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**File: ■ Turmeric (*Curcuma longa*, Zingiberaceae)  
■ Curcumin  
■ Boswellia (*Boswellia serrata*, Burseraceae)  
■ Osteoarthritis**

**HC 021831-588**

**Date: March 15, 2018**

**RE: Combining Curcumin and Boswellic Acid Is More Effective in the Treatment of Osteoarthritis than Curcumin Alone**

Haroyan A, Mukuchyan V, Mkrtchyan N, et al. Efficacy and safety of curcumin and its combination with boswellic acid in osteoarthritis: a comparative, randomized, double-blind, placebo-controlled study. *BMC Complement Altern Med*. January 9, 2018;18(1):7. doi: 10.1186/s12906-017-2062-z.

The symptoms of osteoarthritis (OA), including pain, morning stiffness, joint swelling, limited range of motion, decreased physical function, and restriction of social activities, are treated with analgesic, nonsteroidal anti-inflammatory drugs (NSAIDs), and cortisone. Although those drugs manage the pain and inflammation, they are associated with adverse effects, drug interactions, and contraindications. Curcumin, a component of turmeric (*Curcuma longa*, Zingiberaceae), has been reported to be a potent anti-inflammatory agent. The boswellic acids found in boswellia (*Boswellia serrata*, Burseraceae) possess anti-inflammatory and antiarthritic properties. The primary objective of the comparative, randomized, double-blind, placebo-controlled study reported here was to compare the efficacy of curcumin, a combination of boswellic acid and curcumin, and placebo in treating degenerative joint disease by assessing their effects on joint pain, morning stiffness, and limitations of physical function. The secondary objective was to investigate the safety of the treatments.

The study, which used Curamin® and CuraMed® (both donated by EuroPharma USA, Inc.; Green Bay, Wisconsin), was conducted between September 2014 and May 2016. The study included 201 males and females aged 40 to 77 years who had been diagnosed with degenerative hypertrophic OA of the knee and were patients at Erebuni Medical Center in Yerevan, Armenia. Each 500-mg capsule of the curcumin supplement CuraMed contained 552-578 mg of BCM-95® (DoiCas Biotech, LLC; Landing, New Jersey), a dry turmeric extract with 500 mg curcuminoids and 49-52 mg volatile oil from turmeric rhizome. Inactive excipients (120-149 mg) included phosphatidylcholine, medium-chain triglycerides, glycerol, gelatin, and yellow beeswax. Each 500-mg Curamin capsule contained 350 mg BCM-95 and 150 mg boswellia gum resin extract consisting of 75% boswellic acids and 10% 3-O-acetyl-11-keto-boswellic acid. Each 500-

mg placebo capsule (donated by EuroPharma USA, Inc.) contained maltodextrin, calcium phosphate, gelatin, magnesium stearate, silica dioxide, FD&C yellow 5, FD&C yellow 6, and titanium dioxide.

The patients were randomly assigned to the Curamin (n = 67), CuraMed (n = 66), or placebo group (n = 68). The patients were instructed to take 1 capsule 3 times daily for 12 weeks. No significant differences in demographic or other measured characteristics were observed among the patients at baseline. The mean age was 56.2 years, the average body mass index was 29 kg/m<sup>2</sup>, and 93% of the patients were females.

In the Curamin group, dropouts during the study included 2 patients who did not respond, 1 who lost interest because of lack of improvement, 1 who was injured, and 1 who reported nausea and vomiting. In the placebo group, 3 patients did not respond, 3 lost interest because of lack of improvement, and 3 reported adverse effects (weight gain, stomach pain, dyspepsia, rash, and itching). In the CuraMed group, dropouts included 3 patients who did not respond, 1 who was unable to attend the study visits, 1 who lost interest because of lack of improvement, and 3 who did not trust the medication.

During the study visits at baseline, after 4 weeks, and after 12 weeks, the patients underwent radiography and sonography, completed the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and physical performance measures (PPM) tests, and provided blood samples. The text stated labs differently than the corresponding table, so it is unclear at which visits each of these tests were done.

After 4 weeks of treatment, significant decreases were seen in total WOMAC scores in all groups ( $P < 0.05$  for all). The scores gradually decreased in the Curamin and CuraMed groups until the end of the study; however, in the placebo group, no significant changes were seen at 12 weeks. At the end of the study, the improvements in the CuraMed group ( $P < 0.001$ ) were 3.6-fold greater, and in the Curamin group ( $P < 0.001$ ), 2.7-fold greater, than the improvement seen in the placebo group ( $P = 0.154$ ).

