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Evaluation of Fasting Plasma Glucose, Lipid Profile and Atherogenic Index of Diabetic Rats treated with Aqueous Extract of *Uvaria chamae* Leaves

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Abstract: **Diabetes mellitus is one of the oldest non-communicable diseases affecting a greater proportion of the world's population. *Uvaria chamae* is a medicinal plant with various health benefits. The study evaluated the fasting plasma glucose (FPG), lipid profile and atherogenic index of plasma (AIP) in diabetic rats treated with aqueous extract of *U. chamae* leaves. Diabetes was induced with alloxan monohydrate (150mg/kg body weight) intraperitoneally. Thirty (30) albino wistar rats were randomly assigned into 5 groups (I-V) of 6 rats each. Groups I and II were the control (non-diabetic) and diabetic groups respectively, and received 0.5ml distilled water. Groups III, IV and V were diabetic rats treated with 100mg/kg, 300mg/kg and 500mg/kg of aqueous extract of *U. chamae* leaves respectively for 28 days. The leaves were washed, air-dried, pulverized and macerated in distilled water for 48 hours with intermittent agitations followed by sieving and evaporation of the filtrate to dryness, and reconstitution with distilled water prior to oral administration in the rats. The mean FPG level of group II was significantly higher when compared with groups I, III, IV and V ($p<0.05$). Additionally, there was a dose-dependent reduction in the FPG levels of rats treated with the extract. The mean levels of total cholesterol (TC), low density lipoprotein cholesterol (LDLC), very low density lipoprotein cholesterol (VLDLC), triglyceride (TG) and AIP were significantly higher while high density lipoprotein cholesterol (HDLC) was significantly lower in group II when compared with group I ($p<0.05$). There were significant reductions in TC, LDLC, TG and AIP as well as a significant increase in HDLC in group V when compared with groups II, III and IV ($p<0.05$), although the reduction in VLDLC and TG were not significant in group V compared with that of group IV. The aqueous extract of *U. chamae* leaves may possess anti-diabetic and anti-atherogenic properties, hence, may be useful in the management of diabetes and reduction of cardiovascular disease risk.**

Keywords: **Fasting Plasma Glucose, *Uvaria chamae*, Lipid Profile, Diabetes mellitus, Atherogenic Index of Plasma.**

I. INTRODUCTION

Diabetes mellitus is one of the age old non-communicable diseases affecting a greater proportion of the world's population. It is perceived to be of greater public health concern in low and middle income countries as it is a prominent cause of death in these parts of the world [1]. Diabetes mellitus is characterized by persistent hyperglycemia with accompanying

biochemical and pathological alterations [2]. The hyperglycemic state may result from the destruction of the pancreatic B-cells, B-cell dysfunction or insulin resistance [3]. Poor glycemic control or uncontrolled hyperglycemia predisposes to microvascular (nephropathy, neuropathy, and retinopathy) and macrovascular (cardiovascular disease (CVD)) complications, and diabetes mellitus is regarded as one of the major risk factors for the development of CVD. It is therefore pertinent to keep blood glucose in check in order to reduce the risk of CVD in diabetes. However, the cost of medications, possible side effects, and/or unresponsiveness to treatments with respect to diabetic therapy has led to the quest for a cost effective and readily available alternatives with minimal or no side effects for the treatment and management of diabetes.

These alternatives include certain medicinal plants whose health benefits may be attributed to their phytochemical constituents. Although previous studies have reported some health benefits of *Uvaria chamae* (also known as bush banana), including anti-fungal [4], anti-malarial [5], anti-inflammatory [6], and anti-diabetic [7] effects, there is paucity of data on the effect of this plant on lipids and atherogenic indices. This study is therefore aimed at evaluating the FPG, lipid profile and AIP of diabetic rats treated with aqueous extract of *U. chamae* leaves.

II. MATERIALS AND METHODS

Plants

The Leaves of *U. chamae* were obtained from a farmland located within Enugu metropolis. They were identified by a Taxonomist of Botany Department, University of Nigeria Nsukka, and a voucher specimen deposited at the Herbarium. The fresh leaves were washed with clean tap water, and dried at room temperature after which they were pulverized and soaked in distilled water for 2 days with intermittent stirring. The suspension was first filtered through a muslin cloth followed by Whatmann filter paper (No 1). The filtrate was evaporated to dryness, and the extract stored in a refrigerator ready for use.

