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REVIEW

DERLEME

## Efficacy of Herbal Remedies in the Treatment of Cardiovascular Diseases in Human and Animals

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### S U M M A R Y

Cardiovascular diseases are the most important causes of death and organ failure in industrialized countries. There is widespread use of herbal treatments in patients suffering from cardiovascular diseases all over the world. The discussion about the benefit of these drugs is still controversial because of lack of scientific evidence. Lifestyle interventions, including dietary supplement with natural compounds possessing known lipid-lowering effects, are strongly supported by the international guidelines for cardiovascular disease prevention. This review provides important knowledge both insights on issues concerning the safety of the most commonly used dietary supplements and nutraceuticals with demonstrated lipid-lowering actions and their applicability in the field of veterinary medicine.

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### İnsan ve Hayvanlarda Kalp Hastalıklarının Tedavisinde Bitkisel İlaçların Etkinliği

### ÖZET

Kardiyovasküler hastalıklar sanayileşmiş ülkelerde ölüm ve organ yetersizliklerinin en önemli nedenidir. Dünya çapında kardiyovasküler hastalıklardan müzdarip hastalarda bitkisel tedaviler yaygın olarak kullanılmaktadır. Bu ilaçların faydaları hakkındaki tartışmalar, bilimsel verilerin yetersizliği nedeniyle hala tartışma konusudur. Lipid düşürücü etkileri nedeniyle diyetlere bileşiklerin eklenmesini içeren yaşam tarzı, kardiyovasküler hastalıklardan korunmak için uluslar arası otoriteler tarafından şiddetle önerilmektedir. Bu derleme, en yaygın kullanılan lipid düşürücü etkili nütrosötikler ve diyet ilave ürünleri ve veteriner hekimlik alanında uygulanabilirliği hakkında önemli bilgiler sağlamaktadır.

#### Key Words

Cardiovascular Diseases  
Herbal Treatment

#### Anahtar Kelimeler

Kardiyovasküler Hastalıklar  
Bitkisel Tedavi

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## INTRODUCTION

Cardiovascular disease is a category of chronic noncommunicable diseases causing high global mortality and has a heavy social burden in many countries (Bleske et al. 2007). The Medical Herbalist recognizes a broad range of relevant herbs for the cardiovascular system. They are known as cardiac remedies group. This is a general term for herbs that have an action on the heart. Some of the remedies in this group are powerful cardio-active agents such as Foxglove, while others are gentler and safer cardiac tonics such as Hawthorn and Linden Flowers. Cardio-actives owe their effects on the heart to active substances such as cardiac glycosides, thus having both the strengths and drawbacks of these constituents (Bleske et al. 2007, Daniele et al. 2006).

*Crataegus* spp. (hawthorn) monopreparations are predominantly used for treating congestive heart failure (Daniele et al. 2006). Hawthorn extract (*Crataegus* sp.) is a botanical complementary and alternative medicine is often used to treat heart failure. Hawthorn extract had no effect on the immunomodulatory markers measured in a study (Bleske et al. 2007), although there appeared to be a trend suggesting suppression of IL-2 plasma concentrations. The mechanism(s) by which hawthorn extract may treat heart failure is unknown but may include, theoretically, immunological effects. In this study, animal model of heart failure hawthorn extract failed to significantly affect the immunomodulatory response characterized after 6 months of pressure overload at a time when approximately 50% mortality was exhibited. Mechanisms other than immunological agents may better define hawthorn's effect in treating heart failure.

The results of a recent study provide the evidence that extract of hawthorn (*Crataegus* sp.) may have benefits in left ventricular systolic dysfunction. It was claimed that oligomeric procyanidins from hawthorn extract are as supplementary therapy on contractility of impaired myocardium has been proved in patients with left ventricle systolic dysfunction. It was reported that this kind of supplementary therapy was well tolerated and no interactions with the other compounds for heart failure were reported (Rechcinski and Kurpesa 2005).

Otherwise, symptoms such as dyspnea and fatigue improved significantly with hawthorn treatment as compared with placebo. Reported

adverse events were infrequent, mild, and transient; they included nausea, dizziness, and cardiac and gastrointestinal complaints (Pittler et al 2003). Although these adverse events, it was suggest that there was a significant benefit from hawthorn extract as an adjunctive treatment for chronic heart failure (Pittler et al 2003, Pittler et al 2008).

