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Vasodilator effect of ethanolic extracts of *Passiflora vitifolia* and *Passiflora edulis* f. *edulis* seeds

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ABSTRACT

Hypertension (HTA) is one of the primary risk factors in cardiovascular diseases and is considered one of the main causes of morbidity and mortality worldwide. Therapeutic alternatives focused on natural products and phytocompounds obtain more interest in the treatment of this type of disease, and species of *Passiflora* gender have presented scientific interest due to their chemical composition and the different bioactivities that their compounds have reported. This study aimed to evaluate the antihypertensive potential of extracts obtained from seeds of *Passiflora vitifolia* and *Passiflora edulis* f. *edulis*; for this, extraction was carried out by maceration with 97% ethanol of the seed flour of the two species; the extracts were characterized by qualitative and quantitative tests and UHPLC. Its cytotoxicity, *in vivo* antihypertensive potential, vasodilator effect, and possible mechanisms of action *in vitro* models were evaluated. The extracts did not show apparent toxicity, but showed a preventive effect of HTA, inhibited angiotensin-II (AT-II) contraction, and presented relaxation of contracted aortic rings with phenylephrine and KCl, and this was partially reversed in the presence of L-NAME. The results highlight the potential of these *Passifloras* as a source of extracts with antihypertensive capacity, having as possible mechanisms of action the synthesis of NO and inhibition or antagonism of AT-II.

INTRODUCTION

Cardiovascular diseases (CVDs) have gained a relevant role worldwide by becoming the leading cause of morbidity and mortality, generating around 17.7 million deaths in 2015, which represents 31% of all deaths recorded in the world for that year (World Health Organization, 2015). Among CVDs, arterial hypertension (HTA) stands out, which is a chronic disease that generates alterations in the organism (damage to arteries, brain, heart, eyes, kidneys, sexual dysfunction, and others) and causes 49% of related deaths with CVD. At present, HTA is controlled by the prolonged use of drugs with only one pharmacological target (angiotensin-converting enzyme inhibitors, β-blockers, diuretics, calcium blockers, ARA II, and others), which generate secondary short and long alterations, causing deterioration in the quality of life of the patients (Brown and Bussell, 2011; Piepoli *et al*., 2016; Rojas, 2009; Tedla and Bautista, 2016), what makes it essential to search for new alternatives such as the use of phytotherapy, diets, supplements, and functional foods that prevent condition and control symptoms without serious side effects (Mantovani *et al*., 2017; Shouk *et al*., 2014).In this regard, plants and fruits such as those belonging to the Passifloraceae family, with numerous species, of which various secondary metabolites have been reported among them, alkaloids (harman, harmine, harmalol, and harmaline), flavonoids (vitexin, isovitexin, orientin, vicenin, and isoorientin), saponins (passiflorin and quadranguloside), cyanogenic compounds (passicoriacin and epipassicoriacin), and terpenes (Alvarez *et al*., 2019; Alves *et al*., 2020; Ballesteros-Vivas *et al*., 2019; Ingale and Kasture, 2014; Viganó *et al*., 2020; Wosch *et al*., 2015; 2017) have presented different biological activities such as sedative, antihypertensive, antiparkinsonian, antispasmodic, antioxidant, and antiproliferative (Aguillón *et al*., 2013; Alves *et al*., 2020; Ballesteros-Vivas *et al*., 2019; Contreras *et al*., 2011; Dhawan *et al*., 2004; Ingale and Kasture, 2014; Ocampo *et al*., 2010; Pinzón

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et al., 2007; Rudnicki *et al*., 2007; Viganó *et al*., 2020). Colombia is recognized worldwide as the center of diversity of *Passiflora* and the country with the highest number of records, 172 species (58 endemic); among them, *Passiflora vitifolia* Kunth (gulupa de monte) and *Passiflora edulis* f. *edulis* Sims (gulupa) are studied. They are part of wild and cultivated species, of which their possible bioactivities and chemical composition are not fully known, especially their agroindustrial waste (80% of the fresh fruit).

Therefore, this work focused on characterizing chemically and biologically extracts obtained from *P. vitifolia* and *P. edulis* f. *edulis*, evaluating its cytotoxicity, relaxing capacity, vasodilator potential *in vivo* and *in vitro*, and possible mechanisms of antihypertensive action.

