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Anti-hyperglycemic activity of the alcoholic extract of *Aralia cachemirica* Decne roots

Z. A. Bhat, S. H. Ansari*, H. M. Mukhtar, T. Naved, N. A. Khan[1], I. A. Chashoo[1]

1. Department of Pharmaceutical Sciences, University of Kashmir, Hazratbal, Srinagar-190006, Kashmir (J&K), India
Department of Pharmacognosy and Phytochemistry, Faculty of Pharmacy, Jamia Hamdard, (Hamdard University), Hamdard Nagar, New Delhi-110 062, India

Abstract

Objective: To evaluate the anti-hyperglycemic activity of alcoholic extract of *Aralia cachemirica* Decne roots. Materials and methods: The alcoholic extract of *Aralia cachemirica* 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 h in normal fasted rats at 0, 30 and 90 min in glucose loaded rats; at 0, 1 and 3 h 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. Results: 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. Conclusion: *Aralia cachemirica* posses statistically significant anti-hyperglycemic activity in both acute and sub-acute studies of alloxan induced diabetes and also has an enhanced glucose tolerance activity.

Key words: *Aralia cachemirica* Decne, roots, anti-hyperglycemic, glucose tolerance.

1. Introduction

Many medicinal plants found in the valley of Kashmir have different medicinal properties. One such plant reported to have antidiabetic potential is *Aralia cachemirica* Decne. It is known as khoree in Kashmiri and is found distributed in the temperate Himalayas from Kashmir to Sikkim at 2100 to 4000m and belongs to the family Araliaceae [1]. It has already been reported that most of the members of the family have high molecular weight polysaccharides known as glycans. These polysaccharides stored in their roots have hypoglycemic and immunomodulatory activity [2-5]. Several species of genus Aralia and their isolated constituents have shown promising hypoglycemic activity [6-9]. It has also been reported that the chemical constituents of genus Aralia are very similar to Ginseng [10], which is a well-known hypoglycemic drug. On these basis it was found worthwhile to investigate

* Corresponding author
E-mail: shansari189@rediffmail.com

this rare and only specie of Aralia growing in high altitude areas of Kashmir (J&K) India [11].

The following phytoconstituents have already been isolated from the plant; Octadec-6-enoic acid, 8-primara-14, 15-diene-19-oic acid, Aralosides A&B [12] Nonane, a hexacosane derivative, petroselinic acid, stigmasterol and β-sitosterol [13]. Anti-inflammatory activity of this plant has also been reported [1].

2. Materials and methods

2.1 Plant material

The roots of *Aralia cachemirica* Decne (Araliaceae) 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.

2.2 Preparation of the extract

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

2.3 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 h before experiment but allowed free access to water.

3. Studies in normal fasted rats

Effect of *A. cachemirica* 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 h. respectively. Serum was separated and glucose level estimated by glucose oxidase method [14].

4. Effect of *A. cachemirica* 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 2g/kg of glucose. Blood samples were collected from the tip of the tail just prior to drug administration and at 30 and 90 min after glucose loading. Serum was separated and blood glucose levels were measured immediately by glucose oxidase method [14].

Table 1.
Effect of ethanolic extract of *A. cachemirica* 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)	68.00±2.56	93.8* ±1.08	73.20* ±1.86

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

Table 2.
Effect of acute treatment of *A. cachemirica*, ethanolic root 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 h
		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	10.7
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.

5. 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 [15]. 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 h 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 [14]. 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.

6. Results and discussion

Effect of alcoholic extract of *A. cachemirica* 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 *(A. cachemirica)* 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 1 h and remained upto 3 h (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 (15) and gliclazide requires more than 30 % functional pancreas for the effect.

Table 3.
Effect of sub-acute treatment of *A. cachemirica*, ethanolic root 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
		Basal value	Day 1	Day 3	Day 7	Day 10	reductio/ 10 days
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*	26.60
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.

Sub-acute treatment with alcoholic extract of *A. cachemirica* 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.

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 *A. cachemirica* exert a direct effect in diabetic rats. In conclusion, it may be stated that our observations are suggestive of the fact that *A. cachemirica* 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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