REVIEW ARTICLE

# Cardioprotective Effects of Garlic

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## Abstract

Alternative health care using herbal therapy has become increasingly popular due to its positive effects discovered in recent medicinal studies. Herbs, in particular garlic, have been found to contain an active phytochemical to treat cardiovascular and other metabolic diseases. From experimental usage, garlic shows promise as an effective antiatherosclerotic, antihypertensive, antidiabetic as well as having cholesterol lowering effects. Furthermore, garlic has been reported to be a cardioprotective agent which can counteract free radical damage associated with atherogenesis and myocardial damage seen in ischaemic and reperfusion injury. These biological actions may explain the benefits gained from the use of garlic to treat cardiac disorders associated with coronary heart disease.

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**Keywords**: Herbal therapy; Garlic; Cardioprotective effect

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# ผลในการป้องกันโรคหัวใจของกระเทียม

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## บทคัดย่อ

การใช้สมุนไพรเพื่อดูแลสุขภาพ เป็นทางเลือกที่ได้รับความนิยมมากขึ้นในปัจจุบัน จากการศึกษาที่ผ่านมาพบว่า สมุนไพรให้ผลดีในการรักษา และป้องกันโรคต่างๆ สมุนไพร เช่น กระเทียม มีส่วนประกอบทางเคมีที่ใช้ในการรักษาโรคหัวใจและหลอดเลือด กระเทียมสามารถป้องกันการเกิดโรคหลอดเลือดแข็งตัว ลดความดันโลหิต ลดระดับคอเลสเตอรอล และ ลดระดับน้ำตาลในกระแสเลือดในกรณีของโรคเบาหวาน นอกจากนี้ มีรายงานว่า กรณีการเกิดหลอดเลือดหัวใจอุดตัน สารต่อต้านอนุมูลอิสระในกระเทียม สามารถใช้ในการป้องกันการเกิดความเสียหายของกล้ามเนื้อหัวใจ ซึ่งคุณสมบัตินี้ มีประโยชน์ในการใช้กระเทียมเพื่อป้องกันและรักษาโรคหลอดเลือดหัวใจได้

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## Introduction

Sudden cardiac death (SCD) is a major cause of death worldwide [1]. In recent years, an alternative health care using herbal therapies and dietary supplements provides promising medicinal properties [2]. Growing evidence suggests the therapeutic effects of phytochemicals in foods such as cholesterol-lowering, fibrinolytic, antiatherosclerotic, antihypertensive, hypoglycemic, antioxidant, antimicrobial and cardio-protective effects [3, 4]. The well-known phytochemicals are organosulfur compounds in alliums species, mostly found in garlic [3]. This review mainly focuses on the cardioprotective effects of garlic in both human and animal studies.

## Garlic products and their active ingredients

The key therapeutic effects of garlic are attributed to its pungent aroma and taste. It has been shown that the biological activity of garlic depends on the process of its preparation [5]. Raw garlic homogenate at room temperature contains the active ingredients e.g. alliin and allicin [6]. In garlic, the enzyme allinase converts alliin to allicin and then allicin is broken down into hydrogen sulphide ($H_2S$). Allicin is inactivated by heat (temperatures in excess 60$^{\circ}$C). However, the processed garlic such as heat-treated garlic, garlic powder and garlic oil demonstrated a lack of ability to generate $H_2S$ but to retain

all other biological and antioxidant properties [7]. The organosulphur compounds of garlic including thiosulfinate compounds, complex sulphinyl component and $H_2S$ have been shown to possess the potential effects on cardiovascular disease and other metabolic disorders [7-13].

## Biological mechanisms of garlic and its components

The therapeutic actions for cardiovascular diseases of organosulphur compounds in garlic present in different preparations [3]. The individual effects such as cholesterol-lowering, fibrinolytic, platelet aggregation inhibiting, blood pressure and blood glucose lowering, cardioprotective and anti-arrhythmic are summarized in the following section.

### *Cholesterol-lowering effect*

The cholesterol-lowering effect of garlic is much more evident than other biological effects. About half of clinical trial studies have shown positive effect in lipid reduction of 9-15% from the baseline [14]. Many studies suggested that sulphur compounds in garlic may be the principle source of inhibition of cholesterol synthesis [6, 14, 15]. Chronic intake for 4 weeks of garlic in its raw and processed forms was found to reduce plasma lipid level. Cholesterol-lowering effect of garlic is summarized in **Table 1**.

