Soluble Curcumin: A Promising Oral Supplement For Health Management

Puneet Gandhi, Zeba Khan and Nivedita Chakraverty

ABSTRACT

Curcumin, the most active polyphenolic constituent of turmeric curcuminoids obtained from the rhizome Curcuma longa, holds a high place in ayurvedic medicine but its role in conventional disease management has also been established. However, it has poor bioavailability due to insolubility in water becomes a limiting factor. Increasing its solubility followed by assessment of effect of oral consumption of soluble curcumin on pathological parameters on healthy human volunteers, sixteen healthy subjects comprising of nine females and seven males in the age group of 24-45 years, was undertaken. Oral administration was done in the form of 500 mg capsule, twice a day, for 15 days. Complete blood profile, levels of blood glucose, lipid profile, renal function tests and liver function tests were performed in subjects before the start and at the end of the study. Soluble curcumin was found to improve the liver functions, kidney functions and ameliorated the lipid profile, blood glucose in healthy volunteers, only in 15 days of oral consumption. Enhanced bioavailability of soluble curcumin in the near future is likely to bring this promising natural product to the forefront of therapeutic agents for treatment of human diseases, especially age related problems.

Key words: Soluble curcumin, oral administration, blood glucose, lipid profile, bioavailability.

INTRODUCTION

Turmeric is a popular spice frequently used in Indian foods and curry. Curcumin (1, 7-bis [4-hydroxy-3-methoxyphenyl]-1, 6-heptadiene-3, 5-Dione) is the most active constituent of turmeric curcuminoids obtained from the rhizome Curcuma longa (Kurien et al., 2009). Curcumin is classified as a polyphenol compound that gives turmeric its bright yellow color. Besides being a popular dietary supplement, it is used as a food coloring agent. Curcumin holds a high place in ayurvedic medicine as a “cleanser of the body,” and today, science has documented several diseased conditions that can be healed by the active ingredients of turmeric (Mishra et al., 2008; Nair et al., 2010). Curcumin has been found to have antioxidant, anti-tumor, anti-inflammatory, antiviral, antibacterial, antifungal properties and thus has a potential against various diseases including diabetes, asthma, allergies, arthritis, atherosclerosis, neurodegenerative diseases, and other chronic illnesses like cancer (Sandur et al., 2007; Lin et al., 2008). Curcuma longa is an ingredient in Indian functional foods but the amount required for disease management i.e. a minimum of 8 g., pose problems particularly because of the taste (Wickenberg et al., 2010). Another issue is the bioavailability of curcumin. It has been shown in recent studies that curcumin has poor bioavailability because of its poor absorption and rapid metabolism. Several studies have indicated that the amount of curcumin in the serum after an intake of 4-8 g is only 0.4-3.6 µM (Anand et al., 2007; Kidd, 2009; Dhillon et al., 2008). The limited literature evidence devoted to show improvements in curcumin bioavailability reveals that the curcumin bioavailability enhancement has not gained significant attention. Novel delivery strategies including those of nanoparticles, liposomes, and defined phospholipid complexes offer significant promise and are worthy of further exploration in attempts to enhance the bioavailability, medicinal value, and application of this interesting molecule from mother nature. It has also been documented that
Figure 1. Effect of soluble curcumin (500 mg/twice a day) on lipid profile in healthy volunteers.

**Figure 1.1. Total Cholesterol**
- Average Value: 230 mg/dL
- Start: 180-300 mg/dL
- After: 100-200 mg/dL
- Volunteers recorded on first day of study and after 15 days.
- Approximately 60% of subjects show lowering of total cholesterol level and these values were within normal concentration range.

**Figure 1.2. LDL Cholesterol**
- Average Value: 130 mg/dL
- Start: 160-200 mg/dL
- After: 120-160 mg/dL
- Volunteers recorded on first day of study and after 15 days.
- 68% of subjects show lowering of LDL level and concentrations lay within range.

**Figure 1.3. Triglycerides**
- Average Value: 150 mg/dL
- Start: 180-250 mg/dL
- After: 120-180 mg/dL
- Volunteers recorded on first day of study and after 15 days.
- All the values of triglycerides lie within range.

**Figure 1.4. HDL Cholesterol**
- Average Value: 35 mg/dL
- Start: 30-40 mg/dL
- After: 35-45 mg/dL
- Volunteers recorded on first day of study and after 15 days.
- HDL levels are slightly raised in 60% of subjects but within range.

