DOI: 10.7860/JCDR/2017/27430.9859

Experimental Research

Pharmacology Setion

Hypolipidaemic Effects of *Gymnema sylvestre* on High Fat Diet Induced Dyslipidaemia in Wistar Rats

DHEERAJ KUMAR SINGH[1], NARENDRA KUMAR[2], ANJULA SACHAN[3], PREET LAKHANI[4], SACHIN TUTU[5], RAJENDRA NATH[6], AMOD KUMAR SACHAN[7], RAKESH KUMAR DIXIT[8]

ABSTRACT

Introduction: Hyperlipidaemia is a well known risk factor for cardiovascular diseases. Lifestyle modification can be the initial step to reduce cholesterol levels. There are various drugs which are used to control dyslipidaemia. Treatment of lipid abnormalities is a lifelong battle. Moreover, the safety and effectiveness of long term lipid lowering treatment are questionable. *Gymnema Sylvestre* (GS) is a well known herb with various medicinal properties.

Aim: To explore the hypolipidaemic activity of *GS* leaves extract.

Materials and Methods: Adult healthy female wistar rats, 30 in number, divided into five groups, weighing 150- 200 g were used. Dyslipidaemia was induced in rats by feeding them on high fat diet for four weeks. For the next four weeks GS extract was used as test drug while Atorvastatin was used as standard drug. Blood sample was collected for estimation of lipid profile on day 0, week 4 and week 8.

Data was recorded as mean±SEM (Standard error of mean). Paired t-test and one way Analysis of Variance (ANOVA) followed by Dunnett's post hoc test was used for comparison. A p-value <0.05 was considered statistically significant. SPSS Statistics 20 (IBM software) was used for the analysis.

Results: Feeding rats with high fat diet for four weeks led to obesity and dyslipidaemia in rats. GS at both the doses (100mg/kg and 200mg/kg) significantly improved the lipid profile. Total Cholesterol (TC), Triglycerides (TG), Very Low Density Lipoprotein (VLDL) and Low Density Lipoprotein (LDL) values reduced significantly while that of High Density Lipoprotein (HDL) increased significantly. GS 200 mg/kg was found more effective than GS 100 mg/kg. GS improved the value of lipid profile significantly but the effect was found inferior to Atorvastatin.

Conclusion: From the present study it can be concluded that GS possess an effective hypolipidaemic effect. Hence it can be included as an add on therapy in dyslipidaemia after further confirmatory studies.

Keywords: Cholesterol, Extract, Lipid profile

INTRODUCTION

Hyperlipidaemia attributes to around one third of Cardiovascular Diseases (CVD) worldwide [1]. Clinically, it is mainly defined by elevated TC and/or Low-Density Lipoprotein Cholesterol (LDL-C), but the definition is also often extended to include non optimal levels of High Density Lipoprotein Cholesterol (HDL-C), TG, apolipoprotein B [2-4]. Lipid disorders can be mainly classified into primary or secondary to some underlying cause like environmental factors (diet rich in saturated fat and trans fat or a sedentary lifestyle), diseases (type 2 diabetes, chronic kidney disease, hypothyroidism, etc.,) and even medications (thiazide, β-blockers, progestins, anabolic steroids etc.,) [5,6].

There are various evidences in support of the fact that successful treatment of dyslipidaemia reduces morbidity and mortality from CVD. It is therefore desired to make a comprehensive strategy which includes various ways to control lipid levels and to also address associated metabolic abnormalities and modifiable risk factors such as obesity, hypertension, diabetes, and cigarette smoking.

Lifestyle modification can be the initial step to reduce cholesterol levels [7]. Besides this there are various drugs (statins, fibrates, nicotinic acid etc.,) which are effective in correcting dyslipidaemia [8,9]. Treatment of lipid abnormalities is considered as a lifelong battle as about three fourth of the patients discontinues their medication after two years. Moreover, the safety and effectiveness of long term lipid lowering treatment are questionable.

