Garlic for arterial hypertension and hypercholesterolemia Review of literature and clinical studies

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Abstract

Garlic is a widely known and widely used plant. Due to its taste, it is used in the preparation of many dishes. Garlic is also used in the treatment of bacterial, viral, fungal and parasitic infections. There are many chemical compounds in garlic, but those responsible for its health-promoting effect include, first of all, those containing sulfur. These compounds are characterized by many mechanisms of action, such as antioxidant, cardioprotective and anti-inflammatory effects. Many mechanisms of action of organosulfur compounds influencing the regulation of blood pressure and lipid metabolism have been demonstrated. Many clinical studies and meta-analyses are assessing the effect of garlic on blood pressure and lipid profile in various groups of patients in the literature. This article aims to present the current knowledge on the influence of garlic on blood pressure and lipid metabolism.

Key words: garlic, blood pressure, lipids, arterial hypertension, hypercholesterolemia

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Hypertension and hypercholesterolemia in Poland

Hypertension and hypercholesterolemia are the most common factors of cardiovascular risk in Poland. According to the WOBASZ II (Wieloośrodkowe Badanie Stanu Zdrowia Ludności, Multicentre Study of Population health), the prevalence of hypertension among adult Poles is 42.7%, while that of hypercholesterolemia is 67.2% [1, 2]. In addition, the WOBASZ II study revealed that 34.6% of patients suffer from both hypertension and hypercholesterolemia [3].

Such a high prevalence and concomitance of hypertension and hypercholesterolemia stems from, among other things, insufficient social awareness regarding the impact of an unhealthy lifestyle on cardiovascular function [4, 5]. Numerous studies have shown that dietary habits have a significant impact on blood pressure and plasma lipid levels [6–8].

This paper aims to present current biochemical and clinical knowledge on the impact of commonly consumed garlic and garlic supplements on blood pressure and lipid concentration in plasma.

Garlic — characteristics, properties and differences

Garlic (*Allium L.*) belongs to the *Amaryllidaceae* family and is among the oldest plants cultivated by man, not only due to its culinary value, but also medicinal properties. Garlic comes from Asia and has been known for approximately 5,000 years. Ancient documents from Egypt, Greece, Rome, China and India confirm that garlic was used in medicine [9]. Currently, garlic and its supplements are used to treat
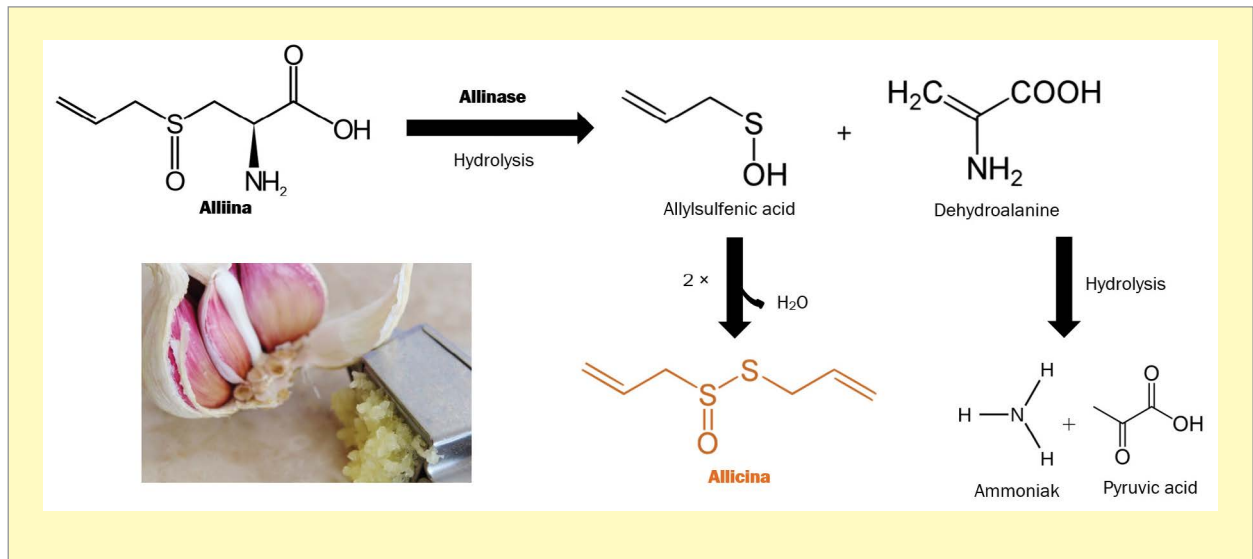
Figure 1. Formation of allicin from alliin by the enzyme alliinase

