Pharmaciana
Vol.15, No.1, March 2025, Page. 29-39
ISSN: 2088 4559; e-ISSN: 2477 0256
DOI: 10.12928/pharmaciana.v15i1.24513

Impact of Black Garlic extract on cardio-renal protection in hypertensive animal models

Patonah Hasimun*, Hendra Mahakam Putra, Fitriani Choerunnisa
Faculty of Pharmacy, Bhakti Kencana University, Bandung,
Jl. Soekarno-Hatta no. 754, Cipadung Kidul, Panyileukan, Bandung, West Java, Indonesia

Submitted: 22-07-2022 ***Reviewed: 21-02-2024*** ***Accepted: 08-03-2025***

ABSTRACT

A strong link exists between arterial stiffening and cardiovascular conditions, particularly hypertension. Hypertension, a significant contributor to mortality rates, particularly affects elderly populations. The processed form of Allium sativum, known as black garlic, is renowned for its medicinal properties, including its ability to lower blood pressure. This study examined the blood pressure-lowering effects of black garlic extract, employing male Wistar rats aged two to three months.The experiment involved six distinct rat groups, each comprising of four animals. The two groups served as controls, whereas the remaining four underwent different treatments. Captopril was administered to one group at a dose of 2.5 mg/kg, whilst the remaining three groups were given black garlic extract as BG50, BG100, and BG200. All groups, with the exception of the control normal, underwent a 28-day induction protocol that included 25% fructose in drinking water, cholesterol (200 mg/kg), and propylthiouracil (12.5 mg/kg). The test substances were administered starting on day 14 concurrently with the induction phase. The evaluated parameters included blood pressure, arterial stiffness, nitric oxide (NO) levels, and renal histopathology. Black garlic extract significantly lowered blood pressure, enhanced arterial elasticity, and increased NO levels ($p < 0.05$) compared with the controls. Renal histopathological analysis revealed protective effects, suggesting prevention of kidney damage. These findings suggest that black garlic may have cardiorenal protective effects and could be useful for managing hypertension and arterial stiffness.

Keywords: arterial stiffness, Black garlic, hypertension, Cardio-renal protection

Corresponding author:
Patonah Hasimun
Faculty of Pharmacy, Bhakti Kencana University
Jl. Soekarno-Hatta no. 754, Cipadung Kidul, Panyileukan, Bandung, West Java, Indonesia
Email: patonah@bku.ac.id

INTRODUCTION

An estimated 26% of the global population will have high blood pressure by 2025, with a predicted rise to 29% (Kearney et al., 2005). Hypertension, a leading contributor to global mortality, is a crucial indicator of cardiovascular disease and stroke risk. Hypertension complications affect 9.4 million people globally each year, causing at least 45% of heart disease deaths and 51% of stroke fatalities (Feigin et al., 2015).

Endothelial dysfunction leads to arterial stiffness, which exhibits a strong correlation with hypertension. Under hypertensive conditions, the progression of arterial stiffness occurs through enhanced inflammatory processes, alterations in fibrotic tissue, and an increase in arterial wall thickness (James et al., 2014). Increased arterial stiffness is associated with a higher risk of cardiovascular events and is often indicated by an enlarged frontal QRS-T angle in the heart. This specific angular measurement is a novel marker for evaluating ventricular repolarisation mechanisms (Oehler et al., 2014). Left ventricular hypertrophy, a condition common in hypertensive individuals, causes an increase in the QRS-T angles. This enlargement is generally linked to changes in the structure and function of the heart's ventricles (Dilaveris et al., 2001; Jaroszyński et al., 2019).

Garlic (*Allium sativum* L.) is a widely used ingredient in culinary arts, traditional practices, and contemporary medical practices, and is known for its unique and strong flavour (Ried & Fakler, 2014). It possesses various health benefits including anticancer, antioxidant, antimicrobial, antihyperlipidemic, antidiabetic, and antihypertensive properties (Chidinma, 2019).

The extensive utilisation of unprocessed garlic is often hindered by its pungent odour and potential digestive discomfort. Nevertheless, the development of black garlic (BG) has been accomplished by subjecting raw garlic to precise thermal processing for designated durations. This modified product offers a palatable taste and aroma while also enhancing its beneficial health effects. Allicin, a component found in raw garlic, can trigger a range of adverse reactions, including malodorous breath, nausea, vomiting, bloating, and diarrhoea. In contrast, S-allyl cysteine (SAC), which is found at higher concentrations in black garlic, is a stable compound derived from the less stable allicin. The transformation of regular garlic into black garlic occurs through a fermentation technique that involves elevated temperatures and moisture. This process induces non-enzymatic browning reactions, which are responsible for the dark colour of the final product. This process includes caramelisation, phenol oxidation, and Maillard reaction. Although the physicochemical properties of garlic change during fermentation, the levels of beneficial compounds also increase (Kimura et al., 2017).

Research has demonstrated that black garlic can exert antihypertensive effects by regulating nitric oxide (NO) levels in the body, improving arterial elasticity, and decreasing the enlarged frontal QRS-T angle (Hasimun et al., 2020). Nevertheless, the impact of BG on renal and aortic function in relation to its blood pressure-lowering effects remains uncertain in studies involving animals. The research sought to investigate the blood pressure-lowering properties of BG, examining its influence on nitric oxide regulation, the elasticity of arteries, and its effects on renal and aortic function in experimental animal models.

