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Crude *Aloe vera* gel Reverses Polyphagia, Polydipsia, Hyperglycemia and Increases Body Weight in Alloxan - Induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author NVU designed the study, coordinated the research, and wrote the first draft of the manuscript. Author PUA managed the analysis and interpretation of data. Author OEO wrote the protocol and managed the literature searches. Author OEE supervised and guided the entire experimental procedure. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims: This study was embarked upon to determine the effect of diabetes mellitus on food intake, water intake and body weight, and to ascertain the impact of treatment with crude *Aloe vera* gel on diabetic animals.
Methodology: The phyto-constituents and median lethal dose of crude *Aloe vera* gel were determined before administration. 32 albino wistar rats were divided into four groups thus, control, diabetic untreated group (DM), diabetic group treated with crude *Aloe vera* gel (DMT) and crude *Aloe vera* gel treated control group. Food intake, water intake, body weight and fasting blood glucose levels were measured during the research work.
Results: Food intake, water intake, and fasting blood glucose levels were significantly (P<0.001) increased in DM group compared to control, DMT and CT group. Body weight was significantly (P<0.001) increased in CT group compared to control. DM group had a significantly (P<0.001) lower body weight compared to control, DMT (P<0.001) and CT

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(*P*<0.001) group at the end of the research work. Consequently, the body weight change in DM group was significantly lower (*P*<0.001) compared to control, DMT and CT group.
Conclusion: Crude *Aloe vera* gel reversed polyphagia, polydipsia and hyperglycemia in diabetic rats. Additionally, crude *Aloe vera* gel increased body weight in diabetic rats and can therefore be used to mitigate weight loss in type 1 diabetes mellitus.

Keywords: Aloe vera; blood glucose; body weight; diabetes mellitus.

1. INTRODUCTION

Diabetes is a complex and multifarious group of disorders characterized by hyperglycemia, that has reached epidemic proportions [1]. Several drugs are presently available to reduce hyperglycemia in Diabetes Mellitus. These drugs have side effects, thus search for a new class of compounds is essential to overcome these problems [2]. Since diabetes is a metabolic disorder, it is important to investigate and understand the impact of the disease on the energy needs of the body.

Aloe is a cactus-like, succulent perennial plant with over 500 species, belonging to family Liliaceae (sub-family of the Asphodelaceae), native to North Africa and cultivated in warm climatic areas [3]. *Aloe vera* barbadensis is the species that is most effective therapeutically [4].

Aloe can be utilized therapeutically, mainly in two basic forms – Gel and Latex. *Aloe vera* gel is the thin, clear, jelly-like substance that can be scraped from the inner part of the fleshy leaf. Aloe latex is obtained from specialized cells (called pericyclic tubule) lining the inner skin of the leaf. The latex is extracted as a liquid then dried into a yellow powder. It is a very potent laxative [5].

It is desirable to make *Aloe vera* gel as pure as possible because the latex contains the anthraquinone glycosides aloin A and B, which are potent laxatives [5]. A third and less popular form in which *Aloe vera* is used is the extract which is made by blending the whole leaves of the plant. That way, the latex and the gel are both consumed.

The efficacy of *Aloe vera* products depend on the type of ailment and the part of the plant used – whether the gel extract, juice extract or whole leaf extract. *Aloe vera* gel is used externally for the treatment of skin irritations, burns, scalds, sunburn, wounds, eczema, psoriasis, acne, dermatitis, ulcers, and also helps to stimulate cell regeneration [6,7,8,9].

Aloe vera latex, a yellow, bitter liquid derived from the skin of the Aloe leaf, is responsible for Aloe's powerful laxative effect. However, it can cause painful abdominal cramps and is not safe for use indiscriminately and so should be taken at low doses [10].

Aloe vera is reputed for a number of therapeutic properties. It has been found helpful in the following systems - respiratory system [11], cardiovascular system [12,13,14], endocrine system [14,15], blood and immune system [14,15].

The mechanism by which *Aloe vera* exerts its previously reported hypoglycemic effect is yet unclear. This study was therefore embarked upon with a view to assess the effect of type 1 diabetes mellitus and treatment with crude *Aloe vera* gel on body weight.

