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An overview on Phytochemistry and Pharmacological properties of *Gmelina arborea*

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ABSTRACT

Gmelina arborea an important medicinal plant is one of the most widely cultivated species of the family Verbenaceae. It is highly valued from time immemorial because of its vast medicinal properties. The present article provides all necessary information regarding its phytochemical investigations, pharmacological actions and medicinal properties like anemia, anxiety, asthma, blood impurities, diarrhea, fever headaches, antioxidants, cardioprotective, antidiabetic, immunomodulatory, antipyretic and analgesic, antimicrobial, diuretic and many other activities. This review emphasizes on the detailed phytochemical components and medicinal uses along with pharmacological properties of different parts of Gmelina arborea.

Keywords: *Gmelina arborea*, gmelinosides, isolation, Phytochemical, toxicity, Pharmacological.

INTRODUCTION

In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects (1). Nature has provided a complete storehouse of remedies to cure all ailments of mankind. About 80% of the world population depending on herbal based alternative system of medicine (Ayurveda, Unani medicine & Chinese traditional medicine). Herbal drugs have played a vital role in curing diseases throughout history of mankind. Despite the major advances in the modern medicine, the development of new drugs from natural products is still considered important. An estimated 70,000 plants (including lower plants) are used medicinally. Ayurveda utilizes about 2000 plants to cure different ailments. There are very few medicinal herbs of commercial importance, which are not cultivated in our country. Approximately 1250 Indian medicinal plants are used in formulating therapeutic preparations, according to Ayurveda and other traditional systems of medicine (2).

The evaluation of various plant products according to their traditional uses and medicinal value based on their therapeutic efficacy leads to the discovery of newer and recent drugs for treating various ailments. This fact forms the basis for the development of new drugs from various plant sources. One of such plants of medicinal value is *Gmelina arborea*, belonging to the family Verbenaceae, commonly known as 'Gamhar' . *Gmelina i*s one of the important genera of the family, consisting of about 33 species. It is a beautiful fast growing deciduous tree, which is

a vital ingredient of the "*dasamula*"(3). It is a popular commercial timber grows naturally in the warm temperate regions of Mediterranean and South Asia. The plant is commonly found in abundance on the hills and in the Andaman Islands of India.

Taxonomic classification

Botanical name : *Gmelina arborea*
Kingdom : Plantae
Division : Magnoliophyta
Class : Dicotyledons
Order : Lamiales
Family : Verbenaceae
Genus : *Gmelina*
Species : *arborea*

Botanical description

Synonyms

Kannada : Shivane mara, kulimavu, kumbuda,
Sanskrit : Gambhari
Bengali : Gamari, Gambar
Gujarathi : Shewan, Sivan
Hindi : Gamhar,
Malayalam : kumbil, kumbulu
Oriya : Gambari,
Tamil : Kumla,
Telugu : Gummadi,
Kasmiri : Shivani
Marathi : Shivan, Siwan
English : White teak

Geographical Source

Gmelina arborea Roxb belonging to the family Verbenaceae fast growing deciduous tree found throughout India and also in Pakistan, Bangladesh, China, Japan, Myanmar, Nepal, Pakistan, Sri Lanka, Thailand. It is a one of the herbs mentioned in all ancient scriptures of Ayurveda. It is known to have been used in traditional Indian medicine. It is an important timber-yielding tree that grows naturally in the tropical and subtropical regions of Southeast Asia and has also been introduced as a plantation species outside these regions (4, 5).

Morphology

It is deciduous tree 12–30 m high and 60–100 cm in diameter. Bark light gray or gray-yellow, smooth, thin, somewhat corking, becoming brown and rough; twigs stout, often slightly 4-angled. Leaves opposite, broadly ovate. Flowers are many, short-stalked, nodding, densely hairy. The drupe is fleshy, ovoid with 1 or 2 seeds (4).

