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File: ■ English Hawthorn (*Crataegus laevigata* syn. *C. oxyacantha*, Rosaceae)
■ Angina Pectoris
■ Cardiovascular Disease

HC 021661-540

Date: March 15, 2016

RE: Hawthorn Extract Reduces Inflammatory Cell Adhesion Molecules in Patients with Stable Angina

Jalaly L, Sharifi G, Faramarzi M, et al. Comparison of the effects of *Crataegus oxyacantha* extract, aerobic exercise and their combination on the serum levels of ICAM-1 and E-selectin in patients with stable angina pectoris. *Daru*. December 19, 2015;23:54. doi: 10.1186/s40199-015-0137-2.

Stable angina (angina pectoris) refers to heart pain caused by a lack of oxygen availability, and is preceded by inflammation and atherosclerosis. Cell adhesion molecules (CAMs) facilitate the inflammation process with white blood cell recruitment, and can negatively affect cellular and tissue function. Previous studies have shown English hawthorn (*Crataegus laevigata* syn. *C. oxyacantha*, Rosaceae), and other species of *Crataegus*, to be useful in treating symptoms of heart failure.[1] This randomized, double-blind, placebo-controlled trial investigated the impact of hawthorn consumption, combined with aerobic exercise (also shown to reduce CAMs), on intercellular adhesion molecule-1 (ICAM-1) and E-selectin. These CAMs have been shown to be important in the pathology of cardiovascular disease.

English hawthorn leaf and flower extract (EPO Istituto Farmochimico Fitoterapico S.r.l.; Milan, Italy) was used for this study. The product Cratagol (provided by Goldaru; Isfahan, Iran), consisting of 240 mg of extract per tablet standardized to 4-6 mg of vitexin-2-ramnozide, was used. These tablets also contained microcrystalline cellulose, corn (*Zea mays*, Poaceae) starch, talc, and magnesium stearate. Placebo tablets (Goldaru) consisted of lactose with identical coating. Two tablets were administered per day with water, prior to meals, for 12 weeks.

Patients diagnosed with stable angina were recruited from the Imam Ali Clinic in Shahrekord, Iran. Patients were included if they had received angina testing between 1-12 months prior to the study, < 50% atherosclerosis, treatment within 3 months prior to the study, and if they were 45-65 years old. Those with severe heart failure, "lack of accessibility," or who were taking medications, including digoxin, cisapride, anticoagulants, or antiarrhythmics, were not included. In total, 80 patients were randomly assigned to 1 of 4 groups with 20 patients in each (11 men and 9 women) as follows: (1)

exercise with placebo, (2) hawthorn extract alone, (3) exercise and hawthorn extract together, and (4) control (no exercise, hawthorn extract, or placebo). At baseline, there were no differences in age, sex, weight, or body mass index among groups. Exercise, nutrition, smoking and drinking habits, and angina symptoms were monitored.

Throughout the study, all patients received 50 mg/day of Methoral, 80 mg/day of aspirin, and nitroglycerine as needed for pain. Exercise consisted of a treadmill protocol of 40-60% of heart rate reserve and an 11-13 rating of perceived exertion using the Borg scale (this scale ranges from 6 to 20, where 20 indicates maximal exertion). The exercise protocol was done for 20-30 minutes twice per week for 12 weeks. If patients had chest pain, asthma, dizziness, fatigue, or decreased systolic blood pressure by > 10 mmHg, exercise was halted. Fasting blood was collected at baseline (24 hours prior to the study) and at the end of the study. Enzyme-linked immunosorbent assay (ELISA) kits were used to measure serum concentrations of ICAM-1 and E-selectin.

None of the patients dropped out. At baseline, ICAM-1 and E-selectin were not different among groups. At the end of the study, ICAM-1 significantly decreased compared to baseline concentrations in the exercise group (65.5 ± 39.7 ng/ml vs. 20.8 ± 2.7 ng/ml, P=0.001), hawthorn extract group (61.3 ± 38.1 ng/ml vs. 23.1 ± 3.7 ng/ml, P=0.001), and the exercise and hawthorn extract combined group (90 ± 53.5 ng/ml vs. 21.9 ± 3.9 ng/ml, P=0.001). No significant differences were noted in the control group. Also, as compared to baseline, E-selectin concentrations were significantly decreased in the exercise group (3.2 ± 1.5 ng/ml vs. 1.8 ± 1 ng/ml, P=0.001), hawthorn extract group (3.4 ± 1.9 ng/ml vs. 2.2 ± 1.3 ng/ml, P=0.003), and the exercise and hawthorn extract combined group (3.5 ± 1.3 ng/ml vs. 1.8 ± 0.7 ng/ml, P=0.001). No differences were seen in the control group.

The ICAM-1 serum concentrations of those in the exercise and hawthorn extract combined group were significantly lower than those taking hawthorn extract alone (P=0.021) and the control group (P<0.05), but not the exercise-only group. Also, E-selectin concentrations were lower in the combination group than in the hawthorn extract-only group and the control group (P=0.021 and P<0.05, respectively), but not the exercise-only group. No adverse side effects were noted.

In summary, this study shows that both English hawthorn extract and exercise were effective in attenuating the concentration of ICAM-1 and E-selectin. This may be due to the alleviation of downstream inflammation markers or general bioactivity associated with the antioxidant potential of hawthorn. It is curious that the control group in this study did not receive the placebo; this somewhat confounds the results. However, English hawthorn extract may be an effective adjuvant treatment, with or without exercise, for those suffering from stable angina.

—Amy C. Keller, PhD

Reference

[1]Veveris M, Koch E, Chatterjee SS. *Crataegus* special extract WS® 1442 improves cardiac function and reduces infarct size in a rat model of prolonged coronary ischemia and reperfusion. *Life Sci*. February 27, 2004;74(15):1945-1955.

Referenced article can be accessed at http://darujps.biomedcentral.com/articles/10.1186/s40199-015-0137-2.

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