GS an indigenous herb belongs to the family Asclepiadaceae. The plant is also known as Gurmar in Hindi which means "destroyer of sugar" [10]. Powdered extract of its leaves is known to possess various properties: astringent, anti-inflammatory, diuretic, digestive, liver tonic, emetic, stimulant, antihelminthic, laxative, expectorant, antipyretic and diuretic. Various animal and human studies have shown the anti-diabetic properties of GS [11-13].

Some of the studies have been conducted in the past to explore the hypolipidaemic activity of this plant. But any conclusive inferences could not be drawn from those as some favoured the hypolipidaemic activity while others showed its absence. The various animal models that had been used were streptozocin induced diabetes and alloxan induced diabetic models. Present study was designed to explore and support the hypolipidaemic property of GS using High Fat Diet (HFD) rodent model and to further compare it with the standard drug Atorvastatin.

MATERIALS AND METHODS

Before commencing this animal experimental work ethical approval was taken from Institutional Animal Ethics Committee (IAEC), King George's Medical University, Lucknow, Uttar Pradesh, India (Research project No. 69/IAEC/2015).

A total of 30 adult healthy female wistar rats, weighing 150-200 g, were procured from the Indian Institute of Toxicology Research (IITR), Lucknow. They were kept at Institutional animal house of King George's Medical University, Lucknow, Uttar Pradesh, India. Standard conditions of temperature (25±2ºC), humidity (55±05%) and proper light dark cycle controlled environment were maintained throughout the work. Rats were given pellet diet and free access to drinking water.

After a period of acclimatisation for seven days, they were randomly divided into five groups with six rats in each group. On day 0, blood sample was collected for the estimation of lipid profile. During phase I (for four weeks) of the study, Group 1 (Normal Control) was given normal chow while Group 2 to 5 were kept on a HFD. HFD was provided by Bharat Science Solution Company, Lok Nagar, Unnao, Uttar Pradesh. It contained crude fat 25%, crude protein 18%, carbohydrate 44%, fiber 13%, moisture 8%, vitamins, minerals and other ingredients in appropriate quantity.

During phase II of the study (from fifth week to eighth week), Group 1 was continued on normal chow diet while Group 2 was continued on HFD. Other groups were given HFD along with respective drugs. Group 3 was given GS (100 mg/kg), Group 4 was on GS (200 mg/kg), Group 5 was given Atorvastatin (10 mg/kg). The drugs were given as a suspension in distilled water by oral route.

Test Drug

GS: Powdered extract was obtained from Ekgaon Company, New Delhi. The drug was administered in a dose of 100 and 200 mg/kg [14].

Standard Drug

Atorvastatin was given in a dose of 10 mg/kg [15].

Measurement of Body Weight

The body weight of rats was measured using digital weighing machine.

Collection of Blood Sample

By retro-orbital route after anaesthetising animals by using Pentobarbital (50 mg/kg, intraperitoneal).

Estimation of Plasma Lipid Profile

For estimation of TC, TG, HDL-C, Selectra E, a fully automated clinical chemistry analyser, manufactured by Vital scientific N.V. Netherlands and commercial kits based on enzymatic assay method (manufactured by Elitech Clinical Systems, France) were used.

Estimation of LDL-C and VLDL-C was done indirectly by using the formula:

$$LDL = TC - (HDL + TG/5)$$

$$VLDL = TG/5$$

STATISTICAL ANALYSIS

All the analyses was performed by SPSS Statistics 20 (IBM software). Data was recorded as mean±SEM (Standard error of mean). Paired t-test was used to compare a single group at different point of time. To make intergroup comparison, one way ANOVA followed by Dunnett's post hoc test was used. A p-value<0.05 was considered statistically significant.

RESULTS

On Day 0 all the rats were weighed and their blood sample was taken for lipid profile estimation. On applying ANOVA it was found that all the groups were comparable in terms of body weight and lipid profile with no significant difference among the groups [Table/Fig-1].

