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(Research Article)

Anti-diabetic Potential of *Quisqualis indica* Linn in Rats

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ABSTRACT

The present study was conceived to evaluate the effect of methanolic extract of flowers of Quisqualis indica Linn. on alloxan induced diabetes. Diabetic rats were treated with methanolic extract of flowers of Quisqualis indica Linn. at doses of 100, 200 and 400 mg/kg, p.o. for 43 days. The methanolic extract of flowers of Quisqualis indica Linn. at doses of 200 and 400 mg/kg, p.o. showed significant decrease in the biochemical parameters, glucose, triglyceride, total cholesterol, HDL-cholesterol, LDL-cholesterol levels as compared to diabetic control group. The methanolic extract of flowers of Quisqualis indica Linn. at doses of 200 and 400 mg/kg, also proved to be effective in normalizing the levels of triglyceride and cholesterol levels in heart homogenates as compared with diabetic control. Hence, it may be concluded, that the methanolic extract of flowers of Quisqualis indica Linn. may be beneficial in the treatment of diabetes.

Key Words: *Quisqualis indica* Linn., Oxidative stress, Diabetes mellitus, Hyperglycemia, Verbenaceae

INTRODUCTION

The prevalence of diabetes mellitus increases with age, and the numbers of older persons with diabetes are expected to grow as the elderly population increases in number. The National Health and Nutrition Examination Survey (NHANES III) demonstrated that in the population over 65 years old, almost 18% to 20% have diabetes[1]. Epidemiological studies in India have shown that prevalence and manifestation of diabetes is very high. At present 18-20 million people are diabetic in India and it is projected that in 2025 there will be 20-60 million diabetic in India and it will be the second country to having the largest number of diabetics in the world[2].

Diabetes mellitus has been a common problem of world form the centuries. It is a disease related to the sweetness, characterized by presence of excessive sugar in blood and urine due to deficiency in the production of insulin by pancreas or presence of ineffective insulin. The growth of disease is rapid due to the heredity, endocrine imbalance, dietary imprudence, severe and continued mental stress, and reduction in physical labour and differences in social structure etc., which is providing a productive atmosphere to diabetes[3].

Quisqualis indica Linn. commonly known as Lalchameli distributed throughout India, is cultivated in gardens for its attractive and fragrant flowers. It is large woody shrub indigenous to tropical Africa and tropical Indo-Malaysian region. *Quisqualis indica* Linn. has been documented in Ayurveda, Siddha, Unnani and other medicinal system. Almost all of its parts are used individually, or mixed with other ingredients, as remedy to different ailments like antiflatulence[4], coughs, diarrhea[5], body pains, antlelmintic, toothache[6], cardiovascular system[7]. Herbs that are rich in flavonoids, vitamin C, or the carotenoids may enhance immune function[8]. A number of pharmacological studies reported on *Quisqualis indica* Linn. Immunomodulatory[9], larvicidal[10], nematicidal[11], antibacterial and antioxidant[12], antipyretic, anthelmintic[13] and antirrhumatic properties[14]. This *Quisqualis indica* Linn. also used in treatment of diabetes in Ayurveda, but activity of which is not reported till

today preclinically. Thus the present investigation was done on antidiabetic potential of flowers *Quisqualis indica* Linn in alloxan induced diabetes in rats.

MATERIALS AND METHODS

Plant Material Collection

The plant material was collected from the Malegaon city of Dist. Nasik, Maharashtra, in the month of September- 2009 at the time of collection, flowers were collected. The plant was authenticated accession no is 0781 by Mr. Arvind S. Dhabe (Herbarium-In charge), Assistant professor of Department of botany. Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, Maharashtra India. It was then filtered and the solvent was evaporated under vacuum. The yield of methanol extract of flowers of *Quisqualis indica* (QI) was 5.7% w/w.

QI was tested for the presence of flavonoids, β-sitosterol, Quercetin, Lupeol and tannins, using standard phytochemical test procedures[15].

Animals

Wistar rats of either sex weighing 150-200 g were obtained from central animal house of Padmavati college of Pharmacy. Institutional Animal Ethics Committee approved the experimental protocol. Rats were housed under standard laboratory conditions with free access to standard pellet diet and water ad libitum.

