www.jahm.in
(ISSN-2321-1563)

ORIGINAL RESEARCH ARTICLE

RANDOMIZED CONTROLLED, OPEN LABELED STUDY OF A HERBAL PREPARATION, LEKHANEEYA MAHAKASHAYA GHANAVATI IN DYSLIPIDEMIA PATIENTS

DEEPAK BSR[1] JADHAV LAKSHMIPRASAD[2] GIRISH KJ[3] NARAYANA PRAKASH

ABSTRACT:

Background: Research over the past 4 decades has consistently shown the burden of dyslipidemia to be very high in terms of morbidity, mortality and medical costs. Dyslipidemia, being a chronic disorder, needs to be managed with safe and effective medicines. The current study compares the efficacy of two herbal preparations, Lekhaneeya Mahakashaya Ghanavati and Shuddha Guggulu Vati in the management of dyslipidemia. **Objective:** To evaluate and compare the efficacy of Lekhaneeya Mahakashaya Ghanavati versus Shuddha Guggulu Vati in the management of dyslipidemia. **Materials and Methods:** In this randomized, interventional, active controlled, open-labeled study, a total of 29 dyslipidemic patients were randomly assigned to receive either Lekhaneeya Mahakashaya Ghanavati (LMG; n = 15)or Shuddha Guggulu Vati (SGV; n = 14) for a duration of 4 weeks. The findings with respect to assessment criteria were recorded at baseline and at end of 4 weeks and assessed for the efficacy of the interventions. **Results:** LMG elicited significant results in Total cholesterol, LDL cholesterol, HDLcholesterol. SGV elicited significant results in Triglycerides. Both the drugs elicited significant results in anthropometric measurements like weight, BMI, various body circumferences and skinfold thickness. However, there was no statistically significant difference between the effects elicited by LMG and SGV on all the parameters.**Conclusion:** The trial drug, Lekhaneeya Mahakashaya Ghanavati is effective in par with Shuddha Guggulu Vati in the management of dyslipidemia. Further randomized and large multicentric studies are recommended.

Key Words: Ayurveda, Dyslipidemia, Lekhaneeya Mahakashaya Ghanavati; Shuddha Guggulu Vati, Commiphora mukul

[1]Postgraduate Scholar, [3]Professor, [4]Professor and Head, Department of Kayachikitsa, Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Thanniruhalla, Hassan-573201, Karnataka, India

[2]Professor and Head, Department of Roganidana, Ashwini Ayurvedic Medical College, Tumakur, India.

Corresponding author email: deepak.ayurveda@gmail.com Access this article online: www.jahm.in

INTRODUCTION:

Research over the past four decades has consistently shown the burden of dyslipidemia to be very high in terms of morbidity, mortality and medical costs. Dyslipidemia is a major risk factor for coronary heart disease (CHD), which is the leading cause of death in the United States. The World Health Organization estimates that dyslipidemia is associated with more than half of global cases of ischemic heart disease and more than 4 million deaths per year. [1]

Dyslipidemia is a broad term that refers to a number of lipid disorders. Most (80%) lipid disorders are related to diet and lifestyle, although familial disorders (20%) are important as well. The basic categories of dyslipidemias include: elevated low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), excess lipoprotein(a), hypertriglyceridemia, atherogenic dyslipidemia, and mixed lipid disorders.[2] Most patients with CHD have mixed dyslipidemia (e.g., elevated LDL-C and low HDL-C).

The literature on the epidemiology and economics of dyslipidemia is extensive. Quite literally, thousands of papers have been written on dyslipidemia, with more than 700 considering costs and more than 100 considering the costs of dyslipidemia alongside stroke or DM. Costs of cardiovascular disease and stroke vary widely around the world, but in every instance, costs are substantial. [1]

Dyslipidemia, being a chronic disorder, needs to be managed with safe and effective medicines. Ayurveda has a wide range of herbal drugs which have great potential in the management of dyslipidemia. Presently there has been a revived interest in this system of medicine and there is a necessity of revalidating these facts by systematic scientific studies.

In the context of dyslipidemia, it has been recommended by earlier studies that it must be treated on the lines of *apatarpana* and the drugs administered must possess *laghu, ruksha, ushna, chedaneeya*and*lekhaneeya* properties.[3,4]The drugs constituting the*Lekhaneeya Mahakashaya* illustrated in the *CharakaSamhita*[5], possess the above properties. The hypolipidemic actions of all these drugs are also well documented in various experimental studies.[6-14]A number of clinical trials have been conducted to evaluate the hypolipidemic effect of Guggulu and gugulipid. Most of these studies were carried out in India and one in the United States. Consistent with the preclinical data, most of these studies demonstrated hypolipidemic activity of guggulu or gugulipid with an average of 10–30% and 10–20% decrease in

total cholesterol and triglyceride, respectively.[15]

Based on the above facts, the present randomized, active controlled, open-labeled study on the efficacy of Lekhaneeya Mahakashaya Ghanavati(LMG)in comparison with that of Shuddha Guggulu Vati(SGV)in the management of dyslipidemia was planned.

MATERIALS AND METHODS

Research design: Interventional, randomized, active controlled open-labeled clinical trial.

Study Population: An accessible population of dyslipidemic patients in and around Hassan, who were representative of target population, participated in the study.

Sampling: Simple random sampling technique was followed using lottery method. Group allocation was done by simple random allocation (complete randomization). For this purpose, an online resource 'Research Randomizer' was used, which generated the random sequence of allocation of the recruited patients to the two groups.

Study sample: Previously known or freshly identified patients of dyslipidemia from in and around Hassan.

Sample size: A total of 29 patients of dyslipidemia, willingly participating in the study from in and around Hassan after a preliminary screening. Determination of sample size was not done priorly as this was a pilot scale study.

Study setting: The study was carried out in Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital (SDMCA&H), Hassan, Karnataka, South India, from June 2014 to March 2015. Hassan is a district headquarters with population of about 1,47,000.

Diagnostic Criteria: The diagnosis was based on serological investigation i.e. serum lipid profile as per ATP III Guidelines [16] (Total cholesterol>200 mg/dL; LDL-cholesterol >100 mg/dL; Triglycerides >150 mg/dL; HDL-cholesterol < 40 mg/dL)

Inclusion Criteria: Patients in the age group of 18-60 years, belonging to either gender, irrespective of caste, religion & socio-economic status with one or more of the diagnostic criteria of dyslipidemiaand consciously willing to participate.

Exclusion Criteria: Cardiovascular conditions or cardiac surgery within the prior 6 months, pregnant and lactating women, other systemic disorders viz., thyroid disorders, renal disorders, cerebro-vascular accident, PCOSand those who were consciously not willing to participate.

Ethical considerations: Ethical clearance was obtained from the institutional ethics committee (IEC) of SDM College of Ayurveda and Hospital, Hassan, Karnataka (IEC No: SDMCAH / IEC / 76 / 13-14; dt. 10th April, 2013). Informed consent was obtained from the participating patients.

Time and Duration of the Study: The total study period was 9 months i.e. June 2014 to March 2015. The duration of the clinical trial was 4weeks.

Selection of drug: Trial drug LMG is a poly herbal formulation in the form of tablet. Nine constituent drugs of *Lekhaneeya Mahakashaya*[Table 1]weresubstituted to pharmaceutical modification to get concentrated medicament in order to facilitate the easy administration and defined dosage form.

Control drug: SGV in the form of 500 mg tablets was administered as control drug. The constituent drugs of SGV are presented in Table 2.

Table 1. Constituent drugs of Lekhaneeya Mahakashaya Ghanavati

Sl.No	Sanskrit Name	Botanical Name	Part Used	Proportion
1	Musta	*Cyperusrotundus*Linn.	Rhizome	1 part
2	Kushta	*Saussurealappa*C.B. Clarke	Root	1 part
3	Haridra	*Curcuma longa* Linn.	Rhizome	1 part
4	Daruharidra	*Berberisaristata*DC.	Stem	1 part
5	Vacha	*Acoruscalamus*Linn.	Rhizome	1 part
6	Ativisha	*Aconitum heterophyllum*Wall.ex.Royle.	Root	1 part
7	Katurohini	*Picrorhizakurroa*Royle ex Benth.	Rhizome	1 part
8	Chitraka	*Plumbagozeylanica*Linn.	Root	1 part
9	Chirabilva	*Holopteleaintegrifolia (Roxb.)*	Stem Bark	1 part

Table 2.Constituent drugs of Shuddha Guggulu Vati

Sanskrit Name	Botanical Name / English Name	Part Used	Proportion
Guggulu	*Commiphora wightii* (Arn.) Bhand	Exudate	1 part
Gomutra	Cow urine	-	QS

Procurement of the drugs: The raw drugs of both LMG and SGV were procured from Dr. SP Kajrekar, raw drug dealer, Belgaum and authenticated in the Department of Dravyaguna, SDM Collegeof Ayurveda, Hassan.

