

The Use of *Convallaria* and *Crataegus* in the Treatment of Cardiac Dysfunction

Jill Stansbury, ND^a
 Paul Saunders, PhD^b
 David Winston, RH(AHG)^c
 Eugene R. Zampieron, ND^d

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 DOI 10.14200/jrm.2012.1.1012

ABSTRACT

Herbal medicines have been effectively used for the treatment of cardiovascular diseases for many years. Herbs such as *Convallaria* (Lily of the Valley) root and *Crataegus* (Hawthorne) have shown significant benefits as adjunctive or stand alone therapies for the treatment of cardiac disorders such as arrhythmia, mitral valve prolapse and shortness of breath. *Convallaria* has been used for the treatment of congestive heart failure and cardiomyopathy, whereas *Crataegus* contains flavonoids with anti-inflammatory, anti-oxidant and protective cardiac effects. *Crataegus* functions as a natural angiotensin converting enzyme inhibitor, and it is therefore beneficial for the treatment of hypertension. *Convallaria* and *Crataegus* have been used in combination with other herbal remedies such as *Selenocereus* (Night Blooming Cereus), *Leonorus* (Motherwort), *Melissa* (Lemon Balm), *Lepidium* (Maca), and *Ginkgo* (Ginkgo). *Convallaria* may interact with digoxin and should not be used during pregnancy, whereas *Crataegus* is a safe herb when used as indicated. Although accidental poisoning resulting from the ingestion of *Convallaria* has been reported, toxicity from this medicinal herb is rare because of its poor absorption and short half life. Studies have shown that at the appropriate doses, *Convallaria* and *Crataegus* are safe and effective alternative treatments for the management of cardiac dysfunction.

Keywords: Cardiac dysfunction, *Convallaria*, *Crataegus*, Arrhythmia

CLINICAL IMPLICATIONS

There are effective herbal remedies to treat cardiac dysfunctions (*e.g.*, arrhythmias) that may complement or replace standard pharmaceutical options. In the 20th century, researchers have demonstrated that some herbal remedies not only improve cardiac health, but may even decrease the symptoms of cardiac dysfunction such that medications may be unnecessary (or the dosages reduced). Herbs used by Complementary Alternative Medicine (CAM) practitioners (such as *Convallaria* and *Crataegus*) are generally considered safe supplements. Modern clinical research suggests a significant benefit in symptom control and physiologic outcomes when *Crataegus* is used as an adjunctive treatment in patients with chronic heart failure.

KEY HERBS DISCUSSED

Convallaria (Lily of the Valley) root; *Crataegus* (Hawthorne) leaf, flower, and berry

PRIMARY INDICATIONS

tachycardia, mitral valve prolapse, shortness of breath, arrhythmia

ADJUNCTIVE OR STAND-ALONE TREATMENT

Both

DOSE OF BIOACTIVE CONSTITUENTS

Hawthorne (*Crataegus*) (whole plant extracts) 80-900 mg per day; containing 1.5 mg Vitexin (*Crataegus* flavanoid) *bid*
 Lily of the Valley Root (*Convallaria*) 100-400 mg per day, containing Convallatoxin (*Convallaria* alkaloid) 0.4 mg *bid*

SYNERGISTIC HERBAL FORMULA

Lily of the Valley (*Convallaria*), Hawthorne (*Crataegus*) Night Blooming Cereus (*Selenocereus*), Motherwort (*Leonorus*), Lemon Balm (*Melissa*), Maca (*Lepidium*), Ginkgo (*Ginkgo*) and bioflavonoids are among the herbal agents that may be complementary.

SIDE EFFECTS (AND CAUTIONS)

Hawthorne (*Crataegus*) can be safely consumed when used appropriately.

Lily of the Valley (*Convallaria*) should not be taken during pregnancy.

Convallaria may interact with digoxin. Cardiac patients being treated with herbal remedies specifically for *Convallaria* along with cardiac medications such as Digoxin should be evaluated for interactions to ensure pharmaceutical dosages are still appropriate. Other than the medical setting in which the drug Digoxin is administered, acute intoxications from cardiac glycosides is rare. There has been a few cases of reported accidental deaths from eating digitails (the plant which Digoxin is made from). However reported adverse reactions reported from *Convallaria* is very rare with no reported deaths. The most common cause of adverse reaction is acute accidental poisoning of eating *Convallaria*. Symptoms of mild to moderate intoxication of cardiac glycoside poisoning based on the drug Digoxin is fatigue, ventricular ectopic beats, bradycardia, and ventricular tachycardia. Toxicity from *Convallaria* as a medicinal herb is very rare partly due to its poor absorption and fast half life.

