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Antihyperglycemic and hypolipidemic potential of *Caesalpinia decapetala* in alloxan-induced diabetic rabbits

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Abstract

The anti-hyperglycemic, anti-hyperlipidemic, kidney and hepatoprotective potential of *Caesalpinia decapetala* were evaluated in alloxan-induced diabetic rabbits. The plant extract showed concentration dependant significant ($p<0.001$) therapeutic potential in diabetic rabbits revealing improvement in lipid profile and liver and kidney functions. 300 and 500 mg/kg oral extract were able to reduce average blood glucose levels from 250.6 to 204.2 and 188.2 mg/dL respectively during 14 days period, in compa-rison to 183.8 mg/dL of glibenclamide. There was no significant synergistic effect found, upon co-administration of both drug and extract representing the competitive binding to sulphonyl urea (SUR1), revealing possible mechanism of action for compounds in extract. Extract was found to be nephroprotective, hepatoprotective and improved lipid profile of alloxan-treated rabbits.

Introduction

Diabetes mellitus may be treated by the use of insulin or hypoglycemic agents. Herbal and natural products for diabetes are considered to be safer and widely being evaluated for their therapeutic and safety potential (Khan and Safdar, 2003). Apart from being consumed as such, natural products have also been a superior source of effective drug candidates. In case of diabetes, a larger number of active principles, derived from plants origin have shown activity in treating (non-insulin dependent diabetes mellitus) NIDDM (Jayasri et al., 2008).

Caesalpinia decapetala (Roth) Alston (Caesalpiniaceae) is commonly found throughout the Africa and different Asian regions of China, Pakistan, Bangladesh, Nepal, Bhutan and India (Coetzer and Neser, 1999). It is a shrub and can climb up to 25 m in height. The leaves are used in treatment of biliousness, burns, and stomach disorder. It is, locally used as antipyretic, tonic, laxative and carminative. Leaves and root of *C. decapetala* act as emmenagogue and purgative. *C. decapetala* has also been locally claimed to be effective as anti-inflammatory, antidiabetic and even effective in diabetic wound healing, but scientific studies to evaluate its antihyperglycemic activities were still being awaited (Sandhya et al., 2011). The present study was designed to assess the antidiabetic and hypolipidemic activity of *C. decapetala* in alloxan-induced diabetic rabbit models including effects on liver, kidney and lipid profile.

Materials and Methods

Plant material and preparation of extract

The plant *C. decapelata* was collected from hilly areas of District Swat, Pakistan. This plant was identified by Dr. Ilyas Iqbal, Assistant professor, University of Malakand with voucher identification number UMLCD019. The leaves and whole plant were completely dried under the shade and grinded to fine powder. The powdered material was stored in well closed cellophane bags at room temperature. An aqueous methanolic extract of *C. decapetala* was prepared using the powder material ex-

tracted with water and methanol (70:30) by maceration for 7 days, afterward the extract was filtered and solvent was evaporated by rotary evaporator (Stuart, Bibby Steriline Ltd. UK) to obtain crude extract.

Experimental animals

Healthy adult rabbits of a local strain (*Oryctolagus cuniculus*) weighing 1-1.5 kg were kept at animal house of the Department of Pharmacy, Government College University, and Faisalabad. None of the animal had any clinical infection. The animals were housed in stainless cages under standard laboratory condition (light period: 8:00 am to 8:00 pm, 21 ± 2°C, relative humidity 55% with free access to green fodder and water). Ethical guidelines of American Psychological Association were followed regarding use of animals in present research. Approval was taken from Ethical Research committee of Advance studies and Research Board (ASRB) of Govt. College University, Faisalabad. Approved document with reference no. GCU-Pharm-023-2013 was deposited in official record of Research Board.

Induction of diabetes

Each group except controls was fasted for 16 hours prior to intravenous injection of alloxan. Alloxan 150 mg/kg was dissolved in isotonic saline to induce diabetes (Razi et al., 2011). The control group A only received the same volume of isotonic saline. 72 hours after alloxan administration, diabetes was confirmed by measuring blood glucose level via glucometer (Optium Xceed, Abbot Laboratories, USA). Rabbits with blood glucose ≥250 mg/dL were included for further study. The *C. decapelata* treated diabetic rabbits received extract daily for 14 days after induction of diabetes was confirmed. Drug was given orally by making uniform suspension in normal saline and same was the case with plant extract but it was dissolved in water.

