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The Hypoglycaemic Activity of the Aqueous Extract of *Stachytarpheta angustifolia* (Verbanaceae) in Normoglycaemic and Alloxan-Induced Diabetic Rats

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Abstract: The hypoglycaemic activity of the aqueous extract of *Stachytarpheta angustifolia* (Verbanaceae) was studied in normoglycaemic and alloxan-induced diabetic rats. The extract was administered orally to the rats and blood glucose level was monitored for 7 h. Results indicate that the aqueous extract (750 mg kg^{-1}) produced a significant blood glucose reduction in both normoglycaemic and alloxan-induced diabetic rats ($p<0.05$). The present result therefore appears to support the use of the plant aqueous extract for the management of type 2 diabetes by traditional medical practitioners in Northern Nigeria. The mechanism of action of the aqueous extract needs to be studied.

Key words: *Stachytarpheta angustifolia*, diabetes, hypoglycaemia, alloxan, blood glucose

INTRODUCTION

Diabetes arises from a deficient production of insulin by the β-cells of the pancreatic islets. Insufficient insulin results in hyperglycaemia and the symptoms of diabetes, namely, an excess sugar in the blood and urine, hunger, thirst and a gradual loss of weight. The disease is estimated to affect 4-5% of the population and patients are generally diabetics (type 1) or non-insulin dependent diabetics (type 2). Individuals in the former category lack functional β-cells necessary to synthesize the hormone and insulin therapy is the only satisfactory treatment. On the other hand type 2 diabetics have functional pancreatic β-cells but there is nevertheless, a deficiency in insulin production. In many cases a suitable diet and exercise can control the type 2 condition but if it is not successful treatment with oral hypoglycaemic is instituted.

Use of herbs has been practiced for centuries in all parts of the world in various systems of medicine like Ayurveda, Siddha, Unani and Neuropathy etc. Recently more works are being published on the hypoglycaemic effect of various plants in response to WHO recommendation on Diabetes mellitus (WHO Expert Committee on Diabetes, 1980; Dash *et al*., 2001; Suba *et al*., 2004).

The production of drugs and other preparation based on indigenous systems of medicine has increased many folds during the past few decades. The number of plant based crude drug findings regular use is put around four hundred and its number is increasing. According to (Momin, 1987), plant drugs are frequently considered to be less toxic and freer from side effects in clinical experience and relatively low costs herbal drugs are prescribed widely even when their biologically active compounds are unknown (Valiathan, 1998).

Management of diabetes without any side effects is still a challenge to the medical system. There is an increasing demand by patients to use natural products with anti-diabetic activity, because insulin and oral hypoglycaemic agents (OHA) have so many side effects. The promising OHA Metformin, which gained its popularity in recent years, got its structure from a compound galegine, isolated from the plant *Galega* (Cusi and Defonzo, 1998). Many scholars had earlier made valuable contribution to the field of indigenous drug trial in diabetes. These workers (Ivorra *et al*., 1989) mentioned the anti-diabetic activities of different plant products and their active ingredients. Presently many laboratories are involved in isolating new herbal oral hypoglycaemic agents.

It is important however to appreciate that there are also many plants and plant extracts, which possess marked hypoglycaemic activity, one of which is *Stachytarpheta angustifolia* (verbanaceae). It is widely distributed in the West tropical Africa (Dalziel, 1937). The plant, which is an herb, has been used by a number of

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traditional medical practitioners in the treatment of diabetes with reported success by some of their patients. Several searches were made from the NAPRALERT database but none showed any study of the hypoglycaemic activity of the plant. There were not any previous scientific findings on the plant from the database.

We therefore report the hypoglycaemic activity of the aqueous extract of *Stachytarpheta angustifolia* (verbanaceae) to ascertain the hypoglycaemia of the folkloric claims of the use of the aqueous extract of the plant by the traditional medical practitioners.

MATERIALS AND METHODS

Plant material: The fresh plant (herb) of *Stachytarpheta angustifolia* (Verbanaceae) was collected from the moist areas of Ahmadu Bello University Dam, Zaria, Nigeria. It was identified and authenticated at the herbarium section of the Biological Sciences Department, Ahmadu Belo University, Zaria, Nigeria where a voucher specimen was deposited (No. 20112). The air-dried herb was powdered, sieved and referred to the powdered material.

