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HYPOGLYCEMIC EFFECT OF THE AQUEOUS STEM BARK EXTRACT OF *Boswellia dalzielii* hutch

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ABSTRACT
Boswellia dalzielii Hutch is frankincense producing tree plant, belonging to the family Burseraceae and found in West Africa. The stem bark is used in ethnomedicine for the treatment of fever, rheumatism and gastrointestinal troubles and has also been reported to possess anti-ulcer, antidiarrhoeal, antibacterial and antifungal activities, but there is no record of its hypoglycemic activity in the literature. The hypoglycemic effect of the aqueous stem bark extract of *Boswellia dalzielii* was therefore studied in this work using male albino mice weighing between 15-40g and was compared to that of chlorpropamide, a standard hypoglycemic agent. The extract lowered blood glucose concentration significantly in both normal and alloxan induced hyperglycemic animals at doses of 153mg/kg and 297mg/kg corresponding to 17% and 33% of the LD_{50} (median lethal dose). Phytochemical screening of the extract showed the presence of saponins, tannins and flavonoids.The result gave evidence that the aqueous stem bark extract of *Boswellia dalzielii* possess hypoglycemic effect, similar to that of chorpropamide and can therefore be used in the treatment of diabetes mellitus.

KEYWORDS: *Boswellia dalzielii*, hypoglycemic effect, male albino mice, chlorpropamide, alloxan.

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INTRODUCTION

Hyperglycemia is a condition which signifies high blood sugar levels and is highly implicated in the disease condition known as diabetes mellitus.

Diabetes mellitus can be classified into two major classes: type 1 and type 2 diabetes. In type 1 diabetes, patients must administer insulin medication regularly in order to survive. (Samreen, 2009; WHO, 1999). Type 2 diabetes is the most common type of diabetes (Samreen, 2009; WHO, 1999), oral hypoglycemic agents, such as sulfonylureas e.g chlorpropamide can be used in the management of this type of diabetes.

Despite the presence of oral, hypoglycemic agents in the pharmaceutical market, diabetes and the related complications continued to be a major medical problem (Neelesh *et al*., 2010). Also, synthetic antidiabetic agents produce undesirable side effects, such as hypoglycemia. Therefore search for a novel antidiabetic drug from plants, is needed, since they have well been recorgnized as an important source of providing new drugs (Chauhan *et al*., 2010).

Boswellia dalzielii is a frankincense producing tree growing to 13 metre high of the wooded savanna, with characteristically pale papery bark and belongs to the family Burseraceae. The stem bark of *Boswellia dalzielii* has found various uses in ethnomedicine, including the treatment of fever, rheumatism and gastrointestinal troubles (Burkill, 1965; Evans, 1989). It has also been reported to possess anti-ulcer (Nwinyi *et al*., 2004), antidiarrhoeal (Etuk *et al*., 2006), antibacterial and antifungal activities (Ntiejumokwu and Alemika, 1991; Adelakun *et al*., 2001).

Compounds isolated from the stem bark of *Boswellia dalzielii* includes: Protocateuchuic acid, gallic acid and ethyl gallate, a diterpenoid- incensole, and a triterpenoid- 3-O-acetyl-11-keto-β-boswellic acid (Alemika, 2001). Very little is

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known of the antidiabetic activity of the stem bark of *Boswellia dalzielii*, therefore this study is aimed at evaluating the antidiabetic effect of the aqueous stem bark extract of *Boswellia dalzielii*.

MATERIALS AND METHOD

Collection and Preparation of Plant Material

The plant material was collected from Jos, Plateau State, Nigeria and was authenticated by comparing with voucher specimen (Number: UJ/PCG/HSP/89B13), deposited at the herbarium of the Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, University of Jos, Nigeria. The stem bark of *Boswellia dalzielii* collected was chopped into small pieces with the aid of a cutlass and air-dried to obtain the dried plant material. 2kg of the dried plant material was weighed out and soaked in 3.5 litres of distilled water (50^{o}C). This was filtered after 24hours (infusion). The filtrate obtained was freeze-dried with a LYOBAC GT-2 freeze-dryer at the National Institute for Pharmaceutical Research and Development (NIPRD), Abuja, Nigeria and stored in an air tight container.

Experimental Animals

Male albino mice with weight between 15-40g obtained from the National Veterinary Research Institute, Vom, Plataeu State, Nigeria were used for this research. The animals were allowed free access to food and water for a period of one week (acclimatization) prior to the commencement of the experiment.

Experimental Design

Median Lethal Dose Determination

Median lethal dose (LD_{50}) determination was carried out according to the method of Lorke, (1983).

Test for Hypoglycemic Activity

The test for hypoglycemic activity was carried out in normal and alloxan induced hyperglycemic animals. For the normal (normoglycemic animals), 20 animals were divided into four(4) groups of five(5) animals each (Group A-D). The animals were allowed water only for 12 hours. They were then treated as shown in Table 1. The individual treatment was administered intraperitoneally.

