Pharmacognostic and Phytopharmacological Overview on Bombax ceiba

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ABSTRACT
Plants have been an important source of medicines since the beginning of cultivation. There is a growing demand for plant-based medicines, health products, pharmaceuticals, food supplements, cosmetics etc. Bombax ceiba Linn. (Bombacaceae) is a tall tree buttressed at the base that is widely distributed throughout India, Ceylon and Malaya, upto 1500 m of altitude. Many parts of the plant (root, stem bark, gum, leaf, prickles, flower, fruit, seed and heartwood) are used by various tribal communities and forest dwellers for the treatment of a variety of ailments. The plant literature survey shows the plant possesses astringent, cooling, stimulant, diuretic, aphrodisiac, demulcent and tonic effects and also helps in dysentery. It also possesses important pharmacological activity such as aphrodisiac, anti-inflammatory and hepatoprotective activity in addition to anticancer and anti-HIV activity, anti-Helicobacter pylori, antiangiogenic, analgesic and antioxidant activity and hypotensive, hypoglycemic and antimicrobial activity. It is reported to contain important phytoconstituents such as naphthol, naphthoquinones, polysaccharides, anthocyanins, shamin and lupeol.

Key words: Bombax ceiba, Ethnobotanical uses, Phytochemistry, Pharmacological activities.

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INTRODUCTION
Natural products are an important source of new compounds leading to drugs in all major disease areas. They represent a pool of structures that have been optimized by evolution to interact with proteins and other molecules. The starting materials for about one-half of the medicines we use today come from natural sources. The future of higher plants as sources of medicinal agents for use in investigation, prevention and treatment of diseases is also very promising.

Natural products have provided some of the important lifesaving drugs used in the armamentarium of modern medicine. However, among the estimated 250,000–400,000 plant species, only 6% have been studied for biological activity and 15% have been investigated phytochemically. This illustrates the need for planned activity guided phyto-pharmacological evaluation of herbal drugs.

This article aims to provide an overview of the chemical constituents present in various parts of Bombax ceiba and their ethnobotanical and pharmacological actions. It has been claimed in Ayurveda, that Bombax ceiba possesses proven medicinal properties and is the ingredient of many formulations.

HABITAT AND DISTRIBUTION
Bombax ceiba Linnaeus belongs to the family Bombacaceae which contains about 26 genera and nearly 140 pantropical species. It is commonly known as Semal, Simbal, Simul, Indian kapok, Katsavar, Indian bombax or Red Silk cotton tree. It is widely found in temperate Asia, Tropical Asia, Africa and Australia. In India, it can be found at altitudes up to 1500 m.

In peninsular India, the tree is very common in the dry as well as moist deciduous forests and near rivers. The tree is a strong light-demander and fast growing. It grows best on deep sandy loams or other well-drained soils, particularly in valleys, in regions receiving 50 to 460 cm annual rainfall well distributed throughout the year.

MORPHOLOGY
Semal is a lofty, deciduous tree up to 40 m tall with horizontally spreading branches and young stems covered with hard prickles. (Figure 1)

Bark - grey brown or silver grey colored with hard sharp conicles prickles

Leaves - are large, spreading, glabrous, leaflets lanceolate, 3-7 and margin entire

Flowers - are red numerous, appearing when the tree is bare of leaves, stamens many arranged in five bundles of 9-12 each and an inner bundle of 15.

Fruits - The fruits are brown capsule-like up to 15 mm long, filled with numerous black seeds.

Seeds - are smooth, black or grey embedded in long white wool, which are irregular obovoid in shape, smooth and oily with dense silky hair.

Gum - Light brown to opaque or dark brown called as semul gum.

TAXONOMICAL CLASSIFICATION
Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Malvales
Family: Bombacaceae
Genus: Bombax
Species: ceiba
Binomial name: Bombax ceiba L.; Bombax malabaricum D.C.; Salmalia malabarica (D.C.) Schott and Endl.

