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## Evaluation of the hypoglycemic and hypolipidemic activity of *Butea monosperma* fruit in diabetic human subjects

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**Abstract:** Evaluation of the hypoglycemic activity of local *Butea monosperma* (*Palas papra*) fruit in normal and diabetic human volunteers was conducted. Sampling was accomplished in and around the city of Faisalabad, especially at the Khadija Mahmood Trust Hospital and at the University of Agriculture, Faisalabad, Pakistan. Volunteers were categorized into normal and diabetic subjects on the basis of their blood glucose levels. Male and female diabetic volunteers aged between 30 and 60 years participated in the study. All the diabetic volunteers suffered from diabetes type II, i.e. non-insulin-dependent diabetes mellitus (NIDDM). The subjects were divided into 5 groups as follows: Group A - Untreated normal subjects; Group B - Normal subjects who received powdered *B. monosperma* (3 g) in 30 mL of water for 30 days, orally; Group C - Control diabetic subjects; Group D - Diabetic subjects who received powdered (3 g) in 30 mL of water for 30 days, orally; and Group E - Diabetic subjects who received a 5-mg tablet b. I. d. of Daonil® (a standard oral antidiabetic drug) in 30 mL of water for 30 days. The oral administration of *B. monosperma* fruit to diabetic and normal subjects for 30 days decreased ( $P < 0.05$ ) blood glucose, urine sugar, and plasma glycoprotein levels, as well as the lipid profile and the activity of liver enzymes. In conclusion, the powder of the medicinal plant *B. monosperma* fruit can be considered an effective and alternative treatment for diabetes.

**Key words:** *Butea monosperma* fruit, glucose level, diabetic human volunteers

### Diyabetik insan deneklerinde *Butea monosperma* meyvesinin hipoglisemik ve hipolipidemik aktivitelerinin değerlendirilmesi

**Özet:** Normal ve diyabetik gönüllü insanlarda yerel *Butea monosperma* (*Palas papra*) meyvesinin hipoglisemik aktivitesinin değerlendirilmesi çalışılmıştır. Örnekleme Faisalabad şehri çevresindeki özellikle Khadija Mahmood Vakıf Hastanesi ve Pakistan, Faisalabad, Ziraat Üniversitesinde yapılmıştır. Gönüllüler, kan glukoz seviyelerine göre normal ve diyabetik denekler olarak kategorize edildi. 30 ve 60 yaş arası erkek ve kadın diyabetik gönüllüler çalışmaya katıldı. Tüm diyabetik gönüllüler tip II diyabetli yani insüline bağımlı olmayan diyabetliydi (NIDDM). Denekler 5 gruba ayrıldı. Grup A - Muamele görmemiş normal denekler; Grup B - *B. monosperma* meyvesini 30 gün boyunca toz halinde 30 mL su içinde 3 g olarak ağızdan alan normal denekler; Grup C - Kontrol diyabetik denekler; Grup D - 30 gün boyunca toz halinde 30 mL su içinde 3 g olarak ağızdan alan diyabetik denekler; Grup E - 30 gün boyunca 30 mL su içinde 5 mg Daonil® tablet (oral olarak alınan standart bir antidiyabetik ilaç) alan diyabetik denekler. 30 gün boyunca diyabetik ve normal denekler tarafından *B. monosperma* meyvesinin ağızdan alınımı, lipid profili ve karaciğer enzim aktivitesi kadar kan şekeri, idrar şekeri ve plazma glikoprotein düzeylerini azaltmıştır ( $P < 0,05$ ). Sonuç olarak, tıbbi bitki *B. monosperma* meyvesinin toz hali şeker hastalığı tedavisi için etkili ve alternatif bir yöntemi olarak düşünülebilir.

