

Article

Unveiling the Antidiabetic Potential of *Parmentiera edulis*: From Polyphenols to Molecular Interaction

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Abstract

Background/Objectives: *Parmentiera edulis*, traditionally called “cuajilote”, is a medicinal plant used to treat infections, indigestion, kidney problems, and diabetes. Although all parts of the plant are utilized, there is little scientific evidence available on its phytochemical composition to explain its medicinal properties. This exploratory study aims to characterize and identify phytochemicals in hydromethanolic extracts of leaves, stems, and fruits; determine their antioxidant capacity, and evaluate in vitro and in silico inhibition of α -glucosidase and α -amylase, enzymes involved in glycemic control. **Methods:** Total phenolic and flavonoid contents were determined, and antioxidant capacity was evaluated using different assays. Phenolic acids were tentatively identified by UPLC-qTOF-MS/MS. Enzyme inhibition assays against α -glucosidase and α -amylase were performed in vitro, and molecular docking was used to explore enzyme–ligand interactions. **Results:** The total phenolic content was significantly higher in the fruit (552.9 mg GAE/100 g dw), while flavonoids were more abundant in leaves (119.84 mg QE/100 g dw). Antioxidant capacity varied among plant parts, depending on the assay used. Caffeic, chlorogenic, coumaric, ferulic, gallic, and quinic acids were identified. The highest concentrations were observed for chlorogenic, ferulic, and quinic acids. Among the analyzed parts, leaf extracts showed the most potent inhibitory effect on α -glucosidase (IC₅₀: 0.85 mg/mL) and α -amylase (IC₅₀: 1.38 mg/mL). Molecular docking revealed that chlorogenic and quinic acids interacted with the catalytic sites of α -amylase (Glu233, Asp197, and Asp300), whereas in α -glucosidase, interactions were observed at allosteric sites. **Conclusions:** These results suggest that *Parmentiera edulis* possesses bioactive compounds that could explain its therapeutic use.

Keywords: *Parmentiera edulis*; cuajilote; medicinal plant; plant extract; phytochemical analysis; molecular docking; α -glucosidase inhibition; α -amylase inhibition; bioactive compounds

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1. Introduction

Diabetes mellitus is one of the most prevalent noncommunicable diseases worldwide and represents a major public health concern. According to the International Diabetes Federation, approximately 463 million adults were living with diabetes in 2019, a number projected to rise to 700 million by 2045 [1]. This metabolic disorder manifests as type 1 when insulin production is inadequate and as type 2 when insulin resistance is present; the latter accounts for up to 95% of cases [2,3]. For the treatment of diabetes, the most used pharmacological approaches include dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose cotransporter-2 (SGLT2) inhibitors, thiazolidinediones, sulfonylureas, meglitinides, biguanides, and α -glucosidase inhibitors. However, their prolonged use can generate some adverse effects, such as taste disturbances, diarrhea, abdominal distension, flatulence, risk of hypoglycemia, weight gain or fluid retention, and other abnormalities, in some cases, high economic cost [4]. One of the primary alternatives is the use of medicinal plants, which are defined as those used for therapeutic purposes, either for their bioactive compounds or as a basis for drug synthesis. They generally represent a lower-cost option and, in some cases, have fewer adverse effects [5]. Around 80% of the world's population is estimated to use medicinal plants as their main therapeutic option, mainly in the form of extracts [6]. Compounds from medicinal plants with antidiabetic properties, such as phenolic compounds, flavonoids, alkaloids, carotenoids, saponins, and tannins, have been shown to increase insulin secretion or decrease glucose absorption [7]. Mexico, recognized for its exceptional biodiversity, is home to around 4000 species of medicinal plants. However, only 5% have been the subject of formal chemical, pharmacological, and biomedical studies [8]. In Central America, *Parmentiera edulis* (*P. edulis*), commonly known as “cuajilote”, is used empirically to treat kidney disease, infections, indigestion, and diabetes, among other conditions. All plant parts, such as fruits, leaves, roots, bark, stems, and flowers, are used [9]. However, there are few studies on its phytochemical composition, which could explain its therapeutic attributes. Previous studies on *P. edulis* have reported hypoglycemic effects from fruit extracts, as well as preliminary phytochemical screenings indicating the presence of phenolic compounds, flavonoids, alkaloids, saponins, and other metabolite classes [10–12]. In this context, available studies have mainly focused on individual plant parts and have addressed bioactive effects in isolation, while information on the antioxidant potential and the tentative characterization of bioactive constituents of *P. edulis* remains scarce. Phenolic acids constitute a widely distributed group of plant secondary metabolites and are consistently associated with antioxidant and antidiabetic biological activities. Furthermore, they serve as metabolic precursors for other classes of bioactive compounds [13]. In this study, we focused on fruits, leaves, and stems because these are the most reported and traditionally used parts of the plant. To the best of our knowledge, this is the first integrative and exploratory study on *P. edulis* that combines phytochemical screening, quantification of antioxidant capacity, phenolic acid profiling by UPLC-qTOF-MS/MS, enzymatic inhibition (α -glucosidase and α -amylase), and molecular docking analysis. This research seeks to contribute new knowledge of the pharmacological potential of this underexplored plant, support its traditional use, and promote the revalorization of *P. edulis* as a valuable source of bioactive natural products.

2. Materials and Methods

2.1. Plant Material

Fifteen *Parmentiera edulis* trees were monitored for 6 months (July–December) in Cuiliacán, Sinaloa. The plants were grown under domestic backyard conditions and without agronomic management practices. Subsequently, three trees exhibiting fruiting stages were selected from this group in January 2021. The identification was carried out by the

biologists C. Cortes and A. Servin in the herbarium of the Botanical Garden of Culiacán, “HJBC”, under catalog number ID: 1629. Leaves, fruits, and stems were collected and immediately transported to the Laboratory of Functional Foods and Nutraceuticals at the Food and Development Research Center (CIAD), Culiacán unit. Subsequently, *P. edulis* leaves, fruits, and stems were washed with a 50 ppm chlorine solution, and a selection was made to exclude any damaged or physical defects; fruits were harvest at the physiological maturity stage, characterized by full development and the initial transition of peel color from green to yellow, and leaves were collected as fully expanded, healthy leaves from different positions, excluding young shoots. All selected material was freeze-dried (Labconco FreeZone Bulk Tray Dryer, Kansas City, MO, USA) under the operating conditions recommended for plant material (−50 °C, 0.080 mbar).

2.2. Phytochemical Screening

Extractions with hexane, methanol, and water were performed for the qualitative phytochemical screening. Freeze-dried samples (fruit, leaves, and stems) were previously milled (IKA M20 laboratory mill, Wilmington, NC, USA). Subsequently, 0.5 g of the milled samples was weighed and suspended in 20 mL of the respective solvent. Then, a stirring process was carried out for 24 h at 200 rpm at room temperature. The mixture was centrifuged (10,000 rpm, 4 °C, 15 min) to recover the supernatant for analysis. Finally, the presence [+] or absence [−] for various secondary metabolites was determined through specific qualitative phytochemical tests, including alkaloids (Dragendorff, Wagner's and Mayer's tests), terpenes (Liebermann–Burchard and Salkowski tests), flavonoids (Shinoda test), tannins (Ferric chloride test), coumarins (Sodium hydroxide test), and saponins (Foam test) [14,15]

2.3. Phytochemical Assays

2.3.1. Extraction

For the preparation of extracts from the different parts of *P. edulis*, 80% methanol was selected due to its intermediate polarity, which facilitates the solubilization of phenolic compounds of interest in this research [16]. To extract leaf, fruit, and stem from *P. edulis*, 0.5 g of the previously lyophilized and milled (IKA M20 laboratory mill, Wilmington, NC, USA) sample was mixed with 10 mL of 80% methanol. Afterward, the mixture was stirred for 24 h at 200 rpm at room temperature and then centrifuged (10,000 rpm, 4 °C, 15 min) to recover the supernatant, which was stored at −20 °C for the determination of total phenolic content, total flavonoid content, antioxidant capacity, and chromatographic analyses by UPLC-qTOF-MS/MS.

