

***PTEROCARPUS MARSUPIUM*: A VALUABLE MEDICINAL PLANT IN DIABETES
MANAGEMENT***¹Patil Udaysing Hari and Dattatraya K. Gaikwad²^{*1}Bhogawati Mahavidyalaya Kurukali, Tal-Karveer, District- Kolhapur, Maharashtra [India]²Department of Botany, Shivaji University, Kolhapur, Maharashtra [India]-416004

ABSTRACT : *Pterocarpus marsupium* (Roxb.) is large deciduous tree, commonly called as Indian Kino or Malabar Kino, belonging to the family fabaceae (Leguminosae). The tree is scard with novel antidiabetic properties. Along with as an antidiabetic drug, it is also used as astringent, anti-inflammatory, haemostatic, anthelmintic, in chest pain, body pain and in indigestion, in diabetic anaemia, elephantiasis, erysipelas, urethrorrhea and ophthalmopathy etc. Phytochemically, many phenolic constituents of which flavonoid comprising major pool, are forming the basis of most pharmacological activities possessed by *Pterocarpus marsupium*. The present review summarizes the phyto-pharmacological role of this valuable medicinal plant.

Key words: *Pterocarpus marsupium*, anti-inflammatory, antidiabetic drug, diabetic anaemia and phyto-pharmacological.

BOTANY

Pterocarpus marsupium (Roxb.) is a deciduous tree, commonly called as Indian Kino tree or Malabar Kino, belonging to the family fabaceae. It is a medium to large sized tree reaching height up to 15-20 meter with dark brown to grey bark having swallow cracks. The bark exudes a red gummy substance called 'Gum Kino' when injured. Leaves are compound and imparipinnate. Flowers are yellow in terminal panicles. Fruit is circular, flat, winged pod. Seed is convex and bony (Warrier, 1995). Tree flowers and fruits in the month of March to June (Yadav and Sardesai, 2002)

DISTRIBUTION

Pterocarpus marsupium is distributed in deciduous forest throughout the India (Varghese, 1996). It is found to grow in parts of states such as Andhra Pradesh, Bihar, Gujarat, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Orissa, Rajasthan, Tamilnadu, Uttar Pradesh, West Bengal and Goa (Sanjappa, 2000).

ETHNOBOTANY

Leaves are used for food and manure. The flowers are used in the treatment of fever. *Pterocarpus marsupium* is a multipurpose leguminous tree. Heart wood is astringent, bitter, acrid, cooling, anti-inflammatory, depurative, haemostatic, revulsive, anthelmintic, constipating and rejuvenating (Warrier, 1995). The wood is useful in chest pain, body pain, and indigestion (Bressers, 1951). The paste of seed and wood is useful in diabetic anaemia (Trivedi, 2006). The paste of heart wood is useful in body pain and diabetes (Yesodharan and Sujana, 2007). Wood of the tree is useful in making the water glasses of the diabetic patients (Reddy, 2008). Bark is useful in vitiated condition of *kapha* and *pitta*, elephantiasis, erysipelas, urethrorrhea, rectalgia, ophthalmopathy, hemorrhages, dysentery, cough and grayness of hair. Aqueous infusions of the bark possess antidiabetic potential (Anonymous, 19689). The powdered bark is mixed with *Schleichera oleosa* and taken with cold water to treat dysentery (Mohanta, 2006). The juice of the bark is applied in the mouth (Prusti and Behera, 2007). Tribal people residing in the Jodhalal forest of Karnataka use stem bark to treat the wounds, fever, stomachache, diabetes and elephantiasis (Mankani et al., 2005). Bark is useful in urinary discharge and piles. The gum Kino is externally applied to leucorrhoea (Pullaiah, 1999). Gum Kino is used in the treatment of polyurea and inordinate night sweat and phthisis pulmonalis.

The Kino powder may be dusted on ulcers and bleeding surfaces (<http://www.henriettesherbal.com>, 2009). The gum is used in the toothache (Chopra et al., 1956) and leaves paste is applied in wounds (<http://www.milliontreedream.org>, 2009). Bruised leaves are useful in boils sores, skin diseases, stomachic and cholera (Jain, 1991). Leaf juice is given in purulent discharges from ear, plant is useful in snakebite and scorpion sting. Fruit cures biliousness and kapha (Kirtikar and Basu, 1975). Flowers are bitter, sweet, cooling, appetizing and febrifuge (Warrier, 1995) and used in fever (Pullaiah, 1999).