MATERIALS AND METHOD

Collection of plants

Fresh garlic (*Allium sativum* L.) was cultivated on lowland farms in Tegal, Central Java, Indonesia. The specimens were identified and verified at the Laboratory of the School of Life Sciences and Technology at the Bandung Institute of Technology. The garlic examination findings are documented in Document Number 865/II.CO2.2/PL/2020.

Fermented garlic and black garlic extraction

Raw garlic was exposed to thermal processing in an oven maintained at 70°C for a duration of 15 days, with assessments carried out at five-day intervals. Following this, the resultant BG underwent extraction through maceration, utilising a 70% ethanol solution as the extracting agent, for 3d at room temperature. The obtained filtrate was then concentrated at 50°C using a rotary evaporator, operating at approximately 90 rpm, until a viscous extract was produced. The extraction process yielded 34.50% of the final product.

Preparation of test animals

For this investigation, male Wistar rats aged two months, with weights ranging from 225 to 290 g, were selected. The rats were maintained in enclosures over a 14-day period, during which they were supplied with regular feed and permitted continuous access to water. The rats were subjected to a circadian rhythm comprising equal periods of light and darkness, each lasting 12 hours. The Ethics Committee of the Faculty of Medicine at Padjadjaran University in Bandung reviewed and approved the study protocol, assigning it the reference number 424/UN6.KEP/EC/2021. This research involved 24 rats, which were randomly assigned to six distinct groups. The first group was the negative control, and the second was the positive control. The third group received 2.5 mg/kg of captopril. The fourth, fifth, and sixth groups were given black garlic extract at doses of 50 (BG50), 100 (BG100), and 200 mg/kg (BG200) respectively. The experimental protocol consisted of a 15-day induction phase, followed by a fortnight of daily treatment administration. The induction protocol, implemented for all experimental groups barring the negative control, encompassed a 28-day regimen. This procedure entailed the provision of fructose-enriched drinking water (25%), the administration of a 200 mg/kg oil emulsion containing cholesterol (4%) and colic acid (0.2%), and the oral delivery of propylthiouracil suspension at 12.5 mg/kg.

Evaluating the effects of black garlic on blood pressure

Blood pressure (systolic and diastolic) was measured using the non-invasive CODA® system by Kent Scientific Corporation. Measurements were conducted at intervals of 0, 7, 14, 21, and 28 days**.** The device employs tail cuffs consisting of two key components: an occlusion cuff and a Volume Pressure Recorder (VPR). The VPR serves as a specialised sensor for detecting blood volume changes. To obtain consistent blood pressure measurements, the cuff was positioned near the rat's tail base, with the animals maintained in a temperature-controlled setting. This apparatus operates by automatically inflating the cuff, applying pressure to the tail, thus enabling precise blood flow measurement.

Impact of Black Garlic on cardiovascular function

Cardiovascular function parameters, including heart QRS-T angle, arterial stiffness, and heart rate, are measured using non-invasive methods. Non-invasive techniques were utilised to evaluate arterial stiffness and heart rate, as outlined by (Hasimun et al., 2020), employing electrocardiogram (ECG) and photoplethysmography (PPG) sensors. The QRS-T frontal angle was determined using a device equipped with two ECG channels for capturing frontal electrocardiogram leads. The heart rate was determined by calculating the interval between the R peaks in the PQRST wave of the electrocardiogram.

Assessment of nitric oxide levels in blood serum

The Griess technique, which relies on diazotisation, was employed to measure the nitric oxide levels in serum specimens (Garmana et al., 2018). The process began with the deproteinisation of 100 µL of serum by introducing 20 µL of 20% ZnSO4, followed by centrifugation. Subsequently, the obtained filtrate underwent a reaction with 6% Cd for 15 min. After adding 50 µl of Griess reagent, the mixture was left to incubate for an hour. The samples' absorbance was then analysed using UV-Vis spectrophotometry at a wavelength of 535 nm.

Histology of kidney and aortic tissues

Histological analysis using Haematoxylin-eosin staining was conducted to examine the treatment's impact on renal and vascular health. This technique enables the observation of alterations in kidney tubule cells and the formation of foam cells within aortic tissue. Through the analysis of these structural changes and cellular reactions, the investigators sought to obtain a thorough insight into how the treatment affects these crucial physiological systems.

Data Analysis

SPSS version 20.0 was employed for the statistical analysis to examine the impact of black garlic compared to the control group. Treatment groups were considered statistically significant when their p-values fell below the established threshold of $p < 0.05$.

RESULT AND DISCUSSION

Analysis of the phytochemical composition of black garlic extract identified various secondary metabolites, including flavonoids, saponins, tannins, and terpenoids. Further examination of the proximate composition yielded specific measurements: water-soluble extract comprised 22%, ethanol-soluble extract accounted for 18%, total flavonoid content measured 139.6 mmol/100 g, and total antioxidant content was determined to be 3.286 mg QE/g of extract.

Table 1 showed the systolic blood pressure measurements for each treatment group over a 28-day period. Rats subjected to a fructose- and cholesterol-rich diet for 28 days exhibited a marked increase in systolic pressure when compared to the negative control. In contrast, the groups treated with BG50, BG100, and BG200 showed a decrease in systolic pressure. Notably, the reduction in blood pressure observed in the BG50 group was not statistically different from that of the captopril group ($p > 0.05$). Furthermore, the groups administered BG100 and BG200 exhibited significantly lower systolic pressure compared to the captopril group ($p < 0.05$).

