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Evaluation of antihypertensive effect of *Stellaria media* and *Beta vulgaris* on Albino rats

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ABSTRACT

This study was carried out to evaluateanti-hypertensive effect of aqueous extracts of Beta vulgaris (BV) (bulb) and Stellaria media (SM)(leaf) onAlbino rats. Fifty-five Albino rats were used and randomly distributed into eleven (11) groups of 5 animals each. Hypertension was induced in animals using 18% sodium chloride (NaCl) orally at the dose of 10 ml/kg. The animals were treated for 28 days before they were sacrificed. Under chloroform anaesthesia blood samples were collected in a plain tube from jugular vein for analysis. The mean blood pressure (BP) values on day 1 for both systolic blood pressure (SBP) and diastolic blood pressure (DBP) in all groups were not significantly ($p>0.05$) lower. As the treatments continued to day 28, SBP (119.67±1.15mmHg) and DBP (78.68±2.08mmHg) lowering effect of the extracts was the highest in group 10 (rat administered 300mg/kg BV + 150mg/kg SM) which was significantly ($p<0.05$) lower from other groups, followed by group 6 (rats administered 450mg/kg BV) with SBP (120.33±0.577mmHg) and DBP (81.67±1.53mmHg). The BP lowering effect of the extracts were dosage and duration dependent with high dosage of BV giving the best BP lowering effect. High blood pressure inhibition may be associated with the presence of some phytochemicals in the extract such as Alkaloid, flavonoid and phenolics. The study showed that Stellaria media and Beta vulgaris extract were able to inhibit the development of hypertension. Different combinations and high single dosage administration of the different extracts at a given duration (28 days) gave desirable results in BP assays.

Keywords: Hypertension, Blood pressure, Stellaria *media*, *Beta vulgaris*, phytochemicals

INTRODUCTION

Hypertension is a major public health problem due to its high prevalence around the globe (Abebe*et al.,* 2015). By 2025, 1.56 billion adults are anticipated to be hypertensive (Tabrizi et al., 2016). High blood pressure is associated to chronic heart disease, stroke, and coronary heart disease. High blood pressure may put a person at risk of stroke and coronary heart disease. Its effects include heart failure, peripheral vascular disease, renal impairment, retinal hemorrhage, and visual impairment, in addition

to coronary heart disease and stroke (Turaket *et al.,* 2014). When blood pressure is consistently low, it is called hypotension; when blood pressure is continually high, it is called hypertension; and when blood pressure is constantly normal, it is called normotension (Salat, 2012). A systolic blood pressure of less than 120 mmHg and a diastolic blood pressure of less than 80 mmHg are considered normal (Chobania *et al.,* 2003). A systolic blood pressure of 140 mmHg or a diastolic blood pressure of 90 mmHg is considered hypertension. Prehypertension is defined as a range of 120-139 mmHg systolic blood pressure and 80-89 mmHg diastolic blood pressure (Chobania *et al.,* 2003; Kim *et al.,* 2018). Long-term hypertension puts you at risk for a variety of ailments, including stroke, heart disease, and kidney failure. A long history of hypertension is more common than a long history of hypotension (Grim, 2016). Despite the fact that prehypertension is not a medical condition in and of itself, those who are pre-hypertensive are more prone to develop hypertension (HTN) (Erem *et al.,* 2009). It is a silent killer since there are no signs until a catastrophic medical crisis, such as a heart attack, stroke, or chronic renal failure, occurs (Millett et al., 2013). Because most people are unaware of elevated blood pressure, it can only be detected through measurement. Although most persons with hypertension are asymptomatic, others suffer from headaches, lightheadedness, vertigo, impaired vision, or fainting spells (Williams, 2001). Ethno-therapies are no longer considered unscientific in many parts of the world; in fact, they are gaining favor due to the perception that natural therapies are healthier. Herbal remedies are recommended by the World Health Organization for a number of local health conditions, particularly in developing countries (Yakubu *et al.,* 2017). As it is with most medicinal plants, *Stellaria media* and *Stellaria media* have been presumed to have blood pressure lowering properties though it has not been scientifically validated (Lee *et al.,* 2009; Oladeji and Oyebamiji, 2020). Photochemicals (functional non-nutrient dietary components) found in vegetables and fruits are useful in boosting health and illness prevention (Melbyb *et al.,* 2004). Carotenoids are phytochemicals that have been reported to be present in Beta vulgaris, however there is insufficient information on Stelaria medium. Excess reactive oxygen species (ROS) are linked to inflammation, growth, and vasoconstriction, all of which contribute to vascular injury in a number of cardiovascular diseases such as hypertension, hyperlipidemia, and diabetes (Monroy-Ruiz et al., 2011). Reactive oxygen species (ROS) play an important pathophysiological function in hypertension. Carotenoids, for example, reduce the generation of reactive oxygen species (ROS) by NAD(P)H oxides, improve endothelial function, increase the production of nitric oxide (NO), and lower blood pressure in hypertensive people (Monroy-Ruiz *et al.,* 2011).