Method of preparation: Thepreparation of LMG was done in Agasthya Herbal Health Care, a GMP certified pharmacy, Honnavar, Karnataka. *Kwatha* (decoction) of above drugs (coarse powder) taken in equalproportions

was prepared by adding 1 part of drug to 8 parts of water andreducing to 1/4th. This *Kwatha* was further heated till it became semi solid in consistency (method of preparation of *rasakriya*).[17]Tablets of 500 mg (drug weight) were punched and packed in air tight plastic containers. SGV was manufactured in theteaching pharmacy attached to SDM College of Ayurveda, Hassan. *Ashodhita* (non-purified) *guggulu*was broken into small pieces and bundled in a piece of the cloth andboiled in a vessel containing *gomutra* (cow urine). The boiling was continued till the guggulu became a soft mass. The impurities left behind in the cloth were discarded. Purified guggulu percolated through the clothwas taken out and spread overa smooth wooden board smeared with ghee. Then it was ground in a stone mortar (*khalva*), rolled into pills of 500mg each and dried insunlight. The pills were packed in air tight plastic containers.

Technique of Data Collection: After an initial screening, patients fulfilling the diagnostic and inclusion criteria were included in the study with due written consent of the participating patients. They were thoroughly interrogated; history and facts were noted in a specialized structured clinical proforma. General vital information about chief complaints, history of present and past illness, family history, personal history to get information on diet, appetite, bladder habits, bowel habits, allergies, addictions if any, along with treatment history was noted. Examinations included anthropometry, general physical examinations, systemic examinations along with *dashavidha pareeksha*.[18]Mechanical devices such as height weight scale, measuring tape and vernier's calipers were used as aids in collection of data.

Treatment methodology and schedule: The selected patients as per inclusion criteria were randomly allocated to control group (SGV-G) and trial groups (LMG-G). Methodology of treatment for each group is summarized in table 3.

Table 3. Methodology of interventions in control and study groups

Control group (SGV-G)	Trial group (LMG-G)
Two tablets of SGV(500 mg each) thrice daily orally after food with water for a period of 4 weeks with no alteration in diet habits	Two tablets of LMG(500 mg each) twice daily orally after food with water for a period of 4 weeks with no alteration in diet habits

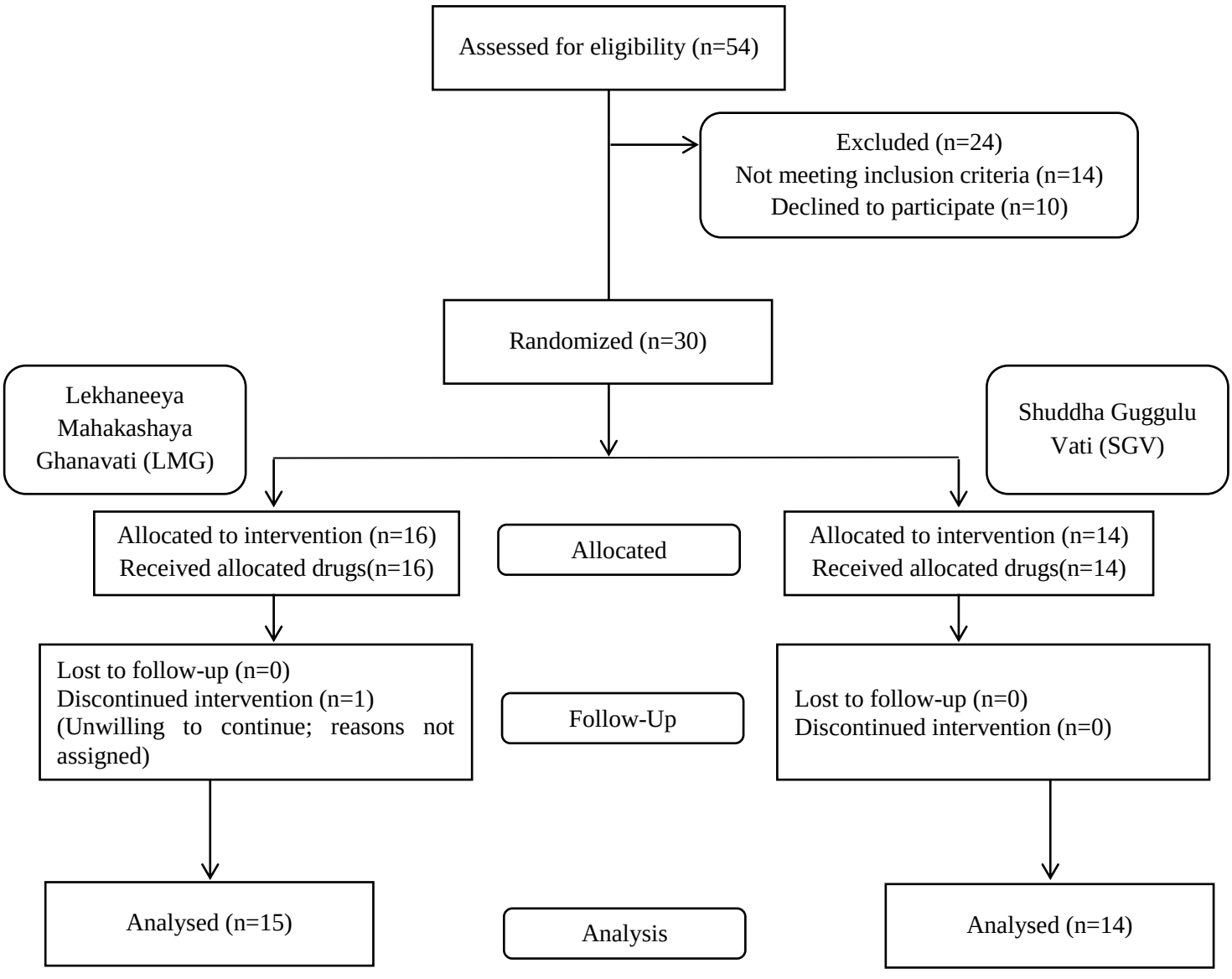
Assessment criteria: Both the groups were assessed before and after the studyon the basis of objective criteria with regards to lipid profile [total cholesterol(mg/dl), low density lipoprotein (mg/dl), triglycerides (mg/dl), high density lipoprotein (mg/dl), very low density lipoprotein (mg/dl)]; anthropometric measurements viz., weight in kg, BMI in kg/m^2,

chest circumference, abdominal circumference, waist circumference, hip circumference, mid-arm circumference, mid-thigh circumference, mid-calf circumference, waist-hip ratio, skinfold thicknesses of biceps, triceps and abdomen in centimeters

Adverse effect evaluation criteria: Evaluation and reporting of adverse effect was done as per the guidelines of national pharmacovigilence program for Ayurveda, Siddha and Unani (ASU) drugs. However there was no adverse effect noted in any patients.

Data analysis: Statistical evaluation of the data obtained was done using means, mean difference, standard deviation, 95% confidence interval, paired samples t test and independent samples t test, using SPSS version 20. The obtained results were interpreted in the statistical terms asnot significant (NS): $p > 0.05$, significant (S): $p < 0.05$ and highly significant (HS): $p < 0.001$

Flow Diagram



OBSERVATIONS AND RESULTS

A total of 30 patients of dyslipidemiaparticipated in the clinical trial with one patient dropping out in the course of study. There was more number of patients (46.7%) between the age group of 40 to 50 years. Among the participating patients, 43.3% were males and 56.7% were females. Majority (86.7%) of the registered patients was Hindus and 96.7% were married. Majority (50%) had completed their education upto level of graduation and above. Majority of patients (50%) were housewives. Most of them (83.3%) belonged to middle class. 86.7% of patients consumed a mixed diet. Maximum (56.7%) were habituated to tea/coffee. Majority (70.6%) of the female patients had already attained menopause.*Ahara* (diet) was found to be dominant in *madhurarasa*(sweet taste)(86.7%), *snigdha guna* (unctuous property) (53.3%) and*sheetaveerya* (~cold potency) (86.7%). Majority (60%) were habituated to *adhyashana*, followed by *samashana* (26.7%), *vishamashana* (6.7%), *ajeernashana* and *viruddhashana* (3.3%). Among 30 patients, 66.7% had practice of *diwaswapna*(day-sleep). 33.3% of the patients were interested in *shayyasanasukha*(sedentary lifestyle). On a daily basis, majority (56.7) performed mild physical work and the rest 43.3% of patients performed moderate physical work. Maximum (50%) patients performed no exercise at all; followed by 43.3% performing exercise irregularly. 23.3% of the patients were known cases of type 2 diabetes mellitus and 16.7% had association of hypertension. Analysis of *prakruti* (physical and mental disposition) revealed that 40% of patients were of *vata-pitta prakruti*, 36.7% that of *vata-kapha* and 23.3% that of *pitta-kapha*.70% among the registered patients had *dushti*(derangement)of *kapha dosha*, followed by 26.7% with that of *pitta dosha* and 3.3% of *vata dosha*.Majority (66.7%) of the patients had *dushti lakshanas*(features of derangement) of *meda dhatu*, 26.7% those of *rasa dhatu* and 6.7% those of *rakta dhatu*.96.7% of patients had *madhyama satwa*.All patients had *madhyama sara*.96.7% had *madhyama satmya*.66.7% had*madhyama samhanana*.96.7% of patients had *madhyama aharashakti*.All patients had *madhyama vyayamashakti*.

