EFFECT OF *BUTEA MONOSPERMA* (*PALAS PAPRA*) FRUIT ON BLOOD GLUCOSE AND LIPID PROFILES OF NORMAL AND DIABETIC HUMAN VOLUNTEERS

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Summary

Butea monosperma fruit is used for different medicinal purposes. However, the scientific studies to evaluate its effect on blood glucose levels and lipid profiles in normal and diabetic human volunteers have not been conducted so far. Groups of 16 normal and 16 diabetic subjects were used in this study. Each group was further divided into four sub groups. Three sub groups in each group received an oral dose of 1, 2 & 3 gm of powdered *Butea monosperma*, while one normal subgroup received carboxy methyl cellulose (CMC) and one diabetic sub group was given Daonil®. The blood glucose and lipid profiles were estimated on 0, 8, 15 and 21 days post dose. This study indicated a significant decrease ($P<0.05$) in 2 hr post prandial blood glucose on 21st day in the diabetic sub groups treated with 2 and 3gm of powdered *B. monosperma*. While oral administration of *B. monosperma* did not produce any significant change in the blood glucose of normal volunteers. A significant decrease in total cholesterol was observed in normal and diabetic sub groups on day 21st after treatment with 2 and 3 gm of powder. The triglycerides levels of diabetic patients treated with 2 and 3 gm of powdered *B. monosperma* were significantly reduced at day 15 and 21 post treatment. Both normal and diabetic groups (who received 2 and 3 gm of plant powder) exhibited a significant decrease in total lipids on day 21st. One normal and diabetic sub group (who received 3 gm of plant drug) indicated significant lower LDL-cholesterol at day 21. In contrast, one normal and diabetic sub group treated with same dose exhibited a significant rise in HDL-cholesterol. This study indicates that *Butea monosperma* might have important hypoglycemic & hypolipidemic properties that may ultimately be used as successful therapies for treatment of diabetes and obesity in the general public.

Key words: *Butea monosperma*, diabetes, lipids, cholesterol, humans.

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Introduction

Diabetes mellitus has been found to be one of the major health problems in Pakistan and a well established major risk factor of coronary heart disease (CHD). In Pakistan, 5-7% of adult population has appeared to be more affected (1). The report of the International Conference on Nutrition (2) has suggested that an "apparent epidemic of diabetes has occurred in adults of 30-62 years of age throughout the world and the trend is strongly related to life style and socio-economic change which concerns mainly NIDDM. A high prevalence (10-20 per cent) is seen in some urban Indian and Chinese societies. Currently, nutritional guide-lines for the management of diabetes have focused attention on the importance of increasing the carbohydrate and fibre in the diet. Experimental studies have indicated that both these measures may be very valuable in achieving better diabetic control and reducing serum lipids. Lipids are the building blocks of any of the fats or fatty substances found in animals and plants. Lipids are used as hormones that play roles in regulating metabolism of our body (3). Lipid levels may be affected by diet, exercise, smoking, certain medication e.g. beta blockers, thiazide diuretics, glucocorticoids and concurrent disease states, e.g. kidney and liver diseases.

A lipid profile usually include total lipids, triglycerides, total cholesterol, low density lipoprotein cholesterol (LDL-cholesterol), high density lipoprotein cholesterol (HDL-cholesterol). Factors such as age, sex, and genetics influence lipid profile (4). Certain aspects of lifestyle, including diet, level of physical activity, level of diabetes control, and smoking status, also affect lipid profile. Some medical conditions can raise or lower cholesterol and triglycerides levels.

Modern researches on indigenous medicinal plants have revealed the presence of active principles which could prove useful for treating many diseases including diabetes (5, 6). However, still a substantial number of our indigenous plants and herbs await exploration by the modern screening methods, especially in the human patients. *Butea monosperma,* commonly known as Palas papra has been commonly used for different medicinal purposes including diabetes mellitus and coronary heart disease (CHD). However, the scientific studies to evaluate its hypoglycemic/ hypolipidemic properties are still awaited in human volunteers.

