

RESEARCH ARTICLE

Evaluation and comparison of hypolipidemic effect of *Curcuma longa* Linn. with atorvastatin in albino rats

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ABSTRACT


Background: Hyperlipidemia is one of the most common causes of atherosclerosis. Secondary hyperlipidemia could be due to obesity, diabetes mellitus, alcohol consumption, kidney failure, nephrotic syndrome, etc. It does not cause any symptoms and may go unnoticed for years. Dietary modifications along with medications are the mainstay of treatment in moderate to severe causes of hyperlipidemia. Statins are one of the most widely used drugs for the treatment of this disorder. Myopathy and persistent liver enzyme abnormalities are the most deleterious adverse effects of statins. The use of phytochemicals would minimize the adverse effects encountered with statins. In the present study, we studied and compared the hypolipidemic effect of *Curcuma longa* Linn. with atorvastatin in obese hyperlipidemic rats. **Aims and Objectives:** The present study was done to evaluate the hypolipidemic effect of turmeric (*C. longa* Linn.) and to compare it with atorvastatin in albino rats. **Materials and Methods:** Wistar albino rats weighing 120–150 g were utilized for the present study. The ethanolic extract of *C. longa* Linn. was administered orally to obese rats for 8 weeks. Serial estimation of lipid profile was done at 2, 4, 6, and 8 weeks, respectively. Lipid profile was assessed using serum cholesterol, serum high-density lipoproteins (HDLs), serum low-density lipoproteins (LDLs), and serum triglycerides (TGs) as parameters. **Results:** Statistically significant improvement in lipid profile ($P < 0.05$) was seen after administration of *C. longa* in obese rats. There was significant reduction in serum cholesterol, serum LDL, and serum TGs. However, serum HDL did not show a significant increase. **Conclusion:** *C. longa* Linn. had a hypolipidemic effect.

KEY WORDS: Hyperlipidemia; Myopathy; Statins

INTRODUCTION

Hyperlipidemia is defined as an elevation of lipid levels in the blood. It is also known as hyperlipidemia, lipemia, or lipedema, and includes elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and total triglyceride (TG) levels in the blood.^[1] It is broadly classified into primary and

secondary hyperlipidemias. Primary/Familial hyperlipidemia is due to a genetic defect which could be a single gene defect (monogenic) or multiple gene defects (polygenic). Secondary hyperlipidemia/acquired hyperlipidemia is caused by disorders such as diabetes, nephritic syndrome, chronic alcoholism, and hypothyroidism and with the use of drugs such as corticosteroids, beta-blockers, and oral contraceptives.^[2] Hyperlipidemia is associated with number of complications which include atherosclerosis, coronary artery disease, myocardial infarction, and ischemic stroke. It is associated with an increase in oxidative stress leading to the production of oxygen free radicals. These oxygen free radicals lead to oxidative modifications in LDLs, which play a major role in the initiation and progression of atherosclerosis and associated cardiovascular diseases.^[3] Hyperlipidemia is

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usually asymptomatic and is detected during a routine blood workup or following a cardiovascular event such as stroke or heart attack.^[4] Treatment of hyperlipidemia is divided into non-pharmacologic and pharmacologic therapy. Non-pharmacologic therapy includes dietary modifications, weight loss, and exercise.^[5] Pharmacologic therapy includes five major classes of antihyperlipidemic drugs, namely statins, fibric acid derivatives, bile acid binding resins, nicotinic acid derivatives, and drugs that inhibit cholesterol absorption.^[6] Among the various classes of drugs available, statins are the most commonly prescribed class of lipid-lowering drugs which include atorvastatin, rosuvastatin, simvastatin, and lovastatin.^[7]

Statins are structural analogs of 3-hydroxy-3-methylglutaryl-coenzyme A. They competitively inhibit the enzyme HMG-CoA reductase responsible for the first step in sterol biosynthesis. They have a predominant effect on reducing LDL-C. The anti-atherogenic effects of statins, beyond lowering LDL-C levels, seem to be related to their ability to reduce ROS production.^[8,9] Use of statins is associated with various adverse effects such as headache, constipation, diarrhea, flatulence, hyperglycemia, hepatotoxicity, and muscle toxicity which are the most important adverse effects.^[10,11]

