JOURNAL OF MEDICINAL FOOD
J Med Food 24 (1) 2021, 28–32

DOI: 10.1089/jmf.2020.0024

Effect of *Gymnema sylvestre* Administration on Glycemic Control, Insulin Secretion, and Insulin Sensitivity in Patients with Impaired Glucose Tolerance

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ABSTRACT *Gymnema sylvestre*, a plant typical of India, has long been known for its hypoglycemic effects. The objective of this study was to evaluate the effect of *G. sylvestr*e administration on glycemic control, insulin secretion, and insulin sensitivity in patients with impaired glucose tolerance (IGT). A randomized, double-blind, placebo-controlled clinical trial was conducted in 30 patients with IGT. Fifteen patients randomly received *G. sylvestre* in doses of 300 mg b.i.d. and the other 15 received placebo in the same way. Before and after the intervention, anthropometric and metabolic measurements were taken, including 2-h oral glucose tolerance test (2-h OGTT), fasting plasma glucose, glycated hemoglobin A1c (A1C), and the lipid profile panel. Areas under the curve of glucose and insulin were calculated, as well as the insulinogenic, Stumvoll, and Matsuda indices. Wilcoxon, Mann–Whitney U, and chi-square or Fisher's exact tests were performed, and a P-value ≤.05 was considered statistically significant. There was a significant reduction in 2-h OGTT (9.1 ± 1.2 vs. 7.8 ± 1.7 mmol/L, $P = .003$), A1C ($5.8 \pm 0.3\%$ vs. $5.4 \pm 0.4\%$, $P = .025$), body weight, body mass index, and low-density lipoprotein cholesterol levels in the *G. sylvestre* group, with an increment in the Matsuda index (1.8 ± 0.8 vs. 2.4 ± 1.2, $P = .008$). At the end of the intervention, 46.7% of the patients obtained normal values in A1C. In conclusion, *G. sylvestre* administration in patients with IGT decreased 2-h OGTT and A1C, increasing insulin sensitivity. There were also improvements in anthropometric measures and the lipid profile.

KEYWORDS: • ***alternative medicine*** • **Gymnema sylvestre** • ***impaired glucose tolerance*** • ***insulin secretion*** • ***insulin sensitivity*** • ***prediabetes***

INTRODUCTION

IMPAIRED GLUCOSE TOLERANCE (IGT) is a transition state to type 2 diabetes mellitus (T2DM). IGT is related to insulin resistance in the liver and normal insulin sensitivity in the muscle, in addition to a severe decrease in the secretion of insulin.[1,2]

Several studies have linked IGT with a significant increase in the risk of developing T2DM, as well as in the prevalence of cardiovascular diseases compared with normoglycemic individuals.[3]

One of the most recommended medications to treat IGT is metformin; however, new strategies are needed to improve insulin resistance and limit the secretory demand of insulin in beta cells to stop or postpone the conversion of prediabetes to T2DM.[4]

Complementary and alternative medicine has attracted attention in the treatment of diabetes with several therapeutic agents that modulate glucose levels because they are relatively accessible and many of them have been used for decades or centuries without showing serious side effects. It is estimated that ∼35%–48% of the world's population use this type of treatment.[5]

Gymnema sylvestre is an ancient medicinal plant belonging to the Asclepiadaceae family, and it is used in Ayurvedic medicine as well as in complementary and alternative medicine. Its leaves exhibit a wide range of therapeutic effects due to gymnemic acids (main compounds). Furthermore, *G. sylvestre* is widely used as a naturopathic treatment for diabetes, and it has also demonstrated other important uses, such as hypolipidemic, antiviral, diuretic, antiallergic, antibiotic, and as a weight loss supplement.[6,7] However, these findings have not been studied in patients with IGT; although it has been used in diabetes, its effect on insulin is not clear, either through improving insulin sensitivity or insulin secretion. Therefore, due to the mechanisms attributed to improve glucose metabolism, the main objective of this study was to evaluate the effect of *G. sylvestre*

Manuscript received 22 January 2020. Revision accepted 15 March 2020.

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administration on glycemic control, insulin secretion, and insulin sensitivity in patients with IGT.

