

Hawthorn

Species (Family)

- (i) *Crataegus laevigata* (Pois) DC. (Rosaceae)
- (ii) *Crataegus monogyna* Jacq.

Synonym(s)

Whitethorn

Part(s) Used

Fruit

Pharmacopoeial and Other Monographs

American Herbal Pharmacopoeia^(G1)
BHP 1996^(G9)
BP 2001^(G15)
Complete German Commission E^(G3)
ESCOP 1999^(G52)
Martindale 32nd edition^(G43)
Mills and Bone^(G50)
PDR for Herbal Medicines 2nd edition^(G36)
Ph Eur 2002^(G28)

Legal Category (Licensed Products)

Hawthorn is not included in the GSL.^(G37)

Constituents^(G1, G2, G22, G62, G64)

Amines Phenylethylamine, *O*-methoxyphenethylamine and tyramine.⁽¹⁾

Flavonoids Flavonol (e.g. kaempferol, quercetin) and flavone (e.g. apigenin, luteolin) derivatives, rutin, hyperoside, vitexin glycosides, orientin glycosides⁽²⁻⁵⁾ and procyanidins.^(6,7)

Tannins Pharmacopoeial standard not less than 1.0% procyanidins, condensed (proanthocyanidins).

Other constituents Cyanogenetic glycosides and saponins.

Food Use

Hawthorn is not commonly used in foods. It is listed by the Council of Europe as a natural source of food flavouring (category N2). This category indicates

that hawthorn can be added to foodstuffs in small quantities, with a possible limitation of an active principle (as yet unspecified) in the final product.^(G16)

Herbal Use^(G2, G3, G7, G43, G52)

Hawthorn is stated to possess cardiotonic, coronary vasodilator and hypotensive properties. Traditionally, it has been used for cardiac failure, myocardial weakness, paroxysmal tachycardia, hypertension, arteriosclerosis and Buerger's disease. The German Commission E did not approve therapeutic use.^(G3)

Dosage

Dried fruit 0.3–1.0 g or by infusion three times daily.^(G7)

Liquid extract 0.5–1.0 mL (1:1 in 25% alcohol) three times daily.^(G7)

Tincture 1–2 mL (1:5 in 45% alcohol) three times daily.^(G7)

Pharmacological Actions

In vitro and animal studies

Cardiovascular activity has been documented for hawthorn and attributed to the flavonoid components, in particular the procyanidins. Hawthorn extracts have been documented to increase coronary blood flow both *in vitro* (in the guinea-pig heart) and *in vivo* (in the cat, dog and rabbit), reduce blood pressure *in vivo* (in the cat, dog, rabbit and rat), increase (head, skeletal muscle and kidney) and reduce (skin, gastrointestinal tract) peripheral blood flow *in vivo* (in the dog) and reduce peripheral resistance *in vivo* (in the dog).^(6,8-13) The hypotensive activity of hawthorn has been attributed to a vasodilation action rather than via adrenergic, muscarinic or histaminergic receptors.⁽¹²⁾ Beta-adrenoceptor blocking activity (versus adrenaline-induced tachycardia) has been exhibited *in vivo* in the dog and *in vitro* in the frog heart using flower, leaf and fruit extracts standardised on their procyanidin content.⁽⁶⁾ The authors reported a direct relationship between the concentration of procyanidin and observed actions.

Negative chronotropic and positive inotropic actions have been observed *in vitro* using the guinea-pig heart and attributed to flavonoid and proanthocyanidin fractions.⁽¹⁴⁾ A positive inotropic effect has also been exhibited by amine constituents *in vitro* using guinea-pig papillary muscle.⁽¹⁾

Hawthorn extracts have also been reported to lack any effect on the heart rate and muscle contractility in studies that have observed an effect on blood pressure in the dog and rat.^(11,12) Hawthorn extracts have exhibited some prophylactic anti-arrhythmic activity in rabbits administered intravenous aconitine.⁽¹⁵⁾ Extracts infused after aconitine did not affect the induced arrhythmias. *In vitro*, vitexin rhamnoside has been reported to have no effect on the action of ouabain and aconitine.⁽¹⁵⁾ A crude extract of *Crataegus pinnatifida* Bge. var *major* N.E.Br. and the flavonoid vitexin rhamnoside have been reported to exert a protective action on experimental ischaemic myocardium in anaesthetised dogs.⁽¹⁶⁾ The extracts were observed to decrease left ventricular work, decrease the consumption of oxygen index, and increase coronary sinus blood oxygen concentrations, resulting in a decrease in oxygen consumption and balance of oxygen metabolism. In contrast to other studies, an increase in coronary blood flow was not observed. The authors attributed these opposing results to the variation in concentrations of active constituents between the different plant parts. *In vitro*, vitexin rhamnoside has been reported to exert a protective action towards cardiac cells deprived of oxygen and glucose.⁽¹⁷⁾

A mild CNS-depressant effect has been documented in mice that received oral administration of hawthorn flower extracts.⁽¹⁸⁾ An increase in barbiturate sleeping time and a decrease in spontaneous basal motility were the most noticeable effects.