Table 1. Systolic blood pressure measurements (mmHg) were recorded at baseline (day 0), as well as on days 14 and 28 after administering black garlic extract

Group	Systolic Blood Pressure (mmHg) ± standard deviation on day		
	T0	T14	T28
Negative control	105.0 ± 1.7	105.3 ± 0.5 $^{\alpha\beta}$	109.0 ± 1.0 $^{\alpha\beta}$
Positive Control	114.6 ± 2.6	166.6 ± 2.3*	186.3 ± 2.0*$^{\alpha}$
Captopril 2.5 mg/kg	112.3 ± 3.5	169.3 ± 3.7*	119.6 ± 0.5*$^{\beta}$
BG50	107.0 ± 3.0	168.3 ± 0.5*	121.6 ± 3.0*$^{\beta}$
BG100	114.3 ± 2.5	167.6 ± 1.5*	112.3 ± 3.0 $^{\alpha\beta}$
BG200	111.0 ± 2.3	168.6 ± 2.0*	111.0 ± 1.7 $^{\alpha\beta}$

Statistically significant difference ($p < 0.05$) in comparison to: the negative control (*), (α) captopril 2.5 mg/kg (α), the positive control (β).

The diastolic pressure measurements for all treatment groups over a 28-day period are presented in Table 2. Diastolic pressure significantly increased in rats after 28 days on a high-fructose, high-cholesterol diet. Rats given BG50, BG100, or BG200 showed a decrease in diastolic pressure. The group receiving BG50 showed a reduction in diastolic pressure similar to the captopril group ($p > 0.05$). Conversely, the BG100 and BG200 treatment groups showed reductions in diastolic pressure that were statistically distinct from the captopril group ($p < 0.05$).

Mean arterial pressure (MAP) represents the average pressure during a complete cardiac cycle. It is determined by combining one-third of the systolic blood pressure with two-thirds of the diastolic pressure (Kundu et al., 2017). Table 3 provides a comprehensive overview of MAP readings for all experimental groups throughout the 28-day study period. After 28 days, rats on a high fructose and cholesterol diet had significantly higher MAP than the control group. However, the introduction of

BG50, BG100, and BG200 was associated with a decline in MAP measurements. The MAP reduction in the BG50 group was comparable to the captopril group ($p > 0.05$). In contrast, the groups administered BG100 and BG200 exhibited MAP decreases that were significantly distinct from the captopril group ($p < 0.05$).

Table 2. Effects of BG extract on diastolic pressure (mmHg) at 0, 14, and 28 days post-treatment

Group	Diastolic Pressure (mmHg) ± standard deviation on day		
	T0	T14	T28
Negative Control	85.0 ± 1.7	85.0 ± 1.0 $^{\alpha\beta}$	87.3 ± 1.1 $^{\alpha\beta}$
Positive Control	85.3 ± 2.0	127.3 ± 1.5*	151.3 ± 1.1*$^{\alpha}$
Captopril 2.5 mg/kg	85.6 ± 2.0	128.0 ± 3.0*	94.0 ± 1.0*$^{\beta}$
BG50	84.3 ± 2.3	128.6 ± 0.5*	93.6 ± 0.5*$^{\beta}$
BG100	85.3 ± 2.5	128.0 ± 2.0*	87.0 ± 2.6 $^{\alpha\beta}$
BG200	85.6 ± 2.0	128.3 ± 1.5*	89.0 ± 1.7 $^{\alpha\beta}$

Statistically significant difference ($p < 0.05$) in comparison to: the negative control (*), (α) captopril 2.5 mg/kg (α), the positive control (β)

Table 3. Effect of black garlic extract on mean arterial pressure (mmHg) measured on days 0, 14, and 28 post treatments

Group	Mean Arterial Pressure (mmHg) ± standard deviation on day		
	T0	T14	T28
Negative Control	91.3 ± 1.5	92.0 ± 1.0 $^{\alpha\beta}$	94.3 ± 1.1 $^{\alpha\beta}$
Positive Control	99.0 ± 3.6	140.6 ± 1.5*	163.0 ±1.0*$^{\alpha}$
Captopril 2.5 mg/kg	96.6 ± 3.5	141.6 ± 3.5*	102.3 ± 0.5*$^{\beta}$
BG50	92.0 ± 2.0	141.6 ± 0.5*	103.0 ± 1.0*$^{\beta}$
BG100	99.3 ± 0.5	141.0 ± 2.0*	95.3 ± 3.0 $^{\alpha\beta}$
BG200	96.0 ± 3.0	141.6 ± 2.0*	96.0 ± 1.0 $^{\alpha\beta}$

Statistically significant difference ($p < 0.05$) in comparison to: the negative control (*), (α) captopril 2.5 mg/kg (α), the positive control (β).

The pulse wave velocity (PWV) data presented in Table 4 elucidate the impact of black garlic on arterial stiffness. A significant elevation in PWV measurements was observed following a 28-day high-fructose, high-cholesterol diet regimen, as compared to the negative control group ($p < 0.05$), suggesting increased arterial rigidity. The group that received BG50, BG100, and BG200 showed a significant reduction in arterial stiffness. This advantageous effect was demonstrated by the diminished PWV values in contrast to the positive control ($p < 0.05$).

