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Acute oral toxicity study of ethanol extract of *Ceiba pentandra* leaves as a glucose lowering agent in diabetic rats

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ABSTRACT

Objective: To evaluate the use of *Ceiba pentandra* (*C. pentandra*) as a glucose lowering agent and the attendant physiological changes in albino rats.

Methods: Acute oral toxicity study of the extract was carried out by the administration of 10, 100, 1 000, 1 600, 2 900, and 5 000 mg/kg body weight of *C. pentandra* to rats in their respective groups. Twenty healthy albino rats weighing between 140 and 150 g were randomly allotted to five groups of four rats each. 100 mg/kg body weight of alloxan monohydrate was *i.p.* administered to rats and rats with blood glucose $\geq$ 200 mg/dL were considered diabetic. 5 mg/kg body weight of standard drug, 200 and 400 mg/kg body weight of ethanol extract of *C. pentandra* were orally administered to diabetic rats in their respective groups once daily for 12 days while the control groups received 0.1 mL of normal saline for the same period. The blood glucose was checked after every 4 days and the experiment was terminated on the 17th day.

Results: The safe dose (LD_{50}) of the extract was greater than 5 000 mg/kg body weight. The extract treated groups exhibited a remarkable reduction in blood glucose [(87.72 ± 7.67) mg/dL for 200 mg/kg body weight dose and (86.33 ± 4.54) mg/dL for 400 mg/kg body weight dose] competitively with the normoglycemic group [(88.71 ± 4.56) mg/dL]. The body weight of the extract and standard drug treated groups appreciated significantly ($P < 0.05$) as compared with normoglycemic group. High density lipoprotein increased significantly in the extract treated groups with the 400 mg/kg body weight having the highest value of (18.61 ± 3.44) mg/dL and a concomitant reduction in the concentrations of low density lipoprotein, triacylglycerol, and cholesterol of same group. The 400 mg/kg body weight dose of the extract also demonstrated the highest reduction in the activities of aspartate transaminase [(59.66 ± 3.45) IU/L], alanine aminotransferase [(33.33 ± 4.34) IU/L] and alkaline phosphatase [(48.36 ± 3.41) IU/L] that elevated as a result of diabetes. The two extract treated groups demonstrated a marked reduction in Cl^-, and elevation in HCO_3^- and Na^+ levels. K^+, urea, creatinine, total and conjugated bilirubin that were elevated in the diabetic untreated group were all ameliorated in the treatment groups.

Conclusions: Ethanol extract of *C. pentandra* has glucose lowering effect and can ameliorate the biochemical abnormalities associated with diabetes mellitus.

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All experimental procedures involving animals were conducted in accordance to Ethical clearance given and approved by Federal University of Technology, Minna/Nigerian Ethical Review Board (CUERB) in accordance with internationally accepted principles for laboratory animal use and care as contained in the Canadian Council on Animal Care Guidelines and Protocol Review.

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1. Introduction

Glucose is the most important controller of insulin secretion, and insulin secretion is exerted by a feedback effect of blood glucose on the β cell of the pancreas. When blood glucose concentration rises above fasting levels, insulin secretion increases and stimulates glucose uptake by the liver and the peripheral tissues thereby returning glucose to the normal levels. This provides an important negative feedback mechanism for controlling the blood glucose concentration. Diabetes mellitus is a chronic disease due primarily to a disorder in carbohydrate metabolism, as a result of deficiency or diminished effectiveness of insulin, resulting in hyperglycemia and glycosuria[1]. Diabetes affects more than 100 million people worldwide (6% of the population) and in the next 10 years is projected to affect five times more people than it does now[2]. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs. The disease may present with classical characteristic features such as blurring of vision, excessive thirst (polydypsia), excessive feeding (polyphagia), excessive urination (polyuria), and weight loss. In its most severe form, ketoacidosis may develop leading to stupor, coma and in absence of effective treatment, death ensues[3]. In conventional therapy, type 1 diabetes is treated with exogenous insulin, while type 2 is treated with oral hypoglycemic agent like biguanides and sulphonylureas[4]. Although these agents provide a good glycemic control, they can do little to prevent secondary complications. Besides, they are also associated with side-effects or diminution in response after prolonged use[5]. According to World Health Organization (WHO)[6], more than 80% of the world population depends on the traditional medicine for their primary health care and this practice is recommended especially in countries where access to conventional treatment of diabetes is inadequate. WHO however emphasizes the fact that safety should be an overriding criterion in the selection of herbal medicine for the use in health care programme. The medicinal potentials of *Ceiba pentandra* (*C. pentandra*) may be due to the presence of bioactive compounds (secondary metabolites) that produce definite physiological action in the human body. They are produced by specific parts of the plant and translocated to other parts for storage[7]. Alloxan is a cytotoxic glucose analogue widely used to induce diabetes in experimental animal models. It destroys the pancreatic β-cells with specific selectivity and produces selective necrosis of β-cells of islets of Langerhans when injected into animals[8].

