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Original article

Antidiabetic, hypolipidemic and histopathological analysis of *Gymnema sylvestre* (R. Br) leaves extract on streptozotocin induced diabetic rats

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ABSTRACT

Objective: To investigate antidiabetic, hypolipidemic histopathological analysis of *Gymnema sylvestre* methanolic extract (GSME) in streptozotocin induced diabetic rat by administering oral doses (100, 200 and 400 mg/kg body weight).
Methods: Blood glucose levels were measured using blood glucose test strips with elegance glucometer on weekly intervals till the end of study (*i.e.* four weeks). Blood glucose, urine sugar, triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL) and very low density lipoprotein (VLDL) were determined in normal and streptozotocin induced diabetic rats after oral administration of the extract for 28 days. Histopathological changes in diabetic rat organs (pancreas, liver, and kidney) were also observed after extract treatment.
Results: Daily oral administration GSME (100, 200 and 400 mg/kg body weight) and glibenclamide (5 mg/kg) showed beneficial effects on blood glucose level ($P < 0.01$) and hyperlipidaemia due to diabetes. The extract treatment also showed to enhance serum insulin level and body weight of diabetic rats as compared to diabetic control group. Furthermore, the extract has a favorable effect on the histopathological studies, in streptozotocin induced diabetes.
Conclusions: *G. sylvestre* possesses antidiabetic property as well improve body weight, and total lipid levels. GSME has also favorable effect to inhibit the histopathological changes in streptozotocin-induced diabetes.

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1. Introduction

Diabetes mellitus has been known since ages and the sweetness of diabetic urine has been mentioned in Ayurvetha by Sushruta. Its pharmacotherapy however is over 80 years old. The world diabetes coined by the Greek physicians Aeretaeus in the first century A.D. In the 17th century, will is observed that the urine of diabetics as wonderfully sweet as imbued with honey or sugar. The presence of sugar in the urine of diabetics was demonstrated by Dobson in 1755 [1].

Diabetes mellitus is the common endocrine disorder. More than 150 million people are suffering from it. Worldwide [2] and it is likely to increase to 300 million by the year 2005. More than one-fifth of them are Indians and the International Diabetes Federation declared India as "Diabetic Capital of the World". Synthetic antidiabetic agents can produce serious side effects and they are not suitable for using during pregnancy. In view of the adverse effects associated with the synthetic drugs and considering natural medicine safer, cheaper and effective, traditional antidiabetic plants can be explored [3]. Furthermore, after the recommendation made by WHO on diabetes mellitus, investigations on hypoglycemic agents from medicinal plants have become more important [4].

Gymnema sylvestre (R.Br) (family: Asclepiadaceae), commonly known as sakkaraikolli, is a woody climber annual climbing plant, abundant in hills region. It is native to India. It reported to contain alkaloids, saponins, flavonoids and tannins. Traditionally, it is used in the treatment of gastrointestinal disorders, bronchial and respiratory disease, kidney stones and diabetes. It also exhibits anxiolytic, analgesic, antipyretic and inflammatory activities.

The medicinally active parts of the plants are the leaves and the roots although the exact mechanism is unknown. Besides impairing the ability to discriminative sweet taste, increase enzyme activity responsible for the glucose uptake and utilization. It may

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stimulate pancreatic β-cell function, increase β-cell number and increase insulin release by increasing cell permeability to insulin [5]. Drug interaction occurs from the additive effect when used concomitantly with hypolipidemic agent. Hence in the present study an attempt is made to elucidate the possible antidiabetic and hypolipidemic activity of *G. sylvestre* methanol extract on both normal and streptozotocin induced diabetic rats.

2. Materials and methods

2.1. Plant material

The fresh and fully mature leaves of *G. sylvestre* were collected from Suruli hills, Theni reserve forest, Theni district during the month of October 2013. Plant species was identified and taxonomically authenticated by Dr. John Brito, Taxonomist, Rabinot Research Herbarium Center, Trichy, and South India. A voucher specimen of the plant has been deposited in the Institutional Herbarium with the accession number SP001.

