

A Review: Garlic Effects on the Cardiovascular System



Madaj Paul M* and Budoff Matthew J

Los Angeles Biomedical Institute at Harbor-UCLA, USA

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***Corresponding author:** Madaj Paul M, Los Angeles Biomedical Institute at Harbor-UCLA, USA, Email: paul_madaj@yahoo.com

Abstract

Coronary Artery Disease (CAD) is one of the leading causes of morbidity and mortality in the world. Detection as well as modification of risk factors for cardiovascular disease (CVD) has been the topics research over several decades. Multiple drugs have been studied and used in clinical practice with people seeking “natural” alternatives. When evaluating for optimal treatment options and the multiple risk factors associated CAD (e.g. diabetes, hypertension, etc.), garlic can play a prominent role. Studies have shown promising results in treating hypertension, altering the lipid profile, prevention and even treatment of coronary atherosclerosis and its systemic anti-oxidant properties.

Garlic also has positive effects outside the cardiovascular system (e.g. immune system). It can be used stand-alone or as an adjunct to current medical therapy. No clinically significant side effects have been reported, thus providing a safe treatment option to be considered. Coronary Artery Disease (CAD) is one of the leading causes of morbidity and mortality in the world. Detection as well as modification of risk factors for cardiovascular disease (CVD) has been the topics research over several decades. Multiple drugs have been studied and used in clinical practice with people seeking “natural” alternatives. Some well-known alternatives include pomegranate juice, green tea, and garlic [1-3]. Our focus will be on the utility of garlic. Multiple myths and beliefs over thousands of years exist where garlic is a key element in treatment and prevention of illness (e.g. common cold) as well as increasing strength and endurance.

It was even used as a performance enhancer in ancient Olympics. In recent years, garlic has been a major area of focus in prevention and treatment of CAD and associated risk factors. We will review the role garlic has played in the modification of hypertension, hyperlipidemia, inflammatory markers and coronary artery calcium [3-7]. Garlic can provide an alternative to conventional medication without significant side effects.

Abbreviations: TAG: Triglycerides; RLPs : Remnant Lipoproteins; CAD: Coronary Artery Disease; CVD: Cardiovascular Disease; CAC: Coronary Artery Calcium; LAP: Low Attenuated Plaque

Lipid Profile

Multiple studies have implemented garlic’s effect of the lipid profile. Of all the components of the lipid panel, well known are the effects of LDL, triglycerides, total cholesterol and their role in CAD. In a meta-analysis by Reinhart et al examined the role of garlic on reduction of total cholesterol, driven mostly by reduction in triglycerides (TAG) [8]. In fact, the component most potent for creating a proinflammatory state is the remnant lipoprotein cholesterol [9]. Remnant lipoproteins (RLPs) are products of partially catabolized chylomicrons and very-low-density lipoprotein, from which some triglycerides have been removed, that are found to be highly atherogenic.

Remnants are known to cross the endothelial barrier and due to their larger size, they carry 5 to 20 times as much cholesterol per particle as LDL [10]. Remnant (apo A1 remnant ratio) association with short and intermediate term

mortality was shown to be a significant predictor, especially in women above 50 years of age [11]. In a study by de Vries et al. [12], chylomicrons were shown to be more potent in causing inflammation when compared to hypertriglyceridemia [12,13]. Of note, Matsuo et al showed remnant lipoprotein levels being linked to coronary plaque vulnerability, which is characterized by high necrotic and low fibrotic components [14].

Thus, remnant lipoproteins are well known and becoming more established as risk factors for CAD [13]. Nakamura et al. [15] was also able to establish the role of insulin resistance as also contributing to postprandial hyperlipidemia, especially in those with CAD, thus possibly requiring more aggressive treatment of such states [15,16]. Well known at this time the various treatment options and preventative measure for hyperlipidemia (e.g. diet, exercise, statins, fibrates, etc.)

Hypertension

Hypertension is also another well-known cardiovascular disease risk factor. Garlic has shown to have a role in treatment of hypertension. Reid et al. [17] in the AGE at Heart trial was able to establish a direct link of garlic on central and peripheral hypertension; as an adjunct or stand-alone treatment. Mean blood pressure was significantly reduced by 5.0 ± 2.1 mmHg ($P=0.016$) systolic, and in responders by 11.5 ± 1.9 mmHg systolic and 6.3 ± 1.1 mmHg diastolic compared to placebo ($P<0.001$) [17,18]. Thus, establishing a role in the reduction of both central and peripheral blood pressure.