MATERIALS AND METHODS

Plant material

Passiflora vitifolia was collected in the Alejandro Von Humboldt Botanical Garden of the University of Tolima (N 4° 15′–N 4° 40′ and W 75° 00′–75° 30′) municipality of Ibagué (Tolima, Colombia); *P. edulis* f. *edulis* was collected in the Buenos Aires farm (4° 26′27″ N and 75° 25′40″ W) municipality of Cajamarca (Tolima, Colombia); ripe fruits were collected for the extraction of seeds, as well as complete specimens (stem, leaves, tendrils, flower, and fruit) for their taxonomic determination in the Colombian National Herbarium, where they were determined as *P. edulis* Sims (COL. 592023) and *P. vitifolia* Kunth (COL. 592024).

Preparation of extract

The seeds were dried in an air circulation oven at 45°C ± 2°C and ground, obtaining a flour that was degreased. Ethanolic extracts were obtained by maceration of the flour and degreased with 97% ethanol; the mixture was vacuum filtered to obtain the crude extract, which was dried under reduced pressure and stored at −20°C (Jiménez *et al*., 2013); preliminary phytochemical characterization was carried out using colorimetric tests (Dominguez, 1973; Murillo and Méndez, 2012).

Quantitative analysis

Determination of total phenolic compounds and tannins

Total phenolic and tannin contents of extracts were determined according to the method described by Viganó *et al*. (2020) with some modifications. 50 µl of each solution was mixed with 800 µl of water and 50 µl of 15% Na_2CO_3 and was stirred and allowed to stand for 8 minutes. Then, 100 µl of Folin–Ciocalteu reagent was added. After 2 hours, absorbance was measured by a microplate lector (Multiskan™ GO Thermo scientific™) at 725 nm. The results were expressed as gallic acid equivalents (g.GAE/100 g sample). In tannins, previously, the sample was incubated with polyvinylpyrrolidone (PVPP 100 mg/ml of sample) at 4°C/4 hours. The mixture was centrifuged at 3,000 rpm for 10 minutes and the supernatant was determined by the method described above. The results were expressed as tannic acid equivalents (g.TAE/100 g sample) (Da Silva *et al*., 2019).

DETERMINATION OF FLAVONOIDS

Flavonoids in the extracts were determined according to the method described by Karapetsas *et al*. (2019) with some modifications. 1 ml of each solution was mixed with 150 µl of 5% sodium nitrite and incubated for 5 minutes at room temperature. 150 µl of 10% $AlCl_3$ ethanolic solution and 2 ml of 4% sodium hydroxide were added; the solution was gauged to 5 ml with distilled water and incubated for 15 minutes at room temperature. Absorbance was measured by a microplate spectrophotometer (Multiskan™ GO; Thermo Scientific™) at 510 nm. Total flavonoid content was calculated as equivalents of g Quercetin (g.QE/100 g sample).

Extract characterization (HPLC-UV)

This was carried out using high-performance liquid chromatographic analysis on a Waters Alliance 2,695 separation module system, coupled to a dual-channel (320 and 280 nm) absorbance k detector, and a Waters Atlantis dC18 column (5 µm; 2.1 × 150 mm) using a gradient system with the conditions used by Delpino-Rius *et al*. (2015). The following metabolites in the extracts were quantified: chlorogenic acid, caffeic acid, coumaric acid, epicatechin, catechin, gallic acid, isoquercetin, quercetin, rutin, synaptic acid, vitexin, isovitexin, orientin, and isoorientin; by means of the elaboration of calibration curves with standards for their correct quantification.

Toxicity of extract

Acute toxicity study

The acute toxicity test of extracts was carried out according to the Organization of Economic Cooperation and Development (OECD) guidelines 423 (Schlede *et al*., 2005). Albino mice ($n = 6$) were treated orally with the extracts prepared in the vehicle [polyethylene glycol:glycerol:Milli-Q water (10:10:80)] control group. The fixed-dose (2,000 mg/kg) method OECD guidelines 423 specified by CPCSEA were implemented for toxicity studies. After the administration of extracts, animals were observed for toxic effect, if any, for the first 4 hours and once daily for 15 days (Saleem *et al*., 2017).

Cytotoxic activity of the extracts [methyl thiazole tetrazolium (MTT) assay]

The MTT assay (Mosmann, 1983) was carried out using human polymorphonuclear leukocytes (PMNs) obtained from human peripheral blood, evaluating the extracts at different concentrations (500, 1,000, 2,000, and 4,000 µg/ml) (Cárdenas *et al*., 2012).

