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RESEARCH ARTICLE

ANTIHYPERLIPIDEMIC EFFECT OF KOMOOTHIRA SILASATHU PARPAM IN TRITON-INDUCED ANTI DYSLIPIDEMIC RATS

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Abstract: Background: Cardiovascular disease (CVD) is known to be associated with hyperlipidemia. The statin medicine class inhibits a stage that limits the production of cholesterol at a certain pace, although all statins have negative effects on the musculoskeletal system. The current interest has led to a hunt for novel lipid-lowering drugs with little to no side effects among traditional sources of siddha. Objective: The primary goal of this study is to assess the siddha formulation Komoothira silasathu parpam (KSP)'s antityperlipidemic capability in triton-induced dyslipidemic rats. Methods: Triton was used for the induction of hyperlipidemia in the experimental animals. The animals were divided into control, disease control and treatment groups. Rats belongs to treatment groups were administered test drug KSP at doses of 250 and 500 mg/kg/p.o. Results: The data of the present investigation clearly emphasise that the body weight, total cholesterol, HDL, LDL, VLDL, and triglyceride levels of the triton group demonstrate a significant increase in comparison with normal control rats. Treatment with the siddha formulation KSP at 250 and 500 mg/kg doses results in a significant decrease in the total lipid profile and body weight of the experimental animals, Furthermore, the KSP treatment causes a Consistent decrease in the internal organ weight (heart and liver) of the animals. Histological examination of the liver sample confirms the existence of inflammatory changes in triton treatment, and treatment with PVC reveals a restorative nature in both the dose level. Conclusion: In conclusion, the data of the present study show that the siddha formulation KSP reveals promising antihyperlipidemic activity in Triton induced dyslipidemic rats. Hence KSP type formulations may be the good drug of choice in the clinical management of hyperlipidemia

Keywords: *Hyperlipidemia, Siddha, Komoothira silasathu parpam, Lipid profile, Body weight, Histopathology*.

INTRODUCTION

Hyperlipidemia, a metabolic disorder characterized by elevated levels of lipids in the blood, significantly increases the risk of cardiovascular diseases such as atherosclerosis, coronary artery disease, and stroke. The global rise in hyperlipidemia prevalence is largely attributed to lifestyle factors including poor dietary habits, physical inactivity, and obesity, alongside genetic predispositions [1-3].

Standard medical treatments primarily involve statins and other lipid-lowering agents, which, despite their efficacy, can lead to adverse effects and long-term dependency.

Given these limitations, there is growing interest in alternative and complementary therapies, particularly traditional medicine systems. The Siddha system of medicine, one of the oldest holistic health systems originating from South India, provides a unique approach to managing hyperlipidemia through its diverse array of herbal formulations, dietary regulations, and lifestyle modifications [4-6].

Siddha medicine's holistic approach aims to balance the body's physical, mental, and spiritual aspects, which may offer

comprehensive benefits beyond lipid lowering. This research article aims to investigate the efficacy and mechanisms of Siddha medicine in the treatment of hyperlipidemia [7-10].

By integrating traditional knowledge with contemporary scientific research, this study will provide a detailed analysis of Siddha interventions and their potential benefits in managing lipid disorders. The review will encompass an examination of key Siddha formulations, their pharmacological properties, and their impact on lipid profiles as evidenced by clinical and preclinical studies [11-15].

By systematically reviewing existing literature and clinical data, this article seeks to evaluate the overall safety and efficacy of Siddha treatments compared to conventional hyperlipidemic therapies. The ultimate goal is to bridge the gap between traditional and modern medicine, demonstrating how ancient practices can contribute to contemporary health challenges. Through this exploration, the study aims to promote integrative and personalized healthcare approaches that enhance patient outcomes and support cardiovascular health [16-22].

MATERIALS AND METHODS

Ingredients & Collection of Drugs

The following Raw materials were collected from Ramasamy chetty traders, Paris, Chennai.

Komoothirasilasathu (Asphalt mineral pitch) -84 (20 varagan)
Kadukkai (Terminalia Chebula.Retz)-42 gm (10.varagan)
Thandrithol (Terminalia bellarica. Rob) -42gm (10 varagan)
Nellimulli (Emblicaofficinalis. Linn) -42gm (10 varagan)

Authentication

The above raw materials were authenticated by post graduate department of gunapadam and medicinal botany Government siddha medical college, palayamkottai.

Purification of the Materials

Komoothirasilasathu: Komoothirasilasathu is finely grind with milk, and keep it until it get dry.

