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Original Research Article

AN EVALUATION OF HYPOLIPIDEMIC EFFECT OF CURCUMIN: A DOUBLE BLIND, PLACEBO CONTROLLED, RANDOMIZED TRIAL

M. Purna Chandrakala,[1*] Kranti Tekulapally[2]

[1*]Professor, Department of Pharmacology, Malla Reddy Medical College for Women, Suraram, Hyderabad

[*]Assistant Professor, Department of Pharmacology, Malla Reddy Medical College for Women, Suraram, Hyderabad;

Corresponding Author: Dr. M. PurnaChandrakala

ABSTRACT:
Background: Curcumin is the principal constituent of turmeric, yellow coloring spice routinely used in Indian Cuisine. Hypolipidemic effect of curcumin is well demonstrated but not that of turmeric that contains about 250mg curcumin/teaspoon. The present study was therefore planned to identify a naturally occurring hypolipidemic agent which when incorporated in diet, may be beneficial in controlling hypercholesterolemia and prevent its adverse consequences. **Materials and methods:** The study was double blind, placebo controlled, randomized trial. Forty five subjects with fasting serum total cholesterol in the range of 200 – 350 mg/dl and triglycerides less than 300mg/dl and with no history of coronary heart disease, diabetes and secondary hypercholesterolemia were randomized into three groups. The three groups received curcumin 500 mg/day, turmeric 500mg/day and placebo 500mg/day (equal proportions of Rice and Bengal gram powder)respectively in addition to dietary advice. The Lipid profiles were assessed at baseline, day 11 and day 31. Later the patients were advised to stop the treatment and the lipid parameters were reassessed after 30 days, day 61 of the study period. Results obtained were analyzed statistically using ANOVA. **Results:** Curcumin significantly reduced the total cholesterol levels, triglycerides and LDL cholesterol ($p < 0.001$) and slightly increased the levels of HDL-C after 30 days of treatment in comparison to the turmeric and control group. The effects of curcumin were more significant than turmeric in lowering total cholesterol, LDL-C and triglycerides but were comparable to each other in increasing HDL- C and decreasing VLDL. **Conclusion:** The results show that Curcumin has significant hypolipidemic effects compared to turmeric
Keywords: Curcumin, Hypolipidemic, Turmeric

INTRODUCTION

Dyslipidemias, which includes hyperlipidemia and low HDL cholesterol levels, is a major cause of atherosclerosis and atherosclerosis- induced conditions such as coronary heart disease (CHD), ischaemiccerebrovascular disease and peripheral vascular disease. CHD accounts for about one third of all deaths of persons in the middle aged and older adults. In the early controlled trials employing drug regimens that reduced LDL-Cholesterol like the statins, the incidence of fatal and

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nonfatal CHD events were reduced by as much as 30-40%. [1]
The first line therapy for elevated LDL Cholesterol in both primary and secondary prevention is dietary modification that includes reduction in the intake of saturated fatty acids and cholesterol. Hypolipidemic drug therapy consists of statins, compounds that inhibit HMG CoAreductase enzyme in the cholesterol biosynthesis pathway; fibrates by activating hepatic lipoprotein lipase decrease the production and increase the degradation of triglycerides; niacin inhibits lipoprotein lipase enzyme in the adipose tissue leading to a decrease of triglyceride hydrolysis in adipose tissue and the hepatic synthesis of triglycerides, also increases HDL cholesterol levels; ezetimibe, cholesterol absorption inhibitor and bile acid sequestrants. Certain herbs, foods and additives like plant stanol esters, psyllium and soya protein, fenugreek are also associated with modest reductions in plasma cholesterol levels.[2]

Despite being efficacious, hypolipidemic drugs are costly and are associated with high side effect profile. Some of the patients, even after treatment, continue to be hypercholesterolemic. [2]

The search to develop safe, efficacious and economical hypolipidemic drugs is on. Recently, Herbal drugs, the naturally occurring substances are being increasingly explored for therapeutic use because of their low adverse effect profile.

Turmeric is the dried rhizome of *Curcuma longa* belonging to the family of *Zingiberaceae*, cultivated widely in the South East Asian countries.[3]

Turmeric contains about 5% diarylheptanoid coloring materials known as curcuminoids, the chief of which is curcumin or diferuloylmethane(82%). The others are dimethoxymethane (15%) and bismethoxycurcumin(3%), the derivatives of curcumin. The rhizomes also contain volatile oils (5%) arabinose (1%), fructose (12%) and glucose (2%).[3]

Turmeric has a long history of use in food as a spice, mainly as an ingredient in many varieties of curry powders and sauces. It has also been used traditionally in Ayurvedic medicine for the treatment of certain diseases like arthritis, ulcers, jaundice, wounds, trauma and also in hepatitis.