Traditional Uses

The whole plant is medicinally very important. Folklore states that it promotes digestive power, improves memory and is useful alteration of fever, heart disease, nervous disorders and piles. The drug has been known to be used for snake-bites and scorpion-stings. The root of *Gmelina arborea* Linn. is one of the ingredients of "*dashmuladikwath*" and "*bhrahatpanchamool*" of ayurveda, which constitutes a number of ayurvedic preparations, used as tonics (6).
The roots are used as demulcent, lactagogue, refrigerant, stomachic, galactogogue, laxative, anthelmintic, anti-inflammatory and tonic. The roots alleviate vata and kapha, have hot potency and heavy attribute. It is used against anthrax, blood disorders, cholera, colic, convulsions, diarrhea, dropsy, epilepsy, fever, gout, headache, intoxication, rheumatism, sore throat, burning sensations, and snakebite. The root decoction is used for abdominal tumors. Fruits are sweet, alternative, aphrodisiac, astringent, diuretic and tonic. Fruits are used for heart diseases, leprosy, vomiting and burning sensations. Flowers are sweet, cooling, bitter, acrid and astringent. They are useful in leprosy and blood diseases. Paste of leaves used in fever, headache and in burning sensations. Root and Bark are useful in

hallucination, piles, abdominal pains, burning sensations, fevers, 'tridosha' and urinary discharge. Leaf paste is applied to relieve headache and juice is used as a wash for ulcers (7,8).

Phytochemical investigations:

- Rao et al (1967)., isolated from the air-dried leaves were extracted successively with petroleum ether, $CHCl_3$ and EtOH. The alcoholic extract was concentrated to remove the alcohol and the remaining aqueous liquid was successively extracted with petroleum ether, Et_2O and CHCl3. The Et_2O extract yielded a crystal substance which after recrystallization from alcohol gave tetrahydroxyflavone with the agreement of spectral analysis of standard and also another compound isolated, confirmed that the unknown compound was luteolin (9).

- Rao et al (1970)., were isolated apigenin, luteolin, quercetin, hentriacontanol and *β*-sitosterol from *Gmelina arborea*. The presence of glycosides of flavones were also indicated (10).

- Ventaka (1970)., reported the chemical examination of the polar extracts of the leaves of *Gmelina arborea* was carried out and isolated the four crystalline constituents such as apigenin, luteolin, quercetin, hentriacontanol and *β*-sitosterol. They also identified the presence of flavones glycosides (11).

- Govindachari et al (1971)., reported from the roots of L. grandis and the heart-wood of G. arborea, a new long chain ester was isolated. This was shown to be the hitherto unknown cluytyl ferulate by spectral studies and by synthesis. This is the first report of the occurrence of cluytyl ferulate as a natural product (12).

- Anjaneyulu et al (1975)., Isolation and elucidation the structure of Gummadiol, a new lignan from the heartwood of *Gmelina arborea* was reported by Anjaneyulu et al. Gummadiol is structural isomers of arboreols, it has two hydroxyl groups and gave a diacetate. The hydroxyl group of gummadiol was hemi-acetal, it was observed by when it was treated with methanol containing a few drops of hydrochloric acid. The structure of isolated compound was characterized on the basis of ^{1}H NMR and ^{13}C NMR (13).

- Anjaneyulu et al (1975)., isolated the six new lignans from the ethyl acetate soluble portion of the methanol extract of heartwood of *Gmelina arborea*. They were identified to be 6“ - bromo - isoarboreol, 4 - hydroxysesamin, 4,8 - dihydroxysesamin, 1,4 – dihydroxysesamin (gummadiol), 2 - piperonyl - 3 - hydroxymethyl-4- (α-hydroxy-3,4-methylenedioxybenzyl) - 4 - hydroxytetrahydrofuran, and the 4 - O - glucoside of 4 - epigummadiol. The structure of these compounds and their derivatives were established by ^{1}H and ^{13}C NMR and mass spectra (14).

