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RESEARCH ARTICLE

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Hypoglycaemic effect of the stem-bark extract of *Commiphora Kerstingii* Engl. on experimental hyperglycaemia

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ABSTRACT

Diabetes mellitus is a syndrome with disordered metabolism and inappropriate hyperglycaemia due to either a deficiency of insulin secretion or to a combination of insulin resistance and inadequate insulin secretion to compensate. Commiphora kerstingii is a tree of 10m high that grows in savanna from Togo to Nigeria, and on to Central African Republic, and it belongs to the family Burseraceae. In Zaria Nigeria, the stem-bark is used traditionally for managing diabetes mellitus. Phytochemical screening was carried out in accordance with the standard protocol as described by Trease and Evans and the oral LD_{50} of the extract in rats was conducted according to the method described by Lorke. Glucose, nicotine and dexamethasone were used to in induce hyperglycaemia. The dose of 400 mg/kg of the extract significantly ($p < 0.02$) prevented an elevation in blood glucose at the 2nd and 3rd hours in the oral glucose load model. In the nicotine-induced hyperglycaemic model 100 mg dose of the extract significantly ($p < 0.05$) lowered the BGL only at the 5th hour, while 200 mg/kg and 400mg/kg doses lowered the BGL at the 4th and the 5th hours. Dexamethasone was administered subcutaneously at a dose of 10 mg/kg/day for ten days consecutively. All doses of the extract used significantly ($p < 0.05$) lowered the Blood Glucose Level when compared with the group that was administered dexamethasone alone on all the days monitored.

Keywords: *Commiphora kerstingii*, glucose, nicotine, dexamethasone, hyperglycaemia

INTRODUCTION

Diabetes mellitus (DM) consist of a group of syndromes characterized by hyperglycaemia, altered metabolism of lipids, carbohydrates, and protein; and an increased risk of complications from vascular disease [1]. DM is a syndrome with disordered metabolism and inappropriate hyperglycaemia due to either a deficiency of insulin secretion or to a combination of insulin resistance and inadequate insulin secretion to compensate [2]. DM is the world's largest endocrine disease with altered carbohydrate, fat and protein metabolism [3]. The increasing prevalence of diabetes has reached epidemic proportion worldwide. According to the World Health Organization (WHO) report, approximately 150 million people have diabetes worldwide, and this figure may double by the year 2025. Diabetes is a major threat to global health that is rapidly increasing [4]. The greatest increase in prevalence is however expected to occur in Asia and Africa, where most patients will probably be found by 2030. The increase in incidence in diabetes in developing countries follows the trend of urbanization and lifestyle changes.

Dexamethasone at a dose of 2mg/kg intraperitoneally was used to induce Sprague Dawley halothane anaesthetized rats [5]. Four days after administration, the plasma glucose level was observed to be 159% greater than in normal rats. Nicotine has been shown to stimulate the adrenal gland resulting in the discharge of adrenaline. The rush of adrenaline stimulates the body and causes a sudden release of glucose.

Commiphora kerstingii is a tree of 10m high that grows in savanna from Togo to Nigeria, and on to Central African Republic, and it belongs to the family *Burseraceae*. The wood is soft it is used to make saddle and is sometimes hollowed out to make quivers in Yola area of Northern Nigeria. The evergreen bark seems to have engendered an idea that the tree is little likely to burn, so that it has acquired vernacular names suggestive of protection against fire, and survival of property and therefore of inheritance. The bark is sometimes used as an antidote to arrow-poison. Fulani herdsmen feed the leaves to goats, and in a superstitious token lay sticks of the plant across graves, perhaps in the same sense of conferring protection [6]. In Zaria Nigeria, the stem-bark is used traditionally for managing diabetes mellitus. The aim of the study is to scientifically evaluate the antidiabetic effect of the stem-bark extract in Wistar rats.

MATERIALS AND METHODS

Plant preparation and experimental animals

The fresh stem-bark of *Commiphora kerstingii* was collected in Samaru, Zaria, Kaduna State of Nigeria in the month of November of 2008. The plant was authenticated at the Herbarium, Department of Biological Sciences, Ahmadu Bello University (ABU), Zaria, Kaduna state, Nigeria. A voucher specimen number of 006 were deposited at the herbarium for future reference.

Male and female Wistar rats weighing 150-200g were used in the study; they were obtained from the Department of Pharmacology and Therapeutics Ahmadu Bello University Zaria. The animals were maintained on standard laboratory animal feed and water *ad libitum*, and housed in polypropylene cages at room temperature and a 12 h light-dark cycle throughout the study. These studies were carried in accordance with the rules governing the use of laboratory animals as accepted internationally [7].