2. MATERIALS AND METHODS

2.1 Plant Material and Preparation of Crude *Aloe vera* gel

Mature, fresh (above 2 years old) *Aloe vera* plant with leaves within 40 – 60cm long was obtained from University of Calabar Botanical Garden and identified by the Chief Herbarium Officer of Botany Department of University of Calabar. A knife was used to slice each leaf longitudinally. This made the *Aloe vera* gel visible. The gel was gently scraped into an electric blender to shatter the block. After blending, the *Aloe vera* gel was administered immediately. This preparation was done daily; there was no form of storage, to ensure that the constituents of the crude *Aloe vera* gel were not compromised. The median lethal dose (LD_{50}) of the plant extract was determined by method of Lorke [16] and found to be non-toxic at the highest tested dose of 64 ml/kg body weight. The lowest tested dose of 2 ml/kg body weight was adopted for this study to determine the effect of the smallest dose on diabetic and normal animals.

2.2 Animal Preparation and Protocol

Thirty two albino wistar rats were used. Each animal was placed in its own separate metabolic cage containing its food and water. The metabolic cages were well ventilated, exposed to normal temperature and 12/12 hours light/dark cycle. After fourteen days of acclimatization, the animals were randomly divided into four groups such that each group contained eight animals, thus, control group, alloxan – induced diabetic untreated group (DM), alloxan – induced diabetic group; treated (DMT) with crude *Aloe vera* gel (0.2ml/100g body weight) orally and control group; treated (CT) with crude *Aloe vera* gel (0.2ml/100g body weight) orally.

2.2.1 Induction of diabetes

Induction of diabetes was achieved by intraperitoneal injection of alloxan. The dose used in this study was 120 mg/kg body weight. Alloxan was given within 10 minutes of preparation to avoid atmospheric oxidation and loss of efficacy due to long standing. Fasting blood glucose level of each animal was taken before alloxan administration. 48 hours after alloxan administration, diabetes was confirmed in the groups administered by using the Finetest glucose meter (IMFOMED IMPEX, INDIA) to measure the blood glucose levels. Animals with blood glucose level >125 mg/dl after 24 hours fast were considered diabetic.

2.2.2 Extract administration

Treatment of diabetes with crude *Aloe* vera gel commenced 48 hours after successful diabetes induction. The extract was orally administered to the DMT and CT groups at a dose of 0.2ml/100g body weight twice daily for 21 days. Administration was facilitated by the use of a syringe and orogastric tube. All experiments were examined and approved by the appropriate ethics committee and were therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

2.3 Determination of Food Intake

The food intake was obtained by giving a measured quantity of palletized Guinea feed, (Guinea Feed Ltd, Nigeria) each day and weighing the quantity remaining, same time the

next day. The difference in quantity was recorded as the food intake. The recording was done at the same time daily to ensure consistency and accuracy.

2.4 Determination of Water Intake

Water intake was obtained using a measuring cylinder and a calibrated conical flask. The daily water intake was obtained by subtracting the volume of water remaining at the end of 24 hours of feeding from the initial amount in the cylinder at the start of each day's feeding.

2.5 Determination of Body Weight

The body weight of the animals was determined by using a weighing balance. The initial weight of each animal was recorded after random grouping, before commencement of administration. The rats were subsequently weighed every two days until the end of the study. The weight was recorded and differences in weight was statistically analyzed.

2.6 Determination of Blood Glucose Levels

The blood glucose level of each animal was measured by the use of the Finetest glucose meter (INFOMED IMPEX, INDIA). Blood used for the test was obtained by pricking the distal end of the tail and placing the drop of blood on the test strip. Blood glucose level before and 48 hours after alloxan administration was determined and recorded in all the groups. Blood glucose level was also measured at the end of the experiment.

2.7 Statistical Analysis

All results are presented as mean $\pm$ standard error of mean. The One – way Analysis of Variance (ANOVA) was used to determine the differences between means, followed by post hoc multiple comparisons, with P=.05 considered significant. Computer software SPSS version 17.0 and Excel Analyzer was used for the analysis.

3. RESULTS

3.1 Daily Food Intake

The mean food intake for day one in the control, DM, DMT and CT group was 20.26 $\pm$ 2.79g/day, 30.40 $\pm$ 1.54g/day, 30.33 $\pm$ 0.72g/day and 22.03 $\pm$ 1.48g/day respectively. The daily food intake in the DM and DMT group was significantly higher ($P<0.01$) compared to control and CT group (Fig. 1).

