Spice Up Your Lipids: The Effects of Curcumin on Lipids in Humans

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ABSTRACT:

Curcumin has been lauded for its antioxidant, anti-inflammatory, and anti-cancer properties in various research studies, but its effects on cholesterol levels are not as well-understood. This review paper aims to consolidate the findings from three recent investigations on curcumin's reputed hypolipidemic effect in humans by Pungcharoenkul, Alwi, and Baum. No consistent effect was noted in healthy subjects receiving a 500mg or 6,000mg daily dose of curcumin, in patients with acute coronary syndrome receiving a daily supplementation of 45-180mg curcumin, or in subjects with cognitive decline given 1,000mg or 4,000mg curcumin per day, as compared with controls. Two earlier studies generated enthusiasm regarding curcumin's ability to lower apo B/apo A ratio, serum cholesterol, and lipid peroxides in healthy humans, but those were flawed and less rigorous trials. Pungcharoenkul showed that daily curcumin dosages of 500mg and 6,000mg significantly decreased subjects' cholesterol levels, but this hypolipidemic effect was not noted across the different populations and dosages in the other two recent studies.

BACKGROUND OF CURCUMIN AND HYPERLIPIDEMIA:

Curcumin is a polyphenolic molecule that can be extracted from turmeric (*Curcuma longa*) and temulawak (*Curcuma xanthorrhizae*), which are native Indonesian plants that belong to the ginger family (*Zingiberaceae*).[1,2] These plants are commonly used in traditional medicines of many Asian cultures. In the Western world, turmeric is more commonly known for providing the yellow color to mustards and curries. Curcumin makes up about 5% of turmeric, giving turmeric its yellow color but not contributing much to its flavor.

Earlier research studies have revealed that curcumin might decrease absorption of cholesterol and increase the activity of cholesterol-7α-hydroxylase.[3,4] Curcumin first was shown to lower total cholesterol in various animals. For example, it can decrease serum cholesterol in rodents,[5,6] inhibit LDL oxidation in atherosclerotic rabbits,[7] and lower LDL/HDL ratio in hamsters.[8] Several studies have also shown curcumin's hypolipidemic effect in humans. Ramirez-Bosca et al. found that a daily oral dose of about 20mg of curcumin extract decreased LDL and increased HDL in healthy individuals and might even be able to ward off atherosclerosis.[9] The Soni and Kuttan study revealed that giving human volunteers 500mg/day of curcumin for just one week lowered their total cholesterol by 12% and increased HDL by 29%.[10] Recently, three additional sets of results which vary by dosage, length of study, and subject population have been published using curcumin as a dietary supplement to lower cholesterol. Pungcharoenkul et al. studied curcumin's effect on healthy subjects, Alwi et al. involved acute coronary syndrome patients, and Baum et al. recruited patients with cognitive decline. Their results suggest that curcumin does not have consistently significant lipid-related effects in different subject populations.

THE PUNGCHAROENKUL STUDY – CURCUMIN AND LIPIDS IN HEALTHY SUBJECTS:

Pungcharoenkul and Thongnopnua conducted a study on curcumin's effect on the cholesterol levels of healthy humans.[11] They recruited 24 healthy subjects in Thailand whose mean age was roughly 29. To be included in the study, participants were required to have no history of any major organ disease, no medications taken within one week of beginning the study, and no dietary supplements (especially curcumin or vitamin E) for at least four weeks before the study. The participants were randomized into three groups: Group A consumed 500mg of curcumin per day, Group B consumed 6,000mg of curcumin per day, while Group C consumed no curcumin and instead took 200IU of vitamin E per day. The study lasted for seven days and sought to measure both plasma antioxidant capacity and serum cholesterol levels. Subjects also recorded each meal they ate throughout the study, but the researchers did not mention whether their diets included curcumin. The subjects were blinded, but the researchers were not. Study subjects took their supplement each morning for up to seven days, and they had their blood drawn after fasting on days one and seven. Compared to the Baum and Alwi studies, this clinical trial involved younger subjects and there was no follow-up after the short seven-day trial.

