Phytochemical and pharmacological profile of *Pterocarpus marsupium*: A review

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Abstract
Natural Products have been prescribed since ages for the treatment of various ailments. Numerous traditional systems of medicine have utilized the potential of medicinal plants. *Pterocarpus marsupium* Roxb. (Fabaceae) is one such herbal drug which finds its place in Ayurveda, Unani and Homeopathic system of medicine. Nature has bestowed this herb with a high versatility due to which it exhibits a wide range of Pharmacological actions. *Pterocarpus marsupium* commonly known as Indian Kino tree or Asana or Vijayasar is a large deciduous tree found in the subtropical regions of the world. It is highly enriched with an array of phytoconstituents including pterosupin, pterostilbene, liquiritigenin, isoliquiritigenin, epicatechin, koin, kinotannic acid, kino-red beta-eudesmol, carsupin, marsupol, marsupinol and so on. Many of these constituents have been explored for numerous biological actions like analgesic, anti-bacterial, anti-cancer, anti-cataract, anti-diabetic, anti-fungal, anti-hyperlipidemic, anti-inflammatory, anti-oxidant, aphrodisiac, cardiotonic, hepatoprotective etc. Thus, the current review aims to provide the complete phytochemical and pharmacological profile of *Pterocarpus marsupium* which would surely be beneficial for future researchers.

Keywords: *Pterocarpus marsupium*, Phytochemical, Pharmacological, Anti-diabetic.

Introduction
The history of herbal medicine is as old as human civilization and even in the current scenario; near about 75-80% of the world population relies on the medicinal plants for primary health care [1]. The reason being that they are easily available, cheap and devoid of side effects [3]. WHO states that the herbs are used two to three times more than the conventional drugs as remedies for various ailments [3]. Various plants have been used since ages as medicine. *Pterocarpus marsupium* is one such plant which has proved itself as versatile plant with a broad spectrum of pharmacological actions. It has been mentioned in various traditional systems of medicine like Ayurvedic, Unani and Homeopathic systems of medicine [4]. *Pterocarpus marsupium* Roxb.-Fabaceae (PM) known as Indian Kino Tree or Malabar Tree in English; Vijayasar or Bija in Hindi and Asana in Sanskrit is indigenous to India, Nepal and Sri Lanka [5, 6]. It is found specifically in the areas of the Western Ghats, in the Karnataka-Kerala region, in the states of Gujarat, Madhya Pradesh, Bihar and Orissa [7]. PM find its place in the Rasayans group of Ayurveda [9]. Due to the exploitation of the tree for its timber and medicinal bark, its population is decreasing in the wild and thus, it has been mentioned in the red data book [9]. PM is a medium to large sized deciduous tree growing upto 30m in height and 2.5 m in girth [10], with dark brown to grey bark having superficial fissures; leaves compound and imparipinnate; flowers yellow in terminal panicles; fruit circular, flat, winged pod; seed convex & bony [11]. Flowering and fruiting duration of the tree is from March to June [12]. The major phytoconstituents of PM are pterostilbene and marsupin [13, 14]. Others being liquiritigenin, iso liquiritigenin, pterosupin, p-hydroxybenzaldehyde, 7, 4’-dihydroxy flavone [14], propertol [15], marsupol [16], carsupin [17] and so on. Different plant parts of PM have been used for various diseases like leaves for boils, sores, skin diseases and stomach pain; flowers for fever; Gum-Kino for diarrhea, dysentery, leucorrhoea etc. and bark as astringent & for toothache [18, 19]. Decoctions of bark and resin have been used traditionally for the treatment of tumours of the gland, urethral discharges and as abortifacient [20]. The heartwood possesses astringent, anti-inflammatory, anti-diabetic and anodyne properties [21].