On feeding rats of Group 2 to 5 with HFD for four weeks, their body weight increased significantly and there were significant changes in the lipid profile as calculated by paired t-test. TC, TG, VLDL and LDL increased significantly from their respective values at day 0 while HDL fell significantly [Table/Fig-2].

Effect on Body Weight

During phase II of the study (between fifth and eighth week) all the groups were given their respective diet and drugs. In Group 2 (on HFD only) and Group 5 (Atorvastatin) body weight increased further while body weight reduced significantly (p-value <0.01) in Group 3 and 4. GS (100 mg/kg) and GS (200 mg/kg) caused 32.9% and 38.1% reduction in body weight when compared to the Group 2 (Disease control/HFD group).

At the end of eighth week Dunnett's post hoc test with Group 2 as comparison group showed that test drugs reduced body weight significantly [Table/Fig-3]. When compared to Group 1 no significant difference was found in Group 3 and 4.

Effect on TC

On feeding Groups 2 to 5 with HFD, the value of TC increased significantly after four weeks while there was no significant change in Group 1 [Table/Fig-4]. Further on giving drug treatment, the value of TC reduced significantly (p-value< 0.01) in all the drug groups (Group 3 to 5). Highest reduction (40.2%) in the value of TC occurred in Group 5 (Atorvastatin group) followed by 21.8% in Group 4 (GS-200 mg/kg) and 15.8% in Group 3 (GS-100 mg/kg).

On comparing with disease control (by Dunnett's post hoc test), TC decreased significantly in all the drug groups. But when compared to Atorvastatin control, significant difference was found. This showed that the test drug reduced the value of TC but it was not as much as that by Atorvastatin [Table/Fig-5].

Effect on Triglycerides

After giving HFD for four weeks to Group 2 to 5, the value of TG increased significantly. Introduction of drug treatment after fourth week lead to decrease in the value of TG in all the groups on drug (Group 3 to 5). Atorvastatin (Group 5) lead to highest reduction (37.4%) in TG followed by GS-200 mg/kg in Group 4 by 23.6% and GS-100 mg/kg in Group 3 by 18.0% [Table/Fig-6].

On applying Dunnett's post hoc test at the end of eighth week with Group 2 as comparison group, it was found that the value of TG fell significantly in all the drug groups as compared to disease control (Group 2). On comparing with Group 5 (Atorvastatin group), significant difference was found [Table/Fig-7]. Hence it can be said that although test drugs reduced the value of TG significantly yet it was found inferior to Atorvastatin.

Effect on HDL-C

HFD for four weeks caused HDL values to fall significantly in Groups 2 to 5 as shown in [Table/Fig-8]. After fourth week drug treatment was started. This lead to increase in the value of HFD in all the drug groups while it further decreased in HFD group (Group 2). Highest increase in the value of HDL occurred in Group 5 (76.3%) followed by in Group 4 (39.4%) and in Group 3 (30.3%) as compared to disease control group (Group 2).

Comparing with disease control (Group 2), HDL increased in all the drug groups but this effect was found inferior to the Atorvastatin as shown by Dunnett's post hoc test [Table/Fig-9].

Effect on VLDL

Feeding rats with HFD lead to increase in the value of VLDL in Groups 2 to 5. On starting drug treatment after fourth week, value of VLDL decreased significantly in Groups 3 to 5 while it further increased in HFD group (Group 2). Atorvastatin lead to highest reduction (37.5%) in VLDL value followed by GS-200 mg/kg (23.7%) and GS-100 mg/kg (18.1%) [Table/Fig-10].

Dunnett's post hoc test with Group 2 as comparison group showed that all the drugs reduced the value of VLDL significantly but when compared to Group 5, VLDL reducing effect of test drug was found inferior to Atorvastatin [Table/Fig-11].

