

Original Research

Hypoglycemic effect of inositol (IP6 as nutritional supplement) on streptozotocin induced type II diabetes mellitus in rats

Authors:

Harry Thomas Rodriguez A,
Muthukumar N and
A John de britto

Institution:

1. Associate Professor,
Department of
Pharmaceutical
Biotechnology, Chilkur
Balaji College of Pharmacy,
Hyderabad.

2. Associate Professor,
Department of Botany,
St. Xaviers College,
Tirunelveli.

3. Research Scholar,
Department of Botany,
St. Xaviers College,
Tirunelveli

Corresponding author:

Harry Thomas Rodriguez
A

ABSTRACT:

In this research, a water soluble vitamin B8 (Inositol) sometimes referred to as phytic acid which has been shown to be effective in treating diabetes mellitus was used to study the hypoglycemic effect. Banana, grapes and orange are the rich inositol food source. The study shows that inositol has anti-diabetic effect on streptozotocin induced diabetic rats and has potential use as a hypoglycemic agent.

Keywords:

Inositol, Hypoglycemic activity.

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INTRODUCTION

Diabetes is an inherited metabolic ailment portrayed by Hypoglycemia that results from utter comparative inadequacy of Insulin secretion (Kuppusamy *et al.*, 2011). Diabetes is auto-immune, hormonal and metabolic disorders, along with hyperphagia (obesity, a particular loss of pancreatic islet Beta cell mass, high blood glucose level and micro vascular complications (Adkeouu *et al.* 2004; Yamac *et al.*, 2008). It is the third most threatening disease whose mortality is directly after malignancy and cardiovascular diseases. Diabetes emerging as a worldwide health care problem that threatens to achieve pandemic level by 2030; the number of individuals with diabetes worldwide is anticipated to increment from 171 million out of 2000 to 366 million by 2030 (Lin *et al.*, 2007; Wildy *et al.*, 2004).

Research against diabetes and its difficulties have been getting an ever increasing number of considerations. Anyhow, at present accessible medications for diabetes mellitus have various constraints, for example, antagonistic impacts, restricted viability and high rates of secondary failure. As of now, there is a solid necessity develop new natural hypoglycemic agents, and the quest for proper hypoglycemic agents has as recently centered of numerous plants and fruits utilized in traditional medicine (Kim *et al.*, 2006; Tsai *et al.* 2006; Sharon and Nutrients, 2005).

The inositol (phytic acid) isolated from fruits of grapes, orange and banana have been reported to exhibit a variety of biological activities, including Alzheimer's disease, insomnia, bipolar mood disorder, retinopathy of prematurity and diabetes. In the present study, we investigated the hypoglycemic effect of inositol (Sigma-Aldrich) on streptozotocin induced diabetic rats. The results showed that inositol can significantly reduce blood glucose level and increase the insulin level in streptozotocin induced diabetes rats and has potential

use as an anti-diabetic agent.

MATERIALS AND METHODS

Standard inositol, streptozocin, blood glucose meters, insulin kit were purchased from Sigma-Aldrich bangalore. All the other chemicals used were of analytical grade.

Experiment animal

Male albino wistar rats (body weight 150-200 g) used for experiments were used for this experiments with the permission of experimental center Sastra University, Thanjavur, Tamilnadu. The rats were acclimatized before being used for the experiment. Before and during the experiment the rats were housed under controlled environmental conditions of temperature ($24\pm 2^{\circ}\text{C}$) and a 12 h light and dark cycle, and maintained on (unless otherwise stated) standard food pellets and water add limited.

Experimental design

The diabetic rats were prompted by the intra peritoneal (i.p.) injection of STZ freshly at a portion of 60 mg/kg body weight. Three days post STZ treatment, sera were collected for estimation of blood glucose from the tail vein. The rodents were marked as hyperglycemia (blood glucose level at 16.7 mmol) and were utilized as the diabetic rats for further investigation.

The STZ induced rats were haphazardly divided into four groups (6 rats per group), and normal rats were used as the control.

Group I (n=6): normal control (NC), normal rats were allowed to free access to a normal diet and treated with saline for 28 days.

Group II (n=6): diabetic control (DC) the diabetic rats were allowed to free access to a normal diet and treated with saline for 28 days.

Group III (n=6): Inositol 100, the diabetic rats were put on a normal diet and treated with 100 mg/kg of inositol for 28 days.

