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Beneficial Effects of *Passiflora edulis* on Blood Pressure and Reduction of Oxidative Stress

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Abstract

Objective: To evaluated the effect of consuming *P. edulis* juice on blood pressure, activity of the Angiotensin-Converting Enzyme (ACE), and antioxidant capacity in hypertensive patients. **Methods/Statistical Analysis**: The study included two groups of patients, one received *Passiflora. edulis* (*P. edulis*) juice (2 g/day, in 2 ml) during four weeks and the other did not. To determine if differences exist among the results found for each group, parametric or non-parametric test were used. **Findings:** This intervention reduced systolic and diastolic pressure (142.4 to 125.2 mmHg and 79 to 76.1 mmHg, respectively) compared to the group not intervened (139.5 to 134.9 and 89.7 to 84.0 mmHg, respectively), ($p < 0.05$); in addition, higher anti oxidative capacity was found of the serum for the group intervened. Contrary to expectations, ACE increased in these patients. **Application/Improvements:** *P. edulis* juice diminished blood pressure and oxidative stress of patients who consumed it; however, the mechanisms through which both effects occur must be studied.

Keywords: Hemolysis, Hypertension, *Passiflora edulis*, Passion Fruit, Lipids, Oxidative Stress, TBARS

1. Introduction

Hypertension is a global epidemic, a chronic health problem, and cause of a high risk factor for myocardial infarction, arteriosclerosis, cerebrovascular accident and terminal kidney disease. Nearly 25% of the world's adult population suffers hypertension and it is likely that this number will increase to 30% by authors[1,2].

Blood Pressure (BP) is controlled by several mechanisms, like neuronal, endocrine, renal mechanisms or Nitric Oxide (NO), among others. For these reasons, several antihypertensive agents have been designed to control hypertension, like diuretics, β-blockers, calcium channel blockers, and blockers and inhibitors of the Renin Angiotensin Aldosterone System (RAAS)[3,4].

These drugs have demonstrated safety and effectiveness in reducing blood pressure, but many of them cause side effects, like reduced kidney function, angioedema, or cough[5]. Hence, management of hypertension through herbal medicine emerges as a complementary alternative to these medications[6]. However, it is also worth mentioning that it is necessary to monitor the collateral damage of medicinal plant extracts, given that these are not always innocuous.

Furthermore, oxidative stress has been related with a broad spectrum of diseases, like Parkinson, Alzheimer, multiple sclerosis, atherosclerosis, and cancer, among others[7], considered a cell damage process derived from the aerobic metabolism. This damage is produced by an imbalance in favor of the generation of Reactive Oxygen Species (ROS) in relation to the presence of antioxidant molecules, which leads to altering the structure of macromolecules, like lipids, proteins, and nucleic acid, fundamental for optimal cell functioning and, thus, the organism.

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Diverse substances of natural origin exist, which are used as antioxidants and antihypertensive agents[8, 9], among these the juice and extracts from leaves and fruits from *Passiflora edulis,* also called passion fruit[10].

One of the properties of greatest importance attributed to *P. edulis* is that of reducing BP, which has been confirmed by *in vitro* studies with lab mice and humans[10–12]. The study by author[11], supplied *P. edulis* juice as co-adjuvant in the hypertension treatment and it was demonstrated that groups receiving Enalapril plus *P. edulis* had a reduction of 6.73 mmHg in systolic pressure and 5.75 mmHg for the diastolic pressure, compared to the group receiving Enalapril plus placebo[11].

