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Hypoglycaemic and Hypolipidaemic Effects of Feed Formulated with *Ceiba Pentandra* Leaves in Alloxan Induced Diabetic Rats

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Abstract: In this study, the hypoglycaemic and hypolipidaemic effects of feed prepared with *Ceiba pentandra* leaves was investigated in alloxan induced diabetic rats. Twenty five (25) Wister albino male rats weighing 105-162g assigned into 5 groups (I-V) of 5 rats per group were investigated. Diabetes was induced in Groups I-IV by intraperitoneal injection of alloxan (200 mg/Kg body weight) while rats in group V were normal. While animals in groups I, II and III received experimental feeds containing 10 %, 15 % and 20 % dry powdered leaves of *Ceiba pentandra* respectively, for a period of three (3) weeks, those in groups IV and V received normal rat feeds and acted as diabetic and non-diabetic controls respectively. In addition to plasma glucose, plasma lipids {total cholesterol (TC), triglyceride (Tg), high density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoproteins (VLDL)}, total protein and albumin were determined by standard laboratory techniques. Plasma glucose was found to be significantly ($p < 0.05$) lower in the treated rats when compared with the controls, with feed containing 20 % of the leaves having the greatest effect. All the groups showed increases in body weight, which was least in group that received 20 % of the experimental feed. However while HDL was elevated ($p < 0.05$) in the treated animals, LDL, VLDL and Tg showed significant ($p <0.05$) decreases. Also total protein and albumin were elevated ($p > 0.05$) in the treated groups compared with the controls. The result therefore demonstrates that *C. pentandra* leaves at moderate concentrations, exert both hypoglycaemic and hypolipidaemic effects in alloxan induced diabetic rats in a dose dependent fashion. Therefore, *C. pentandra* leaves could be of importance in the treatment of diabetes and its associated complications such as coronary artery disease.

Key words: *Ceiba pentandra,* Alloxan induced diabetic rats, Hypoglycemic, Lipid profile, Coronary heart diseases

INTRODUCTION

Diabetes mellitus, a metabolic disorder characterised by derangement in carbohydrate, protein and fat metabolism is caused by complete or relative insulin deficiency and/or insulin resistance, which ultimately leads to hyperglycaemia (Bulkau *et al.,* 2000, Edem *et al.,* 2009). Approximately 140 million people Worldwide suffer from diabetes mellitus (WHO, 1999). The disease has been recognised as an important public health problem in developing countries, where its prevalence is increasing steadily and adequate treatment is often expensive and unaffordable (Djrolo *et al.,* 1998). Due to inability of the modern therapy to control all the pathophysiological aspects of the disorder, as well as the enormous costs it poses on the economy of the

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developing nations of the World, alternative strategies are urgently needed (WHO, 2002). Plants used in traditional medicine to treat diabetes mellitus represent a valuable alternative for the management of this disease. The use of medicinal plants plays an important role in the lives of rural people, particularly in remote parts of developing countries which are poorly served with health facilities. *Ceiba pentandra* (L) Gaertner (Bombacaceae), known as silk cotton tree or locally as *dum* is widely reputed in the African traditional medicine (Ueda *et al.,* 2002). Various morphological parts of the plant have been reported to be useful as effective remedies against diabetes (Ueda *et al.,* 2002), hypertension (Noumi *et al.,* 1999), headache, dizziness, constipation, mental diseases, fever, peptic ulcer (Noumi and Dibakto, 2000) and leprosy. It is also used as diuretics and to expel evil spirits (Ueda *et al*., 2002, Noumi and Techakonang, 2001). The hypoglycaemic activity of the aqueous extract of *Ceiba pentandra* stem's bark at high doses has been reported (Olusola *et al.,* 2003). The objective of this study is therefore to investigate the possible effect of the leaves of *C.pentandra* on body weight, plasma glucose and lipid profile of alloxan induced diabetic rats. The result of the study is hoped to give the scientific basis for possible use of the leaves in the management of diabetic conditions and coronary heart diseases.

