Acta Scientiarum
http://periodicos.uem.br/ojs
ISSN on-line: 1807-8664
Doi: 10.4025/actascitechnol.v46i1.66447

Lychee peel extract obtained by ultrasound-assisted extraction: bioactive compounds and functional properties

Marcia Regina Rodrigues Tanaka[1], Leonardo de Souza Mataruco[1], Elionio Galvão Frota[3], Bruno Emanuel Souza Coelho[4], Marcos dos Santos Lima[5], Tatiana Colombo Pimentel[2] and Carlos Eduardo Barão[1,2*]

[1]Departamento de Agronomia, Universidade Estadual de Maringá, Maringá, Paraná, Brazil. [2]Instituto Federal do Paraná, Campus Paranavaí, Av. José Felipe Tequinha, 1400, 87703-536, Jardim das Nacoes, Paranavaí, Paraná, Brazil. [3]Laboratório de Biomoléculas Microbianas, Faculdade de Ciências Farmacêuticas, Universidade de São Paulo, São Paulo, Brazil. [4]Programa de Pós-Graduação em Agronomia, Produção Vegetal, Universidade Federal do Vale do São Francisco, Petrolina, Pernambuco, Brazil. [5]Departamento de Tecnologia de Alimentos, Instituto Federal do Sertão de Pernambuco, Petrolina, Pernambuco, Brazil. *Author for correspondence. E-mail: carlos.barao@ifpr.edu.br

ABSTRACT. The purpose of this study was to evaluate the impact of extracting solvent composition on the concentration of bioactive compounds and functional properties of lychee peel extracts obtained by ultrasound-assisted extraction. Five conditions were evaluated with different solvent proportions: 100% water, 25% ethanol and 75% water, 50% ethanol and 50% water, 75% ethanol and 25% water, and 100% ethanol. The use of an equitable mixture of water and ethanol (50% ethanol and 50% water) resulted in extracts with a higher content of total phenolic compounds (10964.3 mg EAG 100 g^{-1}), antioxidant activity (27.40%), and inhibition of α-glucosidase (94.31%), α-amylase (33.49%) and angiotensin-converting enzyme (ACE, 51.82%). This extract showed a diversity of phenolic compounds (quercetin 3-glucoside, procyanidin A2, B1, and B2, epicatechin, catechin, kaempferol 3-glucoside, trans-resveratrol, myricetin, and gallic acid). Therefore, extracts of lychee peel with potential anti-diabetic and anti-hypertensive activity can be obtained by ultrasound-assisted extraction. 50% water and 50% ethanol may be suggested as the extracting solvent.

Keywords: *Litchi chinensis*; phenolic compounds; α-amylase inhibitory activity; α-glucosidase inhibition; angiotensin-converting enzyme.

Received on December 26, 2022.
Accepted on June 6 2023.

Introduction

Lychee (*Litchi chinensis*) is a fruit predominantly from subtropical and tropical climates, with an estimated annual world production of 3.5 million tons (Morales-Trejo et al., 2022). It consists of seeds, a white and sweet edible pulp with a gelatinous characteristic, and a rough, red, and slightly rigid shell. Lychee is commonly consumed fresh, but it can be processed to obtain dried fruits, wines, and juices to meet market demand for new products and extend their shelf life (Zhao, Wang, Wang, Zhu, & Hu, 2020).

Consumption and processing of lychee generate many by-products (30-40% of the dry weight), with 10-20% being seeds and 15-20% peels (Chukwuma et al., 2021; Punia & Kumar, 2021). Lychee peel has significant concentrations of bioactive compounds, including phenolic compounds, anthocyanins, flavonoids, lignans, triterpenes, and sesquiterpenes. These compounds are associated with functional properties such as antitumor, anti-inflammatory, antioxidant, antidiabetic, antihyperlipidemic, antihyperglycemic, anti-hypertensive, and antiviral activities (Yao et al., 2021).

The profile and concentration of bioactive compounds in fruit peel extracts depend on cultivars and fruit maturation stage, environmental factors, and extraction methods (Yao et al., 2021). Extracts are commonly obtained using conventional solid-liquid extraction methods with organic solvents. However, these methods may change the chemical composition of the extracts and use high volumes of solvents (Silva, Garcia, & Franciscato, 2016).

The ultrasound-assisted extraction technique may have several advantages: shorter process time, higher yields, low-temperature extractions, and maintenance of the composition and bioactivity of the extracts (Kumar, Srivastav, & Sharanagat, 2021). Furthermore, it can be considered "environmentally friendly" regarding reagent and energy consumption compared to conventional extraction techniques (Živković,

Šavikin, Janković, Ćujić, & Menković, 2018). The parameters of the extraction process are important in the quality of the obtained extract, such as sonication power, extraction time, frequency, ultrasonic wave distribution, type of solvent, solid-liquid ratio, particle size, and temperature, among others (Chemat et al., 2017; Ez zoubi et al., 2021).

Among the process parameters, the type of solvent was reported as the most critical variable, compared to temperature and process time (Silva et al., 2016). Extractions using only water as a solvent may have low yields, and mixing water with organic solvents, such as ethanol, is recommended. Ethanol has a high affinity with phenolic compounds and is the most recommended solvent for extracting these compounds from agro-industrial by-products. In addition, it has other advantages, such as being obtained from a plant source (sugar cane), low cost, and having GRAS (Generally Recognized as Safe) certification (Kumar et al., 2021). The rise in the proportion of ethanol in solvent mixtures is related to an increase in the concentrations of phenolic compounds in the extracts, up to a maximum limit, followed by a reduction in yield (Kumar et al., 2021). Thus, studying solvent composition (water and ethanol mixture) is important for evaluating ultrasound-assisted extraction processes.

The ultrasound-assisted extraction technique has been used in the extraction of bioactive compounds from agro-industrial by-products, such as grape pomace (Bruno Romanini et al., 2021), leaves of *Phyllanthus amarus* (Sousa et al., 2016), olive tree (Khemakhem et al., 2017), stevia (Raspe et al., 2021) and jabuticaba peels (Rodrigues, Fernandes, de Brito, Sousa, & Narain, 2015). However, only one study evaluated its application in lychee peels (Silva et al., 2016), and it evaluated only antioxidant activity and total phenolic compounds.

