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Evaluation of Antidiabetic Activity of Ethanolic Extract of *Solanum Melongena* Roots in Experimental Rats

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ABSTRACT:

This study explored the antidiabetic effects of an alcoholic extract from the roots of *Solanum melongena* (SMRE) in rats. A preliminary phytochemical analysis of the extract identified flavonoids, phenols, alkaloids, and saponins. Diabetes was induced in Wistar albino rats using intraperitoneal injections of Alloxan (100 mg/kg) and Streptozotocin (50 mg/kg). Two oral doses of SMRE, 200 mg/kg and 400 mg/kg, were tested, alongside Glibenclamide (5 mg/kg) as a reference drug. The investigation measured various biochemical markers, such as fasting blood glucose (FBG), serum cholesterol, triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL). Both doses of SMRE led to a significant reduction in blood glucose levels, with the effect increasing in a dose-dependent manner. These results were similar to those observed with the standard drug, Glibenclamide. Consequently, this research suggests that the ethanolic extract of *Solanum melongena* roots might be effective in managing diabetes induced by Alloxan and Streptozotocin.

Keywords: Alloxan, Anti-diabetic activity, *Solanum melongena* (Root), Streptozotocin.

Introduction:

Diabetes mellitus (DM) is a prolonged metabolic disorder catagarized by chronically high blood glucose levels due to either insufficient insulin production or improper insulin utilization by the body. Without effective treatment and control, the condition heightens the risk of developing both macrovascular complications, such as cardiac disease, and microvascular complications, affecting smaller blood vessels. Preventative measures and consistent management are key to reducing these risks and ensuring better health outcomes for those with diabetes [1]. The three major categories of diabetes mellitus (DM) include Type 1 Diabetes (T1DM), Type 2 Diabetes (T2DM), and gestational diabetes. These conditions emerge from issues with either the body's production of insulin, its sensitivity to insulin, or both. T1DM is often diagnosed in younger individuals, such as children or adolescents, while T2DM tends to develop later in life, usually as a consequence of long-term high blood sugar levels resulting from poor lifestyle choices and dietary habits. Gestational diabetes occurs specifically during pregnancy and generally resolves after childbirth, although it requires attention to prevent future health risks [2]. India’s diabetes crisis is expected to worsen in the coming years by 2025, some estimates project that there will be 134.3 million Indians are diabetic [3]. The high rates of illness and death caused by diabetes and its complications create substantial healthcare challenges for both families and society [4].

For countless centuries, plants have been regarded as fundamental sources of powerful remedies for diabetes. In many developing regions, medicinal plants hold particular importance in managing diabetes, providing a more accessible and cost-effective alternative to conventional pharmaceuticals. Recently, there has been a surge of interest in harnessing these plants for diabetes treatment, as they are known to contain an array of bioactive substances, including flavonoids, terpenoids, saponins, carotenoids, alkaloids, and glycosides, which are believed to have potent antidiabetic properties [5]. Ethnomedicine is drawing increasing attention for its advantages, such as its proven efficacy and low risk of side effects. Additionally, it holds significant value due to its deep-rooted historical, cultural, and economic importance [6].

Managing diabetes mellitus (DM) remains a critical public health issue. A long-term study from the Diabetes Prevention Program (DPP) demonstrated that changes in lifestyle, such as healthier eating habits and increased physical activity, reduced diabetes risk by 31–58%. Recent advancements in understanding the disease's underlying biology have also contributed to the development of new drug therapies [7]. In addition, various herbal extracts have exhibited hypoglycemic effects in studies involving both humans and animals with type 2 diabetes. The World Health Organization's Expert Committee on diabetes has encouraged further investigation into traditional medicinal plants to explore their potential in diabetes treatment [8].