Free radicals have been linked with the ageing process. When fed to mice, a hawthorn fruit (*C. pinnatifida*) extract has been reported to enhance the action of superoxide dismutase (SOD), which promotes the scavenging of free radicals.⁽¹⁹⁾ An inhibition of lipid peroxidation, which can be caused by highly reactive free radicals was also documented.⁽¹⁹⁾ The pharmacological actions of leaf with flowers include increase in cardiac contractility, increase in coronary blood flow and myocardial circulation, protection from ischaemic damage and decrease of peripheral vascular resistance.^(G52)

Clinical studies

The effects of a commercial preparation containing 30 mg hawthorn extract standardised to 1 mg procyanidins were assessed in a double-blind, placebo-controlled study involving 80 patients.⁽²⁰⁾ Haw-

thorn extract was reported to exhibit greater overall improvement of cardiac function and of subjective symptoms, such as dyspnoea and palpitations, compared with placebo. Improvements in ECG recordings were not found to differ between the two groups.

A commercial product containing hawthorn, valerian, camphor and cereus was given to 2243 patients with functional cardiovascular disorders and/or hypotension or meteorosensitivity in an open multicentre study.⁽²¹⁾ An improvement in 84% of treated individuals was reported.

In a randomised, double-blind, controlled trial involving 60 patients with stable angina, a commercial hawthorn preparation (60 mg three times daily) was reported to increase coronary perfusion and to economise myocardial oxygen consumption.⁽²²⁾

A commercial hawthorn/passionflower extract (standardised on flavone and proanthocyanidin content) 6 mL daily for 42 days has been assessed in a randomised, double-blind, placebo-controlled trial involving 40 patients with chronic heart failure.⁽²³⁾ Significant improvements were noted for the active group, compared with placebo, in exercise capacity, heart rate at rest, diastolic blood pressure at rest, and concentrations of total plasma cholesterol and low-density lipids. Non-significant improvements were noted in the active group for maximum exercise capacity, breathlessness, and physical performance. The authors commented that a higher dose of the extract administered over a longer period was necessary for further investigation of the observed improvements.⁽²³⁾ Clinical studies with standardised extracts of leaf with flowers have demonstrated beneficial effects in patients with cardiac insufficiency.^(G52)

Side-effects, Toxicity

Nausea⁽²⁰⁾ and fatigue, sweating and rash on the hands⁽²³⁾ have been reported as side-effects in clinical trials using commercial preparations of hawthorn.⁽²⁰⁾

General symptoms of acute toxicity observed in a number of animal models (e.g. guinea-pig, frog, tortoise, cat, rabbit, rat) have been documented as bradycardia and respiratory depression leading to cardiac arrest and respiratory paralysis.⁽⁸⁻¹⁰⁾ Acute toxicity (LD₅₀) of isolated constituents (mainly flavonoids) has been documented as 50–2600 mg/kg (by intravenous injection) and 6 g/kg (by mouth) in various animal preparations.⁽⁸⁻¹⁰⁾ The documented acute toxicity of commercial hawthorn preparations has also been reviewed.⁽⁸⁻¹⁰⁾

Contra-indications, Warnings

Hawthorn has been reported to exhibit many cardiovascular activities and as such may affect the existing therapy of patients with various cardiovascular disorders such as hypertension, hypotension and cardiac disorders. These patient groups are likely to be most susceptible to the pharmacological actions of hawthorn.

Pregnancy and lactation *In vivo* and *in vitro* utero-activity (reduction in tone and motility) has been documented for hawthorn extracts.⁽⁸⁻¹⁰⁾ In view of the pharmacological activities described for hawthorn, it should not be taken during pregnancy and lactation.

Pharmaceutical Comment

Hawthorn is characterised by its phenolic constituents, in particular the flavonoid components to which many of the pharmacological properties associated with hawthorn have been attributed. Pharmacological actions documented in both animal and human studies support the traditional actions of hawthorn and include cardioactive, hypotensive and coronary vasodilator.⁽²⁴⁾ Separate monographs for the fruit (berries) and leaf with flowers appear in the British Pharmacopoeia and European Pharmacopoeia.^(G15,G28) The German Commission E did not approve the use of fruit for therapeutic purposes on the grounds of insufficient evidence. There is some evidence from clinical trials to support the use of the standardised extracts of leaf with flower for cardiac insufficiency. In view of the nature of the actions documented for hawthorn, it is not suitable for self-medication.

References

See also General References G1, G2, G3, G9, G15, G16, G18, G22, G28, G31, G32, G36, G43, G50, G52, G56, G62 and G64.

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