







ISSN: 2455-2976

DOI: https://dx.doi.org/10.17352/jcm/

Research Article

Garlic supplement lowers blood pressure in 40-60 years old hypertensive individuals, regulates oxidative stress, plasma cholesterol and protrombin index

Olexandr M Kravchuk¹, Yulia V Goshovska^{2*}, Yulia P Korkach² and Vadym F Sagach²

¹Kozyatyn Central District Hospital of Kozyanyn District Council, Vinnytsya region, Ukraine

²Bogomoletz Institute of Physiology, National Academy of Science of Ukraine, Kyiv, Ukraine

Received: 10 May, 2021 Accepted: 21 May, 2021 Published: 24 May, 2021

*Corresponding author: Dr. Yulia V Goshovska, PhD, Bogomoletz Institute of Physiology, National Academy of Science of Ukraine, Kyiv, Ukraine, Tel: +380442562485; Fax: +380442562400;

 $\hbox{E-mail: pokutt@gmail.com, goshovska@biph.kiev.ua}\\$

ORCID: https://orcid.org/0000-0003-3308-9091

Keywords: Arterial hypertension; Peripheral vascular resistance; Garlic; Hydrogen sulfide; Nitric oxide; Oxidative stress; Cholesterol

https://www.peertechzpublications.com



Abstract

Background: Arterial hypertension is associated with tissue remodeling, oxidative stress and decreased production of such vasorelaxants as nitric oxide (NO) and hydrogen sulfide (H_2S). Garlic shows promises in treatment of hypertension and could be used as an antioxidative agent and a source/precursor of H_2S for decreasing of blood vessel stiffness.

Objective: The aim was to study the effectiveness of garlic supplement in the treatment of grade II hypertension in male patients.

Methods: The study was carried out in Kozyatyn Central District Hospital (Kozyatyn, Vinnytsia region, Ukraine). Patients with grade II hypertension (40-60 years old men) and healthy individuals of the same age and gender were included into study (n = 10 in each group). Garlic supplement (400mg per day) was included to the treatment after 10 day of standard antihypertensive therapy (angiotensin converting enzyme inhibitors, beta blockers). Echocardiography, biochemical control of blood, determination of plasma H₂S level and markers of oxidative-nitrozative stress were performed during study period.

Results: It was found that 30 days of garlic supplement on the background of a standard antihypertensive therapy reduced both systolic and diastolic blood pressure by 16.5 and 12.5 mmHg respectively (P<0,01 for both). The plasma H_2S level was significantly increased after 30 days of treatment. There was a positive effect of garlic supplement consumption on blood vessels in the form of a decrease in total peripheral vascular resistance by 10% (P<0,01). The production of reactive oxygen species and malonic dialdehyde was significantly reduced in blood plasma indicating antioxidative effect of garlic. Importantly, activity of constitutive NO synthase was restored and inducible NO synthase activity was inhibited. There was a decrease in plasma cholesterol by 30% and prothrombin index (P<0,001 for both). No significant changes in urea, creatinine, glucose, and erythrocyte counts were observed.

Conclusion: The results of our study indicate the effectiveness of garlic supplement consumption as a hypotensive, cholesterol-lowering and mild antithrombotic agent in the treatment of hypertension in elderly patients. Garlic supplement consumption likely improves H₂S and NO synthesis in hypertensive patients.

Introduction

Cardiovascular diseases, especially arterial hypertension, are the most common afflictions in the elderly cohort worldwide. Aging is accompanied by significant tissue remodelling of

the cardiovascular system which is based on the processes of systemic inflammation, programmed cell death, fibrosis and oxidative and nitrosative stress in the cells of the heart and blood vessels [1]. Chronic oxidative stress is a characteristic feature of the metabolic state of tissues of old organisms and can cause