Table I

Treatment schedule for each group of rabbits

Group A	Normal control (Receiving saline)
Group B	Alloxan treated control (150 mg/kg)
Group C	Alloxan (150 mg/kg) + *Caesalpinia decapelata* aqueous methanolic extract (300 mg/kg oral)
Group D	Alloxan (150 mg/kg) + *Caesalpinia decapelata* aqueous methanolic extract (500 mg/kg oral)
Group E	Alloxan (150 mg/kg) + Glibenclamide (5 mg/kg, oral)
Group F	Alloxan (150 mg/kg) + Glibenclamide (5 mg/kg, oral) + Extract (300 mg/kg, oral)
Group G	Alloxan (150 mg/kg) + Glibenclamide (5 mg/kg, oral) + Extract (500 mg/kg, oral)
Group H	Normal control (Receiving extract only 300 mg/kg oral)

Experimental design

Animals were divided in eight groups, normal rabbits receiving saline as control, and normal rabbits receiving extract to see the hypogly-cemic effects (Sharma et al., 2003). Diabetic rabbits were given extract at two doses 300 and 500 mg/kg, with and without standard drug i.e. glibenclamide to elucidate the possible target of plant extract (Table I).

Biochemical analysis

Wooden rabbit holders were used for collection of blood sample of experimental animals from marginal vein of ear. Blood samples were collected before and after the administration of the drug. In order to protect rabbits from infections, the pricked site was rubbed with cotton swabs soaked in 70%alcohol. The parameters like Serum total cholesterol, triglyceride, serum glutamate pyruvatate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), serum urea and creatinine were determined by enzymatic test kit (Fluitest) by means of micro lab 300 (Merck). The plasma LDLs level was determined with the formula:

LDL = Total cholesterol - HDL - (Triglyceride) / 5

Statistical analysis

The data was represented as mean ± standard deviation (SD) and analyzed by using two factor completely randomized design (CRD). Least Significant difference test (LSD) at 5% level of significance was applied. Microsoft Excel (2007) and Minitab was used to check difference among means.

Results

Blood glucose level in previously received alloxan-treated with extract 300, 500 mg/kg and glibencla-mide (5 mg/kg) for 14 days showed decreased its level (Table II).

Total cholesterol, triglyceride and low density lipoprotein (LDL) level increased significantly ($p<0.01$) in diabetic rabbits, while high density lipoprotein (HDL) level decreased ($p<0.01$). Treatment with *C. decapetala* significantly decreased ($p<0.01$) the elevated level of total cholesterol, triglyceride and low density lipoprotein (LDL) level and increased high density lipoprotein (HDL) level (Table III).

There is significant increase in ALT and AST level in alloxanised rabbits. *C. decapetala* significantly ($p<0.01$) decreased SGPT and SGOT level in diabetic rabbits (Table III).

Table II

Effect of Caesalpinia decapetala on blood glucose level

Group	Glucose (mg/dL)				
	Pre-treatment	Day 0	Day 1	Day 7	Day 14
Control	120.7 ± 4.1	115.0 ± 1.4	112.7 ± 3.0	110.7 ± 2.3	120.7 ± 4.1
Alloxan	119.0 ± 5.6	285.3 ± 4.9	277.3 ± 3.7	286.2 ± 0.9	285.1 ± 1.6
Extract (300 mg)	129.3 ± 4.4	261.5 ± 3.7	249.3 ± 2.0	203.7 ± 2.3	180.1 ± 3.9
Extract (500 mg)	125.8 ± 4.6	249.8 ± 4.0	220.8 ± 3.1	188.0 ± 1.2	156.7 ± 2.4
Glibenclamide (5 mg/kg)	124.3 ± 3.2	245.5 ± 2.0	215.2 ± 2.0	184.0 ± 6.0	150.3 ± 2.0
Glibenclamide (5 mg/kg) + Extract (300 mg)	127.6 ± 1.9	258.1 ± 3.2	242.8 ± 2.5	199.2 ± 2.9	182.9 ± 3.4
Glibenclamide (5 mg/kg) + Extract (500 mg)	130.5 ± 3.6	261.3 ± 2.1	235.4 ± 2.3	187.3 ± 3.3	181.2 ± 2.8
Normal with extract (300 mg)	119.3 ± 2.7	120.5 ± 3.6	115.6 ± 2.6	126.0 ± 1.9	122.4 ± 2.2