Vernacular names [5, 22, 18, 23, 24]:
Assam. - Ajar
Beng. - Piyasala, Pitasala
The major phytoconstituents of PM are pterosuprin, pterostilbene, liquiritigenin, isoliquiritigenin, epicatechin, koino, kinotannic acid, kino-red, beta-eudesmol, carsupin, marusupol and marusupinol [3].

Isolation of components from the aqueous extract of PM heartwood yielded a few novel flavonoid C-glycosides: 2,6-dihydroxy-2-(4-hydroxybenzyl)-benzofuran-7-C-b-d-glucopyranoside(1), 3-(a-methoxy-4-hydroxybenzylidene)-6-hydroxy benzo-2(3H)-furane-7-C-b-d-glucopyranoside(2), 2-hydroxy-2-p-hydroxybenzyl-3(2H)-6-hydroxybenzo furane-7-C-b-d-glucopyranoside (4), 8-(C-b-d-glucopyranosyl)-7,30,40-trihydroxyflavone (5) and 1,2-bis (2,4-dihydroxy-3-C-glycopropionate)-ethanediene (6) and two known compounds C-b-d-glucopyranosyl-2,6-dihydroxyl benzene (7) and sesquiterpene (8) [28].

Another new phytoconstituent 6,7,3',4'-tetraoxygenated homoiso flavonoid characterized as 6-hydroxy-7-O-methyl-3 (3-hydroxy-4-O-methylbenzyl) chronan-4-one was isolated from ether soluble fractions of PM heartwood while a flavonol glycoside from the roots [29]. An isoaurone C- glycoside was obtained from the aqueous extract of PM heartwood [30]. Two interconvertible diasteriomeremic epimers 2α/ 2β-hydroxy-2-Phydroxybenzyl-3(2H) benzofuran-7-C-β-D-glucopyranoside have also been reported [31]. The findings of various indicated that PM contains numerous polyphenolic compounds [32], terpenoids [33], fluorescent pigment, phenol glucosides [34] and pterostilbene [35].

A number of phytoconstituents have been isolated from extracts of PM: viz. stilbene [33], catechin, epicatechin [36], beta-eudesmol, triterpene alcohol, erythrodil-3-monoacetate [37], 5,4'-dimethoxy-8-methylisoflavone, retusin 7-glucoside, irsodiol7-rhamnoside and 5,7-dihydroxy-6-methoxyisorhamnoside-7-rhamnose, eudesmane type sesquiterpene alcohol [38], marusupol (4,4'-di hydroxy-Lmethylhydrobenzo) and a novel 2-hydroxy-2 benzylcoumaranone, carpucin, characterized as 2-benzyl 2,4',6-trihydroxy-4-methoxybenzo(b) furan-3(2H)one [16], propterol (1,3-bis(4-hydroxyphenyl)propan-2-ol pseudobaptigenin) [15], garbanzol, liquiritigenin, 5 deoxykaempferol, isoliquiritigenin, pterosuprin, phydroxybenzaldehyde chalcone, dihydrochalcone and aromatic aldehyde [39], 8-C-D-glucopyranosyl-3', 7, 4 trihydroxyflavone; 3, 7, 4'-tetrahydroxyflavone; 3'-C-D glucopyranosylhydroxydihydrochalcone and other phenolic compounds [40]. Two aurone glycosides 4, 6, 4'- trihydroxyaurone 6-O-rhamnopyranoside and 4, 6,4'- trihydroxy-7-methylaurone 4-O-rhamnopyranoside have been characterized from PM flowers and another two 6, 4'- dihydroxy-7-methylaurone 6-O rhamnopyranoside and 4, 6, 3',4'- tetrahydroxyaurone 6-O-rhamnopyranoside from its heartwood [41]. Its roots yielded two flavone glycosides, 7 hydroxy-6, 8-dimethyl flavanon-7-O-a-L-arabinopyranoside and 7, 8, 4'-trihydroxy-3', 5'-dimethoxyflavone-4'-O-beta Dglucopyranoside [42].