PHYTOCHEMISTRY

Mitra and Joshi (1982) isolated an isoflavon glycoside from the heart wood of the *Pterocaepus marsupium* and identified it as 5, 4'-dimethoxy-8-methylisoflavone. Three isoflavon glycosides namely retusin 7-glucoside, irisolidone 7-rhamnoside and 5, 7-dihydroxy-6-methoxyisoflavone-7-rhamnoside were isolated by Mitra and Joshi (1983). A eudesmane type sesquiterpene alcohol, selin-4(15)-en-1 β , 11-diol was reported from the heart wood of the *P. marsupium* (Adinarayana and Syamsundar, 1982). Subba Rao and Mathew (1982) characterized a naturally occurring hydrobenzoin, marsupol, 4, 4'-dihydroxy-a-methylhydrobenzoin and a novel 2-hydroxy-2-benzylcoumaranone, carpucin, characterized as 2-benzyl-2,4',6-trihydroxy-4-methoxybenzo(b) furan-3(2H)one from the *P. marsupium* heart wood. From the heart wood, propterol-B-1-(2, 4-dihydroxyphenyl)-3-(4-hydroxyphenyl) propan-2-ol identified by Mathew and Subba Rao (1983). Subba Rao et al., (1984) isolated propterol: A 1, 3-bis (4-hydroxyphenyl) propan-2-ol as one of the extractive of heart wood. Bezuidenhout et al., (1987) reported two flavonoid analogue, 8-C- β -D-glucopyranosyl-3, 7, 4-trihydroxyflavone and 3, 7, 4'-tetrahydroxyflavone from the heart wood which are representatives of the first 5-deoxy- C-C-coupled flavonol glucosides, and rare 3'-C- β -D-glucopyranosyl- α -hydroxydihydrochalcone. A novel 6,7,3',4-tetraoxygenated homoisoflavonoid, which has been characterized as 6-hydroxy-7-O-methyl-3-(3-hydroxy-4-O-methylbenzyl) chronan-4-one from ether soluble fractions of *Pterocarpus marsupium* heart wood^[27] and 6-hydroxy-3, 5, 7, 4'-tetramethoxyflavone 6-O-rhamnopyranoside, a flavonol glycoside was characterised from the root (Yadav and Singh, 1998). An aqueous extract of heart wood yielded a isoaurone C- glycoside (Handa et al., 2000).

Grover et al., (2004) reported two interconvertible diastereomeric epimers 2 α / 2 β -hydroxy-2-*P*-hydroxybenzyl-3(2H)-benzofuranone-7-C- β -D-glucopyranoside from the heart wood. Five new glycosides reported from the aqueous extract of *P. marsupium* by Maurya et al., (2004) are –

- 1) 6-hydroxy-2-(4-hydroxybenzyl)-benzofuran-7-C- β -D-glucopyranoside.
- 2) 3-(α -methoxy-4-hydroxybenzylidene)-6-hydroxy-benzo-2(3H)-furanone-7-C- β -D-glucopyranoside.
- 3) 2-hydroxy-2-*P*-hydroxybenzyl-3(2H)-6-hydroxybenzofuranone-7-C- β -D-glucopyranoside.
- 4) 8-(C- β -D-glucopyranosyl)-7,3',4'-trihydroxy flavone
- 5) 1,2-bis-(2,4-dihydroxy-3-C-glucopyranosyl)-ethane dione.

