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RESEARCH ARTICLE

PRELIMINARY EVALUATION OF THE ANTIHYPERGLYCAEMIC PROPERTIES OF MEDICINAL PLANTS IN NSUKKA AREA, ENUGU STATE, NIGERIA

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ABSTRACT

The anti hyperglycemic potentials of seven medicinal plants used in Nsukka area of Enugu state, Nigeria namely *Bridellia micrantha, Oxythinia Abyssinia, Ixora brachypoda, Gmelina aborrea, Terminalia catappa, Hymenocardia acida* and *Cassytha filiformis* were investigated on alloxan induced diabetic mice. The oral LD50 of the methanolic extracts in mice were greater than 2000 mg/kg. Phytochemical analysis of the extract revealed the presence of high levels of alkaloids, tannins, flavonoids, glycosides and saponins. Extracts of the plants screened for anti-diabetic activity in mice significantly ($p<0.01$) reduced the fasting blood glucose levels in alloxan diabetic mice. The leaves of *Bridellia micrantha* reduced the blood glucose levels by about 57.8%, *Cassaytha filiformis* by 46.8%, *Terminalia catappa* by 59%, *Oxythina abyssinia* by 71.5%, *Ixora brachypoda* by 67.6% , *Gmelina aborrea* by 30.1% while *Hymenocardia acida* provoked the highest anti-diabetic activity (72%) which appeared comparable to the standard control, Glibenclamide (71.7%).

INTRODUCTION

Diabetes mellitus which seems to be an alarming disease all over the world today, is a metabolic disease characterized by hyperglycemia and is a genetically and clinically a heterogeneous group of disorders with common feature of glucose intolerance (WHO, 1994).

This disorder concerns genetic and exogenic factors (viral, chemical) and damages the β cells of Langerhans, in the pancreas (Kadja, 1998). As a result, the body becomes unable to produce insulin, a pancreatic hypoglycaemic hormone. This disorder is characterized by polyuria,polydypsia, glycosuria and hyperglycaemia. Diabetes comes with other complications of the kidney and eyes. Diabetes is a major cause of disability and death (Dièye *et al*., 2007). Diabetes exists everywhere in the world and interests approximately 6 % of the world population (N'guessan *et al.*, 2009). This prevalence rate places the diabetes like most frequent of endocrine diseases (Gentilini, 1993). In modern medicine, the beneficial effects of standard medications on glycaemic levels are well documented; the preventive activity of medications against the progressive nature of diabetes and its complications was the modest but not always effective. Insulin therapy affords glycaemic control in type 1diabetes, yet its shortcomings such as ineffectiveness on oral administration, short shelf life, the requirement of constant refrigeration, fatal hypoglycemia in event of excess dosage, reluctance of patients to take insulin injection and above all the resistance due to prolonged administration limits its usage (Kasiviswanath *et al.*, 2005). Similarly, treatment of type 2 diabetes patients with sulfonylureas and biguanides is always associated with side effects (Grandhipuram *et al.,* 2006). Hence, search for a drug with low cost, more potential and without adverse side effect is being pursued in several laboratories around the world.

In Africa and in most of the developing countries, plants' properties are empirically appreciated. In connection with the cure's techniques, they require plants and mystic powers. Despite these traditional health care methods, African medicine is used by 80 % of the rural populations and appears like a sure mean of eradication of diseases (Adeyemi *et al.*,2009; Sofowora, 1996). Also, many urban populations turn to treatments using plants. The reason is that traditional medicine is a medicine of proximity, less constraining and non expensive (Gbéassor *et al*., 1989; Pousset, 1989). Many traditional plant treatments for diabetes mellitus are used throughout the world (Marles and Farnswort, 1995). Management of diabetes without any side effect is still a challenge to the medical system. This has led to an increasing demand for

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natural products with antidiabetic activity and fewer side effects (Kameswara *et al.,* 1999).

Alloxan (2,4,5,6-tetraoxypyrimidine), an oxygenated pyrimidine derivative, capable of producing reactive oxygen species (ROS) free radicals which selectively destroy pancreatic β-cell (Sies, 1997; Fischer, 1985). Athough, problems exists with the use of alloxan such as chemical instability, rapid metabolism, thiol reactivity, effects of other factors such as diet, age, and animal species; it is still a preferred model for the induction of type 2 diabetes. The aim of this experiment was therefore to screen some plants with traditional claims of hypoglycaemia potentials in Nsukka area of Enugu state.