2.3.2. Total Phenolic Content

Total phenolic content (TPC) was determined using the Folin–Ciocalteu method described by Swain and Hillis [17], with slight modifications. Briefly, 10 µL of extract was mixed with 230 µL of distilled water and 10 µL of Folin–Ciocalteu reagent, and the mixture was incubated at room temperature for 3 min. Then, 25 µL of 4 N sodium carbonate (Na_2CO_3) was added, and the mixture was incubated for 2 h at room temperature. Afterward, the absorbance at 725 nm was measured using a microplate reader (Synergy HT, BioTek, Winooski, VT, USA). Results were expressed as mg gallic acid equivalents (GAE)/100 g dry weight (dw). All measurements were performed in triplicate ($n = 3$).

2.3.3. Total Flavonoid Content

Total flavonoid content (TFC) was determined following the methodology described by Ghasemi, et al. [18], with slight modifications. The assay was carried out by adding 10

μL of the extract, 250 μL of distilled water, 10 μL of aluminum chloride (AlCl_3 , 10%), and 10 μL of potassium acetate ($\text{CH}_3\text{CO}_2\text{K}$, 1 M). The mixture was incubated for 30 min at room temperature. The absorbance at 415 nm was then measured using a microplate reader (Synergy HT, BioTek, Winooski, VT, USA). The results were expressed as mg of quercetin equivalents (QE)/100 g dw. All measurements were performed in triplicate ($n = 3$).

2.3.4. Phenolic Acid Profile by UPLC-qTOF-MS/MS

Among the vast diversity of plant secondary metabolites, phenolic acids represent a structurally defined and widely distributed group with recognized functional relevance in biological activity, making them suitable for an initial level of phytochemical characterization. Therefore, the UPLC-QToF-MS/MS analysis was designed as a phenolic acid-focused approach, enabling initial phytochemical identification. The tentative identification and quantification of phenolic acids in leaf, fruit, and stem extract of *P. edulis* were carried out using an Acquity H-Class UPLC system (Waters Corp., Milford, MA, USA) coupled to a G2-XS QToF mass analyzer equipped with electrospray ionization (ESI). Instrument settings were as follows: cone voltage 30 V, capillary voltage 1.5 kV, desolvation gas flow 800 L/h at 500 °C, and collision energy of 10 V. For chromatographic separation, an Acquity UPLC BEH C18 column (1.7 μm 2.1 $\times$ 100 mm) was used and maintained at 40 °C, with a 1 μL injection volume. The mobile phase consisted of a binary system: acidified water with 0.1% formic acid (phase A) and acetonitrile (phase B), with a flow of 0.3 mL/min, with the following gradient elution: 0 min, 95% A; 5 min, 70% A; 9 min, 30% A; 10 min, 0% A; 10.5 min, 0% A; 11 min, 95% A; and 11.5 min, 95% A, based on the method described in [19], with modifications. For the quantification of phenolic acids, external calibration curves of caffeic acid, chlorogenic acid, *p*-coumaric acid, ferulic acid, gallic acid, and quinic acid (Sigma-Aldrich, Burbank, CA, USA) were used. Chromatographic Peaks were tentatively identified by comparison with standards based on retention time, mass-to-charge ratio, and fragmentation patterns. Results were expressed as $\mu\text{g/g}$ dw. All measurements were performed in triplicate ($n = 3$).

2.3.5. DPPH Antioxidant Capacity

The antioxidant capacity was determined using the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging capacity method as described by Brand-Williams, et al. [20], with slight modifications. Briefly, 20 μL of the extract was mixed with 280 μL of a DPPH solution (100 μM) in a 96-well microplate and incubated for 30 min at room temperature. Absorbance was measured at 540 nm using a microplate reader (Synergy HT, BioTek, USA). A blank sample was used to correct the absorbance of the extracts before antioxidant capacity calculations. Results were expressed as the extract concentration (mg extract/mL) required to inhibit 50% of the radical activity (IC_{50}). All measurements were performed in triplicate ($n = 3$).

2.3.6. FRAP Antioxidant Capacity

The antioxidant capacity was determined by the FRAP (Ferric Reducing Antioxidant Power) assay, following the methodology described by Benzie and Strain [21], with slight modifications. The assay was carried out with a mixture of 30 μL of extract and 110 μL of FRAP reagent prepared in a 10:1:1 ratio ($v/v/v$) of the solutions: 300 mM sodium acetate buffer, pH 3.6, 10 mM 2,4,6-tripyridyl-s-triazine (TPTZ), and 20 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, respectively. Afterward, the mixture was incubated at room temperature for 5 min. Absorbance was measured at 630 nm using a microplate reader (Synergy HT, BioTek, Winooski, VT, USA). A blank sample was used to correct the absorbance of the extracts prior to antioxidant capacity calculations. Results were expressed as the extract concentration (mg

extract/mL) required to achieve 50% of the maximal ferric reducing response (IC₅₀). All measurements were performed in triplicate (n = 3).

2.3.7. ORAC Antioxidant Capacity

The Oxygen Radical Absorbance Capacity (ORAC) assay was performed following the method described by Huang, et al. [22], with slight modifications. A reaction mixture containing 25 µL of extract or phosphate buffer (blank), 25 µL of 75 mM phosphate buffer (pH 7.4), and 200 µL of 0.106 µM fluorescein was incubated at 37 °C for 15 min. After incubation, 75 µL of 0.8 M AAPH (2,2'-azobis (2-amidino-propane) dihydrochloride) was added to initiate the reaction. Fluorescence was measured every 70 s for 70 min at 485 nm (emission) and 580 nm (excitation) using a microplate reader (Synergy HT, BioTek, Winoosky, VT, USA). Antioxidant capacity was calculated from the area under the fluorescence decay curve (AUC) and expressed as µmol Trolox equivalent (TE)/100 g dry weight (dw), based on a calibration curve of Trolox ranging from 6.25 to 125 µmol TE/g. Net AUC values were calculated by subtracting the corresponding blank. All measurements were performed in triplicate (n = 3).

2.4. Enzymatic Assays

2.4.1. Inhibition of α-Glucosidase

The α-glucosidase inhibitory activity was evaluated following the procedure described by Cuevas-Juárez et al. [23], with slight modifications. In 96-well microplates, 50 µL of extracts or phosphate buffer (blank, 0.1 M, pH 6.9) with 100 µL of α-glucosidase from *Saccharomyces cerevisiae* (0.6 U/mL) in phosphate buffer (0.1 M, pH 6.9) were incubated at 37 °C for 10 min. Then, 50 µL of 3 mM p-nitrophenyl-α-D-glucopyranoside (pNPG) prepared in the same buffer was added, and the mixture was incubated again at 37 °C for 10 min. Enzyme activity was assessed by measuring the absorbance of the released P-nitrophenol at 405 nm using a microplate reader (Synergy HT, BioTek, Winoosky, VT, USA). Acarbose was used as a positive control at a fixed concentration (50 µL, 1 mg/mL) to validate assay performance. The percentage inhibition was calculated using the following equation: $Inhibition(\%) = [(Ac - Ae) / Ac] \times 100$; where Ac is the absorbance of the control (without extract), and Ae is the absorbance in the presence of the extract. A blank sample was considered to correct the absorbance of the extracts prior to inhibition calculations. For each extract of *P. edulis*, the half maximal inhibitory concentration (IC₅₀) was determined. All measurements were performed in triplicate (n = 3).

2.4.2. Inhibition of α-Amylase

The Inhibition of α-amylase was performed according to the methodology described in Worthington Enzyme Manual [24], with some modifications. The reaction consisted of 50 µL of the extract or phosphate buffer (blank) mixed with 50 µL of porcine pancreas α-amylase (13 U/mL), prepared in phosphate-buffered saline (PBS, pH 7.0). The mixture was incubated for 10 min at 37 °C. Subsequently, 50 µL of soluble starch solution (1% w/v) was added to initiate the reaction, and the mixture was incubated for 10 min at 37 °C. Immediately, 1 mL of 3,5-dinitrosalicylic acid (DNS) was added, and the mixture was heated at 85 °C for 15 min. Subsequently, the tubes were cooled in an ice bath and diluted with 1 mL of distilled water. 250 µL of the mixture was placed in a 96-well microplate for reading. The enzyme activity was determined by measuring the absorbance of the DNS reagent at 540 nm using a microplate reader (Synergy HT, BioTek, Winoosky, VT, USA). Acarbose was used as a positive control at a fixed concentration (50 µL, 1 mg/mL) to validate assay performance. The percentage inhibition was calculated using the following equation: $Inhibition(\%) = [(Ac - Ae) / Ac] \times 100$; where Ac is the absorbance of the control (without extract), and Ae is the absorbance in the presence of the extract. A blank

sample was used to correct the absorbance of the extracts prior to inhibition calculations. For each extract of *P. edulis*, the half maximal inhibitory concentration (IC₅₀) was determined. All measurements were performed in triplicate (n = 3).