Eight compounds, pterostilben, isoliquiritigenin, liquiritigenin, carpucin, propterol, propterol-B, oleanolic acid and marsupol were isolated from the heart wood of *Pterocarpus marsupium* (<http://www.silbinol.com>, 2009). Mohan and Joshi (1989) analyzed flower of *P. marsupium* and reported two aurone glycosides, 4, 6, 4'-trihydroxyaurone 6-O-rhamnopyranoside and 4, 6, 4'-trihydroxy-7-methylaurone 4-O-rhamnopyranoside. They also reported another two aurone glycoside from the heart wood and characterised as 6,4'-dihydroxy-7-methylaurone 6-O-rhamnopyranoside and 4,6,3',4'-tetrahydroxyaurone 6-O-rhamnopyranoside. From the roots of this plant, Tripathi and Joshi (1988) isolated two flavone glycosides, 7-hydroxy-6, 8-dimethyl flavanon-7-O- α -L-arbinopyranoside and 7,8,4'-trihydroxy-3',5'-dimethoxyflavanone-4'-O-beta-D-glucopyranoside. Srikrishna and Mathew (2009) synthesized a dimethyl ether of marsupin.

PHARMACOLOGY

In the Indian system of medicine many plants have been used to treat diabetes; of which, *Pterocarpus marsupium* popularly known as Bijasar is one of the most potent species (Rastogi and Mehrotra, 1989; Sivarajan and Balchandran, 1994; and Grover et al., 2002a). Its heart wood is official part used as antidiabetic drug (Shah, 1967). Many workers have studied the antidiabetic potential of *Pterocarpus marsupium*. According to Joshi et al., (2004) *P. marsupium* decreased the blood glucose levels both in normal and non-insulin dependent diabetic (NIDDM) rats. In NIDDM rats the propensity was increased to gastric ulcer which was induced by cold resistant stress, aspirin, and ethanol and pylorus ligation. They observed that the *Pterocarpus marsupium* did not show significant protection from the gastric ulcer in case of normal rats due to above inducers, but it protected the mucosa in NIDDM rats by affecting the mucosal offensive and defensive factors. Ahamad et al. (1991a) studied the hypoglycemic activity of the wood. Vats et al., (2002) found that absolute ethanol extract fraction dissolved in ethyl acetate was protective in lowering the blood sugar level and increased the insulin level in the blood sugar in alloxan diabetic rats while, aqueous extract of *P. marsupium* lowered blood sugar level from 72.32 ± 5.62 to 61.35 ± 1.2 mg in alloxan diabetic rats. The drug also lowered the blood glucose level from 202 ± 5.44 to 85.11 ± 11.28 mg when administered daily (Vats et al., 2002). Kar et al., (2003), also evaluated the hypoglycemic activity of vacuum dried 95% ethanolic extract, when administered at a dose 250mg/ounce, twice or thrice daily found effective in lowering the glucose level in the blood to normal in alloxan diabetic rats. Vats et al., (2002) reported the anti-cataract activity of the *P. marsupium* and *Trigonella foenum* seed extract. They noticed that administration of aqueous extract of *P. marsupium* decreased the opacity index, indicating anticataract potential of the plant. Further, they also noticed that in cataract examined rats, it showed significant effect on body weight and blood glucose values.

Administration of three Phenolic compounds in hyperglycemic rats significantly minimized the blood sugar level. Marsupin and pterostilben are more effective than Pterospin and when compared with metoformin (Manikam et al., 1997). ICMR study group (ICMR, 1998) also studied the antidiabetic potential of *P. marsupium* at multi-center level and hypothesized that, the plant significantly reduced blood glucose level without any side effects in non-insulin dependent diabetes mellitus or newly diagnosed mellitus. ICMR study group (2005) has evaluated the efficacy of Vijaysar (*P. marsupium*) in newly non-insulin dependent diabetes mellitus. They reported that blood glucose level and mean HbA1c levels were decreased significantly from 151-216mg/dl to 32-45mg/dl and 9.8 to 9.4 % respectively indicating the utility of Vijaysar in NIDDM patients. Rizvi et al., (1995) reported the insulin like activity of (-) epicatechin by studying the effect on erythrocyte osmotic fragility. Though the mechanism of action of both (-) epicatechin and insulin are different, they illicit their protective role on red cell osmotic fragility (Rizvi et al., 1995). Ahamad et al., (1989) also described the insulin like effects of (-) epicatechin. According to Ahamad et al., (1991b) (-) epicatechin increases the c-AMP content of the islets and insulin release. They observed that the conversion of proinsulin to insulin have been due to (-) epicatechin and the effect of (-) epicatechin was more in one month old rats than mature (12 month old rats). Sheehan et al., (1983) studied antidiabetic potential of epicatechin in alloxan diabetic rats. In this rats no measurable effects have been noticed in control and (-) epicatechin treated rats and in already attained diabetic condition, the effect of (-) epicatechin was found to be nil. Gayathri and Kannabiran (2008) evaluated the ameliorative potential of aqueous extract of *P. marsupium* bark in streptozotocin (STZ) induced diabetic rats. Oral administration of aqueous extract normalized the glycosylated hemoglobin, total cholesterol, triglycerides and LDL-cholesterol. Increased levels of various enzymes such as aspartate transaminase, alanine transaminase, alkaline phosphatase, glutamyle transferase and ceratine kinase were brought to normal level. They also indicated that the prominent effect of metabolic alterations in experimentally induced diabetes mellitus was due to restoration of the plasma insulin and liver glycogen levels. Rizvi and Zaid (2001) studied the effect of insulin and (-) epicatechin on glutathione content in normal and Type-2 diabetic erythrocytes.