or support the treatment of bacterial, viral, fungal and parasitic infections [9].

Garlic is a vegetable that is commonly imported to Poland. According to the data of Statistics Poland (GUS, *Główny Urząd Statystyczny*), garlic imports to Poland amounted to 11,600 tonnes, and its value reached PLN 72.4 million. The data indicate that the largest amounts of garlic were imported from Spain, Egypt, China and Portugal.

Fresh garlic contains water (62–68%), carbohydrates (26–30%), proteins (1.5–2.1%), amino acids (1–1.5%), organosulfur compounds (1.1–3.5%), and fibre (1.5%) [10]. The health-promoting properties of garlic are primarily attributed to the organic sulfur compounds that it contains. The best-studied biologically active organosulfur compounds in garlic are diallyl disulfide, diallyl trisulfide, methyl diallyl trisulfide, S-allyl cysteine, and alliin [10]. It should be mentioned that the chemical composition of garlic changes when it is processed. The most important chemical reaction that occurs, for example, during the crushing of garlic cloves is the production of allicin from alliin under the influence of the enzyme alliinase (EC 4.4.1.4) (Figure 1). It is worth mentioning that allicin is responsible for the characteristic smell of crushed garlic cloves [11].

The organosulfur compounds found in garlic have numerous health-promoting properties, such as antioxidant (especially strong due to their chemical structure), cardioprotective, antimicrobial, and anti-inflammatory activity [11]. It should be mentioned that garlic shows potent bactericidal activity against numerous Gram (+) and Gram (–) microorganisms, including antibiotic-resistant strains [12]. The exact biochemical mechanism of action of organosulfur compounds found in garlic is presented in Figure 2.

