

Name of Herb or Supplement: Hawthorn



Scientific and Common names:

Most common species: *Crataegus monogyna*, *Crataegus oxyacantha* (aka *laevigata*)¹
Common names: English Hawthorn^{2,3}, One-seed Hawthorn², Haw²⁻³, May², Maybush,²⁻³ whitethorn,²⁻³ *Crataegi Folium cum flore*.²

Description of active ingredients:

The active ingredients include triterpene acid,³⁻⁴ oligomeric procyanidins (OPCs)¹⁻³ and flavonoids:¹⁻³ vitexin,¹⁻² quercetin,¹ hyperoside¹⁻² and rutin.¹⁻² Non-active components include: cardiogenic amines, pectin, crategolic acid, citric acid, chlorogenic acid, tartaric acid, tannins, triterpenoids and coumarins.¹ It is thought that all portions of the Hawthorn plant contain the same active ingredients but in different proportions.¹

MOA:

Hawthorn is used to treat a variety of cardiovascular problems. Such problems include an arrhythmic, mild to moderate heart failure, high cholesterol, and to raise or lower blood pressure. The flavonoids in Hawthorn are thought to interrupt the angiotensin converting enzymes, causing vasodilation and improved circulation.¹ Rutin (a flavonoid) and other unknown components are thought to re-build the collagen fibers in the outer layers of the blood vessels.^{1,3} This would improve the integrity of the blood vessels.^{1,3} The antioxidants are thought to prevent further deterioration, promote blood vessel health and reduce inflammation.¹ Triterpenoids, like triterpene carboxylic acid and the flavonoids are thought to be vasodilators.^{1,3} The triterpene carboxylic acid is thought to vasodilate the coronary blood vessels.³ One study identified the OPCs as the major cause of vasodilation induction.⁴ The flavonoids dilate blood vessels by activating the endothelium derived relaxing factor (nitric oxide) and by inhibiting phosphodiesterase.³ Vasodilation decreases peripheral vascular resistance³. The inhibition of phosphodiesterase causes an increase in cAMP.² The increased cAMP leads to vasodilation, increased coronary blood flow and positive inotropic effects.² The positive inotropic effects are thought to be caused by increasing the intracellular concentrations of calcium,^{3,5} inhibiting 3', 5'-cyclic adenosine monophosphate phosphodiesterase³ and/or possibly inhibiting the sodium/potassium adenosine

Original Author Christa Dierking

Reviewed 5/12/03 Susan Paulsen Pharm D

triphosphatase pump.⁵ Hawthorn has been shown to have an anti-arrhythmic effect by prolonging the refractory period in animals,³⁻⁵ but it is controversial whether this is a true prolongation or if hawthorn just has less pro-arrhythmic actions when compared to other positive inotropic agents.³ OPCs are thought to function as free-radical scavengers.³

Hawthorn has been shown to decrease total cholesterol, triglycerides and low-density lipoprotein (LDL) levels.¹⁻⁵ This may be due to several possible mechanisms: stimulating an up-regulation of LDL receptors, increased breakdown of cholesterol to bile acids and suppressed cholesterol synthesis.³⁻⁵ These effects are possibly caused by select OPCs, triterpene saponins and quercetin.⁴ A few components have been reported to inhibit human LDL oxidation.⁴ These components include epicatechin (OPC), rutin, hyperoside and isoquercitrin.⁴

Current indications and efficacy:

Only the leaf/ flower combination has been shown to be efficacious in the early stages of heart failure^{1,9}. The majority of clinical trials involving hawthorn examine its role in NYHA stage II heart failure.³⁻⁴ Of the randomized, double-blind, placebo controlled studies, the patients taking hawthorn reported experiencing fewer symptoms, had improved exercise tolerance and a slightly improved blood pressure to heart rate product.³⁻⁴ Symptoms include dyspnea, fatigue and palpitations. Specific symptoms for each study were not included and the primary research was not available. These trials included few patients 30-136 and had durations of eight weeks or less.³⁻⁴ One multi-center, double-blind trial compared hawthorn (extract LI 132) 300mg tid to captopril 12.5mg tid in patients with NYHA functional class II heart failure over an eight week period.^{3,5} Both groups significantly improved in exercise tolerance as evaluated by bicycle ergometry, decreased in blood pressure to heart rate product and decreased frequency of symptoms by 50% when compared to patients baseline characteristics.³ There were no statistically significant differences between the captopril and hawthorn groups.³ The increased exercise tolerance was statistically significant ($p < 0.001$), but clinical significance was not mentioned.³ Unfortunately, this article is only published in German, and was not available for more specific details.