Preparation of the plant extract

The stem-bark was washed and air-dried under shade until a constant weight was obtained on three separate weighing and then size-reduced into powder with a pestle and mortar. About 100g of the powdered stem-bark was macerated with 500ml methanol for 72hour with occasional shaking. The extract was concentrated *in vacuo* and subsequently referred to as methanolic stem-bark extract of *Commiphora kerstingii* (CKMSE). Solutions of the extract were prepared freshly for each study.

Phytochemical screening

The screening was carried out in accordance with the standard protocol as described by [8].

Acute toxicity study

The oral LD_{50} of the extract in rats was conducted according to the method described by [9]. Briefly, the method was divided into two phases. In the initial phase, animals were randomly divided into 3 groups of three rats each. Group I, II and III were treated with 10, 100 and 1000 mg/kg body weight orally of the extract and observed for signs of toxicity and death for 24 hours. In the second phase, 4 groups each containing one mouse was administered with four more specific doses of the extract based on the results obtained during the first phase. The LD_{50} value was calculated by taking geometric mean of the lowest dose that caused death and the highest dose that did not produce death.

Oral Glucose-induced Hyperglycaemia Model

In this model described by [10], 12- 14 h fasted rats were randomly divided into 5 groups of 5 rats each. Group V served as the model control and were pretreated with 1mg/kg glibenclamide 1 hour before the oral administration of 3 g/kg of D-glucose. Groups I – IV were administered 10ml/kg/oral distilled water, 100 mg/kg, 200 mg/kg and 400 mg/kg of methanol stem bark extract of *C. kerstingii* respectively, 1 hour before treatment with 3 g/kg/oral D-glucose.

The blood glucose level of the animals was recorded at 0 hour and then after every one hour for the following six hours using an acucheck glucometer with compatible strips. A drop of blood was collected from the tail tip of the animals.

Nicotine-induced Hyperglycaemia Model
The same experimental procedure as described above was used for this model, but nicotine 50ug/kg was administered intraperitoneally instead of glucose as described by [11].

Dexamethasone Induced Insulin Resistance Model
For this model described by [12, 13, and 14], thirty-six male rats were divided into 5 groups of 5 animals. The grouping is as follows:

Group I: Dexamethasone sodium phosphate 10 mg/kg, once daily/SC + Normal saline
Group II: Dexamethasone 10 mg/kg/SC + 100 mg/kg/oral of methanol stem bark extract of *T. indica*
Group III: Dexamethasone 10 mg/kg/SC + 200 mg/kg/oral of methanol stem bark extract of *T. indica*
Group IV: Dexamethasone 10 mg/kg/SC + 400 mg/kg/oral of methanol stem bark extract of *T. indica*
Group V: Dexamethasone 10 mg/kg/SC + 1mg/kg glibenclamide

Animals in all the groups were treated daily for ten consecutive days. The blood glucose levels, was recorded on the 1st, 3rd, 6th, 8th, and 10th days.

RESULTS

The oral acute toxicity test (LD_{50}) of the extract was found to be greater than 5,000 mg/kg body weight.

Phytochemical test of the methanol stem-bark extract of *Commiphora kerstingii* Engl. showed the extract to contain carbohydrate, saponins, flavonoids, alkaloids, and steroids.

The dose of 400 mg/kg of the extract significantly ($p < 0.02$) prevented an elevation in blood glucose at the 2nd and 3rd hours. The 200 mg/kg and 100mg/kg doses of the extract significantly ($p < 0.05$) prevented a rise in the blood glucose from the 2nd to the 5th hour. The standard drug (glibenclamide) significantly ($p < 0.02$) lowered the blood glucose level at the 3rd, 4th and 5th hours (table 1).

Table 1: Effect of methanolic stem-bark extract of *C. kerstingii* on Oral Glucose-induced hyperglycaemic Wistar rats

Treatment	Time (hr)					
	0	1	2	3	4	5
Normal saline	73.4±4	77.0±4	130.3±13	160.3±13	108.5±1	105.0±2
CK 100mg/kg	79.0±2	82.0±2	81.0±2*	79.8±3*	77.3±3*	76.3±4*
CK 200mg/kg	74.5±4	77.5±4	76.5±4*	82.8±3*	84.5±2*	85.8±3*
CK 400mg/kg	78.5±2	83.8±2	82.8±2**	84.8±3**	83.0±4*	81.0±4*
Glibenclamide 1mg/kg	78.3±6	80.3±6	79.3±6*	77.5±5**	76.5±5**	74.5±5**

*n = 5 * = significant at p < 0.05 Vs Normal saline (group I) Student's T-test ** = significant at p < 0.02 Vs Normal saline (group I) CK = Commiphora kerstingii*

The 100 mg dose of the extract significantly ($p < 0.05$) lowered the BGL only at the 5th hour, while 200 mg/kg and 400mg/kg doses lowered the BGL at the 4th and the 5th hours. The standard agent used (glibenclamide) used significantly ($p < 0.02$) lowered the BGL at the 4th and 5th hours (table 2).

