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Original Research Article

Comparative effects of *Portulaca Oleracea* and Metformin in Diabetes Mellitus Rat induced with Alloxan

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ABSTRACT

The present study compared the effects of aqueous extracts of *Portulaca oleracea* and metformin in an alloxan induced diabetic rats. The experimental rats were divided into three groups. The normal control (positive control) was fed with normal feed and water daily for 21 days, second group was treated with 200mg/kg of *Portulaca oleracea* extract and fed with normal feed and water for 21 days following induction with alloxan monohydrate whilst the last experimental group was treated with 250mg of metformin and fed with normal feed and water for 21 days after induction with alloxan monohydrate. The statistical significance of the treatment effects was analyzed using one way analysis of variance (ANOVA). Results showed that the body weight of normal rats (group 1) was significantly ($P<0.05$) increased after 7 days interval and the body weight of groups 2 treated with *Portulaca oleracea* showed mild decrease after 7 days interval. Metformin treated groups 3 showed significant ($P<0.05$) decrease after 7 days interval. Fasting blood glucose level of normal rats (group 1) was not significantly ($P<0.05$) changed as compared with control for the period however, mild fluctuation was observed. Further, there was moderate significant decrease ($P<0.05$) in fasting blood glucose level of groups 2 rats treated with *Portulaca oleracea*, compared with control. Metformin treated rats showed moderate significant decrease ($P<0.05$), when compared with control. Results from this study indicate, administration of *Portulaca oleracea* has more protective effects than metformin against alloxan-induced diabetic state. We postulate, this significant protection of *Portulaca oleracea* may be due to synergistic effect of the constituents of the plant extract.

Keyword: Diabetics; Portulaca oleracea; plant extracts; metformin

INTRODUCTION

Phytomedicine, with its holistic systems approach supported by experiments, can be innovative and powerful for the discovery of newer, safer and affordable medicines [1]. Thus

not suprising that in recent times there has been an increasing interest in the ethnopharmacological studies on medicinal plants, evident by numerous scientific publications and reports [1].

Diabetes is a complex disease characterized mainly by insulin resistance and pancreatic β-cell dysfunction [2]. It is associated with increased oxidative stress resulting from increased free radical formation [1-3], and decreased antioxidant status [3, 4]. In spite of the numerous preventive and therapeutic strategies, the management of type 2 diabetes remains badly insufficient [5]. Hence, progressive needs to adapt multiple therapies as glycemic targets for monotherapy continue to be inadequate [6]. Consequently, the cost of treatment has also become a real problem, thus, the need for more effective and cheaper management of type 2 diabetes using herbal remedies is an attractive option more so, because of their effectiveness, less side effects and relatively low costs [7].

Portulaca oleracea, an edible plant with different medicinal, pharma-cological effects, including anti-oxidative stress activity [8]. Previous studies with animal models of type 2-diabetes have established that protection against oxidative stress ameliorates the severity of diabetes progression [9, 10, 2]. Thus, it is of public health interests elucidating whether *Portulaca oleracea* have an antidiabetic effects on type 2 diabetic animal model and to also, evaluate the expected antidiabetic effect obtainable with *Portulaca oleracea* in relation to its, synergistic with standard antihyperglycemic treatment using a known antidiabetic drug, such as metformin.

Metformin (1,1-dimethylbiguanide), an orally administered drug used to lower blood glucose concentrations in patients with type 2 diabetes mellitus. Metformin is considered a cornerstone in the treatment of diabetes and is one of the most frequently prescribed first line therapy for individuals with type 2 diabetes [11]. Metformin has various beneficial metabolic effects, including antihyperglycemic actions by suppressing hepatic glucose output and increasing insulin-mediated glucose disposal, without weight gain [11]. It has also be shown to improves, lipid profile by reducing hyper-triglyceridemia, lowering plasma fatty acids and LDL-cholesterol, and raising HDL-cholesterol in some patients [10, 12]. Moreover, metformin improves insulin sensitivity by decreasing endogenous and exogenous insulin requirements and reducing basal plasma insulin concentrations [12], for instance, in the adipose tissue, metformin promotes the re-esterification of free fatty acids and inhibits lipolysis, indirectly improving insulin sensitivity through reduced lipotoxicity [13]. Although, the exact mechanisms of action of metformin, is yet to be fully understood but it is thought to includes suppression of endogenous glucose output by the liver and increased sensitivity in skeletal muscle [13]

MATERIALS AND METHODS

Plant identification

Fresh leaves of *Portulaca oleracea* identified as such, was locally sourced.