MATERIALS AND METHODS

A randomized, double-blind, placebo-controlled clinical trial was performed in 30 patients of both genders between 30 and 59 years old, with a diagnosis of IGT according to the American Diabetes Association[8] (defined as a 2-h postload plasma glucose [2-h PG] concentration between 7.8 and 11.1 mmol/L). In both study groups, subjects were considered sedentary (they usually performed light or moderate physical activity as much as 15 min a day and with less than three sessions per week during the last 3 months), nonsmokers, and with a body mass index (BMI) ranging between 25 and 39.9 kg/m^2 and a stable body weight (BWt), considering up to 5% changes in BWt for at least 3 months before the study.

None of the included patients had used any pharmacological treatment, medicinal herbs, or supplements with an effect on glycemic control for at least 3 months before enrollment in the study. Exclusion criteria were prior T2DM diagnosis; hypertension; renal, heart, thyroid, or hepatic disease; and women who were pregnant or breastfeeding.

Enrolled subjects underwent assessments at baseline and at the end of the study (12 weeks). Weight and height were measured with the subject standing barefoot and with the head aligned in the Frankfort horizontal plane with an electric bioimpedance scale (Model TBF-300 A; Tanita Corporation of America Inc., Arlington Heights, IL). BMI was calculated as BWt (kg) divided by the square of body height (m^2). Waist circumference was measured using a flexible tape at the midline between the lowest rib and the highest point of the iliac crest in the midaxillary line at the end of a normal expiration. All anthropometric measurements were performed with the individuals wearing light clothing without shoes and after evacuation of the bladder.

Blood pressure was evaluated after a 15-min resting period with the individual sitting using a digital sphygmomanometer (OMRON model HEM-7130), and a bracelet was adjusted 3 cm above the fold of the elbow of the left arm. The mean of three systolic and diastolic blood pressure measurements was considered.

Blood samples were collected from an antecubital vein after insertion of a catheter to determine fasting plasma glucose, glycated hemoglobin A1c (A1C), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and fasting insulin concentrations. Subsequently, a 2-h oral glucose tolerance test (2-h OGTT) by consuming 75 g of a dextrose load was performed, and two blood samples were obtained at 30, 60, 90, and 120 min after glucose administration. The blood was centrifuged, and the first sample was used to determine plasma glucose immediately, and the second sample was frozen at −20°C for insulin determinations within the next 30 days.

Before clinical and laboratory evaluations, all subjects were instructed to maintain their usual physical activity, which consisted of light or moderate physical activity as much as 15 min a day and with less than three sessions per week during the last 3 months. To ensure proper insulin secretion, patients received an isocaloric diet 3 days before the 2-h OGTT, containing a minimum of 250 g of carbohydrates per day. All females were tested during the first phase of their menstrual cycle (days 3–8).

Glucose, TG, TC, and HDL-C levels were measured by colorimetric methods using an automated analyzer (Erba XL 100®), with an intra- and inter-assay coefficients of variation (CV) of <1% and 2%, respectively. The A1C percentage was measured using ion-exchange high-performance liquid chromatography (Bio-Rad Laboratories, Hercules, CA), with an intra- and inter-assay CV of 0.4% and 1.6%, respectively. Insulin concentrations were measured using a chemiluminescent immunoassay technique (DRG International, Inc.,), with an intra- and inter-assay CV of 2.6% and 2.88%, respectively. The areas under the curve (AUC) of glucose and insulin were obtained using the trapezoidal integration.[9]

Total insulin secretion was calculated with the insulinogenic index [Δ AUC insulin/(Δ AUC glucose)],[10] the first phase insulin secretion using the Stumvoll index ($1283 + 1.829 \times$ insulin $30' - 138.7 \times$ glucose $30' + 3.772 \times$ insulin $0'$),[11] and insulin sensitivity with the Matsuda index [10,000/square root of (glucose $0' \times$ insulin $0') \times$ (mean glucose × mean insulin during 2-h OGTT)].[12] Low-density lipoprotein cholesterol (LDL-C) levels were calculated with the Friedewald equation: LDL-C (mmol/L) = TC (mmol/L) − HDL-C (mmol/L) − [TG (mmol/L)/2.2], and the very low-density lipoprotein with the proportion of TG (mmol/L)/2.2.