Table 2: Effect of the methanol stem-bark extract of *C. kerstingii* on nicotine-induced hyperglycaemic Wistar rats

Treatment	Time (hr)					
	0	1	2	3	4	5
Normal saline	78.5±2	78.5±2	87.5±2	96.5±2	105.5±2	110.5±2
CK 100 mg/kg	78.3±6	79.8±6	88.8±6	93.3±6	90.3±6	89.3±6*
CK 200 mg/kg	74.3±4	75.5±4	86.3±4	91.3±4	88.3±4*	86.3±4*
CK 400 mg/kg	74.5±4	76.0±4	85.0±4	90.0±4	87.0±4*	85.0±4*
Glibenclamide 1mg/kg	79.0±2	78.5±2	83.6±2	87.3±2*	76.3±2**	73.3±2**

*n = 5 * = significant at p < 0.05 Vs Normal saline (group I) Student's T-test ** = significant at p < 0.02 Vs Normal saline (group I) CK = Commiphora kerstingii*

Dexamethasone was administered subcutaneously at a dose of 10 mg/kg/day for ten days consecutively. In table 3 all doses of the extract used significantly ($p < 0.05$) lowered the Blood Glucose Level (BGL) when compared with the group that was administered dexamethasone alone on all the days monitored. Glibenclamide the standard agent used significantly ($P < 0.02$) lowered the BGL.

Table 3: Effect of methanol stem-bark extract of *T. indica* on blood glucose on dexamethasone-induced hyperglycaemia

Treatment	Days				
	1	3	6	8	10
Normal saline	88.0±0	107.3±1	114.3±1	130.8±3	112.0±1
CK 100 mg/kg	88.0±1	90.0±1*	95.0±1*	95.0±1*	98.0±1
CK 200 mg/kg	82.0±0	84.8±3*	89.8±3*	89.8±3*	92.8±3*
CK 400 mg/kg	88.0±2	90.0±2*	96.0±2*	96.0±2*	99.0±2
Glibenclamide 1mg/kg	83.0±6	90.0±5*	89.0±6**	89.0±6**	91.0±3*

*n = 5 * = significant at p < 0.05 Vs Normal saline (group I) Student's T-test ** = significant at p < 0.02 Vs Normal saline (group I)*
CK = Commiphora kerstingii

DISCUSSION

The study seeks to demonstrate the efficacy of *Commiphora kerstingii* Engl. in lowering an elevated blood glucose concentration as well as to investigate the ability of the extract at preventing a rise in blood glucose level.

Several reports have shown that phenolic compounds (e.g. tannins, coumarins, and flavonoids), triterpenoids and a host of other secondary metabolites posses' hypoglycaemic effects in various experimental animals [15, 16], and 17]. The phytochemical screening of the methanolic stem-bark extract of *Commiphora kerstingii* revealed the presence of carbohydrate, glycosides, cardiac glycosides, steroids and terpenoid, flavonoids, tannins and alkaloids. The observed hypoglycaemic effects of *Commiphora kerstingii* could be due to the presence of one or combination of the active chemical constituents in the extract.

An acute toxicity study in animals is important to drug development. In most cases the study tries to establish a precise median lethal dose (LD_{50}) in laboratory animals. The oral median lethal dose of methanol stem-bark extract of *Commiphora kerstingii* in rat was found to be greater than 5,000 mg/kg. This suggests that the stem-bark extract is non-toxic when administered orally.

The post absorptive state of glucose is marked by postprandial hyperglycaemic state which is often accompanied by increased pancreatic insulin secretion, particularly in the first few hours postprandial [18]. In this study, graded doses of the extract prevented this increase and at the 5th hour lowered the glucose concentration close to the level at zero hour. The 100 mg/kg and 200 mg/kg doses significantly ($p < 0.05$) prevented the elevation from the 3rd to the 5th hours. Glibenclamide gave significant ($p < 0.02$) reduction from the 3rd to 5th hours. It is hereby suggested that the extract produced its hypoglycaemic effect by inhibiting intestinal glucose uptake like the α-glucosidase inhibitors.