Thus, the aim of the present article was to evaluate the effect of different concentrations of ethanol and water as a solvent on the functional properties and concentration of bioactive compounds of lychee peel extracts obtained by ultrasound-assisted extraction.

Material and methods

Raw material and processing of the lychee peels

The lychee fruits at commercial maturation were purchased in the city of Maringá – PR, Brazil (harvest of 2020/2021), sanitized and selected based on the absence of injuries. Subsequently, they were manually peeled, and the peels were dried at 45°C for 24h in a drying oven with air circulation. Afterward, they were ground in a mill (SL-30, Solab, SP, Brazil) (Silva et al., 2016), and the peel flour was standardized using Tyler series sieves, with an average diameter of 0.85 cm (20 mesh sieve).

Chemical composition of lychee peel flour (LPF)

The chemical composition of LPF was determined according to AOAC (2012). Moisture was determined in an oven at 105°C until constant weight (AOAC 934.06), lipids by Soxhlet using ethyl ether as the solvent (AOAC 920.39), ash by incineration at 550°C (AOAC 940.26), protein content by the micro-Kjeldahl method with a factor of 6.25 (AOAC 960.52) and carbohydrates by difference.

Ultrasound-assisted extraction

The extraction was performed using an ultrasonic bath of 2.8 L at a frequency of 40 kHz (USC 1400 A, Unique, SP. Brazil). The process parameters were a solid-liquid ratio of 1:20 (m/v) and an extraction time of 10 min. These parameters were selected based on previous studies with extracts of citrus (Ma, Chen, Liu, & Ye, 2009), pomegranate (Sharayei, Azarpazhooh, Zomorodi, & Ramaswamy, 2019), and jaboticaba (Rodrigues et al., 2015) peel. These studies reported maximized extraction of target compounds at these conditions, including phenolic compounds. Five conditions were tested, using water and ethanol as solvents in different proportions, being 100% water, 25% ethanol and 75% water, 50% ethanol and 50% water, 75% ethanol and 25% water and 100% ethanol.

Content of phenolic compounds, organic acids and functional properties

The content of total phenolic compounds (TPC) was realized by the Folin-Ciocalteu method, with gallic acid as a standard, according to Singleton and Rossi (1965). The antioxidant activity was determined by ABTS (2,2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) and DPPH (2,2-diphenyl-1-picrylhydrazy) methods and the results were expressed as radical inhibition (%) (Saraiva, Vital, Anjo, Ribas, & Matumoto Pintro,

2019). The ACE inhibitory activity was calculated according to Ramchandran and Shah (2010), and the results expressed as % ACE inhibition. The results of α-glucosidase and α-amylase inhibition assays (Lavelli, Sri Harsha, Ferranti, Scarafoni, & Iametti, 2016) were expressed as % inhibition of enzymes.

The profiles of phenolic compounds and organic acids were determined for the condition that presented the highest TPC, and ACE, α-glucosidase and α-amylase inhibitory activities. The profile of phenolic compounds was determined according to Padilha et al. (2017). The samples were centrifuged (15 min. 3500 rpm^{-1}) (Solab, São Paulo State, Brazil), and the supernatant was collected. Then, an aliquot (1 mL) was filtered at 0.45 µm (Millex-HA, Millipore Co., Bedford, MA), and phenolic compounds were quantified. For this, the extract (20 µL) was injected into a chromatography using a diode array detector – DAD, a pre-column (Zorbax C18 - 12.6 × 4, 6 mm, 5 µm) and a column (Zorbax Eclipse Plus RP-C18 - 100 × 4.6 mm, 3.5 µm). The flow rate and the column temperature were 0.8 mL min^{-1} and 35°C, respectively. The mobile phases were methanol acidified with 0.5% phosphoric acid (phase A) and water acidified with 0.1 mM phosphoric acid (phase B, pH 2,0).

The peaks of phenolic compounds were verified by comparing their retention times to external standards. It were used as standards: gallic, chlorogenic, p-coumaric, syringic, and caffeic acids, epicatechin, catechin, naringenin, hesperidin, procyanidin B1 and B2, cyanidin 3,5-diglucoside, delphinidin 3-glucoside, cyanidin 3-glucoside, malvidin 3-glucoside, pelargonidin 3,5-diglucoside, malvidin 3,5- diglucoside, from Sigma-Aldrich (St. Louis, USA); cis-resveratrol and trans-resveratrol from Cayman Chemical Company (Ann Arbor, MI, USA); and quercetin 3-rutinoside (rutin), procyanidin A2, quercetin 3-glycoside, pelargonidin 3-glycoside, kaempferol 3-glycoside, myricetin, epigallocatechin gallate, epicatechin gallate, peonidin 3-O-glycosides, and petunidin 3-glycoside from Extrasynthesis (Genay, France). The detection of compounds was performed at 220, 280, 320 and 360 nm, according to chromatogram (Figure 1). External standard calibration curves were used to quantify phenolic compounds (Padilha et al., 2017). The Threshold tool was used to guarantee identification accuracy compared to the external standard. All compounds showed calibration curves with $R^2 \geqslant 0.998$. The Open LAB CDS Chem Station Edition TM software (Agilent Technologies, Inc., Santa Clara, CA) was used for data processing.