041

the development of many diseases of the cardiovascular system [2,3]. In the progression of oxidative stress during aging, an important role is played by the suppression of the antioxidant defense system. This is evidenced by a significant decrease in the content and synthesis of glutathione in the tissues of the cardiovascular system [4-6]. The levels of glutathione correlate positively with the endothelial-depended vasodilatation, which is greatly depressed with aging and hypertensive patients [7-9]. Increased vascular tone and increased resistance of the vascular wall to blood flow with age may occur due to impaired synthesis of vasodilator molecules, in particular such as Nitric Oxide (NO) and hydrogen sulfide (H,S). It has been shown that under oxidative stress, which progresses with hypertension and aging, the production of gas transmitters is significantly reduced [10-12]. Therefore, in the work aimed at the treatment or prevention of these diseases, decrease of markers of oxidative stress and restoration of glutathione levels is considered a promising target. Previously, we showed a significant positive effect of stimulation of glutathione synthesis on the cardiovascular system in rats [13,14]. Garlic has been used as a nutrient and valuable therapeutic cure thousands of years. Phytopreparates or supplements based on garlic might be used as the approaches with a pronounced anti-inflammatory and antioxidant effect which affect the antioxidant system, including glutathione [15-17]. Fresh extracts, dry preparations and active compounds isolated from garlic are now considered as a nutraceutical panacea with a wide range of applications and promising use for the prevention and treatment of chronic pathologies associated with inflammatory processes [15]. Garlic is rich in organosulfur compounds and bioflavonoids, which seems to have synergistic effects. It has been shown that some active components of garlic have the ability to scavenge radicals oxygen species, thus realizing their antioxidant action [18,19]. Previously we showed the positive effect of long-term use of garlic on the functional parameters of the cardiovascular system in young hypertensive patients [20]. The aim of the present work was study the effect of garlic supplementation on biochemical parameters of blood, markers of oxidativenitrosative stress, arterial blood pressure and vessels resistance in elderly hypertensive patients.

Materials and methods

The study was carried out in Kozyatyn Central District Hospital (Kozyatyn, Vinnytsia region, Ukraine). Two groups of male patients (40-60 years old) were included in the study. The first group included persons who were diagnosed with grade II hypertension at the initial examination (n = 10); the second group included healthy persons (n = 10). The study was performed according to the guidelines of the Helsinki Declaration.

Criteria for inclusion in the study groups

Subjects were included to the group of healthy individuals if they 1) were men of 40-60 years old; 2) had systolic blood pressure <140mmHg; 3) had no chronic diseases. Subjects were included to the hypertensive group if they 1) were men of 40-60 years old; 2) had systolic blood pressure >140mmHg; 3) had no chronic cardiovascular, renal or other diseases associated with systemic inflammation, 4) did not take any blood pressure medication for at least 2 months.

Exclusion criteria

Female patients of any age and pregnancy status were not included into the study to avoid secondary hypertension induced by hormonal imbalance and fetal development. We excluded patients with vascular diseases including coronary heart disease, myocarditis, arthritis or blood diseases (anemia, leucosis etc). Patients were not included if they were in unstable conditions, including dementia or mental disorders. Patients were also excluded if they were not able to give informed

Ethical clearance

Ethical clearance was obtained from the ethical review committee. Informed written informed consent was obtained from all patients.

Echo cardiography and cardihemodynamic parameters

All patients were assessed by echocardiography with ULTIMAPA apparatus, then alterations in the echocardiographic variables were compared between the two groups. The following parameters of systemic cardiohemodynamics were studied: end-diastolic volume (EDV), end-systolic volume (ESV), heart rate. If no structural alterations were observed, EDV and ESV were estimated by linear dimensions in the left parasternal position along the long axis; in case of structural changes, Simpson's technique was used in the IV and II chamber positions from the top access. Stroke volume was calculated as EDV and ESV difference. The ejection fraction (EF) was defined as the percentage of stroke volume from EDV. Cardiac output was calculated as product of heart rate on stroke volume. Systolic and diastolic arterial pressure (BPs and BPd) was evaluated by method of Korotkoff. Total peripheral vascular resistance (TVR) was calculated by the formula: TVR = mean BP·1,333·60/Cardiac output, where mean BP=BPs-BPd/3+BPd, 1,333 – coefficient for conversion to dyn·s/cm⁵; 60 – coefficient for conversion of min to sec.

Laboratory investigation

Laboratory tests included a general blood test (hemoglobin, erythrocytes, leukocytes, erythrocyte sedimentation rate); determination of glucose, cholesterol, urea, creatinine using the GBG StatFax 1904 Plus device and prothrombin index by Quick method.

H₂S estimation

Blood was collected from elbow vein, centrifuged at 3000 g and plasma separated for H₂S content determination. Briefly, 0.5 ml of 1% solution of zinc acetate was added to the aliquot of the samples and incubated at 37.5°C for 10 minutes. Then, 0.5ml of 20 mmol/l of N, N-DPD (dimethyl-p-phenylenediamine) and 0.5ml of 30 mmol/l FeCl, solution were added. After the incubation in the cold and dark for 10 min the optic density was measured at λ = 670 nm. The quantity of H₂S in the samples was determined by calibration graph made for NaHS [21].

Oxidative-nitrozative stress markers

The intensity of oxidative metabolism was assessed by changes in markers of oxidative stress in blood plasma. We measured the rate of generation of superoxide anion radical (•O₂-), hydroxyl radical (•OH), hydrogen peroxide and the final product of lipid peroxidation malonic dialdehyde (MDA).