2.5. Molecular Docking

Blind molecular docking studies were performed using the AutoDock Tool v1.5.7 software encompassing the entire protein surface of the enzymes α -amylase and α -glucosidase. Ferulic, chlorogenic, and quinic acids were selected based on their abundance in the different *P. edulis* parts. The structures of these phenolic acids were designed using ChemDraw v16. The 3D optimization was performed in Avogadro v1.2.0 using the MMFF94 method to obtain the minimum energy conformation. Polar hydrogens and Gasteiger charges were assigned to the ligands with AutoDock Tool v1.5.7. Ligand protonation states were assigned using default AutoDock Tools settings. The crystallized structures of α -amylase (PDB:5E0F) and α -glucosidase (PDB:5NN8) with resolutions of 1.40 and 2.45 Å were downloaded from the RCSB protein data bank (<https://www.rcsb.org>). The selection of these enzyme models was based on defined structural and functional criteria, including experimentally resolved active sites with conserved catalytic residues and their extensive use as reference structures in docking studies of digestive enzyme inhibitors. Ligands and water molecules were removed in Chimera v1.18, and polar hydrogens and the Kollman charges were assigned for further analysis. In the case of α -amylase, the grid box center was set at −8.374, 21.617, and −18.886 Å (x, y, and z) with a grid of 126, 126, in each direction (x, y, and z). While α -glucosidase, the grid site was set at 1.346, −26.507, and 86.422 Å (x, y, and z) with a grid of 126, 126, and 126 points (x, y, and z) and a 0.375 Å spacing in both cases. Coupling calculations were performed using a Lamarckian genetic algorithm to search for the conformation with the lowest binding energy. The conditions for the analysis consisted of 270,000 generations, a genetic mutation rate of 0.02, and a crossover rate of 0.8. The docking results were reported as binding energies (Kcal/mol) and an interaction profile of the ligands with the protein site, specifically the lower-energy conformations. The docking analysis was used to support the discussion of relative binding behavior and interaction patterns of the major phenolic acids identified in *P. edulis*. These results were examined using Accelrys, Discovery, and Studio Visualizer [25,26].

2.6. Statistical Analysis

Statistical analysis was performed using a one-way analysis of variance (ANOVA) with three levels (plant parts: leaf, stem, and fruit) and three replications. The evaluated variables included total phenolic content, total flavonoid content, antioxidant capacity, phenolic acid profiles, and enzyme inhibition (α -glucosidase and α -amylase). Differences among means were evaluated using Tukey's test at a significance level of $\alpha = 0.05$. Data were analyzed using Minitab version 17.

3. Results

3.1. Phytochemical Screening

The results of the phytochemical screening are shown in Table 1. Alkaloids were not detected in any part of the *P. edulis*. In contrast, terpenes were detected in all analyzed tissues, and in leaves, they were identified in all three solvents. Flavonoids were identified in the methanol and water solvents in all parts of the plant. Likewise, tannins and coumarins were found in the fruit and stem, while saponins were present in all the parts analyzed. Overall, the qualitative analysis revealed the presence of different metabolites.

Table 1. Results of phytochemical screening.

Plant part	Solvent	Alkaloids	Terpenes	Flavonoids	Tannins	Coumarins	Saponins
Fruit	Hexane	–	+	–	–	–	–
	Methanol	–	–	+	+	+	+
	Water	–	–	+	+	+	+
Leaf	Hexane	–	+	–	–	–	–
	Methanol	–	+	+	–	–	+
	Water	–	+	+	–	–	+
Stem	Hexane	–	–	–	–	–	–
	Methanol	–	+	–	+	+	+
	Water	–	+	–	+	+	+

All tests were performed in triplicate; presence [+], absence [–]. Alkaloids were detected using Dragendorff, Mayer, and Wagner tests; terpenes by Liebermann–Burchard and Salkowski tests; flavonoids by Shinoda test; tannins by Ferric chloride test; coumarins by sodium hydroxide test; saponins by foam test.

3.2. Total Phenolic Content

The total content of phenolic compounds was highest in the fruit (552.9 mg GAE/100 g dw), followed by stem (344.8 mg GAE/100 g dw) and leaf (277.9 mg GAE/100 g dw) (Figure 1a). Significant differences ($p < 0.05$) were found among plant parts. The fruit exhibited a total phenolic content approximately twice that of the leaves and 1.5 times that of the stem, indicating a precise distribution of phenolic compounds among the plant parts analyzed.

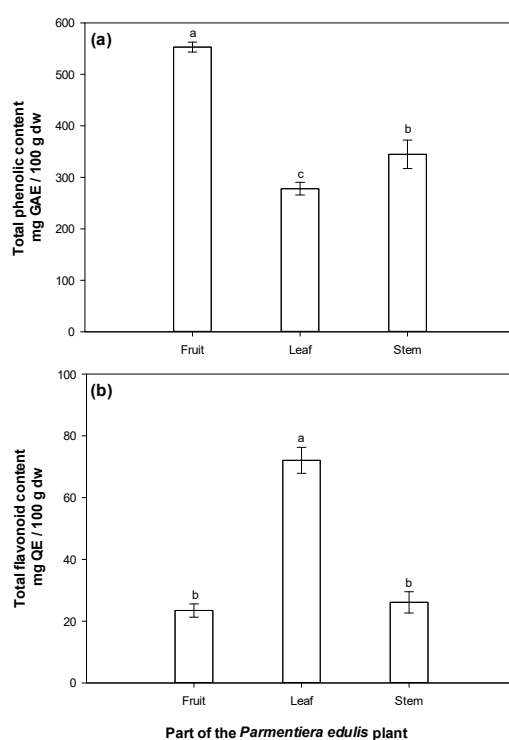


Figure 1. (a) Total phenolic content ($n = 3 \pm \text{SD}$); (b) Total flavonoid content ($n = 3 \pm \text{SD}$). Different letters in the error bars represent significant differences according to the Tukey test ($\alpha < 0.05$). GAE: Equivalents of gallic acid, QE: Equivalents of quercetin.

3.3. Total Flavonoid Content

Figure 1b shows the total content of flavonoids in the different parts of *P. edulis*. The leaf exhibited the highest content (72.06 mg QE/100 g dw, $p < 0.05$), approximately three times higher than that of the stem (26.10 mg QE/100 g dw) and fruit (23.43 mg QE/100 g dw). Therefore, the leaf presented significant differences ($p < 0.05$) compared to the stem and fruit. Leaf extracts showed the highest levels of flavonoids, with values approximately three times higher than those observed in the stem and fruit.

3.4. Antioxidant Capacity ORAC, DPPH, and FRAP

The antioxidant capacity of *P. edulis* extracts was evaluated using ORAC, DPPH, and FRAP assays, and the results are shown in Table 2, revealing differences among plant parts across the assay methods. The fruit had the highest antioxidant capacity, as measured by the ORAC assay, with values at least twice those of the stem and leaf. All the plant parts analyzed showed significant differences ($p < 0.05$). The results of the antioxidant capacity, determined by the DPPH method, showed that the lowest IC₅₀ was observed in the leaves, followed by the stems and the fruit. All parts of the *P. edulis* plant showed significant differences ($p < 0.05$). The ferric reducing antioxidant power (FRAP) assay showed the highest antioxidant capacity (lowest IC₅₀) in the stem (0.15 mg/mL), followed by the leaf and fruit. Significant differences ($p < 0.05$) were observed among all plant parts. Generally, different plant parts exhibited varying antioxidant capacities, depending on the assay used.