TRADITIONAL USES
Ayurveda, the traditional Indian medicine, describes the excellence of plants by combining both the Pharmacognosy (properties) and Pharmacology (action). These traditional parameters reflect not only the quality but also efficacy of the plants. Some of its medicinal uses and formulations as mentioned in Ayurveda are being described here.
Charak samhita
Semal has been described among top ten drugs used as styptic, bowel regulator and tissue regenerator in Ayurveda. Pedicel/petiole of the plant or gum is used as enema in ulcerative colitis and dysentery.⁶,⁷

Sushruta samhita
Stem bark is said to be useful in hemorrhagic disorders, wound healing, removing pimples/acne and have a cooling effect in burning sensations. It is also used in hyperpigmentation, wounds, burns and stomatitis as a topical therapeutic agent.⁸

Ashtang hridya
Mocharasa of the plant is widely used in various Ayurvedic formulations for tissue regeneration, wound healing and antidysenteric effects.⁹

Bhava prakash
Powder of root (Semal-musli) with sugar is considered to be a good aphrodisiac. Root is also considered to possess antiaging, anabolic and nutritive properties. Paste of leaves is applied in arthritis and on glandular swellings. Flowers of B. ceiba with seeds of Papaver somniferum, sugar and milk are prescribed to cure piles. Gum (Mocharasa) of the plant is cold in potency, absorbent, demulcent, aphrodisiac and astringent in taste and cures dysentery, diarrhoea, retained undigested food, burning sensation, various menstrual diseases and diseases of Kapha, Pitta and Rakta.¹⁰

Dravyaguna vijnana
A traditional formulation “Shalmali ghrita” prepared with flowers of B. ceiba is used as Pramehagna and to cure polyurea, spermatorrhea, leucorrhea and menorrhagia.¹¹

INDIAN MATERIAL MEDICA
In painful micturition, a preparation called Trinetra rasa is given with a decoction in milk made of juice of Cynodon dactylon, liquorice root, gum of Bombex malabaricum and Tribulus terrestris.¹²

PHYTOCHEMICAL STUDIES
B. ceiba flowers have been shown to contain the β-D’ glucoside of β-sitosterol, free β-sitosterol, hentriacontane, hentriacontanol, traces of an essential oil, kaempferol and quercetin.¹³ (Figure 2)

Shamimin, a newly discovered flavonol C-glycoside has been isolated as a pale yellow powder from the ethanolic extract of fresh, undried leaves of B. ceiba. Its structure has been elucidated as 2-(2, 4, 5-trihydroxyphenyl)-3, 5, 7-trihydroxy-6-C-glucopyranosyl-9H-xanthen-9-One (II), 4-C-β-D Glucopyronosyl-1, 6, 8-trihydroxy-3, 7-di-O-(4”-hydroxybenzoyl)-9H-xanthen-9-One (I), 2-C-β-D Glucopyranosyl-1, 3, 6, 8-tetrahydroxy-3-O-(4”-hydroxyphenyl)-3, 5, 7-trihydroxy-6-C-glucopyranosyloxy-4H-1-benzothaquinone.¹⁴

Three new compounds [4-C-β-D Glucopyronosyl(1-4)-α-L-rhamnopyranoside, n-hexacosanol and palmitic acid isolated from seeds, lactone isolated from root bark, polysaccharide isolated from flowers-had a continuous backbone of 4(1-4)-β-linked D-galactopyranosyl and 2 (1-3)-β-linked L-arabinopyranose units with β-linked D- galactose and α-linked L-rhamnose and L-arabinose units as end groups.¹⁵

As a sesquiterpene lactone isolated from the roots of a plant species identified as Salmalia malbaricum (syn Bombax ceiba) was previously identified as hemigossypol and palmitic acid isolated from seeds, lactone isolated from root bark, polysaccharide isolated from flowers-had a continuous backbone of 4(1-4)-β-linked D-galactopyranosyl and 2 (1-3)-β-linked L-arabinopyranose units with β-linked D- galactose and α-linked L-rhamnose and L-arabinose units as end groups.²²