Kadukkai: Remove the seed from kadukkai.

Thadrithol: Remove the seed from thandrikai.

Nellimulli: Remove the seed from Nellikai.

Process of Preparation

Dried pericarp of Terminalia chebula, Terminalia bellarica, Emblica officinalis each weighing about 42 gm taken in a clean pot and add 1600ml of water. It was boiled and reduced upto 200ml and filtered this devotion.And then 84 gms of purified komoothira silasathu is placed in a stone mortar and triturated with above prepared decoction for about 3 hours and made onto small cakes and dried.

Then dried cakes (villai) were placed with in a earthern plate and covered with another earthen plate subjected into incineration process by using dried cow dung cakes. After incineration process it is allowed to cool, black colored komoothirasilasathu parpam is obtained. It is kept in a stone mortar and grind into fine powder and stored in a container.

Human Dose: 488 mgs.

Materials: Animals: Male albino wistar rats (180-220gm)

Drugs: Powder of ***KSP***

Animals

Wistar albino adult male rats weighing 150-200gm from animal housing facility of Vels University were housed in polypropylene cages maintained with temperature 27°C ±1°C and 12 hrs light and dark cycles. The animals were allowed to adapt to the environment for seven days and supplied with a standard pellet diet (Sai Durga foods, Bangalore) and water *ad libitum*. The experimental protocol has got the approval IAEC bearing no.

Pharmacological Evaluation

All animals starved for 18 hours and provided water *ad libitum* before the experiment. The animals were divided into five groups of six rats each. Group I served as normal control administered with 2% CMC only. Group II served as anti dyslipidemic control given a single dose of triton was administered 400 mg/kg only. Group III and IV served as test groups received KC 250mg/kg and KC 500mg/kg

respectively. Group V served as Lovastatin (10mg/kg/day) considered as standard. All the groups except the normal control group. administered a single dose of Triton dissolved in 0.9% Normal saline intraperitonially. After inducing the hyperlipidemia, the respective treatment was continued for 7 days. Animals were given standard pellet diet and water *adlibitum*.

Collection of Blood

The next day after the completion of experimental study, the blood was taken from the rats under mild anesthetic state by retro orbital sinus puncture. The collected blood samples were centrifuged (2500 rpm) for 10 minutes. Then serum samples were separated and it was used for various biochemical analyses. Then animals were sacrificed and the liver, heart and kidney were taken for histopathological study and for the analysis of organ weight.

Liver Lipid Extraction

The liver was homogenized in cold 0.15M KCl and extracted with CHCl3: CH3OH (2% *v/v*). This lipid extract was used for the estimation of lipid parameters.

Biochemical Analysis

The serum and liver were analyzed for serum total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) by standard enzymatic calorimetric methods.

Histopathology

All rats were sacrificed after the collection of blood sample. Liver was excised from the rats to visually detect gross lesions, and weighed to determine weight variation and preserved in 10% neutral formalin for histopathological assessment. The tissue was embedded in paraffin, and then sectioned, stained with haematoxylin and eosin and were examined microscopically.

RESULT

The effect of KSP on body weight, Blood lipid profile, liver lipid profile, on SGOT, SGPT Totalprotein, Urea and Blood glucose levels of Triton-induced anti dyslipidemic rat are tabulated in Table 1, 2,3 and 4.

Table 1: Effect of KSP on body weight of Triton-induced anti dyslipidemic rat

Groups	Body Weight (gm.)				
	Initial	1st Week	2nd Week	3rd Week	4th Week
G1 Normal control	155±0.87	157±1.3	159.25±1.03**	161.5±2.72**	163.6±3.17**
Dyslipidemic Control	157.17±0.87	159±1.04	170.17 ±1.7	198.5±0.66	216±1.1
G3 Lovastatin (10mg/kg/day)	156±1.59	159.17±1.08	164.5±1.18**	163.17±0.91**	167.5±0.8**
KSP250mg/kg	155.63±0.9	158±0.97	164.75±1.47*	167.42±1.23**	170.83±2.3**
KSP 500mg/kg	156.5±0.67	159.5±1.89	164.33±0.80*	164.67±0.76**	168.83±0.7**

*Values are as mean ± SEM (n=6). Values are statistically significant at *P<0.05, **P<0.01, ***P<0.001. Comparison made between Group II Vs Group I and Group III, IV, V Vs Group II.*

Table 2: Effect of *KSP on* blood lipid profile of triton-induced dyslipidemic rats

