Anti-diabetic Effects of the Aqueous and Ethanol Extracts of *Ipomoea batatas* Tubers on Alloxan Induced Diabetes in Wistar Albino Rats

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Authors' contributions

Article Information

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ABSTRACT

Background: Diabetes mellitus continues to remain the number one cause of mortality among the low- and mid-income populations. Hence, the need for cost-effective, available and accessible novel drug agents for improved health outcomes. This study was undertaken to investigate the antidiabetic effects of the aqueous and ethanol extracts of *Ipomoea batatas* tubers on alloxan induced diabetes in Wistar albino rats.
Methods: Proximate analysis was conducted directly on the sweet potato tubers using the method of AOAC (2004) while ethanol and aqueous extracts obtained from the *Ipomoea batatas* tubers were subjected to phytochemical analysis using various standard methods. Seven groups of 5 albino Wistar rats each were used for the study as follows: the negative control group, the standard drug group treated with Glibenclamide, the 200 mg/kg aqueous extract group, the 400 mg/kg aqueous extract group, the 200 mg/kg ethanol extract group, the 400 mg/kg ethanol extract group and the untreated group. The rats were induced to diabetes by administering alloxan (130 mg/kg) intraperitoneally. Further, the extracts were orally administered to the four treatment groups while

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changes in both weights and blood glucose levels were closely monitored. After 28 days, blood samples were collected and assayed for the activities of superoxide dismutase, glutathione peroxidase and catalase. Data were further subjected to statistical analysis using ANOVA (Analysis of Variance).

Results: The proximate analysis of *I. batatas* showed a high carbohydrate content of 86.37 ± 0.04 while the fat amount was lowest with 0.58 ± 0.18. The phytochemical analysis indicated a high tannin concentration for both aqueous and ethanol extracts at 87.83 ± 2.91 and 89.05 ± 2.53 respectively whereas the lowest content was found for terpernoids in the aqueous extract and total flavonoids in the ethanol extract. Remarkable recovery from weight loss was more rapid in the 400 mg/kg ethanol extract group (29.09% increase) than the other groups. There was no significant difference ($P > 0.05$) in the initial and final weights of the animals. The difference in final glucose levels were significant ($P < 0.05$) across treatment groups when compared with the negative control group. The 400 mg/kg ethanol extract had the highest percentage reduction in glucose level (53.21%) in 28 days, even more than the standard drug group (24.74 %). The 200 mg/kg ethanol extract gave the least percentage reduction. The results showed that there was no significant difference ($P > 0.05$) in the activities of the three antioxidant enzymes across treatment groups.

Conclusion: The relatively rapid recovery of weight and reduction in blood glucose levels of the animals observed with the 400 mg/kg ethanol extract showed that it is more potent in the management of diabetes mellitus when compared with the other dosage preparations.

1. INTRODUCTION

Diabetes mellitus (DM) is one of the leading causes of death worldwide. It is a group of metabolic diseases characterized majorly by hyperglycemia due to the inability of the body to produce enough insulin or because cells do not respond to insulin that is produced [1] and other occurrences like polyuria and glucosuria.

According to recent statistics, the prevalence figure published by the International Diabetes Federation (IDF) [2] is 425 million persons living with DM worldwide, with nearly 50% of these undiagnosed [2] and the figure is projected to double in the next two decades [3]. The developing economies of Africa and Asia contribute a significant fraction to this figure. There is also a rising burden from the complications of DM alongside the ever-increasing prevalence of the disease. In Nigeria, the prevalence of DM among adults aged 20-69 years is reported to be 1.7% of the IDF published Fig. [4].

Though, conventional synthetic drugs have made considerable progress in the management of diabetes, traditional plant treatments for diabetes are also being used throughout the world and the search for natural anti-diabetes plant produces for controlling diabetes is on-going [5]. Modern synthetic drugs like; biguanides, pioglitazone and alpha glucosidase inhibitors are very effective in managing diabetes but have side effects like gastrointestinal tract disturbance, hypoglycemia and abdominal bloating respectively. Obesity, water intoxication and hyponatremia are also caused by other antidiabetic drugs [4]. In addition to these side effects, most of these drugs come with very with high cost which makes them almost unaffordable for the low-income class. Therefore, the search for medicinal plants with very low cost and little or no side effects becomes a task of global importance.

Ipomoea batatas is one of the medicinal plants with reported vast medicinal properties. It has been documented to possess antidiabetic properties as among the Yorubas in the South-West Nigeria, hot water infusion of the plant of *Ipomoea batatas* continues to be highly valued in the local management of diabetes because of its effectiveness in the control of blood glucose and its low cost [1]. It was also shown by other researchers to decrease blood glucose levels, increase high density lipoproteins and reduces low density lipoproteins levels all due to the presence of dietary fibers with low glycemic index [6,7]. This all-important ethnobotanical value of *I. batatas* predisposes the plant for a scientific evaluation of its potentials, hence the need to study the antidiabetic activities of the aqueous and ethanol extract of *I. batatas* tubers. The aim of this research is to investigate the antidiabetic effects of the aqueous and ethanol extracts of *I. batatas* tubers on alloxan-induced diabetes in Wistar albino rats.