The method for •O₂- determination was based on the ability of cytochrome c to oxidize •O, - to O, after 30 min of incubation at 37°C, detected at 550 nm and the amount of superoxide was determined using molar absorption coefficient 28,000 mol⁻¹·cm⁻¹ [22].

For ·OH generation rate determination, the following mixture was prepared (in mmol/l): deoxyribose - 20; H₂O₂ - 1; sodium-phosphate buffer - 20, pH=7,4. The probe was incubated at 37 °C for 60 min, then 0,5 ml of 1% solution of tiobarbituric acid in NaOH (50 mM) and 0,5 ml of 2,8% trichloroacetic acid solution were added. The resulting mixture was kept in a water bath for 20 min, cooled and recorded the amount of extinction at λ = 532 nm. The amount of ·OH radical generated was expressed in conventional units of ΔE * 102 per 60 min per 1 mg of protein [23].

The method for hydroperoxide (H₂O₂) determination was based on the indirect registration of H2O2 consumption in the course of iodide (I-) oxidation to iodine (I3-) in the presence of excess lactoperoxidase I3- formation was followed spectrophotometrically at 353 nm and the amount was determined using molar absorption coefficient 26,000 mol-1.cm-1 [24].

The method for MDA determination was based on reaction of MDA with 2'-thiobarbituric acid and formation of trimetin complex as red derivative that was detected at 532 nm. The amount of MDA was determined using molar absorption coefficient 15,600 mol⁻¹·cm⁻¹ [25].

The method for cNOS and iNOS activity was based on the ability of NOS to utilize the L-arginine as substrate with the production of L-citrulline [26,27]. The aliquots were mixed with reaction mixture (final concentrations: 1 mM NADPH, 2 mM L-arginine and 50 mM KH₂PO₂, 1 mM MgCl₂, 2 mM CaCl₃ and incubated at 37°C for 60 min to determine the levels of summary NOS activity. Duplicate samples were incubated in the similar reaction mixture with addition of EGTA (5 mM) instead of CaCl, to determine the levels of Ca2+-independent iNOS activity. Reaction was stopped by adding 300 µl of 2N HClO, Then, the mixture was centrifuged (3,500 g for 10 min) and 1 ml of the supernatant was collected for L-citrulline measurement. The method included addition of urease, chromogenic solution (diacetyl monoxime, FeCl₂, thiosemicarbazide), boiling at 100°C for 10 min and measurement of absorbance at 492 nm. The concentration of L-citrulline was found from the calibration curves. Ca2+-dependent NOS activity (cNOS) was calculated as: NOS activity in 2 mM Ca2+ (total NOS activity) - NOS activity in 5mM EDTA (iNOS activity). The activity of enzymes was expressed in picomoles of newly formed L-citrulline for 1 min per 1 mg of total protein in the sample.

Treatment and supplement

Hypertensive patients received standard antihypertensive drugs: angiotensin converting enzyme inhibitors (enalapril, ramipril, perindopril) and beta blockers (nebivalol, concor, bisoprolol). After 10 days, the use of garlic supplement (Full Spectrum Garlic, 400 mg, Swanson Health Products, USA) was added to the standard treatment in a dose of 1 capsule per day. After 14 and 30 days of treatment all tests were repeated and compared with the baseline values.

Justification statement regarding the size of groups

Since the participation in the study was voluntary, some of patients were excluded in the course of the study because they did not complete the doctor's instructions or did not visit the final testing. Thus, the final n of patients in hypertensive group was equal 10 as well as in group of healthy donors.

Statistical analysis

We used Shapiro-Wilk test to evaluate the normality of distribution of data in each group. Data are present as mean ± SEM. To evaluate the difference between healthy individuals and hypertensive patients, data were analyzed by unpaired t test. To evaluate changes of cardiohemodynamic and biochemical parameters due to garlic supplement consumption in the group of patients with hypertension, data were analyzed by paired t-test. A P value < 0.05 was be considered statistically significant.

Results

H₂S level in the plasma of hypertensive patients after garlic supplement consumption The results of our study showed that the content of H₂S was twice lower in the blood of hypertensive patients aged 40-60 years comparing to healthy individuals of the same age (Figure 1). Our data are consistent with data of others that indicate a decrease in H₃S level of in the blood of in animal model of hypertension in rats [21], patients with arterial hypertension and coronary heart disease that allow to propose the endogenous level of H₂S as a maker of disturbances of cardiovascular system [28,29]. Interestingly, standard antihypertensive therapy reduced H2S levels by 32%, but the use of garlic supplement gradually increased H₂S level and by the 30th day its content was significantly higher than before treatment, however it did not reach the values of healthy donors. The results of laboratory investigation of patients with hypertension and the effect of garlic supplement consumption. Biochemical control of blood did not reveal significant differences in hemoglobin, erythrocytes, erythrocytes sedimentation rate between healthy individuals and hypertensive group. These parameters remained stable within the reference values range in healthy individuals as well as in hypertensive patients throughout the study period (Table 1). Protein metabolism (creatinine, urea) and blood glucose levels also did not changed significantly during treatment.