Pomegranate juice is a polyphenol-rich fruit juice with high antioxidant capacity along with significant antiatherogenic, antioxidant, antihypertensive, and anti-inflammatory effects. Pomegranate juice significantly reduces atherosclerotic lesion areas in immune-deficient mice and intima media thickness in cardiac patients on medications. It also decreases lipid peroxidation in patients with type 2 diabetes, systolic blood pressure and serum angiotensin converting enzyme activity in hypertensive patients (Aviram et al 2000, Basu and Penugonda 2009, Stowe 2011). Cardioprotective effects of various plants are generally attributed to their antioxidant activity. The whole fruit extract of pomegranate (WFEP), *Punica granatum* L. (Punicaceae), has a potent antioxidant activity (Aviram et al 2000). Results of a recent study indicated that cardioprotective effect of WFEP against doxorubicin (Dox)-induced cardiotoxicity in rats (Hassanpour et al 2011), however Jadeja et al (2010) proved as a first scientific report that of supplementation of Pomegranate juice against isoproterenol-induced cardiac necrosis in rats has protective effect. Davidson et al (2009) claimed that pomegranate juice consumption had no significant effect on overall anterior and posterior carotid intima-media thickness (CIMT) progression rate but might have slowed CIMT progression in subjects with increased oxidative stress and disturbances in the TG-rich lipoprotein/HDL axis.

Aviram et al. (2008) had analyzed in vivo and in vitro the antiatherogenic properties and mechanisms of action of all pomegranate fruit parts: peels (POMxl, POMxp), arils (POMa), seeds (POMo), and flowers (POMf), in comparison to whole fruit juice (PJ). They concluded that attenuation of atherosclerosis development by some of the POM extracts and, in particular, POMf could be related to the combined beneficial effects on serum lipid levels and on macrophage atherogenic properties. Otherwise, daily consumption of pomegranate juice might improve stress-induced myocardial ischemia in patients who have coronary heart disease (Sumner et al 2005).

Green tea (from the plant *Camellia sinensis*), a beverage whose consumption started 5000 years ago in China, has important biological and pharmacological properties. The beneficial effects of green tea have been attributed to the presence of phenolic compounds that are powerful anti-oxidants and free iron scavengers (Mak 2012). The results of a recent study with Rooibos, a unique South African herbal tea (Pantsi et al 2011) showed that the rooibos supplemented hearts significantly improved aortic output recovery after reperfusion when compared to the green tea supplemented hearts. Additionally, it was showed that the rooibos extracts, containing the highest amount of flavonols, significantly decreased the level of cleaved caspase-3 and PARP (Poly (ADP-ribose) polymerase), both pro-apoptotic proteins, during reperfusion when compared to green tea.

Ischemia-reperfusion injury is among the most serious problems in cardiac surgery. Oral pretreatment with epigallocatechin-3-gallate, a major polyphenolic component of green tea, preserved cardiac function after ischemia-reperfusion, an effect that may involve its antioxidative, antiapoptotic properties, although a high dose did not lead to dramatic improvement in cardiac function (Yanagi et al 2011, Moore et al 2009). Similarly, green tea catechins are dietary antioxidant compounds that have been shown to protect against myocardial ischemia-reperfusion injury by catechins can induce phase 2 enzymes in cultured cells and some organs (Kuriyama 2010). Wang et al (2010) declared that green tea consumption can protect against the development of coronary atherosclerosis in male patients, and Hsieh et al (2009) validated the novel action of green tea polyphenols protecting against myocardial damage and enhancing cardiac contractility by modulating myofilament Ca(2+) sensitivity in post-MI rats while Clement (2009) claimed that green tea might also attenuated the risk factors association with the development of atherosclerosis thus reducing the incidence of cardiovascular events and stroke. Nantz et al (2009) declared that green tea (*Camellia sinensis*) was effective for decreasing, in as quickly as 3 wk, blood pressure, LDL cholesterol, oxidative stress, and a marker of chronic inflammation, all independent cardiovascular risk factors. According to Ikeda et al (2007) continuous ingestion of green tea catechins from an early age prevented the development of spontaneous stroke in malignant stroke-prone spontaneously hypertensive in rats, probably by inhibiting the further development of high blood pressure at later ages.

