



HYPOGLYCEMIC AND HYPOLIPIDEMIC ACTIVITY OF LEAVES OF *GARDENIA TAITENSIS* ON STREPTOZOTOCIN INDUCED DIABETIC RATS

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ABSTRACT

The present study was aimed to evaluate the anti diabetic - activity potential of *Gardenia taitensis* leaves against streptozotocin (STZ) induced experimental rats. Ethanolic extract of leaves of *Gardenia taitensis* was administered to streptozotocin induced rats. Glibenclamide was used as a standard drug. Blood glucose levels were determined after oral administration of a dose of *Gardenia taitensis* (400 mg/kg b. wt) in diabetic groups. Blood glucose levels were determined on 0, 7th, 14th and 21st day after oral administration of ethanolic extracts of *Gardenia taitensis* (400 mg/kg). An ethanolic extract of *Gardenia taitensis* was found to reduce blood sugar in streptozotocin induced diabetic rats. Reduction in blood sugar could be seen from 7th day after continuous administration of the extract. The effect of extracts of *Gardenia taitensis* on serum lipid profile like Total cholesterol, triglycerides, low density, very low density and high density lipoprotein were also measured in the diabetic and non diabetic rats. There was significant reduction in Total cholesterol, LDL cholesterol, VLDL cholesterol and improvement in HDL cholesterol in diabetic rats. These results indicated that *Gardenia taitensis* possesses a hypoglycemic and hypolipidemic effect.

Key words: *Gardenia taitensis*, Glibenclamide, Hypoglycemia, Hypolipidemic, Streptozotocin.

INTRODUCTION

Diabetes mellitus is a complex disorder that characterized by hyperglycemia resulting from malfunction in insulin secretion and/or insulin action both causing by impaired metabolism of glucose, lipids and protein [1]. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs [2]. In diabetic rats, the utilization of impaired carbohydrate leads to accelerate lipolysis, resulted in hyperlipidemia [3, 4]. Despite the presence of known hypoglycemic medicine in the pharmaceutical market, diabetes and the related complications continued to be a major medical problem. Recently, some medicinal plants have been reported to be useful in diabetes worldwide and have been used empirically as hypoglycemic and hypolipidemic remedies [5-10]. Diabetes mellitus is known to cause hyperlipidemia through various metabolic derangements. Among several metabolic derangements, insulin deficiency has been known to stimulate lipolysis in the adipose tissue and gives rise to

hyperlipidemia and fatty liver. Thus, in diabetes hypercholesterolemia and hypertriglyceridemia often occurs [11]. More than 400 plant species having hypoglycemic activity have been available in literature [12, 13]; however, searching for new hypoglycemic drugs from natural plants is still attractive because they contain substances which take alternative and safe effect on diabetes mellitus. Most of plants contain glycosides, alkaloids, terpenoids, flavonoids, cartenoids, etc., that are frequently implicated as having hypoglycemic effect [14]. *Gardenia taitensis* is a herbaceous member of the family Rubiaceae. It is a shrub or small tree to 6 m high with conspicuous stipules. Leaves are opposite, petiolate, broadly elliptical, up to 15 cm long. Flowers are showy, white, fragrant, borne singly on stems arising from upper leaf axils. Fruit a yellowish-green sub-globose-to-ellipsoid capsule up to 5 cm long containing numerous whitish seeds surrounded by an orangish pulp. Flowers available throughout the year, fruit often rare.

It is common along coastal limestone rock and occasionally in coastal forest near the shore. It is also widely cultivated in villages. It is native to the South-West Pacific Islands of Fiji, Vanuatu, Tonga, and nearby islands, and widely cultivated and naturalized on many other islands in the South Pacific. It contains 9,19 Cyclolanostane-3, 23-dione [15]. Cook Islanders merely smell the flowers to relieve headaches. Migraine headaches may be cured by immersing the head in a solution with the crushed flowers. The flowers are also used to treat childhood diseases. In American Samoa, a medicine including the leaves of this plant is used to purify the blood in prenatal care and diabetes treatment. The plant is also used in treating inflammations in children. In Futuna, however, it is thought that an infusion of the bark can be used to induce an abortion. Vaginal bleeding is treated with an infusion of the leaves [15-16]. However, no simultaneous hypoglycemic and hypolipidemic activity on the leaves of *Gardenia taitensis* was scientifically available. Therefore, the present study has been carried out to explore the hypoglycemic and hypolipidemic activity of *Gardenia taitensis*.