MATERIALS AND METHODS

Animals:

Male Wister albino rats (n = 25), weighing 105-162 g purchased from animal house of the Department of Pharmacy, University of Nigeria, Nsukka were randomly assigned into five (5) groups (I-V) of five (5) rats per group. The animals were allowed free access to feed and water *ad libitu* for a period of one week to allow them acclimatise. All the rats received human care in accordance with the National Institute of Health guidelines for the care and use of laboratory animals (NRC, 1985).

Preparation of Experimental Feed:

Fresh *Ceiba pentandra* leaves were collected in a farm land from Ugwulangwu, in Ohaozara Local Government Area of Ebonyi State. The leaves were identified and certified at the Department of Botany, University of Nigeria, Nsukka. The leaves were sun-dried to a constant weight and ground into powder with a mortar. The resulting powder was sieved and stored in polyethylene bags at room temperature. The experimental feed was prepared by mixing 10g/90g, 15g/85g and 20g/80 w/w of the powder and feed, representing 10 %, 15 % and 20 % respectively. A little quantity of water was added to get the feed in pellet form.

Induction of Diabetes:

Diabetes mellitus was induced in rats in groups I-IV by intraperitoneal injection of 200 mg/Kg body weight of alloxan dissolved in distilled water. Fasting blood glucose levels were determined after three days of alloxan injection with a glucometer (ACCUTREND GC (Boerhinger, Mannheim, Germany), using blood from the tail tips and diabetes mellitus was confirmed by elevated blood glucose >7.8 mmol/l.

Experimental Feeding of the Animals:

One week after the induction of diabetes, fasting blood glucose was determined in all the animals with a glucometer (ACCUTREND GC, Boerhinger, Mannheim, Germany) using blood from the tail tips. Thereafter the animals in groups I, II and III received the experimental feed, containing 10 %, 15 %, and 20 % of *Ceiba pentandra* leaves respectively. Animals in groups IV and V received normal feed and acted as diabetic control and non diabetic control respectively. The treatment lasted for three weeks after which the animals were sacrificed and blood collected for biochemical analyses.

Biochemical Analyses:

Plasma glucose was determined by glucose oxidase method (Barham and Trinder, 1972), total cholesterol and triglyceride were determined by colorimetric method as described previously (Siedel *et al.,* 1983, Negele *et al.,* 1984) while high density lipoprotein (HDL) was determined enzymatically after precipitation of other lipoproteins as described by Warnic *et al.* (1982). Low density lipoprotein and very low density lipoprotein were calculated using Friedewald equation (1972). Plasma total protein was estimated by Biuret method as described by Weichselbaum (1995) and albumin was determined by bromocresol green as described by Doumas *et al.* 1971).

Statistical Analysis:

Data were analysed for mean and standard deviation. Comparison of parameters among groups was done by one-way analysis of variance (ANOVA) and p value less than 0.05 was considered as statistically significant.

Results:

Table 1 shows that there were generally increases in the body weight of the animals, irrespective of treatment, but the weight gain was least in the groups that received diet containing 20 % of the *Ceiba pentandra* powder.

From table 2, plasma glucose levels were significantly ($p < 0.05$) reduced in animals treated with *Ceiba pentandra* supplement when compared with either the diabetic control or the non-diabetic control, with highest reduction (44.4%) recorded in the group that received feed containing 20 % of the supplement.

There were generally statistically significant ($p < 0.05$) decreases in the plasma lipids in diabetic animals fed with diet containing *Ceiba pentandra* powder when compared with diabetic control or the non-diabetic control except for high density lipoprotein (HDL) which showed increases (table 3). However, both effects were highest in the diabetic group that received feed containing 20 % of the supplement. As for plasma protein, there was no significant difference in the treated and non-treated groups.

