

Review Article

Anti- Hyperlipidemia Properties of Curcumin

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Abstract

Aim: To evaluate the effects of Curcumin on total cholesterol, LDL cholesterol, HDL cholesterol, and Triglyceride in acute hyperlipidemia.

Introduction: Dyslipidemias, (Including hyperlipidemia and low HDL cholesterol levels) is a major cause of atherosclerosis and atherosclerosis-induced Coronary Heart Disease (CHD), and accounts for about one third of all deaths in the middle aged and older adults. (M. Purna Chandrakala 2014) One fifth of the deaths in young Indians are from coronary heart disease.

Ayurvedic herbs appeared to have been helpful in the management of Hypercholesterolemia & Metabolic disorder. One of its active ingredients, Curcumin has been widely studied for its anti-inflammatory and antioxidant benefits. Curcumin protects against the oxidation of cholesterol. Studies have shown that, Curcumin significantly reduced the level of lipid profile and slightly increased the levels of HDL-C. It has demonstrated efficacy in treating hypercholesterolemia. The available experimental evidences clearly showed that though the acceptable daily intake of curcumin as an additive had been defined by the WHO as 0-3 mg/kg body weight, it was well tolerated in human subjects in a dose as high as 12,000 mg/day.

Bioavailability: The systemic bioavailability of orally administered Curcumin is low in humans. Oral administration of Curcumin furnishes trace levels of the parent compound and its metabolites in the liver and portal circulation. Factors limiting the bioavailability of Curcumin include poor absorption, rapid metabolism, and rapid systemic elimination [1-4]. Adjuvant's (Such as, Piperine) has been reported to increase the bioavailability of Curcumin [5,6]. The bioavailability of Curcumin ingested in foods may be increased as a result of cooking or dissolution in oil [7]. The study conducted by, Mohanty and Sahoo stated that nanoparticulate Curcumin is readily dispersed in aqueous medium unlike the free Curcumin [8].

Result: The trial results have shown conflicting results, where the Pungcharoenk ul, RamirezBosca et al. & Soni & Kuttan studies have shown some significant decrease in the Total cholesterol & Triglyceride. Whereas the trials conducted by Alwi et al. & Baum et al. are contradictory.

Introduction

Natural plant products have been used as the foundation of several medical treatments in humans & continues to be used as remedies as an alternative medicine throughout the world. It is estimated that 80% of individuals in developing countries depend primarily on natural products to meet their healthcare needs [5].

Ayurvedic herbs appeared to have been helpful in the management of Hypercholesterolemia & Metabolic disorder. (Diabetes) One of its active ingredients, Curcumin has been widely studied for its anti-inflammatory and antioxidant benefits. Curcumin protects against the oxidation of cholesterol. (LDL) It's also been shown to promote the HDL (Good cholesterol) hence achieving healthy total cholesterol.

Studies show, Curcumin significantly reduces the level of lipid profile and increases the levels of HDL-C after 30 days of treatment in comparison to plain turmeric. The effects of Curcumin is more significant than the house hold turmeric alone. Curcumin has demonstrated some efficacy in treating hypercholesterolemia. One small study found that daily administration of 500 mg of curcumin

for 7 days resulted in reduction in the total cholesterol by 11.63%, and increase in HDL cholesterol by 29%. Thus suggesting a chemo preventive agent against atherosclerosis [4]. A phase I clinical trials show's Curcumin as a safe drug even at high doses (12 g/day) in humans [5] but it's poor bioavailability largely limits its pharmacological activity.

Mechanism

Curcumin attenuates diet-induced hypercholesterolemia by increasing the rate of cholesterol catabolism through conversion of cholesterol to bile acids in the liver, and increases fecal excretion. The conversion is enhanced in order to replenish the loss in bile acids; the conversion of cholesterol to bile acids is the major pathway of cholesterol elimination and accounts for about 50% of daily cholesterol excretion. Curcumin supplementation increased Cholesterol 7 α -hydroxylase (CYP7A1) which is a liver-specific enzyme that catalyzes the rate-limiting step in the biosynthesis of bile acid from cholesterol in the liver. Moreover, as a mechanism, effect of curcumin on enterocytes inhibits re-absorption of excreted cholesterol as bile acids from digestive tract. Thus, increasing the

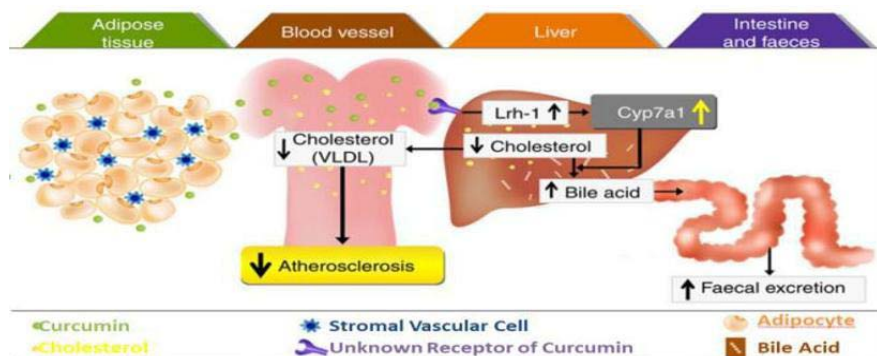


Figure 1: Suppresses expression of low-density lipoprotein (LDL) receptor, leading to the inhibition of LDL- induced activation of hepatic stellate cells/Qiaohua Kang and Anping Chen [11,12].