Soluble curcumin as compared to crude extract of turmeric shows better results for management of various health parameters with enhanced antioxidant activity (Inoue et al., 2008) as well as effective cytoprotective and a potential chemotherapeutic agent for treatment of human leukemia (Anuchapreeda et al., 2008; Jeong et al., 2006). Clinical trials of curcumin in humans have been promising. Phase 1 studies demonstrated virtually no toxicity in humans consuming up to 8 g curcumin per day for 3 months or a single dose of up to 12 g. Based on the encouraging preclinical and phase 1 clinical data, several additional human trials have been initiated and are currently enrolling patients. This includes trials testing the activity of curcumin in patients with colon cancer, pancreatic cancer, multiple myeloma, and myelodisplasia (Jiao et al., 2009).

Extensive investigations over the last five decades have indicated that curcumin reduces blood cholesterol (Yuan et al., 2008), prevents LDL oxidation (Mahfouz et al., 2009), inhibits platelet aggregation (Mayanglambam et al., 2010), suppresses thrombosis and myocardial infarction (Kim et al., 2008), suppresses symptoms associated with type II diabetes (Rungeesantisavivon et al., 2010), rheumatoid arthritis (Park et al., 2007), multiple sclerosis (Bright, 2007) and Alzheimer (Bauma et al., 2007), inhibits HIV replication, enhances wound healing, protects against liver injury, increases bile secretion, protects against cataract formation and pulmonary toxicity and fibrosis, antileishmaniasis and acts as an anti-atherosclerotic (Shishodia et al., 2007). There has been a lack of studies about the effect of curcumin on metabolic factors and usually the studies are conducted for experimental animals. The present study evaluates the effect of soluble curcumin on all parameters of blood and serum chemistry of healthy volunteers, as a part of serial studies about the effect of soluble curcumin on metabolic factors in volunteers having healthy profile and its possible use as an oral supplement for management of a good health status.

**EXPERIMENTAL DESIGN**

This study was a randomized single blind controlled trial, which was designed to evaluate the effect of soluble curcumin with...
constant dose 500 gm/ twice daily, on lipid profile, renal function tests, levels of blood glucose, liver function tests and hematological parameters in healthy volunteers. Soluble curcumin was given for 15 days. The study was conducted at CIMS, Bhopal and approval of the study was obtained from the Institutional Ethical Committee as per the norms of Indian Council of Medical Research for the same.

Study subjects
Subjects of the study were 16 healthy volunteers, who had not visited a physician with a medical complaint in the past six months. They were divided into two groups of nine females and seven males in the age group of 24-45 years. The healthy volunteers’ informed consents were obtained after they had been explained the study design and purpose by the investigators. On the initiation of the pilot study, sixteen volunteers were examined for various hematological and biochemical parameters and proven to have all values within normal range.

Parameters
Clinical history including age, sex, education level, ethnicity, personal habits including smoking and alcohol consumption, previous medical treatment if any, physical examination, blood pressure, BMI was recorded to ensure healthy status of subjects. Pathological profile included: total protein, albumin, globulin, neutrophils, lymphocytes, hemoglobin (Hb), fasting blood glucose, total cholesterol, direct LDL cholesterol, HDL cholesterol and triglycerides, urea, creatinine, total bilirubin, ALP (Alkaline phosphatase), SGOT (Serum glutamic oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase).

Data collection
For blood test and blood chemistry test, samples of peripheral venous blood were taken as per approved protocol, after a fasting period of 12 hours, before and after 15 days of study and sent according to the standard procedure to the clinical laboratory for profiling. The data of pathological parameters were computed in sigmakast and plot.

Curcumin
Purified curcumin capsules, trade mark CUR-500 manufactured by UNICO Pharmaceuticals, Ludhiana, India were procured from the INDSAFF, Batala, India. Each capsule contained extract of Curcuma longa containing curcumin (>95%) per 500 mg. To increase the solubility of purified curcumin, it was extracted in 30% of ethanol and redissolved in sterile distilled water and vacuum dried as per protocol of Kar et al (unpublished work). 500mg of this soluble curcumin was then packed into empty gelatin capsules for oral consumption to avoid dosage variation.

RESULT
Healthy volunteers who were fed the soluble curcumin (500 mg/twice a day) showed a significantly decreased total cholesterol level in comparison with the values recorded at zeroth hours on first day of study (Figure 1.1). The soluble curcumin also significantly lowered serum triglycerides and LDL cholesterol in 35% and 68% of subjects respectively, compared to the values recorded on first day (Figure 1.2 & 1.3). Serum HDL cholesterol level was not significantly affected by soluble curcumin supplementation (Figure 1.4). However, blood glucose was significantly decreased in soluble curcumin supplemented 75% of healthy volunteers in comparison with normal value (Figure 2).