Materials and Methods

Fruit of *Butea monosperma*, commonly known as Palas papra in Pakisatn, was obtained from local herbal market of Faisalabad (Pakistan). They were carefully washed with tap water, dried under the shade, powdered in metallic pastille mortar and stored in the well closed cellophane bags at 4ºC in a refrigerator. The mutagenecity and carcinogenic potential tests for living cells of *Butea monosperma* fruit have been done at National Institute for Biotechnology and Genetic Engineering, Faisalabad, Pakistan.

For the determination of blood glucose levels, groups of 16 normal and 16 diabetic subjects were selected randomly from University of Agriculture Faisalabad and Khadija Memorial Trust Hospital Faisalabad city respectively. Normal subjects were apparently healthy and showed normal glucose tolerance and lipid profiles.

The diabetic volunteers were of both sexes and their ages ranged from 30-60 years. All the volunteers were suffering from the type II i.e. non-insulin dependent diabetes mellitus (NIDDM). They were found to be mostly on different oral hypoglycaemic agent (s), while others on the dietary control only. History of each patient was recorded in a proper performa and the diagnosis was confirmed with the proper laboratory tests. Outdoor diabetic human volunteers suffering from type 2 diabetes mellitus were motivated for better treatment. The normal human volunteers were divided into 4 groups comprising of four volunteers in each group. Carboxy Methyl Cellulose (CMC) Fiber was given to one group while other groups were treated orally with 1, 2 and 3 grams of *B. monosperma* fruit powder, respectively with 30 ml of water.

The diabetic human volunteers were also divided into 4 subgroups, each comprising of 4 diabetic volunteers. The diabetic volunteers of one sub-group were kept as control and received Daonil® 5mg tablet b.i.d orally. The diabetic human volunteers of other three groups were treated orally with 1, 2 and 3 grams of *B. monosperma* fruit powder, respectively. The two hours post breakfast blood glucose levels of the volunteers were determined (0 day). Subsequently, 2-hours post-prandial blood glucose levels were determined with Glucotrend Glucometer, Roche milpitus, California, USA on post treatment days 8, 15 & 21 after the continuous daily oral intake of *B. monosperma* fruit powder in the prescribed dosage.

Lipid profile parameters included total lipids, triglycerides, total cholesterol, high density lipoprotein cholesterol (HDL- Cholesterol) and low density lipoprotein cholesterol (LDL-Cholesterol) were determined with reagent kits RANDOX, UK. Total lipids were determined with the help of reagent kit method as described by Zoeliner (7). Triglycerides were determined with reagent kit method as given by Trinder (8). Total cholesterol was determined with the help of reagent kit method according to Richmond (9). HDL - Cholesterol was determined with reagent kit method as described by Lopes-virella (10). LDL cholesterol was determined by calculation method with the help of Fried-Wald *et al.* (11) formula (LDL cholesterol = Total cholesterol – Triglycerides/5 – HDL cholesterol). The data has been expressed as standard error of means (Mean ± SEM), and was analyzed statistically, applying the difference between means of two samples by "t- test".

Results

Two hours post-prandial blood glucose levels (Mean ± SEM) in normal and diabetic human volunteers on various days' intervals after treatment with three different doses of powdered *B. monosperma* are presented in Figure 1a & 1b. The oral administration of the carboxy methyl cellulose (CMC) did not alter the blood glucose levels in normal volunteers. Similarly, treatment with 1, 2 and 3 grams of *B. monosperma* did not produce any significant change in blood glucose of normal volunteers. However, treatments with 2 and 3 gm of *B. monosperma* in diabetic patients caused a significant decrease in blood glucose levels at 15 and 21 day (Fig. 1b). Mean ± SEM blood glucose levels of the diabetic group treated with 2 gram of the powdered plant at 0, 8, 15 and 21 day were 194.2 ± 27.01, 185.2 ± 32.43, 178.2 ± 32.12, 172.2 ± 20.37 mg/dl while that with 3 gram of plant powder the glucose levels at above days were 203.0 ± 19.49, 187 ± 31.52, 180 ± 33.66 and 165.7 ± 48.83 mg/dl respectively. The diabetic patients treated with Donail® did not reveal any decrease in their blood glucose levels on various days' intervals.

