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HYPOGLYCAEMIC EFFECT OF AQUEOUS EXTRACT OF *BENINCASA HISPIDA* IN RABBITS

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ABSTRACT

Present study was designed to evaluate hypoglycaemic effect of aqueous extracts of *Benincasa hispida* stem. Rabbits of either sex weighing 2 – 2.5 kg were included in the study. Alloxan monohydrate was given 120mg/kg i.p. to induce experimental diabetes. The animals with fasting blood glucose levels 200-250mg/dl were included in the study. The animals were divided into five groups. Group one and two received 1ml of normal saline (negative control), 0.5mg/kg of glibenclamide (Positive control) and the other three groups were received graded doses of aqueous extract of test drug (*Benincasa Hispida*) i.e., 50mg/kg, 100mg/kg and 200mg/kg respectively. The glucose estimation was done by a glucometer (Accu-Chek, Roche Diagnostics, USA) and the blood was obtained by puncturing marginal vein of the rabbit's ear. The extracts showed dose-dependent significant ($P < 0.05$) reduction in the blood glucose levels, when compared with that of the control rabbits. The most effective percentage reductions in blood glucose level were observed at 200mg/kg. From the experimental findings, it is possible to conclude that aqueous extracts of *Benincasa hispida* studied exhibited promising hypoglycaemic activity in alloxan-induced diabetic rabbits.

Keywords: *Benincasa hispida,* hypoglycaemia, alloxan induced diabetic rabbits

INTRODUCTION

Diabetes has been known in India for centuries as a disease of the affluent class. India faces a grave health care burden due to the high prevalence of type2 diabetes and its sequalae, as a result of societal influences and changing lifestyles.[1] It is apparent that due to the side effects of the currently used drugs, there is a need for safe agents with minimal adverse effects, which can be taken for longer duration. Recently, the search for appropriate hypoglycemic agents has been focused on plants used in traditional medicine partly because of leads provided by traditional medicine to natural products that may be better treatments than currently used drugs.[2]

Benincasa hispida belonging to cucurbitaceous family is employed as a main ingredient in *kusmanda lehyam*, in *Ayurvedic* system of medicine. The *leyham* is used as rejuvenate agent and also in numerous nervous disorders. Many empirical applications have been used in India centuries for various ailments such as dyspepsia, burning sensation, heart disease, vermifuge, and urinary disease.[3, 4] Certain scientific studies carried out reveal its anti inflammatory activity[5], diuretic activity[6], hypoglycaemic[7], Anti Alzheimer's[8], antidiarrheal[9], antioxidant[10], antiulcer[11,] antiobesity[12], antihistaminic[13] and anti cancer property.[14] However there is no report on its hypoglycemic activity of aqueous extracts of *Benincasa hispida* stem in

rabbits. In the light of the above information the present investigation was undertaken to evaluate the hypoglycaemic potential of *Benincasa hispida* stem.

MATERIALS AND METHODS

Benincasa hispida stem were collected from Khammam district, Andhra Pradesh. Sample was authenticated by botanist of Govt. Degree College at Khammam; Voucher sample is deposited at Dept. of Pharmacology, Mamata Medical College hospital, Khammam.

Animals

Rabbits of either sex weighing 2 – 2.5 kg were procured from the institutional animal house. The animals had free access to food and water ad libitum under strict hygienic conditions and maintained in room temperature of 25±1°C, relative humidity 45- 55% and a 12:12h light/dark cycle. All the experiments were conducted in strict compliance according to ethical principles and guidelines provided by CPCSEA and the study protocol was approved by the institutional animal ethical committee.

Preparation of extract

The preparation of extract from the stem of *Benincasa hispida* was done in the department of Pharmacology, Mamata Medical College at Khammam. Shade dried stem of *Benincasa hispida* without leaves was cut into small pieces and was then finely powdered. The powdered stem was extracted with aqueous by process of simple maceration.[15]

Preliminary Chemical test

The aqueous extract of *Benincasa hispida* stem was subjected to qualitative chemical investigation for the identification of phyto constituents[16] like steroids, tannins, alkaloids, carbohydrates, flavonoids and glycosides using appropriate reagents.