Extracts preparation

The fresh leaves as purchased were sun-dried and made into powder and, the dry powder, weighed (500g). This was soaked in 1500 ml distilled water, 72 hours. The extract was obtained using a rotary evaporator with, solvent extracted at a temperature of 45^{o}C with water pressure of 60 mmHg. Paste-like extract obtained was oven dried and grinded to smooth powdered.

Experimental animals and design

Fifteen (15) adult Wistar rats weighing between 120g-200g (Animal House Department of Physiology, Delta State University, Abraka, Nigeria) were used, following approval of institutional animal ethical committee. The

animals were housed in standard animal cage, at room temperature with access to water in accordance with the international guide for the care and use of laboratory animals. They were maintained under controlled environmental condition with a 12 hour dark: light cycle.These twenty-one (21) male albino rats of Wistar strain were, divided into three (3) groups and, seven (7) rats in a group (group A – C). Group A (positive control) was fed with normal feed and water daily,for 21 days; Group B, was treated with 200mg/kg of *Portulaca oleracea* extract, fed with normal feed and water for 21 days following induction with alloxan monohydrate. Group C, was treated 250 250 mg of metformin and fed with normal feed and water for 21 days after induction with alloxan monohydrate. Experimental rats in the different groups A-C were marked blue, black, green and red at different parts of their body for identification. Extract was given to diabetic group B and metformin was given to diabetic group C according to their body weight. The control group A was given normal feed and water throughout the experimental life cycle. The rat body weights were determined before alloxan induction, after induction, every week and day before sacrificing using a digital balance and recorded in grams. The experimental animals were observed for signs and abnormalities throughout study life cycle.

Diabetes Induction

Each rat, group B and C received a single intravenous injection of alloxan monohydrate (40 mg/kg) after fasting for 24 hours, following standard feeding and water an hour later. Before induction, all rats were weighed and blood glucose level taken using Accu-check active blood glucometer and after 72 hours of induction, they were weighed and blood glucose level was taken using Accu-check active blood glucose monitor and lancet (Roche diagnostic, Germany) and, 200 mg/dl glucose level was considered diabetic.

Blood Glucose Level Determination

Using Accu-check (Roche diagnostic, Germany) active glucometer machine, the blood glucose level of the experimental rats was determined. The tip of the animals' tail was pricked using a sterile needle blade. A drop of the blood from the lateral tail vein was spotted on the test spot region of the glucose strip after inserting it into the glucometer. The value obtained was recorded immediately and expressed in mg/dl. The glucose level determination was done early in the morning after the withdrawal from food overnight and before extracts and drug (metformin) administered in the morning.

Statistical Analysis

The results were expressed as mean ± SEM (standard error of the mean) following similar studies [14, 15], and statistical significance of the treatment effect was analysed using one way analysis of variance (ANOVA) followed by Duncan's multiple range test using SPSS 10.0 computer software package (SPSS Inc., Chicago, U.S.A), for the group means. The least significant difference or probability were carried out when: $F_{cal} > F_{tab}$, and significance between mean values was determined using the critical values of p at 0.05 being the Pearson correlation coefficient and test of significant level of probability.

RESULTS

The present study was designed to determine and compare the combine therapy, *Portulaca oleracea* to antidiabetic therapy of metformin drug using alloxan induce rats with diabetic disease phenotypes as a model. Individual antidiabetic potential of *Portulaca oleracea* and metfomin have been studied however, detailed biochemical explanation on, benefits (thereof) of combined regimen of *Portulaca oleracea* and of metformin in experimental rats with diabetes mellitus remain, largely deficient.