The epidemiological, clinical, and laboratory data have proved that garlic contains many biologically and pharmacologically important compounds, which are beneficial for human health from cardiovascular, neoplastic, and to the several other diseases (Agarwal 1996). Garlic did not influence other lipid parameters, including low-density lipoprotein cholesterol, high-density lipoprotein cholesterol (HDL-C), apolipoprotein B, and total cholesterol (TC)/HDL-C ratio, but it could reduce serum TC and TG levels, and garlic therapy should benefit to patients with risk of cardiovascular diseases (Chan et al 2012, Zeng et al 2012). Garlic-derived polysulfides were being designed and investigated for the treatment of cardiovascular conditions, specifically myocardial ischaemic disease reported by Layu et al (2011). The results of the study showed that anti-apoptotic, anti-inflammatory and antioxidant effects of H<sub>2</sub>S (hydrogen sulfide), has demonstrated significant cardioprotection, only by additional studies would perform we understand more about the role of this intriguing molecule in the treatment of cardiovascular disease.

Ginkgo biloba extract is an important natural product for treatment of cerebral and cardiovascular diseases, whereas ginkgolide B (GB) is a main component of it (Hao et al 2009). Ginkgo biloba extract 50 (GBE50), a new multicomponent drug with polyvalent action extracted from the leave of *Ginkgo biloba*, could alleviate the electrophysiological heterogeneity of ischemic myocardium, which may attenuate myocardial ischemia and block the onset of arrhythmia (Liu and Zhang 2010). Bao et al (2010) similarly detected GBE50 could decreased the content of IL-6 and increase the content of IL-4 in myocardium after ischemia-reperfusion injury. They suggested that GBE50 could regulate the inflammatory reaction after ischemia-reperfusion injury via inhibiting inflammatory cytokines and promoting anti-inflammatory cytokines. The results of a recent study showed also the effects of Ginkgolide on hemodynamics and myocardial oxygen metabolism in acute myocardial ischemic dogs showed that Ginkgolide improved the hemodynamic conditions and oxygen metabolism of myocardial ischemic dogs (Yin et al 2010). Some researchers (Liu et al 2008, Panda and Naik 2008) had demonstrated that the cardioprotective effects of Ginkgo biloba derivatives in doxorubicin and isoproterenol-induced oxidative myocardial damage in rats might be due to an augmentation of the endogenous antioxidants and inhibition of lipid peroxidation of membrane.

Flaxseed is a rich source of 3 components demonstrated cardioprotective effects: the omega-3 fatty acid alpha-linolenic acid (ALA), dietary fibre, and phytoestrogen lignans. It is suggested that the dietary fibre and (or) lignan content of flaxseed provides the hypocholesterolemic action. The omega-3 ALA found in the flaxseed oil fraction also contributes to the antiatherogenic effects of flaxseed via anti-inflammatory and antiproliferative mechanisms. Dietary flaxseed may also protect against ischemic heart disease by improving vascular relaxation responses and by inhibiting the incidence of ventricular fibrillation (Bassett et al 2009, Prasad 2009).

## CONCLUSION

Ginkgo is mainly used to treat in vascular dementia and peripheral vascular disease. Garlic shows a modest lipid-lowering effect in the same range as a low-cholesterol diet. Effect on blood pressure seems to be at best minor. Crataegus is often used in patients with heart failure because of its positive inotropic effect. Additionally, crataegus acts as an antiarrhythmic substance by prolonging refractory period of the action potential. Flaxseed suppresses oxygen radical production by white blood cells, prolongs bleeding time, and higher doses of it suppresses serum levels of inflammatory mediators and does not lower serum lipids. Pomegranate juice is a polyphenol-rich fruit juice with high antioxidant capacity along with significant antiatherogenic, antioxidant, antihypertensive, and anti-inflammatory effects. The beneficial effects of green tea have been attributed to the presence of phenolic compounds that are powerful anti-oxidants and free iron scavengers. Although there are a lot of data available from experimental and clinical studies related to herbal treatments, unfortunately not always adhering to the criteria of evidence based medicine. According to this review, we suggested that a lot of scientific studies should be made related to herbal treatment according to criteria of evidence based on veterinary medicine.

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