Herbal medicine is increasingly embraced across the globe, in both emerging and developed nations, due to its natural source and minimal side effects. Numerous traditional remedies are sourced from medicinal plants. Herbal ingredients are favoured for their lower toxicity, reduced risk of adverse effects, cost-efficiency, and broader availability compared to conventional drugs [6]. One such plant *Solanum melongena* belongs to Solanaceae originated, cultivated in India and adjoining districts. The root concentrates of *Solanum melongena* contained steroids, alkaloids, tannins, flavonoids, saponins and

glycosides. The roots, leaves, stem, flowers are extensively having antimicrobial, cytotoxic and antidiabetic activity [9]. However, current literature survey revealed that there is no scientific data documented for the effect of roots of *Solanum melongena* for antidiabetic effect. Hence, the present study has been designed to evaluate *Solanum melongena* root extract for the antidiabetic potential using experimental animal models [10].

Methodology:

***Drugs and Chemicals*:**

Chemicals such as Alloxan monohydrate, Streptozotocin and Glibenclamide were of pure analytical grade and procured from a local supplier.

Preparation of ethanolic extract of root

The fresh root of *Solanum melongena* were washed in running water, cut into small pieces, and shade dried. Dried sample was grounded to powder using mechanical grinder. The obtained powder was used for the preparation of ethanolic extract. 30g of powder was packed into Soxhlet extractor with sufficient volume of ethanol for adequate cycles. The extract was concentrated by evaporation. The final extract was preserved in a refrigerator. The percentage of yield was found to be 14.4%.

Preliminary phytochemical screening of alcoholic extract

The ethanolic extract of *Solanum melongena* was subjected to preliminary phytochemical screening as per the standard procedure.

Experimental Animals

Wistar Albino rats (175 to 225 g) of either sex were used for this study. They were maintained under standard conditions (temperature 22 ± 2°C, relative humidity 60±5% and 12 h light/dark cycle) and had free access to standard pellet diet and water and libitum. The animals were housed in sanitized polypropylene cages containing sterile paddy husk as bedding. The Institutional Animal Ethics Committee reviewed and approved the experimental protocol (Approval no: SCP/IAEC/F150/P198/2022). All the procedures were performed in accordance with Institutional Animal ethics committee constituted as per the direction of the Committee for Control and Supervision of Experiments on Animals (CCSEA) [11].

Evaluation of antidiabetic activity

Alloxan Induced Diabetic Activity in Rats:

The Wistar albino rats (175-225g) of either sex were randomly divided into five groups of six each. The different groups were assigned as follows.

Group I: Normal control (Vehicle)

Group II: Diabetic control (Alloxan 100 mg/kg, i.p)

Group III: (Alloxan 100 mg/kg, i.p + standard Glibenclamide 5 mg/kg, p.o)

Group IV: Diabetic animals (Alloxan 100 mg/kg, i.p + *S. melongena* root extract 200 mg/Kg, p.o)

Group V: Diabetic animals (Alloxan 100 mg/kg, i.p + *S. melongena* root Extract 400 mg/Kg, p.o)

Treatment:

All the animals except group I was made diabetic by a single intra peritoneal injection of Alloxan monohydrate (100mg/kg body weight) in normal saline. After two days of Alloxan injection the blood glucose level was assessed using glucometer and the animals having blood sugar level >200 mg/dl were selected for the study. Plant extract was orally administered. All the treatment was given orally once daily for entire 30 days.

Evaluation:

Blood samples were taken on days 0, 7, 14, and 21 of the treatment from the tail vein of the animals under mild anesthesia. Fasting blood glucose levels were assessed using a glucometer. On the 30th day, the animals were anesthetized with ether, and blood was collected through retro-orbital puncture. The samples were then centrifuged at 2500 rpm for 15 minutes. Biochemical analyses, including measurements of fasting glucose, total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol, were conducted using kits from Agape Diagnostics Pvt. Ltd., with the results evaluated through a semi-automated analyzer based on the color intensity of the formed complexes. After completing the experimental protocol, the animals were sacrificed, and additional blood samples were collected via retro-orbital puncture for final biochemical assessments**.**