At the end of 21 days, the mean daily food intake in the DM group; 34.71 ± 0.73g/day was significantly higher ($P<0.001$) compared to control; 23.51 ± 0.58g/day, DMT; 28.15 ± 0.76g/day and CT; 24.62 ± 0.80g/day group (Fig. 1).

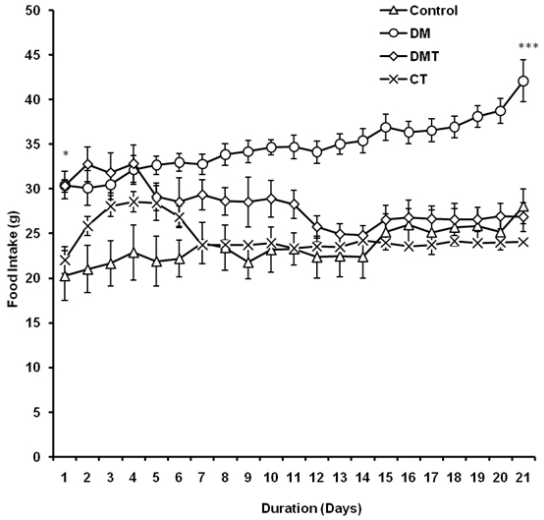

Fig. 1. Comparison of daily food intake in the different experimental groups
Values are mean ± SEM. n = 8
**P<0.01 vs Control and CT. ***P<0.001 vs Control, DMT and CT.*

3.2 Daily Water Intake

The mean daily water intake in the control, DM, DMT and CT group was 25.78 ± 0.37ml/day, 36.72 ± 2.87ml/day, 29.22 ± 0.78ml/day and 22.58 ± 0.56ml/day respectively. Mean daily water intake was significantly higher (P<0.001) in the DM group compared to control. DMT and CT group had significantly lower (P<0.001) mean daily water intake compared to DM group (Fig. 2).

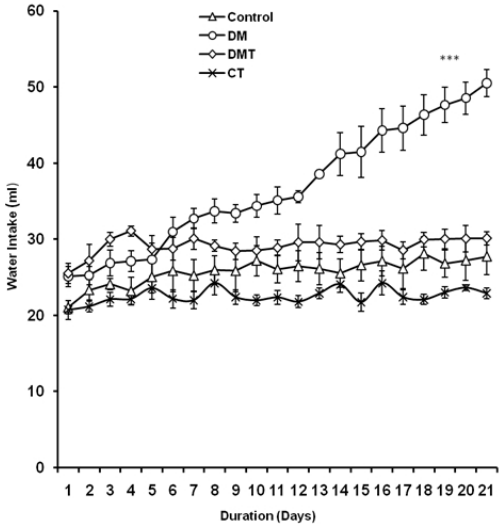

Fig. 2. Comparison of daily water intake of the different experimental groups.
Values are mean ± SEM. n = 8
**** P<0.001 vs Control, DMT and CT.*

3.3 Body Weight Change

The DM group (-41.25 ± 6.4086g) showed retarded growth (P<0.001) compared to control (10.0 ± 0.6904g) which showed an accelerated growth. DMT group (22.5 ± 10.3509g) and CT group (30.0 ± 5.3452g) showed a significant increase in body weight change (P<0.001) compared to DM group. (Figs. 3a and 3b).

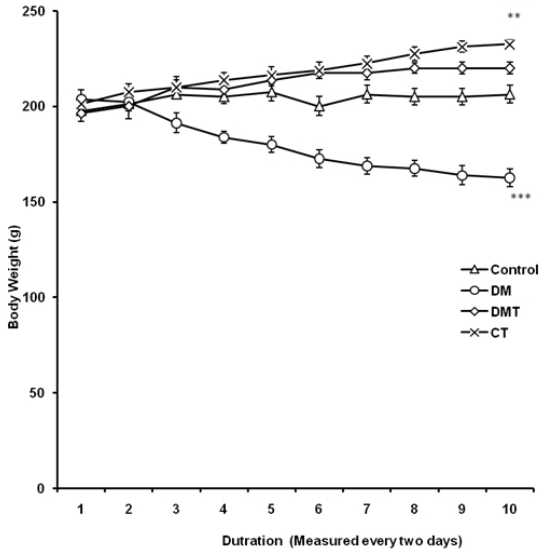

Fig. 3a. Comparison of daily body weight of the different experimental groups. Values are mean ± SEM. n = 8
***P<0.01, ***P<0.001 vs Control*