Table 2. Antioxidant capacity of the different parts of the *Parmentiera edulis* plant.

Part of the Plant	ORAC	DPPH	FRAP
Fruit	34,646.00 ± 895.69 ^a	5.90 ± 0.03 ^a	0.60 ± 0.008 ^a
Leaf	12,806.51 ± 35.66 ^c	1.78 ± 0.12 ^c	0.17 ± 0.004 ^b
Stem	17,404.27 ± 875.84 ^b	3.49 ± 0.15 ^b	0.15 ± 0.002 ^c

Results were expressed as mean ± SD (n = 3), with the following units: ORAC: µmol ET/100 g dw; DPPH: IC₅₀ mg extract/mL; FRAP: IC₅₀ mg extract/mL. Different letters in the same column represent significant differences according to the Tukey test ($\alpha < 0.05$).

3.5. Phenolic Acid Profile by UPLC-qTOF-MS/MS

Phenolic acids in *P. edulis* were tentatively identified by comparing retention times and molecular ions with those of standards and by mass spectral analysis using the Mass Bank database of North America (MoNA). Representative chromatograms and mass spectra for these identifications are provided in the Supplementary Material (Figures S1–S3). Six compounds of interest were tentatively identified in the fruit, leaves, and stem of *P. edulis*, as analyzed (Table 3), which consisted of ferulic, chlorogenic, caffeic, and coumaric acids (hydroxycinnamic acids), gallic acid (hydroxybenzoic acid), and quinic acid (cyclohexanecarboxylic acid). Statistically significant differences ($p < 0.05$) were observed among plant parts. In general, phenolic acid concentrations showed a tissue-dependent distribution pattern. The highest concentrations of phenolic acids were found in the fruit. Hydroxycinnamic acids represented the predominant class in all parts of the plant, with chlorogenic acid showing the highest concentration in both fruit and leaf extracts. In the fruit, chlorogenic acid showed the highest concentration (378.09 µg/g dw), followed by ferulic (280.04 µg/g dw) and quinic (273.54 µg/g dw) acids. Likewise, in the stem, ferulic (55.09 µg/g dw), chlorogenic (23.93 µg/g dw), and quinic (35.24 µg/g dw) acids were the most abundant. In the leaf, chlorogenic acid represented a markedly higher concentration (526.49 µg/g dw), whereas the remaining phenolic acids were present at substantially lower levels. From a general perspective, these results indicate that the phenolic acid

profile of *P. edulis* varies among plant parts, both in terms of abundance and relative composition.

Table 3. Phenolic acids in extracts from different parts of the *Parmentiera edulis* plant.

Compound Name	Type of Compound	Exact Mass	[M-H] ⁻	Identified Mass	* RT (min)	Part of the <i>Parmentiera edulis</i> (µg/g dw)		
						Fruit	Leaf	Stem
Quinic acid	Cyclohexanecarboxylic acid	192.063	191.063	191.063	0.87	273.54 ± 9.81 ^a	0.06 ± 0.04 ^c	35.24 ± 0.75 ^b
Ferulic acid	Hydroxycinnamic acid	194.057	193.057	193.057	0.88	280.04 ± 14.36 ^a	5.85 ± 1.01 ^c	55.09 ± 3.15 ^b
Gallic acid	Hydroxybenzoic acid	170.021	169.021	169.021	1.02	1.30 ± 0.02 ^a	0.29 ± 0.03 ^b	1.13 ± 0.39 ^a
Chlorogenic acid	Hydroxycinnamic acid	354.098	353.098	353.084	3.60	378.09 ± 23.22 ^b	526.49 ± 19.70 ^a	23.93 ± 2.83 ^c
Caffeic acid	Hydroxycinnamic acid	180.042	179.042	179.042	4.10	1.50 ± 0.02 ^a	0.25 ± 0.05 ^c	0.37 ± 0.02 ^b
Coumaric acid	Hydroxycinnamic acid	164.047	163.047	163.047	5.00	2.33 ± 0.10 ^a	0.08 ± 0.01 ^c	0.29 ± 0.03 ^b

* RT: retention time; Different letters in the same row for each acid indicate significant differences between the means ($n = 3 \pm \text{SD}$) for the Tukey test ($\alpha < 0.05$).

3.6. Inhibition of α -Glucosidase

The α -glucosidase inhibitory activity of various extracts from the *P. edulis* plant is presented in Table 4. Differences were observed in the inhibition capacity of the different parts of the plant, with the leaf extract showing the most potent inhibition. The leaf extract exhibited the lowest IC₅₀ (0.85 mg/mL), which was significantly lower ($p < 0.05$) than those obtained for the fruit and stem extracts. In contrast, the fruit and stem extracts exhibited markedly lower inhibitory activity, with similar IC₅₀ values of 22.66 mg/mL and 23.64 mg/mL, respectively, and no statistically significant differences between them.

Table 4. Inhibitory effect of the different parts of the *Parmentiera edulis* plant on α -glucosidase and α -amylase.

Part of the Plant	α -Glucosidase	α -Amylase
Fruit	22.66 ± 0.62 ^a	20.61 ± 2.18 ^a
Leaf	0.85 ± 0.04 ^b	1.38 ± 0.01 ^c
Stem	23.64 ± 0.66 ^a	7.23 ± 0.39 ^b
% inhibition of acarbose	53.90 ± 3.8%	65.12 ± 0.5%

Results were expressed as mean ± SD ($n = 3$), with the following units: α -glucosidase: IC₅₀ (mg/mL); α -amylase: IC₅₀ (mg/mL). Different letters in the same column represent significant differences according to the Tukey test ($\alpha < 0.05$); Values for acarbose correspond to the inhibition observed at a fixed concentration (1 mg/mL).

3.7. Inhibition of α -Amylase

The inhibitory effects of *P. edulis* extracts against α -amylase are shown in Table 4. Significant differences were observed among all plant parts analyzed. The leaf extract exhibited the most potent inhibitory activity, showing the lowest IC₅₀ value (1.38 mg/mL), followed by the stem (7.23 mg/mL) and fruit (20.61 mg/mL) extracts. Thus, inhibitory activity decreased in the order leaf > stem > fruit.

3.8. Molecular Docking

After phytochemical characterization and in vitro inhibition studies, a molecular docking analysis was performed to evaluate whether the major compounds identified in *P. edulis*, ferulic, chlorogenic, and quinic acids, could interact with α -amylase (PDB: 5E0F) and α -glucosidase (PDB: 5NN8). The docking analysis focused on binding energies and interaction profiles to identify ligand-enzyme interaction sites. The docking results concerning the binding energy for α -amylase were -6.4 , -6.4 , and -8.5 kcal/mol (Table 5). Although all evaluated compounds interacted with α -amylase, quinic and chlorogenic acids interacted at the enzyme's active site, similar to acarbose (Figure 2), with chlorogenic acid showing the highest affinity, comparable to that of acarbose (-9.0 kcal/mol). Ferulic acid only presented interactions with allosteric site residues, specifically Arg252, Ser289, Pro332, and Arg421, through conventional and carbon-hydrogen bonding (Figure 2). On the other hand, quinic acid was found bound to catalytic and biologically relevant residues by polar hydrogen, and hydrophobic bonds, these interactions were between H-O $\cdots$ H-N Arg195 (2.54 Å), O-H $\cdots$ O=C Asp197 (2.12 Å), O-H $\cdots$ O=C Glu233 (2.72 Å), C $\cdots$ Ring A Trp59 (4.5 Å), C $\cdots$ Ring B Trp59 (5.18 Å) and C $\cdots$ Ring A Tyr62 (5.00 Å) (Figure 3a). Similarly, chlorogenic acid was also bound to catalytic and biological relevance residues with interactions like O-H $\cdots$ O=C Glu233 (1.92 Å), C=O $\cdots$ H-N His101 (2.63 Å), O-H $\cdots$ O=C Gln63 (2.3 Å), Ring A $\cdots$ Ring A Trp59 (4.05 Å), Ring A $\cdots$ Ring B Trp59 (3.96 Å) (Figure 3b). Although quinic acid presented two interactions in the active site with catalytic residues (Asp197 and Glu233), chlorogenic acid showed the highest affinity energy with only one interaction in the active site (Glu233). The bond distance with Glu233 in chlorogenic acid (1.92 Å) was less than that of quinic acid (2.72 Å).

