_2H_2O	$C_{20}H_{17}BrO_8$	896.58 g/mol			TLC, silica gel as stationary phase and benzene-ethyl acetate as eluent	
5.	Ketolignans arborone	C_2H_2O	$C_{20}H_{18}O_8$	86.34 g/mol			TLC, silica gel as stationary phase and benzene-ethyl acetate as eluent	(27)
6.	Arborone diacetate	C_2H_2O	$C_{24}H_{22}O_{10}$	470.42 g/mol			TLC, silica gel as stationary phase and benzene-ethyl acetate as eluent	
7.	7-oxo-dihydro gmelinol	C_3H_3O	$C_{24}H_{26}O_8$	442.84 g/mol		Heartwood	TLC, silica gel as stationary phase and benzene-ethyl acetate as eluent	
8.	7-oxo-dihydrogmelinol acetate	C_3H_3O	$C_{24}H_{24}O_9$	456.44 g/mol		Heartwood	TLC, silica gel as stationary phase and benzene-ethyl acetate as eluent	
9.	Arboreol	C_2H_2O	$C_{20}H_{18}O_8$	386.4 g/mol		Heartwood	TLC, silica gel as stationary phase and benzene-ethyl acetate as eluent	(28, 29)
10.	(+)7'O-ethyl arboreol	C_2H_2O	$C_{22}H_{22}O_8$	414.4 g/mol		Heartwood	HPLC, stationary phase C18 reversed-phase column and n-hexane-$CHCl_3$-MeOH, 80:12:8, v/v/v as mobile phase	(30, 31)
11.	(+) Paulownin	C_3H_2O	$C_{20}H_{18}O_7$	370.4 g/mol		Heartwood	HPLC, stationary phase C18 reversed-phase column and n-hexane-$CHCl_3$-MeOH, 80:12:8, v/v/v as mobile phase	(31)

12.	(+) Gmelinol	C_3H_4O	$C_{22}H_{26}O_7$	402.4 g/mol		Heartwood	UPLC with mass detectors	(25, 31)
13.	(+)-balanophonin	C_2H_2O	$C_{20}H_{20}O_6$	356.4 g/mol		Heartwood	HPLC, C18 column as stationary phase and (MeOH: H_2O, 20:80, MeOH: H_2O, 30:70, MeOH: H_2O, 45:55) (v/v) as mobile phase	(24, 31)
14.	(+) Epieudesmin	C_3H_4O	$C_{22}H_{26}O_6$	386.4 g/mol		Heartwood	HPLC, C18 column as stationary phase and (MeOH: H_2O, 20:80, MeOH: H_2O, 30:70, MeOH: H_2O. 45:55) (v/v) as mobile phase	(24, 31)



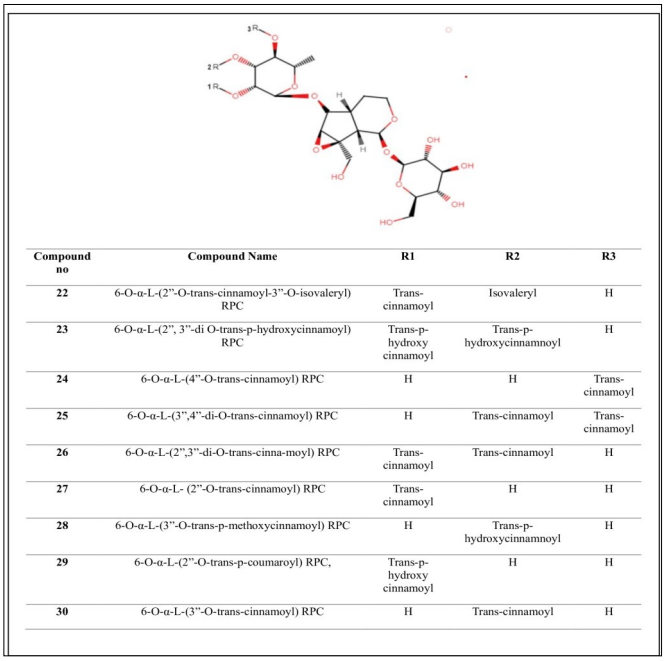
Compound no	Compound Name	R1	R2	R3	R4	R5
1	6-O-α-L-rhamno-pyranosyl-catalpol	H	H	H	H	H
2	Gmelinoside A	H	H	H	H	O-trans-cinnamoyl
3	Gmelinoside B	Ac	Ac	H	H	O-trans-cinnamoyl
4	Gmelinoside C	H	H	H	H	Coumaroyl
5	Gmelinoside D	H	H	H	H	Di hydroxycinnamoyl
6	Gmelinoside E	Ac	H	Ac	H	4-hydroxy acetophenone crotonyl
7	Gmelinoside F	H	H	H	Ac	4-hydroxy-acetophenone
8	Gmelinoside G	4-hydroxy acetophenone crotonyl	4-hydroxy acetophenone crotonyl	H	H	H
9	Gmelinoside H	4-hydroxy acetophenone crotonyl	4-hydroxy acetophenone crotonyl	Ac	H	H
10	Gmelinoside I	Coumaroyl	H	Coumaroyl	H	H
11	Gmelinoside J	Acetophenone	H	Acetophenone	H	H
12	Gmelinoside K	H	Acetophenone	Acetophenone	H	H
13	Gmelinoside L	H	Ac	O-trans-cinnamoyl	H	H
14	6-O-(3''-O-transferuloyl)-α-L-RPC	H	4-hydroxy acetophenone crotonyl	H	H	H
15	6-O-(2''-O-acetyl-3'',4''-O-di-trans-cinnamoyl)-α-L RPC	Ac	O-trans-cinnamoyl	O-trans-cinnamoyl	H	H