In hypertensive patients, leukocytes, cholesterol and prothrombin index were significantly increased by 52, 20 and 8,5% respectively, although they did not exceed reference values.

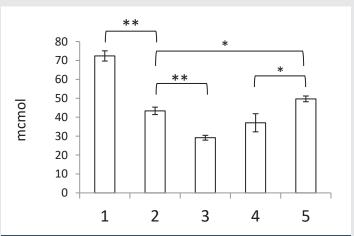


Figure 1: H_2S content in blood plasma of healthy donors (1), hypertensive patients at the initial examination (2), hypertensive patients after 10 days of standard treatment (3), hypertensive patients after 10 days of standard treatment and 14 days of garlic supplement consumption (4), hypertensive patients after 10 days of standard treatment and 30 days of garlic supplement consumption (5). The comparison between healthy donors and hypertensive patients was made by unpaired t test. The comparison in group of hypertensive patients was made by paired t test. *P<0,05, **P<0,01.

Despite the fact that there was no pronounced inflammatory process in hypertensive patients, garlic supplement significantly reduced the number of leukocytes after 14 days of consumption. However, the number of leukocytes returned to baseline after 30 days of treatment. Antihypertensive therapy with garlic supplement reduced blood cholesterol by 14.8% at the 14th day and by another 5% on the 30th day of treatment (P<0,001 for both compared to baseline). Detailed analysis of lipid metabolism would provide a better understanding of the effects of garlic supplement but decrease in total cholesterol may indicate a normalizing effect of garlic on lipid metabolism in hypertensive patients.

Significant decrease in the prothrombin index after 30 days of garlic consumption is of particular interest. Although the values of prothrombin index before and after therapy were within the range of reference values, this suggests the possibility of garlic usage as a mild antithrombotic agent in patients with hypertension and hypercholesterolemia. Our data correlate with those obtained earlier in hypertensive patients of younger age (20–39 years old) who showed reduced cholesterol

Table 1: The results of laboratory investigations of patients 40-60 years old.

Parameter	Healthy donors, n=10	Hypertensive patients, n=10					
			Ref. values				
		Baseline	10 days	+14 day of garlic supplement	+30 days of garlic supplement	Ref. Values	
Hemoglibin, g/L	133,8±5,3	124,8±1,7	122,2±1,1	126,8±2,5	130±1,4	110-130	
Erythrocytes, x1012	4,8±0,11	4,48±0,07	4,51±0,06	4,54±0,09	4,33±0,13	4-5,1	
Leukocytes, ×10 ⁹	5,1±0,6	7,3±0,40*	6,7±0,27cc	5,9±0,15*.#	7,0±0,15 ^{&&}	4-9	
Erythrocytes sedimentation rate	5,3±0,26	5,6±0,7	5,3±0,6	4,7±0,47	5±0,57	>8	
Prothrombin index	89,2±2,6	96,8±1,16*	97,8±0,9	83,8±2,7 +++,###	83,7±3,4 ***.##	78-142	
Cholesterol, mmoles	5,7±0,41	6,85±0,19*	6,93±0,15	5,15±0,16 ***,###	4,83±0,20 ***.##	3,0-6,2	
Creatinine, mcmoles	93,0±1,4	86,9±2,17	89,8±1+,20	85,7±1,55	88,6±1,20	53-110	
Urea, mmoles	5,1±0,30	4,02±0,14*	4,31±0,11	4,51±0,08+	4,16±0,08 ^{&}	2,0-8,3	
Glucose, mmoles	4,9±0,14	3,88±0,18*	4,31±0,19	4,74±0,17++	4,26±0,17	4,2-6,4	

The comparison between healthy donors and hypertensive patients was made by unpaired t test. The comparison in group of hypertensive patients was made by paired t test. *P<0,05, comparing to healthy donors, *P<0,05, **P<0,01, ***P<0,01 comparing to baseline in hypertensive group; *P<0,05, **P<0,01, ***P<0,001 comparing to 10 days of a standard therapy + 14 days of garlic supplementation

Table 2: Effect of garlic consumption on cardiohemodynamic parameters of hypertensive patients.

