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The antihypertensive effect of the ethanol seed extract of *Persea americana* Mill in albino Wistar rats

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Abstract

Aim: Hypertension is a medical condition in which the arterial blood pressure is persistently elevated. This condition can lead to multiple complications, organ damage and death. The aim of this study was to assess the antihypertensive effects of ethanol seed extracts of *Persea americana mill*

Method: Wister rats used were divided into 14 groups of which 13 groups were induced with cadmium chloride for 2weeks and made hypertensive, a group not induced used as negative control. Thereafter *Persea americana mill* extract and fractions were administered to 8 groups of experimental rats at 200mg/kg bodyweight and 400mg/kg body weight via oral gavage. Four groups of the experimental animals were given standard Antihypertensive while a group was used as positive control

Results: Findings show that after 2weeks of the treatment with the ethanol seed extracts of *Persea americana mill* and it's fractions,the blood pressure of all animals were reduced significantly compared to standard antihypertensive drugs with the exception of animals treated with 400mg/kg methanol fractions whose blood pressure reduction was not significant compared to ones treated with standard antihypertensive drugs

Conclusion: Therefore, Avocado seeds (*Persea americana* mill) can be used as local or traditional antihypertensive.

Keywords: Hypertension; Antihypertensive; *Persea Americana*; Blood pressure; Wistar rats

1. Introduction

Hypertension is the most common cardiovascular diseases and affect almost two-third of adults aged 60 years or older [1]. Sustained arterial hypertension damages blood vessels in kidney, heart and brain which leads to an increased incidence of renal failure, coronary diseases, heart failure and stroke [2]. It is a major cause of premature death worldwide with upward of 1 in 4 men and 1 in 5 women over a billion people having the condition [3]. The burden of

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hypertension is felt disproportionately in low and middle income countries, where two –thirds of cases are found, largely due to increased risk factors in those populations in recent decades [4]. Long term high blood pressure, is a major risk factor for coronary artery disease, stroke, heart failure, peripheral artery disease, vision loss, chronic kidney disease and dementia.

Medicinal plants have over the years constituted indispensable tools for research and development of new drugs [5, 6], and coupled with the fact that there are still many plants whose medicinal values have not been exploited, it is reasonable to describe the plant kingdom as a sleeping giant for potential drug development [7].

The avocado tree has shiny evergreen, elliptical leaves about 10-20cm long. It is a branched, medium sized tree cultivated for its delicious and highly nutritious fruits. The pear shaped fruit is about 7-20cm (2.8-7.9 inches) long, weighs between 100 and 1000g. The skin may be yellow-green, deep green or very dark green, reddish-purple or very dark purple as to appear almost black and is sometimes speckled with tiny yellow dots. Beneath the skin is a thin layer of soft, bright- green flesh or generally pale to rich yellow buttery and bland flavor [8].It has a large central seed,5-6cm (2-2.5 inches) ,hard, ivory in colour but enclosed in two brown thin, papery seed coats often adhering to the fleshy cavity, while the seed slips out readily. The avocado seed makes up about 13-18 percent of the fruit, and a byproduct generally not utilized [8].Several biological activities of the avocado seed have been reported such as antioxidant, larvicidal, fungicidal, hypolipidemic ,amoebicidal and giardicidal activities [9].

In spite of all this, the avocado seed is largely considered a waste product and therefore underutilized [10] Persea americana Mill (Lauraceae) is one of the emerging plants of interest in the management of hypertension. It is commonly known as the avocado pear tree and is widely distributed in tropical countries.

2. Material and methods

2.1. Collection of the fruits

The fruits of *Persea americana* mill were obtained from Osumenyi community in Nnewi south local government Area, Anambra state, Nigeria, in the fruiting season of June, 2019. The fruit was identified and authenticated by Mr. Egboka Tochukwu, a staff of the department of botany, Nnamdi Azikiwe University where a herbarium specimen exists.