Table 1 shows the mean effect of alloxan induced diabetes mellitus and, the ameliorative

Table 1: Mean body weight effects change of *Portulaca oleracea* and Metformin treated rats with alloxan monohydrate-induced hyperglycemia state

Body Weight (g)						
Groups	**Initial**	**After induction**	**Week 1**	**Week 2**	**Week 3**	**Week 4**
Control	±3.25	±3.59	±4.17	±4.72	±5.35	±5.59[f]
Portulaca oleracea	±4.30	±2.86	±0.63	±1.94	±4.23	±4.79
Metformin	±7.74	±5.95	±6.29	±6.87	±9.13	±10.43

Values are expressed as mean ± standard error of mean (S.E.M), n=4 [f]p<0.05: significant increase and [e]p<0.05: significant decrease when body weight were initial and final values compared.

Table 2: The mean effects of *Portulaca oleracea* and Metformin drug on the fasting blood glucose level of alloxan monohydrate-induced hyperglycemia state in experimental rats

Fasting Blood Sugar Level (mg/dL)						
Groups	**Initial**	**After induction**	**Week 1**	**Week 2**	**Week 3**	**Week 4**
Control	±4.94	±6.01	±9.95	±5.75	±4.96	±4.44
Portulaca oleracea	±2.016	±51.45	±60.76	±51.47	±70.63	±18.74^
Metformin	±0.75	±82.24	±121.76	±87.34	±76.65	±112.15

*Values are expressed as mean ± standard error of mean (S.E.M), n=5 ^ P<0.05: significant increase and * P<0.05: significant decrease when fasting blood glucose level (FBGL) were compared in 7 day interval*

effect of *Portlaca oleracea* and Metformin on the body weight of the experimental rats, expressed in mean ± SEM. The body weight of normal rats (group A) was significantly (P<0.05) increasing as compared, 7 days interval for the period. In the body weight of groups B treated with *Portulaca oleracea*, there was mild decrease, compared in 7 days interval, but in not treated, there was observed significantly (P<0.05), and metformin groups C treated shows significant (P<0.05) decrease when compared in 7 days interval. The percentage changes in body weight (between before treatment, and after treatment) are represented in Figure 1. From (Figure 1) the percentage body weight change of the experimental rats before and after induction for non-treated, *portlaca oleraca* treated and metformin was found to be 15.12%, 0.42% and 9.82% respectively.

Conversely, Table 2 shows the mean effects of alloxan induce diabetes in rats with, ameliorative effects of *Portulaca oleracea* and metformin drug on the fasting blood glucose level (express in mean ± SEM). From Table 2, fasting blood glucose level of normal rats (group A) there was no significantly (P<0.05) changes, compared in 7 days interval for the period. Albeit mild fluctuation was observe. There was moderate significant decrease (P<0.05), in fasting blood glucose level of groups B (treated with *Portulaca oleracea*), when compared in 7 days interval and group C (metformin treated), there was moderate significant decrease (P<0.05), compared in 7

days interval, showing that *Portulaca oleracea* hyperglycemic state induced with alloxan-monohydrate in experimental rats. The percentage (see Fig 2) change in fasting blood glucose level (between after induction and after treatment) was 14.83%, 95.79% and 160.9% and metformin significantly reduced respectively. These results, shows that metformin decreases the hyperglycemic state more than aqueous leaves extract of *Portulaca oleracea*.

