

**ANTI-DIABETIC ACTIVITY OF *CENTRATHERUM ANTHELMINTICUM* KUNTZE
ON ALLOXAN INDUCED DIABETIC RATS**

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Summary

The antidiabetic activity of *Centratherum anthelminticum* Kuntze (Compositae) was investigated in a model of Alloxan-induced diabetic rats. Extracts were administered daily at the doses 200 mg/kg and 500 mg/kg p.o., 14 days after alloxan administration (150 mg/kg). The aqueous extract of the drug showed significant dose dependent percentage blood glucose reduction in diabetic rats (35.61% at 200 mg/kg dose, 40.1% at 500 mg/kg dose). The antidiabetic effect of *C.anthelminticum* was compared with the reference standard drug Glibenclamide (5 mg/kg body weight) which showed 48.65% decrease in blood glucose level after the study of one week. The drug was found promising in management of diabetes and in overcoming the secondary effects of diabetes like fatigue and thirst.

Keywords: Diabetes, Glibenclamide, GOD-POD, Kalijiri.

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Introduction

Centratherum anthelminticum Kuntz (Hindi- Kalijiri) previously known as *Vernonia anthelmintica* belongs to family compositae(1). It has a good anthelmintic property and used for the treatment of various skin infections. It is also reported to be used in asthma, kidney troubles, cough and also used to remove blood from liver(2) . But no work has been done uptill now to establish its antidiabetic potential. The major classes of chemical constituent present in this plant are glycosides(3), carbohydrates(4) , phenolic compounds and tannins(5) , flavanoids(6) , proteins, saponins(7), sterols(8,9) , lipids(10) and fats(11).

In this work the effect of its aqueous extract on the blood glucose lowering effect of alloxan induced diabetic rats as been investigated, which is one of the main parameter for checking the potential of drug in the management of Diabetes mellitus. Diabetes mellitus is a group of syndromes characterized by hyperglycemia, altered metabolism of lipid, carbohydrate and proteins, and an increased risk of complication from vascular diseases.

Non Insulin dependent diabetes mellitus [NIDDM] i.e. Type II diabetes is the most common form of diabetes in which survival (except in emergencies) does not depend upon insulin therapy. NIDDM is associated with morbidity and mortality, resulting from its microvascular, macrovascular and neuropathic complications. Some Classical Features of diabetes mellitus are Polyuria, Polydypsia, Polyphagia, and Wasting (12).

Method

Animals. The animals used for the study were adult albino rats of either sex, weighing 150-200 gm. All animals were procured from Institute of Pharmacy, and approved by the Institutional Ethics Committee, Bundelkhand University, Jhansi.

The animals were housed in polypropylene cages, 4 per cage, with free access to standard laboratory diet and water were provided *ad libitum*. The rats were maintained under standard laboratory condition at $25 \pm 2^\circ\text{C}$, relative humidity $50 \pm 15\%$ and normal photo period (12h dark/12h light) were used for experiment.

Determination of plasma blood glucose level: In the experiment the blood glucose level of the animals were estimated by Glucose Oxidase-Peroxidase Enzymatic Method (GOD-POD). Blood from the tail vein was collected. About 100 μl of blood was taken in Epindroff's tube (1.5 ml capacity) to which anticoagulant (potassium EDTA + sodium fluoride, 2:1) was previously added. Blood was mixed properly and centrifuged at 3000 rpm for 10 min. Out of it 10 μl of plasma was further used with 1ml of enzyme solution. Thoroughly mixed plasma and enzyme were incubated at 37°C for 15 min. Then the absorbance of pink colored solution formed was noted at 500 nm. Further glucose value was calculated using 100 mg/dl standard solution of glucose.
Glucose conc. (mg/dl) = Absorbance (sample) / Absorbance (standard) X 100

Drugs: Alloxan was obtained from Central Drug House, New Delhi, India, Glibenclamide was purchased from Ultratech, New Mumbai, India and The enzyme was purchased from Beacon Diagnostics Pvt Ltd, Kabilpore, Navasari, India. All drugs were suspended in distilled water for oral administration.