Animals: Locally bred adult wistar rats of both sexes, weighing 120-150 g were used for the acute toxicity studies while only male wistar rats weighing 150-200 mg were used for the hypoglycaemic activity studies which were carried out in research laboratory, Department of Pharmacology and Clinical Pharmacy, Ahmadu Bello University, Zaria, Nigeria. The animals were fed on standard rats' pellets and water was supplied *ad libitum*. They were allowed to acclimatize before the test and were also conditioned at an ambient temperature of 22±2°C. The University ethical committee reviewed the protocols, which are consistent with the international animal welfare guidelines.

Preparation of the extract: The powdered material (200 g) was extracted with 2 L of hot water, on a hot plate for 30 min. The extract was concentrated on a rotarvapour after cooling and filtration to a brown sticky mass (34.3 g) and in an oven at a temperature of 20°C for 2 h. The brown dried material (29.2 g) was size-reduced using a mortar and pestle and packed in an airtight container (to protect it from moisture) and now referred to as the extract.

LD_{50} determination: The per oral (p.o.) route was used for the determination of the acute toxicity (LD_{50}) of the aqueous extract in adult wistar rats of both sexes. Forty rats, divided into eight groups of five rats each were used for assessing the LD_{50}. Varying doses of the extract (ranging from 500-5000 mg kg^{-1} body weight for the oral route) were given to the animals as single doses. The control group received 0.9% w/v saline solution. After the administration of the extract, animals were observed for mortality over 24 h.

Diabetes induction: Diabetes was induced in male wistar rats weighing 150-200gm by intraperitoneal administration of aqueous alloxan monohydrate, 150 mg kg^{-1} body weight (Rao *et al*., 1999). From the 5th day onwards fasting blood samples were collected from the rats through the caudal vein and the blood glucose was measured to know the induction of diabetes. From the 10th day of injection of alloxan, fasting blood glucose levels were increased to a level higher than normal. After a fortnight, rats with marked hyperglycaemia (> 250 mg dL^{-1}) were selected and used for the study. All animals were allowed free drinking water and pellet diet and maintained at room temperature in plastic cages.

PROTOCOLS

Effects of extract on the blood glucose levels of normoglycaemic rats: Five groups of five rats each were fasted overnight but allowed access to water. To a dose-effect profile, the aqueous extract was administered orally at doses of 250, 500, 750 and 1000 mg kg^{-1} body weight to each of the four groups of rats respectively while the fifth group which served as control was administered 0.9% saline solution. Blood samples were collected at 0, 3, 5 and 7 h after administration of the extract orally. Blood glucose levels were measured using glucose advantage test strips with Accu-chek Glucometer (Fig. 1).

Studies on the hypoglycaemic activity of aqueous extract of *Stachytarpheta angustifolia* on blood glucose levels of alloxan-induced diabetic rats: Induction and confirmation of diabetes was as above and the aqueous extract of the plant was administered at doses as described earlier, while the fifth group which served as control was given 0.9% w/v saline solution. Blood samples were collected at 0, 3, 5 and 7 h after administration of the extract orally and measured using the test strips with Accu-chek Glucometer (Fig. 2).

Comparative studies on the hypoglycaemic activity of aqueous extract of *Stachytarpheta angustifolia* with some selected oral hypoglycaemic agents on blood glucose level on alloxan-induced diabetic rats: The same method of diabetes induction and confirmation was employed as above. After diabetes confirmation, the

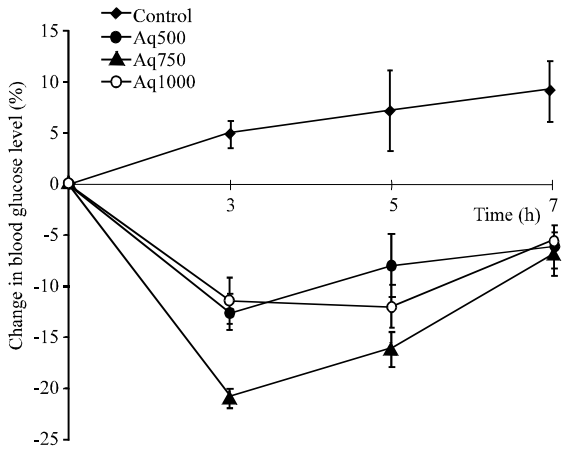

Fig. 1: Percent change in blood glucose levels vs time (h) after administration of various doses of aqueous extract of *Stachytarpheta angustifolia* on normoglycaemic rats

