

Hypoglycemic property of *solanum nigrum*

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Abstract : In recent times, focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional systems. *Solanum nigrum* (commonly called Makoi) is also a medicinal plant. A dietary intake of *S. nigrum* supplies our body with nutrients that offer protection against numerous diseases. All parts of this plant are used in the traditional medicine as a remedy for treating various diseases like, cough, cold, asthma, skin diseases and liver problem. The objective of this study is to induce experimental diabetes mellitus using Alloxan monohydrate in normal adult albino rats and study the anti-diabetic activity of changes in body weight, consumption of food and water, volume of urine and levels of glucose between normal and diabetic rats. The hypoglycemic potential of aqueous (100, 200 mg/kg) extract of leaves of *S. nigrum* Linn. (Solanaceae) was evaluated by normoglycemic rats followed by alloxan and glucose loaded hyperglycemic rats by single oral administration. The plant extract was subjected to the study of presence of different phytoconstituents by using standard qualitative chemical methods. The preliminary antioxidant potential of the extract was evaluated by spectrophotometric method. This is a metabolic disorder characterized by disarrangements in carbohydrate, protein and fat metabolism caused by the complete or relative insufficiency of insulin secretion and/or action. This is due to defective or deficient insulin secretory response. This results into impaired glucose use, which is a characteristic feature of diabetes mellitus i.e. resultant hyperglycemia. Elevated blood glucose level causes dehydration of the tissue cells as glucose does not diffuse easily through the pores of cell membrane and increased osmotic pressure. Present investigation is therefore designed to determine the effect of crude ethanolic extract of *S. nigrum* on blood sugar of albino rat after daily oral administration of dose at the level of 200

mg/kg b. wt. for five and seven days respectively. The hematological, biochemical and loss of body weight study report are in good agreement with the activity and safety profile of the plant extract. The experimental results of the above studies indicate that the aqueous extract of the leaves of *S. nigrum* Linn. endowed with potential anti-hyperglycemic activity presumably due to free radical scavenging potential of the test extract.

(Keywords: *Solanum nigrum*, Hypoglycemic, Albino rats, Blood Sugar, Alloxan)

Introduction

Diabetes mellitus (DM) is common endocrine disorder affecting more than 150 million people worldwide and this number is likely to increase to 300 million by the year 2025, out of which more than one-fifth are Indians. In recent times, focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional systems. *Solanum nigrum* is also a medicinal plant. It has been used widely as medicinal and food plants despite their reputation for being poisonous¹. The unripe fruit of *S. nigrum* contain the highest concentration of toxin particularly Solanine. The level of toxin in the berries is greatly reduced by ripening. The ripe berries are eaten raw as fruits and are used in pies and preservative in many regions of the world. All parts of this plant are used in the traditional medicine as a remedy for treating various diseases like, cough, cold, asthma, skin diseases and liver disorder².

World Health Organization has suggested the evaluation of the potential of plants as effective therapeutic agents, especially in areas in which we lack safe modern drugs. Elevated blood glucose level causes dehydration of the tissue cells as glucose does not diffuse easily through the pores of cell membrane and increased osmotic pressure. Present investigation is therefore designed to determine the effect of crude ethanolic extract of *S. nigrum* on blood sugar of albino rat after daily oral administration of dose at the level of 250 mg/kg b. wt. for five and seven days respectively³. It was noticed that the chronic administration for longer duration leads to significant decrease in blood sugar compared to control.

Experimental

Materials and Methods

Plant Material

The mature entire plant was collected from the place named as Botanical garden, BHU, Varanasi authenticated by Dr. A.K. Singh, Taxonomist of the Department of Botany, Kadir P.G. College Chakke, Jaunpur. A voucher specimen has been preserved in the institution herbarium. After the authentication, fresh matured leaves were collected from well-grown plants at the same place and cleaned thoroughly to remove adherent from the leaves under running tap water. The cleaned leaf materials were subsequently dried under shade. The shade dried leaves were powdered in an electrical grinder and passed under sieve No. 40 to get coarse powder of the leaves for further study.

Preparation of extract

The powdered leaf materials are defatted using petroleum ether (40:60) as solvent. The defatted powdered plant material (550 g) was refluxed with 1500 ml of methanol for 22h followed by filtration and the filtrate was concentrated under vacuum. A dark brown sticky residue was obtained with yield value 21.52% (w/w).

Animals

The healthy Wistar albino rats, weighing 150-200g body weight of either sex were selected and housed in acrylic cages in standard laboratory conditions and were standard rodent diet with water ad libitum. The experiments on animals were conducted in accordance with the standard experimental procedure and the animals were used as per the experimental protocol duly approved by the Institutional Ethical Committee, Institute of Medical Sciences, Banaras Hindu University, Varanasi (India).