For curcumin's effect on lipid levels, this clinical trial showed a significant, dose-dependent decrease in subjects' serum cholesterol and triglyceride levels. Group A subjects (curcumin 500mg/day) had the largest decreases in serum cholesterol and triglyceride levels, which were 17% ($p=0.003$) and 47% ($p=0.016$), respectively. Group B subjects (curcumin 6,000mg/day) had a 5% decrease in cholesterol ($p=0.039$) and a non-significant 15% decrease in triglyceride ($p=0.323$), while Group C subjects (vitamin E 200IU/day) showed a 6% and 4% decrease in cholesterol and triglyceride levels, respectively. Group B subjects had their AST and ALT levels measured throughout the study and there were no statistically significant increases in their levels, so curcumin seems to have little liver toxicity at this high dose. However, the high dose of curcumin used in this study was less hypolipidemic than the lower dose, which suggests that too much of a good thing is not necessarily beneficial. Curcumin's mechanism of action may involve cholesterol absorption, breakdown, or elimination, but the relatively small hypolipidemic effect of a proven antioxidant such as vitamin E suggests that curcumin's effect on lipids is likely distinct from its antioxidant properties.

THE ALWI STUDY – CURCUMIN AND LIPIDS IN ACUTE CORONARY DISEASE:

The Alwi et al. study was a double-blind randomized control trial (RCT) that investigated curcumin's effects on levels of total cholesterol, LDL, HDL, and triglycerides.[1] In this study the patient population had acute coronary syndrome (ACS), which often involved dyslipidemia. The 75 patients were hospitalized at one of four ICCUs in Indonesia: 67 at Cipto Mangunkusumo Hospital, 6 at Persahabatan Hospital, and 2 at MMC Hospital. Only 63 patients followed through with the trial to its end. They met the criteria for ACS with an onset of less than 72 hours and were followed for up to two months after their hospital admission to study their inflammatory response and metabolic factors upon administration of curcumin. ACS was defined as experiencing a cardiac crisis involving ST elevation myocardial infarction, non-ST elevation myocardial infarction, or unstable angina pectoris (based on the Canadian classification of angina). The curcumin extract came from turmeric root and its concentration was analyzed with the HPLC method. Patients were randomized to one of four groups for two months: high-dose curcumin (60mg three times a day), moderate-dose (30mg three times a day), low-dose (15mg three times a day), or placebo (0mg). The form in which the curcumin was administered (e.g.,

capsule or powder) was not specified. At regular intervals, peripheral venous blood was sampled after 10-12 hours of fasting, followed by a two-hour post-prandial blood glucose measurement.

The results demonstrated no statistically significant difference between the curcumin groups and the placebo group. Total cholesterol and LDL levels did not change between the low-dose curcumin (2.10% [p=0.40] and 8.60% [p=0.92], respectively), moderate-dose curcumin (0.20% [p=0.34] and 3.40% [p=0.76]), high-dose curcumin (0.30% [p=0.99] and 15.40% [p=0.66]), and placebo (2.40% [p=0.61] and 11.60% [p=0.66]) groups following the curcumin intervention. HDL was also not statistically significantly changed (11.30% in low-dose group [p=0.36], 7.70% in moderate-dose [p=0.09], 7.70% in high-dose [p=0.23], 10% in placebo [p=0.39]). No dose response was evident as the low-dose curcumin group had the largest drop in total cholesterol and LDL levels and the largest increase in HDL levels. The level of triglycerides increased in all groups but to a non-significant degree, with the lowest increase in the moderate-dose group (18% in low-dose group [p=0.64], 10.30% in moderate-dose [p=0.55], 20.40% in high-dose [p=0.95], 14.90% in placebo [p=0.57]). This study was limited by a small sample size that was likely experiencing co-interventions when the patients were in the various ICCUs. The study did not specify how much curcumin was already in each patient's diet. The daily dosage levels of the Alwi study (45-180mg) were also orders of magnitude smaller than the dosage levels in the studies of Pungcharoenkul (500-6,000mg) and Baum (1,000-4,000mg).