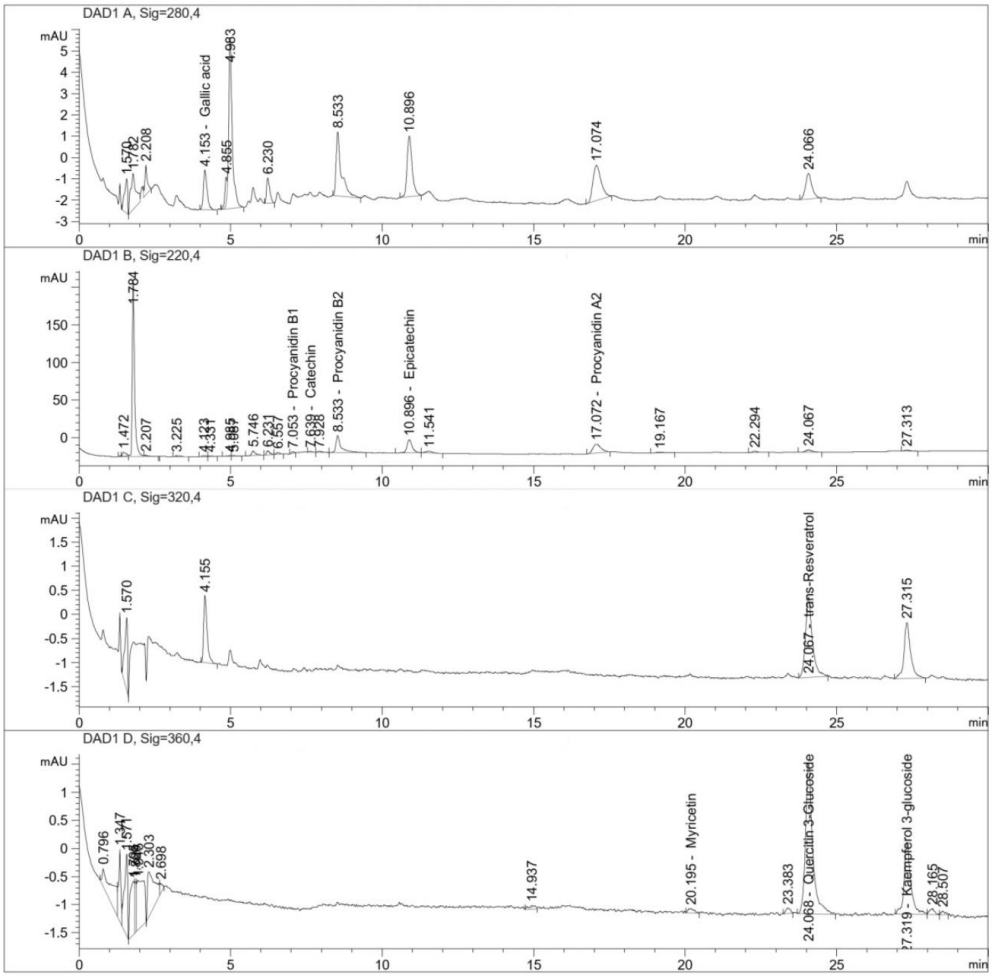

Figure 1. Chromatogram of phenolic compounds profile.

The content of organic acids was determined according to Donkor, Henriksson, Vasiljevic, and Shah (2006). It was analyzed using a High-Performance Liquid Chromatography (Chromaster, Hitachi, Japan) with a quaternary solvent pump, automatic injection and a diode array detector - DAD. The flow rate and the column temperature were 0.5 mL $min.^{-1}$ and 40°C, respectively for 15 min. Detection was performed in Phenomenex Luna C18 (4.6 × 150 mm, 5 µm). The mobile phase was water: methanol solution (97.5:2.5) acidified with phosphoric acid (pH 2,2). To identify organic acids, the standards used were citric, tartaric, malic, acetic, succinic, formic, butyric, propionic, and lactic acids (Sigma-Aldrich). External standard calibration curves following validated methods were used to quantify the organic acids (Padilha et al., 2017). The data were processed with EZ Crom software in GALAXIE Chromatography Data System (Figure 2).