2.2. Extraction of the seeds

The seeds *P. americana* were removed from the pulp and chopped into small pieces and air dried for five days at room temperature. The seeds were then ground into powder using a mill. Five hundred gram (500 g) of the powder was weighed and macerated in 2.5 litres of ethanol 72 hours with frequent agitation to soften and to ensure sufficient extraction of the active secondary metabolite [11]. The ethanol extract was later filtered using Whatman No 1 filter paper and the filtrate, concentrated to dryness under reduced pressure in a rotary evaporator at 40^0c. The extract yield was kept cold in a refrigerator. The extract was thereafter, dissolved in an appropriate volume of distilled water to obtain a solution from which calculated doses were given to the animals orally during the experiment.

2.3. Animals used for the experiment

Eighty four (84) Albino Wister rats weighing 140-220 g, of either sex were obtained from university of Nigeria Enugu campus in the animal research laboratory and caged sex-wise separately in fourteen cages of six animal each to prevent mating and pregnancy. They were fed with rat chow (Vital feeds, Nigerian Ltd) and clean water *ad libitum*. The rats were allowed to acclimatize for 2 weeks during which the rat local restrainer in form of an open cone was included in their cages to prepare the rat for blood pressure measurement. The cone was used to restrain the movement of the rat (immobilize) before blood pressure measurement. The rats were maintained according to the national institute of health (NIH) guidelines for care and use of laboratory animals [12].

2.4. Phytochemical screening

Simple chemical tests were used to perform phytochemical screening of the extract in order to determine whether secondary ingredients were present or absent, as described in the literature [13].

2.5. Acute toxicity test

Acute toxicity of P. americana seed extract was determined by Lorke [14]. Rats were divided into two phases. In the first phase of the study, 9 rats were divided into 3 groups of 3 rats and they were given ethanol extract of P. americanal through oral route at the doses of 10 mg/kg, 100 mg/kg and 1000 mg/kg respectively. Mortality and clinical signs of

toxicity were monitored in the animals for the first 4 h and periodically until 24 h. The animals were observed for signs of toxicity which includes; paw licking, weakness, feeling sleepy, respiratory distress, hyperactivity, coma and death for the first 4 hours, and subsequently 24 hours. Since no signs of toxicity were observed, the second phase was initiated. In this phase, 4 rats were also grouped into 4 with one rat per cage. Higher doses were selected and orally administered; 1600 mg/kg, 2900 mg/kg, 5000 mg/kg and 10 mL/kg of distilled water. The animals were observed for signs of toxicity and mortality for 48 hours and thereafter 72 hours for late toxicity.

2.6. Induction of Hypertension and Blood Pressure Measurements in Rats

Hypertension was induced in the rats via intraperitoneal injection of 1mg/kg /day dose of 1%cadmuim chloride dissolved in distilled water, for a period of 2 weeks. CdCl-induced hypertension is thought to be due to endothelial dysfunction and increased oxidative stress which have been demonstrated to occur even in low-dose exposure models [15]. The induction process was according to Balarama *et al*., [16] Badyal et al.,[17], who reported an increase in blood pressure of rat using cadmium chloride for 14 days and they were mated with the test material without stopping the induction. In this study, hypertension was induced with 1% Cdcl for 14 days. A rat weighing 140g was given 0.14mls of 1% Cdcl once daily for 14 days. Thereafter, blood pressure reading of the rats were monitored and recorded using the non- invasive method of measurement of blood pressure. (That was to ensure they became hypertensive). The blood pressure was measured in Wister rats using tail cuff plethysmography (non-invasive), method. Normal rat blood pressure is 80-120mmHg of systolic while 60-80mmHg of diastolic blood pressure. The blood pressure apparatus used was CODA-6 Kent Scientific, Torrington, CT, USA, via the non-invasive method of measurement of blood pressure through the tail. (Kent Scientific Corporation)

2.7. Procedure of the blood pressure measurement

At the start of the measurements cycle, blood was pushed from the tail by the volume pressure recording (VPR) cuff and then the occlusion cuff inflates to prevent blood flow back into the tail. When the occlusion cuff deflates, blood begins to flow back into the tail, increasing the tail volume. The occlusion cuff pressure at which the tail volume increases is the systolic blood pressure. The tail volume will continue to increase as the occlusion cuff deflates until blood flow into and out of the tail equalizes, the occlusion cuff pressure at this point is the diastolic blood pressure.