Fig. 3. Structures of iridoid glycosides isolated from the leaves of *G. arborea* (33).



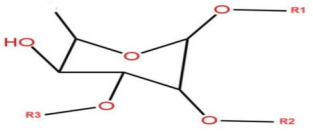
Compound no	Compound Name	R1	R2
16	6-O-(3''-O-benzoyl)-α-L-RPC	H	O-benzoyl
17	6-O-(3''-O-trans-cinnamoyl)-α-L-RPC	H	O-trans-cinnamoyl
18	6-O-(3''-O-cis-cinnamoyl)-α-L-RPC	H	O-cis-cinnamoyl
19	6-O-(3'',4''-O-dibenzoyl)-α-L RPC- heptaacetate	Ac	O-benzoyl
20	6-O-(3''-O-transcinnamoyl)-α-L- RPC-heptaacetate	Ac	O-trans-cinnamoyl
21	6-O-(3''-O-cis-cinnamoyl)-α-L- RPC heptaacetate	Ac	O-cis-cinnamoyl

Fig. 4. Structures of iridoid glycosides isolated from the leaves of *G. arborea* (34).



Compound no	Compound Name	R1	R2	R3
22	6-O-α-L-(2''-O-trans-cinnamoyl-3''-O-isovaleryl) RPC	Trans-cinnamoyl	Isovaleryl	H
23	6-O-α-L-(2'', 3''-di O-trans-p-hydroxycinnamoyl) RPC	Trans-p-hydroxy cinnamoyl	Trans-p-hydroxycinnamnoyl	H
24	6-O-α-L-(4''-O-trans-cinnamoyl) RPC	H	H	Trans-cinnamoyl
25	6-O-α-L-(3'',4''-di-O-trans-cinnamoyl) RPC	H	Trans-cinnamoyl	Trans-cinnamoyl
26	6-O-α-L-(2'',3''-di-O-trans-cinna-moyl) RPC	Trans-cinnamoyl	Trans-cinnamoyl	H
27	6-O-α-L- (2''-O-trans-cinnamoyl) RPC	Trans-cinnamoyl	H	H
28	6-O-α-L-(3''-O-trans-p-methoxycinnamoyl) RPC	H	Trans-p-hydroxycinnamnoyl	H
29	6-O-α-L-(2''-O-trans-p-coumaroyl) RPC,	Trans-p-hydroxy cinnamoyl	H	H
30	6-O-α-L-(3''-O-trans-cinnamoyl) RPC	H	Trans-cinnamoyl	H

Fig. 5. Structures of iridoid glycosides isolated from the flowers of *G. arborea* (35).