Several authors have found that *P. edulis* pulp and leaf extracts contain tannins, flavonoids, carotenoids, and cardiotonic glycosides[10, 13]; this latter work also found that the ethanolic leaf extract and juice of *P. edulis* had high antioxidant activity (EC50 = 0.096 mg/ml and EC50 = 0.022 mg/ml, respectively) and all extracts inhibited over 98% the hemolysis induced by H_2O_2. Likewise, other works by the same group have reported that the fruit juice and the ethanolic extract from the *P. edulis* leaves showed inhibition percentages above the ACE of 26.8 ± 3.3% and 36.8 ± 6.4%, respectively[13]. Additionally, high cytotoxic and anti-proliferative capacity has been shown of the aqueous extract from the leaves against SW620 carcinogenic cells with (CI_{50} = 340 µg/ml and CI_{50} 415 µg/ml, respectively); while in SW480 cells, it was (CI_{50} 444 µg/ml)[10]. This prompted this work sought to study the effect of the *P. edulis* juice on blood pressure, antioxidant capacity, and inhibition of the serum ACE activity of hypertensive adults recently diagnosed (*de-novo* hypertensive) without traditional drug treatment.

2. Materials and Methods

2.1 Experimental Design

2.1.1 Population

University workers, professors, and/or students called on to participate through billboards integrated to the cardiovascular day carried out by the university's medical students. Screening was conducted on 173 men, with recent diagnosis of hypertension (maximum two months after the diagnosis) and with a maximum of two years of evolution of the hypertension, with traditional treatment.

2.1.2 Type of Study

This study lasted five weeks. For all the individuals, the first week was about sensitization and medical revision. The four weeks remaining were used for the intervention (consumption of *P. edulis* juice. The individuals were distributed into two groups; group one: *de-novo* hypertensive individuals, who were provided with juice, extract (2 g/day in 2 ml/for 30 days). Group two: individuals with hypertension and in traditional treatment who continued with this according to that approved by their physicians (they were not given *P. edulis* juice). The criterion to which group to enter was defined by the time of the hypertension diagnosis and if they were or not in treatment.

2.1.3 Inclusion Criteria

Elderly individuals with recent diagnosis of hypertension, who could be managed with diet and exercise without placing their health at risk during the four weeks the study lasts, according to the clinical practice guide on primary arterial hypertension by the Colombian Ministry of Health and Social Protection (2015), who voluntarily decided to participate in the study and whose clinical condition permitted their consuming the *P. edulis* juice extract during four weeks under medical supervision. The study also included hypertensive individuals with treatment recommended by their treating physician, which they maintained throughout the intervention.

2.1.4 Exclusion Criteria

Kidney or cardiac disease diagnosed, use of tobacco and alcohol more than two times a week, use of food supplements different from multivitamins and uncontrolled chronic hypertension.

2.1.5 Intervention

During the intervention period, the volunteers received weekly 20 ml of the *P. edulis* juice extract in dosages of 2 ml (2 g/day). They were requested to consume the extract in the mornings. Each subject avoided consuming during the intervention *P. edulis* juice and foods rich in carotenoids (they were instructed which these were).

At the start, middle, and end of the intervention period, both groups were subjected to medical care and blood samples were taken for the biochemical determinations. This protocol was approved in accordance with the ethical standards of the Universidad del Quindío and with

the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The participants signed an informed consent, followed by a physical exam and filling out a complete clinical history.

Information was gathered from the primary source with an instrument designed for said purpose with all the study variables. Patients were scheduled for an initial evaluation, clinical follow-up after two weeks and at the end of the intervention.

2.2 Blood Pressure

This was measured by the participants by using a digital tensiometer (Beurer Medical BM20), in accordance with standard procedures.

2.3 *P. edulis* Fruit Extract

This was extracted through mechanical methods, strained to eliminate seeds and filtered (1-mm mesh) to guarantee its homogeneity; thereafter, it was packaged and stored at -80 °C, in asepsis conditions for human consumption.

2.4 Phytochemical Analysis

Qualitative analysis was performed in a prior work to identify secondary metabolites [10].