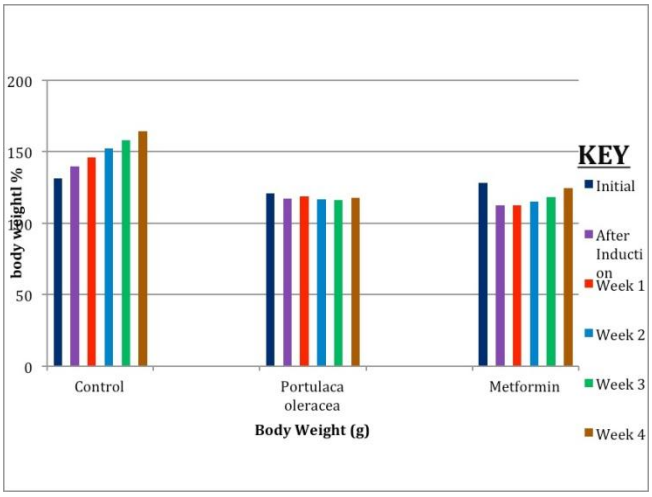

Fig 1: Body weight changes before and after induction monitored (4 weeks)

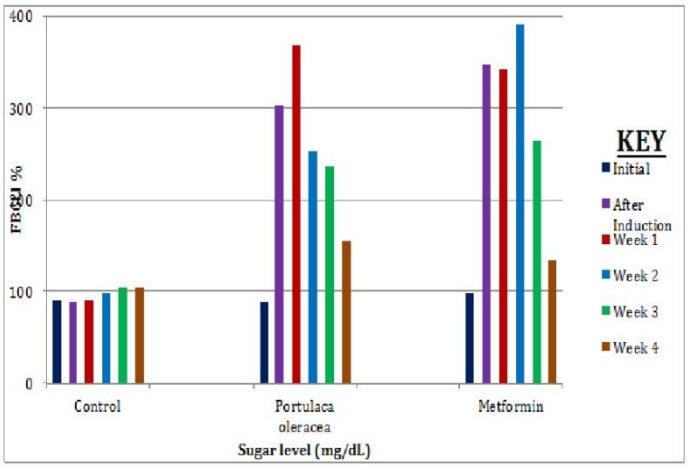

Fig 2: Percentage fasting blood sugar level (FBGL) over experiment life cycle (4 weeks)

DISCUSSION

Diabetes mellitus is a common disorder of metabolism in which the body (pancreas) does not produce or properly use insulin, characterized by excess sugar in the body, hyperglycemia, [16]. In diabetes mellitus, it is thought that cells are exposed to oxidative stress due to increased formation of reactive oxygen species produced by glucose auto-oxidation and protein-glycation [17]. During the early stage of diabetes mellitus, there is increased production of free radicals and a decreased total anti oxidative capacity of the cells [18], leading to lipid peroxidation and to the development of late diabetes complications

[18]. Largely, two types of diabetics are; diabetes mellitus and diabetes insipidus [16].

Once diabetes is diagnosed, treatment consists of controlling the amount of glucose in the blood and preventing complications. There are several complications of diabetics and hypercholesterolemia is one common complication of diabetes, depending on the type of diabetes and degree of control [19]. Generally, insulin is self-administered by patients via injection or with automatic drug injectors containing a cartridge of insulin, which can be carried in the pocket for ease and speed of treatment [20, 21]. Also, herbal remedies can be used to treat diabetes mellitus [22]. Thus, it is of public health importance that plants with phytomedical properties are properly researched with a view to harnessing such properties.

Plant extracts have been used over the years, in food preservation, pharmaceuticals, alternative medicine and natural therapeutics. In our findings, there was a balanced significant increase in body weight of rats used as control (see Fig 1A), whilst for the *Portulaca oleracea* administered rats, there was a steady decrease in the weights of the rats (Fig 1 and Table 1). For rats administered with metformin, there was decrease in the weight at one week, with a corresponding increase after two weeks of administration of metformin (Table 1 and Fig 1). Generally, metformin had a more significant effect on the body weight of the rats (9.82% change in weight) than *Portulaca oleracea* (caused 0.43% change in body weight) see Fig 1. It is very plausible; the difference in the body weight might be due to the toxic fallout of metformin to the rats. However, in the rats administered with *Portulaca oleracea*, the presence of other phytochemicals including, β-sitosterol, β-sitosterol-glucoside, phenolic alkaloids; oleracein A, oleracein B, and oleracein E [23, 24], could make *Portulaca oleracea* less toxic to the rats, explaining, the less changes in the body weight of *Portulaca oleracea* administered rats with alloxan-induced diabetic, but there was a significant change (see table 1 and fig 1), in metformin administered rats.

