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# Antidiabetic effect of *Crossopteryx febrifuga* methanolic leaf extract in alloxan induced diabetic rats

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**Abstract**
Diabetes mellitus is a potentially morbid condition with high prevalence worldwide thus the disease constitutes a major health concern. Presently, it is an incurable metabolic disorder which affects about 2.8% of the global population. This study, investigate the antidiabetic effect of methanolic leaf extract of *Crossopteryx febrifuga* in alloxan induced diabetes rats. The plant was found to be safe with an LD 50 value of 5000mg/kg and phytochemical screening reveal the presence of flavonoids, tannins, saponins and carbohydrates. The plant significantly decreased blood glucose level at $p < 0.05$ from 139 to 83 mg/dl but body weight of treated rat and control slightly increased significantly after seven days of administration of the extract. The result from this study shows possible beneficial effects of *Crossopteryx febrifuga* in the management of diabetes.

*Keywords*: Diabetes mellitus; *Crossopteryx febrifuga*; Alloxan; Blood glucose; Diabetic rats

## INTRODUCTION

Diabetes mellitus is a complex, chronic disease. It is a condition characterized by an elevation of the level of glucose in the blood. Insulin, a hormone produced by the pancreas controls the blood glucose level by regulating the production and storage of glucose. In diabetes there may be a decrease in the body's ability to respond to insulin or a decrease in the insulin produced by the pancreas which leads to abnormalities in the metabolism of carbohydrates, proteins and fats. The resulting hyperglycemia may lead to acute metabolic complications including ketoacidosis and in the long term contribute to chronic micro-vascular complications (Yim *et al.*, 2007).

Joseph and Jini (2011) defined diabetes mellitus as a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid and protein metabolism which cause hyperglycemia resulting from insufficient insulin secretion, insulin action or both. It is classified basically into Type 1 or primary or Insulin Dependent Diabetes Mellitus (IDDM) and Type 2 or secondary or Non-Insulin Dependent Diabetes Mellitus (NIDDM) with the secondary type accounting for barely 1 to 2%. (Chuhwak and Pam, 2007).

African indigenous herbal medicine is widely used throughout the African continent, despite an apparent lack of scientific evidence for their quality, safety and efficacy (Amos *et*

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*al.,* 2002*). Crossopteryx febrifuga* belongs to the family Rubiaceae. The English name is African bark and Ordeal tree. The Yoruba people call it *Ayeye* while Hausa call it *Kasfiya*. *Crossopteryx febrifuga* is used for the symptomatic relief of dry cough and for treatment of respiratory infection, fever, dysentery and pain (Odungbemi, 2006). In Northern Nigeria the plant has been used for treatment of pain and malaria for many years and its efficacy is widely acclaimed among the Hausa communities (Audu, 1989). The crude extract of the plant has been shown to contain biologically active substances with potential values in the treatment of trypanosomiasis, malaria and *Staphylococci aureus* infection. (Hostettmann *et al.,* 2000), (Yusuf *et al.,* 2004) have reported that the extract possesses analgesic, antipyretic and anti-inflammatory activities. It also has gastro protective effect (Salawu *et al.,* 2011). Ojewale *at al.* (2014) reported that the ethanolic root extract of *Crossopteryx febrifuga* has hypoglycemic and hypolipidemic activity.

There are claims by some herbal practitioners in Kogi state, Nigeria that the aqueous leaf extract of *Crossopteryx febrifuga* is effective in the management in the management of diabetes mellitus and diabetic complications. However, the scientific evidence to back the claim is lacking. In view of this, the aim of this study is to evaluate the antidiabetic effect of the methanolic leaf extract of *Crossopteryx febrifuga* on alloxan-induced diabetic rats.

## EXPERIMENTAL

**Plant collection and preparation.** The leaves were collected from Kogi State, Nigeria on May 27$^{th,}$ 2015. It was then identified appropriately by a taxonomist, Mr. Azila of the College of Forestry, Jos. The leaves were then dried for seven days at room temperature under the shade after which it was reduced to a coarse powder using a mortar and pestle.