There has only been one trial in humans specifically regarding hawthorn's effects on lipids.³ Lipid effects were a primary outcome in this trial.¹⁰ Among the thirty patients involved, there was a statistically significant decrease in total cholesterol, LDL and HDL, with a $p < 0.001$.¹⁰ The hawthorn preparation contained several other antioxidants, so this study has unknown bearing on hawthorn's specific activities.³ The drink studied contained haw flavones, sugar, low levels of potassium, sodium, calcium, magnesium, copper and vitamin C, medium levels of zinc, iron, vitamin B1 and B2.¹⁰ This study reported an average decrease in LDL of 16mg/dL, an increase in HDL of about 3mg/dL, and a decrease in total cholesterol of 45mg/dL.¹⁰ All other trials were conducted in animals or were secondary endpoints in human trials.³⁻⁴ There are no trials examining arrhythmic activities in humans.³⁻⁴

Suggested uses include: angina pectoris,^{1,3-5} arrhythmias (mild),^{1,3-5} arteriosclerosis/ dyslipidemia,^{1,3-5} arthritis,¹ balance blood pressure,¹ improve circulation,¹ fluid retention,^{1,3-4} hypertension,⁵ heart palpitations,¹ heart weakness (myocardial insufficiency),^{1,4} hemorrhoids,¹ mild mitral valve stenosis,¹ phlebitis,¹ sore throat,¹ varicose ulcers,¹ and varicose veins.¹

Original Author Christa Dierking

Reviewed 5/12/03 Susan Paulsen Pharm D

Contraindications/ allergies

Hawthorn is contraindicated if patient has a known allergy (rash or allergic rhinitis symptoms).⁶ It is contraindicated in pregnancy as it may relax organ smooth muscle (uterus);² however, a different source recommended low doses in pregnancy as it may aid in controlling high blood pressure, varicose veins, irregular heartbeat and thrombosis.¹ No known data on teratogenicity and lactation. No data available on efficacy in more advanced stages of heart failure.

Dosage forms, recommended doses, duration

Powder generally standardized to 2.2% flavonoid or 18.75% oligomeric procyanidins¹; can vary between 3.5-19.8 mg total flavonoids calculated as hyperoside, or 30-160mg procyanidins².

Dosage form	Adults (>12yo)	7-12 yo	3-7	< 3 yo	Alternative adult dose
Tincture (for everyday/ long-term use) ¹	5ml tincture diluted into 25ml water bid-tid. ¹	half adult dose: 2.5 ml diluted into 25ml bid-tid ¹	quarter adult dose: 1.25ml diluted in 25ml bid-tid ¹	2-5 drops daily 1. ¹	20 drops bid-tid ²
Decoction or infusion (tea) ¹	2-3cups qd ¹	half adult dose (1-1.5 cups) qd ¹	quarter adult dose (0.5-0.75cups) qd ¹	a few sips up to 30ml/day ¹	Tea: 1tsp leaves and flowers, steep 20 min, bid-tid (strain before drinking) ²
Capsules: contain 250-350 mg powdered herb ¹	2 capsules bid-qid ¹	1capsule bid-qid ¹	1capsule qd-bid. Do not give to children under 5 yo. ¹	do not give to children under 5 ¹	200-500 mg powder tid or dry extract 160-900mg divided bid-tid. ²
Syrup ¹	6-12tbsp (90-180ml) qd ¹	half adult dose, 3-7tbsp (45-90ml) qd ¹	quarter adult dose: 1.5-3tbsp (22.5-45ml) qd ¹	5-15ml qd ¹	
Dried Fruit	300-1000mg tid ²				
LI 132 (Faros 300, Lichtwer Pharma) ³	300mg tid ³ Or 100mg tid				

