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Turmeric with Its Curcumin as a Natural Lipid Lowering Nutritional Supplement in Subjects with Hyperlipidemia

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Abstract
Atherosclerosis represents one of the most problematic inflammatory consequences that predisposing to cardiovascular diseases. Although, statins listed on the top treatment of atherosclerosis cardiovascular disease (ASCVD), they possess several adverse effects like rhabdomyolysis, loss of cognition, and hepatic dysfunction.
The present study evaluates the role of natural turmeric (the rhizome of curcuma longa) in lowering plasma lipid in subjects with hyperlipidemia.
The study was performed on 60 subjects (age:23-46 years), (BMI: 26-33 kg/m²) diagnosed with hyperlipidemia, according to American College of Cardiology/American Heart Association guidelines and National Cholesterol Education Program. They were divided randomly into two equal groups, the 1st group were given 1500 mg turmeric per day in three divided doses before meal, and the 2nd group were given 1500 mg of turmeric with 10mg of bioperine thrice per day. All participants continued to take the prescribed regimen doses for 120 days, and the blood samplewere collected (13 hours of fasting time) at 0,30,60,90, and 120 days. The paired sample t-test was used to compare the changes in lipid profile of each group during the 120 days of herbal supplementation but independent t-test was used to compare changes between the two groups. P-value < 0.05 considered significant. The results showed that turmeric treated patients displayed a significant decrease in total cholesterol, LDL-C, and triglyceride (P < 0.001; 90 days of treatment) and a significant rise of HDL-C level (p.value< 0.001; 120 days of treatment). Nevertheless, The substantial decline in total cholesterol, LDL-C, and triglyceride p.value< 0.001 in patients in the second group who were given turmeric with bioperine began after 60 days of treatment, which was also the same length needed for significant elevation p.value< 0.001 of HDL-C.
Between the two comparison groups, there were no significant variations in anthropometric and clinical parameters. Furthermore, despite the fact that there were no significant differences p.value> 0.05 on day 0 in terms of (total cholesterol, LDL-C, HDL-C, and triglycerides), significant differences began to emerge after 60 days of treatment between the two comparative groups, in which total cholesterol, LDL-C, and triglycerides began to decrease significantly in subjects given turmeric with bioperine compared to subjects given turmeric without bioperine. In addition, there was no significant difference in HDL-C until 120 days of treatment, when HDL-C began to rise considerably in participants who took turmeric plus bioperine compared to those who took turmeric alone.
ASCVD is strongly associated with morbidity and mortality that required high attention to provide multiple save, effective, and well-tolerated therapy.Curcuma longa may meets the ambition, and can find in what looking for.
The study concluded that, turmeric the natural and well tolerates especially if it taken with bioperine may act as a better natural herbal supplement surrogate with lipid lowering performance.
Keywords: Turmeric, Bioperine, Natural supplement, Atherosclerosis cardiovascular disease, Hyperlipidemia, Lipid lowering agents

1. INTRODUCTION

Cardio Vascular Disease (CVD) considered one of the major leading causes of death, the single most important predisposing causes of CVD is the deposition of inappropriate quantities of lipid in blood vessels in particular Low Density Lipoprotein-Cholesterol (LDL-C) resulted in atherosclerosis cardiovascular diseases (ASCVD)[1][2][3][4].ASCVD on the top of cardiovascular disease as a causative factor of death, and yet it can be prevented, avoided or even cure by changing the life style and using lipid lowering agents particularly statin to

reduce lipid and especially the cholesterol.[5][6][7][8][9] The centerpiece of the ASCVD risk revolves around LDL-C , as the LDL-C reduced by statin treatment; the ASCVD risk will be reduced subsequently.[10]

Statins, the lipid lowering agents considered the first line drug of choice treatment of cholesterol elevation. However, they have many adverse effects as rhabdomyolysis, loss of cognition, nerve conductance disorder, hepatic and pancreatic dysfunction, and last but not least sexual dysfunction. Moreover, many patients cannot get the desire outcome at the tolerated doses, add to that, the statins adverse effects are dose dependent and can be potentiate by drug interaction. [11] For these reasons, the present study assess the role of the natural turmeric in lowering plasma lipid.

