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File: ■ Lemon Verbena (*Aloysia citriodora*)

■ Fish Oil

■ Arthritis

HC 011264-444

Date: March 15, 2012

RE: Joint Status Improved by Lemon Verbena Extract Combined with Fish Oil

Caturla N, Funes L, Pérez-Fons L, Micol V. A randomized, double-blinded, placebo-controlled study of the effect of a combination of lemon verbena extract and fish oil omega-3 fatty acid on joint management. *J Altern Complement Med.* November 2011;17(11):1051-1063.

Arthritis is characterized by inflammation of the joints, and there are 2 general types of the disease. Osteoarthritis (OA) is associated with age-related joint degeneration, while rheumatoid arthritis (RA) is caused by autoimmune joint inflammation. Cartilage destruction, synovial fluid disruption, mitochondrial dysfunction, and other joint-related problems have been found to be caused by reactive oxygen and nitrogen species (RONS). Many plants used medicinally have antioxidant activity, and many plant antioxidant compounds alleviate diseases caused by inflammation.

Lemon verbena (*Aloysia citriodora* syn. *A. triphylla* and *Lippia citriodora*), used traditionally for a variety of ailments, contains the potent antioxidant and anti-inflammatory phenylpropanoid compound verbascoside. In addition, the long chain omega-3 polyunsaturated fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), found in cold-water fish oil, have been shown to affect the immune system. This double-blind, placebo-controlled, randomized study investigated the effects of a mixture of lemon verbena extract and fish oil omega-3 fatty acids on patients with joint pain and dysfunction. In addition, the antioxidant capacity of both the extract and treatment mixture was assessed in vitro.

The lemon verbena extract was dissolved with water (5 mg/ml), and the verbascoside content of the extract was analyzed using high-performance liquid chromatography (HPLC). Antioxidant activity was measured using the oxygen radical absorbance capacity (ORAC) assay and data expressed as μ mole of Trolox equivalents (TE) per gram; in this particular assay, a higher ORAC value indicates stronger antioxidant activity.

Included patients were diagnosed by a physician as having joint discomfort and pain in knees, hips, elbows, hands, or shoulders for 3 months or more. Patients were excluded if they used medication other than for high cholesterol, or antihypertonic or antiarrhythmic agents. Patients were also excluded if they had plant, herbal medicine, vitamin, or mineral allergies. Patients were randomized to either supplement (n=23) or placebo (n=22) groups

for the 9-week study. A capsule of the supplement (0.6 g) consisted of 370 mg of fish oil powder containing a ratio of 10:8 EPA to DHA, and 230 mg of lemon verbena extract containing 14% w/w verbascoside. All patients took 6 capsules daily of placebo or supplement, 2 before each meal from week 1 to week 5. At the beginning of week 6, patients took 3 capsules per day before meals until week 9. The dose per day of verbascoside from weeks 1-5 was 193 mg, and 97 mg for weeks 6-9.

The primary endpoints were joint pain, stiffness, and function. These were assessed using the Western Ontario McMaster (WOMAC) and Lequesne's surveys. The WOMAC questionnaire is designed to measure pain/stiffness and physical dysfunction, while Lequesne's assesses pain, discomfort, maximum distance walked, and daily activities. Reduced severity of these arthritis factors is indicated in a low score for both questionnaires. Surveys were completed by patients at baseline and at least once per week during the study.

It was found that verbascoside was the most common phenylpropanoid in the lemon verbena extract and occurred at $14.75 \pm 0.85\%$ w/w. Isolated verbascoside had an ORAC value of $11,710 \pm 106 \mu\text{mol TE/g}$, while the extract was $5,183 \pm 300 \mu\text{mol TE/g}$. The total supplement was found to have antioxidant activity of $1,065 \pm 122 \mu\text{mol TE/g}$. It is surmised that excipients associated with the omega-3 fatty acids may have interfered in the assay, resulting in a value lower than expected. Of the 45 total patients randomized, 31 completed the study ($n=12$ for the placebo group and $n=19$ in the supplement group). No significant differences were seen between groups at baseline, and the majority of patients maintained normal physical activity. Only 1 adverse side effect was found in each group; these patients were dropped from the study, supplementation discontinued, and no complications ensued.

The WOMAC scores in the supplement group declined steadily throughout the study, and the pain/stiffness and function scores of the test first significantly differed from the placebo group at weeks 3 ($P \leq 0.01$) and 4 ($P \leq 0.05$), respectively. Also, the total WOMAC score of the supplement group at 9 weeks was 53% lower than the baseline score. No significant changes were observed in the WOMAC score of the placebo group. In addition, the Lequesne's score of the supplement group was significantly different from the placebo group at week 4 ($P \leq 0.05$) and remained significant from weeks 5-9 ($P \leq 0.01$). By the end, the score had decreased by 78% as compared to the baseline score. No significant differences were seen in the Lequesne's scores of the placebo group.

The combination supplement of lemon verbena extract and omega-3 fatty acids significantly improved arthritis symptoms in this study. Many previous studies have shown that a diet rich in antioxidants may improve disorders caused by exercise-induced free radicals and other RONS-caused inflammation problems. Lemon verbena extract and compounds therein demonstrate antioxidant activity, and omega-3 fatty acids have been shown to benefit those suffering from joint problems; therefore, this tested mixture is worthy of future investigation into the treatment of arthritis and other inflammation diseases.

—Amy C. Keller, PhD

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