Turmeric Phosphatidylcholine Complex

Stephen F. Olmstead, MD

INTRODUCTION
Turmeric (Curcuma longa) is an herb from India and southeast Asia used for centuries in cooking as a spice, colorant, and food preservative as well as a prized botanical in traditional Indian Ayurvedic medicine. 1,2 Turmeric is part of the ginger family of herbs, the Zingiberaceae. The root and rhizome are dried, crushed, and powdered. 2 The active component of turmeric is the polyphenol curcumin, which usually comprises 2% to 5% of the herb by weight. In addition to curcumin, turmeric contains other curcuminoids such as demethoxycurcumin, bisdemethoxycurcumin, and cyclocurcumin which have substantially less biological activity to no biological activity. Curcumin is an astonishingly pleiotropic molecule with a plethora of physiologic activities. 3 Curcumin directly targets over 100 protein kinases, transcription factors, enzymes, growth factors, adhesion molecules, and proteins associated with apoptosis. It scavenges free radicals and hydroxyl ions. It binds cationic metals such as iron and copper. Since 1949, nearly 9,000 papers have been published detailing the beneficial activities of curcumin in vitro and in vivo as an effective anti-inflammatory, antiproliferative, antimutagenic, antibacterial, antifungal, antiviral, and proapoptotic agent. 3,4

CURCUMIN BIOAVAILABILITY
Translation of the myriad potential benefits of curcumin from the laboratory to the clinic has been severely constrained by the biochemical properties of curcumin. It is essentially insoluble in water and ether, but soluble in acetone and ethanol. 2 Curcumin displays marked hydrolytic instability at physiologic pH. 5 It has exceedingly poor bioavailability after an oral dose, is rapidly metabolized, and efficiently excreted. 6 Following oral doses as high as 12 g daily, only 1 of 6 volunteers had detectable serum curcumin levels. In all the other subjects only the conjugates curcumin glucuronide or sulfate were detected. Despite curcumin’s very poor bioavailability, many human studies suggest its benefit in cardiovascular, metabolic, neurodegenerative, pulmonary, autoimmune, inflammatory bowel, and neoplastic diseases. 6

Realization of the full clinical spectrum of curcumin’s benefits depends on the formulation of a safe, highly bioavailable form of curcumin. The pharmaceutical approach is to develop and patent a curcumin analog. 7 This is an active area of pharmaceutical research. An alternative strategy is to combine curcumin with an adjuvant that enhances curcumin’s absorption after an oral dose. 8 Such adjuvants have included piperine or quercetin. 9 The best documented of these adjuvants is curcumin-piperine. 10 Piperine is one of the alkaloids responsible for pepper’s pungent taste and is a powerful intestinal and hepatic inhibitor of phase-1 and phase-2 xenobiotic detoxifying enzymes. Piperine nearly doubles the bioavailability of curcumin, but does so at the risk of increasing herb-drug interaction. 9 A final approach has been to combine curcumin with a lipophilic matrix (liposomes, phytosomes, and lipid micro- and nanoparticles). 9 In animal studies many of these formulas increase curcumin bioavailability, but have been poorly documented in humans.

BEST DOCUMENTED BIOAVAILABILITY
The clinical promises of curcumin stand ready to be fulfilled by a unique standardized ethyl acetate extract of turmeric complexed with phosphatidylcholine. 9 The curcumin-phosphatidylcholine complex is the best documented curcumin formulation that safely and dramatically increases curcumin and curcuminoid bioavailability. In a pharmacokinetic study involving nine volunteers, following ingestion of the curcumin-phosphatidylcholine phytosome complex the average absorption of curcumin was found to be approximately 18-fold higher than from the control unformulated curcumin-curcuminoid extract. 9 Moreover, curcuminoid absorption was about 29-fold higher for the curcumin-phosphatidylcholine phytosome complex compared to the unformulated reference, since the plasma concentrations of demethoxycurcumin and bisdemethoxycurcumin were 50- to 60-fold higher relative to the unformulated curcumin-curcuminoids. Complexing curcumin with phosphatidylcholine stabilizes the curcumin at physiological pH and promotes its absorption via pinocytosis. The curcumin-phosphatidylcholine phytosome complex has now been studied in a number of clinical trials and registries involving a variety of disorders.