Fig 1. Beetroot (*Beta vulga*ris)

Fig 2. Chickweed (*Stelleria media*)

Sources:https://www.theresiliencyinstitute.net.

MATERIAL AND METHODS

All materials, chemicals and reagent used were of analytical standard.

Instrument and Apparatus

Automatic blood pressure monitor KD-595 and #.1 philips (M1870A) Cuff was use for the examination of the blood pressure levels, glass wares were washed with deionized water and rinsed with distilled water to minimize the chances of interference during phytochemical extraction. .ATOM electronic compact scale was use to weigh samples.

Plant Sample Collection and Preparation

Beta vulgaris was purchased from building material market in Jos, Plateau State, Nigeria, while *Stellaria media* was obtained from Kwararafa area, Wukari LGA., Taraba state. The plants were identified at University of Jos, Department of Botanical Science, Nigeria by a botanist. The plant was air dried for two weeks in the shade at room temperature (25ºC) before being pulverized into fine powder with a mortar and pestle. The powder was sieved and kept in airtight containers until needed.

Sample Digestion

The extraction was carried using cold maceration method in the ratio 1:5 grams to volume of distilled water. Each sample powder (100g) was weighed using a top loading balance before being put into a large extraction flask (bottles) containing 500ml of distilled water and left at room temperature for 24 hours with constant agitation and stirring with a sterile glass rod. The suspension was then filtered using a sterile muslin cloth before being filtered once more with Whatman No.1 filter paper inserted in a funnel, as reported by Stojiljkovi et al. (2016).

Research Design

Albino rats (4-5 weeks) were obtained from the Department of Biology and Physiology, Faculty of Sciences, University of Jos, Nigeria. The rats were kept in the animal house of the Department of Biology, Faculty of Natural and Applied Sciences, University of Jos, Nigeria, in plastic and wooden cages. The animals were given two weeks to acclimate before being offered critical feed and water ad libitum. Normal and hypertensive rats were randomly assigned into ten (10) groups of five (5) animals each. Fifty (50) Wistar Albino rats were divided into five (5) groups and given 10mg/kg/day of 18% sodium chloride (NaCl) for 28 days to develop hypertension (Tokaç *et al.,* 2013). The animals' blood pressures (BP) (diastolic and systolic) were measured non-invasively. To reduce stress, the rats' legs were placed in the holder and allowed to move freely. Each rat was given 5 minutes to acclimate without being touched or making any noise. A proper tail cuff was chosen and inserted at the base of the tail. The (#.1) philips (M1870A) cuff (sensors) was linked to the automatic blood pressure monitor-KD595, and the BP monitor received and presented the readings electronically (Jepson *et al.,* 2005).

The rat treatment groups were as follows with different solvent in mg/kg body weight.

Group 1- Normal control 10ml/kg/day received distilled water.