The binding energy results for the analyzed compounds, as determined by α -glucosidase (Table 5), ranged from -5.8 to -7.9 kcal/mol, within the same range as that found for acarbose (-7.1 kcal/mol). The interaction profile obtained for α -glucosidase revealed that all evaluated compounds interacted only at allosteric sites, indicating a distinct mechanism of action compared to acarbose (Figure 4). Analyzing the interaction of the evaluated compounds, quinic acid presented a smaller number of interactions (two) than ferulic acid (eight), and this compound presented fewer interactions than chlorogenic acid (ten). This information corresponds to the binding energy values (-5.8 , -6.5 , -7.9 kcal/mol). Specifically, quinic acid presented polar hydrogen interactions between O-H $\cdots$ O=C Ile823 (2.32 Å) and O-H $\cdots$ O=C Arg854 (2.68 Å) (Figure 5a). Ferulic acid presented polar hydrogen, carbon hydrogen, electrostatic and hydrophobic bonds between H-O $\cdots$ H-N Arg725 (2.33 Å), O-H $\cdots$ O-OC Glu748 (2.13 Å), O-H $\cdots$ O=C Glu856 (2.43 Å), CH₃-O $\cdots$ H₂-C Gly855 (3.62 Å), Ring A $\cdots$ O-OC Glu856 (4.29 Å), Ring A $\cdots$ Ring A His708 (4.97 Å), O-H₃C $\cdots$ C- H₃ Ala749 (4.00 Å) and O-H₃C $\cdots$ ring A Tyr822 (4.60 Å) (Figure 5b). Furthermore, chlorogenic acid presented polar hydrogen, carbon hydrogen, electrostatic and hydrophobic bonds between C=O $\cdots$ H-N Arg725 (2.40 and 1.96 Å), O-H $\cdots$ O=C Ile823 (2.48 Å), O-H $\cdots$ O=C Arg854 (2.86 Å), O-H $\cdots$ O-OC Glu748 (1.86 and 2.74 Å), OH $\cdots$ H₂-C Pro825 (3.53 Å), Ring A $\cdots$ N-Ring A His708 (4.56 Å), Ring A $\cdots$ O-OC Glu856 (4.90 Å) and Ring A $\cdots$ Ring A His708 (4.55 Å) (Figure 5c).

Table 5. Molecular docking analysis of ferulic, quinic, and chlorogenic acids against α -glucosidase and α -amylase.

Compounds Evaluated	EU (Kcal/mol) α -Glucosidase	Interactions with α -Glucosidase	EU (Kcal/mol) α -Amylase	Interactions with α -Amylase
Ferulic acid	-6.5	Hydrogen bond: Arg725, Glu478, Glu856 Carbon-hydrogen bond: Gly855	-6.4	Hydrogen bond: Arg252, Arg421. Carbon-hydrogen bond: Ser289, Pro332

		Electrostatic bond: Glu856 Hydrophobic bond: His708, Ala749, Tyr822			
Quinic acid	−5.8	Hydrogen bond: Ile823, Arg854	−6.4	Hydrogen bond: Arg195, Asp197, Glu233. Hydrophobic bond: Trp59, Tyr69	
Chlorogenic acid	−7.9	Hydrogen bond: Ile823, Arg854, Glu748, Arg725 Carbon-hydrogen bond: Pro825 Electrostatic bond: His708, Glu748 Hydrophobic bond: His708	−8.5	Hydrogen bond: Gln63, His101, Glu233. Hydrophobic bond: Trp59. Hydrogen bond: Trp59, Gln63, His101, Lys200, Glu233, Asp197, Asp300. Carbon-hydrogen bond: Asp197, His201, Glu233, Asp300 Hydrophobic bond: His101, Leu162	
Acarbose [#]	−7.1	Hydrogen bond: Phe252, Arg281, Asp282, Arg600, Trp376	−9.0		

EU: Binding energy between the enzyme and each compound; [#] Acarbose: was included as a representative standard antidiabetic drug.

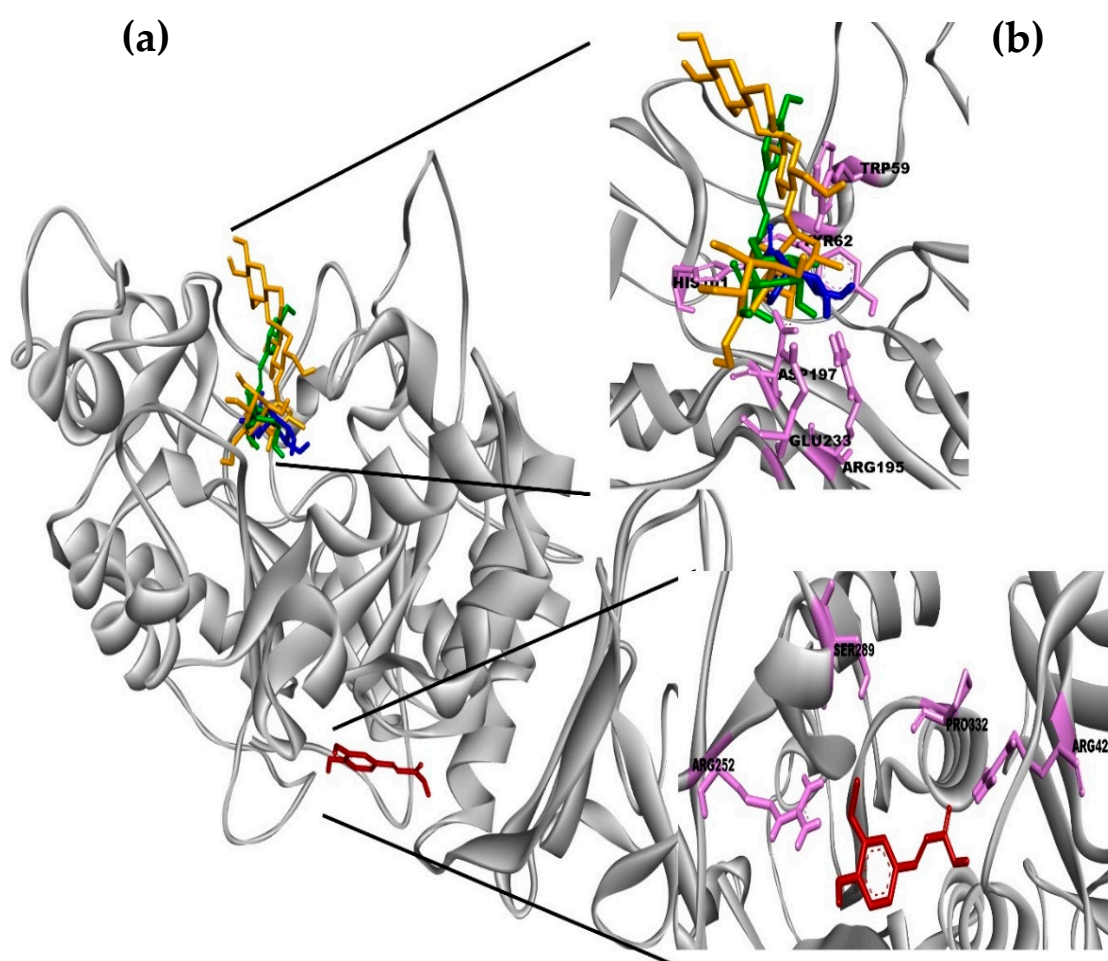


Figure 2. Blind molecular docking of ferulic (red), chlorogenic (green), quinic (blue) acids, and acarbose (orange) against α -amylase (PDB: 5E0F), showing interacting amino acid residues (pink) (a) General location of evaluated compounds in α -amylase; this panel shows that quinic and chlorogenic acid are in the main pocket of the enzyme, same as the reference drug; and ferulic acid is in

an allosteric site of α -amylase. (b) Visualization of the binding site and nearby residues of evaluated compounds and the enzyme. This panel shows the possible interaction of chlorogenic and quinic acids with biological relevance and catalytic residues of amino acids like Asp197, Glu233, Arg195, His101, etc., in the active site. Otherwise, ferulic acid shows possible interactions with amino acid residues such as Arg252, Ser289, Pro332, and Arg421 in the allosteric site.