2. MATERIALS AND METHODS

2.1 Study Site

This research was carried out at Natural Products Research and Development Laboratory, Special Research Centre, Nnamdi Azikiwe University, Awka.

2.2 Collection and Identification of Sample

Fresh tubers of *I. batatas (Linn.) Lam* were purchased from Western Research Farm, National Root Crop Research Institute, Umudike, Abia state. The samples were identified and authenticated with Voucher Number Cab No 2 Shelf No 49 at Herbarium Unit in the Department of Botany, Nnamdi Azikiwe University, Awka.

2.3 Preparation of Sample

The *Ipomoea batatas* tubers were washed to get rid of dust and dirt. Afterwards, they were chopped into small pieces and left to dry in the open, away from direct sunlight. The tubers were ground into powder form and stored at room temperature in a clean, dry transparent plastic bottle. The powdered samples were stored in air-tight container until further analysis. Each powdered sample were extracted in hydro-ethanol by soaking 1 kg of each part separately in 1 litre of 70 % ethanol. They were allowed to stand for 48 hours at room temperature with intermittent shaking and later filtered using three layers of muslin cloth followed by Whatman No 4-filter paper. The filtrates were further concentrated by evaporation to dryness using a rotary evaporator.

2.4 Proximate Analysis

The moisture, ash, crude fiber and crude fat were determined using standard methods according of the Association of Official Analytical Chemists [8]. Crude protein was determined by the Micro-Kjeldahl method as proposed by AOAC [8]. The total percent carbohydrate content was estimated by the difference of 100 of the other proximate components as reported by Yerima and Adamu [9] using the following formula:

Total Carbohydrate (%) = 100 - (% Moisture + % Ash + % Crude fibre + % Crude protein + % Fat)

2.5 Phytochemical Analysis

The qualitative phytochemical screening was carried out according to the method of Usunobun et al. [10]. The terpenoid content was determined using the method of Indumathi et al. [11]. The quantity of alkaloid present was determined using the method of Harborne [12]. The flavonoids content was determined by the use of a slightly modified colorimetry method described previously by Barros *et al.* [13]. Tannin content was determined using the AOAC method [8]. The total phenol content of the samples was determined using the method of Barros *et al.* [13]. The amount of oxalate was determined using the method of Osagie [14]. Saponin and cardiac glycoside determinations were done using the method of AOAC [15]. The phytate content was determined using the method of Young and Greaves [16].

2.6 Experimental Animals

Thirty-five rats of Wistar strain were purchased from Onyewuchi Farms, Ifite, Awka, Anambra State. The animals were kept in well aerated cages at the Department of Applied Biochemistry Laboratory, Nnamdi Azikiwe University, Awka and allowed to acclimatize for one week before the experiment. They were maintained under standard environmental conditions of 27°C ± 3°C, 12-hour light/dark cycle according to the National Institute of Health Guide on the Use and Care of Experimental Animals. The animals were fed *ad libitum* with Vital grower's mash pellets purchased from Vital Feed Distributor, Awka. At the end of the acclimatization period, the animals were weighed and grouped accordingly.

2.6.1 Grouping of animals

The rats were divided into seven different groups of five rats each as follows:

Negative control group - induced and received only the normal feed and water;
Positive control or standard drug group - induced and treated with 5mg/75kg glibenclamide;
200 mg/kg aqueous group - received 200 mg/kg *b/w* of the aqueous extract after induction;
400 mg/kg aqueous group - received 400 mg/kg *b/w* of the aqueous extract after induction;
200 mg/kg ethanol group - received 200mg/kg *b/w* of the ethanol extract after induction;
400 mg/kg ethanol group - received 400mg/kg *b/w* of the ethanol extract after induction and
Untreated group - Induced and not treated.

2.7 Acute Toxicity Study

Acute toxicity study was carried out on the two extracts by adopting the method as described by

Lorke [17]. A total of eighteen rats were used for the study. The rats were randomized into six groups: three rats each for the first phase were given 10, 100 and 1000 mg/kg *b/w* and one rat each for the second phase which were given 50, 100, 200 and 400 mg/kg *b/w*. The animals were monitored for changes in behavior and mortality within 2 hours, 24 hours and 14 days after single administration of the extracts.

2.8 Induction of Diabetes

The induction of diabetes was done by administering alloxan intraperitoneally. Erhirhie et al. [18] concluded that the alloxan standard dosage for inducing rats is 150 mg/kg. However, after a pilot study, the dosage was modified to 130 mg/kg. Alloxan was dissolved in 0.9% normal saline solution before administering to the rats according to their individual weights. Afterwards, the animals were fed 5% glucose to achieve diabetes faster. The blood glucose levels of the animals were monitored and after 48 hours it was determined that they have all become diabetic at 200 mg/dl and above.

