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Research Article

EVALUATION OF ANTIHYPERGLYCAEMIC EFFECT OF *BUTEA MONOSPERMA* LEAF EXTRACT ON ADRENALIN INDUCED AND HIGH GLUCOSE FEED ANIMAL MODEL

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ABSTRACT

Objective: As per the ethnopharmacological information has *Butea monosperma* been used to treat diabetes mellitus by the tribal people of tropical and subtropical areas. However, there is no much more scientific report available about the antidiabetic property of the leaves of the plant. Hence, the study was undertaken to evaluate the antidiabetic effect of ethanolic extract of *B. monosperma* on blood levels of adrenaline-induced and glucose feed diabetic rabbits.

Methods: The three different doses of the extracts (100, 200, and 400 mg/kg) were administered orally to an experimental animal. The animals were induced diabetics by adrenaline and high glucose diet. Blood glucose level was measured accordingly. For antidiabetic activity, photocolorimeter was used to monitoring the blood glucose level with crest kit box (GOP-POD method).

Results: The extracts showed considerable dose-dependent activity. However, the dose 400 mg/kg showed considerable lower of blood glucose level. $p<0.01$ indicates the significance result. 8 hrs reading 182.5±3.83 for 400 mg does is most effective for reducing blood sugar.

Conclusion: The study indicates that the ethanolic extract of *B. monosperma* leaves possesses antidiabetic properties which suggest the presence of biologically active components.

Keywords: Glucose, Adrenaline, Leaf extract, Hyperglycemia.

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by high glucose concentration (hyperglycemias) due to impaired insulin secretion and or insulin resistance [1]. It is a metabolic disorder in which there is an inability to metabolize carbohydrate due to disturbances in insulin function and secretion. Diabetes is one of the oldest known diseases of the man whose devastating effect is increasing by the day and severity almost at an epidemic level. The identification parameter and treatment protocol are becoming complicated day-by-day. Diabetes is always associated with many other complications which may or may not be preexisting. The number of people suffering from the disease worldwide is increasing at an alarming rate with a projected 366 million peoples likely to be diabetic by the year 2030 as against 191 million estimated in 2000 (Wild *et al*., 2004). Developing countries are the most affected because of expansive and inadequate treatments (djr olo etd, 1998), coupled with the side effect associated with these drug [2].

Thus the search of a new drug with low cost, more potential and without adverse effect becomes inevitable. A great number of medicinal plants have been used in the treatment of diabetes in a different part of the world. Many herbal products are the mixture of different plant extract used for a therapeutic purpose which is based on its ethnobotanical information. Many times plant product are subjected to animal screening but sometimes these product used by following traditional information on the basis of traditional use. Evaluation of the antidiabetic potentials of these plants becomes necessary to provide scientific proof and justify their uses in ethnomedicine.

Butea monosperma is a species of Butea native to tropical and subtropical parts of the Indian Subcontinent and Southeast Asia, ranging across India, Bangladesh, Nepal, Pakistan, Sri Lanka, Myanmar, Thailand, Laos, Cambodia, Vietnam, Malaysia, and western Indonesia 4,5. In this study, the different doses of leaf extracts were screened for antidiabetic study [3].

METHODS

Collection and leaf extract preparation

The plant leaves were collected based on local ethnobotanical information. The collected plant materials were subjected to authenticated identification using the standard of nomenclature and classification. The authentification has been certified by the Scientist, Botanical Survey of India (BSI), Kolkata.

The leaves were dried in the shade and powdered to get a coarse powder. About 800 g of dry, coarse powder was subjected to extraction with ethanol using Soxhlet apparatus. The residue of the extract obtained evaporated to dried mass and then the residue of the extract obtained was taken for the experiment [4,5].

Chemicals and reagent uses

All chemicals and drugs were obtained commercially and were of analytical grade. All the reagent kits were obtained from crest India Ltd.

Instrument used

For antidiabetic activity photocolorimeter was used to monitoring the blood glucose level with crest kit box (GOP-POD method).

