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Effect of Hydro-Alcoholic Extract of Cucurbita Maxima, Fruit Juice and Glibenclamide on Blood Glucose in Diabetic Rats

[1]Lal, V.K., [2]P.P. Gupta, [3]Awanish Pandey and [3]P. Tripathi
[1]Department of Pharmacy, S.I.T.M., Barabanki, U.P.
[2]Department of Pharmacology, B.R.D.M. College, Gorakhpur, U.P.
[3]Department of Pharmacy, ITM, AL-1,
Sec-7, GIDA, Gorakhpur, Uttar Pradesh, 273209, India

Abstract: Problem statement: Cucurbita maxima has been used traditionally in Mexico, China and India as antidiabetic agents. **Approach:** The present study was to evaluate the hypoglycemic activity of fruit juice and hydro-alcoholic extract of Cucurbita maxima for validation of its folkloric use. **Results:** Hypoglycemic activity was evaluated on streptozotocin induced diabetic rats at the doses of 100 and 200 mg kg^{-1} for 28 days. Blood glucose level was evaluated on 0, 7, 14, 21 and 28 days. Oral daily administration of both fruit juice and extract led to significant decrease in hyperglycemia as compared to unfed diabetic control. High dose of both the treatment is more effective than low dose. Extract show more hypoglycemic effect than fruit juice. **Conclusion/Recommendations:** The result of this study scientifically proved the folkloric use of Cucurbita maxima as hypoglycemic agent. Thus the plant can be key contributor in alternative remedy in the treatment of diabetes.

Key words: Diabetes, cucurbita, hypoglycemic activity, hyperglycemia

INTRODUCTION

Focus on plant research has increased worldwide in recent times and a large body of evidence has been collected to show the immense potential of medicinal plant used in various traditional system. There is a estimation that 12.1% of adult in the united states used herbal medicine in 1997 Ang-Lee *et al.* (2001). In 2001 17.8 billion was spent on dietary supplement, 23.6% of it for herbal remedies Marcus and Grollman (2002). In developing countries, all over the world 80% population continues to use traditional medicine in primary medical problem Grover and Yadav (2004). Medicinal plants use has turned out to be an alternative method for the treatment of disease such as diabetes mellitus.

Diabetes Mellitus (DM) is a major chronic life-threatening disorder, in which homeostasis of carbohydrate and lipid metabolism is improperly regulated by the pancreatic hormone, insulin; resulting in an increased blood glucose level. DM is a serious metabolic disease that has a significant impact on the health, quality of life and life expectancy of patients, as well as on the health care system Sancheti *et al*. (2009). It is also one of the most prevalent (the estimated lifetime risk of developing diabetes for individuals born in 2000 is 32.8% for males and 38.5% for females) and costly chronic diseases, which significantly reduces life expectancy. In the year 2000, the total number of people with DM was 151 million and the number is projected to increase by 46% to reach 221 million by the year 2010 and 300 million in 2025 Al-Shamsi *et al*. (2007).

Oral hypoglycemic agents and \or insulin are commonly practiced pharmacological treatment for diabetes mellitus (Charpentier, 2002; Scheen, 1997) but synthetic hypoglycemic agents can produce serious side effects including hematological effects, hypoglycemic coma and disturbance in kidney. In additions they are not suitable for pregnancy Scheen and Lefebvre (1998). In spite of the fact that insulin has become one of the most important therapeutic drugs for diabetes, efforts are ongoing to find insulin substitutes from other sources. In fact, aside from classical chemically prepared antihyperglycemics, the use of traditional medicinal plants with hypoglycemic effect has recently gained popularity world-wide. More than 400 traditional plant treatments for Diabetes Mellitus (DM) have been reported, but only a small number of these have received scientific and medical evaluation Dallak *et al.* (2009). Herbal preparations are frequently considered to be less toxic with fewer side effects.