Pharmacological administration

Simple randomization was performed by a random number table. Fifteen individuals per group received either oral capsules of *G. sylvestre* (Swanson Superior Herbs) or homologated placebo, 300 mg b.i.d. before breakfast and dinner (for a total 600 mg/day) for 12 weeks. Presence of adverse events and adherence to the intervention were evaluated monthly. Adherence was evaluated by capsule countbacks (adherence of at least 80% was considered good). All patients were asked to register the appearance of adverse effects in their daily treatment diary, and they were instructed to maintain their habitual physical activity. Finally, patients also received general nutritional recommendations during the study period.

Statistical analysis

Sample size was calculated using a formula for mean differences[13] for each of the primary variables with a statistical confidence of 95% and a statistical power of 80%. According to the largest sample size calculated from 2-h PG with a standard deviation (SD) of 0.8 mmol/L[14] and an expected difference between groups of at least 1.0 mmol/L, a total of 15 subjects per group was obtained, including 20% of expected loss. Data were analyzed using SPSS software (ver. 25; SPSS, Inc., Chicago, IL).

Continuous variables are presented as mean ± SD, and categorical variables are presented as frequencies and

percentages. Values are presented according to the International System of Units. After assessing normality with the Shapiro–Wilk test, continuous data were compared using nonparametric tests; Wilcoxon signed-rank test and Mann–Whitney U test were used to evaluate intra- and intergroup differences, respectively, and chi-square or Fisher's exact test was used to assess the differences in nominal variables. Intention-to-treat analysis was performed. Dropout cases were not replaced, and a P-value ≤.05 was considered statistically significant.

Ethical considerations

The present study was performed in accordance with ethical principles for medical research involving humans described in the international guidelines for Good Clinical Practices and the Declaration of Helsinki. Informed consent was obtained from all participants before the intervention and after being accurately informed regarding the nature, purpose, risks, and benefits of the study by the principal investigator. The protocol was registered at ClinicalTrials.gov as NCT02708966.

RESULTS

Every group consisted of 11 women and 4 men. Four patients, two per group, withdrew from the study for reasons unrelated to the intervention before the first week at the beginning of the investigation. At baseline, both study groups had similar clinical and laboratory characteristics (Table 1).

After the administration of *G. sylvestre*, a significant decrease was observed in 2-h PG, A1C, LDL-C, BWt, and BMI, as well as an increase in the Matsuda index. There were no differences in the placebo group. There were no intergroup differences in all variables at the end of the intervention (Table 1).

In the *G. sylvestre* group, the A1C values considered for the diagnosis of patients with prediabetes were normalized in 46.7%, meanwhile in the placebo group, A1C values were not normalized in any of the patients ($P = .003$).

There were no statistically significant differences in the prevalence of adverse events between the intervention groups; the most common adverse events were headache and gastrointestinal symptoms.

DISCUSSION

The administration of *G. sylvestre* improved glucose metabolism in patients with IGT by significantly decreasing 2-h PG and A1C and increasing insulin sensitivity. Moreover, it promoted a decrease in BWt, BMI, and LDL-C. It is important to note that this is the first study aimed at determining the effect of *G. sylvestre* in patients with IGT.

A large number of studies (*in vitro*, *in vivo*, and clinical trials) have postulated their findings on the hypoglycemic effects of *G. sylvestre*,[6,14–20] and although their mechanisms of action continue to be investigated, several theories suggest that they could act on different pathways between them by reducing the absorption of glucose in the small intestine because the gymnemic acid occupies the receptors in the outer layer of the intestine and thus prevents the absorption of glucose molecules.[14–16] Another mechanism proposed is the inhibition of the enzyme α-glucosidase, which would also contribute to the decrease or delay of carbohydrate digestion.[21]

