

## Hypoglycemic activity of *Pterocarpus marsupium* in patients with Type 2 diabetes mellitus

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### ABSTRACT

**Background:** Type 2 diabetes mellitus is a chronic disorder, and it requires drug treatment over a long period of time. Apart from synthetic drugs available in the market for the management of diabetes, there is voluminous literature pouring on indigenous medicine with claim for the utility in diabetes mellitus. *Pterocarpus marsupium* is one of the traditional medicinal plants with hypoglycemic activity, used by a lot of patients on a large scale. The objectives of the study were to compare the blood glucose lowering effect of *P. marsupium* as add-on therapy with oral hypoglycemic drugs in patients with Type 2 diabetes mellitus and to determine adverse events (if any).

**Methods:** The study was carried out at tertiary care hospital of Gwalior, Madhya Pradesh. Total of 56 old uncontrolled hyperglycemic (Type 2 diabetes mellitus) patients already taking oral hypoglycemic drugs were enrolled on the basis of inclusion and exclusion criteria. The duration of treatment with *P. marsupium* as add-on therapy with glimepiride+metformin or glimepiride+metformin+pioglitazone was 12 weeks with 4 weekly clinical attendances for review and collection of the drug. It was prospective, open, non-randomized, interventional, efficacy, and safety type of study, the dosage of *P. marsupium* wood powder being 2-4 g/day.

**Results:** At the end of treatment (12 weeks) with *P. marsupium* as add-on therapy, mean fasting blood glucose, postprandial blood glucose, and glycosylated hemoglobin were compared with baseline using student's paired t-test. Calculated p value for all parameter is <0.05, i.e., it is statistically significant.

**Conclusions:** *P. marsupium* is highly effective blood glucose lowering Indian traditional plant agent, its glycemic effect being comparable as add-on therapy in patients with Type 2 diabetes mellitus and free from any adverse event.

**Keywords:** *Pterocarpus marsupium*, Type 2 diabetes mellitus, Glimepiride, Metformin, Pioglitazone

### INTRODUCTION

The prevalence of diabetes mellitus is rapidly increasing all over the world, and it has become a global public health crisis.<sup>1</sup> According to International Diabetes Federation, 387 million people worldwide have diabetes and it is projected to reach 592 million by 2035.<sup>2</sup> Diabetes mellitus increases with aging. In 2010, the prevalence of diabetes mellitus in the United States was estimated to be 0.2% in individuals aged <20 years and 11.3% in individuals aged >20 years. In individuals aged >65 years, the prevalence of diabetes mellitus was 26.9%. Diabetes is a major cause of mortality, but several studies indicated that diabetes is likely unreported as a cause of death. In the United States, diabetes

was listed as the 7th leading cause of death in 2007; a recent estimate suggested that diabetes was the fifth leading cause of death worldwide and was responsible for almost 4 million deaths in 2010.<sup>3</sup>

A number of medicinal plants, traditionally used for over 1000 years named Rasayana are present in herbal preparations of the Indian traditional health care systems.<sup>4</sup> The World Health Organization has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as "Botanical Garden of the World."<sup>5</sup> In Indian systems of

medicine, most practitioners formulate and dispense their own recipes. More than one-third of Canadians are using complementary and alternative medicine (CAM) therapies, often without consulting or even informing their family physicians. It is important for family physicians to ask patients about their CAM use and provide evidence-based information about the safety and efficacy of commonly used CAM therapies.<sup>6</sup>

*Pterocarpus marsupium* has a long history of use in India as a treatment for diabetes. It is also known as the Indian kino tree or Malabar kino tree. It belongs to family Fabaceae of Plantae kingdom. Parts (heartwood, bark, leaves, and flowers) of the *P. marsupium* have long been believed to have medicinal properties in Ayurveda. The bark contains l-epicatechin. The heartwood yields liquiritigenin, isoliquiritigenin, alkaloid (0.017%), and resin (0.9%).<sup>7</sup> Ethyl acetate extract of powdered dried heartwood of *P. marsupium* revealed the presence of following constituents: (-) epicatechin (a flavonoid), pterosupin (a dihydrochalcone), marsupin (a benzofuranone), pterostilbene, liquiritigenin (a stilbene), isoliquiritigenin, (2S)-7-hydroxyflavanone, 7, 4'-dihydroxyflavone, p-hydroxybenzaldehyde, (2R)-3-(p-hydroxyphenyl)-lactic acid, and pm-33.<sup>8</sup> Pterostilbene, a constituent derived from wood of this plant caused hypoglycemia in dogs<sup>9,10</sup> showed that the hypoglycemic activity of this extract is because of presence of tannates in the extract. Flavonoid (epicatechin) fraction from *P. marsupium* has been shown to cause pancreatic  $\beta$ -cell regeneration.<sup>11</sup> Other mechanism of *P. marsupium* may be increase release of insulin from  $\beta$ -cells,<sup>12</sup> prevent insulin resistance<sup>13</sup> and hindering the absorption of glucose from intestine.<sup>10</sup>

## Objectives

1. Blood glucose lowering effect (change in fasting and postprandial blood glucose (PBG) and glycosylated hemoglobin (HbA1c) from baseline to 3 months of follow-up) of dry wood powder of *P. marsupium* as add-on therapy in patients of Type 2 diabetes mellitus.
2. To evaluate the number of patients reporting adverse events to study medication, type and duration of adverse events reported.

