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# Hawthorn (*Crataegus oxyacantha*)

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## General Features

Hawthorn is a spiny shrub or tree, and is a member of the crataegus family. It has been used medicinally since ancient times and during the first century, Roman physicians used Hawthorn as a drug to treat a variety of heart and cardiovascular conditions. During the Middle Ages Hawthorn was used for the treatment of congestive heart failure (dropsy), an application that has proven to be valid according to modern day evidence-based research.<sup>1,11,12,13,14</sup>

## Principle Active Constituents

Hawthorn flowers, berries, and leaves contain flavonoid compounds that appear to account for its positive effects on cardiac function. These flavonoids account for the red color of Hawthorn berries. The flavonoids found in Hawthorn include oligomeric procyanidins (OPCs), vitexin, vitexin 4 – 0 – rhamnoside, quercetin, and hyperoside. Standardized extracts of Hawthorn are usually validated by their vitexin and procyanidin content, which ensure that sufficient levels of flavonoids are present to yield the desired outcomes on cardiovascular health.<sup>11,12,13,14</sup>

Hawthorn flower extract is the primary compound used medicinally and is particularly rich in the following flavonoids:

- Quercetin
- Quercetin-3-galactoside
- Vitexin
- Vitexin-4-rhamnoside

In addition to proanthocyanidins, Hawthorn extract also contains cardiogenic amines, which include:

- Phenylethylamine
- Methoxyphenylamine
- Tyramine
- Isobutylamine<sup>1,2,3</sup>

## Clinical Application and Mechanism of Action

### 1. Cardiovascular Effects:

Angina: Dilation of Coronary Vessels - Evidence exists to show that Hawthorn extract may improve coronary artery blood flow and strengthen the contractions of the heart muscle. This has led to findings that Hawthorn extract can benefit patients with a history of angina by preventing or reducing angina attacks and improving other indices of cardiovascular function, according to a small number of clinical trials.<sup>4,5,6,7,8,15,16</sup>

Congestive Heart Failure: Hawthorn increases cyclic AMP (adenosine monophosphate) in the Myocardium (heart muscle) due to its effects on inhibiting the enzyme phosphodiesterase, which breaks down cyclic AMP (cAMP). The oral administration of Hawthorn extract results in higher myocardial concentrations of cAMP in patients suffering from various cardiomyopathies (heart conditions). As cAMP can be further

phosphorylated to ADP (adenosine diphosphate) and then to ATP (adenosine triphosphate—the energy source used by the heart muscle to pump blood through the system), higher myocardial concentrations of cAMP enables the heart muscle to pump more efficiently. The net result is an increase in the heart muscle's force of contraction. This effect has been shown to be of great benefit for patients with congestive heart failure, who by definition, have a weakened heart muscle. A number of well-controlled clinical trials have demonstrated that Hawthorn extract can reverse many cases of congestive heart failure via its inotropic effect (increasing the amount of available energy) on cardiac muscle.<sup>9,10,11.</sup>

High Blood Pressure: Inhibits Angiotensin – Converting Enzyme (acting as an ACE-inhibitor) – by inhibiting the angiotensin-converting enzyme Hawthorn extract reduces the conversion of angiotensin I to angiotensin II, which is a potent constrictor of blood vessels and stimulates adrenal production of aldosterone. Thus, in a similar fashion to ACE-inhibitor drugs, Hawthorn extract has been shown to exert a blood pressure lowering effect. However, Hawthorn has been shown to have a modest effect on lowering blood pressure in hypertensive patients relative to more powerful ACE-inhibitor medications. In one study, systolic blood pressure dropped from 205 to 148 mm Hg, but other studies have shown a more modest reduction in blood pressure (e.g., systolic decline from 160 – 150 mm Hg, diastolic decline from 89 – 84 mm Hg) with Hawthorn extract supplementation.<sup>7,11,15</sup>

Clinical trials show that Hawthorn extract can be an effective adjunct to the lowering of high blood pressure, but its hypotensive effects often require two to four weeks to manifest themselves. Hawthorn does not further lower blood pressure in subjects who demonstrate normal blood pressure, but rather selectively appears to reduce blood pressure only in hypertensive individuals.<sup>23</sup>

Thus, the cardiovascular conditions that may be responsive to Hawthorn include congestive heart, angina, and high blood pressure. In particular, Hawthorn has a long history of use in the treatment of congestive heart failure.

Congestive Heart Failure Clinical Trials: At least 8 double-blind, placebo-controlled trials, involving a total of more than 400 participants, have shown that Hawthorn extract is an effective intervention for mild to moderate congestive heart failure.<sup>17</sup> One study, involving more than 200 patients, found that Hawthorn extract was helpful in more severe congestive heart failure cases.<sup>18</sup> Even in more severe cases of congestive heart failure patients receiving high dose Hawthorn extract reported improvement in subjective symptoms (shortness of breath, fatigue, etc.) as well as objective improvement in exercise capacity.<sup>18</sup> A comparative study has indicated that Hawthorn extract is about as effective as low dose captopril, a drug commonly used to treat congestive heart failure.<sup>19</sup>