- Anjaneyulu ASR, et al (1975)., reported the structures of 2 new 2,3,4-trisubstituted THF lignans arborone (I) and 7-oxodihydrogmelinol (II), isolated from the heartwood of *Gmelina arborea*. In addition, 2 known furofuran lignans, paulownin acetate and epieudesmin, were isolated along with Me trans-p-methoxycinnamate and trans-p-hydroxycinnamic acid. The conversion of I into arboreol were also reported (15).

- Nair et al (1975)., reported the Quercetagetin and other glycosides of kaempferol, apigenin, and luteolin were isolated from *G. arborea* and *G. asiatica* (16).

- Anjaneyulu et al (1976)., isolated the five new lignans were isolated from the heartwood of *Gmelina arborea* Linn. The parent compound arboreol was identified to be 2a, 6e-dipiperonyl-1e, 2e-dihydroxy-3, 7-dioxabicyclo-[3, 3, 0] octanes. It was accompanied by its 2-O-methyl ether, the 2-O-ethyl ether and its 2-epimer, isoarboreol. The fifth substance, gmelanone, was the first example of a lignan derived from 3, 6-dioxabicyclo-[3, 2, 1]-octane.The structures of arboreol (I, R1 = OH), 2-O-methylarboreol (I, R1 = OMe), 2-O-ethylarboreol (I, R1 = OEt), isoarboreol (II) and gmelanone III were detected from chemical and spectral data. Gmelinol (IV), paulownin (V), and *β*-sitosterol were also isolated from *Gmelina arborea* (17).

- Krishna et al (1977)., Monobromo derivative of isoarboreol, is a bromine containing lignan were isolated from *Gmelina arborea*. The structure of isolated compound was characterized on the basis of NMR and other spectral studies (18).

• Joshi KC et al (1980)., isolated the hentriacontanol-1, a sesquiterpene, ceryl alcohol, β-sitosterol and octacosanol from the light petroleum extract of the roots of *Gmelina arborea*, and in addition from an aqueous extract gave gmelinol (19).

• Ukkonen (1982) ., reported the nonsaponifiable fraction from the *G. arborea* wood contained C18-C30 wax alcohols with C_{28} and C_{30} predominating (33.1 and 14.7%, resp.), sterols (β-sitosterol, stigmasterol, stigmastanol, campesterol, and α2-sitosterol), and triterpene alcs. (betulinol, a $C_{30}H_{50}O$ and others). Among the wax alcohols were small amounts of odd-numbered C chain representatives (C27 and C29). The saponifiables were fatty acids, with oleic and linoleic dominating and with a relative high amount of saturated fatty acids (20).

• Sosanwo et al (1984)., isolated the four alkyl and one carbonyl resorcinol from benzene extracts of *Gmelina arborea* by column chromatography and their structures were elucidated by chemical analysis and IR, NMR, and mass spectroscopy (21).

• Satyanarayana et al (1985)., reported the isolation Apiose-containing coumarin glycoside i.e Umbelliferone 7-apiosylglucoside from the methanolic extract of root of *Gmelina arborea*(22).

• Joseph et al (1989)., were reported the gross heat of combustion of holocellulose, α-cellulose, lignin, from *Gmelina aborea* was 19,715; 19,704; 25,383; and 25,137 kJ/kg, resp. The bark and leaves which contained relatively high proportions of lignin and extractables had the highest heat of combustion on dry, ash-free basis (23).

• Adeyeye et al (1991)., isolated the fatty acid compound (lauric, myristic, palmitic, stearic, oleic, linoleic, linolenic, and arachidic acids from the *G. arborea* and *T. grandis* seed oils by chromatography of their Methyl esters. Both seed oils showed low oil content with a high degree of unsaturation with linoleic acid >53% (24).