Phytochemical screening

The ethanolic extract of the leaves obtained was subjected to preliminary phytochemical screening to identify the chemical constituents. The methods of analysis employed were those described by Trease and Evans (1989) [6].

The presence of various constituent has been screened in a different chemical test using different chemical reagent. The finding of different chemical constituents is evidence for different pharmacological activity [7].

Dose selection
The three test drug dose and standard drug dose were selected by acute toxicity study (LD_{50}).

Animals and induction of diabetes mellitus
Healthy albino rabbits of either sex, inbred in the departmental animal house, weighing between 2 and 2.5 kg, aged between 6 months and 1 year were used for this study. The animals were kept properly and maintain required condition suitable for experiment before and during experiment. Adrenaline diabetes can be produced by intravenous, intramuscular, subcutaneous, administration of different doses. In this study, adrenaline 8 mg/kg by intravenous route has been sued as the route is least toxic. The protocol of the study was approved by IAEC, Gayatri College of Pharmacy, Sambalpur, India, bearing Regd. No1339/ac/10/CPCSEA.

Experimental design
Method used by Mohan *et al*. (1978) was followed to study the affect of BMLE on the fasting plasma glucose (FPG) at different hour's intervals. Adrenaline was administered in the dose 0.8 mg/kg for induction of diabetics. In addition, high carbohydrate diet has been employed for experimental animal to maintain the good diabetic model. Adrenaline is responsible for hyperglycemia in an animal model, and high carbohydrate diet plays a synergistic role for maintaining diabetes [8,9]. The diabetic rabbits with FPG level 200-250 mg/dl were divided into different groups of six animals each in the following manner. The detail is present in Table 1.

Determination of blood glucose levels
Blood samples from the overnight fasted diabetic rabbits were collected. Then, the drug and the vehicles in their indicated doses were administered orally to the respective groups. The effect of BMLE on FPG was compared to that of their respective vehicle and glibenclamide, the standard antihyperglycemia drug at different time interval by photocolorimeter. The detail is present in respective table.

Statistical analysis
Blood glucose levels were expressed in mg/dl as mean ± SEM. The data were statistically analyzed using ANOVA with multiple comparisons versus control group. The values of $p<0.01$ were considered as significant [10].

RESULT AND DISCUSSION

Adrenaline-induced hyperglycemia has been described as a useful experimental model to study the activity of antidiabetic agents as adrenaline is responsible for elevated glucose label by producing glycogenolysis. The following table shows the result of the effect of three doses (100, 200, and 400 mg/kg) of the ethanolic extract of *B. monosperma* leaves.

BM leaf extract administered in doses of 100, 200, and 400 mg/dl to three different group of diabetic rabbits whose FPG was estimated just before (Ohr) and 2, 4 as well as 8 hrs after the drug administration. In Table 2, the effect of vehicle on FPG has been noted. This table bears the report of the FPG of the diabetic rabbits 0 hr (before) and 2, 4 and 8 hrs intervals after administrations of different vehicles. Here, $p<0.05$ after analysis by one-way ANOVA. There is no significant difference between the mean FPG of all groups. Hence, none of the vehicles have any significant action. In Table 3, the effect of different doses of BM leaf extract on adrenaline-induced diabetic animal has been mentioned. BM leaf extract at 100, 200, and 400 mg/kg dose has been administered and glucose level has been monitored at 0 hr (before) and 2 hrs, 4 hrs and 8 hrs intervals after administration. One-way ANOVA analysis shows $p<0.01$ which indicates statistical significance. At 4 hrs reading and 8 hrs reading there is a significant lowering of FPG. In 8 hrs reading the lowering of FPG is very prominent. Table 4 is a consolidated table showing the effect of BMLE at 3 dose level and glibenclamide 0.5 mg/kg on mean FPG of different groups of rabbits as compared to their respective vehicles at 0, 2, 4, and 8 hrs interval of drug administration. Statistical analysis by one-way ANOVA followed by paired t-test indicates the significant of result which has been mentioned in the respective table. The highly significant result has been indicated as triple star within the table. BMLE 100 mg dose at 8-hour interval achieve 203.5±3.92.200 mg dose at 8 hrs interval achieve 191.33±5.14.