The findings from the 28-day observation period regarding heart rate measurements are summarized in Table 5. The positive control group showed a significant increase in heart rate compared to the negative control group ($p < 0.05$). The groups receiving BG extract showed a significant decrease in heart rate compared to the positive control ($p < 0.05$). However, the study found no statistically significant distinctions among the BG50, BG100, and BG200 treatment groups in terms of heart rate.

Table 4. Effects of black garlic extract on pulse wave velocity (PWV) (cm/s) measured on days 0, 7, 14, 21, and 28 following treatments

Group	Pulse Wave Velocity (cm/sec) ± standard deviation on day		
	T0	T14	T28
Negative Control	456.0 ± 7.2	415.1 ± 8.1 $^{\alpha\beta}$	467.8 ± 6.4 $^{\alpha\beta}$
Positive Control	445.8 ± 3.5	577.3 ± 3.0*	630.7 ± 10.0*$^{\alpha}$
Captopril 2.5 mg/kg	432.8 ± 2.3	570.6 ± 14.0*	570.2 ± 8.7*$^{\beta}$
BG50	392.6 ± 4.3	572.8 ± 10.3*	509.6 ± 1.5 $^{\alpha\beta}$
BG100	428.2 ± 5.0	562.9 ± 14.1*	460.1 ± 4.1 $^{\alpha\beta}$
BG200	428.2 ± 5.0	570.8 ± 13.8*	413.8 ± 2.6*$^{\beta}$

Statistically significant difference ($p < 0.05$) in comparison to: the negative control (*), (α) captopril 2.5 mg/kg (α), the positive control (β).

Table 5. Effect of black garlic extract on heart rate (bpm) recorded on 0, 7, 14, 21, and 28 days post-treatment

Group	Heart Rate (bpm) ± standard deviation on day		
	T0	T14	T28
Negative Control	390.5 ± 5.1	394.0 ± 4.9 $^{\alpha\beta}$	424.2 ± 7.9 $^{\alpha\beta}$
Positive Control	351.6 ± 3.0	562.8 ± 15.9*	597.2 ± 1.3*$^{\alpha}$
Captopril 2.5 mg/kg	362.7 ± 3.2	545.0 ± 19.5*	553.8 ± 11.1*$^{\beta}$
BG50	353.6 ± 4.2	561.3 ± 9.3*	439.6 ± 19.9 $^{\alpha\beta}$
BG100	364.7 ± 5.3	560.0 ± 2.4*	437.0 ± 4.9 $^{\alpha\beta}$
BG200	364.7 ± 5.3	550.9 ± 8.7*	415.5 ± 13.4 $^{\alpha\beta}$

Statistically significant difference ($p < 0.05$) in comparison to: the negative control (*), (α) captopril 2.5 mg/kg (α), the positive control (β)

The impact of BG extract on the heart's QRS-T angle is shown in Table 6, with doses of BG50, BG100, and BG200 being examined. The study showed a significant reduction in the QRS-T angle after two weeks of black garlic extract treatment compared to the positive control group ($p<0.05$).

Table 6. Effect of black garlic extract on the frontal QRS-T angle (°) measured on days 0, 7, 14, 21, and 28 following treatments

Group	frontal QRS-T angle (°) ± SD on the day		
	T0	T14	T28
Negative Control	51.6 ± 7.6	50.0 ± 8.6 $^{\alpha\beta}$	50.0 ± 8.6 $^{\alpha\beta}$
Positive Control	46.6 ± 2.8	116.6 ± 5.7*	145.0 ± 5.0*$^{\alpha}$
Captopril 2.5 mg/kg	41.6 ± 2.8	120.0 ± 10.0*	130.0 ± 10.0*$^{\beta}$
BG50	46.6 ± 12.5	123.3 ± 5.7*	63.3 ± 5.7*$^{\beta}$
BG100	43.3 ± 7.6	123.3 ± 5.7*	60.0 ± 10.0 $^{\alpha\beta}$
BG200	43.3 ± 7.6	123.3 ± 15.2*	46.6 ± 2.8 $^{\alpha\beta}$

Statistically significant difference ($p < 0.05$) compared to: the negative control (*), (α) captopril 2.5 mg/kg (α), the positive control (β).

Figure 1 demonstrates the vasodilatory impact of black garlic extract administration by showing increased blood nitric oxide (NO) levels. Rats fed a high-fructose, high-cholesterol diet showed a decrease in NO concentrations compared to the negative control group ($p < 0.05$). Conversely, the BG50 and BG200 treatment groups displayed markedly higher NO levels in comparison to the positive control group ($p < 0.05$).

