

# Hawthorn SAP

Science-based Hawthorn for Cardiovascular Health\*

Widely recorded in traditional medicine for its medicinal properties, hawthorn (*Crataegus laevigata*) has been extensively studied for its beneficial effects in cardiovascular health.\* Its unique chemical composition rich in flavonoids and oligomeric proanthocyanidins, especially vitexin are suggested to exert antiarrhythmic, hypotensive and hypolipidemic effects.\* Preclinical evidence shows support for the cholesterol lowering effects of hawthorn with a positive inotropic effect, in addition to its antioxidant effect exhibited by lowering reactive oxygen species and reducing expression of pro-inflammatory cytokines.\* Clinical studies show improvement of coronary heart disease markers in diabetic patients, combined with hypotensive effects.\* In addition, research evidence indicates the potential of hawthorn in reducing incidence of cardiac death in patients with congestive heart failure.\* Some of the postulated mechanisms of action purported to the benefits of hawthorn include inhibition of phosphodiesterase activity, increasing the levels of cAMP in cardiac cells, inhibition of angiotensin converting enzyme which exerts a vasodilating and hypotensive effect, lowering levels of LDL cholesterol by increasing LDL breakdown through hepatic receptors, antioxidant effect by increasing nitric oxide production, and inhibition of the Na<sup>+</sup>/K<sup>+</sup>-ATPase pump in cardiac muscles.\*

**Hawthorn SAP** provides high quality hawthorn berry extract standardized to vitexin that can help maintain and support cardiovascular health, manage hypertension and improve inflammatory responses.\*

## SUPPLEMENT FACTS

Serving Size: 1 Capsule

	Amount Per Serving	% Daily Value
Hawthorn ( <i>Crataegus laevigata</i> ) berry extract providing 1.8% Vitexin	300 mg	**
Hawthorn berry ( <i>Crataegus laevigata</i> )	200 mg	**

\*\*Daily Value not established

**Other ingredients:** Hypromellose, purified water, vegetable magnesium stearate, and silicon dioxide.

**Contains no:** Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, starch, or sugar.

**This product is non-GMO and vegan friendly.**

**Hawthorn SAP** contains 90 capsules per bottle.

## DIRECTIONS FOR USE

**Adults:** 1-3 capsules daily or as directed by your healthcare practitioner. Use for a minimum of two months to see beneficial effects.

## INDICATIONS

**Hawthorn SAP** can help

- Maintain and support cardiovascular health.\*
- Manage elevated blood pressure levels.\*
- Promote a healthy inflammatory response.\*

## CAUTIONS AND WARNINGS

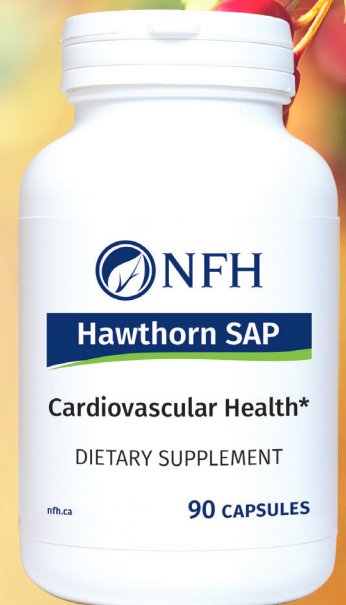
Consult a healthcare practitioner if symptoms persist or worsen. Consult a healthcare practitioner prior to use if you are taking cardiac glycosides such as digitalis/digoxin, or blood pressure medication.

**Do not use if seal is broken. Keep out of reach of children.**

## PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **Hawthorn SAP** have been tested by an ISO 17025 accredited third-party laboratory for identity, potency and purity.

\* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health



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**HAWTHORN- PHYTOCHEMISTRY AND MECHANISMS OF ACTION**

Hawthorn (*Crataegus laevigata*) is a member of the Rosaceae family and is also known by the common names such as English hawthorn, Maytree and Whitethorn. It is a fruit-bearing plant distributed in Europe, Asia, and North America with red berries being the most common. Hawthorn has a long history of traditional medicine use that ranges from treatment of diarrhea, diuretic, treating kidney stones and gall bladder disease, anti-spasmodic agent, and even treatment of insomnia and even asthma. [1] However, the most studied clinical application of this plant, as supported by preclinical and human clinical studies has been focused on its therapeutic potential in the mitigation of cardiovascular diseases. [1] Hawthorn has several bioactive compounds such as flavonoids (hyperoside, quercetin, quercitrin, hyperine), flavon-C-glycosides (vitexin, isovitexin, orientin, isoorientin), catechins, amines, triterpene saponins, and oligomeric proanthocyanidins (OPCs) which are suggested to contribute to its health benefits. Vitexin is specifically known for its cardiotoxic activity, while flavonoids and OPCs are generally responsible for antiarrhythmic, hypotensive and hypolipidemic activity of hawthorn. [2]