## METHODS

The study was conducted in tertiary care hospital, Gwalior, Madhya Pradesh, India, after approval of the protocol by Institutional Ethical Committee of Gajra Raja Medical College, Gwalior, Madhya Pradesh, India. The study was prospective, open, non-randomized, interventional, efficacy, and safety type of study.

### Patient selection

Patients were enrolled from Department of Medicine outpatient on the basis of inclusion and exclusion criteria.

### Inclusion criteria

1. Patients willing to give written informed consent and ready to come regularly for follow-up
2. Patients with Type 2 diabetes mellitus taking <50% of maximum dose of oral hypoglycemic drugs for last 3 months but with uncontrolled blood glucose level
3. Patients of >30 years of either gender
4. Fasting blood glucose (FBG) >126 mg/dl
5. PBG >180 mg/dl
6. HbA1c >7%.

### Exclusion criteria

1. Type 2 diabetes mellitus patients taking insulin
2. Type 1 diabetes mellitus patients
3. Patients of age of <30 years
4. FBG >230 mg/dl
5. Body mass index <18.5 kg/m<sup>2</sup>
6. Pregnant and lactating women
7. Patients with severe liver and/or kidney disease
8. Patients with complications of diabetes like retinopathy, nephropathy, diabetic foot, and coronary artery disease (CAD).

### Materials

Wood of *P. marsupium* was collected from an ayurvedic herb store at Gwalior, (Madhya Pradesh) and identified by research officer (botany) and confirmed by a test. It was to be made in fine powder form by grinding and provided to patients without encapsulation in air tight container with a capacity of 1 g spoon.

### Study design

The study was prospective, open, and non-randomized. The duration of drug treatment was 12 weeks, with 4 weekly clinical attendances for assessment and drug collection. The recommended dietary schedule was advocated to avoid dietary aberration. The patients were instructed to avoid the use of other drugs for any ailment without consulting the treating physician. If the patient developed any major ailment that required the institution of new treatment modalities, he/she was to be withdrawn from the trial.

The patients were enrolled after considering selection criteria. Free and written informed consent was obtained from each patient before entering the study. Patients were advised primary investigations (fasting and postprandial plasma glucose), secondary investigation (HbA1c), and some other investigations whichever are required at the start of the study. During the study, patients were advised to stick to their previous drug regimen (metformin 500 mg+glimepiride 1 mg daily or metformin 500 mg+glimepiride 1 mg+Pioglitazone 15 mg daily) prescribed by the physician. *P. marsupium* wood powder (starting dose 2 g/day in divided doses) was

added as add-on therapy and advice to take with previous drug regimen 30 minutes before meal. At each 4 weekly follow-up visit, primary measurements (FBG and PBG) were estimated and any adverse event(s) if encountered was thoroughly evaluated by a concerned physician and separately reported. Patients who tolerated *P. marsupium* powder with oral hypoglycemic drugs and have controlled blood glucose were continued on the same dose until the end of the study. Dose of *P. marsupium* was increased from 2 to 4 g/day (in divided doses) in unresponsive patients. After completion of 12 weeks therapy, each patient was advised for FBG, PBG and glycosylated hemoglobin (HbA1c). Total 56 patients were recruited for the study. Out of these, 4 patients dropped out from the study due to an unknown reason.

### Statistical analysis

The data of 52 patients were recorded in the structured proforma. Student's paired t-test was used to compare the mean of initial (baseline) 3 values of fasting and PBG (before the start of the study) with the mean 3 values of fasting and PBG (after the start of the study) and also to compare the value of HbA1c. Mean and standard deviation were obtained, and data are expressed as mean $\pm$ SD. p value was calculated using Epicalc statistical software. p<0.05 was considered as statistically significant and p<0.001 as statistically highly significant result.