MATERIALS AND METHOD

Animals

Out bred Albino Swiss mice of both sexes weighing between 16 and 42 g were purchased from the Laboratory Animal Facility of the Department of Veterinary Physiology and Pharmacology, University of Nigeria, Nsukka, and served as experimental animals. They were housed in clean plastic cages, supplied clean drinking water and fed with standard commercial pelleted feed (Guniea Feed®, Nigeria).

Plant Collection and Extraction

Based on folklore and with the assistance of traditional healers in Nsukka area of Enugu State, fresh samples of some Nigerian plants were collected. These plants materials were collected between November 2008 and January 2009, from various locations in Enugu State, Nigeria and were identified and authenticated by Mr. A. O. Ozioko, a taxonomist with the International Centre for Ethnomedicine and Drug Development (ICEDD), Nsukka. These plant materials included: The leaves of *Bridellia micrantha, Oxythinia Abyssinia, Ixora brachypoda, Gmelina aborrea, Terminalia catappa and Hymenocardia acida;* as well as the stem-bark of *Cassytha filiformis.* Voucher specimens were kept in the herbarium of ICEDD, Nsukka. The plants were dried under mild sunlight and subsequently pulverized into coarse powder.

Two hundred grams of each dried powdered plant material was macerated with 80% methanol in distilled water for 48 h at room temperature with intermittent shaking. Each extract was filtered through Whatmann No.1 filter paper and the filtrates dried in oven at 50^{o}C and stored on the bench pending use.

Acute Toxicity Testing

The plants were assessed for acute toxic effect using modified Up and Down procedures (OECD, 2001) and the LD_{50} extrapolated. Five male Swiss mice were randomly selected and housed individually. A test dose of 2000 mg/kg (b. wt.) was administered orally in a single dose one after another by gavage using a gastric tube. After the dosing of each animal; food was withheld for further three hours before feeding the animals. In the first day of dosing, the first animal is dosed and observed immediately for signs of toxicity for about an hour. On the survival of the first animal after 48 h, other four animals were subsequently and sequentially dosed at 48 h intervals.

Anti-diabetes Test

Hyperglycaemia was induced using the method described by Iwueke and Nwodo, 2008. The fasting blood glucose was determined before the mice were made diabetic by a single intraperitoneal injection of 150 mg/kg of freshly prepared alloxan monohydrate. Ten (10) days after, diabetes was confirmed in alloxan treated mice with fasting blood glucose levels of 6.4 mmol/L and above. Blood samples were collected at 0, 30 and 60 mins post oral treatment with 600 mg/kg of the various extracts. Fifty four Swiss mice were randomly selected, examined thoroughly to ensure that they were healthy and divided into 9 groups (n=6). The animals were housed in clean stainless steel cages. Eighteen (18) hours (overnight) prior to the experiment, food was withdrawn but water remained available *ad libitum*. Groups A-G served as test groups and received methanolic extracts of *Bridellia micrantha* (Leaves)*, Oxythina abyssinia* (Leaves)*, Ixora brachypoda* (Leaves)*, Gmelina aborrea* (Leaves)*, Cassytha filiformis* (Stem-bark)*, Terminalia catappa* (Leaves) and *Hymenocardia acida* (Leaves) respectively, while Group H served as treated (positive) control receiving Glibenclamide (2mg/kg) *per os*, Group I, served as untreated (negative) control and received equal volume of distilled water orally. The blood glucose levels were determined by dropping blood samples obtained from the cut tail tip of each mouse on the glucose strip (Accu- Chek Advantage II) which was already inserted into an electronic glucose meter (Accu- Chek Advantage) to display the blood glucose level on a screen.