Animals

Thirty (30) albino wistar rats weighing between 150g and 190g were procured and housed at the animal house of College of Medicine, University of Nigeria, Enugu Campus. The rats were allowed to acclimatize for 2 weeks, and were maintained on standard poultry diet (Vital Feeds, Jos) and water ad libitum. These experimental animals were handled according to the institutional and international guidelines for the use and care of laboratory animals.

The 30 albino wistar rats were randomly assigned into five groups of 6 rats each. Groups I and II were the control (non-diabetic) and diabetic groups given distilled water while groups III, IV and V were diabetic groups given a daily dose of 100mg/kg, 300mg/kg and 500mg/kg of the plant extract respectively for 28 days by oral gavage.

Induction of Diabetes

Experimental diabetes was induced in groups II-V by intraperitoneal administration of a single dose of 150mg/kg body weight of alloxan monohydrate (Sigma-Aldrich) dissolved in normal saline. Blood glucose level was measured after 72 hours of the induction, and blood glucose level of >200mg/dl was considered diabetic.

Blood Sample Collection and Biochemical Analyses

At the end of 28days, 4mL of fasting blood sample was collected from each animal from the retro-orbital plexus, and dispensed into fluoride oxalate and plain tubes for FPG and lipid profile assays respectively.

FPG, TC, HDLC and TG were determined using enzymatic methods as described by [8], [9], [10], and [11] respectively. LDLC and VLDLC were calculated using Friedewald's formula [12] while AIP was calculated as the logarithm ratio of molar concentration of TG to HDLC [13].

Determination of Median Lethal Dose (LD_{50})

In this study, the LD_{50} was determined using the method described by [15] with slight modifications. Nine rats were randomly assigned into 3 groups of 3 rats each. Groups I, II and III were orally administered 1000mg/kg, 2000mg/kg and 3000mg/kg body weight of the extract, the rats were then monitored at intervals for signs of toxicity over the next 24 hours. With the administration of the aqueous extract up to 3000mg/kg, the rats showed no signs of toxicity or mortality. Thus, the LD_{50} value of the aqueous extract was recorded as >3000mg/kg body weight. An LD_{50} of >5000mg/kg body weight of aqueous extract of *U. chamae* leaves in wistar rats has also been reported [14].

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Statistical Analyses

Data were analysed using the Statistical Package for Social Sciences (SPSS) version 23.0, and all values were expressed as mean ± standard error of mean (SEM). One way analysis of variance (ANOVA) was used to assess the mean differences among groups, and Post hoc test was used to assess the intergroup variability. Statistical significance was considered at $p<0.05$.

III. RESULTS

The results of this study are shown in Table 1 and Figs. 1-7. It was observed that the FPG level of group II was significantly higher when compared with those of groups I, III, IV and V ($p<0.05$). Additionally, the FPG levels of groups III, IV and V were significantly higher when compared with that of group I ($p<0.05$). The mean serum levels of TC, LDLC, VLDLC, TG and AIP of group II were significantly higher while HDLC was significantly lower when compared with groups I and V, and in groups III and IV when compared with group V ($p<0.05$). However, the mean serum TG and VLDLC levels were not significant in group IV when compared with group V ($p>0.05$).

There were no significant differences in the mean serum levels of TC, HDLC, LDLC, VLDLC, TG and AIP in group II when compared with groups III and IV, and in group III when compared with group IV ($p>0.05$).

Table 1: FPG, Lipid Profile and AIP in Control and Diabetic Rats treated with Aqueous Extract of *U. chamae* Leaves.

Parameters	Group I Non-diabetic Control	Group II Diabetic	Group III 100mg/kg	Group IV 300mg/kg	Group V 500mg/kg	p-value
FPG(mmol/l)	$4.14 \pm 0.95^{a,b,c,d}$	$11.19 \pm 0.95^{a,b,c}$	$9.67 \pm 0.95^{c,d}$	6.98 ± 0.11^{d}	5.78 ± 0.27	0.0001
TC(mmol/l)	$2.31 \pm 0.03^{a,b,c,d}$	3.91 ± 0.04^{d}	3.89 ± 0.04^{d}	3.76 ± 0.05^{d}	3.19 ± 0.09	0.0001
HDLC(mmol/l)	$0.97 \pm 0.01^{a,b,c,d}$	0.69 ± 0.01^{d}	0.74 ± 0.03^{d}	0.75 ± 0.03^{d}	0.86 ± 0.03	0.0001
LDLC(mmol/l)	$0.93 \pm 0.03^{a,b,c,d}$	2.62 ± 0.04^{d}	2.57 ± 0.06^{d}	2.44 ± 0.06^{d}	1.79 ± 0.11	0.0001
VLDLC(mmol/l)	$0.41 \pm 0.01^{a,b,c,d}$	0.60 ± 0.01^{d}	0.59 ± 0.01^{d}	0.58 ± 0.01	0.55 ± 0.01	0.0001
TG(mmol/l)	$0.90 \pm 0.01^{a,b,c,d}$	1.31 ± 0.02^{d}	1.29 ± 0.02^{d}	1.26 ± 0.02	1.20 ± 0.01	0.0001
AIP	$-0.04 \pm 0.01^{a,b,c,d}$	0.28 ± 0.01^{d}	0.24 ± 0.02^{d}	0.25 ± 0.03^{d}	0.14 ± 0.01	0.0001