Corresponding Author: Awanish Pandey, Department of Pharmacy, ITM, AL-1, Sec-7, GIDA, Gorakhpur, Uttar Pradesh, 273209, India

Pumpkin is one such plant that is frequently being used as food as well as traditional medicine for long days. The pumpkin, Cucurbita maxima belongs to family cucurbiteaceae. It is large climbing herb, annual or perennial. Its aerial part consist of flexible succulent stem with trifoliate leaves Hardman *et al*. (2001). It is widely cultivated throughout the India and other warm regions of world for use as vegetable as well as medicine.

This plant has been traditionally used as antidiabetic, antitumor, antihypertensive, anti-inflammatory, immunomodulatory and antibacterial agent (Kirtikar and Basu, 1996; Jia *et al*., 2003; Andrade-Cetto and Heinrich, 2005). Popularity of pumpkin in various traditional system of medicine for several ailments focused investigators attention on this plant.

This study seeks to evaluate the effect of fruit juice and hydro alcoholic extract of aerial part of Cucurbita maxima in glycemic control in streptozotocin induced diabetic rats.

METERIALS AND METHODS

Preparation of Fruit Juice and extract - Mature fruits of Cucurbita maxima were obtained from local market of Gorakhpur and identified by the NBRI, Lucknow, India. A voucher specimen no is 97374. Mature fruits of *C. maxima* were cut in halves. Fibers and seeds were removed and just pulp was used. The juice was obtained with electronic extractor.

The aerial part of the plant Cucurbita maximawere shade dried, milled and ground into coarse powder with the help of a mixer. The powdered material was subjected to cold maceration using sufficient quantity of ethanol and distilled water (1: 1) for 10 days with intermittent shaking in a round bottomed flask. On 10th day, it was strained and marcs were pressed. The expressed liquids were added to the strained liquids and the combined liquids were clarified by filtration and the filtrate was subjected to distillation at temperature 60°C for removing ethanol and water. After distillation, the semi solid obtained was kept for experiment Rajanandh and Kavitha (2010).

Experimental animals-healthy wistar albino rats were used for the study. They were maintained at standard laboratory condition and fed with commercial pellet diet and water ad libitum. The animals were acclimatized to laboratory condition for one week before commencement of experiment.

Acute oral toxicity study of *C. maxima* extract and Fruit Juice- In present study observation of acute toxicity study carried according to OECD guideline 423, none of the rats showed observable signs of toxicity upon single administration of *C. maxima* extract and fruit juice (2 g kg^{-1}, p.o.) on day one. Observations twice daily for 14 days also did not reveal any drug related observable changes. The study was repeated with another set of animals for 14 days and no signs of toxicity were observed.

Induction of diabetes-rats was fasted overnight before inducing diabetes with streptozotocin. The rats were given an intraperitoneal injection of streptozotocin (50 mg kg^{-1}) freshly prepared in 0.1M sodium citrate buffer. The diabetic state was confirmed 48 h after streptozotocin injection. Threshold value of fasting blood glucose was taken as > 200 mg dL^{-1}.

Control and diabetic rats were weighed matched for body weight and divided into following group consisting five animals each.

- Group I-Non diabetic control
- Group II-Diabetic Control
- Group III-Diabetic rats administered with Glibenclamide at dose of 0.5 mg kg^{-1}
- Group IV-Diabetic rats administered with fruit juice in dose of 100 mg kg^{-1}
- Group V-Diabetic rats administered with fruit juice in dose of 200 mg kg^{-1}
- Group VI-Diabetic rats administered with Cucurbita extract in dose of 100 mg kg^{-1}
- Group VII-Diabetic rats administered with Cucurbita extract in dose of 200 mg kg^{-1}

Blood Glucose estimation-blood sample was obtained through puncture tail vein and glucose was estimated on 0, 7, 14, 21 and 28th day by Accu-Check Glucometer.

Statistical analysis-result were expressed as mean ± SEM. Statistical analysis was carried out by using one way analysis of variance followed by Dunnet multiple comparison test. A value of $p<0.05$, $p<0.01$ were considered significant.

RESULTS

In acute oral toxicity studies fruit juice and hydro-alcoholic extract did not show any mortality and toxic effects up to the dose of 2000 mg kg^{-1} body weight. So 1\20th and 1\10th of safe dose is used for the experiments Fig. 1.