Group 2- HBP induced (Negative control) 18% NaCl 10mg/kg/day

Group 3-HBP induced +Ramipril (Altace) 10 mg/kg/day

Group 4- HBP induced +*Beta vulgaris* extract 150mg/kg/day

Group 5- HBP induced +*Beta vulgaris* extract 300mg/kg/day

Group 6-HBP induced + *Beta vulgaris* extract 450mg/kg/day

Group 7- HBP induced +*Stellaria media* extract 150mg/kg/day

Group 8- HBP induced +*Stellaria media* extract 300mg/kg/day

Group 9- HBP induced +*Stellaria media* extract 450mg/kg/day

Group 10- HBP induced +*Beta vulgaris* extract 300mg/kg/day + *Stellaria media* extract 150mg/kg/day

Group 11- HBP induced+*Beta vulgaris* extract 150mg/kg/day + *Stellaria media* extract 300mg/kg/day

This experimental protocol follows up to 28 days after the test groups have been confirmed hypertensive (Lee *et al.,* 2009).

Statistical Analysis

The statistical analysis was performed using statistical package for social science (SPSS) version 23 and significant was at $p<0.05$. Statistical analysis was carried out using analysis of variant (ANOVA) and Duncan's multiple comparison test. Results were expressed as mean ± standard deviation.

RESULT AND DISCUSSION

Table 1: Qualitative phytochemical screening results of *B. vulgaris* and *S. media*

Constituents	Beta vulgaris (beet roots)	Sterellia media (zakibanza)
Alkaloids	++	+
Saponins	++	++
Tannins	+++	+++
Flavonoids	+	++
Carbohydrates	++	-
phenols	+++	+++
Steroids	+	-
Anthraquinones	++	-
Cardial glycosides	-	-
Terpenoids	-	-
Percentage yield	55.22	30.64

Were - = Absent, + = slightly present ++ = more present +++ =highly present

Percentage yield of *Beta vulgaris* (%) = 55.22 %

Percentage yield of *Sterellia media* (%) = 30.64 %

Table 2: Result showing the systolic blood pressure (mmHg)of Albino rats treated with *B.vulgaris and S. media.*

	SYS T O L I C				
Groups/Treatments mg/kg/day	SBP(DAY1)	SBP(DAY7)	SBP(DAY14)	SBP(DAY21)	SBP(DAY28)
Normal control	116.67±5.86^{a}	120.00±0.00^{a}	122.67±1.53^{a}	120.00±0.00^{a}	122.33±4.04^{ab}
Negative control	145.33±11.72^{b}	148.33±8.50^{d}	162.00±19.29^{d}	182.67±29.69^{c}	209.33±16.77^{d}
Positive control (Ramipril)	142.33±2.52^{b}	138.00±1.00^{bc}	129.67±4.04^{abc}	124.00±2.00^{ab}	115.67±1.15^{a}
150 *B. vulgaris*	146.67±1.53^{b}	142.33±2.08^{c}	140.33±1.53^{c}	138.67±1.53^{b}	136.33±1.15^{c}
300 *B. vulgaris*	143.33±2.08^{b}	138.67±0.58^{bc}	130.33±1.53^{abc}	126.33±1.53^{ab}	121.67±2.08^{ab}
450 *B. vulgaris*	141.67±1.53^{b}	135.67±2.52^{b}	127.67±0.58^{ab}	124.67±2.08^{ab}	120.33±0.577^{ab}
150 *S. media*	142.33±2.52^{b}	140.33±0.58^{bc}	140.67±0.58^{c}	140.00±0.00^{b}	138.00±1.00^{c}
300 *S. media*	144.67±1.53^{b}	140.33±2.52^{bc}	138.00±1.00^{bc}	135.00±1.00^{ab}	128.67±1.15^{bc}
450 *S. media*	141.67±0.58^{b}	135.67±1.53^{b}	132.00±2.00^{abc}	128.00±1.00^{ab}	123.67±2.52^{ab}
300 *B.vulgaris* +150 *S.media*	144.67±1.53^{b}	139.33±1.53^{bc}	131.00±2.00^{abc}	123.00±1.00^{ab}	119.67±1.15^{ab}
300 *S.media* +150 *B.vulgaris*	144.33±1.53^{b}	140.00±1.00^{bc}	134.00±2.00^{abc}	129.00±1.73^{ab}	124.00±2.00^{ab}

The Results were expressed as mean±standard deviation. Results with the same alphabet superscript

shows no significant difference while results with different alphabet superscript within the row shows significant difference at p<0.05.