2.9 Administration of Extracts and Glibenclamide

The animals were orally fed with 130 mg/kg of the extracts according to the method of Erhirhie *et al.* [18]. The animals received the doses according to their various weights. Glibenclamide (5 mg/75kg) was only administered to the standard drug group (positive control) while the untreated group received no treatment. The negative control group received neither the extracts nor glibenclamide.

2.10 Monitoring of Blood Glucose and Body Weights

The glucose levels of the animals were monitored using a Fine Test Glucometer and the weights were measured using a SearchTech weighing balance. Before induction, the weights and blood glucose levels of the animals were measured and then afterwards recorded on a seven-day interval until the end of the experiment.

2.11 Animal Sacrifice and Blood Collection

The animals were anaesthetized with chloroform and blood samples collected via cardiac puncture. The samples were collected into the

universal bottles and allowed to clot, after which they were centrifuged for 10 minutes at 4000 rpm. The sera obtained were transferred into another set of test tubes. The sera were used for the biochemical analysis on the same day.

2.12 Antioxidant Enzyme Assays

2.12.1 Determination of superoxide dismutase activity

Superoxide dismutase activity was determined by its ability to inhibit the auto-oxidation of epinephrine determined by the increase in absorbance at 480 nm as described by Sun and Zigma [19]. The reaction mixture (3 ml) containing 2.95 ml of 0.05 M sodium carbonate buffer pH 10.2, 0.02 ml of the serum and 0.03 ml of 0.3 mM adrenaline in 0.005 N HCl was used to initiate the reaction. The reference cuvette contained 2.95 ml buffer, 0.03 ml of substrate (epinephrine) and 0.02 ml of water. Enzyme activity was calculated by measuring the change in absorbance at 480 nm for 3 min. $\sum = 4020 M^{-1} cm^{-1}$.

2.12.2 Determination of catalase activity

Catalase activity was determined according to Sinha [20]. It was assayed colorimetrically at 620 nm and expressed as µmoles of H_2O_2 consumed/min/mg protein at 25^0C. The reaction mixture (1.5 ml) contained 1.0 ml of 0.01M phosphate buffer (pH 7.0), 0.1 ml of the serum and 0.4 ml of 2M H_2O_2. The reaction was stopped by the addition of 2.0 ml of dichromate-acetic acid reagent (5% potassium dichromate and glacial acetic acid were mixed in 1:3 ratio). The absorbance was recorded at 620 nm using UV-Vis Spectrophotometer and the catalase activity was calculated using $\sum = 40 M^{-1} cm^{-1}$.

2.12.3 Determination of glutathione peroxidase activity

The GSH-Px activity of sera was determined according to a modification of the method proposed by Paglia and Valentine [21]. The reaction medium was composed of potassium phosphate buffer (171 mM), sodium azide (4.28 mM), EDTA (2.14 mM), reduced glutathione (6 mM), NADPH (0.9 mM), and glutathione reductase (2 U.mL^{-1}). The reaction took place at 22°C (±1), starting with the addition of H_2O_2 (0.72 mM). The absorbances of the samples were measured at 340 nm using a spectrophotometer. The measurements were taken every 15

seconds for 300 seconds. The GSH-Px enzymatic activity can be expressed in enzymatic units per mL of sample ($U.mL^{-1}$), $U. L^{-1}$, $U.g^{-1}$ of tissue, $U.g^{-1}$ of protein, or $U.mg^{-1}$ of hemoglobin (PUNCHARD; KELLY, 1996). In the present study, the GSH-Px enzymatic activity was expressed as $U.g^{-1}$ of the blood samples and was calculated using

$$U/g = \Delta A/min \times F$$

Where F is a constant used for converting absorbance per minute ($\Delta A/min$) into enzymatic units (U). F was calculated by the following:

$$F = \left(\frac{RV}{SV}\right) \times 5/6.22\cdot$$

Where RV is the reaction volume (in mL); SV is the sample volume (in mL); 5 is the volume (in mL) used to dilute 1 g of tissue during the enzyme extraction; and 6.22 is the NADPH molar extinction coefficient (in $Mm.cm^{-1}$).

2.13 Data Analysis

Data was analyzed using SPSS statistical software package (SPSS for Windows, version 23, IBM Corporation, NY, USA). One-way Analysis of Variance was used to test for variability between the mean values while Tukey's HSD *post-hoc* test was employed for multiple comparisons. Data was presented as the mean ± Standard deviation of triplicate determinations. Values were considered significantly different at $p = 0.05$.

3. RESULTS

3.1 Proximate Analysis of *I. batatas* Tubers

The proximate analysis of the tubers of *I. batatas* is presented in Table 1. The findings are expressed as Mean ± Standard deviation of triplicate determinations. The percentage of ash, moisture, crude fiber and crude protein with mean values of 1.12 ± 0.03, 8.87 ± 0.28, 1.07 ± 0.17 and 1.97 ± 0.22 respectively. Total carbohydrate was found to be the highest concentration with mean value of 86.37 ± 0.04 explaining *I. batatas* is classified a high energy-yielding food.