Compound no	Compound Name	R1	R2	R3
31	2-O-trans-cinnamoyl-α-L-RP	H	Trans-cinnamoyl	H
32	3-O-trans-cinnamoyl-α-L-RP	H	H	Trans-cinnamoyl
33	2-O-cis-cinnamoyl-α-L-RP	H	Cis- cinnamoyl	H
34	1-O-transcinnamoyl-α-L-RP	Trans-cinnamoyl	H	H
35	3-O-trans-p-methoxycinnamoyl-α-L-RP	H	H	Trans-p-methoxycinnamnoyl

Fig. 6. Structures of α -L-rhamnopyranoses isolated from the flowers of *G. arborea.*

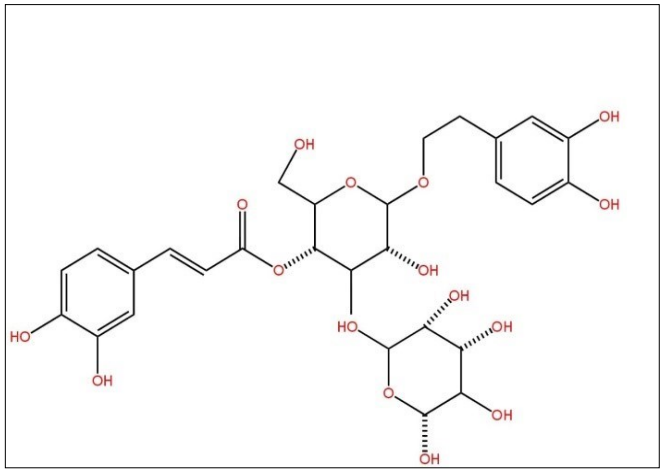


Fig. 7. Verbascoside.

Flavonoids, Flavones and Flavone Glycosides

A research study isolated 7 flavonoids from the leaves of *G. arborea*, which have been shown to possess well-established pharmacological characteristics. Notable flavonoid identified include rutin, luteolin, kaempferol and isoquercetin (37, 38). Table 3 provides detailed information on the structure and molecular description of these flavonoid compounds **[1-7]** extracted from the leaves of *G. arborea*.

It has also been reported that the roots of the plant contain flavone glycosides such as apigenin-7-rutinoside, luteolin-7-glucuronide, quercetin and apigenin. Additionally, other flavone glycosides, including apigenin-3-rutinoside, luteolin-7-glucuronide and coumarin glycosides are present in the roots of *G. arborea* (38). The HPTLC method was employed to quantify apigenin in desiccated root powder of *G. arborea* (39).

Sterols

During the investigation, sterols such as sitosterol **[1]**, stigmasterol **[2]**, β-sitosterol **[3]**, campesterol **[4]** and -α-sitosterol were isolated from the heartwood of *G. arborea* (42). The structure and chemical properties of these sterols are detailed in Table 4.

Hydrocarbons and Terpenoids

The saponifiable fraction primarily consisted of oleic and linoleic acids, with a relatively high concentration of saturated fatty acids. Additionally, fatty acid compounds derived from *G. arborea* included lauric, myristic, stearic, linolenic, oleic, linoleic, palmitic and arachidic acids (44).

Miscellaneous compounds

G. arborea has been found to contain premnazole **[1]**, an isoxazole alkaloid known for its anti-inflammatory properties (45, 46). The acetone extract from the barks was fractionated using n-hexane, diethyl ether and ethyl acetate and then further separated by chromatography, leading to the isolation of 4 distinct compounds. The diethyl ether-soluble fraction yielded several compounds, including 2,6-dimethoxy-p-benzoquinone **[2]**, tyrosol **[3]**, 3,4,5-trimethoxyphenol **[4]**, a phenylethanoid glycoside called balanophonin **[5]**, gmelinol **[6]** and phydroxyphenylethyl [5'aEuro-(3)-O-(3,4-dimethoxycinnamoyl)-β-dapiofuranosyl (1, 6)] **[7]** (47).

These compounds, derived from various parts of *G. arborea* are detailed in the Table 5, which provided their structures and chemical properties.

