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Full Length Research Paper

Evaluation of hypoglycaemic and antihyperglycaemic activity of methanolic wholeplant extract of *Schwenckia americana* (Solanacae) in normal and alloxan-induced diabetic rats

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Powdered whole plant of *Schwenckia americana* (family Solanacae) is used traditionally (in combination with other herbs) for treating diabetes mellitus in Northern Nigeria. Therefore, in the current study, the traditional claim was evaluated by testing the effects of methanolic extract of *S. americana* whole plant on blood glucose in normal, alloxan-induced sub-diabetic and alloxan-induced diabetic rats. The median lethal dose after oral administration of the extract in rats was found to be above 5,000 mg per kilogram of body weight. The extract significantly lowered blood glucose in normal and alloxan-induced subdiabetic rats but not in alloxan-induced diabetic rats. It is concluded that *S. americana* may reduce blood sugar in type 2 diabetes, thus vindicating the traditional claim of its antidiabetic property.

Key words: *Schwenckia americana*, blood sugar, rats.

INTRODUCTION

Diabetes mellitus is one of the most prevalent chronic diseases worldwide, which is accompanied by high mortality and morbidity. The global prevalence of the disease is expected to rise from 6.4% (equivalent to 285 million people) in 2010 to 7.7% (equivalent to 439 million people) in 2030 (Shaw et al., 2010). Of all the regions in the world, Africa is predicted to witness the greatest increase in the number of adults with diabetes from 12.1 million in 2010 to 23.9 million in 2030 (Shaw et al., 2010). Ancient records from the Ebers papyrus have indicated that traditional practices, particularly the use of plants, have been applied by Man to treat diabetes mellitus as far back as 1550 BC. Such traditional approaches remain the only therapeutic option available prior to the discovery of insulin (Swanston et al., 1990). Currently, despite availability of various drug options for its treatment, an ideal drug for the condition that is both effective and well tolerated is yet to be discovered, thus warranting continuing exploration of such possibility from the biodiversity of nature.

Schwenckia americana is a perennial plant that belongs to the family Solanacae. Although the plant originated in South and Central America, it is currently widely distributed in Asia (particularly India) and Africa (mainly West and Central Africa) (Bosch, 2008). In Northern Nigeria, the plant is traditionally used for treating rheumatism, fungal infections and diabetes mellitus (in combination with other herbs). Although the analgesic, anti-inflammatory and antimicrobial effects of the plant have been reported (Asusheyi et al., 2010; Jimoh et al., 2011), to the best of our knowledge, no study has investigated its antidiabetic effect. This study

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was thus undertaken with the aim of evaluating hypoglycaemic and antihyperglycaemic activity of the methanolic whole plant extract of the herb in normal, alloxan-induced subdiabetic and diabetic rats. The acute toxicity of the extract was also investigated.

MATERIALS AND METHODS

Plant

Fresh whole plant of *S. americana* was obtained from a local herbalist in Birnin Kebbi, Kebbi state, Northern Nigeria and identified by Mallam Awwali, a taxonomist in botany department, Faculty of biological sciences. A dried specimen (Voucher specimen no.43) was kept at the herbarium, Botany department, for future reference.

Preparation of extract

The whole plant of *S. americana* was shade-dried to constant weight, ground to powder and then subjected to Soxhlet extraction using methanol as solvent. The methanolic extract was then evaporated in an aerated oven set at 40°C. The residue obtained (yield = 20%) was stored at 4°C until ready for use.

Chemicals and drugs

Methanol, alloxan monohydrate (Burgoyne Burbidges & Co. Mumbai, India) and glibenclamide (Daonil, Thailand) were purchased from reputable pharmaceutical stores.

Animals

Male Wistar rats weighing 200 to 250 g were purchased from biological sciences, Faculty of science, Usmanu Danfodiyo university, Sokoto. They were acclimatized for 2 weeks on standard chow and water *ad libitum*. The study was conducted according to established international guidelines for the handling of animals and was approved by the research ethics committee, Usmanu Danfodiyo University, Sokoto.

Phytochemical analysis

The extract was tested for the presence of saponins, alkaloids, flavonoids, tannins, cardiac glycosides and steroids using the methods of Harbone (1973) and Trease and Evans (2005).

Acute toxicity

The acute toxicity study of the methanolic extract of *S. americana* was conducted using the upper limit dose of 5000 mg/kg body weight (BW) in accordance with the Organisation for Economic Cooperation and Development (OECD) guidelines (2001). For 14 days, the animals were observed for any death or sign of toxicity, frequently within the first 48 h and then daily for the remaining 12 days.

Induction of diabetes in rats

A freshly prepared aqueous solution of alloxan monohydrate (150 mg/kg) was administered intraperitoneally to overnight-fasted rats followed by addition of glucose to the drinking water to prevent the animals from developing hypoglycaemia (Prince et al., 1998). Baseline fasting blood sugar (FBS) for the rats was measured just before the induction of diabetes and then 1 week thereafter. Animals with near normal FBS level (< 130 mg/dl) but exhibiting abnormal oral glucose tolerance test were considered subdiabetic (Shukla et al., 1994; Kesari et al., 2005). Rats with fasting blood sugar ≥ 200 mg/dl were regarded as diabetic.