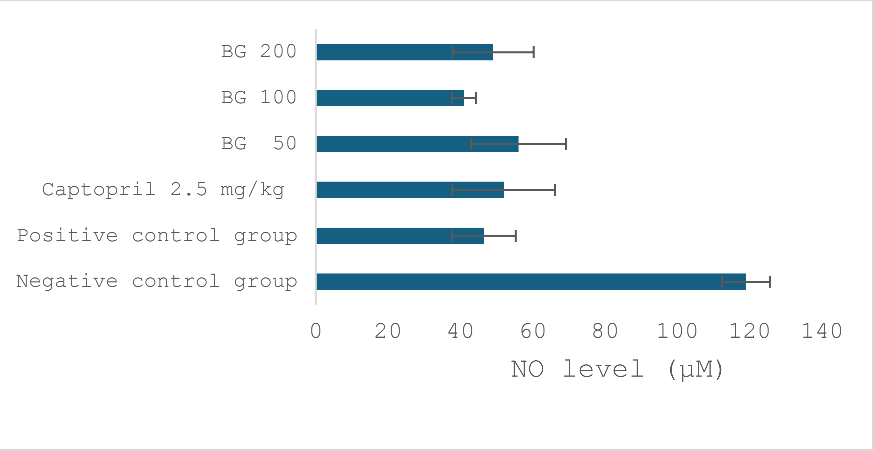

Figure 1. Effect of black garlic extract on serum nitric oxide levels (µM) measured on day 28 following treatment

The histological examination of kidney tissue samples is depicted in Figure 2. Analysis revealed significant changes in the tubular cells of subjects exposed to a diet high in fructose and cholesterol for 28 days, compared to the negative control. Interestingly, the tubules' structural integrity remained intact, indicating that BG200 treatment might offer protective effects against kidney damage.

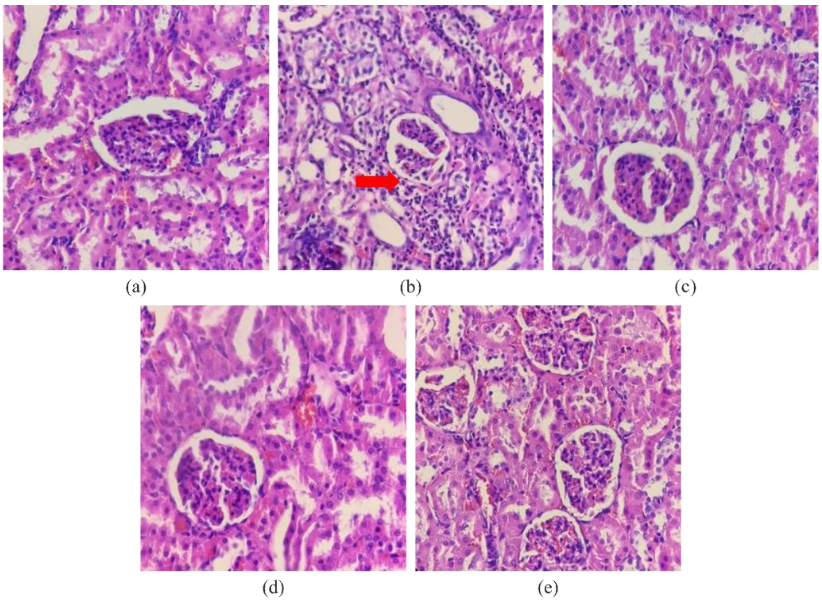

Figure 2. Effects of BG extract on renal tubular cells in preventing nephrotoxicity across all groups during the 28 days of treatment.

Description: a: Negative control, b: Positive control, c-e: BG50, BG100, and BG200, respectively. The red arrow highlights changes in tubular cells (haematoxylin-eosin staining at 400x magnification).

As illustrated in Figure 3, the aortic tissues were examined for foam cell presence. Interestingly, the group subjected to a 28-day diet rich in fructose and cholesterol exhibited no significant foam cell development. The effects of BG50, BG100, and BG200 on the aortic tissues were observed to be comparable to those in the control group.

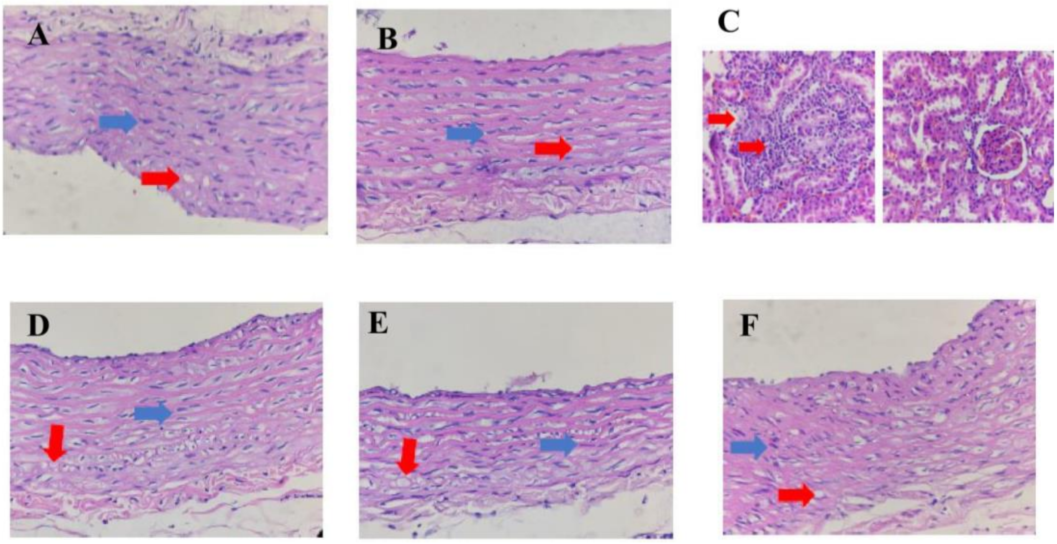

Figure 3. Aortic histology with haematoxylin and eosin (H&E) staining across all treatment groups

Description: A: Negative control; B: Positive control; C: Captopril 2.5 mg/kg; D: Black garlic extract 50 mg/kg; E: Black garlic extract 100 mg/kg; F: Black garlic extract 200 mg/kg. The blue arrow highlights the cell nucleus, while the red arrow indicates the foam cell (haematoxylin-eosin staining at 400x magnification).