Acute Toxicity Study

Acute toxicity of methanolic extract of leaves of *Quisqualis indica* Linn was determined using Albino rats of Wistar strain (150-180 g) according to the procedure of OECD guidelines no. 425 (Organization for Economic Co-operation and Development). The animals were observed for mortality for 48 h, and QI was found to be safe upto a dose of 5000 mg/kg. b.w.

Induction of Diabetes in Animals

Alloxan was used for experimental induction of diabetes. Diabetes was induced by a single intraperitonial injection of prestandardised dose of 140 mg/kg, i.p. alloxan monohydrate in citrate buffer (pH 5.5). The diabetic state was confirmed 48 hr after alloxan injection by hyperglycemia. Surviving rats with fasting blood glucose level higher than 250 mg/dl were included in the study[16-18].

Experimental Design

After randomization into various groups, the rats were acclimatized for a period of 2-3 days before initiation of experiment. The animals were randomized in the following groups:

Rats in group I were nondiabetic and received 1% gum acacia (1 ml/kg, p.o., o.d.), and served as control. Rats in groups II-VII were diabetic. Group II received 1% gum acacia (1 ml/kg, p.o., o.d.) and served as a diabetic control. Group III received glimepride (0.09 mg/kg, p.o., o.d.) for 42 days. Group V, VI, VII were treated for 42 days with three different doses of methanolic extracts of flowers of *Quisqualis indica* Linn. 100, 200, 400 mg/kg, p.o., o.d. respectively.

Sample Collection

Fasting blood samples were collected on day 1 and day 43 of the treatment from retro-orbital plexus under light ether anesthesia in two Eppendorff tubes; one containing anticoagulant (Heparin sodium, 100 I.U. /ml of blood) for separation of plasma. Plasma was separated in a high speed C-24 tabletop centrifuge (Remi Udyog, New Delhi) at 2,000 rpm for 20 min by centrifugation.

Biochemical Analysis in Blood

On day 1 and 43 plasma glucose, triglyceride, total cholesterol, LDL cholesterol, HDL cholesterol along with total cholesterol, and triglyceride levels in heart homogenates were estimated by using commercially available diagnostic kits (Biolab Diagnostics Pvt. Ltd, India).

Statistical Analysis

The results were expressed as mean ± SEM and statistically analyzed by one way ANOVA followed by Dunnett test, with level of significance set at $p<0.05$.

RESULT AND DISCUSSION

Diabetic control group exhibited significant hyperglycemia and dyslipidemia ($p<0.01$) when compared with normal control. The serum glucose, triglyceride, LDL-cholesterol and total cholesterol levels were increased and HDL-cholesterol level was decreased significantly ($p<0.01$) in the diabetic control group when compared to normal control. In the methanolic extracts of flowers of *Quisqualis indica* Linn. treated groups (200 and 400 mg/kg), there was significant decrease in the serum glucose, triglyceride, and total cholesterol levels as compared to diabetic control ($p<0.01$). The methanolic extracts of flowers of *Quisqualis indica* Linn. treated groups (200 and 400 mg/kg) showed significant reduction ($p<0.01$) in the triglyceride and cholesterol levels.

Alloxan is commonly used to produce diabetes mellitus in experimental animals due to its ability to destroy the β-cells of pancreas possibly by generating excess reactive oxygen species such as H_2O_2, $O^{\bullet}_2$ and $HO^{\bullet}$, which leads to persistent hyperglycemia. Reactive oxygen species play an important role in the etiology and pathogenesis of diabetes mellitus and its complications because of generation of oxidative stress[19]. Alloxan induced diabetes in experimental animal shows structural and functional changes in liver and kidney similar to the once observed in severe diabetes mellitus. Alloxan induced rats produce cardinal signs of diabetes mellitus such as polydypsia, polyphagia, increase in blood pressure, decrease in heart rate and loss of body weight[20,21].