They found that the glutathione content was lower in Type-2 diabetic erythrocytes than normal while, the insulin treatment both at 1mm and 10mm increased the glutathione level in normal and diabetic Type-2 patient. They also noticed that the (-) epicatechin treatment also increased the glutathione content at 1mm but did not show dose dependent effect like insulin and was ineffective below 1mm concentration. The effect of (-) epicatechin was remarkable at 1mm and 10mm when compared to insulin (Rizvi and Zaid, 2001). The effect of aqueous extract of *P. marsupium* on glycogen content of tissue was studied by Grover et al., (2002b). According to Grover et al., (200b) increase in glycogen content in renal and decrease in glycogen content in hepatic and skeletal muscle was partly prevented by aqueous extract of *Pterocarpus* treatment. Alterations in the activities of hexokinase, glucokinase and phosphofructokinase in diabetic and control were corrected by *Pterocarpus marsupium* extract (Grover et al., 200b). Zaid et al., (2002) reported that lowered activities of erythrocytic membrane Ca^{++} -ATPase leads to cardiomyopathy indicated by reduction in contractibility, relaxation, cardiac work and diastolic complications in Type-2 diabetes mellitus. When the normal and diabetic type -2 patients treated with 1mm (-) epicatechin, the Ca^{++} -ATPase activity increased both in normal and diabetic type-2 patients (Zaid et al., 2002). Apart from this many other researchers proved the antidiabetic nature of the *Pterocarpus marsupium* (Sharma and Kumar, 2007).

Anti-hyperlipidemic effect of ethanolic extract of heartwood of *Pterocarpus marsupium* and its flavonoid constituents marsupin, pterosupin, and liquiritigenin are studied by Jahromi and Ray (1993). They observed that ethanol extract decreased the serum triglyceride, total cholesterol and LDL and VLDL cholesterol levels without affecting the HDL cholesterol level. They found significant effect of liquiritigenin and pterosupin in lowering the serum cholesterol, LDL cholesterol and atherogenic index while; pterosupin was satisfactory in reducing the triglyceride level. Cardiotoxic activities of aqueous extract of heart wood have been evaluated by Mohire et al., (2007). The extract *Pterocarpus marsupium* protects cardiac muscle at 4mg/ml, as compared to standard drug Digoxin (0.5mg/ml). 5, 7, 2-4 tetrahydroxy isoflavone 6-6-glucosides which is protective in cardiovascular diseases (Mohire et al., 2007).

Anti-cancerous potential of pterostilben has been studied by Pan et al., (2007). Further, stilbens isolated from berries and grapes possess anticancer properties and used to cure colon cancer in men and women (Rimando and Suh, 2008). Mankani et al., (2005) studied the hepato-protective activity of aqueous and methanolic extract of marsupium wood against carbon tetrachloride induced hepatotoxicity. They found marked increase in total bilirubin, serum transaminase and serum alkaline phosphatase activity caused due to carbon tetrachloride toxicity were restored by aqueous and methanolic extract and later it was more effective in restoring the altered levels of these parameters (Manakani et al., 2005). Rajalakshmi et al., (2008) studied the antioxidant activity of *P. marsupium* on isolated frog heart and found that the plant extract protected the cardiac muscles from oxidative stress induced by H_2O_2 . While, the cardiac arrest time was prolonged by 14 minutes in the presence of plant extract than control, indicating the antioxidant activity of the methanolic extract of marsupium bark.

