# Potential benefits of garlic and other dietary supplements for the management of hypertension (Review)

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Received August 8, 2019; Accepted September 12, 2019

DOI: 10.3892/etm.2019.8375

**Abstract.** Elevated blood pressure is a major risk factor for cardiovascular diseases. Although some effective drug treatments are available, a relatively large proportion of patients have uncontrolled blood pressure. Dietary supplements are used for the prevention and treatment of hypertension as complementary and alternative medicines. Of the various dietary supplements, antioxidants, fish oil and diverse herbal products are commonly used. Within this context, it is important to determine the actual effectiveness and possible side-effects of these supplements; however, some of the products have been poorly investigated for their effects and safety. In the current review, we focus on garlic and several other dietary supplements, such as coenzyme Q10, fish oil and probiotics, that have exhibited significant beneficial effects on blood pressure in clinical trials. In addition, we discuss the possible mechanisms of action responsible for their anti-hypertensive effects, as well as the safety, active ingredients and their potential use as adjunct therapies for uncontrolled hypertension.

**Contents**



## 1. Introduction

Hypertension is a major risk factor of cardiovascular diseases (CVD), which are the predominant cause of morbidity and mortality worldwide (1,2). The treatment and control of hypertension are extremely important for the prevention of CVD and its related diseases (3). Generally, several types of drugs are recommended as first-line anti-hypertensive medications, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), dihydropyridine calcium channel blockers and thiazide diuretics (4,5). When blood pressure cannot be controlled with one drug, treatment with multiple anti-hypertensive agents, such as combinations of ACE inhibitors or ARBs with dihydropyridine calcium channel blockers or thiazide diuretics is required (6). In spite of those well-established anti-hypertensive medications for high blood pressure, uncontrolled hypertension remains prevalent worldwide (7). In a cross-sectional study of 153,996 adults from 17 countries, more than half of the participants were unaware of their hypertension and blood pressure was controlled by the drug treatments in only 32.5% of the patients (8). The prevalence of uncontrolled hypertension in the United States decreased to approximately 50% from 1999 to 2010, but it has since not been improved further (9). It is clear that uncontrolled hypertension should be treated by alternative means to prevent subsequent morbidity and mortality.

## 2. Dietary supplements

There has been a growing awareness of complementary and alternative approaches in the prevention and treatment of CVD. According to the 2012 National Health Interview Survey, the most popular healthcare approaches are natural products, which are widely marketed and are often sold as dietary supplements (10). Dietary supplements used for the management of hypertension include coenzyme Q10 (CoQ10), vitamins and minerals, fish oil and various herbal products (11). In addition, a recent review highlighted that manipulating the gut microbiota using probiotics may be a valuable adjuvant to traditional anti-hypertensive therapy (12). Although a large variety of dietary supplements are used worldwide, only a few products have been investigated extensively for their effectiveness, safety and potential interactions with other medicines and dietary supplements. Furthermore, food-based preparations contain a large number of constituents, the amounts of which may vary according to the raw material, the manufacturing process and several other factors. This type of complexity can cause the inconsistency between the results in different clinical studies.

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*Key words:* garlic, dietary supplements, hypertension, antioxidants, probiotics

The use of the following dietary supplements has been reported to lead to a significant reduction in blood pressure without severe side-effects in multiple clinical trials (Table I).

### 3. Antioxidants and fish oil

*Coenzyme Q10*. CoQ10 is a potent antioxidant and an essential component of the mitochondrial electron transport chain (13). A number of studies have indicated that the plasma level of CoQ10 is associated with CVD, including hypertension and CoQ10 supplementation has been shown to be protective against such diseases (14,15). In a 10-week trial with hypertensive patients, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly reduced by 17.8 mmHg and 12.0 mmHg, respectively (16). A randomized, double-blind study examining the anti-hypertensive effect of CoQ10 in patients with hypertension and coronary artery disease (CAD) demonstrated that SBP, DBP and heart rate were significantly decreased, and that the plasma levels of antioxidants, such as vitamins A and E were significantly increased after 8 weeks of treatment (17). Moreover, patients taking CoQ10 were able to reduce the dosage or the number of anti-hypertensive drugs in several studies (15,17). The postulated principal mechanism underlying the beneficial effects of CoQ10 on hypertension is the decrease in peripheral resistance as a consequence of vasodilatation by preserving nitric oxide (NO) availability (18).