Hawthorn appears to act in a similar manner as other cardiac glycoside drugs, such as digoxin and digitalis, which exert an inotropic effect on the myocardium; enhancing ATP production through bioenergetic pathways. Studies reveal that Hawthorn provides similar benefits as these drugs, and exhibits a much safer profile. Digoxin and related cardiac glycoside prescription drugs increase the strength of the heart pump, but also increase the likelihood of dangerous arrhythmias. This occurs because these drugs shorten the refractory period between heartbeats (the period in which the heart can not contract between beats), which increases the chances of premature beats arising from areas outside or inside the heart's natural pacemaker. In turn, this disturbs the necessary synchronized and rhythmic contraction

pattern that the heart muscle must follow to perform its function properly. The result is the development of cardiac arrhythmia, which can be life threatening. It is well documented that digoxin and related drugs have a narrow index of safety for this reason. In contrast to this, Hawthorn extract is able to strengthen the heart muscle, and has been shown to lengthen the refractory period between heartbeats, which reduces the likelihood of developing cardiac arrhythmias. As well, Hawthorn exhibits much lower toxicity than digoxin and is reported to have an enormously large range of safety, in regards to daily dosage (a number of studies have used doses as high as 600 mg per day with no significant side effects reported).<sup>20,21,22, 13, 15</sup>

The major precautionary note pertains to the fact that it is not known if Hawthorn can be used safely with other cardiac glycoside drugs or with other medications (usually ACE- inhibitors) that are now more commonly prescribed in the treatment of congestive heart failure.<sup>13</sup> Some authorities suggest that Hawthorn's effects are synergistic to the biological actions of cardiac glycoside drugs and ACE-inhibitors, indicating that they can be used concurrently as long as the attending physician is able to monitor patient response and adjust the dosing of these drugs accordingly.<sup>15</sup> From an historical standpoint, Hawthorn has been used alone and in combination with other cardiac glycoside drugs in the management of congestive heart failure.<sup>11, 15</sup>

Anti- Aging: (Author's Note) Hawthorn may be an important herb in the prevention of cardiovascular disease and age-related cardiac decline leading to the development of congestive heart failure. Studies demonstrate that after the age of 35- 40 the heart muscle appears to make less ATP energy in a certain percentage of individuals. This has been shown to result from a marked reduction in Coenzyme Q10 synthesis, which is required to maximize the conversion of ADP to ATP. Theoretically, supplementation with both Coenzyme Q10 and Hawthorn extract may help to stave off age-related declines in ATP production, due to their known inotropic effects on heart muscle. Many practitioners involved in anti-aging medicine subscribe to this practice and recommend these supplements on a preventive basis to their patients over 40 – 50 years of age. (see also Coenzyme Q10 in this document).

### Dosage and Standardized Grade

Hawthorn flower extract should be standardized to contain 18 - 20 percent procyanidins or 2 – 5% flavonoid content, of which at least 1.5% is the flavonoid vitexin.<sup>11,12,13,14,15</sup>

1. Congestive Heart Failure: In a 1993 study of 30 patients with congestive heart failure 80 mg of standardized Hawthorn extract taken twice per day for eight weeks showed a statistically significant improvement in heart function vs. the placebo. There were no side effects (Leuchtgens H, 1993). Blood pressure was also mildly reduced.<sup>10</sup> However, other studies have used 300 – 600 mg of Hawthorn extract, three times per day, and have shown good results in cases of congestive heart failure without generating any side effects. Thus, the dosage range for this application is vast, ranging from 80 to 600 mg, two to three times per day, and is based upon the severity of the condition; as more severe congestive heart failure has been shown to respond better to higher doses.<sup>11,12,13,14,15</sup>
2. Angina: 180 mg per day (e.g., 60 mg, three times per day)<sup>15</sup>
3. High Blood Pressure: 100 – 250 mg, one to three times per day<sup>23</sup>
4. Anti- Aging: For general prevention purposes 70-100 mg of standardized Hawthorn extract may be appropriate after age 40 – 50<sup>1,2,3,4,5,6,7</sup>

## Adverse Side Effects, Toxicity and Contraindications

Hawthorn is regarded as being very safe. The German Commission E lists no known risks, contraindications, or drug interactions with Hawthorn. Animals given very large doses of Hawthorn extract have not shown any signs of toxicity. In clinical trials with congestive heart failure and other cardiovascular patients, reported side effects have been rare, consisting of stomach upset and occasional allergic skin reaction.<sup>1,13,14,15</sup>

## Drug-Nutrient Interactions

Hawthorn may potentiate the action of the following drugs, and therefore, requires appropriate physician monitoring if taken concurrently with these medications. This is extremely important in the case of digitalis, digoxin and other cardiac glycoside drugs, as it is plausible that a drug nutrient interaction of this nature could lead to life threatening consequences.

Interactions of concern include:

1. Digitalis, digoxin and other cardiac glycoside medications<sup>24</sup>
2. Antiarrhythmic Medications<sup>25</sup>
3. Anti-hypertensive Medications: As Hawthorn extract is known to lower high blood pressure to some degree, it may work synergistically with a variety of antihypertensive drugs, reducing the required dosage of the drug.<sup>26, 27</sup>

### *Pregnancy and Lactation*

*During pregnancy and lactation, the only supplements that are considered safe include standard prenatal vitamin and mineral supplements. All other supplements or dose alterations may pose a threat to the developing fetus and there is generally insufficient evidence at this time to determine an absolute level of safety for most dietary supplements other than a prenatal supplement. Any supplementation practices beyond a prenatal supplement should involve the cooperation of the attending physician (e.g., magnesium and the treatment of preeclampsia.)*

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