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File: ■ Chinese Skullcap (*Scutellaria baicalensis*)
■ Cutch Tree (*Acacia catechu*)
■ Osteoarthritis

HC 041423-505

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RE: Short-term Supplementation with Chinese Skullcap and Catechu Helps Relieve Osteoarthritic Knee Pain and Stiffness

Arjmandi BH, Ormsbee LT, Elam ML, et al. A combination of *Scutellaria baicalensis* and *Acacia catechu* extracts for short-term symptomatic relief of joint discomfort associated with osteoarthritis of the knee. *J Med Food*. June 2014;17(6):707-713.

Osteoarthritis is caused by the degradation of joint cartilage and is characterized by joint swelling, pain, and a decrease in joint mobility. Osteoarthritis is generally treated with prescription medications, but alternative and complementary medicines are also commonly used. Complementary medicines high in flavonoids have been shown to have positive effects on the symptoms of osteoarthritis. Flavonoids are thought to reduce inflammation by inhibiting the expression of interleukins, tumor necrosis factor-α (TNF-α), and cyclooxygenase 2. UP446 is a proprietary dietary supplement containing extracts of Chinese skullcap (*Scutellaria baicalensis*) and cutch tree (*Acacia catechu*) (plant parts not included in article) with a ratio of 85 to 15 free-B-ring flavonoids to flavans. UP446 (Unigen, Inc.; Seattle, Washington) has been shown to be effective in alleviating joint pain and stiffness in patients with osteoarthritis after treatment for over 4 to 12 weeks. In this double-blind, randomized study, the short-term (1 week) effect of UP446 on osteoarthritis symptoms and inflammation biomarkers was measured. The non-steroidal anti-inflammatory drug, naproxen, was used as a positive control.

Patients with mild-to-moderate osteoarthritis in 1 or both knees were recruited in Tallahassee, Florida. Patients were between the ages of 40 and 90 years old and had experienced knee pain for at least 6 months. The patients who responded were all overweight or obese with body mass indexes (BMIs) of around 30 kg/m^2. Patients were excluded if they had a history of liver or kidney disease or other diseases known to affect osteoarthritis, had knee surgery, cortisone or hyaluronan injections within 2 months prior to the study, or were allergic to shellfish or naproxen. The study was conducted at the Human Performance Laboratory at Florida State University's Department of Nutrition, Food, and Exercise Science. Eighty-four patients met the study criteria and were randomly divided between the UP446 (500 mg/d) treatment (n = 45) and the naproxen (440 mg/d) positive control group (n = 39). Five patients from the control group did not complete the study. Four had schedule conflicts, and 1 developed headaches and dizziness. BMI, heart rate, blood pressure, knee range of motion (ROM), and distance covered in 6 minutes of walking were measured at the beginning and end of the study. Fasting blood samples were collected at

the start and end of the study, and C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-1β (IL-1β), TNF-α, and hyaluronic acid (HA) concentrations were measured. Pain, stiffness, and mobility were measured every 2 days with the Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain assessment. Physical activity and sleep patterns were assessed at the beginning and end of the study with the Five-City Project Physical Activity Recall. Data were compared with analysis of variance (ANOVA).

No statistically significant differences were found between the test groups at the beginning of the study. There was a significant reduction in time spent on hard activity in the naproxen group from the beginning to the end of the study ($P < 0.001$) and this was significantly different from the UP446 treatment group ($P < 0.05$), where no change in time spent on hard activity was observed. There was a significant reduction in pain from baseline in the UP446 treatment group ($P = 0.009$), but there was no difference in the naproxen group. Both groups experienced a significant decrease in joint stiffness (UP446, $P = 0.0021$, and naproxen, $P = 0.0081$). The UP446 treatment group also had a significant 6% increase in ROM over the course of the study ($P = 0.036$). However, there was a significant difference in the pro-inflammatory biomarker IL-1β, which was higher after 1 week of treatment in the UP446 group but had decreased in the naproxen group ($P = 0.02$); TNF-α increased significantly in both groups ($P = 0.0007$ for UP446 and $P = 0.02$ for naproxen). The reason for the increase in IL-1β and TNF-α after UP446 administration unclear. No other significant changes in blood biomarkers were found.

This study provides preliminary evidence that the proprietary mix of Chinese skullcap and cutch tree, UP446, may be helpful in the short-term for treating the symptoms of osteoarthritis of the knee. In addition, UP446 showed greater efficacy than naproxen in relieving some osteoarthritis symptoms, but the 440 mg/day dose of naproxen was lower than the 500-1000 mg/day commonly recommended for osteoarthritis. There was a significant reduction in pain and stiffness with UP446 supplementation that, in turn, resulted in an increase in knee ROM and no significant loss in hard physical activity over the course of 1 week. Naproxen treatment also resulted in a decrease in knee stiffness, but this did not correspond to an increase in ROM or maintenance of physical activity level. Two other studies of Chinese skullcap and cutch tree have shown a decrease in knee stiffness over 30 days and a decrease in time needed to walk a set distance over 6 to 12 weeks. In one of the studies, Chinese skullcap and cutch tree were found to affect older patients and patients with less severe osteoarthritis more than younger patients or patients with severe osteoarthritis. The pro-inflammatory biomarker, TNF-α, increased in both study groups. The authors note that older patients with osteoarthritis tend to have high concentrations of pro-inflammatory markers, though the extract group average age was only about 3 years greater than the control group (63.8 vs. 60.9, respectively). They suggest that further mechanistic studies are needed. They also suggest studies of UP446 at varying dosages.

—Cheryl McCutchan, PhD

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