2.2. Preparation of methanol extract

The fresh leaves of *G. sylvestre* were washed with distilled water immediately after collection and air-dried for 14 days at room temperature. The collected leaves were chopped into small pieces and ground into coarse powder with a mechanical grinder (Miyako 3 in one blender, China) and stored in an airtight container. Dried 246 g powder was soaked into 750 mL 95% pure methanol for seven days at room temperature (25 ± 1) °C with occasional stirring. After seven days, methanol extract was filtered with Whatman no. 1 filter paper. The extract was concentrated under reduced pressure below 50 °C through rotary evaporator (RE 200, Bibby Sterling, UK). The concentrated extract was collected in a petri dish and allowed to air-dry for complete evaporation of methanol. Blackish-green semisolid extract (19.15 g, yield 7.78% w/w) was preserved at 4 °C until further use [6].

2.3. Chemicals

Streptozotocin was purchased sigma-Alrich St. Louis, USA. Total cholesterol (TC), serum high-density lipoprotein (HDL), serum creatinine (SC), serum urea (SU), serum alkalin phosphate (SAP), and triglyceride (TG) were assayed using standard kits from Erba Diagnostics Mannheim Gambh, Germany and blood glucose level was measured using elegance glucose meter (CT-X10) of convergent Technologies, Germany.

2.4. Experimental animals

Albino Wistar male rats 7–8 weeks old, weighing 150–200 g, were purchased from GSA animal farm, Chennai, Tamil Nadu, India used for the present study. The animals were fed with standard pellet diet (Chakan Oil Mills, Sangli) and water *ad libitum*. Ethical clearance was obtained from Institutional Animal Ethics Committee and conducted according to the Indian National Science Academy guidelines for the use and care of experimental animals (CPCSEA/265).

2.5. Drug administration

After seven days of streptozotocin on induction, the methanol leaf extract was administered orally through intragastric tube at the following doses of 100, 200 and 400 mg kg body weight.

2.6. Experimental induction of diabetes

The rats were injected intraperitoneally with streptozotocin dissolved in sterile normal saline at a dose of 150 mg kg^{-1} body weight. Blood samples were collected before the administration of Streptozotocin and after seven days of streptozotocin administration. Diabetic state was confirmed when the blood sugar level was above 200 mg/dL. The rats with moderate diabetes and hypolipidemia were used for the experiment.

2.7. Animal allotment

After the induction of diabetes the rats were divided in to a four groups of six rats. Each group has six animals using different drug ratio:

- group 1: normal saline;
- group 2: diabetic control (streptozotocin);
- group 3: *G. sylvestre* 100 mg/mL;
- group 4: *G. sylvestre* 200 mg/mL;
- group 5: *G. sylvestre* 400 mg/mL;
- group 6: glibenclamide 5 g/kg.

2.8. Experimental procedure

During the study period, the animals were deprived of food overnight. Blood was collected from tail vein into two separate tubes. One tube containing potassium oxalate and sodium fluoride was used for the estimation of glucose, the other tube containing the blood was allowed to clot at room temperature and the serum obtained after centrifugation was used for estimation lipid. Apart from this fasting blood glucose [7], plasma protein [8], total hemoglobin [9], serum cholesterol [10], serum phospholipids [11], free fatty acids in serum [12] were also estimated.

2.9. Statistical analysis

All the data were statistically evaluated and the significance of various treatments was calculated. All the results were expressed as mean ± standard error of mean (S.E.M) and comparison between the groups were made by Analysis of variance (ANOVA), followed by Student *t* test. A value of $P < 0.01$ was considered significant.

3. Result

3.1. Body weight

Body weight increased significantly and all animals except diabetic rat. All animals ingested normal amounts of food and water during the study period (Table 1).

3.2. Determination of blood sugar and urine sugar

In the present study, oral feeding of methanol extracts of suspension cells (GSME1, GSME2, and GSME3) as well as field and wild grown plant leaves (GBL) for two days was found to reduce hyperglycemia, SC, phospholipids, and free fatty acids and increase body weight, plasma protein, total hemoglobin in streptozotocin induced rats as compared to untreated diabetic rats. Administration of the extracts was found to reverse the blood glucose considerably. The same trend was observed in urine sugar levels also (Table 2).