Most of the activity of turmeric in the treatment of various ailments was shown to be due to *Curcumin*, its principle coloring agent.

Curcumin is the product obtained by solvent extraction of turmeric and purification of the extract by crystallization. It is an oil soluble orange yellow crystalline powder, practically insoluble in water and soluble in alkali.[3]A number of properties of curcumin have been explored in research includes anti-inflammatory, anticancer, antioxidant, neuroprotective, hypoglycemic, antiobesity, antiprotein aggregatory and antiinfective properties.

Hypolipidemic effect of curcumin has been demonstrated both in experimental animals and humans.SubbaRao et al supplemented the diet of rats with 0.5 %, 0.15 and 0.25% curcuminand found that all the three doses lowered serum cholesterol levels without statistical significant difference between them. [4]In high fat diet fed hamsters, supplementation of 0.05gm curcumin /100 g diet significantly lowered total cholesterol, LDL Cholesterol and Triglycerides while the HDL levels were increased.[5]In streptozotocin induced diabetic rats maintained on 0.5% curcumin containing diet, there was decrease in the levels of LDL and triglycerides. [6]

Wang and Michelle consolidated the findings from three investigations on curcumin's hypolipidemic effect in humans by Puncharoenkul, Alwi and Baum and reported that there is no consistent lipid lowering effect in healthy subjects and also in acute coronary syndrome patients.[7]Larry Baum et al reported that consumption of 1gm/day and even 4 gm/day of curcumin did not significantly affect the triglycerides or total, LDL and HDL cholesterol.[8]

The results of previous clinical studies on hypolipidemic effects of Curcumin were inconsistent and there are no studies comparing the lipid lowering effect of curcumin with turmeric. Turmeric is relatively inexpensive spice used regularly in diet. One teaspoon of turmeric contains about 250mg of curcumin. So healthy amounts of curcumin can be easily incorporated in our daily dietary regimen and thus control hypercholesterolemia and its untoward consequences.

MATERIALS AND METHODS

Subjects: The study was a double blind, placebo controlled randomized trial. Forty five subjects in the age group of 45 – 65 years were included in the study after obtaining informed consent. Subjects with fasting serum total cholesterol levels in the range of 200-350 mg/dl, triglycerides levels less than 300 mg/dl and with no history of coronary artery disease were recruited in the study. The patients were randomized into three groups of fifteen each. Because of non-compliance to treatment and dropouts, we could complete the study with 15 patients in group 1 (curcumin group), 12 and 10 patients in group II (turmeric) and group III (placebo) respectively. The subjects were recruited from the outpatient clinic, Department of Cardiology, Gandhi Medical College, Secunderabad. Institutional Ethical Committee of Gandhi Medical College approved the trial.

Exclusion criteria were patients who had myocardial infarction, who underwent coronary artery bypass surgery or angioplasty within previous 3 months, patients with unstable angina, cardiac or renal failure, hepatic disease, diabetes mellitus or secondary hypercholesterolemia. Patients who were already on lipid lowering therapies were also excluded from the study.

Experimental Protocol:Turmeric and Curcumin powder were obtained on gratis form Kancor Flavors and Extracts Limited, Cochin, India. Placebo powder was made with equal proportions of rice and Bengal gram. The powders were weighed and 500 mg of each powder wasfilled in coded empty gelatin capsules.

Prior to intervention, all the subjects underwent baseline general physical examination and certain investigations like complete blood picture, lipid profiles, liver function tests, renal function tests and echocardiography to exclude cardiovascular diseases. The patients were then randomly divided into three groups – group 1 received 500mg of curcumin, group II – 500mg of turmeric and group III –500mg placebo. The patients were given coded capsules and advised to take the capsules once daily for 30 days before breakfast. The compliance of the subjects to the ingestion of capsules was documented using a capsule calendar. All the subjects were provided with standard dietary advices restricting their daily calorie intake to 1300 – 1500 Kcal/ day, increase the intake of raw vegetables, fresh fruits, white meat like fish and decrease the intake of fat.

After 30 days of treatment, subjects were advised to stop the medications, continue to follow the same dietary instructions for another 30days.

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Biochemical measurements: Fasting serum lipid profiles were measured at baseline, day 11, day 31 and day 61 of the study period. Total Cholesterol, Triglycerides and HDL cholesterol were estimated using diagnostic kits and values read from semi automated analyzer, RA-50 while LDL and VLDL cholesterol levels were calculated from the primary measurements.

