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Original Article

Anti-hyperglycaemic activity of tuber extract of *Chlorophytum alismifolium* Baker in streptozotocin-induced hyperglycaemic rats

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ABSTRACT

The tubers of *Chlorophytum alismifolium* (Liliaceae) are widely used in Nigerian Herbal Medicine to treat diabetes mellitus and their efficacy is widely acclaimed among the rural communities of Northern Nigeria. This study was aimed at investigating the antihyperglycaemic potential of the tuber extract of *Chlorophytum alismifolium* (CAE) in streptozotocin-induced hyperglycaemic rats. Phytochemical screening and oral median lethal dose (LD_{50}) estimation of CAE in rats were carried out. Antihyperglycaemic screening of the extract (at oral doses of 150, 300 and 600 mg/kg) was performed using normal and streptozotocin-induced hyperglycaemic rats for 28 days. Fasting blood glucose levels were measured and serum lipids were analyzed. Liver, kidney, heart and pancreatic tissues were examined for histopathological damages using standard histological processing. Phytochemical screening revealed the presence alkaloids, saponins, flavonoids, triterpenes and glycosides. Oral LD_{50} was estimated to be > 5000 mg/kg body weight in rats. *C. alismifolium* extract at all the doses tested showed blood glucose lowering effect. Statistical significant ($p < .01$) blood glucose lowering effect at 150 mg/kg on day 21, at 300 mg/kg on days 21 and 28 ($p < .001$ and $p < .01$ respectively) and 600 mg/kg on days 7, 14, 21 and 28 ($p < .05$, $p < .01$, $p < .001$ and $p < .01$ respectively) was produced by the extract. The extract also reduced the levels of total cholesterol, triglycerides and low density lipoprotein. Histopathological examination of the pancreas showed restoration of pancreatic islet cells at the doses of 300 and 600 mg/kg of the extract. In conclusion, the results obtained suggest the tuber extract of *Chlorophytum alismifolium* possesses antihyperglycaemic activity.

1. Introduction

Diabetes mellitus (DM) is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or cells do not respond to the insulin that is produced [1]. The global prevalence of diabetes among adults has risen from 4.7% in 1980 to 8.5% in 2014 [2]. In 2012, diabetes was the direct cause of 1.5 million deaths and hyperglycaemia was the cause of another 2.2 million deaths [2]. DM is also associated with complications such as retinopathy, nephropathy, peripheral neuropathy, ketoacidosis, non-ketotic coma, cardiovascular diseases and genito-urinary complications [3]. Among several metabolic derangements, insulin deficiency stimulates lipolysis in the adipose tissues and results in hyperlipidemia [4].

Insulin and oral anti hyperglycaemic agents are not only expensive but also known to produce serious side effects such as hypoglycaemia, anorexia nervosa, brain atrophy and fatty liver [5] following chronic treatment. Biguanides and sulphonylureas are valuable in the management of type 2 DM but their use is also limited by side effects such as lactic acidosis, gastrointestinal tract disturbances and hypoglycaemia [6]. Therefore the search for cheaper, safer and effective agents for the management of DM has continued to be an important area of investigation [7].

The study of medicinal plants has led to the discovery of new chemicals for potential development as drugs that act on new or known therapeutic targets [8]. There has been a focus on the search for new drugs from medicinal plants that will be useful in management of DM [9]. The genus Chlorophytum contains 198 species which are valuable medicinal plants widely distributed in the tropical regions of the world especially in Africa and India [10]. The tubers of these species are the medicinally useful parts [11]. *Chlorophytum borivilianum* for example has been reported to possess anti hyperglycaemic, hypolipidemic and

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antimicrobial properties [12,13]. Similarly, *Chlorophytum nimmoni* possesses antidiabetic and hypolipidemic properties [14].

Chlorophytum alismifolium (Baker), a member of Liliaceae family is a short stem herb with tuberous root stocks and white flowers found around stony sites in forest streams [15]. It is commonly known as Alimsa-Ground lilly and locally known as *Rogon makwarwa* (Hausa) and *Cigorodi* (Fufulde). The tubers of *Chlorophytum alismifolium* are used in herbal medicine in Northern Nigeria for the treatment of DM, bacterial infections, arthritis, erectile dysfunction, pain and inflammation [16]. The efficacy of *Chlorophytum alismifolium* tubers in management of DM is widely acclaimed among the rural communities of Northern Nigeria; however, there is no scientific report to justify the folkloric claim for such use, hence this research was carried out to validate the aforementioned claim using experimental animal model.