On an average, half of the healthy volunteers showed slightly decreased serum activities of glutamicoxaloacetic transaminase (GOT), glutamate-pyruvate transaminase (GPT) and Alkaline phosphatase (Figure 3.1, 3.2 & 3.3). Total bilirubin was also found to be low in 75% of healthy volunteers (Figure 3.4). Figure 4.1 & 4.2, indicates the levels of urea and creatinine on first day recorded values and last day of the study. Results indicate that the levels of creatinine and urea showed a significant decrease in 87% and 68% of the subjects respectively. However, hematological parameters like lymphocytes and neutrophils levels showed no significant variations (Figure 5.1 & 5.2) but there was a significant increase in the haemoglobin level of the healthy volunteers (Figure 5.3).

**DISCUSSION**

The aim of this study was to assess the effect of soluble curcumin, a component of turmeric which is a regular ingredient of all Indian cuisines. Blood chemistry, glucose and cholesterol levels along with the other parameters like serum urea, serum creatinine, Hb, lymphocytes, neutrophils, SGOT, SGPT, ALP and total bilirubin levels in healthy human subjects were investigated. Our results showed that oral ingestion of 500 gm of soluble curcumin twice a day, lowered serum triglycerides and LDL cholesterol. Serum HDL cholesterol level was not significantly affected by curcumin supplementation. However, the results of the present study provide substantial support for the protective and hypolipidemic effects of curcumin in human subjects since most of the earlier studies are either *in vitro* or in animal models. Alwi et
al., in 2008 have reported that oral administration of curcumin extract taken from the root (rhizome) of turmeric (Curcuma domestica) (45 mg/day given as 15 mg three times daily) reduces total cholesterol and LDL cholesterol level in patients with acute coronary syndrome. Arun et al., 2002 also reported a decrease in blood glucose and glycosylated hemoglobin levels when 0.08 g curcumin/kg body weight or 1 g C. longa /kg body weight was administered to diabetic rats daily for three weeks. The study showed that curcumin was effective in diabetes mellitus. In a similar study on diabetic rats given curcumin for two weeks (15 mg/kg and 30 mg/kg), a decrease in renal dysfunction was observed (measured as reductions in creatinine and urea clearance), proteinuria, together with a decrease in oxidative stress (measured as decreased activities of the key anti-oxidant enzymes) (Sharma et al., 2006). This indicates that curcumin may offer protection against diabetic nephropathy.

Our results indicate that the levels of creatinine and urea showed a significant decrease in 87% and 68% of the subjects respectively. Tirkey et al., in 2005 have reported curcumin significantly and dose-dependently improved creatinine and urea clearance, and decreased the elevated levels of serum creatinine and BUN (Blood Urea Nitrogen). Jagadeesh et al., in 2009 reported the carcinogen exposed rats treated with curcumin and embelin respectively showed an amelioration of the altered biochemical parameters (urea, creatinine) towards normalcy giving an indication of the protective effect of these 2 compounds during DENA/PB-induced hepatocarcinogenesis in rats. The result showed hemoglobin levels are also found to be increased in soluble curcumin supplement healthy volunteers. Kumari et al., in 2007 also reported increased hemoglobin level in curcumin fed broiler birds. In the assessment of liver functioning after supplementation of soluble curcumin SGOT, SGPT, ALP was determined. In this study, decreased in the activities of SGOT,
SGPT and ALP in serum evidenced the positive effect of curcumin on liver. Rajesh et al., in 2010 also reported that crude extract of *C. longa* (250 g) is bioactive agent, recruits the damage of the liver and deduced the liver fat and necrotic condition from alcoholic erosion in swiss albino mice. Pari et al., in 2005 also reported that administration of 80 mg/kg body weight tetrahydrocurcumin is an antioxidative substance, derived from curcumin, for 8 days in female wistar rats treated with hepatotoxic compound chloroquine. SGOT, SGPT, ALP and total bilirubin levels were found to be significantly decreased in rats after supplemented with curcumin. In our study we did not found any significant results on lymphocytes and neutrophils. This might because of small sample size or short time duration.

**CONCLUSION**

Soluble curcumin was given orally to 16 healthy volunteers of both sexes at a dose of 500 mg/twice a day. No pathological, behavioral abnormalities or lethality was observed. Soluble curcumin can serve as a promising oral supplement for good health management especially for age related problems like liver, kidney and heart ailments even when administered for a very short duration. There is also a need for estimating the bioavailability of soluble curcumin which will corroborate the findings of this study. An elaborate study to comprehend underlying mechanistics in a larger sample size is underway.

**REFERENCES**


