

# Hawthorn Extract: Is It Time to Turn Over a New Leaf?

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**H**awthorn (*Crataegus oxyacantha*), also known as haw, maybush, or whitehorn, is a fruit-bearing shrub with thorny branches, deciduous leaves, and white flowers that contain flavonoids, amines, triterpene, saponins, and oligomeric procyanidins (1). These compounds have inotropic, vasodilating, lipid-lowering, antioxidant, and anti-inflammatory properties, which may protect against reperfusion-related myocardial damage and arrhythmias (2,3). This herbal remedy has limited apparent adverse effects, including rash, sweating, palpitations, dizziness, agitation, sleepiness, and gastrointestinal symptoms. Although hawthorn extract has been used for various medical complaints for more than 700 years, it has only been recently evaluated systematically for heart disease, particularly chronic heart failure.

In this issue of *The American Journal of Medicine*, Pittler et al. (4) present a meta-analysis of randomized clinical trials of hawthorn extract in patients with chronic heart failure (New York Heart Association class I to III). They found that use of hawthorn extract was associated with a modest improvement in maximal exercise workload. By performing a thorough search of eligible studies and by restricting their analysis to double-blind, randomized, controlled trials, the authors minimized bias and enhanced the validity of their analysis.

Should we, however, exchange digitalis leaf for hawthorn extract? Despite the positive results of the meta-analysis, there are lingering concerns. First, use of angiotensin-converting enzyme inhibitors was either not allowed or not reported in four trials included in the meta-analysis. There has been only one trial comparing hawthorn extract with an established agent in the treatment of heart failure (5). Whether hawthorn extract provides clinical benefits beyond those of proven heart failure drugs remains uncertain. Second, the observed improvement in maximal exercise workload was derived from a total of 310 randomized patients with only 3 to 16 weeks of follow-up. There has been no long-term randomized trial of this agent, and many inotropic predecessors have improved symptoms and exercise capacity in

the short term at the expense of increased mortality with continued use (6). Studies involving larger samples and a longer follow-up will be required to assess the effects of hawthorn extract on mortality as well as on quality of life and hospitalization. To that end, the Survival and Prognosis: Investigation of Crataegus Extract—WS1442 (SPICE) trial will enroll approximately 2300 patients from 120 international centers and evaluate the long-term effects (24 months) of a standard preparation of hawthorn extract, as compared with placebo, on hospitalizations and mortality in patients with modest heart failure and an established standard medical regimen (7). Results of this trial, which are expected to be available during 2003–2004, should help determine if hawthorn extract is appropriate as therapy for heart failure.

Herbal therapy is currently estimated to be used by 12.1% to 14% of the U.S. population, an increase from 2.5% in 1990 (8,9). Approximately 16% to 18.4% of patients taking prescription medication also take herbal remedies. Unfortunately, less than 40% of these patients inform their physicians that they are taking herbal treatments (8,9). Hence, it is important that physicians inquire about their patients' use of alternative therapies and become knowledgeable about the effects and potential adverse effects of commonly used agents. In addition, despite the limited profit motive for rigorous investigation of these agents because of less easily obtained patent protection to those companies studying or manufacturing herbal compounds (10), we must evaluate herbal agents as carefully as we do newly synthesized drugs. Finally, we cannot allow herbal treatments to be unregulated, exposing patients to false claims and increased medical risk based on nonstandard preparations and contaminants in these products.

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