

**ANTIDIABETIC ACTIVITY OF COCCINTIA GRANDIS IN ALLOXAN INDUCED
DIABETIC RATS****Shubham G. Suryawanshi*¹, Kalyani R. Shinde¹, Prof. P. N. Folane¹, Prof. S. L. Khedekar² and
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ABSTRACT

Diabetes mellitus is lifestyle disease rapidly spreading in India. It has been major health issue in south-east Asia and world's largest numbers of diabetics are found in India. By 2019, 60.8 million diabetics are found and this will rise up to 97 million by 2030. Therefore looking at the scenario and possible complications of uncontrolled B.G.L, different modes of therapy have been practiced. The present work is an effort to study Antidiabetic's activity of coccintia grandis in alloxan induced diabetic rats. Coccintia grandis is commonly known as Gram (ivy gourd. Family- CCucurbitaceae). A single dose of (150 mg/kg) alloxan prepared in normal saline solution was injected intraperitoneally to induce diabetes in rats. The age matched control rats receives an equal volume of citrate buffer and used along with diabetic animals. Diabetes was confirmed after 48 hr of alloxan injection. The rats having plasma glucose level more than 300 mg/dl were selected and study was conducted for 21 days. The rats were divided into six groups and serum glucose levels were assessed by GOD - PAP method. The BGL and body weights were taken at day 1, day 3, day 7 and day 21. This investigation proves that coccintia grandis shows beneficial effect in diabetes. It is found to reduce the BGL and prevented loss of Body weight in diabetic rats and does not have any effect on normal glycemic level. Thus, it can be concluded that coccintia grandis can be used as supportive therapy for diabetes mellitus.

KEYWORDS: Alloxan, Antidiabetic, 5% Glucose, Metformin, Ethanol.**INTRODUCTION**

Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia. It is associated with abnormalities in carbohydrate, fat and protein metabolism and results in chronic complications including microvascular, macrovascular and neuropathic disorders. Several distinct types of DM exist and are caused by a complex interaction of genetics, environmental factors and life-style choices. Depending on the etiology of the DM, factors contributing to hyperglycemia may include reduced insulin secretion, decreased glucose utilization and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiological changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.

Coccinia grandis, a member of Family – Cucurbitaceae. Also Known as Scarlet gourd, tindora and Kowai fruit. It grows primarily in tropical climates and is commonly found in the southern Indian State. Coccintia grandis is cooked as a vegetable.

The Fruit of Coccinia grandis per 100g edible Portion has 93.5g- Water, 1.2g-Protein, 3.1g- Carbohydrate, 1.6g-fibre, 40mg-Ca, 30mg-P, 1.4mg- Fe, 0.07mg-thiamin, 0.08mg- riboflavin, 0.7mg-niacin, 1.4mg- ascorbic acid. Some chemical Constituents : B- Amyrin Acetate, Lupeol, cucurbitacin B, Teraxerone, Teraxrol, B-Carotene, Lycopene, cryptoxanthin, stigmas- 7- en-3- one. The study conducted Coccinia grandis having Hypoglycemic, analgesic, antipyretic, hepatoprotective, tuberculosis, eczema, antidiabetic and anti-inflammatory effects significantly on Patients.

MATERIALS AND METHODS**Collection and authentication of the plants**

The fruit of the Plant Coccintia grandis was collected from the local market of Buldhana District. They were authenticated by Head of Department of botany Shri. Shivaji Science College chikhli, District Buldana, Maharashtra. (India).

Chemicals

Alloxan (Ozone international mumbai), Ethanol, Normal saline solution was procured and used, Metformin, 5% Glucose, Tween 80.

Instruments: Glucometer-Accu-Cheak Instant.

Extraction of the Plant

Coccinia grandis: Coccintia grandis fruit was collected, air-dried and powdered. 1500 gm of the powdered seeds was extracted in soxhlet apparatus with 70% of ethanol

Preparation of Coccintia grandis

The individual extract of Coccintia grandis was prepared in Pharmacognosy lab-1 at Anuradha college of pharmacy, Chikhli.

Experimental designing

36 Healthy adult albino Wistar rats of either sex, 8-10 weeks old, weighing about 150-200 gm were used in the experiments. Animals were housed in polypropylene cages maintained under standard condition (12 hours light / dark cycle; 25 ± 3 °C, 45-65% humidity) and had free access to standard rat feed (Hindustan Lever Ltd., India) and water. All the animals were acclimatized to laboratory condition for a week before commencement of the experiment.

Study (OECD Guideline 423 Acute Toxicity)

Animals were fasted prior to dosing, food but not water was withheld overnight. Following the period of fasting, the animals were weighed and test substance was administered. After the substance had been administered, food was withheld for further 3-4 hours. As a dose was administered in fractions over a period, it was necessary to provide the animals with food and water depending on the length of the period. (Ghosh MN, 1984; Turner R, 1965)

Three animals were used for each step. The dose level of the extract to be used as the starting dose was selected from one of the four fixed dose levels 500, 1000, 1500 and 2000mg/kg body weight (Lorke D, 1983). The starting dose levels such that which was most likely to produce mortality in some of the dosed animals. After administration of the test sample, the animals were observed continuously for first four hours for behavioral changes and at the end of 48 hour for mortality, if any.