**Anahtar sözcükler:** *Butea monosperma* meyvesi, glukoz seviyesi, diyabetik insan gönüllüleri

## Introduction

Diabetes mellitus is a major world health problem that currently affects an estimated 143 million people worldwide, and this number is growing rapidly (1). This disease is also a major health problem in Pakistan, where it is locally/popularly known as “sugar” disease. Between 5% and 7% of the adult population in Pakistan is affected by diabetes (2). This illness is a complex disorder characterized by hyperglycemia caused by the impaired metabolism of glucose, lipids, proteins, and glycoproteins, which in turn results from impaired insulin secretion and/or insulin action. Diabetes leads to structural changes in a range of cells, which later result in the long-term complications of this condition (3-5). There are 2 major types of diabetes, namely type I, the insulin-dependent diabetes mellitus (IDDM), and type II, the non-insulin-dependent diabetes mellitus (NIDDM). Subjects with IDDM abruptly start to manifest several symptoms, thus requiring insulin to control their condition. NIDDM develops insidiously, has milder symptoms, and can be frequently controlled by diet alone (6). The causes of both types of diabetes remain unknown, but current evidence suggests that both IDDM and NIDDM are a heterogeneous disorder that is expressed with age or via the influence of other factors such as obesity, diet, and sedentary lifestyle (7). Diagnosis of the disease is usually accomplished by measuring fasting plasma glucose levels (8). The range of normal plasma glucose level is considered to fall within the range 70 to 115 mg/dL (9), whereas the fasting plasma glucose level in diabetic patients is reported to be higher than 140 mg/dL (10).

Glycoproteins are carbohydrate-linked protein macromolecules present on the cell surface, the main component of animal cells. It is well documented that the oligosaccharide moieties of glycol proteins—i.e. hexose, hexosamine, fucose, and sialic acid—play an important role in protein stability, function, and turnover (11). A previous literature report has shown a significant rise in serum mucoprotein, hexosamine, sialic acid, and fucose levels in diabetic patients, and a parallel rise in glycoprotein has been observed with increasing severity of the disease (12). Analysis of the human diabetic basement membrane has shown both an absolute increase in glycoprotein levels and a different composition compared with the normal

human basement membrane. It has been reported that glucose is employed in insulin-independent pathways in diabetic individuals, leading to the synthesis of glycoproteins, and even mild insulin deficiency results in the thickening of the basement membrane (13).

Despite the availability of well-established antidiabetic drugs on the market, diabetes and its related complications remain a major medical problem. Recently, some medicinal plants have been reported to be useful in the treatment of diabetes worldwide, and they have been empirically employed as antidiabetic and antihyperlipidemic remedies (14,15). The antihyperglycemic effects of these plants are attributed to their ability to restore the function of the pancreatic tissues through increased insulin output. It is also thought that these plants can inhibit the intestinal absorption of glucose and facilitate the elimination of metabolites in insulin-dependent processes. More than 400 plant species exhibiting hypoglycemic activity have been reported in the literature, but only a small number of these plants have had their efficacy evaluated from a scientific and medical perspective (16,17). These herbal plants are widely prescribed because of their effectiveness, fewer side effects, and relatively low cost (18).

*Butea monosperma* belongs to the family *Fabaceae*. Its English name is “Bastard teak”, its vernacular name is “Parasa”, and it is commonly known as *Palaspapra* (19). It is frequently employed in central Asia as a herb and also in folk medicine. The fruit of *Buteamonosperma* has been shown to be rich in phytochemical substances such as butrin; butein; 3', 4', 7-trihydroxyflavone; palasonin; and stigmastrol-3  $\beta$ -D-glucopyranoside, which stimulate the stomach and the pancreas (20). Due to these active ingredients, this plant may be useful in the treatment of diabetes mellitus, which is not curable by conventional drugs. However, no scientific studies have been carried out in order to establish the hypoglycemic effects of *B. monosperma* (*Palas papra*) fruits. Thus, the present study examines the effects of powdered *B. monosperma* (*Palas papra*) fruits on serum glucose, Glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), lactate dehydrogenase (LDH), and plasma glycoprotein levels in normal and diabetic human volunteers.

## Materials and methods

### Plant material

Fruit of the *B. monosperma* plant was acquired from the local herbal market. The material was carefully washed with tap water, dried in the shade, powdered by means of a metallic pestle and mortar, packed inside sealed cellophane bags, and stored at 4 °C in a refrigerator for further study.

