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Pterocarpus Marsupium for the Treatment of Diabetes and Other Disorders

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Abstract

Pterocarpus marsupium Roxb., is a deciduous tree commonly grows in India and Sri Lanka. It is well known to Ayurvedic medicine because of its curative and lenitive properties. The heartwood extract of *P. marsupium* is reported to have many pharmacological compounds and used in treatment of various disorders. Literature was collected via electronic search (PubMed, ScienceDirect) from published articles that reports medicinal properties of *P. marsupium*. A significant research of antidiabetic activities and other medicinal properties of *P. marsupium* combined with bioactive compounds isolated from the plant will provide leads for the discovery of new drugs for the management of many disorders with minimal side effects.

Keywords: *Pterocarpus marsupium;* Vijayasar; Anti-diabetic; Antioxidant

Introduction

Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. The increasing worldwide incidence of diabetes mellitus in adults constitutes a global public health burden. Out of the two types of diabetes, the incidence of non-insulin dependent diabetes mellitus is much higher than the insulin dependent diabetes mellitus. Even insulin therapy does not reinstate a permanent normal pattern of glucose homeostasis and carries an increased risk of atherogenesis and hypoglycemia. Plants are used as traditional remedies in one or other form for the treatment of diabetes. There has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Drugs derived from natural products have played a major role in the development of pharmaceutical treatments for diabetes. *Pterocarpus marsupium* Roxb., is a deciduous tree commonly grows in Sri Lanka and India [1]. It is popularly known as Vijaysar in Hindi and is a valuable medicinal plant, used mainly in Ayurveda, for the treatment of diabetes [2-4]. It is well known to Ayurvedic medicine because of its curative and lenitive properties. Its flowers are employed against fever, its heartwood as depurative, hemostatic, and rejuvenating, its wood is used for chest and body pain as well as indigestion, etc. The gum (kino) obtained from the tree is used in diarrhea, pyrosis and toothache. Bruised leaves are used externally for boils, sores, and various skin diseases. The water kept in tumblers made out of the wood of this plant is said to be beneficial for chest pain and diabetes. The bark of *P. marsupium* is very effective in preventing cataract formation and reducing hyperglycemia in alloxanized diabetic rats [1] and the heartwood is useful as hypolglycemic agents [5].

Methodology

A systematic search was carried out in Pub Med, Scopus and Web of Sciences using a combination of Boolean operators. Peer reviewed papers in English on the keyword *Pterocarpus marsupium* were retrieved and evaluated based on titles and abstracts. The retrieved papers were managed using Mendeley and the data were consolidated.

Anti-diabetic activity

Aqueous extract of heartwood of *Pterocarpus marsupium* was given orally to alloxan induced type-2 diabetic rabbit model (Pradhan et al., 2017). Both the fasting blood glucose (194.8±12.7 vs. 155.2±16.3) and postprandial blood glucose (191.6±23.2 vs. 149.2±14.5) were decreased indicating the hypoglycaemic effect of *P. marsupium*. Incubation of red blood cells with glucose in the presence of alcoholic extract of *P. marsupium* under high glucose conditions lead to reduction in the accumulation of intracellular sorbitol in a dose dependent manner. There was 50% reduction of sorbitol accumulation with alcoholic extract of was observed with IC50 151.00µg/ml and 105.12µg/ml for ascorbic acid [6]. Ethanolic extract of *P. marsupium* heartwood have antihyperglycemic activity in streptozotocin treated diabetic rats [7]. At 100 mg/kg dose levels, fasting blood glucose, oral glucose tolerance and serum insulin levels were recorded as 113±3.40mg/dl, 35930±102.9

AUC and 160±31.3ng/l respectively. Blood glucose lowering effect of *P. marsupium* heartwood was also reported. Anti-diabetic activity of *P. marsupium* Roxb. heartwood in alloxan induced diabetic rats using extracts obtained by optimized conventional and non-conventional extraction methods was evaluated by Devgan et al. [8]. Ultrasound-assisted extraction was proved to enhance the antidiabetic activity of *P. marsupium.* Mohan Kumar et al. [9] reported that the exposure of mouse pancreatic and muscle tissues to *P. marsupium* extract stimulated the insulin secretion and glucose uptake, respectively, in a concentration-dependent manner. Gairola et al. [10] found that the aqueous extract significantly reduces type 2 diabetes in rats and can prevent hyperinsulinemia and hypertriglyceridemia. Aqueous extract of *P. marsupium* has significantly decreased the fasting blood glucose (182.5±4.1mg/dL) in type 2 diabetic rat. It also decreased the postprandial hyperglycemia significantly (112.3±2.8mg/dL) as compared to diabetic control group (301.4±5mg/dL). *P. marsupium* modulated the inflammatory cytokine TNF-α in type 2 diabetic rats [11]. Dhanabal et al. [12] studied the antidiabetic activity of various subfractions of the alcohol extract of the bark of *Pterocarpus marsupium* Roxb. in alloxan-induced diabetic rats. The butanol subfraction of the alcohol extract of *P. marsupium* exhibits significant antidiabetic activity and corrects the metabolic alterations in diabetic rats. Mukhtar et al. [13] reported the hypoglycemic activity of *P. marsupium* wood at an oral dose of 250mg/kg in alloxan induced diabetic rats. The aqueous extract of *P. marsupium* significantly ($P<0.001$) reduced the blood sugar levels from 72.32±5.62 to 61.35±1.2mg% 2 h after oral administration of the extract and also significantly lowered the blood glucose in alloxan diabetic rats from 202.91±5.44 to 85.22±11.28mg% 21 days after daily oral administration of the extract [14]. Alloxan-diabetic rats fed with the ethanolic extract of *P. marsupium* wood for 5 days resulted in a significant lowering of fasting blood sugar level. There was a 5-fold increase in blood glucose level of alloxan to rats after injection compared to normal controls and feeding of the extract to alloxan-diabetic animals lowered the blood sugar by 70% as compared to the alloxan-diabetic controls [15].