Which is very effective and 400 mg achieve 182.5±3.83 which is very effective for reducing blood glucose level in the experimental animal.

The peak effect with each dose was observed at 8 hrs with low dose the onset of antihyperglycemic action was delayed whereas with high dose an early response was observed [11,12].

Table 1: Details of Drug, Vehicle and Routes of Administration

Drug/vehicle	Dose per kg body weight	Route of administration	Nature of use
5% Tween 80	2 ml	Oral	Vehicle for SRLE
Glibenclamide	0.5 mg	Oral	Standard antihyperglycemic drug
SRLE	100, 200 and 400 mg	Oral	Indigenous test drug
Adrenaline	0.8 mg	I.V	Diabetes inducing agent

Table 2: Effect of vehicles on fasting plasma glucose in adrenaline-induced diabetic rabbits (acute study)

S. No.	FPG (mg/dl)											
	Distilled water				2% gum acacia				5% Tween 80			
	0 hrs	2 hrs	4 hrs	8 hrs	0 hrs	2 hrs	4 hrs	8 hrs	0 hrs	2 hrs	4 hrs	8 hrs
1	239	239	231	224	236	232	228	219	245	241	243	239
2	237	234	238	225	238	234	236	238	235	236	231	225
3	232	227	223	232	231	224	223	225	232	229	233	224
4	244	228	237	238	243	238	237	231	234	233	235	231
5	231	228	231	226	230	226	229	227	219	215	221	213
6	226	233	228	226	225	228	227	223	227	229	224	233
Mean	234.83	231.5	231.33	228.5	233.8	230.3	230.0	227.17	230.0	230.5	231.2	227.5

One-way ANOVA $p>0.05$ns, ns: Not significant. This table bears the report of the FPG of the diabetic rabbits 0 hr (before) and 2, 4 and 8 hrs intervals after administrations of different vehicles. There is no significant difference between the mean FPG of all groups. Hence, none of the vehicles have any significant action on FPG levels of diabetic rabbits, and there is no significant difference among the effects of these three vehicles

Table 3: Effect of BMLE on FPG in adrenaline-induced diabetic rabbits (acute study)

S. No.	FPG (mg/dl)																			
	0 hr					2 hrs					4 hrs					8 hrs				
	T-80	B-100	B-200	B-400	GL	T-80	B-100	B-200	B-400	GL	T-80	B-100	B-200	B-400	GL	T-80	B-100	B-200	B-400	GL
1	232	224	238	239	236	229	219	229	227	213	233	208	205	204	162	224	198	197	186	171
2	234	235	225	243	228	233	234	221	230	209	235	224	201	217	156	231	209	188	192	162
3	227	238	243	233	239	229	221	228	219	213	224	210	219	201	164	233	201	210	184	169
4	245	239	219	228	241	241	237	208	215	215	243	228	195	178	173	239	218	172	178	175
5	235	219	233	245	221	236	215	221	231	196	231	202	201	215	150	225	190	194	189	157
6	219	233	228	221	227	215	229	225	209	201	221	221	199	182	176	213	205	187	166	183
Mean	232.0	231.33	231.0	234.8	232.0	230.5	225.8	222.0	221.8	207.8	231.2	215.5	203.3	199.5	163.5	227.5	203.5	191.33	182.5	169.5
SEM	3.54	3.3	3.59	2.78	3.2	3.61	3.60	3.12	3.64	3.12	3.23	4.19	3.40	6.68	4.03	3.67	3.92	5.14	3.83	3.78