Results are represented as mean ± SD; n=5 in each group

Urea and creatinine level were significantly decreased after the administration of *C. decapetala* extract.

Discussion

Methanolic extract was obtained from wood and pericap of *C. decapetala* and were investigated for decrease in blood glucose level in experimental animals as compared to control glibenclamide. *C. decapetala* belongs to family *Caesalpiniacae,* traditionally it is used as purgatives. Constituents like Flavonoids and phenols also showed the decrease in oxidative stress associated with diabetes (Jayasri et al., 2008). Other plants from same family are investigated for presence of these constituents (Srinivas et al., 2003). Antidiabetic activity may be due to flavonoids, tannins or polyphenols, which need to be further explored for structure and phytochemical analysis. In group F and G, when extract was given in combination with standard SUR receptor binder, i.e. glibenclamide, then no synergistic effects of drug and extract were observed, indicating the same target is being shared for both for anti-diabetic activity. Competitive binding to SUR receptor is proposed mechanism of action. When drug was given alone to normal rabbits, then blood gluclose levels were normal and showed no hypoglycemic effects. Extract showed dose dependant reduction of anti-hyperglycemic effects in diabetic rabbits of group C and D which are very much comparable to standard drug given alone in

Table III

Effect of various groups of Caesalpinia decapetala on serum profile in alloxan-treated diabetic rabbits for 14 days

Group	Total cholesterol (mg/dL)	Triglyceride (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	SGPT (IU/L)	SGOT (IU/L)	Urea (mg/dL)	Creatinine (mg/dL)
Control	46.8 ± 0.6	70.7 ± 0.5	32.7 ± 0.6	3.1 ± 0.1	101.7 ± 1.5	117.5 ± 1.6	45.0 ± 0.6	1.2 ± 0.0
Alloxan	61.8 ± 1.8	128.3 ± 6.1	31.4 ± 0.7	6.3 ± 0.3	211.7 ± 8.2	174.8 ± 6.7	67.5 ± 2.4	1.6 ± 0.0
Extract (300 mg)	57.4 ± 1.1	123.5 ± 5.7	34.6 ± 0.8	6.0 ± 0.3	182.5 ± 2.0	151.5 ± 2.2	53.7 ± 1.6	1.5 ± 0.0
Extract (500 mg)	56.5 ± 1.2	116.1 ± 6.7	36.7 ± 1.6	5.7 ± 0.3	173.2 ± 2.5	146.0 ± 2.2	47.4 ± 1.9	1.4 ± 0.0
Glibenclamide (5 mg/kg)	46.6 ± 1.1	114.1 ± 5.4	38.2 ± 1.7	4.9 ± 0.2	161.8 ± 6.2	139.7 ± 5.1	47.3 ± 2.1	1.5 ± 0.0
Glibenclamide (5 mg/kg) + Extract (300 mg)	55.3 ± 1.2	110 ± 2.1	35.2 ± 1.5	6.4 ± 0.2	169.7 ± 5.6	148.3 ± 3.6	51.2 ± 1.2	1.4 ± 0.1
Glibenclamide (5 mg/kg) + Extract (500 mg)	48.2 ± 2.5	118.2 ± 4.3	33.5 ± 1.0	5.21 ± 0.1	158.0 ± 4.2	139.3 ± 4.6	46.9 ± 0.7	1.5 ± 0.1
Normal with extract (300 mg)	45.2 ± 0.3	69.6 ± 0.6	31.5 ± 1.0	3.15 ± 0.1	99.9 ± 2.4	115.2 ± 1.0	43.5 ± 0.3	1.2 ± 0.1

group E. In isolated form these effects may be more prominent with small dose even.