Pharmacology

Anti-inflammatory activity

The protective mechanisms against apoptosis and inflammation in the stem barks of *G. arborea* are being investigated using albino Wistar rats. The study evaluates the impact on the nervous system by assessing motor impairments, locomotor activity and performace in the forced swim test. Additionally, it examines various brain oxidative stress biomarkers, including lipid peroxidation, superoxide dismutase, catalase levels, glutathione levels, total calcium levels and sodium-potassium-ATPase. These findings suggest that the extract may offer potential mechanisms for preventing ischemic reperfusion injury (48).

The roots of *G. arborea* are also being used to assess the anti-inflammatory activities in Wistar rats. The anti-inflammatory efficacy of *G. arborea* was compared to that of the standard pharmaceutical medication aspirin. For acute inflammation, parameters included evaluating the reduction in inflammation and calculating the % inhibition of paw edema. For sub-acute inflammation, the % inhibition of dry granuloma weight was used. Results indicate that both low and high doses of *G. arborea* root extract showed significant anti-inflammatory effects compared to the control group. High doses of *G. arborea* extract yielded results comparable to the aspirin-treated group in reducing inflammation, inhibiting paw edema and decreasing the weight of dry granulomas in both the acute carrageenan paw edema and sub-acute inflammation cotton pellet granuloma models (49).

Stem bark extracts of *G. arborea* demonstrated strong *in vivo* anti-inflammatory action in rats. The study aimed to assess the anti-inflammatory effects of a methanol extract and its fractions using a carrageenan-induced paw edema model. Administration of a 500 mg/kg dose of methanol extract and a 50 mg/kg dose of its ethyl acetate fraction resulted in a significant reduction in paw swelling compared to the standard medication (50).

Antioxidant activity

To explore the antioxidant activity of *G. arborea,* various quantities of its extract were dissolved in a DPPH solution. The absorbance was measured at a wavelength of 517 nm using a spectrophotometer, a method commonly employed to estimate the antioxidant characteristics, specifically the plant's

Table 3. Structures of flavonoids isolated from *G. arborea* along with the molecular description, chemical structures, isolated part and isolation process.

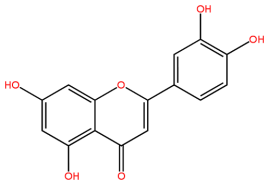
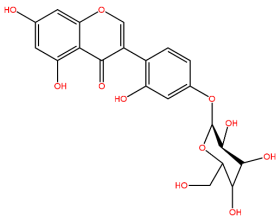
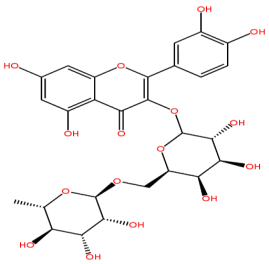
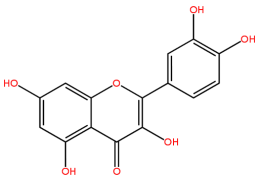
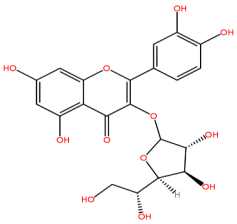
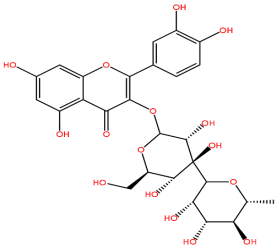
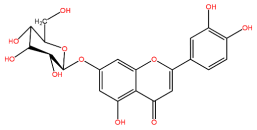
Sl. No.	Trivial name of the compound	Empirical formula	Formula weight / Molecular weight	Chemical structure	Plant part from which isolated	Process of isolation	References
1.	Luteolin	C_2HO	Molecular Formula: $C_{15}H_{10}O_6$ Molecular weight: 286.24 g/mol		Leaves	HPLC and HPTLC, TLC plates are used as the stationary phase and CHCl: MeOH is used as the mobile phase	(36, 40)
2.	Luteolin-4'-O-β - D-4 C1 – galactoside	C_2H_2O	Molecular Formula:$C_{21}H_{20}O_{11}$ Molecular weight: 448.4 g/mol		Leaves	HPTLC, TLC plates are used as the stationary phase and CHCl: MeOH is used as the mobile phase	(36)
3.	Quercetin-3-O-robinobioside	CH_2O	Molecular Formula: $C_{27}H_{30}O_{16}$ Molecular weight: 610.5 g/mol		Leaves	HPTLC and TLC plates are used as the stationary phase and CHCl: MeOH is used as the mobile phase	(36)
4.	Kaempferol	C_2H_2O	Molecular Formula: $C_{15}H_{10}O_6$ Molecularweight: 286.24 g/mol		Leaves	HPLC, Chromolith Performance RP-18e 2.0 × 100 mm column as stationary phase and distil water and acetonitrile (0.1 % formic acid) as mobile phase	(36, 41)
5.	Quercetin -3 - O - β- D - 4 C 1- glucopyranoside (Isoquercetin)	C_2H_2O	Molecular Formula: $C_{21}H_{20}O_{12}$ Molecular weight: 464.4 g/mol		Leaves	HPTLC, TLC plates as stationary phase and CHCl: MeOH as mobile phase	(36)
6.	Quercetin - 3 - O – α-1 C4 - L - rhamnopyranosyl - (1'' - 6'') -O -β - D4 C1 – glucopyranoside (rutin)	CH_2O	Molecular Formula: $C_{27}H_{30}O_{16}$ Molecular weight: 610.5 g/mol		Leaves	HPTLC, TLC plates as stationary phase and CHCl: MeOH as mobile phase	
7.	Luteolin-7-O- β -D- 4 C1 -galactoside	CHO	Molecular Formula: $C_{21}H_{20}O_{11}$ Molecular weight: 448.4 g/mol		Leaves	HPTLC, TLC plates as stationary phase and CHCl: MeOH as mobile phase	(36)