Since garlic is grown in many climatic zones and thus is exposed to different environmental factors, its different varieties (e.g., Polish garlic "Harnaś", Chinese and Portuguese garlic, Spanish garlic "Violetta" or Italian garlic "white or savoury") may differ not only in terms of their morphology but also in terms of the content of biologically active substances, which may translate into their biological properties. Rybczynska et al. [13] used an in vitro culture of human vascular endothelial cells (HUVEC) to investigate the impact of Polish and Chinese garlic extracts on the expression of adhesive molecules — soluble vascular cell adhesion molecule 1 (sVCAM-1), soluble intercellular adhesive molecule 1 (sICAM-1) as well as the expression of metalloproteinases ADAM10 (ADAM metallopeptidase domain 10) and ADAM 17 (ADAM metallopeptidase domain 17) in these cells. It was demonstrated that extracts from both varieties of garlic reduced the expression of these proteins, with the extract from the Chinese variety showing a stronger effect [13]. Furthermore, Matysiak et al. [14] demonstrated that chemical substances contained in the aqueous extract from Chinese garlic had a greater ability to neutralize the DPPH free radical, cation radical ABTS+ and chelated copper (II) ions. They also inhibited the growth of the *Saccharomyces cerevisiae* fungi much more strongly than those contained in the aqueous extract from Polish garlic. On the other hand, chemical substances contained in an aqueous extract from Polish garlic chelated iron (II) ions more strongly [14]. Another study by Matysiak et al. revealed that varieties of garlic from China, Poland and Spain had different antioxidant properties [15]. Gaweł-Bęben et al. [16] also observed that among such varieties of garlic as Polish garlic "Harnaś", Chinese, Uzbek, Portuguese garlic, Spanish garlic "Violetta"
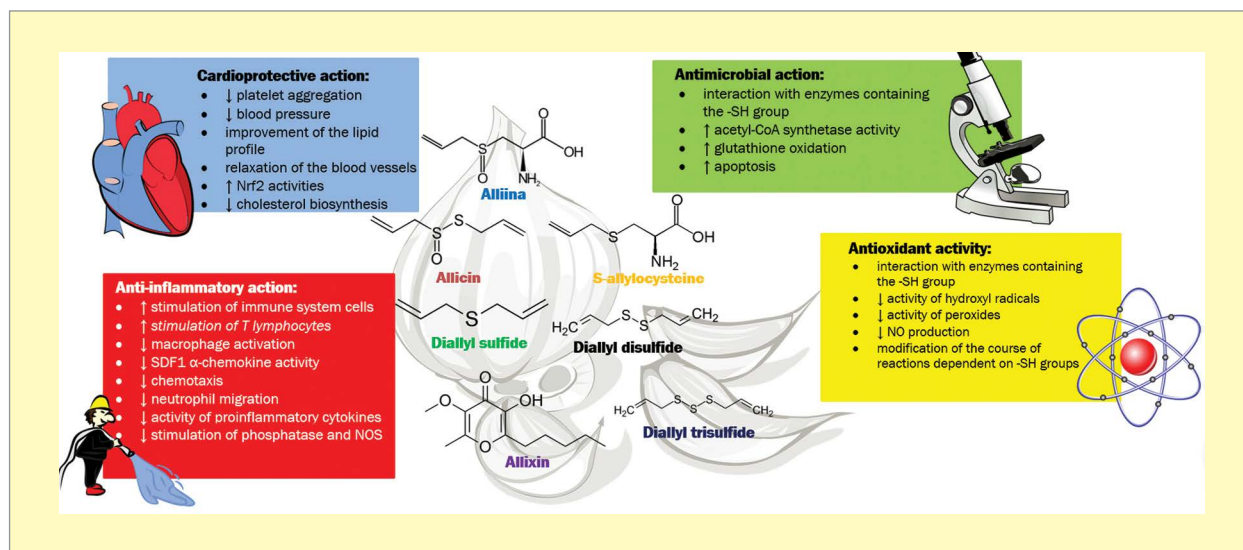
Figure 2. Effects of garlic on human health (based on [11]) Nrf2 — nuclear factor erythroid; SDF-1 — stromal cell-derived factor 1; NOS — nitric oxide synthase; -SH group — thiol group

and Italian "white or savoury" garlic, it was the Italian varieties that showed the strongest antifungal effect against *Saccharomyces cerevisiae.* Magnetic resonance imaging (MRI) analysis of the content of organic sulfur compounds in individual garlic extracts showed that the tested varieties of garlic differed in terms of their content of biologically active compounds, such as allicin [16].

In conclusion, garlic is a popular vegetable used for both culinary and medicinal purposes. It contains many chemical compounds and its health-promoting properties are primarily attributed to organosulfur compounds, such as acillin. Different varieties of garlic originating from different geographical areas have different biological properties.

Garlic for blood pressure and lipid metabolism regulation — biochemical mechanisms

It seems that the mechanisms of the antihypertensive properties of garlic are not yet fully understood. In their review of literature, Borghi and Cicero [17] attempted to summarize the knowledge on the impact of various nutraceuticals, including garlic, on blood pressure. According to the authors, the most likely mechanisms responsible for garlic-induced lowering of blood pressure include increased production of nitrogen oxide (NO) by vascular endothelial cells, increased production of Hydrogen sulfide (H$_2$S), increased production of bradykinin, decreased sensitivity of tissues to catecholamines, reduced activity of the angiotensin-converting enzyme (ACE), as well as blocking of calcium channels [17].