Parameter	Healthy donors, n=10	Hypertensive patients, n=10		
Parameter	nealthy donors, n=10	Baseline	Standard therapy + 30 days of garlic supplement	
Systolic blood pressure, mmHg	135±3,1	158,0±2,0**	141,5±1,7**	
Diastolic blood pressure, mmHg	85±2,6 98,0±2,5**		85,5±1,6**	
Mean BP, mmHg	114±3,4	117,0±2,25	104,1±1,4++	
End-diastolic volume, ml	129,5±9,6	138,6±11,1	138,2±10,1	
End-systolic volume, ml	56,8±5,7	65,0±8,0	61,8±7,6	
Stroke volume, ml	62,8±2,6	73,6±3,7*	76,4±3,5	
Ejection fraction, %	59,4±2,1	54,4±2,3	56,5±2,3	
Heart rate, beat/min	71,8±1,3	72,4±1,7	68,2±1,8 ⁺⁺	
Cardiac output, I/ min	4,52±0,44	5,33±0,34	5,22±0,29	
Total peripheral vascular resistance, dyn s/cm⁵	1712±98	1835±125	1653±117++	

^{*}P<0,05, comparing to healthy donors, * P<0,05, ** P<0,01 comparing to baseline in group of hypertensive patients

044

level, prothrombin index, as well as the number of leukocytes in the blood serum after garlic consumption [20].

Effect of garlic consumption on cardihemodynamiecs parameters of hypertensive patients. BPs, BPd and stroke volume were significantly increased in hypertensive patients comparing to healthy donors. 30 days of garlic consumption decreased both BPs and BPd by 16.5 and 12.5 mm Hg respectively (Table 2). There was a slight decrease in ESV and a slight increase in stroke volume; however, ejection fraction and cardiac output did not changed significantly under the treatment. It is important to note a significant decrease in heart rate and TVR by 10% (P<0,01 for both).

Effect of garlic supplement consumption on oxidativenitrozative stress in hypertensive patients. The results of biochemical studies showed that markers of oxidative stress were increased in blood plasma of hypertensive patients comparing to healthy donors (Table 3). In particular, the generation rates of superoxide and hydroxyl radicals were increased by 3,8 and 2,6 times respectively and the content of hydrogen peroxide was increased by 2 times. The marker of oxidative stress MDA was increased by 3,3 times indicating intensified lipid peroxidation. Activity of cNOS was decrease by 57% and activity of iNOS was increase by 75,4% in hypertensive patients. This data might indicate the damaging effect of oxidative stress on NO production.

10 days of the standard antihypertensive therapy decreased the markers of oxidative stress in the blood plasma: the rate of generation of superoxide and hydroxyl radicals decreased by 60 and 67% respectively (P<0,001 and P<0,01), H₂O₂ and MDA were decreased by 47 and 27,5% respectively (P<0,01 and P<0,05). It is important to note that the activity of iNOS decreased by 35,2% (P<0,001), and the activity of cNOS increased 2-fold comparing to baseline value (P<0,001) indicating positive effect of the standart treatment (Table 3).

Interestingly, 14 days of garlic supplement consumption was accompanied by 2,2-fold increased in H₂O₂ content (P<0,01) and MDA was increased by 45% (n/s). At the same time, the activity of iNOS increased by 11,7% (P <0,05) and the activity of cNOS decreased by 10% (P<0,05) compared with the data obtained after 10 days of the standard therapy. However, the rate of superoxide and hydroxyl radicals generation remained

significantly lower than baseline values. In addition, positive changes were observed in the biochemical analysis on the 30th day of garlic supplement consumption: MDA, H2O2 and iNOS activity were significantly reduced compared to the 14th day, thus, all the indicators reached the values of healthy donors.

Discussion

The problem of high blood pressure in the progression of arterial hypertension is especially acute in the elderly. Screening for effective antihypertensive drugs is the most urgent task of preclinical and clinical studies. In 2015, a metaanalysis of 7 randomized trials revealed the hypotensive effect of garlic in patients with hypertension [30]. Garlic consumption appears to modulate inflammatory response thus limiting the progression of cardiovascular diseases. Indeed, in 2019, the results of a meta-analysis of 20 studies found that hypotensive effect of garlic consumption for 2 weeks was accompanied by a decrease in interleukin 6, TNF and c reactive protein in serum [31]. The latter is produced by the liver in response to proinflammatory cytokines, including TNF and is a major risk factor for cardiovascular disease and atherosclerosis.

Another meta-analysis of 12 clinical studies showed that the use of garlic for 2 - 24 weeks increases the overall antioxidant properties of blood, superoxide dismutase activity and reduces the level of malonic dialdehyde [17]. In addition, the use of garlic by patients with hypertension lowers cholesterol and affects the immune system increasing the number of killer cells, macrophage activity and increasing the production of T and B cells [32]. Thus, garlic preparations have proven to be hypotensive drugs with anti-inflammatory and immunostimulatory properties.