The incidence of various adverse effects associated with statins has increased the need to discover natural agents as alternatives to currently available treatments.^[12]

Turmeric (*Curcuma longa*) is well-known condiment in the world. It is a prime ingredient in curry powder and is used widely in Asian cuisines, known as “Golden spice” of India. *C. longa* is a herbaceous perennial plant, belonging to the Zingiberaceae family. It is extensively used in Ayurveda, Unani, and Siddha medicinal systems since Vedic-ages and also as a home remedy for various ailments. The various medicinal properties of turmeric include anti-inflammatory, antifungal, antimutagenic, anticarcinogenic, anticoagulant, antihepatotoxic, antifertility, antiprotozoal, antiviral, antifibrotic, antivenom, antiulcer, antidiabetic,

and hypolipidemic properties.^[13] Turmeric is widely used in therapeutic preparations against anorexia, rhinitis, herpes zoster, acne, cough, urinary tract diseases, diabetic wounds, hepatic disorder, rheumatism, and sinusitis.^[14]

Very few studies have been conducted on the hypolipidemic effect of turmeric using multiple doses. Furthermore, there is limited number of studies where the hypolipidemic effect of turmeric has been compared with a standard hypolipidemic drug. Taking into consideration the numerous adverse effects associated with the use of statins, the present study was undertaken to evaluate the hypolipidemic effect of turmeric in comparison with atorvastatin albino rats.

Aim

The aim of the study was to evaluate the hypolipidemic effect of turmeric and compare it with that of atorvastatin in albino rats.

Objectives

The objectives are as follows:

1. To evaluate the hypolipidemic effect of turmeric in albino rats.
2. To compare the hypolipidemic effect of turmeric with atorvastatin in albino rats.

MATERIALS AND METHODS

Duration of Study

The duration of the study was 8 weeks.

Sample Size

There were 36 albino rats used in the study.

Type of Study

This was an experimental study.

Locus of Study

The study was being carried out in Animal House, Department of Pharmacology, Jawaharlal Nehru Medical College, Wardha.

The study was undertaken after approval from the Institutional Animal Ethical Committee Ref. No – DMIMSDU/IAEC/2016-17/12.

Wistar albino rats of either sex weighing 150–200 g were utilized for the study. The experiment was performed after due permission from the Institutional Animal Ethics Committee. As shown in Table 1 experimental animals were divided into 6 groups.

Table 1: Experimental animals were grouped

Group	Treatment to be given	Duration
I	Normal diet	8 weeks
II	High-fat diet	8 weeks
III	High-fat diet along with atorvastatin 40 mg/kg PO daily	8 weeks
IV	High-fat diet along with 300 mg alcoholic extract of turmeric PO daily	8 weeks
V	High-fat diet along with 500 mg alcoholic extract of turmeric PO daily	8 weeks
VI	High-fat diet along with atorvastatin 40 mg/kg daily PO and 500 mg alcoholic extract of turmeric daily	8 weeks

All rats were kept under observation for 1 week before the experiment to permit the animals to adjust to the environment. The high-fat diet consisted of coconut oil with vanaspati ghee added to the daily diet of experimental rats. Blood samples were collected through retro-orbital puncture a day before starting the study and at 2, 4, 6, and 8 weeks, respectively. These samples were centrifuged for 10 min at 3000 rpm and sera were obtained. These were analyzed for serum TC, serum (TG), and serum high-density lipoprotein (HDL) using lipid profile kit marketed by Priman Instruments, New Delhi. All specimens of sera were stored at -200°C until use. Results were measured using a spectrophotometer.

RESULTS

Statistical analysis was done using descriptive and inferential statistics using one-way ANOVA and Multiple comparison Tukey test and software used in the analysis was SPSS 17.0 version and $P < 0.05$ is considered as the level of significance.

Mean value of serum TC in Group I was 132.38 ± 27.66 , Group II was 164.35 ± 7.01 , Group III was 75.08 ± 6.92 , Group IV was 66.58 ± 3.23 , Group V was 62.51 ± 2.96 , and Group VI was 51.47 ± 2.32 . Using one-way ANOVA statistically significant difference was found in mean serum TC levels among six groups ($F = 83.656$, $P = 0.0001$). On comparing serum TC levels in six groups using Multiple comparisons Tukey test statistically significant variation was found in mean serum TC levels among Groups I and II, Groups I and III, Groups I and IV, Groups I and V, and Groups I and VI ($P < 0.05$). Furthermore, statistically significant variation was found in mean serum TC levels among Groups II and III, Groups II and IV, Groups II and V,

and Groups II and VI ($P < 0.05$). No significant variation was found between Groups III, IV, V, and VI [Table 2].