Experimental protocol

The same protocol was followed for the 4 experiments. Oral glucose tolerance and fasting blood sugar were measured in untreated and treated normal rats in order to test the hypoglycaemic effect of the plant extract, while alloxan-induced subdiabetic and diabetic rats were used to assess its antidiabetic property. For each experiment, 25 male albino rats fasted overnight for 14 h were randomly (using computer random numbers from STATS software) divided into five groups consisting of five animals each. Two groups of rats (1 and 2) received either distilled water or aqueous suspension of glibenclamide (0.6 mg/kg) to serve as negative and positive controls, respectively. Methanolic whole plant extract of the plant suspended in distilled water (100, 200 and 300 mg/kg body weight) was given to the remaining three groups (III to V). Each rat in the groups received 5 ml/kg of the vehicle (distilled water) or one of the treatments orally using gavage needle.

Hypoglycaemic activity in normal rats

Determination of blood glucose levels normal fasted rats was performed at an hourly interval for 3 h.

Oral glucose tolerance in normal rats

In this experiment, normal fasted rats in all the groups received 3 g/kg of glucose thirty minutes following extract or drug administration. Serum glucose level of the animals was determined just prior to glucose administration and then at 1, 2 and 3 h after glucose loading.

Oral glucose tolerance in subdiabetic rats

Alloxan-induced subdiabetic rats were used for this experiment following the same protocol described above for normal rats.

Hypoglycaemic activity in diabetic rats

The same protocol described above for normal rats was applied in this experiment. Alloxan-injected rats confirmed to develop diabetes (> 200 mg/dl) were used.

Collection of blood sample

Blood was obtained from the animals' tail veins by excision and the glucose level determined using one touch glucometer (Accucheck, Rouche).

Statistics

The data were subjected to statistical analysis using Analyse-it for excel software and the values were expressed as mean ± standard

Table 1. Fasting blood sugar in normal rats.

Treatment groups (n=5)	Mean blood glucose concentration ± SD (mg/dl)			
	Baseline	1 h	2 h	3 h
CNT	84.6±6.6	84.6±6.7^{NS}	84.2±6.2^{NS}	82.0±6.5^{NS}
Glb (0.6 mg/kg)	70.0±4.3	65.8±5.5^{NS}	59.4±2.1**	55.8±2.9**
SA (100 mg/kg)	78.4±4.3	75.6±4.0^{NS}	73.0±3.9^{NS}	72.4±4.4^{NS}
SA (200 mg/kg)	81.4±4.6	76.2±4.3^{NS}	68.4±8.6*	72.0±3.2**
SA (300 mg/kg)	80.8±3.5	75.6±2.7*	72.4±4.2**	74.4±2.9*

CNT = control; Glb = glibenclamide; SA= methanolic wholeplant extract of *Schwenckia americana*; SD = standard deviation. NS, * and ** denote *p* values > 0.05(not significant), < 0.05 and < 0.01, respectively compared to baseline using Student's t test.

Table 2. Fasting blood sugar in diabetic rats.

Treatment groups (n=5)	Mean blood glucose concentration ± SD (mg/dl)			
	Baseline	1 h	2 h	3 h
CNT	348.6±54.7	385.0±57.9	356.8±62.2	355.6±53.9
Glb (0.6 mg/kg)	310.0±63.0	269.4±63.5	231.6±55.9	181.0±21.9**
SA (100 mg/kg)	285.0±65.5	275.6±58.8	261.4±63.8	267.8±61.8
SA (200 mg/kg)	327.8±81.6	323.6±74.4	299.4±78.5	302.6±81.9
SA (300 mg/kg)	290.0±42.9	280.2±41.8	273.8±41.9	276.4±38.1

CNT = control; Glb = glibenclamide; SA = methanolic wholeplant extract of *S. americana*; SD = standard deviation. ** denotes *p* value < 0.01 compared to baseline using Student's t test.

Table 3. Oral glucose tolerance test in normal fasted rats.

Treatment groups (n=5)	Mean blood glucose concentration ± SD (mg/dl)			
	Baseline	Δ BGL at 1 h	Δ BGL at 2 h	Δ BGL at 3 h
CNT	69.0±5.4	+46.4±8.8	17.8±7.4	-5.8±5.4
Glb (0.6 mg/kg)	60.2±6.0^{NS}	+14.8±6.4**	15.8±5.9	-2.2±2.3
SA (100 mg/kg)	66.4±7.7^{NS}	+20.4±2.5**	10.2±1.3	1.6±4.3
SA (200 mg/kg)	62.6±3.9^{NS}	+18.6±5.8**	15.2±4.2	4.6±2.2
SA (300 mg/kg)	71.4±6.9^{NS}	+16.8±4.3**	-0.6±3.4**	-7.8±4.3

CNT = control; Glb = glibenclamide; SA = methanolic wholeplant extract of *Schwenckia americana*; SD = standard deviation. Δ BGL = Change in blood glucose level as compared to baseline. NS and ** denotes *p* value > 0.05 (not significant) and < 0.01, respectively compared to control using Dunnet post test.

deviation (SD) (since any difference in readings was assumed to be due to biological variation). Statistical significance between groups was determined using one- way analysis of variance (ANOVA) followed by Dunnett's test or Student's t-test as appropriate. Differences were considered significant at $p < 0.05$.

