

Effects of garlic supplementation on blood pressure

Marjan Mahdaviroshan^{*1}, Javad Nasrollahzadeh², Elham Khodadadi³

¹ National Nutrition and Food Technology Research Institute, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

² Department of Clinical Nutrition & Dietetics, National Nutrition and Food Technology Research Institute, Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

³ Proteomics Research Center, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

*Corresponding Author: email address: mahdaviroshan@yahoo.com (M. Mahdaviroshan)

ABSTRACT

Hypertension is one of the major risk factor for cardiovascular morbidity and mortality. One of primary management of hypertension include dietary changes which could incorporate dietary supplementation ,also use of non pharmacological treatment options is high in patients with high blood pressure .Garlic has played an important dietary as well as medicinal role in human history and it has been on the top ten lists of herbal sales among people.

For evaluating the effect of garlic on blood pressure ,we reviewed clinical trials published from 1982 until 2013 by searching in informative bank such as PubMed ,Ovid , Elsevier Science , Google Scholar with keywords garlic , blood pressure, hypertension and herbal supplement. The result of this review article showed that several clinical trials have suggested garlic lowers systolic and or diastolic blood pressure and has beneficial effect in controlling hypertension, but negative results also have been obtained in some of trials .Blood pressure reducing properties of garlic have been linked to its hydrogen sulphide production and allicin content , liberated from alliin and the enzyme alliinase. large scale trials are needed to investigate whether standardized garlic preparations could provide a safe alternative or complementary treatment option for hypertension in clinical practice.

Keyword: Garlic; Hypertension; Blood pressure; Herbal supplement

INTRODUCTION

Hypertension that defined as a systolic blood pressure Greater than 140 mmHg and or a diastolic blood pressure Greater than 90 mmHg, is one of the major risk factors for cardiovascular morbidities including coronary artery disease , myocardial infarction and kidney disease, as well as for mortality [1] .Hypertension affects one billion or one in three adults worldwide, and attributes to about 40% of cardiovascular related deaths , unfortunately more than 50% of hypertensive individuals are unaware of their condition [2] .

There are several factors that have been associated with hypertension such as smoking, obesity, inappropriate lifestyle and some chronic

disease. Primary management of hypertension should include relevant lifestyle modifications such as increased exercise, weight loss and dietary changes which could incorporate dietary supplementation [1].Current medication therapy with standard antihypertensive medication is not always effective and leading to a large proportion of uncontrolled hypertension . In addition, side effects of treatment may be influence treatment adherence. For this reason, use of complementary and alternative therapies is high in patients with high blood pressure [2] .

Garlic (*Allium sativum*) has a long history of use as a pungent spice and as a foodstuff in numerous countries. It has also been used for various medicinal purposes [3]. Garlic has historically

been used to treat earaches, severe diarrhea, leprosy, deafness, constipation and parasitic infections, fever, fight infections and relieve stomach [4].

The name "allium sativum" is derived from the Celtic word "all", meaning burning or stinging, and the Latin "sativum" meaning planted or cultivated. The English word, garlic, is derived from the Anglo-Saxon "gar-leac" or spear plant, referring to its flowering stalk [5].

In Traditional Chinese Medicine, garlic is known as da suan. It is considered a warm, bitter herb with particular effects on the Large Intestine, Spleen and Stomach meridians. Garlic has been on the top ten lists of herbal sales for several years [6].

Over the last 30 years, numerous clinical studies have been carried out to examine the effects of various garlic-based products containing dried garlic powder, garlic oil or garlic extract as the basal component on health. This paper will review the effect of Garlic on Blood pressure.

MATERIALS AND METHODS

Articles used in this study, were collected by searching in informative bank such as PubMed, Ovid, Elsevier Science, Google Scholar. From 1982 until 2013. The keywords "Garlic, Blood pressure, Hypertension and Herbal supplement" were used for searching. Studies were limited to English languages and clinicaltrials.gov was searched for ongoing trials. From related articles, 37 articles related to the effect of garlic and blood pressure were extracted.

RESULT

Chemical and biochemical structure of garlic

Garlic contains Thirty-three sulfur compounds, several enzymes, seventeen amino acids, and minerals [7]. It contains a higher concentration of sulfur compounds than any other Allium species. The sulfur compounds are responsible both for garlic's medical effects and its pungent odor. Dried, powdered garlic contains approximately one percent alliin [7]. One of the most biologically active compounds, allicin (diallyl disulfide) does not exist in garlic until it is crushed or cut, injury to the garlic bulb activates the enzyme allinase, which metabolizes alliin to

allicin. Allicin is further metabolized to vinylthiins [8]. Garlic is rich source of highly bioavailable selenium, which is thought to account, in part, for garlic's antioxidant that is important for health. Some growers add selenium to the soil to enhance garlic's selenium content [9]. Allicin and alliin is thought to be the most beneficial compound in terms of cardiovascular risk factors [10]. Various garlic-based products are used in studies. Raw garlic homogenate has been the major preparation of garlic subjected to scientific study, as because it is the commonest way of garlic consumption. Raw garlic homogenate is essentially same as aqueous extract of garlic, which has been used in various scientific studies [11].