Previously we showed that garlic supplement consumption for 30 days provided antioxidant and hypotensive effects in patients aged 20-39 years with grade II hypertension [20]. We have found the normalization of plasma H,S levels and restoration of constitutive NO synthesis. Improvement of H₂S and NO production were accompanied with decrease in total peripheral vascular resistance. To our knowledge the vasorelaxing effect of garlic supplement was shown for the the first time.

In the present study, we tested the ability of garlic supplement to improve the functional parameters of the

Table 3: Effect of garlic supplement consumption on markers of oxidative-nitrozative stress in blood plasma of hypertensive patients

	Haaliby damana	Hypertensive patients, n=10			
Parameter	Healthy donors, n=10	Baseline	Standard therapy		
			10 days	+14 days of garlic supplement	+ 30 days of garlic supplement
Generation rates of superoxide anion radical, nmol/min/mg	1,11±0,28	4,26±0,1**	1,74±0,28	1,23±0,22	0,89±0,06
of protein			+++	***	***,#
Malone dialdehyde, nmol/mg of protein	1,74±0,09	5,82±0,23**	4,22±0,48+	6,13±0,68	3,81±0,12***, ^{&}
Generation rates of OH, nmol/min/mg of protein	2,62±0,16	6,96±0,88**	2,28±0,07++	1,91±0,12**	2,16±0,04**
Generation rates H ₂ O ₂ , mcmol/min/mg of protein	2,02±0,09	4,21±0,37**	2,23±0,16++	4,95±0,44##	2,14±0,07++,&&
Activity of inducible NOS, pmol/min/mg of protein	10,03±0,64	17,6±0,27**	11,4±0,35	12,74±0,29	10,0±0,05
Activity of inducible NOS, pholymin/mg of protein			++	****,#	+++ # &&
Activity of constitutive NOS, pmol/min/mg of protein	19,07±1,11	8,18±0,26**	16,9±0,09	15,2±0,45 ***,#	16,5±0,21***

*P<0,05, comparing to healthy donors, * P<0,05, ** P<0,01, *** P<0,01 comparing to baseline in group of hypertensive patients, *P<0,05, **P<0,05, **P<0,01 comparing to 10 days of a standard therapy, &P<0,05, &&P<0,01 comparing to 10 days of a standard therapy + 14 days of garlic supplementation

cardiovascular system of hypertensive patients 40-60 years old who demonstrate the hypertensive changes associated with age-dependent remodeling of cardiovascular tissues. It turned out that garlic supplement comsumption for 30 days significantly decreased BPs and BPd by 16.5 and 12.5 mmHg that was even greater than in younger patients (by 9 and 8 mm Hg) [20]. It is important to note that the hypotensive effect of the garlic was realized due to the reduction of oxidative stress and decrease of the peripheral vascular resistance. Such changes may be due to the re-coupling of cNOS activity, iNOS inhibition as well as increasing in the plasma H₂S content in patients after 30 days of garlic supplement consumption.

With age, disturbances of lipid metabolism and progression of atherosclerosis aggravate hypertensive patient's condition and might require the use of additional pharmacological drugs. In our study, garlic supplement consumption decreased cholesterol and prothrombin index which may also contribute to lowering of blood pressure and decrease of total peripheral vascular resistance. In addition to these mechanisms, garlic is likely to affect other molecular targets including calcium management, redox regulation and smooth and cardiac smooth muscle production in these patients, which require further research.

Conclusion

Garlic supplement consumption for 30 days likely improved H₃S and NO synthesis in hypertensive patients. The results of our clinical, biochemical and functional examinations indicate the effectiveness of garlic supplement as an alternative hypotensive, cholesterol-lowering and mild antithrombotic agent in the treatment of hypertension in elderly patients.