MATERIALS AND METHODS

Materials:

The leaves of *Gardenia taitensis* was collected from adjoining areas of collected from Tirunelveli District, in the Month of August 2010. The plant was authenticated by Dr.V. Chelladurai, Research Officer Botany. C.C.R.A.S., Govt. of India., by carrying out macroscopic and microscopic evaluation.

Animals:

Male Wistar rats of body wt. 180–200 g were obtained from Sree Vidyanikethan College of Pharmacy, Sree Sainathnagar, Chandragiri (M), Tirupati, Andhra Pradesh. The animals were fed on standard pellet diet (Hindustan Lever, Mumbai, India) and water ad libitum. The rats used in the present study were maintained in accordance with guidelines of the CPCSEA, India and the study approved by the ethical committee.

Preparation of the root extract:

The shade dried leaves was powdered to get a coarse granule. About 250 g of dried powder were extracted with 90% ethanol by continuous hot percolation, using soxhlet apparatus. The resulted dark – brown extract was concentrated up to 100 ml on Rota vapour under reduced pressure. The concentrated crude extracts were lyophilized in to powder and used for the study.

The preliminary phytochemical analysis:

The preliminary phytochemical studies were performed for testing different chemical groups present in

ethanolic extract [17]. Phytochemical screening gave positive test for alkaloids.

Toxicity studies:

The animals were divided into six groups separately and were treated orally with ethanolic extracts of *Gardenia taitensis* at 100, 200 and 400 mg/kg, body weight doses. The animals were continuously observed for 1 hr., then frequently for 14 days. The parameters observed were grooming, hyperactivity, sedation, loss of righting reflex, respiratory rate and convulsion [18].

Streptozotocin-induced diabetic rats:

Streptozotocin (STZ), was dissolved in ice-cold normal saline immediately before use. Diabetes was induced in rats by intraperitoneal (i.p) injection of streptozotocin at a dose of 50 mg/kg [19]. Forty eight hours after streptozotocin administration, blood samples were drawn from tail and glucose levels determined to confirm diabetes. The rats were divided into 4 groups as follows, first group served as normal control, received food and water. Second group served as diabetic control, received 0.5 ml of 5% Tween 80; third group served as (diabetic control), received glibenclamide (0.5 mg/kg p.o.), and fourth groups, (diabetic rats) received 400 mg/kg, b.wt. of ethanolic extracts of *Bruguiera gymnorrhiza*. The treatment was continued daily for 21days. Blood drop was collected from the tail for glucose estimation, just before drug administration on 1st day and 1 h after sample administration on days 7, 14 and 21 (Table 1).

Biochemical parameters:

Triglycerides, cholesterol, HDL-cholesterol, and LDL-cholesterol were estimated from the serum by using standard kits [20-22].

Statistical evaluation:

All the data are presented as mean \pm SEM. The differences between group were evaluated by one-way analysis of variance (ANOVA) followed by the Dunnett's multiple comparisons test's <0.01 was considered to be significant.

RESULTS AND DISCUSSION

Phytochemical screening:

Phytochemical screening of both the plant extracts revealed that the presence of alkaloids, phytosterols, carbohydrates and saponins.

Toxicity studies:

In performing preliminary test for pharmacological activity in rats, ethanolic extract did not produce any significant changes in the behavioral or neurological

responses upto 400 mg/kg body weight. Acute toxicity studies revealed the non-toxic nature of the ethanolic extracts of *Gardenia taitensis*. The result obtained from the LD50 study indicates that ethanolic extract of *Gardenia taitensis* is safer to use in animals even at a dose of 400 mg/kg p.o.

Hypoglycemic Effects:

Effect of ethanolic extract of *Gardenia taitensis* on serum glucose levels in diabetic rats was depicted in Table 1. In animals treated with streptozotocin (50 mg/kg i.p) (Group II), a significant increase in serum glucose level was observed on 7th, 14th, 21st, and 28th day when compared with normal rats (Group I). Group III received glibenclamide (0.5 mg/kg p.o.) showed decrease in serum glucose level when compared with diabetic control rats (Group II). After the oral administration of ethanolic extract of *Gardenia taitensis* in diabetic control rats, a significant reduction in blood glucose level was observed on the 7th, 14th, 21st, and 28th day compared with diabetic control rats (Group II).