High-fructose diets may precipitate hypertension through the formation of conjugated aldehydes during fructose catabolism. These aldehydes interact with protein membranes, compromising calcium channel function. Such disruption results in heightened calcium levels, enhanced peripheral resistance, and consequently, elevated blood pressure (Vasdev et al., 2004). This research utilized both extrinsic and intrinsic methods to develop animal models. Extrinsic induction of metabolic disorders was achieved through diets high in cholesterol and colic acid (Muniz et al., 2019). The experimental approach utilized Propylthiouracil (PTU) as an endogenous trigger to inhibit thioperoxidase enzyme activity, thereby suppressing the synthesis of T4 and T3 thyroid hormones. The introduction of PTU induces hypothyroidism, which subsequently leads to a range of metabolic disturbances. This method causes oxidative stress, which occurs when reactive oxygen species (ROS) production exceeds the organism's ability to neutralize them or repair the cellular damage. This state occurs when ROS generation surpasses the biological system's ability to neutralize these destructive agents or rectify the ensuing cellular injury (Ivanovic & Tadic, 2015).

The regulation of vascular tone relies heavily on nitric oxide (NO), a crucial component in maintaining cardiovascular homeostasis. The proper production of NO is fundamental for the normal functioning of the cardiovascular system (Tousoulis et al., 2012). A reduction in nitric oxide (NO) availability can lead to compromised endothelial function and heightened salt sensitivity. Moreover, elevated angiotensin II activity, which is closely associated with hypertension, results in decreased production of endothelial nitric oxide synthase (eNOS), a crucial enzyme for maintaining proper endothelial function (De Bruyne et al., 2019). The administration of black garlic extract was found to ameliorate endothelial dysfunction by elevating nitrite oxide concentrations in the serum (Figure 1). Studies show that increased inflammation and oxidative stress can lead to vascular rigidity. These mechanisms lead to endothelial dysfunction, which is believed to result from the generation of free radicals by nitric oxide synthase (Tsao & Vasan, 2015).

The evaluation of arterial stiffness serves as an effective method for assessing cardiovascular health, with non-invasive pulse wave velocity (PWV) techniques providing reliable measurements. Studies have shown that powerful antihypertensive medications offer a two-pronged benefit: they not only lower blood pressure but also improve arterial elasticity. This dual action results in a reduced likelihood of cardiovascular incidents, highlighting the significant role these drugs play in maintaining heart health (Grassi, 2020).

The animal models in this investigation exhibited heightened vulnerability to atherosclerosis, partially attributed to increased heart rates. Evidence suggests that the formation of atherosclerotic plaques in blood vessels is associated with heightened oxidative stress and diminished endothelial-dependent vasodilation, consequently leading to accelerated cardiac rhythms. As the heart rate rises, it prompts sympathetic vascular responses, resulting in an increase in pulse wave velocity (PWV). PWV is regarded as the benchmark for assessing arterial elasticity Value of the frontal planar QRS-T angle on cardiac (Li et al., 2013).

The frontal QRS-T angle of the heart was utilized to assess the impact of induction on cardiac electrical conduction modifications. This angle denotes the directional disparity between ventricular depolarization and repolarization processes. In this context, a broad QRS-T angle functions as an indicator for several cardiac disorders, including coronary artery disease, ventricular dysrhythmias, cardiac failure, and the risk of acute myocardial infarction (Czompa et al., 2018). The results confirm earlier findings that black garlic can reduce the breadth of the frontal QRS-T angle (Miao et al., 2014).

Studies have demonstrated that black garlic possesses the ability to reduce blood pressure, heart rate, and pulse wave velocity (PWV). The antioxidant components present in black garlic, such as S-allyl-L-cysteine, polyphenols, ajoene, and flavonoids, are believed to be more effective than those in fresh garlic. The observed decrease in blood pressure may be attributed to either the inhibition of angiotensin-converting enzyme (ACE) or the suppression of angiotensin II production (Hasimun et al., 2020; Ried & Fakler, 2014).

Following a fortnight of fermentation, the levels of S-allyl-l-cysteine (SAC) were observed to rise. SAC exhibits hypotensive effects by stimulating the generation of intracellular nitric oxide (NO) and hydrogen sulfide (H2S). Moreover, this compound promotes vasodilation and suppresses the formation of angiotensin II. The anti-inflammatory characteristics of SAC also contribute to its ability to combat atherosclerosis. This is achieved through the enhancement of NO production within endothelial cells, coupled with a reduction in the expression of inducible nitric oxide synthase (iNOS) in macrophages (Qurbany, 2015). Moreover, ajoene is believed to contribute to lowering blood pressure by inhibiting the entry of calcium ions into cells. This reduction in cellular calcium levels results in hyperpolarization, leading to the relaxation of smooth muscle cells in blood vessels (Qurbany, 2015).