Parameters	F-value	p-value
Body weight	0.266	0.897
TC	0.337	0.850
TG	0.303	0.873
HDL	0.124	0.972
VLDL	0.303	0.873
LDL	1.036	0.408

[Table/Fig-1]: Comparison of different groups by ANOVA at day 0.

GROUPS	DAY 0	WEEK 4	WEEK 8	% change at week 8 as compared to Group 2
Group 1	196.6±3.11	198.2±4.2	203.3±2.7	32.7
Group 2	197.1±7.5	292.0±3.7*	331.8±5.0#$	-
Group 3	188.2±8.6	284.9±7.4*	222.7±3.3#$	32.9
Group 4	188.4±11.7	283.8±9.2*	205.5±9.0#$	38.1
Group 5	189.9±9.4	285.5±9.0*	300.7±7.7#$	9.37

[Table/Fig-2]: Body weight (g) of all the Groups (mean ± SEM, n=6).
*Significant as compared to baseline (Day 0)
#Significant as compared to week 4
$Significant as compared to baseline (Day 0)

Y	X					
	Group 1 (Normal Control)		Group 2 (Disease Control)		Group 5 (Atorvastatin Control)	
	Mean Difference (Y–Group 1)	p-value	Mean Difference (Y–Group 2)	p-value	Mean Difference (Y–Group 5)	p-value
Group 1	-	-	-128.5*	<0.01	-97.4*	<0.01
Group 2	128.5*	<0.01			31.1*	<0.01
Group 3	19.4	0.10	-109.1*	<0.01	-78.0*	<0.01
Group 4	2.2	1.00	-126.3*	<0.01	-95.3*	<0.01
Group 5	97.4*	<0.01	-31.1*	<0.01	-	-

[Table/Fig-3]: ANOVA followed by Dunnett's post hoc test (comparison Groups- 2 and 5) at the end of eighth week for body weight.
*Significant.

GROUPS	DAY 0	WEEK 4	WEEK 8	% change at week 8 as compared to Group 2
Group 1	81.3±2.5	81.3±2.8	81.2±2.1	52.2
Group 2	80.9±2.4	152.6±2.7*	170.0±3.0#$	-
Group 3	78.5±3.1	155.4±2.9*	143.1±2.6#$	15.8
Group 4	83.8±3.2	154.8±3.3*	133.0±2.6#$	21.8
Group 5	80.4±4.6	155.5±2.6*	101.6±2.2#$	40.2

[Table/Fig-4]: Pre and post treatment Total Cholesterol (mg/dl) of all the Groups (mean ± SEM, n=6).
*Significant as compared to baseline (Day 0)
#Significant as compared to week 4
$Significant as compared to baseline (Day 0)

Y	X					
	Group 1 (Normal Control)		Group 2 (Disease Control)		Group 5 (Atorvastatin Control)	
	Mean Difference (Y–Group 1)	p- value	Mean Difference (Y–Group 2)	p- value	Mean Difference (Y–Group 5)	p-value
Group 1	-	-	-88.9*	<0.01	-20.4*	<0.01
Group 2	88.9*	<0.01			68.4*	<0.01
Group 3	62.0*	<0.01	-26.9*	<0.01	41.6*	<0.01
Group 4	51.8*	<0.01	-37.1*	<0.01	31.4*	<0.01
Group 5	20.4*	<0.01	-68.4*	<0.01	-	-

[Table/Fig-5]: ANOVA followed by Dunnett's post hoc test (comparison Groups- 2 and 5) at the end of eighth week for Total Cholesterol.
*Significant.

