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ANTIHYPERLIPIDEMIC EFFECT OF SIDDHA FORMULATION KAMALAIKU KASHAYAM IN HIGH FAT DIET INDUCED HYPERLIPIDEMIC RATS

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ABSTRACT

Hyperlipidemia is a medical disorder defined by an increase in plasma lipids such as triglycerides, cholesterol, cholesterol esters, phospholipids, and/or plasma lipoproteins. Statins, nicotinic acids, and bile acid sequestrants have been found to be effective in patients for avoiding stroke, cardiovascular disease, and acute cardiac events. Due to frequent side effect encountered upon usage of statin in long term, it's a right time to explore the drugs from alternate traditional sources. Numerous traditional remedies have been demonstrated to be useful in the treatment of hyperlipidemia. The main aim of the present investigation is to evaluate the anti-hyperlipidemic potential of High fat diet the formulation Kamalaiku Kashayam in high fat diet induced hyperlipidemia rat model. (HFD) induced hyperlipidaemia is a well-established model to evaluate the anti-hyperlipidemic potential of the test drugs. From the data's of the study it was evident that significant increase in serum cholesterol, LDL, VLDL and triglyceride level of the rats belongs to HFD group in comparison with control group. Treatment with KK at both the dose level shown measurable decrease in serum cholesterol, LDL, VLDL and triglyceride level, Further increase in HDL level was observed in treatment group when compare to that of HFD group rats. From the data's of the present investigation it was concluded that the siddha formulation Kamalaiku Kashayam reveals significant anti-hyperlipidemic property may due to existence of versatile phytocomponents present in the formulation, Further therapeutic recommendation of the drug Kamalaiku Kashayam for the management of hyperlipidaemia shall be warranted with prior clinical validation.

KEY WORDS: ***Hyperlipidemia, Siddha, Kamalaiku Kashayam, Statins, High fat diet, Anti-hyperlipidemic potential***

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1. Introduction

Hyperlipidemia has been identified as a major risk factor for the development and progression of coronary heart disease [1]. In industrialized nations, coronary heart disease, stroke, atherosclerosis, and hyperlipidemia are the leading causes of mortality. [2] Hyperlipidemia is defined by an increase in blood total cholesterol, low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) cholesterol, and a reduction in serum high-density lipoprotein (HDL) cholesterol. Lipid problems linked with hyperlipidemia are thought to contribute to atherosclerotic cardiovascular disease [3]. According to World Health Organization data, the most major risk factors for CVD are hypertension, high cholesterol, alcohol use, and cigarette use [4] Dyslipidemia, is a significant risk factor for cardiovascular disease (CVD). It is widely established that an increase in LDL-C is a risk factor for CVD [5]. A 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase is a regulatory enzyme that catalyzes the production of mevalonate from HMG-CoA in the liver. As a result, antihyperlipidemic medications target HMG-CoA reductase (HMGR) [6]. Statins limit cholesterol production by inhibiting HMGR [7]. However, statins have a number of adverse effects, including digestive disorders, myopathy, and teratogenicity [8].

Currently, a number of synthetic hypolipidemic drugs are available and are effective but the associated side effects such as diarrhea, nausea, myositis and abnormal liver function severely handicap their application. Some patients are resistant to or are intolerant of conventional pharmacotherapy. Therefore, alternative approaches are eagerly needed [9].

Herbal medicines are being used by an increasing number of people because they are thought to have no or minimal side effects. In Asian and African countries, traditional medicine serves as the primary source of care for 80 percent of the population. Herbal medicines are the most profitable type of traditional medicine, bringing in billions of dollars. Traditional medicines are used as a guide by researchers because 40 percent of the plants contain key ingredients that can be used in prescription drugs [10]. According to reports, the Indian herbal industry is worth approximately Rs 16,000 crores (US$ 4,000 million) [11].

Siddha medicine possess numerous advantage in managing dyslipidemia, secondary metabolites commonly known as phytotherapeutics plays a pivotal role in limiting the serum cholesterol level through versatile pharmacological activity. The main aim of the present investigation is to evaluate the anti-hyperlipidemic potential of the formulation Kamalaiku Kashayam in high fat diet induced hyperlipidemia rat model.

