Anti-Hyperglycemic Activity of Alcoholic Extract of *Swertia Tetragona* Edgew

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Summary

The alcoholic extract of ***Swertia tetragona*** Edgew was tested for anti-hyperglycemic activity on normal fasted, glucose loaded and alloxan induced diabetic rats. Blood glucose levels were evaluated at 0,1 and 3 hours in normal fasted rats; at 0, 30 and 90 minutes in glucose loaded rats; at 0, 1 and 3 hours in acute, and at days 1, 3, 7 and 10 in sub-acute studies of alloxan induced diabetic rats after extract administration of 250 mg/kg. In both acute and sub acute-studies the ethanolic extract showed statistically significant anti-hyperglycemic and an enhanced glucose tolerance activity while it had no effect on normal fasted rats.

Key words: ***Swertia tetragona*** Edgew, anti-hyperglycemic, glucose tolerance.

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Introduction

The genus Swertia comprises of 170 species and most of them are found in India growing at a high altitude in the temperate Himalayas from Kashmir to Bhutan and also in Khasi and Western Ghat Hills (1). Swertia species are of high pharmacological interest. Different plant extracts have been studied for their therapeutic efficacies and found to be highly effective. Xanthonoids are the major class of compounds among the chemical constituents of this genus and since they often exhibit multidirectional biological activities, this spectacular segment of natural products has created a stir among pharmacologist and biologist. Particularly the tetraoxygenated xanthones have been reported to exhibit hypoglycaemic, antihepatotoxic, antimalarial, anti-inflammatory, antioxidant, antimicrobial and antitumour properties, among others (2).

Swerchirin and bellidifolin are two well known hypoglycemic compounds reported from various species of Swertia (3)(4)(5). One such specie of Swertia reported to have antidiabetic activity is *Swertia tetragona.* It is an annual, erect, solitary or tufted branched herb and found distributed in temperate Himalayas from Kashmir to Sikkim at 1900 to 3100m (7).

Materials and methods

Plant material

Whole plants of ***Swertia tetragona*** Edgew were collected from Aharbal region of Kashmir (J&K), India, in presence of Dr. A.R.Naqshi, Taxonomist, Department of Botany, Faculty of Science, University of Kashmir. A voucher specimen is deposited in the laboratory of Pharmacognosy, Department of Pharmaceutical Sciences, University of Kashmir.

Preparation of the extract

Dried roots of ***Swertia tetragona*** were macerated with ethanol (95%), filtered and dried under reduced pressure and a solid extract (12.5 %w/w) was obtained

Animals

Male Wistar rats (160-200 g), were used in the experiment. They were procured from Central Animal House, Jamia Hamdard, New Delhi (173/CPCSEA), after approval under project number 151. They were maintained under standard environmental conditions and had free access to feed (Hindustan Lever, India) and tap water *ad libitum* during the quarantine period. The animals were fasted for 16 hours before experiment but allowed free access to water.

Studies in normal fasted rats

Effect of ***Swertia tetragona*** extract on normal fasted rats

Fasted rats were divided into three groups of five animals each. Group 1 served as normal control and received distilled water only. Group II served as standard control and received standard drug, gliclazide at an oral dose of 25 mg/kg. Group III received drug extract at an oral dose of 250 mg/kg. Blood samples were collected from the tip of the tail just prior to drug/ extract administration and at 1 and 3 hr. respectively. Serum was separated and glucose level estimated by glucose oxidase method (8)

Effect of *Swertia tetragona* on glucose loaded animals

Fasted rats were divided into three groups of five animals each. Group 1 served as normal control and received distilled water only. Group II served as standard control and received standard drug, gliclazide at an oral dose of 25 mg/kg. Group III received drug extract at an oral dose of 250 mg/kg. After thirty minutes of drug administration the rats of all the groups were orally treated with 2 g /kg of glucose. Blood samples were collected from the tip of the tail just prior to drug administration and at 30 and 90 minutes after glucose loading. Serum was separated and blood glucose levels were measured immediately by glucose oxidase method (8)

Induction of experimental hyperglycemia

Hyperglycemia was induced by a single i.p. injection of 120 mg/kg of alloxan monohydrate (s.d.fine-chem. Ltd., Mumbai, India) in sterile saline (9). At 5th day of alloxan injection, the diabetic rats (glucose level>300 mg/dl) were separated and divided into three groups of five diabetic animals each. Group I served as diabetic control and was given distilled water. Group II received standard anti-diabetic drug gliclazide at an oral dose of 25 mg/ kg (Panacea Biotech Ltd., Batch No. 01030513). Group III was treated orally with ethanolic extract at a dose of 250 mg/kg. Normal group was previously chosen from amongst normal animals. In the acute treatment, blood samples were collected from the tip of the tail just prior to and 1 and 3 hours after the extract/drug administration.

In sub-acute treatment, the administration of extract/drug was continued, once daily, for 10 days. Blood samples were collected from the tip of the tail just prior to and on days 1, 3, 7 and 10 of the extract/drug administration. The blood glucose levels were estimated for all the samples by glucose-oxidase method [Varley et al. 1976].