The screening for the levels of inorganic contents of PM bark yielded Nitrogen (1.50-3.13%), calcium (0.60-1.848%), magnesium (0.21-0.339%) and Phosphorus (0.023-0.163%); trace elements : iron (11.38-44.34mg/100gm), manganese (2.0-4.94mg/100gm), zinc(1.98-3.62mg/100gm) and cobalt(0.68-3.2mg/100gm) [43]. A bioactive flavonol 7-O-a-L-rhamnopyranosyl oxy-4'-methoxy-5-hydroxy isoflavone was characterized form the methanolic extract of PM and evaluated for its influence on cellular targets Glut-4, PPARγ and PI3 kinase [44].

Cyclic voltammetry study was used for the electrochemical investigation of resorcinol in PM [45]. Chemical structures of some of the phytoconstituents are depicted in Table 1.
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**Ayurvedic Profile** \([46]\)**

**Medicinal Properties:**

- **Guna (Qualities)** - Laghu (light to digest), Ruksha (dry)
- **Rasa (Taste)** - Kashaya (astringent), Tikta (bitter)
- **Vipaka (post-digestive taste)** - pungent
- **Veerya (Sheeta)** - Coolant
- **Effect on tridosha** – balances kapha and pitta dosha
- **Dosage** – Decoction 50-100 ml; powder 3-6 gm

**Pterocarpus marsupium uses**

- Keshya – improves hair strength, promotes hair growth
- Medohara – reduces fat and cholesterol levels
- Rasayana – anti-ageing, causes cell and tissue rejuvenation

**Indicated in**

- Raktapitta – bleeding disorders such as nasal bleeding, heavy periods etc.
- Krumi - worm infestation
- Visarpa – herpes
- Kushtha – skin diseases
- Shivita – leucoderma, vitiligo
- Meha – diabetes, urinary tract infections
- Gala dosha – throat disorders
- Raktamandala – ring worm infestation

**Ayurvedic medicines with Beejak as ingredient**

- Asana manjishtadi taila – for treatment of headache and eye disorders
- Asana cladi taila – for treatment of headache, ear and eye disorders
- Asana vilwadi taila – for treatment of headache, ear and eye disorders
- Narasimha Rasayan – for treatment of weakness, weight gain, hair growth and rejuvenation

**Classical Categorization**

- Susruta – Salaasaradi gna
- Vabhata – Asanadi Gana
- Kaiyadeva Nighantu – Oshadhi Varga
- Dhanvantari Nighantu – Amradi Varga
- Bhavaprakasha – Vatadi Varga
- Rajanighantu – Prabhadradi Varga

**Pharmacological activities:**

**Analgesic Activity**

In an investigation, PM leaves were successively extracted with petroleum ether, ethyl acetate and methanol. Then these extracts were utilized for studying the analgesic activity by acetic acid induced writhing assay in Swiss albino mice.
Significant analgesic activity was shown—methanol extract being most potent followed by ethyl acetate and petroleum ether extracts [47].

The central analgesic activity of PM bark extract studied using the hot-plate method showed that the pain threshold reduced and the response latency period to thermal stimulus in mice increased in the same manner as that of the reference drug-Pentazocine [48].

**Anti-bacterial Activity**

The antibacterial activity of PM stem methanolic extract was tested against gram positive bacteria-Bacillus coagulans and gram negative bacteria- Escherichia coli using the paper disc diffusion method. 100mg/ml concentration significantly inhibited the growth of both the bacteria [49]. The Hexane, ethyl acetate and methanol extracts of PM bark and leaves have shown antimicrobial activity against four selected Gram positive and Gram negative bacteria [50].

In vitro studies have shown that PM inhibits Pseudomonas aeruginosa, Streptococcus pyrogens and Staphylococcus aureus [51].

Another research investigation showed positive indications for anti-microbial activity against two gram positive (Enterococci and Staphylococcus aureus) and negative (Escherichia coli and Pseudomonas aeruginosa) microbial organisms and a fungal strain Candida albicans [52].