***Streptozotocin Induced Diabetic Activity in Rats* [11,12]:**

The Wistar albino rats (175-225 g) of either sex were randomly divided into five groups of six each. The different groups were assigned as follows

Group I: Normal control (Vehicle)

Group II: Diabetic control (Streptozotocin 50 mg/kg, i.p)

Group III: (Streptozotocin 50 mg/kg, i.p + Standard Glibenclamide 5 mg/Kg, p.o)

Group IV: Diabetic animals (Streptozotocin 50 mg/kg, i.p +*S. melongena* root Extract 200mg/Kg, p.o)

Group V: Diabetic animals (Streptozotocin 50mg/kg, i.p + *S. melongena* root Extract 400mg/Kg, p.o)

Treatment

All the animals except group I was made diabetic by a single intra peritoneal injection of Streptozotocin (50 mg/kg body weight) in normal saline. After two days of Streptozotocin injection the blood glucose level was assessed using glucometer and the animals having blood sugar level >200 mg/dl was selected for the study. Plant extract was orally administered. All the treatment was given orally once daily for entire 30 days.

Evaluation

Blood samples were taken on days 0, 7, 14, and 21 of the treatment from the tail vein of the animals under mild anesthesia. Fasting blood glucose levels were assessed using a glucometer. On the 30th day, the animals were anesthetized with ether, and blood was collected through retro-orbital puncture. The samples were then centrifuged at 2500 rpm for 15 minutes. Biochemical analyses, including measurements of fasting glucose, total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol, were conducted using kits from Agape Diagnostics Pvt. Ltd., with the results evaluated through a semi-automated analyzer based on the color intensity of the formed complexes. After completing the experimental protocol, the animals were sacrificed, and additional blood samples were collected via retro-orbital puncture for final biochemical assessments.

Methods for estimation of biomarkers

The biochemical parameters were estimated as per the standard procedure prescribed by the manufacturer's instruction manual provided in the kit using semi-autoanalyzer [13].

Statistical analysis

All data were expressed as Mean ± SEM. The statistical significance between groups were compared using one-way ANOVA, followed by Dunnett's multiple comparison test.

Result

Preliminary phytochemical screening

The preliminary phytochemical test of *Solanum melongena* root extract is performed and the results showed the presence of alkaloids, flavonoids, cardiac glycosides, terpenoids, saponins, tannins, volatile oils.

Alloxan induced antidiabetic activity:

Fasting blood glucose level (FBG) was within the range of 70-100 mg/dl in all the groups at day 0. Treatment with alloxan in normal saline (100 mg/kg. i.p) had increased the FBG level more than 200 mg/dl after 48 h. Changes in FBG level in different groups after repeated dose administration are tabulated in Table No. 01. Diabetic control group has showed significant increase in fasting blood glucose during the study period. Glibenclamide (5 mg/kg) significantly ($p< 0.01$) reduced FBG after repeated administration as compared to diabetic control group. Whereas treatment with SME at dose 200 mg/kg and 400 mg/kg has significantly ($p< 0.01$) decreased FBG as compared to diabetic control on 7th, 14th, 21st and 30th day.

Table no 1: Effect of ethanolic extract of *S. melongena* extract on blood glucose level in alloxan induced diabetic rat