• Barik BR et al (1992)., isolated the Premnazole, from the leaves of the Premna integrifolia and *Gmelina arborea*. It had an anti-inflammatory activity comparable to that of phenylbutazone in reducing cotton pellet-induced granuloma formation in rats. Tests indicated that Premnazole probably acts by regulating the activity of ACTH (25)

• Mohammed and John (1998)., reported the isolation of 12 new acylated iridoid glycoside named Gmelinosides A-L (2-13) from a water soluble portion of the methanolic extract of leaves of *Gmelina arborea*. These compounds were structurally characterized using a variety of spectral methods (UV, IR, ^{1}H, ^{13}C NMR) (26).

• Olatunji, Gabriel (1999)., A furanoresorcinol was isolated from the benzene extract of the heartwood of *Gmelina arborea*. The identity of furanoresorcinol was confirmed by means of its spectral data (27).

• Shrutika et al (2005)., reported the induced hairy roots in *Gmelina arborea* for the increased production of verbascoside. The dried extract of the roots and the medium in which hairy root culture was developed, root culture dissolved in methanol and estimated for verbascoside by HPLC (28).

• Vidya et al (2007)., reported a sensitive HPTLC method for quantification of apigenin in dried root powder from *Gmelina arborea* Linn. A dried root of *G.alborea* was successively extracted with chloroform (purity 99.00%), acetone (purity 99.00%), formic acid (purity 85.00%) and methanol (purity 99.00%). A stock solution of apigenin was prepared by mixing 10mg apigenin standard with methanol. Chromatographic separation was performed on silica gel plates with chloroform-acetone-formic acid, 7.6:1.6:0.8 (*v* / *v*), as mobile phase. The plates were scanned densitometrically at 340 nm.(29, 31)

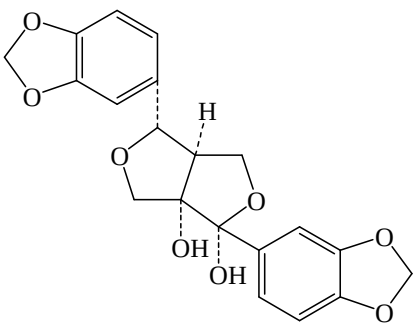
• Tiwari et al (2008)., isolated the three new iridoid glycosides in their acetate form from n-butanol soluble portion of the methanolic extract of aerial parts of *Gmelina arborea*. The structures of these compounds were established on the basis of spectroscopic studies. Apart from these, a known iridoid 6-*O*-(3″, 4″-*O*-dibenzoyl)-α-L-rhamnopyranosylcatalpol was isolated and identified (30).

• Akhilesh KY et al (2008)., a sensitive, selective and robust qualitative and quantitative densitometric HPTLC method was developed and validated for the determination of iridoid glycoside in the aerial part of *Gmelina arborea*

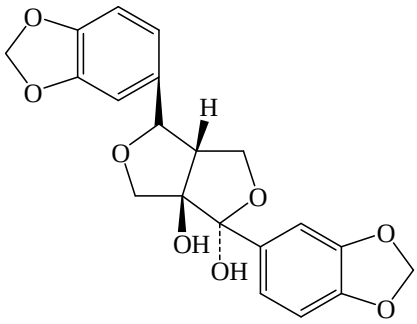
by Akhilesh et al**.** Iridoid glycoside 6-*O*-(2″, 3″-dibenzoyl)-α-L-rhamnopyranosylcatalpol (IG) was used as a chemical marker for the standardization of *G. arborea* plant extracts. The separation was performed on aluminum Kieselgel 60F_{254} TLC plates using chloroform–methanol as mobile phase. The quantitation of IG was carried out using the densitometric reflection/absorption mode at 240 and 430 nm after post-chromatographic derivatization with vanillin–sulphuric acid reagent. Specificity of quantitation was confirmed using retention factor (R_f), uv–vis spectral correlation factor and ESI-MS spectra of a marker compound (IG) in sample track (31).