Table 3: Result showing the diastolic blood pressure (mmHg)of Albino rat treated with *B.vulgaris* and *S.media.*

	DIASTOLIC				
Groups/Treatments mg/kg/day	DBP(DAY1)	DBP(DAY7)	DBP(DAY14)	DBP(DAY21)	DBP(DAY28)
Normal control	76.00±9.53^{a}	81.33±2.31^{a}	77.67±2.51^{a}	79.67±0.57^{a}	80.00±0.00^{a}
Negative control	98.00±1.00^{c}	101.00±3.61^{g}	103.33±15.27^{d}	120.00±30.27^{b}	154.67±10.78^{c}
Positive control (Ramipril)	94.67±1.52^{bc}	89.66±0.58^{cd}	86.67±1.53^{ab}	80.66±1.53^{a}	77.67±1.52^{a}
150 *B. vulgaris*	96.67±1.53^{ab}	95.67±1.53^{f}	90.33±0.58^{c}	84.33±3.79^{a}	82.00±2.00^{ab}
300 *B.vulgaris*	95.67±2.52^{bc}	82.33±1.53^{a}	80.00±1.00^{a}	79.00±2.64^{a}	83.00±2.64^{ab}
450 *B.vulgaris*	95.00±2.00^{bc}	87.66±2.52^{bcd}	85.67±2.31^{ab}	84.33±2.08^{a}	81.67±1.53^{a}
150 *S.media*	94.67±1.51^{bc}	87.66±1.15^{bcd}	89.66±1.53^{c}	89.66±0.58^{a}	88.67±0.57^{b}
300 *S.media*	96.66±0.58^{bc}	93.33±0.58^{ef}	90.00±1.00^{c}	87.66±1.52^{a}	84.66±2.08^{ab}
450 *S.media*	90.66±o.57^{b}	86.00±1.00^{b}	85.00±1.00^{ab}	83.00±1.00^{a}	80.00±2.64^{a}
300 *B.vulgaris* +150 *S.media*	92.33±1.53^{bc}	86.66±1.53^{bc}	84.00±2.00^{ac}	81.00±2.65^{a}	78.68±2.08^{a}
300 *S.media* +150 *B.vulgaris*	94.66±1.50^{bc}	90.33±1.53^{de}	87.00±2.00^{ab}	84.00±2.00^{a}	80.33±2.08^{a}

The Results were expressed as mean±standard deviation. Results with the same alphabet superscript shows no significant difference while results with different alphabet superscript within the row shows significant difference at p<0.05.

Result interpretation and Discussion

The objective of this study was to investigate the anti-hypertensive effect of aqueous extracts of *Beta vulgaris* (bulb) and *Stellaria media* (leaf) on Albino rats model which could be used to mirror similar

effect in human use of *B.vulgaris* and *S.media*. This research stems from claims by folk medicinal practice in some parts of Nigeria in which *S. media* (leaf) and *B. vulgaris* (bulb) were used in treatment of cardiovascular ailment most especially high blood pressure and other blood related diseases(Mirmiran *et al.,* 2020; Cavender, 2021). In folk medicine, *Stellaria media* and *Beta vulgaris* are mostly consumed as tea and believed to lower blood pressure. Accordingly, several available tea products with similar claims from plants parts were extracted using aqueous methods and consumed as tea. From the entire literature search conducted before this research, the anti-hypertensive effect of *Beta vulgaris* and *Stelleria media* has not been investigated. From the qualitative phytochemical screening results (Table 1), the study revealed the present of some phytochemicals in *B. vulgaris*and *S.media*, Qualitatively, the phytochemicals that appear to be more present in *B.vulgaris* are; Alkaloids, Saponins, Carbohydrates and Anthraquinones. Tannins and phenols were highly present, while Steroids and Flavonoids were slightly present. In *S. media,* saponin and flavonoid appeared to be more present, phenols and tannins were highly present and Alkaloid was slightly present. Carbohydrates, Anthraquinones and Steroids were absent in *S. media*