Antihypertensive activity in vivo

Experimental animals

The Bioethics Committee of the Faculty of Sciences, National University of Colombia, Bogotá headquarters, endorsed the implementation of the project under Act 16 of September 13, 2016. Wistar rats (males and females) 9–11 weeks old, with weights between 250 and 320 g, were supplied by the Bioterium of the Pharmacy Department (Science Faculty), Universidad Nacional de Colombia, Bogotá headquarters, keeping them under controlled conditions (temperature 22°C, humidity 70%, and light/dark 12/12 hours).

In vivo antihypertensive potential of *P. vitifolia* and *P. edulis* extracts

This was carried out using the methodology proposed by Bareño *et al*. (2017). The experimental animals were randomly divided into groups ($n = 6$), taking into account the treatments that were going to be used (Table 1). Every 48 hours for 7 weeks, the extracts and enalapril (reference drug) were administered orally and L-NAME (nitric oxide synthase inhibitor) was administered intraperitoneally. The measurement of systolic blood pressure (SBP) was made by the tail-cuff method (Tail-Cuff) in an ultrasound transducer (PANLAB-LE 5002) (Bareño *et al*., 2017; Vanvliet *et al*., 2000).

Model of vasodilation in isolated aortic rings

Preparation of the rings

By thoracotomy, the thoracic aortic artery was removed after the animal was sacrificed in a CO_2 camera. It was cleaned of connective tissue and it was divided into 4–5 mm rings that were kept in Krebs solution (NaCl 118.7; KCl 4.7; CaCl2 2.5; NaHC03 25.0; MgS04.7H20 1.2; glucose 11.0; and ascorbic acid 0.1, nM) at 37°C with carbogen mixture of 95% O_2 and 5% CO_2. The measurement of the tension was made by fixing the rings to the base in the organ chambers containing 10 ml of Krebs solution maintained at 37°C, pH 7.4 ± 0.2, and carbogen and to the isometric transducer coupled to a signal amplification system and computerized recording (Data Trax 2, WPI) (Torres *et al*., 2012).

Relaxation induced by extracts of *P. vitifolia* and *P. edulis* f. *edulis*

Phenylephrine (10^{-6} M) or KCl (60 mM) was added to the organ chamber, compounds with which a stable signal of contraction was reached, to each bath; subsequently, the ethanolic extracts dissolved in Dimethyl sulfoxide (DMSO) (0.1%) were administered in cumulative concentrations (1, 10, 30, 100, and 300 µg/ml). As a control, 0.1% DMSO was used (Bareño *et al*., 2017; Cupitra *et al*., 2020).

Effect of acetylcholine (ACh) and sodium nitroprusside (NPS) in aortic rings of hypertensive rats treated with the extracts

Aortic rings from hypertensive rats treated with the extracts and the reference drug were coupled in the organ chambers and contracted with phenylephrine (10^{-6} M) until a maximum contraction was obtained; subsequently, cumulative concentrations of ACh were added ($1.0*10^{-4}$, $1.0*10^{-3}$, $5.0*10^{-3}$, $1.0*10^{-2}$, $5.0*10^{-2}$, $8.0*10^{-2}$, $1.0*10^{-1}$, $3.0*10^{-1}$, $5.0*10^{-1}$, 1.0, 5.0, 10, 50, and 100 µM) and NPS ($5.0*10^{-5}$, $1.0*10^{-4}$, $1.0*10^{-3}$, $5.0*10^{-3}$, $1.0*10^{-2}$, $5.0*10^{-2}$, $1.0*10^{-1}$, $5.0*10^{-1}$, 1.0, 5, and 10 µM), observing the relaxing potential of these in the different rings.

Table 1. Distribution of groups and treatments administered.

Group	Treatment 1	Treatment 2
1	Extract *P. edulis* (150 mg/kg)	L-NAME (30 mg/kg)
2	Extract *P. vitifolia* (150 mg/kg)	L-NAME (30 mg/kg)
3	Vehicle	Vehicle
4	Vehicle	L-NAME (30 mg/kg)
5	Enalapril (10 mg/kg)	L-NAME (30 mg/kg)

Vehicle: polyethylene glycol: glycerol: Milli-Q water (10:10:80).