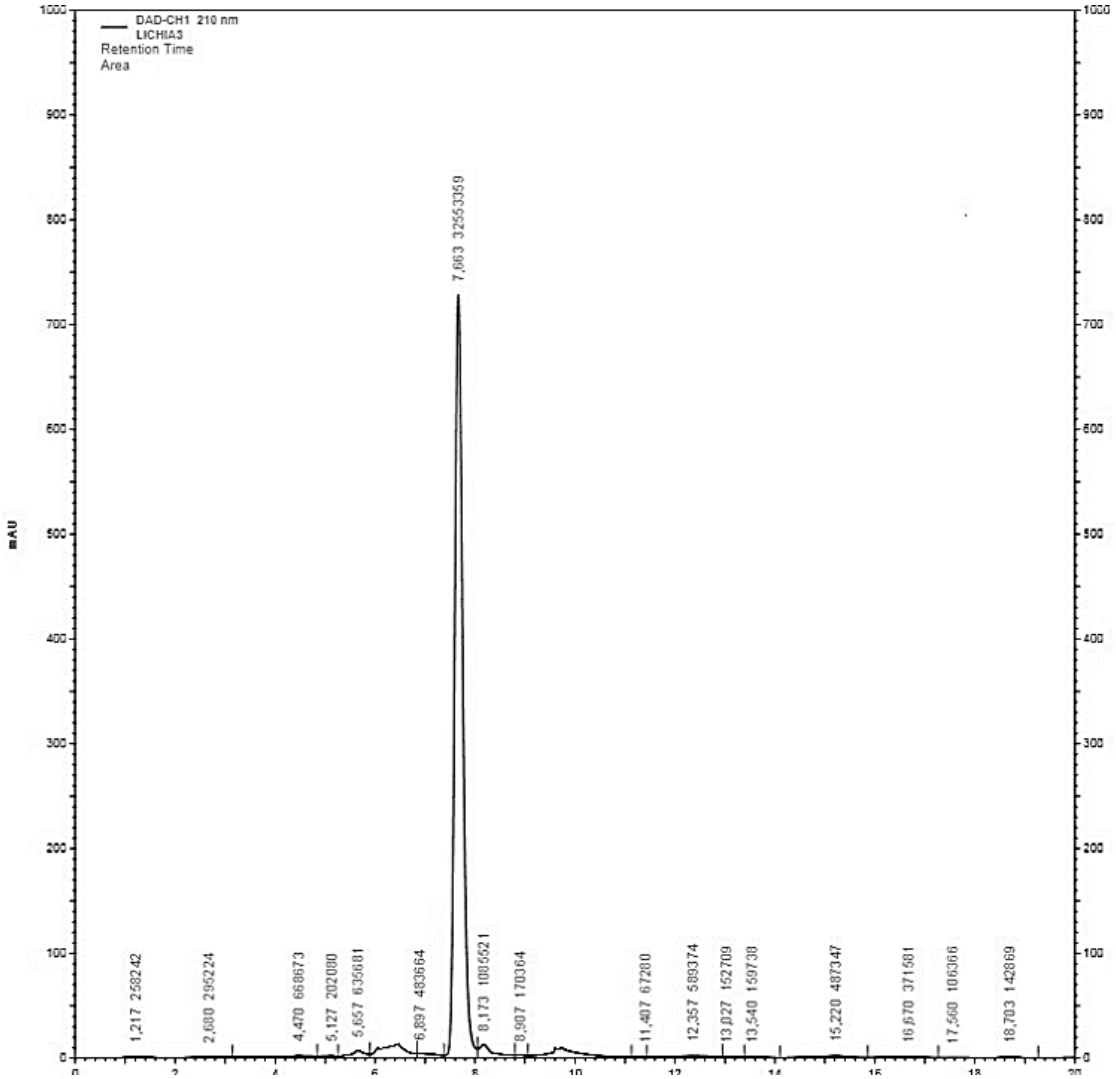

Figure 2. Chromatogram of organic acids.

Statistical analysis and experimental design

The experiment followed a completely randomized design with two replications. Analyzes were realized in triplicate. The TPC data, antioxidant, and enzyme inhibitory activities were submitted to Analysis of Variance (ANOVA) and Tukey or Fisher's multiple comparison test (p=0.05) using the XLXTAT 2022 software (Adinsoft, Paris, France).

Results and discussion

Chemical composition of LPF

The chemical composition of LPF is shown in Table 1. The LPF had a moisture content of 10.64 g 100 g^{-1} and a carbohydrate concentration of 74.17 g 100 g^{-1}, which was the primary nutrient in LPF. The carbohydrate

content is intrinsically linked to the production of compounds by the tissues that make up the pericarp or epicarp of fruits for protection, such as polysaccharides (pectin, cellulose, and hemicellulose) and dietary fibers (Pareek, 2016; Queiroz, Abreu, Santos, & Simão, 2015). Studies involving the characterization of litchi peel are still scarce (Chukwuma et al., 2021), and significant concentrations of phenolic compounds have been reported, such as procyanidins, anthocyanins, and flavones (Liu et al., 2021).

However, the composition may change the extracts based on the extraction method and process parameters (Devequi-Nunes, 2018; Lazarjani, Young, Kebede, & Seyfoddin, 2021). In this way, LPF may have important nutrients associated with health benefits to consumers, suggesting its utilization as a raw material for extracts.

Table 1. Chemical composition of lychee peel flour.

Parameter	Quantity (g 100 g^{-1})
Moisture	10.64 ± 0.77
Protein	5.30 ± 0.37
Lipid	7.68 ± 1.27
Ash	2.28 ± 0.33
Carbohydrate	74.17 ± 2.12

*Data are presented as mean ± standard deviation.

TPC, phenolic compounds profile, antioxidant activity (DPPH and ABTS) and organic acids of lychee peel extracts

The total phenolic compounds and antioxidant activity (DPPH and ABTS) of lychee peel extracts are shown in Table 2, while the inhibitory effect on α-glucosidase, α-amylase and ACE enzymes is shown in Table 3.

Table 2. Content of total phenolic compounds and antioxidant activity of lychee peel extracts.

Conditions	Total phenolic compounds (mg GAE 100 g^{-1})	DPPH (%)	ABTS (%)
100% water	9019.4 ± 129.8^{b}	88.12 ± 1.55^{a}	18.39 ± 2.28^{c}
25% ethanol and 75% water	9365.1 ± 618.8^{b}	86.22 ± 1.48^{a}	26.19 ± 1.14^{a}
50% water and 50% ethanol	10964.3 ± 960.9^{a}	87.25 ± 2.4^{a}	27.40 ± 1.62^{a}
75% ethanol and 25% water	8651.9 ± 175.7^{b}	90.89 ± 2.81^{a}	22.19 ± 0.31^{b}
100% ethanol	6426.1 ± 114.6^{c}	90.73 ± 0.63^{a}	16.61 ± 0.72^{c}

Data are presented as mean ± standard deviation. Values followed by different letters in the column indicate a significant difference ($p < 0.05$, $n = 6$).

The extracts showed TPC of 6426.1 to 10,964.4 mg EAG 100 g^{-1}, values close to those reported in tangerine extracts, 14,000 mg EAG 100 g^{-1} (Nipornram, Tochampa, Rattanatraiwong, & Singanusong, 2018) and higher than those reported for mango, 400 mg EAG 100 g^{-1} (Sánchez-Camargo et al., 2021), araticum, 489 to706 mg EAG 100 g^{-1} (Arruda et al., 2019) and orange, 46 to 149 mg EAG 100 g^{-1} (Barrales et al., 2018). Furthermore, the extracts showed antioxidant activity of 86.22 to 90.89% of radical inhibition in the DPPH analysis and 16.61 to 27.40% of radical inhibition in the ABTS analysis.

Table 3. Inhibitory activity of lychee peel extracts on alpha-amylase and angiotensin-converting enzyme (ACE).

Conditions	α-amylase inhibitory activity (%)	α-glucosidase inhibitory activity (%)	ACE inhibitory activity (%)
100% water	30.51 ± 0.17^{bc}	73.92 ± 1.04^{d}	33.93 ± 1.89^{d}
25% ethanol and 75% water	31.53 ± 1.96^{ab}	90.31 ± 1.21^{b}	44.55 ± 2.22^{b}
50% water and 50% ethanol	33.49 ± 0.48^{a}	94.31 ± 1.09^{a}	51.82 ± 3.74^{a}
75% ethanol and 25% water	31.46 ± 1.12^{ab}	82.51 ± 1.55^{c}	41.20 ± 1.05^{c}
100% ethanol	28.63 ± 1.68^{c}	74.22 ± 1.19^{d}	34.21 ± 2.09^{d}

Data are presented as mean ± standard deviation. Values followed by different letters in the column indicate a significant difference ($p < 0.05$, $n = 6$).