^aCorresponding author: Battle Ground Healing Arts, 408 E Main Street, Battle Ground, WA 98604, USA

^bDundas Naturopathic Centre, Dundas L9H 1V6, Canada

^cDavid Winston's Center for Herbal Studies, Broadway, NJ 08808, USA

^d413 Grassy Hill, Woodbury, CT 06798, USA

DISCUSSION

Convallaria and *Crataegus* have been used for centuries by herbalists in the treatment of certain cardiac dysfunctions. *Convallaria* has been used for congestive heart failure and cardiomyopathy, while *Crataegus* has been used as an all-purpose cardiac and vascular tonic.

Positive inotropic effects may also be accomplished with *Crataegus* and some other herbs. In these plants, the primary mechanism involves cyclic AMP (adenosine monophosphate). When stimulated, receptors on the outsides of muscle cell membrane enable the synthesis of adenylyl cyclase, the enzyme that catalyzes the production of intracellular cAMP. The presence of cAMP activates the calcium channels in the muscle cell membranes. In heart muscle cells, calcium influx promotes increased heart contractility. When epinephrine and norepinephrine bind to membrane receptors, a chain reaction is initiated; the increased calcium level results in increased inotropic capacity.

CRATAEGUS AS A TREATMENT FOR CARDIAC DYSFUNCTION

Crataegus (Hawthorne Tree) species are actually several varieties of the Hawthorne tree, and it was used in early European medicine for a wide variety of cardiac and vascular conditions. As this tree (in the rose family) flowers in Europe in May, it became commonly known as the “Mayflower”.

Crataegus does not contain cardiac glycosides, but rather a group of flavonoids. These flavonoids have anti-inflammatory, anti-oxidant, and protective cardiac effects. The berries and other constituents present in the buds of the flowers have particularly positive effects. *Crataegus* contains large amounts of flavonoid anthocyanidins and proanthocyanidins, as well as condensed polyphenolic tannins known as *procyanidolic oligomers* (PCOs). The flavonoids have a stabilizing effect on capillaries,¹ and serve to reduce vascular permeability and fragility. *Crataegus* extracts (and particularly their flavonoids) may support cardiac mitochondrial respiration.²

Crataegus flower buds contain quercetin, other anti-inflammatory flavonoids, and volatile amines. Haw-

thorne berries also contain sugar, pectin, Vitamin C, and glycosides. The leaves contain catechins and traces of sterols. Chemically, these procyanidins (such as 1-epicatechol) are small dimers of epicatechin (a tannin derivative). Other flavonoids found in *Crataegus* include vitexin-4-rhamnoside, rutin, and quercetin. Other constituents include ursolic, oleanic, and cinnamic organic acids, along with sterols, purines, triterpenes, and cardiogenic amines including trimethylamine, isobutylamine, and tyramine. Currently, many *Crataegus* supplements are standardized to 10-28% PCO content.

The procyanidins found in *Crataegus* also inhibit phosphodiesterase,³ the enzyme that degrades cAMP into inactive AMP. Since the breakdown of cAMP is prevented by *Crataegus*, calcium levels remain high; this leads to sustained myocardial contractility. While elevations in cAMP and intracellular calcium promote contractions of coronary



Convallaria majallis of the Liliacea family
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muscle, the same conditions promote relaxation of blood vessel smooth muscle. Thus, blood flow through the heart is not impaired due to vasoconstriction. *Crataegus* enhances myocardial contractility, yet coronary arteries are dilated rather than contracted.⁴⁻⁵

Extracts of *Crataegus* leaf, flower, and berry have been shown to promote calcium influx via effects on sodium and potassium ATPase mechanisms,⁶ and to promote calcium concentrations affecting myocontractility.⁷

CRATAEGUS AS AN ACE INHIBITOR

Crataegus constituents act as natural angiotensin converting enzyme (ACE) inhibitors.⁸ ACE is an important enzyme involved with blood pres-

sure regulation and also sodium and electrolyte balance in tissues. Inhibiting ACE also serves to lower blood pressure and strengthen heart muscle function. *Crataegus* inhibits ACE, presumably due to its procyanidin oligomers. When this enzyme is inhibited, angiotensin I is not converted to angiotensin II. As a result, the production of aldosterone is reduced. Since aldosterone promotes water and sodium retention, sodium and water (in the absence of aldosterone) are more easily excreted. Additionally, angiotensin II promotes vasoconstriction and inactivates bradykinin—a polypeptide with vasodilating action. When ACE is inhibited, bradykinin promotes the release of other vasodilatory prostaglandins which, in turn, improve blood flow and oxygen delivery to the heart muscle. (Fig 1)