3.2 Phytochemistry of *I. batatas* Tubers

The phytochemical analysis of the tubers of *I. batatas* plant is presented in Table 2 below. Generally, from the investigations, both extracts of the tubers expressed considerable amounts and presence of phytochemicals. Terpenoids were seen to be totally absent in the aqueous extract while the ethanol extract had 16.08 ± 0.25 µg/g of terpenoids. Both extracts were also rich in tannins with mean values of 87.83 ± 2.91 and 89.05 ± 2.53 respectively, indicating a possibility for high antioxidant potential in both extract media. There was a significant difference in terpenoids, oxalates, saponins, phytates and cardiac glycosides when the two extracts were compared ($P = 0.05$).

Table 1. Proximate analysis of *I. batatas* tubers

Proximate parameters	Amount (%)
Ash	1.12 ± 0.03
Moisture	8.87 ± 0.28
Crude fiber	1.07 ± 0.17
Fat	0.58 ± 0.18
Crude protein	1.97 ± 0.22
Total carbohydrate	86.37 ± 0.04

Results are expressed as Mean ± Standard deviation of triplicate determinations

Table 2. Phytochemical analysis of the aqueous and ethanol extracts of *I. batatas* tubers

Phytochemicals	Aqueous	Ethanol
Total alkaloids (%)	0.20 ± 0.08	0.32 ± 0.08
Total flavonoids (mgCE/g)	0.12 ± 0.00	0.02 ± 0.00
Tannins (mgTAE/g)	87.83 ± 2.91	89.05 ± 2.53
Total phenol (mgGAE/g)	4.27 ± 0.04	4.54 ± 0.11
Oxalate (mg/g)	3.11 ± 0.14	2.43 ± 0.27
Saponin (%)	0.19 ± 0.07	5.00 ± 0.32
Phytate (%)	0.35 ± 0.01	0.19 ± 0.00
Cardiac glycosides (%)	1.93 ± 0.50	0.32 ± 0.00
Terpenoids (ug/g)	0.00 ± 0.00	16.08 ± 0.25

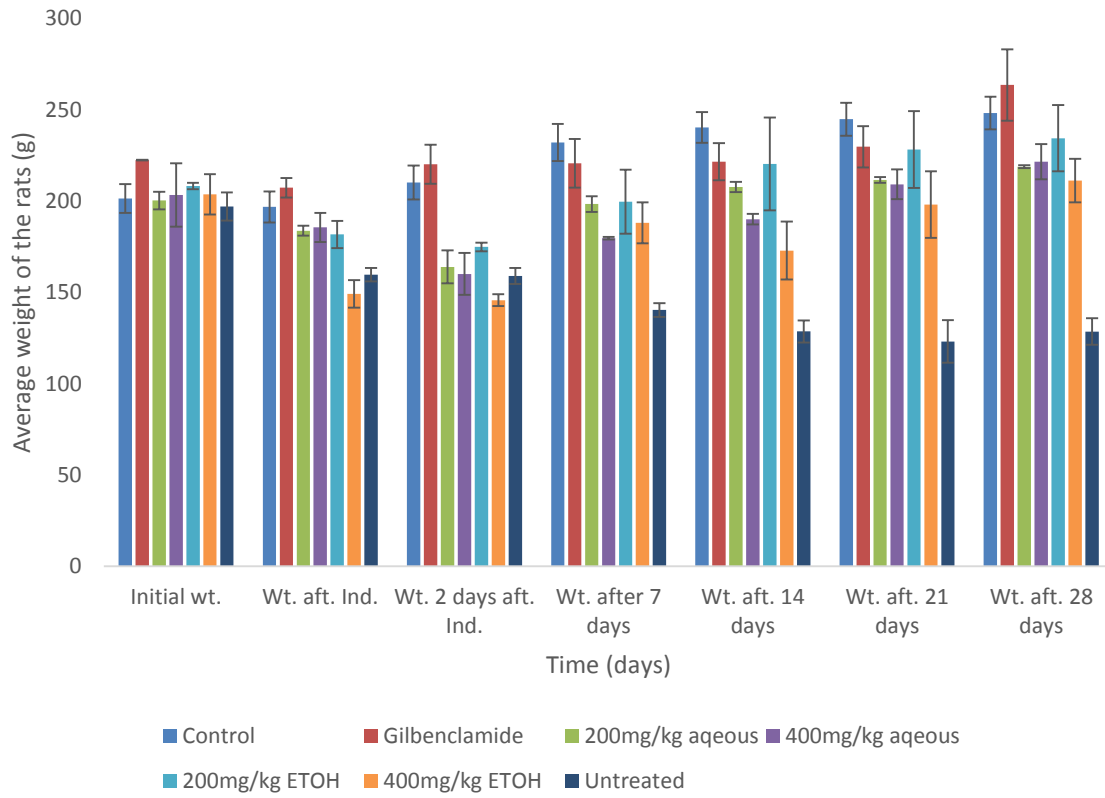*Results are expressed as Mean ± Standard deviation of triplicate determinations*