Acute Toxicity Studies

Healthy adult Wistar albino rats of either sex, starved overnight were divided into five groups and were orally fed with the methanol and aqueous extract of *Solanum nigrum* in increasing dose levels of 100 and 200, mg/kg body weight⁴. The rats were observed continuously for 2h for behavioural, neurological and autonomic profiles and after a period of 24 and 72h for any lethality or death.

Induction of diabetes

Hyperglycemia was induced by injecting alloxan monohydrate at a dose of 120 mg/kg intraperitoneally. The animals were kept under observation and after 48 hrs were tested for hyperglycemia using glucometer.

Group I (control): This group was kept as normal control animals without any treatment.

Group II (Diabetic control): This group was taken as diabetic control with the injection of Alloxan monohydrate.

Group III: This group was taken as Standard control with the injection of Alloxan and the Standard glibenclamide.

Group IV: This group was treated with *Solanum nigrum* methanol extract was mixed with alloxan at 100 & 200 mg.

Group V: This group was treated with *Solanum nigrum* water extract was mixed with alloxan at 100 & 200 mg.

Oral Glucose Tolerance Test in normal rats (OGTT):

Rats were divided into five groups and were administered normal saline and dose of 500 mg/kg oral of aqueous extract. Glucose solution 2 g/kg was administered 30 min after the administration of the extract. Blood samples were withdrawn from retro-orbital at intervals of 30, 60 and 120 min of glucose administration and the level of blood glucose was measured⁵.

Experimental Design

Body weights and blood glucose level of individual animals were recorded before and the period of study in week interval. The end of the 21st day, the experimental animals were sacrificed along with their control group. The animals were fasted overnight, sacrificed by decapitation and blood was collected from individual animals and the serum was obtained from the clotted blood samples for Biochemical studies^{6,7}. The Liver and other organs were immediately excised, after perfusing with physiological saline the organs were blotted dried and it is used for further analysis^{8,9}.

Collection of Blood Sample

Blood samples were collected from the tail vein puncture of treated rats. The samples were taken in to tubes with anticoagulant. From these samples blood sugar was estimated by a standard method.

Estimation of Lipid Profile in Blood sample

Blood samples were collected by tail vein puncture in the morning hours before the mice were fed and watered and were immediately processed for the blood serum separation. Clear

serum was separated and kept at 20°C till used for biochemical analysis⁹.

A rise in blood creatinine level is observed only with marked damage to functioning nephrons. Therefore, this test is not suitable for detecting early-stage kidney disease. A better estimation of kidney function is given by the creatinine clearance (CrCl) test. Creatinine clearance can be accurately calculated using serum creatinine concentration and some or all of the following variables: sex, age, weight and rice, as suggested by the American Diabetes Association without a 24-hour urine collection^{10,11}.

Estimation of total protein in Blood sample:

Serum globulin was calculated as the difference between total protein and albumin. The estimation of serum total cholesterol was done by Wxbenga and Pileggi's method by using cholesterol kit manufactured by M/s Mediprob Laboratories Pvt. Ltd., Hyderabad, India^{12,13}.

Results & Discussion

The effect of single oral administration of water and methanolic extracts of *S. nigrum* are shown in (Table-1). An experimental study reveals that the Methanolic and water extracts from *Solanum nigrum* (100 and 200 mg/kg) orally administered produced a significant decrease in the blood glucose level in the model of alloxan-induced diabetes in rats. Methanol extract is effective even at a higher dose (200 mg/kg) in decreasing blood sugar level in alloxan treated rats. The plant extract almost brought down blood glucose level by 50% in diabetic animals¹⁴.

Thus, it may be effective like tolubtamide. This study reports for the first time, the anti-hyperglycemic effect of *S. nigrum* suggests that the active principle from this plant could be effective in the treatment of diabetes.

Table-1:
Effect of *Solanum* Plant extract on blood glucose in multi-dose treated in alloxan induced diabetic rats in oral route

Groups	Treatment		Blood Glucose Level (mg/dl)			
			Initial	Day 7	Day 14	Day 21
I	Normal control		90.46±3.80	92.82±2.92	94.32±1.73	91.29±3.44
II	Diabetic control		293.8±5.27	286.91±5.05	291.8±5.41	289.41±9.75
III	Alloxan + Glibenclamide		285.86±6.92	205.25±7.06	183.18±6.15	178.13±9.75
IV	Alloxan + methanol extract	100 mg	284.48±5.32	277.76±5.65	265.76±2.60	253.75±0.19
		200 mg	287.48±5.32	262.98±7.08	234.90±32.0	198.70±60.99
V	Alloxan + water extract	100 mg	285.48±5.32	273.90±76.9	268.87±90.07	255.67±0.70
		200 mg	283.86±6.92	265.90±6.98	233.90±7.67	200.02±6.23

Note: Values are given as mean±S.E.M. from six rats in each group.