Figure 2a shows that normal human volunteers treated with 2 and 3 gram of powdered *B. monosperma* had a statistically significant reduction in total cholesterol levels at 15 and 21 day post treatment. While, the diabetic patients treated with 2 and 3 gram of powdered *B. monosperma* indicated a significant reduction in their total cholesterol levels at day 21 post treatment only (Fig. 2b).

Figure 3a and 3b give the Mean ± SEM triglycerides levels of normal and diabetic human volunteers receiving three different doses of powdered *B. monosperma.* Treatment with CMC and Donail® in normal and diabetic groups respectively, did not significantly reduce triglycerides levels at any time interval. The normal human treated with 3 gram of powdered plant indicated a significant decrease in their triglycerides levels on 21 day while the triglycerides levels of diabetic patients treated with 2 and 3 gram of powdered *B. monosperma* were significantly reduced at day 15 and 21 post treatment (Fig. 3b).

Table 1 showed that total lipids of normal human volunteer treated with 2 & 3 gram of powdered *B. monosperma* had a significant ($P<0.05$) decrease in total lipids at day 15 and 21 of treatment. While that, diabetic patients treated with similar doses of powdered plant caused a significant reduction in total lipids at day 21 of treatment only.

The levels of high density lipoprotein cholesterol in normal and diabetic human are given in Table 2. It is clear from the data that 3 gram of powdered *B. monosperma* produced a significant increase in HDL cholesterol both in normal as well as diabetic humans on day 21 of treatment.

Similarly Table 3 gives the levels of LDL cholesterol in normal and diabetic human volunteers treated with various doses of powdered plant. This is evident in the table that the highest dose of 3 gram of powdered *B. monosperma* resulted in significant reduction in LDL cholesterol at 21 day of treatment in both normal and diabetic humans.

Discussion

The use of herbs is not rare among diabetic and obese patients. Certain scientists such as Al-Rowais (12) have encouraged their patients regarding the use of herbs, as it might affect the outcomes and management of these diseases. *Butea monosperma* is a well known indigenous medicinal plant that has been used in traditional medicines for various diseases including diabetes mellitus. However, no scientific research work has been carried out to assess the hypoglycemic/ hypolipidemic activities of this indigenous plant in normal and diabetic human volunteers. Therefore, in the present investigation the powdered fruit of *Butea monosperma* were administered to normal and diabetic human volunteers. For comparison, the effects of a standard oral hypoglycemic drug Daonil® were also recorded on the blood glucose and lipid profiles of normal and diabetic human volunteers suffering from non insulin dependent diabetes mellietus.

