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Research Article

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Abstract

Gymnema lactiferum var. lactiferum is a climber distributed in many South Asian countries. It is reported that the diabetic patients in Sri Lanka use *G. lactiferum* leaves as a treatment for diabetes. However, scientific data is not available on this plant. A clinical trial was conducted including 26, type 2 diabetic patients with hypercholesterolemia. The treatment group received a suspension of *G. lactiferum* leaf powder twice daily for four weeks. Blood parameters of both groups (treated and control) were determined at the beginning and the end of the study period. Study indicates significant effects on fasting blood sugar (p=0.002), cholesterol (p=0.004), and LDL lowering (p=0.023) and a significant postprandial glucose lowering effect (p=0.026 for 60 min and p=0.022 for 120 min, after four weeks). In spite of the short study period, a significant reduction (p=0.012) in HbA_{1C} levels was also observed.

Introduction

Gymnema lactiferum var. lactiferum is a woody branched climber which belongs to the family *Asclapiadaceae*. It is known as "Kurincha" in Sinhala and "Kshirakakoli" in Sanskrit. The plant is distributed in Assam, Malay Peninsula, Malaysia and Sri Lanka (Dassanayake and Fosberg, 1983).

The leaves of *G. lactiferum* are used as a green leafy vegetable in salads, curries and in herbal gruels. Further it has been reported that *G. lactiferum* leaves possess cooling, anabolic, rehydrating, spermiogenic (Ayurveda Pharmacopia, 1961) and wormicide properties (forlkloric). *G. lactiferum* leaves have been used as a supportive treatment for diabetes by people in Jaffna, Sri Lanka for several decades.

The present report describes the effects of this plant material on glycemic and lipidemic status of type 2 diabetic patients. No scientific studies on this plant have been found in the literature.

Materials and Methods

Identification, collection and preparation of the leaf powder

The plant was identified at the National Herbarium, Sri Lanka. Plants were grown in Jaffna, Sri Lanka. They were grown with organic composts avoiding the use of synthetic fertilizers, insecticides and fungicides. After washing, mature leaves were dried hygienically in sunlight for 4-5 days within an enclosure covered with a glass roof. After grinding and sieving, the leaf powder was packed into 100 g packets.

Selection of patients

Patients were selected from the Out-Patient Wing of the Bangladesh Institute for Research and Rehabilitation in Diabetes Endocrine and Metabolic Disorders (BIRDEM), Dhaka.

Diabetes was diagnosed according to WHO (1999) criteria. Hypercholesterolemia was detected according to

the lipid profile levels of the patients. Type 2 diabetic patients (n = 12, age 30-60 years) with hypercholesterol-emia were included in the test group. Patients of more than 60 years of age, suffering from serious recurrent illnesses, hypertension or any other endocrinological diseases were excluded from the study. Patients with a serum creatinine level of more than 1.7 mg/dL and the patients on any dislipidemic drug were also excluded. Another group of type 2 diabetics (n = 14) with hyper-cholesterolemia served as the control group.

Informed consent of each patient was obtained after explaining the purpose and the procedure of the study. Patients had to fulfill four visits (one visit/ week) during the study period. Body weights were recorded on the day zero and on the 29th day. Patients complaints (if any) on gastric discomfort, generalized weakness, headache, vertigo, twinging sensation of the limbs, nausea, drowsiness, dryness of mouth, ano-rexia and flatulence etc. were recorded during each visit.

Sample collection

Fasting blood samples of 10 mL were drawn from the antecubital vein (0 hour). The test group patients received a suspension of *G. lactiferum* leaf powder (3.5 g dissolved in 30 mL of water) before their breakfast which was supplied according to their diet charts. Blood samples were drawn at 1 and 2 hours time intervals. Patients were provided with individual leaf powder doses (wrapped in a paper pack and sealed in a polythene bag) for the rest of the week. They were requested to take the preparation just before breakfast and just before dinner each day for one month.

Fasting blood (1 mL) was transferred in an EDTA containing tube to be used in the determination of HbA_{1C}.

The rest of the blood was centrifuged at 4,000 rpm for 10 min and serum was transferred to new Eppendorff tubes and re-centrifuged at 3,000 rpm for 5 min and the supernatant was separated. Serum samples were analyzed for fasting glucose, serum total cholesterol, triglyceride, HDL- cholesterol, SGPT and creatinine. The same procedure was followed on the last day where the above biochemical parameters were tested.