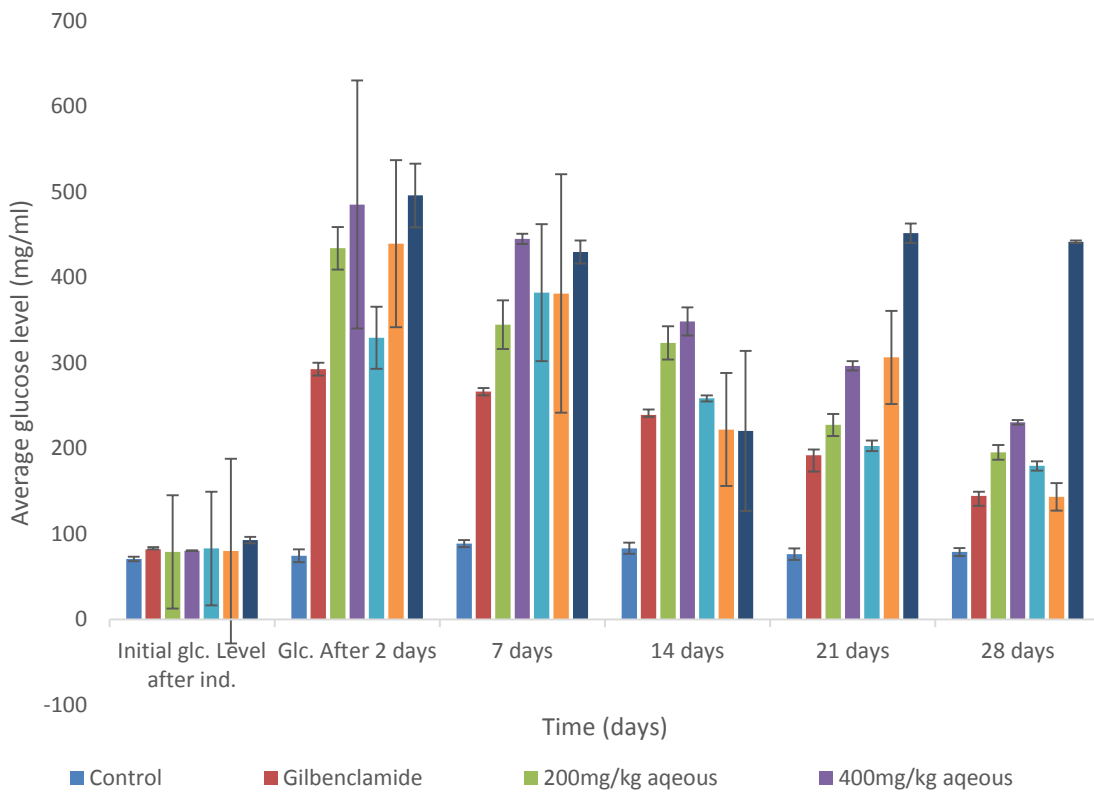**Fig. 1. The average body weights of the animals through the experiment**

Fig. 2. The mean blood glucose levels of the rats through the experiment

3.3 Effect of the Aqueous and Ethanol Extracts of *I. batatas* on Body Weights of the Rats

In Fig. 1, the clustered columns/bars were used to show the average weights of each of the rat groups. Each cluster represents a particular period of observation while each column represents the average weight for a particular group. The varying lengths of the columns in successive clusters show the changes in body weights of the rats over the period of the experiment. There was no significant difference in the initial weights of the animals ($P > 0.05$). The untreated group had the least average initial weight (197.05 ± 7.72 g) while the glibenclamide group had the highest (222.41 ± 0.175 g). After the induction of diabetes using alloxan, there was a drastic reduction in weights in days 1 and 2 in all the groups except the glibenclamide group. Their weights began to increase from day 7 till the end of the experiment except in the untreated group. The increase in weight was more rapid in the 400 mg/kg ethanol extract group (29.09% increase) than the other groups.

3.4 Effect of the Aqueous and Ethanol Extracts of *I. batatas* on Blood Glucose Levels of the Rats

Fig. 2 shows the mean blood glucose levels in the various rat groups over the period of the experiment. The control group remained below 100 mg/dl throughout the experiment while the other groups clearly increased markedly above 200 mg/dl after two days of successful induction of diabetes. Aside from the untreated group, mean blood glucose levels were observed to markedly decrease till the end of the experiment. By the last day of administration, the blood glucose levels in some of the groups had decreased below 200 mg/dl. The untreated group had the highest final glucose levels (441.50 ± 1.50 mg/dl) while the control was the least (78.80 ± 4.70 mg/dl). The difference in final glucose levels were also significant ($P = 0.05$) when all the treatment groups were compared with the negative control. By the 28th day of experiment, the rat groups administered 400 mg/kg aqueous and ethanol extracts showed a 52.47% and 67.3% drop in mean blood glucose levels respectively, which was observed to be significant between the two extracts ($P = 0.05$). Similarly, the 200 mg/kg aqueous and ethanol extract administered *I. batatas* rat groups showed 55% and 45.48% decrease in mean blood glucose levels respectively not statistically significant ($P = 0.05$) between the two rat groups.