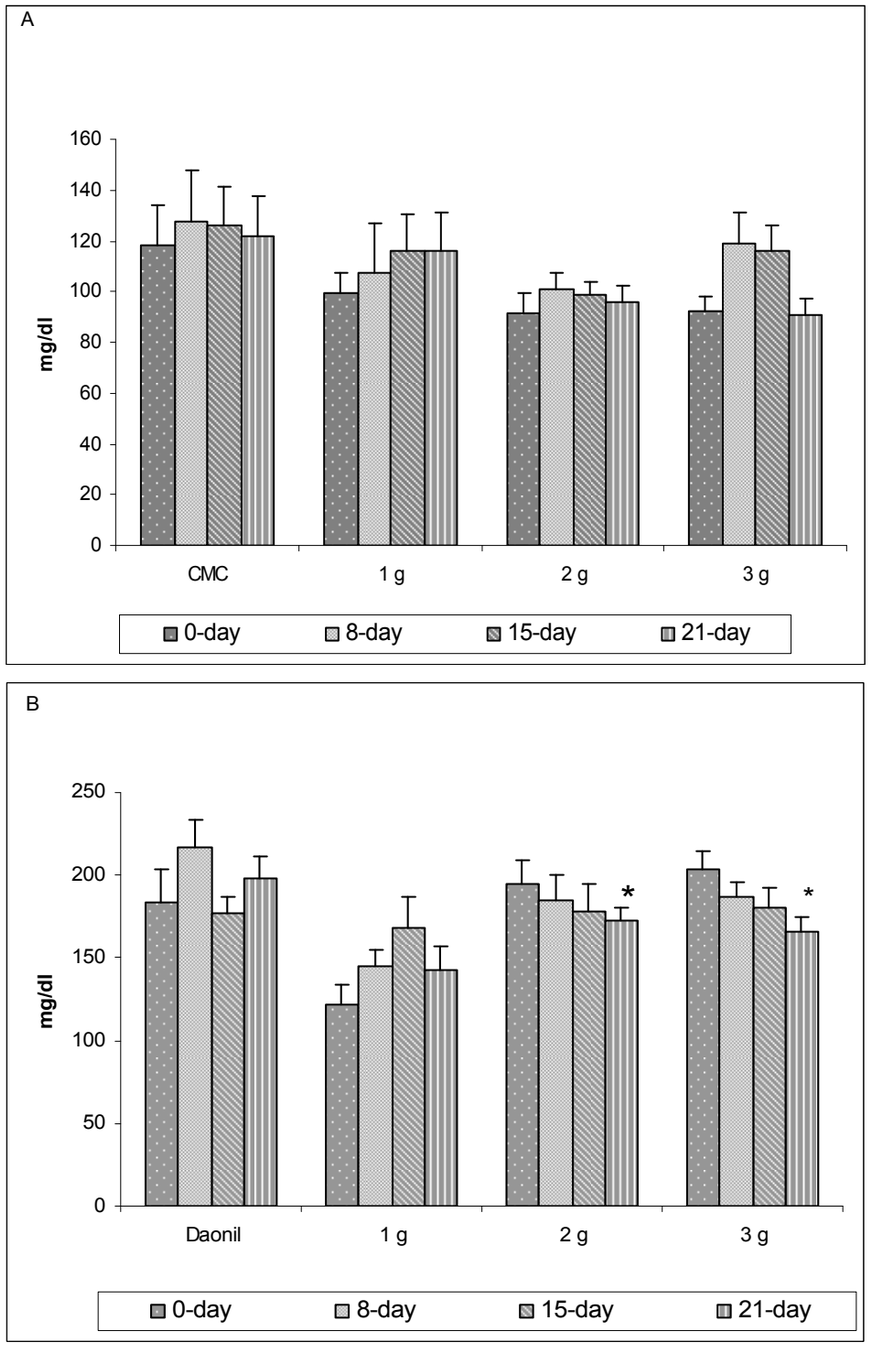
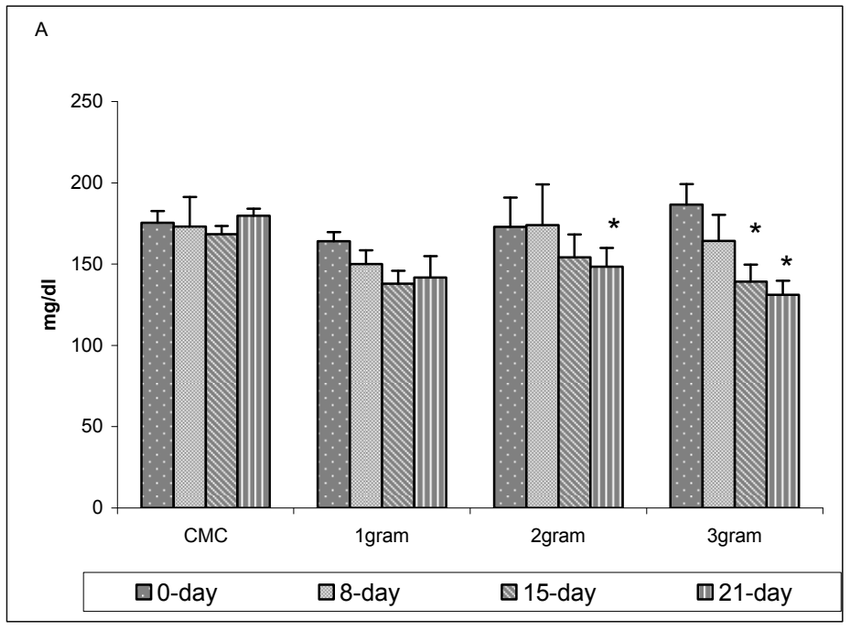