Research has shown that consuming a diet high in fructose leads to changes in the tubular architecture of kidney tissue, as observed through histological examination (Saleh et al., 2017). The described diet causes kidney enlargement due to tubular cell proliferation and damage to renal microvascular endothelial cells in the tubulointerstitial region. Additionally, increased uric acid concentrations aggravate kidney disorders by triggering glomerular hypertension and diminishing blood supply to the kidneys (Sánchez-Lozada et al., 2007). Nevertheless, this study did not measure uric acid levels; consequently, further investigation is required to confirm these results.

Black garlic has been found to possess potential nephroprotective properties, according to previous investigations. Its antioxidant constituents, including S-allyl-L-cysteine (SAC), polyphenols, and flavonoids, exhibit anti-inflammatory characteristics that affect nitric oxide production by inhibition of pro-inflammatory factors. The results of this research support to earlier studies, suggesting that black garlic extract may function as a protective agent against nephrotoxicity (Lee et al., 2019).

Research has revealed that this induction heightens cardiovascular risk by expanding the frontal QRS-T angle and elevating heart rate, owing to increased arterial stiffness. Animal studies focusing on hypertension and atherosclerosis might require an extended treatment duration. The investigation demonstrated that black garlic extract possesses the ability to counteract the induction's effects.

CONCLUSION

The research findings underscore the advantageous effects of BG extracts on cardiovascular and renal health. These extracts demonstrated efficacy in counteracting the deleterious impacts of a diet rich in fructose and cholesterol. Notably, the extract yielded substantial reductions in blood pressure, cardiac rate, and arterial rigidity. Moreover, it elevated serum nitric oxide (NO) concentrations, which are essential for maintaining vascular integrity. Black garlic also exhibited renoprotective properties, shielding the kidneys from harm associated with hypertension and vascular stiffness.

ACKNOWLEDGEMENT

The authors extend their appreciation to the Institute of Research and Community Service at Bhakti Kencana University for provided funding through a research excellence scheme grant.

REFERENCES

Chidinma, O. (2019). Therapeutic effects of garlic: a review. *Scientific Journal of Biology & Life Sciences*, *1*(1),1-5. https://doi.org/10.33552/SJBLS.2019.01.000502

Czompa, A., Szoke, K., Prokisch, J., Gyongyosi, A., Bak, I., Balla, G., Tosaki, A., & Lekli, I. (2018). Aged (Black) versus raw garlic against ischemia/reperfusion-induced cardiac complications. *International Journal of Molecular Sciences*, *19*(4), 1017. https://doi.org/10.3390/ijms19041017

De Bruyne, T., Steenput, B., Roth, L., De Meyer, G. R. Y., Santos, C. N. dos, Valentová, K., Dambrova, M., & Hermans, N. (2019). Dietary polyphenols targeting arterial stiffness: interplay of contributing mechanisms and gut microbiome-related metabolism. *Nutrients*, *11*(3), 578. https://doi.org/10.3390/nu11030578

Dilaveris, P., Gialafos, E., Pantazis, A., Synetos, A., Triposkiadis, F., & Gialafos, J. (2001). The spatial QRS-T angle as a marker of ventricular repolarisation in hypertension. *Journal of Human Hypertension*, *15*(1), 63–70. https://doi.org/10.1038/sj.jhh.1001129

Feigin, V. L., Krishnamurthi, R. V., Parmar, P., Norrving, B., Mensah, G. A., Bennett, D. A., Barker-Collo, S., Moran, A. E., Sacco, R. L., Truelsen, T., Davis, S., Pandian, J. D., Naghavi, M., Forouzanfar, M. H., Nguyen, G., Johnson, C. O., Vos, T., Meretoja, A., Murray, C. J. L., & Roth, G. A. (2015). Update on the global burden of ischemic and hemorrhagic Stroke in 1990-2013: the GBD 2013 study. *Neuroepidemiology*, *45*(3), 161–176. https://doi.org/10.1159/000441085

Garmana, A. N., Sukandar, E. Y., & Fidrianny, I. (2018). Antihypertension study of anredera cordifolia (ten). V. Steenis extract and its fractions in rats through dexamethasone induction and nitric oxide release. *Asian Journal of Pharmaceutical and Clinical Research*, *11*(1), 278. https://doi.org/10.22159/ajpcr.2017.v11i1.22312

Grassi, G. (2020). Impact of heart rate on arterial stiffness: virtual vs. real assessment. *Journal of Hypertension*, *38*(12), 2382–2383. https://doi.org/10.1097/HJH.0000000000002603

Hasimun, P., Mulyani, Y., Rehulina, E., & Zakaria, H. (2020). Impact of Black Garlic on biomarkers of arterial stiffness and frontal QRS-T angle on hypertensive animal nodel. *Journal of Young Pharmacists*, *12*(4), 338–342. https://doi.org/10.5530/jyp.2020.12.88

Ivanovic, B., & Tadic, M. (2015). Hypercholesterolemia and Hypertension: two sides of the same coin. *American Journal of Cardiovascular Drugs*, *15*(6), 403–414. https://doi.org/10.1007/s40256-015-0128-1