Garlic oil also is used in studies, it is mostly prepared by steam-distillation process. Steam-distilled garlic oil consists of the diallyl (57%), allyl methyl (37%) and dimethyl (6%) mono to hexa sulfides. A typical commercial preparation of garlic oil contains diallyl disulfide (26%), diallyl trisulfide (19%), allyl methyl trisulfide (15%), allyl methyl disulfide (13%), diallyl tetrasulfide (8%), allyl methyl tetrasulfide (6%), dimethyl trisulfide (3%), penta sulfide (4%) and hexa sulfide (1%) [12]. Another widely studied garlic preparation is aged garlic extract (AGE). Sliced raw garlic stored in 15–20% ethanol for 20 months is referred to as AGE. This whole process is supposed to cause considerable loss of allicin and increased activity of certain newer compounds, like S-allylcysteine, S-allylmercaptocysteine, allixin and selenium which are stable, highly bioavailable and significantly antioxidant [13]. Another recently identified antioxidant compound of AGE is N-alpha-L-arginine that is not present in raw garlic [12].

Effect of garlic on blood pressure

Many studies have explored effect of garlic on controlling blood pressure. In a meta-analysis of seven placebo-controlled clinical trials using garlic powder supplementation, three studies showed a significant reduction in systolic blood pressure and four in diastolic blood pressure. The overall pooled mean difference in the change in systolic blood pressure was 5-7% greater in the subjects who were treated with garlic than in those treated with placebo. The reduction in

diastolic blood pressure in the garlic-treated subjects was slightly smaller [14].

Table 1. Summaries of human studies about effect of garlic on blood pressure

References	Intervention	subjects	Duration	Dose	Result
Ried K 2013 [2]	aged garlic extract	hypertensive patients	12 weeks	960 mg/day	reduction in systolic blood pressure -10.2±4.3 mmHg, $P=0.03$)
Nakasone Y 2013[17]	dried garlic homogenate	prehypertensive and mild hypertensive subjects	12 weeks	300 mg/day	↓ hypertension in mild hypertensive subjects (4.6%; $P<0.01$)
Sobenin IA 2009 [27]	garlic powder tablets	men with mild or moderate hypertension	8-week	600 mg	reduction of both systolic and diastolic blood pressures by 7.0 mm Hg and 3.8 mm Hg respectively
Turner B 2004 [28]	Dried garlic powder	Healthy middle-aged individuals	12-week	230 mg/day	No changes
Ziaei 2001 [29]	Garlic tablet (Garlet)	pregnant women	3 months	800 mg/day	during the third trimester of pregnancy garlet was effective in reducing the occurrence of hypertension ($P=0.043$), but it was no effective in preventing of preeclampsia.
Qidwai, 2000 [30]	Garlic in diet	Healthy subjects	Chronic intake	134gm/month	individuals with blood pressures on the lower side consume more garlic in their diets
Siegel G 1999 [18]	garlic powder	Cardiovascular disease patients	4-year	900 mg/day	↓ BP (lowering in blood pressure by 7%)
McCrindle 1998 [31]	Kwai(garlic pill)	pediatric patients, aged 8 to 18 years, who had familial hyperlipidemia	8 weeks	900 mg/day	No changes
Steiner 1996 [32]	Aged garlic extract	moderately hypercholesterolemic men	6 months	7.2 gm/day	5.5% decrease in systolic blood pressure and a modest reduction of diastolic blood pressure
Simons 1995 [33]	Kwai(garlic pill)	subjects with mild to moderate hypercholesterolaemia and hypertension	12 weeks	900 mg/day	No changes
Jain 1993 [34]	Kwai(garlic pill)	healthy adults	12 weeks	900 mg/day	No changes
Mcmahan, 1993 [35]	Garlic powder	patients with severe hypertension	Acute	2400 mg	significant decrease in diastolic blood pressure ($p < 0.05$) from 5-14 hours after the dose
Kiesewetter 1991[36]	Garlic powder	Cardiovascular disease patients	4 weeks	800 mg/day	diastolic blood pressure decreased 9.5% (from 74 +/- 9 to 67 +/- 5 mmHg)
Auer 1990 [37]	Kwai(garlic pill)	patients with mild hypertension	12 weeks	600 mg/day	diastolic blood pressure fell from 102 to 89 mmHg (p less than 0.01)
Zimmerman1990[38]	Kwai (garlic pill)	hypertensive patients	3 weeks	900 mg/day	No changes

One trial study included 47 hypertensive patients showed that garlic significantly reduces mean systolic blood pressure by 12 mmHg (95% CI 0.56 to 23.44 mmHg, $p=0.04$) and mean diastolic blood pressure by 9 mmHg (95% CI 2.49 to 15.51 mmHg, $p=0.007$) versus placebo[15].