Antioxidant activity

Many recent studies reveal that antioxidants capable of neutralizing free radicals are effective in preventing experimentally induced diabetes in animal models. In DPPH scavenging activity and ABTS·+ scavenging activity, IC50 values were found to be 138.3, 12.4, 13.5 and 47.8, 3.9, 4.2μg/mL for aqueous, methanolic extract of *P. marsupium* and standard ascorbic acid respectively. In α-amylase inhibition assay and α-glucosidase inhibition assay, IC50 values for standard Acarbose, aqueous and methanolic extract of heartwood were 44.09, 166.72, 48.20 and 45.17, 172.32, 48.12 respectively [16]. The effects of different fractions of heart wood of *Pterocarpus marsupium* on antioxidant enzyme like protein thiols and the efficacy of the extract for the protection of the renal function in alloxan induced diabetic rats was evaluated by Bhata, Nayak [17]. *P. marsupium* extract showed a promising antioxidant effect, as well as hypoglycemic activity. Aqueous extract of *P. marsupium* showed high antioxidant activity in all different assays used and also protected mitochondria against oxidative damage. It significantly reduced lactate dehydrogenase release along with reduction of lipid peroxidation [18]. The herbal extract mixture of *P. marsupium* and O. sanctum has succeeded in not only rectifying dyslipidemia but also in restoring the endogenous antioxidant levels to the pre-diabetic status in non-diabetic and alloxan induced diabetic adult female Wistar rats [19].

Anticancer activity

The cytotoxicity of *P. marsupium* aqueous extract was evaluated by Gosetti et al. [20] using calcein acetoxymethyl ester (calcein-AM) assays. Different cell lines were incubated for 24h with different concentrations of the aqueous heartwood extract. The IC50 values for cancer cells are comparable among the cell lines and are significantly lower (at least 50%) for the cancer cell lines than for non-tumoral cell lines, highlighting a selective cytotoxicity of the extract towards the cancer cells. α-dihydroxychalcone-glycoside (α-DHC) isolated from *P. marsupium* has effectively reduced nitric oxide and cytokine production by the LPS stimulated RAW 264.7 mouse macrophage cell line. The compound effectively attenuated the expression of inflammation-mediating enzymes COX-2 and iNOS at the mRNA as well as protein levels in a concentration dependent manner [21]. Pterostilbene isolated from *P. marsupium* was found to cause apoptosis in breast (MCF-7) and prostate (PC3) cancer cell lines. It also inhibited Matrix metalloproteinase 9 (MMP9) and α-methylacyl-CoA recemase (AMACR), two very well-known metastasis inducers [22].

Reproductive effects

Hugar et al. [23] has reported that *Pterocarpus marsupium* showed potential reproductive effects on testosterone propionate induced Polycystic Ovary Syndrome (PCOS) female albino rats and could be used as an alternative therapy in the treatment of PCOS.

Activity against cataract

The protective effect of *Pterocarpus marsupium* bark extracts against cataract in streptozotocin-induced diabetic male albino rats was investigated by Xu et al. [24]. The blood glucose was reduced up to 36% following treatment with bark extracts. The blood insulin and tissue GSH contents were substantially increased more than 100% in diabetic rats following treatment with extracts. Aldose reductase activity was reduced up to 79.3% in diabetic rats following treatment with extracts. he findings concluded that the use of *P. marsupium* bark extracts could be the potential therapeutic approach for the reduction of aldose reductase against diabetic cataract.