Turmeric, the native Indian plant, the rhizome of curcuma longa; belongs to the ginger family (Zingiberaceae). Turmeric has been used by Indians since ancient times as a food additives awing to its spice nature and specific color.[12] It can be considered as one of the most known dietary supplement because it contains effective compounds that are not only important in nutrition, but also as herbal medicinal preparations.[13]The importance of turmeric from medical point of view caught attention after it was discovered that it contains many specific compounds; the most significant are the curcuminoids in which the main bioactive constituent is the polyphenol curcumin in addition to other volatile oils. It also contains minerals, carbohydrates, proteins, and essential volatile oils[14][15][16] Curcumin (the naturally yellow distinctive pigment) although it represents a small percentage may not exceed 5%.[17] but, it is considered the main bioactive constituent of the raw material of turmeric.[18][19]The remarkable importance of curcumin owing to its polyphenolic characteristics make it capable therapeutically to treat a wide range of many diseases, it is considered antioxidant, anti-inflammatory, antimutagenic, cardiovascular protective, and many other wide range of therapeutic effects.[20][21][22][23] The bioavailability of curcumin is relatively low because of poorly absorption and/or the rapid metabolism in intestine and liver that will make it lose many of its therapeutic effects so, to increase its absorption either by accompanied to bioperine (black pepper extract) or taken orally with fatty meal.[24]

Cardiovascular disease correlates directly with the mortality rate, as this disease is the main cause of death in united states and European countries in which, low density lipoprotein-cholesterol (LDL-C) represents as a predisposing factor.[25][26] High abnormal lipid in particular cholesterol will deposits in the vascular walls causing endothelial injury by induction of inflammation leading to atherosclerosis.[27]

2. MATERIAL AND METHODS

Formulation of the turmeric

Turmeric used as a capsule from Puritan′s Pride, USA. This study has been taken two types of capsules, each capsule contains either Turmeric (Curcuma longa) (root) 450 mg, Turmeric Extract (Curcuma longa) (root) 50 mg (Standardized to contain 95% Curcuminoids), or Turmeric (Curcuma longa) (root) 450 mg, Turmeric Extract (Curcuma longa) (root) 50 mg (standardized to contain 95% Curcuminoids) with 10 mg Black Pepper Fruit Extract (BioPerine®).

Study design

The present study is randomized case control study. The subjects have been obtained from obesity and nutritional outpatient clinics; the subjects were counseled. Before testing, they signed a written informed consent.

The study was performed on 60 subjects (23-46 years) and (BMI 26-33 kg/m²) of hyperlipidemia diagnosed according toAmerican College of Cardiology/American Heart Association (ACC/AHA) and National Cholesterol Education Program(NCEP) guideline[6].The subjects were free of cardiovascular diseases,and renal diseases according to clinical feature, biochemical investigations, and imaging study. Moreover, they are not yet on any lipid lowering agents and/or other related herbs at least till the study accomplished. In addition, the patients selected who were not alcoholics, not smokers, and not on the program of weight reduction.

The dose administered for each subject was three capsules 3 times daily for a total of 1500 mg per day for 120 days, and the dose was given according to the type of constituents assigned to each group.

The blood samples were collected from the subjects for measuring and follow up of lipid profile started from day 0, and each 30 days till 120 days. i.e., 0,30,60,90, and 120 days after 13 hrs. fasting.

Statistical analysis

All statistical calculations were performed by the using of SPSS software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp. USA) and Microsoft Excel (2010, Microsoft Corp. USA). The results have been expressed as mean ± SD. A $p < 0.001$ was considered statistically significant.Paired-Sample t-test was employed to evaluate the presence of significant difference pre and post treatment within the same group. While, independent-sample t-test was employed to evaluate the presence of significant difference between the two groups andp.value< 0.05 considered significant.

3. RESULTS

Two comparable groups were taken in this study; each group contains 30 subjects with hyperlipidemia. There were no significant differences between the two groups regarding the demographic parameters as shown in table-1. Furthermore, there were no significant differences also concerning Total Cholesterol (TC), Low Density Lipoprotein-Cholesterol (LDL-C), Triglycerides TGs (TGs), and High Density Lipoprotein-Cholesterol (HDL-C) in the two comparable studied groups immediately prior to the starting of the study. i.e., at day 0 as shown in table-2.

Table 1: Demographic parameters of the subjects in studied groups.

Demographic Parameter	**Turmeric only** n=30		**Turmeric with Bioperine** n=30	
	no.	%	no.	%
Age				
<= 30	7	23.3	7	23.3
31 - 39	11	36.7	10	33.3
40+	12	40	13	43.3
Mean±SD	36±6.57		35.97±6.36	
P.value	0.984			
Sex				
male	20	66.7	18	60
female	10	33.3	12	40
BMI				
Mean±SD	29.17±2.18		29.23±2.21	
P.value	0.91			

Table 2: Lipid profile subsequent alterations in the two groups received the nutritional supplements starting from day 0 through day 120.

