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ANTIHYPERLIPIDEMIC EFFECT OF PANCHATIKTA GHANA AND SHUDDHA GUGGULU: AN EXPERIMENTAL STUDY

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Abstract:

Hyperlipidemia is emerging as major health problem in the modern era. Hyperlipidemia leads to coronary artery disease, myocardial infarction and cerebrovascular accidents (CVA).Coronary heart disease (CHD) is the number one killer among the diseases and it accounts for 37% of adult deaths in the US every year. Nikolai Anichkov in 1912 discovered the role of cholesterol in CHD, currently the world's most deadly disease. An experimental study was done on albino rats to evaluate the effect of Panchatikta Ghana (combination of *Adhatoda vesica*, *Azadirachta indica*, *Tinospora cordifolia*, *Solanum xanthocarpum* and *Trichosanthes dioica*) and Shuddha Guggulu (*Commiphora mukul*) in hyperlipidemia induced albino rats. The study showed that Shuddha Guggulu has cardioprotective activity as it has increased the HDL Level and this drug also reduced the serum triglycerides to significant level and thus gave antihypertriglyceridaemic activity too. Both of the drugs were free from any side effects. Shuddha Guggulu was having better effect in reducing the body weight of the albino rats than Panchatikta Ghana.

Key words: Hyperlipidemia, Medoroga, Albino rats, Panchatikta Ghana, Shuddha Guggulu (purified Guggulu)

Introduction:

Hyperlipidemia is emerging as major health problem in the modern era. Hyperlipidemia leads to coronary artery disease, myocardial infarction and cerebrovascular accidents (CVA). Coronary heart disease (CHD) is the number one killer among the diseases and it accounts for 37% of adult deaths in the US every year[1]. Coronary heart disease (CHD) is the number one killer among the diseases and it accounts for 37% of adult deaths in the US every year.[1] Nikolai Anichkov in 1912 discovered the role of cholesterol in CHD, currently the world's most deadly disease. CHD is the commonest cause of death in the UK. Average level of cholesterol is 12% higher in the UK population than in the USA and 80% of UK adults have a total cholesterol level above 200mg/dl.[2] In India, persons suffering from the CHD are doubled in the last 20 years.[3] In South India, CHD incidences are 7.4% in rural area and 13.9% in urban area, which is higher than North India (rural 3% and urban 9.7%).[4]

Hyperlipidemia is a condition in which the levels of lipids in plasma are increased. It is of utmost significance because it leads to atherosclerosis of vessels (arterial walls) leading to vascular accidents. Blood levels of cholesterol and triglycerides are uniformly distributed in general population, graphically presenting bell-shaped curves without any indication of cut-off points between normal and abnormal. In newborn, plasma cholesterol is around 100 mg/dl, which slowly rises to about 160 mg/dl during 1st year of life. Plasma cholesterol levels tend to rise slowly after 4th decade of live in men

and in postmenopausal women. Also, the cholesterol levels of plasma may be elevated during the period of menstruation in females.[5-6]

Hyperlipidemia is not a single condition but a range of disorders with a variety of genetic and environmental determinants. It can be caused or modified by a wide range of other disorders, and its presence can affect many different organs and systems. The presence of Hyperlipidemia is a key factor in the development of atherosclerosis and endothelial dysfunction. It is essential that everyone with hyperlipidemia have a full clinical assessment, as well as appropriate treatment, so that other important factors and co-morbidities can be identified and assessed. Hyperlipidemia can be secondarily due to diabetes mellitus, hypothyroidism, renal disease[7-8] liver disorder, ethanol consumption, frequent coffee intake,[9] gout, obesity[10] and drugs. Stress is one of the factors for increased level of lipoproteins.[11-16]

Ischaemic heart disease is number one killer among the all disorders and hyperlipidemia is one of the risk factor for it. Hyperlipidemia is mainly due to two factors-hereditary and dietary factors. It is difficult to treat and the person has to take medicine throughout his life. However, antihyperlipidemic drugs are having the side effects. Present study was conducted to evaluate the antihyperlipidemic effect of Panchatikta Ghana and Shuddha Guggulu on albino rats. The previous research work was done on Sthaulya (obesity) patients with Panchatikta Ghana at Institute for Post Graduate Teaching & Research in Ayurveda (IPGT & RA) have shown good results. Thus to evaluate the effect of Panchatikta on hyperlipidemia induced albino rats this study was started.[17] Vasa Ghana also produced significant decrease in lipids in previous study.[18]

Aims and Objectives:

The present study was undertaken with the following aims and objectives:

1. Pharmacological evaluation of Panchatikta Ghana (PTG) (test drug) to assess its effect on lipid profile of albino rats for possible use as hypolipidaemic drug.
2. Pharmacological evaluation of Gomutra Shodhita Guggulu (GSG) to assess its effect on lipid profile of albino rats for possible use as standard hypolipidaemic drug.