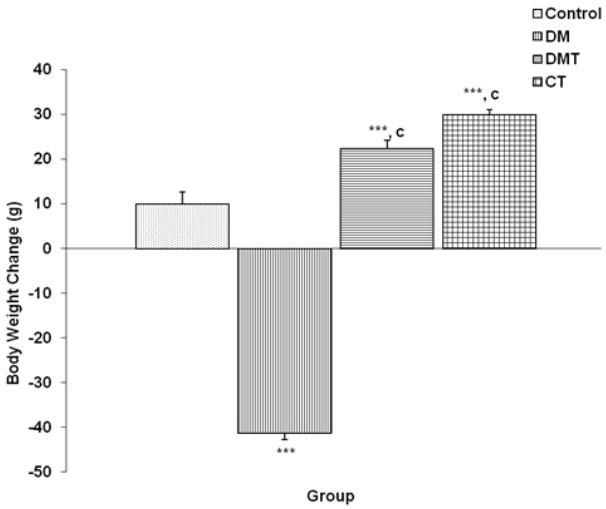

Fig. 3b. Comparison of body weight change of the different experimental groups. Values are mean ± SEM, n = 8
****P<0.001 vs control; c = P<0.001 vs DM.*

3.4 Fasting Blood Glucose After Treatment With Crude *Aloe vera* Gel

At the end of 21days, the fasting blood glucose of animals in the control, DM, DMT and CT group was 70 ± 0.8mg/dL, 112 ± 1.9mg/dL, 72 ± 3.1mg/dL and 75 ± 0.8mg/dL respectively. DM group showed a significant increase (P<0.001) in fasting blood glucose level compared to control. DMT and CT group showed a decrease in blood glucose level (P<0.001) compared to DM group, (Fig. 4).

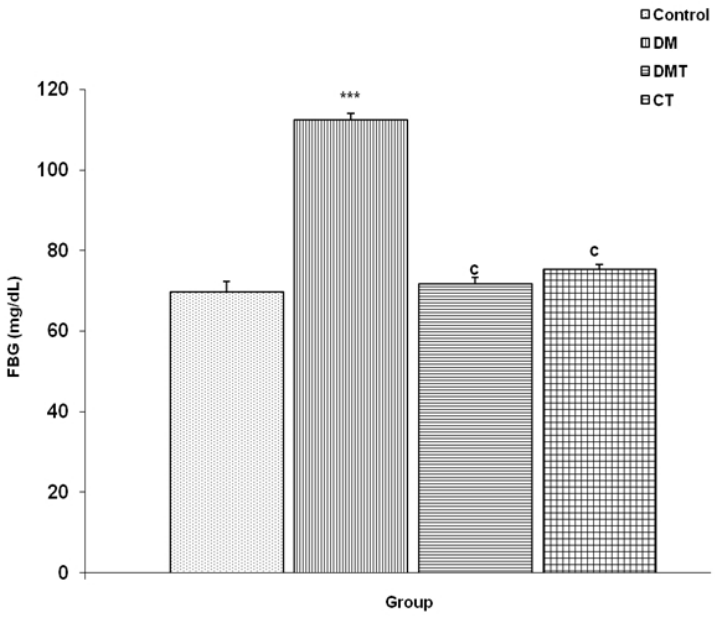

Fig. 4. Comparison of fasting blood glucose (FBG) of the different experimental groups at the end of the experiment.

*Values are mean ± SEM, n = 8; ***P<0.001 vs control; c = P<0.001 vs DM.*

4. DISCUSSION

Diabetes mellitus, a group of metabolic disorder with multiple etiologies, is characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism due to defect in insulin secretion, insulin action or both [17]. Determination of fasting blood glucose level in the control group, diabetic untreated group (DM), diabetic treated group (DMT) and control treated (CT) group 48 hours after alloxan administration confirmed hyperglycemia in the test groups (DM and DMT), thus suggesting that the insulin – producing pancreatic beta cells were destroyed by alloxan, a cytotoxic compound [18] administered for the induction of type 1 diabetes mellitus in these groups. Alloxan is a urea derivative which causes selective necrosis of the β - cells of pancreatic islets [19,20]. It is a hydrophilic and unstable chemical compound which has similar shape as that of glucose. Similarity in the shape favours it transport into the cytosol by the glucose transporter (GLUT2) in the plasma membrane of beta cells [21,22]. Alloxan's presence in the cytosol results in series of reactions that destroy the beta cells.