Study	Study type	N	Sample Population	Intervention	Duration of Study	Mean Total Cholesterol	Mean LDL	Mean HDL	Mean TGL	Summary of Findings
Puncharoenkul and Thonnopras (2011)	SBRC T	24	Healthy subjects in Thailand	Daily dose of 500mg or 6g of Curcumin	7 days	500mg=-17% (p=0.003), 6g=-5% (p=0.039)	N/A	N/A	500mg=-47% (p=0.016), 6g=-15% (p=0.323)	Low dose Curcumin significantly reduced serum Cholesterol & triglyceride more than the high dose Curcumin
Alwi et al. (2008)	DBRC T	75	Patients with ACS hospitalized in the ICCU in Indonesian hospital	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=0.610)	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=0.4% (p=0.95), Placebo=14.9% (p=0.57)	All Curcumin effects were not significantly different from placebo.
Baum et al. (2007)	DBRC T	36	Chinese's in Hong Kong, ≥50 years old, 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=5.8% (p=0.98), Placebo=-5.6%	1g=15.8% (p=0.35), 4g=9.4% (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. (2006)	CT	12	43-70 year old men in good health, LDL>150mg/dL, had managerial or scientific/technical jobs	2 tablets of 10mg Curcumin extract each	30 days	N/A	LDL=-38% (p=0.01), apo-B=-16.9% (p=0.05), apo-B/apo-A=-33.4% (p<0.01)	HDL=72.3% (p<0.01), apo-A=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 study.

Figure 2: SB RCT: Single Blinded Randomized Controlled Trial; DB RCT: Double Blinded Randomized Controlled Trial; CT: Clinical Trial; N/A: Not Applicable LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; Apo B: Apolipoprotein B; Apo A: Apolipoprotein A

hepatic CYP7A1 gene expression and suppressing of NPC1L1 gene expression in the intestinal cells (Figure 1). The mechanism partially accounts for the hypo-cholesterolemic effect of curcumin, and involve in cholesterol homeostasis.

Conclusion

The trial results studied show conflicting results, where the Puncharoenkul, Ramirez Bosca et al. & Soni & Kuttan studies have shown some significant decrease in the Total cholesterol & Triglyceride, whereas Alwi et al. & Baum et al. gives an unfavourable result. It is imperative to note that all the studies conducted and studied were conducted using the conventional form of Curcumin that would have Impended its bioavailability. Hence it would be interesting to study the effects of Curcumin (95% extract Curcuminoid) using a different drug delivery system. Researchers have come up with methods, to increase the bioavailability of Curcumin.

In one such method, Piperine has reported to significantly increase the bioavailability of Curcumin. In another one, it is reported that, Nano-particulate Curcumin is more bioavailable and has a longer half-life than the native Curcumin, suggesting the use of additive to achieve the desired protective and a therapeutic properties.

Avenues for Future Research

The historical use of Curcumin as a therapeutic natural plant product dates back hundreds of years ago, but the most recent advances regarding this agent have extended the possibilities of its use as therapy.

Research on Curcumin for its chemoprophylaxis and anti-inflammatory properties has been on the rise rapidly in the last decade. In 2008 there were at least twelve active clinical trials of Curcumin in the United States, Israel, and Hong Kong [1]. As of July

2012, there have been observations from 67 clinical trials that have been published, with another 35 clinical trials, which were in progress at that time [7]. Clinical Trials Registry India (CTRI) itself has listed more than 50 trials by Nov. 2018.

Curcumin trials & data regarding its role in reducing lipid profile and dyslipidemia, is limited with mixed results where Pungcharoenkul; Alwi et al. & Baum et al., demonstrate disappointing outcomes, whereas trials by Soni; Kuttan & Ramirez Bosca et al. show's significant promising results.

With extensive research on Curcumin's efficacy, safety, and pharmacokinetics, it has been recognized that Curcumin does not cause any significant short or long-term adverse events. There are some concerning issues, in particular its poor bioavailability. Because of which its concentrations are rarely achieved in humans, let alone its sustenance in circulation, limiting its chemotherapeutic potential. Most trials have only gathered results studying the conventional form of Curcumin, which is already struggling with its low availability hurdle in the systemic circulation. Future research in improving the bioavailability of Curcumin have shown that changing the drug delivery technique may lead in resolving the low availability concerns for its lipid lowering effect [9,12].

Literature Review

See Figure 2.

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