Groups	Level of lipid profile (mean±SD)				
	0 day	**30 days**	**60 days**	**90 days**	**120 days**
Total Cholesterol					
Turmeric	236.63±9.1	236.23±8.92	236.03±8.81**	233.47±8.37** ' **	222.5±8.5* ' **
Turmeric with	237.77±8.63	237.5±8.48	222.83±8.1*	197.3±7.1*	180.53±7.34*

Bioperine					
LDL-C					
Turmeric	171.77±12.99	171.47±12.8	171.6±12.8**	168.1±10.56* ' **	164.13±12.52* ' **
Turmeric with Bioperine	173.63±9.1	173.53±9.1	162.13±10.78*	143.03±9.4*	126.73±9.4*
TGs					
Turmeric	226.7±14.37	226.5±14.16	226.6±14.26**	224.7±13.1* ' **	219.97±13.97* ' **
Turmeric with Bioperine	228.53±13.127	228.4±12.95	219.43±13.4*	206.43±12.32*	184.03±12.629*
HDL-C					
Turmeric	47.78±14.23	48.11±13.01	48.8±11.5	49.3±11.2	49.9±10.7* ' **
Turmeric with Bioperine	46.9±13.8	47.9±12.6	49.1±10.7*	51.13±10.11*	51.9±11.4*

Group one, took 1.5 gm of turmeric in three divided doses per day. Group two took 1.5 gm of turmeric with bioperine in the same manner.

*Significant difference ($p<0.001$) in lipid profile compared to the lipid status at day 0 within the same group.

**Significant difference ($p<0.05$) in lipid status between the two groups.

4. TREATMENT CONSEQUENCES

On total cholesterol

The significant decrease ($p<0.001$) began at 90th day of treatment (233.47±8.37) compared to the status at 0th day (236.63±9.1) in the subjects of group 1 were taken turmeric. While the significant decrease ($p<0.001$) in total cholesterol started at day 60th of treatment (222.83±8.1) compared to the status at 0th day (237.77±8.63) in the subjects of group two were taken turmeric with bioperine. Meanwhile, there was a significant reduction ($p<0.05$) of total cholesterol in-grouptwo subjects (222.83±8.1) compared to group one (236.03±8.81) starting at the 60th day of treatment, table-2.

On LDL-C

The significant decrease ($p<0.001$) began at 90th day of treatment (168.1±10.56) compared to the status at 0th day (171.77±12.99) in the subjects of group 1 were taken turmeric. While the significant decrease ($p<0.001$) in LDL-C started at day 60th of treatment (162.13±10.78) compared to the status at 0th day (173.63±9.1) in the subjects of group two were taken turmeric with bioperine. Meanwhile, there was a significant reduction ($p<0.05$) of LDL-Cin-grouptwo subjects (162.13±10.78) compared to group one (171.6±12.8) starting at the 60th day of treatment, table-2.

On TGs

The significant decrease ($p<0.001$) began at 90th day of treatment (224.7±13.1) compared to the status at 0th day (226.7±14.37) in the subjects of group 1 were taken turmeric. While the significant decrease ($p<0.001$) in TGs started at day 60th of treatment (219.43±13.4) compared to the status at 0th day (228.53±13.127) in the subjects of group two were taken turmeric with bioperine. Meanwhile, there was a significant reduction ($p<0.05$) of TGsin-grouptwo subjects (219.43±13.4) compared to group one (226.6±14.26) starting at the 60th day of treatment, table-2.

On HDL-C

The effect of turmeric and/or turmeric with bioperine on their specific groups regarding this lipid type biomarker were relatively less than other lipid profile stated above. The significant increase ($p<0.001$) began at 120th day of

treatment (49.9±10.7) compared to the status at 0th day (47.78±14.23) in the subjects of group 1 were taken turmeric. While the significant increase ($p<0.001$) in HDL-C started at day 60th of treatment (49.1±10.7) compared to the status at 0th day (46.9±13.8) in the subjects of group 2 were taken turmeric with bioperine. Meanwhile, there was a significant elevation ($p<0.05$) of HDL-C in group 2 subjects (51.9±11.4) compared to group 1 (49.9±10.7) starting at the 120th day of treatment; table-2. The effect of turmeric with bioperine was stronger and faster compared to turmeric, figure-1.