Clinical studies have indicated that CoQ10 treatment causes few adverse effects and minimal drug interactions. According to a meta-analysis by Rosenfeldt *et al*, side-effects were observed in only 0.8% in 12 studies with 3,500 patients (19). CoQ10 however, may increase the risk of bleeding in patients taking antiplatelet drugs due to its effect on platelet function (20). Overall, CoQ10 is a safe dietary supplement and can be a potent adjuvant for anti-hypertensives medication.

*Vitamin C*. Researchers have investigated the potential effects of vitamin C supplementation in the management of hypertension. The blood pressure-lowering effect of vitamin C was previously observed following treatment with 500 mg daily for 4 to 6 weeks in patients with hypertension (21,22). A meta-analysis including 29 clinical trials reported that vitamin C supplementation for 8 weeks on average reduced SBP and DBP by 3.8 mmHg and 1.5 mmHg, respectively (23). Of note, a clinical study with 77 mostly normotensive participants suggested that the intravenous administration of high-dose vitamin C led to an acute reduction in blood pressure, particularly in prehypertensive patients (24). Furthermore, Mahajan *et al* reported that concomitant treatment with vitamin C and the anti-hypertensive drug, amlodipine, provided additional benefits, namely a lower SBP and higher serum level of superoxide dismutase (25). The anti-hypertensive effect of vitamin C is probably ascribed to the improvement of endothelial function by directly scavenging free radicals, which causes vascular damage in hypertensive patients. Padayatty *et al* surveyed 172 practitioners who administered vitamin C to 20,109 patients and reported that the side-effects of vitamin C appeared to be relatively minor (26).

*Fish oil*. Fish oil contains long-chain and highly polyunsaturated n-3 fatty acids (n-3 PUFAs), such as eicosapentaenoic acid and docosahexaenoic acid. The consumption of fish oil or n-3 PUFAs is inversely associated with mortality from CVD (27,28). The majority of clinical studies exploring the effects of fish oil on hypertensive participants indicated that fish oil intervention caused a modest, but significant reduction in both SBP and DBP (29,30). Conversely, there was no effect on blood pressure in studies with normotensive subjects (31). A meta-analysis of 31 placebo-controlled trials concluded that the dose-dependent effect of fish oil on blood pressure was dependent on the treatment period and subject type (32). The consistent effect of fish oil can be manifested by a study design with hypertensive patients treated for more than 3 weeks. It has been reported that n-3 PUFAs induce endothelial NO synthase (eNOS) expression and activation, leading to endothelium-dependent vasorelaxation (33). In addition, n-3 PUFAs appear to have a variety of beneficial effects on cardiometabolic risk factors, such as blood lipid levels, platelet function and inflammatory markers (34). To date, at least to the best of our knowledge, there are no studies available reporting the adverse effects of fish oil supplementation.

### 4. Herbal products

*Ginseng*. Ginseng is one of the most commonly used herbal products for the prevention and treatment of hypertension. This herb has been reported to exert beneficial effects on atherosclerosis and CVD, as well as hypertension (35,36). Jovanovski *et al* demonstrated that Korean red ginseng (*Panax Ginseng*), rich in ginsenoside Rg3, acutely decreased central and peripheral blood pressure in 23 young, healthy individuals (35). Significant reductions were observed in central SBP and DBP (-5.7 mmHg and -5.1 mmHg, respectively), as well as the augmentation index (-4.3%) at 3 h following the administration of a 400 mg dose. American ginseng (*Panax quinquefolius*), another major form of ginseng, has been shown to significantly decrease SBP by 11.7% and arterial stiffness by 5.3% in 64 individuals with essential hypertension and type 2 diabetes receiving 3 g of ginseng extract for 12 weeks (36). The main active components of ginseng are considered to be ginsenosides, which have been reported to exert beneficial effects on the cardiovascular system (37,38). As regards the mode of action, the improvement of vascular function by ginseng has been attributed to the increase in the production of NO through the eNOS-dependent mechanism (36,39). By contrast, others have concluded that ginseng does not affect either arterial stiffness or blood pressure in subjects with hypertension (40). These inconsistent results may be due to the differences in the ginsenoside concentrations in ginseng preparations, the study population and the measurement methods. Systematic reviews evaluating the safety have concluded that ginseng has a good safety profile with no specific adverse events (39,41).