2.8. Treatment of Animals

- Group 1 being negative control rats were fed with rat chow and clean water freely and there was no induction and no treatment.
- Group 2 which is hypertensive control-rats were fed with rat chow and clean water freely and were induced with 1mg/kg/body weight/ day of 1 % Cdcl via intraperitoneal route once daily for 14 days without treatment.
- Group 3 rats were induced with 1 mg /kg /body weight/day with 1% Cdcl for 14 days and subsequently treated with 1mg/kg /day Amlodipine for 2 weeks.
- Group 4 rats were induced with 1mg /kg/bw/day of 1% Cdcl for 14 days and treated with 0.75mg/kg/day Hydralazine.
- Group 5 rats were induced with 1mg/kg/b.w/day using 1% Cdcl for 14days and treated with 0.07mg/kg/day Lisinopril.
- Group 6 rats were induced using 1mg/kg/bw of 1% Cdcl for 14 days and treated with 2mg/kg/day hydrochlorothiazide.
- Group 7 rats were induced with 1% Cdcl for 14 days and treated with 200 mg/kg/b.w of the ethanol seed extract of *P. americana* mill.
- Group 8 rats were induced with 1% Cdcl and treated with 400 mg/kg/b.w of the ethanol seed extract of *P. americana* mill.

2.9. Statistical Analysis

Results were expressed as means ± SEM and analyzed with statistical products and services solution (SPSS version 20) by using one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test. A difference in the mean $P < 0.05$ was considered statistically significant.

3. Results

3.1. Phytochemical analysis

The ethanol seed extract prepared with ethanol underwent phytochemical screening, which identified the presence of alkaloids, cardiac glycosides, saponins, tannins, flavonoids, terpenoids, steroids, while resin was not detected.

3.2. Acute toxicity tests

Seventy-two hours following the ethanol leaf extract administration, no observable alterations, mortality, or toxicological indicators were noted. During the course of the investigation, every animal remained robust and energetic. As a result, it was discovered that the median lethal dose (LD50) was more than 5000 mg/kg.

3.3. Effect of Extract and Drug on mean systolic blood pressure (SBP)

Effects of the extract and standard drugs on rats' systolic blood pressure (SBP). This result indicates that the extract significantly ($p < 0.05$) lowered the rats' systolic blood pressure. There was statistically significant reductive effects by Amlodipine and Hydralazine (Table 1).

Table 1 Effect of Extract and Drug on mean systolic blood pressure (SBP)

Treatment	Dose (mg/kg)	Induced	Treated
Control	10 mL/kg	142.20±18.45	159.40±0.45
Hypertensive control	10 mL/kg	151.27±9.04	130.70±7.75
Amlodipine	1mg/kg	164.03±7.50	139.53±12.74*
Hydralazine	0.75 mg/kg	164.40±6.40	131.13±7.14*
Lisinopril	0.7mg/kg	155.47±16.09	104.20±14.40
Hydrochlorothiazide	2 mg/kg	152.03±10.96	140.30±4.71
P. Americana	200 mg/kg	148.30±6.73	130.90±2.19*
P. Americana	400 mg/kg	161.30±7.85	130.47±11.96*

Results are expressed as mean±SEM; Significant at P≤ 0.05 compared with control

3.4. Effect of the Extract and Drug on mean diastolic blood pressure (DBP)

Table 2 showed the effect of the extract and standard drugs on rats' diastolic blood pressure (DBP). This result indicates that the ethanol extract significantly ($p < 0.05$) reduced the DBP from the induced levels. Only the hydrochlorothiazide significantly reduced the DBP.