### Test subjects

For determination of all the blood parameters, normal human volunteers were selected from the Division of Education and Extension, University of Agriculture, Faisalabad; diabetic subjects were randomly selected from the Khadija Memorial Trust Hospital, Faisalabad (Punjab), Pakistan. This study was carried out in the period 2004-2005. Normal subjects were apparently healthy and had a normal glucose tolerance profile. Male and female diabetic volunteers were aged between 30 and 60 years, and they all suffered from diabetes type II, i.e. NIDDM. Most of the diabetic subjects were on different oral hypoglycemic agent(s), while others were on dietary control only.

### Experimental Design

The patient's history was recorded in the proper form, and diagnosis was confirmed by means of routine laboratory tests. Outside diabetic human volunteers suffering from diabetes type 2 and normal human volunteers participated in the experimental study. A total of 30 individuals were included in the study. These individuals were divided into 5 groups of 6 individuals each, as follows:

Group A: Untreated normal subjects.

Group B: Normal subjects who received powdered *B. monosperma* (3 g) in 30 mL of water for 30 days, orally.

Note: Our previous study proved that 3 g of *B. monosperma* fruit powder was a more effective dose than was 1 or 2 g in diabetic subjects (unpublished data).

Group C: Control diabetic subjects.

Group D: Diabetic subjects who received powdered *B. monosperma* (3 g) in 30 mL of water for 30 days, orally.

Group E: Diabetic subjects who received 5-mg tablet b.i.d. Daonil® (oral standard antidiabetic drug) in 30 mL of water for 30 days.

### Blood sample collection

Blood samples (5 mL) were collected in a syringe after 12-h fasting and were usually drawn from a vein from the back of the hand. The blood sample was allowed to clot for 20 min at refrigerator temperature and was then placed in a clean centrifuge tube. Lithium heparin was added, and the withdrawn blood was separated by centrifugation at 4000 rpm for 10 min to obtain plasma and serum. The processed blood was then placed in small clean bottles with the aid of a micropipette. The bottles were stored in a freezer until analysis.

### Biochemical analysis

Blood glucose was determined by means of a glucometer (Glucotrend Glucometer, Roche Milpitas, California, USA). Urine glucose was assessed in fresh urine by employing glucose indicator sticks (Boehringer Mannheim, Germany). The plasma insulin was assayed by the ELISA method (Awareness Technologies, USA), using the Boehringer Mannheim kit. Hexose and hexosamine were estimated by the colorimetric method (21). Sialic acid and fucose were also determined (22,23).

Glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), and lactate dehydrogenase (LDH) were measured using a photometer CH-100 plus (Dae Guang Meditech. Ltd). GOT and GPT were estimated using the NADH oxidation reaction method (24). The serum (0.1 mL) was added to 1.0 mL of auto-reagent and incubated at 37 °C for 1 min. The absorbance was measured at 340 nm, and the values were expressed as unit L<sup>-1</sup>. LDH was determined by spectrophotometry (25). To this end, 1 mL of the auto-reagent was added to 0.025 mL of the serum, and the resulting mixture was incubated at 37 °C for 1 min. The absorbance was measured at 340 nm, and the value was expressed as unit L<sup>-1</sup>.

Plasma lipid peroxidation was spectrophotometrically assayed by the thiobarbitonic acid reactive substances (TBARS) method (26). Triglycerides (TGLs) were determined by the enzymatic calorimetric method (27). Cholesterol was also measured by the same method (28). Low-density

lipoproteins (LDLs) were precipitated by adding phosphotungstic acid and magnesium ions to the sample. Centrifugation left only the high-density lipoproteins (HDLs) in the supernatant; the cholesterol content was then determined (29). These tests were carried out in the laboratory of the Khadija Memorial Trust Hospital in Faisalabad, by using the auto-analyzer Express plus, Ciba Corning USA. The calculations were accomplished automatically.

**Chemical analysis**

Random samples of the test *B. monosperma* powder were further ground and analyzed for moisture, crude protein, crude fat, crude fiber, total ash, and total soluble carbohydrates, in the Food Testing Laboratory, Institute of Animal Nutrition and Food Technology, University of Agriculture, Faisalabad (30). The mutagenicity and carcinogenic potential tests carried out on living cells of *B. monosperma* fruits were performed at the National Institute for Biotechnology and Genetics Engineering, Faisalabad, Pakistan. The study was planned with the permission of the University’s ethical committee for human care.