Another key feature that sets hawthorn apart is the high pectin content (about 20.5%). Pectin oligosaccharides in hawthorn have shown antibiotic, antioxidant, antiglycation and lipid lowering properties. [3] Several mechanisms of action have been proposed through which these phytochemicals exert their effects on the cardiovascular system. Some of these mechanisms include inhibition of phosphodiesterase activity, increasing the levels of cAMP in cardiac cells, inhibition of angiotensin converting enzyme which exerts a vasodilating and hypotensive effect, lowering levels of LDL cholesterol by increasing LDL breakdown through hepatic receptors, antioxidant effect by increasing nitric oxide production, and inhibition of the Na<sup>+</sup>/K<sup>+</sup>-ATPase pump in cardiac muscles. [4]

**PRECLINICAL EVIDENCE**

These mechanisms of action have been studied extensively through preclinical studies. Hawthorn administration has shown a positive effect by reducing intravascular cholesterol levels in a preclinical model. [5] These cholesterol-lowering effects may be due to the catechins and triterpene saponins in hawthorn through up-regulation of hepatic LDL receptors, enhancement of the breakdown of cholesterol to form bile acids, and suppression of cholesterol synthesis as possible mechanisms of action. [5] Using an automated *in vivo* platform with the aid of high-speed confocal microscopy, researchers were able to confirm the anti-hypercholesterolemic effect of hawthorn extract and its positive inotropic effect (the ability to increase the integrity of the blood vessel wall and improve coronary blood flow, and positive effects on oxygen utilization). [6]

*In vitro* testing of hawthorn on human keratinocytes stimulated by lipopolysaccharide showed a reduction in production of reactive oxygen species, with lower mRNA expression of pro-inflammatory cytokines and interleukins. [7] These anti-inflammatory effects have been previously observed on human neutrophils as well, where administration with hawthorn not only reduced lipopolysaccharide induced increase in tumor necrosis factor- $\alpha$  and interleukin-8, but also reduced extracellular calcium entry into neutrophils and increased elastase release, providing multiple functional benefits for the management of cardiovascular diseases. [8] In addition to cardiovascular benefits, hawthorn extract administration at 200 mg/kg in animal models showed significant reduction in paw edema, provided gastro-protective effect and even showed anti-microbial effects against gram positive bacteria such as *Listeria monocytogenes*, *Bacillus subtilis*, and *Micrococcus flavus*. [4]

**CLINICAL STUDIES**

Clinical studies, although few, show promising results with regards to the cardio-protective effects of hawthorn. In a recently conducted randomized double-blinded placebo-controlled trial, administration of 400 mg thrice daily of hawthorn extract to 49 diabetic participants for 6 months showed a significant reduction in neutrophil elastase (a biomarker of coronary heart disease) compared to the placebo. Additionally, hawthorn in conjunction with statins appeared to lower LDL cholesterol and non-HDL cholesterol, showing promising effects in diabetic patients suffering from cardiovascular diseases. [9] Another randomized, double-blind, placebo-controlled trial showed that administration of 900 mg daily of

hawthorn extract for 24 months in 1338 patients indicated that hawthorn administration may help reduce the risk towards sudden cardiac death in patients with congestive heart failure with no adverse reactions. [11]

In a multicenter, double-blind, placebo-controlled trial hawthorn extract (80 mg) was administered to 136 patients with NYHA (New York Heart Association) functional class II CHF or placebo twice daily for eight weeks. The extract showed a significant improvement in cardiac performance compared to the placebo including a significant difference in the patients' self-assessment of shortness of breath and ankle edema. [12, 13] In a high dosage study using a placebo-controlled, double-blind design, 78 patients with NYHA functional class II CHF were randomized to receive either a hawthorn extract at 200 mg three times daily or placebo for eight weeks. Using a bicycle exercise tolerance test, efficacy was assessed. The study results showed that patients who received the extract had significantly improved exercise tolerance, decreased systolic blood pressure and decreased heart rate, where no changes were observed in the placebo group. [13, 14]

In another high dosage randomized, double-blind study in 72 patients with moderately reduced left ventricular ejection fraction, hawthorn extract dosed at 300 mg three times daily compared to placebo improved oxygen uptake and increased the duration to reach the anaerobic threshold while exercising. [15]

**HYPOTENSIVE EFFECTS**

A pilot double blind study that observed the hypotensive effect of hawthorn extract showed that administration of 500-600 mg of hawthorn extract daily for 10 weeks had a promising trend of lowering resting diastolic blood pressure with a reduction in anxiety at week 10 (n=19). These findings although not statistically significant, point to the therapeutic potential of hawthorn as an anti-hypertensive adjunct. [10] Results from this pilot study were however further corroborated with a larger cohort in a randomized controlled trial, where 39 patients were assigned 1200mg daily hawthorn extract, and compared with 40 placebo participants for 16 weeks. The hawthorn administered group showed significantly greater reductions in mean diastolic blood pressure, with no herb-drug interactions or adverse reactions observed. [16]

Overall, the current evidence suggests that hawthorn extract could be a valuable and safe adjunct in cardiovascular therapy. However, more studies are warranted to confirm the existing evidence and also explore other benefits and clinical applications of hawthorn.

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