Glucose Tolerance Test

Animals were fasted for 24 hours before experiment but were allowed free access to water. Fasted rats were divided into three groups of 6 animals each (WHO, 1999)

Group I - Control animals received 5% Tween 80 in distilled water at 5ml/kg b.w.p.o.

Group II - 100 mg/kg b.w. of Coccintia grandis p.o.

Group III - 200 mg/kg b.w. of Coccintia grandis p.o.

Group IV - 400 mg/kg b.w. of Coccintia grandis p.o.

to the animals. Blood samples were collected from tail just prior to glucose administration and at 60, 120 and 180 minutes after glucose loading. The glucose levels were estimated for all the three groups by tail tipping method using Accu-check glucometer. After 30 minutes of the treatment to the Groups I, II and III, 2gm/kg body weight glucose was given orally

Effect of Formulation on Blood Glucose Levels in Alloxan Induced Diabetic Rats

36 male Wistar rats (150-200g) were made diabetic by a single i.p injection of Alloxan at a dose of 120 mg/kg i.p. after dissolving it in freshly prepared 0.1M citrate buffer (pH 4.5). The rats were maintained on 5 % glucose solution for next 24 hour to prevent hypoglycemia. Five days later blood samples were drawn from tail vein and glucose levels were determined to confirm the development of diabetes (>300mg/dl). The diabetic rats were divided into six groups, each containing six animals.

Group I- Normal control rats received 5% Tween 80 in distilled water p.o. at 5 ml/kg b.w.

Group II - Diabetic control rats received 5% Tween 80 in distilled water p.o.

Group III - Diabetic rats received Coccintia grandis 100mg/kg b.w., p.o.

Group IV - Diabetic rats received Coccintia grandis 200mg/kg b.w., p.o.

Group V - Diabetic rats received Coccintia grandis 400mg/kg b.w., p.o.

Group VI - Diabetic received Metformin at the dose of 5mg/kg b.w., p.o.

The administrations of extracts were continued for 21 days, once daily. Blood samples were collected through the tail vein on days 1, 7, 14 and 21 after drug administration and the blood glucose levels were estimated using Accu-check Glucometer

Statistical Analysis

Results were expressed as Mean \pm SEM. Statistical analysis were performed with Graph pad prism 5 software using one way analysis of variance (ANOVA) followed by Dunnett's t test. P values less than * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ was considered to be statistically significant, when compared with control and standard group as applicable (Diabetes and Metabolism 1989).

RESULTS

Dried powdered parts of the respective plant was extracted using soxhlet method and percentage yield of the extract are tabulated in table 1.

Table 1: Percentage yield of extract.

Sr no.	Plant Extract	Part used	Extraction Method	Solvent used	%yield of extract(w/w)
1.	Coccintia grandis	Fruit	soxhlation	ethanol	12.7%

Effect of Coccintia grandis on Blood Glucose Levels

21 days treatment of Coccintia grandis at the dose of 100mg/kg, 200mg/kg, 400mg/kg showed significant

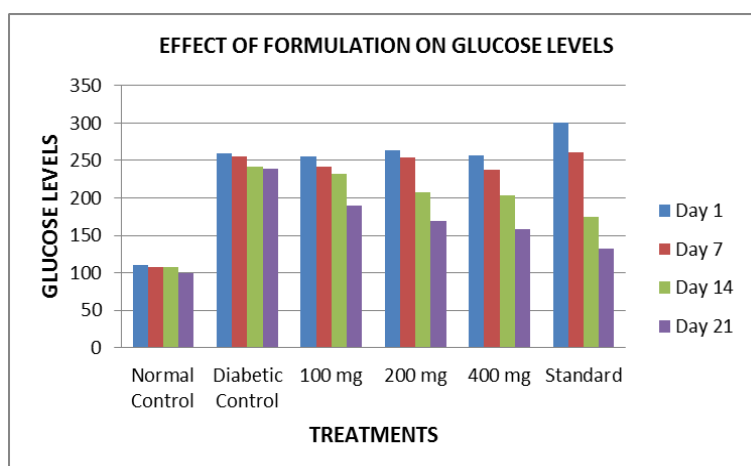
decrease in blood glucose level on days 7 & 21 as compared to diabetic control group. The result was found to be dose and time dependent. The result obtained with

Coccintia grandis on blood glucose levels are given in table 2 and illustrated in Graph 1.

Table 2: Effect of Coccintia grandis on Blood Glucose Level.