Figure 1: **Blood glucose levels in normal (A) and diabetic (B) human subjects after oral administration of different doses of powdered *Butea monosperma*.**

CMC (carboxy methyl cellulose) treated group
Daonil ® treated group
1, 2, 3 g (groups treated with 1, 2 & 3 gram of powdered *Butea monosperma*)
* Significantly different at ($P<0.05$)



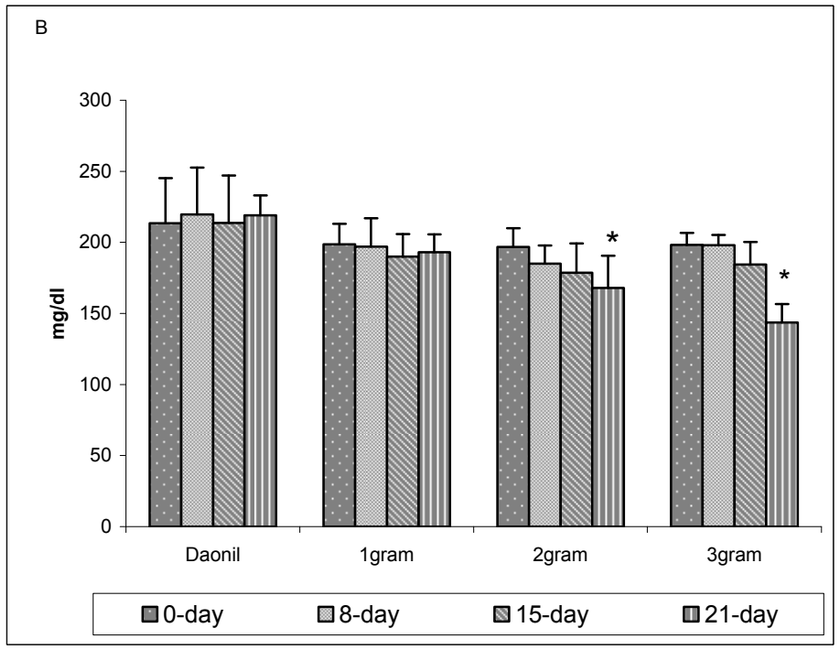


Figure:2 Total cholesterol levels in normal (A) and diabetic (B) human subjects after oral administration of different doses of powdered *Butea monosperma*.

CMC (carboxy methyl cellulose) treated group
Daonil ® treated group
1, 2, 3 gram (groups treated with 1, 2 and 3 grams of powdered *Butea monosperma*)
* Significantly different at ($P<0.05$)