GROUPS	DAY 0	WEEK 4	WEEK 8	% change at week 8 as compared to Group 2
Group 1	67.2±3.3	69.5±3.2	67.6±1.7	55.5
Group 2	69.3±3.0	138.3±1.5*	152.0±1.8#$	-
Group 3	68.7±4.1	138.6±2.3*	124.7±2.4#$	18.0
Group 4	72.8±3.7	138.6±2.4*	116.2±1.9#$	23.6
Group 5	69.6±4.5	138.4±2.6*	95.2±2.9#$	37.4

[Table/Fig-6]: Pre and post treatment TG (mg/dl) of all the groups (mean±SEM, n=6).
*Significant as compared to baseline (Day 0)
#Significant as compared to week 4
$Significant as compared to baseline (Day 0)

Y	X					
	Group 1 (Normal Control)		Group 2 (Disease Control)		Group 5 (Atorvastatin Control)	
	Mean Difference (Y–Group 1)	p- value	Mean Difference (Y–Group 2)	p- value	Mean Difference (Y–Group 5)	p-value
Group 1	-	-	-84.4*	<0.01	-27.6*	<0.01
Group 2	84.4*	<0.01			56.8*	<0.01
Group 3	57.0*	<0.01	-27.4*	<0.01	29.4*	<0.01
Group 4	48.6*	<0.01	-35.8*	<0.01	21.0*	<0.01
Group 5	27.6*	<0.01	-56.8*	<0.01	-	-

[Table/Fig-7]: ANOVA followed by Dunnett's post hoc test (comparison Groups- 2 and 5) at the end of eighth week for Triglycerides.
*Significant

GROUPS	DAY 0	WEEK 4	WEEK 8	% change at week 8 as compared to Group 2
Group 1	33.4±1.0	33.8±1.3	32.8±1.1	65.7
Group 2	33.2±1.3	22.4±1.0*	19.8±0.9#$	-
Group 3	32.5±1.2	22.8±1.1*	25.8±0.9#$	30.3
Group 4	33.0±1.6	23.1±1.1*	27.6±1.0#$	39.4
Group 5	33.8±1.5	23.6±0.9*	34.9±1.3#$	76.3

[Table/Fig-8]: Pre and post treatment HDL (mg/dl) of all the groups (Mean±SEM, n=6).
*Significant as compared to baseline (Day 0)
#Significant as compared to week 4
$Significant as compared to baseline (Day 0)

Y	X					
	Group 1 (Normal Control)		Group 2 (Disease Control)		Group 5 (Atorvastatin Control)	
	Mean Difference (Y–Group 1)	p- value	Mean Difference (Y–Group 2)	p- value	Mean Difference (Y–Group 5)	p-value
Group 1	-	-	13.0*	<0.001	-2.1	0.447
Group 2	-13.0*	<0.01			-15.0*	<0.01
Group 3	-7.0*	<0.01	6.0*	0.002	-9.1*	<0.01
Group 4	-5.2*	<0.01	7.7*	<0.001	-7.3*	<0.01
Group 5	2.1	0.447	15.0*	<0.001	-	-

[Table/Fig-9]: ANOVA followed by Dunnett's post-hoc test (comparison Groups- 2 and 5) at the end of eighth week for HDL.
*Significant

GROUPS	DAY 0	WEEK 4	WEEK 8	% change at week 8 as compared to Group 5
Group 1	13.4±0.7	13.9±0.6	13.6±0.3	55.6
Group 2	13.9±0.6	27.7±0.3*	30.4±0.4#$	-
Group 3	13.7±0.8	27.7±0.5*	24.9±0.7#$	18.1
Group 4	14.6±0.7	27.7±0.5*	23.2±0.4#$	23.7
Group 5	13.9±0.9	27.7±0.5*	19.1±0.6#$	37.5

[Table/Fig-10]: Pre and post treatment VLDL (mg/dl) of all the groups (Mean±SEM, n=6).
*Significant as compared to baseline (Day 0)
#Significant as compared to week 4
$Significant as compared to baseline (Day 0)

