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Anti-Diabetic Activity of *Ipomoea batatas* Leaves Extract: Effects on Hepatic Enzymes in Alloxan-Induced Diabetic Rats

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ABSTRACT

Diabetes mellitus is the most common endocrine disorder of man, whose devastating effect is increasing by the day and severity almost at epidemic level. This study was carried out to investigate the anti-diabetic activity of *Ipomoea batatas* (sweet potato) leaves extract and its effect on hepatic enzymes, total protein and albumin in alloxan induced diabetic rats. A total of twenty animals was divided into four experimental groups consisting of five animals each. The groups included a positive control, negative control, diabetic-treated *Ipomoea batatas* and Diabetic-treated tolbutamide for 14 days. All were fed normal diet *ad libitum*. After the treatment a significant reduction was observed in fasting serum glucose levels in the treated diabetics' rats. There was a significant ($p<0.05$) reduction of feed and water intakes by the animals after the treatment with *Ipomoea batatas* and tolbutamide. Treatment also improved the weight gain compared to untreated diabetic rats. Alkaline phosphatase activity in the diabetes untreated is significantly higher compared to that normal and treated animal and others treated with extract and tolbutamide. A Similar trend was observed in the Aspartate transaminase and Alanine transaminase activity, respectively, the reversed was observed in the albumin and total protein level, respectively. Hence, the result shows that the extract is not toxic and possesses anti-diabetic properties.

Key words: *Ipomoea batatas*, anti-diabetic, hepatic enzymes, alloxan, albumin

INTRODUCTION

Diabetes Mellitus (DM), a common endocrine disorder of man, is considered one of the major health concerns all over the world today (Rohilla and Ali, 2012). It is a disease of disordered metabolism of carbohydrate, protein and fat, caused by the complete or relative insufficiency of insulin secretion and/or insulin action (Ivorra *et al*., 1989). The number of people suffering from the disease worldwide is increasing at an alarming rate, according to the World Health Organization (WHO), more than 180 million people worldwide have diabetes and that this number is likely to double by 2030 (Wild *et al*., 2004). This increase in incidence follows the trends of urbanization and lifestyle changes, perhaps most importantly a Western-style diet. The greatest increase in prevalence is however expected to occur in Asia and Africa, where most patients will probably be found by 2030 (Wild *et al*., 2004).

One of the most potent methods to induce experimental diabetes mellitus is chemical induction by alloxan, a well-know diabetogenic agent. Alloxan is a urea derivative, which causes selective

necrosis of the β-cells of pancreatic islets. Its toxic action on pancreatic β-cells involve oxidation of essential sulfhydryl (-SH) groups, inhibition of glucokinase enzyme, generation of free radicals and disturbances in intracellular calcium homeostasis resulting in diabetic mellitus disease (Rohilla and Ali, 2012). Diabetes can be managed by exercise, diet and pharmaceutical drugs like tolbutamide, which are either too expensive or have undesirable sides effects or contraindications (Serrano, 1990). Thus, the search for new drugs with low cost, more potential and without adverse effects becomes inevitable.

A great number of medicinal plants have been used in the treatment of diabetes in different parts of the world, some of which are without scientific scrutiny. The World Health Organization has also encouraged and recommended the use of plants as an alternative therapy for diabetes especially in countries where access to the conventional treatment of diabetes is not adequate (WHO., 1980). Sweet potatoes (*Ipomoea batatas*) are excellent sources of plant proteins with very low calories. Unlike other starchy root vegetables, it is used in folk medicine for the treatments of metabolic diseases (Niwa *et al*., 2011). Its leaves, the by-products, possess activities of accelerating metabolism, preventing atherosclerosis, protecting eyesight, hypoglycemia and anti-oxidant (Islam, 2006). *Ipomoea batatas* is used for the treatments of diabetes, although its mechanism of action is enigmatic. The present study was therefore intended to investigate the anti-diabetic activity of *Ipomoea batatas* leaves extract and its effect on hepatic enzymes in alloxan induced diabetic rats.