In the present investigation, rats in the diabetic control group had characteristic hyperglycemia, hyperlipidemia and decreased HDL-cholesterol level when compared with normal control. The plasma glucose on day 43 revealed that methanolic extracts of flowers of *Quisqualis indica* Linn. produced significant antihyperglycemic activity.

In the present investigation, the antihyperglycemic activity of the Methanolic extracts of flowers of *Quisqualis indica* Linn. in alloxan-induced diabetic animals could possibly be due to inhibition of the intestinal absorption of glucose or by suppressing enzymes involved in gluconeogenesis or by stimulating glucose uptake in the peripheral tissues or due to increased insulin sensitivity or by increasing either the pancreatic secretion of insulin from β-cells of islets of langerhan's or its release from the bound form.

Apart from the regulation of carbohydrate metabolism, insulin also plays an important role in the metabolism of lipids. Chronic diabetes is always associated with derangement in lipid metabolism. In diabetes, enhanced activity of the hormone sensitive lipases increases lipolysis and releases more free fatty acids in to the circulation. Increased fatty acid concentration also increases the β-oxidation of fatty acids, producing more acetyl-coA, and cholesterol during diabetes[22,23]. Since insulin inhibits the activity of the hormone sensitive lipases in adipose tissue and suppresses the release of free fatty acids, it is potent inhibitor of lipolysis. Insulin has an inhibitory action on HMG-COA Reductase, a key enzyme that acts as a rate limiting enzyme in the metabolism of LDL-cholesterol[24]. In normal condition, insulin increases the receptor-mediated removal of LDL-cholesterol and decreased activity of insulin during diabetes causes hypercholesterolemia. Diabetes-induced hyperlipedemia is attributed to excess mobilization of fat from adipose due to less utilization of glucose[25]. Hypercholesterolemia and hypertriglyceridemia have been reported to occur in diabetic rats. The increased concentration of cholesterol could result in a relative molecular ordering of the residual phospholipids resulting in decrease in the membrane fluidity. In diabetes, level of HDL is decreased and due to decrease in level of HDL chances of heart disease increases[26,27].

Accumulation of triglycerides is one of the risk factors in coronary heart disease (CHD). In the present investigation there was significant increase in the level of triglycerides in diabetic control rats[28]. Methanolic extracts of flowers of *Quisqualis indica* Linn. significantly reduced the triglyceride level in alloxan-induced diabetic rats. Diabetic animal treated with Methanolic extracts of flowers of *Quisqualis indica* Linn., and glimepride showed significant decrease in the triglyceride level possible mechanism for triglyceride lowering activity of Methanolic extracts of flowers of *Quisqualis indica* Linn. may be either due to increase in uptake and utilization of glucose leading to subsequent inhibition of lipolysis. In the present study all diabetic Methanolic extracts of flowers of *Quisqualis indica* Linn. treated groups showed significant and dose dependant reduction in levels of plasma cholesterol and LDL-cholesterol, and improvement in HDL-cholesterol levels, which may be due to decrease in lipolysis by direct action of Methanolic extracts of flowers of *Quisqualis indica* Linn. on lipoprotein lipase and increase in removal of LDL so, this activity also may have played role in hypocholesteremic activity of Methanolic extracts of flowers of *Quisqualis indica* Linn.

Insulin is the main regulator of glycogenesis in muscle and liver. There is decrease in the hepatic and skeletal muscle glycogen content in diabetic rats[29,30]. One possible effect of antidiabetic drugs can be improvement of glycogenesis[31]. Administration of Methanolic extracts of flowers of *Quisqualis indica* Linn. for 43 days in diabetic rats resulted in significant and dose dependant elevation of the liver glycogen content. This focuses one possible way of antidiabetic action of Methanolic extracts of flowers of *Quisqualis indica* Linn., and is by improvement of glycogenesis process in liver.

Hence, the results obtained in the present study indicate that methanolic extracts of flowers of *Quisqualis indica* Linn has the potential to treat diabetes mellitus.

Table-1 : Effect of methanolic extracts of flowers of *Quisqualis Indica* Linn. on plasma glucose and triglyceride levels in non diabetic and alloxan induced diabetic rats.