• Vidya D et al (2011)., a simple, fast and precise reverse phase high performance liquid chromatography method is developed for the quantitative determination of apigenin, a flavonoid from the dried root powder of *Gmelina arborea*. Apigenin was extracted from root powder of *Gmelina arborea* by using warm methanol. The quantization of apigenin was carried out on an Inertsil ODS-3V-C18, (25 cm × 4.6 mm internal diameter 5µm) column, using acetonitrile and distilled water in vol. ratio of (45:55), as the mobile phase. The detection of the compound was carried out at 340 nm, using UV-Visible detector, which is reported to be the wavelength of max. absorption of the standard apigenin (32).

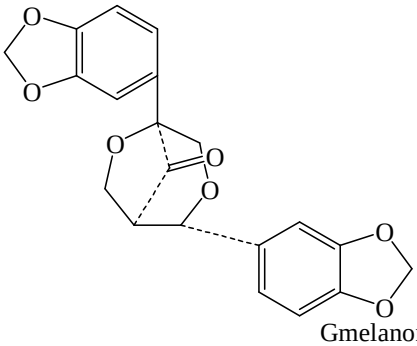
• Niyati et al (2012)., reported a high-performance thin-layer chromatography (HPTLC) method for the quantitative analysis of roots using *β*-sitosterol as a chemical Marker. Validated HPTLC method developed can be used as a tool for standardization of roots in different formulations using *β*-sitosterol as a marker (33).



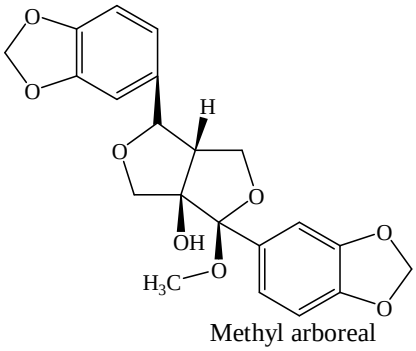
Arboreol



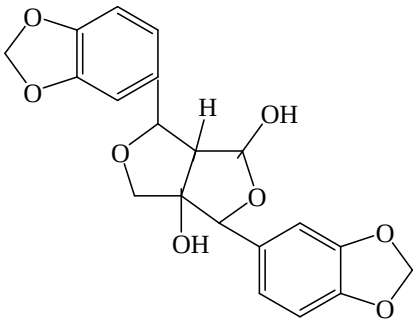
Isoarboreol



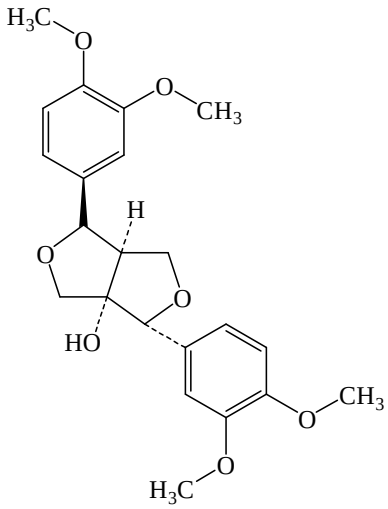
Gmelanone



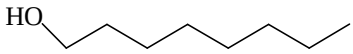
Methyl arboreal



Gummadiol



Gmelinol



N-Octanol

Pharmacological investigations

Anthelmintic activity

- Ambujakshi et al (2009)., investigated the anthelmintic activity of alcoholic and aqueous leaves extracts of *Gmelina arborea* Roxb exhibited anthelmintic activity in dose dependent manner giving shortest time of paralysis and death compared to piperazine citrate especially with 100mg/ml concentration for *Pheretima posthuma* and *Ascardia galii* worms by increasing chloride ion conduction of worm muscle membrane produces hyperpolarization and reduces excitability that leads to muscle to relaxation and flaccid paralysis (34).

