Crataegus oxyacantha (Hawthorn) Monograph

Introduction

Crataegus oxyacantha has been used traditionally as a cardiac tonic since the first century A.D., as noted by the Greek herbalist, Dioscorides, and became even more popular among European and American herbalists in the late 19th century. Currently it is used as a cardiotonic for a variety of functional heart disorders. Recent research shows Crataegus extracts exert a wide range of positive actions on heart function, supporting and validating historical observations.

Description

C. oxyacantha is a thorny deciduous tree found primarily in Europe, North America, and Western Asia, growing to heights of 25-30 feet. The tree is a member of the Rosaceae family and common names include hawthorn, English hawthorn, May bush, and whitehorn. Large bunches of fragrant white or pink flowers bloom in the spring and develop into small, bright red, apple-shaped fruit in the autumn.

Active Constituents

The primary cardiovascular protective activity of the plant is generally attributed to its flavonoid content, particularly the oligomeric proanthocyanidins (OPCs). The OPCs are highly concentrated in the leaves, berries, and flowers and are responsible for providing the pigment that colors the berries. These flavonoids have very strong vitamin P (also known as citrin bioflavonoid) activity, working synergistically with vitamin C to promote capillary stability. Other constituents of Crataegus include quercetin, quercetrin, triterpene saponins, vitamin C, and several cardioactive amines.

Mechanisms of Action

Because of its high flavonoid content, particularly the OPCs, Crataegus has significant antioxidant activity. Crataegus oxyacantha extract has been shown to reduce oxidative stress in reperfused myocardium and appears to inhibit apoptosis, resulting in a cardioprotective effect.

In addition, Crataegus increases coronary blood flow, enhancing oxygen flow and utilization by the heart. Crataegus extracts also have a positive inotropic effect on the contraction amplitude of myocytes. Crataegus exerts a simultaneous cardiotropic and vasodilatory action. Because of these actions, it can be safely and effectively utilized for cardiac conditions for which digitalis is not yet indicated. Due to the flavonoid content, extracts of this herb exert considerable collagen-stabilizing effects, enhancing integrity of blood vessels. In rats fed a hyperlipidemic diet, extracts of Crataegus prevented elevation of plasma lipids, including total cholesterol, triglycerides, and...
LDL- and VLDL-fractions.\textsuperscript{13} Crataegus up-regulates hepatic LDL-receptors, resulting in greater influx of plasma LDL-cholesterol into the liver. It also prevents the accumulation of cholesterol in the liver by enhancing cholesterol degradation to bile acids, promoting bile flow, and suppressing cholesterol biosynthesis.\textsuperscript{14}

**Clinical Indications**

Crataegus provides effective and low-risk phytotherapy for patients with coronary heart disease, atherosclerosis, hypertension, or hypercholesterolemia.

**Congestive Heart Failure**

Research indicates administration of Crataegus provides subjective and objective benefits in individuals with signs and symptoms of mild congestive heart failure (CHF) New York Heart Association stage II (NYHA-II). Over a period of eight weeks, supplementation with Crataegus resulted in a clear improvement in the performance of the heart. Patients reported improvement in subjective symptoms, such as reduced performance, shortness of breath, and ankle edema.\textsuperscript{5} A large multi-center observational study demonstrated 450 mg Crataegus extract WS\textsuperscript{®} 1442 (standardized to 18.75\% OPC) given twice daily for 24 weeks signifcantly improved exercise tolerance and dyspnea, fatigue, blood pressure, ejection fraction, and resting pulse in 1,011 patients with NYHA-II cardiac insuffciency. Ankle edema and nocturia also were signifcantly decreased.

Physicians reported treatment was well tolerated in most patients and had a good or very good efficacy.\textsuperscript{15}

In a randomized, placebo-controlled trial, 209 Germans (average age, 67.6 years) with NYHA-III cardiac insuffciency were supplemented with 1,800 mg Crataegus extract WS 1442 daily for 16 weeks. Compared to placebo, Crataegus resulted in a statistically significant improvement in maximal tolerated workload during exercise under standardized loading on a bicycle ergometer.\textsuperscript{16}

In the SPICE trial, a long-term, randomized, double-blind, placebo-controlled, multi-center study, 2,681 patients with NYHA-II or -III CHF and left ventricular ejection fraction (LVEF) ≤35 percent received 900 mg WS 1422 or placebo daily for 24 months in addition to regular treatments (beta-blockers, angiotensin converting enzyme [ACE] inhibitors, diuretics, and digoxin). Primary endpoint was time until first cardiac event. For those in the treatment group the average time to first cardiac event was 620 days, compared to 606 days for those in the placebo group. Although the difference between the two groups did not reach statistical significance for the primary endpoint, a trend toward cardiac mortality reduction was observed in the treatment group. Furthermore, in a subgroup of 1,139 patients with initial LVEF between 25 and 35 percent, cardiac mortality was decreased by 20 percent and sudden cardiac death by 39.7 percent compared to placebo. The treatment was well tolerated with no significant side effects or drug interactions reported.\textsuperscript{17}