3.3. Lipid profile

The lipid profiles in control and experimental rats are depicted in (Table 3). In streptozotocin induced diabetic rats, there was a

Table 1
Effect of *Gymnema sylvestre* methanolic leaf extract on the changes of body weight of control and experimental rat observed for 28 days.

Serial no.	Groups	Body weight (g)				
		Initial (0 day)	Day 7	Day 14	Day 21	Final (28 days)
1	Control	205.15 ± 19.12	207.18 ± 18.21	216.12 ± 12.11	223.14 ± 11.41	230.21 ± 19.14
2	Diabetic (streptozotocin)	182.04 ± 1.2	174.02 ± 1.82	161.2.6 ± 3.02	153.11 ± 12.21	149.11 ± 11.4*
3	Diabetic + *G. sylvestre* methanolic leaf extract (100 mg/kg bw)	183.05 ± 2.41	185.05 ± 3.02	187.19 ± 2.45	187.02 ± 1.2	188.19 ± 2.45
4	Diabetic + *G. sylvestre* methanolic leaf extract (200 mg/kg bw)	190.13 ± 18.11*	192.14 ± 13.21	192.01 ± 1.2	193.25 ± 12.01	195.14 ± 12.21*
5	Diabetic + *G. sylvestre* methanolic leaf extract (400 mg/kg bw)	198.06 ± 19.43*	207.13 ± 14.21	216.12 ± 15.26	221.02 ± 10.26	229.02 ± 11.41**
6	Glibenclamide (5 mg/kg)	202 ± 11.25**	208 ± 10.21	214 ± 12.26	220 ± 11.32	225 ± 12.35**

Values are given as mean ± S.D ($n = 6$ rats).
* $P < 0.05$ *vs.* control.
** $P < 0.01$ *vs.* control by Student *t* test.

significant increase of TC, TG, phospholipids, low density lipoprotein (LDL) and very low-density lipoprotein (VLDL) cholesterol and significant decrease in HDL cholesterol in serum compared with normal control. The plant extract used in the study significantly decreased the level of cholesterol, TG, phospholipids, and LDL and VLDL cholesterol and significantly increased HDL cholesterol.

3.4. Histopathological investigation

Histopathology of the liver (Fig. 1) in control animals showed normal hepatic cells with well-preserved cytoplasm, nucleus, nucleolus, and central vein. In diabetic control, liver section showed that the lobular architecture was maintained, but there was also severe fatty change, sinusoidal dilation and congestion, mild periportal inflammation fibrosis, severe feathery degeneration and necrosis. In diabetic rats treated with GSME1, liver section maintained lobular architecture and had mild fatty change, mild sinusoidal congestion mild periportal inflammation fibrosis, and severe feathery degeneration. In normal animal treated with GSME1, liver section showed normal hepatic cells with well-preserved cytoplasm, nucleus, nucleolus, and central vein. In which normal hepatic structure was maintained.

Histopathology of the pancreas (Fig. 2) in control animal showed normal pancreatic parenchyma cells and islet cells. In diabetic control, pancreas section showed moderate hyperplasia of islet cells, severe congestion in pancreatic parenchyma, and mild infiltration

