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Hypoglycemic, Anticholesterolemic and Body Weight-Lowering Effects of Aqueous Leaves Extract of *Olea hochstetteri* Bak. in Rats

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Abstract: In cognizance of the traditional use of the leaves extract of *Olea hochstetteri* Bak. against several diseases including non-insulin dependent diabetes mellitus, this study was carried out to determine the effect of prolonged oral administration of aqueous leaves extract of the plant on serum glucose and total cholesterol levels and body weight of rats. Sixty apparently healthy Wistar strain albino rats were separated into 4 equal groups (labeled A-D) and used in the experiment. Rats in groups B-D were given daily oral dose of 250, 500 and 1000 mg kg^{-1} of aqueous leaves extract of *O. hochstetteri* Bak., respectively for 21 days while those in group A served as control. At the end of each week, five rats from each group were humanely sacrificed to collect serum for analyses for glucose and total cholesterol. The body weights of the rats were also determined weekly. The result of the study revealed that the extract caused significant ($p<0.05$) decrease in serum glucose and total cholesterol and body weight of the rats throughout the period of treatment. It was concluded that the extract had hypoglycemic, anticholesterolemic and body weight lowering effects and may be potentially useful against diabetes mellitus, hypercholesterolemia and obesity. Further studies to elaborate more on these effects and on the toxicity of the plant were recommended.

Key words: Aqueous extract, *Olea* hochstetteri Bak., serum, total cholesterol, glucose, body weight, Wistar rats

INTRODUCTION

Hyperglycemia is the primary manifestation of diabetes mellitus. The condition is been implicated as the major cause of a cascade of a series of pathological entities among which is hypercholesterolemia. Diabetes mellitus-induced hypercholesterolemia markedly increases predisposition to atherosclerosis (Cotran *et al*., 1999) and coronary heart diseases (Iweala and Okeke, 2005); these hyperglycemia-induced cardiovascular diseases associated with alteration in serum lipid profile are among the common causes of mortalities (Adaramoye *et al*., 2008).

Lipid lowering therapy is indicated in the primary and secondary prevention of cardiovascular diseases in addition to the management of other risk factors (Jessani *et al*., 2006). Drugs used for antihyperlipidemic therapy includes fibrates, bile acid sequestrants and statins (HMG CoA inhibitors) however, there are serious side effects reported with the use of these drugs. This has led to the withdrawal of statins from the market by one of its manufacturers. There is also an increasing quest for natural products that has lipid-lowering potential while presenting very minimal or no side effects (Adaramoye *et al*., 2008). Furthermore, the high level of treatment failures coupled with unpleasant side effects associated with oral antidiabetic drugs has led to the search for alternative drugs (Iweala and Okeke, 2005) hence, emphasis on management of diabetes is gradually shifting towards the use of plant products, diet management and exercise (Grover *et al*., 2002). Several plant species have been reported to have hypoglycemic and/or antidiabetic activity (Bnouham *et al*., 2006; Moshi and Mbwambo, 2002; Chattopadhyay and Bandyopadhyay, 2005; Iweala and Okeke, 2005; Jelodar *et al*., 2005; Talpur *et al*., 2005; Adeneye and Agbaje, 2008) and cholesterol-lowering effect (Ghasi *et al*., 2000; Mehta *et al*., 2003; Andreadou *et al*., 2006; Banu *et al*., 2007; Adaramoye *et al*., 2008; Vijaya *et al*., 2009).

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Olea hochstetteri Bak. (English-East African olive) belong to the family Oleaceae (Hutchingson and Dalziel, 1958). It is a small tree (6-15 m high) with dense crown and ascending branches that has dark green leathery leaves and thick, smooth, grayish bark (Keay *et al*., 1964). The plant has been mentioned by the FAO among the species of trees of ethnomedicinal significance used by the Mukogodo Maasai people of Kenya (Ngethe *et al*., 1998). It is also used in traditional medicine against many disease conditions in northeastern Nigeria (Aji *et al*., 2010) and by traditional healers of Morogoro region of Tanzania in the management of non-insulin dependent diabetes mellitus (Moshi and Mbwambo, 2002).

The objective of this study was to determine the effect of prolong oral administration of the aqueous leaves extract of *Olea hochstetteri* Bak. on serum glucose, total cholesterol and body weight of rats.