Table 1. Effect of Inositol in diabetic induced rats

S. No	Group	Blood glucose (mg/ dL)				
		0 day	7 th day	14 th day	21 st day	28 th day
1	Normal	82.3 ±0.01	82.1 ±0.27	81.1 ±0.30	82.3 ±1.20	82.2 ±1.64
2	Diabetic control	339.41 ±1.02	341.10 ±1.21	360.1 ±1.26	371.14 ±0.91	381.50 ±1.11
3	Inositol (100mg/Kg)	340.24 ±1.16	332.10 ±21.60	330.61 ±1.16	328.22 ±1.96	196.92 ±1.99
4	Inositol (200 mg/Kg)	343.21 ±1.92	301.12 ±1.91	261.14 ±1.24	181.16 ±1.90	158.67 ±1.96
5	Metformin	341.16 ±1.15	150.42 ±1.91	120.26 ±1.72	82.40 ±1.65	82.21 ±1.11

Data represent mean ±SD (n=6) for each group.

Group IV (n=6): Inositol 200, the diabetic rats were put on a normal diet and treated with 200 mg/kg of inositol for 28 days.

Group V (n=6): Metformin, the diabetic rats were put on a normal diet and treated with 200 mg/kg: metformin for 28 days.

On the last day of the study the animals were denied for food overnight sacrificed and yielded by cervical dislocation. Blood was gathered in polystyrene tubes without the anticoagulant. Serum was quickly isolated by centrifugation at 3000 rpm at room temperature for 10 min. samples were put away at -70°C until examined. The pancreas were removed immediately, cleaned and washed in ice cold normal saline for further biochemical examination. Pancreatic tissue was fixed in formaldehyde solution and embedded in paraffin. Sections were stained with hematoxylin and eosin and evaluated under light microscope by experienced pathologist.

RESULTS AND DISCUSSION

In recent years new information has emerged that inositol compounds regulates β -cells. Streptozotocin is one of the most commonly used substances to introduce diabetes in the rats. This toxin causes the death of pancreatic β -cells by alkylation of DNA resulting in reduced synthesis of insulin (Montilla et al., 2004). The effect of inositol on blood glucose level in STZ – induced diabetic rats were shown in

Table 1. The blood glucose level in normal rat's maintained constant during four weeks and was significantly lower than those induced diabetic rats of the rest four groups. The daily administration of inositol (100 and 200 mg/kg) in STZ-induced diabetic rats caused a significant reduction in the blood glucose level as compared to diabetic control group.

At fourth week, the mean decrease in the percentage of blood glucose level caused by inositol at the dose of 100 mg was 165.251± 1mg/dL. The result showed that lower dose inositol was a little more effect in reducing blood glucose range than Metformin on STZ –induced diabetic rats. However, no significant difference was observed between inositol and standard drug. The effects of inositol on insulin level in STZ-induced diabetic rats were shown in Table 2. The insulin level in diabetic control rats was significantly lower than that of normal group. After four weeks insulin level increased significantly in inositol treated groups. Pancreatic β -cells are highly specialized cells which are responsible for producing all of the insulin required by an organism to maintain glucose homeostasis. Defects in development, maintenance or expansion of β - cells could results in impaired glucose metabolism and diabetes (Ackermann and Gannaon, 2007).

The immunohistochemical staining of the pancreatic tissues showed that strong insulin antigen positivity was detected in the β -cells of the islets in healthy rats and islets maintained a normal rounded

Table 2. Effect of inositol on insulin level in STZ induced diabetic rats

	Normal control (1U/mL)	Diabetic control (1U/mL)	Inositol (100mg/1U/mL)	Inositol (200mg 1U/mL)	Standard metformin
Plasma insulin (1U/mL)	16.78±1.01	6.91±1.2	20.76±1.32	19.51±1.96	18.01±1.76

Data represent mean ±SD (n=6) for each group.

appearance. Anyhow, there was week insulin immune reactivity in a few β -cells in the islets of diabetic control rodents. Insulin-positive cells were disorganized. Inositol treatment extensively expanded the insulin antigenicity of β -cells of islets and had an ordinary appearance, proposing the likelihood of β -cells proliferation and recovery by inositol treatment. The result additionally demonstrated that the quantity of cells expanded essentially in inositol treated groups. Other than this inositol has the capability of remediating destruction of pancreatic islets. Further, treatment of STZ-induced diabetic group with inositol could significantly prevent the development of diabetes. The hypoglycemic effect of inositol was not dose dependent. Hence inositol could be considered as a potential in controlling blood glucose level.

CONCLUSION

The aim of the review was to highlight known and potential role of inositol in β -cells stimulation. The biochemical assays suggest that inositol 100 200 mg/kg body weight administered orally in STZ-induced diabetic rats could significantly reduce blood glucose level, increase the insulin level and remediating the damaged pancreas beta-cells. More interesting, it was not dose dependent. WHO could recommend the drug inositol as a single drug, new ant diabetic-agent.

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