In table 2 above, oral administration of 150, 300 and 450 mg/kg of *B.vulgaris* (BV) and *S. media* (SM) aqueous extracts and also the synergistic effect of their composite administration (300 mg/kg BV +150mg/kg SM and 300mg/kg SM + 150 mg/kg BV) on Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) over a period of twenty-eight (28) days showed appreciable varied antihypertensive effects. On days 1, 14 and 28, the negative control (group 2) showed SBP (145.33±11.72, 162.00±19.29, 209.33±16.77 mmHg) and DBP values (98.00±1.00, 103.33±15.27, 154.67±10.78mmHg) indicating high blood pressure in the untreated but induced BP rats. The positive control (group 3) on days, 1, 14, and 28 showed a SBP (142.33±2.52, 129.67±4.04, 115.67±1.15mmHg) and DBP values (94.67±1.52, 86.67±1.53, 77.67±1.52mmHg) whose blood pressure decreased appreciably compared to the negative control; an indication that the ramipril drug is an effective antihypertensive drug with which we intent to compare our treatment groups.Among the treatment groups; experimental group 10 (hypertensive rats administered 300mg/kg BV +150mg/kg SM) on days 1, 14 and 28, showed SBP values (144.67±1.53 ,131.00±2.00 , 119.67±1.15mmHg) in which the BP was significantly ($p \leq 0.0.05$) the least among the treatment groups indicating that the administered composite extracts as shown in group 10 had the best antihypertensive constituents. Down the column in day 1, there was no significant difference ($p \geq 0.05$) in BP among all the groups except the normal control which was not induced and thus non hypertensive. On day 14, group 6 (rats administered 450mg/kg BV), 5(rats administered 300 mg/kg BV) and 4 (rats administered 150mg/kg BV) showed SBP (127.67±0.58, 130.33±1.53, 140.33±1.53mmHg) and DBP (85.67±2.31, 80.00±1.00, 90.33±0.58mmHg) values which are significantly ($p \leq 0.05$) different in terms of their SBP and DBP. This shows that within two weeks of administration of extracts, there was reduction in BP which was dosage dependent as shown in group 6. On day 28, group 6, 5 and 4 SBP (120.33±0.577, 121.67±2.08,136.33±1.15mmHg) and DBP (82.00±2.00, 83.00±2.64, 81.67±1.53mmHg) values showed that there were no significantly ($p \geq 0.05$) different between groups 5 and 4 but group 6 was significantly ($p \leq 0.05$) different from the rest. Comparing the results of 14 days administration to those of the 28 days administration of BV extracts, it could be inferred that there was general reduction in BP value which was both duration and dosage dependent.On day 14, group 9 (rats administered 450mg/kg SM), 8(rats administered 300 mg/kg SM) and 7 (rats administered 150mg/kg SM) showed SBP (132.00 ± 2.00 mmHg , 138.00±1.00·140.67±0.58mmHg) and DBP (85.00±1.00, 90.00±1.00, 89.66±1.53mmHg) values which are significantly ($p \leq 0.05$) different in terms of their SBP and DBP except for the DBP of groups 7 and 8. This shows that within two weeks of administration of extracts, there was reduction in BP