Statistical analyses: Lipid values are presented as mean ± SD. Statistical analysis was carried out using ANOVA test. Single factor was used between groups and two factors, without replication for different time points. The significance level was set at $p<0.05$. At the baseline, there is no statistically significant difference in the lipid parameters in all the three groups.

RESULTS

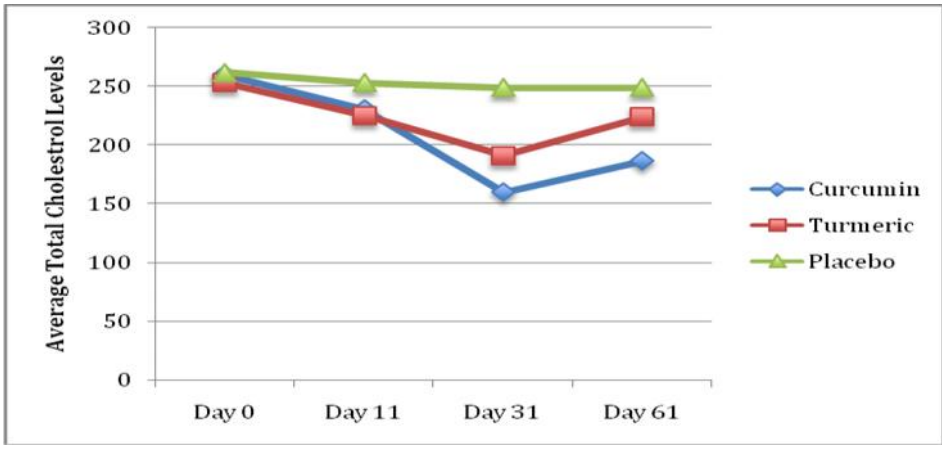

Figure 1. AVERAGE SERUM TOTAL CHOLESTEROL LEVELS

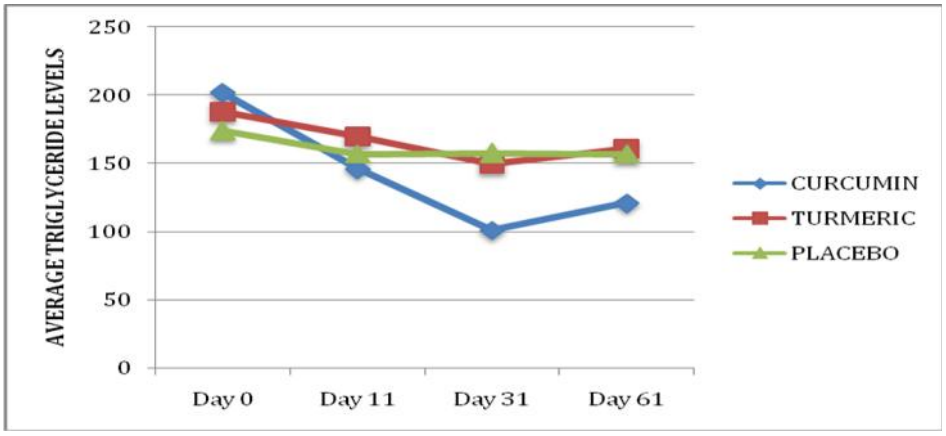

Figure 2. AVERAGE TRIGLYCERIDE LEVELS

Table 1. BIOCHEMICAL PARAMETES OF THE SUBJECTS AT DAY 0,11,31,AND 61

PARAMETERS	Day 0	Day 11	Day 31	Day 61
TOTAL CHOLESTEROL				
GROUP 1	260.00 ± 30.7	231.00 ± 35.8#	160.00 ± 18.1#	187.00 ± 27.8#
GROUP 2	253.00 ± 31.6	225.00 ± 31.3	191.00 ± 35.1	224.00 ± 31.4ns
GROUP 3	262.00 ± 23.6	253.00 ± 21.9	249.00 ± 24.7	249.00 ± 24.5
F ratio	0.66	2.49	34.46	14.90
p value	>0.05ns	>0.05ns	<0.001***	<0.001***
TRIGLYCERIDES				
GROUP 1	202.00 ± 56.0	146.00 ± 51.9#	101.00 ± 21.0#	121.00 ± 37.0#
GROUP 2	188.00 ± 36.5	170.00 ± 35.8#	150.00 ± 34.8#	161.00 ± 30.0#
GROUP 3	174.00 ± 43.8	157.00 ± 41.4#	158.00 ± 46.4#	157.00 ± 41.0#