Hypercholesterolemia and hypertriglyceridemia have been reported to occur in alloxan induced diabetic rabbits (Wojtowicz et al., 2003) and same was observed in this study. Oral administration of *C. decapetala* extract decreased the total cholesterol and triglyceride level in diabetic groups. HDL level decreases in type 2 diabetic patients that eventually causes atheromatous disease (Rang et al., 2003). It was observed that oral administration of *C. decapetala* extract increased HDL and decreases LDL levels in diabetic rabbits. The antihyperlipidemic effects of *C. decapetala* extract might be due to inhibition of fatty acid synthesis (Jayasri et al., 2008). The strong hypolipidemic effects might be through its control of diabetes, as this is a main determinant of total cholesterol, triglyceride and LDL levels (Laakso, 1995).

The present study showed that *C. decapetala* treatment significantly decreased the elevated levels of SGPT and SGOT levels in diabetic groups, which showed that *C. decapetala* may reduce the risk of liver failure associated with diabetes. *C. decapetala* extract also significantly decreased the elevated levels of serum urea and serum creatinine which showed that this may act as crucial trigger for kidney to revert to their metabolic homeostasis. The antidiabetic effects of aqueous methanolic extract of *C. decapetala*is possibly may be due to polyphenol and flavonoids that have the anti-oxidant activity and are very effective in preventing oxidative damage and protecting beta cells of pancreas.

Conclusion

C. decapetalai showed significant potential of reducing the blood glucose and cholesterol levels as well as protective activity for both liver and kidney, which indicate the safety associated with use of crude drug.

References

Coetzer W, Neser S. Biological control initiatives against the invasive *Oriental legume*, *Caesalpinia decapetala* (Roth) alston (*Mauritius thorn*), in South Africa. Biological control of weeds in South Africa (1990-1998) Afr Entomol Memoir. 1999; 1: 145-52.

Dhasarathan P, Theriappan P. Evaluation of anti-diabetic activity of *Strychonous potatorum* in alloxan induced diabetic rats. J Med Med Sci. 2011; 2: 670-74.

Jayasri M, Gunasekaran S, Radha A, Mathew T. Antidiabetic effect of *Costus pictus* leaves in normal and streptozotocin-induced diabetic rats. J Diabet Metabol. 2008; 16: 117-22.

Khan A, Safdar M. Role of diet, nutrients, spices and natural products in diabetes mellitus. Pakistan J Nutr. 2003; 2: 1-12.

Laakso M. Epidemiology of diabetic dyslipidemia. Diabetes Rev. 1995; 3: 408-22.

Rang H. Atherosclerosis and lipoprotein metabolism. In: Pharmacology. Rang H, Dale M, Ritter J, Moore PK. (eds). 5th ed. England, Churchill Livingstone, 2003, pp 306-10.

Razi MT, Saadullah M, Murtaza G, Hassan W. Determination of the anti-diabetic effect of methanolic extract of *Sphaeranthus indicus* L. on alloxan induced diabetic rabbits. Lat Am J Pharm. 2011; 30.

Sandhya S, Kumar PS, Vinod K, Banji D, Kumar K. Plants as potent antidiabetic and wound healing agents: A review. Hygeia JD Med. 2011; 3: 11-19.

Sharma S, Nasir A, Prabhu K, Murthy P, Dev G. Hypoglycaemic and hypolipidemic effect of ethanolic extract of seeds of *Eugenia jambolana* in alloxan-induced diabetic rabbits. J Ethnopharmacol. 2003; 85: 201-06.

Srinivas KV, Rao YK, Mahender I, Das B, Krishna KR, Kishore KH, Murty US. Flavanoids from *Caesalpinia pulcherrima*. Phytochemistry 2003; 63: 789-93.

Wojtowicz Z, Wrona W, Kiś G, Błaszczak M, Solecka A, editors. Serum total cholesterol, triglycerides and high density lipoproteins (HDL) levels in rabbit during the course of experimental diabetes. Annales Universitatis Mariae Curie-Sklodowska Sectio D, Medicina, 2003.

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