Table 4. Structures of sterols compounds isolated from *G. arborea* along with a molecular description, chemical structures, isolated part and isolation process.

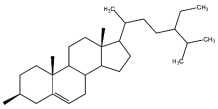
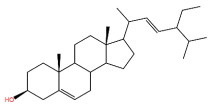
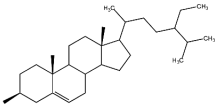
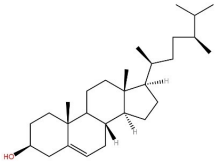
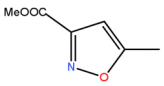
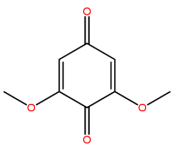
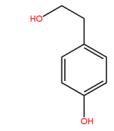
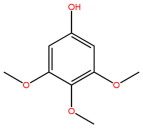
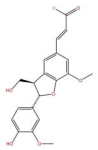
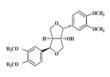
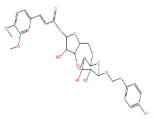
Sl. No.	Trivial name of the compound	Empirical formula	Molecular formula	Formula weight / Molecular weight	Chemical structure	Plant part from which isolated	Process of isolation	References
1.	Sitosterol		$C_{29}H_{50}O$	414.7 g/mol		Leaves	HPTLC, TLC plates as stationary phase and CHCl: MeOH as mobile phase	
2.	Stigmasterol		$C_{29}H_{48}O$	412.7 g/mol		Root	HPTLC, TLC plates as stationary phase and CHCl: MeOH as mobile phase	(43)
3.	β-sitosterol		$C_{29}H_{50}O$	414.7 g/mol		Heartwood	TLC, TLC plates as stationary phase and CHCl: MeOH as mobile phase	(42)
4.	Campesterol		$C_{28}H_{48}O$	400.7 g/mol		Heartwood	TLC, TLC plates as stationary phase and CHCl: MeOH as mobile phase	(42)

Table 5. Structures of miscellaneous compounds isolated from *G. arborea* along with molecular description, chemical structures, isolated part and process of isolation.