**Statistical analysis**

All data are expressed as means ± S.E. Significant differences among the groups were determined by one way analysis of variance (ANOVA) using the SPSS version 9.5 (SPSS, Cary, NC, USA) statistical analysis program. A P value of <0.05 was considered a significant difference among groups.

**Results**

The chemical composition of the *B. monosperma* fruit powder is given in Table 1. Chemical analyses indicate that the fruit does not have any carbohydrate

Table 1. Proximate composition (on dry matter basis) of the *Butea monosperma* fruit powder.

Items	Percentage
Moisture	5.87
Ash	6.6
Proteins	0.64
Carbohydrates	Nil
Fats	Traces

or fat contents; however, it contains 6.6% total ash. The plant material appeared to be a relatively safe drug for human use as it is devoid of any mutagenic activity.

A significant decrease in the blood glucose and urine sugar levels as well as a rise in the plasma insulin level were observed in *B. monosperma*-treated individuals compared with the corresponding control subjects. Treatment of diabetic individuals with *B. monosperma* and Daonil® tended to bring these levels close to normal values (Table 2). The effect of the *B. monosperma* powder (3g) was found to be more pronounced than that of Daonil® (5 mg tablet).

Table 2. Effect of the *Butea monosperma* powder on changes in the levels of blood glucose, plasma insulin, and urine sugar of normal and diabetic individuals following fasting.

Groups*	Blood glucose mg dL <sup>-1</sup>	Plasma insulin μU mL <sup>-1</sup>	Urine sugar
A	88.8 ± 8.50 <sup>d</sup>	25.75 ± 2.50 <sup>a</sup>	NIL
B	77.61 ± 6.70 <sup>e</sup>	26.00 ± 2.60 <sup>a</sup>	NIL
C	170.5 ± 15.7 <sup>a</sup>	11.50 ± 1.02 <sup>d</sup>	+++
D	91.20 ± 6.98 <sup>c</sup>	23.01 ± 2.15 <sup>b</sup>	NIL
E	99.50 ± 5.97 <sup>b</sup>	20.25 ± 2.0 <sup>c</sup>	Traces

Means in the same columns bearing different superscripts were significantly (P < 0.05) different

+++ : Indicates more than 2% sugar

- \* A: Untreated normal subjects;
- B: Normal subjects who received *B. monosperma* (3 g);
- C: Control diabetic subjects;
- D: Diabetic subjects who received *B. monosperma* (3 g);
- E: Diabetic subjects who received Daonil®.

The results depicted in Table 2 indicate that there was a significant (P < 0.05) effect of the *B. monosperma* fruit powder on the lipid profile of diabetic individuals. Upon treatment with the fruit powder, the LDL levels significantly (P < 0.05) increased, whereas the HDL-cholesterol levels markedly (P < 0.05) decreased in diabetic subjects (Table 3). When the diabetic participants were treated with *B. monosperma* powder or Daonil® for 30 days, the LDL level decreased (P < 0.05), whereas the HDL-cholesterol level increased (P < 0.05), in both cases.

Table 3. Effect of the *Butea monosperma* powder on changes in the serum lipid profile of normal and diabetic individuals following fasting.

Lipid Profile (mg dL <sup>-1</sup> )	GROUPS*				
	A	B	C	D	E
Lipid Peroxidation	25.5 <sup>bc</sup> ± 4.5	22.3 <sup>c</sup> ± 3.8	41.0 <sup>a</sup> ± 7.1	31.4 <sup>b</sup> ± 2.8	32.8 <sup>b</sup> ± 5.7
Cholesterol	155 <sup>b</sup> ± 4.80	148.40 <sup>b</sup> ± 7.50	200.8 <sup>a</sup> ± 24.25	158 <sup>b</sup> ± 8.78	165 <sup>b</sup> ± 7.50
Triglycerides	150 <sup>b</sup> ± 20.0	134 <sup>b</sup> ± 13.51	209.19 <sup>a</sup> ± 24.0	175 <sup>b</sup> ± 19.30	190.40 <sup>b</sup> ± 25.00
HDL	55.09 <sup>a</sup> ± 1.70	59.10 <sup>a</sup> ± 2.00	36.08 <sup>c</sup> ± 8.10	45.00 <sup>b</sup> ± 13.8	42.10 <sup>b</sup> ± 3.30
LDL	70.30 <sup>b</sup> ± 30.00	65.20 <sup>b</sup> ± 18.10	112.05 <sup>a</sup> ± 30.00	72.90 <sup>b</sup> ± 20.00	82.25 <sup>b</sup> ± 21.00

Means in the same rows bearing different superscripts were significantly ( $P < 0.05$ ) different

\* A: Untreated normal subjects; B: Normal subjects who received *B. monosperma* (3 g); C: Control diabetic subjects; D: Diabetic subjects who received *B. monosperma* (3g); E: Diabetic subjects who received Daonil®.