Data were expressed as ± SE, n=5. Statistical significance was determined by using, one-way analysis of variance (ANOVA) followed by Dunnet's t-test. $P<0.05$ indicates significant differences between group means.

Results

Effect of alcoholic extract of ***Swertia tetragona*** on glucose tolerance is shown in Table 1. Administration of gliclazide (25 mg/kg) prior to glucose loading induced time dependent and statistically significant ($p<0.001$) hypoglycemic effect. The test drug (***Swertia tetragona***) showed statistically significant ($p<0.05$) antihyperglycemic effect on blood glucose levels in the same study.

In the acute studies of alloxan-induced diabetes, oral administration of the alcoholic extract led to significant ($p<0.01$) blood glucose lowering effect (Table 2). The fall was seen at 1hr and remained upto 3 hr (22.4% reduction) after administration of the extract, whereas the fall in case of gliclazide administration was marginal because alloxan treatment causes permanent destruction of β cells (9) and gliclazide requires more than 30 % functional pancreas for the effect.

Sub-acute treatment with alcoholic extract of ***S. tetragona*** on alloxan-induced hyperglycemic rats produced consistent reduction ($p<0.001$) in the blood glucose levels (Table 3). The fall in blood glucose was seen from day I till the end of the study i.e. 10 days (45.60% reduction). Again the hypoglycemia shown by gliclazide was marginal as observed in the acute treatment.

Table-1 Effect of ethanolic extract of *Swertia tetragona* on Glucose tolerance test[a]

Group	Treatment	Basal value	30 min	90 min
I	Normal Control (Distilled water only)	69.33 ±2.24	110.6 ±1.20	89.6 ± 2.62
II	Standard group (gliclazide)	65.83 ±1.47	84.20*** ±2.85	54.40*** ± 1.86
III	Test group (extract)	70.6 ±1.202	90.0 ±1.733**	75.0 ±1.231**

[a]Values are means ± S.E.; n = 5, ***p<0.001, *p<0.05, vs. group I.

Table-2 Effect of acute treatment o*f Swertia tetragona*, ethanolic extract (250 mg/kg, p.o.), on blood glucose level in alloxan induced diabetic rats[a]

Group	Treatment	Blood Glucose (mg/dl)			%age reduction / 3 hr
		Basal value	1 h	3 h	
I	Normal Control (Distilled water only)	75.60 ± 1.24	77.00 ± 1.87	74.80 ± 2.08	
II	Diabetic Control (Alloxan only)	321.00 ±9.22	323.20 ± 8.67	295.60 ± 7.22	
III	Standard (Alloxan+Std. drug)	329.00 ±10.85	315.60 ±10.26*	308.20 ±9.58^{NS}	6.4
IV	Test (Alloxan+extract)	300.40 ± 8.26	278.60 ±7.30**	233.00 ±6.42**	22.4

[a]Values are means ± S.E.; n = 5, *p<0.05, **p<0.01, NS, not significant vs. group II.

Table-3 Effect of sub-acute treatment of *Swertia tetragona*, ethanolic extract (250 mg/kg, p.o., once daily), on blood glucose level in alloxan induced diabetic rats[a]

Group	Treatment	Blood Glucose (mg/dl)					%age reduction/ 10 days
		Basal value	Day 1	Day 3	Day 7	Day 10	
I	Normal Control (Distilled water only)	75.60 ± 1.24	93.80 ± 6.08	88.20 ± 5.45	91.80 ± 3.48	92.20 ± 1.77	
II	Diabetic Control (Alloxan only)	353.80 ±18.29	353.40 ± 10.20	353.60 ± 9.65	354.40 ± 10.15	354.80 ± 10.83	
III	Standard (Alloxan+Std. drug)	329.00 ±10.85	303.80 ±11.62*	306.40 ±10.77*	304.40 ± 10.09*	304.60 ±11.40*	07.60
IV	Test (Alloxan+extract)	358.00 ± 8.42	294.00 ±11.40**	241.30 ±8.47***	212.20 ±11.55***	195.20 ±7.75***	45.60

[a]Values are means ± S.E.; n = 6, ***p<0.001, **p<0.01, *p<0.05 vs. group II.

Discussion

It is generally accepted that sulphonylureas, including gliclazide produce hypoglycemia in normal animals by stimulating the pancreatic β-cells to release more insulin. These drugs, however, do not release blood glucose in alloxan diabetic animals. In contrast to the oral anti-diabetic agents, the exogenous administration of insulin is known to produce hypoglycemia in both normal and alloxan-induced rats. It is, therefore, conceivable that the hypoglycemic principle (s) in the alcoholic extract of ***Swertia tetragona*** exert a direct effect in diabetic rats. In conclusion, it may be stated that our observations are suggestive of the fact that ***Swertia tetragona*** posses a significant antihyperglycemic activity. Further studies are in progress to identify the active principle(s) responsible for the antihyperglycemic effect and to understand mechanism of action involved in it.

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