***P < 0.001 significant from normal and diabetic control animals.

The positive effect of methanol and water extracts was also studied in other biochemical parameters (TC, LDL, HDL, VLDL and TAG)¹⁵. Normally diabetic rats tend to lose weight but after treatment with the two extracts, the body weight did not decline significantly. It

is therefore clear that *Solanum nigrum* are a good for reducing not only the overall physiological and biochemical effects due to diabetes but also physical effects like body weight food and water intake¹⁶.

Table-2 demonstrates that the effect of the methanol and water extract on total protein. Methanol extract was effective even at a higher dose (200 mg/kg) in decreasing level in alloxan treated rats.

Table-2
Effect of *Solanum* Plant extract on total protein in Alloxanised rats on 21th Day of Study

Groups	Treatment	Total protein (g/dl)	Albumin (g/dl)	Globulin (g/dl)	HB (%)
A	Normal control	6.0	3.9	2.0	8.2
B	Diabetic control	6.2	4.1	2.2	9.2
C	Alloxan + Glibenclamide	6.4	3.4	3.0	8.8
D	Alloxan + <i>Solanum</i> Methanol extract	6.2	3.4	2.1	8.2
E	Alloxan + <i>Solanum</i> Water extract	6.4	3.7	2.2	8.0

In this study, we discuss about the hypoglycemic and antidiabetic effects of the *S. nigrum* on normal and Alloxan-induced diabetic rats. Acute toxicity studies revealed the non-toxic nature of the *S. nigrum* plant extract.

There was no lethality or any toxic reactions found with the selected dose until the end of the study period. The dose of the test drug

has been selected on the basis of dose calibration curve. The results of the study have shown that the methanol extract of *S. nigrum* at a dose of 200 mg/kg body weight has a marked hypoglycemic activity by improvement of the glucose tolerance test in normoglycemic rats and by lowering the blood glucose levels in Alloxan induced-diabetic rats¹⁶.

The results of the study have shown a significant difference between the initial and anal fasting glucose levels of methanol extract of *S. nigrum* and glibenclamide treated group. Induction of diabetes by alloxan leads to loss of body weight due to the increased muscle wasting and loss of tissue proteins⁸. The results obtained with the methanol extract treatment in chronic diabetic model further clarified the antidiabetic effect of the extract¹⁰.

After 21 days of plant extract treatment, gain in the body weight was observed in diabetic rats and the results were comparable with that of the standard drug glibenclamide. Methanol extract of *S. nigrum* showed significant increase in serum insulin level. Animals treated with plant extract indicated a significant decrease in the glycosylated hemoglobin level which could be due to an improvement in insulin secretion. In conclusion, it can be stated, that the methanol extract of *Solanum nigrum* has beneficial effects, in reducing the elevated blood glucose level and lipid profile of alloxan-induced-diabetic rats, but has no effect on normal rats. From this preliminary investigation, it has been concluded that the leaves of *S. nigrum* have significant hypoglycemic activity¹⁷.

Liver glycogen study suggest the values for the relative rates of synthesis which very

similar in all the diabetic groups, indicating that the rate of synthesis of the enzyme increased early in diabetes and is maintained at the increased rate throughout the time period studied. The value for rate of degradation and synthesis suggest that liver glycogen synthase in diabetic animal's turns over more rapidly than normal ones¹¹.

Total percentage of glucose level of the diabetes induced rat at the time intervals after administration of *S. nigrum* extracts were tabulated. Upon analysis of protein, electrolytes, lipids, urea & creatinine there is a decrease in these values found when compared with the normal ones. The difference in blood glucose level of different rat in between control versus standard drug and the test is calculated. Active constituent present in aqueous extract or methanol extract of *S. nigrum* with hypoglycemic properties would be effective in the management of diabetes mellitus. This protective effect of extract may be mainly attributed to steroidal saponins which may possess antioxidant and detoxifying effects. Therefore a dietary intake of *S. nigrum* fruits supplies our body with nutrients that offer protection against numerous diseases. Further studies are warranted to elucidate the mechanisms of action and to explore its medicinal value.

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