Activity against Ulcerative colitis

The effect of *P. marsupium* on acetic acid induced ulcerative colitis in rats was studied by Mathew et al. [25]. *P. marsupium*

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had significantly reduced colon inflammation and mucosal damage in the treated group. The COX-1/2 selective inhibitory activity of *P. Marsupium* (PM) extract was investigated by Hougee et al. [26]. PM extract, pterostilbene and resveratrol inhibited PGE2 production from LPS-stimulated human Peripheral Blood Mononuclear Cells (PBMC) with IC50 values of 3.2 +/- 1.3 microg/mL, 1.0 +/- 0.6 micro M and 3.2 +/- 1.4 micro M, respectively. In a COX-1 Whole Blood Assay (WBA) PM extract was not effective while in a COX-2 WBA, PM extract decreased PGE2 production indicating COX-2 specific inhibition (Table 1 & Table 2) [27-56].

Table 1: Pharmacological Activity of *Pterocarpus marsupium*

Activity	References
Antidiabetic	Bose and Sepaha [27]
Anti-diabetic	Sheehan et al. [5]
Anti-hyperlipidemic	Jahromi et al. [28]
Anti-hyperglycemic	Manickam et al. [29]
Antihyperglycemic	Vat et al. [14]
Hypoglycemic property	Dhanabal et al. [12]
COX-2 inhibition	Hougee et al. [26]
Hepatoprotective	Devipriya et al. [30]
Cardiotonic	Mohire et al. [31]
Hypoglycemic property	Karanjit et al. [32]
Regeneration of beta cells in pancreas	Badkhane et al. [33]
Anti-diabetic	Halagappa et al. [11]
Antihyperglycemic	Patil and Dattatraya [34]
Antihyperglycemic	Waghmare et al. [35]
Astringent property	Rizvi and Mishra [36]
Antidiabetic	Devgan et al. [8]
Regeneration of beta cells in pancreas	Khan et al. [37]
Antihyperlipidemic	Hilal, Kalyanaraman [38]
Hypoglycaemic	Pradhan et al. [39]
In-vitro lipid lowering	Singh et al. [40]

Table 2: Bioactive Compounds isolated from *Pterocarpus marsupium*.

Isolated compound	References
Pterostilbene	Haranath et al. [41]
5,4′-dimethoxy-8-methylisoflavonen (Isoflavone)	Mitra and Joshi [42]
selin-4(15)-en-1β,11-diol, β-eudesmol, erythrodiol-3-monoacetate and pterostilbene (sesquiterpene alcohol)	Adinarayana, Syamasundar [43]
Epicatechin	Sheehan et al. [5]
Epicatechin	Chakravarthy, Gode [44]
7-Hydroxy-6, 8-dimethyl flavanone-7-O-alpha-L-arabinopyranoside and 7,8,4′-trihydroxy-3′, 5′-dimethoxy flavanone-4′-O-beta-D-glucopyranoside	Tripathi, Joshi [45]
4,6,4′-trihydroxyaurone 6-O-rhamnopyranoside, 4,6,4′-trihydroxy-7-methylaurone 4-O-rhamnopyranoside (Aurone glycosides)	Mohan, Joshi [46]
Marsupsin, pterosupin, pterostilbene and liquiritigenin	Jahromi et al. [28]
Marsupsin, pterosupin, pterostilbene and liquiritigenin	Manickam et al. [29]
6-hydroxy-7-O-methyl-3-(3-hydroxy-4-O-methyl benzyl) chronan-4-one (Homoisofalvonoid)	Jain et al. [47]
2-hydroxy-2-benzylcoumaranone	Mathew, Subba Rao [48]
6-hydroxy-3,5,7,4′-tetramethoxyflavone 6-rhamnoside (flavonol glycoside)	Yadav, Singh [49]
Pterocarposide	Handa et al. [50]
Flavonoid C-glycosides	Maurya et al. [51]
7-O-alpha-L-rhamnopyranosyl oxy-4′-methoxy-5-hydroxy isoflavone	Anandharajan et al. [52]
Pterostilbene	Chakraborty et al. [22]
Pterolinus K and pterolinus L (phenanthrenedione and chalcone)	Wu et al. [53]

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Marsupsin, pterocarpin	Thara et al. [54]
Bijayasaline	Joshi et al. [55]
α-Dihydroxychalcone-glycoside	Chakraborty et al. [21]
Volatile compounds	Gosetti et al. [20]
3'-Hydroxypterostilbene	Majeed et al. [56]
Liquiritigenin	Yadav, Mishra [16]
Marsuposide	Singh et al. [40]

Conclusion

Major hindrance in amalgamation of herbal medicine in modern medical practices is lack of scientific and clinical data proving their efficacy and safety. This review article showed the anti-diabetic potential of a *P. Marsupium* for the management of hyperglycemia, along with good antioxidant activity. However limited data were available about the collective pharmaceutical property of *P. Marsupium*. This plant may provide leads for the discovery of new drugs for the management of many disorders with minimal side effects.

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