Treatment Group	Blood Glucose Level (mg/dl)				Comments
	Day 1	Day 7	Day 14	Day 21	
Normal	110±7.40	108±8.25	107±7.39	99.83±6.39	–
Diabetic Control	259±8.24	256±9.84	242±13.81	239±9.84	Blood sugar level increases
Coccintia grandis 100 mg/kg p.o	255±1.69	242±2.05	232±2.54	190±2.05	Blood sugar level reduced as compared to diabetic control
Coccintia grandis 200 mg/kg p.o	263±1.24	254±2.44*	208±2.05**	169±1.63**	Blood sugar level reduced as compared to last table
Coccintia grandis 400 mg/kg p.o	257±4.21	238±2.38*	204±2.94**	158±3.78**	Blood sugar level reduced as compared to last table
Standard Metformin 5mg/kg b.w., p.o	301±11.62	261.33±9.76*	174.5±8.03**	132.17±9.08**	

Values are expressed as Mean±SEM (n=6); *P<0.05, **P<0.01, ***P<0.001 was considered significant with respect to control group using ANOVA followed by Dunnett's t-test.



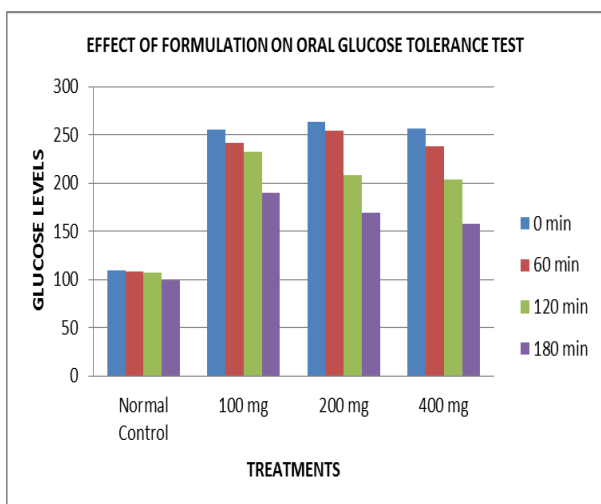
Graph 1: Values are expressed as Mean±SD *<0.01 was considered significant with respect to control group using ANOVA followed by Dunnett's t-test.

The result obtained with oral glucose tolerance test on blood glucose levels are given in table 3 and illustrated in Graph 2. The result of the test indicated significant decrease in blood glucose level on Days 1, 3, 5, 21. In extract treated group as compared to control treated group.

Table 3: Oral Glucose Tolerance Test.

Treatment group	Blood Glucose Level (mg/dl)			
	0 min	60 min	120 min	180 min
Normal	93.67±3.87	156.54±9.21	189.08±8.99	247.72±10.22
Coccintia Grandis 100 mg/kg p.o	86.78±4.92	127.39±6.87**	97.64±5.81**	90.39±4.85**
Coccintia Grandis 200 mg/kg p.o	91.56±4.63	119.02±7.62**	95.37±5.83**	87.65±3.91**
Coccintia Grandis 400 mg/kg p.o	87.64±5.23	117.04 ±8.65**	93.23±7.45**	85.53 ±5.63**

Values are expressed as Mean±SEM (n=6); *P<0.05, **P<0.01, ***P<0.001 was considered significant with respect to control group using ANOVA followed by Dunnett's t-test.



Graph 2: Values are expressed as Mean±SD * <0.01 was considered significant with respect to control group using ANOVA followed by Dunnett's t-test.

DISCUSSION

Diabetes mellitus is now recognized as one of the major killer diseases and a leading cause of death, claiming many lives world over. Oral hypoglycemic agent especially the sulphonylureas and biguanides have been commonly used in the diseases management especially type II diabetes but not without serious side effects. Consequently, attention has been focused on the use of plants/herbal remedies believed to be safer and devoid of serious side effect as alternative in the treatment of diabetics. The *Coccintia grandis* fruit is one of such herbal remedies used to evaluate antidiabetic activity. The extraction value of *Coccintia grandis* was 12.7% w/w. The Maximum Tolerated Dose (MTD) of the drug preparation was determined to be 2000 mg/kg b.w. for p.o. as there was no lethal effect at the dose. Thus, the test dose was decided as 200 mg/kg b.w.p.o. (1/10th of MTD) and 400 mg/kg b.w. p.o. was also decided for the experimental study.

The antihyperglycemic activity of one of the *coccintia grandis* was screened using glucose tolerance test. The *coccintia grandis* tested for this activity exhibited significant antihyperglycemic activity at a dose level 400mg/kg b.w. (93.67 ± 3.87) as compared to control (247.72 ± 10.22) at 180 min. The *coccintia grandis* drug was effective in decreasing the blood glucose levels in diabetic rats at both the low and high dose significantly. In this present investigation showed significant antihyperglycemic. So it can be used as an agent for treatment of diabetic effect of *Coccintia grandis* may be due to increase in insulin secretion or decrease in insulin resistance or increased glucose absorption.

CONCLUSION

The WHO has recommended and encouraged the use of alternative therapy especially in countries where access to the conventional treatment of diabetes is not adequate. The *Coccintia grandis* is used in various systems of

medicine for a wide range of properties. In addition to antidiabetic activity.

On the basis of these results, It could be concluded that *coccintia grandis*, exerts a significant antidiabetic effect. The *coccintia grandis* may be considered as safe supplementary therapy for a long term and effective management of diabetic patient thus, further studies can be done to identify the exact chemical constituents and mechanism of action which are responsible for the said activity. In conclusion, the overall result of this study have clearly shown that *coccintia grandis* could be used as antidiabetic activity.

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