Group	Treatment	T.C.	T.G.	LDL	HDL	VLDL
I	Normal Control	72.81±1.1**	60.17±1.7**	52.83±1.8* *	35.3±1.3	19.3±1.2**
II	Triton Control	174.17±1.35	115.17±1.4 9	120.17±1.2 5	28.17±1.08	20.83±1.11
III	KSP 250mg/kg	72.5±1.23**	69.67±0.99**	71.17±1.38 **	40.33±0.88 *	14.33±0.80 **

IV	KSP 500mg/kg	67.30±1.45**	56.83±0.90**	56.33±1.02 **	42.17±1.14 **	11.17±1.25 **
V	Lovastatin	54.5±1.12**	54.3±1.30* *	46.33±1.15 **	44.33±1.36 **	12.5±1.87* *

*Values are as mean ± SEM (n=6). Values are statistically significant at *P<0.05, **P<0.01, ***P<0.001. Comparison made between Group II Vs Group I and Group III, IV, V Vs Group II.*

Table 3: Effect of *KSP on* liver lipid profile of Triton-induced anti dyslipidemic rats

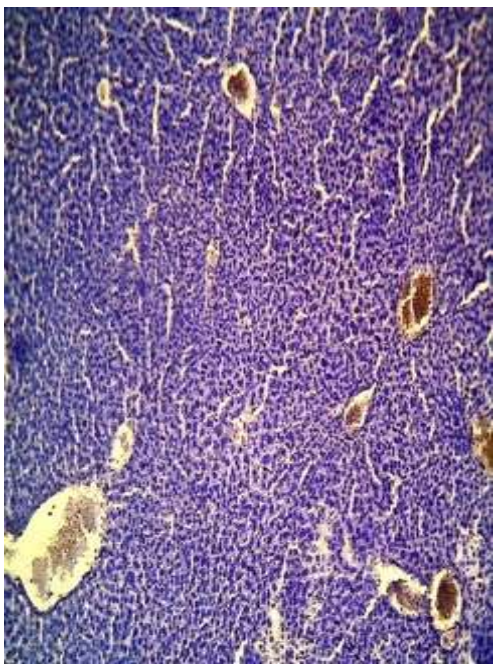
Group	Treatment	T.C.	T.G.	LDL	HDL	VLDL
I	**Normal Control**	74.17±0.87**	70.75±1.93* *	26.17±1.70* *	36.17±0.91	13.58±1.24**
II	**Triton Control**	155.17±1.08	178.82±1.46	105.25±2.42	18.15±1.05	35.1±0.93
III	**KSP250mg/ kg**	82.15±0.92**	64.15±1.03* *	23.12±1.01* *	35.9±0.86	12.22±0.25**
IV	**KSP 500mg/kg**	75.3±0.85**	64.12±0.97* *	20.3±1.06**	44.05±1.4*	12.88±1.12**
V	**Lovastatin (10mg/kg/d ay)**	67.05±0.97**	57.25±1.15* *	17.93±1.31* *	50.1±0.99*	12.1±0.91**

*Values are as mean ± SEM (n=6). Values are statistically significant at *P<0.05, **P<0.01,***P<0.001. Comparison made between Group II Vs Group I and Group III, IV, V Vs Group II.*

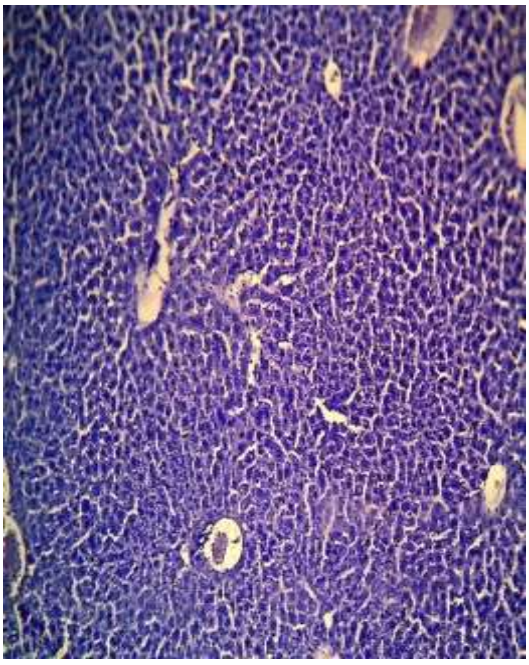
Table 4: Effect of *KSP on* SGOT, SGPT Total protein, Urea and Blood glucose levels of Triton-induced dyslipidemic rats