Y	X					
	Group 1 (Normal Control)		Group 2 (Disease Control)		Group 5 (Atorvastatin Control)	
	Mean Difference (Y–Group 1)	p-value	Mean Difference (Y–Group 2)	p-value	Mean Difference (Y–Group 5)	p-value
Group 1	-	-	-16.9*	<0.01	-5.5*	<0.01
Group 2	16.9*	<0.01			11.4*	<0.01
Group 3	11.4*	<0.01	-5.5*	<0.01	5.9*	<0.01
Group 4	9.7*	<0.01	-7.2*	<0.01	4.2*	<0.01
Group 5	5.5*	<0.01	-11.45*	<0.01	-	-

[Table/Fig-11]: ANOVA followed by Dunnett's post hoc test (comparison Groups-2 and 5) at the end of eighth week for VLDL.
*Significant.

GROUPS	DAY 0	WEEK 4	WEEK 8	% change at week 8 as compared to Group 2
Group 1	34.5±1.5	33.5±1.9	34.9±1.9	70.9
Group 2	33.8±1.0	102.6±2.0$^{\$}$	119.8±2.2$^{\#\$}$	-
Group 3	32.3±1.6	104.9±1.8$^{\$}$	92.4±1.7$^{\#\$}$	22.9
Group 4	36.3±1.3	104.0±2.6$^{\$}$	82.2±1.8$^{\#\$}$	31.4
Group 5	32.7±2.2	104.2±1.9$^{\$}$	47.7±1.3$^{\#\$}$	60.2

[Table/Fig-12]: Pre and post treatment LDL (mg/dl) of all the groups (Mean±SEM, n=6).
$^{\$}$Significant as compared to baseline (Day 0)
$^{\#}$Significant as compared to week 4
$^{\$}$Significant as compared to baseline (Day 0)

Y	X					
	Group 1 (Normal Control)		Group 2 (Disease Control)		Group 5 (Atorvastatin Control)	
	Mean Difference (Y–Group 1)	p- value	Mean Difference (Y–Group 2)	p- value	Mean Difference (Y–Group 5)	p-value
Group 1	-	-	-84.9*	<0.01	-12.8*	<0.01
Group 2	84.9*	<0.01	-	-	72.1*	<0.01
Group 3	57.5*	<0.01	-27.3*	<0.01	44.7*	<0.01
Group 4	47.3*	<0.01	-37.6*	<0.01	34.5*	<0.01
Group 5	12.8*	<0.01	-72.1*	<0.01	-	-

[Table/Fig-13]: ANOVA followed by Dunnett's post hoc test (comparison Groups-2 and 5) at the end of eighth week for LDL.
*Significant.

Effect on LDL

HFD for four weeks lead to derangement of lipid profile. Value of LDL increased in all the groups on HFD. After starting drugs, value of LDL decreased in Group 3 to 5. Maximum reduction occurred in Group 5 on Atorvastatin (60.2%) followed by Group 4 (31.4%) and Group 3 (22.9%) [Table/Fig-12].

When compared to Group 2 (by Dunnett's post hoc test at the end of eighth week) it was found that all the drugs reduced LDL values significantly. On considering Group 5 as comparison group, significant difference was found. Thus the LDL reducing effect of test drugs was found inferior to Atorvastatin (10 mg/kg) [Table/Fig-13].

DISCUSSION

Diet rich in fats (HFD) given to rats for four weeks induced significant weight gain along with derangement of lipid profile. TC, TG, VLDL and LDL values increased significantly while that of HDL fell significantly. These findings suggest that the rats fed with HFD can act as a model of obesity and dyslipidaemia.

Powdered extract of GS was given to rats in two doses of 100 mg/kg and 200 mg/kg and effect was compared to that of Atorvastatin. GS at both the doses reduced TC but effect was inferior to Atorvastatin. Value of TG also decreased significantly but not equivalent to that of standard drug. The extract of *Gymnema* also improved the value of HDL-C significantly yet effect was lower as compared to Atorvastatin. GS also decreased the value of LDL and VLDL significantly but the effect was inferior to the standard drug Atorvastatin. The findings of present study are in accordance with some of the previous studies [16]. Mall GK et al., investigated the antidiabetic and hypolipidaemic activity of aqueous leaf extract in Alloxan induced diabetic rats at variable dosage [12].