Induction of Diabetes

The overnight fasted animals were administered with inj. Alloxan monohydrate reconstituted in sterile normal saline (120mg/kg body weight, intra peritoneal) after taking their fasting blood glucose values. Then they were allowed to have free access to food and water. After 1 week of alloxan induction the animals with fasting blood glucose levels between 200-250mg/dl were included in the study.

Experimental Design

5 groups of animals, each group consisting of 6 animals, with fasting blood glucose levels 200-250mg/dl were included in the study. 1st group was considered as control and was administered with 1ml of sterile normal saline. 2nd group was considered as standard and was administered with 0.5mg/kg of glibenclamide dissolved in distilled water. The other three groups were administered with 50mg/kg, 100mg/kg and 200mg/kg of aqueous extract of test drug. An orogastric tube for feeding the experimental drugs was inserted into esophagus. When it is certain that the tube was at desired level, the drug was pushed into stomach. Then they were allowed to have food and water *ad libitum.*

Estimation of Blood Glucose

The blood glucose levels were estimated alter 12h of fasting and then the doses were administered and blood glucose estimation was done at 2nd, 4th, 6th, 8th, 12th & 24th hourly. The glucose estimation was done by a glucometer (Accu-Chek, Roche Diagnostics, USA) and the blood was obtained by puncturing marginal vein of the rabbit's ear.

Stastical Analysis

The statistical analysis was done by paired *t*-test and wilcoxon signed rank test. All the data reported are expressed as mean ± SEM. The values were considered as significant when the p value was <0.05.

RESULTS

Preliminary Chemical test

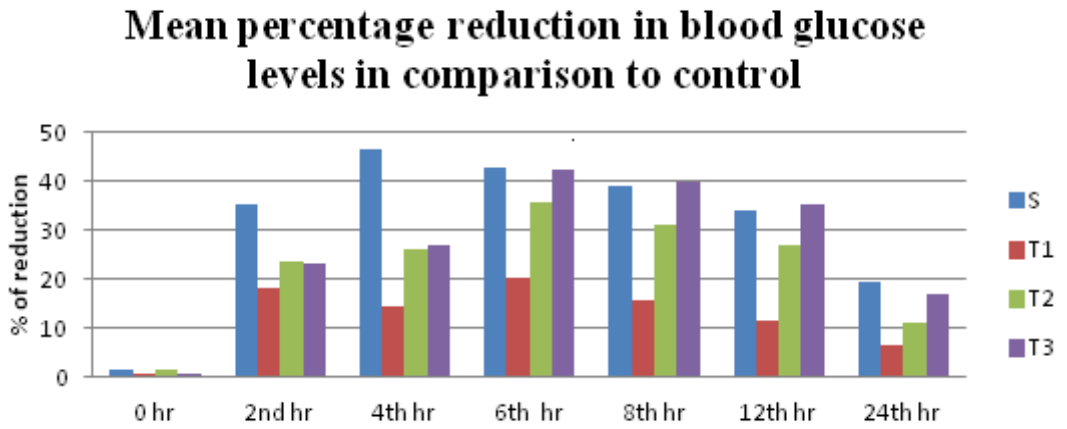
The chemical tests indicate the presence of flavonoids, carbohydrates, tannins, phenols, glycosides and alkaloids in the aqueous extract.