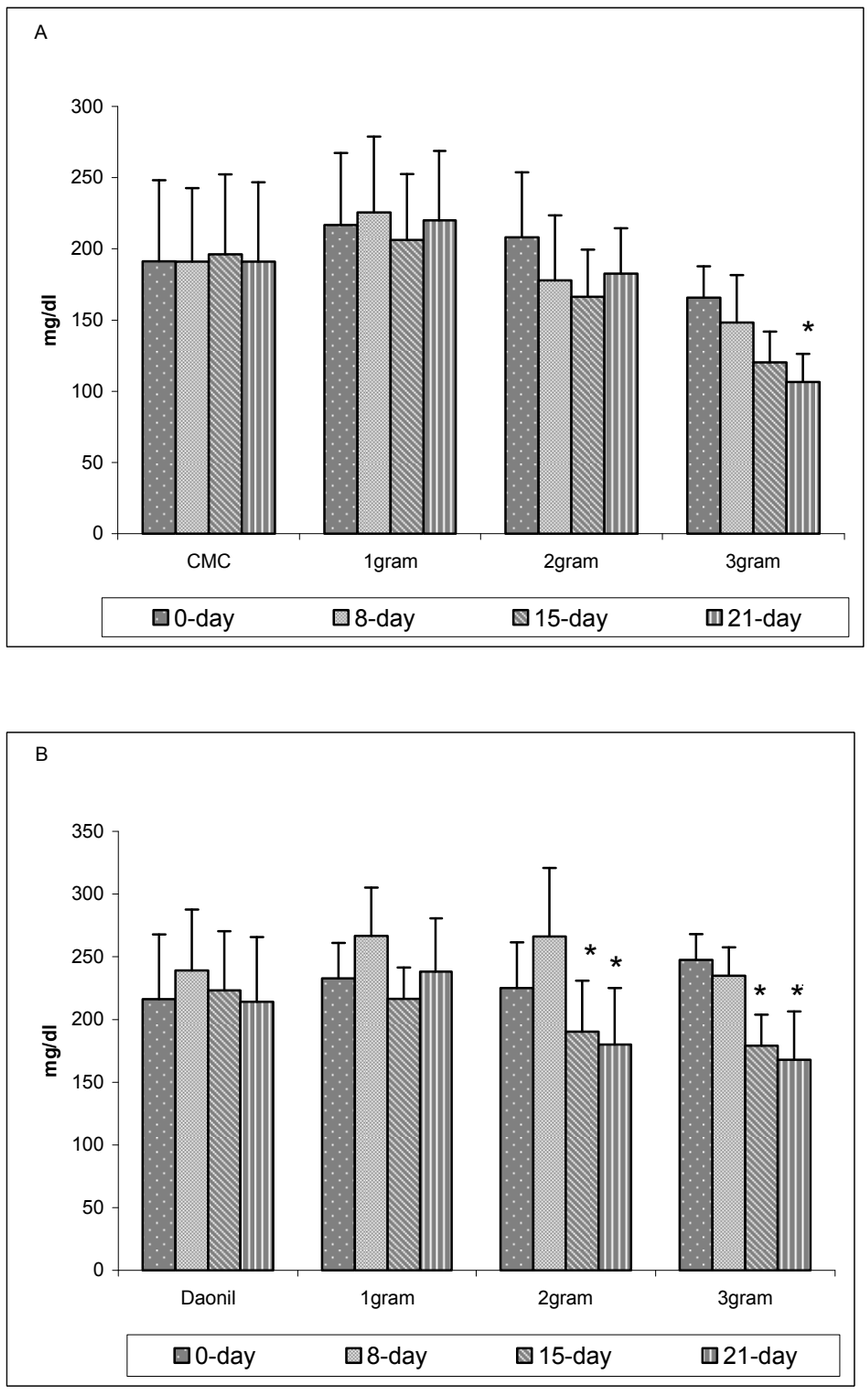


Figure:3. Triglyceride levels in normal (A) and diabetic (B) human subjects after oral administration of different doses of powdered *Butea monosperma*.

CMC (carboxy methyl cellulose) treated group
Daonil ® treated group
1, 2, 3 gram (groups treated with 1, 2 and 3 grams of powdered *Butea monosperma*)
* Significantly different at ($P<0.05$)

Table 1: Mean ± SEM total lipids levels (mg/dl) of normal and diabetic human volunteers on various days intervals after treatment with three different concentrations (1, 2 and 3 gram) of powder Palas papra *(Butea monosperma)*

Treatment	Time Intervals (days)			
	0	8	15	21
Normal				
CMC	527.2 ± 8.04	521.2 ± 9.37	505.5 ± 6.02	539.2 ± 4.92
1 gram	492.0 ± 6.97	375.0 ± 9.17	414.2 ± 17.2	425.2 ± 18.54
2 gram	549.7 ± 19.57	522.7 ± 28.82	462.7 ± 14.16*	445.5 ± 15.32*
3 gram	560.2 ± 13.14	492.7 ± 19.64	417.7 ± 7.21*	393.7 ± 8.38*
Diabetic				
Daonil®	640.5 ± 24.70	659.2 ± 29.86	641.2 ± 31.12	660.0 ± 37.35
1 gram	596.2 ± 14.38	591.0 ± 20.23	570.7 ± 16.60	579.0 ± 13.07
2 gram	515.2 ± 35.50	555.0 ± 13.96	499.2 ± 23.07	471.0 ± 26.87*
3 gram	594.7 ± 8.60	594.0 ± 7.14	553.5 ± 17.01	431.2 ± 17.97*