Markedly lower hexose and hexosamine, sialic acid, and fucose levels were recorded in the plasma of *B. monosperma*-treated groups compared with control diabetic subjects (Table 4). Oral treatment with *B. monosperma* and Daonil® significantly ( $P < 0.05$ ) restored the altered levels of glycoprotein components in diabetic individuals.

Treatment with the *B. monosperma* powder reduced ( $P < 0.05$ ) the GOT, GPT, and LDH activities in groups B and D compared with the corresponding controls (groups A and C, Table 5). Administration of the *B. monosperma* powder to group B individuals brought the GOT, GPT, and LDH values down by 5.12%, 4.48%, and 8.51%, respectively. The tested plant also decreased GOT, GPT, and LDH values in group D subjects by

70%, 49.7%, and 76%, respectively. Similarly, the standard drug reduced the GOT, GPT, and LDH values of group E individuals to almost normal, by 64%, 44.85%, and 71.6%, respectively.

## Discussion

Herbal medicine has always played a key role in the health system, and so we decided to study the hypoglycemic effect of *B. monosperma* fruit, in order to ratify its traditional use for the control of diabetes mellitus in humans. Countless studies have demonstrated that a variety of medicinal plants effectively lower glucose levels in diabetic animals (31,32).

Table 4. Effect of the *Butea monosperma* powder on changes in the plasma glycoprotein levels of normal and diabetic individuals following fasting.

Glycoprotein Components (mg dL <sup>-1</sup> )	GROUPS*				
	A	B	C	D	E
Hexose	99.20 <sup>d</sup> ± 3.88	97.80 <sup>d</sup> ± 6.50	150.8 <sup>a</sup> ± 7.10	117.40 <sup>b</sup> ± 4.95	110.55 <sup>c</sup> ± 4.50
Hexosamine	80.25 <sup>d</sup> ± 3.90	78.40 <sup>d</sup> ± 3.51	106.19 <sup>a</sup> ± 7.12	90.20 <sup>b</sup> ± 3.70	96.40 <sup>c</sup> ± 3.65
Sialic acid	60.01 <sup>d</sup> ± 2.70	58.12 <sup>d</sup> ± 3.50	80.05 <sup>a</sup> ± 4.10	65.90 <sup>b</sup> ± 2.48	69.20 <sup>c</sup> ± 3.30
Fucose	34.35 <sup>d</sup> ± 1.75	32.23 <sup>d</sup> ± 1.75	49.25 <sup>a</sup> ± 2.45	40.09 <sup>b</sup> ± 1.70	44.15 <sup>c</sup> ± 1.96

Means in the same rows bearing different superscripts were significantly ( $P < 0.05$ ) different

\* A: Untreated normal subjects; B: Normal subjects who received *B. monosperma* (3 g); C: Control diabetic subjects; D: Diabetic subjects who received *B. monosperma* (3 g); E: Diabetic subjects who received Daonil®.

Table 5. Effect of the *Butea monosperma* fruit powder on glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, and lactate dehydrogenase in normal and diabetic subjects following fasting.