MATERIALS AND METHODS

Collection of plant materials and preparation of extract: *Ipomoea batatas* were collected between May and June in Yaba area of Lagos State, Nigeria and identified and authenticated in the Department of Botany, Lagos State University, Ojo-Lagos, Nigeria. The fresh plant material was air-dried for 4 weeks at room temperature and ground into a powder. The plant powder (500 g) was decocted in 4 L of distilled water for 15 min. This was repeated four times, until the resulting extract gave no further colouration. The aqueous extract was then filtered and evaporated to dryness in an oven at 40°C to obtain 100 g of crude residue (yield: 20%).

Experimental animals: Three month old male Wistar Albino rats weighing between 160-200 g were obtained from the animal house of the laboratory of Biochemistry, Department of Biochemistry, Lagos State University, Ojo-Lagos, Nigeria. They were acclimatized for two weeks, fed with standard rat feed supplied by Animal Care Ltd., Nigeria.

Experimental induction of diabetes: Diabetes was induced in the animals 14 days before commencement of treatment. The animals were fasted overnight and then injected with alloxan monohydrate dissolved in sterile normal saline at a dose of 150 mg kg^{-1} body weight, intraperitoneally. Since, alloxan is capable of producing fatal hypoglycaemia as a result of the massive pancreatic insulin release, rats were treated with 20% glucose solution intraperitoneally after 6 h. The animals were then allowed to drink 5% glucose solution for the next 24 h to prevent hypoglycaemia (Dhandapani *et al*., 2002). After a fortnight, rats with marked hyperglycaemia were selected and used for the study.

Experimental design: In the experiment, a total of 20 rats were divided into 4 groups with five animals in each group:

- **Group A:** Positive Control-normal rats
- **Group B:** Negative Control-Diabetic untreated rats
- **Group C:** Diabetic rats treated with *Ipomoea batatas* leaves extract (150 mg kg^{-1} body weight) for 14 days (Li *et al*., 2009)
- **Group D:** Diabetic rats treated with tolbutamide (80 mg kg^{-1} body weight) for 14 days

All the rats had access to water. Every 7 days (1, 7, 14) the water, feed, body weight and blood glucose of the animals were carefully monitored and after 14 days of treatment, the rats were sacrificed by cervical dislocation under ether anaesthesia after an overnight fasting. Blood samples were drawn at weekly intervals till the end of the study and processed for the estimation of serum glucose, total protein, Alkaline phosphate (ALP), Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT) and albumin. All the experimental animals were conducted according to the ethical norms approved by the Guide for the Care and Use of Laboratory Animals (NIH., 1985) and was approved by the Animal Ethical Committee of the Department of Biochemistry, Lagos State University, Ojo-Lagos, Nigeria.

Biochemical assay: The blood glucose levels was determined for all the samples by the glucose-oxidase method (Varley *et al*., 1976). Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) activities were assayed at 546 nm (Schmidt and Schmidt, 1963). The activity of alkaline phosphatase (ALP) was determined using phenolphthalein mono-phosphate method (Wright *et al*., 1972). Serum total protein concentration was determined at 540 nm using the Biuret method (Plummer, 1978). Serum albumin determination was done using the method of Doumas *et al*. (1971).

Statistical analysis: The data were analyzed using one-way ANOVA followed by Turkey Honest Significant Difference (THSD). The differences were considered statistical significant at $p<0.05$.

RESULTS

Water, feed intakes and body weight: Table 1 shows a significant ($p<0.001$) increase in the index of water intakes of negative diabetic rats compared to positive control-control rats,

Table 1: Effect of tolbutamide and *Ipomoea balatas* leaves extract on the intakes (mL rat^{-1} day^{-1}) and feed intake (g rat^{-1} day^{-1}) of alloxan-induces diabetic animals