MATERIALS AND METHODS

Collection and identification of plant material: Fresh leaves of *Olea hochstetteri* Bak. were collected from Mafa local government area of Borno state in Nigeria and were identified and authenticated by a taxonomist in the Department of Biological Sciences, University of Maiduguri, Nigeria. Voucher specimen (Species Vet. 206 A) was deposited at the University Herbarium for reference.

Preparation of extract: The leaves were air-dried, crushed and pulverized and then kept in cellophane bags. The aqueous leaves extract was prepared according to the methods of Mittal *et al*. (1981) and Fernando *et al*. (1989). The 200 g of the powdered leaves was mixed with 1 L of water in a 5 L beaker. The mixture was steamed at 65°C for 1 h allowed to cool and mixed vigorously. It was filtered using Whatman no.1 filter paper. The aqueous extract was then concentrated by evaporation at 60°C in a water bath and finally stored at 4°C. The extract yield was 6.1% (w/w). A concentration of 0.5 g mL^{-1} was prepared as a stock solution for administration to rats.

The animals: The sixty Wistar strain albino rats of both sexes weighing between 90-128 g were used in the experiment which lasted for 3 weeks. They were housed in plastic rat cages in the Research Laboratory of the Department of Veterinary Physiology, Pharmacology and Biochemistry, University of Maiduguri, Nigeria. They were given feed and water *ad libitum* and allowed to adjust for 3 weeks before the commencement of the experiment.

Treatment of animals with the plant extract and collection of samples: The rats were separated into 4 groups (A-D) of fifteen rats per group at random. Rats in groups B-D were treated with daily oral dose of aqueous extract at 250, 500 and 1000 mg kg^{-1} body weight, respectively for 21 days while rats in group A served as control. At the end of each week, five rats were picked at random from each group and humanely sacrificed by decapitation. Blood samples were collected into sterile sample bottles without anticoagulant. The formed sera were collected and their glucose and total cholesterol levels were determined.

Determination of serum total cholesterol and glucose: The enzymatic endpoint method based on the principles described by Trinder (1969) was adopted for the determination of blood cholesterol using Randox Laboratoy® test kits and documented procedures. The enzymatic calorimetric test method without deproteinization was adopted for the determination of glucose using Human® Gmbh test kits based on the principles described by Barhem and Trinder (1972).

Determination of body weight: The body weights of rats in each group were determined using triple beam balance on the 1st day of the experiment and repeated weekly until the 3rd week.

Statistical analysis: Data obtained from the studies were analyzed using computer software (GraphPad InStat, Instant Biostatistics, Version 3, GraphPad software Inc®., USA, 2002). Results were presented as mean and standard deviation and the differences between means were analyzed using ANOVA. Level of significance was considered at $p \leq 0.05$.

RESULTS AND DISCUSSION

The serum glucose levels of rats treated with aqueous leaves extract of *O. hochstetteri* Bak. are showed in Table 1. Daily treatment with extract dosage of 250, 500 and 1000 mg kg^{-1} all produced significant ($p<0.01$) decreases in the blood glucose levels of

Table 1: Effects of aqueous leaves extract of *Olea hochstetteri* Bak. on serum glucose levels of rats

	Concentration (mg dL^{-1}) of glucose in serum (mean±SD) (days)		
Groups (n = 5)	7	14	21
A (control)	77.80±0.70	72.60±0.53	76.10±0.50
B (250 mg kg^{-1})	65.20±1.01*	65.80±0.66*	61.80±0.70*
C (500 mg kg^{-1})	65.00±0.38*	63.80±0.19*	57.20±0.64*
D (1000 mg kg^{-1})	49.00±0.95*	49.40±0.86*	43.40±0.25*

*Significant ($p<0.05$) compared with control

Table 2: Effects of aqueous leaves extract of *Olea hochstetteri* Bak. on serum cholesterol of rats

	Concentration (mg L^{-1}) of cholesterol in serum (mean±SD) (days)		
Groups (n = 5)	7	14	21
A (control)	28.80±0.13	26.90±0.10	28.00±0.35
B (250 mg kg^{-1})	21.40±0.50*	20.00±0.16*	17.00±0.21*
C (500 mg kg^{-1})	20.60±0.31*	20.50±0.35*	18.20±0.43*
D (1000 mg kg^{-1})	18.70±0.60*	15.60±0.40*	15.00±0.23*