2.5 ACE Activity

Determination of the ACE activity in serum was conducted as already described[13, 14], briefly: the method is based on the enzymatic hydrolysis of Furilacryloyl-L-phenylalanyl-glycyl-glycine (FAPGG), by the serum ACE, to Furilacryloyl-L-phenyl (FAP) and glycyl-glycine (Gly-Gly): 225 µl of distilled water and 250 µl of buffer (0.8 mM FAPGG, 400 mM NaCl, 50 mM of HEPES pH 8.25) were added to each of two tubes with 25 µl of serum.

As target, we used another tube containing exactly the same, plus EDTA 3.3 mM as ACE inhibitor. In addition, Quinapril was used as positive control. The tubes were incubated at 37 °C for 20 min and left to rest in ice to stop the enzymatic reaction. Finally, absorbance of each was measured at 345 nm in a spectrophotometer (Milton Roy Genesis 5).

2.6 Total Antiox idant Capacity in Serum

2.6.1 TBARS Method

This was determined by using the protocol described by Koracevic et al.[15], which measures the serum's capacity to inhibit production of reactive substrates of thiobarbituric acid, using the following formula:

Antioxidant activity = AOA = (UAC)(K-A)/(K-UA) (1)

Where: UAC = Uric acid concentration, A = Absorbance of the sample (A1 –A0),
K = Absorbance of the control (K1-K0) and UA = Absorbance of the uric acid standard (UA1-UA2)

2.7 Protection of Erythrocytes Against Hemolysis

This was conducted through the method described by Nabavi et al.[16]; blood samples were obtained by venipuncture in tube without anticoagulant. This was centrifuged at 2500 rpm for 10 minutes and the serum and leucocytes were removed. The red cells were washed three times with isotonic saline phosphate buffer (PBS: Na_2HPO_4 22.2 mM, KH_2PO_4 5.6 mM, NaCl 123.3 mM, and glucose 10 mM in distilled water at pH 7.4).

Thereafter, 200 µl aliquots were taken of erythrocytes at 5% (v/v) in 3800 µl PBS at pH 7.4; then, 200 µl of H_2O_2 1 mM were added, through inversion mixing.

The tubes were incubated at 37 °C under constant movement (in shaker) during 3 h. After this time, 6 ml of PBS were added and centrifuged at 2500 rpm during 10 min; 1 ml of the supernatant (hemoglobin released) obtained through centrifuge was measured via spectrophotometry at 540 nm.

The percentage of protection against hemolysis was calculated thus:

% = {(Ac-A)/Ac} x 100 (2)

where:

Ac = Absorbance of the negative control, A = Absorbance of the sample for negative control, blood was processed from a chronic hypertensive individual treated with synthetic antihypertensive medication (Losartan).

2.8 Statistical Analysis

The results were expressed as the mean ± the standard deviation (SD), the statistical significance was established at $p < 0.5$ and 95%CI was included. To determine if differences exist among the results found for each group, a Student's t test was carried out for the parametric results; the Kruskal Wallis test was conducted for the non-parametric results, using the SPSS v.18 statistical package.

3. Results and Discussion

This study researched the effect of *P. edulis* juice on blood pressure, angiotensin converting enzyme activity, oxidative stress and blood lipids in non-chronic hypertensive patients.

3.1 Patients, Characteristic

The study included 173 men between 18 and 71 years of age, (students, employees, and professors from the University), all with hypertension at the moment of screening. Figure 1 shows the flow chart of patient selection.

Results showed an age difference between both study groups, with the youngest being the group intervened with juice; however, Body Mass Index (BMI) and blood pressure values were similar at the beginning (Table 1).

It is known that hypertension prevalence increases with age, to the point that over half of the people between 60 and 69 years of age, and approximately three quarters of those over 70 are affected[17]. It is interesting that the older group had pharmacological treatment and it was expected for the values to be lower. This fact has been related in other research with very low adherence to pharmacological treatment or to measures of lifestyle changes or the ineffectiveness of the medications[18]; among others, these are some of the reasons for the poor control of BP in many individuals, as shown by these results.