Success in the treatment was assessed by charting the improvements in lipid profile values as well as in the anthropometric

measurements. The response of therapy within trial group (LMG-G) and control group (SGV-G) for lipid profile and anthropometric measurements [table 4, table 5,table6 and table 7], betweenthe groups for lipid profileand anthropometric measurements [Table 8, Table 9 and Figure 1,Figure 2,Figure 3,Figure 4] are studied before and after trial.

Table 4. Effect of Lekhaneeya Mahakashaya Ghanavati on Lipid Parameters

Parameters	Means (mg/dl)		Diff. in Means (BT-AT)	Paired 't' Test				95% Confidence Interval of the Difference		Remarks
				S.D.	S.E.M	't' value	p value	Lower	Upper	
Total Cholesterol	BT AT	231.46 219.97	11.486	16.86	4.353	2.638	0.019	2.1488	20.8244	S
HDL Cholesterol	BT AT	44.073 46.313	- 2.240	3.376	0.871	-2.569	0.022	-4.1099	-0.37001	S
LDL Cholesterol	BT AT	130.91 120.06	10.853	13.06	3.374	3.217	0.006	3.61667	18.0900	S
VLDL Cholesterol	BT AT	56.393 57.113	- 0.720	8.240	2.127	-0.338	0.740	-5.2836	3.84363	NS
Tri-glycerides	BT AT	232.03 227.86	4.166	41.76	10.78	0.386	0.705	-18.96	27.2942	NS

HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, VLDL: Very Low-Density Lipoprotein,
BT: Before Treatment, AT: After Treatment, SD: Standard Deviation, SEM: Standard Error Mean, S: Significant, NS: Not Significant

Table 5. Effect of Lekhaneeya Mahakashaya Ghanavati on anthropometric measurements

Parameters	Means		Diff. in Means (BT-AT)	Paired 't' Test				95% Confidence Interval of the Difference		Re-marks
				S.D.	S.E.M	't' value	p value	Lower	Upper	
Weight (kg)	BT AT	66.816 66.102	0.714	0.425	0.109	6.508	<0.001	0.4791	0.9502	HS
BMI (kg/m^2)	BT AT	27.205 26.865	0.340	0.277	0.071	4.745	<0.001	0.1863	0.49370	HS
Chest Circumference (cm)	BT AT	95.1333 94.4267	0.7066	1.220	0.3152	2.242	0.042	0.0305	1.382	S
Abdominal Circumference (cm)	BT AT	95.733 95.066	0.6667	0.6172	0.15936	4.183	0.001	0.3248	1.0084	S
Waist Circumference (cm)	BT AT	93.833 92.733	1.100	1.929	0.4980	2.208	0.044	0.0317	2.168	S
Hip Circumference (cm)	BT AT	101.733 101.100	0.633	1.368	0.353	1.792	0.095	-0.124	1.391	NS
Mid-arm Circumference (cm)	BT AT	28.300 27.733	0.5666	0.9423	0.2433	2.329	0.035	0.04479	1.08854	S
Mid-thigh Circumference (cm)	BT AT	46.633 45.933	0.7000	0.8823	0.2278	3.073	0.008	0.2113	1.18864	S
Mid-calf Circumference (cm)	BT AT	31.666 30.533	1.1333	1.0601	0.2737	4.141	0.001	0.5462	1.7204	S
Waist-Hip Ratio (cm)	BT AT	0.9147 0.9087	0.006	0.027	0.00696	0.863	0.403	-0.0089	0.0209	NS
Bicepsskinfold thickness (cm)	BT AT	1.718 1.700	0.018	0.0161 2	0.0041	4.323	0.001	0.0090	0.0269	S
Triceps skinfold thickness (cm)	BT AT	2.169 2.125	0.044	0.0396	0.0102	4.303	0.001	0.0220	0.0659	S
Abdomen skinfold thickness (cm)	BT AT	2.505 2.456	0.0486	0.0405	0.0104	4.653	<001	0.0262	0.0711	HS

BMI: Body Mass Index, BT: Before Treatment, AT: After Treatment, SD: Standard Deviation, SEM: Standard Error Mean, S: Significant, NS: Not Significant, HS: Highly Significant

Table 6. Effect of Shuddha Guggulu Vati on Lipid Parameters

Parameters		Means (mg/dl)	Diff. in Means (BT-AT)	Paired 't' Test				95% Confidence Interval of the Difference		Re-marks
				S.D	S.E.M	't' value	p value	Lower	Upper	
Total Cholesterol	**BT**	222.80	3.535	8.162	2.1814	1.621	0.129	-1.176	8.24841	NS
	AT	219.26								
HDL Cholesterol	**BT**	45.807	-1.657	5.044	1.3480	-1.229	0.241	-4.569	1.25522	NS
	AT	47.464								
LDL Cholesterol	**BT**	130.62	13.25	23.339	6.2378	2.125	0.053	-0.2188	26.7331	NS
	AT	117.36								
VLDL Cholesterol	**BT**	46.421	1.978	5.3130	1.4199	1.393	0.187	-1.089	5.04621	NS
	AT	44.442								
Tri-glycerides	**BT**	230.75	23.39	28.860	7.7134	3.033	0.010	6.7290	40.0566	S
	AT	207.36								

HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, VLDL: Very Low-Density Lipoprotein,
BT: Before Treatment, AT: After Treatment, SD: Standard Deviation, SEM: Standard Error Mean, S: Significant, NS: Not Significant

Table 7. Effect of Shuddha Guggulu Vati on anthropometric measurements

Parameters	Means		Diff. in Means (BT-AT)	Paired 't' Test				95% Confidence Interval of the Difference		Re-marks
				S.D.	S.E.M	't'value	p value	Lower	Upper	
Weight (kg)	BT	73.664	0.8428	0.7917	0.2116	3.983	0.002	0.3857	1.300	S
	AT	72.821								
BMI (kg/m^2)	BT	27.822	0.3190	0.2624	0.0701	4.550	0.001	0.1675	0.4706	S
	AT	27.503								
Chest Circumference (cm)	BT	98.428	0.500	0.6504	0.1738	2.876	0.013	0.1244	0.8755	S
	AT	97.928								
Abdominal Circumference (cm)	BT	100.85	1.1428	1.6574	0.4429	2.580	0.023	0.18585	2.09986	S
	AT	99.714								
Waist Circumference (cm)	BT	100.57	1.4286	1.3986	0.3738	3.822	0.002	0.62105	2.23609	S
	AT	99.142								
Hip Circumference (cm)	BT	104.928	0.643	1.1507	0.3075	2.090	0.057	-0.021	1.307	NS
	AT	104.285								
Mid-arm Circumference (cm)	BT	31.36	0.571	1.0164	0.2716	2.104	0.055	-0.015	1.158	NS
	AT	30.786								
Mid-thigh Circumference (cm)	BT	48.393	1.3214	1.1369	0.3038	4.349	0.001	0.66499	1.97787	S
	AT	47.071								
Mid-calf Circumference (cm)	BT	33.714	0.5714	0.7559	0.2020	2.828	0.014	0.13497	1.00789	S
	AT	33.142								
Waist-Hip Ratio (cm)	BT	0.9529	0.00786	0.021	0.0055	1.412	0.181	-0.0041	0.0198	NS
	AT	0.9450								
Bicepsskinfold thickness (cm)	BT	1.741	0.0207	0.0168	0.0045	4.599	<001	0.01098	0.03045	HS
	AT	1.720								
Triceps skinfold thickness (cm)	BT	2.062	0.0364	0.0358	0.0096	3.801	0.002	0.01572	0.05714	S
	AT	2.026								
Abdomen skinfold thickness (cm)	BT	2.478	0.0528	0.0499	0.0133	3.956	0.002	0.02399	0.08172	S
	AT	2.425								

BMI: Body Mass Index, BT: Before Treatment, AT: After Treatment, SD: Standard Deviation, SEM: Standard Error Mean, S: Significant, NS: Not Significant, HS: Highly Significant

Table 8. Effect of trial group in comparison with control group on lipid profile parameters

Para-meter	Group	N	Means BT-AT (mg/dl)	Diff. in mean BT-AT (mg/dl)	Unpaired 't' test					Re-marks
					Std. Err. Diff.	95% Confidence Interval of the Difference		't' value	p value	
						Lower	Upper			
TC	SGV-G	14	3.5357	-7.95	4.869	-18.092	2.1905	-1.633	0.118	NS
	LMG-G	15	11.486							
HDL	SGV-G	14	-1.6571	0.5828	1.583	-2.666	3.832	0.368	0.716	NS
	LMG-G	15	-2.2400							