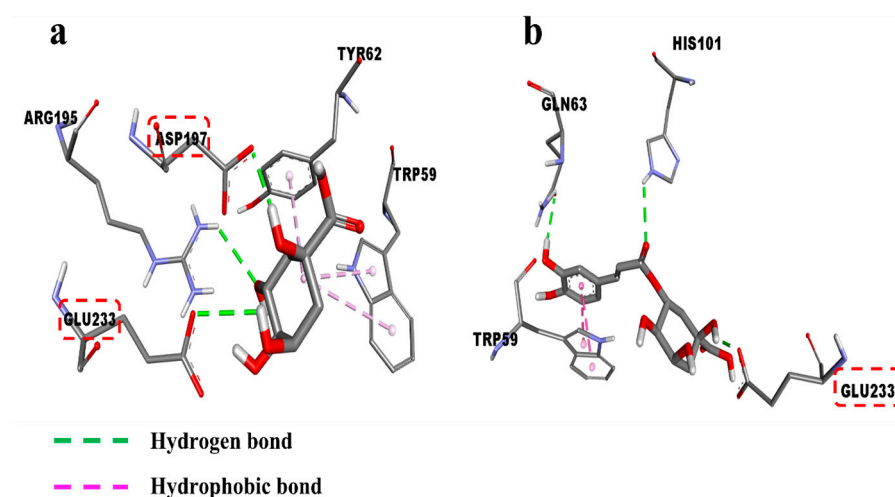


Figure 3. Interaction profile of quinic and chlorogenic acids in the active site of α -amylase. (a) The interaction profile of quinic acid in the active site shows three polar hydrogen bonds with catalytic residues, where the hydroxyl groups of the phenolic acid are of relevance for the interaction; further, the structural ring shows hydrophobic bonds with Trp59 and Tyr62. (b) The interaction profile of chlorogenic acid in the active site shows three polar hydrogen bonds (one with catalytic residues) and a hydrophobic bond with Trp59. Hydrogen bonds are represented by green dashed lines, hydrophobic interactions by purple dashed lines, and catalytic residues are indicated by red dotted boxes, and atoms are shown with oxygen in red, nitrogen in blue, carbon in gray, and hydrogen in white.

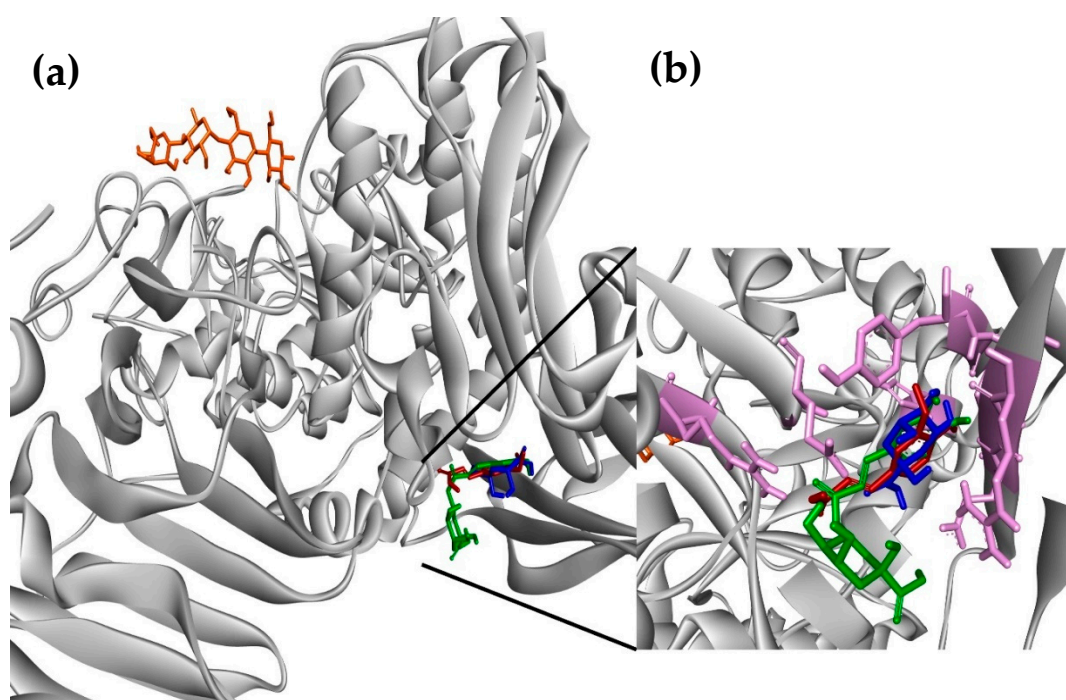


Figure 4. Blind molecular docking of ferulic (red), chlorogenic (green), quinic (blue) acids, and acarbose (orange) against α -glucosidase (PDB: 5NN8), showing interacting amino acid residues (pink).

(a) General location of evaluated compounds in α -glucosidase; this panel shows that all compounds are located in an allosteric site of the enzyme, different from the reference drug, which suggests a different mechanism of action. (b) Visualization of binding site and nearby residues of evaluated compounds and α -glucosidase, this panel shows the possible interaction of ferulic, chlorogenic, and quinic acids with biological relevance residues of amino acids like His708, Arg725, Glu748, Tyr822, Ile823, Pro825, Ala749, Arg854, Gly855, Glu856, etc., in the allosteric site.

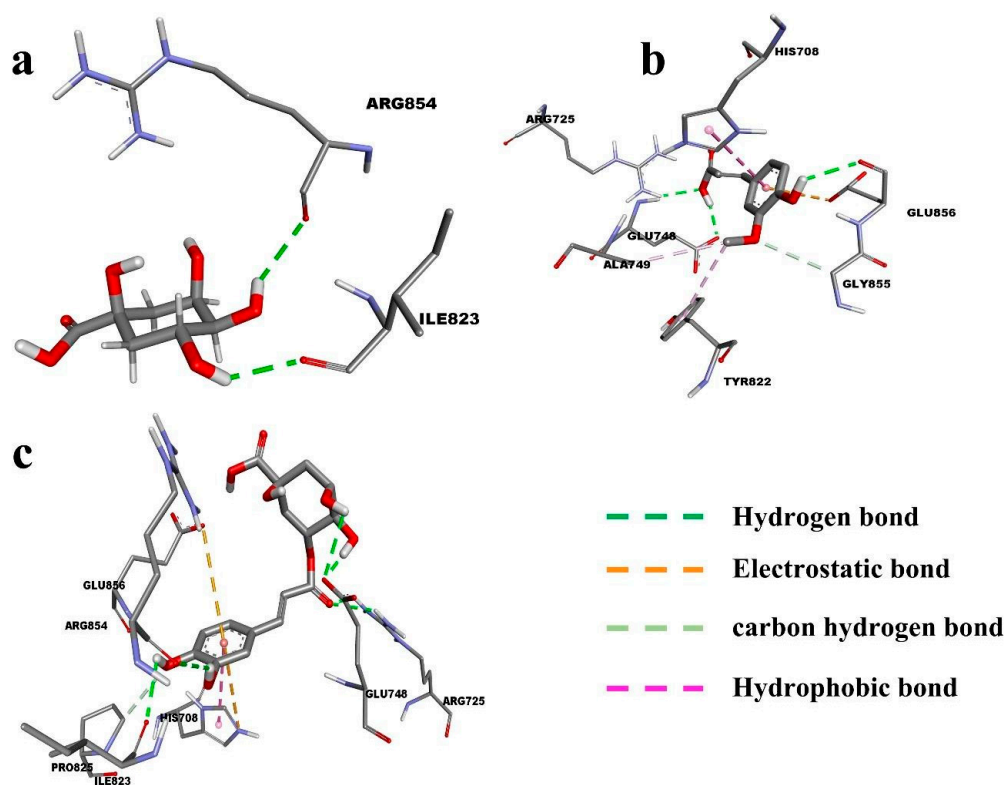


Figure 5. Interaction profile of phenolic acids in the allosteric site of α -glucosidase. (a) The interaction profile of quinic acid at the allosteric site shows two polar hydrogen bonds with allosteric residues like Ile823 and Arg854, where the hydroxyl groups of the structure present relevance for the interaction. (b) Interaction profile of ferulic acid in the allosteric site shows three polar hydrogen bonds and one carbon hydrogen bond with allosteric residues like Arg725, Glu748, Glu856, and Gly855, respectively; additionally, it presents electrostatic and hydrophobic bonds with Glu856, His708, Ala749, and Tyr822. (c) Chlorogenic acid presents six polar hydrogen bonds and one carbon hydrogen bond with allosteric residues like Arg725, Ile823, Arg854, Glu748, and Pro825; it also shows electrostatic and hydrophobic bonds with His708 and Glu856. Hydrogen bonds are represented by green dashed lines, electrostatic interactions by orange dashed lines, carbon-hydrogen bonds by light green dashed lines, hydrophobic interactions by pink dashed lines, and atoms are shown with oxygen in red, nitrogen in blue, carbon in gray, and hydrogen in white.