**Table 1.** Cholesterol-lowering Effects of Garlic

| Study type | Preparation | Duration | Dose | Major finding | References |
|---|---|---|---|---|---|
| **Clinical trial** (CHD patients with cholesterol level above 200 mg/dl; n=51) | Allicor | 12 months | 150 mg Twice daily | Reduce the cardiovascular risk by lowering LDL cholesterol levels | Sobenin *et al*., 2010 [39] |
| **Clinical trial** (70 subjects) | Oily macerated garlic | 30 days | 0.54 mg of allicin tid | Reduced plasma lipid | Duda *et al*., 2008 [40] |
| **Clinical trial** (n=192) | Raw and commercial garlic (Garlic powder) | 24 weeks | 1.4 g (12.8 mg allicin) | Lower low-density lipoprotein cholesterol (LDL-C) or other plasma lipid in subjects with moderate hypercholesterolemia | Gardner *et al*., 2007 [41] |

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**Table 1.** Cholesterol-lowering Effects of Garlic

| Study type | Preparation | Duration | Dose | Major finding | References |
|---|---|---|---|---|---|
| **Animal model** Wistar male rats fed cholesterol-containing diet | Raw and cooked at 100°C for 20, 40 and 60 min garlic samples | 30 days | 500 mg (25 mg of lyophilized garlic/1 kg body weight) | Raw and cooked at 100 C for 20 min garlic samples contain high quantities of bioactive compounds and total antioxidant potential Lower plasma lipid levels and plasma antioxidant activity | Jastrzebski *et al*., 2007 [42] |
| **Animal model** (Wistar male rats) | Raw and commercial garlic (Lyophilized garlic) | 4 weeks | 500, 750, and 1000 mg/kg body weight | Positive influences of commercial garlic on plasma lipids, and indicators of blood coagulation are dose-dependent | Gorinstein *et al*., 2007 [43] |

***Fibrinolytic, platelet aggregation inhibiting and antiatherosclerotic effects***

The activity of coagulation and fibrinolytic mechanisms in the vessels are important factor in the development of thrombosis and ischemia. Garlic has the capacity to inhibit the mechanism of platelet formation such as inhibiting uptake of calcium into platelets, or inhibiting the synthesis of clot formation [16]. All studies of garlic preparations that demonstrate effects on fibrinolytic and atherosclerosis prevention are due to its lipid lowering effects in the arterial wall [17, 18] as summarized in **Table 2**.

**Table 2.** Fibrinolytic, Inhibition of Platelet Aggregation and Antiatherosclerotic Effects

| Study type | Preparation | Duration | Dose | Major finding | References |
|---|---|---|---|---|---|
| **Clinical trial** (n=23) | AGE | 1 year | 1200 mg | Slow coronary artery calcification Garlic effect may be related to the reduction of multiple risk factors in CVD, such as LDL, homocysteine, and blood coagulation | Budoff, *et al*., 2006 [44] |
| **Animal model** (Albino wistar rats) | Fresh garlic (homogenised) | 10 weeks | 0.5% by weight | Vasorelaxant Reduced the atherogenic properties of cholesterol | Ashraf, *et al*., 2005 [17] |

*Continued*

**Table 2.** Fibrinolytic, Inhibition of Platelet Aggregation and Antiatherosclerotic Effects

| Study type | Preparation | Duration | Dose | Major finding | References |
|---|---|---|---|---|---|
| ***In vitro*** (Human T cell and Human umbilical vein endothelial cells) | Allicin | Acute effect | 20 µM or 50 µM | Reduced the formation of fatty streaks (atherosclerosis) in blood vessels | Sela *et al*., 2004 [45] |
| **Animal model** (Isolated rat aorta) | Fresh garlic | Acute effect | 3700µg allicine, 7200µg alliin, 105µg ajoene, 210µg adenosine, 435µg 1,3-vinyl dilhiines, and 170 µg 1,2-vinyldilhiine | Effects on endothelium vasorelaxation through EDHFs and cycloxygenase pathways | Ashraf, *et al*., 2004 [46] |
| **Clinical trial** (n=50) | Garlic powder | 3 months | 800 mg/day | Anti platelet aggregation | Ziaei *et al*., 2001 [47] |

***Blood pressure and blood glucose lowering effects***

Previous studies have demonstrated that garlic can reduce blood pressure by decreasing peripheral vascular resistance and releasing nitric oxide (NO), depending on relaxation in arterial wall [19]. Allicin, the major thiosulfinate compounds in homogenised garlic extract and other sulphur compounds in garlic oil showed antihypertensive and antioxidant properties in a variety of doses [20-22]. High blood glucose levels increase the risk for sudden cardiac death associated with coronary heart diseases [23]. A protective property of garlic as an antidiabetic agent is believed to be active via its allicor components in tablet form [24-26]. Animal model studies have suggested that garlic reduces blood glucose by lowering plasma insulin, triglyceride levels and blood pressure [23]. The effects are summarized in **Table 3**.

