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File: ■ Turmeric (*Curcuma longa*, Zingiberaceae)
■ Curcuminoids
■ Osteoarthritis

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RE: Curcuminoid Supplementation Improves Knee Osteoarthritis Symptoms

Panahi Y, Rahimnia AR, Sharafi M, Alishiri G, Saburi A, Sahebkar A. Curcuminoid treatment for knee osteoarthritis: a randomized double-blind placebo-controlled trial. *Phytother Res*. November 2014;28(11):1625-1631.

The most common joint disease in adults, osteoarthritis (OA) is characterized by chronic joint pain, inflammation, stiffness, and limited mobility. Standard treatment is the prescription of analgesics and non-steroidal anti-inflammatory drugs (NSAIDs); however, NSAIDs are only partially effective and may cause adverse gastrointestinal, renal, and cardiovascular effects. Experimental studies have found that the curcuminoid constituents (2-5%) of turmeric (*Curcuma longa*, Zingiberaceae) have significant analgesic, anti-inflammatory, and antioxidant properties. Preliminary clinical evidence suggests curcuminoids may be an effective alternative or adjunct treatment for OA. In this randomized, double-blind, placebo-controlled pilot study, the effect of curcuminoid supplementation on clinical measures of knee OA symptoms was measured.

Patients under the age of 80 with mild-to-moderate knee OA (n=60) were recruited from Baqiyatallah University Clinic in Tehran, Iran. Diagnoses of knee OA were based on the clinical and radiological criteria of the American College of Rheumatology and a minimum score of 40 mm on a 100 mm visual analog scale (VAS) of joint pain. The exclusion criteria were as follows: known allergy to curcuminoids or other herbs; candidates for knee replacement or any other surgery; OA secondary to trauma; rheumatoid arthritis, inflammatory disorders, or hemophilia; malabsorption disorders; active, generalized inflammatory conditions; heart, renal, or liver failure; history of psychological disorders; using >10 mg/day corticosteroids in the prior 3 months; and intra-articular injections in the last 3 months.

The eligible consenting patients (n=53) were consecutively randomly assigned to receive either 500 mg 3x/day (1500 mg/day) of curcuminoids (n=27; C3 Complex®; Sami Labs Ltd; Bangalore, India) or a size- and shape-matched placebo (n=26; inert starch) for 6 weeks. Each C3 Complex capsule contained 500 mg curcuminoids and 5 mg BioPerine® (Sami Labs Ltd). BioPerine is a standardized extract of black pepper (*Piper nigrum*, Piperaceae) and/or long pepper (*Piper longum*) containing at least 95% piperine, which has been shown to increase the absorption of curcuminoids. All patients were allowed to use an escape medication (naproxen) when they had intolerable pain.

The change in OA symptoms was measured with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), OA pain severity rating on VAS, and the 5-item Lequesne's Pain Functional Index (LPFI). Adverse effects were recorded using a pre-designed checklist.

Forty patients completed the study with 19 in the treatment group and 21 in the placebo group. Eight patients in the treatment group and 5 patients in the placebo group were lost to follow-up. No reasons for the losses in either group were given. All patients were taking NSAIDs at baseline.

At the end of the study, there were significant reductions in the global WOMAC score and the pain, physical function, and stiffness subcategory scores in the treatment group ($P < 0.001$, $P < 0.001$, $P < 0.001$, and $P = 0.043$, respectively) compared to baseline. The scores for the WOMAC pain and stiffness subcategories were also significantly reduced in the placebo group ($P = 0.025$ and $P = 0.009$, respectively) compared to baseline. However, the global WOMAC score and scores for the subcategories of pain and physical function were all significantly lower in the treatment group compared to the placebo group at the end of the study ($P = 0.001$, $P < 0.002$, and $P < 0.001$, respectively). There was no significant difference between the treatment and placebo groups in the WOMAC stiffness subcategory.

Treatment with curcuminoids (but not placebo) significantly improved both the VAS and LPFI scores ($P < 0.001$ for both) compared to baseline. Compared to the placebo group, the magnitude of reduction in VAS and LPFI scores was significantly greater in the treatment group ($P = 0.013$ and $P < 0.001$, respectively). There was also a significant reduction ($P < 0.001$) in the use of NSAIDs in the treatment group (84%) compared to the placebo group (19%). No serious adverse events (AEs) were reported, and none of the dropouts were due to AEs. The most common AE was gastrointestinal distress with 7 patients in the treatment group and 4 in the placebo group affected.

Six weeks of curcuminoid supplementation resulted in marked improvement in symptoms of knee OA compared to the placebo. In addition, there was a significant reduction in the use of NSAIDs in the group taking curcuminoid supplements. The authors suggest that a plausible mechanism is the potent anti-inflammatory and antioxidant properties of curcuminoids. Curcuminoids have been shown to reduce the release of pro-inflammatory cytokines in cultured chondrocytes, increase chondrocyte survival, inhibit the production of reactive oxygen species which impair joint components, and scavenge free radicals which disrupt the cartilage matrix and promote the production of pain mediators.

The authors note several limitations of the study, including the small sample size and short duration, as well as the facts that the optimum dose and dose-response relationship were not determined and only patients with mild-to-moderate OA were evaluated. Based upon the positive safety and efficacy findings in this study, the authors conclude that larger scale (Phase III) trials should be conducted to confirm the results and investigate whether the effect is independent of analgesic mechanisms.

–Cheryl McCutchan, PhD

The American Botanical Council has chosen not to include the original article.