Groups	SGOT(U/I)	SGPT(U/I)	Tota Protein (gm/dl)	Urea (mg/dl)	Blood Glucose (mg/dl)
Normal control	148.17±1.08	61.17±0.87	5.9±0.86*	36±0.97	85.83±0.79
Anti dyslipidemic Control	190.33±1.12	120.5±0.76	6.0±0.97	45±1.1	92.14±0.74
KSP 250mg/kg	176.5±1.67	71±2.03	5.68±1.08*	32.02±1.1	86.83±1.08
KSP 500mg/kg	150±1.18**	70.37±0.89**	5.17±1.02	32.6±1.2**	85.08±1.30 **
Lovastatn (10mg/kg/day)	155.52±1.74	64.05±1.35	5.13±0.90	28.67±0.6	85.17±0.87

*Values are as mean ± SEM (n=6). Values are statistically significant at *P<0.05, **P<0.01,***P<0.001. Comparison made between Group II Vs Group I and Group III, IV, V Vs Group II.*



Hyper Lipidemic-Normal



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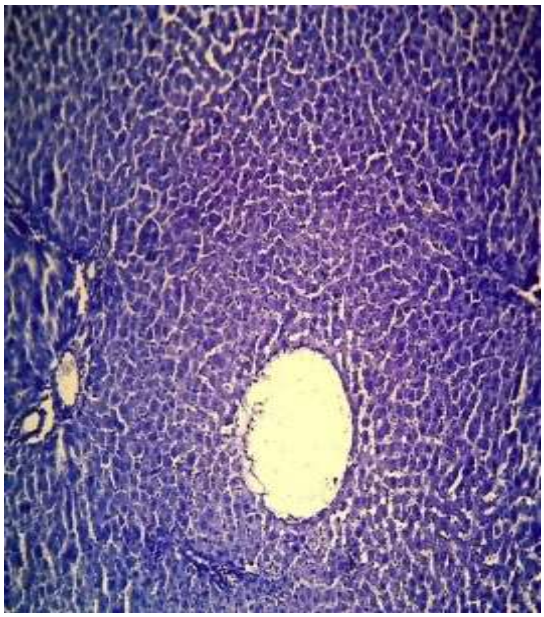
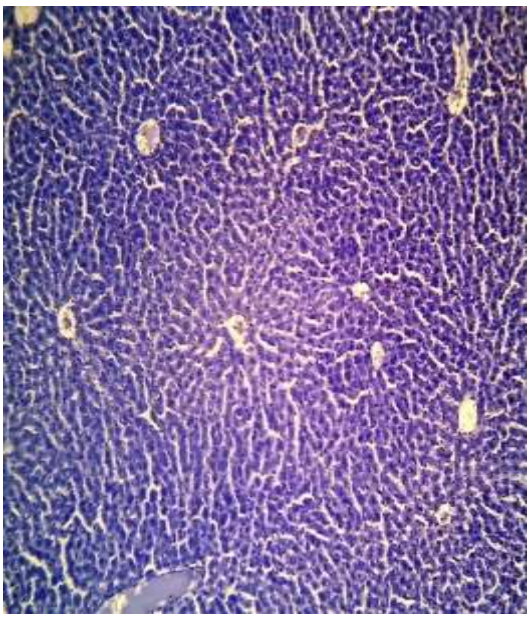
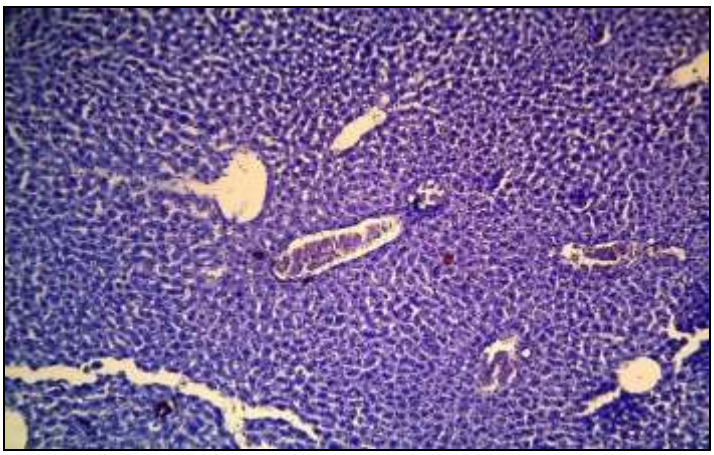


Anti Dyslipidemic-STD/Control



Anti Dislipidemic-Low Dose



Anti Dislipidemic-High Dose

DISCUSSION

The level of serum lipids are usually elevated in diabetes mellitus, and such an elevation represents the risk of coronary heart disease (CHD). Lowering of serum lipids concentration through diet or drug therapy seems to be associated with a decrease in the risk of vascular disease. The abnormal high concentration of serum lipids in diabetic subject is mainly due to increased mobilization of free fatty acids from the peripheral fat depots, since insulin inhibits the hormone sensitive lipase.