Immunomodulatory activity

- Shukla et al (2010) ., investigated the immunomodulatory effects of methanolic extract of the roots of *Gmelina arborea* Linn. (MEGA) and its ethyl acetate fraction (EAFME) in albino rats. The modulating effect was evaluated on humoral and cell-mediated immune response using animal models like cyclophosphamide-induced myelosuppression, delayed-type hypersensitivity (DTH) response and humoral antibody (HA) titre. These extract were found induce a significant increase in HA titre, DTH response and levels of total white blood cell count (35).

Antimicrobial activity

- Mahmood et al (2010)., investigated the antimicrobial activity of leaves and bark extract of *G. arborea* were investigated againt pathogenic bacterial strains like *Escherichia coli*, *Klebsiella pneumonieae*, *Proteus mirabilis*, *Shigella dysenteriea* and *Salmonella typhi*. The dried powdered plant samples were soaked separately in 100 ml of distilled water, ethanol, acetone, chloroform and hexane respectively. The *in vitro* antimicrobial activity was performed by agar diffusion method using standard antibiotic- tetracycline. The crude extracts of the leaf and stem bark of the plant inhibited the growth of bacteria used. Phytochemical screening of the *Gmelina arborea* revealed the presence of carbohydrates, alkaloids, saponins, tannins, anthraquinones and

cardiac glycosides. The presence of these bioactive compounds in plants was linked to its biological activity (36).

In vivo rodent micronucleus assay

- Sahu Rohit et al (2010)., investigate the effect of genotoxic potential of G. arborea in bone marrow cells obtained from Swiss albino mice using micronuclei formation as the toxicological endpoints. Aqueous extract of G. arborea (AEGA) was tested at the dose of 286 & 667 mg/kg body weight. Cyclophosphamide (CPZ) 25 mg/kg b. w. was used as positive control in micronucleus test. The AEGA significantly increased the % micronucleated polychrometics at doses of 286mg/kg and 667mg/kg, after 24, 48 72h time interval and also decreased the PCE/NCE ratio after 24, 48 and 72 h as compared to the solvent control group. In this study, author investigated the effect of G. arborea on mammalian bone marrow cells using micronuclei formation to assess the genotoxicity of the herb (37).

Diuretic activity

- Sravani et al (2011) ., reported the diuretic activity of *G.arborea* methanolic extract on albino rats. The test extracts were given in the dose of 250 mg/kg and 500 mg/kg body weight. Sodium (Na+), Potassium (K+) and chloride (Cl+) output in urine markedly increased as compared to normal saline. The *G.arborea* extract exerted its diuretic activity due to synergistic action of the [HCO3 −/Cl−], [HCO3 +/H+] exchangers and the [N+/H+] antiporter by inhibiting tubular reabsorption of water and accompanying anions to cause diuresis. There was an increase in the ratio of concentration of excreted sodium and potassium ions after methanolic extract of *Gmelina arborea* treatment. This indicates that the extract increases sodium excretion to larger extent than potassium which leads to hyperkalaemic side effect (38).

Cardioprotective

- Vijay e al (2011)., reported the ethanolic extract of *G.arborea* shown potential protective effect against doxorubicin (DOX) induced cardiac toxicity by increasing cardiac markers activities in plasma. The significant increases the activities of cardiac markers such as SGOT, SGPT and ALP in plasma of DOX (20 mg/kg) treated rats might be due to enhanced susceptibility of myocardial cell membrane to the isoproterenol mediated peroxidation damage resulting in increased release of these diagnostic marker enzyme into the systemic circulation (39).

Anti diabetic activity

- Pattanayak et al (2011)., investigated the antidiabetic activity of ethanolic extract of *G.arborea* bark at dose of 420 mg/kg and chlorpropamide at dose of 200 mg/kg ($P< 0.05$) was found to reduce the increase of blood sugar in streptozotacin (50 mg/kg) induced diabetes due to the increased blood GSH levels reinforcing the role of GSH as free radical scavenger and in the repair of free radical caused biological damage (40).