Groups	**Blood Glucose level (mg/kg)**				
	Initial	**Day 7**	**Day 14**	**Day 21**	**Day 30**
Normal control	91.17 ± 1.195	91.50 ± 1.232	91.33 ± 1.202	90.98 ± 1.182	90.87 ± 1.352
Diabetic control	292.2 ± 1.138$^{\#}$	294.5 ± 1.310$^{\#}$	302.8 ± 5.718$^{\#}$	304.0 ± 6.836$^{\#}$	308.7 ± 8.456$^{\#}$
Glibenclamide (5mg/kg)	285.0 ±3.225	206.3 ± 2.985**	199.8 ± 6.215***	168.5 ± 2.693***	136.8 ± 5.665***
SMRE (200mg/kg)	292.2 ± 1.990	287.3 ± 2.848*	277.5 ± 6.607*	259.5 ± 4.272**	199.3 ± 6.469**
SMRE (400mg/kg)	291.8 ± 1.973	278.7 ± 4.485*	267.8 ± 2.762**	247.7 ± 2.771**	247.7 ± 2.771**
Values are expressed as mean± S.E.M, n=6 in all group except in diabetic control, one way ANOVA followed by Dunette's t- test *p<0.05, **p<0.01, ***p<0.001, when compared with diabetic control rats. # p<0.001, Values are significantly different from normal with control group.					

STZ induces anti diabetic activity

Fasting blood glucose (FBG) level was within the range of 70-100 mg/dl in all the groups at day 0. Treatment with STZ in normal saline (50 mg/kg, i.p.) had increased the FBG level more than 200 mg/dl after 48 hr. Changes in FBG level in different groups after repeated dose of drug administration are

tabulated in Table No. 02. Diabetic control group has showed significant increase in fasting blood glucose during the study period. Glibenclamide (5 mg/kg) significantly ($p<0.01$) reduced FBG after repeated administration as compared to diabetic control group. Whereas treatment with SME 200 mg/kg and 400 mg/kg has significantly ($p<0.05$) decreased FBG as compared to diabetic control on 7th, 14th, 21 stand 30th day.

Table no 2: Effect of ethanolic extract of *S. melongena* extract on blood glucose level in STZ induces diabetic rats

Groups	**Blood Glucose level (mg/kg)**				
	Initial	**Day 7**	**Day 14**	**Day 21**	**Day 30**
Normal control	91.77 ± 132	91.15 ± 1.066	90.70 ± 1.854	90.81 ± 1.167	90.78 ± 1.444
Diabetic control	253.8 ± 1.376#	260.7 ± 2.060#	265.4 ± 1.304#	274.5 ± 2.765#	284.3 ± 3.712#
Glibenclamide (5mg/kg)	257.5 ± 2.717	225.5 ± 5.506**	192.8 ± 1.447**	165.0 ± 3.596***	123.3 ± 2.985***
SMRE (200mg/kg)	267.5± 2.719	254.3 ± 5.213*	241.9 ± 1.172**	236.7 ± 3.818**	191.7 ± 2.028**
SMRE (400mg/kg)	275.2 ± 1.447	260.8 ± 2.023*	239.3 ± 2.906**	221.3 ± 4.810**	183.7 ± 3.051**
Values are expressed as mean± S.E.M, n=6 in all group except in diabetic control, one way ANOVA followed by Dunette's t- test *p<0.05, **p<0.01, ***p<0.001, when compared with diabetic control rats. # p<0.001, Values are significantly different from normal with control group.					

Table no 3: Bodyweight in Alloxan induced diabetic rats.

Groups	**Body Weight (g)**				
	Initial	**Day 7**	**Day 14**	**Day 21**	**Day 30**
Normal control	206.5 ±1.500	209.8 ±4.246	213.2 ± 7.485	214.8 ± 9.130	216.5 ± 1.473
Diabetic control	209 ± 4.308	199.0 ± 1.211	190.0 ± 2.236	187.5 ± 2.814	181.7 ± 4.216
Glibenclamide (5mg/kg)	205.8 ± 2.151***	203.8 ±1.956***	204.8 ± 2.626***	207.3 ± 4.828***	209.0 ± 6.419***
SMRE (200mg/kg)	208.7 ± 2.319	203.8 ± 1.956	204.2 ± 2.104	204.2 ± 2.224*	206.8 ± 4.693**
SMRE (400mg/kg)	205.7 ± 2.201	203.7 ± 1.333	202.3 ± 0.8028	203.2 ± 1.493*	206.5 ± 4.738**
Values are expressed as Mean± S.E.M, n=6 in all group except in diabetic control, one way ANOVA followed by Dunette's t- test *p<0.05, **p<0.01, when compared with diabetic control.					