RESULTS

Phytochemical analysis of the whole plant of methanolic extract of *S. americana* revealed the presence of saponins, alkaloids, flavonoids, tannins, steroids and cardiac glycosides. Neither mortality nor sign of toxicity was observed in any of the rats administered single dose of 5,000 mg/kg body weight of the extract. Methanolic extract of *S. americana* exhibited a significant but nondose-dependent hypoglycaemic effect in normal rats as illustrated in Table 1. On the other hand, no significant hypoglycaemic effect was observed in alloxan-induced diabetic rats following the administration of the extract (Table 2). However, treatment with glibenclamide resulted in a significant hypoglycaemic effect. Furthermore, as shown in Tables 3 and 4, all the 3 doses of the extract exhibited significant improvement in glucose tolerance in normal and subdiabetic rats, with the effect being dose-related in the former and nondose-dependent in the latter.

Table 4. Oral glucose tolerance tests in subdiabetic rats.

Treatment groups (n=5)	Mean blood glucose concentration ± SD (mg/dl)			
	Baseline	Δ BGL at 1 h	Δ BGL at 2 h	Δ BGL at 3 h
CNT	115.0±6.0	145.0±2.0	83.0±2.0	-15.0±1.0
Glb (0.6 mg/kg)	120.0±8.0^{NS}	59.6±1.5**	2.8±6.6**	--15.0±1.6
SA (100 mg/kg)	114.4±5.1^{NS}	130.2±3.2	56.4±3.8*	-32.4±3.2*
SA (200 mg/kg)	121.0±7.9^{NS}	118.0±17.6 *	68.4±24.6	-27.2±13.6
SA (300 mg/kg)	102.2±12.1^{NS}	121.0±23.8*	57.0± 22.8*	-8.4±12.4

CNT = control; Glb = glibenclamide; SA= methanolic wholeplant extract of *Schwenckia americana*; SD = standard deviation. Δ BGL = Change in blood glucose level as compared to baseline. NS, * and ** denote *p* values >0.05(not significant), < 0.05 and < 0.01, respectively compared to control using Dunnet post test.

DISCUSSION

In this study, methanolic extract of *S. americana* whole plant was found to be very safe in rats with oral LD_{50} above 5,000 mg/kg body weight (BW). The extract was also as effective as glibenclamide in reducing blood sugar level in normal rats, but only moderately active in subdiabetic animals and inactive in insulin-deficient rats. It is well established that alloxan induces type 1 diabetes by destroying pancreatic beta cells resulting in insulin deficiency and hyperglycaemia (Rerup, 1970). However, following its administration, some of the animals may regenerate their pancreatic cells - a good model of type 2 diabetes (Shukla et al., 1994). Also, depending on the degree of pancreatic destruction, alloxan-induced animals with fetal bovine serum (FBS) above 200 mg/kg may possess either type 1 or type 2 diabetes (Shukla et al., 1994). Although the exact mechanism of action of the plant extract could not be determined in this study, these findings suggest that it might involve stimulation of insulin release from pancreatic beta cells, just like the sulfonylureas. The greater effectiveness of glibenclamide in reducing blood sugar in moderate than in severe diabetes, as observed in the current study, has been previously documented (Ivorra et al., 1988; Sharma et al., 1997). Some of the effects exhibited by the extract are nondose-dependent - a finding that conforms with some ethnopharmacological studies (Kesari et al., 2005, 2006; Singh et al., 2007, 2009; Rai et al., 2008).

The findings of this study also indicate that the extract is not effective in type 1 diabetes. However, it is well known that various factors including humidity, type of soil (Evans, 1996), geographical location of the plant (Eldridge and Kwolek, 1983), the season in which the plant was collected (Salminen et al., 2004), the part of the plant used (Eldridge and Kwolek, 1983) as well as the method of extraction used (Shan et al., 2007), may have an effect on phytochemical constituents. It has also been documented that some activities of a plant may only be evident following prolonged administration (Pepato et al., 2001). In addition, since this herb is traditionally combined with other herbs for treatment of diabetes in Northwestern Nigeria, the antidiabetic effect may be due to synergistic effect of a particular herbal formula.

The hypoglycaemic effect of the extract may have been contributed by the presence of at least one of these 3 phytochemicals previously reported to possess anti-diabetic property, namely flavonoids (Vessal et al., 2003), tannins (Teotia and Singh, 1997), or saponins (Yoshikawa et al., 2001), either individually or in combination. More studies are needed to confirm these findings and assumptions as well as to clarify the contribution of the various factors mentioned above to the antidiabetic activity of the plant.

Conclusion

S. americana reduces blood sugar in type 2 but not type 1 diabetic animals, thus vindicating the traditional claim of its antidiabetic property.

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