Drug interactions and Drug-disease interactions

Hawthorn may potentiate the effects of *hypertension medications*.¹⁻⁵ Recommend not using this with *beta-blocker* therapy because of the potential to increase BP.¹ Caution should be taken when combining with other herbs containing *cardiac glycosides* such as Foxglove (*digitalis*),¹⁻² Lily-of-the-Valley (*convallaria*),¹⁻² black hellebore,² Canadian hemp root,² *digitalis* leaf,² hedge mustard,² figwort,² motherwort,² oleander leaf,² pheasant's eye plant,² pleurisy root,² squill bulb leaf scales,² and *strophanthus* seeds.² Use with caution when combining *other herbs* that have cardiovascular activities: calamus, cereus, cola, coltsfoot, devil's claw, European mistletoe, fenugreek, fumitory, ginger, Panax ginseng, white horehound, mate, parsley, quassia, scotch broom flower, shepherd's purse and wild carrot.² Hawthorn may potentiate *CNS depressants* and *digoxin*.² Hawthorn may interfere with cardiovascular diseases and the treatments for these diseases; patients should be monitored closely.^{1-5, 7}

Hawthorn has also been shown to inhibit the second stage of platelet aggregation.⁸ The second phase of platelet aggregation involves granule release of serotonin, ADP and ATP to further potentiate the clot.⁸ Tannins can also interfere with platelet aggregation, but the inhibition continued after the tannins were removed.⁸ In vitro, the hawthorn extract inhibited platelet aggregation up to 15% and serotonin release by up to 85%.⁸ Caution should be used in patients on *anticoagulant* or *antiplatelet* therapy.⁵ There are no case reports of bleed.⁵

Other Safety issues

No pharmacokinetic information is available for humans.^{4,9} Teas are not standardized as they can be made from a variety of sources, including fresh plant sources. Adverse effects may include mild rash, headache, sweating, dizziness, palpitations, sleepiness, agitation, and gastrointestinal symptoms.^{2,3}

References

1. Davies JR. Hawthorn. Shaftesbury, Dorset: Element Books; 2000.
2. Therapeutic Research Faculty (US). Natural Medicines Comprehensive Database. Stockton, CA: Therapeutic Research Faculty; 1999. p. 427-429.
3. Rigelsky JM, Sweet BV. Hawthorn: Pharmacology and therapeutic uses. Am J Health-Syst Pharm 2002; 59: 417-422.
4. Chang Q, Zuo Z, Harrison F, Chow MS. Hawthorn. J Clin Pharmacol 2002; 42: 605-612.
5. Dennehy C. Botanicals in cardiovascular health. Clin Obstet & Gyn. 2001; 44: 814-823.
6. Steinman HK, Lovell CR, Cronin E. Immediate-type hypersensitivity to *Crataegus monogyna* (hawthorn). Contact Dermatitis 1984; 11: 321.
7. DeSmet PA. Herbal Remedies. N Engl J Med 2002; 347: 2051.
8. Rogers KL, Grice ID, Griffiths LR. Inhibition of platelet aggregation and 5-HT release by extracts of Australian plants used traditionally as headache treatments. Eur J Pharm Sci 2000; 9: 355-363.

9. Blumenthal M, editor. The Complete German Commission E Monographs: Therapeutic guide to herbal medicines. Austin, TX: American Botanical Council. 1998. p.142-144.
10. Chen JD, Wu YZ, Tao ZL, Chen ZM, Liu XP. Hawthorn (Shan Zha) drink and its lowering effect on blood lipid levels in humans and rats. World Rev Nutr Diet 1995; 77:147-154.
Conversion of cholesterol results from mmol to mg/dL are based on the information from <http://heart.kumu.org/cholcomp.html>

(Other comments)

I would not recommend the use of this herb without the physician's knowledge. Hawthorn does appear efficacious; however, the patients most likely to need this drug are also likely to be taking medications that can potentially interact with it. These patients should be closely monitored for blood pressure changes, symptoms of worsening heart failure and changes in thrombosis formation. Counseling tips may include BP self-monitoring, increased bleeding/ bruising, heart rate and rhythm. Patients should discontinue the medication if no effect is noticed after six weeks of use or they develop signs/symptoms of worsening heart function or MI. The problem is that the herb may take several weeks to work, yet it has not been tested for longer than eight weeks. There is another investigation that has not been finished/published yet called the Survival and Prognosis Investigation of Crataegus Extract trial examining the addition of hawthorn to conventional drug treatments.⁹ This may provide insight into appropriate length of therapy.

A brief description of select trials on Hawthorn can be accessed at <http://floraleads.net/hawthorninfo.htm> This website has short abstracts of several trials, some of which are translated from German. This may be a good referral website if patients are interested in finding out more about Hawthorn. Be aware that the website does not include specifics, only statistically significant results. It does not mention any clinical significance of findings.