Materials and Methods:

Drug Procurement:

Guduchi, Vasa, Kantakari were collected fresh from Jamnagar (dated 2-3-2006), Nimba was taken from pharmacy of IPGT&RA. Patola was procured from BHU, Varanasi. Shuddha Guggulu was procured from Prashant Pharmacy, Rajpipala, Narmada district, Gujarat. Both drugs Panchatikta Ghana and Shuddha Guggulu were prepared in Pharmacy of IPGT& RA, Gujarat Ayurved University (GAU), Jamnagar.

***Animals*:**

Wistar strain albino rats of either sex weighing 170 to 290 g attached to the Pharmacology Laboratory, IPGT&RA, GAU, Jamnagar and maintained in ambient conditions on a normal 12 h light / dark cycle were used in the experimentation (male and female animals were kept in separate cage to avoid the possibility of pregnancy during the 22 days study). Standard rat chow of Amrut brand (Nav Maharashtra Chakan Oil Mill) and tap water was provided ad libitum. The room temperature during the experiment was 21±2°C. All procedures and experiments were conducted in day time according to specification of the Indian National Science Academy (INSA). The experiments were carried out after obtaining the permission of Institutional Animal Ethics Committee of Institute.

Animal Grouping:

The animals were grouped at random irrespective of sex into three groups. Group PTG and GSG were treated with Panchatikta Ghana and Gomutra Shodhita Guggulu respectively and third group was kept as control and tap water was administered to the animals in this group.

Dose Fixation and Schedule:

The dose of the formulations was calculated by extrapolating the therapeutic dose to rat dose on the basis of body surface area ratio by referring to the table of Paget and Barnes (1979)

(a) Human dose X conversion factor (0.018) for rat = 'x' / 200 g

(b) 'X' x 5 = 'Y' / kg dose

a. So, by calculating this way, the rat doses of the following formulations are

i. Panchatikta Ghana (PTG): 270mg /kg

ii. Gomutra Shodhita Guggulu (GSG):`270mg /kg

The drug solutions were administered orally with the help of gastric catheter of suitable size sleeved on to a syringe nozzle to all the groups. The animal of control group received equal volume of tap water.

Preparation of Test Drug:

Both drugs were crushed into fine powder and dissolved in distilled water to obtain suitable concentration to administer at a volume of 0.5 ml/100g body wt., while the animals of control group were given only tap water in an equal volume. The drug solutions and tap water were administered with the help of gastric catheter.

The test drug has administered at morning hours and hyperlipidaemic diet was given at evening hours.

Statistical Analysis:

The data generated during the study was subjected to Students' 't' test for unpaired data to assess the statistical significance. A 'p' value <0.05 was considered as statistically significant

Experimental Protocol:

The selected rats of either sex were assigned to three groups. To first group(I), Panchatikta Ghana (PTG) was administered orally in the dose of 270 mg kg $^{-1}$ body weight; to the second group (II), Gomutra Shodhita Guggulu (GSG) was administered orally in the same dose as in Group I. Third group receiving equal volume of tap water served as the control group (cholesterol control). The drug administration was done at morning hours and continued for 22 days. Similarly hydrogenated vegetable oil (Vanaspati Ghee - ('Raag' brand, Batch No. (AO) VA02, Adani Wilmar Ltd., Gujarat) and Cholesterol extrapure powder (Batch No. 5593 Suvidhnath Laboratories, Baroda) made suspension in 20% coconut oil (Parachute coconut oil, Batch No. GGER019, Goa) were administered in the dose of 0.5 ml/100 g body weight of rats respectively daily for 22 days (at evening hours) to all the rats. On the 23rd day after overnight fasting, the rats were sacrificed by stunning and severing of jugular vessels, blood was collected and sent for biochemical investigations. From the sacrificed animals' liver, kidney, heart and aorta were excised out and transferred to fixing solution (10% formation). The tissues were processed for histopathological examinations following standard procedure to note down cytoarchitectural disturbances if any.

Parameters Studied:

Ponderal changes:

Body weight, weight of liver, heart and kidney

Biochemical parameters:

Serum was collected from blood for Biochemical investigations. The investigations were carried out at Biochemical laboratory, IPGT&RA of GAU, Jamnagar.