Table no 4: Bodyweight in STZ induced diabetic rats.

Groups	**Body Weight (g)**				
	Initial	**Day 7**	**Day 14**	**Day 21**	**Day 30**
Normal control	201.7± 0.4216	203.0 ± 3.615	205.7 ± 5.277	207.0 ± 8.606	210.3 ± 1.194
Diabetic control	200.0 ± 2.049	190.3 ± 0.5578	184.8 ± 2.982	180.8 ± 3.005	178.3 ± 2.108
Glibenclamide (5mg/kg)	200.8 ± 1.922***	201.5 ± 3.547***	203.8 ± 6.858***	204.2 ± 1.018***	205 ± 1.208***
SMRE (200mg/kg)	196.3 ± 1.022	192.5 ± 2.460	192.5 ± 2.460	193.2 ± 1.078*	194.8 ± 1.352*
SMRE (400mg/kg)	195.0 ± 0.8563	193.3 ± 0.9545	193.2 ± 0.9098	194.0 ± 1.461*	195.7 ±2.985*
Values are expressed as Mean± S.E.M, n=6 in all group except in diabetic control, one way ANOVA followed by Dunette's t-test *p<0.05, **p<0.01, when compared with diabetic control.					

Effect of S. melongena root extract on serum cholesterol, triglycerides, HDL and LDL in alloxan and STZ induced diabetic rats:

All doses of SMRE significantly ($p<0.05$) decreased the elevated levels of TC, TG, and LDL and increased HDL level in the diabetic rats. These parameters were significantly ($p<0.05$) different in the diabetic treated rats when compared to the diabetic control groups. Results are summarized in Table No. 05 and 06.

Table no 5: Effect of *S. melongena* root extract on serum cholesterol, triglycerides, HDL, and LDL, in Alloxan induced diabetic rats.

Groups	**SERUM**			
	Cholesterol (mg/kg)	**Triglyceride (mg/kg)**	**HDL (mg/kg)**	**LDL (mg/kg)**
Normal control	106.2 ± 1.990	147.3 ± 2.741	38.0 ± 1.506	41.17 ± 0.792
Diabetic control	205.2 ± 1,302#	178.0 ± 2.517#	30.33 ± 1.961#	144.0 ± 3.933#
Glibenclamide (5mg/kg)	66.33 ± 1.406**	99.33 ± 6.173**	39.17 ± 1.376**	80.33 ± 1.98**
SMRE (200mg/kg)	146.7 ±1.258**	97.50 ± 1.962**	33.67 ± 1.382*	141.7 ± 1.971**
SMRE (400mg/kg)	108.2 ± 2.688**	165.7 ± 2.909**	32.50 ± 1.522**	89.17 ± 3.664**
Values are expressed as Mean± S.E.M (n=6). One way ANOVA followed by Dunette's t- test. *p<0.05, **p<0.01 when compared with diabetic control group. #p<0.00. Values are significantly different from normal with control group.				

Table no 06: Effect of *S. melongena* extract on serum cholesterol, triglycerides, HDL, and LDL in STZ induced diabetic rat

Groups	**SERUM**			
	Cholesterol (mg/kg)	**Triglyceride (mg/kg)**	**HDL (mg/kg)**	**LDL (mg/kg)**
Normal control	67.32 ± 2.25	57.48 ± 0.09	47.65 ± 1.54	46.26 ± 3.28
Diabetic control	162.5 ± 1.013#	215.8 ± 5.069#	46.00 ± 3.00#	75.67 ±2.974#
Glibenclamide (5mg/kg)	156.7 ± 2.824***	95.4 ±1.390***	59.33 ± 5.897***	71.50 ± 2.668***
SMRE (200mg/kg)	127.2 ± 2.750*	210.2 ±3.420**	35.50 ± 2.986*	127.5 ± 4.581*
SMRE (400mg/kg)	108.7 ± 4.394**	198.7 ± 2.333**	39.50 ± 4.169**	76.67 ± 4.723**
Values are expressed as Mean± S.E.M (n=6). One way ANOVA followed by Dunette's t- test. *p<0.05, **p<0.01 when compared with diabetic control group. #p<0.00. Values are significantly different from normal with control group.				