GROUPS	(Unit L <sup>-1</sup> )		
	GOT	GPT	LDH
A	78 ± 3.0 <sup>d</sup>	67 ± 4.3 <sup>d</sup>	47 ± 8.1 <sup>d</sup>
B	74 ± 4.5 <sup>d</sup>	64 ± 2.6 <sup>d</sup>	43 ± 2.8 <sup>d</sup>
C	290 ± 2.1 <sup>a</sup>	165 ± 2.7 <sup>a</sup>	317 ± 25.9 <sup>a</sup>
D	87 ± 4.1 <sup>c</sup>	83 ± 6.0 <sup>c</sup>	76 ± 13.5 <sup>c</sup>
E	104 ± 11.3 <sup>b</sup>	91 ± 3.8 <sup>b</sup>	90 ± 10.5 <sup>b</sup>

Means in the same rows bearing different superscripts were significantly ( $P < 0.05$ ) different

\* A: Untreated normal subjects;

B: Normal subjects who received *B. monosperma* (3 g);

C: Control diabetic subjects;

D: Diabetic subjects who received *B. monosperma* (3 g);

E: Diabetic subjects who received Daonil®.

The oral treatment of diabetic subjects with the *B. monosperma* fruit powder for 30 days caused a significant ( $P < 0.05$ ) antihyperglycemic effect. The capacity of the *B. monosperma* fruit to significantly decrease elevated blood glucose levels to almost normal levels is an essential trigger for the liver to reverse to its normal homeostasis in experimental diabetic patients. Moreover, this fact indirectly indicates that the antidiabetic effect of the *B. monosperma* fruit is partly due to insulin release from the existing cells of the pancreas. In another study, a traditional plant (*Artemisia herba-alba*) was employed for the conventional therapy of diabetes mellitus, and this plant was reported to produce a significant ( $P < 0.05$ ) hypoglycemic effect in both normal and diabetic rabbits (33). The aforementioned study indicated that the said plant acts as a hypoglycemic agent, either by stimulating pancreatic  $\beta$  cells to release more insulin into the bloodstream, thereby increasing glycogen deposition in the liver and reducing glucose levels, or by increasing the number of insulin receptors (34,35). The *B. monosperma* fruit might produce the same effect in terms of the prevention of hyperglycemia, and it can significantly reduce the blood glucose levels in normoglycemic and hyperglycemic subjects. The

possible action mechanism of the *Buteamonosperma* fruit could be correlated with the reminiscent effect of the hypoglycemic sulfonylurease, which promotes insulin secretion by closure of  $K^+$  —ATP channels, membrane depolarization, and stimulation of  $Ca^{2+}$  influx, an initial key step in insulin secretion.

Clinical and experimental evidence suggests that free-radical-mediated oxidative processes are involved in the pathogenesis of diabetic complications. An increase in free radical production can lead to a hyperglycemia-induced enhancement in glucose autoxidation and protein glycation. There is growing evidence that oxidative stress is implicated in cardiac dysfunction, culminating with heart failure in diabetes (36). It has been observed that over 75% of early deaths in diabetes are related to coronary artery disease caused by abnormal lipid metabolism, which often leads to an altered lipid profile in the victim (37). In this study, administration of the *B. monosperma* fruit for 30 days altered ( $P < 0.05$ ) the lipid profile of the diabetic individuals compared with untreated groups. The diabetic subjects had higher ( $P < 0.05$ ) serum triglycerides, LDL-cholesterol, and total cholesterol levels compared with normal subjects. This is consistent with the findings of another study (38) reporting elevated levels of total cholesterol and LDL-cholesterol in STZ-diabetic rats. In that study, these biochemical indices decreased ( $P < 0.05$ ) in diabetic rats following administration of the *Cocculus hirsutus* extract. Increased lipid accumulation in the diabetic group and its decrease in the treated groups show a parallelism with the insulin effect on lipid metabolism. While insulin deficiency causes the usage of lipid stores in the adipose tissue, it also results in lipid accumulation in the liver by increasing the amount of triglyceride stores there. Lipid peroxidation is one of the characteristic features of chronic diabetes. The excess free radicals may react with polyunsaturated fatty acids in cell membranes, leading to lipid peroxidation and consequent elevated free radical production. Insulin secretion is also closely associated with lipoxygenase-derived peroxides. Low lipoxygenase-derived peroxide levels stimulate insulin secretion. However, uncontrolled lipid peroxidation may take place when the concentration of endogenous peroxides increases, thus resulting in cellular infiltration and islet cell damage in diabetes (39). In agreement with previous studies that have used the

TBARS assay as an index of lipid peroxidation (40), we found an increase in TBARS levels in diabetic patients. In the present study, the *Buteamonosperma* fruit-treated diabetic individuals had lower ( $P < 0.05$ ) TBARS levels compared with those of untreated groups.