PM ethanolic extract was evaluated for antimicrobial potential against Bacillus polymyxa, Vibrio cholera and Candida albicans using cyclic voltammetry. The low anodic current and low anodic peak potential were obtained indicating the good reducing ability of the molecules resulting in good antioxidant activity of the extract. The results depicted the significant antimicrobial activity at different dosages [53].

**Anti-cancer Activity**

Pterostilbene [54] and Stilbene [55] have been found to exhibit the anti-cancer potential. An investigation showed that Pterostilbene inhibited the cell proliferating factors like Akt, Bcl-2 and induced the mitochondrial apoptotic signals like Bax, and the series of caspases. It was also found to inhibit two important metastasis inducers-Matrix Metalloproteinase 9 (MMP) and α-Methyl Acyl CoA racemase (AMACR). Thus, Pterostilbene has manifold target sites to induce apoptosis and it can be used for the treatment of breast and prostate cancer [56]. Resveratrol has also been reported to possess anticancer potential [57].

**Anti-cataract Activity**

An investigation showed that the aqueous extract of PM bark reduced the opacity index in the alloxan induced diabetic rats, thus it possesses the anti-cataract activity [58, 59].

**Anti-diabetic Activity**

PM has been used as a highly potent anti-diabetic agent since ancient times. It possesses blood glucose lowering, beta cell protective and regenerative properties. Numerous experimental studies have been conducted on various animal species viz., rats, dogs, and rabbits to study the hypoglycemic effect of PM. The results have shown that PM restored the normal insulin secretion by reversing the damage to the beta cells and by repopulating the islets [58, 60-73]. In a study, alcoholic extract and various fractions of PM (toluene, chloroform, ethyl acetate and butanol were found to possess beneficial effects on blood glucose levels [74].

The findings of a clinical trial (flexible dose double blind multicenter randomized controlled trial) revealed that PM is an effective blood sugar lowering agent [75].

Three phenolic compounds were evaluated for their anti-diabetic potential and it was found that marsupin and pterostilben were more effective than pterospin on comparison with metformin [61].

A study group of ICMR investigated the antidiabetic activity of PM at multi-center level and found that the blood glucose level significantly decreased without any side effects [76].

Another ICMR study group also proved the utility of PM in diabetes. Their findings indicated a significant reduction in blood glucose level and mean HbA1c levels from 151-216mg/dl to 32-45mg/dl and 9.8 to 9.4% respectively [77].

The aqueous extract of PM bark has exhibited its ameliorative potential in STZ (streptozotocin) induced diabetes. The glycosylated hemoglobin, total cholesterol, triglycerides and LDL cholesterol were normalized and the elevated levels of numerous enzymes like ceratine kinase, glutamyl transferase, aspartate transaminase, alanine transaminase, alkaline phosphatase were also brought to usual range [50].

Another study suggested the ability of methanolic extract of PM to improve STZ-induced chronic stress by rectifying the glycosylated hemoglobin (HbA1c), serum protein, albumin, insulin, acid and alkaline phosphatase [78].

Ethyl acetate extract of PM was utilized in another study to evaluate its anti-hyperglycemic action and it was concluded that its activity might be due its free radical scavenging property [79].

Optimized conventional (infusion, decoction, maceration and percolation) and non-conventional extraction as ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE) methods were used in an investigation to prepare ethanolic and aqueous extracts of PM heartwood and assess their anti-diabetic activity in alloxan induced diabetic rats. The findings verified the use of conventional methods and suggested that the antidiabetic action of PM can be improved by extracting the heartwood by non-conventional method of UAE [80].

A high molecular weight fraction was obtained by Bio-assay-guided fractionation of PM which exhibited potent antidiabetic properties in vitro and in vivo by stimulating the insulin secretion and glucose uptake, respectively, in a concentration-dependent manner [81].