Extract of GS are rich in phytochemicals, gymnemic acids and gurmarin are the active one [17]. Gurmarin is known to block the ability to taste sweet and bitter flavors thus reduces craving for food [18]. Palatal taste buds are innervated by greater petrosal nerve; gurmarin acts on it and decreases the phasic response to sugars [19]. Along with glucose it also decreases the intestinal absorbtion of histidine and oleic acids [20]. Gymnemagenin present in the leaf extracts increases the fecal excretion of cholesterol, neutral steroids and bile acids [21].

Aziza AM et al., demonstrated that treatment of streptozocin induced diabetic rats with leaf extract of GS significantly reduced the blood glucose, TC, LDL-C levels and increased insulin and HDL-C levels [22]. Rachh PR et al., showed that treating rats with leaf extract of GS increased the value of HDL and reduced TC, TG, LDL and VLDL [14]. The present study shows that leaf extract of GS possess significant hypolipidaemic action and strengthens the findings of some of the studies conducted to explore the lipid lowering action of GS.

LIMITATION

The present work is an animal experimental study to strengthen the effects of GS on lipid profile in animals. The results are limited to only two doses. This study has limitation of proper dose response relationship of GS on lipid profile. The use of only single model is another limitation. The number of animals in each group was six which may be another constraint.

CONCLUSION

The findings of the present study affirm that GS at both the doses (100 and 200 mg/kg) has a significant hypolipidaemic action but the effects were inferior to the standard drug Atorvastatin. It can be considered to use the active constituents of this plant as an add on therapy for hyperlipidaemia. Herbal drugs are considered safer and cheaper alternatives. Hence it would be to prudent to promote more studies on higher animals and humans so as to affirm the findings of present study.

REFERENCES

[1] National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the national cholesterol education program (ncep) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel iii) final report. Circulation. 2002;106:3143–421.
[2] Sniderman AD. Applying apoB to the diagnosis and therapy of the atherogenic dyslipoproteinemias: a clinical diagnostic algorithm. Curr Opin Lipidol. 2004;15:433– 38.
[3] Brunzell JD. Increased apo B in small dense LDL particles predicts premature coronary artery disease. Arterioscler Thromb Vasc Biol. 2005;25:474–75.
[4] Durrington P. Dyslipidaemia. Lancet. 2003;362:717.
[5] Smellie WS. Hypertriglyceridaemia in diabetes. BMJ. 2006;333:1257.
[6] Fonarow GC, Deedwania P, Fonseca V, Nesto RW, Watson K, Tarka E, et al. Differential effects of extended release carvedilol and extended release metoprolol on lipid profiles in patients with hypertension: results of the Extended Release Carvedilol Lipid Trial. J Am Soc Hypertens. 2009;3:210.
[7] Ballantyne CM, Grundy SM, Oberman A, Kreisberg RA, Havel RJ, Frost PH, et al. Hyperlipidemia: diagnostic and therapeutic perspectives. J Clin Endocrinol Metab. 2000;85:2089.
[8] Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high risk individuals: a randomised placebo controlled trial. Lancet. 2002;360:7.
[9] Brunzell JD. Clinical practice. Hypertriglyceridemia. N Engl J Med. 2007;357:1009.
[10] Arya Vaidya Shala, "Indian Medicinal Plants" A Compendium of 500 species, Vol.,Orient Longman Ltd., Madras. 1997;3:107-09.