THE BAUM STUDY – CURCUMIN AND LIPIDS IN ALZHEIMER'S DISEASE:

Curcumin has been studied in animal models of Alzheimer's Disease (AD) and shown to reverse cognitive deficits in rodents.[12,13] Baum et al. sought to determine whether the same benefits applied to humans by studying curcumin's effect on the blood lipid profiles of ethnic Chinese individuals living in Hong Kong, at least 50 years old and whose cognitive function and memory had been progressively declining for at least six months to the point where they had a NINCDS-ADRDA diagnosis of probable or possible Alzheimer's Disease.[2] This double-blind RCT lasted six months and included 31 subjects randomized to three different daily curcumin doses: 1,000mg of curcumin, 4,000mg of curcumin, or placebo. Subjects could choose whether they wanted to consume the curcumin as 10 capsules after a meal or as a packet of powder that could be mixed with food. The curcumin packets were from Kancor Flavours, while the capsules were from Arjuna Natural Extracts. Although both companies were based in Kerala, India, they were still separate entities with different manufacturing practices. The investigators did not measure the curcumin, demethoxycurcumin, and bisdemethoxycurcumin composition of the products. Similar to the Alwi study, this trial involved co-interventions since subjects continued to take any drugs or other medical treatments prescribed by their physicians. For example, all subjects were also given one capsule of 120mg ginkgo leaf extract (24% flavone glycosides and 6% terpene lactones) daily as a standard Alzheimer's Disease treatment. It is not well known whether ginkgo extract affects cholesterol and thereby may obscure curcumin's effect on cholesterol.

Baum et al. found that curcumin did not appear to significantly change serum cholesterol or triglyceride concentrations, which challenges previous claims of curcumin's cholesterol-lowering properties. Total cholesterol slightly increased in the 1,000mg group (5.78%, p=0.15) and decreased in the 4,000mg group (1.02%, p=0.29) and placebo group (6.66%); LDL levels increased in the 1,000mg group (1.37%, p=0.57) and placebo group (2.38%) and decreased in the 4,000mg group (3.36%, p=0.71); while triglycerides did not change in the 1,000mg group (0.00%, p=0.50), increased in the 4,000mg group (9.41%, p=0.19), and decreased in the placebo

group (29.59%). HDL levels tended toward decrease in the placebo group (5.57%), but HDL increased in the 1,000mg and 4,000mg groups (15.79% [p=0.35] and 5.77% [p=0.98], respectively), which might be due to curcumin's reported ability to increase expression of ABCG1 and thereby increase plasma HDL levels by increasing lipid efflux. The absorbed concentration of curcumin correlated positively with cholesterol concentration, which indicated that curcumin might even increase cholesterol concentration instead of decreasing it. Unfortunately, the small sample size of this study did not have the power to detect small differences that resulted from the curcumin treatment. Another caveat to consider is that food may affect the absorption of curcumin and its metabolites, so consuming the curcumin as powder with food may have different effects from taking the same dosage in capsule form. Curcumin's mechanism of action may involve targeting dietary cholesterol absorption and not cholesterol synthesis. Capsules or fasting seemed to increase the absorption but not metabolism of curcumin compared to the consumption of curcumin with food, for capsules/fasting yielded higher plasma concentrations of curcumin, demethoxycurcumin, and bisdemethoxycurcumin but not of curcumin's metabolites (tetrahydrocurcumin, ferulic acid, and vanillic acid). The positive correlation between absorbed concentration of curcumin and cholesterol concentration suggested that curcumin was less hypolipidemic and even potentially hyperlipidemic at higher doses. These results could be due to the specific curcumin doses used, the characteristics of the sample population, or the long duration of the trial.

DISCUSSION:

Earlier human studies reported curcumin's significantly hypolipidemic effect, but those trials were not placebo-controlled and blinded. The Pungcharoenkul, Alwi, and Baum studies continued the investigation of curcumin's effect on lipid levels in human subjects by comparing different dosages in different populations. Pungcharoenkul did show a significant decrease in the cholesterol levels of healthy subjects taking 500mg and 6,000mg curcumin daily, but the other two studies were unable to substantiate any significant effect of curcumin on lipids.