3.5 Effect of Aqueous and Ethanol Extracts of *I. batatas* on *In Vivo* Antioxidant Enzymes of the Rats

Fig. 3 illustrates the antioxidant enzymes activities in the various rat groups. There was no significant difference in the activities of all the antioxidant enzymes when statistically compared ($P > 0.05$). The 200 mg/kg ethanol extract group had the highest SOD activity of 1.69 ± 0.53 µ/l while the 400 mg/kg aqueous extract group had the least of 0.79 ± 0.01 µ/l. The 200 mg/kg aqueous extract group had the highest GPx activity of 6.58 ± 1.28 µ/l while glibenclamide group had the least of 2.47 ± 0.21 µ/l. The 400 mg/kg aqueous extract group had the highest catalase activity expressed as 1.23 ± 0.28 µ/l while the control group had the least mean value of 0.38 ± 0.03 µ/l.

4. DISCUSSION

The proximate analysis of the tubers of *I. batatas* showed a moisture content of 8.87 ± 0.27 % and carbohydrate content of 86.37 ± 0.04%. This is in contrast to the findings of Alam et al. [22] who observed that the tubers had relatively high moisture content (70.95 ± 0.70%) and relatively low carbohydrate (25.50 ± 0.13%). In another contrasting result, Adepoju and Adejumo [23] showed that the tubers had relatively low carbohydrate content (26.84%) and also relatively high moisture content of 69.80%. It is important to note that Adepoju and Adejumo [23] carried out an analysis on non-dried sweet potato tubers. However, in a result similar to the one obtained in this study, Dusuki et al. [24] stated that dried samples of purple fleshed sweet potatoes contained low amount of moisture (6.02 ± 0.42%) and high amount of carbohydrate (75.07%). The method of sample preparation may have influenced their various moisture contents. Dried tubers have the tendency to show little moisture content while non dried ones have the tendency to show high moisture content. Low moisture content is an indication that the tubers would likely have a very good shelf life. However, the tubers are only susceptible to bacterial attack if not dried and stored properly.
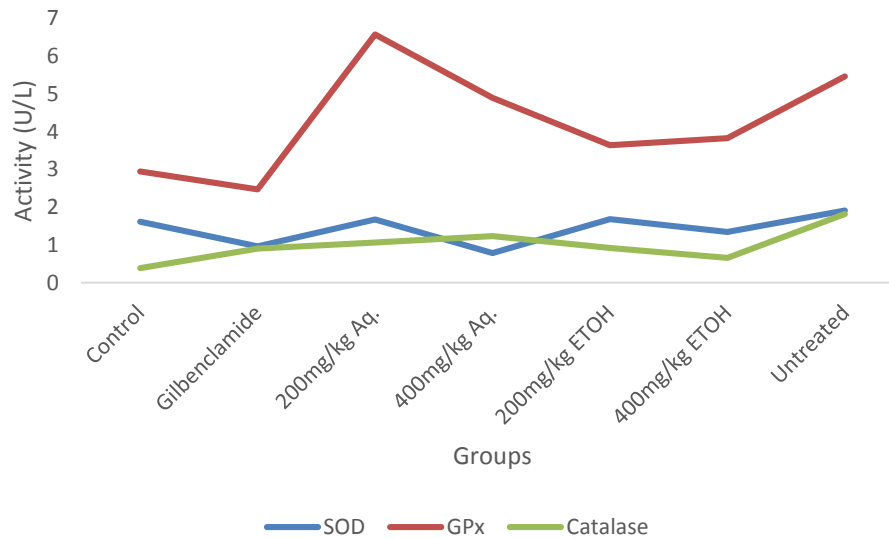
Fig. 3. The mean *in vivo* antioxidant enzyme activities of the rat groups

The high carbohydrate content shows that it is a very good source of energy. It had a low protein content of $1.97 \pm 0.22\%$ which is normal for most tubers since they are high starch containing foods. Dusuki et al. [24] reported $0 \pm 0.00\%$ protein content, while the tubers analyzed by Adepoju and Adejumo [23] had 0.46% proteins. It had a very low-fat content and normal ash content as when compared with other food crops.

The ash content is a measure of the quantity of inorganic matter present in food materials. These results are in line with the findings of Taira et al. [25] who observed I. batatas tubers contained no saturated fats or cholesterol and is a rich source of dietary fiber, antioxidants, vitamins and minerals. Its energy content normally comes from starch, a complex carbohydrate. Taira et al. [25] also reported that it contained a higher amylose to amylopectin ratio and amylose is recommended as a healthy food substance even for patients with diabetes. *I. batatas* is a rich source of vital minerals such as iron, calcium, magnesium, manganese and potassium that are essential for enzyme, protein and carbohydrate metabolism [26].