Xiong et al. [19] in a meta-analysis on 7 randomized, placebo controlled trials since 2014 was able to establish a similar link on the role of garlic on hypertension. This meta-analysis revealed a significant lowering effect of garlic on both systolic BP (WMD: -6.71 mmHg; 95% CI: -12.44 to -0.99 ; $P=0.02$) and diastolic BP (WMD: -4.79 mmHg; 95% CI: -6.60 to -2.99 ; $P < 0.00001$). Hosseini et al. [20] was able to establish a similar link in addition to the effect on lipid profile as well as anti-diabetic effect. Despite this link, more research is required to establish garlic as a stand along treatment of hypertension. At this time, it can be used as an adjunct to conventional means.

Coronary Atherosclerosis

Garlic has also to have a role in prevention and treatment of coronary atherosclerosis. Multiple randomized trials were able to demonstrate a significant reduction in Coronary Artery Calcium (CAC) progression [4]. This is demonstrated through its direct role on the atherosclerotic process [21,22]. In a study by Budoff et al. & Ahmadi et al. [21,22], aged garlic extract supplemented with B vitamins, folic acid and L-arginine had a positive role in not only reducing atherosclerosis but improvement in oxidative biomarkers and vascular function.

Matsumoto et al. [23] was able to establish the role of aged garlic extract and its role in coronary plaque. The % low attenuated plaque (LAP) change in the study was significantly reduced in the AGE group compared with the placebo group ($-1.5\% \pm 2.3\%$ compared with $0.2\% \pm 2.0\%$, $P=0.0049$). Multivariable linear regression analysis found a beneficial effect of AGE on %LAP regression (β : -1.61 ; 95% CI: -2.79 , -0.43 ; $P=0.008$) [23]. Thus, demonstrating the inhibitory role on the progression of non-calcified plaque. Recently, Madaj et al. [24] demonstrated garlic's positive effects on coronary artery calcium, to supplement those earlier studies. Karagodin et al. [25] after evaluation of the Atherosclerosis Monitoring and Atherogenicity Reduction Study was able to show reduction of cardiovascular risk after use of garlic.

Twelve-month treatment lowered 10-years prognostic risk of coronary artery disease by 13.2% in men ($P=0.005$), and by 7.1% in women ($P=0.040$). Ten-year prognostic risk of acute myocardial infarction and sudden coronary death was

lowered by 26.1% in men ($P=0.025$) [25]. Studied here was also the progression of carotid atherosclerosis in asymptomatic men which can one can indirectly infer its effect on coronary artery atherosclerosis. Mahdavi-Roshan et al. [26] were able to demonstrate lack of progression of carotid intima media thickness with the use of garlic. After 3 months of taking garlic tablets, CIMT values had minor variations (0.009 ± 0.007 mm reduction from baseline), while in the placebo group, an increase in CIMT values was observed (0.04 ± 0.01 mm increase from baseline). Zeb et al. & Ahmadi et al. [27,28] were also able to demonstrate the use of garlic in the prevention of coronary artery disease. Thus, garlic has been shown to have positive effects on coronary atherosclerosis either as a stand-alone treatment or adjunct to conventional therapy.

Inflammatory Markers

Garlic has been found in studies to have a prominent role in affecting inflammatory markers. Despite its systemic anti-oxidant effects, we will limit our discussion to its effects on the cardiovascular system. This link has been demonstrated predominantly by decreased levels of CRP and IL-17A27, thus allowing garlic to have a direct role on the atherosclerotic process [21,22]. In a study by Budoff et al & Ahmadi et al. [21,22], aged garlic extract supplemented with B vitamins, folic acid and L-arginine had a positive role in not only reducing atherosclerosis but improvement in oxidative biomarkers and vascular function. Ried et al. [17] in the AGE at Heart trial were also able to demonstrate a reduction in inflammatory markers. TNF α was reduced in the garlic group compared to placebo with borderline significance ($P=0.05$), while changes in IL-1 β were not significant, but greater reduction was observed in the garlic group [17]. Results to date are very promising in establishing this relationship, but further work is needed to validate and expand on the progress made on the link between garlic and its anti-oxidant properties.

Conclusion

When evaluating for optimal treatment options and the multiple risk factors associated CAD (e.g. diabetes, hypertension, etc.), garlic can play a prominent role. Studies have shown promising results in treating hypertension, altering the lipid profile, prevention and even treatment of coronary atherosclerosis and its systemic anti-oxidant properties. Garlic also has positive effects outside the cardiovascular system (e.g. immune system). It can be used stand-alone or as an adjunct to current medical therapy. No clinically significant side effects have been reported, thus providing a safe treatment option. Despite the promising results, further studies are needed along to evaluate and validate the role of garlic on the various components of the atherosclerotic process, especially on its role in event reduction.

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