Psoriasis Study
Sixty-three people with psoriasis were randomized to topical corticosteroids or topical corticosteroids together with 2 g/d of the curcumin-phosphatidylcholine phytosome complex. 12 People receiving the curcumin-phosphatidylcholine formulation had improved PASI assessment of psoriasis severity as well as significantly lower interleukin (IL)-22 levels. The curcumin-phosphatidylcholine phytosome complex was well-tolerated and only one subject reported an adverse effect which was diarrhea, most likely related to gastroenteritis.

Exercise Study
In a registry supplement study, the curcumin-phosphatidylcholine phytosome complex has been shown to improve strength and exercise capacity in elderly people complaining of fatigue and weakness. 13 In young, healthy males the curcumin-phosphatidylcholine phytosome complex showed the potential to prevent delayed onset muscle soreness following eccentric continuous exercise. 14 Subjects receiving the curcumin formulation reported less muscle pain and had significantly lower IL-8 levels two hours after exercise.

Knee Osteoarthritis Study
An observational study of people with knee osteoarthritis found that the addition of the curcumin-phosphatidylcholine phytosome complex to glucosamine resulted in significantly improved Karnofsky Index and WOMAC score (both in the physical and emotional domains) compared to glucosamine plus chondroitin sulfate. 15,16 Walking distance on treadmill was better and sustained after one month. The need for additional antiarthritic drugs and medical attention was reduced in people receiving the curcumin formulation. In another study, 2 g of the curcumin-phosphatidylcholine phytosome complex demonstrated analgesic activity comparable to a standard 1 g dose of acetaminophen but less than
that of a therapeutic 100 mg dose of the nonsteroidal nimesulide, which has been associated with severe hepatotoxicity.17

**Diabetic Microangiopathy Study**

Two studies have explored the utility of the curcumin-phosphatidylcholine phytosome complex in preventing diabetic microangiopathy. In a study involving 38 people with diabetes, retinal edema, and peripheral microangiography, four weeks of the curcumin formulation resulted in less retina edema, an improved venoarteriolar response, and sharper visual acuity.18 A pilot trial involving 25 people with diabetes found that 2 g/d of the curcumin-phosphatidylcholine phytosome complex decreased skin flux and edema as well as improving the venoarteriolar response indicating improved microvascular rheology.19 The curcumin formulation also increased tissue oxygen concentrations.

**Visual Acuity Study**

The curcumin-phosphatidylcholine phytosome complex may have a role in the management of central serous chorioretinopathy, a disease characterized by focal leakage at the level of the retinal pigment epithelium and hyperpermeability of the choroid.20 Administration of the curcumin phytosome complex stabilized visual acuity in 39% of 18 eyes (12 subjects) and 61% showed statistically significant improvement. In 95% of eyes, neuroretinal or retinal pigment epithelium detachment was reduced.

**Prostatic Hypertrophy Study**

The antiproliferative effects of the curcumin-phosphatidylcholine phytosome complex have been studied in a group of 63 men with symptomatic benign prostatic hyperplasia.21 Curcumin phytosome complex administered at 2 g/d compared to best medical management improved all scores on the International Prostate Symptom Score (IPSS) except stream weakness. Quality of life was better and the number of urinary tract infections and obstructions were lower in men receiving the curcumin phytosome complex.

**SUMMARY**

The curcumin-phosphatidylcholine phytosome complex results in the greatest bioavailability of oral administered curcumin and curcuminoids while being safely tolerated. Clinical evidence is accumulating as to its broad applications as an anti-inflammatory and antiproliferative agent.

**REFERENCES**