Table 1: Effect of hydro-alcoholic extract of cucurbita maxima, fruit juice and Glibenclamide on blood glucose in diabetic rats

	Blood glucose				
Groups	0 Day	7 Day	14 Day	21 Day	28 Day
Normal control	85±1.09	83±2.07	83±1.13	84±2.39	85±3.6
Diabetic control	254±6.3	283±3.78	310±3.9	325±6.8	342±3.9
Diabetic+ Glibenclamide	252±3.9	235±6.1**	180±3.1**	145±6.1**	101±2.8**
Diabetic + juice low dose	255±4.8	221±3.8*	198±5.3*	169±3.8*	147±6.2*
Diabetic + juice high dose	252±3.8	210±3.1**	181±3.5**	156±4.8**	124±3.8**
Diabetic + extract low dose	265±2.8	210±3.8**	178±4.8**	139±2.7**	111±5.8**
Diabetic + extract high dose	260±3.2	192±5.8**	151±2.9**	119±4.7**	100±3.3**

All values are expressed as mean ± SEM (n=5) *: p<0.05, **: p<0.01 as compared to diabetic control. One-way ANOVA followed by Dunnet Multiple Comparison test.

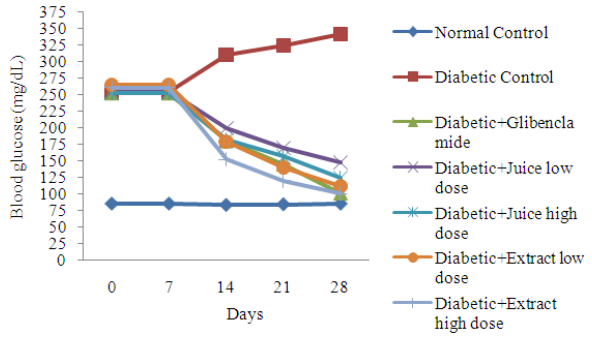

Fig. 1: Effect of hydro-alcoholic extract of Cucurbita maxima,fruit juice and glibenclamide on blood glucose in diabetic rats

STZ-induced diabetic rats exhibiting persistent hyperglycemia (Blood Glucose>200 mg dL^{-1}) were selected for assessing the effect of *C. maxima* fruit juice and *C. maxima* aerial part extract. Oral daily administered dose of 100 and 200 mg kg^{-1} of both fruit juice and extract led to significant decrease in hyperglycemia as shown in Table 1. High dose of both treatments is more effective than low dose. Extract show more effect than fruit juice. All treatment show highly significant ($p<0.01$) decrease in blood glucose except low dose of fruit juice ($p<0.05$) as compared to unfed diabetic control. So it is concluded from the study that *C. maxima* fruit juice and extract show significant decrease in blood glucose of diabetic rats and extract is more effective than fruit juice.

DISCUSSION

Streptozotocin is a valuable agent for the production of diabetes because it allows the consistent production of diabetic states with mild, moderate and severe hyperglycemia, where animals with mild or moderate diabetes have provided an opportunity to study the influence of oral hypoglycemic agents and streptozotocin induced diabetic rats have been widely used as a model for diabetes mellitus in experimental animal Murphy and Anderson (1974).

This research was performed for (a) to characterize the hypoglycemic effect of fruit pulp of Cucurbita maxima (b) to determine the hypoglycemic effect of hydro alcoholic extract of its plant by its daily administration for 28 days. In both cases the result showed significant hypoglycemic effect and hypoglycemic effect was found more with hydro alcoholic extract of plant than fruit juice. C. maxima are considered as an edible resources. Neverthless, people who consume these fruits and plant prepare different dishes. These process may have altered some components in the fruit and plant, thus reducing its effect.

CONCLUSION

In conclusion result of the present study showed that the fruit pulp and hydro-alcoholic extract of Cucurbita have orally produced hypoglycemic effect on streptozotocin induced diabetic rats and extract is more effective than fruit juice. It is necessary to do further study using Cucurbita maxima in order to know if the active component of this plant represents an alternative therapy for the control of blood glucose level in diabetic patients.

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