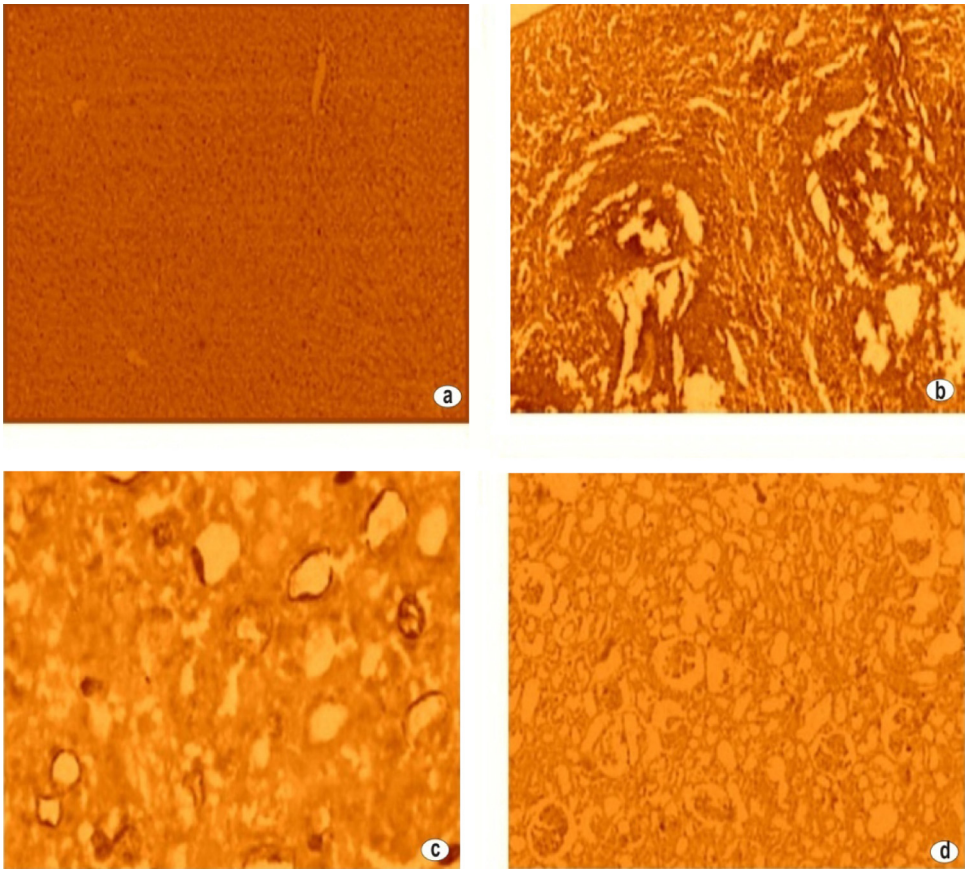

Fig. 1. Histopathology study of the liver : a: liver of control animal showing hepatic structure; b: liver of diabetic animal showing severe fatty changes, sinusoidal dilation, feathery degeneration, and necrosis; c: liver of diabetic animal treated with methanol leaf extract of *Gymnema sylvestre* showing mild fatty change, mild sinusoidal dilation, and congestion; d: liver of normal animal treated with methanol leaf extract of *Gymnema sylvestre* showing normal hepatic structure.

Table 2
Effect of *Gymnema sylvestre* methanolic leaf extract on the levels of blood glucose, plasma insulin, hemoglobin and urine sugar in control and experimental rats.

Serial no.	Groups	Blood glucose (mg/dL)	Plasma insulin (μg/mL) increase	Total hemoglobin (g/dL)	Urine sugar
1	NC	86.44 ± 8.81	16.27 ± 0.13	12.47 ± 1.35	Nil
2	DC (streptozotocin)	285.11 ± 19.33	7.28 ± 1.54	8.97 ± 0.49	++
3	GSME1 (100 mg/kg bw)	108.14 ± 4.57*	11.06 ± 1.21*	11.88 ± 0.45*	Nil
4	GSME2 (200 mg/kg bw)	103.11 ± 4.57*	14.05 ± 1.21*	13.07 ± 1.58*	Nil
5	GSME3 (400 mg/kg bw)	90.04 ± 3.12**	17.26 ± 1.05**	13.99 ± 0.45**	Nil
6	GNC (5 mg/kg)	84.27 ± 6.23**	15.16 ± 2.43**	14.88 ± 3.12**	Nil

GSME: *Gymnema sylvestre* methanolic extract; NC: normal control; DC: diabetic control; GNC: glibenclamide.
Values are given as mean ± S.D ($n = 6$ rats).
* $P < 0.05$ *vs.* control.
** $P < 0.01$ *vs.* control by Student *t* test.