The lowest daily dose of curcumin was used by Ramirez-Bosca et al. in healthy subjects (20mg), followed by Alwi et al. with ACS patients (45mg, 90mg, 180mg), then Soni and Kuttan with healthy subjects (500mg), Pungcharoenkul and Thongnopnua with healthy subjects (500mg, 6,000mg), and Baum et al. with subjects who had cognitive decline (1,000mg, 4,000mg). Pungcharoenkul reported that lower doses (500mg) and higher doses (6,000mg) of curcumin both exerted a pronounced hypolipidemic effect. Soni and Kuttan's earlier study was very similar to Pungcharoenkul's study in that both clinical trials involved small numbers of healthy subjects, lasted for only a week, and used a curcumin dose of 500 mg/day. Both groups of researchers found that using this dose, which is higher than that used in the Alwi study (45-180mg) and lower than that in the Baum study (1,000-4,000mg), significantly decreased total cholesterol levels. These significant results could be a factor of the dose or the health of their subjects. Ramirez-Bosca found a significant LDL-lowering and HDL-raising effect at a low dose (20mg), but Alwi found no such significant effect at doses between 20mg and 500mg. Moreover, Baum did not have statistically significant results at the high doses of 1,000mg and 4,000mg, even though Pungcharoenkul observed a significant decrease in the total cholesterol of subjects taking 6,000mg curcumin daily. The studies that did showcase significant hypolipidemic effects all involved healthy individuals. More rigorous studies are needed to investigate further the validity of curcumin's potential hypolipidemic effect. Without further studies, it cannot be determined

whether curcumin has any consistently significant effect on total cholesterol, LDL, HDL, or triglycerides at the daily dose range from 20mg to 6,000mg.

The aforementioned studies do have a number of limitations. Most of these studies were conducted in Asian countries (China, Indonesia, and Thailand) with small numbers of subjects from relatively homogenous populations, and the lengths of the trials varied from one week to six months. It is difficult to compare AD, ACS, and healthy individuals directly, though the investigators did perform effective randomizations to ensure that the experimental groups were similar at baseline. The researchers did not seem to rigorously control for curcumin consumed in subjects' diets, and it is likely that Eastern populations consume more turmeric on a regular basis than Western populations, but the diet's contribution would not be as significant when working with high interventional doses involving thousands of milligrams of curcumin. The form in which the dose of curcumin was consumed was either not specified or differed from study to study (e.g., powder versus capsule). Finally, the studies had widely divergent dosages of curcumin (e.g., 45-180mg in Alwi study compared with 1,000-4,000mg in Baum study).

The results of these three studies are inconclusive and inconsistent, but they do demonstrate that even at "high" doses of curcumin study subjects did not seem to suffer from any significant side effects, so curcumin appears to be quite safe for subsequent human trials. Cheng et al.'s phase 1 trial showed no side effects in patients with advanced cancer who took 180mg of curcuma extract daily for four months,[14] which Alwi et al. claimed to be "the highest curcumin dose that had ever been used in clinical trial for human."[1] Alwi et al. must not have seen the Baum et al. publication, which involved giving patients up to 4,000mg of curcumin daily for six months, and neither Baum (up to 4,000mg/day) nor Pungcharoenkul (up to 6,000mg/day) reported subjects suffering from any major side effects.

CONCLUSION AND SUGGESTED FUTURE RESEARCH:

These three recent studies show conflicting evidence of curcumin's effect on cholesterol levels in humans, so further research is needed to substantiate any alleged hypolipidemic effect. The Pungcharoenkul study showed that curcumin at a dose of 500 mg/day could significantly reduce cholesterol and triglyceride levels in healthy subjects and also suggested that a higher dosage (6,000mg/day) was not more effective. The Alwi study did not find statistically significant benefit at dosages in the range of 45-180mg/day for patients with acute coronary syndrome, and the Baum study suggested that curcumin at dosages of 1,000-4,000mg had no significant effects on cholesterol levels in patients with cognitive decline. Given the findings of these studies, the future direction of study in this area should focus on (1) refining the optimal dosage, specifically focusing on the range between 20mg and 1,000mg daily; (2) controlling for dietary curcumin consumption; (3) recruiting more subjects; (4) extending follow-up; and (5) standardizing the form of delivery (e.g., capsule, powder, or as part of turmeric). It may also be worth further investigating whether curcumin works more effectively at lowering lipid levels in healthy individuals compared to people with medical conditions such as ACS and AD. The benefits of curcumin are especially important given that it can easily and realistically be worked into people’s diets. Turmeric is a relatively inexpensive spice and just one teaspoon of it contains approximately 250mg of curcumin, so this research can provide practical advice for incorporating healthy amounts of curcumin into one’s regular cooking. Should the benefits of curcumin be substantiated by future RCTs and the most effective dosages determined, curcumin would be lauded for much more than its contribution to delicious curry.

