

Anti-hyperglycaemic and Insulin Release Effects of *Coccinia grandis* (L.) Voigt Leaves in Normal and Alloxan Diabetic Rats

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ABSTRACT

Coccinia grandis (L.) Voigt (Cucurbitaceae), occurs throughout the world and has intensive popular use in the treatment of infections. The main aim of the present work was to investigate the antidiabetic effects of aqueous extracts of leaves of *C. grandis* obtained by Decoction method. Graded doses of the aqueous extract were administered to normal and experimental diabetic rats for 10 days. Significant ($p < 0.05$) reduction in fasting blood glucose levels were observed in the normal as well as in the treated diabetic animals. Serum insulin levels were not stimulated in the animals treated with the extract. The changes in body weight, serum lipid profiles, liver glycogen levels were assessed in the extract treated diabetic rats and compared with diabetic control and normal animals.

Key words: Antidiabetic activity, alloxan monohydrate, Gliben clamide, *Coccinia grandis*.

INTRODUCTION

Diabetes mellitus (DM) is a serious health problem with high rates of incidence and mortality. DM is characterized by elevated plasma glucose concentrations resulting from insufficient insulin, insulin resistance or both leading to metabolic abnormalities in carbohydrates, lipids and proteins (Hernandez-galicia *et al.*, 2002). According to the World Health Organization, more than 70% of the world's population must use traditional medicine to satisfy their principal health needs (Farnsworth *et al.*, 1985). A great number of medicinal plants used in the control of the DM have been reported (Baily & Day 1989; Marles & Farnsworth, 1994). However these plants represent alternatives to developing new oral hypoglycemic agents, appropriate ethnobotanical information is scarce, obscure and ambiguous.

Coccinia grandis (L.) Voigt. (Family: Cucurbitaceae) is a climbing perennial herb distributed almost all over the world. The leaves of the plant possess antidiabetic, anti-inflammatory, antipyretic, analgesic, antispasmodic, antimicrobial, cathartic and expectorant activities (Asolkar *et al.*, 1992; Nadkami and Nadkami, 1992). The leaves contain Triterpenoids, alkaloids and tannins (Rastogi. and Mehrota, 1990). The objective of the present work is to make an analysis of the ethnobotanical information on *Coccinia grandis* used in South Indian region for diabetes mellitus control.

MATERIAL AND METHODS

Plant material and decoction preparation

The leaves of *C. grandis* were collected in December 2007 from Coimbatore district, Tamilnadu, India and authenticated by Botanical Survey of India (Southern circle), Coimbatore, Tamil Nadu, India. A voucher specimen is being maintained in the RVS College of Arts and Science and RVS Medical & Ayurvedic foundation, Coimbatore. The leaves were shade dried and powdered.

About 150 g of dried powdered leaves were boiled in 1 liter of water for 5 min, allowing the decoction to stand for 30 min and filtered through Whatman no.1 filter paper which yielded a decoction with a 15% higher concentration than that of produced by the method described by Teixeira *et al.*, (1990).

Test animals

The test animals used in the study were procured from Karpagam Medical and Research Foundation. Six Albino rats of wistar strain weighing 150 - 200 g bred in Animal Tissue Culture Lab, Karpagam Arts and Science College. They were individually housed in polypropylene cages in well-ventilated rooms, under hygienic conditions. Animals were given water *ad libitum* and fed with rat pellet feed.

Induction of Experimental Diabetes and Treatment

Alloxan monohydrate solution of 10 mg/ml was prepared in ice-cold citrate buffer 0.1 M, pH 4.5 and was administered to the rats within 5 min at a dose of 50 mg/kg body weight intraperitoneally. After 48 h of alloxan monohydrate administration, rats with moderate diabetes having glycosuria and hyperglycemia were taken for the experiment.

Rats weighing 150 – 160 g, fasted over night were used for induction of diabetes. Rats were divided into two sets; diabetic and non-diabetic. Group I received normal diet and served as normal control. Group II consists of alloxan-induced rats receiving normal diet and serving as diabetic control. Group III consists of alloxan induced rats receiving Gliben clamide (synthetic antidiabetic drug) at 0.5 mg/kg body weight once a day orally for 10 days. Group IV consists of alloxan-induced rats receiving *C. grandis* (1 ml) once a day orally for 10 days. Group V consists of normal rats receiving *C. grandis* (1 ml) once a day orally for 10 days.