Discussion

This study aimed to explore the impact of *Solanum melongena* root extract on blood glucose levels and lipid profiles in diabetic rats. The findings revealed that Alloxan monohydrate specifically targeted and destroyed the pancreatic beta cells in the rats, leading to significant damage to the islets of Langerhans. This destruction reduced insulin production and impaired glucose conversion to glycogen, resulting in elevated blood sugar levels (hyperglycaemia) in the diabetic rats [14,15]. Similarly, Streptozotocin induces diabetes by selectively damaging insulin-secreting beta cells, which reduces their activity and impairs glucose utilization by body tissues [16,17].

Glibenclamide was used as a standard because it is a second-generation sulfonylurea derivative, oral hypoglycaemic agent and found to be effective in diabetic rats that retain functioning of islet β -cells. Hence the principle mechanism of action is to stimulate the production and secretion of insulin by the β -cells of pancreas. This drug may lower down the output of glucose from the liver by insulin independent mechanism [18].

The extract of *Solanum melongena* root showed significant ($p<0.01$) antidiabetic activity in both the experimentally induced diabetes models, which were compared to standard Glibenclamide. The results in the present study indicate that the root extract of *Solanum melongena* were found to be effective against both alloxan and streptozotocin induced diabetes.

In diabetic control rats, there was an increase in total cholesterol, triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C), while high-density lipoprotein cholesterol (HDL-C) levels were lower. Treatment with all doses of *S. melongena* and Glibenclamide significantly ($p<0.05$) reduced levels of

cholesterol, triglycerides, and LDL-C, and significantly increased HDL-C levels in the treated rats. These observations suggest that the root extract of *S. melongena* effectively lowers lipid levels in diabetic rats.

The phytochemical screening of *Solanum melongena* root extract revealed the presence of alkaloids, flavonoids, cardiac glycosides, tannins, saponins, volatile oils, and terpenoids. Previous research on diabetes suggests that alkaloids, terpenoids, and flavonoids play a role in antidiabetic activity. Alkaloids may enhance hepatic glycogen production, while flavonoids are recognized for their bioactive antidiabetic properties. The antidiabetic effects observed in *Solanum melongena* roots could be attributed to these compounds. Although the precise mechanism remains unclear, it is hypothesized that the root extract may improve serum insulin activity by either stimulating insulin secretion from pancreatic β-cells or enhancing glucose utilization and inhibiting intestinal glucose absorption. Further research is required to isolate and identify the active components and elucidate the exact mechanisms behind its antidiabetic effects.

Conclusion

Many herbal medicines have been recommended for the treatment of diabetes, In the present study the extract of the plant *Solanum melongena* root was studied for its antidiabetic potentials. The preliminary phytochemical screening of the plant *Solanum melongena* root extract revealed the presence of Alkaloids, Flavonoids, Cardiac glycosides, Tannins, Saponins, Volatile oil and Terpenoids. The observed anti- diabetic activity might be due to the presence of these phytoconstituents. From experimental data it can be concluded that the extract of the *Solanum melongena* root showed significant, dose-dependent anti-diabetic activities in both alloxan and STZ induced diabetic models. The possible mechanism of action might be due to the regeneration of pancreatic β- cells, which may increase the insulin level or by increasing the peripheral utilization of glucose. Though the extract showed significant anti-diabetic activity, further study is needed to isolate the bioactive compounds responsible for this activity with exact mechanism of action involved in the same.

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