Mean value of serum TG in Group I was 93.67 ± 12.44 , Group II was 110.70 ± 13.48 , Group III was 51.79 ± 12.13 , Group IV was 49.09 ± 10.32 , Group V was 47.84 ± 9.65 , and Group VI was 31.67 ± 2.81 . Using one-way ANOVA statistically significant difference was found in mean serum TG levels among six groups ($F = 49.31$, $P = 0.0001$). On comparing serum, TG levels in six groups using Multiple comparisons Tukey test statistically significant variation were found in mean serum TG levels among Groups I and II ($P < 0.05$). Statistically significant variation was also seen among Groups II and III, Groups II and IV, Groups II and V, and Groups II and VI ($P < 0.05$). No significant variation was found between Groups III, IV, V, and VI [Table 3].

Mean serum HDL in Group I was 57.60 ± 5.67 , Group II was 33.75 ± 2.25 , Group III was 35.00 ± 2.23 , Group IV was 35.6778 ± 2.75 , Group V was 36.15 ± 2.42 , and Group VI was 36.91 ± 2.41 . Using one-way ANOVA statistically significant variation was found in mean serum HDL levels among six groups ($F = 48.23$, $P = 0.0001$). On comparing serum, HDL levels in six groups using Multiple comparisons Tukey test statistically significant difference were found in mean serum HDL levels among Groups I and II ($P < 0.05$). HDL-C decreased in the group receiving a high-fat diet. No significant variation was found between Groups III, IV, V, and VI. However, there was an increase in HDL-C levels in Groups III, IV, V, and VI when compared to Group II ($P > 0.05$) [Table 4].

Table 2: Comparison of serum total cholesterol in six groups

Group	n	Mean \pm SD	Standard error	95% confidence interval for mean		Minimum	Maximum
				Lower bound	Upper bound		
I	6	132.39 \pm 27.66	11.29	103.35	161.42	114.12	188.00
II	6	164.35 \pm 7.01	2.86	156.98	171.71	152.88	172.70
III	6	75.08 \pm 6.92	2.82	67.81	82.35	63.65	81.46
IV	6	66.58 \pm 3.23	1.32	63.19	69.98	61.62	70.12
V	6	62.51 \pm 2.96	1.21	59.40	65.63	58.13	65.87
VI	6	51.47 \pm 2.32	0.94	49.03	53.91	48.64	54.32

Table 3: Comparison of serum triglycerides in six groups

Group	n	Mean \pm SD	Standard error	95% confidence interval for mean		Minimum	Maximum
				Lower bound	Upper bound		
I	6	93.67 \pm 12.44	5.08	80.61	106.73	82.16	112.18
II	6	110.70 \pm 13.48	5.50	96.54	124.85	97.54	128.81
III	6	51.79 \pm 12.13	4.95	39.05	64.53	33.35	65.13
IV	6	49.09 \pm 10.32	4.21	38.26	59.92	34.21	58.60
V	6	47.84 \pm 9.65	3.94	37.71	57.97	34.13	56.80
VI	6	31.67 \pm 2.81	1.15	28.71	34.63	28.34	35.12

Table 4: Comparison of serum HDL in six groups

Group	n	Mean \pm SD	Standard error	95% confidence interval for mean		Minimum	Maximum
				Lower bound	Upper bound		
I	6	57.60 \pm 5.67	2.31	51.64	63.55	51.47	65.56
II	6	33.75 \pm 2.25	0.91	31.39	36.12	31.25	37.11
III	6	35.00 \pm 2.23	0.91	32.66	37.35	32.18	38.00
IV	6	35.67 \pm 2.75	1.12	32.78	38.56	31.16	39.18
V	6	36.15 \pm 2.42	0.99	33.61	38.70	32.34	39.67
VI	6	36.91 \pm 2.41	0.98	34.37	39.45	33.12	40.21

HDL: High-density lipoprotein

DISCUSSION

In the present study, to evaluate and compare the hypolipidemic effect of turmeric with atorvastatin, 36 albino Wistar rats of either sex were included. Experimental animals were grouped, and intervention was given as per the study protocol. Lipid profile was estimated in all experimental rats a day before the start of study followed by serial estimations at 2, 4, 6, and 8 weeks, respectively. It was observed that experimental animals treated with ethanolic extract of turmeric showed a significant reduction in serum TC and serum TGs. No significant increase in serum HDL-C was observed.