1. Serum total cholesterol
2. Serum triglyceride
3. Serum HDL cholesterol
4. Serum LDL cholesterol[19]
5. Serum VLDL cholesterol[19]
6. Blood sugar
7. Blood urea
8. Serum creatinine
9. Serum total protein
10. Serum albumin
11. Serum globulin
12. A/G ratio
13. S.G.O.T.
14. S.G.P.T.
15. Serum alkaline phosphatase

Observations and Results:

Ponderal changes:

Table 1
Effect of Panchatikta Ghana and Gomutra Shodhita Guggulu on body weight in albino rats

Group	Dose (mg/kg)	Body weight (g)					
		Initial body wt.	After treatment	Weight gain	% Change	% Change of weight	% Change
Cholesterol control (n=6)	Q.S	218.33 ± 16.62	253.67 ± 16.95	35.30 ± 06.50	---	16.69 ±03.03	---
P.T.G.(n=6)	270	233.33 ± 18.74	255.00 ± 21.56	31.70 ± 06.01	10.19 ↓	14.18 ± 02.54	15.03 ↓
G.S.G. (n=5)	270	244.00 ± 18.60	272.80 ± 20.34	28.80 ± 07.31	18.41 ↓	12.00 ± 02.74	28.10 ↓

Data: Mean ±SEM, ↑-Increase; ↓-Decrease

The data related to the effect of drug on body weight have been shown in Table 1. Analysis of the data shows the decrease in body weight in both PTG and GSG in comparison to control group but the observed decrease is statistically not significant.

Table 2

Effect of Panchatikta Ghana and Gomutra Shodhita Guggulu on liver weight in albino rats

Group	Dose (mg/kg)	Weight of liver (g)			
		Absolute wt. (g)	% change	Relative weight	% change
Cholesterol control(n=6)	Q.S	06.4 ± 00.62	----	02.51±00.09	----
P.T.G.(n=6)	270	06.78±00.40	05.41↑	02.7 ±00.10	07.57↑
G.S.G. (n=5)	270	07.26±00.69	12.96↑	02.65±00.10	05.58↑

Data: Mean ±SEM; ↑-Increase; ↓-Decrease

The data related to the effect of drug on liver weight have been shown in Table 2. Analysis of the data shows increase in both absolute and relative liver weight in the test drug and Shuddha Guggulu group in comparison to control group but the observed increase is not statistically significant.

Table 3

Effect of Panchatikta Ghana and Gomutra shodhita Guggulu on heart weight in albino rats

Group	Dose (mg/kg)	Weight of heart (g)			
		Absolute wt. (g)	% change	Relative weight	% Change
Cholesterol control(n=6)	Q.S	0.795±0.063	----	0.31 ± 0.01	----
P.T.G.(n=6)	270	0.908±0.065	14.21 ↑	0.36 ± 0.02	16.13 ↑
G.S.G. (n=5)	270	0.888±0.055	11.70 ↑	0.33 ± 0.01	6.45 ↑

Data: Mean ±SEM; ↑-Increase; ↓-Decrease

The data related to the effect of drug on heart weight have been shown in Table 3. Analysis of the data shows increase in both absolute and relative heart weight in the test drug and Shuddha Guggulu group in comparison to control group but the observed increase is not statistically significant.

Table 4

Effect of Panchatikta Ghana and Gomutra shodhita Guggulu on kidney weight in albino rats

Group	Dose (mg/kg)	Weight of Kidney (g)			
		Absolute wt. (g)	% Change	Relative weight	% Change
Cholesterol control(n=6)	Q.S	1.33 ± 0.138	-	0.52 ± 0.02	-
P.T.G.(n=6)	270	1.47 ± 0.146	10.88↑	0.58 ± 0.02	11.54↑
G.S.G. (n=5)	270	1.56 ± 0.163	17.70↑	0.57 ± 0.02	9.62↑

Data: Mean ±SEM ↑-Increase; ↓-Decrease

The data related to the effect of drug on kidney weight have been shown in Table 4. Analysis of the data shows increase in both absolute and relative kidney weight in the test drug and Shuddha Guggulu group in comparison to control group but the observed increase is not statistically significant.

Biochemical parameters:

Table 5

Effect of Panchatikta Ghana and Gomutra Shodhita Guggulu on serum total cholesterol in albino rats

Group	Dose (mg/kg)	Serum total cholesterol (mg/dl)	% Change
Normal control	Q.S	58.83 ± 07.09	
Cholesterol control (n=6)	Q.S	093.50 ± 06.32*** $^{@}$	
P.T.G.(n=6)	270	108.30 ± 04.82	15.8 ↑
G.S.G. (n=5)	270	105.0 0±12.24	12.3 ↑

Data: Mean ±SEM ↑ - Increase; ↓ - Decrease *** $^{@}$ P <0.001 in comparison to normal control

The data related to the effect of test drugs on serum total cholesterol can be seen in Table 5. Feeding of hyperlipidaemic diet leads significant increase in the serum total cholesterol level in comparison to normal control rats. This elevation was not antagonized by the administration of test drugs. In contrast a mild elevation was observed in these groups.