Anti-hyperlipidaemic activity:

The lipid profiles in control and experimental rats are depicted in Table 2 in STZ induced diabetic rats. The diabetic control rats (Group II) showed significant increase in serum triglycerides, Total cholesterol, very low density lipoproteins (VLDL), low density lipoproteins (LDL), and High density lipoproteins (HDL) when compared with normal (Group I). Standard glibenclamide (Group III) also reduced triglycerides, Total cholesterol, very low density lipoproteins (VLDL), low density lipoproteins (LDL), and increased High density lipoproteins (HDL) when compared with normal (Group I). The ethanolic extract showed significant decrease ($p < 0.001$) in Total cholesterol, LDL, VLDL, Triglycerides and significant increase ($p < 0.001$) in HDL when compared with diabetic control group (Group II). All these effects were observed on day 14th, 21st, and 28th. The present experimental result indicated that ethanolic extracts exhibited a potent blood glucose lowering properties in STZ diabetic rats.

Tab 1: Anti-hyperglycemic activity of extracts of *Gardenia taitensis* on STZ induced diabetic rats.

Groups	0 day (mg/ml)	After 7days (mg/ml)	After 14days (mg/ml)	After 21days (mg/ml)	After 28days (mg/ml)
Normal control	64.57±1.47	98.87±1.06	87.35±2.25	81.57±2.09	68.17±2.13
Diabetic control	226 ±1.47	216.5±2.60*	213 ±2.45*	210.12 ± 1.54*	204± 3.12*
Glibenclamide (0.5mg/kg)	234.32±1.92***	186.23 ±2.84***	131.54 ±1.68 ***	94.57±2.06 ***	94.14±2.21***
Ethanolic extract (400mg/kg)	235 ±1.24***	192±1.15***	135.67 ±1.57 ***	100.47±2.24 ***	90.04±2.25***

The values are mean ± SEM, n=6, When compared with diabetic control * $p < 0.05$, ** $p < 0.001$, *** $p < 0.001$ (One way ANOVA followed by Dunnett's, multiple comparison test).

Tab 2: Hypolipidemic activity of extracts of *Gardenia taitensis* on STZ induced diabetic rats.

Groups	TC	TG	HDL C	LDL C	VLDL C
Normal control	84 ±1.05	68.37 ±1.75	37.40±0.29	45±2.54	17.03±0.55
Diabetic control	139.13 ±1.95*	135±1.58*	27.42±1.05*	88.46±2.55*	28.54±1.07*
Glibenclamide (0.5mg/kg)	95.45 ±3.72**	85.02 ±2.45**	33.23±5.42**	58.23±1.09**	22.54±0.54**
Ethanolic extract (400mg/kg)	97.14 ±2.56**	84 ±2.09**	34.57±1.03**	57.13±1.64**	23.47±1.37**

The values are mean ± SEM n = 6, when compared with diabetic control, * = $p < 0.05$, ** = $p < 0.01$, (One way ANOVA followed by Dunnett's, multiple comparison tests).

DISCUSSION

Diabetes mellitus is one of the leading causes of death, illness and economic loss all over the world. Insulin-dependent (Type I, IDDM) diabetes is characterized by juvenile onset and by absolute insulin deficiency. Non-insulin-dependent (Type II, NIDDM) diabetes is characterized by mature onset, by varying basal insulin levels and a frequent association with obesity. We found an elevated blood glucose concentration accompanied by increase in total cholesterol, triglycerides, LDL, VLDL and decrease in HDL cholesterol in streptozotocin induced

diabetic rats as compared to control animals. Oral administration of ethanolic extract of *Gardenia taitensis* normalized the levels of blood glucose. The potent hypoglycemic effect of the plant extract suggests the presence of potent hypoglycemic active principles, which produced antihyperglycemic effect in diabetic rats. In recent years, considerable interest has been directed towards the investigation of plasma lipids and lipoproteins pattern in diabetes mellitus due to the fact that abnormal lipid level leads to the development of coronary artery disease in diabetic patients [23]. Reduced insulin secretion and defect

in insulin function resulted in enhanced metabolism of lipids from adipose tissue to the plasma. Impairment in insulin sensitivity due to high concentration of lipids in the cells is responsible for the elevated cardiovascular risk in diabetes mellitus [24]. Thus, the altered lipid and lipoprotein pattern observed in diabetic rats could be due to defect in insulin secretion and/or action. Hypercholesterolemia and hypertriglyceridemia have been reported to occur in alloxan

induced diabetic rats. Accumulation of cholesterol and phospholipids in liver due to elevated plasma free fatty acids has been reported in diabetic rats. In the present study, ethanolic extract of *Gardenia taitensis* had significantly decreased Total Cholesterol, Triglycerides, VLDL, and LDL with increase in HDL which is having a protective function for the heart compared with diabetic control group [25].

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