In a study of 20 normal adults, garlic powder supplements significantly increased the diameter of conjunctival venules and arterioles [16]. Study on 34 subjects with prehypertension and 47 with mild hypertension that were treated with a daily dose of GH diet (300 mg as dried garlic homogenate ; $n=16$ and 23 , respectively) or placebo ($n=18$ and 24 , respectively) for 12 weeks, have demonstrated that a daily 300 mg as dehydrated garlic homogenate dose, lowered systolic blood pressure by 6.6–7.5 mmHg and diastolic blood pressure by 4.6–5.2 mmHg in subjects with mild hypertension, but not in those with prehypertension , following an 8 or 12 week treatment[17]. In a four-year clinical trial of atherosclerotic adults, receiving standardized garlic powder supplementation (900 mg daily) lowered blood pressure by 7% ($P<0.05$) [18]. A meta analysis of eight controlled trials (seven placebo controlled) with a total of 415 subjects that all tested the same brand of dried garlic tablets, showed only small reductions in blood pressure. In this meta analysis only three of these trials were in hypertensive patients [10]. Simons and coworkers, in a systematic review on the influence of trial quality on the effect of garlic on blood pressure conclude the effect of garlic on blood pressure cannot be ascertained [19]. Summaries of other human studies has been shown in table 1. In experimental animals, intravenous injection of garlic extracts produced slight reductions in both systolic and diastolic pressures [20,21] Oral administration of garlic reduced experimentally induced hypertension, bringing blood pressure back to the normal range. Studies showed that garlic extracts reduce blood pressure in rats and dogs [22]. In anesthetized dogs, for example, gastric administration of encapsulated garlic powder induced dose-dependent natriuretic and diuretic responses which reached a maximum 30-40 minutes after garlic administration and decreased to basal levels after 100-150 minutes[23].

In rabbits, intravenous administration of garlic extracts elicited a dose-dependent diuretic-natriuretic response and a gradual decrease in heart rate, but not in arterial blood pressure [24]. Elkayam and coworkers in their study showed , Allicin lower blood pressure and triglyceride levels in spontaneously hypertensive rats[25].

In vitro data, In isolated strips of canine carotid arteries and in isolated rat aorta, garlic exerted direct vasodilating effects .Garlic also activated the synthesis of nitric oxide, which is a potent endogenous vasodilator [26].

DISCUSSION

Several human and animal clinical trials have suggested that garlic lowers systolic and or diastolic blood pressure and has beneficial effect in controlling blood pressure . Mechanisms of antihypertensive action of garlic are related to its prostaglandin like effects, which decreases peripheral vascular resistance [11] .Garlic reduce prostaglandin E_2 and thromboxane B_2 level and thereby can reduce hypertension [39]. The gamma-glutamylcysteines are the compounds in garlic ,they inhibit angiotensin-converting enzyme and for this mechanism, garlic can lower blood pressure [11]. Garlic also inhibited endothelin-1 induced contraction in a dose-dependent manner [39]. Allicin and ajoene in Garlic appear to inhibit inducible nitric oxide synthase in macrophages, reducing nitrite accumulation in atherosclerotic plaques and in hypoxic tissues [40]. Zalejska-Fiolka and coworkers reported that garlic-fed rats had improved antioxidant status, less lipid peroxidation and fewer atherosclerotic changes than controls[41]. Garlic modulates the production and function of both endothelium derived relaxing and constricting factors and this may contribute to its protective effect against hypoxic pulmonary vasoconstriction [42,43]. Garlic elicits nitric-oxide-dependent relaxation in pulmonary arteries. But another study reported that pulmonary vasodilatory effect of allicin are independent of the synthesis of NO, ATP-sensitive (K^+) channel, activation of cyclooxygenase enzyme [44]. In contrast some trials have reported that garlic has not significant effect on blood pressure. One reason for different

result in studies may be related to varied dose or varied types of garlic preparation (dried garlic powder, garlic oil or garlic extract) that may contain widely varying types of sulfur-containing phytochemicals due to the different methods of producing the preparations, for example minimal allicin compounds are found in aged garlic extract or heat treated garlic, which may limit its hypotensive properties [45,46]. In positive studies daily dose of 600 mg and 900 mg dried garlic powder equivalent to 1.8–2.7 gram or approximately 1–3 cloves fresh garlic (as a food supplement) are recommended for controlling blood pressure [47].

Possible adverse Effects

Herbs, can trigger side effects and can interact with other supplements or medications. For these reasons, they should be taken with care. Garlic is listed as Generally Recognized as Safe (GRAS) by the United State Food and Drug Administration [48]. Relatively few side effects were reported in clinical studies using garlic and its preparations. Most of the reported side effects

were non-specific. Reported side effects included bloating, headache, dizziness, esophageal and abdominal pain and profuse sweating [11,49,50]. Also ingestion of too much fresh garlic and garlic powder may have additive effects with anticoagulants or platelet aggregation inhibitors including warfarin (Coumadin), clopidogrel (Plavix) and aspirin [51,52]. The frequency of adverse effects and whether they varied by particular preparations were not studied.

CONCLUSION

Although several clinical trials have suggested that garlic lowers systolic and or diastolic blood pressure and has beneficial effect in controlling blood pressure, negative results also have been obtained in some of trials. Future large scale trials are needed to investigate whether standardized garlic preparations could provide a safe alternative or complementary treatment option for hypertension in clinical practice.

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