Estimation of blood parameters

Serum glucose levels were estimated using GOD POD Enzymatic kit (Randox Laboratories Ltd, UK) using Auto analyzer Auto Lab (Kunst et al., 1984). Serum total cholesterol levels were estimated using CHOD-PAP (Randox Laboratories Ltd, UK) reagent kit (Allain et al., 1974). High-density lipoproteins were separated from chylomicrons, VLDL and LDL by the addition of precipitating reagent (phosphotungstic-magnesium chloride) to serum (Hainline et al., 1980). After centrifugation, the cholesterol content of HDL fraction which remains in the supernatant was determined by the enzymatic colorimetric method using the total cholesterol, CHOD-PAP kit. Serum TG was estimated by enzymatic GPO-PAP (Randox Laboratories Ltd, UK) kit (Tietz, 1990) and Serum LDL- cholesterol was calculated by using the Friedewald formula (Friedewald et al., 1972). The serum alanine aminotransferase (SGPT) levels were estimated by using ALT (GPT) Opt. (Randox Laboratories Ltd, UK) kit (International Federation of Clinical Chemistry, 1980) using the Auto analyzer, Auto Lab. Serum creatinine levels were measured by the alkaline picric acid colorimetric method (Toro and Ackermann, 1975). The level of HbA_{1C} (in whole blood) was analyzed by using VARIANT Hemoglobin A_{1C} program (Mayer and Freedman, 1983).

Statistical analysis

Results are presented as mean ± standard deviation (SD). Groups of data were compared using student t-test. Differences were considered significant at $p < 0.05$.

Results

All 26 patients enrolled in the study had similar baseline characteristics (Table I). All patients were on oral hypoglycemic agents but any dose adjustments were not made during the study. Since it was not possible to conduct a double blind experiment, the patients were aware of who were the tests and who were the controls. The patients were expected to continue their normal dietary habits. However, control patients were reported to follow dietary controls. Despite this, *G. lactiferum* therapy indicated many beneficial effects on the glycemic and lipidimic status of the patients.

The body weight of the *Gymnema* treated group had reduced by 0.7% in comparison to their day zero values

Table I			
Baseline characteristic of the patients included in the study			
Demographics	*Gymnema lactiferum* (n = 12)	Control (n = 14)	p value
Age in years	47 ± 10	45 ± 11	0.505
No. of males	7	5	
Mean Body Mass Index (kg/m² ± SD)	26.8 ± 6.3	25.4 ± 2.9	0.464
Mean HbA$_{1C}$ (% ± SD)	7.9 ± 1.7	7.6 ± 1.7	0.626
Mean fasting blood sugar (mmol/L)	8.1 ± 1.8	7.5 ± 1.8	0.426
Mean total cholesterol (mg/dL)	235.8 ± 26.4	235.7 ± 32.9	0.992
Mean creatinine (mg/dL)	1.1 ± 0.2	1.0 ± 0.1	0.396
Mean SGPT (IU/L)	28.9 ± 12.2	25.6 ± 13.4	0.523

Table II			
Effect of *G. lactiferum* leaf powder on fasting serum glucose levels of type 2 diabetes patients			
Group	Fasting serum glucose levels (mmol/L)		
	Day 0	Day 15	Day 29
Control (n = 14)	7.5 ± 1.8	7.1 ± 1.6	6.8 ± 2.2
Gymnema treated group (n = 12)	8.1 ± 1.8	7.2 ± 1.6	6.6 ± 1.3[a]
Data are Mean ± SD; [a]p= 0.002 in comparison to day zero			

Table III			
Effect of *G. lactiferum* leaf powder on postprandial blood glucose levels of type 2 diabetes patients			
Group	Serum glucose levels (mmol/L)		
	After 60 min		After 120 min	
	Day 0	Day 29	Day 0	Day 29
Control (n= 14)	12.4 ± 3.0	11.8 ± 3.3	12.5 ± 3.6	11.2 ± 3.9
Gymnema treated group (n= 12)	13.8 ± 2.7	11.8 ± 1.7[a]	14.9 ± 3.0	12.4 ± 2.9[b]
Data are Mean ± SD ; [a]p= 0.026, [b]p= 0.022 in comparison to day zero				

(66.9 ± 12.1 Vs 67.4 ± 12.6, p= 0.089) and 0.4% reduction of the same parameter was observed in the control group (62.6 ± 10.8 Vs 62.9 ± 11.3, p= 0.204). However, those changes were insignificant.

The effect of *G. lactiferum* leaf powder on fasting serum glucose levels has been shown in Table II. A gradual reduction was observed in the *Gymnema* treated group. There was a 10.7% reduction on day 15. The reduction became significant (p= 0.002) on day 29 (with an 18.2% reduction).