Table 1: Comparison of blood glucose values in Control(C), Standard(S) and Test groups i.e., *Benincasa* 50mg/kg (T1), 100mg/kg (T2), 200mg/kg (T3)

Hour	C	S	T1	T2	T3
0	228.83±6.7	225.66±6.4	229.16±4.7	225.66±6.3	227.83± 6.3
2	270.5±5.6	175.33±2.8	221.33±4.3	206±6.5	208.16± 5.0
4	260±6.8	139.5±4.4	212.33±3.4	192±5.2	188 ± 4.7
6	255.33±6.2	146±4.4	203.66±3.3	164.66±2.1	147.66 ± 3.0
8	249.5±6.2	152.33±4.2	210.66±3.1	171.83±3.2	154.5±3.7
12	244.66±5.6	160.66±4.2	216.5±2.6	178.66±2.5	164.16±3.8
24	237.5±8.4	191.16±6.7	222.66±3.1	211.66±6.5	184.83±1.3

All the data reported are expressed as mean ± S.E.M, P-value <0.05

Figure 1: Comparison of mean % reduction in blood glucose values of Standard(S), *Benincasa*50mg/kg (T1), *Benincasa*100mg/kg (T2), and *Benincasa* 200mg/kg (T3) when compared to Control(C)



DISCUSSION

Numerous oral hypoglycaemic drugs exist alongside insulin but still there is no promising drug therapy to cure diabetes.[17] In recent years, many traditional medicinal plants were tested for their antidiabetic potential in the experimental animals.[18] Although some of these plants have great reputation in the indigenous system of medicine for their antidiabetic activities, many remain to be scientifically established. In the light of the literature of the cucurbitaceous family, an attempt was made to study the hypoglycaemic effect of *Benincasa hispida* aqueous extract.

The present showed that aqueous extract of *Benincasa hispida* stem has significantly decreased the elevated blood glucose levels in Alloxan induce hyperglycemia in rabbit model. Test drug caused variable reductions in blood glucose levels with the three different doses. The mean blood glucose values were significantly decreased with 200mg/kg ($p<0.002$) when compared to control group and it was comparable with that of standard ($p<0.237$). With the doses of 50 and 100mg/kg also there was significant difference in mean blood glucose levels when compared to control ($p<0.005$ & 0.003 respectively) but they were lesser than standard drug ($p<0.018$ & 0.028 respectively). The aqueous extract of *Benincasa hispida* produced a marked decrease in blood glucose levels at 200 mg/kg and the maximum antihyperglycemic effect of standard drug Glibenclamide was seen after 4th hour its administration, whereas the peak action for aqueous extract of *Benincasa* was seen at

6th hour of its administration.[Table 1 and Figure 1]

The hypoglycaemic action of aqueous extract may be due to potentiating the insulin effect of plasma by stimulating insulin release from the remnant pancreatic β-cells or its release from the bound form.[19] Besides, it might involve an extra-pancreatic action in these alloxan-diabetic rabbits, which might include the stimulation of peripheral glucose utilization or enhancing glycolytic and glycogenic processes with concomitant decrease in glycogenolysis and gluconeogenesis.[20] The antihyperglycemic activity of aqueous extract may also be due to the presence of phyto constituents present in the plant.

The preliminary phyto chemical investigation of aqueous extract of *Benincasa* revealed the presence of flavonoids, carbohydrates, tannins, phenols, glycosides and alkaloids. These phytoconstituents have been associated with hypoglycaemic activity.[21] As reported by Glauce *et al*.,[22] flavonoids like myricetin, a polyhydroxylated flavonol has insulinomimetic properties and stimulates lipogenesis and glucose transport in the adipocytes, hence lowering blood sugar. Similar studies on *Pterocarpus marsupium* found epicatechin and catechin flavonoids to have anti-diabetic properties.[23] The alkaloid 1-ephedrine promotes the regeneration of pancreas islets following destruction of the beta cells, hence restoring the secretion of insulin and thus corrects hyperglycaemia.[21] The tannin epigallo-catechin-3-gallate exhibits anti-diabetic activity as demonstrated by Broadhurst *et al*.[24]

CONCLUSION

The mechanism of the hypoglycaemic effects of *Benincasa hispida* extract remains speculative; therefore further studies are required to unravel the pathway of its hypoglycaemic action and to shed more light on the hypoglycaemic constituents of the plants. It is however evident from this research that *Benincasa hispida* extracts studied contains hypoglycaemic agents capable of lowering blood glucose level in alloxan diabetic rabbits.

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