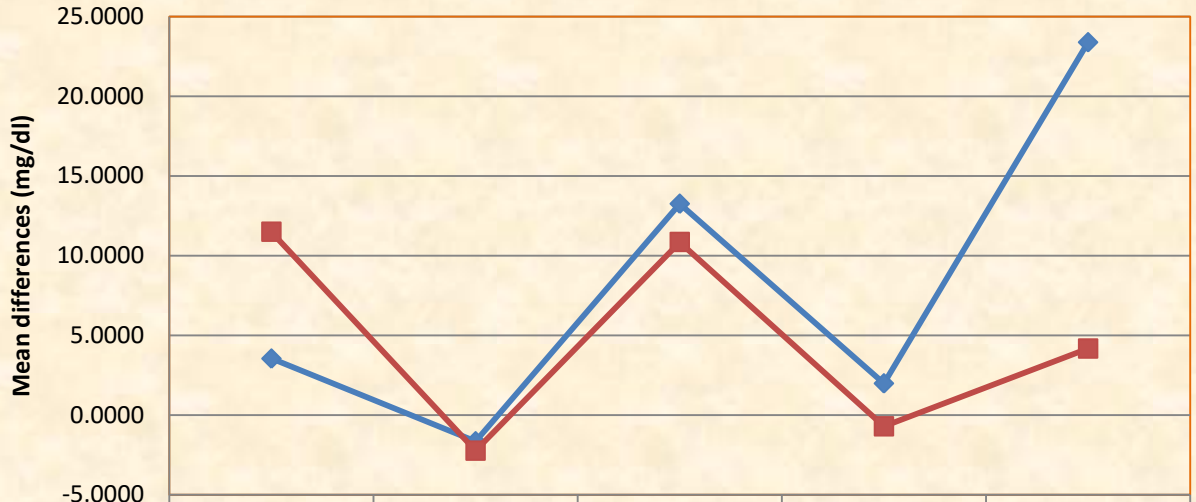
LDL	SGV-G	14	13.2571	2.4038	7.091	-12.383	17.1915	0.339	0.738	NS
	LMG-G	15	10.8533							
VLDL	SGV-G	14	1.9786	2.6985	2.596	-2.6281	8.0253	1.039	0.308	NS
	LMG-G	15	-0.720							
TG	SGV-G	14	23.3929	19.226	13.42	-8.3228	46.7752	1.432	0.164	NS
	LMG-G	15	4.1667							

TC: Total Cholesterol, HDL: High-Density Lipoprotein Cholesterol, LDL: Low-Density Lipoprotein Cholesterol, VLDL: Very Low-Density Lipoprotein Cholesterol, TG: Triglycerides, SGV-G:Shuddha Guggulu Vati group, LMG-G:Lekhaneeya Mahakashaya Ghanavati group, BT: Before Treatment, AT: After Treatment, Std. Err. Diff: Standard Error difference, NS: Not Significant

Table 9. Effect of trial group in comparison with control group on anthropometric measurements

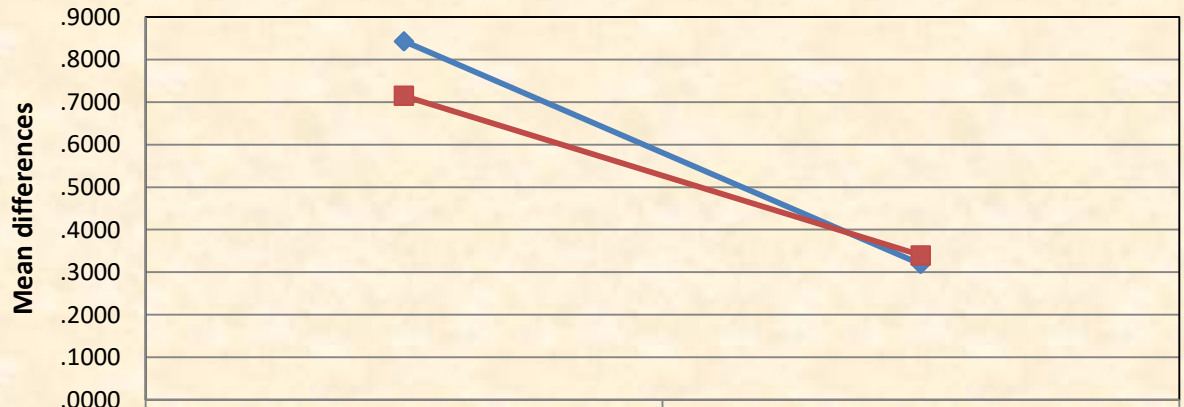
Parameter	Group	N	Means BT-AT (mg/dl)	Diff. in mean BT-AT (mg/dl)	Unpaired 't' test					Re-marks
					Std. Err. Diff.	95% Confidence Interval of the Difference		't' value	p value	
						Lower	Upper			
Weight (kg)	SGV-G	14	0.8429	0.1281	0.233	-0.3514	0.60778	0.548	0.588	NS
	LMG-G	15	0.7147							
BMI (kg/m^2)	SGV-G	14	0.3193	-0.02071	0.100	-0.2268	0.18540	-0.206	0.838	NS
	LMG-G	15	0.3400							
Chest Circumference (cm)	SGV-G	14	0.5000	-0.2066	0.3672	-0.9601	0.5468	-0.563	0.578	NS
	LMG-G	15	0.7067							
Abdominal Circumference (cm)	SGV-G	14	1.1429	0.4761	0.458	-0.4639	1.41633	1.039	0.308	NS
	LMG-G	15	0.6667							
Waist Circumference (cm)	SGV-G	14	1.428	0.3285	0.6297	-0.9634	1.62062	0.522	0.606	NS
	LMG-G	15	1.100							
Hip Circumference (cm)	SGV-G	14	0.6429	0.00952	0.471	-0.9577	0.9767	0.020	0.984	NS
	LMG-G	15	0.6333							
Mid-arm Circumference (cm)	SGV-G	14	0.5714	0.00476	0.363	-0.7414	0.7510	0.013	0.990	NS
	LMG-G	15	0.5667							
Mid-thigh Circumference (cm)	SGV-G	14	1.3214	0.6214	0.376	-0.1509	1.39378	1.651	0.110	NS
	LMG-G	15	0.7000							
Mid-calf Circumference (cm)	SGV-G	14	0.5714	-0.5619	0.344	-1.2681	0.1443	-1.633	0.114	NS
	LMG-G	15	1.1333							
Waist-Hip Ratio (cm)	SGV-G	14	0.0079	0.00186	0.0089	-0.0165	0.0203	0.207	0.838	NS
	LMG-G	15	0.0060							
Bicepsskinfold thickness (cm)	SGV-G	14	0.0207	0.00271	0.006	-0.0098	0.01528	0.443	0.661	NS
	LMG-G	15	0.0180							
Triceps skinfold thickness (cm)	SGV-G	14	0.0364	-0.00757	0.014	-0.0364	0.02129	-0.538	0.595	NS
	LMG-G	15	0.0440							
Abdomen skinfold thickness (cm)	SGV-G	14	0.0529	0.00419	.0168	-0.0303	0.03875	0.249	0.805	NS
	LMG-G	15	0.0487							

BMI: Body Mass Index, SGV-G:Shuddha Guggulu Vati group, LMG-G:Lekhaneeya Mahakashaya Ghanavati group, BT: Before Treatment, AT: After Treatment, Std. Err. Diff: Standard Error difference, NS: Not Significant



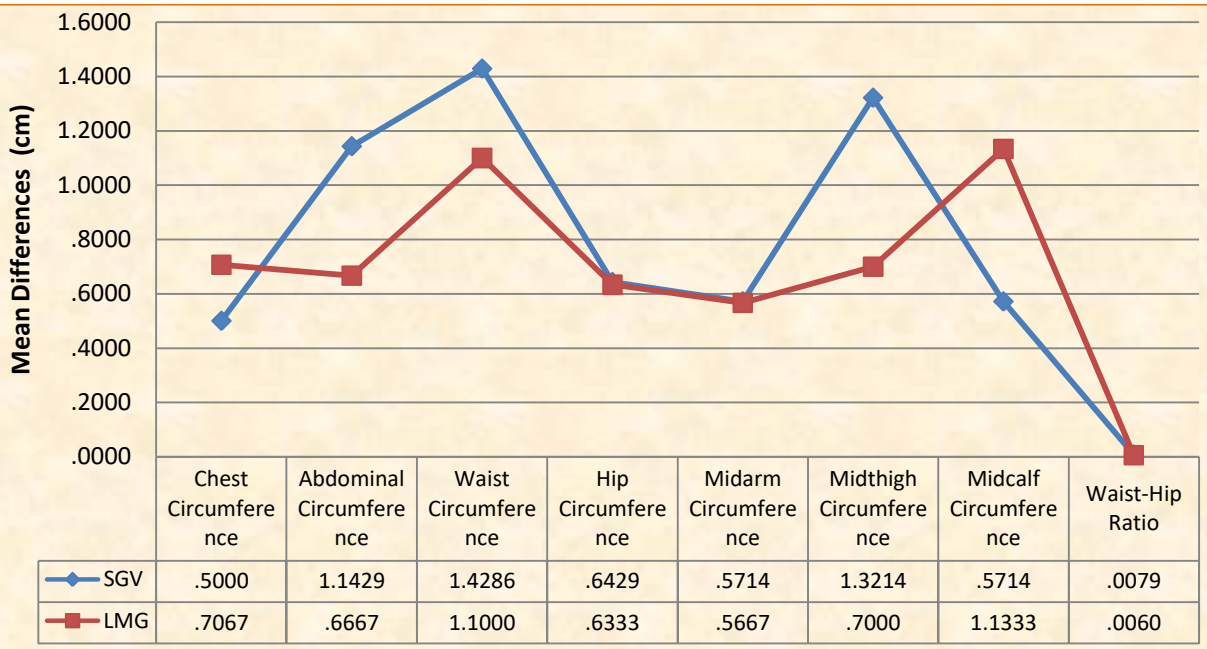
	Total Cholesterol	HDL Cholesterol	LDL Cholesterol	VLDL Cholesterol	Triglycerides
SGV	3.5357	-1.6571	13.2571	1.9786	23.3929
LMG	11.4867	-2.2400	10.8533	-.7200	4.1667