*Garlic*. Garlic (*Allium sativum*) has been used globally since ancient times for its diverse effects, and in particular for its cardioprotective properties, including its blood pressure-lowering effects. The findings from different meta-analyses of clinical studies on the anti-hypertensive effects of garlic are inconsistent (42-44); however, the most recently published analysis indicated that garlic supplements are effective for subjects

Table I. Dietary supplements used for the management of hypertension.

| Dietary supplement | Participants | No. of participants | Dose (per day) | Period (weeks) | SBP (mmHg) | | | DBP (mmHg) | | | Author/(Refs.) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Baseline | Final | Change | Baseline | Final | Change | |
| Coenzyme Q10 | HT | 109 | 225 mg | >52 | 159.2 | 147.8 | -11.4 | 94.4 | 85.4 | -9.0 | Langsjoen and Langsjoen (15) |
| | HT | 26 | 100 mg | 10 | 164.5 | 146.7 | -17.8 | 98.1 | 86.1 | -12.0 | Digiesi *et al* (16) |
| | HT, CAD | 59 | 120 mg | 8 | 168 | 152 | -16 | 106 | 97 | -9 | Singh *et al* (17) |
| Vitamin C | HT | 39 | 500 mg | 4 | 155 | 142 | -13 | - | - | - | Duffy *et al* (21) |
| | HT | 70 | 500 mg | 6 | 142.2 | 129.1 | -13.1 | 89.3 | 84.5 | -4.8 | Afrose *et al* (22) |
| Fish oil | HT | 32 | 4 g | 16 | 154 | 146 | -8 | 97 | 91 | -6 | Prisco *et al* (29) |
| | HT | 156 | 6 g | 10 | 144.9 | 140.3 | -4.6 | 95.0 | 92.0 | -3.0 | Bønaa *et al* (30) |
| | Healthy | 162 | 3.6 g | 12 | 122.4 | - | -2.2%[a] | 74.6 | - | -3.8%[a] | Rasmussen *et al* (31) |
| Ginseng | | | | | | | | | | | |
| Korean red ginseng | Healthy | 23 | 400 mg | (3 h) | 100.2 | 94.5 | -5.7 | 71.1 | 66.0 | -5.1 | Jovanovski *et al* (35) |
| American ginseng | HT, Diabetes | 64 | 3 g | 12 | 148.5 | 131.1 | -17.4 | 84.9 | 77.8 | -7.1 | Mucalo *et al* (36) |
| Garlic | | | | | | | | | | | |
| Kwai garlic powder | HT | 84 | 900 mg | 8 | 152.1 | 146.7 | -5.4 | 96.4 | 95.4 | -1.0 | Sobenin *et al* (46) |
| Garlic homogenate diet | HT | 40 | 300 mg | 12 | 142.7 | 136.1 | -6.6 | 90.2 | 85.6 | -4.6 | Nakasone *et al* (47) |
| Aged garlic extract | HT | 88 | 1.2 g | 12 | 148.7 | 141.7 | -7.0 | 89.9 | 86.1 | -3.8 | Ried *et al* (50) |
| Probiotics | | | | | | | | | | | |
| *Lactobacillus plantarum* | Healthy | 36 | $2x10^8$ CFU | 6 | 134 | 121 | -13 | 89 | 85 | -4 | Naruszewicz *et al* (66) |
| Fermented milk with *Lactobacillus helveticus* and *Saccharomyces cerevisiae* | HT | 46 | 160 g | 4 | 147.6 | 142.5 | -5.1 | 95.3 | 92.4 | -2.9 | Mizushima *et al* (67) |
| Fermented milk with *Lactobacillus casei* and *Lactococcus lactis* | HT | 39 | 100 ml | 12 | 155.1 | 137.7 | -17.4 | 93.3 | 86.1 | -7.2 | Inoue *et al* (68) |

[a]These values are in percentages, as only these values were available. SBP, systolic blood pressure; DBP, diastolic blood pressure; HT, hypertension; CAD, coronary artery disease; CFU, colony forming unit.

with hypertension and slightly elevated cholesterol levels (45). More than 10 studies performed using Kwai garlic powder have suggested that garlic supplement in doses ranging from 600 to 900 mg/day exert potent effects on blood pressure in hypertensive individuals, but not in normotensive individuals (46). Likewise, in the clinical study by Nakasone *et al*, treatment with a garlic homogenate-based supplementary diet for 12 weeks resulted in a significant reduction in both SBP and DBP only in patients with hypertension (47). The most consistent effects were observed in studies using aged garlic extract (AGE), another garlic preparation produced through natural aging for >10 months (48). AGE has been shown to significantly reduce blood pressure in patients with uncontrolled hypertension, suggesting that it may be used as a potent adjunct therapy for uncontrolled hypertension (49,50). Intriguingly, Ried *et al* demonstrated that AGE lowered arterial stiffness, decreased inflammation and improved gut microbiota beneficially for cardiovascular health (51). AGE has also been shown to improve peripheral circulation in hypertensive rats, increase the plasma level of NO in mice and induce endothelium-dependent vasorelaxation of isolated rat aortic rings (52-54).