Antipyretic and analgesic activity

- Pravat et al (2011) ., the effect of bark extract of *G.arborea* was evaluated and the ethanolic and aqueous extract found to reduce the hyperthermia at a dose of 420 mg/kg body weight 1hrs after administration and its effect is comparable to that of the standard antipyretic drug paracetamol at a dose of 50 mg/kg body weight. Whereas chloroform and benzene extract reduced the temperature 3h after their administration but have mild effects. However the analgesic activity of test compounds was found to be more significant on acetic acid induced test than tail flick test as compared to standard diclofenac sodium at a dose of 25 mg/kg and thus it appears that the test compounds inhibit predominantly the peripheral pain mechanism (41).

Ameliorating effect

- Anthony et al (2012)., investigated the phytochemical screening of stem bark and leaves and the effect of aqueous and ethanolic extracts of *Gmelina arborea* stem bark on hepatic and renal insufficiency in rats were investigated. Phytochemical screening results show the presence of alkaloid, flavonoid, tannin, saponin, cyanogenic glycoside, phytate, and carbohydrate. Saponin and carbohydrate were shown to be much higher in concentration than other phytochemicals. All the *Gmelina arborea* extracts and extract mixture administered to both paracetamol and cisplatin treated animals, significantly lowers both the activities of the SGOT and SGPT, and the levels of serum creatinine and urea (42).

Antifungal activity

- Kawamura et al (2004) ., reported the effect of antifungal activity of constituents from the heartwood of the *Gmelina arborea* against Trametes versicolor and Fomitopsis palustris was investigated. A sensitive bioassay system for antifungal activity against basidiomycetes was developed which uses a medium in which homogenized hyphae were dispersed. Ethyl acetate-solubles from the heartwood showed the highest activity against both fungi, although the activity against F. palustris was quite weak. Spots exhibiting antifungal activity against T. versicolor were specified by bioautography of Ethyl acetate-solubles and 5 constituents were isolated and identified as (+)-7'-O-Et arboreol, (+)-paulownin, (+)-gmelinol, (+)-epieudesmin, and (-)-*β*-sitosterol. The 4 lignans showed antifungal activity, whereas *β*-sitosterol did not. From the comparison of antifungal activity, it was concluded that the piperonyl nucleus contributed to the activity of lignans. Of the four lignans isolated, gmelinol appeared to be an important antifungal constituent, since it was rich in the heartwood of *G. arborea.* Furthermore, the synergism by coexistence of these 5 compounds were confirmed (43).
- Kawamura F, Ohara S (2005)., reported the iridoid glycosides were isolated from the heartwood of *Gmelina arborea* showed antifungal activity against *Trametes versicolor* of these compound was assayed by using a medium in which homogenized hyphae were dispersed (44).

Antioxidant activity

- Patil et al (2009) ., investigated the antioxidant effect and free radical scavenging activity of defatted and fractionated methanol extract of stem bark of *Gmelina arborea* (MEGA) was evaluated by using various in vitro assays. Ascorbic acid was used as a reference antioxidant compound. The reduced power of assay with increase in absorbance was observed in a dose dependent manner. Measurement of total phenolic content using Folin-Ciocalteu phenol reagent showed that 1 mg of the extract contained 85.95 µg/mL total phenolics equivalent to gallic acid. The results obtained in the present study indicate that MEGA can be a potential source of natural antioxidants and the activity may due to the presence of phenolics (45).