Fig 1. Comparison between mean differences of Shuddha Guggulu Vati and Lekhaneeya Mahakashaya Ghanavati Groups in Lipid Profile



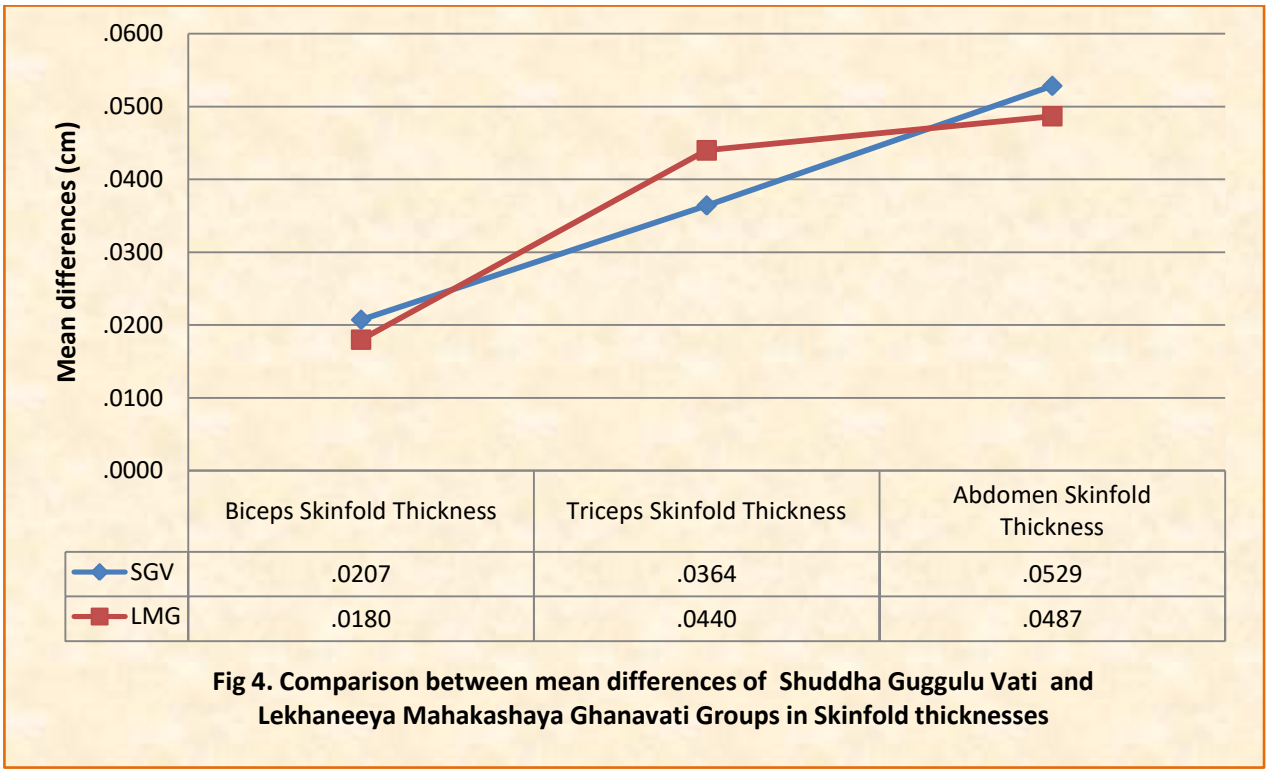
	Weight (kg)	BMI (kg/m2)
SGV	.8429	.3193
LMG	.7147	.3400

Fig 2. Comparison between mean differences of Shuddha Guggulu Vati and Lekhaneeya Mahakashaya Ghanavati Groups in Weight and BMI



	Chest Circumference	Abdominal Circumference	Waist Circumference	Hip Circumference	Midarm Circumference	Midthigh Circumference	Midcalf Circumference	Waist-Hip Ratio
SGV	.5000	1.1429	1.4286	.6429	.5714	1.3214	.5714	.0079
LMG	.7067	.6667	1.1000	.6333	.5667	.7000	1.1333	.0060

Fig 3. Comparison between mean differences of Shuddha Guggulu Vati and Lekhaneeya Mahakashaya Ghanavati Groups in Anthropometric Measurements



	Biceps Skinfold Thickness	Triceps Skinfold Thickness	Abdomen Skinfold Thickness
SGV	.0207	.0364	.0529
LMG	.0180	.0440	.0487

Fig 4. Comparison between mean differences of Shuddha Guggulu Vati and Lekhaneeya Mahakashaya Ghanavati Groups in Skinfold thicknesses

DISCUSSION:

Previously, various experimental and clinical studies have been carried out on the hypolipidemic activity of the control drug and the constituent drugs of the trial drug. Most of the animal studies were conducted in rats. Consistent results wereobtained with guggulsterone at doses ranging from 5 to 100 mg/kg of body weight.[15] In onestudy,guggulsterone, 25 mg/kg per oral, lowered serum cholesterol and triglycerides by 27% and30%, respectively, after a treatment period as short as 10 days. Along with the decrease in cholesterol and triglycerides, low-density lipoprotein (LDL) binding tohepatic cell membranes was significantly increased.[19,15]The lipid loweringaction of guggulsterone was also investigated in rats with hyperlipidemia induced by tritonor cholesterol-feeding.[20,15] In triton-fed rats guggulsterone, at a dose of 50mg/kg p.o., significantly decreased serum lipids. In cholesterol-fed rats guggulsterone, at adose of 5 mg/kg per oral for 30 days, decreased lipids, LDL, and very low-density lipoprotein(VLDL) levels. In addition, it was found that guggulsterone treatment increased lipolyticenzyme activity as well as receptor-mediated catabolism of LDL.[20,15]With the hypolipidemic efficacy in rats being proven, guggulsterone was used as a positive control to assess the hypolipidemic activity of other chemical compounds.[21,22,15]

A number of clinical trials have also been conducted to evaluate the hypolipidemic effect of guggulu and gugulipid.[15]In one such study, a total of 205 patients who werehypercholesterolemic or hypertriglyceridemic were enrolled.When these patients were treated with500 mg gugulipid daily for 12 weeks, total serum cholesterol and triglycerides decreased by24% and 23%, respectively. It should bementioned that such hypolipidemic effectswere observedin 70–80% patients with no effect in the remaining subjects. No detailed descriptionfor those nonresponderswas given, for example,whether or not theywere obese.[23,15]A crossover follow-up study to this preliminary investigation was conducted to compare gugulipid with an antihyperlipidemic drug clofibrate in a total of 233 patients**.** [23,15]One hundred and twenty five patients were treated with gugulipid at 500 mg daily for 12 weeks, whereas 108 patients were treated with clofibrate at the same dose. At the end of the study, gugulipid significantly decreased total serum cholesterol by 11% and triglycerides by 17%. These effects were comparable to those of clofibrate (10% and 22% reduction in cholesterol and triglyceride levels, respectively). The beneficial effects of gugulipid became evident within the first 3–4

weeks of the study. In addition, HDL level was increased in 60% of the responders to gugulipid therapy, whereas clofibrate had no effect on HDL levels. More detailed analysis of the results indicated that hypercholesterolemic patients responded better to the gugulipid therapy than did hypertriglyceridemic patients, and vice versa for clofibrate. The study clearly demonstrated the benefits of guggulu therapy in reducing cholesterol and lipid levels in hypercholesterolemic and hypertriglyceridemic patients.[23,15]

Various studies establishing the hypolipidemic activity of the constituents of LMG have been conducted. *Cyperusrotundus* was investigated for hypolipidemic activity in CCl_4 Induced dyslipidemia in male albino rats of Wistar strain. The fine powder of *Cyperusrotundus* rhizome was dissolved in distilled water and administered orally.In the study group, rats were treated with *Cyperusrotundus* (through intragastric tube) at the dose of 500 mg/kg body weight every day in addition to CCl_4 suspension every alternate day for 15 consecutive days. *Cyperus rotundus* significantly decreased the level of LDL, increased the level of HDL when compared to untreated and significantly restored in the level of lipid profile in CCl_4 induced dyslipidemia in rats.[24]