Action mechanisms of the extracts of *P. vitifolia* and *P. edulis* f. *edulis*

They were evaluated using the organ chambers model in aortic rings incubated for 15 minutes with the following agents: atropine (muscarinic antagonist), indomethacin (cyclooxygenase inhibitor), propranolol (beta antagonist), L-NAME (nitric oxide inhibitor synthase), and methylene blue (guanylate cyclase inhibitor) (Brunton *et al*., 2006; Lorenzo *et al*., 2008; Torres *et al*., 2012). Subsequently, the extracts were supplied under the aforementioned conditions and their effect in the presence and absence of the mentioned agents was compared, by adding angiotensin-II (AT-II) to the bath in cumulative concentrations ($1*10^{-5}$, $5*10^{-5}$, $1*10^{-4}$, $5*10^{-4}$, $1*10^{-3}$, $5*10^{-3}$, $1*10^{-2}$, $5*10^{-2}$, $1*10^{-1}$, and $5*10^{-1}$ until 1 µM); a contraction curve was established in the rings; the extract effect was verified by incubation for 15 minutes with them at 30 and 300 µg/ml, repeating the contraction curve with AT-II and comparing the contraction results obtained in the presence and absence of those extracts.

Data analysis

Data were expressed as the mean ± SEM. Statistical analysis was carried out using analysis of variance (two-way parametric), followed by Tukey's multiple difference test ($p \leq 0.05$), using the GraphPad Prism 6 program.

RESULTS AND DISCUSSION

Toxicity of extract

Acute toxicity

In the acute toxicity test, there were no deaths or toxic signs after administration. The weight gain did not vary in the treated groups compared to the control group. The necropsy did not reveal any macroscopic alteration of the organs and tissues examined.

The extracts of *P. vitifolia* and *P. edulis* f. *edulis* are framed in the category of not classified according to the Toxicity Classes of the European Community (Commission of the European Communities, 1992), since no mortality or toxic signs are attributable to its administration. According to this result, we can affirm that the evaluated extracts did not produce significant toxicity at the limit dose in the acute toxicity test.

In vitro *cytotoxic activity of the extracts (MTT Assay)*

Cell viability was established with respect to the vehicle to which a 100% survival was assigned. In Figure 1, it is evident that extracts at the evaluated concentrations did not show cell viability less than 80%; therefore, these can be considered safe, complying with the parameters proposed by Rodríguez *et al.* (2004); on the other hand, during the time of administration of the extracts to the animals, they did not present symptoms of apparent toxicity. It is possible that the type and concentration of metabolites present are related to high levels of cell viability, since, for example, under the conditions of this study, it was not possible to detect saponins, which are reported in other plant

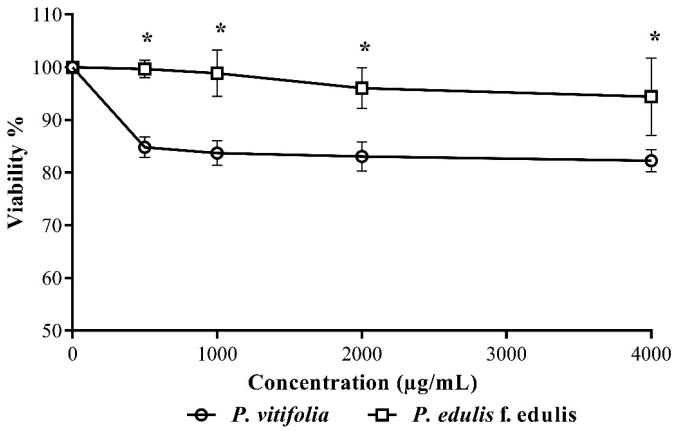

Figure 1. Cytotoxic effect of the extracts against PMNs. Each point represents the mean % viability ± SD of each treatment. * Indicate significant differences ($p \leq 0.05$).

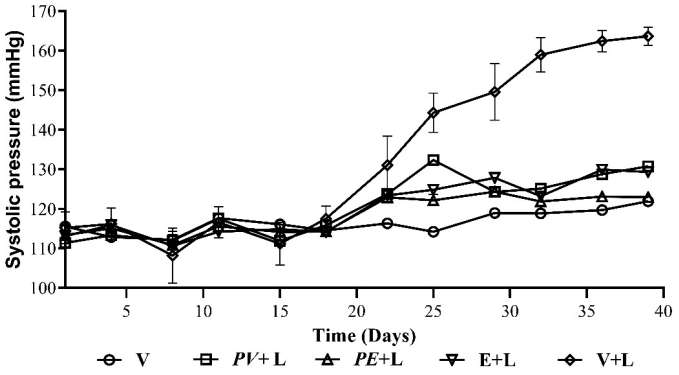

Figure 2. Antihypertensive potential of the extracts, PAS of hypertensive rats induced by L-NAME. Each point represents the mean of the SP ± SEM.

organs (Table 1) and have been reported as toxic in cell models and if the presence of polyphenols is evident (Table 2) which are reported as antioxidants with a cellular protective effect (Orhan *et al*., 2003; Podolak *et al*., 2010).