**Table 3.** Lower Blood Pressure and Reduction in Blood Glucose Effect

| Study type | Preparation | Duration | Dose | Major finding | References |
|---|---|---|---|---|---|
| **Clinical trial** (n=70) | Oily macerated garlic | 30 days | 0.54 mg of allicin three times daily | No effect on arterial blood pressure<br>Anti-oxidant properties | Duda *et al*., 2008 [40] |

*Continued*

**Table 3.** Lower Blood Pressure and Reduction in Blood Glucose Effect

| Study type | Preparation | Duration | Dose | Major finding | References |
|---|---|---|---|---|---|
| **Clinical trial** (n=40) | Garlic oil | 8 weeks | 5 mg/day | Reduced blood pressure Counteracted oxidative stress | Dhawan and Jain, 2005 [21] |
| **Clinical trial** (n=75) | Garlic powder | 12 weeks | 920 mg (10.8 mg alliin | No clinical association with blood pressure-lowering effects in middle-aged, normo-lipidaemic subjects | Turner *et al*., 2004 [48] |
| **Animal model** (2K1C hypertensive rats) | Homogenized garlic extract | 4 weeks | 50 mg/kg/day | Blood pressure lowering effect, which could partly be mediated by reduction in ACE activity | Cruz *et al*., 2006 [22] |
| **Animal model** (2K1C hypertensive rats) | Homogenized garlic extract | 7 days | 50 mg/kg/day | Garlic reduces blood pressure by an interaction of prostanoids, NHE-1 and sodium pump in 2K1C rats | Al-Qattan *et al*., 2003 [19] |
| **Clinical trial** (n=101) | Garlic in diet | Chronic intake | 134 gm/mth | Reduced systolic blood pressure | Qidwai, 2001 [49] |
| **Animal model** (Alloxan-diabetic rats) | Aqueous garlic extract | 4 weeks | 1 ml/kg/day i.p. injection of garlic extract | Relieved diabetes associated metabolic disorders by lowering the plasma levels of glucose, total cholesterol, triglyceride, and alkaline phosphatase activities in blood of diabetic animals | Hfaiedh *et al*., 2010 [50] |

***Cardioprotective and Anti-arrhythmic effects***

The health effects of garlic on cardiovascular diseases have been studied for decades. The major cardioprotective effects of garlic include: protecting against coronary heart diseases, preventing drug induced cardiac injury and protecting the rat heart from *in vitro* ischemic reperfusion injury [9, 20, 27, 28]. Within experimental studies, garlic has often used in two major forms [i.e., fresh crushed and garlic homogenate). It has been proposed that many of the medicinal properties of garlic are associated with its antioxidant properties [29]. Recently, antiarrhythmic drugs and antihypertensive agents were derived from herbal extracts. Many studies demonstrated the antiarrhythmic effects of garlic in both ventricular and supraventricular arrhythmias by decreasing the positive inotropic and chronotropic effects of isopronalin in a dose dependent manner [30, 31]. It has been proposed that one of the factors which leads to the changes in the metabolism of mitochondrial membrane may be related to the cardiac protection effect of garlic [32]. The summary effects are presented in **Table 4 and 5**, respectively.

**Table 4.** Cardioprotective Effects of Garlic

| Study type | Preparation | Duration | Dose | Major finding | References |
|---|---|---|---|---|---|
| Animal model Wistar female albino rats: (i) fructose induced hypertension (ii) isoproterenol induced myocardial damage | Garlic homogenate | 3 weeks | 125, 250 and 500 mg/kg/day | Garlic in moderate dose (250 mg/kg) with added Hydrochlothiazide has synergistic cardioprotective and antihypertensive properties against fructose- and isoproterenol-induced toxicities | Asdaq *et al*., 2011 [20] |
| **Animal model** (Isoproterenol induced MI in Wistar female albino rats) | Garlic homogenate | 3 weeks | 125, 250 and 500 mg/kg/day | Combination of garlic in moderate doses and propranolol resulted in beneficial effect during treatment of hypertensive animals with myocardial damage Increased bioavailability and half life along with decreased clearance and elimination rate constant of propanolol when taken orally | Asdaq *et al*., 2010 [51] |
| **Animal model** (Doxorubicin (DXR) induced cardiotoxicity in Wistar albino male rats) | AGE | 6 weeks | 3ml/kg daily | Prevent doxorubicin (DXR)-induced cardiac injury | Demirkaya *et al*., 2009 [9] |