Isolation and characterization resulted in the identification of two compounds from the extracts of stem barks of B. ceiba. These were lup-20 (29) en-3b-ol, named BC-1 and 2-hexyl-7, 8-dimethyl-1, 4-naphthaquinone, named ceibanaphthaquinone.¹⁹

Phytochemical investigation was carried out on the gynaeceum part of the flower of B. ceiba plant. Chromatographical techniques were employed to isolate the compound quercetagetin glycoside from the ethyl acetate fraction of an ethanolic extract of the gynaeceum part of the flowers. The structure of the isolated compound was elucidated by spectroscopic methods including UV, 1H and 13 CNMR.¹⁸

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A detailed exploration of phytochemical properties along with the TLC ratios of various extracts of B. ceiba was also conducted which showed that the alcoholic and water extracts indicate the presence of alkaloids, flavonoids, glycosides, coumarins, proteins and amino acids.¹⁷

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Bark contains lupeol, saponins, tannins, gums and 4,5,7-trihydroxyflavone-3-O-β-D-glucopyranosyl(1-4)-α-L-rhamnopyranoside, nhexacosanol and palmitic acid isolated from seeds, lactone isolated from root bark, polysaccharide isolated from flowers-had a continuous backbone of 4(1-4)-β-linked D-galactopyranosyl and 2 (1-3)-β-linked L-arabinopyranose units with β-linked D- galactose and α-linked L-rhamnose and L-arabinose units as end groups.²⁰ (Figure 2)

Hemigossypol-6-methyl ether was isolated from the root bark of B.malabaricum along with isohemigossypol-1-methyl ether.²¹

The structures of these compounds were elucidated by spectroscopic
were quantified by high performance liquids chromatography (HPLC).

The total phenolic content present in water extracts of

extract was 264 μg/ml. The extract showed very low toxicity toward Vero
drug-resistant E. coli and S. aureus. The extract showed strong activity against multi-drug resistant
Klebsiella pneumoniae and P. aeruginosa. The extract was shown to be active against
Salmonella typhimurium, Salmonella typhi and Shigella flexneri. The extract was also shown to be active against
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Antimicrobial and antibacterial activity
Plant extracts (methanol and aqueous) were assayed for their activity against multi-drug resistant Salmonella typhimurium. Strong antibacterial activity was shown by the methanol extracts of Salmalicia malabarica. Plant extracts were shown to be active against Klebsiella pneumoniae, Salmonella typhi and Shigella flexneri. The extracts were also shown to be active against E. coli and S. aureus.

Anticycotoxicity
Aqueous extracts of the plants were screened for their cytotoxicity using the brine shrimp lethality test. The present study supports that brine shrimp bioassay is simple, reliable and convenient method for assessment of bioactivity of medicinal plants and lends support for their use in traditional medicine.

Figure 2: Structures of Phyto-constituents present in Bombax ceiba.

analysis and comparison with literature data as: quercetin-3-O-β-D-glucuronopyranoside, chlorogenic acid, rutin, sexanguaretin-3-O-sophoroside, vitexin, isovitexin, kaempferol-3-O-rutinoside, kaempferol-3-O-β-D-glucuronopyranoside, isomangiferin and 7-O-methyl mangiferin, esculetin, scopoletin, fraxetin, scopolin, blumenol C, glucoside, benzyl-β-D-glucopyranoside, phenylethyl-rutinoside, protocatechulic acid, methyl chlorogenate and vanillic acid. Of these, were isolated from this plant.

PHYTOPHARMACOLOGICAL STUDIES

Hyptensive activity
Shamimin along with lupeol (lup-20 (29) en-3b-ol), which possesses potent hypotensive activity, have been isolated from B. ceiba stem bark. BCBMM (filtrate from BCBM (Methanolic extract of defatted stem bark)) of one of the most active fractions has revealed its adverse effects on heart, liver and kidneys of mice at the dose of 1000 mg/kg/d.