Table 3
Effect of *Gymnema sylvestre* methanolic leaf extract on lipid profile of control experimental rats.

Serial no.	Treatment	TG (mg/dL)	HDL (mg/dL)	VLDL (mg/dL)	LDL (mg/dL)	Total C cholesterol	Serum phospho-lipid (mg/dL)
1	Control	77.15 ± 6.68	39.6 ± 2.71	17.03 ± 1.51	43.9 ± 4.25	98.16 ± 8.76	106.61 ± 5.09
2	Diabetic (streptozotocin)	133.32 ± 10.05	25.31 ± 1.64	32.14 ± 2.86	96.47 ± 8.12	215.2 ± 7.23	67.18 ± 4.27
3	Diabetic + *G. sylvestre* methanolic extract (100 mg/kg bw)	104.45 ± 11.14	27.56 ± 2.62	31.24 ± 1.64	94.19 ± 6.77	182.86 ± 10.05	71.12 ± 5.17
4	Diabetic + *G. sylvestre* methanolic extract (200 mg/kg bw)	94.18 ± 8.76*	37.23 ± 3.06*	30.19 ± 2.8*	88.41 ± 2.34	172.3 ± 5.12*	87.51 ± 4.19*
5	Diabetic + *G. sylvestre* methanolic extract (400 mg/kg bw)	89.49 ± 7.45**	38.27 ± 2.56**	21.52 ± 3.4**	71.27 ± 5.28**	115.6 ± 6.90**	93.48 ± 5.36**
6	Glibenclamide (5 mg/kg)	82.04 ± 6.71**	38.91 ± 5.14**	16.92 ± 1.34**	33.9 ± 2.66**	96.2 ± 4.8**	99.73 ± 5.44**

TG: triglycerides; HDL: high-density lipoprotein; VLDL: very low-density lipoprotein; LDL: low-density lipoprotein.
Values are given as mean ± S.D ($n = 6$ rats).
* $P < 0.05$ *vs.* control.
** $P < 0.01$ *vs.* control by Student *t* test.