Table 1. Characteristics Before and After the Intervention

	Placebo		Gymnema sylvestre	
Characteristic	*Baseline* (n = *15*)	*12 Weeks* (n = *13*)	*Baseline* (n = *15*)	*12 Weeks* (n = *13*)
BWt, kg	79.1 ± 16.8	77.7 ± 13.2	79.6 ± 11.9	77.4 ± 11.6**
BMI, kg/m^2	29.8 ± 5.2	29.3 ± 4.4	31.1 ± 3.7	30.3 ± 3.6**
WC, cm	98.8 ± 9.8	99 ± 7.6	97.3 ± 6.9	97.3 ± 7.7
SBP, mmHg	119 ± 12	120 ± 14	117 ± 12	120 ± 15
DBP, mmHg	77 ± 8	77 ± 8	77 ± 13	75 ± 10
TG, mmol/L	1.5 ± 0.7	1.6 ± 0.7	1.8 ± 1.3	1.7 ± 0.9
TC, mmol/L	5.2 ± 0.9	5.4 ± 1.0	5.1 ± 0.1	4.7 ± 1.2
HDL-C, mmol/L	0.9 ± 0.3	1.0 ± 0.3	1.0 ± 0.1	0.9 ± 0.2
LDL-C, mmol/L	3.5 ± 0.5	3.2 ± 1.6	3.5 ± 0.8	2.5 ± 1.3*
VLDL, mmol/L	0.3 ± 0.1	0.3 ± 0.1	0.4 ± 0.3	0.3 ± 0.2
FPG, mmol/L	5.6 ± 0.4	5.5 ± 0.5	5.9 ± 0.4	6.0 ± 0.8
2 h-PG, mmol/L	8.6 ± 0.8	7.9 ± 1.1	9.1 ± 1.2	7.8 ± 1.7**
A1C, %	5.6 ± 0.2	5.7 ± 0.5	5.8 ± 0.3	5.4 ± 0.4*
AUCG, mmol/L	1078 ± 137	1018 ± 158	1157 ± 147	1075 ± 253
AUCI, pmol/L	63,544 ± 28,041	53,374 ± 20,663	68,348 ± 20,329	56,968 ± 20,787
Insulinogenic index	0.54 ± 0.22	0.49 ± 0.18	0.56 ± 0.20	0.51 ± 0.21
Stumvoll index	1391 ± 712	1528 ± 677	1297 ± 550	1399 ± 552
Matsuda index	2.5 ± 1.5	2.5 ± 1.2	1.8 ± 0.8	2.4 ± 1.2**

*$P < .05$, **$P < .01$ between baseline and 12-week measurement within the *G. sylvestre* group (Wilcoxon rank test).

2 h-PG, 2-hour postload plasma glucose; A1C, glycated hemoglobin A1c; AUCG, area under the curve of glucose; AUCI, area under the curve of insulin; BMI, body mass index; BWt, body weight; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; VLDL, very low-density lipoprotein; WC, waist circumference.

However, it has been widely described in the literature that *G. sylvestre* is a potent modulator of the incretin effect, the latter being a powerful stimulant for insulin secretion, specifically after glucose intake, which would contribute to its subsequent decrease of the oral glucose load.[22,23]

Finally, in a study in which a glucose tolerance test was carried out in obese mice that were given *G. sylvestre*, a significant decrease in glucose levels was observed at 90 and 120 min, which reinforces the findings of our study on the acute effect of the administration of this phytodrug.[24]

Within our study, after the administration of *G. sylvestre* in a dose of 600 mg/day, an important hypoglycemic effect in 2-h PG was shown, a finding that is in agreement with the aforementioned evidence.

With respect to A1C, the administration of *G. sylvestre* showed a significant decrease at the end of the intervention compared with baseline. This finding was also reported by Shanmugasundaram *et al.*[25] when performing a clinical trial in which *G. sylvestre* extract was administered in 27 patients with T2DM, and they found an improvement in glycemic control demonstrated by a decrease in A1C levels. However, they also found that C-peptide levels were increased after the intervention, which they interpreted as an improvement in beta-cell function associated with the administration of *G. sylvestre*.

Related to insulin sensitivity, Bhansali *et al.*,[19] administered gymnemic acids to three groups of six rats in doses of 50, 100, and 200 mg/kg orally for 40 days. They found a decrease in insulin resistance estimated by the homeostatic model of insulin resistance evaluation (HOMA-IR) at the end of the study. In our study, we analyzed insulin sensitivity using the Matsuda index, where there was a statistically significant increase.

Furthermore, El Shafey *et al.*[16] developed an *in vivo* study where they demonstrated that *G. sylvestre* promotes BWt loss because of its ability to reduce cravings for sweets and block glucose absorption during digestion. *G. sylvestre* may regulate BWt gain and fat accumulation in adipose tissue because it acts to prevent adipocyte hypertrophy and hyperplasia.[26] In a preclinical study in adult male Wistar rats that received *G. sylvestre* for 28 days, BMI and BWt gain decreased significantly compared with those rats of the untreated group.[27] In a clinical trial conducted within our study group by Zuñiga *et al.*,[6] where patients with metabolic syndrome were studied, we found a significant decrease in BWt and BMI. In this study, we found a significant decrease in BWt and BMI in a concordant manner. Therefore, this article constitutes a strong confirmation of the beneficial effect of *G. sylvestre* on BWt in humans.