## Organosulfur compound in animal models of cardiovascular diseases

The effects of organosulfur compounds such as sulfinate groups, sodium hydrogen sulphide (NaHS) and hydrogen sulphide ($H_2S$), have been investigated over the past few years as shown in **Table 6**. The effects of organosulfur compounds from garlic extract on reduced hypertension in hypertensive

**Table 5.** Anti-arrhythmic Effects of Garlic

| Study type | Preparation | Duration | Dose | Major finding | References |
|---|---|---|---|---|---|
| **Animal model** (Intracardiac catheterization in juvenile pigs) | Garlic powder (1.3% alicin) | Acute effect | 20 mg/kg or 40 mg/kg i.v. drip | - Extend the refractory period in a dose dependent manner<br>- Improved defibrillation efficacy:<br>(i) decrease in the degree of dispersion of refractoriness in the ventricles<br>(ii) prevention of reentrant propagation | Sungnoon *et al*., 2008 [52] |
| **Animal model** Anaesthetized dogs and on isolated left rat atria | Garlic dialysate | Acute effect | 0.83% w/w | - Negative inotropic effect of garlic is related to concentraton of extracellular $Ca^{2+}$ | Martin *et al*., 1997 [53] |
| **Animal model** Anaesthetized dogs and on isolated left rat atria | Garlic dialysate | Acute effect | 0.83% w/w | - Significant anti-arrhythmic effect in both ventricular and supraventricular arrhythmias<br>- Prolongation of ERP and SNRT in dose dependent manner | Martin *et al*., 1994 [37] |
| **Animal model** Anaesthetized dogs and on isolated left rat atria | Garlic dialysate | Acute effect | 0.83% w/w | - Beta- adrenoceptor blocking action | Martin *et al*., 1992 [54] |

and high cholesterol diet rat have been studied [19, 22, 27]. It has been shown that $H_2S$ demonstrates similar biological effects to preserve mitochondrial structure and function as nitric oxide (NO) and carbon monoxide (CO) [33-37]. The cardioprotective actions of $H_2S$ involved in opening $K_{ATP}$ channels and activation of cardiac extracellular signal regulated kinase or Akt pathway [38].

## Summary

Herbal therapies have been used for centuries and their medicinal effects have been identified by experimental usage. Sulphur containing compounds in garlic have been shown to have beneficial effects

**Table 6.** Organosulfur Compound in Animals Models of Cardiovascular Diseases

| Study type | Preparation | Duration | Dose | Major finding | References |
|---|---|---|---|---|---|
| **Animal model** (Male Sprague–Dawley rats) | NaHS | 6 weeks | 37.5 mg/kg daily i.p. | - Inhibition of apoptosis of cardiac myocytes through the mitochondrial pathway to improve the survival and ventricular dysfunction in the developing HF model | Wang *et al*., 2011 [55] |
| **Animal model** (Fructose Fed Rats; FFR) | Thiosulfinates and allicin | 6 weeks | 150 mg/kg daily | Effect on prevention of oxidative stress and vascular remodeling in rats with metabolic syndrome | Vazquez-Prietov *et al*., 2010 [3] |
| **Animal model** (Male C57BL6/J mice; model of ischemia induced heart failure) | Sodium sulfide ($Na_2S$) | 7 days | 100 µg/kg intracardiac at the time of reperfusion or i.v. daily | - Provided therapeutic benefit in the treatment of ischemia-induced heart failure by reducing oxidative stress and attenuating mitochondrial dysfunction | Calvert *et al*., 2010 [56] |
| **Animal model** (porcine model of myocardial ischemia and reperfusion injury) | NaHS | Acute effect | 0.2 mg/ kg Bolus injection over 10 seconds or 2 mg.kg/h infusion | Provided biochemical myocardial protection via attenuation of caspase-independent apoptosis and autophagy in the setting of cardiopulmonary bypass (CP/CPB) | Osipov *et al.*, 2010 [57] |
| ***In vitro*** (Cardiac myocytes of adult male Sprague–Dawley rats) | NaHS | 5 minutes | 100 µM | Negative regulation of β-adrenergic function via inhibition of adenylylcyclase | Yong *et al*., 2008 [58] |

to reduce the risk of cardiovascular disease progression. These include having cholesterol lowering, fibrinolytic, antiatherosclerotic, antioxidant, antihypertensive, antidiabetic and, anti-arrhythmic effects, which supports its long history of use in preventing and treating cardiovascular disease.

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