Table 6

Effect of Panchatikta Ghana and Gomutra shodhita Guggulu on serum triglycerides in albino rats

Group	Dose (mg/kg)	Serum total Triglyceride (mg/dl)	% Change
Normal control		117.50 ± 15.53	
Cholesterol control(n=6)	Q.S	208.50 ± 22.25*** $^{@}$	
P.T.G.(n=6)	270	211.00 ± 26.83	01.20↑
G.S.G. (n=5)	270	151.60 ± 15.74	27.29↓

Data: Mean ±SEM; ↑-Increase; ↓-Decrease; $^{**@}$P <0.01 in comparison to normal control

The data related to the effect of test drugs on serum triglycerides level can be seen in Table-6. Feeding of hyperlipidaemic diet leads to significant increase in the serum triglycerides level in comparison to normal control rats. This elevation was not antagonized by the administration of PTG. However administration of Shuddha Guggulu lead to significant decrease in serum triglycerides level in comparison to hyperlipidaemic diet given control rats.

Table 7

Effect of Panchatikta Ghana and Gomutra Shodhita Guggulu on serum HDL in albino rats

Group	Dose (mg/kg)	Serum HDL cholesterol (mg/dl)	% Change
Normal control	Q.S	±	
Cholesterol control(n=6)	Q.S	39.67 ± 00.99	
P.T.G.(n=6)	270	45.00 ± 04.54	13.44↑
G.S.G. (n=5)	270	48.40 ± 05.10	22.00*↑

Data: Mean ±SEM; ↑-Increase; ↓-Decrease; P<0.01

The data related to the effect of test drugs on serum HDL level can be seen in Table 7. Feeding of hyperlipidaemic diet leads significant increase in the serum HDL level in

comparison to normal control rats. This elevation was not antagonized by the administration of PTG. Also administration of Shuddha Guggulu and PTG lead to increase in serum HDL level in comparison to hyperlipidaemic diet given control rats but the observed increase is not statistically significant.

Table 8
Effect of Panchatikta Ghana and Gomutra Shodhita Guggulu on serum VLDL in albino rats

Group	Dose (mg/kg)	Serum VLDL cholesterol (mg/dl)	% Change with normal control	% Change with cholesterol control
Normal control		±	-	-
Cholesterol control(n=6)	Q.S	40.17 ± 04.45		-
P.T.G.(n=6)	270	42.20 ± 05.37		01.20↑
G.S.G. (n=5)	270	30.32 ± 03.15		27.29↓

Data: Mean ±SEM; ↑-Increase; ↓-Decrease

The data related to the effect of test drugs on serum VLDL level can be seen in Table 8. Administration of PTG lead to increase in serum VLDL level in comparison to hyperlipidaemic diet given control rats but the observed increase is not statistically significant. However administration of Shuddha Guggulu leads to decrease in serum VLDL level in comparison to hyperlipidaemic diet given control rats but the observed decrease is not statistically significant.

Discussion:

The Panchatikta drug was taken for the present study as test drug because of the properties of Tikta Rasa to reduce the Meda and Kapha. [20] Guggulu has proven anti-hyperlipidemic effect as shown in various studies.[21-24] Various postgraduate and doctorate level studies have shown good effect of Shudha Guggulu and other Ayurvdic formulations like Amritadi Yoga, Navaka Guggulu, Methika Beeja, Lekhaniya Mahakshaya, Krishnadi Churna and Trishila Guggulu on hyperlipdemia.[25-34] In this study, PTG reduced the body weight (Table 1) by 15.03% whereas in GSG group, the reduction was 28.10%. Gugggulu has shown better effect because of presence of resin in it and it has Medohara effect as per Ayurveda texts. Administration of Shuddha Guggulu lead to significant decrease in triglycerides level and VLDL level (27.29%) in comparison to hyperlipidaemic diet given albino rats. This shows that the test drug GSG has hypotriglyceridaemic activity, which can be considered as a part of hypolipidaemic activity.

PTG produced moderate eleation in serum HDL-cholesteol level and GSG produced significant elevation in serum HDL-cholesteol level. This can be considered as a significant finding of this study. Based on the results obtained it can be suggested that GSG has good anti- -hypertriglyceridaemic activity. It may prove useful in the treatment of patients with hypertriglyceridaemia, especially patients with Type - I, IV and V hypertriglyceridaemia. HDL prevents or reduces the build-up of plaque in the arterial wall and appears to be a significant cardiovascular risk factor independent of whether LDL is low or high.

Conclusion:

Shuddha Guggulu is having cardio-protective action as observed in the present study. It can be concluded that GSG produced anti-hyperlipidaemic effect against hyperlipidaemic diet induced elevation in serum triglyceride level.

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