**Hypertension**

Crataegus exerts mild blood pressure-lowering activity, which appears to be a result of a number of diverse pharmacological effects. It dilates coronary vessels,\textsuperscript{18} inhibits ACE,\textsuperscript{13} acts as an inotropic agent,\textsuperscript{19} and possesses mild diuretic activity.\textsuperscript{4} A randomized, placebo-controlled, pilot study of 36 untreated, mildly hypertensive, middle-aged subjects (18 males, 18 females) investigated the hypotensive effects of a standardized Crataegus extract and magnesium (both separately and in combination) for 10 weeks. Subjects were divided into four groups: 600 mg magnesium daily, 500 mg Crataegus extract daily, a two-tablet combination of magnesium and Crataegus (same dosages as in groups 1 and 2), or cellulose placebo. Subjects were assessed at baseline and at five and 10 weeks for anthropometric measurement, dietary patterns, and blood pressure. Both systolic and diastolic blood pressure decreased in all treatment groups, but analysis revealed no clear benefit of one group over another. However, when looking at resting diastolic blood pressure alone, subjects receiving Crataegus extract demonstrated a significant decrease at week 10 compared to the other groups. Interestingly, this group also showed a trend toward reduced anxiety episodes compared to the other groups.\textsuperscript{20}

Crataegus extract has also been shown to lower blood pressure in type 2 diabetics taking prescription medications for hyperglycemia. In a randomized, double-blind, parallel, placebo-controlled trial, 80 type 2 diabetics (mean age, 60) with diastolic blood pressures between 85-95 mmHg and systolic blood pressures between 145-165 mmHg were randomized to receive 1,200 mg Crataegus extract (n=40) or placebo (n=40) daily.\textsuperscript{21} Study length was 16 weeks and patients were assessed at baseline and at eight and 16 weeks for anthropometric...
measurements and blood pressure (primary outcome was diastolic blood pressure). Subjects were also assessed for electrolytes, liver and kidney function, blood glucose, hemoglobin A1C, and fructosamine at baseline and 16 weeks. At 16 weeks those in the Crataegus group showed a statistically significant (although perhaps not clinically significant) reduction of 2.6 mmHg in diastolic blood pressure compared to placebo. No other statistically significant differences were reported between the placebo and treatment groups. The Crataegus extract was well tolerated and no adverse effects or drug interactions were reported.

**Hyperlipidemia**

Crataegus extract demonstrates a lipid-lowering effect in mouse and rat models of hyperlipidemia. In a mouse study, group A mice (n=6) were fed a normal diet and served as the negative control, while group B mice (n=6) were fed a high cholesterol diet (HCD) and demonstrated higher blood lipid levels compared to group A, thus serving as the positive control. Group C mice (n=6) were fed an HCD and simvastatin, and group D mice (n=6) were fed an HCD and a Crataegus fruit-kiwi fruit extract for eight weeks. Mice in groups C and D both demonstrated a significant reduction in triglyceride levels as well as the LDL- to total-cholesterol ratio. Only mice in the Crataegus-kiwi extract group demonstrated a reduction in LDL levels.22 Another study in mice investigated the mechanism behind hawthorn flavonoids’ effect on blood lipid levels and found they significantly up-regulate adipogenesis gene expression and modulate both lipogenesis and lipolysis, resulting in decreased blood lipid concentrations.23

**Drug-Botanical Interactions**

The root, leaves, fruit, and flowers of Crataegus contain cardioactive compounds. Crataegus preparations may have a potentiating effect on digitalis, anti-hypertensive agents, and lipid-lowering medications, and concomitant use may necessitate a reduction in the dosage of these drugs.24

**Side Effects and Toxicity**

Crataegus has been shown to have low toxicity, with an LD₅₀ of 25 mg/kg.25 The German Commission E monograph states that mice and rats have been safely given a standardized extract at doses up to 3 g/kg body weight.26 Serious side effects are not associated with use of Crataegus extracts, although mild, transient side effects including dizziness, gastrointestinal complaints, headaches, and heart palpitations have occasionally been reported.27

**Dosage**

Positive effects from supplementation will usually be observed within the first two weeks. In most instances, as a cardiac tonic, Crataegus is administered for prolonged intervals. Dosages vary depending on the concentration of the extract. A typical therapeutic dose of an extract standardized to contain 1.8 percent vitexin-4 rhamnoside is 100-250 mg three times daily. A standardized extract containing 18-percent OPCs is dosed in the range of 250-500 mg daily.

**References**