CMC (carboxy methyl cellulose) treated group
Daonil ® treated group
1, 2, 3 gram (groups treated with 1, 2 and 3 grams of powdered *Butea monosperma*)
* Significantly different at ($P<0.05$)

The blood glucose data obtained in normal and diabetic human volunteers (Figures 1a, 1b) clearly show that powdered *B.monosperma* can produce significant hypoglycemic effects in diabetic patients. This plant did not produce hypoglycemia in normal subjects. This observation indicates that hypoglycemic principles in whole powdered *B. monosperma* may be similar to Metformin® (biguanides) whose pharmacological effects are mediated, at least in part, through a time-dependent, self-limiting inhibition of the respiratory chain that restrains hepatic gluconeogenesis while increasing glucose utilization in peripheral tissues (13). It has been reported earlier that biguanides produce hypoglycemia by increasing the glycolysis and uptake of glucose in muscles and by decreasing gluconeogenesis in the liver and absorption of glucose in the intestine. However, biguanides do not produce hypoglycemia in normal subjects because the increase in peripheral glucose utilization is compensated by an increase in hepatic glucose output (14). Therefore, it would appear that the active principles in *B. monosperma* act like biguanides as the blood glucose levels was decreased only in diabetic subjects and not in normal volunteers. The present finding is in agreement with Somani *et al* (15) who studied the antihyperglycemic activity of the ethanolic extract of *B. monosperma* (BMEE) in glucose-loaded and alloxan-induced diabetic rats. In this study, single dose treatment of BMEE (200 mg/kg, p.o.) significantly improved glucose tolerance and caused reduction in blood glucose level in alloxan-induced diabetic rats.

Table 2: Mean ± SEM high density lipoprotein (HDL) cholesterol levels (mg/dl) of normal and diabetic human volunteers on various days intervals after treatment with three different concentrations (1, 2 and 3 gram) of powder Palas papra *(Butea monosperma)*

Treatment	Time Intervals (days)			
	0	8	15	21
Normal				
CMC	40.7 ± 4.19	667 ± 2.52	66.0 ± 65.31	64.2 ± 67.97
1 gram	39.5 ± 3.27	38.0 ± 14.09	37.0 ± 6.62	38.5 ± 1.50
2 gram	43.7 ± 14.78	42.2 ± 14.78	49.7 ± 12.56	57.2 ± 5.95
3 gram	43.5 ± 14.36	39.7 ± 14.36	58.2 ± 5.80	67.2 ± 2.55*
Diabetic				
Daonil®	47.5 ± 22.31	49.5 ± 18.84	48.2 ± 20.05	47.2 ± 22.64
1 gram	45.0 ± 15.50	49.0 ± 11.66	46.0 ± 13.86	43.5 ± 16.20
2 gram	44.0 ± 17.90	44.0± 15.64	51.5 ± 25.31	68.0 ± 21.16
3 gram	47.0 ± 11.52	47.0 ± 8.33	68.5 ± 10.31	76.2 ± 16.95*

CMC (carboxy methyl cellulose) treated group
Daonil ® treated group
1, 2, 3 gram (groups treated with 1, 2 and 3 grams of powdered *Butea monosperma*)
* Significantly different at ($P<0.05$)

Figures 2a, 2b show that oral administration of 2 and 3 grams of powdered *B. monosperma* produced significant decrease in total cholesterol levels on 21 day of treatment in both normal and diabetic individuals. It has been reported that repeated oral treatment with *B. monosperma* ethanolic extract (200 mg/kg/day) for 2 weeks significantly reduced serum cholesterol in alloxan-induced diabetic rats (15). These results are in accordance with the findings of He *et al*., (16) and Hernandes *et al*. (17) who reported that lower serum cholesterol was associated with higher intakes of fiber. The product (*B. monosperma*) which was used in the present study also contained higher fiber. In majority of individuals with diabetes it can be best done with a diet that was low in fat and high in carbohydrate (18). Similar findings were reported by Wahlquist (19) and Vessby *et al*. (20).