2. Materials and Methods

2.1. Animals

Healthy adult wistar albino rats of either sex weighing between 200-220 g were used for the study. The animals were housed in poly propylene cages and were kept in well ventilated with 100% fresh air by air handling unit. A 12 light / dark cycle were maintained. Room temperature was maintained between 22 ¬+ 2o C and relative humidity 50–65%. They were provided with food (Sai feeds, Bangalore, India) and water ad libitum. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. The experimental protocol was approved by The Institutional Animal Ethics Committee of Sathyabama Institute of science and technology, Chennai, Tamil Nadu, India. SU/CLATR/IAEC/XVII/184/2021

2.2. Experimental Methodology [12,13]

The animals were grouped into four groups of 6 animals each. Group I (Control group) -received normal saline, Group II – Administered with high-fat diet (HFD) comprises of Powdered Normal Chow, 365 g; lard, 310 g; casein, 250 g; cholesterol, 10 g; vitamin mix and mineral mix, 60 g; DL methionine, 0.3 g; yeast powder, 0.1 g; and NaCl, 0.1 g were mixed to prepare 1.0 kg of HFD. The high fat diet contained 5.33 kcal/g. Animal will be treated with HFD for the period of twelve weeks along with low and high dose of the test drug. Group III (Treatment group Low Dose)- Administered with HFD and treated with 250 mg/kg of Kamalaiku Kashayam (KK) , p.o prior to HFD for the period of twelve weeks .Group IV (High dose treated group): Hemorrhoid rats was treated with 500mg/kg of KK, p.o prior to HFD for the period of twelve weeks. Animal will be treated with HFD for the period of twelve weeks along with low and high dose of the test drug. At the end of the study all rats will be

sacrificed and the serum will be collected for lipid profile estimation. Weight per ml of the study drug KK was found to be 1.025 gm/ml.

2.3. Biochemical analysis [14]

Serum samples were analyzed for High Density Lipoprotein (HDL), Low density Lipoprotein (LDL), Very low density Lipoprotein (VLDL), Triglycerides (TGL) and Total Cholesterol using Mind ray auto analyzer model BS 120.

2.4. Sample Collection

At the end of the study, before sacrifice, the animals were fasted for overnight with free access to water. Animals were sacrificed with excess anesthesia. Liver tissue was removed weighed and subjected to histological examination.

2.5. Histopathological Analysis [15]

Sample obtained were immersed in 10% formalin for 24 h-48h for histopathological examination. After standard processing, the cut tissue was embedded in paraffin (Leica TP1020 tissue processor) and cut into 5 µm thick sections in a rotary microtome (Leica RM2255 - Fully Automated Rotary Microtome). The sections were stained with haematoxylin-eosin (Merck). Histological measurement and photographs were taken with Olympus CX31, Trinocular Biological Microscope (magnification 10x & 40 x).

2.6. Statistical Method

The statistical analysis was carried by one-way analysis of variance ANOVA. Results are expressed as ±SEM. The data were statistically analyzed by ONE WAY ANOVA followed by Dunnett's multiple comparison test. Probability P values < 0.05 were considered as significant

3. Results

3.1Effect of KK on Body weight of Rats treated with HFD

From the result analysis of the present investigation it was clear that the body weight of the rats belongs to HFD group have shown significant increase when compare to group I. Treatment with KK at both the dose level shown measurable decrease in the body weight of the rats in the treatment group. Similar pattern were observed in the heart and liver weight of the rats, significant decrease in the organs weights were observed in the treatment group of KK at both the dose level. As shown in Table 1.

Table 1: Table 1: Effect of KK on Body weight of Rats treated with HFD

Group	Initial Body Wt in gms	Final Body Wt in gms	Weight of Heart in gms	Weight of Liver in gms
Group I-Control	205.3 ± 1.476	271.5 ± 3.16	0.58 ± 0.04	5.11 ± 0.14
Group II-HFD	207 ± 2.08	330.3 ± 1.726**	0.98 ± 0.02	7.55 ± 0.29*
Group III-HFD + 250 mg/kg KK	201.2 ± 3.17	314.5 ± 1.11	0.82 ± 0.03*	6.78 ± 0.15
Group IV-HFD + 400 mg/kg KK	206.2 ± 1.47	281.8 ± 8.89*	0.67 ± 0.02*	5.75 ± 0.12*

Values represent mean ± SEM of 6 experimental animals. * P< 0.05; ** P< 0.01; *** P < 0.001.

3.2. Effect of KK on Lipid profile of Rats treated with HFD

From the data's of the study it was evident that significant increase in serum cholesterol, LDL, VLDL and triglyceride level of the rats belongs to HFD group in comparison with control group I. Treatment with KK at both the dose level shown measurable decrease in serum cholesterol, LDL, VLDL and triglyceride level, Further increase in HDL level was observed in treatment group when compare to that of HFD group rats. As shown in Table 2.As shown in Table 2.