Antioxidant activity
The antioxidant activity of a methanolic extract of B. ceiba was evaluated using several antioxidant assays, in terms of its: (i) ability to scavenge DPPH (1,1-diphenyl-2-picrylhydrazyl) and hydroxyl free radicals; (ii) action against lipid peroxidation (in rat liver microsomes and soy bean phosphatidylcholine liposomes), induced by ascorbyl radicals and peroxynitrite; and (iii) effect on myeloperoxidase activity. The cytotoxicity was monitored through the mitochondrial activity in the Vero cell line. The extract showed antioxidant activity in all assays. The EC_{50} for DPPH was 87 μg/ml; lipid peroxidation of microsomes and soy bean liposomes induced by ascorbyl radicals were 141 μg/ml and 105 μg/ml, respectively and by peroxynitrite were 115 μg/ml and 77 μg/ml, respectively. The K (0.5) value for myeloperoxidase activity inhibition by the extract was 264 μg/ml. The extract showed very low toxicity toward Vero cells.

The total phenolic content present in water extracts of B. ceiba (ela imbul; gum), was determined by Folin-Ciocalteau method. Caffeine and gallic acid were quantified by high performance liquids chromatography (HPLC). Total free radical scavenging activity of each ingredient was investigated by 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging method and the values were compared with phenolic and gallic acid present in each plant. The polyphenol content of B. ceiba were 32.57 ± 5.04% of total extractable. Detectable levels of gallic acid were present only in B. ceiba (1.46 mg/g of total extractable). The EC_{50} values for DPPH radical scavenging activity for B. ceiba were 15.47 ± 1.80 μg cm-3. The mean values of EC_{50} (y) for DPPH radical scavenging activity were correlated with total phenolics (x) present in plant extracts (y = -35.417x + 1428; R = 0.9887).41

Analgesic activity
Mangiferin, 2-beta-D-glucopyranosyl-1,3,6,7-tetrahydroxy- 9H-xanthen-9-one, obtained directly from methanolic extracts of B. ceiba leaves demonstrated strong antioxidant activity (EC_{50} 5.8 (+/-) 0.96 μg/ml) using DPPH assay. The acetyl and cinnamonyl derivatives were found to be less active than mangiferin whereas methyl and 3, 6, 7-trimethyl ether tetraacetate derivatives were inactive implying that for antioxidant activity, free hydroxyl groups and catechol moiety are essential. Moreover, mangiferin showed hepatoprotective activity against carbon tetrachloride induced liver injury further supporting the free radical scavenging property in the in vivo system. Additionally, crude plant extracts and purified mangiferin failed to exhibit acute anti-inflammatory activity whereas, displays significant analgesic effect in acetic acid-induced writhing and hot plate tests in mice. Using nalozone, it was revealed that plant extract induced analgesia was independent of the opioid receptor; whereas, mangiferin demonstrated significant interaction with the receptor at a peripheral site, with a slight contribution at the neuronal level.52

Antiangiogenic activity
A methanol extract of the stem barks of B. ceiba was found to exhibit a significant antiangiogenic activity on in vitro tube formation of human umbilical venous endothelial cells (HUVEC). Bioactivity-guided fractionation and isolation carried out on this extract identified lupeol as an active principle. At 50 and 30 μg/ml, lupeol showed a marked inhibitory activity on HUVEC tube formation while it did not affect the growth of human umbilical venous endothelial cells (HUVEC). The extract was shown to be active against multi-drug resistant K. pneumoniae and P. aeruginosa. The extract was also shown to be active against E. coli and S. aureus.

Hypotensive and hypoglycaemic activity
Shamimin, a C-flavonol glucoside from B. ceiba leaves showed significant potency as a hypotensive agent at the doses of 15 mg/kg, 3 mg/kg, 1 mg/kg and significant hypoglycaemic activity at 500 mg/kg in Sprague Dawley rats.44

Antimicrobial and antibacterial activity
Plant extracts (methanol and aqueous) were assayed for their activity against multi-drug resistant Salmonella typhi. Strong antibacterial activity was shown by the methanol extracts of Salmalicia malabarica. Plant or plant parts were collected, dried, homogenized and extracted in two organic solvents viz. methanol and acetone. The antibacterial activity against Klebsiella pneumoniae was done by agar disc diffusion method. The activity was compared with standard antimicrobials Amikacin and Piperacillin.46