BIOLOGICAL EFFECTS OF CRATAEGUS AND ACE INHIBITORS

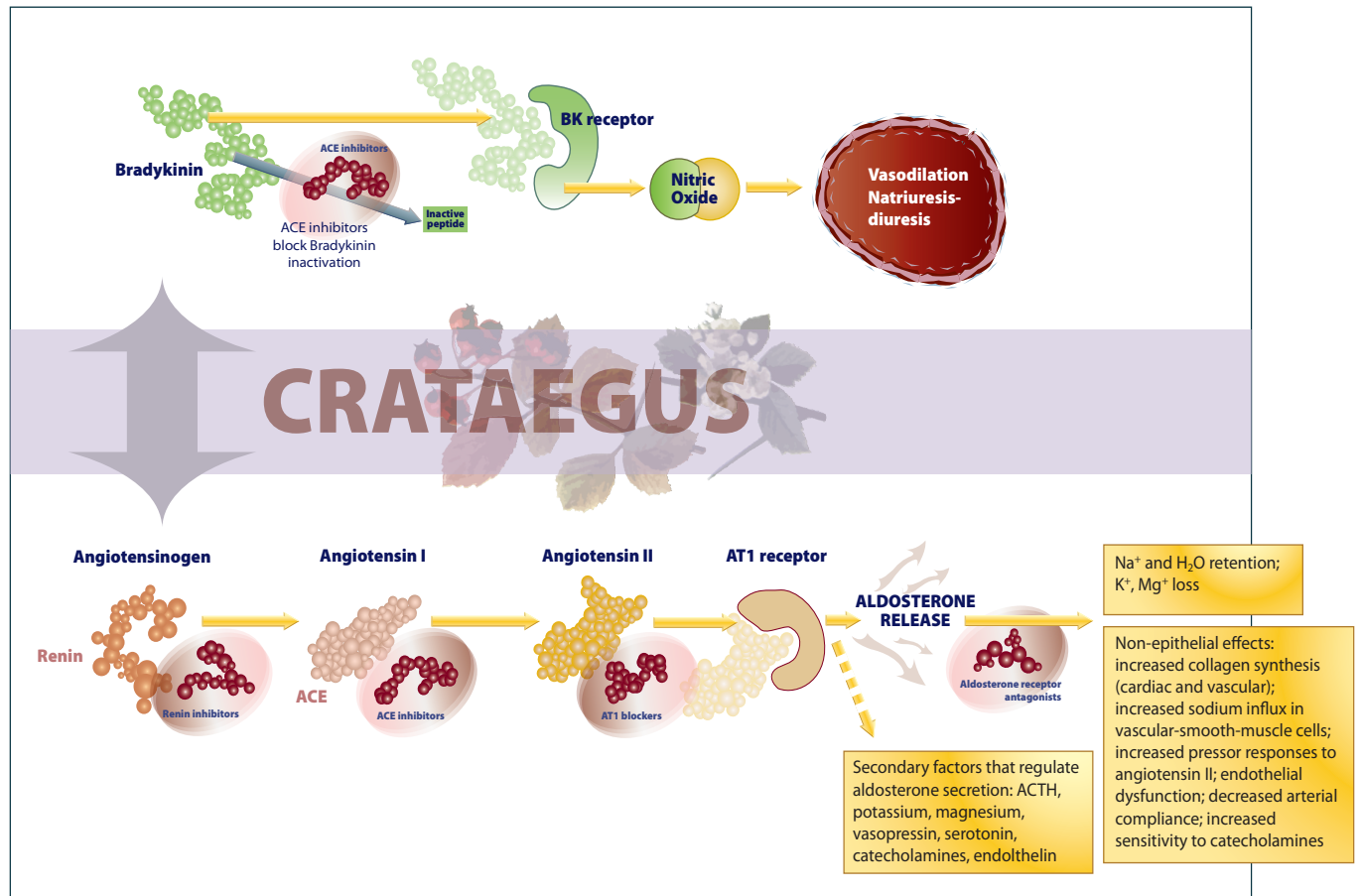


Figure 1

CRATAEGUS FOR BLOOD PRESSURE CONTROL

Crataegus has long been used as a heart tonic for both hyper- and hypotension. Researchers have demonstrated that *Crataegus* may also be helpful in treating elevated cholesterol levels, high blood pressure, angina pectoris, and atherosclerosis.⁹⁻¹⁰ *Crataegus* may also regulate heart rhythm in patients with heart failure.¹¹ There have been clinical trials using *Crataegus* extracts in patients with Congestive Heart Failure (CHF) showing significant improvements in symptoms.¹² In animal models, studies have shown *Crataegus* to improve aortic contractility in heart failure.¹³

Studies on the use of *Crataegus* along with standard pharmaceutical treatments for heart failure have not revealed any negative drug-herb interactions, and have suggested that *Crataegus* may slow the progression of heart failure.¹⁴ One study reported that the addition of *Crataegus* to the overall protocol for heart failure patients reduced the incidence of sudden cardiac death.¹⁵

CONVALLARIA (LILY OF THE VALLEY)

In cardiomyopathy, the heart muscle progressively weakens and becomes increasingly ineffective at pumping blood. Typical chronic management is with chemical pharmaceuticals, and the only definitive cure is by heart transplant. Many medications used to treat cardiomyopathy have stemmed from *Digitalis* and its cardiac glycosides (*e.g.*, digoxin and digitalin).

Cardiac glycosides (steroid-like molecules that act on cardiac smooth muscle) are sometimes termed “positive inotropic agents” because they positively affect the flow of ions across cardiac muscle cell membranes. Muscle cells (including cardiac muscle cells) need to be able to contract and expand—and it is the flow of charged calcium, potassium and other ions across the cell membrane that serves to establish electrical currents, enabling depolarization and repolarization.

Convallaria majallus (Lily of the Valley) contains cardiac glycosides. For centuries, many herbalists and medical practitioners considered *Convallaria majallus* to be safer than *Digitalis*. For centuries, herbalists have considered the roots of the *Conval-*