Table 1: Treatment Administered to Normoglycemic Animals.

Group	Treatment	Dose
A	Distilled water	Equivolume with group C
B	Crude extract	153mg/kg body weight (17% of LD_{50})
C	Crude extract	297mg/kg body weight (33% of LD_{50})
D	Chlorpropamide (reference drug)	400mg/kg body weght

The same procedure was followed to test for hypoglycemic effect in alloxan induced hyperglycemic animals, except that the animals were induced intraperitoneally with 150mg/kg body weight of alloxan monohydrate (single dose) and given a three day resting period (to enable the development of hyperglycemia) before treatment.

Determination of Blood Glucose

Immediately after treatment, blood glucose concentration (BGC) was determined at 0,2,4,8 and 24 hours, using a Life scan, one touch ultra easy glucometer, manufactured by Lifescan inc., Milipitas, USA.

Phytochemical Screening

Phytochemical screening was carried out for the presence of alkaloids, saponins, tannins, anthraquinones, cardiac glycosides, steroids and flavonoids. The tests were carried out as described by Trease and Evans, (1978) and Sofowora, (1982).

Statistical Analysis

Data for hypoglycemic activity was expressed as mean ± standard error of mean (mean±SEM). Statistical analysis was done using the student t-test. Significance was checked at 0.05 and 0.01 levels of significance.

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Table 2: Blood Glucose Concentration (BGC) in mg/dl of Normoglycemic Animals expressed as Mean±SEM; n=5;

Group	Treatment Admnistered	0 hour	2 hours	4 hours	8 hours	24 hours
A	Distilled water	79.92±0.53	104.04±0.45	64.08±0.33	108.00±0.63	67.68±0.44
B	153mg/kg extract	109.44±1.45 NS	48.24±1.06*	21.24±0.18**	27.72±0.25**	43.92±0.70 NS
C	297mg/kg extract	79.56±1.19 NS	39.60±0.34**	18.00±0.00**	41.40±0.70**	73.80±0.50 NS
D	400mg/kg chlorpropamide	55.44±0.46*	33.12±0.22**	36.36±0.18**	62.28±0.50**	83.16±0.15*

NS-not significant, *p<0.05, **P<0.01VS group A (control group)

Table 3: Blood Glucose Concentration (BGC) in mg/dl of Hyperglycemic Animals expressed as Mean±SEM; n=3;

Group	Treatment Admnistered	0 hour	2 hours	4 hours	8 hours	24 hours
A	Alloxan +Distilled water	451.80±6.87	422.46±8.53	417.06±8.83	423.54±8.47	392.94±7.27
B	Alloxan+153mg/kg extract	197.46±1.23 NS	169.74±3.07 *	49.14±0.87**	18.00±0.00**	64.80±0.90*
C	Alloxan+297mg/kg extract	182.34±0.48 NS	94.68±0.24 **	24.66±0.37**	18.00±0.00**	31.68±0.03**
D	Alloxan+ 400mg/kg chlorpropamide	423.54±1.33NS	232.20±2.60 NS	91.08±0.83 **	100.80±0.40**	474.97±5.50NS

NS-not significant, *P<0.05, **P<0.01 VS group A (control group).

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RESULTS AND DISCUSSION

The blood glucose concentration (BGC) of both normoglycemic and hyperglycemic control animals were virtually unchanged throughout the 24 hour experimental period. Also, for both normoglycemic and hyperglycemic animals, group B (administered153mg/kg body weight of extract) and C (admnistered 297mg/kg body weight of extract) showed significant decrease ($P<0.05$ and $P<0.01$) in BGC, with that at the 2nd hour being significant at only $P<0.05$. In the hyperglycemic group D, administered with the reference drug (400mg/kg chlorpropamide), the BGC reduced up to the 4th hour and was still significant at the 8th hour after administration. Thereafter, the BGC returned to baseline levels at the end of the 24th hour. Table 2 and Figure 1 summarises the result of test on normoglycemic animals while Table 3 and Figure 2 summarises the result of test on hyperglycemic animals.

Hyperglycemia was successfully induced as shown by the higher blood sugar levels recorded for the alloxan induced hyperglycemic group. Alloxan (a pyrimidine derivative, 2,4,5,6-tetraoxypyrimidine) (Wohler and Liebig, 1838) is selectively toxic to beta cells because it preferentially accumulate in beta cells as a glucose analogue through uptake via the GLUT2 glucose transporter (glucose transporter 2) (Reup, 1970; Losert *et al*., 1971). In the presence of intracellular thiols, especially glutathione, alloxan generates reactive oxygen species (ROS) in a cyclic reaction with its reduction product, dialuric acid. Autoxidation of dialuric acid generates superoxide radicals ($O_2^{\cdot}$), hydrogen peroxde (H_2O_2) and, in a final iron catalysed reaction step, hydroxyl radicals ($OH^{\cdot}$). These hydroxyl radicals are ultimately responsible for the death of the beta cells (Lenzen and Panten, 1988; Meglasson *et al*., 1986; Lenzen and Munday, 1991). The extract therefore, possibly acts as an antioxidant, i.e., it blocks the formation of ROS.