Table 3: Effect of aqueous leaves extract of *Olea hochstetteri* Bak. on the body weight of rats

	Body weight (g) (mean±SD) (days)			
Groups (n = 5)	1	7	14	21
A (control)	115.00±13.64	140.74±13.16	181.09±11.37	201.56±18.00
B (250 mg kg^{-1})	116.37±10.11	126.80±11.17	129.91±18.09*	127.92±14.31*
C (500 mg kg^{-1})	110.54±11.54	123.86±16.01	129.91±19.45*	109.39±11.21*
D (1000 mg kg^{-1})	105.30±14.92	103.19±18.52*	100.30±15.69*	86.62±17.66*

*Significant ($p<0.05$) compared with control

rats by day 7, 14 and 21, respectively. The effect of the extract on serum total cholesterol levels of the rats are shown in Table 2. Rats treated with all the dosages (250, 500 and 1000 mg kg^{-1}) of the aqueous extract showed significant ($p<0.01$) dose and time-dependent progressive decreases in their serum levels of cholesterol with the least cholesterol level (15.00 mg L^{-1}) attained by day 21st following daily treatment of rats with 1000 mg kg^{-1} of extract.

The above findings revealed that the extract had hypoglycemic and anticholesterolemic activities which possibly suggests its potential usefulness in cases of diabetes mellitus and hypercholesterolemia. Diabetes mellitus which is a chronic disorder of carbohydrate, lipid and protein metabolism is characterized by persistent elevation of fasting blood glucose above 200 mg dL^{-1} due to insufficient or complete cessation of insulin synthesis or secretion and/or peripheral resistance to insulin action (Murray and Pizzorno, 1997) and alterations in serum lipid profile leading to hypercholesterolemia (Massing *et al*., 2001) that markedly increases predisposition to atherosclerosis (Cotran *et al*., 1999) and coronary heart disease (Iweala and Okeke, 2005).

Conversely when the level of serum cholesterol are lowered by diet or drugs, the rate of progression of atherosclerotic diseases is slowed, some atherosclerotic plaques regress and the risk of cardiovascular events is reduced (Gotto Jr., 1997). Some phytochemicals are known to be associated with biological activities such as hypoglycaemia, hypolipidaemia, hypotention and hypoazotemia. Among these are alkaloids and flavonoids (Sudheesh *et al*., 2005). The presence of alkaloids and also flavonoids in the aqueous leaf extract of *O. hochstetteri* Bak. was previously reported (Aji *et al*., 2010). These phytochemicals could possibly account for the hypoglycemic and anticholesterolemic effects of the extract observed in the treated group of rats. The result of the effect of the extract on the body weight of rats is showed in Table 3. The body weight of rats treated with 250 and 500 mg kg^{-1} of the extract were significantly ($p<0.01$) lower when compared with the control group at day 14 and 21st. Rats treated with 1000 mg kg^{-1} of the extract however had significantly ($p<0.01$) decreased body weights throughout the 21 days treatment period when compared with the control rats.

The extract's body weight lowering effect observed in the experimental rats in this study may not be unconnected with the extract's effect on blood glucose and cholesterol levels since high carbohydrate (glucose) intake and increased cholesterol levels are known to be associated with increased body fats, body weight and obesity (Murray *et al*., 2006).

Increased serum cholesterol especially the low density fraction is known to be associated with obesity and increased risk of diseases such as diabetes, atherosclerosis and coronary heart disease among others (Cotran *et al*., 1999).

Decreased feed intake was also observed in the group of rats that were treated with the extract although, feed intake was not quantitatively determined in the study. This could have further accounted for the decreased body weight observed in the rats. Therefore, the effect of the extract on body weight may be pointing at its potential usefulness against obesity and its consequences on health.

CONCLUSION

It is therefore founded from the result of this study that aqueous leaves extract of *O. hochstetteri* Bak. decreased serum glucose, serum total cholesterol and body weight of rats. Therefore, we recommend detailed

studies on the extract's hypoglycemic and anticholesterolemic activities and also its effect on diabetic subjects with the view to unveiling its possible benefit against these diseases conditions. We also recommend toxicity studies on this plant.

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