The liver is primarily responsible for producing a large amount of glycoproteins present in the blood. The biosynthesis of the carbohydrate moieties of glycoproteins forms the insulin-independent pathways for glucose-6-phosphate utilization. However, insulin deficiency during diabetes produces derangement of glycoprotein metabolism, resulting in the thickening of the basal membrane. The increased glucose availability in diabetic individuals accelerates glycoprotein synthesis, thereby enhancing hexose, hexoamine, and fucose formation and consequent glycoprotein accumulation (41).

Changes in the glycoprotein concentration and composition of various proteins in diabetic patients have been correlated with hyperglycemia, which in turn causes the early functional alterations in the peripheral nerves, kidney, and retina that precede the development of characteristic diabetic pathology in these susceptible sites (12). A study has reported that streptozotocin-induced diabetic rats exhibit a significant modification in the connective tissue macromolecules, and insulin has been shown to increase the incorporation of glucose in the rat submaxillary gland (13). The requirement of insulin for the biosynthesis of the carbohydrate moiety of mucoproteins from glucose is thus evident. Previous reports suggest that the plasma concentrations of glycoproteins are significantly increased in diabetic animals (13,42). The elevated levels of plasma glycoprotein components in the present study may be due to their secretion from cell membrane glycoconjugates into the circulation.

The elevation of serum glycoprotein levels with a disproportionate increase in the level of serum protein-bound fucose has been reported. Studies have also indicated that serum and hepatic fucosyltransferase and fucosidase activities are increased in streptozotocin-induced diabetic rats (43). In diabetes, 3 serum proteins, namely haptoglobin, alpha 1-acid glycoprotein, and alpha 1-antitrypsin, synthesized in the liver are mainly responsible for the

increase in bound fucose levels (44). The present study also suggests that the enhanced levels of fucosylated proteins in diabetic subjects could be due to increased synthesis and decreased degradation of these proteins.

Sialic acids represent a group of 30 derivatives of neuraminic acid with different substituents at the amino residue and alcoholic hydroxyl groups. They are located at the nonreducing ends of glycoproteins, glycolipids, and polysaccharides (45). Alteration in sialic acid contents in certain tissues and in the serum of diabetic patients and animals has been reported (46). In diabetes mellitus, the serum concentration of sialic acid was found to increase significantly, especially in poorly controlled and long-term cases (46). A significantly higher level of plasma total sialic acid was observed in our diabetic subjects compared with the treated groups. Various factors might cause an elevation in the concentration of plasma sialic acid. Among them is an increase in the synthesis of this acid in insulin-independent tissues such as the liver and the brain and an increase in the activity of sialyltransferase, which transfers the sialic acid residues to the glycolipids and glycoproteins (47). In the present study, treatment with the *B. monosperma* fruit powder reduced the sialic acid content in the plasma of diabetic individuals. The antidiabetic action of the *B. monosperma* fruit powder is mediated via an enhancement in insulin action, which is allowed by the increased insulin levels in diabetic subjects treated with the *B. monosperma* fruit powder. This mechanism may be responsible for the reversal of changes in carbohydrate moieties of glycoproteins.

In diabetes, protein synthesis ceases and protein catabolism increases. Liver cell destruction itself impairs the permeability of the liver cell membrane. As a result, cytoplasmic enzymes such as GOT, GPT, and LDH pass into blood plasma, and their activities in the serum are enhanced (48). The increase in the serum activities of the secretion enzymes GOT, GPT, and LDH, which are formed in the liver and released into the bile, provides evidence that the liver has lost its secretion function (49). In the present study, a decrease in the serum GOT, GPT, and LDH levels of diabetic subjects treated with the *B. monosperma* fruit powder may prevent hepatic injury associated with diabetes.



## Conclusion

Administration of the *B. monosperma* fruit powder to diabetic subjects has a beneficial effect on the carbohydrate moieties of glycoproteins, in addition to its antidiabetic effect. Our results revealed the potential application of the *B. monosperma* fruit powder as an alternative medicine for the better control, management, and prevention of diabetic mellitus progression. Further biochemical and pharmacological investigations are needed to elucidate the precise action mechanism of this medicinal plant.

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