The findings of an investigation suggested that the antidiabetic potential of PM might be due to its ability to inhibit the glucose diffusion across the bio-membrane [82].

An investigation was carried out to study the effect of (-) epicatechin and insulin on glutathione content in normal and Type-2 diabetic erythrocytes. It was observed that (-) epicatechin increased the glutathione content (which was lower in Type-2 diabetic erythrocytes) [83]. Treatment with aqueous extract of PM caused an increase in renal glycogen content and prevented decrease in glycogen content of hepatic and skeletal muscles. PM was also able to rectify the alterations in activities of glucokinase, hexokinase and phosphofructokinase [84].

(-)-Epicatechin has been reported to possess insulin like activity [85] and illicit protective effect on erythrocyte osmotic fragility [86]. It has been observed that (-)-Epicatechin causes insulin release (by increasing c-AMP content of the islets) and converts proinsulin to insulin [87].

PM has been beneficial in combination for amelioration of associated diabetic manifestations/dys regulations [88, 89] and
some of its potent poly herbal formulations include Diabecon [90], Diabeta [91], DRF/AY/5001 [92] and D-400 [93].

**Anti-fungal Activity**

PM showed beneficial effects as a topical agent against *T. cruris* and *T. corporis*. Good response was obtained within 3 days after first application [94].

**Anti-hyperlipidemic Activity**

Numerous natural products including PM have been screened for their hypolipidemic potential [95]. The ethanolic extract of PM heartwood and its flavonoid phytoconstituents marsupin, pterosupin, and liquiritigenin have shown anti-hyperlipidemic effect. The experimental observations proved that the extract was able to reduce serum triglyceride, total cholesterol, LDL- and VLDL- cholesterol without any significant effect on the level of HDL-cholesterol. It was also shown that liquiritigenin and pterosupin lowered the serum cholesterol, LDL cholesterol and antherogenic index while pterostilbene also reduced the triglyceride level [96]. Another investigation proved the utility of aqueous extract of PM bark in hypertriglyceridaemia [97].

**Anti-inflammatory Activity**

PM is also a potent anti-inflammatory agent. Extract containing pterostilbene was investigated for its PGE2-inhibitory activity in LPS-stimulated PBMC and for COX-1/2 selective inhibitory activity [98, 99]. Aqueous extract of PM at doses of 100mg/kg and 200mg/kg was found to reduce the elevated inflammatory cytokine, tumor necrosis factor TNF-α level in type 2 diabetic rats [100]. The methanolic and aqueous extract of PM stem bark, both at the doses of 100mg/kg showed positive results for anti-inflammatory activity in carrageenan induced rat paw oedema model [101]. The herbal hydrogels containing hydro-alcoholic extracts of *Pterocarpus marsupium*, *Pterocarpus santalinus* and *Glycyrrhiza glabra* exhibited significant anti-inflammatory activity (43.70%) when compared with the standard (17.03%) [102].

**Anti-oxidant Activity**

The anti-oxidant potential of PM bark (aqueous, methanol and ethyl acetate extract) has been investigated with the aid of numerous antioxidant models, viz DPPH, ABTS, NO, OH, SO and inhibition of in vitro lipid peroxidation. The findings indicated the free radical scavenging potential of PM [103]. 1,1-diphenyl-2-picrylhydrazyl assay was used to evaluate the in vitro anti-oxidant potential of PM bark extract and the results were expressed as IC50. PM showed the IC50 of 53.0 μg/ml as compared to that of ascorbic acid (standard) with IC50 of 34.0 μg/ml [48]. In a study, PM extract sheltered the cardiac muscles against the oxidative stress induced by H2O2 [104].

**Aphrodisiac Activity**

A review has stated the utility of PM as Vajikaran rasayana of Ayurveda or Aphrodisiac of Modern concept [105].