Finally, the extracts showed 28.63 to 33.49% inhibition of α-amylase, 73.92 to 94.31% inhibition of α-glucosidase, and 33.93 to 51.82% inhibition of ACE. Inhibition of α-glucosidase and α-amylase promotes a reduction in the rate of glucose absorption in the small intestine, decreasing postprandial hyperglycemia (Aleixandre, Gil, Sineiro, & Rosell, 2022). At the same time, ACE is an enzyme that plays a vital physiological role in the degradation of the vasodilator bradykinin leading to hypertension and in the regulation of blood pressure by converting angiotensin-I to angiotensin-II, a potent vasoconstrictor. For this reason, there is a demand for foods with ACE-inhibitory activity (Kessy, Wang, Zhao, Zhou, & Hu, 2018; Rong et al., 2018). The higher inhibition of α-glucosidase compared to α-amylase is desired, as strong or complete inhibition of the

latter may cause undesirable side effects after consumption of the extract (Oboh, Ademiluyi, Agunloye, Ademosun, & Ogunsakin, 2018). Our results demonstrate that the extraction process used in the present study could extract the bioactive compounds commonly reported for lychee peel, resulting in an extract with important antioxidant activity and potential anti-diabetic and anti-hypertensive properties.

The increase in the concentration of ethanol in the solvent mixture caused an increase in TPC and antioxidant activity (ABTS) up to a concentration of 50%, with a subsequent decrease ($p < 0.05$). It was observed the same behavior for the inhibition of α-amylase, α-glucosidase, and ACE enzymes. Therefore, to obtain an extract with higher antioxidant activity and anti-diabetic and anti-hypertensive properties, it would be interesting to use a mixture of 50% water and 50% ethanol as solvent. The increase in ethanol concentration promotes an increase in the diffusivity and solubility of phenolic compounds in the plant matrix due to the reduction in the dielectric constant of the solvent. However, high ethanol concentrations can cause protein denaturation and dehydration of plant tissue, resulting in reduced yields (Kumar et al., 2021). The presence of ethanol in the solvent promotes the recovery of bioactive compounds. When used together (binary systems), it turns out that fewer polar compounds are extracted in ethanol, while polar compounds are better recovered with water. When water and ethanol are used together, there is an advantage over their pure constituents since a synergistic effect is obtained for both solvents in the phytochemical extraction (Lim, Cabajar, Lobarbio, Taboada, & Lacks, 2019).

Our results demonstrate the importance of evaluating the type and composition of solvents, as increases of 17.08 to 66.42% radical inhibition were observed in the antioxidant activities of 50% water and 50% ethanol condition concerning the other conditions. Furthermore, increases of 1.96 to 4.86% in α-amylase inhibition, 4.00 to 20.39% in α-glucosidase inhibition, and 7.27 to 17.89% in ACE inhibition were observed for this condition.

Thus, the 50% water and 50% ethanol condition was used to evaluate phenolic compounds and organic acid profiles to correlate its composition with the observed potential health effects. The phenolic compound profile is presented in Table 4.

Table 4. Profile of the phenolic compounds (mg 100 g^{-1}) and organic acids (mg ml^{-1}) of the 50% water and 50% ethanol condition.

Compound	Quantity
Galic acid	0.526 ± 0.02
Procyanidin B1	0.422 ± 0.01
Catechin	1.062 ± 0.01
Procyanidin B2	5.070 ± 0.63
Epicatechin	4.147 ± 0.03
Procyanidin A2	6.796 ± 0.08
Trans-resveratrol	0.450 ± 0.001
Myricetin	0.208 ± 0.001
Quercetin 3-glucoside	2.693 ± 0.03
Kampeferol 3-glucoside	2.240 ± 0.03
Malic Acid	17.08 ± 0.73

Data are presented as mean ± standard deviation.

The lychee peel extract showed the highest concentration of procyanidin A2, followed by procyanidin B2, epicatechin, quercetin 3-glucoside, kaempferol 3-glucoside, catechin, gallic acid, trans-resveratrol, procyanidin B1 and myricetin. Procyanidin oligomers are compounds commonly reported in lychee peels, including epicatechin and procyanidins A (mainly A2) (Yao et al., 2021). Quercetin and its derivatives, epicatechin, catechin, procyanidins A, and epigallocatechin gallate, have been reported to be the phenolic compounds with the most significant α-amylase inhibitory activity. At the same time, procyanidins A2 would have a high capacity to inhibit α-glucosidase (Chukwuma et al., 2021). Finally, some flavonoids (rutin, quercetin, procyanidins, catechin, and epicatechin) and gallic acid have exhibited inhibitory action on the ACE enzyme (Kessy et al., 2018; Yao et al., 2021).

The suggested mechanisms of action of phenolic compounds on antioxidant, antidiabetic, and anti-hypertensive properties have been studied. Procyanidin oligomers may reduce oxidative processes through the chelation of metal ions and the sequestration of reactive oxygen species, resulting in high antioxidant activities (Chukwuma et al., 2021). It has been described that A-type dimeric procyanidins (procyanidins A2) could have a greater antioxidant activity due to the number of hydroxyls in their structures (Zhang et al., 2020). Kaempferol 3-glucoside may show antioxidant activity due to a hydroxyl group in the C ring, contributing to its radical scavenging activity (Mukemre, Konczak, Uzun, & Dalar, 2020).

Procyanidin oligomers may also inhibit α-glucosidase and α-amylase by binding to their active sites (Chumsri, Chaijan, & Panpipat, 2021), resulting in improved glucose homeostasis, suppressing glucose production in the liver, modulating protein expression, and increasing glycolysis. Procyanidins A showed more significant activity than procyanidins B (Yao et al., 2021). The inhibition of α-glucosidase may be related to the molecular structure of the phenolic compound and glycosylation, and lower glycosylation and smaller molecular structures show higher inhibitory activity (Zhao et al., 2020). The anti-hypertensive activity of phenolic compounds is related to the number of hydroxyl groups, their position, and the presence of double bonds in the rings, resulting in stable complexes that chelate zinc in the ACE-I active site (Escher et al., 2020). Furthermore, phenolic compounds may interact with the disulfide bridge residue at the protein's active site (ACE), resulting in enzymatic inhibition (Oboh et al., 2018). Thus, the higher concentration of procyanidins, mainly procyanidin A2, in the 50% water and 50% ethanol extract (6.786 mg 100 g-1) may be related to the observed antioxidant, α-glucosidase and α-amylase inhibitory activities. Therefore, the present study demonstrated that lychee peel extract has phenolic compounds that could exert antidiabetic and anti-hypertensive activity.

