

PHARMACOLOGICAL EVALUATION OF HERBOTRIM FOR ITS ANTI-ATHEROGENIC PROPERTY USING ANIMAL MODELS

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ABSTRACT

Obesity is an abnormal or excessive fat accumulation that causes risk to health. In severe case weight gain leads to various risks in the general health. Several classical formulations of ayurveda and other modern medicines give only time bound recovery. Hence treatment of obesity has been remained as a challenging problem to the medical field. The test drug herbotrim is a polyherbal formulation has showed promising results in reducing the elevated serum cholesterol and lipids by correcting lipid metabolism. It also prevents atherosclerosis of blood vessels and fatty infiltration of vital organs thereby protecting from cardiovascular and cerebrovascular diseases. It can be used as an excellent supplement for the patients of myocardial infarction, coronary artery diseases and diabetes mellitus. Acute toxicity study carried out as per the Globally Harmonized system has proved that herbotrim is absolutely safe and no side effects even at high doses. Hence it is very important in this era to discover this type of multi beneficiary drugs to cure obese patients with no side effects. Histopathological studies of the drug proved that herbotrim having tissue protective activities against fatty infiltration and tissue damage. So that herbotrim tablets can serve as a potent ayurvedic medicine for the prevention of heart diseases.

Keywords: Herbotrim, Acute toxicity, antiobesity, Globally Harmonized System.

INTRODUCTION

Obesity is found to be a major problem of modern population. It is associated with many hazards and is recognized as risk factor in the etiology of premature death, diabetes mellitus, hypertension, atherosclerosis, gall bladder problems and certain type of cancers¹. Athero-sclerosis, major complication associated with obesity. Elevated levels of cholesterol and triglycerides are known to cause athero sclerosis. It is responsible for more deaths in the U.S. than any other condition. Atherosclerotic heart diseases involving the coronary arteries (coronary heart disease), is the most common cause of death, accounting for one-third of all deaths. Atherosclerotic interference with blood supply to the brain (stroke) is the third most common cause of death after cancer. Ayurveda is a major traditional system of Indian medicine that is still being successfully used in many countries. According to the World Health Organization (WHO), approximately 80% of the world's population currently uses herbal medicines in healing different ailments. Among the estimated 400,000 plant species, only 6% have been studied for biological activity, and about 15% have been investigated phytochemically²⁻³. Hence evaluation more herbal formulation is needed to assess the anti obesity properties of the drug. The time-tested evidences vouch immense therapeutic benefits for ayurvedic herbs and formulations. Herbotrim is a polyherbal proprietary ayurvedic drug prescribed for obese patients. Obesity is a major health problem and as a result, it is reasonable to consider pharmacological approaches along side, approaches involving diet, physical activity and life style change. The current available drugs, sibutramine and orlistat result in modest, clinically worthwhile weight loss, with demonstrable improvement in co-morbidity, but do not meet the often unrealistic expectations of patients and health care professionals managing obese patients. There is insufficient data to support the efficacy or safety of these drugs.

The risk of IHD (Ischaemic Heart Disease) is also more in obese patients. Hence the therapy for atherosclerosis and other complications should aim at reducing the obesity and lipid contents of the blood. In ayurveda, obesity is referred as "Sthoulya" the treatment of obesity has been described in ancient Ayurvedic classics. This particular product is designed as per the reference given in classical text books. It contained about ten different herbs having Medohara, Kapha and Vatahara properties. Present

investigation is our attempt for pharmacological evaluation of atherogenic properties of polyherbal drug herbotrim.

MATERIALS AND METHODS

Herbotrim is a proprietary ayurvedic polyherbal drug procured from Muniyal Ayurvedic Research Center at Manipal. Acute Oral Toxicity Test done as per the OECD Guidelines 423. This is a stepwise procedure with three animals of a single sex per step. Depending on the mortality and/ or moribund status of the animals, on an average 2- 4 steps are necessary to allow judgement on the acute toxicity of the test substance. The method used with defined doses (5, 50, 500, 2000mg/kg b.wt.) and the results are allow the substance to be ranked and classified according to Globally Harmonized Systems (GHS) for the classification of chemical which cause acute toxicity.

Hypolipidemic activity assessment

Male wistar (body weight 150-200g) rats are used for the study. Rats were divided into three groups of six rats each. Group 1 is control group, group second hyper cholestremic diet and group third was diet with test drug. Hypercholestremia is induced by supplementing atherogenic diet comprising 40% groundnut powder, 20% cholesterol, 40% normal rat food. Hypocholestremic diet is administered for 45 days. Then profile was carried out for all the animals in order to confirm elevated cholesterol level. All hypercholestremic rats are then subjected to the drug treatment for next 15 days. At 16 th day blood sample is withdrawn from the retro-orbital plexus of overnight fasted rats, serum is separated and total cholesterol, HDL, LDL and triglycerides are estimated using commercially available kits. Finally, the animals are dissected and the aorta is removed and kept in formol-saline for histopathological observation.