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Study	Study Type	N	Sample Pop.	Intervention	Duration	Mean Total Cholesterol	Mean LDL	Mean HDL	Mean Triglyceride	Summary of Findings
Pungcharoenkul and Thongnopnua (2011)	SB RCT[1]	24	Healthy subjects in Thailand	Daily doses of 500mg or 6g of curcumin, or 200IU of vitamin E	7 days	500mg = -17% (p = 0.003), 6g = -5% (p = 0.039)	N/A[2]	N/A	500mg = -47% (p = 0.016), 6g = -15% (p = 0.323)	Low-dose curcumin significantly reduced serum cholesterol and triglyceride more than did high-dose curcumin
Alwi et al. (2008)	DB RCT[3]	75	Patients with ACS hospitalized in the ICCU of 1 of 3 Indonesian hospitals	3 daily doses of 15mg (45mg/day), 30mg (90mg/day), or 60mg (180mg/day) of curcumin or placebo	2 months	45mg = -2.1% (p = 0.40), 90mg = -0.2% (p = 0.34), 180mg = 0.3% (p = 0.99), Placebo = -2.4% (p = 0.61)	45mg = -8.6% (p = 0.92), 90mg = -3.4% (p = 0.76), 180mg = 15.4% (p = 0.66), Placebo = -11.6% (p = 0.66)	45mg = 11.3% (p = 0.36), 90mg = 7.7% (p = 0.09), 180mg = 7.7% (p = 0.23), Placebo = 10% (p = 0.39)	45mg = 18% (p = 0.64), 90mg = 10.3% (p = 0.55), 180mg = 20.4% (p = 0.95) Placebo = 14.9% (p = 0.57)	All curcumin effects were not significantly different from placebo
Baum et al. (2007)	DB RCT	36	Chinese in Hong Kong, ≥50 YO, cognitive decline	3 daily oral doses of curcumin, 1g or 4g or placebo, capsule or powder	6 months	1g = 5.8% (p = 0.15), 4g = -1.0% (p = 0.29), Placebo = -6.7%	1g = 1.4% (p = 0.57), 4g = -3.4% (p = 0.71), Placebo = 2.4%	1g = 15.8% (p = 0.35), 4g = 5.8% (p = 0.98), Placebo = -5.6%	1g = 0.0% (p = 0.50), 4g = 9.4% (p = 0.19), Placebo = -29.6%	No significant change in serum cholesterol or triglyceride

Ramirez-Bosca et al. (2000)	CT[4]	12	43-70 YO men in good health, LDL > 150mg/dL, had managerial or scientific/technical jobs	2 tablets of ~10mg of curcumin extract each	30 days	N/A	LDL[5] = -38.4% ($p < 0.01$), apo B[7] = -16.9% ($p < 0.05$), apo B/apo A = -33.4% ($p < 0.01$)	HDL[6] = 72.3% ($p < 0.01$), apo A[8] = 24.1% ($p < 0.01$)	N/A	Subjects had a decrease in LDL and apo B levels, an increase in HDL and apo A levels, and a significant decrease in their mean apo B/apo A ratio
Soni & Kuttan (1992)	CT	10	Human volunteers	500mg/day of curcumin	7 days	-12% (statistically significant, no p-values given)	N/A	29% (statistically significant, no p-values given)	N/A	Subjects had significantly decreased total cholesterol and increased HDL by the end of the study

[1]SB RCT: single-blinded randomized controlled trial
[2]N/A: not applicable
[3]DB RCT: double-blinded randomized controlled trial
[4]CT: clinical trial
[5]LDL: low-density lipoprotein
[6]HDL: high-density lipoprotein
[7]apo B: apolipoprotein B
[8]apo A: apolipoprotein A