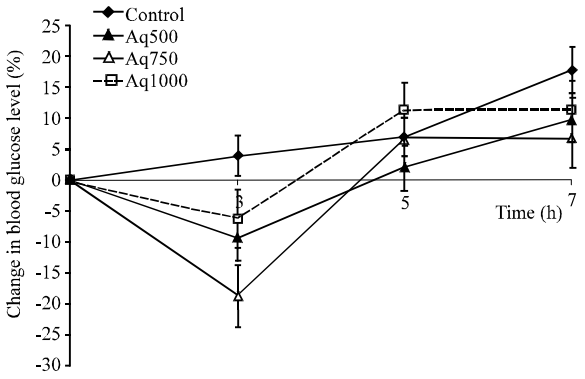

Fig. 2: Percent change in blood glucose levels vs time (h) after administration of various doses of aqueous extract of *Stachytarpheta angustifolia* on alloxan-induced diabetic rats

aqueous extract (750 mg kg^{-1} body weight) of the plant was administered orally to a group of rats using gastric intubations. Similarly, three other groups of five rats each were given 250 mg kg^{-1} of chlorpropamide, 1 mg kg^{-1} of glibenclamide and 500 mg kg^{-1} metformin, respectively, while the fifth group (control) was given 0.9% w/v saline solution. Aqueous suspensions of the oral hypoglycaemic agents were freshly prepared. All rats were fasted overnight before the administration of the extract and the agents and no food was given on the day blood samples were collected. Blood samples were collected at 0, 3, 5 and 7 h from each rat and the blood glucose levels were measured using the strips with Accu-chek Glucometer (Fig. 3).

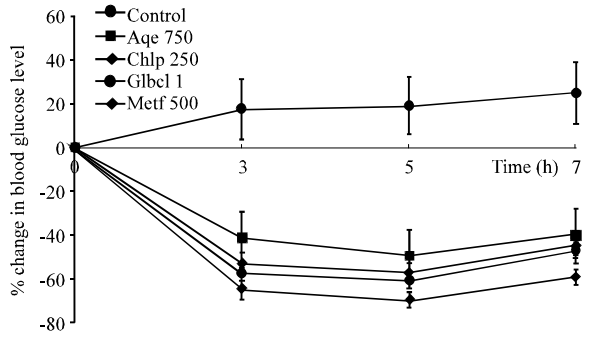

Fig. 3: Percent change blood glucose levels vs time (h) after administration of aqueous extract of *Stachytarpheta angustifoliain* comparison with some selected oral hypoglycaemic agents, Aqe = Aqueous extract Chlp = Chlorpropamide, Glbcl = Glibenclamide, Metf = Metformin

RESULTS

The LD_{50} of the aqueous extract for the oral route was found to be 5000 mg kg^{-1} body weight indicating that it is safe and of no practical value (Lorke, 1983).

Figure 1 and 2 summarised the results of the hypoglycaemic activity of the extracts of the plant on normoglycaemic and alloxan-induced diabetes respectively while Fig. 3 showed the result of the comparative studies on the hypoglycaemic activity of the aqueous extract with some selected Oral Hypoglycaemic Agents (OHA) on alloxan-induced diabetic rats.

Effects of the aqueous extract on the blood glucose levels of normoglycaemic rats: The effects of different doses of aqueous extract of *Stachytarpheta angustifolia* on the fasting blood glucose levels of normoglycaemic rats are shown in Fig. 1. In normoglycaemic rats, aqueous extract at a dosage of 750 mg kg^{-1} body weight elicited a maximum of 20.76% hypoglycaemic activity after 3 h of extract administration. The blood glucose levels started increasing after the 3rd h of administration in the animals.