Preparation of dose of plant extract: The dried seeds of plant were collected from the local market of Jhansi and authenticated by 'Dr.H.B.Singh, Head, Raw Material, Herbarium and Museum' NISCAIR, New Delhi, and sample was submitted in the museum. (Ref. No. –

NISCAIR/RHM/F-3/2004/Conslt/626/106). Shade dried seeds of *C. anthelminticum* were extracted with distilled water by soxhlation. The crude extract was evaporated at reduced pressure in rotary evaporator (STRIKE-102) and dried further in vacuume dessicator with phosphorus pentaoxide. The dose of 200mg/kg and 500mg/kg was used for the test. The extract was suspended in 5% Tween 80 solution for oral administration(13).

Induction of experimental diabetes: Total of 40 rats were kept at laboratory conditions for 10 days for adaptation of environment. After this the animals allowed to fast for 18 hrs were injected with alloxan monohydrate dissolved in distilled water at a dose of 150 mg/ kg body weight intraperitoneally(14).

The general behavior and blood glucose level were checked for 14 days at constant intervals. After completion of specified days a stabilized increased blood glucose level were registered and animals having more than 250 mg/dl blood glucose were separated and opted for experimentation. During the period of induction 20% death were registered and about 11-12 % of animals did not responded to alloxan.

Experimental Procedure: In the experiment total 30 surviving rats were used, which were further divided into 5 groups

Group - 1. Normal control treated with water

Group - 2. Diabetic control treated with vehicle (Water: Tween 80, 9:1)

Group - 3. Treated with 200 mg/kg body wt extract solution orally

Group - 4. Treated with 500 mg/kg body wt extract solution orally

Group - 5. Treated with Glibenclamide 5mg./kg., p.o. as standard

The treatment was continued for one week. During this period food and water was supplied *ad libitum*. The oral administration of all doses done with orogastric tube. The drug was given once daily in the morning time. The blood glucose was estimated daily for 7 days in fasting condition in the morning by the method described before. The general behavior of the animals were registered daily.

Statistics: All the data were expressed as mean \pm S.D. (Table 1.), and analysis of variance (ANOVA) was used for the statistical analysis. The values were considered to be significant when the *p* value was less than 0.05.

Table 1. Effect of extract of *C. anthelminticum*. on Fasting Blood Glucose Levels of Alloxan Induced Diabetic Rats

Group	Dose (mg/kg)	Blood Glucose Level (mg/dl) at Different Days with Treatment						
		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day7
Normal	-	92.3 \pm 1.4	90.5 \pm 1.1	91.4 \pm 1.3	90.4 \pm 1.3	88.2 \pm 1.4	89.6 \pm 1.5	87.5 \pm 1.2
D.C	-	291.4 \pm 1	288.3 \pm 1	284.4 \pm 1	285.3 \pm 1	284.1 \pm 1	290.3 \pm 1	289.1 \pm 1
Extract	200	0.8	2.6	1.2	2.8	1.4	3.5	2.9
Extract	500	273.2 \pm 1	260.5 \pm 1	243.3 \pm 1	219.2 \pm 1	192.1 \pm 1	180.4 \pm 1	175.9 \pm 1
Glibinclam ide	5	2.6	3.4	1.1	2.4	5.2	4.5	5.1
		301.3 \pm 1	282.8 \pm 1	264.1 \pm 1	241.4 \pm 1	231.7 \pm 1	225.1 \pm 1	185.4 \pm 8.
		5.2	4.9	7.8	6.2	1.3	3.5	1
		320.8 \pm 6.	298.4 \pm 7.	273.5 \pm 5.	246.1 \pm 6.	215.6 \pm 4.	190.1 \pm 6.	164.8 \pm 5.
		1	3	8	4	3	4	2

D.C Diabetic Control

Results

The management of diabetes is more concerning inspite of its treatment. Many synthetic drugs are in the flow for its management but due to side effects, attention toward herbal treatment is increasing day by day. The effect of aqueous extract of seeds were studied on rats for antidiabetic effect. The doses used were 200 mg/ kg body weight and 500 mg/kg body wt. Both the doses were showed marked decrease in the blood glucose level during the study of one week. The standard drug used for the comparison was glibenclamide which showed 48.63% decrease in the blood glucose level. 200 mg dose showed 35.61% decrease and 500 mg dose showed 40.1% decrease in the blood glucose level within one week and there comparisons are presented graphically (Figure 1). In Diabetic controlled group rats there was no significant decrease in the blood glucose level. Simultaneously general behavior of the animals were also recorded during the study and it was found that complications during diabetes like thirst, fatigue, irritation etc. were very less in the animals feed with herbal drug in comparison to diabetic controlled rats and rats which received glibenclamide.