Terpenoids are phytochemicals well known to have antibacterial, antifungal activity and wound healing properties [27]. Other important therapeutic uses of terpenoids include antimicrobial, antiviral, antiparasitic, immunomodulatory and as skin permeation enhancer. In the present study, terpenoids were observed in the ethanol extract than the aqueous

extract indicating a more potent property of antimicrobial, antifungal and other activities. Terpenoids have been implicated in lowering of blood glucose as shown by previous studies by inhibiting enzymes responsible for the development of insulin resistance, normalization of plasma glucose and insulin levels and glucose metabolism [3]. They can act as agents in the treatment of diabetic retinopathy, neuropathy and nephropathy or in impaired wound healing by inhibiting several pathways involved in diabetes and associated complications. Some other mechanisms of actions for the antidiabetic property of *I. batatas* may be through the inhibition of α-glucosidase, plasma lipase, aldose reductase, tyrosine phosphatase-1B and α-amylase leading to increased uptake of glucose and glycogen synthesis [6].

Tannins were the major phytochemical constituent of the two extracts. This was in contrast to the findings of Ijaola et al. [1] who noted that the major phytochemicals were alkaloids. Tannins as antinutrients are known to reduce the absorption of proteins in the gastrointestinal tract but have been shown to have antidiabetic activity. This means that the two extracts would have good antidiabetic activity. This blood lowering property as observed by the current study may be due to the presence of tannins, which were identified in high concentration in the root plant acting through mechanisms that induce phosphorylation of the insulin receptor and translocation of glucose transporter 4 (GLUT4) involved in the signaling

pathway of glucose transport mediated by insulin [28]. In other studies, they have been observed to enhance the glucose uptake through the mediators of the insulin-signaling pathways, such as PI3K (Phosphoinositol-3-kinase) and P38 MAPK (Mitogen-activated protein kinase) activation as well as GLUT-4 translocation. The reduction in glycemia (blood glucose levels) caused by phenol compounds has been attributed to such actions as a reduction in the absorption of nutrients [29], reduction in food intake, induction of beta cell regeneration and a direct action on adipose cells that enhances insulin activity. Tannins establish a coordinated net of metabolic sensors which integrates lipid metabolism, inflammation, drug metabolism, bile acid synthesis and glucose homeostasis among other processes [29].

The importance of cardiac glycosides in these extracts lie on their role in the treatment of cardiac failure [30]. In cardiac failure, or congestive heart failure, the heart cannot pump sufficient blood to maintain body needs. During each heart contraction, there is an influx of Na^+ and an outflow of K^+. Before the next contraction, Na^+/K^+-ATPase must re-establish the concentration gradient pumping Na^+ into the cell against a concentration gradient. This process requires energy which is obtained from hydrolysis of ATP to ADP by Na^+/K^+-ATPase. Cardiac glycosides inhibit Na^+/K^+-ATPase, and consequently increase the force of myocardial contraction [30]. Some cardiac glycosides have been reported to have antitumor activity and inhibitor activity against the rhinovirus.

Oxalates are naturally occurring substances found in plants, plant extracts and in the human body [28]. It belongs to a group of molecules called organic acids. Certain body tissues routinely convert other substances into oxalate, which is an end product of human metabolism. For example, vitamin C can be converted into oxalate [31]. Food and drug oxalate content is a predictor of urinary oxalate excretion, which in turn has been directly linked to kidney stone formation [32]. These oxalates may crystallize as oxalate stones in the urinary tract in some people [33].

The presence of phytates in foods and plant extracts comes with its benefits and adverse effects. Dietary phytate has been reported to prevent kidney stone formation, protect against diabetes mellitus, caries, atherosclerosis and coronary heart disease as well as against a variety of cancers [34]. The levels of phytate and its dephosphorylation products in urine, plasma and other biological fluids fluctuate with ingestion or deprivation of phytate in the human diet [34]. Therefore, the reduction of phytate intake in developed countries compared to developing countries might be one factor responsible for the increase in diseases typical for western societies such as: diabetes mellitus, cancer and coronary heart diseases. Adversely, phytates have been reported to form complexes with proteins at both low and high pH values. These complex formations alter the protein structure which may result in decreased protein solubility, enzyme activity and proteolytic digestibility. The phytate degrading enzyme, phytase, is in vogue for degrading phytate during food processing and in the gastrointestinal tract. Another major concern about the presence of phytates in food and plant extracts is its negative effect on mineral uptake [35]. Phytate decreases calcium bioavailability and the calcium-phytate molar ratio has been proposed as an indicator of calcium bioavailability. The critical molar ratio of calcium-phytate is reported to be 6:1 [34].