KEY: a = Significant when compared with group II. b = Significant when compared with group III.
c = Significant when compared with group IV d = Significant when compared with group V

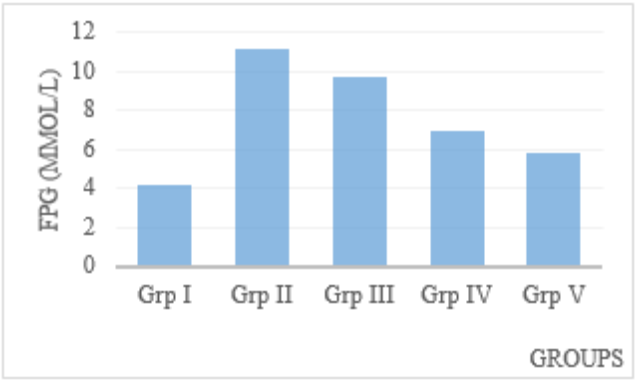

Fig 1: Mean FPG Levels of Control and Diabetic Groups

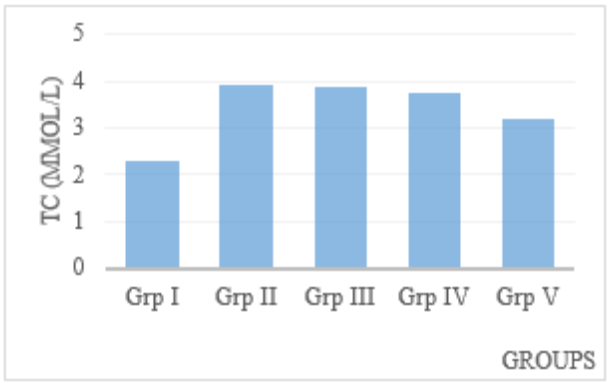

Fig 2: Mean TC Levels of Control and Diabetic Groups

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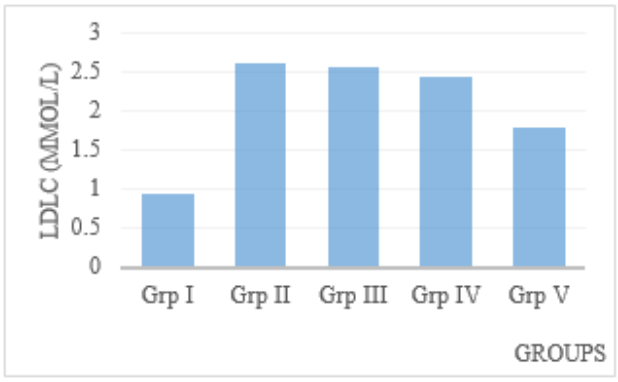