4. Discussion

All the identified compounds (terpenes, flavonoids, tannins, coumarins, and saponins) are secondary metabolites distributed across various plant organs, including stems, flowers, roots, fruits, seeds, and leaves. These compounds generally participate in plant communication, defense, and regulation processes. They are currently of interest due to their biological activities, including antioxidant, antibacterial, antidiabetic, antihyperglycemic, and hypoglycemic effects [27]. Similar results have been reported by Estanislao, et al. [28], who analyzed aqueous, acetonc, and hexane extracts of *P. edulis* bark and identified flavonoids, steroids, terpenes, quinones, and coumarins. Furthermore, similar

qualitative screenings in the fruits of other members of the Bignoniaceae family, such as *Kigelia africana*, have revealed the presence of flavonoids, tannins, saponins, glycosides, coumarins, terpenoids, and alkaloids [29]. In addition, within the tribe Crescentieae, which belongs to the Bignoniaceae family, the leaves of *Crescentia cujete* have also been shown to contain flavonoids, saponins, tannins, and anthraquinones in qualitative analyses [30]. Our qualitative screenings demonstrate that the secondary metabolite composition of *P. edulis* is consistent with phytochemical trends observed in other members of the Bignoniaceae family. As is well known, various factors influence these metabolites, ranging from the species to environmental conditions [31]. However, despite limited information on *P. edulis*, the results suggest that this species naturally produces a variety of secondary metabolites across its different parts, which could be of scientific interest, as the bioactive properties of plants are closely related to their phytochemical diversity.

For its part, the results on quantifying total phenolic content provide additional evidence of the distribution of phenolic compounds in *P. edulis* tissues. The values are comparable to those reported in dragon fruit (*Hylocereus undatus* and *Hylocereus polyrhizus*), which range between 270 and 390 mg GAE/100 g dw [32]. Similarly, the values found are within the range reported for native Mexican plants, such as the nopal (*Opuntia* spp.), with contents from <200 to 1990 mg GAE/100 g dw [33]. In the same way, comparing the values found in this investigation with some plants of regular consumption considered as medicinal, *P. edulis* has a higher content of total phenols than *Turnera diffusa* (254–470 mg GAE/100 g dw), but lower levels than *Eucalyptus camaldulensis* (956–1412 mg GAE/100 g dw) [34], *Piper auritum* (1552 mg GAE/100 g dw) [35], and the leaves of *Moringa oleifera* (71.08–76.63 mg GAE/g dw) [36]. Within the plant kingdom, phenolic compounds represent the second most abundant group of organic compounds. They include phenolic acids, flavonoids, tannins, stilbenes, and lignans, derivatives of secondary metabolism (the shikimic acid and malonic acid pathways). Their consumption is related to possible health benefits against non-communicable diseases. These compounds also contribute to plants' bitterness, color, and flavor and serve as a support and protection against various types of stress. Moreover, phenolic compounds are ubiquitously distributed in most plant tissues [37]; for this reason, we found them in all parts of the *P. edulis* analyzed, where they perform different functions, at concentrations that could be of interest for pharmaceutical or industrial purposes.

In addition, flavonoids exhibited significant accumulation in leaves compared to stems and fruits. The flavonoid content of *P. edulis* is higher than that of several medicinal plants used in India, such as *Acacia catechu*, *Acacia sinuate*, *Aerva lanata*, *Caesalpinia sappan*, *Jasminum grandiflorum*, among others (0.25–7.58 mg QE/100 g). It has values similar to those reported for *Senna tora*, with 21.58 mg QE/100 g [38]. Likewise, certain peppers such as jalapeño, serrano, and habanero are comparable (47–97 mg QE/100 g) [39], as well as fruits such as litchi, tangerine and dragon fruit (29–55 mg of catechin/100 g), but less than guava, carambola or durian (96–722 mg of catechin/100 g) [40]. The values found are also lower than those reported for *Hibiscus sabdariffa* (1866 mg/100 g) [41] and for the different parts of *Moringa oleifera* (leaf, bark, stem, and pods), where its content ranges from 265 to 9867 mg QE/100 g [42]. A similar behavior was reported for eggplant, where the leaf had the highest total flavonoid content among plant parts (leaf, stem, and fruit) [43]. In this sense, the distribution of phytochemicals such as flavonoids, to which some activities such as anticancer, antimicrobial, antiviral, antioxidant, and antitumoral effects are attributed [44], could be of interest when evaluating the potential pharmacological effects for each part of the plant of *P. edulis*.

Antioxidant compounds play a crucial role in controlling, delaying, or preventing oxidative stress. Therefore, they are relevant for preventing and treating various diseases. In this context, it is essential to determine the total antioxidant capacity of new plants,

such as *P. edulis*. Therefore, the antioxidant capacity of *P. edulis* was evaluated using complementary assays to allow comparative interpretation with other plant matrices.

The ORAC values found in this study (Table 2) are higher than those reported for some fruits, such as guava (11,763.9 $\mu\text{mol ET}/100\text{ g dw}$), and red apple (18,748.8 $\mu\text{mol ET}/100\text{ g dw}$), but lower than those of strawberry (35,741.3 $\mu\text{mol ET}/100\text{ g dw}$) [45]. Likewise, the leaf has values similar to those reported in other plants such as *M. oleifera* (15,471–182,313 $\mu\text{mol ET}/100\text{ g dw}$) [36], although lower than those of *Mhenta australis* and *Mhenta spicata* (155,110–172,720 $\mu\text{mol ET}/100\text{ g dw}$) [46]. In contrast, the results of the antioxidant capacity, determined by the DPPH assay, showed that the IC_{50} values obtained were lower than those reported for some industrial by-products, such as avocado peel, orange peel, pomegranate skin, and pineapple peel, which have values ranging from 14.5 to 39.8 $\mu\text{g/mL}$ [47]. Likewise, in a study analyzing different types of *Averrhoa carambola* leaf and fruit extracts, the reported IC_{50} values ranged from 0.075 to 1.106 mg/mL [48]. On the other hand, some medicinal plants, such as the leaf extract of *Sonchus arvensis* (31.55 $\mu\text{g/mL}$) [49], showed lower IC_{50} values than *P. edulis*. A similar pattern was observed in a study examining different parts of the dragon fruit, with the stem showing the lowest IC_{50} value, followed by the peel and flesh, ranging from 2.69 to 94.17 $\mu\text{g/mL}$ [50]. For their part, in the FRAP assay, the IC_{50} values of the fruit found in this study are lower than those reported for fruits such as *Vitis vinifera* (0.98 mg/mL), *Citrus aurantium* (3.82 mg/mL), and *Opuntia ficus-indica* (8.04 mg/mL) [51]. Similarly, the IC_{50} values reported in leaves of medicinal plants such as *Ficus exasperata* (5.16 mg/mL), *M. oleifera* (3.19 mg/mL), and *Jatropha tanjorensis* (3.16 mg/mL) were higher than those found in the leaves of *P. edulis* [52]. In addition, similar IC_{50} values have been reported for *P. edulis* on *Jatropha podagrica* stem bark (0.426–0.614 mg/mL) [53]. In general, it is worth noting that each antioxidant capacity assay highlights different parts of the plant (fruit in ORAC, leaf in DPPH, and stem in FRAP). Because each assay is based on a different reaction mechanism, the patterns observed across different plant organs reflect characteristic differences in antioxidant behavior. These results demonstrate that the *P. edulis* plant exhibits values of interest comparable to those of common or medicinal plants. The antioxidant capacity and differences observed across plant parts may be attributed to the presence of compounds with antioxidant properties, such as total phenols, flavonoids, terpenes, tannins, coumarins, and saponins, among others. Since different plant parts are expected to contain distinct profiles of bioactive compounds, variations in antioxidant capacity are consistent with their phytochemical diversity. Therefore, the antioxidant potential of *P. edulis* could not be attributed to a single class of compounds, but rather to the combined and complementary action of multiple metabolite groups. Such antioxidant-rich plant matrices have been reported to be associated with the inhibition of carbohydrate-hydrolyzing enzymes involved in glucose metabolism [54].