Ethanolic extract of *Saussurea lappa*(EESL) was tested for its hypolipidemic activity. Hyperlipidemia was induced in male wistar rats by the oral administration of cholesterol (400 mg/kg) along with cholic acid (50 mg/kg) in coconut oil for 20 days, once daily. The rats with elevated cholesterol level were divided into 5 groups of 6 animals each and given drug/vehicle treatment for 7 days. During these 10 days all groups also received cholesterol in same dose as earlier. High fat diet fed rats showed significant increase ($p<0.001$) in Serum cholesterol, triglyceride, LDL-C, but significant decrease ($p<0.001$) in HDL-C level as compared to 0 day and normal control rats. Treatment with EESL (200mg/kg) exhibited significant reduction ($p<0.05$) in triglyceride and LDL-C. Treatment with EESL (400mg/kg) showed significant reduction ($p<0.001$) in TC, LDL and Triglyceride ($p<0.001$), but significant increase ($p<0.01$) in HDL-C as compared to high cholesterol diet fed rats.[25]

Curcuma longa's protective properties on the cardiovascular system include lowering cholesterol and triglyceride levels, decreasing susceptibility of low density lipoprotein (LDL) to lipid peroxidation and inhibiting platelet aggregation. In various studies, *Curcuma longa* extract demonstrated decreased susceptibility of LDL to lipid peroxidation, in addition to

lower plasma cholesterol and triglyceride levels.[26]

Effect of *Berberisaristata* on lipid profile and coagulation parameters after high cholesterol diet (HCD) for 45 days was investigated in 14 healthy white rabbits of either sex. All animals were equally divided into 2 groups. After 45 days of HCD, animals of treated group were administered *B. aristata* orally for period of 30 days in the dose of 25 mg/kg during the first phase of study, while animals of control group were administered normal saline through same route equivalent to the volume of respective doses according to their body weight. Body weights of the animals were measured weekly. During the second phase of study, animals of treated group were further administered *B. aristata*for 15 more days making a total period of 45 days and compared with control for the same period. Blood samples were collected thrice from the ear vein of animals, first after 45 days of HCD then again after 30 and 45 days dosing of *B. aristata*. Rabbits which received *B. aristata* in a dose of 25 mg/kg for a period of 45 days showed highly significant decrease in the levels of triglycerides and LDL-C and in comparison to control values, while cholesterol was significantly decreased as compared to control.[27]

Male adult albino rats (180–200 g) randomly bred in the animal house of C.U. Shah College of Pharmacy, Mumbai, India, were used in an experimental study which tested the hypolipidemic activity of *Acoruscalamus*. Administration of the 50% ethanolic extract (100 and 200 mg/kg) as well as saponins (10 mg/kg) isolated from the extract demonstrated significant hypolipidemic activity. On the contrary, the aqueous extract showed hypolipidemic activity only at a dose of 200 mg/kg.[28]

The alcoholic, chloroform and aqueous root extracts of *Picrorhizakurroa*Royle ex Benth were screened for its antihyperlipidemic activity in Triton wr-1339 induced albino rats. Atorlip-20 was used as reference standard. The results showed significant decrease in triglyceride and cholesterol level when compared with the hypolipemic groups by using different doses: low (50mg/kg), high (200mg/kg) and standard Atorlip-20(4mg/kg bw) and by treating for 7 hr and 24 hr.[29]

A study examined the antihyperlipidemic effect of the aqueous extract of *Plumbagozeylanica* Linn. (Plumbaginaceae) roots in diet-induced hyperlipidemic rats. The oral administration of the aqueous extract at the dose of 20, 40, and 80 mg/kg were found to ameliorate the hyperlipidemic condition as evidenced by a reduction of cholesterol and triglyceride levels. The standards fenofibrate (20 mg kg−1) and atorvastatin (8 mg kg−1) were also found to exhibit significant ($p < 0.05$)

cholesterol and triglyceride lowering effect. Further, the aqueous extract at all doses demonstrated a significant ($p < 0.05$) increase in fecal cholesterol excretion indicating a reduction in intestinal cholesterol absorption. e cholesterogenesis. The aqueous extract (20, 40 and 80 mg kg−1) also significantly ($p < 0.05$) reduced the total lipid content in the liver. Thus the results suggest a beneficial role of aqueous extract of *Plumbagozeylanica* roots in ameliorating the hyperlipidemic condition leading to atherosclerosis.[30]

Hypolipidemic effect of *Holoptelia integrifolia* and its mechanism in diet-induced obese rat model was investigated. After 4 weeks of oral administration, blood samples were collected for the estimation of serum lipids, lecithin cholesterolacyltransferase

(LCAT),apolipoproteins (apo) and liver for HMG-CoA reductase (HMGR) assay. The faecal samples were also collected to estimate the faecal fat content. The *H. integrifolia* treatment markedly lowered body weight, serum lipids and apo B and increase high-density lipoprotein-cholesterol and apo A1 concentrations. In this study, HMGR activity was enormously reduced, which helps to reduce cholesterol biosynthesis and an increase in LCAT activity was also observed. The detailed faecal analysis showed a remarkable increase in faecal lipids, which indicates the ability to inhibit intestinal fat

Additionally, the activity of lipogenic enzymes like HMGCoAreductase in the liver remained significantly ($p < 0.05$) low on treatment of aqueous extract (80 mg kg−1), thus decreasing th

absorption. The methanol fraction of H. integrifolia on LC-MS and tandem mass spectrometry analysis shows the presence of a compound, 3-(7 -ethoxy-4-methyl-2-oxo-2H-chromen-3-yl)propanoate (C1). The result showed that the significant hypolipidemic effect of *H. integrifolia* may be linked to its ability to inhibit HMGR activity and block intestinal fat absorption.[31]

In the current study, the diet of the dyslipidemic patients enrolled for the trial was found to be dominant in *madhura rasa* (sweet taste), *snigdha guna* (unctuous property) and *sheetaveerya* (~cold potency). Majority were habituated to *adhyashana*(eatingrepeatedly). Majority followed sedentary lifestyle (depicted by majority of patients who performed mild physical work and no exercise at all). These factors are known to increase *kapha dosha, medo dhatu* and*ama*which was quite evident by the *dosha* and *dhatu* assessment, suggesting their role in pathogenesis of dyslipidemia. It is known that derangementof *kapha* and *medas* must be corrected by the principles of *apatarpana*.This provides evidence for the rationale of selection of the trial drug based on the hypothesis that

dyslipidemia must be managed on the lines of *apatarpana.*LDL is the most abundant and clearly evident atherogenic lipoprotein[16]which has been significantly reduced by LMG. HDL is inversely related to total body cholesterol and a reduction of plasma HDL concentration may accelerate the development of atherosclerosis, leading to ischemic heart disease, by impairing the clearance of cholesterol from the arterial wall.[28]LMG has brought about significant increase in the HDL-cholesterol levels. Thus, LMG can be considered as a promising cardio-protective drug in the management of coronary artery disease.

When triglyceride levels are ≥200 mg/dL, the presence of increased quantities of atherogenic remnant lipoproteins can heighten CHD risk substantially beyond that predicted by LDL cholesterol alone. Elevated triglycerides represent one factor within a set of risk-factor targets in persons who are overweight, obese, sedentary, or cigarette smokers. [32] With these facts in view, the significant reduction of triglyceride levels by SGV is of great importance.

Both the drugs have shown promising results on most of the objective parameters related to obesity (i.e., body weight, BMI, body circumferences and skin-fold thickness), which shows the depletory action on *vruddha sthayi medo dhatu*.[33]Overweight and obesity not only predispose to CHD, stroke and numerous other conditions, but also are associated with greater all-cause mortality. People who are overweight or obese have a high burden of other CHD risk factors including dyslipidemia (high LDL cholesterol, low HDL cholesterol and high VLDL and triglycerides), type 2 diabetes and hypertension.[16]With these facts in background, the results seen in the current study are quite encouraging and suggest that the drugs can be effectively used to manage the conditions of over-weight and obesity associated with dyslipidemia.

Probable mode of action of LMG:

Normally hepatocytes initiate synthesis of triglycerides and cholesterol during states of increased free fatty acid flux to the liver (e.g., after the fatty meal or in the situation of increased lipolysis). LMG's effect on cholesterol levels may be due to decreased cholesterol uptake in the intestines. By virtue of LMG, there may be inability of hepatocytes to increase cholesterol synthesis and decrease hepatocyte cholesterol concentration by increasing the catabolic conversion of cholesterol to bile acids in liver.

Curcumin, the chief phyto-chemical of *haridra,* one of the constituent of LMG, mobilizes α-tocopherol from adipose tissue, which results in protection against oxidative damage produced during atherosclerosis development. Curcumin increases VLDL cholesterol transport

in plasma, which results in increasing levels of α-tocopherol.[26]

Saponins and tannins present in some of the constituent drugs of LMG, are known to prevent cholesterol absorption, interfere with its entero-hepatic circulation and increase its fecal excretion and fecal bile acid excretion, thereby leading to reduction in cholesterol levels.[28]

LMG has predominance of *katu, tikta rasa;laghu, ruksha guna;ushnaveerya andkatuvipaka.*It pacifies the vitiated *kapha dosha* and *medo dhatu*, which are dominant in the pathogenesis of dyslipidemia. It also depletes the excessively produced *rasa, meda, vasa, sweda and kleda,* which are all similar in attributes to *kapha dosha*. Thus, it has the potential to act against the *santarpanottha* pathogenesis of dyslipidemia and also bring about reduction in *vruddha sthayi medo dhatu* which is reflected by the results in anthropometric measurements, weight and BMI.