**Extraction.** The bulk powder **(**200 g) was macerated in 70% methanol for 72 Hours. The extract was filtered, and concentrated under reduced pressure at a temperature of 40$^{o}$C.

**Animals.** Thirty-eight albino rats (Wistar strain) weighing between 100-150g were obtained from the University of Jos Animal Experimental Unit, where they were kept and maintained on water ad libitum and Grower's mash prior to being used for the experiments.

**Acute toxicity test ($LD_{50}$).** The oral acute toxicity of the methanol extract of *Crossopteryx febrifuga* was determined in rats as described by Lorke (1983).

**Phytochemical screening.** The Phytochemical screening was carried out according to protocols described in Trease and Evans (1983).

**Induction of diabetes.** The animals were fasted for 24hrs but given water *ad libitum*. Diabetes was induced by intraperitoneal injection of alloxan monohydrate (100 mg/kg body weight). After 48 hours, blood was withdrawn from the caudal vein tip for blood glucose estimation monitored with a glucometer. The animals with blood glucose level $\geq$ 120mg/dl were considered diabetic and included in the experiment.

**Hypoglycemic effect of the extract on diabetic rats.** The twenty-five rats were divided into five groups, with five rats in each group. The following drugs were administered orally to each group: Group 1 received 0.5ml Normal Saline, group 2 Gilbenclamide 5mg/kg, group 3, 4, 5 received 200, 400, 800mg/kg of the extract respectively. Blood samples were collected from the tail vein of the rat and then applied on the glucose test strip in the glucometer on day 1, 4 and 7 after administration of the extract and standard drugs. The values

displayed on the glucometer were noted and recorded as blood glucose level for each observation.

**Statistical analysis.** Data generated from the experiment were entered into (SPSS) version 2.0 based on pre-coded format. Descriptive statistics (mean and standard error mean were used to compute weight and blood glucose concentration for each study group. Paired T-test was used to compare changes in weight from day 0 to day 7 for each group while Analysis of Variance (ANOVA) turkey post hoc test was used to investigate mean change in blood glucose across the study groups. *P* value set at < 0.05 was used as test for significance, between extract treated groups and vehicle control group.

## RESULTS

**Phytochemical screening.** The result shows that the plant contains tannins, saponins, flavonoids, and carbohydrates but alkaloids, steroids, anthraquinones and cardiac glycosides are absent.

**Acute toxicity.** The acute toxicity $LD_{50}$ showed that none of the animal died at a high dose of 5000 mg/kg.

Table 1 above shows the weight of the rat there was slight significant increase in weight of the rat for both the extract and standard at the end of seven days when compared with control there was significant decrease in weight.

Table 2 shows a decrease in blood glucose concentration in the glibenclamide and extract group, while there was an increase in the normal saline group.

**Table 1**: Showing effect of the hydromethanolic extract of *Crossopteryx febrifuga* on mean body weight of alloxan-treated rats.

| Treatment | Dose (mg/kg) | Weight (g) | |
|---|---|---|---|
| | | Day 0 | Day 7 |
| Normal saline | 0.5 ml | 136.94 ± 6.12 | 116.23 ± 7.22 |
| Extract | 200 | 154.34 ± 2.80 | 161.54 ± 5.43 |
| Extract | 400 | 162.48 ± 4.28 | 175.16 ± 4.67 |
| Extract | 800 | 116.68 ± 2.00 | 129.53 ± 2.40* |
| Glibenclamide | 5 | 162.86 ± 2.40 | 174.42 ± 3.48* |