The incidence of these compounds implies that the extracts obtained are potential sources for isolating bioactive compounds that may have important therapeutic properties for numerous diseases. Pharmacological perspectives include antioxidant, hypolipidemic, antidiabetic, anticancer, anti-inflammatory, neuroprotective, and antimicrobial properties possibly mediated by its constituent polyphenols (Chukwuma et al., 2021).

Malic acid, a dicarboxylic organic acid, is naturally present in vegetables and fruits such as pears and apples and was the predominant acid in the 50% water and 50% ethanol extract (17.08 mg mL-1). During the Krebs cycle, it is produced in the body, helping the body to produce energy (Muhamed, Moussa, Aboasy, & Gaweesh, 2022) enhancing the activities of digestive enzymes and could aid digestion and absorption by various chelating cations (Ren et al., 2021). Other effects of malic acid have been reported by different authors, such as decreasing the quantity of glucose absorbed by the gastrointestinal system (Guevarra & Panlasigui, 2000), stimulating insulin secretion (Édouard & Kouassi, 2009), and decreasing the absorption of glucose through inhibition of the α-glucosidase enzyme (Gou et al., 2015).

Conclusion

This is the first study to verify the effect of solvent type (water and ethanol mixtures) on the concentration of bioactive compounds and functional properties of ultrasonic lychee peel extract. A combination of 50% water and 50% ethanol is recommended, resulting in extracts with a greater content of total phenolic compounds, inhibition activity of α-amylase, α-glucosidase, ACE and antioxidant activity. In addition, this extract was presented as a source of phenolic compounds (kaempferol 3-glucoside, procyanidin A2, B1, and B2, epicatechin, catechin, quercetin 3-glucoside, trans-resveratrol, myricetin, and gallic acid). Therefore, the extract obtained could be recommended for glycemic control and arterial hypertension. However, *in vivo* studies are needed to prove these effects.

Acknowledgements

The authors are grateful to CAPES, the Federal Institute of Parana (IFPR) and the Araucária Foundation (FA/PR).

References

AOAC International. (2012). *Official Methods of Analysis* (19th ed.). Gaithersburg, MD: AOAC.

Aleixandre, A., Gil, J. V., Sineiro, J., & Rosell, C. M. (2022). Understanding phenolic acids inhibition of α-amylase and α-glucosidase and influence of reaction conditions. *Food Chemistry, 372,* 131231. DOI: https://doi.org/10.1016/j.foodchem.2021.131231

Arruda, H. S., Silva, E. K., Pereira, G. A., Angolini, C. F. F., Eberlin, M. N., Meireles, M. A. A., & Pastore, G. M. (2019). Effects of high-intensity ultrasound process parameters on the phenolic compounds recovery from araticum peel. *Ultrasonics Sonochemistry, 50*, 82-95. DOI: https://doi.org/10.1016/j.ultsonch.2018.09.002

Barrales, F. M., Silveira, P., Barbosa, P. P. M., Ruviaro, A. R., Paulino, B. N., Pastore, G. M., ... Martinez, J. (2018). Recovery of phenolic compounds from citrus by-products using pressurized liquids — An application to orange peel. *Food and Bioproducts Processing, 112*, 9-21. DOI: https://doi.org/10.1016/j.fbp.2018.08.006

Bruno Romanini, E., Misturini Rodrigues, L., Finger, A., Perez Cantuaria Chierrito, T., Scapim, M. R. S., & Scaramal Madrona, G. (2021). Ultrasound assisted extraction of bioactive compounds from BRS Violet grape pomace followed by alginate-Ca^{2+} encapsulation. *Food Chemistry, 338*, 128101. DOI: https://doi.org/10.1016/j.foodchem.2020.128101

Chemat, F., Rombaut, N., Sicaire, A. G., Meullemiestre, A., Fabiano-Tixier, A. S., & Abert-Vian, M. (2017). Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. *Ultrasonics Sonochemistry, 34*, 540-560. DOI: https://doi.org/10.1016/j.ultsonch.2016.06.035

Chukwuma, C. I., Izu, G. O., Chukwuma, M. S., Samson, M. S., Makhafola, T. J., & Erukainure, O. L. (2021). A review on the medicinal potential, toxicology, and phytochemistry of litchi fruit peel and seed. *Journal of Food Biochemistry, 45*(12). DOI: https://doi.org/10.1111/jfbc.13997

Chumsri, P., Chaijan, M., & Panpipat, W. (2021). A comparison of nutritional values, physicochemical features and in vitro bioactivities of Southern Thai short-grain brown rice with commercial long-grain varieties. *International Journal of Food Science and Technology*, *56*(12), 6515-6526. DOI: https://doi.org/10.1111/ijfs.15371

Devequi-Nunes, D., Machado, B. A. S., Barreto, G. D. A., Rebouças Silva, J., Silva, D. F., Rocha, J. L. C., ... Umsza-Guez, M. A. (2018). Chemical characterization and biological activity of six different extracts of propolis through conventional methods and supercritical extraction. *PLoS One*, *13*(12). DOI: https://doi.org/10.1371/journal.pone.0207676

Donkor, O. N., Henriksson, A., Vasiljevic, T., & Shah, N. P. (2006). Effect of acidification on the activity of probiotics in yoghurt during cold storage. *International Dairy Journal*, *16*(10), 1181-1189. DOI: https://doi.org/10.1016/j.idairyj.2005.10.008

Édouard, K. K., & Kouassi, K. C. (2009). Ethnobotanical study of plants used to treat diabetes, in traditional medicine, by Abbey and Krobou people of Agboville (Côte-d'Ivoire). *American Journal of Scientific Research*, *4*, 45-58.