Probable mode of action of SGV: Guggulsterone, the bioactive constituent of guggulu has been identified as an antagonist at the nuclear receptor farnesoid x receptor (FXR).[34,35,15], a key transcriptional regulator for the maintenance of cholesterol and bile acid homeostasis.[36,37,38,15]Subsequent studies also found that guggulsterone is a potent antagonist at the mineralocorticoid receptor (MR), glucocorticoid receptor (GR) and androgen receptor (AR), and an agonist at pregnane x receptor (PXR), progesterone receptor (PR) and estrogen receptor (ERα).[35,39,40,41,15]

In the liver, the conversion of cholesterol to bile acids is initiated by the rate-limiting enzyme, cholesterol 7α-hydroxylase (CYP7A1), whereas removal of bile acids from the liver is mediated by the rate limiting bile acid transporter bile salt export pump (BSEP).[42,43,15] A study demonstrated that guggulsteroneupregulates the expression of the bile salt export pump (BSEP), a rate-limiting efflux transporter for eliminating cholesterol metabolites bile acids from the liver. Such upregulation is possibly mediated through the activating protein 1 (AP-1) signaling pathway.[44,15]

The FXR antagonism and enhanced BSEP expression have been proposed as possible mechanisms for the hypolipidemic effect of guggulsterone.[34,44,15] In addition, guggulsterone has been found to be a potent inhibitor of the nuclear factor-κB (NF-κB),[45,46,47,15] a key regulator for inflammatory responses. Such repression of NF-κB activation may represent a mechanism for the anti-inflammatory effect of guggelsterone.

Pharmacological studies revealed that the pure guggulsterone isomers had pronounced hypolipidemic activity.[48,49,15] Therefore, it is

generally accepted that guggulsterone is the bioactive constituent in guggulu and gugulipid responsible for the therapeutic effects.

Although the antioxidant effect of guggul and guggulsterone has been demonstrated in vitro and in vivo, the underlying mechanism remains largely to be determined. It has been well established that LDL is atherogenic and accumulates in atherosclerotic lesions. Although it is not clear how LDL is oxidized in vivo, accumulating evidence indicates that LDL oxidation is essential for atherogenesis.[50,51,15]Antioxidants that prevent this oxidation may either delay or prevent atherogenesis. The antioxidant activity of guggulsterone was first reported in the 1990s.[52,53,15] In those studies, the ability of guggulsterone to prevent oxidation of LDL was demonstrated in vitro[15]

Recent studies have proved that cow urine, which has been used for *shodhana* of Guggulu in the current study, exhibits antioxidant activity and that cow urine could be a potential source of natural antioxidant that could have greater importance as supportive therapy in preventing or slowing oxidative stress related degenerative diseases.[54]The recent findings related to cow urine was its role as a bio-enhancer. It is an activity enhancer and availability facilitator for bio active molecules.[55] By virtue of its being a bio-enhancer, it may facilitate and enhance the action of Guggulu.

SGV has predominance of *katu, tiktarasa;laghu, ruksha, sara, vishada, ushna andteekshna guna; ushnaveerya andkatuvipaka.*It is *kapha vata shamaka*and brings about*karshana*by its *medohara* property. These properties might be the reason for its effect on the weight, BMI, body circumferences and skin fold thicknesses.

CONCLUSION

In the current study, most of the dyslipidemic patients were of *vata-pitta* and *vata-kaphaprakruti*. The diet was found to be dominant in *madhura rasa* (sweet taste), *snigdha guna* (unctuous property) and *sheetaveerya* (~cold potency). Majority were habituated to *adhyashana*(eating repeatedly) and followed sedentary lifestyle, suggesting the role of these factors in causing dyslipidemia and also justifying the rationale of treating dyslipidemia on the lines of *apatarpana.* LMG elicited mean reductions in Total cholesterol (11.486 mg/dl), LDL cholesterol (10.853 mg/dl) and mean increase in HDL cholesterol (2.240 mg/dl) in comparison with baseline values which was statistically significant ($p < 0.05$). SGV elicited statistically significant ($p < 0.05$) mean reduction in Triglycerides (23.39 mg/dl), in comparison with baseline values. Both LMG and SGV were efficacious in parameters of

weight, BMI and other anthropometric measurements as specified in the tables. The effect elicited by LMG (trial drug)in the management of dyslipidemia and the morbid conditions associated with it like overweight and obesity was in par with that elicited by SGV (control drug) and there was no significant difference between the effects elicited by both the groups. Thus LMG can be a promising drug in the overall management of dyslipidemia. With due consideration of the limitations of the current trial, this study can serve as a basis for further exhaustive trials on similar topics.

Limitations: Sample size of the study is small and the study is limited to a single geographical area. Duration of the trial was short (4 weeks).

Recommendations for future research

Multi-centric study with a larger sample size needs to be conducted. It would be better to extend the course of the study for 2 to 3 months to assess the long term effects of the drugs.

REFERENCES:

1. Smith DG. Epidemiology of dyslipidemia and economic burden on the healthcare system. Am J Manag Care. 2007 Jun;13Suppl 3:S68–71.
2. Eaton CB. Hyperlipidemia. Prim Care ClinOffPract [Internet]. 2005 Dec [cited 2015 Mar 20];32(4):1027–55. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0095454305000771
3. Dr. ManjiriArunNadkarni, Vyas SN, Baghel MS, Ravishankar B. Clinico-Experimental study of Hyperlipidaemia and its management by Mustadighanavati. [Jamnagar, Gujarat]: Gujarat Ayurved University; 2009.
4. Sapra UK, Thakar AB, Vyas SN, Baghel MS, Ravishankar B. A clinical study of hyperlipidaemia and the effect of panchatiktaghana in its management-a double blind study.Post graduate thesis (Kayachikitsa). [Jamnagar, Gujarat]: Gujarat Ayurved University; 2007.
5. Agnivesha, Charaka, Drudhabala. Sutra Sthana, Chapter 4, Shloka 9. In: AcharyaJadavjiTrikamji, editor. CharakaSamhita with the Ayurveda Deepika Commentary ByChakrapanidatta. Varanasi (India): ChaukhambaSurbharatiPrakashan; 2005. p. 32.
6. Yadav AK, Meena AK, Niranjan U, Singh B, Nagariya AK, Verma M. Review on Cyperusrotundus - A Potential Herb. Int J Pharm Clin Res. 2010;2(1):20–2.
7. Zahara K, Tabassum S, Sabir S, Arshad M, Qureshi R, Amjad MS, et al. A review of therapeutic potential of Saussurealappa-An endangered plant from Himalaya. Asian Pac J Trop Med [Internet]. 2014 Sep [cited 2015 Mar 16];7, Supplement 1:S60–S69. Available from: http://www.sciencedirect.com/science/article/pii/S1995764514602042
8. Halim EM, Ali H. Hypoglycemic, hypolipidemic and antioxidant properties of combination ofCurcuminfromCurcuma longa, Linn, and partially purified product fromAbromaaugusta, Linn. instreptozotocin induced diabetes. Indian J ClinBiochem [Internet]. 2002 Jul [cited 2015 Mar 16];17(2):33–43. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3454113/
9. Mazumder PM, Das S, Das S, Das MK. Phyto-pharmacology of Berberisaristata DC: A review. J

Drug DelivTher [Internet]. 2011 Sep 12 [cited 2015 Mar 16];1(2). Available from: http://jddtonline.info/index.php/jddt/article/view/34