Alloxan induces diabetes in rats by damaging the insulin secreting cells of the pancreas leading to hyperglycemia [36]. There was no significant difference in the initial weights of the animals ($P > 0.05$). This was because the animals were sorted according to similar body weights before the commencement of the experiment. The untreated group had the least average initial weight of 197.05 ± 7.72 g while the glibenclamide group had the highest 222.41 ± 0.175 g. After the induction of diabetes using alloxan, there was a drastic reduction in weights in days 1 and 2 in all the groups except the glibenclamide group. Their weights began to increase from day 7 till the end of the experiment except in the untreated group. This reduction in weight is one of the symptoms of type 2 diabetes mellitus. Diabetes is always accompanied by increased glycogenolysis, lipolysis, gluconeogenesis and these biochemical activities result in muscle wasting and loss of tissue protein thus weight loss. The increase in weight was more rapid in the 400 mg/kg ethanol extract group representing a 29.09% increase than the other groups. It showed the highest ability to prevent the biochemical changes leading to weight loss and thus restored the body weight of the diabetic treated rats back to normalcy. This reduction in weight by alloxan and later restoration by treatment with herbal remedies was in line with the findings of Ewenighi et al. [36].

The glucose levels of the rats were monitored after induction of the animals on a seven days interval. The initial glucose level of the rats represents their glucose levels before induction of the animals. The control was not induced with alloxan thus the normal glucose level. This general increase in glucose levels in the treatment groups was due to the damage of the insulin-secreting cells of the pancreas and thus hyperglycemia. A glucose level of 200 mg/dl and above served as evidence of hyperglycemia. Their final glucose levels were taken on the 28th day. The untreated group had the highest final glucose levels of 441.50 ± 1.50 mg/dl while the control was the least at 78.80 ± 4.70 mg/dl. The difference in final glucose levels were also significant ($P < 0.05$) with this occurring when all the treatment groups were compared with the control.

There was a general reduction in blood glucose levels of the treated groups showing the potency of the extracts in comparison with the standard drug, glibenclamide. The 400 mg/kg ethanol extract had the highest percentage reduction in glucose level (53.21%) in 28 days, even more than the standard drug group (24.74 %) while the 200 mg/kg ethanol extract gave the least percentage reduction. These findings were similar to the findings of Metgud and Kore [37] and Ijaola et al. [1]; where the potato extracts reduced the glucose levels and may be thought to have normalized albumin, globulin and serum liver enzymes activity, increased the level of high-density lipoproteins and decreased protein glycation levels than the standard drug. Glibenclamide belongs to the class of drugs called sulfonylureas. They were the first widely used oral hypoglycemic medications. They are insulin secretagogues, triggering insulin release by direct action on the K^+ATP channel of the pancreatic beta cells [38]. The mechanism behind the antidiabetic potential of the extracts could be due to inhibition of renal glucose reabsorption, alpha amylase inhibition, stimulation of insulin secretion from the beta cells of islets or/and inhibition of degradative processes, regeneration and/or repairing pancreatic beta cells and/or increasing the size and number of cells in the islets of Langerhans [38].

The incidence of diabetes mellitus generates reactive oxygen species. Oxidative stress has been linked to the pathogenesis of various debilitating health conditions in humans [39] and free radicals have been implicated as the major factor responsible for the onset of these pathological ailments such as cancer, inflammation, rheumatoid arthritis, diabetes mellitus among others. Antioxidant enzymes are particularly important in ridding the body of reactive oxygen species and as reported by various studies, *in vitro* antioxidant enzyme activity have been demonstrated to be increased by some plant parts' extracts [40], giving an indication of the potentials in *in vivo* studies. The findings of the assay showed that while the untreated group had the highest SOD and catalase activity due to the induced diabetes, the treatment groups all observed a varying marked reduction in the activity of the antioxidant enzymes owing possibly to the presence of some phytochemicals and antioxidants that may be responsible for the action. However, these findings were not statistically significant across the treatment groups ($P > 0.05$). Since there was no significant difference in the antioxidant enzyme activities between the positive control and treatment groups, it may also mean that the extracts and standard drug, glibenclamide, showed the same degree of antioxidant activity indicating that *I. batatas* extracts can potentially exhibit the same efficacy and degree of mopping up ROS from the body, which is a hallmark indicator of the debilitating effects of diabetes mellitus. These findings similarly agree with the works of Pochapski et al. [41], who noted a higher antioxidant capacity of I. batatas than ascorbic acid and Egbunonu et al [42] who described the effect of C. albidum cotyledon on MSG induced oxidative stress in albino rats. Specifically, the total antioxidant activity of the sweet potatoes may be attributed to their high total phenolic content [43]. Additionally, sweet potatoes have been reported to possess antioxidant activity in all the parts [44].

5. CONCLUSION

The proximate, phytochemical and antidiabetic potentials of the tubers of *I. batatas* were highlighted in this study. The findings showed significant and appreciable concentrations of nutritional and phytochemical constituents of the tubers. Both extracts were also observed to be non-toxic even at the highest dosage and found to be rich in medicinal phytochemicals especially the ethanol extract. Conclusively, the extracts showed good antidiabetic activity owing to the presence of some phytochemicals and antioxidants. Hence, extensive research is required to isolate and characterize these bioactive compounds of antidiabetic importance.

Further investigation into the pharmacokinetics and pharmacodynamics of the extracts are also advocated.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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