The hypolipemic properties of garlic involve several biochemical mechanisms [11]. Chemical compounds present in garlic decrease the activity of enzymes such as fatty acid synthase, glucose-6-phosphate dehydrogenase, and 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMGCoA) [18]. In addition, garlic increases the excretion of acidic and neutral steroids from the organism [19]. It is also suggested that the chemical compounds present in garlic reduced the gene expression of such enzymes as cholesterol ester transfer protein (CETP), Niemann-Pick C1-like 1 protein (NPC1L1), and microsomal triacylglyceride transfer protein (MTP) [20]. Garlic exerts positive effects on high-density lipoprotein (HDL) by regulating the ATP-binding cassette transporters, such as ABCG5, ABCG8 and ABCA1, involved in lipid transport [11].

It should also be mentioned that garlic has been demonstrated to have a positive effect on the composition of the gut microbiota. Disorders in gut microbiota may play a significant role in hypertension pathogenesis and interventions aimed at reducing dysbiosis in this region of the gut have antihypertensive effects [21, 22]. A meta-analysis conducted by Ried [23] investigated the impact of garlic on gut microbiota. It was demonstrated that there was an improvement in gut microbiota, as evidenced by greater microbial diversity, with a significant increase in the number of *Lactobacillus* and *Clostridia* species that was observed after three months of garlic supplementation [23]. In addition, biologically active compounds present in garlic show antimicrobial activity against pathogens contributing to the development of periodontitis or caries, such as *Porphyromonas gingivalis*, *Aggregatibacter*

Table 1. Summary of results of meta-analyses (n = 7) investigating the effects of garlic on blood pressure

Author	Year	Study	Sample size	Results	Impact on BP
Mulawarman et al. [27]	2021	Meta-analysis of RCTs	12 RCTs (503 hypertensive patients)	In the group treated with garlic: • SBP: reduction by **3.62 mm Hg** (95% CI: –5.43 to –1.80 mm Hg, p < 0.0001) • DBP: reduction by **1.40 mm Hg** (95% CI: –2.72 to –0.08 mm Hg, p = 0.04)	:)
Ried [23]	2020	Meta-analysis of RCTs	12 RCTs (553 hypertensive patients)	In the group treated with garlic: • SBP: reduction by **8.32 mm Hg** (95% CI: –10.25 to –6.39 mm Hg, p < 0.00001) • DBP: reduction by **5.48 mm Hg** (95% CI: –7.40 to –3.55, p < 0.00001) The observed BP reduction translated into lowering the cardiovascular risk by **16–40%**	:)
Ried [28]	2016	Meta-analysis of RCTs	20 RCTs (n = 970, including hypertensive patients)	In patients with hypertension: • SBP: reduction by **8.35 mm Hg** (95% CI: –10.58 to –6.11 mm Hg, p < 0.00001) • DBP: reduction by **6.08 mm Hg** (95% CI: –7.33 to –4.48 mm Hg, p < 0.00001) Greater antihypertensive properties were observed in the case of garlic powder (compared to mature garlic extract)	:)
Rohner et al. [29]	2015	Meta-analysis of RCTs	10 RCTs (482 hypertensive patients)	In the group treated with garlic: • SBP: reduction by **9.1 mm Hg** (95% CI: –12.7 to –5.4 mm Hg, p = 0.0006) • DBP: reduction by **3.8 mm Hg** (95% CI: –6.7 to –1.0 mm Hg, p = 0.00001) The effect varied depending on the garlic preparation used	:)
Wang et al. [30]	2015	Meta-analysis of RCTs	17 RCTs (healthy individuals and individuals with hypertension)	Individuals with normal blood pressure: • SBP: not significant • DBP: not significant Hypertensive patients: • SBP: reduction by **4.4 mm Hg** (95% CI: –7.37 to –1.42 mm Hg, p = 0.004) • DBP: not significant	:)
Xiong et al. [31]	2015	Meta-analysis of RCTs	7 RCTs (391 hypertensive patients)	In the group treated with garlic: • SBP: reduction by **6.71 mm Hg** (95% CI: –12.44 to –0.99, p = 0.02) • SBP: reduction by **4.79 mm Hg** (95% CI: –6.60 to –2.99 mm Hg, p < 0.00001)	:)
Kwak et al. [32]	2014	Meta-analysis of RCTs	9/10 RCTs	In the group treated with garlic: • SBP: reduction by **4.34 mm Hg** (95% CI: –8.38 to –0.29 mm Hg, p = 0.036) • DBP: reduction by **2.36 mm Hg** (95% CI: –4.56 to –0.15, p = 0.036)	:)