Allicin has been considered as a major active ingredient in garlic supplementation, since it has been reported to exert angiotensin II-inhibiting and vasodilating effects (55,56). In addition to allicin, γ-glutamyl-*S*-allylcysteine (GSAC) may contribute to the effects by inhibiting ACE and inducing endothelium-dependent and -independent relaxation (47). In AGE, allicin and GSAC are chemically converted to other sulfur compounds including *S*-allylcysteine (SAC) and *S*-1-propenylcysteine (S1PC) during the aging process. SAC has been shown to reduce renal injury and hypertension in 5/6 nephrectomized rats, which was shown to be associated with its antioxidant properties (57). Both the single and repeated administration of S1PC have been shown to significantly lower blood pressure in hypertensive rats by modulating various regulatory molecules, such as histidine, tryptophan and lyso-phosphatidylcholine (58,59). The anti-hypertensive mechanisms of AGE appear to be divergent due to its various active ingredients.

The majority of studies have stated that garlic supplements are very safe. Only a few studies have reported that the use of garlic may cause adverse events, such as malodorous breath, body odor and mild gastrointestinal disturbances (60,61). These side-effects are prominently observed in studies using raw garlic and are alleviated in interventions with AGE (62).

## 5. Probiotics

Recently, probiotics have attracted considerable interest for their health promoting benefits, including the management of blood pressure (12,63). Gut microbial richness and diversity have been shown to be markedly reduced both in animal and human hypertension and this microbiota dysbiosis contributes to the pathogenesis of hypertension (64,65). A growing number of clinical trials have reported that the use of probiotics leads to a moderate or significant reduction in blood pressure, which is associated with the improvement of the gut microbiota (63). For example, the intake of a drink containing *Lactobacillus plantarum* for 6 weeks has been shown to lead to a significant reduction in SBP, leptin, fibrinogen and interleukin-6 in healthy participants (66). In several studies with hypertensive subjects, milk fermented with bacteria, in particular the *Lactobacillus* species, has been shown to significantly decrease blood pressure (67,68). The study by Aoyagi *et al* suggested that the consumption of fermented milk products containing *Lactobacillus casei* at least 3 times a week considerably reduced the incidence of hypertension over a 5-year follow-up period (69). In a comparative study between bacteria, a yoghurt product fermented with one strain of *Enterococcus faecium* and two strains of *Streptococcus thermophilus* more significantly reduced low-density lipoprotein cholesterol and blood pressure than that fermented with less strains or other bacteria in obese participants (70).

It has been demonstrated that probiotics improve lipid levels, reduce blood glucose levels and regulate the renin-angiotensin system, which contributes to the decrease in blood pressure (71-73). In addition, Tanida *et al* demonstrated that the intraduodenal injection of Lactobacilli or its metabolites reduced hypertension and renal sympathetic nerve activity via the central histaminergic system in urethane-anesthetized rats (74). These findings suggest that the anti-hypertensive effects of probiotics are associated with several different mechanisms. No side-effects have been reported in clinical studies to date, at least to the best of our knowledge.

## 6. Conclusion

A number of dietary supplements are available and are used as anti-hypertensive medication worldwide; however, not all the products have been extensively studied in terms of their effects on blood pressure or for any adverse effects. The present review provides an overview of dietary supplements recommended for the prevention and treatment of hypertension from the viewpoint of substantial benefits with minor or no side-effects in clinical studies. Notably, a few garlic preparations and probiotic products can reduce blood pressure by multiple mechanisms. In addition, they have demonstrated various health-promoting properties both in animal and human studies, suggesting that they may be used as beneficial complementary and alternative medications in hypertension therapy. There is still controversy on the association between the supplementation of some products and blood pressure since clinical studies have reported inconsistent conclusions, probably due to the differences in study designs. Larger and longer term trials and cross-sectional analyses are required to determine the substantial benefits and risks associated with the use of these dietary supplements.

## Acknowledgements

The author would like to thank Dr Takami Oka of Wakunaga Pharmaceutical Co., Ltd. for his helpful advice, his encouragement and his critical reading of the manuscript.

## Funding

No funding was received.

## Availability of data and materials

Not applicable.

## Authors' contributions

TM researched the literature, performed the analysis of the data and drafted the manuscript. The author has read and approved the final manuscript.

## Ethics approval and consent to participate

Not applicable.

## Patient consent for publication

Not applicable.

## Competing interests

The author declares that there are no competing interests.

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