	Days		
Treatment groups	0	7	14
Water intakes (mL rat^{-1} day^{-1})			
Positive control-normal rate	16.20±0.42	18.00±0.79	15.00±0.36
Negative control-diabetic untreated rats	77.80±4.16$^{\#}$	87.60±0.76$^{\#}$	79.40±2.28$^{\#}$
Diabetic rats treated with *Ipomoea batatas* leaves extract	80.80±3.93	74.80±0.42***	48.80±0.65***
Diabetic rats treated with tolbutamide	81.80±0.89	53.20±0.96***	41.20±3.15***
Feed intake (g rat^{-1} day^{-1})			
Positive control-normal rate	14.00±0.36	15.60±0.45	15.20±0.23
Negative control-diabetic untreated rats	20.40±1.04$^{\#}$	28.20±0.42$^{\#}$	32.80±0.42$^{\#}$
Diabetic rats treated with *Ipomoea batatas* leaves extract	27.20±0.42	31.60±0.57	25.20±0.42*
Diabetic rats treated with tolbutamide	28.20±0.74	24.40±0.28	20.90±0.98*

Values are Mean±SD for 5 rats in each group. Values having different superscript differ significantly when compared with position control-normal ($^{\#}p<0.001$) and negative control-diabetic untreated rats (***$p<0.001$ and *$p<0.001$)

which was decreased with the administration of *Ipomoea balatas* but further reduction by tolbutamide. This same pattern was observed in the feed intakes.

The effect of tolbutamide and *Ipomoea batatas* leaf extract on body weights (g) in alloxan-induced diabetic animals is depicted in Table 2. Significant ($p<0.001$) weight loss was observed in negative control-diabetic untreated rats compared to positive control-normal rats. Treatment with aqueous extract of *Ipomoea batatas* and tolbutamide improved the weight gain throughout the 14 days but the highest improvement in the weight gain was by *Ipomoea batatas* aqueous leaf extract.

Blood glucose and hepatic enzymes: The change in blood glucose on treatment of diabetic rats with *Ipomoea batatas* and tolbutamide is shown in Table 3. The blood glucose concentration was increased significantly in negative control-diabetics untreated rats compared to positive control-normal rats ($p<0.05$). Administration of *Ipomoea batatas* and tolbutamide led to significant decrease in blood glucose levels in diabetics treated groups ($p<0.001$). In Table 4, the ALP activity in the negative control-diabetic untreated rats was significantly ($p<0.001$) higher compared to that of positive control-normal animal but treatment with *Ipomoea batatas* extract and tolbutamide reduced its activity, although, *Ipomoea batatas* was more potent. This trend was observed in the AST and ALT activities, albumin and total protein levels, respectively.

Table 2: Effect of tolbutamide and *Ipomoea balatas* leaves extract on b.wt. (g) of alloxan-induces diabetic animals

	Days		
Treatment groups	0	7	14
Body weights (g)			
Positive control-normal rate	168.20±3.33	180.00±0.00	186.80±0.36***
Negative control-diabetic untreated rats	176.80±4.29	156.20±0.00	144.40±0.28$^{\#}$
Diabetic rats treated with *Ipomoea batatas* leaves extract	171.60±4.19	197.00±0.00*	200.40±0.65***
Diabetic rats treated with Tolbutamide	169.00±4.47	175.60±0.00	190.80±3.15***

Values are Mean±SD for 5 rats in each group. Values having different superscript differ significantly when compared with position control-normal ($^{\#}p<0.001$) and negative control-diabetic untreated rats (***$p<0.001$ and *$p<0.001$)

Table 3: Effect of tolbutamide and *Ipomoea balatas* leaves extract on the serum glucose concentration (mg dL^{-1}) of alloxan-induces diabetic animals

	Days		
Glucose concentrations (mg dL^{-1})	1	7	14
Positive control-normal rate	84.20±02.66	64.60±2.75	59.00±3.47
Negative control-diabetic untreated rats	244.20±09.66$^{\#}$	257.00±8.35$^{\#}$	268.00±5.23$^{\#}$
Diabetic rats treated with *Ipomoea batatas* leaves extract	247.00±10.40	183.80±3.53***	268.00±5.23$^{\#}$
Diabetic rats treated with tolbutamide	245.00±11.18	162.00±2.75***	114.60±7.83***

Values are Mean±SD for 5 rats in each group. Values having different superscript differ significantly when compared with position control-normal ($^{\#}p<0.001$) and negative control-diabetic untreated rats (***$p<0.001$ and *$p<0.001$)