The effect of oral administration of B. monosperma on the triglyceride levels in normal and diabetic subjects is shown in Figures 3a, 3b. Significant low triglycerides levels are produced in diabetic groups with 2 and 3 grams of plant powder after 2 and 3 week administration. These results are in line with Wahlquist (19) who has studied that low triglyceride level was attained at higher fiber diet. Similarly Pedersen *et al*. (21) reported that individual dietary regulation was still an important part of all form of treatment of diabetes as high fiber diet lowered the triglycerides in diabetic subjects below 100mg/dl.

The oral administration of *B. monosperma* significantly reduced total lipids (Table. 1), LDL-cholesterol (Table,3) and significantly increased HDL-cholesterol (Table-2) in both normal and diabetic subjects with repeated administration of 3 gram of plant powder for three week.

Table 3:Mean ± SEM low density lipoprotein (LDL) cholesterol levels (mg/dl) of normal and diabetic human volunteers on various days intervals after treatment with three different concentrations (1, 2 and 3 gram) of powder Palas papra *(Butea monosperma)*.

Treatment	Time Intervals (days)			
	0	8	15	21
Normal				
CMC	102.5 ± 8.37	104.2 ± 9.48	97.7 ± 15.55	104.2 ± 15.65
1 gram	86.2 ± 2.45	75.2 ± 23.43	64.0 ± 3.38	65.50 ± 20.35
2 gram	98.7 ± 27.90	101.7 ± 22.32	123.7 ± 37.71	84.0 ± 29.53
3 gram	101.0 ± 24.76	91.0 ± 25.43	79.7 ± 15.27	76.2 + 15.61*
Diabetic				
Daonil®	127.5 ± 28.66	129.0 ± 30.04	150.0 ± 54.72	149.2 ± 55.31
1 gram	110.7 ± 25.78	103.5 ± 32.16	128.0 ± 43.36	107 ± 22.70
2 gram	111.7 ± 14.20	99.5 ± 20.14	101.0 ± 24.05	97.2± 27.42
3 gram	109.5 ± 9.30	103.5 ± 16.95	82.5 ± 12.89	71.5 ± 17.88*

CMC (carboxy methyl cellulose) treated group
Daonil ® treated group
1, 2, 3 gram (groups treated with 1, 2 and 3 grams of powdered *Butea monosperma*)
* Significantly different at ($P<0.05$)

Higher HDL blood levels have been correlated with a lower risk for heart disease. HDL-cholesterol appears to benefit the body in two ways; it removes cholesterol from the walls of arteries and returns it to the liver. It helps prevent oxidation of LDL. In fact, it appears to have antioxidant properties on its own. HDL then helps keep arteries open and reduces the risk for heart attack. Less than 35 mg/dl is considered a positive risk factor for coronary artery disease; over 60 mg/dl is considered a negative risk factor (reduces risk of heart disease). Recent studies have shown that low HDL level is the strongest predictor of cardiovasulcar death in women (22). The present study indicates that *B. monosperma* clearly raised the HDL-cholesterol levels well above 60mg/dl in both normal and diabetic subjects.

Obviously the oral hypoglycemic drugs are of no value in the treatment of severe diabetes of any type as their islets have already lost all the potential to secrete insulin. Therefore, till today search for more effective and safer antidiabetic agents has continued to be an area of active research. It is conceivable that this cheap indigenous medicinal plant drug may ultimately prove to be an extra ordinarily valuable anti-diabetic agent since in addition to its non-toxic insulin releasing and for insulin-like activities, it could also compensate for the mineral deficiency that occurs in diabetes due to osmotic diuresis (23).'Virtually, the plant drug has been already reported to be safe for human use as it gave negative results in the mutagenicity testing. However, further comprehensive phytochemical studies followed by pharmacological evaluations in animals and subsequently in the humans, are further required to evaluate and pinpoint the real hypoglycemic principle(s) and to precisely determine the mechanism(s) of its hypoglycaemic action. Simultaneously chronic toxicity studies in laboratory animals must also be carried out to find its ultimate safety for prolonged use in the human beings.

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