3.2 Blood Pressure During the Month of Intervention

Figure 2 reflects the blood pressure variation for both study groups during the month the study lasted. The illustration shows how systolic and diastolic pressure diminishes in individuals intervened with extract compared to patients not intervened in whom both values remain higher. Differences were significant between weeks 1 and 2 ($p = 0.0005$) and weeks 1 and 3 ($p = 0.0004$).

The results indicate that during the second week of intervention with the juice, although a slight increase of diastolic blood pressure was noted, it was similar to the values for the group not intervened; but these values dropped by the fourth week, while the values for the group not intervened were maintained (although the difference was not significant).

Regarding diminished blood pressure in individuals who consumed *P. edulis* juice; our results confirm those by other groups in relation to blood pressure or its control and regulation mechanisms being modified by the *P. edulis* juice extract, peel and leaves[13, 19]. In this sense, it has been demonstrated that *P. edulis* peel, leaf, or fruit extracts [13] and from other medicinal plants, like

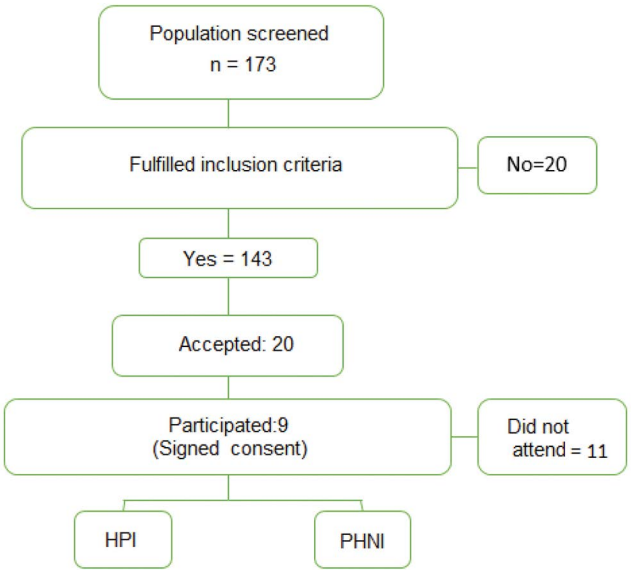

Figure 1. Flow chart for patient selection. HPI: hypertensive patient intervened with *P. edulis* juice. HPI: hypertensive patient intervened; HPNI: hypertensive patient not intervened.

Table 1. Initial anthropometric characteristics of the participating patients

Characteristics	All Patients	HPI	HPNI	P
Age (years)	45.2 ± 17.1	37.5 ± 18.9	52.7 ± 10.4	0.02*
BMI (kg/m^2)	27.4 ± 3.32	27.5 ± 2.09	26.1 ± 3.8	0.182
SBP (mmHg)	141 ± 11.4	142 ± 7.9	139 ± 16.5	0.302
DBP (mmHg)	83.3 ± 10.1	78.2 ± 4.2	89 ± 12.2	0.059

HPI: hypertensive patient intervened with P. *edulis* juice; HPNI: hypertensive patient not intervened; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure

Apium graveolens, Avena sativa, and *Berberis vulgaris*, reduce blood pressure in *in-vitro* models, animals, and humans[9,11,20,21], or are capable of modifying enzyme activity or factors intervening in blood pressure control[9].

The mechanisms through which this occurs still remain under study, given that hypertension is a multifactor disease, however, one of the systems proven to intervene in blood pressure regulation mechanisms is RAAS in which ACE converts Angiotensin I into Angiotensin II, a potent vasoconstrictor. *In-vitro* studies with *P. edulis* extracts have shown this plant's capacity to inhibit ACE[13].

3.3 Angiotensin Converting Enzyme Serum Levels

Figure 3 shows the results of the ACE activity during the four study weeks. Contrary to expectation, ACE levels increased in hypertensive individuals intervened and diminishes in chronic individuals.