There are several reports in the scientific literature showing, *Portulaca oleracea* have noteworthy anti-hyperglycemic and glucose tolerance effect in an experimentally induced diabetic rats [25, and the references therein]. Moreover, *Portulaca oleracea* has been reported to possess hepatoprotective, analgesic and anti-inflammatory [26, 28, antioxidant and antihypertensive [27; 29], anticancer, wound healing [30] bronchodilator, neuroprotective [31, 32], and many other biological activities. Due to the seeming importane of portulaca oleracea, the seeds were analysed and found to contains light green oil (17.4%) with the following constituent fatty acids: palmitic, 10.9; stearic, 3.7; behenic, 1.3; oleic, 28.7; linoleic, 38.9; and linolenic, 9.9%; unsaponifiable fraction yields sitosterol [33-35].

The mechanism of action of *Portulaca oleracea* is thought to be similar to the effects of sulfonylureas, it bolster insulin secretion by closure of the K^{+}-ATPase channels, membrane depolarization and increase in Ca^{++} ions influx [25].

Administration of *Portulaca oleracea* and metformin to alloxan-induced diabetic rats decreases the plasma glucose level (Table 2), this may be, perhaps due to the augmented quantity of insulin in diabetic rats. This study shows, there was, no significant effects on glucose level between *Portulaca oleracea* and metformin (see table 2). Additionally, as *Portulaca oleracea* might improve glucose utilization making adipose tissues more sensitive towards insulin receptors by enhancing the Peroxisome Proliferator-Activated Receptor- γ (PPAR-γ) dependent mRNA expression, reducing cases of insulin resistance [36-38]. Moreover, in a study by [25], using, *Portulaca oleracea* extract on rats with diabetic phenotypes, a marked decrease in the blood glucose level and increased insulin

concentration was observed in alloxan induced diabetic rats in a process that suggest closure of K^+ ATP channels, membrane depolarization and stimulation of Ca^{++} influx. Furthermore, the efficacy of *Portulaca oleracea* to curtail the hyperglycemia seems established, as it have potentials to inhibits cohort of free radicals accountable for destruction of pancreatic β-cell [39], and may thus prevent the hyperglycaemia in diabetic rats [39].

It is most plausible that *Portulaca oleracea* mechanism of action are multifaceted including; due to the activation of PPAR-γ receptor [37, 38] or due to increased insulin secretion from pancreatic β-cells due to closure of K^+ATP [25] channels, or may be attributable to free radical scavenging property to shield β-cell from destruction [39]. In consequence, this research has presented that *Portulaca oleracea* also amends the imperative glucose metabolizing enzymes in liver. Hepatic hexokinase is a prime enzyme that converts glucose into glucose-6-phosphate. Decreased level of hexokinase alloxan-induced diabetic rats can be accountable for diminished glycolysis, which results in decreased utilization of glucose for energy production [40].

CONCLUSION

The general objective of this study was to evaluate the efficacy of *Portulaca oleracea* and compare with metfomin in experimental rat with chemically (alloxan), induced hyperglycaemia. It is worth mentioning that *Portulaca oleracea* efficiently trims down the levels of blood glucose without producing any adverse effect viz. hypoglycemia. The results from the present study indicate the administration of *Portulaca oleracea* has more significantly protective effects than metformin against alloxan-induced diabetic state. This significant protection of *Portulaca oleracea* may be due to synergistic effects of the constituents of *Portulaca oleracea extract.* The antidiabetic effect of *Portulaca oleracea* from the results was effectual than metformin. These finding strengthen the observation/argument that naturally occurring compounds of plant origin properly harnessed could be more effective in controlling diabetes than synthetic oral hypoglycaemic.

CONFLICTS OF INTERESTS

We declare that there are no conflicts of interests.

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