Cytotoxicity
Aqueous extracts of the plants were screened for their cytotoxicity using the brine shrimp lethality test. The present study supports that brine shrimp bioassay is simple, reliable and convenient method for assessment of bioactivity of medicinal plants and lends support for their use in traditional medicine.
Cancer Cell Growth Inhibition

Flowers of *B. ceiba* showed antioxidant effects and antiproliferative activity against seven human cancer cell lines (Michigan Cancer Foundation-7 [MCF-7], HeLa Henrietta Lacks), COR-L23, C32, A375, ACHN and LNCaP cells. The presence of interesting/novel chemical compounds indicates that the plant could serve as “lead” for developing therapeutic value of *B. ceiba*. An extensive literature survey has revealed that *B. ceiba* has a long history of traditional use for a wide range of diseases. Much of the traditional uses have been validated by scientific research. It is an important species that has economic and ecological importance and should be conserved for ecological perspectives. The plant is used in dysentery, affections, chronic inflammation, ulceration of bladder and kidney, and gallic acids acting as astringents which precipitate proteins which decrease in alkaline phosphatase (ALP), alanine transaminases (ALT), aspartate transaminases (AST) and total bilirubin levels, but increase in the level of total protein in comparison to control. The results obtained from the analysis of biochemical parameters and histopathological studies, resulted in the conclusion that the MEBC were not able to completely revert the hepatic injury induced by INH and RIF, but it could limit the effect of INH and RIF to the extent of necrosis.

Hepatoprotective activity

The hepatoprotective activity of a methanolic extract of flowers of *B. ceiba* (MEBC) was investigated against hepatotoxicity produced by administering a combination of two anti-tubercular drugs isoniazid (INH) and rifampicin (RIF) for 10 and 21 days by intraperitoneal route in rats. MEB were administered at three graded dose i.e. 150, 300 and 450 mg/kg i.p. 45 min prior to anti-tubercular challenge for 10 and 21 days. MEB was evident in all doses as there was a significant decrease in alkaline phosphatase (ALP), alanine transaminases (ALT), aspartate transaminases (AST) and total bilirubin levels, but increase in the level of total protein in comparison to control. MEBC significantly decreased the level of TBARS (thiobarbituric acid reactive substances) and elevated the level of GSH (reduced glutathione) at all doses as compared to control. The results obtained from the analysis of bioactive chemical compounds indicates that the plant could serve as “lead” for developing therapeutic value of *B. ceiba*. An extensive literature survey has revealed that *B. ceiba* has a long history of traditional use for a wide range of diseases. Much of the traditional uses have been validated by scientific research. It is an important species that has economic and ecological importance and should be conserved for ecological perspectives. The plant is used in dysentery, affections, chronic inflammation, ulceration of bladder and kidney, and gallic acids acting as astringents which precipitate proteins which decrease in alkaline phosphatase (ALP), alanine transaminases (ALT), aspartate transaminases (AST) and total bilirubin levels, but increase in the level of total protein in comparison to control. The results obtained from the analysis of biochemical parameters and histopathological studies, resulted in the conclusion that the MEBC were not able to completely revert the hepatic injury induced by INH and RIF, but it could limit the effect of INH and RIF to the extent of necrosis.

Inhibitory effects on fatty acid syntheses

Fatty acid syntheses (FAS) had been found to be over express and hyperactive in most cancers. Pharmacological inhibitors of FAS activity preferentially repress cancer cell proliferation and induce cancer cell apoptosis without affecting nonmalignant fibroblasts. These made FAS an excellent drug target for cancer therapy. The FAS activity is the lowest in gastric cancer cell N87 (15.91 ± 3.61 U/mg protein) and the highest in lung cancer cell A549 (127.36 ± 10.14 U/mg protein). The cancer cell A549 was used as a cell model to test the inhibitory effect of flavonoid extracts on FAS. The minimum inhibitory concentration of *B. ceiba* Linn was 247.98 μg/ml.

