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Combined Tulsi Extract and Cinnamon oil Reduce Hypercholesterolemia in Dyslipidemic Rats.

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ABSTRACT

The studies were intended to investigate the possible antihyperlipidemic effect of tulsi and cinnamon oil in high cholesterol diet induced hyperlipidemic rats. Tulsi and cinnamon oil were evaluated for antihyperlipidemic activity using high cholesterol diet induced hyperlipidemia model in male Wistar albino rats(200-250g). A comparison was also made between the action of tulsi(0.5 mg/kg b.w) and cinnamon oil extracts(1.8mg/200g b.w) and antihyperlipidemic drug atorvastatin (0.18mg/200g). Parameters assessed were body weight, total cholesterol, triglyceride, HDL-C, LDL-C. The results of the study are represented by mean ± SEM. Statistical significance of data was assessed by one way analysis of variance (ANOVA) followed by a comparison between different groups using "Tukey - Kramer" test. Oral administration of 0.5 mg/kg of tulsi oil with dist. water and Cinnamon oil of 1.8 mg/200g suspended in tween80 solution exhibited significant reduction ($p < 0.01$) in serum biochemical parameters total cholesterol, triglycerides, low density lipoprotein (LDL), very low density lipoprotein (VLDL) and increase in high density lipoprotein (HDL) levels in hyperlipidemic rats of HC diet model compared to hyperlipidemic positive control. The results demonstrated that tulsi and cinnamon oil extracts possessed significant antihyperlipidemic activity.

Keywords: Tulsi oil, Cinnamon oil, Atorvastatin, High cholesterol diet, Hyperlipidemia.

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INTRODUCTION

Hyperlipidemia is a major risk factor for CAD in patients suffering with cardiovascular disorders. Hyperlipidemia is deeply involved in the etiology of atherosclerosis.[1] Hyperlipidemia in many cases in the modern age is caused by over-consumption of alcohol or fatty foods. Attention is also being paid to treatment of patients with hyperlipidemia using strict management and appropriate exercise.[2] currently available antihyperlipidemic drugs have been associated with a number of side effects[3], naturally available herbal drugs have lesser side effects and are easily available. The literature survey reveals that Ayurvedic drugs are able to reduce the lipid content of blood.[4] The safety of herbal formulation has ensured and most comply with regulatory authorities. Herbal formulations usually are considered as derived of side effects by the general population, however they can cause hepatotoxicity hepatotoxicity, renal failure and allergy etc. Unfortunately the side effect can be due to a variety of other reasons such as poor quality of raw material, misidentified herbs, adulteration or contamination. There can be error in the extract used in formulation & the one claimed in the label.

Tulsi plant is known as holy basil and historically used in ayurvedic medicine. That has various pharmacological activities.[5] The rats fed with *Ocimum sanctum* extract has shown a decrease in hyperlipidemia and thus shown antiatherogenic and cardioprotective actions against hyperlipidemia.[6] Linoleic acid and linolenic acid present in *Ocimum sanctum* as fixed oil were possibly responsible for both lipid lowering and cardiac protective action against hyperlipidemia.[7]

Cinnamon is commercially known as Indian cassia and has been used in traditional medicine as an astringent, stimulant, diuretic, carminative and in cardiac disorders.[8] Cinnamate, a phenolic compound found in inner bark of cinnamon[9], lowers cholesterol level in high fat-fed rats by inhibiting hepatic HMG-CoA reductase activity.[10] Hence, the present study is designed to evaluate the antihyperlipidemic activity using marketed herbal extracts.

MATERIALS AND METHOD

Tulsi oil was procured from Vedic Tulsi Amrit and it is made from pure extract of 5 different types of tulsi leaves as per the claim of manufacturer. Tulsi leaves contain Rama tulsi, Shyama tulsi, Rosary tulsi, Vana tulsi, Shukla tulsi (Each 50mg/ml). Cinnamon oil was purchased from local ayurvedic drug supplier.

High Cholesterol Diet: standard animal diet consisting of Bengal gram flour, wheat flour, maize and jawar flour, 2.5% cholesterol,1% cholic acid and 2 ml coconut oil with adequate quantity of water was fed to animals.[10]

Atorvastatin (Zydus Healthcare) and Diagnostic kits for estimation were purchased from Pathozyme diagnostic kits Kolhapur. All other chemicals were of analytical grade.

Animals

Male Wistar albino rats weighing between 200-250 g were procured from Central animal house, M.R. Medical College, Kalaburagi. They were acclimatized for one week to the laboratory condition in well ventilated room at t temperature 25 ± 2°C and relative humidity of 30-70% with a 12:12 light-dark cycle, and fed with standard pellet supplied by Hindustan lever. Co. Mumbai with water *ad libitum* throughout the course of study. The animals were fasted for 18 h prior to the experiment. All the animal experiments were conducted according to the ethical norms approved by CPCSEA, and ethical clearance was granted by institutional ethical animal committee.(HKESCOP/IAEC/58/2013-14) The present study was conducted in Dept. of Pharmacology H.K.E.S MTRIPS, Kalaburagi.