The results in the present work are contradictory in relation to these findings, because the juice did not manage to reduce ACE levels in patients who consumed it; rather, this enzyme increased by the fourth week of intervention with the juice.

In this respect, a study by Fyhrquist et al.[22] with hypertensive rats, which showed that the ACE activity in serum increased between 2.5 and 3 times after week 12 of treatment with Quinapril, an ACE inhibitor. This was parallel with an increased concentration of the enzyme in lungs obtained from these animals. Said study argues that the Quinapril inhibitor causes an increase in the pulmonary synthesis of the enzyme as compensation to its inhibition. The lungs are the principal source of serum ACE. Although our study obtained a decrease of systolic blood pressure in patients who consumed *P. edulis* juice, it did not achieve a decrease of ACE activity, as had been demonstrated *in vitro*[13]. We are unaware of the mechanisms through which the juice can inhibit the enzyme *in vitro,* but not *in vivo.* Quite possibly, these results suggest that *P. edulis* also acts through other mechanisms to diminish systolic blood pressure besides RAAS; among these mechanisms, we could mention production of nitric oxide and reduction of oxidative stress – the latter, as demonstrated by results with TBAR.

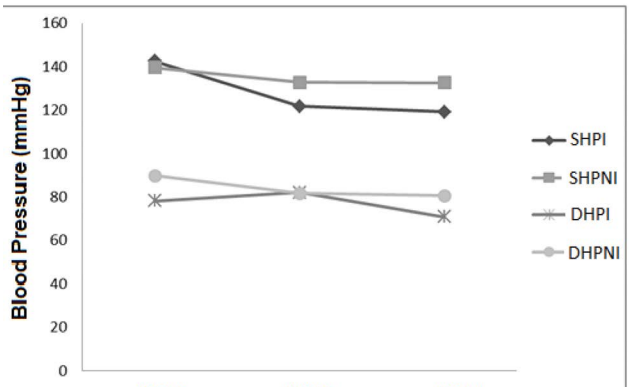

Figure 2. Systolic and diastolic blood pressure during the four weeks in both study groups. SHPI: Systolic pressure hypertensive patient intervened; SHPNI: systolic pressure hypertensive patient not intervened; DHPI: diastolic pressure hypertensive patient intervened; DHPNI: diastolic pressure hypertensive patient not intervened.

3.4 Antioxidant Capacity

3.4.1 TBAR Capacity

Defined as the protection capacity against oxidative damage measured through the thiobarbituric acid method.

Results shows that consuming *P. edulis* juice for 30 days increases the antioxidant capacity of patients' serum, with respect to those not consuming the juice (Figure 4).

3.5 Protection Capacity Against Hemolysis

Consumption of *P. edulis* juice showed no significant difference in relation to protection against hemolysis between both groups of hypertensive patients. Figure 5 shows the results.

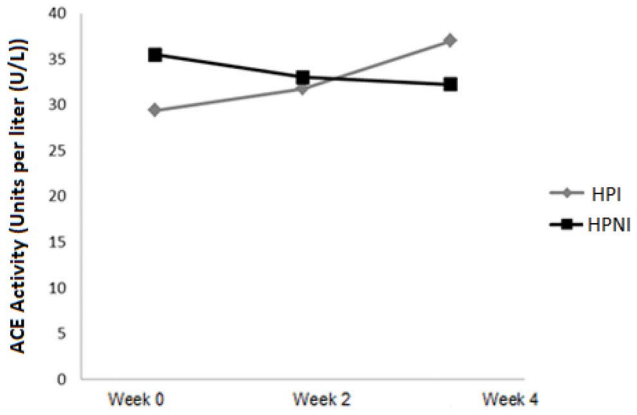

Figure 3. Variation of the ACE activity during the study period. HPI: hypertensive patients intervened; HPNI: hypertensive patients not intervened.