C. pentandra Telugu: is a tropical tree of the order Malvales and the family Malvaceae (previously separated from the family Bombacaceae). It is native to Mexico, Central America and the Caribbean, North-South America, and tropical West Africa[9]. Kapok is the most used common name for the tree and may also be referred to the cotton-like fluff obtained from its seed pods. The tree is also known as the Javacotton, Java kapok, silk-cotton or ceiba. Its bark decoction has been used as a diuretic, aphrodisiac, and to treat headache, as well as type II diabetes. It is used as an additive in some versions of the hallucinogenic drink[10]. Diabetes and its associated complications have become a public health problem of considerable magnitude and is one of the top five global leading causes of death. In the year 2000, the excess global mortality attributable to diabetes and its late complications were estimated to be 2.9 million deaths, equivalent to 5.2% of all deaths. The unaffordability and side effects associated with the conventional antidiabetic drugs have resulted in increased search for alternative medicinal plants. The side effects of the new agent, and its ameliorative potentials on complications associated with diabetes will also be investigated.

2. Materials and methods

2.1. Reagents and chemicals

All the reagents used for the research were of analytical grades and obtained from the Department of Biochemistry, Federal University of Technology, Minna, Nigeria. They include distilled water, ethanol, Randox diagnostic kits and normal saline.

2.2. Apparatus and equipment

These include: reflux extractor, milling machine, rotary evaporator, bucket centrifuge, water bath, Whatman filter paper, measuring cylinders, hand gloves, masking tape, beakers, syringes, spatula, glucometer, and weighing balance.

2.3. Sample collection

2.3.1. Plant sample

Adequate quantities of fresh leaves of *C. pentandra* were collected in July, 2015 from rural area of Gada Oli via Wawa, New-Bussa, Niger State, Nigeria and were identified and authenticated at the Herbarium of Department of Biological Sciences, Federal University of Technology, Minna, Nigeria.

2.3.2. Preparation of plant material

The leaves were washed, blotted and air-dried at room temperature in the Departmental Laboratory for two weeks. They were homogenized into fine powder using milling machine.

2.3.3. Experimental animals

Healthy Swiss albino rats weighing 100–200 g were procured from Animal house of Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria, Kaduna State, Nigeria. The animals were housed and accommodated in groups of four in polypropylene cages with stainless steel grill top and a bedding of clean paddy husk. Standard room temperature of 30–36 °C, 12 h light and dark cycles were also maintained. They were allowed access to commercial grower mesh to feed on *ad libitum*. Acclimatization of the animals to these conditions was for two weeks.

2.3.4. Extraction of plant sample

1500 g of dried powdered sample of *C. pentandra* was weighed and extracted with 300 mL ethanol using reflux method at temperature of 60 °C. The extract was thereof concentrated with rotary evaporator and then evaporated to dryness in a water bath at 100 °C. The crude extract yielded 130.11 g (9.29%) and was stored in a labeled sterile bottle kept at 4 °C in a refrigerator until ready for use.

2.4. Acute toxicity studies

The acute toxicity test of the ethanol extract was carried out by the method of Lorke[11]. Eighteen albino rats were fasted for