Statistical Analysis

The experimental results were collated as mean plus or minus standard deviation (mean± SD) with level of significance set at 1% which is $p<0.01$; although expressed as percentage reduction in blood glucose levels of 60 minutes(T60) from 0 minutes (T0) for clarity,

$$\frac{T0-T60}{T0} \quad X \quad \frac{100}{1}$$

RESULTS

A total of 7 plants were selected for the study from about 20 plants suggested by traditional medicine practitioners (both male and female) in the study area. The choice of these plants was based on their folkloric uses, absence in literature after search and content of bitter principles. Preliminary phytochemical analysis of the methanolic extracts of the plants revealed that they contain alkaloids, tannins, flavonoids, glycosides and saponins. The extracts did not demonstrate any acutely toxic effects as all test animals survived following oral administration of 2000 mg/kg (b. wt.) indicating safety at the dose although, dullness was recorded with *H. acida, C. filiformis* and *T. catappa*. Alloxan monohydrate at 150 mg/kg (b. wt.) induced diabetes with fasting blood glucose levels of 16.3 mmol/L and above in all test animals. After 60 minutes, the methanol extracts of the plants screened for anti-diabetic activity in mice significantly ($p<0.01$) reduced the fasting blood glucose levels in alloxan diabetic mice (Figure 1). The leaves of *Bridellia micrantha* reduced the blood glucose levels by about 57.8%, *Cassaytha filiformis* by 46.8%, *Terminalia catappa* by 59%, *Oxythina abyssinia* by 71.5%, *Ixora brachypoda* by 67.6% and *Gmelina aborrea* by 30.1%. The leaves of *Hymenocardia acida* provoked the highest anti-diabetic activity (72%) which appeared comparable to the standard control, Glibenclamide (71.7%). The order of anti-diabetic activity in the screened plants was thus:

Hymenocardia>Oxythnia>Ixora>Terminalia>Bridellia>Cassaytha>Gmelina.

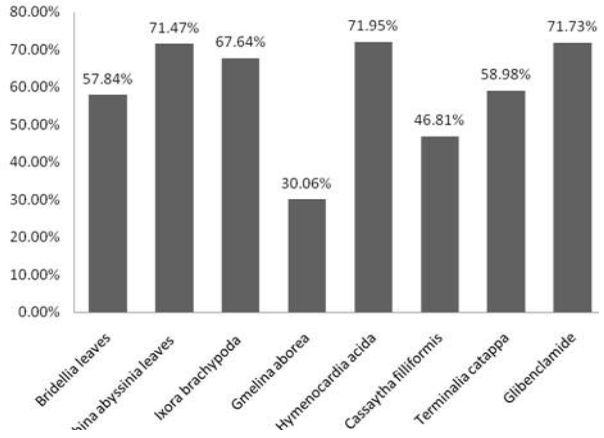

Figure 1. The percent anti-hyperglycaemic activity of methanol extracts of various plants

DISCUSSION

In this study, 7 plants were selected for the study from about 20 plants suggested by herbalists in Nsukka, Enugu State. This number of plant species recorded used traditionally in the treatment of diabetes is an indication of the rich plant diversity in the area, a situation that is being adversely affected by rapid urbanisation and deforestation (Etuk *et al*., 2009). There is an urgent need to therefore screen more medicinal plants available in other parts of Nigeria, as a database of these plants is very important as knowledge of therapeutic, medicinal plants can be lost as traditional societies are supplanted by development (Igoli *et al*., 2003).

Out of the seven plants screened for anti-diabetic activity, *Hymenocardia acida* gave the highest effect of 72% in alloxan induced diabetic rats comparable to the control, glibenclamide (71.7%). Traditionally, a decoction is prepared by soaking these leaves in local gin overnight; or by boiling in water, therefore, 80% methanol in water was preferred for extraction.

The methanol extract of the test leaves did not produce death at doses used in the study. No death was recorded even at a high dose of 2000 mg/kg, which is an indication that the extract was well tolerated by the rats. It showed that the extract was safe at the dose range used in the study. However, the mice showed signs of dullness with *H. acida, C. filiformis* and *T. catappa,* which indicate that these plants extracts may have depressive effects on the central nervous system.

In conclusion, further pharmacological studies to confirm the mechanism of action, effects on lipid profile as well as characterisation of the active principles in some of the plants like *Oxythina abyssinia*, *Ixora brachypoda* and *Hymenocardia acida* which exhibited antidiabetic potentials comparable to the standard control, glibenclamide is highly encouraged. Further screening of plants for their medicinal properties is also recommended.

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