Although *P. edulis* juice consumption does not protect against hemolysis, it is clear that increases the antioxidant capacity of patients' serum. In this regard, several studies by the group showed the antioxidant capacity of *P. edulis*[13]; also Rojas et al.[23] revealed that this plant's methanolic extract had antioxidant activity with a CL50 of 124 µg/mL.

Furthermore, ethno-pharmacological information reveals that *P. edulis* has been used in traditional medicine in diverse parts of the world[24] and that its leaves are rich in polyphenolic compounds[13], and flavonoids were also found in the *P. edulis* juice (Table 2).

Polyphenols, especially flavonoids, have shown antihypertensive effect in different experimental models[25]; thus, for example, in *in-vivo* models, using hypertensive rats, the flavonoid quercetin induced a significant reduction in systolic, diastolic, and mean blood pressure[26]. In another study, polyphenols exhibited a significant blood pressure decrease, explained – in part – by decreased expression of light chains of phosphorylated myosin and by increased urinary excretion of sodium, potassium, and chloride, in addition to increasing the rate of glomerular filtration[11].

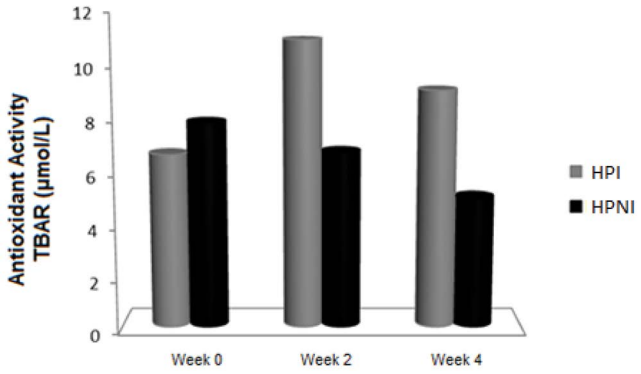

Figure 4. Antioxidant activity of the serum in µmol/L of uric acid in the groups studied. HPI: hypertensive patients intervened; HPNI: hypertensive patients not intervened.

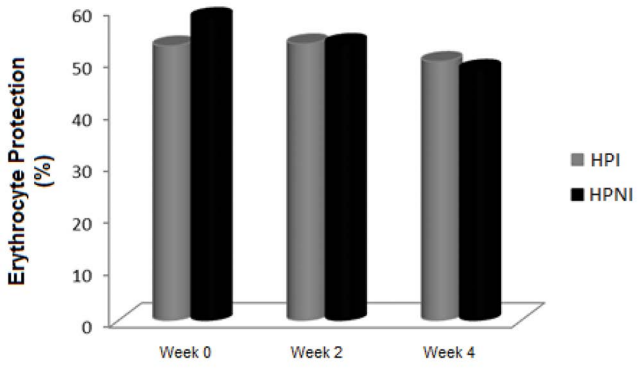

Figure 5. Protection percentage of erythrocytes against hemolysis induced by H_2O_2. HPI: hypertensive patients intervened; HPNI: hypertensive patients not intervened.

Table 2. Phytochemical analysis of the *Passiflora edulis* juice

Phytochemical Constituent	Amount (qualitative)
Tannins	++
Flavonoids	+
Quinones	+
Sterols	+
Saponins	-
Cardiotonic Glycosides	+++
Carotenoids	+++
Carbohydrates	+++

(+) Low presence, (++) medium presence, (+++) high presence, (-) absent

The aforementioned could merely be some of the mechanisms that explain why in our study systolic pressure diminished, although it increased ACE activity.

This study presented some limitations, for example, the limited number of participants. Additionally, the groups were not homogeneous, especially in age, given that older individuals will have more oxidative stress; however, the study demonstrates diminished blood pressure with consumption of *P. edulis*.

4. Conclusions

The data show that consuming *P. edulis* juice diminished blood pressure and oxidative stress of patients who consumed it; however, the mechanisms through which both effects occur must be studied in cell models, animals, or in humans. In humans, this should include a higher number of patients to determine the relevance of the findings in this work.