Table 1: Effect of *Ceiba pentandra* Leaves on Body Weight of Alloxan Induced Diabetic Rats [1]

Body weight (g)	Experimental Groups				
	Group I	Group II	Group III	Group IV (Diabetic control)	Group V (Non-Diabetic control)
Initial	123 ± 1.0	137 ± 2.0	156 ± 1.0	116 ± 1.1	144 ± 1.2
Final	140 ± 1.0	160 ± 2.1	166 ± 1.2	132 ± 1.1	174 ± 2.1
Change in body weight (%)	+17 (13.8)	+23 (16.8)	+10 (6.4)	+16 (13.8)	+30 (20.8)

[1] Values are expressed as mean ± standard deviation (n = 5)

Table 2: Effect of *Ceiba pentandra* Leaves on Glucose Level of Alloxan Induced Diabetic Rats [1, 2]

Blood glucose concentrations	Experimental Groups				
	Group I	Group II	Group III	Group IV (Diabetic control)	Group V (Non-Diabetic control)
Initial (mmol/l)	8.67 ± .12	8.33 ± 0.11	8.89 ± 0.13	8.94 ± 0.31	4.50 ± 0.10
Final (mmol/l)	6.33 ± 0.11^{b}	6.5 ± 0.20^{b}	4.94 ± 0.10^{b}	8.10 ± 0.13^{a}	5.01 ± 0.16
Change in blood glucose (%)	-2.34 (26.5)	-1.83 (22.0)	-3.95 (44.4)	-0.84 (9.4)	+0.51 (11.3)

[1] Values are expressed as mean ± standard deviation (n = 5)

[2] Values carrying different superscripts in a horizontal row are significantly different ($p< 0.05$).

Table 3: Effect of *Ceiba pentandra* Leaves on Plasma Total Protein, Albumin and Lipid Profile of Alloxan Induced Rats[1, 2]

Parameters	Experimental Groups				
	Group I	Group II	Group III	Group IV (Diabetic control)	Group V (Non-Diabetic control)
TC (mg/dl)	60.5 ± 3.1^{b}	60.0 ± 2.0^{b}	51.2 ± 2.1^{b}	69.2 ± 8.5^{a}	71.9 ± 19.0
Tg (mg/dl)	32.7 ± 4.2^{b}	29.9 ± 5.1^{b}	32.7 ± 7.2^{b}	40.8 ± 8.0^{a}	42.5 ± 10.3
HDL (mg/dl)	21.4 ± 2.1^{b}	21.0 ± 3.1^{b}	24.1 ± 3.2^{b}	13.1 ± 4.5^{a}	19.5 ± 2.0
LDL (mg/dl)	32.3 ± 2.9^{b}	33.0 ± 2.1^{b}	20.6 ± 4.1^{b}	37.8 ± 11.1^{a}	32.9 ± 15.6
VLDL (mg/dl)	6.5 ± 1.1^{b}	5.8 ± 2.0^{b}	6.5 ± 3.3^{b}	8.2 ± 1.6^{a}	8.5 ± 2.1
TP (g/dl)	5.4 ± 0.9	5.1 ± 0.51	4.2 ± 0.1	4.6 ± 0.7	5.7 ± .6
Alb (g/dl)	3.9 ± 0.1	3.8 ± 0.1	3.8 ± 0.2	3.1 ± 0.7	4.3 ± 0.3

TC: Total cholesterol; Tg: Triglyceride; HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: Very low density lipoprotein; TP: Total protein; Alb: Albumin.

[1] Values are expressed as mean ± standard deviation

[2] Values with different superscripts in a horizontal row are significantly different ($p < 0.05$).