## RESULTS

**Table 1: Age and gender wise distribution of Type 2 diabetes mellitus patients.**

Age (in years)	n (%)		
	Male	Female	Total
30-40	01 (04)	01 (03.70)	02 (03.83)
41-50	08 (32)	12 (44.44)	20 (38.46)
51-60	07 (28)	08 (29.62)	15 (28.84)
61-70	07 (28)	05 (18.51)	12 (23.07)
>70	02 (08)	01 (03.70)	03 (05.76)
Total	25	27	52

**Table 2: Distribution of Type 2 diabetes mellitus patients according to BMI.**

BMI (kg/m <sup>2</sup> )	n (%)		
	Male	Female	Total
<18.5 (lean)	-	-	-
18.5-24.99 (normal)	11 (44)	16 (59.26)	27 (51.92)
25-29.99 (pre-obese)	11 (44)	11 (40.74)	22 (42.30)
>30 (obese)	03 (12)	-	03 (05.77)
Total	25	27	52

BMI: Body mass index

### Adverse drug reactions

Out of 52 patients, 01 patient reports with the loss of appetite on 1st follow-up visit but not on a subsequent visit and 01 patient with weakness that was last for 7-10 days. Hypoglycemia was not reported in any case.

## DISCUSSION

This prospective, open, and non-randomized trial has ascertained the blood glucose lowering effect of *P. marsupium* as add-on therapy in patients with uncontrolled Type 2 diabetes mellitus. Mean FBG, PBG, and HbA1c at baseline and mean FBG, PBG, and HbA1c at the end of treatment with *P. marsupium* as add-on therapy with conventional oral hypoglycemic drugs was compared and calculated p<0.05 is highly significant for all these parameter. The safety aspect of *P. marsupium* was also established with the dosage up to 4 g/day. There was no episode of hypoglycemia occur in any patient. *P. marsupium* is the important herbal drug of various pharmacological properties and it requires further exploitation.

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**Table 3: Distribution of Type 2 diabetes mellitus patients on the basis of their antidiabetic therapy.**

Antidiabetic therapy	n (%)		
	Male	Female	Total
Glimepiride+metformin+ <i>Pterocarpus marsupium</i>	14 (56)	20 (74.07)	34 (65.38)
Glimepiride+metformin+ pioglitazone+ <i>Pterocarpus marsupium</i>	11 (44)	07 (25.93)	18 (34.62)
Total	25	27	52

**Table 4: Distribution of Type 2 diabetes mellitus patients on the basis of daily dose of *Pterocarpus marsupium* as add-on therapy.**

Daily dose	n (%)		
	Male	Female	Total
2 g	01 (04)	02 (07.40)	03 (05.76)
3 g	16 (64)	12 (44.44)	28 (53.84)
4 g	08 (32)	13 (48.14)	21 (40.38)
Total	25	27	52

**Table 5: Mean blood glucose before and after *Pterocarpus marsupium* as add-on therapy on every visit.**

Blood glucose	Sample size	Before <i>Pterocarpus marsupium</i> (baseline)			After <i>Pterocarpus marsupium</i>		
		8 weeks ago	4 weeks ago	During enrolment	After 4 weeks	After 8 weeks	After 12 weeks
FBG (mg/dl)	52	155.2	161.58	160.67	146.05	130.54	126.61
PBG (mg/dl)	52	227.1	245.36	248.19	212.47	194	189.85
HbA1c (%)	52	-	-	9.39	-	-	8.055

FBG: Fasting blood glucose, PBG: Postprandial blood glucose, HbA1c: Glycosylated hemoglobin

**Table 6: Effect of *Pterocarpus marsupium* as add on with glimepiride+metformin.**

Blood glucose	Sample size	Before (mean±SD)	After (mean±SD)	p-value
FPG (mg/dl)	34	160.12±30.57	135.25±32.35	p<0.05 (significant)
PBG (mg/dl)	34	245.54±70.8	201.82±43.09	p<0.05 (significant)
HbA1c (%)	34	9.40±1.79	7.97±1.23	p<0.001 (highly significant)

FBG: Fasting blood glucose, PBG: Postprandial blood glucose, HbA1c: Glycosylated hemoglobin, SD: Standard deviation

**Table 7: Effect of *Pterocarpus marsupium* as add on to glimepiride+metformin+pioglitazone.**

Blood glucose	Sample size	Before (mean±SD)	After (mean±SD)	p-value
FBG (mg/dl)	18	157.33±30.21	133.65±26.27	p<0.05 (significant)
PBG (mg/dl)	18	230.16±54.24	192.32±31.64	p<0.05 (significant)
HbA1c (%)	18	9.36±1.5	8.2±1.12	p<0.05 (significant)

FBG: Fasting blood glucose, PBG: Postprandial blood glucose, HbA1c: Glycosylated hemoglobin, SD: Standard deviation

**Table 8: Effect of *Pterocarpus marsupium* as add-on therapy.**

Blood glucose	Sample size	Mean±SD		p-value
		Before	After	
FBG (mg/dl)	52	159.15±30.38	134.7±30.31	p<0.001 (highly significant)
PBG (mg/dl)	52	240.22±65.77	198.53±39.66	p<0.001 (highly significant)
HbA1c (%)	52	9.39±1.68	8.05±1.19	p<0.001 (highly significant)

FBG: Fasting blood glucose, PBG: Postprandial blood glucose, HbA1c: Glycosylated hemoglobin, SD: Standard deviation

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