However, glucagon, catecholamines and other hormones enhance lipolysis. The marked hyperlipidemia that characterized the diabetic state may therefore be regarded as a consequence of the uninhibited actions of lipolytic hormones on the fat depots. Triton has been widely used to block the clearance of triglyceride-rich lipoproteins to induce acute hyperlipidemia particularly, in rats it has been used for screening natural or chemical hypolipidemic drugs. The results showed that *KSP* produced a significant reduction in cholesterol level and also it reversed Triton induced hypolipidemic in rats. Similarly, *KSP* at a dose of 250 and 500mg/kg significantly lowered both plasma triglycerides and cholesterol levels.

The reduction of total cholesterol by the *KSP* at the dose level of 250 and 500 mg kg may be associated with a decrease of LDL, which is the ultimate aim of many hypolipidemic agents. This study suggests that cholesterol-lowering activity of the *KSP* may increase the fecal excretion of bile acids and neutral sterols with the consequent reduction of hepatic cholesterol because of its use in the biosynthesis of these bile acids. These fractions also slow down the rate of diffusion

through the intestinal mucosa thereby reducing the absorption of cholesterol and triglycerides. Anti-oxidant constituents of *Kadukkai*, *Nellimuli* and *thandrikai* also prevent the endogenous oxidation of cholesterol result in decrease in the concentration of low density lipoprotein and again confirms the hypolipidemic drug.

Table 2 & 3 shows the KSP has significant anti-dyslipedemic activity and the level of serum total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), Low density lipoprotein(LDL) and phospholipids of normal and experimental animals in each group. The main 'anti-atherogenic' lipoprotein (HDL) is involved in the transport of cholesterol from peripheral tissues into liver and thereby it acts as a protective factor against coronary heart disease (CHD).

In rats treated with both doses of Siddha formulation KSP and Triton there was significant decrease in the content cholesterol TGs, LDL, VLDL and increases HDL when compared with cholesterol controlled rats. KSP has significant Anti dyslipidemic effect.

HISTOPATHOLOGY

Table 5: Histopathology

Group	Description
Group I	Normal section of hepatic cells are seen.
Group II	Showing degeneration of hepatocytes in some were portal zone. This appear more eosinophilic
Group III	Showing normal features of hepatic tissue compared to cholesterol induced group.
Group IV	Showing normal feature of hepatic tissue compared to standard group.
Group V	Normal hepatic cells are seen compared to low dose of KSP.

CONCLUSION

In conclusion, our study demonstrates that the Siddha formulation KSP exhibits significant anti-dyslipidemic activity. Elevated serum lipid levels, a common feature in diabetes mellitus, contribute substantially to the risk of coronary heart disease (CHD). The hyperlipidemia observed in diabetic subjects primarily results from the increased mobilization of free fatty acids due to the uninhibited action of lipolytic hormones, a process normally regulated by insulin.

The administration of Triton to induce hyperlipidemia in rats provided a robust model for evaluating the hypolipidemic potential of KSP. Our findings indicate that KSP at doses of 250 mg/kg and 500 mg/kg effectively reduced plasma triglycerides and cholesterol levels. This reduction in total cholesterol is likely linked to a decrease in low-density lipoprotein (LDL), which is a key target of hypolipidemic agents. The cholesterol-lowering activity of KSP may be attributed to increased fecal excretion of bile acids and neutral sterols, along with a decreased absorption rate of cholesterol and triglycerides through the intestinal mucosa.

Moreover, the antioxidant constituents of Kadukkai, Nellimuli, and Thandrikai in KSP appear to prevent the endogenous oxidation of cholesterol, thereby reducing LDL concentrations. This study also highlighted the ability of KSP to increase high-density lipoprotein (HDL) levels, which plays a crucial role in the reverse transport of cholesterol from peripheral tissues to the liver, offering protective effects against CHD.

Overall, the results underscore the potential of KSP as a natural hypolipidemic agent with significant therapeutic benefits in managing dyslipidemia and reducing the risk of cardiovascular diseases in diabetic patients. Further research is warranted to explore the detailed mechanisms and long-term effects of KSP in clinical settings.

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