Preparation of dose [12]

Tulsi oil: (0.5 mg/200 g b.w p.o) Tulsi oil was taken and dissolved in distilled water. The solution was freshly prepared everyday before dosing the animals.

Cinnamon oil: (1.8 mg/200 g b.w p.o) Cinnamon oil was taken and suspended with 2% tween 80 solution. The solution was freshly prepared every day before dosing the animals.

Preparation of standard drugs

Atorvastatin 0.18mg/200g b.w p.o was used as the reference standard drug for evaluating the antihyperlipidemic activity which was made into suspension in distilled water using Tween-80 as a suspending agent.

High Cholesterol Diet induced hyperlipidemic model

The animals were selected, weighed then marked for individual identification. In this model, rats were made hyperlipidemic by high cholesterol diet feed provided for 7 weeks. The rats were given free access to the feed and water *ad libitum*. The rats were given plant extract and standard drug daily, for 3 weeks except positive control and normal control group. At the end of treatment period, the animals were used for the study for various biochemical parameters. Blood was collected by retro-orbital plexus of rat under mild ether anesthesia and centrifuged at 2000 rpm for 30 min to get serum.

Experimental Design

Male Wistar albino rats weighing between 200-250 g were divided into 5 groups of 6 animals in each group. Group I served as normal control and this group did not receive high cholesterol diet except regular standard pellet diet. Group II was hyperlipidemic control (positive control) and this

group did not receive any treatment except HCdiet for 7 weeks ; Group III received HCdiet for 4 weeks then Tulsi oil(0.5 mg/kg/day p.o) extract was administered for three weeks. Group IV received HCdiet for 4 weeks; then Cinnamon oil (1.8mg/200g b.w/day p.o) extract was administered for three weeks. Group V was administered with standard antihyperlipidemic drug atrovastatin (0.18mg/200g b.w/day p.o) for three weeks after HC diet of 4 weeks. Treatment period of all these groups was 7 weeks in high cholesterol diet induced hyperlipidemia model.

Collection of blood

The blood was collected from orbital sinus with the help of capillary tube under mild ether anesthesia. The collected samples were centrifuged for 15 min.

Biochemical Analysis

The serum was analyzed for total cholesterol, triglycerides, high-density lipoproteins (HDL), low-density lipoproteins (LDL) and very low density lipoproteins (VLDL) using standard diagnostic kits. Cholesterol, triglyceride were estimated by CHOD-PAP method and high density lipoprotein by GPO-PAP method and low density lipoproteins were calculated by using Friedewald formula and VLDL:TG/5 [13,14]respectively.

Statistical analysis

Results were expressed as mean ± SEM. Statistical significance of data was assessed by one way analysis of variance (ANOVA) followed by a comparison between different groups using "Tukey - Kramer" test. A value of $P < 0.05$ was considered to be statistically significant. The HC- diet group was compared with normal control group and all other treatment groups were compared with HC- diet group.

RESULTS AND DISCUSSION

Body weight of animals after 4th week and after 7th week treatment against high cholesterol diet induced hyperlipidemia in rats:

High Cholesterol diet significantly increased the body weight compared to the control group (Normal Rats). Administration of HC-diet significantly increased the body weight after 28 days of the treatment compared to control group. At the 42th day positive control group of rats increased in their weight by 23% as tabulated in Table 1

Table 1: Shows the body weight of rat's treated with high cholesterol diet inducing hyperlipidemia.

Groups	Treatment	Initial Body wt in (g)	Body wt in (g) after 4th week	Body wt in (g) after 7th week
1	Tween 80	221 ± 1.75	224 ± 0.03	226 ± 2.01
2	HCD	232 ± 1.35	247 ± 1.89	267 ± 1.17**
3	HCD + Tulsi oil	228 ± 2.81	245 ± 1.56	249 ± 1.83***
4	HCD + Cinnamon oil	224 ± 2.19	241 ± 2.29	250 ± 1.63**
5	HCD + Atorvastatin	241 ± 2.17	256 ± 3.12	264 ± 2.11***

High cholesterol diet induced hyperlipidemic model

In HCD-induced hyperlipidemic model results showed serum lipid lowering potentials of tulsi and cinnamon oil extracts selected for study. The results are presented in(Fig 1) these results are comparable to standard drug atorvastatin. Both extracts showed significant serum lipid lowering effects in hyperlipidemic rats. Cinnamon oil showed significant effect which brought down total cholesterol 328 ±7 to 258.7 ±8.3, triglycerides 204.4±3.9 to 159.6 ±2.3, LDL-C181.1±2.2 to 164.7 ± 1.3 and increased level of HDL-C 32.3± to 45.9 ± 0.8 at 42th day.