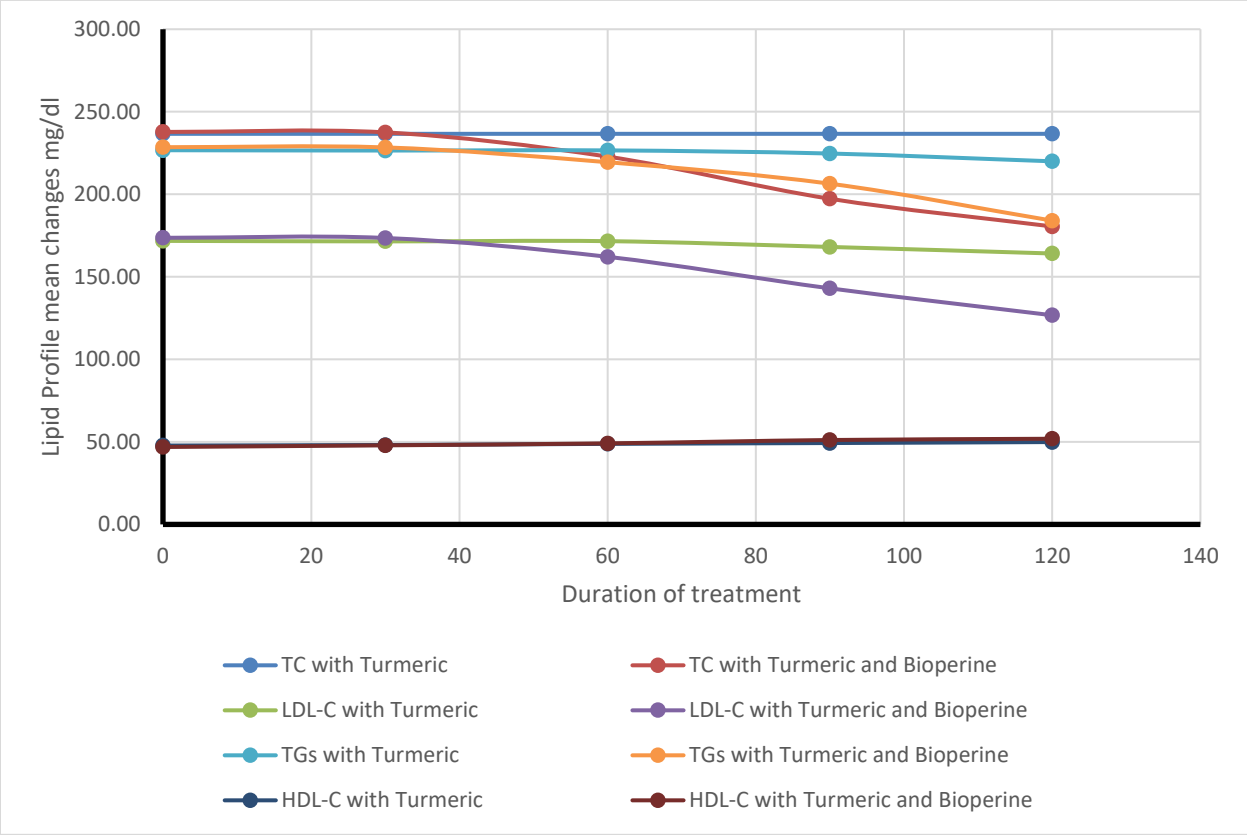

Figure 1: Changes in lipid profile as a consequence of treatment in the two studied groups relative to each other from day 0 to day 120.

Discussion

This study assessed the influence of turmeric in particular its bioavailability on the blood lipid profile. Although it was variable in effect, the reduction of lipid in both groups after the administration of turmeric was significant. Turmeric can affect lipid profile through several mechanisms that can have achieved via its role as:

Antioxidant

Turmeric may acts as scavenging of free radicals and decrease oxidative stress by regulation of certain genetic materials that induce synthesis of antioxidant mediators and so, decrease lipid peroxidation. [28][29]

Enhancer of lipid metabolism

Turmeric can decrease cholesterol by increasing hepatic LDL-C receptors expression and accelerates lipid metabolism in particular TGs via elevation lipoprotein lipase and hepatic TGs lipase, in addition to hormone sensitive lipase. [30][31][32]

Inhibitor of cholesterol absorption from the intestine

Curcumin may lower intestinal absorption of cholesterol bydecrease synthesisof Niemann-Pick C1-like 1, the transmembrane proteinnormally present in the apical of enterocytes which act as a cholesterol transporter from the intestinal lumen.[33]

The administration of turmeric with bioperine had the earlier and the most important was the stronger effect on the lipid profile reduction than the administration of turmeric alone, table-2. Curcumin is a hydrophobic polyphenol that may cause decrease in its absorption causing lowering in systemic bioavailability, that can be improved by either administration of turmeric after fatty meal or most importantly with black pepper (bioperine).[29][34][35].

The study conclude that turmeric lower the bad cholesterol and triglycerides in blood and so can be considered as safe, well tolerated, and effective natural surrogate lipid lowering supplement.

5. CONCLUSION

The study showed that turmeric can be used as a safe, effective, and tolerable natural lipid lowering alternative.

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