Escher, G. B., Marques, M. B., Carmo, M. A. V., Azevedo, L., Furtado, M. M., Sant'Ana, A. S., ... Granato, D. (2020). Clitoria ternatea L. petal bioactive compounds display antioxidant, antihemolytic and antihypertensive effects, inhibit α-amylase and α-glucosidase activities and reduce human LDL cholesterol and DNA induced oxidation. *Food research international*, *128*, 108763. DOI: https://doi.org/10.1016/j.foodres.2019.108763

Ez zoubi, Y., Fadil, M., Bousta, D., el Ouali Lalami, A., Lachkar, M., & Farah, A. (2021). Ultrasound-Assisted Extraction of Phenolic Compounds from Moroccan Lavandula stoechas L.: Optimization Using Response Surface Methodology. *Journal of Chemistry*, *2021*, 1-11. DOI: https://doi.org/10.1155/2021/8830902

Gou, L., Zhan, Y., Lee, J., Li, X., Lü, Z. R., Zhou, H. M., ... Yang, J. M. (2015). Effects of L-malic acid on alpha-glucosidase: inhibition kinetics and computational molecular dynamics simulations. *Applied biochemistry and biotechnology*, *175*(4), 2232-2245. DOI: https://doi.org/10.1007/s12010-014-1429-6

Guevarra, M. T. B., & Panlasigui, L. N. (2000). Blood glucose responses of diabetes mellitus type II patients to some local fruits. *Asia Pacific Journal of Clinical Nutrition*, *9*(4), 303-308. DOI: https://doi.org/10.1046/j.1440-6047.2000.00159.x

Kessy, H. N. E., Wang, K., Zhao, L., Zhou, M., & Hu, Z. (2018). Enrichment and biotransformation of phenolic compounds from litchi pericarps with angiotensin I-converting enzyme (ACE) inhibition activity. *LWT, 87,* 301-309. DOI: https://doi.org/10.1016/j.lwt.2017.09.003

Khemakhem, I., Ahmad-Qasem, M. H., Catalán, E. B., Micol, V., García-Pérez, J. V., Ayadi, M. A., & Bouaziz, M. (2017). Kinetic improvement of olive leaves' bioactive compounds extraction by using power ultrasound in a wide temperature range. *Ultrasonics Sonochemistry, 34*, 466-473. DOI:https://doi.org/10.1016/j.ultsonch.2016.06.010

Kumar, K., Srivastav, S., & Sharanagat, V. S. (2021). Ultrasound assisted extraction (UAE) of bioactive compounds from fruit and vegetable processing by-products: A review. *Ultrasonics Sonochemistry, 70*, 105325. DOI: https://doi.org/10.1016/j.ultsonch.2020.105325

Lazarjani, M. P., Young, O., Kebede, L., & Seyfoddin, A. (2021). Processing and extraction methods of medicinal cannabis: A narrative review. *Journal of Cannabis Research*, *3*(32), 1-15. DOI: https://doi.org/10.1186/s42238-021-00087-9

Lavelli, V., Sri Harsha, P. S. C., Ferranti, P., Scarafoni, A., & Iametti, S. (2016). Grape skin phenolics as inhibitors of mammalian α-glucosidase and α-amylase – effect of food matrix and processing on efficacy. *Food and Function, 7*(3), 1655-1663. DOI: https://doi.org/10.1039/C6FO00073H

Lim, K. J. A., Cabajar, A. A., Lobarbio, C. F. Y., Taboada, E. B., & Lacks, D. J. (2019). Extraction of bioactive compounds from mango (Mangifera indica L. var. Carabao) seed kernel with ethanol–water binary solvent systems. *Journal of Food Science and Technology*, *56*, 2536-2544. DOI: https://doi.org/10.1007/s13197-019-03732-7

Liu, Z., Du, M., Liu, H., Zhang, K., Xu, X., Liu, K., ... Liu, Q. (2021). Chitosan films incorporating litchi peel extract and titanium dioxide nanoparticles and their application as coatings on watercored apples. *Progress in Organic Coatings*, *151*, 106103. DOI: https://doi.org/10.1016/j.porgcoat.2020.106103

Ma, Y. Q., Chen, J. C., Liu, D. H., & Ye, X. Q. (2009). Simultaneous extraction of phenolic compounds of citrus peel extracts: Effect of ultrasound. *Ultrasonics sonochemistry*, *16*, 57-62. DOI: https://doi.org/10.1016/j.ultsonch.2008.04.012

Morales-Trejo, F., Trujillo-Ramírez, D., Aguirre-Mandujano, E., Lobato-Calleros, C., Vernon-Carter, E. J., & Alvarez-Ramirez, J. (2022). Ultrasound-Assisted Extraction of Lychee (*Litchi chinensis* Sonn.) Seed Starch: Physicochemical and Functional Properties. *Starch - Stärke, 74*(1–2), 2100092. DOI: https://doi.org/10.1002/star.202100092

Muhamed, S. A., Moussa, E. M., Aboasy, N. K., & Gaweesh, Y. Y. (2022). Effect of 1% malic acid spray on diabetes mellitus induced xerostomia: A randomized clinical trial. *Oral Diseases*. DOI: https://doi.org/10.1111/odi.14327

Mukemre, M., Konczak, I., Uzun, Y., & Dalar, A. (2020). Phytochemical profile and biological activities of Anatolian Plantain (Plantago anatolica). *Food Bioscience*, *36*, 100658. DOI: https://doi.org/10.1016/j.fbio.2020.100658

Nipornram, S., Tochampa, W., Rattanatraiwong, P., & Singanusong, R. (2018). Optimization of low power ultrasound-assisted extraction of phenolic compounds from mandarin (Citrus reticulata Blanco cv. Sainampueng) peel. Food Chemistry, *241*, 338-345. DOI: https://doi.org/10.1016/j.foodchem.2017.08.114

Oboh, G., Ademiluyi, A. O., Agunloye, O. M., Ademosun, A. O., & Ogunsakin, B. G. (2018). Inhibitory effect of garlic, purple onion, and white onion on key enzymes linked with type 2 diabetes and hypertension. *Journal of Dietary Supplements*, *16*, 1-14. DOI: https://doi.org/10.1080/19390211.2018.1438553

Padilha, C. V. da S., Miskinis, G. A., de Souza, M. E. A. O., Pereira, G. E., de Oliveira, D., Bordignon-Luiz, M. T., & Lima, M. dos S. (2017). Rapid determination of flavonoids and phenolic acids in grape juices and wines by RP-HPLC/DAD: Method validation and characterization of commercial products of the new Brazilian varieties of grape. *Food Chemistry, 228*, 106-115. DOI: https://doi.org/10.1016/j.foodchem.2017.01.137