RCT — randomized controlled trial; SBP — systolic blood pressure; DBP — diastolic blood pressure; CI — confidence interval

Table 2. Summary of results of meta-analyses (n = 8) investigating the effects of garlic on lipid metabolism

Author	Year	Study	Sample size	Results	Effects on lipids
Gyawali et al. [33]	2021	Meta--analysis of RCTs	24 RCTs (n = 1,386, including patients with cardiovascular risk factors)	In the garlic use group: • TC: reduction by **12.45 mg/dL** (95% CI: −18.68 to −6.22 mg/dL, p < 0.00001) • LDL cholesterol: reduction by **10.37 mg/dL** (95% CI: −17.58 to −3.16 mg/dL, p = 0.005) TG: not significant HDL cholesterol: not significant	🙂
Mulawar--man et al. [27]	2021	Meta--analysis of RCTs	12 RCTs (n = 503 individuals including hypertensive pa-tients)	In the group treated with garlic: • TC: reduction by **17.17 mg/dL** (95% CI: −28.57 to −5.78 mg/dL, p < 0.00001)	🙂
Shabani et al. [34]	2019	Meta--analysis of clinical trials	33 clinical trials (n = 1,273 patients with diabetes)	In the group treated with garlic: • TC: reduction by **16.87 mg/dL** (95% CI: −21.01 to −12.73 mg/dL, p = 0.001) • HDL cholesterol: increase by **3.19 mg/dL** (95% CI: 1.85 to 4.53 mg/dL, p = 0.001) • LDL cholesterol: reduction by **9.65 mg/dL** (95% CI: −15.07 to −4.23 mg/dL, p = 0.001) • TG: reduction by **12.44 mg/dL** (95% CI: −18.19 to −6.69 mg/dL, p = 0.001)	🙂
Sun et al. [35]	2018	Meta--analysis of clinical trials	14 clinical trials (n = 1,093 patients with dyslipidemia)	In the group treated with garlic: • TC: reduced concentration (SMD = **−1.26**, 95% CI: −1.86 to −0.66, p < 0.0001) • LDL cholesterol: decreased concentration (SMD = **−1.07**, 95% CI: −1.67 to −0.47, p < 0.0001) • HDL cholesterol: increased concentration (SMD = **0.50**, 95% CI: 0.06 to 0.94, p < 0.0001) • TG: not significant	🙂
Sahebkar et al. [36]	2016	Meta--analysis of RCTs	6 RCTs (n = 286, including patients with dyslipidemia)	In the group treated with garlic: • lipoprotein (a): not significant	😐
Kwak et al. [32]	2014	Meta--analysis of RCTs	22/17/18 RCT	In the group treated with garlic: • TC: reduction by **15.83 mg/dL** (95% CI: −26.64 to −4.63 mg/dL, p = 0.005) • LDL cholesterol: reduction by **9.11 mg/dL** (95% CI: −15.44 to −1.16 mg/dL, p = 0.024) HDL cholesterol: not significant	🙂
Reid et al. [37]	2013	Meta--analysis of RCTs	39 RCTs (n = 2,298 individuals, including patients with dyslipi-demia)	TC: • individuals with TC ≤ 200 mg/dL: not significant • individuals with TC > 200 mg/dL: **17.32 mg/dL** reduction (95% CI: −23.48 to −11.16 mg/dL, p < 0.00001)* LDL cholesterol: • reduction by **6.41 mg/dL** (95% CI: −11.77 to 01.05 mg/dL, p = 0.02) HDL cholesterol: • increased by **1.49 mg/dL** (95% CI: 0.19 to 2.79, p = 0.02) TG: not significant	🙂
Zeng et al. [38]	2012	Meta--analysis of RCTs	26 RCTs	In the group treated with garlic: • TC: reduction by **10.83 mg/dL** (95% CI: −17.40 to −4.25 mg/dL, p = 0.001) • TG: reduction by **11.51 mg/dL** (95% CI: −17.71 to −5.31, p < 0.001) The hypolipemic effect was more pronounced during the longer intervention. Garlic powder and mature garlic extract resulted in a greater reduction in total serum cholesterol, whereas garlic oil resulted in a gre-ater reduction in serum triglycerides	🙂