Table 2 Effect of Extract and Drug on mean diastolic blood pressure (DBP)

Treatment	Dose (mg/kg)	Induced	Treated
Control	10 mL/kg	99.33±12.66	120.20±0.49
Hypertensive control	10 mL/kg	108.33±8.41	98.90±9.17
Amlodipine	1mg/kg	127.97±12.10	115.30±11.22
Hydralazine	0.75 mg/kg	133.20±7.83	103.13±8.46
Lisinopril	0.7mg/kg	130.97±17.41	77.87±13.39
Hydrochlorothiazide	2 mg/kg	127.97±11.00	107.90±8.74*
P. Americana	200 mg/kg	122.60±8.10	106.40±3. 87*
P. Americana	400 mg/kg	120.90±7.27	107.70±11.63*

Results are expressed as mean±SEM; Significant at P≤ 0.05 compared with control

3.5. Effect of the Extract and Drug on mean pressure (MN)

Table 3 showed the effect of the extract and standard drugs on rats mean arterial pressure (MN). This result indicates that the extract significantly reduced ($p < 0.05$) the mean arterial pressure

Table 4 Effect of Extract and Drug on mean Heart Rate (HR)

The effect of standard drugs and extract on the rat's heart rate. There were observed statistical reduction in heart rate by the extract and hydralazine (Table 4)

Table 3 Effect of Extract and Drug on mean diastolic blood pressure (DBP)

Treatment	Dose (mg/kg)	Induced	Treated
Control	10 mL/kg	113.13±14.62	132.80±0.12
Hypertensive control	10 mL/kg	121.20±8.67	109.10±8.51
Amlodipine	1mg/kg	139.60±10.38	123.00±11.62
Hydralazine	0.75 mg/kg	143.40±6.81	112.13±7.24
Lisinopril	0.7mg/kg	138.83±16.94	86.30±13.67
Hydrochlorothiazide	2 mg/kg	135.70±10.94	118.43±7.37
P. Americana	200 mg/kg	131.00±7.59	110.60±5. 79
P. Americana	400 mg/kg	134.10±6.37	114.97±11.66

Results are expressed as mean±SEM; Significant at P≤ 0.05 compared with control

Table 4 Effect of Extract and Drug on mean diastolic blood pressure (DBP)

Treatment	Dose (mg/kg)	Induced	Treated
Control	10 mL/kg	456.40±13.31	449.80±19.11
Hypertensive control	10 mL/kg	327.13±35.44	387.97±52.07
Amlodipine	1mg/kg	437.87±13.94	123.00±11.62
Hydralazine	0.75 mg/kg	423.80±11.63	471.67±12.59
Lisinopril	0.7mg/kg	393.80±11.04	394.00±32.16
Hydrochlorothiazide	2 mg/kg	411.87±16.08	438.07±16.55
P. Americana	200 mg/kg	390.10±18.34	397.10±8. 36
P. Americana	400 mg/kg	416.70±20.03	468.17±14.95

Results are expressed as mean±SEM; Significant at P≤ 0.05 compared with control

4. Discussion

In this study the phytochemistry analysis of the *Persea americana* seed extract showed that it contained alkaloid, flavanoids, saponin, protein, steroid, terpenoid, cardiac glycosides and tannins.

The antihypertensive effects of these extracts may be due to the presence of the above phytochemical components which are known for their vasorelaxant and cardioprotective activities.

Ortega et al., [18] maintained that polyphenols possess vasorelaxant effects. Due to the different content of biologically active compounds, the antioxidant activities of the avocado seed extracts also differed importantly compared to already known data. The extremely high content of proanthocyanin, phenol, reserveratrol, saponin, steroid, terpenoid was

found in methanol fraction compared to other fractions. The polyphenol content of the extract may be responsible for the reduction in blood pressure.

Hypertension was induced, which explained why the mean systolic and diastolic blood pressures of induced rats were significantly higher than that of the normal control. Treatment of hypertensive rats with the ethanol seed extract of *P. americana* over a period of fourteen days resulted in the reduced blood pressure/mean arterial pressure in the rats from 161.33+_ 4.90mmhg to 119.20+_ 4.78mmhg with the highest percentage reduction occurring in rats given 200mg/kg methanol extract.