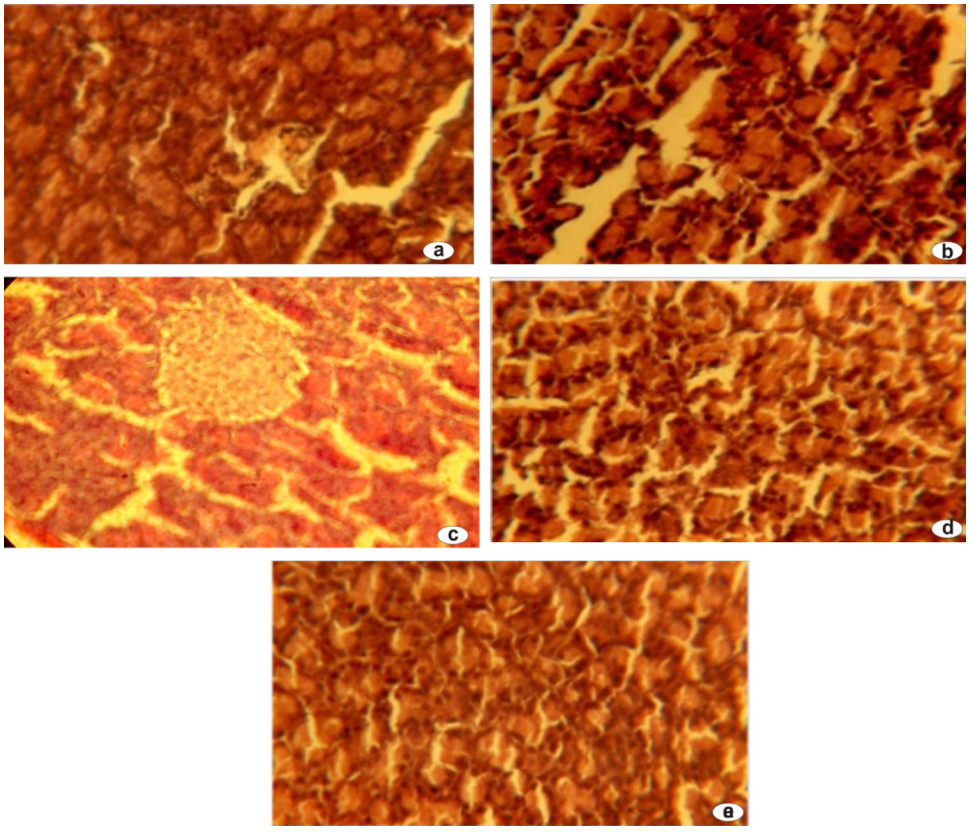

Fig. 2. Histopathology study of the pancreas: a: histopathology of islets of Langerhans normal rat (control); b: histopathology of islets of Langerhans diabetic rat (STZ) induced; c: histopathology of islets of Langerhans of diabetic rat treated with *Gymnema sylvestre* (100 mg/kg); d: histopathology of islets of Langerhans of diabetic rat treated with *Gymnema sylvestre* (200 mg/kg); e: histopathology of islets of Langerhans of diabetic rat treated with glibenclamide (5 g/kg).

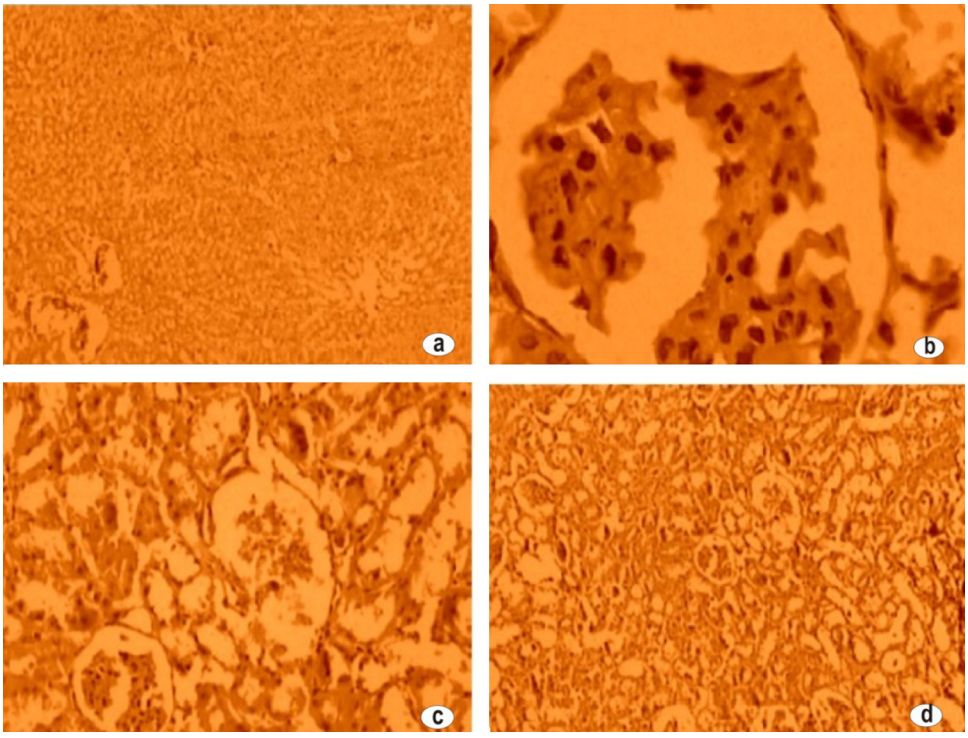

Fig. 3. Histopathology study of the kidney: a: kidney of diabetic animal showing normal histology; b: kidney of diabetic animal showing similar tubular epithelial atrophy, mild mesangial proliferation, mild sclerotic channges in the glomerulus, and moderate congestion of cappilaries; c: kidney of diabetic animal treated with methanol leaf extract of *Gymnema sylvestre* showing mild tubular epithelial atrophy and cogestion of capilaries; d: kidney of normal animal treated with methanol leaf extract of *Gymnema sylvestre* showing normal histological structure.

of inflammatory cells. In diabetic animals treated with GSME, pancreas section showed mild hyperplasia of islet cells and congestion of pancreatic parenchyma. In normal animals treated with GSME, the pancreas section showed normal pancreatic structure.