Antipyretic activity

The methanol extract of *Bombax malabaricum* (syn *Bombax ceiba*) leaves (MEBM) was investigated for the antipyretic activity in rats. MEBM possessed significant antipyretic activity in Baker’s yeast-induced pyrexia. Phytochemical tests showed the presence of steroids, carbohydrates, tannins, triterpenoids, deoxy-sugars, flavonoids and coumarin glycosides.

Aphrodisiac activity

The aphrodisiac activity of *B. ceiba* root extract was investigated. The extract (400 mg/kg body wt/day) was administered orally by gavage for 28 days. Mount latency (ML), intromission latency (IL), ejaculation latency (EL), mounting frequency (MF), intromission frequency (IF), ejaculation frequency (EF) and post-ejaculatory interval (PEI) were the parameters observed before and during the sexual behavior study at day 0, 7, 14, 21 and 28 days. The extract reduced significantly ML, IL, EL and PEI (p < 0.05). The extract also increased significantly MF, IF and EF (p < 0.05). These effects were observed in sexually active and inactive male mice.

Young roots of *B. ceiba* also known as Semal-musli are used traditionally in Indian subcontinent as aphrodisiac. Its juice is considered nutritive, restorative and sexual stimulant. The lyophilized aqueous extract of roots on sexual behavior, spermatogenesis and anabolic effects in male albino rats in presence of female rats. A gain in body weight was achieved and significant improvement in mount, intromission and ejaculation frequencies. Seminal fructose content and epididymal sperm counts were also significantly improved.

Protective Effect in Inflammatory Bowel Disease

The extract of stem bark of *B. ceiba* has significant anti-obesity potential against high-fat diet-induced experimental obesity, possibly due to modulation of FAS and PTP-1B signaling in Wistar rats due to the presence of active flavanoids and lupeol, respectively.

Anti-obesity

Thorn of *Salamalia malabarica* Schott. and Endl has been employed to treat acne of the face. The alcoholic extract of bark and thorns posses very good anti-acne potential against *Propionibacterium acne* with minimum inhibitory concentration (MIC) of 250 μg/ml while MIC value of leaf was 500 μg/ml which was better as compared to MIC of standard clindamycin. All three extracts have been reduced *P. acne*-induced granulomatous inflammation on rats. The thorns of *S. malabarica* are an important ingredient of Himalaya, “Acne-N-Pimple Cream” is a polyherbal formulation recommended for the management of acne vulgaris. The study on cream observed significant reduction in the number of blackheads and whiteheads, in number of inflamed pustules and overall inflammation. “Acne-N-Pimple Cream” is clinically effective and safe in the management of acne vulgaris.

CARDIOPROTECTIVE EFFECT

Root powder of this plant i.e., *B. ceiba* significantly modifies the coronary risk factors such as atherogenic lipids, fibrinogen and oxidative stress in patients with ischemic heart disease. Moreover it has been reported with its antioxidant activity due to high amounts of phenolics and tannins.

CONCLUSION

An extensive literature survey has revealed that *B. ceiba* has a long history of traditional use for a wide range of diseases. Much of the traditional uses have been validated by scientific research. It is an important species that has economic and ecological importance and should be conserved for ecological perspectives. The plant is used in dysentery, menorrhagia, skin troubles, haemorrhoids, for the treatment of snake bite and scorpion sting, boils, leucorrhoea, internal bleeding, calculus affections, chronic inflammation, ulceration of bladder and kidney, gonorrhea, haemoptysis, influenza, enteritis, pulmonary tuberculosis, cystitis and catarrhal affections bleeding piles. The pharmacological and clinical studies reported in the present review confirm the therapeutic value of *B. ceiba*. The presence of interesting/ novel chemical compounds indicates that the plant could serve as “lead” for development of novel agents in disorders in the coming years. In this regard, further studies need to be carried out to explore *B. ceiba* for its potential in preventing and treating diseases.

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CONFLICT OF INTEREST
The authors declare no conflict of interest.

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