laria plant to be a treatment for a weak heart, shortness of breath tachycardia and arrhythmia. *Convallaria majalis* contains at least around 40 cardiac glycosides (including convallarin, convallotoxin, convalloside, convallasaponin, cholestane glycoside, strophanthidin, cannogenol, sarmentogenin, dipindogenin and hydroxysarmentogenin).¹⁶⁻¹⁸

The *Convallaria* plant transforms convalloside (the basic metabolic glycoside) into convallotoxin and other cardiac glycosides.¹⁹ Convallotoxin affects vasoconstriction and vasodilation,²⁰ and cardiac stroke volume, pulse pressure and cAMP activity are all enhanced by *Convallaria*.²¹ Convallamaroside may reduce angiogenesis and have anti-tumor effects.²² *Convallaria* has also been shown to be a lipoxxygenase inhibitor.²³

HERBAL MEDICINE TO MAINTAIN HEART HEALTH

These herbs described hererin may be used alone or in combination to support heart function. A 2008 meta-analysis on a *Crataegus* clinical trial reported no adverse advents, and the only significant side effects to be mild and transient.²⁴ Studies have shown *Crataegus* to be safe when used in tandem with conventional pharmaceutical therapies in the management of congestive heart failure and other cardiac maladies. The use of *Convallaria* and *Crataegus* are both medicinal herbs that in appropriate doses can be used safely and effectively to manage basic cardiac dysfunction.

DISCLOSURE OF INTERESTS

Dr. Saunders reports personal fees related to employment or seeing patients from CCNM, the Dundas Naturopathic Centre, and from Beaumont Health Systems, Troy Hospital, MI, outside the submitted work. Dr. Winston reports personal fees from Herbalist & Alchemist, Inc, outside the submitted work. Dr. Stansbury and Dr. Zampieron have nothing to disclose.

REVIEW ESSAY

Many nutrients and herbs that have not been the subject of randomized controlled studies are used regularly by clinicians. They have also been used

traditionally for hundreds, sometimes thousands of years. Review Essays contain the opinions of professionals and experts in the fields of nutritional and botanical medicine on how to most effectively use herbs and nutrients in clinical practice. The dosages

recommended are based on clinical experience. Side effects that are described in “Unsubstantiated Theoretical Concerns” have not been seen in clinical practice or clinical studies but are speculative based on, for example, possible mechanisms of action.

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