Several sources point out the hypolipidemic effect of *G. sylvestre*. The possible mechanisms are the promotion of decreased lipid absorption at the intestinal level and the decrease of its synthesis. In addition, *G. sylvestre* increases the fecal excretion of cholesterol, as well as it decreases its synthesis due to glycolytic interactions of gymnemic acids with the enzyme glyceraldehyde 3-phosphatase, which decreases its action.[28,29] It has also been found that the decrease in lipids by *G. sylvestre* may be due to the inhibition of pancreatic lipase activity.[30] In this study, after the administration of *G. sylvestre*, there was a significant decrease in LDL-C, which partially coincides with a study performed in patients with type 1 diabetes mellitus with insulin therapy in a 10- to 12-month period, in which each patient received 400 mg/day of *G. sylvestre*, and a significant reduction of TC and TG was observed, as well as free fatty acids,[25] probably due to the use of insulin therapy. However, further studies in humans to confirm its benefits as a hypolipidemic agent are needed.

Regarding the limitations of this study, body composition analysis was not performed; thus, it is not possible to determine if the loss of BWt in each study group was due to the loss of muscle mass, body water, and/or body fat. It is necessary to consider that in our study we used an average dose as reported in the literature, so that higher doses (1 g/day) as well as a longer intervention time could have achieved significant results in other outcome variables, according to reports by other authors, who used the dose already mentioned in their respective clinical trials.

In this research, narrow criteria for the selection of patients were established to obtain a sample with few intervening variables that had an influence on the results, so the results cannot be generalized to an open population with IGT.

In conclusion, *G. sylvestre* administration in subjects with IGT decreased 2-h PG, A1C, increasing insulin sensitivity, and thus, showing its potential as an anti-obesity and hypolipidemic agent.

ACKNOWLEDGMENT

The authors thank L. Michele Brennan-Bourdon, PhD, Executive Editor, Scientific Communications and Brennan Language Editing Services, for the English editorial assistance.

AUTHOR DISCLOSURE STATEMENT

No competing financial interests exist.

FUNDING INFORMATION

No funding was received.

REFERENCES

1. Kanata M, DeFronzo RA, Abdul-Ghani MA: Treatment of prediabetes. *World J Diabetes* 2015;6:1207–1222.
2. Nathan DM, Davidson MB, DeFronzo RA, *et al.:* Impaired fasting glucose and impaired glucose tolerance: implications for care. *Diabetes Care* 2007;30:753–759.
3. Palermo A, Maggi D, Maurizi AR, Pozzilli P, Buzzetti R: Prevention of type 2 diabetes mellitus: Is it feasible? *Diabetes Metab Res Rev* 2014;30(Suppl 1):4–12.
4. Hostalek U, Gwilt M, Hildemann S: Therapeutic use of metformin in prediabetes and diabetes prevention. *Drugs* 2015;75: 1071–1094.
5. Shane-McWhorter L: Epidemiology of CAM supplement use. In: *Complementary and Alternative Medicine (CAM) Supplement*