James, P. A., Oparil, S., Carter, B. L., Cushman, W. C., Dennison-Himmelfarb, C., Handler, J., Lackland, D. T., LeFevre, M. L., MacKenzie, T. D., Ogedegbe, O., Smith, S. C., Svetkey, L. P., Taler, S. J., Townsend, R. R., Wright, J. T., Narva, A. S., & Ortiz, E. (2014). 2014 evidence-based guideline for the management of high blood pressure in adults. *JAMA*, *311*(5), 507.

https://doi.org/10.1001/jama.2013.284427

Jaroszyński, A., Furmaga, J., Zapolski, T., Zaborowski, T., Rudzki, S., & Dąbrowski, W. (2019). The improvement of QRS-T angle as a manifestation of reverse electrical remodeling following renal transplantation in end-stage kidney disease patients on haemodialysis. *BMC Nephrology*, *20*(1), 441. https://doi.org/10.1186/s12882-019-1624-3

Kearney, P. M., Whelton, M., Reynolds, K., Muntner, P., Whelton, P. K., & He, J. (2005). Global burden of hypertension: analysis of worldwide data. *The Lancet*, *365*(9455), 217–223. https://doi.org/10.1016/S0140-6736(05)17741-1

Kimura, S., Tung, Y.-C., Pan, M.-H., Su, N.-W., Lai, Y.-J., & Cheng, K.-C. (2017). Black garlic: a critical review of its production, bioactivity, and application. *Journal of Food and Drug Analysis*, *25*(1), 62–70. https://doi.org/10.1016/j.jfda.2016.11.003

Kundu, R., Biswas, S., & Das, M. (2017). Mean arterial pressure classification: a better tool for statistical interpretation of blood pressure related risk covariates. *Cardiology and Angiology: An International Journal*, *6*(1), 1–7. https://doi.org/10.9734/CA/2017/30255

Lee, T. W., Bae, E., Kim, J. H., Jang, H. N., Cho, H. S., Chang, S.-H., & Park, D. J. (2019). The aqueous extract of aged black garlic ameliorates colistin-induced acute kidney injury in rats. *Renal Failure*, *41*(1), 24–33. https://doi.org/10.1080/0886022X.2018.1561375

Li, Y.-H., Ren, X.-J., Han, Z.-H., Wang, Y.-L., Wang, Y., Zhang, J.-R., & Chen, F. (2013). Value of the frontal planar QRS-T angle on cardiac dysfunction in patients with old myocardial infarction. *International Journal of Clinical and Experimental Medicine*, *6*(8), 688–692.

Miao, Y., Chen, J., Zhou, G., Xu, X., Zhang, Q., & Wang, I. (2014). The antihypertensive effect of black garlic (Allium Sativum) in spontaneously hypertensive rats via Scavening of free radicals. *Research in Health and Nutrition (RHN)*, *2*(1), 5–12.

Muniz, L. B., Alves-Santos, A. M., Camargo, F., Martins, D. B., Celes, M. R. N., & Naves, M. M. V. (2019). High-lard and high-cholesterol diet, but not high-lard diet, leads to metabolic disorders in a modified dyslipidemia model. *Arquivos Brasileiros de Cardiologia*. https://doi.org/10.5935/abc.20190149

Oehler, A., Feldman, T., Henrikson, C. A., & Tereshchenko, L. G. (2014). QRS-T angle: a review. *Annals of Noninvasive Electrocardiology*, *19*(6), 534–542. https://doi.org/10.1111/anec.12206

Qurbany, Z. T. (2015). The benefits of Garlic (Allium sativum) as antihypertension. *Journal Majority*, *4*, 116–121.

Ried, K., & Fakler, P. (2014). Potential of garlic (Allium sativum) in lowering high blood pressure: mechanisms of action and clinical relevance. *Integrated Blood Pressure Control*, 71. https://doi.org/10.2147/IBPC.S51434

Saleh, R., Merghani, B., & Awadin, W. (2017). Effect of high fructose administration on histopathology of kidney, heart and aorta of rats. *Journal of Advanced Veterinary and Animal Research*, *4*(1), 1. Salehhttps://doi.org/10.5455/javar.2017.d193

Sánchez-Lozada, L. G., Tapia, E., Jiménez, A., Bautista, P., Cristóbal, M., Nepomuceno, T., Soto, V., Ávila-Casado, C., Nakagawa, T., Johnson, R. J., Herrera-Acosta, J., & Franco, M. (2007). Fructose-induced metabolic syndrome is associated with glomerular hypertension and renal microvascular damage in rats. *American Journal of Physiology-Renal Physiology*, *292*(1), F423–F429. https://doi.org/10.1152/ajprenal.00124.2006

Tousoulis, D., Kampoli, A.-M., Tentolouris Nikolaos Papageorgiou, C., & Stefanadis, C. (2012). The role of nitric oxide on endothelial function. *Current Vascular Pharmacology*, *10*(1), 4–18. https://doi.org/10.2174/157016112798829760

Tsao, C. W., & Vasan, R. S. (2015). Cohort profile: the framingham heart study (FHS): overview of milestones in cardiovascular epidemiology. *International Journal of Epidemiology*, *44*(6), 1800–1813. https://doi.org/10.1093/ije/dyv337

Vasdev, S., Longerich, L., & Gill, V. (2004). Prevention of fructose-induced hypertension by dietary vitamins. *Clinical Biochemistry*, *37*(1), 1–9. https://doi.org/10.1016/j.clinbiochem.2003.09.003