which was dosage dependent. On day 28, groups 9, 8 and 7 SBP (123.67±2.52, 128.67±1.15,138.00±1.00mmHg) and DBP (80.00±2.64, 84.66±2.08, 88.67±0.57mmHg) values were not significantly ($p \geq 0.05$) different. Comparing the results of 14 days administration to those of the 28 days administration of SM extracts, it could be inferred that there was general reduction in BP value which was only duration but not dosage dependent.On day 14, groups 10 (rats administered 300mg/kg BV +150mg/kg SM) and 11(rats administered 300mg/kg BV +150mg/kg SM) showed SBP (131.00±2.00, 134.00±2.00mmHg) and DBP (84.00±2.00, 87.00±2.00mmHg) values which were not significantly different ($p \geq 0.05$) in terms of their SBP and DBP. This shows that within two weeks of administration of extracts, there was reduction in BP which was not based dosages or duration but their combination. However, the extracts combination with higher concentration of BV showed slightly more reduction in BP values. On day 28, groups 10 (rats administered 300mg/kg BV +150mg/kg SM) and 11(rats administered 300mg/kg SM +150mg/kg BV) SBP (119.67±1.15, 124.00±2.00mmHg) and DBP (78.68±2.08, 80.33±2.08mmHg) values were not significantly different ($p \geq 0.05$). Comparing the results of 14 days administration to those of the 28 days administration of the mixed extracts, there was reduction in BP which was BV dosage dependent and duration dependent. On day 7, down the column, group 2 (negative control) and 4(rats administered 150mg/kg) shows the highest SBP (148.33±8.50, 142.33±2.08 mmHg) and DBP (101.00±3.61, 95.67±1.53 mmHg) value indicating that the rats in the groups were hypertensive. Groups 8 (rats administered 300mg/kg SM) and 9 (rat administered 450mg/kg SM) showed SBP (140.33±0.58, 140.33±2.52 mmHg) and DBP (93.33±0.58, 87.66±1.15mmHg) values are not significantly different ($p \geq 0.05$) in terms of their SBP but significantly ($p \leq 0.05$) different in term of their DBP. On day 21, down the column, groups 2 (negative control) and 7(rats administered 150mg/kg SM) showed the highest SBP (209.33±16.77, 140.00±0.00mmHg) and DBP (120.00±30.27, 89.66±0.58mmHg) values indicating that the rats in that group are hypertensive. Group 6 showed the least SBP (127.67±0.58mmHg) values indicating that administration of 450mg/kg of BV lowers blood pressure more than all other treatment groups. Noni fruit was utilized in the treatment of hypertension generated by ketamine 0.05 ml + epinephrine 0.2 ml, and captopril 2.5 mg was employed as the reference medicine, according to Hermilasari *et al.,* (2020). According to the study, noni fruit extract reduces blood pressure by an average of 58.5 mmHg while captopril reduces blood pressure by 25.5 mmHg, indicating that the fruit extract is more effective than the standard drug. However, the combination of BV and SM extract was not more effective than the standard drug for the duration of time we tried, but it does show a significant reduction in hypertensive Albino rats. From our studies it was observed that the phytochemical compounds present in both extracts may be responsible for the BP-lowering effects observed. *Beta vulgaris* and *Stellaria media*contains other potentially bioactive compounds such as Alkaloids, Tannins, Carbohydrates, Steroids Anthraquinones and others. Saponin and flavonoid have been said to possess antihypertensive effect (Chhatre *et al.,*2014).

Longer saponin exposure may result in saponin buildup in other renal compartments. Saponin found in the artery wall suggested that saponin might infiltrate the granular cell of the afferent arteriole, the location of renin synthesis. As a result, saponin may suppress renin synthesis before it is released from granular cells. Saponin has previously been shown to suppress intracellular renin in cultured cardiac cells (Chen *et al.,* 2013). Flavonoids are polyphenols found in fruits that have antihypertensive properties via boosting nitric oxide (NO) bioavailability, decreasing endothelial cell oxidative stress, and altering vascular ion channel function (Gai *et al.,* 2023).

Base on the result obtain from this research, it was discovered that the BP lowering effect is directly proportional to the dosage administered (the higher the dosage the more the lowering effect) and

duration of administration is in agreement with a previous researched reported elsewhere (Craig et al., 2018). According to Hobbs *et al.* (2012) 250ml and 500ml of nitrate was found to have a peak decrease in SBP from 5.40 to 2.20mmHg and 10.4 to 5.20 mmHg within 2 to 3 hours.