The findings of this study were also similar to the studies of Imafidon and Amaechina [19] who reported the antihypertensive effect of aqueous seed extract of *Persea americana* work at doses of 200,500 and 700mg/kg body weight administered orally, mixed with animal feeds to rats. Anaka *et al.,* [20] also reported an effective minimal dose of the aqueous seed extract of *Persea americana* at 240mg/kg up to a maximum tolerable dose of 260mg/kg intravenously. The findings of Amaechina *et al.,* [21] insisted on blood pressure lowering effect at doses of 0.625 to 2.5mg/kg for rats intravenously.For intravenously administered drugs the bioavailabilty should be 100 percent justifying the reason why intravenously dosing of drugs is usually lower than that of oral route where pharmacokinetic parameters such as first pass effect,tissue binding tend to reduce the bioavailabilty.It was also noted from the result that,with the exception of the 400mg/kg methanol extract whose observed reductive systolic blood pressure (SBP) effect was not statistically significant(z= - 1.23,P=0.153),all the other extracts significantly lowered the rats SBP. Also in comparison with standard antihypertensive, there was statistically significant reductive effects by Amlodipine and hydrallazine.

For the diastolic blood pressure(DBP), this result indicates that with the exception of the crude extracts and 400mg/kg methanol, all extracts significantly reduced the DBP from the induced levels.

The result also showed that hexane, ethyl acetate and 200 mg/kg methanol 200 mg/kg of the ethanol extract significantly reduced the mean pressure. There was also an observed statistical reduction in heart rate by 400mg of the crude extract. 200mg methanol,200mg ethyl acetate and 400mg ethyl acetate extracts. This revealed that the blood pressure lowering effect of aqueous seed extract and its fractions with the highest percentage reduction occurring with the use of 200mg methanol extract from 160.80+-6.86mmhg to 110.90+-8.21mmhg systolic and from 136.43±8.61mmhg to 73.90+-0.24mmhg diastolic.

Consistently.it has shown that 400mg methanol extract was not statistically significant in reducing the SBP, DBP and mean blood pressure.

The findings of this study were also similar to the studies of Amechina.*et al.,* [21] and Dzeufiet.,*et al,.* [22] which showed that extract of persea Americana has blood pressure lowering effect in the rodent specie evaluated. The literature contains a number of scientifically confirmed uses of the parts of Persea americana for example its aqueous leaf extract possessing antihypertensive properties. Alhassan *et al.,* [23], purported the hypotensive effect of the avocado pear seed extract may be due to elemental contents such as calcium, potassium, magnesium, zinc etc which play key roles in blood homeostasis. Various studies have shown the presence of bioactive compounds such as flavonoids, alkaloids, tannin and phenolic compounds in the different medicinal plants. Studies showed that the vasodilatory effect of plant and natural products were mainly correlated with the NO/cGMP pathway or blockage of the calcium channel [24]. Some natural products such as anthocyanin- rich cherries [25] and Prunes [26] showed endothelial-dependant vasorelaxation via the NO / c GMP pathway [27].

Tannins extracted from other plants have attracted considerable attention due to their potential health-promoting benefits through reported vasorelaxant and hypotensive effects; the tannin components of *P. americana* are presumed to also have a vasodilatory effect. It was reported that anothcyanin of red wine caused vasorelaxation. Other studies also reported that polyphenols such as epigallocatechin, resveratrol from grape skin extract increased the phosphorylation of eNoS [28]. The antihypertensive effects of this extract may be due to the presence of the above phytochemical components which are known for their vasorelaxant and cardioprotective activities [22].The mechanisms of the antihypertensive effects of *P. americana* have been considered to be of increases in endothelial NO, the inhibition of angiotensin-Converting enzyme, decreases in platelet adhesion and delay of low-density lipoprotein oxidation [29]. Therefore, *P. americana* appears to have an advantage over other foods or plants because it exhibits vascular relaxant effect via the above various mechanisms. Also, the serum electrolyte urea creatinine assay done revealed that 200mg/kg methanol extract had all the electrolytes reduced (Na, K^+, CL^-, HCO_3) more than other extracts but had ca^{2+} increased more than in other extracts, making it appear to work similar to thiazide diuretics.

For the urea it was lowest in 200mg/hexane and lisinopril (ACE1) which is not surprising since ACE1 and ARB" s lower blood pressure and help to slow kidney damage (It reduces proteinuria which was said to be due to its ability to cause a fall in intraglomerular capillary pressure.