Groups	Plasma Glucose level (mg/dl) at		Plasma Triglyceride (mg/dl)	
	Day 1	Day 41	Day 1	Day 41
Control	79.98±3.88	80.37±4.10	93.75±2.77	94.37±4.06
D Control	298.62±4.38$^{\#\#}$	327.00±6.61$^{\#\#}$	93.00±2.18	172.25±2.51$^{\#\#}$
D + Glim	301.62±5.39	119.75±5.24**	91.37±2.42	128.00±7.36**
D + MFQ-100	300.12±5.35	237.00±7.18*	85.25±2.09	176.62±4.08
D + MFQ-200	291.75±5.44	156.62±6.82**	86.62±1.67	154.25±4.87*
D + MFQ-400	293.75±3.96	129.00±3.57**	88.75±2.39	120.75±3.41**

Values are presented as mean ± SEM. (n=8) ANOVA followed by Dunnett test. $^{\#\#}p<0.01$ when compared with Control; $^{*}p<0.05$, $^{**}p<0.01$ when compared with D Control.

Table-2: Effect of methanolic extract of flowers of *Quisqualis indica* Linn. (MLQ) on plasma LDL-Cholesterol and total Cholesterol levels in non diabetic and alloxan induced diabetic rats.

Groups	Plasma LDL-Cholesterol (mg/dl)		Plasma Total Cholesterol (mg/dl)	
	Day 1	Day 41	Day 1	Day 41
Control	86.25±2.93	86.75±2.81	89.54±4.35	99.36±4.81
D Control	86.00±3.64	150.25±2.63$^{\#\#}$	80.64±5.08	183.29±10.83$^{\#\#}$
D + Glim	85.25±3.57	93.87±3.72**	88.35±4.38	133.66±4.41**
D + MFQ-100	89.25±3.38	152.25±3.3	89.71±6.78	164.83±5.68*
D + MFQ-200	86.62±3.00	123.37±2.28*	98.64±5.36	148.25±4.16**
D + MFQ-400	89.37±3.47	108.12±3.41**	90.16±5.25	128.12±5.72**

Values are presented as mean ± SEM. (n=8) ANOVA followed by Dunnett test. $^{\#\#}p<0.01$ when compared with Control; $^{*}p<0.05$, $^{**}p<0.01$ when compared with D Control.

Table: III Effect of methanolic extract of flowers of *Quisqualis indica* Linn. (MLQ) on plasma HDL-Cholesterol level and % body weight change in non diabetic and alloxan Induced diabetic rats

Groups	Plasma HDL-Cholesterol (mg/dl)	
	Day 1	Day 41
Control	50.87±2.92	54.62±2.88
D Control	52.87±2.98	32.87±1.77$^{\#\#}$
D + Glim	54.87±1.96	49.37±1.62**
D + MFQ-100	52.87±3.37	37.00±3.37
D + MFQ-200	51.37±3.15	42.75±3.15*
D + MFQ-400	55.75±2.4	49.87±3.70**

Values are presented as mean ± SEM. (n=8) ANOVA followed by Dunnett test. $^{\#\#}p<0.01$ when compared with Control; $^{*}p<0.05$, $^{**}p<0.01$ when compared with D Control.

Table IV: Effect of methanolic extract of flowers of *Quisqualis indica* Linn. (MLQ) on total cholesterol and triglyceride levels in heart homogenates of alloxan induced diabetic rats.

Groups	Total Cholesterol (mg/g)	Triglyceride (mg/g)
Control	1.46±0.06	2.23±0.08
D control	2.31±0.09$^{\#\#}$	4.06±0.13$^{\#\#}$
D + Glim	1.86±0.05**	3.52±0.07**
D + MFQ-100	2.27±0.05	3.88±0.05
D + MFQ-200	2.06±0.08*	3.71±0.07*
D + MFQ-400	1.92±0.04**	3.59±0.05**

Values are presented as mean ± SEM. (n=5) ANOVA followed by Dunnett test. $^{\#\#}p<0.01$ when compared with Control; $^{*}p<0.05$, $^{**}p<0.01$ when compared with D Control.

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