BIOTECHNOLOGY AND PHYSIOLOGY

The natural regeneration of *Pterocarpus marsupium* takes place by means of the seed but the germination percentage is only 30% and very low (Kalimuthu and Lakshaman, 1995). The native natural stands of tree are fast disappearing (Wilkins, 1991). The conventional seed and vegetative propagation of the tree has not been very successful due to hard fruit coat, less germinability together with poor viability (Venkataramaiah et al., 1980). Bharmukh and Nikam (2008) studied the seed germination of *Pterocarpus marsupium* and reported that 30 min. scarification treatment with concentrated H_2SO_4 is found fruitful to induce seed germination up to 85% with highest vigour index of 3.3. Due to overexploitation of the tree for its various useful applications coupled with low germinability, *Pterocarpus marsupium* has been included in the list of depleted plant species (Choudhuri and Sarkar, 2002). Inevitably, therefore, its propagation and multiplication through tissue culture technique is urgently needed (Anis et al., 2005). There are some earlier reports on the regeneration of *Pterocarpus marsupium* employing cotyledonary node explants, but reports lacked in the data for number of roots, and their length (Anis et al., 2005 and Chand and Singh, 2004).

Chand and Singh (2004) raised this plant *in vitro* by using cotyledonary nodal explants from 20 day old axenic seedling. They obtained the regeneration frequency 85% and 9.5 shoots per explant on MS medium supplemented with 4.44 μ M BA and 0.26 μ M NAA. Husain et al., (2007) developed a protocol to regenerate the *Pterocarpus marsupium* using 'Thidiazuron'. MS medium supplemented with 0.1-10 μ M thidiazuron successfully produced the multiple shoots from cotyledonary nodes and obtained highest regeneration frequency 90% and much maximum number of shoots 15.2 \pm 0.20 per explant on MS medium supplied with 0.4 μ M thidiazuron. Distabanjong and Geneve (1997) inoculated the nodal explant on the MS medium showing differential response to all the three cytokinins (BA, Kin and 2iP) and noticed that nodal explant taken from the 18 day old axenic seedling showed better response for shoot induction as compared to 6, 12 and 24 days old seedlings. They also noticed that the age of the seedlings plays an important role in morphogenesis. Husain et al., (2008) propagated this plant through tissue culture technique using nodal explants from 18 day old axenic seedling. They obtained highest regeneration frequency (85%) and maximum number of multiple shoots (8.6). The length of the shoot was increased on MS medium supplied with 4.0 μ M 6-benzyl-adenine (BA), 0.5 μ M indol three acetic acid (IAA), and 200 μ M adenine sulphate (ADS).

Raju and Raju (1999) studied the distribution patterns of rare earth metals, thorium and uranium in three species of *Pterocarpus*- *P. santalinus*, *P. marsupium* and *P. dalbergioides*. They reported that, concentration of these metals was highest in the heart wood than the leaves. The concentration of uranium and thorium was quite high in the heart wood of *P. santalinus* than other two species.

SUMMARY

Indian Kino, *Pterocarpus marsupium* belonging to the family fabaceae is scared potential anti-diabetic drug since ancient times. The heart wood of this leguminous tree is medicinally important and posses novel anti-diabetic principle. Different flavons and flavonoids have been isolated and characterized as main phytoconstituents responsible for the well known sugar lowering effect possessed by this plant. The plant possess various pharmacological properties and the drug is used as astringent, anti-inflammatory, haemostatic, anthelmintic, in chest pain, body pain and in indigestion, in diabetic anemia, elephantiasis, erysipelas, urethrorrhea, anti-cataract, hyperglycemic, anti-hyperlipidemic, cardiotoxic activities, hepato-protective and ophthalmopathy. The plant show less germination capacity (30%) due to hard seed coat and less viability and conventional vegetative regenerations methods are not successful. The tree is enrolled in the "Red list" due to over-exploration for its various medicinal applications and is on the verge of extinction. Therefore, the propagation of this natural anti-diabetic drug by employing different techniques has become inevitable and urgent need.

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