[11] Sathya S, Kokilavani R, Gurusamy K. Hypoglycemic effect of Gymnema sylvestre (retz.,) R.Br leaf in normal and alloxan induced diabetic rats. Ancient Science of Life. 2008;28(2):12-14.
[12] Mall GK, Mishra PK, Prakash V. Antidiabetic and Hypolipidemic activity of Gymnema sylvestre in alloxan induced diabetic rats. Global Journal of Biotechnology & Biochemistry. 2009;4(1):37-42.
[13] Suman RK, Borde MK, Mohanty IR, Deshmukh YA. Antidiabetic activity of Gymnema sylvestre leaves extract on streptozocin induced experimental diabetic rats. Indo American Journal of Pharm Research. 2015;5(05):2054-60.
[14] Rachh PR, Rachh MR, Ghadiya NR, Modi DC, Modi KP, Patel NM, et al. Antihyperlipidemic activity of Gymenma sylvestre R.Br. leaf extract on rats fed with high cholesterol diet. International Journal of Pharmacology. 2010;6(2): 138–41.
[15] Reddy GD, Reddy AG, Rao GS, Kumar MV. Pharmacokinetic interaction of garlic and atorvastatin in dyslipidemic rats. Indian Journal of Pharmacology. 2012; 44(2):246-52.
[16] Preuss HG, Bagchi D, Bagchi M, Rao CV, Dey DK, Satyanarayana S. Effects of a natural extract of (-)-hydroxycitric acid (HCA-SX) and a combination of HCA-SX plus niacin-bound chromium and Gymnema sylvestre extract on weight loss. Diabetes Obes Metab. 2004;6(3):171-80.
[17] Khramov VA, Spasov AA, Samokhina MP. Chemical composition of dry extracts of Gymnema sylvestre leaves. Pharmaceutical Chemistry Journal. 2008;42(1): 30–32.
[18] Ninomiya Y, Imoto T. Gurmarin inhibition of sweet taste responses in mice. Am J Physiol. 1995;268:1019-25.
[19] Harada S, Kasahara Y. Inhibitory effect of gurmarin on palatal taste responses to amino acids in the rat. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2000;278(6):R1513-17.
[20] Shimizu K, Iino A, Nakajima J, Tanaka K, Nakajyo S, Urakawa N, et al. Suppression of glucose absorption by some fractions extracted from Gymnema sylvestre leaves. J Vet Med Sci. 1997;59(4):245-51.
[21] Persaud SJ, Majed HA, Raman A, Jones PM. Gymnema sylvestre stimulates insulin release in vitro by increased membrane permeability, J Endocrinol. 1999;163:207-12.
[22] Aziza AM, El Shafey, El-Ezabi MM, Seliem MME, Ouda HHM, Ibrahim D. Effect of Gymnema Sylvestre R.Br. leaves extract on certain physiological parameters of diabetic rats. Journal of King Saud University-Science. 2013;25:135-41.

PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Pharmacology, King George's Medical University, Lucknow, Uttar Pradesh, India.
2. Assistant Professor, Department of Pharmacology, King George's Medical University, Lucknow, Uttar Pradesh, India.
3. Assistant Professor, Department of Pharmacology, Hind Institute of Medical Sciences, Mau, Ataria, Sitapur, Uttar Pradesh, India.
4. Junior Resident, Department of Pharmacology, King George's Medical University, Lucknow, Uttar Pradesh, India.
5. Junior Resident, Department of Pharmacology, King George's Medical University, Lucknow, Uttar Pradesh, India.
6. Professor, Department of Pharmacology, King George's Medical University, Lucknow, Uttar Pradesh, India.
7. Professor, Department of Pharmacology, King George's Medical University, Lucknow, Uttar Pradesh, India.
8. Professor, Department of Pharmacology, King George's Medical University, Lucknow, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Dheeraj Kumar Singh,
Junior Resident, Department of Pharmacology, King George's Medical University,
Lucknow-226003, Uttar Pradesh, India.
E-mail: drdheerajsingh19@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Feb 10, 2017**
Date of Peer Review: **Mar 07, 2017**
Date of Acceptance: **Mar 16, 2017**
Date of Publishing: **May 01, 2017**