- Wansi et al (2012)., investigated the effects *in vivo* Antioxidant and Vasodilating Activities from the *Gmelina arborea* leaves of hexane extract on markers of oxidative stress and its vasorelaxant effects on isolated rat aorta, in order to postulate the possible mechanisms involved in the antihypertensive properties of the plant. To evaluate the antioxidant effects of the extract, rats were randomly divided into four groups of five rats each. With the exception to the group receiving Tween (2.5%), the other groups were treated either with NaCl (900mg/kg/day) alone, NaCl (900mg/kg/day) combined with vitamin C (5mg/kg/day) or *Gmelina arborea* extract (150mg/kg/day). The in vitro vasodilating effects of the extract (0.5-1.5mg/ml) were evaluated using intact and denuded rat thoracic aortic rings or aorta pre-incubated in L-NAME (2µM), indomethacin (2µM) or glibenclamide (2µM) and contracted with phenylephrine (1µM). The in vivo effects of *G. arborea* hexane extract prevented both left ventricular and vascular hypertrophy, it also modulated lipid metabolism. Moreover, the extract prevented lipid peroxidation, increased superoxide dismutase and catalase activity as well as NO level. On isolated rat aortic rings, the extract induced concentration-dependent vasorelaxant effects. Extract-induced vasodilation was reduced by mechanical denudation of the endothelium as well as pre-treatment with L-NAME, indomethacin or glibenclamide. These results indicate that *Gmelina arborea* hexane extract possesses bioactive compounds with antioxidant and vasorelaxant properties (46).

Anti-hyperlipidemic activity

- David P et al (2012)., investigated the antihyperlipidemic effects of ethanolic leaf extract of *Gmelina arborea* (Verbenaceae) in male wistar albino rats was evaluated. The ethanolic extract of *G. arborea* at a dose of 150 mg/kg of body weight and standard drug glibenclamide at the dose of 100µg/kg given to the animal models. The extract exhibited significant hypoglycemic activity in animal models when compared with a standard antidiabetic drug Glibenclamide. The hypoglycemia produced by the extract may be due to increased uptake of glucose at tissue level and or increase in pancreatic β-cell function or due to inhibition of intestinal glucose absorption of glucose. The lipid profile such as TC, TG and LDL levels were significantly increased in diabetic control animals where as HDL levels were decreased when compared to the control rats. The ethanolic extract of *G. arborea* produced significant antihyperglycemic activity in STZ induced diabetic rat which is comparable to that the Glibenclamide (47).

Toxicity studies:

- Kulkarni et al 2013., et al studied the toxicity of alcoholic extract and its analgesic activity in female Swiss albino mice. Alcoholic extract and its fractions did not produce mortality, changes in behavior or any other physiological activities in mice, at selected dose. The alcohol extract at 250 and 500 mg/kg showed a significant decrease in writhes -13.4 ± 0.16 and 12.2 ± 0.22, respectively when compared with control (19.2 ± 0.58). Their observations suggested that alcoholic extract and its fractions are safe after oral administration and also have significant analgesic activity(48).
  The author also reported the administration of ME from the G. arborea bark at 300-5000 mg/kg did not produce mortality or significant changes in the clinical signs and it was found to be safe in acute and repeated dose toxicity studies when tested in mice and rats(49).
- Jabbar Shaila et al (2004)., studied the bioactivity of the individual ingredients of Dashamularishta. The Gmelina arborea exhibited severe toxicity to the brine shrimp (BST) nauplii, wheat rootlet growth (WRG), but it is not toxic to the lettuce seed germination (LSG) bioassay (50).

CONCLUSION

Gmelina arborea is an important medicinal plant indicated in the ancient literature of traditional Indian medicine. *Gmelina arborea*, having potential medicinal values and most widely cultivated species of the family Verbenaceae. Various parts of the plant have been used for human medication. Some of the recent phytochemical and pharmacological investigation of the herb documenting the same trend. The exciting findings of the previous studies must provoke the researchers for determining other pharmacological profile. This review summarizes some important pharmacological studies on *Gmelina arborea* and more emphasizes on the phytochemical investigations and isolated principles from them, which can be investigated further to achieve lead molecules in the search of novel herbal drugs. Toxicity studies of extract indicate that the safe in acute and repeated dose toxicity studies.

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