*Provided that garlic has been consumed for ≥ 2 months; RCT — randomized controlled trial; TC — total cholesterol; CI — confidence interval; LDL — low-density lipoproteins; TG — triglycerides; HDL — high--density lipoproteins; SMD — standardized mean difference

actinomycetemcomitans and *Streptococcus mutans* [24, 25]. It seems that periodontitis constitutes a non-traditional risk factor for the development of hypertension [26]. The antihypertensive properties of garlic may also be related to its effect on maintaining a healthy oral microbiota.

Garlic for hypertension and lipid metabolism — what do results of clinical studies say?

There are many randomized controlled trials (RCT) investigating the impact of garlic on blood pressure and lipid metabolism available in the literature. Results of these studies have been collectively summarized in numerous meta-analyses, the results of which are presented in Table 1 [23, 27–32] and Table 2 [27, 33–38].

Garlic preparations that were most used in clinical trials included garlic powder, mature garlic extract, garlic oil, Japanese garlic powder containing egg yolk, and raw garlic. Doses of individual preparations varied, as did the duration of the intervention (several weeks on average) [23, 27, 38]. In the meta-analysis by Ried [28], it was observed that formulations containing garlic had a high safety profile and were well tolerated.

Garlic has been shown to have antihypertensive and hypolipemic properties that were particularly evident in patients with cardiovascular risk factors [23, 27–38].

A recent meta-analysis conducted by Schoeneck and Iggman [39] evaluated the hypolipemic effect of garlic. It was observed that the impact of garlic on reducing serum low-density lipoprotein (LDL) cholesterol was small to moderate (maximum reduction of its concentration by approx. 15 mg/dL) [39].

A very interesting, randomized controlled and double-blind trial conducted by Wlosinksa et al. [40] investigated the impact of supplementition with mature garlic extract (2,400 mg/day for a year) on the progression of coronary artery calcification. It involved 104 patients who were randomized to receive supplementation with mature garlic extract or placebo. It was demonstrated that the applied intervention had a significant impact on reducing the progression of coronary calcification (p = 0.040). In addition, glucose (p = 0.034) and interleukin 6 (p = 0.049) concentration as well as systolic blood pressure (p = 0.027) were significantly reduced in the study group [40].

In summary, garlic shows antihypertensive and hypolipemic effects, as well as anti-atherosclerotic effects.

Summary

In Poland, where 18 million people suffer from hypercholesterolemia and 11 million have hypertension, it seems that supplementing the diet with ingredients that show hypotensive, hypolipemic, and potentially anti-atherosclerotic effects would

be very beneficial. In this context, the promotion of garlic as a frequent component of the diet should be considered to be cardio- and vaso-protective activity. The lipid-lowering properties of garlic have been noticed in the latest guidelines for the treatment of lipid disorders in Poland. These guidelines indicate that garlic (5–6 g/day dose) may have a mild to moderate reduction in serum LDL cholesterol (5–10% of the baseline concentration). The recommendation for the use of garlic in patients with lipid disorders is class IIa (should be considered) and the level of evidence A (data from many randomized clinical trials or meta-analyses) [41, 42].

Conflict of interest

The authors report no conflicts of interest.

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