Table 2: Effect of KK on Lipid profile of Rats treated with HFD

Group	Total cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	TG (mg/dl)
Group I-Control	137.7 ± 5.41	64 ± 1.57	57 ± 4.09	16.68 ± 1.42	43.33 ± 4.27
Group II-HFD	218 ± 3.40**	33.67 ± 1.54*	132.5 ± 2.46*	51.83 ± 1.96*	122.3 ± 0.88**
Group III-HFD + 250 mg/kg KK	183.1 ± 4.55*	41.17 ± 1.19*	103 ± 3.80**	38.95 ± 1.98*	94 ± 1.91**
Group IV-HFD + 400 mg/kg KK	172.8 ± 3.50*	49.5 ± 1.38*	92.67 ± 1.68*	30.62 ± 1.31*	74.5 ± 5.92*

Values represent mean ± SEM of 6 experimental animals. * P< 0.05; ** P< 0.01; *** P < 0.001.

3.3. Effect of KK on histopathology of rat Liver

The centrilobular hepatocytes appears normal with stained cytoplasm were observed in group I rats. Appearance of terminal hepatic venules (central veins) to the portal tracts was normal in sample belongs to group I. Marginal changes near portal vein was observed with migration of inflammatory cells. Increase in sinusoidal spaces were observed were

observed were observed in HFD alone treated group II rats. Distinct widen hepatic cords that were dorsally radiating from the central vein were observed. Numerous hepatocytes appears with shrunken nucleus were observed in group III rats. Mild discrete cytoplasmic vacuoles and rare foamy cytoplasm were observed in group IV rats. As shown in Fig 1.

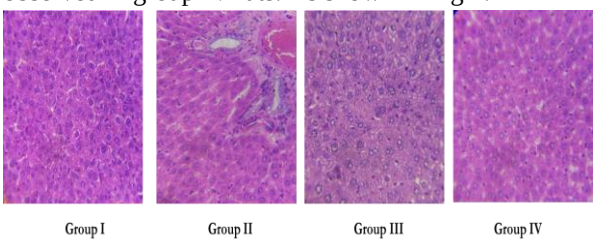

Figure 1: Histopathology of Rat Liver

4. Discussion

Hypercholesterolemia and hypertriglyceridemia, in particular, are strongly associated with ischemic heart disease [16]. The primary goal of hyperlipidemia therapy is to decrease the risk of developing ischemic heart disease or the onset of further cardiovascular or cerebrovascular illness [17]. Numerous adverse effects have been reported with currently available hypolipidemic medications [18]. Synthetic drug usage results in hyperuricemia, diarrhea, nausea, myositis, gastric irritation, flushing, and dry skin, as well as impaired liver function. Numerous studies on the pharmacological characteristics of over thirteen thousand plants have been conducted.

Medicinal plants continue to be important therapeutic agents in both contemporary and traditional medicine. Plants are employed in traditional systems of medicine in many areas of the globe, particularly in rural communities, as powders, extracts, decoctions, or infusions for the control, management, and/or treatment of a wide range of human and animal disorders. As a result of current global trends toward the use of plant-derived natural treatments, there is an urgent need for accurate and up-to-date information on the qualities, applications, efficacy, safety, and quality of medicinal plant products [19]. The plant kingdom has been a focus for global pharma companies looking for physiologically active lead chemicals [20].

Previously, it was shown that the HFD-fed hyperlipidemic rat model was an appropriate in vivo model for evaluating anti-hyperlipidemic medicines [21]. Enhanced fatty foods result in an increase in plasma total and LDL cholesterol. Atherosclerosis is predicted by elevated TC and, more critically, LDL cholesterol levels [22]. Triglycerides are associated with coronary heart disease in a direct or indirect manner, according to research [23].

Cholesterol in the serum is mostly synthesized biologically. The HMG-CoA enzyme is critical for cholesterol production. Inhibiting the enzyme results in a decrease in blood cholesterol levels. HMG-CoA is the target of statin medications, which are commonly used in clinical practice to lower cholesterol. But the chronic usage of statins may leads to undesirable side effects. Siddha formulations expected to significantly lowered blood triglycerides and cholesterol levels.

From the data's of the study it was evident that significant increase in serum cholesterol, LDL, VLDL and triglyceride level of the rats belongs to HFD group in comparison with control group I. Treatment with KK at both the dose level shown measurable decrease in serum cholesterol, LDL, VLDL and triglyceride level, Further increase in HDL level was observed in treatment group when compare to that of HFD group rats.

5. Conclusion

Hyperlipidemia is a dangerous epidemic condition characterized by abnormal lipid metabolism. It is a major risk factor for atherosclerosis and ischemic heart disease. Improved food habits and statin therapy are recommended as the initial therapy for cholesterol reduction. From the data's of the present investigation it was concluded that the siddha formulation Kamalaiku Kashayam reveals significant anti-hyperlipidemic property may due to existence of versatile phytocomponents present in the formulation, Further therapeutic recommendation of the drug Kamalaiku Kashayam for the management of hyperlipidaemia shall be warranted with prior clinical validation.

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