Antihypertensive activity in vivo

The administered extracts showed an effect against the increase of the SBP of animals after the administration of the L-NAME (Fig. 2); it was evident that the basal values of SBP did not increase with the administration of L-NAME; this contrasts with the SBP of hypertensive animals which increased significantly ($p < 0.0001$) compared to animals treated with the extracts, enalapril, and vehicles. This favorable effect of the extracts could be attributed to different metabolites groups identified in the extracts (Table 2), since phenolic compounds (found in high concentration) and *Passiflora* alkaloids have been reported to generate a protective and hypotensive effect in both *in vivo* and *in vitro* models (Carrón *et al*., 2010; Wang *et al*., 2014); it is possible that it should be noted that the rats with the lowest increase in SBP were those treated with the extract of *P. edulis*, which evidenced a higher content of the quantified polyphenols.

Table 2. Phytochemical screening.

Metabolite	Test	Ethanolic extract *P. edulis*	Ethanolic extract *P. vitifolia*
Polyphenols	Folin–Ciocalteu	+++	+++
Flavonoids	Shinoda	+++	+++
	TLC	+++	+++
Tannins	Ferric chloride	+++	+++
Saponins	Rosenthaler	N.D.	N.D.
	Foam	N.D.	N.D.
Anthraquinones	Borntrager	+	+
Terpenes and steroids	Lieberman–Burchard	+++	+++
	Salkowski	+++	+++
	TLC	+++	+++
Alkaloids	Tanred	++	++
	Dragendorff	++	++
	Mayer	++	++
	Valser	N.D.	N.D.
Cardiotonics	Baljet	+	+
Total phenols (g E.A.G/100 g extract)	Folin–Ciocalteu	43.2 ± 1.0	33.07 ± 0.68
Flavonoids (g E.N/100 g extract)	Aluminum trichloride	15.24 ± 0.73	13.64 ± 0.97
Total tannins (g E.A.T/100 g extract)	Folin–Ciocalteu Polyvinyl pyrrolidone	15.08 ± 0.47	10.77 ± 0.42

N.D. indicates no detection of secondary nucleus under these conditions, + indicates low quantity, ++ indicates medium quantity, and +++ indicates high quantity. g E.A.G = equivalent grams of gallic acid; g E.N = equivalent grams of naringenin; g E.A.T = equivalent grams of tannic acid.
Adapted from (Murillo & Méndez, 2012).

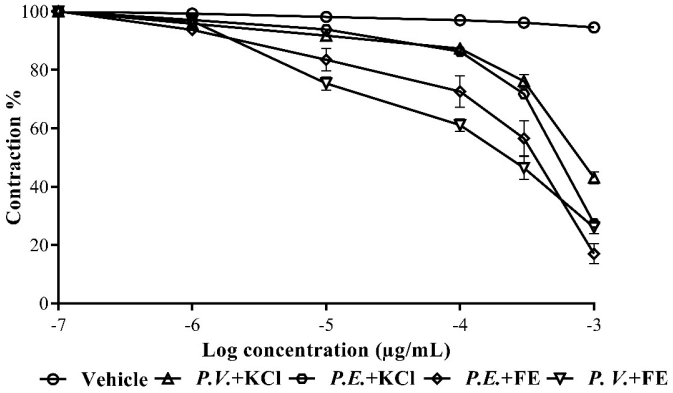

Figure 3. Relaxation exerted by the extracts in aortic rings contracted with FE and KCl. Each point represents the mean ± SEM.

Relaxing effect of the extracts on the contraction exerted by phenylephrine (Phe) and KCl

The extracts showed relaxation in aortic rings contracted with Phe and KCl (Fig. 3), being greater in the rings treated with the extract of *P. edulis*. It was possible to show greater activity on the part of the two extracts in the rings contracted with Phe, finding significant differences in the maximum response between the treatments and the compounds used to contract the rings. The relaxation induced by the extracts of the two species presented concentration response behavior, suggesting that the effects may be linked to intracellular calcium movement stimulated by different mechanisms that act on voltage-dependent Ca^{+2} channels (Clark *et al*., 2001; Costa, 2013; Wang *et al*., 2014).