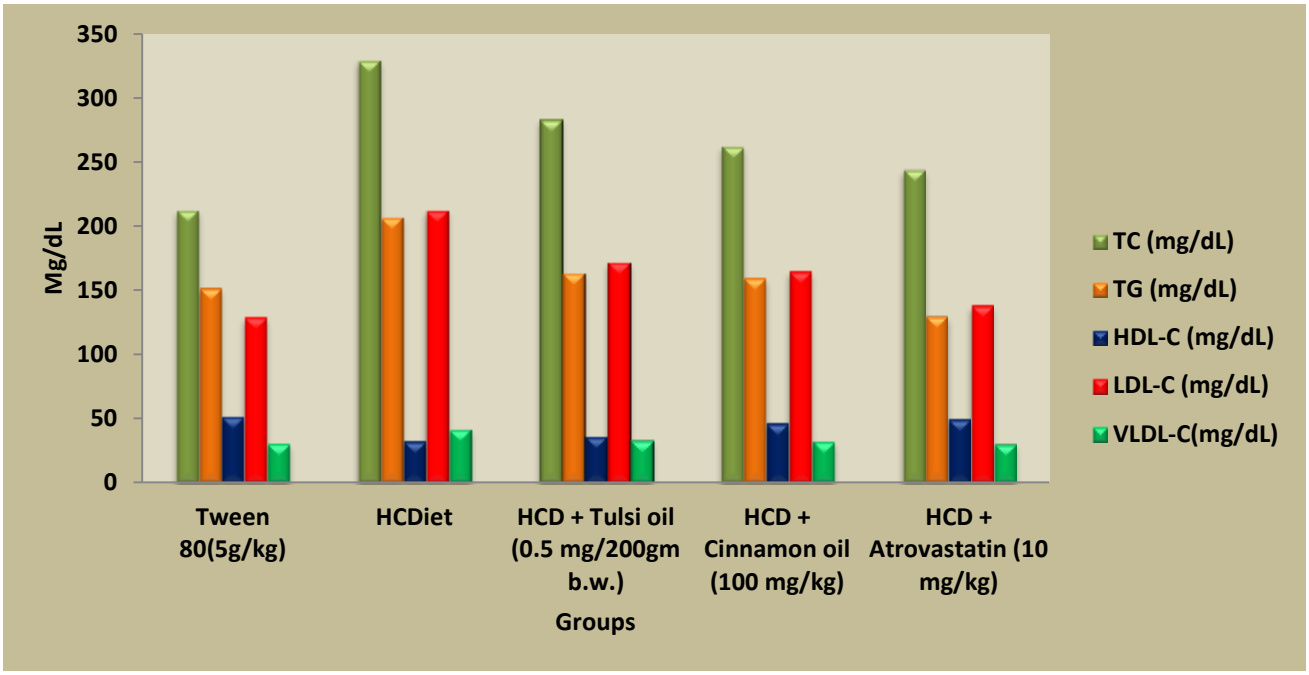

Figure 1: Average percentage change in selected serum biochemical parameters in high cholesterol diet induced hyperlipidemia in rats.

There was marked increase in the level of serum total cholesterol, triglycerides, LDL,VLDL and decrease in the level of good cholesterol carrier HDL-C in the animals treated with high cholesterol diet. Elevated levels of blood cholesterol especially LDL-C was the major risk factor for the coronary heart disease. Treatment with tulsi oil extract (0.5 mg/200g) and cinnamon oil (1.8

mg/200 g) significantly decreased the levels of serum total cholesterol, triglycerides, LDL-C, VLDL-C as compared to hyperlipidemic control. Several preclinical models have been used to explore antihyperlipidemic effects of novel compounds on hyperlipidemia, most frequently the male rat or mice model (for avoiding influence of estrogen on lipid metabolites) is used. This drug may also enhance the synthesis of LDL apoproteins (Apo B) as well as receptor protein to accelerate the turnover of cholesterol. The present investigation with cholesterol fed hyperlipidemic animals shows the stimulation of LDL catabolism.

In the present study, the high cholesterol diet (2.5 % cholesterol, 2 ml coconut oil) with all different flours mix was choosen. It has been reported that cholesterol and fatty acids are main reason for elevated serum cholesterol, triglyceride levels for hypercholesterolemia in rat model as it amplifies the effect of dietary cholesterol. Tulsi oil well known for its therapeutic potential and as medicinal plant is widely used for management of various diseases. Eugenol is major constitute in tulsi leaves but not much acknowledged for the mechanism action. Cinnamate, a phenolic compound found in inner bark of cinnamon, lowers the cholesterol level in high fat fed rats by inhibiting hepatic HMG-CoA reductase activity. Tulsi oil has shown a marked decrease in lipid lowering activity but cinnamon oil has shown a better action in decreasing serum lipid profiles.

CONCLUSION

The results show that Tulsi ($P<0.01$) and cinnamon oil ($P<0.001$) possess antihyperlipidemic activity. Among them cinnamon oil possesses more activity; the results are statically significant compared to atorvastatin ($P<0.01$).

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