References

- 1. Maruyama Y (2012) Aging and arterial-cardiac interactions in the elderly. Int J Cardiol 155: 14-19. Link: https://bit.ly/3fExWPw
- 2. Khansari N, Shakiba Y, Mahmoudi M (2009) Chronic Inflammation and Oxidative Stress as a Major Cause of Age- Related Diseases and Cancer. Recent Pat Inflamm Allergy Drug Discov 3: 73-80. Link: https://bit.ly/3oLqvKz
- 3. Papaconstantinou J (2019) The Role of Signaling Pathways of Inflammation and Oxidative Stress in Development of Senescence and Aging Phenotypes in Cardiovascular Disease. Cells 8: 1383. Link: https://bit.ly/3hKMMgz
- 4. Sekhar RV, Patel SG, Guthikonda AP, Reid M, Balasubramanyam A, et al. (2011) Deficient synthesis of glutathione underlies oxidative stress in aging and can be corrected by dietary cysteine and glycine supplementation. Am J Clin Nutr 94: 847-853. Link: https://bit.ly/3ysf1jA
- 5. Ferguson G, Bridge W (2016) Glutamate cysteine ligase and the age-related decline in cellular glutathione: The therapeutic potential of γ-glutamylcysteine. Arch Biochem Biophys 593: 12-23. Link: https://bit.ly/3yuCMr7
- 6. Szabó R, Hoffmann A, Börzsei D, Kupai K, Veszelka M, et al. (2021) Hormone Replacement Therapy and Aging: A Potential Therapeutic Approach for Age-Related Oxidative Stress and Cardiac Remodeling. Oxid Med Cell Longev 2021: 8364297. Link: https://bit.ly/3yxvZ04
- 7. Lapenna D, Ciofani G, Giamberardino MA (2017) Glutathione metabolic status in the aged rabbit aorta. Exp Gerontol 91: 34-38. Link: https://bit.ly/2RFNrij
- 8. Mys LA, Strutynska NA, Goshovska YV, Sagach VF (2020) Stimulation of the endogenous hydrogen sulfide synthesis suppresses oxidative-nitrosative

- stress and restores endothelial-dependent vasorelaxation in old rats. Can J Physiol Pharmacol 98: 275-281. Link: https://bit.ly/3u9CJhk
- 9. Costa ED, Silva JF, Aires RD, Garcia DC, Kansaon MJ, et al. (2018) Neuronal nitric oxide synthase contributes to the normalization of blood pressure in medicated hypertensive patients. Nitric Oxide 80: 98-107. Link: https://bit.ly/3bKOeWa
- 10. Sahach V, Baziliuk O, Kotsiuruba A, Buzhanevich O (2000) Disorders of Endothelium-Dependent Vascular Reactions and of the Arginase and NOsynthase Pathways of L-arginine Metabolism in Arterial Hypertension. Fiziol Zhurn 46: 3-13. Link: https://bit.ly/3yzp3Qa
- 11. Mys LA, Strutynska NA, Strutynskyi VR, Sagach VF (2017) activation of endogenous hydrogen sulfide synthesis inhibits mitochondrial permeability transition pore opening and restores constitutive no-synthase coupling in old rat heart. Fiziol Zh 63: 16-23. Link: https://bit.ly/2QGnbnn
- 12. Drachuk KO, Kotsjuruba AV, Sagach VF (2015) Hydrogen Sulfide Donor, Nahs, Recovers Constitutive No Synthesis And Endothelium-Dependent Relaxation Of Isolated Aorta In Old Rats. Fiziol Zh 61: 3-10. Link: https://bit.ly/346409J
- 13. Fedichkina R, Goshovska Y, Sagach V (2021) Cardioprotective effect of H2S and glutathione synthesis modulation is mediated by inhibition mitochondrial permeability transition pore opening. Visnyk Lviv Univ Biol Ser 83.
- 14. Sahach V, Shymans'ka T, Hoshovs'ka I (2013) Effects of stimulation and blockade of the synthesis of endogenous hydrogen sulfide at myocardial ischemia-reperfusion. Fiziol Zh 59: 8-15. Link: https://bit.ly/3fwMEbm
- 15. Quesada I, de Paola M, Torres-Palazzolo C, Camargo A, Ferder L, et al. (2020) Effect of Garlic's Active Constituents in Inflammation, Obesity and Cardiovascular Disease. Curr Hypertens Rep 22. Link: https://bit.ly/3f7D4fV
- 16. Nasr AY, Alshali RA (2020) Cytoprotective and antioxidant effects of aged garlic extract against adriamycin-induced cardiotoxicity in adult male rats. Anat Cell Biol 53: 201-215. Link: https://bit.ly/3ueENV8
- 17. Askari M, Mozaffari H, Darooghegi Mofrad M, Jafari A, Surkan PJ, et al. (2021) Effects of garlic supplementation on oxidative stress and antioxidative capacity biomarkers: A systematic review and meta-analysis of randomized controlled trials. Phyther Res. Link: https://bit.ly/3bLKqUq
- 18. Galano A, Francisco-Marquez M (2009) Peroxyl-Radical-Scavenging Activity of Garlic: 2-Propenesulfenic Acid versus Allicin. J Phys Chem B 113: 16077-16081. Link: https://bit.ly/3hYeQXF
- 19. Lynett PT, Butts K, Vaidya V, Garrett GE, Pratt DA (2011) The mechanism of radical-trapping antioxidant activity of plant-derived thiosulfinates. Org Biomol Chem 9. Link: https://rsc.li/3hLHvz4
- 20. Kravchuk OM, Goshovska YV, Korkach YP, Sagach VF (2020) Garlic Lowers Blood Pressure And Reduces Oxidative Stress By Increasing Plasma H2s Content In Patients With Arterial Hypertension. Fiziol Zh 66. Link: https://bit.ly/3oCXT66
- 21. Yan H, Du J, Tang C (2004) The possible role of hydrogen sulfide on the pathogenesis of spontaneous hypertension in rats. Biochem Biophys Res Commun 313: 22-27. Link: https://bit.ly/3vnQ6vP
- 22. Kuthan H, Ullrich V, Estabrook RW (1982) A quantitative test for superoxide radicals produced in biological systems. Biochem J 203: 551-558. Link: https://bit.ly/3hFL0H8
- 23. Humphries KM, Yoo Y, Szweda LI (1998) Inhibition of NADH-Linked Mitochondrial Respiration by 4-Hydroxy-2-nonenal. Biochemistry 37: 552-557. Link: https://bit.ly/2QDZ4pm
- 24. Huwiler M, Kohler H (1984) Pseudo-catalytic degradation of hydrogen peroxide in the lactoperoxidase/H2O2/iodide system. Eur J Biochem 141: 69-74. Link: https://bit.ly/3hQZIeB
- 25. Janero DR (1990) Malondialdehyde and thiobarbituric acid-reactivity as