Effect of ACh and NPS on aortic rings of hypertensive rats treated with the extracts

Chronic exposure to L-NAME generates a decreased vascular response (Bryant *et al*., 1995). In this work, it was not possible to maintain the vascular response of the animals by cumulative action of ACh and NPS (Figs. 4 and 5), since a decrease is observed with respect to that obtained in normotensive rats. It is evidenced that the aortic rings obtained from animals treated with the extracts showed greater relaxation than those treated with

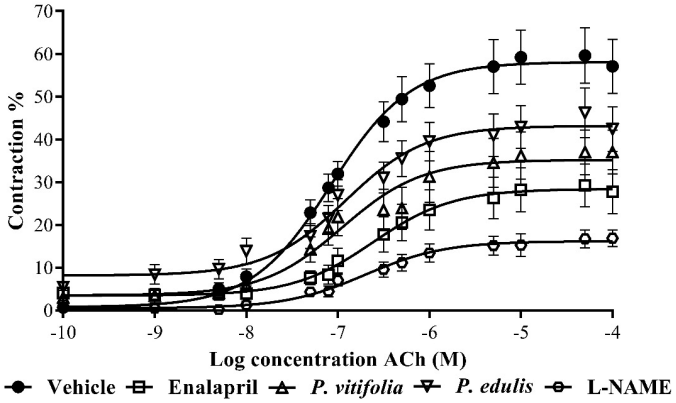

Figure 4. Relaxation by ACh (10^{-10}–10^{-4} M) in aortic rings of hypertensive Wistar rats treated with the extracts of the two species, enalapril, and vehicle (control). Results are expressed as means ± SEM.

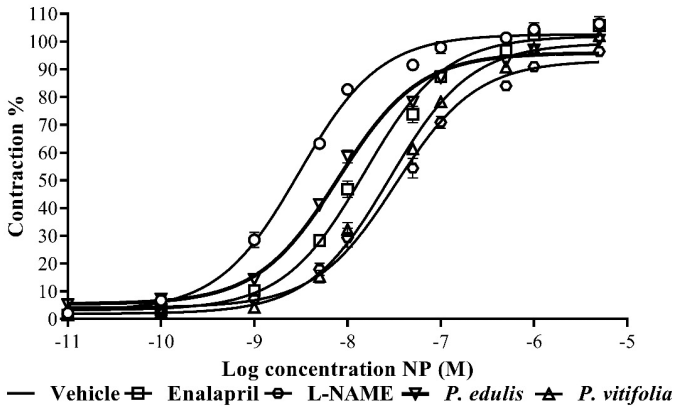

Figure 5. Relaxation by NPS (10^{-11}–10^{-5} M) in aortic rings of hypertensive Wistar rats treated with the extracts of the two species, enalapril, and vehicle. Results are expressed as means ± SEM.

enalapril and hypertensive rats. In both cases, a shift to the right of the curve was observed with respect to the control, which could indicate a decrease in the potency and/or antagonistic action by the extracts to the relaxing action of the two compounds on the aortic rings (Aleixandre and Ortega, 2000).

Extract mechanism of action

Relaxation in the presence of L-NAME

The relaxing action of the two ethanolic extracts on aortic rings precontracted with Phe and incubated with the agents mentioned above did not show significant differences, except for L-NAME, which partially reversed the relaxation compared to rings without the presence of it (Fig. 6). The evaluation of the synthesis of nitric oxide by adding L-NAME to the organ bath showed that this partially reduces the relaxing capacity of the two extracts compared to that produced in its absence, which suggests that the relaxing effect of the extract could be dependent on the endothelium and would be directly related to the synthesis of nitric oxide (Pérez *et al*., 2010; Wang *et al*., 2014).