Table 4: Effect of tolbutamide and *Ipomoea balatas* extract on the serum biochemical indices of alloxan-induces diabetic animals

	Biochemical indices				
Treatment groups	ALP (U L^{-1})	AST (U L^{-1})	ALT (U L^{-1})	Albumin (mg d L^{-1})	Total protein (mg d L^{-1})
Positive control-normal rate	24.840±09.00	8.80±00.82	3.600±0.45	3.72±0.40	7.11±0.42
Negative control-diabetic untreated rats	104.880±20.00$^{\#}$	74.80±10.00$^{\#}$	10.400±1.10$^{\#}$	4.30±0.43$^{\#}$	5.55±0.22$^{\#}$
Diabetic rats treated with *Ipomoea batatas* leaves extract	33.120±06.17**	8.20±01.34***	4.800±0.90***	4.81±0.66	5.86±0.19**
Diabetic rats treated with tolbutamide	44.160±07.56**	7.00±01.54***	5.600±0.45***	4.36±0.19	6.84±0.42**

Values are Mean±SD for 5 rats in each group. Values having different superscript differ significantly when compared with position control-normal ($^{\#}p<0.001$) and negative control-diabetic untreated rats (***$p<0.001$ and *$p<0.001$), ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALT: Alkaline phosphate

DISCUSSION

Available evidence shows that alloxan causes diabetes through its ability to destroy the insulin-producing beta cells of the pancreas, inducing hyperglycaemia and other diseases in animals (Lenzen and Panten, 1998; Ijaola *et al*., 2014). Tolbutamide and some plant drugs were known to influence the effect of diabetes mellitus, however, their anti-diabetic efficacy and hypoglycemic mechanisms are unknown. In the present study, we revealed that while the treatments of *Ipomoea batatas* leaf extract significantly reduced the increased feed and water intakes, there was increase in body weight of the animals which may be due to the regeneration of the adipocytes and muscle tissues to make up for energy in the body. This agrees with the findings of previous workers (Ijaola *et al*., 2014; Niwa *et al*., 2011; Pant *et al*., 1968).

Our finding showed a significant decrease in serum glucose concentration of diabetic animals treated with *Ipomoea batatas* extract compared to treatment with tolbutamide. This observation supports the report of Nishikant *et al*. (2014) and Ijaola *et al*. (2014). The possible mechanism by which aqueous extract of *Ipomoea batatas* brings about its hypoglycaemic action may be, by potentiating the insulin effect, either by increasing the pancreatic secretion of insulin from the cells of islets of Langerhan's or its release from bound insulin, thereby, decreasing the postprandial glucose in animals. This may be the cause of the increased body weight in *Ipomoea batatas* extract treated rats (Oliveira *et al*., 2008; Pandikumar *et al*., 2009).

Some enzymes act as markers and indicators of disease states, thus, their increased activities in serum are indicative of cell damage (Udobre *et al*., 2009). The reduction in ALP activity following *Ipomoea batatas* treatment shows its stability of biliary function against the damage caused by alloxan. The result is similar to what was reported on treatment with *Caralluma fimbriata* (Latha *et al*., 2013). AST and ALT activities act as an indicators of liver function, hence the restoration of these enzymes after administration of *Ipomoea batatas*, indicates that the normal functioning of the liver and the bile duct was restored. This is in consistent with reports of Udayakumar *et al*. (2009) on the *Withania somnifera* extracts.

Albumin constitutes the major component of the Total Protein (TP) and therefore a diagnostic tool for the determination of liver function (Spencer *et al*., 2011). In this present study, while there was an increased in the levels of both albumin and total protein by the administration of *Ipomoea batatas* extract, tolbutamide significantly increased total protein. This observation agreed with the findings of Omoniwa and Luka (2012). The result implied that the liver's synthetic activity and ability to maintain nutrient homeostasis was enhanced as a result of administration of the *Ipomoea batatas* extract.

From the above results, it may be concluded that the *Ipomoea batatas* leaf extracts show no sign of toxicity and possess anti-diabetic activities in alloxan-induced diabetic rats compared to tolbutamide.

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