Sl. No.	Trivial name of the compound	Empirical formula	Formula weight / Molecular weight	Molecular weight	Chemical structure	Plant part from which isolate	Process of isolation	References
1.	Premnazole	C_2H_2NO	Molecular Formula: $C_6H_7NO_3$ Molecular weight:	145.15 g/mol		Bark	HPLC, C18 column as stationary phase and (MeOH: H_2O, 20:80, MeOH: H_2O, 30:70, MeOH: H_2O. 45:55) (v/v) as mobile phase	(46)
2.	2,6-dimethoxy-p-benzoquinone	C_2H_2O	Molecular Formula: $C_8H_8O_4$	168.15 g/mol		Bark	HPLC, C18 column as stationary phase and (MeOH: H_2O, 20:80, MeOH: H_2O, 30:70, MeOH: H_2O. 45:55) (v/v) as mobile phase	
3.	Tyrosol [2-(4-hydroxyphenyl) ethanol]	C_4H_5O	Molecular Formula: $C_8H_{10}O_2$	138.16 g/mol		Bark	HPLC, C18 column as stationary phase and (MeOH: H_2O, 20:80, MeOH: H_2O, 30:70, MeOH: H_2O. 45:55) (v/v) as mobile phase	(47)
4.	3,4,5-trimethoxyphenol	CH_3O	Molecular Formula: $C_9H_{12}O_4$	184.19 g/mol		Bark	HPLC, C18 column as stationary phase, and (MeOH: H_2O, 20:80, MeOH: H_2O, 30:70, MeOH: H_2O. 45:55) (v/v) as mobile phase	
5.	Balanophonin	C_3H_3O	Molecular Formula: $C_{20}H_{20}O_6$	356.4 g/mol		Bark	HPLC, C18 column as stationary phase and (MeOH: H_2O, 20:80, MeOH: H_2O, 30:70, MeOH: H_2O. 45:55) (v/v) as mobile phase	
6.	Gmelinol	C_3H_4O	Molecular Formula: $C_{22}H_{26}O_7$	402.4 g/mol		Bark	HPLC, C18 column as stationary phase and (MeOH: H_2O, 20:80, MeOH: H_2O, 30:70, MeOH: H_2O. 45:55) (v/v) as mobile phase	(32)
7.	Phydroxyphenylethyl [5'aEuro-(3)-O-(3,4-dimethoxycinnamoyl)-β-dapiofuranosyl (1,6)]-ß-d-glucopyranoside	Not found	Molecular formula:			Bark	HPLC, C18 column as stationary phase and (MeOH: H_2O, 20:80, MeOH: H_2O, 30:70, MeOH: H_2O. 45:55) (v/v) as mobile phase	

ability to scavenge free radicals. The results confirmed that *G. arborea* possesses significant antioxidant capabilities, likely due to hydrogen exchange, which is a probable mechanism underlying these properties (51).

Gastroprotective activity

The gastroprotective effects of *G. arborea* are being investigated in Wistar rats with ethanol-induced stomach ulcers. The methanolic extract of the stem bark is used as the test substance, with ranitidine serving as the standard. The experiment's result indicates that *G. arborea* exhibits notable gastroprotective activity. This effect is likely attributed to its antioxidant properties, which protect the gastric mucosa from oxidative damage and its anti-lipid peroxidative activity, which helps maintain the integrity of cell membranes (52).

Hepatoprotective activity

The hepatoprotective and nephroprotective properties of *G. arborea* and *G. umbellifera* are currently under investigation. The study employs gas chromatography-mass spectrometry (GC-MS) techniques to detect the phytoconstituents present in these plants. The analysis has demonstrated that these plants have a protective effect on liver enzymes and renal indicators. The findings suggests that extracts from GA and GU possess strong antioxidant, hepatoprotective and nephroprotective properties, indicating their potential effectiveness in treating liver and kidney injuries resulting from chemical exposure (53).

Anticancer activity

The anticancer activity of *G. arborea* fruit extracts were investigated by integrating into environmentally friendly nanorods. This study focused on the synthesis of MnO_2 nanoparticles (NPs) and their effectiveness in inhibiting the growth of MCF-7 breast cancer cells. The results showed that the nanorods achieved a 96 % inhibition of cancer cell growth at a dose of 400 µg/mL. Therefore, it can be inferred that combination of MnO_2 nanoparticles with *G. arborea* has potential therapeutic applications, provided that further studies on the underlying mechanisms are conducted (54).

Anti-tumour activity

The anti-inflammatory and anti-tumour properties of *G. arborea* were evaluated using a methanolic extract derived from the plant's stem bark. The anti-inflammatory effects were assessed through dextran and formalin-induced inflammatory models, while the anti-tumour efficacy was tested on solid and ascites tumour models in mice. The findings clearly demonstrate that the methanolic extract of *G. arborea* exhibits significant anti-inflammatory and anti-cancer properties. Additionally, the extract showed *in vitro* cytotoxic effect on DLA and EAC cell lines. Further research is necessary to validate the precise mechanism underlying these effects and to identify the specific chemical components responsible for the observed anti-inflammatory and anti-cancer activities (55).