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6. References

1. World Health Organization A global brief on Hypertension - World Health Day; 2013. p. 1–40.
2. World Heart Foundation Cardiovascular disease risk factors - Stress | World Heart Federation [Internet]. [cited 2017 May 30]. Available from: http://www.world-heart-federation.org/cardiovascular-health/cardiovascular-disease-risk-factors/stress/.
3. Vardanyan R, and Hruby V. Synthesis of Best-Seller Drugs. 1st Edition; 2016. p. 329–57. https://doi.org/10.1016/B978-0-12-411492-0.00022-5
4. Charlton M, Thompson JP. Drugs acting on the heart: Antihypertensive drugs. Anaesthesia and Intensive Care Medicine. 2015; 16(5):227–31. https://doi.org/10.1016/j.mpaic.2015.02.007
5. Kiriyama A, Honbo A, Nishimura A, Shibata N, Iga K. Pharmacokinetic-pharmacodynamic analyses of antihypertensive drugs, nifedipine and propranolol, in spontaneously hypertensive rats to investigate characteristics of effect and side effects. Regulatory Toxicology and Pharmacology. 2016; 76:21–9. https://doi.org/10.1016/j.yrtph.2016.01.003. PMid:26773344
6. Leung AA, Daskalopoulou SS, Dasgupta K, McBrien K, Butalia S, Zarnke KB, Nerenberg K. Hypertension Canada's 2017 guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults. Canadian Journal of Cardiology. 2017; 33(5):557–76. https://doi.org/10.1016/j.cjca.2017.03.005. PMid:28449828
7. Poprac P, Jomova K, Simunkova M, Kollar V, Rhodes CJ, Valko M. Targeting free radicals in oxidative stress-related human diseases. Trends in Pharmacological Sciences. 2017; 38(7):592–607. https://doi.org/10.1016/j.tips.2017.04.005. PMid:28551354
8. Popović Z, Matić R, Bojović S, Stefanović M, Vidaković V. Ethnobotany and herbal medicine in modern complementary and alternative medicine: An overview of publications in the field of I&C medicine 2001-2013. Journal Ethnopharmacology. 2016; 181:182–92. https://doi.org/10.1016/j.jep.2016.01.034. PMid:26807912
9. Rawat P, Singh PK, Kumar V. Anti-hypertensive medicinal plants and their mode of action. Journal of Herbal Medicine. 2016; 6(3):107–18. https://doi.org/10.1016/j.hermed.2016.06.001
10. Aguillón J, Maldonado ME, Loango Chamorro N, Arango SAV. Antioxidant and antiproliferative activity of ethanolic and aqueous extracts from leaves and fruits juice of Passiflora edulis. Perspectivas en Nutrición Humana. 2013; 15:13–25.
11. Rojas J, Ronceros S, Palomino R, Salas M, Aza-ero R, Cruz HA. Efecto coadyuvante del extracto liofilizado de Passiflora edulis (maracuyá) en la reducción de la presión arterial en pacientes tratados con enalapril. Anales de la Facultad de Medicina. 2009; 70(2):103–8.https://doi.org/10.15381/anales.v70i2.957
12. Lewis BJ, Herrlinger KA, Craig TA, Mehring-Franklin CE, DeFreitas Z, Hinojosa-Laborde C. Antihypertensive effect of passion fruit peel extract and its major bioactive components following acute supplementation in spontaneously hypertensive rats. Journal of Nutritional Biochemistry. 2013; 24(7):1359–66. https://doi.org/10.1016/j.jnutbio.2012.11.003. PMid:23333089
13. Restrepo RA, Loango N, Moncada MV, Landazuri P. Angiotensin-Converting Enzyme Inhibitory Activity of Passiflora edulis f. flavicarpa and Petroselinum crispum (Mill) Fuss. British Journal of Pharmaceutical Research. 2013; 3(4):776–85. https://doi.org/10.9734/BJPR/2013/3517
14. Ronca Testoni S. Direct spectrophotometric assay for angiotensin-converting enzyme in serum. Clinical Chemistry. 1983; 29(6):1093–96. PMid:6303627
15. Koracevic D, Koracevic G, Djordjevic V, Andrejevic S, Cosic V. Method for the measurement of antioxidant activity in human fluids. Journal of Clinical Pathology. 2001; 54(5):356–61. https://doi.org/10.1136/jcp.54.5.356. PMid:11328833. PMCid:PMC1731414
16. Nabavi SF, Ebrahimzadeh MA, Nabavi SM, Eslami B. Antioxidant activity of flower, stem and leaf extracts of Ferula gummosa Boiss. Grasas y aceites. 2010; 61(3):244–50.https://doi.org/10.3989/gya.110809
17. Cheng HM, Park S, Huang Q, Hoshide S, Wang JG, Kario K. Vascular aging and hypertension: Implications for the clinical application of central blood pressure. International Journal of Cardiology. 2017; 230:209–13. https://doi.org/10.1016/j.ijcard.2016.12.170. PMid:28043670
18. Butler MJ, Tanner RM, Muntner P, Shimbo D, Bress AP, Shallcross AJ. Adherence to antihypertensive medications and associations with blood pressure among African Americans with hypertension in the Jackson Heart Study (JHS). Journal of the American Society of Hypertension. 2017; 11(9):581–8. https://doi.org/10.1016/j.jash.2017.06.011. PMid:28895842. PMCid:PMC5603252
19. Cordova FM, Zibadi S, Watson RR. Antioxidant and anti-inflammatory actions of passion fruit peel extract in modifying osteoarthritis, hypertension, and asthma. Bioactive Food as Dietary Interventions for Arthritis and Related Inflammatory Diseases; 2013. p. 633–9.
20. Restrepo RA, Nieto OA, Aristizabal J, Landazuri P. Angiotensin-converting enzyme inhibition by Phthirusa Pyrifolia (Kunth) Eicher. World Journal of Pharmaceutical Sciences. 2014; 3(6):352–63.
21. Landazuri P, Loango Chamorro N, Restrepo B. Medicinal plants used in the management hypertension. Journal of Analytical and Pharmaceutical Research. 2017; 5(2):5–7.