Use in People with Diabetes: A Clinician's Guide. American Diabetes Association, Alexandria, VA, 2007, pp. 7–9.
6. Zuñiga LY, González-Ortiz M, Martínez-Abundis E: Effect of *Gymnema sylvestre* administration on metabolic syndrome, insulin sensitivity, and insulin secretion. *J Med Food* 2017;20:750–754.
7. Tiwari P, Mishra BN, Sangwan NS: Phytochemical and pharmacological properties of Gymnema sylvestre: An important medicinal plant. *Biomed Res Int* 2014;2014:830285.
8. American Diabetes Association: Classification and diagnosis of diabetes: Standards of medical care in diabetes-2019. *Diabetes Care* 2019; 42(Suppl 1):S13–28.
9. Tai MM: A mathematical model for the determination of total area under glucose tolerance and other metabolic curves. *Diabetes Care* 1994;17:152–154.
10. Dalfrà MG, Pacini G, Parretti E, *et al.:* Elevated insulin sensitivity and β-cell function during pregnancy in mothers of growth-restricted newborns. *Am J Physiol Metab* 201;301:E25–30.
11. Stumvoll M, Mitrakou A, Pimenta W, *et al.:* Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. *Diabetes Care* 2000;23:295–301.
12. Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA: Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. *Diabetes Care* 2007;30:89–94.
13. Jeyaseelan L, Rao PS: Methods of determining sample sizes in clinical trials. *Indian Pediatr* 1989;26:115–121.
14. Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS: Systematic review of herbs and dietary supplements for glycemic control in diabetes. *Diabetes Care* 2003;26:1277–1294.
15. Baskaran K, Kizar Ahamath B, Radha Shanmugasundaram K, Shanmugasundaram ERB: Antidiabetic effect of a leaf extract from Gymnema sylvestre in non-insulin-dependent diabetes mellitus patients. *J Ethnopharmacol* 1990;30:295–300.
16. El Shafey AAM, El-Ezabi MM, Seliem MME, *et al.:* Effect of Gymnema sylvestre R. Br. leaves extract on certain physiological parameters of diabetic rats. *J King Saud Univ - Sci* 2013;25:135–141.
17. Porchezhian E, Dobriyal RM: An overview on the advances of Gymnema sylvestre: Chemistry, pharmacology and patents. *Pharmazie* 2003;58:5–12.
18. Wang Y, Dawid C, Kottra G, Daniel H, Hofmann T: Gymnemic acids inhibit sodium-dependent glucose transporter 1. *J Agric Food Chem* 2014;62:5925–5931.
19. Bhansali S, Shafiq N, Pandhi P, *et al.:* Effect of a deacyl gymnemic acid on glucose homeostasis & metabolic parameters in a rat model of metabolic syndrome. *Indian J Med Res* 2013;137:1174–1179.
20. Bera R, Kundu A, Sen T, Adhikari D, Karmakar S: In vitro metabolic stability and permeability of gymnemagenin and its in vivo pharmacokinetic correlation in rats—A pilot study. *Planta Med* 2016;82:544–550.
21. Chen G, Guo M: Rapid screening for α-glucosidase inhibitors from Gymnema sylvestre by affinity ultrafiltration-hplc-ms. *Front Pharmacol* 2017;8:1–8.
22. Spasov A, Samokhina M, Bulanov A: Antidiabetic properties of gymnema sylvestre (a review). *Pharm Chem J* 2008;42:626–629.
23. Kimura I: Medical benefits of using natural compounds and their derivatives having multiple pharmacological actions. *Yakugaku Zasshi* 2006;126:133–143.
24. Al-Romaiyan A, King AJ, Persaud SJ, Jones PM: A novel extract of Gymnema sylvestre improves glucose tolerance in vivo and stimulates insulin secretion and synthesis in vitro. *Phyther Res* 2013;27:1006–1011.
25. Shanmugasundaram ER, Rajeswari G, Baskaran K, *et al.:* Use of Gymnema sylvestre leaf extract in the control of blood glucose in insulin-dependent diabetes mellitus. *J Ethnopharmacol* 1990;30: 281–294.
26. Kim HJ, Hong SH, Chang SH, *et al.:* Effects of feeding a diet containing Gymnema sylvestre extract: Attenuating progression of obesity in C57BL/6J mice. *Asian Pac J Trop Med* 2016;9:437–444.
27. Kumar V, Bhandari U, Tripathi C, Khanna G: Evaluation of antiobesity and cardioprotective effect of Gymnema sylvestre extract in murine model. *Indian J Pharmacol* 2012;44:607.
28. Shigematsu N, Asano R, Shimosaka M, Okazaki M: Effect of administration with the extract of Gymnema sylvestre R. Br leaves on lipid metabolism in rats. *Biol Pharm Bull* 2001;24: 713–717.
29. Izutani Y, Murai T, Imoto T, *et al.*: Gymnemic acids inhibit rabbit glyceraldehyde-3-phosphate dehydrogenase and induce a smearing of its electrophoretic band and dephosphorylation. *FEBS Lett* 2005;579:4333–4336.
30. Manish K, Aditi K, Renu A, Gajraj S, Poonam M: Anti-obesity property of hexane extract from the leaves of Gymnema sylvestre in high fed cafeteria diet induced obesity rats. *Int Res J Pharm* 2011;2:112–116.