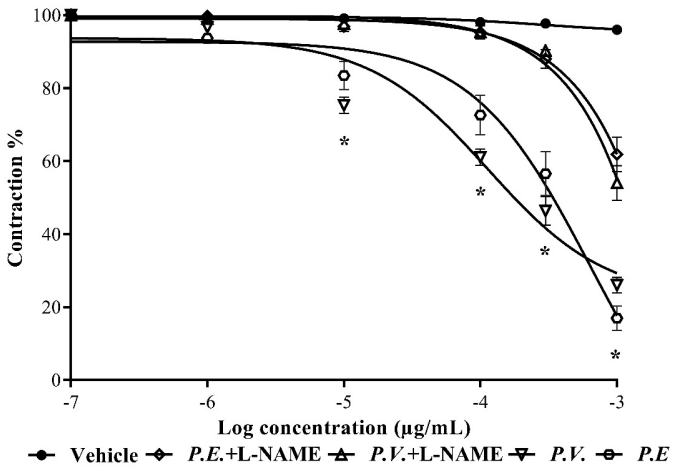

Figure 6. Relaxation of the extracts in the presence and absence of L-NAME. Each point represents the mean ± SEM; *represents differences ($p \leq 0.05$) between treatments in the presence and absence of L-NAME.

Inhibitory effect of the extracts on the contraction exerted by AT-II

Ethanolic extracts of two species inhibited contraction produced by AT-II in aortic rings. It was observed that the extract of *P. edulis* at the two concentrations evaluated presented a greater inhibitory effect than the extract of *P. vitifolia* (Fig. 7). Contraction of the rings by cumulative doses of AT-II in rings preincubated with extracts showed a concentration-dependent effect, being the *P. edulis* extract the one that showed the greatest inhibition of AT-II. When comparing the effect of the extracts with that of Losartan (AT-II inhibitor), higher effectiveness was obtained than that caused by the reference drug, which is a selective inhibitor of the AT1 receptor which reduces the effects of AT-II in the artery

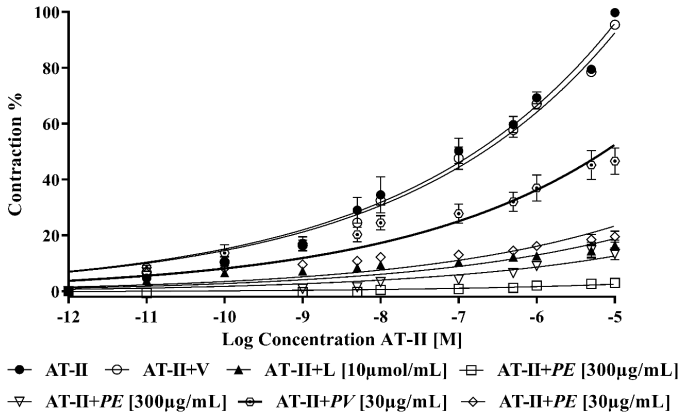

Figure 7. Comparison between contraction exerted by AT-II on aortic rings in the presence and absence of the extracts, Losartan, and vehicle. Each point represents the mean ± SEM.

(Pérez *et al*., 2010). The two extracts could act as possible AT-II inhibitors; however, a greater effect ($p \leq 0.05$) of the extract of *P. edulis* than that produced by *P. vitifolia* is observed; the above could be related to the concentration of phenolic compounds greater in the extract of *P. edulis* (Table 2).

UHPLC-DAD analysis

The results of the characterization of the two extracts by UHPLC-UV can be seen in Table 3 and Figure 8. Chromatographic analysis showed the presence and quantification of vitexin, orientin, isovitexin, isoorientin, coumaric acid, rutin, and quercetin, using curves made with the reference compounds. Other chromatographic signals were evidenced that showed characteristic UV spectra of polyphenols but that could not be identified or quantified because they did not correspond to the standards used. Similarly, quantitation of phenolic compounds (total phenols, total flavonoids, and tannins) revealed the high content of these in the two extracts (Table 2). It should be noted that some c-glycosides flavonoids such as orientin and vitexin are used in *Passiflora* as chemomarkers of the genus; however, these reports refer to extracts obtained from stem and leaves but not from seeds (Gomes *et al*., 2017; Petenatti *et al*., 2014; Sepúlveda *et al*., 2018; Wosch *et al*., 2017; Zeraik and Yariwake, 2010). On the other hand, some authors (Bayard *et al*., 2007; Occhiuto and Limardi, 1994; Occhiuto *et al*., 1990) indicated the positive effect of said compounds on the vascular behavior of animals with HTA and the protective potential they present on target tissues related to pathology (Orhan *et al*., 2003); however, it is necessary to carry out tests that allow the different compounds present in the extracts of the two *Passiflora* to be correlated with the different pharmacological targets related to HTA.