Flavonoids are active components in many medicinal plants and natural products that have a good effect on human health, and saponin content has also been linked to a reduction in heart disease (Feig *et al.,* 2014). It is worth noting in this study that Beta vulgaris and Stellaria media have found great relevance in human traditional medicine and assessment of ethno pharmacological application based on the results obtained from the rat's models following the traditional claims that they have antihypertensive properties, which have been confirmed by this study.

CONCLUSION

The claim of use of *Stellaria media* and *Beta vulgaris* by traditional medicinal practice for lowering blood cholesterol and blood pressure levels was examined in vivo with rat models, using an experimental design to mimic the human use of the herb. The BP lowering effect of the extracts were dosage and duration dependent with high dosage of BV giving the best BP lowering effect. Hence, high blood pressure inhibition may be associated with the presence of some phytochemical (Alkaloid, flavonoid and phenols) in the extracts. The study showed that *Stellaria media* and *Beta vulgaris* extracts were able to inhibit the development of hypertension. Different combinations and high single dosage administration of the different extracts at a given duration (28 days) gave desirable results in BP.

REFERENCE

[1] Cavender, M. A., & Wirka, R. C. (**2021**). Blood pressure lowering in the prevention of type 2 diabetes. *The Lancet*, *398*(10313), 1778-1779.

[2] Chen, M., Long, Z., Wang, Y., Liu, J., Pian, H., Wang, L., & Chen, Z. (**2013**). Protective effects of saponin on a hypertension target organ in spontaneously hypertensive rats. *Experimental and therapeutic medicine*, *5*(2), 429-432.

[3] Chhatre, S., Nesari, T., Somani, G., Kanchan, D., & Sathaye, S. (**2014**). Phytopharmacological overview of Tribulus terrestris. *Pharmacognosy reviews*, *8*(15), 45.

[4] Chobanian, A. V., Bakris, G. L., Black, H. R., Cushman, W. C., Green, L. A., Izzo Jr, J. L., ... & National High Blood Pressure Education Program Coordinating Committee. (**2003**). Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *hypertension*, *42*(6), 1206-1252.

[5] Chobanian, A. V., Bakris, G. L., Black, H. R., Cushman, W. C., Green, L. A., Izzo Jr, J. L., & National High Blood Pressure Education Program Coordinating Committee. (**2003**). The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. Jama, 289(19), 2560-2571.

[6] Craig, J. C., Broxterman, R. M., Smith, J. R., Allen, J. D., & Barstow, T. J. (**2018**). Effect of dietary nitrate supplementation on conduit artery blood flow, muscle oxygenation, and metabolic rate during handgrip exercise. *Journal of applied physiology*, *125*(2), 254-262.

[7] Erem, C., Hacihasanoglu, A., Kocak, M., Deger, O., & Topbas, M. (**2009**). Prevalence of prehypertension and hypertension and associated risk factors among Turkish adults: Trabzon

Hypertension Study. *Journal of public health*, *31*(1), 47-58.

[8] Feig, J. E., Hewing, B., Smith, J. D., Hazen, S. L., & Fisher, E. A. (**2014**). High-density lipoprotein and atherosclerosis regression: evidence from preclinical and clinical studies. *Circulation research*, *114*(1), 205-213.

[9] Gai, Z., Hu, S., Gong, G., & Zhao, J. (**2023**). Recent advances in understanding dietary polyphenols protecting against hypertension. *Trends in Food Science & Technology*.

[10] Grim, C. E., & Grim, C. M. (**2016**). Auscultatory BP: still the gold standard. *Journal of the American Society of Hypertension*, *10*(3), 191-193.

[11] Hermilasari, H., Subair, H., Irianto, I., Armyn, A. A. U., & Hakim, S. (**2020**). Study in vitro and in silico on effectiveness noni fruit extract (Morinda citrifolia) to reducing hypertension. *Canrea Journal: Food Technology, Nutritions, and Culinary Journal*, 57-64.

[12] Jepson, R. E., Hartley, V., Mendl, M., Caney, S. M., & Gould, D. J. (**2005**). A comparison of CAT Doppler and oscillometric Memoprint machines for non-invasive blood pressure measurement in conscious cats. *Journal of Feline Medicine and Surgery*, *7*(3), 147-152.