**Cardiotonic Activity**

The cardiotonic activity of aqueous extract of PM heartwood has been reported. 5, 7, 2-4 tetrahydroxy isoflavone 6-6 glucoside found in the extract is a potent antioxidant and have been supposed to be beneficial in cardiovascular diseases. The isolated frog heart perfusion technique was used to study the cardiotonic effect of highly diluted aqueous extract of PM. The findings of the investigation indicated an excellent cardiotonic activity. PM produced negative chronotropic and positive inotropic effects in frogs [106]. (-)-Epicatechin isolated from PM was evaluated for cardiotonic activity and it was found to exhibit cardiac stimulant activity in perfused frog hearts producing increase in force along with increase in rate [107]. Cardiomyopathy occurs as a result of lowered activities of erythrocytic membrane Ca+-ATPase which leads to decrease in contractibility, relaxation and cardiac work. With (-) - Epicatechin, Ca+-ATPase activity increased both in normal and diabetic type-2 patients [108].

**Hepatoprotective Activity**

Methanolic extract of PM bark shows hepatoprotective potential [109]. An investigation was carried out to evaluate the hepatoprotective activity of PM bark extracts against carbon tetrachloride (CCL4)-induced hepatotoxicity. The biochemical parameters used to assess the liver functions (total bilirubin, serum protein, alanine aminotransaminase, aspartate aminotransaminase, and alkaline phosphatase activities) was found to be controlled in extract treated groups. Histopathological results revealed normal hepatic cords, absence of fatty infiltration and necrosis [110].

**Toxic effects**

PM is not suggested during constipation because of its astringent property [18]. As the herbal treatment for diabetes is given for a longer duration, so the genotoxic assessment of PM was done using both somatic and germ cells. The results indicated that the extract was not genotoxic [111]. (-)-Epicatechin isolated from PM was studied for its action on CNS of frog, rat and mice. The results did not show any toxic effects on heart. Even in higher doses (-)-epicatechin exhibited no untoward effects [107]. A study group of ICMR investigated the anti-diabetic activity of PM at multi-center level and found that the blood glucose level significantly decreased without any side effects [78].

**Conclusion**

PM has been used since ages for the management of various human ailments. Wooden tumblers made from the bark of PM tree are still used to control diabetes and referred to as ‘The miracle cure for diabetes’. The tumbler is filled with water and left overnight. This water when consumed daily twice for 30 days has shown beneficial effects in individuals suffering from diabetes. Ayurvedic texts reveal that PM has the potential to detoxify the body, purify blood, reduce blood sugar and rejuvenate the various cells of the body. It has also been described as a natural way to control overweight, high blood pressure and pain in joints. The current review has focused on the numerous pharmacological activities of PM like analgesic, anti-bacterial, anti-cancer, anti-hyperlipidemic, anti-inflammatory, anti-oxidant, cardiotonic, hepatoprotective and so on. It also indicates that very few investigations have been carried out involving the anti-cataract, anti-fungal and aphrodisiac activities. Most of the studies have utilized the PM extracts while there are a very few clues exhibiting the activity of isolated phytoconstituents like epicatechin, pterostilbene, marsupin, pterosupin, liquiritigenin etc.
Thus, the current review provides a background for the upcoming basic researches on PM which shall involve the isolation and pharmacological investigations to well establish its broad spectrum medicinal potential.

**PHYTOCONSTITUENTS**

- Pterosupin
- Pterostilbene
- Liquiritigenin
- Epicatechin
- Marsupin

**PHARMACOLOGICAL ACTIVITY**

- Analgesic Activity
- Anti-cancer Activity
- Anti-diabetic Activity
- Cardiotonic Activity
- Anti-hyperlipidemic Activity
- Anti-inflammatory Activity
- Anti-bacterial Activity
- Anti-cataract Activity
- Anti-fungal Activity
- Hepatoprotective Activity
- Aphrodisiac Activity
- Anti-oxidant Activity
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