The report of Pfizer labs, 2010 on diabinese® (chlorpropamide) states that diabinese lowers blood sugar by stimulating the release of insulin from the pancrease, an effect dependent upon beta cells in the pancreatic islets. The result suggests that the plant extract acts in a similar way, since the pattern of glucose reduction in animals administered with the plant extract is similar to that obtained in animals administered with chlorpropamide, especially in hyperglycemic animals. The Pfizer labs report also states that diabinese is absorbed rapidly from the GIT. Within one hour after a single dose, it is readily detectable in the blood, and the level reaches a maximum within two to four hours. It exerts hypoglycemic effect in healthy subjects within one hour, becoming maximal at 3 to 6 hours. This report is in agreement with the result obtained from the hyperglycemic group administered 400mg/kg chlorpropamide.

The result is also in agreement with that obtained by Salisu *et al*., 2009. In this case, in hyperglycemic animals administered with chlorpropamide, the BGC reduced significantly upto the 7th hour, and was still significant 9 hours after admnistration, thereafter, it returned to baseline levels at the end of the 24th hour. On the other hand, the maximal reduction in blood glucose concentration occured at the dose of 200mgkg^{-1}, using roots of *Acacia albida* at the 7th hour after oral administration while the maximal reduction in BGC for both normo and hyperglycemic animals occured at the dose of 297mg/kg using the stem bark of *Boswellia dalzielii* at the 4th hour after intraperitoneal administration.

This study showed a similarity between the hypoglycemic effect of chlorpropamide and the plant extract, in that, a repeated and monitored daily dose treatment of diabetic patients with the plant extract will be required in order to maintain normal blood glucose levels, since the blood glucose concentraton returned to higher levels at the 24th hour. Also, if not properly monitored, administration of the plant extract can result in hypoglycemia, just like chlorpropamide.

Phytochemical screening showed the presence of saponins, tannins and flavonoids in the aqueous stem bark extract of *Boswellia dalzielii.*

CONCLUSION

In conclusion, the reduction of blood glucose levels in the normo and hyperglycemic animals showed clearly that the aqueous bark extract of *Boswellia dalzielii* can be used in the treatment of diabetes mellitus, and the plant extract is effective at the two doses administered. The antidiabetic effect may be as a result of the phytochemical constituents, i.e., either saponins, tannins or flavonoids or their combination.

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PLOT OF BLOOD GLUCOSE CONCENTRATION IN MG/DL OF NORMOGLYCEMIC AND HYPERGLYCEMIC ANIMALS AGAINST TIME IN HOURS

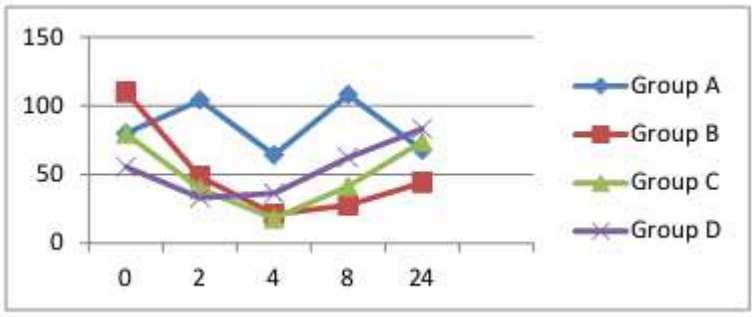


Figure 1: Plot of Blood Glucose Concentration in mg/dl (vertical axis) of Normoglycemic animals against Time in hours (horizontal axis)

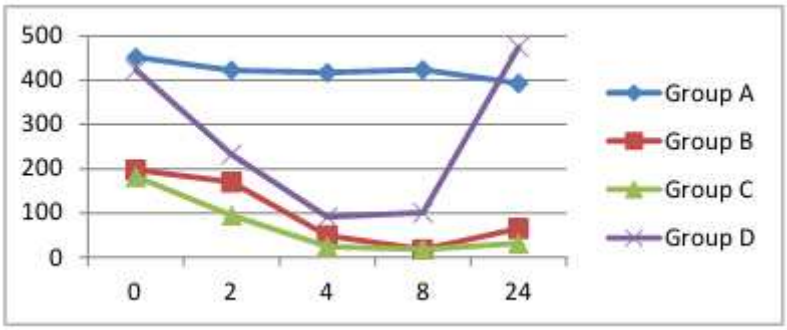


Figure 2: Plot of Blood Glucose Concentration in mg/dl (vertical axis) of Hyperglycemic animals against Time in hours (horizontal axis)

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