2. Materials and methods

2.1. Drugs and chemicals

Streptozotocin (MP Biomedicals M 3219k, France), Glimepiride (Sanofi Aventis, D-65926 Frankfurt, Germany), 10% Dextrose and Normal saline (Dana pharmaceuticals, Nigeria), Glucometer and test strips (Accu-check Active, Roche, Germany), standard kits and photoelectric colorimeter (AC-115 Optima, Japan) for assay of low density lipoprotein (LDL), high density lipoprotein (HDL), triglyceride (TG) and total cholesterol (TC).

2.2. Experimental animals

Wistar albino rats (males) weighing 150–200 g were obtained from the laboratory Animal Facility, Department of Pharmacology and Therapeutics, Ahmadu Bello University, Zaria. The animals were maintained in a well-ventilated room, fed on standard animal feed and granted access to water *ad libitum*. The experimental protocols were approved by the University Animal Ethics Committee (Protocol number: DAC/IW-OT/212–15). The studies performed on the permitted species were in accordance with Ahmadu Bello University Research policy as well as ethic and regulations governing the care and use of experimental animals as contained in “Principles of laboratory animal care” published by the National Institute of Health (NIH Publication No. 85-23, revised, 1996).

2.3. Plant material

The tubers of *Chlorophytum alismifolium* were collected in July 2014 from *Tilden Fulani* River in Toro LGA, Bauchi State, Nigeria. The botanical identification and authentication was done by Mallam Musa Muhammed of the Herbarium Unit of the Department of Botany, Ahmadu Bello University, Zaria, Nigeria. A voucher number of 6785 was obtained and a voucher specimen was kept in the Herbarium for future reference.

2.4. Preparation of the CAE

The tubers were washed and chopped into smaller sizes and then air-dried under shade for three weeks until constant weight was attained. The dried plant was then crushed into fine powder using pestle and mortar. The powdered plant (1 kg) was extracted with 2.5 L of 90% $^{v}/_{v}$ aqueous methanol (90% methanol: 10% water) for 72 h using the soxhlet apparatus. The extract was concentrated to dryness on a water bath set at 50 °C and was stored in a desiccator until required for the main experiment. The extract was reconstituted freshly with distilled water for each study.

2.5. Phytochemical screening

Standard phytochemical screening tests [17,18] were employed in screening the plant extract. The extract was screened for the presence or absence of phytochemicals including alkaloids, flavonoids, saponins, glycosides, cardiac glycosides, tannins, anthraquinones, triterpenes and carbohydrates.

2.6. Extract and drug treatment

Stock solutions of the extract were prepared by dissolving it in deionized water followed by serial dilution to obtain the appropriate concentrations for the studies. Similarly, a stock solution of the standard drug, glimepiride was prepared by dissolving the powder in deionized water to obtain the appropriate concentration. The extracts and standard drug were administered orally using oral gavages. The drug solutions were usually prepared fresh for each day’s experiment to maintain their stability.

2.7. Acute toxicity study

The method described by Lorke [19] was employed in the determination of the oral median lethal dose (LD_{50}) in rats. The test was in two phases; in phase one, three groups of animals (n = 3) were administered widely differing doses of the extract (10, 100 and 1000 mg/kg) and were observed for signs of toxicity and mortality for 24 h. In the second phase, 3 animals were administered 1600, 2900 and 5000 mg/kg of the extract and then observed for signs of toxicity and mortality for 24 h. The LD_{50} was calculated as the geometric mean of the lowest lethal dose and highest non-lethal dose as presented below:

$$LD_{50} = \sqrt{\text{lowest lethal dose} \times \text{highest non-lethal dose}}$$

The doses of the extract used in the main study (150, 300 and 600 mg/kg) were less than 20% of the estimated LD_{50}.

2.8. Experimental induction of **hyperglycaemia**

Experimental hyperglycaemia was induced using the method of Virendra et al. [20]. Streptozotocin (STZ) (50 mg/kg) was dissolved in ice cold citrate buffer (pH 4.5) immediately before use. The solution was injected intraperitoneally at the dose of 50 mg/kg in rats fasted for 12 h. The rats were given 10% glucose solution for 24 h to prevent mortality due to initial hypoglycemia induced by STZ. The animals were given food and water then observed over a period of 72 h for signs of hyperglycemia. The determination of glucose concentration was done using test strips which follows the Glucose Oxidase principles [21]. The animals with blood glucose levels above 200 mg/dL were considered hyperglycaemic and selected for further study.

2.9. Experimental design

The selected STZ-induced hyperglycaemic and normal rats were then assigned accordingly into six groups with each group containing six rats (n = 6). The normal saline, graded doses of CAE and glimepiride were administered orally and daily for 28 days