Histopathology of the kidney (Fig. 3) in control animals revealed normal structure. In diabetic control kidney, sections showed severe tubular epithelial atrophy, mild mesangial proliferation, mild sclerotic changes in the glomerulus, and moderate congestion of capillaries. In diabetic animal treated with GSME, kidney section showed mild tubular epithelial atrophy and congestion of capillaries. In animal treated with GSME, kidney section showed normal histology.

Morphological changes in liver, kidney, and pancreas due to direct toxic effect of streptozotocin as well as diabetic rats were remarkably reduced in rats treated with GSME although unable to prevent them completely (100 mg/mL GSME). GSME on its own did not produce any morphological changes in the organs tested (200 mg/mL GSME). Islet hyperplasia (possibly due to β-cell hyperplasia) due to streptozotocin induced diabetes was less conspicuous in the rats treated with GSME (100 mg/mL).

4. Discussion

Alloxan, a -cytotoxin, induces "chemical diabetes" in a wide variety of animal species by damaging the insulin secreting pancreatic β-cells, resulting in a decrease in endogenous insulin release, which paves the ways for the decreased utilization of glucose by the tissue [13]. In our study, we have observed that *G. sylvestre* decreases fasting blood glucose in streptozotocin diabetic rats that may be due to increase the activity of enzymes responsible for utilization of glucose by insulin-dependent pathway [14] or regenerate cells in pancreatic islets [5]. Like the plant extract, glibenclamide also produced significant reduction in blood glucose levels of alloxan diabetic rats, the present findings appear to be in consonance with the earlier suggestion [15].

In this study, the feeding of *G. sylvestre* leaf extract resulted in significantly decreased total cholesterol and serum triglycerides and significantly increased HDL-cholesterol level. This indicates that leaf extract had favorable effects, on lipid metabolism of diabetic rats. Derangement of glucose, fat, and protein metabolism in diabetes results in the development of hyperlipidemia [16–18].

Significant lowering total cholesterol and rise in HDL cholesterol is a very desirable biochemical state for the prevention of atherosclerosis and ischemic conditions [19]. These findings are correlated with the experiment [20]. Ingestion of *G. sylvestre* produces a significant lowering of cholesterol in a hypertension model [21]. Insulin is potent inhibitor of lipolysis since it inhibits the activity of the hormones sensitive lipases in adipose tissue and suppresses the release of triglycerides [22]. The increase in HDL-cholesterol levels may be beneficial awing to the negative correlation between HDL-cholesterol levels and cardiovascular diseases. This could be due to the presence of other hypolipidemic agents such as -sitosterol in the methanol leaf extract [23].

5. Conclusion

Diabetes mellitus is a well-known clinical entity with various late complications like retinopathy, neuropathy, nephropathy etc. *G. sylvestre* has significant antidiabetic as well as hypolipidemic activity so that it can be used as an adjuvant along with allopathic treatment of medicine to treat diabetes as well as to delay the late complications of diabetes.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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References