Dexamethasone stimulates lipolysis and free fatty acids synthesis which may compete with glucose for intracellular glucose oxidation, leading to insulin resistance through the glucose–fatty acid cycle, [19, 20, 21]. In the present study, dexamethasone administration for 10 days resulted in increased BGL when compared to group I animals (untreated control) similar to a previous study by [22, 3]. The BGL was significantly ($p < 0.05$) reduced in all the doses and with glibenclamide.

Nicotine has been shown to cause an increase in BGL in rats [23, 10] and canines [24, 25]. Nicotine is known to stimulate the nicotinic acetylcholine receptors [26]. In this study hyperglycaemia was induced by administration of 50ug/kg of nicotine to the animals. However, the hyperglycaemic state was attenuated by all the doses of the extract used and the standard agent by the 5th hour. *C. kerstingii* could have mediated this effect by the inhibition of adrenergic homeostatic mechanism.

REFERENCES

[1] Stephen N. D; In Goodman and Gilman's The Pharmacological basis of Therapeutics. **2006** 11th Edition McGraw Hill publishers.

[2] Umesh M; in *Current Medical Diagnosis and Treatment* **2006** 45th Edition pp 1195 - 1203
[3] Shalam M.D., Harish M.S. and Farhana S.A. *Indian Journal of Pharmacology* **2006** vol.8 (6) 419-422.
[4] World Health Organization. Obesity: Preventing and managing the global epidemic. Geneva: WHO Technical Report Series, **2000** No 894.
[5] Thompson M., Gallager D., William J. B., Faizzu A., Paul A. L., and William L. *Anaesthesiology* **2000** (93) 5 1279-84
[6] Dalziel J.M. Useful Plants of West Tropical Africa. Crown Agent for oversea Governments and Administrations London. **1937** Pp 316 – 317.
[7] National Research Council guide for the care and use of laboratory animals **1985**. Publication no. 85 – 23 (rev.) NIH Washington DC
[8] Trease, G.E., and Evans, M.C. *Textbook of Pharmacology* 12th ed., Balliere Tindall, London **1989** pp. 322-383.
[9] Lorke D. *Archives of toxicology* **1983**, 54:275-287.
[10] Sepici A., Gurbuz I., Cevik C. and Yesilada E. (**2004**). *Journal of Ethnopharmacology* **2004** 93: 311 – 318.
[11] Alada R. A; *African Journal of Medicine and Medical Science* **2001** 30: 57 - 59
[12] Kaur N., Sharma N., and Gupta A.K; *Indian Journal of Biochemistry and Biophysiology;* **1989** 26:371-6
[13] Weisenberg I., Chiesi M., Missbach M., Spanka C. and Pignat W; *Molecular Pharmacology* **1998** 53:1131-6.
[14] Mahendran P. and Shyamala Deva C.S; *Indian Journal of Physiology and Pharmacology* **2001** 45:345-50.
[15] Akah P.A. and Okafor C.L; *Phytotherapy Reaserch* **1992** 6:171-173.
[16] Marles R.J. and Farnsworth N.R; *Phytomedicine* **1995** 2:137-189.
[17] Ojewole, J.A.O; *Journal of Ethnopharmacology* **2002** 8: 231-237
[18] Guyton A.C. Secretory Functions of the Alimentary Tract in: Textbook of Medical Physiology **1991,** 8th edition Philadelphia: W.B. Saunders, 709 – 725p.
[19] Randle P. J; *Diabetes and Metabolism Reviews* **1998,** 14, 263 - 283
[20] Venkatesan N., Davidson M.B. and Hutchinson A; *Metabolism* **1987,** 36, 883–891.
[21] Guillaume-Gentil C., Assimacopoulos-Jeannet F., and Jeanrenaud B; *Diabetologia* **1993,** 36, 899–906.
[22] Dai S., Todd S.C., and McNeil J.H; *Journal of Pharmacology and Toxicological Methods* **1995,** 33:101-3.
[23] Oyebola D. D., and Alada R. A; *African Journal of Medical Science* **1993,** 91: 109 - 113
[24] Grayson J. and Oyebola D. D; *British Journal of Pharmacology* **1985,** 85:797 - 804
[25] Milton A.S; *British Journal of Pharmacology* **1996,** 26: 256 - 263
[26] Westfall T. C; In: Tobacco and related compounds **1965,** 1st edition USA Van Euler Pergamon press 179 - 203