22. Fyhrquist F, Forslund T, Tikkanen I, Gronhagen-Riska C. Induction of angiotensin I-converting enzyme in rat's lung with captopril (SQ 14225). European Journal of Pharmacology. 1980; 67(4):473–5. https://doi.org/10.1016/0014-2999(80)90189-2
23. Rojas J, Tomás G. Tamizaje Fitoquímico Y Actividad antioxidante in vitro De Passiflora Edulis Sims (Maracuyá). Revista Peruana de Química e Ingenieria Química. 2010; 13:23–9.
24. Miroddi M, Calapai G, Navarra M, Minciullo PL, Gangemi S. Passiflora incarnata L.: Ethnopharmacology, clinical application, safety and evaluation of clinical trials. Journal of Ethnopharmacology. 2013; 150(3):791–804. https://doi.org/10.1016/j.jep.2013.09.047. PMid:24140586
25. Saravanan S, Arunachalam K, Parimelazhagan T. Antioxidant, analgesic, anti-inflammatory and antipyretic effects of polyphenols from Passiflora subpeltata leaves - A promising species of Passiflora. Industrial Crops and Products. 2014; 54:272–80. https://doi.org/10.1016/j.indcrop.2014.01.038
26. Choi S, Ryu KH, Park SH, Jun JY, Shin BC, Chung JH. Direct vascular actions of quercetin in aorta from renal hypertensive rats. Kidney Research and Clinical Practice. 2015; 351):15–21. https://doi.org/10.1016/j.krcp.2015.12.003. PMid:27069853. PMCid:PMC4811985