Note: The values are mean ±SD, indicate significant change in weight, p<0.05 n=5

**Table 2:** Effect of the hydromethanolic extract of *Crossopteryx febrifuga* on mean blood glucose concentration (mg/dl) in diabetic rats

| Treatment | Dose (mg/kg) | Day 0 | Day 1 | Day 4 | Day 7 |
|---|---|---|---|---|---|
| Normal saline | 0.5 ml | 173.4± 14.6 | 205.40± 28.6 | 217.25± 18.90 | 263.00± 20.93 |
| Extract | 200 | 173.4± 1.93* | 199.80±8.95* | 206.00±10.00 | 156.00±8.91 |
| Extract | 400 | 127.80±0.89 | 131.00±2.55* | 81.00±4.71* | 74.20±3.76* |
| Extract | 800 | 139.20±3.89* | 87.80±3.89* | 113.20±3.29* | 83.20±6.04* |
| Glibenclamide | 5 | 321.40±37.64* | 302.00±31.33* | 302.00±31.33* | 143.41±20.41* |

Results are expressed as mean blood glucose concentration ±SD, *indicates significant difference at $p < 0.05$

## DISCUSSION

The advances made with the use of oral hypoglycaemic agents such as biguanides, sulphonylureas and thiazolidinedione, plant sources for the management of diabetes mellitus has gained wide acceptance for a number of reasons. Investigations showed that plants are more effective in the management of diabetic complications (Li *et al.*, 2004). Herbal medicine as oral anti-diabetic immensely helped to eradicate the discomfort of

continuous insulin infusion or subcutaneous injections in diabetic patients (Silva *et al*., 2002). In addition, attention has been focused on the use of plants and herbal remedies believed to be safe and lack serious side effects as alternative in the management of diabetes mellitus and Diabetic complication. The methanolic leaf extract of *Crossopteryx febrifuga* was found to be safe according to WHO (1966) toxicity grading.

The crude extract was found to contain tannins, saponins, flavonoids and carbohydrate. Flavonoids, tannins and saponins have been found to possess hypoglycemic activity (Sharma *et al*., 2010). This could be responsible for the hypoglycemic activity observed. The root extract of the plant contains alkaloids, glycoside, cardiac glycoside, saponins, flavonoids, terpenoids, anthraquinone derivative and tannins (Ojewale *et al.*, 2014).

The significant slight weight gain observed in the diabetic animals treated with extract clearly stated that it might not have the obesity forming tendency which is one of the undesirable side effects associated with sulphonylureas. The ethanolic root extract of *Crossopteryx febrifuga* also shows similar effects. (Ojewale *et al*., 2013)

The presence of antioxidant compound such as flavonoids, saponins in this plant provides further evidence for the beneficial effects of methanolic leaf extract of *Crossopteryx febrifuga* on the alloxan induce diabetics rat. Over the decades, an expanding body of evidence from epidemiological and laboratory studies have demonstrated that some plant as a whole or their identified ingredients with antioxidant properties have substantial protective effects on diabetes (Sabu and Kuttan, 1982), cardiovascular and renal disorders (Anderson *et al*., 2000) and several other human ailments (Lampee,2003). Bioactive molecules present in indigenous leaves may possibly possess insulin like effect or stimulated the pancreatic beta cells to produce insulin which in turn lowers the blood glucose level (Atawodi, 2005), Similar observations have been reported by other researchers (Akah and Okafo, 1992, Sepici *et al*., 2004). The anti-hyperglycaemic effect observed may be by stimulating the secretion of insulin or increasing the glucose uptake (Nyunni, 2009) or may inhibit glucose absorption in gut (Bhowmik, 2009).

Alloxan is known for its selective pancreatic β cells cytotoxicity and is extensively used to induce diabetes mellitus in animals, (Prince and Menon, 2000). Although the extract mechanism of action is unknown, it is possible to suggest that this extract might play a vital role in improving the diabetic status in terms of blood sugar by restoring the structural and functional properties of β-cells of pancreas, a primary target organ for alloxan. The activities of these substances may have triggered the beta cells to increase insulin production thus leading to glucose uptake, metabolism or by inhibiting gluconeogenesis and utilization by other tissues. Further studies need to be carried out to identify the extract mechanism of action and the compound(s) responsible for the hypoglycaemic activity.

**Conclusion.** The metabolic leaf extract of *Crossopteryx febrifuga* exhibited antidiabetic activity in alloxan induced diabetic rat. The results support the traditional use of this plant.

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