Pareek, S. (2016). Nutritional and Biochemical Composition of Lychee (*Litchi chinensis* Sonn.) Cultivars. *Nutritional Composition of Fruit Cultivars,* 395-418. DOI: https://doi.org/10.1016/B978-0-12-408117-8.00017-9

Punia, S., & Kumar, M. (2021). Litchi (*Litchi chinenis*) seed: Nutritional profile, bioactivities, and its industrial applications. *Trends in Food Science & Technology, 108*, 58-70. DOI: https://doi.org/10.1016/j.tifs.2020.12.005

Queiroz, E. R., Abreu, C. M. P., Santos, C. M., & Simão, A. A. (2015). Composição química e fitoquímica das farinhas da casca e da semente de lichias (*Litchi chinensis* Sonn) cultivar "Bengal." *Ciência Rural, 45*(2), 329-334. DOI: https://doi.org/10.1590/0103-8478cr20140106

Ramchandran, L., & Shah, N. P. (2010). Characterization of functional, biochemical and textural properties of synbiotic low-fat yogurts during refrigerated storage. *LWT - Food Science and Technology, 43*(5), 819-827. DOI: https://doi.org/10.1016/j.lwt.2010.01.012

Raspe, D. T., Ciotta, S. R., Zorzenon, M. R. T., Dacome, A. S., Silva, C., Milani, P. G., & Costa, S. C. (2021). Ultrasound-assisted extraction of compounds from Stevia leaf pretreated with ethanol. *Industrial Crops and Products, 172*, 114035. DOI: https://doi.org/10.1016/j.indcrop.2021.114035

Ren, F., Yang, W., Hu, J., Huang, P., Jiao, X. A., & Huang, J. (2021). Feeding Malic Acid to Chickens at Slaughter Age Improves Microbial Safety with Regard to Campylobacter. *Animals*, *11*(7), 1999. DOI: https://doi.org/10.3390/ani11071999

Rodrigues, S., Fernandes, F. A. N., de Brito, E. S., Sousa, A. D., & Narain, N. (2015). Ultrasound extraction of phenolics and anthocyanins from jabuticaba peel. *Industrial Crops and Products*, *69*, 400-407. DOI: https://doi.org/10.1016/j.indcrop.2015.02.059

Rong, S., Zhao, S., Kai, X., Zhang, L., Zhao, Y., Xiao, X., ... Liu, L. (2018). Procyanidins extracted from the litchi pericarp attenuate atherosclerosis and hyperlipidemia associated with consumption of a high fat diet in apolipoprotein-E knockout mice. *Biomedicine and Pharmacotherapy, 97*, 1639-1644. DOI:https://doi.org/10.1016/j.biopha.2017.10.139

Sánchez-Camargo, A. del P., Ballesteros-Vivas, D., Buelvas-Puello, L. M., Martinez-Correa, H. A., Parada-Alfonso, F., Cifuentes, A., ... Gutiérrez, L.-F. (2021). Microwave-assisted extraction of phenolic compounds with antioxidant and anti-proliferative activities from supercritical CO2 pre-extracted mango peel as valorization strategy. *LWT, 137*, 110414. DOI: https://doi.org/10.1016/j.lwt.2020.110414

Saraiva, B. R., Vital, A. C. P., Anjo, F. A., Ribas, J. C. R., & Matumoto Pintro, P. T. (2019). Effect of yerba mate (*Ilex paraguariensis* A. St.-Hil.) addition on the functional and technological characteristics of fresh cheese. *Journal of Food Science and Technology, 56*(3), 1256-1265. DOI: https://doi.org/10.1007/s13197-019-03589-w

Sharayei, P., Azarpazhooh, E., Zomorodi, S., & Ramaswamy, H. S. (2019). Ultrasound assisted extraction of bioactive compounds from pomegranate (*Punica granatum* L.) peel. *Lwt*, *101*, 342-350. DOI: https://doi.org/10.1016/j.lwt.2018.11.031

Silva, C., Garcia, V. S., & Franciscato, L. S. (2016). Extração assistida por ultrassom de compostos bioativos das cascas de lichia (*Litchi chinensis* Sonn.). *RECEN-Revista Ciências Exatas e Naturais, 18*, 81-96.

Singleton, V. L., & Rossi, J. A. (1965). Colorimetry of Total Phenolics with Phosphomolybdic-Phosphotungstic Acid Reagents. *American Journal of Enology and Viticulture, 16*(3), 144-158. Retrieved from http://www.ajevonline.org/content/16/3/144.abstract

Sousa, A. D., Maia, A. I. V., Rodrigues, T. H. S., Canuto, K. M., Ribeiro, P. R. V., de Cassia Alves Pereira, R., ... Brito, E. S. (2016). Ultrasound-assisted and pressurized liquid extraction of phenolic compounds from Phyllanthus amarus and its composition evaluation by UPLC-QTOF. *Industrial Crops and Products, 79*, 91-103. DOI: https://doi.org/10.1016/j.indcrop.2015.10.045

Yao, P., Gao, Y., Simal-Gandara, J., Farag, M. A., Chen, W., Yao, D., ... Wang, Y. (2021). Litchi (*Litchi chinensis* Sonn.): a comprehensive review of phytochemistry, medicinal properties, and product development. *Food & Function, 12*(20), 9527-9548. DOI: https://doi.org/10.1039/D1FO01148K

Zhao, L., Wang, K., Wang, K., Zhu, J., & Hu, Z. (2020). Nutrient components, health benefits, and safety of litchi (*Litchi chinensis* Sonn.): A review. Comprehensive *Reviews in Food Science and Food Safety, 19*(4), 2139-2163. DOI: https://doi.org/10.1111/1541-4337.12590

Živković, J., Šavikin, K., Janković, T., Ćujić, N., & Menković, N. (2018). Optimization of ultrasound-assisted extraction of polyphenolic compounds from pomegranate peel using response surface methodology. *Separation and Purification Technology*, *194*, 40-47. DOI: https://doi.org/10.1016/j.seppur.2017.11.032