[1] Satoskar RS, Bhandarkar SD, Ainapure SS. Pharmacology and pharmaco therapeutics. Edn. 16 Mumbai: Popular Prakashan; 1999. p. 874.
[2] Tripathi KD. Essentials of medical pharmacology. 3rd edition New Delhi: Jaypee Brothers, Medical Pubhlishers Ltd; 2003. p. 532–42.
[3] Kamboj VP. Herbal medicine. Cur Sci 2000;78(1):35–51.
[4] WHO Expert Committee on diabetes mellitus. Technical reports series. Geneva: World Health Organization; 1980.
[5] Grijesh Kumar Mall, Pankaj Kishor Mishra, Veeru Prakash. Antidiabetic and hypolipidemic activity of *Gymnema sylvestre* in alloxan induced diabetic rats. Global J Biot Bioche 2009;4(1):37–42.
[6] Merina B. (2005). Toxicity studies of the herb *costus pictus* D. Don, Pharmainfo.net (accessed June 2, 2007). http://www.Pharmainfo.net/reviews/toxicity studies-herb-costus-pictus-d-don
[7] Yadav M, Lavanya A, Tomar R, Prasad GB, Jain S, Yadav H. Complementary and comparative study on hypoglycemic and antihyperglycemic activity of various extracts of Eugenia jambolana seed, *Momordica charantia* fruits, *Gymnema sylvestre*, and *Trigonella foenumgraecum* seeds in rats. Appl Biochem Biotechnol 2010;160(8):2388–400.
[8] Lowry OH, Rosenbrough MJ, Farr AL, Randall RJ. Protein measurement with folin-phenol reagent. J Biolchem 1951;193:265–75.
[9] Shiyovich A, Sztarkier I, Nesher L. Toxic hepatitis induced by *Gymnema sylvestre*, a natural remedy for 2 types diabetes mellitus. Am J Med Sci 2010;340(6):514–7.
[10] Quershi RN, Kaal E, Janssen HG, Schoenmakers PJ, Kok WT. Determination of plasma lipoproteins using flow field-flow fractionation coupled to gas chromatography-mass spectrometry. Anal Chim Acta 2011;706(2):361–6.
[11] Zilversmit DB, Davis AK. Microdetermination of plasma phospholipids by trichloroacetic acid precipitation. J Lab Clin Med 1950;35(1):155.
[12] Hron WT, Menahan LA. A sensitive method for the determination of free fatty acids in plasma. J lipid Res 1981;22(2):377–81.
[13] Szkudelski T. The mechanism of alloxan and streptozotocin action in β-cells of the rat pancreas. Physiol Res 2001;50:536–46.
[14] Ananthan R, Muniappan L, Leelavinothan P, Chokkanna GB, Vengatesh NB. Effect of *Gymnema montanumon* blood glucose. Plasma insulin and carbohydrate metabolic enzymes in alloxan-induced diabetic rats. J Med Food 2003;6(1):43–9.
[15] Ling Z, Wang Q, Stange G, Veld PI, Pipeleers D. Glibenclamide treatment recruits β-cell sub population into elevated and sustained basal insulin synthetic activity. Diabetes 2006;55:78–85.
[16] Kraus-Fredmann N. Hormonal regulation of hepatic gluconeogenesis. Physiol Rev 1984;64:170–6.
[17] Austin MA, Hokanson JE. Epidemiology of triglyceride, small dense low-density lipoprotein and lipoprotein (a) risk factors for coronary heart diseases. Med Clin North Am 1994;78:99–115.
[18] Brown MS, Goldstein JL. Lipoprotein receptor in the liver: control signals for plasma cholesterol traffic. J Clin Invest 1983;72:743–7.
[19] Luc G, Fruchart JC. Oxidation of lipoprotein atherosclerosis. Am J Clin Nutr 1991;53:206S–9S.
[20] Juhavekkilainen Mero N, Anjaschweizer Foly K, Rittajasinen M. Effects of naleglinide and glibenclamide on the post prandial lipid and glucose metabolism in type-2 diabetes. Diabetes Metab Res Rev 2002;18(6):484–90.
[21] Kanetkar P, Singhal R, Kamat M. *Gymnema sylvestre*: a memoir. J Clin Biochem Nut 2007;41:77–81.
[22] Shigematsu N, Asano R, Shimosaka M, Okazaki M. Effect of long-term administration with *Gymnema sylvestre* R BR on plasma and liver lipid in rats. Biol Pharm Bull 2001;24:643–64.
[23] Nanthakumar J, Sethumathi P, Malini A, Senguttuvelu S, Duraisamy R, Karthikeyan D, Sivakumar D. Antidiabetic activity of methanolic leaf extract *Costus pictus* D. Don in alloxan induced diabetic rats. J Health Sci 2007;53(6):655–63.