P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

HerbClip™

File: ■ Turmeric (*Curcuma longa*)
■ Curcumin
■ Bioavailability

HC 021461-492

Date: March 14, 2014

RE: Novel Curcumin Formulations with Improved Bioavailability

Schiborr C, Kocher A, Behnam D, Jandasek J, Toelstede S, Frank J. The oral bioavailability of curcumin from micronized powder and liquid micelles is significantly increased in healthy humans and differs between sexes. *Mol Nutr Food Res.* January 9, 2014; [epub ahead of print]. doi: 10.1002/mnfr.201300724.

Curcumin, a compound in turmeric (*Curcuma longa*) root, has been found to have antioxidant, anti-inflammatory, and antitumor bioactivity, among other activities.[1] Limited uptake and rapid metabolism have been problematic to the larger therapeutic potential of curcumin use. To increase solubility of a compound in water, micellation (encapsulation in circular, water-soluble aggregates) or micronization (reduction of particulate size) may be utilized. This single-blind, crossover study compared the bioavailability of micellation and micronization of curcumin with native curcumin, as well as any gender effects, in both healthy men and women.

Subjects (23 total, 13 women and 10 men) had normal blood parameters and ranged in ages from 19-28 years old. Subjects were excluded if they had a body mass index (BMI) of ≥ 30 kg/m^2, diseases, were pregnant or lactating, used drugs, smoked, or drank more than 20 g of alcohol daily, had a restrictive diet, were taking medication or dietary supplements, could not consume curcumin, or exercised more than 5 hours weekly. Included subjects were instructed to continue their normal lifestyles during the study.

The native curcumin used was in powder form and manufactured by Jupiter Leys; Okkal, Kerala State, India. This powder was standardized to curcumin (82%), demethoxycurcumin (DMC, 16%), and bisdemethoxycurcumin (BDMC, 2%). Micronisate of curcumin was manufactured from the powder by RAPS GmbH & Co. KG; Kulmbach, Germany. The curcumin powder (25%) was mixed with triacetin (58%) and panoden (16.7%), and the mixture was sprayed onto silicon dioxide. The micronisate contained 17.2% curcumin powder (14.1% curcumin). The micelles were produced by AQUANOVA AG; Darmstadt, Germany. These contained 7% of curcumin powder (6% curcumin) and 93% Tween®-80 (a detergent).

One week before the study, subjects were instructed to cease any consumption of curcumin, turmeric, or curry, and subjects were given a list of foods to avoid. Also, compliance was ensured by the screening of curcumin, DMC, and BDMC in plasma and urine. After a 12-

hour overnight fast, subjects consumed 500 mg of curcumin (410 mg curcumin, 80 mg DMC, and 10 mg of BDMC) in the form of native curcumin, liquid curcumin micelles, or micronized curcumin powder together with 50 g of woodruff (*Galium odoratum*) syrup in the morning. Treatments were given in randomized order after washout periods of ≥ 1 week. Subjects consumed water ad lib and food at mealtimes during the study day. Subjects' blood was taken at baseline, 0.5, 1, 1.5, 2, 4, 6, 8, and 24 hours following curcumin ingestions. After 1 incident of urination, urine was collected at baseline, 6, 12, and 24 hours. High-performance liquid chromatography (HPLC) was used to detect curcumin, DMC, and BDMC.

At baseline, BMI, height and weight, high-density lipoprotein (HDL) cholesterol, and blood hemoglobin concentrations were significantly different between men and women ($P<0.05$). Liver and kidney function parameters were normal at baseline and 24 hours after curcumin consumption, and no significant differences were seen between preparations. Adverse side effects (ASEs) reported with the native curcumin included flatulence, stomach ache, and yellow stool. ASEs described following micronized curcumin were "yellowish" diarrhea and stool, and greater amount of stool volume. Reported ASEs of the curcumin micelles were nausea, vomiting, fatigue, headache, stomachache, and regurgitation. One male subject dropped out of the study, resulting in 9 male subjects that consumed the curcumin micronisate preparation. The reason for the dropout is not specified.

At baseline, blood samples did not contain curcumin, DMC, or BDMC. There was a greater area under the curve (AUC) for curcumin, DMC, and BDMC of both curcumin micronisate and micelles as compared to native curcumin, with a significant formulation ($P<0.0001$) and gender effect for women ($P<0.04$). There was also a significant formulation effect for the greater amount of maximum concentration (C_{max}) of curcumin, DMC, and BDMC following ingestion of the micronisate and micelles preparation as compared to native curcumin ($P<0.0001$). There was also a gender effect on the curcumin C_{max} with women subjects ($P<0.0314$). A significant formulation effect was seen with the decreased time to C_{max} for curcumin, DMC, and BDMC, with the micelle preparation having the shortest amount of time compared to the other curcumin preparations ($P\leq0.003$). For urinary excretion of curcumin, DMC, and BDMC, there were significant formulation and gender effects (women) on the greater concentrations for the micronisate and micelles preparations as compared to the native curcumin ($P<0.0001$). In the urine samples at 24 hours after curcumin consumption, the average percent of the curcumin detected in urine as compared to the dose was 0.002 ± 0.012% (native curcumin), 0.007 ± 0.005% (curcumin micronized), and 0.151 ± 0.082% (curcumin micelles).

In summary, both preparations greatly increased bioavailable curcumin, DMC, and BDMC over native curcumin, with the micelle preparation being the most effective. It is mentioned that the curcumin micronized preparation had similar efficacy as other reported methods. Although these preparations will ultimately assist with the efficacy of curcumin use for many health conditions, the ASEs reported (as well as dosage and gender effects) should be a central focus of any future studies.

—Amy C. Keller, PhD

Reference

[1]Blumenthal M, Goldberg A, Brinckmann J, eds. *Herbal Medicine: Expanded Commission E Monographs*. Austin, TX: American Botanical Council; Newton, MA: Integrative Medicine Communications; 2000.

Referenced article can be found at http://onlinelibrary.wiley.com/doi/10.1002/mnfr.201300724/pdf.