Statistically significant pain relief was observed in all groups, as reported on the WOMAC. In the placebo group, the pain index decreased significantly after 4 weeks of treatment ( $P < 0.01$ ); however, after 12 weeks, the change was not significant ( $P > 0.05$ ). Significant decreases in pain were seen in the Curamin and CuraMed groups ( $P < 0.001$  for both) after 12 weeks of treatment. The significant decrease in pain reported in the placebo group after 4 weeks is similar to results from other studies that report placebo effects of OA treatments; meta-analyses have indicated that more than 50% of study patients with OA respond positively to placebo treatment.<sup>1,2</sup> Placebo effects can be influenced by the strength of the active treatment, the severity of disease at baseline, the route of medication delivery, and the study's sample size.<sup>1</sup>

After 12 weeks of treatment, patients in the Curamin and CuraMed groups reported significantly less difficulty in moving their knees and less stiffness compared with baseline ( $P < 0.05$  for both groups). In the placebo group, significant improvement was seen only after 4 weeks ( $P < 0.05$ ) of treatment. Differences in changes during the study between the Curamin and placebo groups and between the CuraMed and placebo groups were not significant.

Among the PPM tests was the chair stand test. The maximum number of chair stand repetitions in 30 seconds increased significantly during the study in the Curamin and CuraMed groups ( $P < 0.001$  for both). Significant differences between the Curamin and placebo groups ( $P < 0.05$ ) and between the CuraMed and placebo groups ( $P < 0.01$ ) were observed, with greater improvements in the Curamin and CuraMed groups. A timed walking test (40-m walking speed) revealed significantly increased walking speeds from baseline to week 12 only in the Curamin ( $P < 0.001$ ) and CuraMed ( $P < 0.01$ ) groups. Comparing the changes from baseline among the groups revealed significant differences between the CuraMed and placebo groups ( $P < 0.05$ ) and between the Curamin and placebo groups ( $P < 0.01$ ), with faster speeds reported in the active treatment groups.

Patients were timed as they rose from a chair, walked 3 meters, turned around, walked back to the chair, and sat down. They wore regular footwear and used a walking aid if needed. The time significantly decreased only in the Curamin ( $P < 0.001$ ) and CuraMed ( $P < 0.05$ ) groups. Comparing the changes from baseline to the end of the study revealed greater improvement in the Curamin group compared with the placebo group ( $P < 0.01$ ); improvements in the CuraMed and placebo groups were not significantly different ( $P > 0.05$ ). The time required to go up and down a flight of stairs significantly decreased by week 12 only in the Curamin ( $P < 0.001$ ) and CuraMed ( $P < 0.01$ ) groups. Comparing the changes from baseline to the end of the study revealed greater improvement in the Curamin group compared with the placebo group ( $P < 0.01$ ); improvements in the CuraMed and placebo groups were not significantly different. Blood levels of inflammation markers significantly increased ( $P < 0.05$ ) in all groups compared with baseline, with no significant differences seen among the groups.

Adverse effects were observed in 13 of the 201 patients as follows: 4 in the placebo group, 2 in the Curamin group, and 7 in the CuraMed group. None of those effects were serious. The types and frequency of adverse effects were similar in all groups and were not related to the treatment.

Compared with placebo, Curamin significantly improved the patients' performance on all physical tests and on the factors of the WOMAC. Patients treated with CuraMed saw improvements in 2 physical performance tests and in the WOMAC joint pain index. These results suggest that "these plant extracts are more effective in combination," write the authors, possibly because boswellic acid increases the bioavailability of curcumin. "However, to our knowledge, there is no published study demonstrating the effect of boswellic acid on the bioavailability of curcuminoids." In this study, the 12-week use of a curcumin complex or its combination with boswellic acids reduced pain-related symptoms in patients with OA. The authors conclude that the combination of curcumin and boswellia extract "increases the efficacy of treatment of OA presumably due to synergistic effects of curcumin and boswellic acid."

This study was supported in part by EuroPharma USA, Inc.

—*Shari Henson*

#### **References**

<sup>1</sup>Zhang W, Robertson J, Jones AC, Dieppe PA, Doherty M. The placebo effect and its determinants in osteoarthritis: meta-analysis of randomised controlled trials. *Ann Rheum Dis.* 2008;67(12):1716-1723.

<sup>2</sup>Zou K, Wong J, Abdullah N, et al. Examination of overall treatment effect and the proportion attributable to contextual effect in osteoarthritis: meta-analysis of randomised controlled trials. *Ann Rheum Dis*. 2016;75(11):1964-1970.

Referenced article can be accessed at  
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