A number of plants have been reported to exhibit glycemic control by stimulating insulin release [23]. Crude *Aloe vera* gel significantly reduced (P<0.001) the blood glucose level in the DMT group compared to DM group (Fig. 4). This result is highly correlated with the work of Eman et al. [24] and Okyar et al. [25]. *Aloe vera* leaf extract has been found to be significantly effective in lowering blood glucose in experimental diabetics [25].

It is possible that *Aloe vera* gel may contain some active insulinogenic agents which help in lowering blood glucose level in diabetic rats [26,27,28,28,29].

Although the blood glucose level in the CT group was greater than that of the control and DMT group, this was not significant (Fig. 4). The slight increase in blood glucose level in the CT group however maybe attributed to the monosaccharides and polysaccharides contained in crude *Aloe vera* gel [30,31]. Monosaccharides are the simple sugars which include glucose. The polysaccharides are the more complex long-chain sugars involving glucose and mannose or the gluco-mannans. [14,30,31]. Comparing the DMT group with the control group, it is possible that crude *Aloe vera* gel may be operating through a negative feedback that ensures that as soon as the blood glucose level is restored through the restoration of pancreatic beta cells, the stimulatory effect of *Aloe vera* gel on pancreatic beta cells reduces, so as to maintain the blood glucose level rather than reducing it to a hypoglycemic level which is even more life threatening.

The classical signs of diabetes; polyuria, polyphagia and polydipsia, were observed in DM group. This significantly increased (P<0.001) their food and water intake compared to control, (Figs. 1 and 2). There was no significant difference in food and water intake of CT group when compared to control animals. This indicates that crude *Aloe vera* gel has no effect on food and water intake in normal rats.

There was no significant difference in body weight in the different groups prior to experiment (Fig. 3a). At the end of the research work, CT group showed a significant increase in body weight compared to control (P<0.001), DM group (P<0.001) and DMT group (P<0.01). Body weight was least in the DM group. (Fig. 3b).

The DM group showed a negative change in body weight, significantly different (P<0.001) compared to control which had a positive body weight change (Fig. 3b). This is in line with Cooke and Plotnick's [32] report that type 1 diabetes is associated with weight loss.

The decrease in body weight observed in the DM group may be as a result of excessive depletion of fat stores to produce energy. DMT and CT group had a significant positive body weight change (P<0.001) compared to DM group. Change in body weight and indeed positive change in body weight was highest in the CT group, indicating that crude *Aloe vera* gel increases body weight in normal and diabetic conditions. The increased body weight observed in the CT group compared to control was not proportional to food intake, suggesting that crude *Aloe vera* gel exert its effect on body weight through a mechanism other than influencing food intake. Phytochemical studies on *Aloe vera* has shown that it contains some enzymes like alkaline phosphatase, amylase, carboxypeptidase, catalase, cellulase, lipase and peroxidase, some of which are involved in the breakdown of food sugars and dietary fats [30,31]. These enzymes positively influence digestion of ingested food materials thus making the materials readily available for absorption. This probably accounts for the increased body weight observed in the CT group.

The puzzle however goes thus; since crude *Aloe vera* gel increases body weight in type 1 DMT animals which is known to be associated with weight loss, is it ideal to encourage type 2 DM (associated with obesity) patients to ingest crude *Aloe vera* gel? In view of this, patients of type 2 diabetes mellitus who indulge in self medication with crude *Aloe vera* gel may be exposed to more health hazards secondary to obesity if not closely monitored since crude *Aloe vera* gel increases body weight.

5. CONCLUSION

Previous studies had reported weight loss in type 1 diabetes mellitus. Crude *Aloe vera* gel increases body weight in normal and diabetic rats and can therefore be used to mitigate weight loss in type 1 diabetes mellitus.

CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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