Cardioprotective activity

The cardioprotective activity of *G. arborea* was evaluated in Wistar albino rats using fresh leaf extracts in ethanol. Two different doses, 250 and 500 mg/kg b.w. of the extract were administered orally. Doxorubicin (DOX) 20 mg/kg b.w was used as the standard. The doxorubicin-induced cardiotoxicity assay revealed elevated levels of marker enzyme levels, while the DOX-induced depletion of glutathione (GSH) in cardiac tissues was significantly inhibited by the extract. Additionally, the cardiac activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx) and glutathione reductase (GR) were significantly reduced. Antioxidant assays and histopathological studies further confirmed the protective effects of the ethanolic extracts against DOX-induced cardiotoxicity in rats (56).

Anticonvulsant activity

The methanolic extract of *G. arborea* stem bark has been shown to possess anticonvulsant activity. Oral administration of the extract at a dose of 500 mg/kg b.w. resulted in a reduction in convulsions induced by pentylenetetrazole and strychnine (57).

Antihyperlipidemic activity

The antihyperlipidemic efficacy of *G. arborea* was demonstrated in a study where an ethanolic extract of the leaves (150 mg/kg b.w.) was administered to Wistar rats. Glibenclamide (100 µg/kg b.w.) was used as the standard. The results showed a reduction in blood glucose levels and lipid profile (TG, TC and LDL), along with a corresponding increase in HDL levels (58).

Anthelmintic activity

The anthelmintic activity of *G. arborea* against *Pheretima posthuma* has been reported using ethanolic and petroleum ether extract of plant's root. Various concentrations of each extract were tested, with the paralysis time and death time of the worm being measured. Albendazole (60 mg/mL) was used as the reference standard. The result indicates that both the ethanol and petroleum ether extracts exhibited dose-dependent and significant anthelmintic activity. Notably, petroleum ether extract showed better activity compared to the reference drug, albendazole (59).

Antidiabetic activity

The stem bark of *G. arborea* has traditionally been used as a remedy for diabetes mellitus. The antidiabetic study was performed on stem bark extracts from *Gmelina arborea* and *Pondias pinnata* Kurz. These extracts were incorporated in nanoparticles and were evaluated for their antidiabetic activities using chitosan tripolyphosphate as the polymer. The anti-diabetic properties of the GAE-CS-TPP and SAE-CS-TPP nanoparticles were assessed concerning their effects on α-amylase, α-glucosidase, DPP-IV enzymes, glucose uptake and glucose adsorption assays. The α-glucosidase and DPP-IV enzyme inhibitory activities of GAE-CS-TPP nanoparticles were found to be more potent than those of the *Gmelina arborea* aqueous extract, with increases of 3.89 and 3.12 times respectively, yielding values of 8.09 ± 0.99 and 7.95 ± 0.68 mg/mL. In summary, both GAE-CS-TPP and SAE-CS-TPP nanoparticles demonstrated the ability to reduce high blood sugar levels in diabetes. These nanoparticles could be incorporated into pharmaceutical formulations for effective hyperglycemia treatment (60).

Additionally, the aqueous bark extract of *G. arborea* was evaluated for its anti-diabetic activity in male Wistar rats with streptozotocin-induced diabetes. The diabetic rats were

treated orally with the aqueous bark extract of *G. arborea* and the standard medication Glibenclamide for 30 days. After this period, the treatment with the plant extract resulted in a significant decrease in fasting blood glucose concentration and a significant increase of 57 % and 39 % in serum insulin and C-peptide concentrations respectively ($p < 0.05$). Histological and immuno histochemical analyses of the group treated with the plant extract showed a regenerative effect on the β-cells of the pancreas in diabetic rats. These findings indicate that the aqueous stem bark extract of *G. arborea* positively impacts diabetes mellitus by enhancing β-cell regeneration and insulin production in diabetic rats (61).