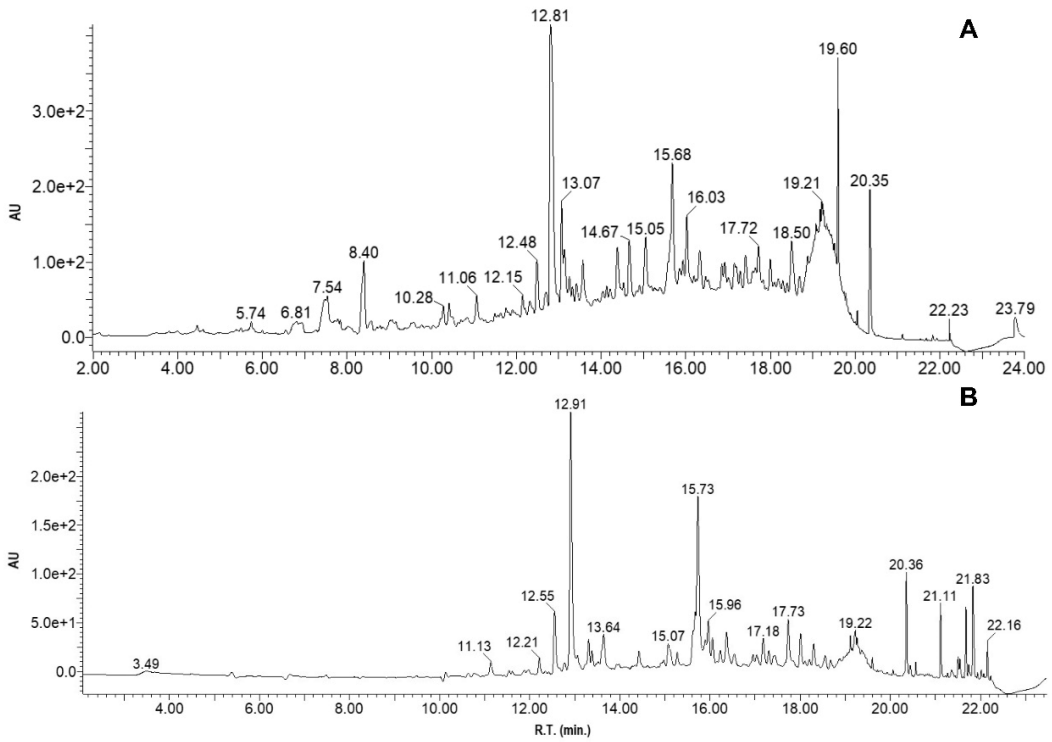

Figure 8. (A) Chromatograms of extracts from *P. vitifolia* and (B) *P. edulis* f. *edulis*, with diode array detection at 340 nm.

Table 3. Phenolic compounds in *P. edulis* and *P. vitifolia* seeds determined by UHPLC-UV.

Compound	R.T. (minutes)	Concentration µg/g	
		P. edulis* f. *edulis	***P. vitifolia***
Isoorientin	2.55	51.79	133.3
Isovitexin	3.59	421.56	368.43
Orientin	4.15	34.80	302.37
Vitexin	5.46	341.59	88.82
Coumaric acid	10.51	54.0	78.4
Rutin	12.22	N.D.	48.8
Quercetin	13.84	99.6	N.D.

N.D. indicates the nondetection of the compound evaluated under the applied conditions.

CONCLUSION

This study demonstrates that the two ethanolic extracts obtained from the seeds of *P. edulis* f. *edulis* and *P. vitifolia* prevented HTA induced by nitric oxide deficit in rats; however, *P. edulis* f. *edulis* had a greater effect, obtaining SBP similar to those of normotensive animals. The possible mechanisms of action for the extracts are primarily related to the synthesis of nitric oxide and inhibition of AT-II; these results, together with the not apparent toxicity in cell, no acute toxicity in mice and the chemical composition, that relates the activity with the presence of phenolic compounds be in agreement to studies previously carried out on seeds of the genus; the above, postulates the two species as a possible source of extracts with antihypertensive potential, reinforcing the ethnobotanical use of the genus Passiflora for the control of hypertension. In addition, this type of results contributes to the generation of added value to the agroindustrial waste of these two species through its use in obtaining extracts with biological potential.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

CONFLICT OF INTEREST

The authors declare no conflict of interest in carrying out this work.

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