F ratio	1.10	0.99	10.77	5.09
p value	>0.05ns	>0.05ns	<0.001***	<0.05**
HDL – C				
GROUP 1	38.00 ± 6.60#	37.86 ± 6.60#	41.20 ± 6.0#	39.21 ± 5.74#
GROUP 2	35.16 ± 3.92#	33.00 ± 3.89#	37.67 ± 3.37#	41.30 ± 6.29#
GROUP 3	41.40 ± 5.93#	41.00 ± 6.42#	41.70 ± 6.2#	41.00 ± 6.29#
F ratio	3.27	5.06	1.86	3.04
p value	>0.05ns	>0.05ns	>0.05ns	>0.05ns
LDL – C				
GROUP 1	187.00 ± 31.8#	164.86 ± 38.00#	97.10 ± 20.5#	125.00 ± 29.3#
GROUP 2	180.00 ± 35.8#	157.00 ± 35.0#	124.00 ± 31.10#	160.34 ± 34.6#
GROUP 3	186.00 ± 25.9#	180. 00 ± 26.00#	176.00 ± 26.1#	177.00 ± 27.0#
F ratio	0.15	1.36	22.90	9.34
p value	>0.05ns	>0.05ns	<0.001***	<0.001***
VLDL – C				
GROUP 1	41.00 ± 10.06#	29.3 ± 10.3#	20.2 ± 4.18#	24.1 ± 7.34#
GROUP 2	37.5 ± 7.30#	34.0 ± 7.15#	29.58 ± 6.45#	31.58 ± 6.45#
GROUP 3	34.7 ± 8.7#	31.14 ± 8.26#	29.58 ± 6.43#	31.58 ± 6.45#
F ratio	1.46	0.94	11.00	7.75
p value	>0.05ns	>0.05ns	<0.001***	<0.001***

Values are expressed in mean ± SD;ns : p > 0.05, ** : p < 0.05, ***: p < 0.001

significant difference at different time points, **p**<0.05

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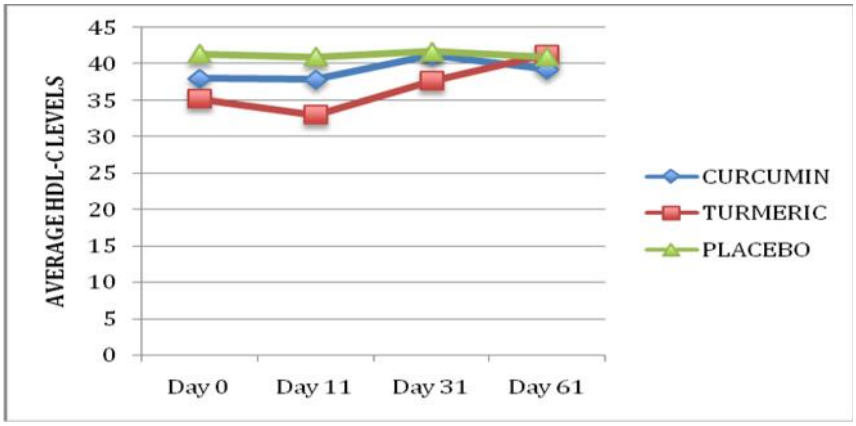