One-way ANOVA p>0.05ns. *p<0.01 statistically significant this table bears the report of the fasting plasma glucose of the diabetic rabbits. 0 hr (before) and 2 hrs, 4 hrs and 8 hrs intervals after administration of BMLE at 100, 200, and 400 mg/kg and gl at doses 0.5 mg/kg. There is a significant difference among the mean FPG value of different groups in each set at 2, 4 as well as 8 hrs interval. Result of post ANOVA tests is represented in next page, table

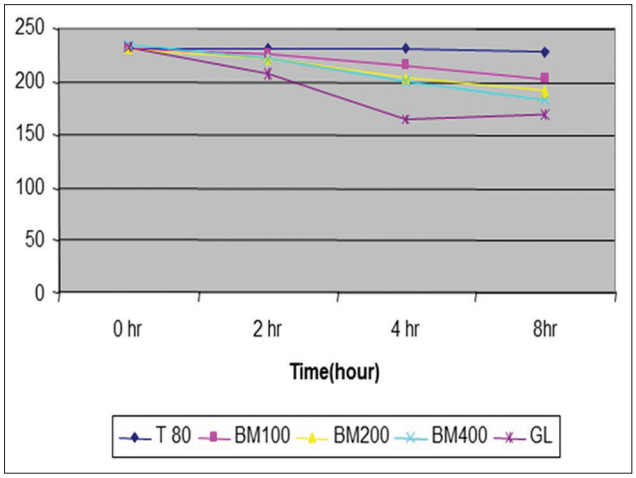
Table 4: Effect of BMLE on mean FPG in diabetic rabbits (acute study)

Group	Treatment	Dose per kg Bd. Wt.	Mean FPG ± SEM (mg/dl)			
			0 hr	2 hr	4 hr	8 hr
I	Glibenclamide	0.5 mg	232.0±3.2	207.8±3.12***	163.5±4.03***	169.5±3.78***
I i	5%tween80	2 ml	232.0±3.4	230.5±3.61	231.2±3.23	227.5±3.67
Iii	BMLE	100 mg	231.33±3.3	225.8±3.60	215.5±4.19	203.5±3.92**
Iv	BMLE	200 mg	231.0±3.59	222.0±3.12	203.3±3.40**	191.33±5.14***
v	BMLE	400 mg	234.8±2.78	221.8±3.64**	199.5±6.68***	182.5±3.83***

This is a consolidated table showing the effect of BMLE at 3 dose level and glibenclamide 0.5 mg/kg on mean FPG of different groups of rabbits as compared to their respective vehicles at 0, 2, 4, and 8 hrs interval of drug administration. 8 hrs reading 182.5±3.83 for 400 mg does is most effective for reducing blood sugar

Post ANOVA paired t-test] Test drug Vs. glibenclamide
**Statistically significant]

**Statistically significant] Test drug /glibenclamide Vs. Vehicle
***Highly significant]



Graph 1: Effect of Bmle on Fpg in Diabetic Rabbit

CONCLUSION

The study indicates that the ethanolic extract of *B. monosperma* leaves possesses antidiabetic properties which suggest the presence of biologically active components. The extract might be promoting glucose uptake and metabolism or inhibiting hepatic gluconeogenesis. BM leaf extract administered in doses of 100, 200, and 400 mg/dl to three different group of diabetic rabbits whose FPG was estimated just before (0 hr) and 2, 4 as well as 8 hrs after the drug administration. The results of this study depicted in Table 2 and Graph 1 reveal that the drug exhibited a significant effect on FPG of diabetic rabbits. Post ANOVA analysis of the data by paired *t*-test reveals that BMLE with 100 mg/kg dose reduced mean FPG levels in diabetic rabbits significantly at 8 hrs; with 200 mg/kg at 4 and 8 hrs; and with 400 mg at 2, 4 as well as at 8 hrs intervals in comparison to its vehicle. The peak effect with each dose was observed at 8 hrs. With low dose, the onset of antihyperglycemic action was delayed whereas with high dose an early response was observed [13].

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