- Peertechz Publications
 - diagnostic indices of lipid peroxidation and peroxidative tissue injury. Free Radic Biol Med 9: 515-540. Link: https://bit.ly/3hHawvD
- 26. Chin SY, Pandey KN, Shi SJ, Kobori H, Moreno C, et al. (1999) Increased activity and expression of Ca 2+ -dependent NOS in renal cortex of ANG II-infused hypertensive rats. Am J Physiol Physiol 277: F797- F 804.
- 27. Salter M, Knowles RG, Moncada S (1991) Widespread tissue distribution, species distribution and changes in activity of Ca 2+ -dependent and Ca 2+ -independent nitric oxide synthases. FEBS Lett 291: 145-149.
- 28. Jiang H, Wu H, Li Z, Geng B, Tang C (2005) Changes of the New Gaseous Transmitter H2S in Patients With Coronary Heart Disease. Di Yi Jun Yi Da Xue Xue Bao 25: 951-954. Link: https://bit.ly/3fC3QMB
- 29. Feng Y, Fan J, Lin X, Yang J, Cui Q, et al. (2017) Facilitating the Measurement

- of Circulatory Hydrogen Sulfide With Fluorescence Probe-Coated Microplates. Beijing Da Xue Xue Bao Yi Xue Ban 49: 1060-1065. Link: https://bit.ly/343VB6v
- 30. Xiong XJ, Wang PQ, Li SJ, Li XK, Zhang YQ, et al. (2015) Garlic for hypertension: A systematic review and meta-analysis of randomized controlled trials. Phytomedicine 22: 352-361. Link: https://bit.ly/2Tc6O2U
- 31. Darooghegi Mofrad M, Milajerdi A, Koohdani F, Surkan PJ, Azadbakht L (2019) Garlic Supplementation Reduces Circulating C-reactive Protein, Tumor Necrosis Factor, and Interleukin-6 in Adults: A Systematic Review and Meta-analysis of Randomized Controlled Trials. J Nutr 149: 605-618. Link: https://bit.ly/3bLEsD1
- 32. Ried K (2016) Garlic Lowers Blood Pressure in Hypertensive Individuals, Regulates Serum Cholesterol, and Stimulates Immunity: An Updated Metaanalysis and Review. J Nutr 146: 389S-396S. Link: https://bit.ly/3oChnYL

Discover a bigger Impact and Visibility of your article publication with **Peertechz Publications**

Highlights

- Signatory publisher of ORCID
- Signatory Publisher of DORA (San Francisco Declaration on Research Assessment)
- Articles archived in worlds' renowned service providers such as Portico, CNKI, AGRIS, TDNet, Base (Bielefeld University Library), CrossRef, Scilit, J-Gate etc.
- Journals indexed in ICMJE, SHERPA/ROMEO, Google Scholar etc.
- OAI-PMH (Open Archives Initiative Protocol for Metadata Harvesting)
- Dedicated Editorial Board for every journal
- Accurate and rapid peer-review process
- Increased citations of published articles through promotions
- Reduced timeline for article publication

Submit your articles and experience a new surge in publication services (https://www.peertechz.com/submission).

Peertechz journals wishes everlasting success in your every endeavours.

Copyright: © 2021 Kravchuk OM, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.