Mean value of serum TC in Group I was 132.38 \pm 27.66, Group II was 164.35 \pm 7.01, Group III was 75.08 \pm 6.92, Group IV was 66.58 \pm 3.23, Group V was 62.51 \pm 2.96, and Group VI was 51.47 \pm 2.32. Groups IV, V, and VI, which received an ethanolic extract of turmeric showed a statistically significant reduction in mean serum TC in comparison with Group II ($P < 0.05$). A study conducted by Santoshkumar *et al.* on diabetic hyperlipidemic rats showed a significant reduction in serum TC at the end of 4 weeks in Group IV and Group V rats who were given turmeric in a dose of 300 mg/kg and 500 mg/kg body weight, respectively. Serum TC level in Group IV was 103.66 \pm 4.24 and in Group V was 83.5 \pm 4.32 in comparison with Group II rats (diabetic hyperlipidemic control group) 144.8 \pm 8.12. Santoshkumar *et al.* reported that turmeric is known to possess hypolipidemic activity that probably results from increased elimination of cholesterol in the form of bile acids, as turmeric increases production and secretion of bile acids. Furthermore, increased hepatic cholesterol 7 α -hydroxylase activity suggest a higher rate of cholesterol catabolism.^[15] Curcumin reduces TC level in the liver along with an increase of α -tocopherol level in rat plasma, suggesting *in vivo* interaction between curcumin and α -tocopherol that may increase the bioavailability of Vitamin E and decrease cholesterol levels.^[16] Mean value of serum TG in Group I was 93.67 \pm 12.44, Group II was 110.70 \pm 13.48, Group III was 51.79 \pm 12.13, Group IV was 49.09 \pm 10.32, Group V was 47.84 \pm 9.65, and Group VI was 31.67 \pm 2.81. These values suggest that Groups IV, V, and VI which received an ethanolic extract of turmeric

showed a statistically significant reduction in mean serum TG level. A study conducted by Santoshkumar *et al.* on diabetic hyperlipidemic rats showed a significant reduction in serum TG level at the end of 4 weeks in Group IV and Group V rats who were given turmeric in a dose of 300 mg/kg and 500 mg/kg body weight, respectively. Serum TG level in Group IV was 109.0 \pm 7.98 and in Group V was 94.33 \pm 5.15 in comparison with Group II rats (diabetic hyperlipidemic control group) 136.33 \pm 3.32.^[15] Maithilikarpagaselvi *et al.* reported that curcumin improves hypertriglyceridemia and insulin sensitivity through the suppression of protein tyrosine phosphatase 1B.^[14] Mean value of serum HDL in Group I was 57.60 \pm 5.67, Group II was 33.75 \pm 2.25, Group III was 35.00 \pm 2.23, Group IV was 35.67 \pm 2.75, Group V was 36.15 \pm 2.42, and in Group VI was 36.91 \pm 2.41. In our study, it was noted that curcumin administration did not have any significant effect on the mean value of serum HDL ($P > 0.05$). In a study conducted by Santoshkumar *et al.* on diabetic hyperlipidemic rats, there was a significant rise in serum HDL levels in diabetic hyperlipidemic rats who received turmeric in a dose of 300 mg/kg and 500 mg/kg, respectively, for 4 weeks. Serum HDL level in Group IV was 22.66 \pm 1.69, in Group V was 35.0 \pm 3.16 in comparison with Group II (diabetic hyperlipidemic control group) 19.5 \pm 1.71.^[15] There was no increase in serum HDL levels in our study.

We studied the effect of ethanolic extract of turmeric in a dose of 300 mg/kg/day and 500 mg/kg/day. The body weight of animals was not recorded.

CONCLUSION

In the present study, ethanolic extract of turmeric has significantly reduced serum TC and serum TG. There was no significant increase in serum HDL-C levels in Groups III, IV, V, and VI.

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