10. Divya G, Gajalakshmi S, Mythili S, Sathiavelu A. Pharmacological Activities of Acoruscalamus: A Review. Asian J Biochem Pharm Res. 2011;1(4):57–64.
11. Ukani MD, Mehta N., Nanavati D. Aconitum Heterophyllum (Ativisha) In Ayurveda. AncSci Life [Internet]. 1996 [cited 2015 Mar 16];16(2):166–71. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3331153/
12. Shetty S, Mengi S, Vaidya R, Vaidya AB. A study of standardized extracts of PicrorhizakurroaRoyle ex Benth in experimental nonalcoholic fatty liver disease. J Ayurveda Integr Med [Internet]. 2010 [cited 2015 Mar 16];1(3):203. Available from: http://www.jaim.in/text.asp?2010/1/3/203/72622
13. Mandavkar YD, Jalalpure SS. A comprehensive review on Plumbagozeylanica Linn. Afr J Pharm Pharmacol. 2011 Dec 30;5(25):2738–47.
14. Pandey HP, Jaya S, Prasad SK, Dwivedi KN. Holopteleaintegrifolia Planch: A potential Ayurvedic medicinal plant. Int J Pharm Sci Rev Res. 2013 Aug;21(2):281–6.
15. Deng R. Therapeutic Effects of Guggul and Its Constituent Guggulsterone: Cardiovascular Benefits. Cardiovasc Drug Rev [Internet]. 2007 Dec 1 [cited 2015 Mar 16];25(4):375–90. Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1527-3466.2007.00023.x/abstract
16. 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 Dec 17;106(25):3143–421.
17. Sharangadhara. Madhyama Khanda, AvalehaKalpana, chapter 8, verse 1. In: Shastri P, editor. SharangadharaSamhita. 5th ed. New Delhi: ChaukhambaOrientalia; 2002. p. 206.
18. Agnivesha, Charaka, Drudhabala. Vimanasthana; Rogabhishagjiteeyam, chapter 8, verse 94. In: AcharyaJadavjiTrikamji, editor. CharakaSamhita with the Ayurveda Deepika Commentary by Chakrapanidatta. Varanasi (India): ChaukhambaSurbharatiPrakashan; 2005. p. 276.
19. Singh V, Kaul S, Chander R, Kapoor NK. Stimulation of low density lipoprotein receptor activity in liver membrane of guggulsterone treated rats. Pharmacol Res. 1990;22:37–44.
20. Chander R, Khanna AK, Kapoor NK. Lipid lowering activity of guggulsterone from Commiphora mukul in hyperlipaemic rats. Phytother Res. 1996;10:508–11.
21. Patra A, Batra S, Bhaduri AP, Khanna A, Chander R, Dikshit M. Isoxazole-based derivatives from Baylis-Hillman chemistry: Assessment of preliminary hypolipidemic activity. Bioorg Med Chem. 2003;11:2269– 2276.
22. Kumari K, Augusti KT. Lipid lowering effect of S-methyl cysteine sulfoxide from Allium cepa Linn in high cholesterol diet fed rats. J Ethnopharmacol. 2007;109:367–71.
23. Nityanand S, Srivastava JS, Asthana OP. Clinical trials with gugulipid. A new hypolipidaemic agent. J Assoc Physicians India. 1989;37:323–8.
24. Dominic AA, Parkavi C, Murugaiah K, Dhanaraj TS. Hypolipidemic Activity of Cyperousrotundus on CCl4 induced Dyslipidemia in Rats. Asian J Pharm Tech. 2012 Jun;2(2):51–3.
25. Anbu J, Ashwini A, Purushothaman K, Sumithra, Suganya S, Bathula NK, et al. Evaluation of

antihyperlipidemic activity of ethanolic extract of saussurealappa in rats. Int J Pharma Bio Sci. 2011 Dec;2(4):550–6.

26. Louay L. Medicinal and pharmacological properties of Turmeric (Curcuma longa): A review. Int J Pharm Biomed Sci. 2014;5(1):17–23.
27. Razzaq FA, Khan RA, Feroz Z, Afroz S. Effect of Berberisaristata on lipid profile and coagulation parameters. Afr J Pharm Pharmacol. 2011 Jul;5(7):943–7.
28. Parab RS, Mengi SA. Hypolipidemic activity of Acoruscalamus L. in rats. Fitoterapia. 2002 Oct;73(6):451–5.
29. Singh V, Chaudhary, Gunjan. Anti-Hyper Lipidemic activity of PicrorhizakurroaRoyle ex Benth Roots. Int J Drug Dev Res. 2012 Sep;4(3):88–91.
30. Pendurkar SR, Mengi SA. Antihyperlipidemic effect of aqueous extract of Plumbagozeylanica roots in diet-induced hyperlipidemic rat. Pharm Biol [Internet]. 2009 Sep 23 [cited 2015 Mar 16];47(10):1004–10. Available from: http://informahealthcare.com/doi/abs/10.1080/13880200902973779
31. Subash AK, Augustine A. Hypolipidaemic effects of methanol extract of Holopteleaintegrifolia (Roxb.) Planchon bark in diet-induced obese rats. ApplBiochemBiotechnol. 2013 Jan;169(2):546–53.
32. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The 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). JAMA J Am Med Assoc. 2001 May 16;285(19):2486–97.
33. Nadkarni MA, Vyas SN, Baghel MS, Ravishankar B. Randomized placebo-controlled trial of Mustadi Ghanavati in hyperlipidemia. Ayu. 2010 Jul;31(3):287–93.
34. Urizar NL, Liverman AB, Dodds DT, Silva FV, Ordentlich P, Yan Y, et al. A natural product that lowers cholesterol as an antagonist ligand for FXR. Science. 2002;296:1703–6.
35. Wu J, Xia C, Meier J, Li S, Hu X, Lala DS. The hypolipidemic natural product guggulsterone acts as an antagonist of the bile acid receptor. MolEndocrinol. 2002;16:1590–7.
36. Ory DS. Nuclear receptor signaling in the control of cholesterol homeostasis: Have the orphans found a home? Circ Res. 2004;95:660–70.
37. Kalaany NY, Mangelsdorf DJ. LXRS and FXR: The yin and yang of cholesterol and fat metabolism. Annu Rev Physiol. 2006;68:159–91.
38. Cai SY, Boyer JL. FXR: A target for cholestatic syndromes? Expert OpinTher Targets. 2006;10:409–21.
39. Owsley E, Chiang JY. Guggulsterone antagonizes farnesoid X receptor induction of bile salt export pump but activates pregnane X receptor to inhibit cholesterol 7alpha-hydroxylase gene. BiochemBiophys Res Commun. 2003;304:191–5.
40. Brobst DE, Ding X, Creech KL, Goodwin B, Kelley B, Staudinger JL. Guggulsterone activates multiple nuclear receptors and induces CYP3A gene expression through the pregnane X receptor. J PharmacolExpTher. 2004;310:528–35.
41. Burris TP, Montrose C, Houck KA, Osborne HE, Bocchinfuso WP, Yaden BC, et al. The hypolipidemic natural product guggulsterone is a promiscuous steroid receptor ligand. MolPharmacol. 2005;67:948–54.
42. Fuchs M. Bile acid regulation of hepatic physiology: III. Regulation of bile acid synthesis: past progress and future challenges. Am J PhysiolGastrointest Liver Physiol. 2003;284:G551–G557.
43. Kullak-Ublick GA, Stieger B, Meier PJ. Enterohepatic bile salt transporters in normal physiology and liver disease. Gastroenterology. 2004;126:322–42.

44. Deng R, Yang D, Radke A, Yang J, Yan B. The hypolipidemic agent guggulsterone regulates the expression of human bile salt export pump: Dominance of transactivation over farsenoidXreceptor-mediated antagonism. J PharmacolExpTher. 2007;320:1153–62.
45. Shishodia S, Aggarwal BB. Guggulsterone inhibits NF-kappaB and IkappaBalpha kinase activation, suppresses expression of anti-apoptotic gene products, and enhances apoptosis. J Biol Chem. 2004;279:47148– 47158.
46. Ichikawa H, Aggarwal BB. Guggulsterone inhibits osteoclastogenesis induced by receptor activator of nuclear factor-kappaB ligand and by tumor cells by suppressing nuclear factor-kappaB activation. Clin Cancer Res. 2006;12:662–8.
47. Cheon JH, Kim JS, Kim JM, Kim N, Jung HC, Song IS. Plant sterol guggulsterone inhibits nuclear factorkappaB signaling in intestinal epithelial cells by blocking IkappaB kinase and ameliorates acute murine colitis. Inflamm Bowel Dis. 2006;12:1152–61.
48. Dev S. A modern look at an age-old Ayurvedic drug-guggul. Sci Age. 1987;1987:13–8.
49. Bajaj AG, Dev S. Chemistry of Ayurvedic crude drugs. Tetrahedron. 1982;38:2949–54.
50. Steinberg D. Lowdensity lipoprotein oxidation and its pathobiological significance. J Biol Chem. 1997;272:20963– 20966.
51. Chisolm GM, Steinberg D. The oxidative modification hypothesis of atherogenesis: An overview. Free RadicBiol Med. 2000;28:1815–26.
52. Singh RB, Niaz MA, Ghosh S. Hypolipidemic and antioxidant effects of Commiphora mukul as an adjunct to dietary therapy in patients with hypercholesterolemia. Cardiovasc Drugs Ther. 1994;8:659–64.
53. Singh K, Chander R, Kapoor NK. Guggulsterone, a potent hypolipidaemic, prevents oxidation of low density lipoprotein. Phytother Res. 1997;11:291–4.
54. Wate S, Dhanjode D, Duragkar N, Tajne M. Antioxidant potential of cow urine and its fractions: A comparative study. Int J Univers Pharm Life Sci. 2011;1(1):146–54.
55. Mohanty I, Senapati MR, Jena D, Palai S. Diversified Uses of Cow Urine. Int J Pharm Pharm Sci. 2014;6(3):20–2.

Cite this article as: Deepak BSR, Jadhav Lakshmiprasad, Girish KJ, Narayana Prakash, Randomized Controlled, Open Labeled Study of A Herbal Preparation, Lekhaneeya Mahakashaya Ghanavati in Dyslipidemia Patients, *J of Ayurveda and Hol Med (JAHM)*.2015;3(4):1-23

Source of support: Nil, Conflict of interest: None Declared.