Discussion

G. arborea is a medicinal plant used in traditional systems of medicine. The plant has demonstrated a broad spectrum of therapeutic properties, including anti-inflammatory (62), antioxidant (63), anti-cancer (64), hepatoprotective (65), cardioprotective, anticonvulsant and anti-hyperlipidemic activities. These effects are attributed to the presence of various phytochemicals in the plants such as lignans, glycosides, flavonoids, terpenoids and sterols present in the plant (66).

The antidiabetic potential of *G. arborea* has been extensively studied, demonstrating hypoglycaemic effects in animal models (67). Research is also focusing on the phytochemicals responsible for these antidiabetic properties. For instance, flavonoids like quercetin activate adenosine monophosphate kinase (AMPK) in skeletal muscles, which in turn stimulates Akt and GLUT4 receptors on the cell membrane. This process facilitates glucose transport into cells via GLUT4 and its subsequent metabolism, helping to regulate glucose levels (68). Kaempferol protects beta cells and inhibits alpha-amylase (69), while flavones such as apigenin also protect beta cells (70). Additionally, luteolin inhibits both alpha -glucosidase and alpha-amylase (71).

The hepatoprotective efficacy of *Gmelina arborea* was also investigated. Verbascoside, a compound found in the flowers and leaves of the plant, demonstrates its hepatoprotective activity by promoting the growth of HepG2.2.15 cells, as determined by the MTT assay (72).

The antioxidant activity of the plant extracts has been well-documented, with the DPPH radical scavenging assay indicating potent free radical scavenging properties (53). The flavonoid compound kaempferol effectively suppresses inflammatory reactions *in vitro*. It achieves this not only by scavenging reactive oxygen species (ROS) but also by directly inhibiting Src, Syk, IRAK1 and IRAK2, which are crucial for the activation of NF-κB and AP-1. Through these mechanisms, kaempferol helps control chronic inflammation (73).

The review also highlights the anticancer and antitumor activities of *G. arborea*. The plant extracts have demonstrated promising inhibitory effects against various cancer cell lines, including MCF-7 breast cancer cells (64). The flavonoid kaempferol has been shown to exhibit antiproliferative effects in numerous *in vitro* studies. This compound disrupts the cell cycle in HT-29 and Caco-2 human colorectal cancer cells by inhibiting DNA production, which leads to decreased expression of cyclins (D1, E and A) as well as CDK2 and CDK4. Consequently, this result in reduced RB phosphorylation and a cell cycle arrest specifically in the G1 phase.

Additional studies on the same colorectal cancer cell lines have demonstrated that kaempferol reduces the activation of the PI3K/Akt and ERK-1/2 pathways by suppressing IGF-IR and ErbB3. Another study on the OVCAR-3 cancer cell line, a type of human ovarian cancer, showed that kaempferol inhibits angiogenesis through both the HIF-dependent pathway (Akt/HIF) and the HIF-independent pathway (ESRRA). Furthermore, kaempferol significantly reduces the invasion capacity of human breast cancer cells by decreasing the expression and activity of metalloproteinase-9 (73). In addition, β-sitosterol and stigmasterol exhibit antitumor properties. β-sitosterol stimulates the tumor-suppressive protein p53, promoting apoptosis and DNA repair while elevating the phosphorylation level of AMPK, which affects tumor cell proliferation and apoptosis (74). Stigmasterol inhibits the proliferation of SMMC-7721 liver cancer cells in a dose and time-dependent manner, downregulating oncogenes (FOS, MYC, RAS, PIM-1, MET, REL) and upregulating tumor-suppressor genes (NF2, MAP2K6) (75).

Advanced analytical technologies, including TLC, HPTLC and HPLC are used to extract and isolate the phytoconstituents present in *G. arborea*, significantly enhancing our understanding of its pharmacology and molecular mechanisms.

Conclusion

This article provides a concise and well-documented overview of the ethnopharmacology, phytochemistry, phytoconstituents characterization and pharmacological properties of *G. arborea*. Although research on the toxicological properties of this plant is limited, it holds significant potential for the discovery of new phytochemicals. These compounds could play a crucial role in combating various diseases, thereby providing scientific validation for its traditional uses.

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None

Authors' contributions

SB carried out the literature review and drafted and edited the manuscript. KD helped in drafting all the tables present in the article. PC contributed to drawing the pictures. DS participated in design and coordination. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interest to declare.

Ethical issues: None

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