5. Conclusion

The results from this study indicate that the ethanol seed extract of *P. americana* possesses blood pressure lowering properties in normotensive Albino Wistar rats. The effect of the extract may be due to reduction in heart rate. The results from this study justify the use of the extract for the management of hypertension in Nigerian herbal medicine.

Compliance with ethical standards

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Disclosure of conflict of interest

Compliance with ethical standards

Statement of ethical approval

All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. Also, all procedures performed in studies involving animals were in accordance with the ethical standards of the institution or practice at which the studies were conducted.

References

[1] Go AS, Bauman MA, Coleman KSM, Fonarow GC, Lawrence W, Williams KA, Sanchez E. An Effective Approach to High Blood Pressure Control. Journal of the American College of Cardiology. 2014; 63(12), 1230–123.

[2] Boulestreau R, van den Born BH, Lip GYH, Gupta A. Malignant Hypertension: Current Perspectives and Challenges. Journal of the American Heart Association. 2022; 11: e023397.

[3] World Health Organization. A global brief on hypertension: silent killer, global public health crisis: World Health Day 2023. Www.who.int. https://www.who.int/publications/i/item/aglobal-brief-on-hypertension-silent-killer-global-public-health-crisis-world-health-day.

[4] Akinlua JT, Meakin R, Umar AM, Freemantle N. Current Prevalence Pattern of Hypertension in Nigeria: ASystematic Review. PLoS ONE. 2015; 10(10).

[5] Akuodor GC, Anyalewechi NA, Udoh FV, Ikoro NC, Akpan JL, Gwotmut MD, Pharmacological evaluation of Verbenahastate leaf extract in the relief of fever. Advanced Pharmacology and Toxicology. 2011; 12 (3):1-8.

[6] Essien AD, Edidara Thomas, Essiet GA, Akuodor GC. Anti-inflammatory, antipyretic and anti-nociceptive activities of the ethanol stem bark extract of Salacia lehmbachii. British Journal of Pharmacology and Toxicology. 2017;8 (2): 9-16.

[7] Ajegi1 IF, Ajegi1 GO, Ajaegbu OC, Nwokike MO, Ramalan MA, Eje VI, Akuodor GC. Evaluation of the antiulcer and antimicrobial activities of methanol leaf extract of Helianthus annuus. Int J Basic Clin Pharmacol. 2023; 12 (2):161-166.

[8] Eduardo, P., Moisés, M., José, M.F. and Socorro, V. (2013). Acute Toxicity and Genotoxic Activity of Avocado Seed Extract (Persea americana Mill.Hass) The Scientific World Journal. 2013; 245828

[9] Bangar SP, Dunno K, Dhull SB, Siroha AK, Changan S, Maqsood S, Rusu AV. Avocado seed discoveries: Chemical composition, biological properties, and industrial food applications. Food Chemistry. 2022; 16:100507.

[10] Dabas D, Shegog R, Ziegler G, Lambert J. Avocado (Perseaamericana) Seed as a Source of BioactivePhytochemicals. Current Pharmaceutical Design. 2013; 19 (34), 6133–6140. https://doi.org/10.2174/1381612811319340007

[11] Azwanida NN. A Review on the Extraction Methods Use in Medicinal Plants, Principle, Strength and Limitation. Medicinal and Aromatic Plants, 4, 3. Scientific Research Publishing. 2015;

[12] National Institutes of Health (NIH). Guide for the Care and Use of Laboratory Animals. 8th ed. Bethesda, MD: NIH; 2011. p. 82-3.

[13] Evans WC. Trease and Evans Pharmacognosy. 15th Edn., Reed Elsevier India Pvt. Ltd., New Delhi, India 2005; 174: 224-535.

[14] Lorke D. A new approach to practical acute toxicity testing. Archives of Toxicology. 1983; 54(4), 275–287.