In this study, aqueous extract of the plant at a dose of 750 mg kg^{-1} could produce a significant fall in blood glucose in normoglycaemic rats. Increasing the dose to 1000 mg kg^{-1} did not seem to increase the hypoglycaemia, implying that the maximum effect was obtained at 750 mg kg^{-1} possibly because most of the receptor sites have been blocked (Clark, 1933). This hypoglycaemia was produced in a related fashion similar to that produced by *Anthocleista vogelli* (Abuh *et al*., 1990). The hypoglycaemic effect which lasted about 7 h in both normoglycaemic and alloxan-induced diabetic rats suggests that the plant extract could be useful in

significantly controlling blood glucose levels in non-insulin dependent and possibly insulin dependent diabetic patients.

Effects of the aqueous extract on the blood levels of alloxan-induced diabetic rats: Figure 2 shows the effect of the various doses of the plant aqueous extract on alloxan-induced diabetic rats. From the Fig. 2, it can be observed that at concentration of 500 mg kg^{-1}, the percentage change in blood glucose level was significant. And at extract concentration of 750 mg kg^{-1}, there was a great decrease of blood glucose level, which was most at the 3rd h.

The mechanism (s) of action of the reduction of blood glucose levels following oral administration of the extract is (are) difficult to explain. Some medicinal plants with hypoglycaemic properties are known to increase circulating insulin levels in rats (Torres and Suarez, 1980; Farjou *et al*., 1987). It is also possible that the extract might have stimulated the residual pancreatic β-cells function or produced the hypoglycemia through an extra-pancreatic mechanism, possibly by increasing peripheral utilization of glucose as postulated by Farjou *et al*. (1987).

Comparative studies on the hypoglycaemic properties of *Stachytarpheta angustifolia* extract and some selected oral hypoglycaemic agents: The hypoglycaemic activity of the aqueous extract in comparison with some selected oral hypoglycaemic agents (Chlorpropamide, Glibenclamide and Metformin) is shown in Fig. 3. The pattern of reduction in the blood glucose levels exhibited by all the drugs (OHA and extract) was similar. However, the level of reduction was comparatively lower than the standard drugs. This is similar to that produced by *Anthocleista* vogelli earlier reported by Abuh *et al*. (1990).

It is also possible that the extract might have stimulated the residual pancreatic β-cells function or produced the hypoglycaemia through an extra-pancreatic mechanism, possibly by increasing peripheral utilization of glucose as postulated by Torres and Suarez (1980).

DISCUSSION

The reduction in both urine output and water intake and also the lowering of blood glucose levels of the laboratory animals (within 7 h) were used to infer the hypoglycaemic activity of the extract. The results of this study indicate that the aqueous extract of *Stachytarpheta angustifolia* (Verbanaceae) exhibits an *in vivo* hypoglycaemic activity in both normoglycaemic and alloxan-induced diabetic rats. The hypoglycaemia was produced in a dose-related fashion from 0 to 3 h after oral administration of the extract. As mentioned above there has not been earlier scientific evidence confirming the hypoglycaemic activity of the plant, but the traditional medical practitioners use it with great success.

The mechanism of action of the reduction of blood glucose levels following oral administration of the extract is difficult to explain in this study. Some medicinal plants with hypoglycaemic activity are known to increase circulating insulin levels in normoglycaemic rats (Abuh *et al*., 1990; Torres and Suarez, 1980). The extract of *Stachytarpheta angustifolia* may be acting like other plants reported to cause hypoglycaemia independent of insulin release (Farjou *et al*., 1987). It is also possible that the extract might have stimulated the residual pancreatic β-cells function or produced the hypoglycaemia through an extra-pancreatic mechanism, possibly by increasing peripheral utilization of glucose as postulated by Torres and Suarez (1980). Jimenez *et al*. (1986) list glycosides, flavonoids, tannins, organic sulphur compounds, catechol and alkaloids as active ingredients in hypoglycaemic plants. Thus, the hypoglycaemic activity produced by *Stachytarpheta angustifolia* (Verbanaceae) may be due to one or more of these secondary metabolites.

Further studies will be required to investigate the pharmacological effects of the plant extract and also the isolation of the active ingredients of the extract need to be investigated. Finally, as a conclusion, the aqueous extract of *Stachytarpheta angustifolia* (Verbanaceae) at a dose of 750 mg kg^{-1} has some beneficial effects on high blood sugar level of both normoglycaemic and alloxan-induced diabetic rats.

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