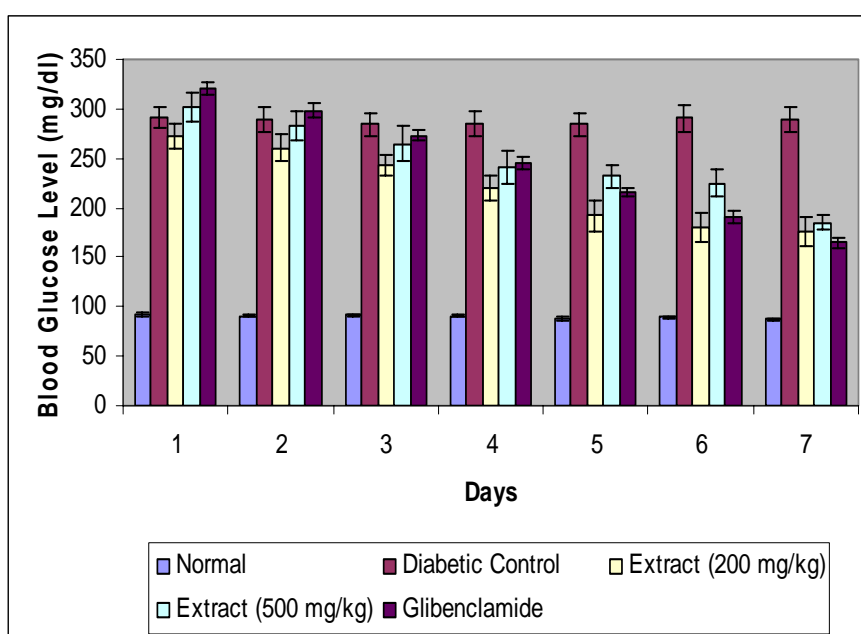


Figure 1. Comparison of Blood Glucose Concentration of Groups in One Week

Discussion

Many of herbal preparations have shown marked potential for the management of diabetes. All forms of diabetes mellitus are due to decrease in the circulating concentration of insulin (insulin deficiency) and a decrease in a response of peripheral tissue to insulin (insulin resistance). These abnormalities lead to alteration in the metabolism of carbohydrates, lipids, ketones and amino acids, the central feature of the syndrome of hyperglycemia.

In the same continuation the effect of *C. anthelminticum* was studied for the management of diabetes mellitus. Alloxan has been observed to cause a massive reduction of the β – cell of the islets of langerhans and induce hyperglycemia(10). The perusal of literature shows that studies were carried out on this plant with regards to other pharmacological properties and phytochemistry but there is no scientific evidence for antidiabetic activity. The plant is credited with flavone glycosides, which in general believed to be responsible for antidiabetic activity. The possible mechanism by which *C. anthelminticum* brings about its hypoglycemic action may be potentiating

the insulin effect of plasma by increasing either the pancreatic secretion of the insulin from the β -cell of islets of langerhans or its release from bound insulin. In this context a number of other plants have also been observed to have hypoglycemic effect . In this study the aqueous extract of *C. anthelminticum* produced a dose dependent percent blood glucose reduction in alloxan induced diabetic rats. After one week treatment, the percent blood glucose reduction produced by the 500 mg/kg dose in diabetic group was greater than 200 mg/kg, although the reduction in the body wt was almost similar in both the groups. As 500 mg/kg treated group showed a greater and persistent fall in blood glucose level till the end, thus it was found more effective than 200 mg/kg dose. So further investigations are going on to target the compound responsible for the antidiabetic potential of the plant. The routine activity of the animals fed with herbal drug was found more normal than the animals treated with standard drug, which could be due to presence of a significant level of steroids present in the plant.

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