Lipid lowering profile of Herbotrim was shown by comparing lipid profiles of hypercholestremic and herbotrim treated rats. Highly significant reduction of TC, LDL, TG, atherogenic index and increase in HDL indicates promising results of Herbotrim as hypocholestremic drug.

RESULTS

Statistical analysis was carried out to assess the hypercholestremia in treated animals. Elevation of cholesterol level shown by increase in TC, TG, LDL and decrease in HDL. Lipid lowering profile of herbotrim was shown by comparing lipid profiles of hypercholestremic and herbotrim treated rats. Marginal reduction in

TC, LDL, TG, atherogenic index and increase in HDL indicates that Herbotrim is a promising drug used for the management of obesity and obesity associated risks.

Table No.1 shows the values of serum lipid profile in normal (before atherogenic diet), cholesterol fed-control group and herbotrim treated groups. Serum total cholesterol, LDL-cholesterol, VLDL cholesterol and triglycerides levels increased significantly ($P<0.001$) after 45 days of cholesterol feeding. Further more, the total cholesterol: HDL – cholesterol ratio and LDL – cholesterol: HDL cholesterol ratio was also increased significantly ($P<0.001$). Administration of Herbotrim Tablets for 15 days in hypercholesteremic rats caused statistically highly significant decrease ($P<0.001$) in the levels of serum total cholesterol and LDL, a moderately significant increase in HDL ($P<0.01$) was also noticed. The ratios of total cholesterol and LDL: HDL- cholesterol and LDL-Cholesterol: HDL-cholesterol were also declined significantly ($P<0.001$) as compared to control group rats.

Histopathology of aorta of hypercholesteremic rats indicated lesion with abnormal overlying endothelium and desquamation. Observation of tissues also showed cholesterol deposits and fatty infiltration. Herbotrim treated rats showed neither infiltration and cholesterol deposit nor desquamation indicating good protection (Plate-1)

DISCUSSION

Hyperlipidemia including hypercholesteremia is mostly associated with obesity (however, there are exceptions) which is correlated with Sthoulya (Obesity) as mentioned in Ayurvedic texts. For the treatment of obesity, classics of Ayurveda, have mentioned medicinal plants like *Premna mucronata* Roxb, *Commiphora mukul* Hook ex Stock, *Emblica officinalis* Gaertn, *Terminalia chebula* Retz, and *Terminalia bellerica* Roxb⁴ Acute toxicity studies have proved that Herbotrim is safer till the dose level of 2000 mg/Kg bwt. It is well documented that elevated total cholesterol and low density lipoprotein cholesterol levels promote atherosclerosis and cardiovascular complications⁵. Hypolipidemic activity of guggule, curcumin of Haridra⁶⁻⁸ and *Embelia ribes* are proved by various experimental studies. Guggulu also has proved anti atherogenic properties. *Emblica officinalis* is a key ingredient in many Ayurvedic preparations, a good adaptogen, antioxidant and anti-inflammatory. Several scientific reports are available on its role in protection of liver, heart and other tissues from various toxicities. Amalaki reduces serum cholesterol levels. Vibheetakai (*Terminalia bellerica*) in experimentally proved that induces atherosclerosis⁹. The drug kulatha also possesses hypolipidemic property. The test drug herbotrim is combination of ten different drugs highly significant in reduction of Total Cholesterol, LDL, Triglycerides, atherogenic index and increase in HDL indicates it as

hypocholesteremic drug. It was observed that elevation of cholesterol level which is shown by significant increase in TC, TG, LDL and decrease in HDL. Lipid lowering profile of Herbotrim was shown by comparing lipid profiles of hypercholesteremic and herbotrim treated rats. Highly significant reduction of TC, LDL, TG, atherogenic index and increase in HDL indicates promising results of Herbotrim as hypocholesteremic drug. Lipid level is marginally decreased in herbotrim treated animals (Table 1 and Fig 1).