Discussion:

This study has shown the potential hypoglycaemic and hypolipidaemic effects of *Ceiba pentandra* on Alloxan induced diabetic rats. Although study on *Ceiba pentandra* is scarce, the significantly decreased plasma glucose in diabetic rats administered feed containing powdered leaves of *Ceiba pentandra* in the present study suggests that the herb has effect on the glucose metabolism. Previously, the hypoglycaemic activity of the aqueous extract of *C. pentandra's* stem bark at high doses has been reported (Olusola *et al.,* 2003). Many plant leaves have been shown to exert hypoglycaemic effect (Maghrani *et al.,* 2005, Jain *et al*., 2010). A number of mechanisms have been suggested by which these plants exert their effects on blood glucose level. These include enhancement of muscle glucose uptake and metabolism (Gray *et al*., 2000), enhancement of insulin production by regeneration of β-cells of the Islet of Langerhans (Ayber *et al.,* 2001 Jelodar *et al.,* 2007, Yadav *et al.,* 2008), possession of insulin-like substance (Gray *et al*. 2000), inhibition of insulinase activity (Gray *et al*., 2000), inhibition of renal glucose reabsorption (Maghrani *et al.,* 2005), inhibition of endogenous glucose production (Eddouks *et al.,* 2003) and through fibre-mediated interference with glucose absorption (Nelson *et al.,* 1991). Although phytochemical investigation was not part of this study, some bioactive products, such as γ-sitosteroline, fatty acids, anthraquinones, tannins and alkaloids have been isolated from plants claimed to have antidiabetic activity (Farswan *et al.,* 2009). It has been shown that β-sistosterol and tannin in leaf of such plants are responsible for their antidiabetic activity. It is therefore speculated that the hypoglycaemia exhibited by diabetic rats treated with feed containing leaf of *C. pentandra* in the present study may be partly attributed to some of these bioactive products, particularly, tannins and sterol as tannins- and sterol-containing drugs have been shown to possess antidiabetic activity (Hatapakki *et al.,* 2005). Although phytochemical analyses of *C. pentandra* have revealed some bioactive products, such as naphtoquinones (Rao *et al.,* 1993) vivain and its glucosides (Noreem *et al.,* 1998), both of which have antimicrobial and inhibitory effect on cyclooxygenase-catalysed prostaglandin biosynthesis respectively (Ueda *et al.,* 2002), the effects of these bioactive products on glucose metabolism are yet to be ascertained. Another mechanism by which *C. pentandra* may have exerted its hypoglycaemic effect in the present study is by fibre-mediated inhibition of intestinal glucose absorption (Nelson *et al.,* 1991), as plant leaves are generally rich in fibres. Additionally, regeneration of β-cells can not be ignored as the probable mechanism by which *C. pentandra* produced a significant reduction in blood glucose in the treated rats. This is because, improved blood glucose in the treated animals suggests either increased insulin release or improved insulin activity, both of which could be attributed to improvement in the intergrity of β –endocrinocytes (Snigur *et al.,* 2008). In addition to hypoglycaemic effect, *C. pentandra* showed a beneficial effect in the maintenance of body weight as less weight gain was observed in animal fed with the experimental feed. This is also evidenced by improvements in plasma lipids in the diabetic rats fed with diet supplemented with powdered leaves of *C. pentandra* in comparison to the diabetic or non diabetic control rats. Interesting to note is the fact that diabetic rats fed with the experimental diet showed significant elevation in HDL-cholesterol, suggesting that the plant has protective effect on the heart. It is well known that in uncontrolled diabetes, the resultant increases in LDL, VLDL, triglyceride and total cholesterol were associated with increased morbidity and mortality from coronary artery disease (Arvind *et al.,* 2002). The protective effect of *C. pentandra* was seen to be extended to the liver in this study, as shown by increases ($p > 0.05$) in total protein and albumin, thus supporting the regenerating capacity of this plant leaves on the pancreatic tissues which are manifested by increased utilization of glucose and protein synthesis. In the light of the hypoglycaemic and hypolipidaemic effects exhibited by *C. pentendra,* coupled with its protective effect on cellular and tissue damage as exemplified by improvement in plasma proteins, it may be considered for use in the management of diabetes and its associated complications. However, more research is desired to identify the bioactive agent (s) responsible for these actions and its/their mode of actions.

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