[13] Kim, S., Goel, R., Kumar, A., Qi, Y., Lobaton, G., Hosaka, K., ... & Raizada, M. K. (**2018**). Imbalance of gut microbiome and intestinal epithelial barrier dysfunction in patients with high blood pressure. *Clinical science*, *132*(6), 701-718.

[14] Lee, J. H., Son, C. W., Kim, M. Y., Kim, M. H., Kim, H. R., Kwak, E. S., ... & Kim, M. R. (**2009**). Red beet (Beta vulgaris L.) leaf supplementation improves antioxidant status in C57BL/6J mice fed high fat high cholesterol diet. *Nutrition research and practice*, *3*(2), 114-121.

[15] Melby, M. K., Murashima, M., & Watanabe, S. (**2004**). Phytochemical intake and relationship to past health history in Japanese women. *Biofactors*, *22*(1-4), 265-269.

[16] Millett, C., Agrawal, S., Sullivan, R., Vaz, M., Kurpad, A., Bharathi, A. V., ... & Indian Migration Study group. (**2013**). Associations between active travel to work and overweight, hypertension, and diabetes in India: a cross-sectional study. *PLoS medicine*, *10*(6), 100-1459.

[17] Mirmiran, P., Houshialsadat, Z., Gaeini, Z., Bahadoran, Z., & Azizi, F. (**2020**). Functional properties of beetroot (Beta vulgaris) in management of cardio-metabolic diseases. *Nutrition & metabolism*, *17*, 1-15.

[18] Monroy-Ruiz, J., Sevilla, M. Á., Carrón, R., & Montero, M. J. (**2011**). Astaxanthin-enriched-diet reduces blood pressure and improves cardiovascular parameters in spontaneously hypertensive rats. *Pharmacological Research*, *63*(1), 44-50.

[19] Oladeji, O. S., & Oyebamiji, A. K. (**2020**). Stellaria media (L.) Vill.-A plant with immense therapeutic potentials: phytochemistry and pharmacology. *Heliyon*, *6*(6).

[20] Salat, D. H., Williams, V. J., Leritz, E. C., Schnyer, D. M., Rudolph, J. L., Lipsitz, L. A., ... & Milberg, W. P. (**2012**). Inter-individual variation in blood pressure is associated with regional white matter integrity in generally healthy older adults. *Neuroimage*, *59*(1), 181-192.

[21] Stojiljković, D., Arsić, I., & Tadić, V. (**2016**). Extracts of wild apple fruit (Malus sylvestris (L.) Mill., Rosaceae) as a source of antioxidant substances for use in production of nutraceuticals and

cosmeceuticals. *Industrial Crops and Products*, *80*, 165-176.

[22] Tokaç, M., Taner, G., Aydın, S., Özkardeş, A. B., Dündar, H. Z., Taşlıpınar, M. Y., ... & Basaran, N. (**2013**). Protective effects of curcumin against oxidative stress parameters and DNA damage in the livers and kidneys of rats with biliary obstruction. *Food and Chemical Toxicology*, *61*, 28-35.

[23] Turak, O., Afsar, B., Ozcan, F., Canpolat, U., Grbovic, E., Mendi, M. A., ... & Kanbay, M. (**2014**). Relationship between elevated morning blood pressure surge, uric acid, and cardiovascular outcomes in hypertensive patients. *The Journal of Clinical Hypertension*, *16*(7), 530-535.

[24] Williams, D. R., & Neighbors, H. (**2001**). Racism, discrimination and hypertension: evidence and needed research. *Ethnicity & disease*, *11*(4), 800-816.

[25] Yakubu, O. E., Olawale, O., Arowora, K. A., & Imo, C. (**2017**). Biochemical changes in haemtological and liver function parameters in intoxicated male Albino rats treated with Hymenocardia acida leaves ethanolic extract. ARCHIVOS DE MEDICINA, 2(2), 10