[15] Camila C. P. Almenara ,Gilson B. Broseghini-Filho, Marcus V. A. Vescovi, Jhuli K. Angeli,Thaís de O. Faria, Ivanita Stefanon, Dalton V. Vassallo,Alessandra S. Padilha. Chronic Cadmium Treatment Promotes Oxidative Stress and Endothelial Damage in Isolated Rat Aorta. PLOS ONE. 2013; 8(7): e68418

[16] Bai G, Zhang J, Zhao C, Wang Y, Qi Y, Zhang B. Adherence to a healthy lifestyle and a DASH-style diet and risk of hypertension in Chinese individuals. Hypertension Research. 2016; 40(2):196–202.

[17] Badyal DK, Lata H, Dadhich AP. Animal model of hypertension and effect of drugs.Indian Journal of Pharmacology 2003; 35: 349-362.

[18] Brai BI, Odetola AA, Agomo PU. Hypoglycemic and hypocholesterolemic potential of Persea americana leaf extracts. Journal of Med. Food. 10: 356 –360. Med. Food. 2007; 10: 356 –360.

[19] Imafidon KE, Amaechina, FC. Effects of Aqueous Seed Extract of Perseaamericana Mill. (Avocado) on Blood Pressure and Lipid Profile in Hypertensive Rats. Advances in Biological Research. 2010; 4:116-121.

[20] Anaka O, Ozolua R, Okpo S. Effect of the aqueous seed extract of Perseaamericana mill (Lauraceae) on the blood pressure of sprague- dawley rats. African Journal of Pharmacy and Pharmacology. 2009; 3(10), 485–490.

[21] Amaechina FC, Uchendu AP, Oboh C, Agokei NI, Eboka CJ, Preliminary Comparative effect of the aqueous extract of Persea Americana seeds on the blood pressure of normotensive rabbits and rats. Journal of Science and Practice of Pharmacy. 2014; 4(1): 177 – 181.

[22] Dzeufiet PDD, Mogueo A, Bilanda DC, Aboubakar BFO, Tédong L, Dimo T, Kamtchouing P. Antihypertensive potential of the aqueous extract which combine leaf of Perseaamericana Mill. (Lauraceae), stems and leaf of Cymbopogoncitratus (D.C) Stap. (Poaceae), fruits of Citrus medical L. (Rutaceae) as well as honey in ethanol and sucrose experimental model. BMC Complementary and Alternative Medicine. 2014; 14(1). https://doi.org/10.1186/1472-6882-14-507

[23] Alhassan AJ, Sule MS, Atiku MK, Wudil AM, Abubakar H, Mohammed, SA. Effects of aqueous avocado pear (Perseaamericana) seed extract on alloxan induced diabetes rats. Greener Journal of Medical Sciences. 2012; 2(1), 005-011.

[24] Tang F, Yan H,Wang LX, Xu J, Peng C, Hui A, Tan Y. Review of Natural Resources WithVasodilation: Traditional Medicinal Plants, Natural Products, and Their Mechanism and Clinical Efficacy. Frontiers in Pharmacology. 2021; 12: 627458.

[25] Markovics A, Biró A, Kun-Nemes A, Fazekas ME, Rácz AA, Paholcsek M, Lukács J, Stündl L, Remenyik J. Effect of Anthocyanin-Rich Extract of Sour Cherry for Hyperglycemia-Induced Inflammatory Response and Impaired Endothelium-Dependent Vasodilation. Nutrients. 2020; 12: 3373.

[26] Sadlera MJ, Gibson S, Whelanc K , Had M, Lovegrove J, Higgs J. Dried fruit and public health – what does the evidence tell us? I nternational Journal of Food Science and Nutrition. 2019; 70(6): 675–687

[27] Chalopin M, Tesse A, Martínez MC, Rognan D, Arnal JF, Andriantsitohaina R. Estrogen Receptor Alpha as a Key Target of Red Wine Polyphenols Action on the Endothelium. PLoS ONE. 2010; 5(1): e8554.

[28] Miller, A. J., and Arnold, A. C. (2018). The renin–angiotensin system in cardiovascular autonomic control: recent developments and clinical implications. Clinical Autonomic Research. 2018; 29(2): 231–243

[29] Martin Berger M, Naseem KM. Oxidised Low-Density Lipoprotein-Induced Platelet Hyperactivity—Receptors and Signalling Mechanisms. International Journal of Molecular Sciences. 2022; 23(16): 9199.