Fig 3: Mean LDLC Levels of Control and Diabetic Groups

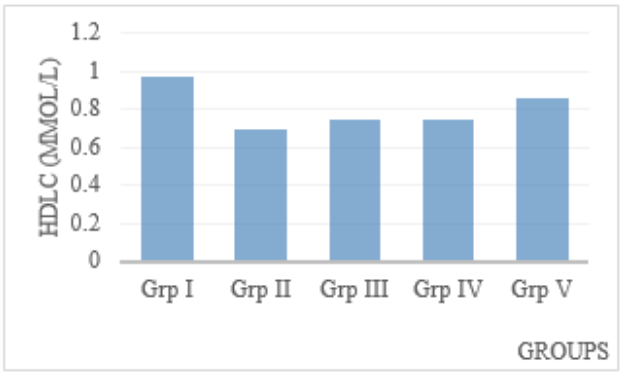

Fig 4: Mean HDLC Levels of Control and Diabetic Groups

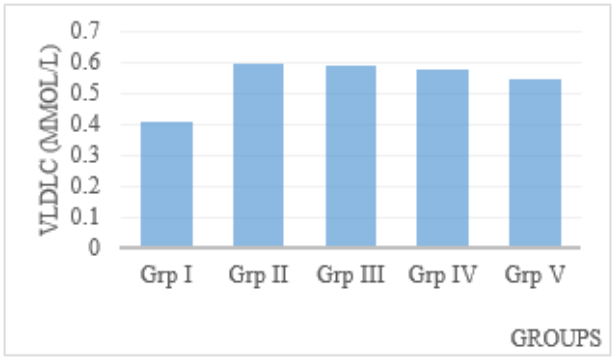

Fig 5: Mean VLDLC Levels of Control and Diabetic Groups

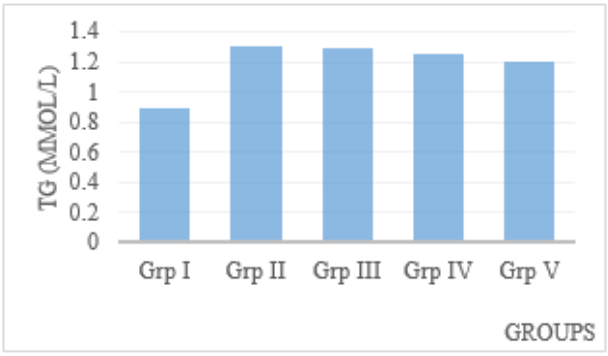

Fig 6: Mean TG Levels of Control and Diabetic Groups

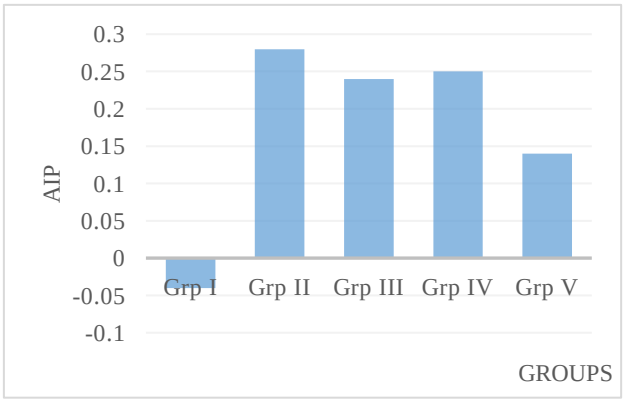

Fig 7: Mean AIP Values of Control and Diabetic Groups

IV. DISCUSSION

The present study evaluated the FPG, lipid profile and atherogenic index of plasma of diabetic rats treated with aqueous extract of *U. chamae* leaves. The higher mean FPG level observed in the diabetic rats may be associated with alloxan-induced damage of the pancreatic B-cells. Since uncontrolled hyperglycemia predisposes to diabetic complications, including CVD which is a leading cause of mortality in diabetic patients [16], treatment of diabetes is therefore aimed at maintaining blood glucose levels within satisfactory limits in order to reduce the risk of developing complications [17]. The result of this study showed dose-dependent reductions in the mean FPG level of diabetic rats treated with different doses of the extract. The observed reduction in plasma glucose may be attributed to the presence of phytochemicals in the leaf extract which may have caused the inhibition of intestinal glucose absorption. This result corresponds with the report of [18] who also observed a reduction in blood glucose levels of diabetic rats treated with ethanolic root extract of *U. chamae*.

Dyslipidemia which is a consequence of derangement in lipid metabolism in diabetic patients was evident in this study as shown by the higher TC, LDLC, VLDLC and TG levels as well as lower HDLC level in the untreated diabetic rats. However, diabetic rats treated with 500mg/kg of the extract showed significant reductions in TC, LDLC, VLDLC, and TG levels with significant increase in HDLC level. This may be associated with the reduction in dietary cholesterol absorption which could result from the inhibition of pancreatic lipase or cholesterol esterase. Emordi and colleagues [18] also reported the hypolipidemic activity of hydroethanolic extracts of *U. chamae* roots. Notably, dyslipidemia and elevated AIP have been reported as possible risk factors for the development of CVD [19]. AIP which may serve as an indication of CVD risk was significantly higher in the untreated diabetic rats which is an indication of the higher risk of developing CVD in diabetes. *U. chamae* extract likewise caused significant reduction of AIP in the diabetic rats treated with 500mg/kg.

V. CONCLUSION

From the findings of this study, *U. chamae* may possess anti-diabetic and anti-atherogenic properties, therefore may be useful in the management of diabetes as well as reduction of CVD in diabetes.

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