Figure 3. AVERAGE HDL-C LEVELS

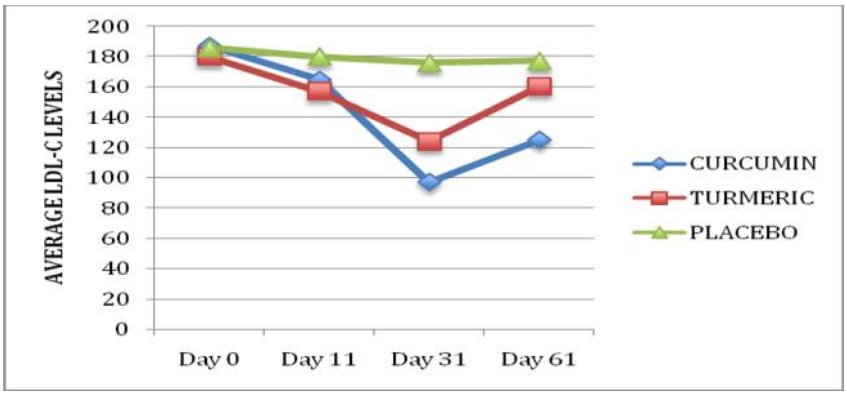

Figure 4. AVERAGE LDL-C LEVELS

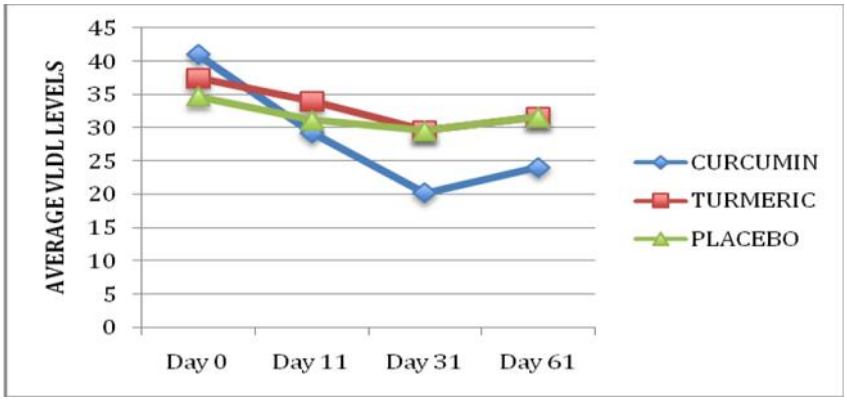

Figure 5. AVERAGE VLDL LEVELS

Administration ofcurcumin and turmeric has significantly lowered the levels of Total cholesterol; LDL cholesterol and triglyceride after 30 days and levels remained the same after the drugs were

stopped. The HDL cholesterol levels showed slight increase after 30 days but the levels decreased after stopping the treatment.
The effects of curcumin were more significant than turmeric in lowering the total Cholesterol, Triglycerides and LDL. In terms of increasing HDL and decreasing VLDL, the effects of curcumin and turmeric are comparable to each other.
In the control group, there is a mild reduction in the levels of cholesterol, triglycerides and LDL levels

DISCUSSION

Spices not only make our food palatable but also give beneficial pharmacological effects when used in judicious quantities. Even though they cannot totally displace the medications, they may be used in conjunction with medications to have better therapeutic potential, to minimize the drug dose with little or no toxic effects as compared to synthetic chemicals and thereby be most cost effective. Therefore in the present study an attempt was made to identify a naturally occurring hypolipidemic agent among the dietary substances that is routinely used in Indian cuisine.

Curcumin is the active coloring principle of Turmeric, a yellow orange powder which is the basic component of curry powders and sauces. There are reports on the hypolipidemic activity of curcumin but none of the previous studies compared its effect to that of turmeric. In the present study hypolipidemic effect of 500mg of curcumin was compared to that of 500mg of Turmeric and placebo. The results of the present study show that curcumin is very effective in lowering total serum cholesterol, to some extent triglyceride and LDL levels while there is a slight increase in the levels of HDL cholesterol after 30 days. It is more effective than turmeric in lowering total cholesterol, Triglycerides and LDL cholesterol. There was mild reduction in the levels of Total cholesterol, triglycerides and LDL levels in the control group which might be due to diet restriction.

There are many mechanisms that are postulated to explain the hypolipidemic effect of curcumin which include antioxidant, increase in bile and cholesterol excretion, increase in cholesterol catabolism.

Curcumin scavenges peroxidase and other free radicals and also regulates the expression of genes involved in free radical scavenging like catalase and hemeoxygenase 1. This antioxidant nature is responsible not only for its lipid lowering effect but also for itsantiatherogenic, anti-inflammatory and antiaging effect.[9] Increased peroxidase levels may cause cardiac arrhythmias. Curcumin can thus also be cardioprotective.[10]

Bile acids are the end products of cholesterol catabolism and the amount of bile excreted is a measure of reduction in tissue cholesterol levels. SubbaRao et al demonstrated an increase in the fecal output of total bile acids in curcumin fed rats and also that of cholesterol itself.Also, the feeding of curcumin with fibers, pectins and other nonnutrient carbohydrates did not lower endogenous cholesterol levels suggesting that curcumin may not allow the added cholesterol to accumulate in liver and prevent concomitant fatty infiltration.[4]

Hepatic Cholesterol 7α hydroxylase enzyme levels were demonstrated to be high in curcumin fed rats. So elevated levels of this enzyme involved in cholesterol catabolism may be responsible for its lipid lowering effect.[6]

From the results of the present study, it can be concluded that curcumin can be safely used to lower the levels of total cholesterol, Triglycerides and LDL. It may be used alone in mild, uncomplicated cases, along with other cholesterol lowering drugs in severe, complicated cases so that the dose of other hypolipidemic drugs can be reduced which in turn will minimize their adverse effects. Compared to curcumin, dietary intake of turmeric will lower the lipid levels to a less extent. So, dietary incorporation of turmeric will show definite hypolipidemic effects.

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