Blood samples were collected through the tail vein just prior to and on days 10 after drug administration. The blood glucose, urea, cholesterol, serum glutamate oxygenate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) were determined for all the samples.

Statistics

The data were analyzed using one-way ANOVA followed by Dunnett's test. The level of significance was set at 0.05.

RESULTS AND DISCUSSION

The extracts of *C. grandis* produced significant changes in the alloxan-induced diabetic rats (Table 1). The aqueous extracts of *C. grandis* reduced the glucose levels considerably. Treatment of the diabetic rats with Gliben clamide (10 mg/kg) also reduced blood glucose level. The prolonged treatment of *C. grandis* extracts on alloxan-induced diabetes rats produced consistent reduction in the blood glucose levels. The aqueous extract also reduced urea, protein and cholesterol during the 10 days treatment period (Tables 1 and 2).

It is possible that the drug may be acting by potentiating the pancreatic secretion or increasing the glucose uptake. Hypercholesterolemia, hypertriglyceridemia and hyperurea have been reported to occur in alloxan diabetic rats (Resmi *et al.*, 2001; Joy and Kuttan, 1999). Increase in glycogen in liver can be brought about by an increase in glycogenesis and/or decrease a glycogenolysis. Therefore, the *C. grandis* extract could have stimulated glycogenesis

and/or inhibited glycogenolysis in diabetic rat liver. The plant extracts treated animals showed non-toxicity of the extract, which indicates that unlike insulin and other common hypoglycemic agents, overdose of the drug may not result in hypoglycemia. The increase in total protein (Table 2) may be due to changes in circulating amino acids levels, hepatic amino acids uptake, and muscle output of amino acid concentrations (Felig *et al.*, 1977). The non-protein nitrogen compound urea is found to be increased when compared to plant extract treated rats. The level of SGPT and SGOT increased remarkably in the *C. grandis* extract-treated rats (Nagappa *et al.*, 2003). Our results support Ghosh *et al.*, (2004) who reported that transaminase activity is increased in serum of diabetics. In diabetic animals, the changes in level of serum enzymes are directly related to changes in the metabolism (Felig *et al.*, 1977).

C. grandis leaf extract showed significant anti-diabetic effect in diabetic rats after oral administration. Thus, the claim made by the Indian systems of medicine regarding the use of leaf extract of this plant in the treatment of diabetes is validated. Present efforts are directed to isolate the active constituents and elucidation of mechanism of action.

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Table 1. Glucose and cholesterol content of serum of control and experimental rat groups.

Parameters	(Group I)	(Group II)	(Group III)	(Group V)	(Group V)
Glucose (mg/dl)	114.71± 1.60	256.39± 7.22***	146.90 ± 1.76**	154.9± 14.3c***	160± 17.10.5d***
Cholesterol (mg/dl)	120± 2.5	244.80± 6.28***	115± 3.40b***	112.2± 7.1c***	117± 5.9dNS

Table 2. The Concentrations of urea, total protein, SGOT and SGPT in serum of control and experimental groups.

Parameters	(Group I)	(Group II)	(Group III)	(Group IV)	(Group V)
Urea (mg/dl)	44±2.8	61.5±5.0a***	56.0±5.0b***	88 ±3.2c***	50.0±2.8d**
SGOT (U/L)	23.3±1.2	24.2± 3.8a***	28.0±3.4b***	31.5±2.7c***	41.6±3.6d***
SGPT (U/L)	24.6±2.1	28.0±3.4a***	32.0±2.8b***	38.5±1.0c***	42.0±7.1d***
Total protein (g/dl)	6.95±0.42	3.9±0.6a***	2.4±0.5b***	7.3±1.0c***	7.9±0.8d*

Values are taken as mean of five individual's experiments and expressed as Mean ± S.D.

***p< 0.001, **p< 0.01 and *p< 0.05. NS = Not Significant.

Group I & II - Normal and Diabetic control

Group III - Diabetic treated with Synthetic drug

Group IV - Diabetic treated with Plant drug

Group V - Plant drug