As shown in Table III there were significant reductions (p= 0.026 for 60 min and p= 0.022 for 120 min) in postprandial serum glucose levels in the *Gymnema* treated group on day 29 in comparison to day zero.

Though the study period was four weeks, there was a

significant (p=0.012) reduction (11.6%) in HbA$_{1C}$ levels in comparison to the day zero values in the *Gymnema* treated group (7.0 ± 0.9 Vs 7.9 ± 1.7). However, such a reduction was not observed in the control group (7.4 ± 1.2 Vs 7.6 ± 1.7, p= 0.316).

The serum total cholesterol levels of the *Gymnema* treated group reduced significantly (p=0.004) by the 29th day (Table IV). There was a 12.3% reduction in comparison to the day zero value. However, the serum HDL levels remained steady (p= 0.417) throughout the study period. As shown in Table IV, there was a significant reduction (p=0.023) in the serum LDL levels in the *Gymnema* treated group on day 29 in comparison to day zero. The reduction was 15.5%. However, this therapy did not produce any significant reduction (p= 0.380) in serum triglyceride levels (Table IV).

Serum ALT (p=0.261) and creatinine (p=0.797) levels remained steady in both groups throughout the study period (data not shown). On the day zero the serum mean ALT level (U/I) in the treated group was 28.9 ± 12.2 and on the day 29 it was 31.7 ± 15.0. In the control group the relevant values of this parameter was 25.6 ± 13.4 Vs 28.6 ± 15.3. The mean serum creatinine level (mg/dL) of the treated group was 1.1 ± 0.2 Vs 1.1 ± 0.2, whereas in the control group this was 1.0 ± 0.1 Vs 1.1 ± 0.1.

Discussion

Although *G. lactiferum* leaf powder did not produce any acute blood glucose lowering effect, its chronic consumption led to a gradual reduction in FBS and after four weeks of treatment the reduction was significant (p= 0.002). The patients of both groups were on their conventional oral hypoglycemic drugs. Therefore this indicates the added advantage of *G. lactiferum* therapy on the patient's glycemic status. Though the postprandial blood glucose (PPG) levels did not show any significant reduction in the acute experiments, after treating the patients with leaf powder for four weeks their PPG levels went down significantly in comparison to day zero levels. This suggests that the leaf powder

Table IV								
Effect of *G. lactiferum* leaf powder on serum total cholesterol, HDL, LDL and triglyceride levels of type 2 diabetes patients								
Group	Serum levels (mg/dL)							
	Total cholesterol		HDL		LDL		Triglyceride	
	Day 0	Day 29	Day 0	Day 29	Day 0	Day 29	Day 0	Day 29
Control (n = 14)	235.7 ± 32.9	218.3 ± 38.4	37.5 ± 7.4	35.2 ± 8.2	155 ± 36	140 ± 44	218.1 ± 104.2	213.9 ± 99.9
Gymnema treated group (n = 12)	235.8 ± 26.4	206.8 ± 35.7[a]	36.8 ± 7.4	34.7 ± 6.2	155 ± 20	131 ± 33[b]	222.8 ± 81.1	207.2 ±105.4
Data are mean ± SD; [a]p= 0.004, [b]p= 0.023 (in comparison to day zero)								

could overcome postprandial hyperglycemia which is one of the major causes for the initiation and progression of many diabetic complications. Further the chronic consumption of leaf powder produced a significant decline (p=0.004) in serum total cholesterol levels and serum LDL levels (p=0.023). However, there was no significant changes in serum HDL (p=0.417) and TG (p=0.380). The insignificant serum ALT (p=0.261) and creatinine (p=0.797) levels indicated that there was no detrimental effects on the liver and kidneys of the patients.

The body weights of patients' did not show significant changes (p=0.089) throughout the study period. No complaints were made by the patients while consuming the leaf powder. Some patients had a history of generalized weakness, gastric discomfort and constipation prior to the treatment. All the above complaints were alleviated and gradually subsided while being fed on the leaf powder.

From the data obtained it could be concluded that *G. lactiferum* leaf powder possesses pronounced hypoglycemic effects and favorable effects on the lipid profiles on type 2 diabetic patients and it would therefore make a good functional food. The hypoglycemic effect may be due to stimulation of insulin secretion, enhancement of the activity of insulin or inhibition of glucose absorption.

Conclusion

The hypocholesterolemic effect may probably be due to the indirect effect of lowering of blood glucose or due to any other active principle which can inhibit cholesterol synthesis or increase cholesterol or bile salt excretion.

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Ethical Issue

The study was approved by the Ethical Committee of the Institute.

Conflict of Interest

Authors declare no conflict of interest.

Acknowledgement

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