Histopathology of hypercholesteremic rat indicates lesion with abnormal overlying endothelium and desquamation. Observation of tissues also showed cholesterol deposits and fatty infiltration. Herbotrim treated rats showed neither infiltration and cholesterol deposit nor desquamation indicating good protection (Plate-1). Being its antiobesity activity is experimentally proven and drug is safe even in high dosage, herbotrim can be a good herbal drug for the management of risks of obesity. The reduction in atherogenic index and prevention of fatty infiltration and atherosclerosis suggest the possibility of using herbotrim tablets as a promising, safe ayurvedic supplement for the prevention of heart diseases.

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Table 1: Lipid lowering profile of Herbotrim

Lipid profile	Before Atherogenic diet (Normal)	After Atherogenic diet (Hypercholesteremic)	After Herbotrim treatment
TC	51.40±6.24	128±12.32a**	62.20±9.74b**
HDL	19.40±3.63	10.2±2.04a*	16±1.88b*
LDL	23.1±4.18	106±19.06a**	36±7.38b**
VLDL	8.05±0.98	12.5±2.06a*	9.25±0.86b*
TG	45±9.86	60±14.02a*	50.5±11.52b*
Atherogenic index	1.64	11.5	2.88

Statistical significance based on paired 't' test. Results are expressed as Mean ±S.E.M of 6 numbers of animals.

a-comparison made between normal and hypercholesteremic rats.

b-comparison made between hypercholesteremic and herbotrim treated rats.

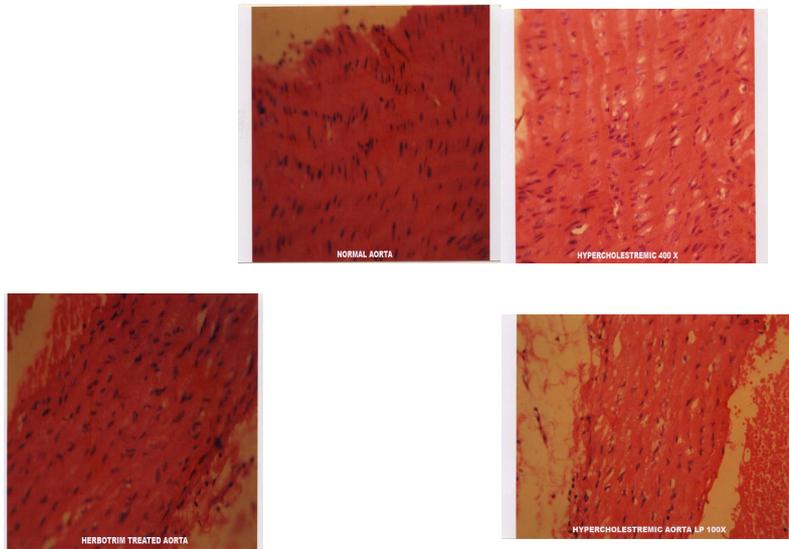
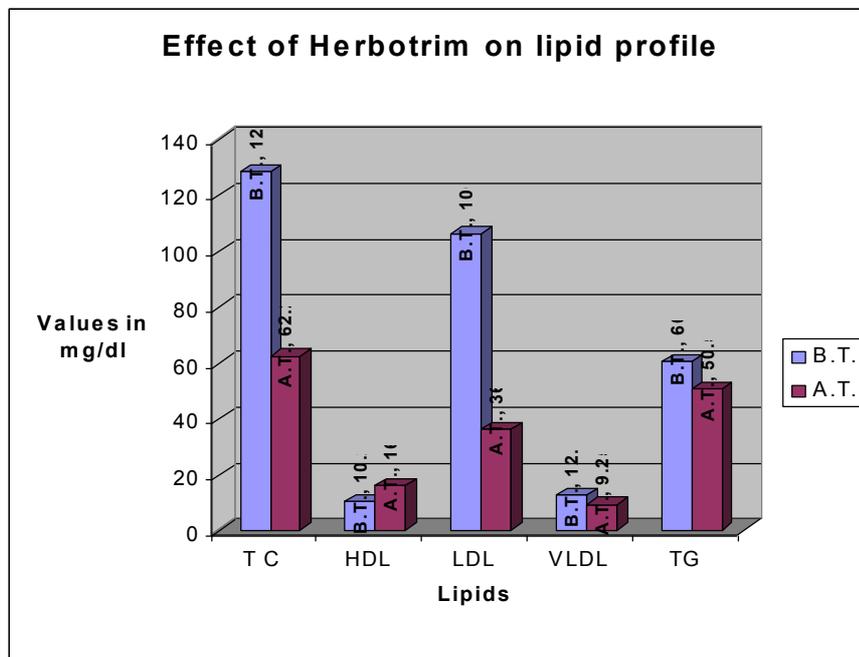


Plate -1.Effect of Herbotrim on atherogenic Index



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