Due to their widespread distribution and biological significance among plant secondary metabolites, phenolic acids were selected for detailed analysis. They play essential roles in plant defense and antioxidant mechanisms. Phenolic acids also contribute to nutrient uptake, protein synthesis, enzymatic activity, photosynthesis, structural integrity, and allelopathy. Furthermore, they are precursors to other classes of bioactive compounds, such as flavonoids, tannins, and lignans. This highlights the biological importance of studying them. Phenolic acids are characterized by a structure made up of a phenol with a carboxylic acid group and are mainly linked to other compounds by ester, ether, or acetal bonds, but a small amount is found as free acids. These compounds have attracted particular interest due to their potential to protect against diseases related to oxidative stress, such as cancer, diabetes, and cardiovascular disease [13]. In this regard, several studies within the genus *Parmentiera* and other members of the Bignoniaceae family have reported the presence of phenolic acids. For example, Abdel-Wahab, et al. [55]

the methanolic extracts of leaves and stems of the species *Parmentiera cereifera* Seem. were analyzed, managing to isolate and elucidate hydroxybenzoic acids such as isovanillic, vanillic, and p-hydroxybenzoic acid; they also reported two new glycosylated acids called parmentin A and parmentin B. Likewise, within the Bignoniaceae family, some plants considered medicinal have been analyzed; the presence of phenolic acids has been reported, such as in *Arrabidaea chica*, where Gemelli, et al. [56], found gallic and ellagic acid. In another study by Torres, et al. [57], they evaluated the antioxidant, anti-inflammatory, and antimicrobial capacities of seven plants of this family; they found that the species *Cuspidaria convoluta* was the best assessed, and the main phenolic compounds found were coumaric and hydroxybenzoic acid derivatives and three flavonoids. In *Crescentia cujete* leaves, chlorogenic, p-hydroxybenzoic, and protocatechuic acids have also been identified [58]. In the fruit, a study using UPLC-MS/MS-based molecular networking and NMR structural determination for untargeted phytochemical characterization reported 23 phenolic acid derivatives [59]. Likewise Ferraz-Filha, et al. [60], analyzed *Tabebuia roseoalba* (Bignoniaceae) leaf extracts using HPLC-UV/DAD, finding caffeic acid and chlorogenic acid, to which their possible anti-inflammatory effect is attributed. Similarly, using HPLC-ESI-MS, caffeic, p-coumaric, and ferulic acids were identified in *Kigelia africana* [61]. In general, six bioactive compounds were tentatively identified in *P. edulis*, which have also been reported in other species of *Parmentiera* and in many plants of the Bignoniaceae family. This suggests they share a similar phytochemical profile, particularly in phenolic acids. Furthermore, the combination of chlorogenic, ferulic, and quinic acids in this studied species is interesting, as it could contribute to its therapeutic potential. However, it is still necessary to expand studies on the characterization of other bioactive compounds.

The enzyme α -glucosidase is a key enzyme in carbohydrate digestion; it catalyzes the hydrolysis of glycosidic bonds in polysaccharides and glycoconjugates. This enzyme is of interest because its inhibition is one of the treatments against diabetes mellitus, as it delays glucose absorption and reduces postprandial plasma glucose levels and hyperglycemia. Over the years, interest in the study of medicinal plants has grown, as it has been shown that various phytochemicals, such as flavonoids, terpenoids, alkaloids, and phenolic compounds, among others, can inhibit α -glucosidase [62]. In this regard, the inhibitory activity observed in *P. edulis* can be placed within the range reported for other medicinal plant extracts. Arslan and Çam [63], have reported the inhibitory capacity of extracts from medicinal plants, such as peppermint, spearmint, thyme, sage, lavender, yarrow, echinacea, and lemon balm, with IC_{50} values like those observed in this study (1.18–47.45 mg/mL). In other studies, lower IC_{50} values (15.80 μ g/mL) have been reported for extracts of *Bougainvillea glabra* flowers; this effect was attributed to the secondary metabolite content of the extracts [64]. Likewise, extracts of oregano (*Hedeoma patens*, *Lippia graveolens*, and *Lippia palmeri*), a plant with a rich medical tradition, have demonstrated inhibitory effects on α -glucosidases, which are related to the flavonoid and phenolic acid content of the extracts [65]. Other Mexican medicinal plants, such as *Justicia spicigera* (268 μ g/mL), *Leucaena collinsii* (323 μ g/mL), and *Tagetes nelsonii* (193 μ g/mL) [66] have demonstrated greater inhibitory effects than *P. edulis*. It has been described that flavonoids are compounds with α -glucosidase inhibitory activity. Their potential depends on the structure, position, and number of OH groups. For example, hydroxylation in rings A (positions 5, 7, and 8) or B (3' and 4'), and a double bond in the C ring (C2-C3), are structural characteristics that could increase inhibitory activity [67]. In the case of phenolic acids, it has been documented that caffeoylquinic acids exhibit strong inhibitory potential, whereas hydroxycinnamic, ferulic, and gallic acids exhibit lower inhibitory potential [68]. Our results show that *P. edulis* leaves contain higher levels of flavonoids ($p < 0.05$) and chlorogenic acid ($p < 0.05$), which could partially explain their greater inhibitory capacity against α -glucosidase. It is important to note that the α -glucosidase assay used in this study

employed the enzyme *Saccharomyces cerevisiae*, which differs from mammalian α -glucosidase; therefore, the observed inhibitory effects should be interpreted in the context of an in vitro assay.

The enzyme α -amylase, produced by the salivary glands and the pancreas, plays a key role in the digestion of starch and other carbohydrate polymers by catalyzing the hydrolysis of the α -1-4-D-glycosidic linkages to obtain smaller products such as dextrin, maltose, and glucose; therefore, the activity of the enzyme is related to postprandial hyperglycemia and high blood glucose levels. Thus, inhibiting α -amylase activity is a therapeutic objective in the treatment of diabetes mellitus [69]. The inhibitory activity observed for *P. edulis* extracts can be compared with reports of other medicinal plants. Magaji, et al. [70] analyzed different extracts of seeds, leaves, and roots of *M. oleifera* with various solvents such as water, methanol, hexane, and ethyl acetate, obtaining the highest α -amylase inhibitory capacity in the methanolic and hexanic leaf extracts with IC_{50} values of 8.217 mg/mL and 9.397 mg/mL, respectively. In another study, hydroalcoholic extracts of the mesocarp, endocarp, pericarp, and whole fruit of *Opuntia oligacantha* variety Ulapa showed inhibition percentages ranging from 50.97% to 56.39% at 15 mg/mL [71]. In addition, a variety of plant extracts have been described with inhibitory effects against α -amylase, such as *Valeriana dioscoridis* [72] and *Ocimum basilicum* [73], among others. The inhibitory effect of plant extracts on amylase is attributed to the content and variety of secondary metabolites, including phenolics, phenolic acids, terpenoids, tannins, and alkaloids. It has been described that some structural characteristics of polyphenols can improve the inhibitory power such as the hydroxylation of flavonoids and the presence of an unsaturation in the 2–3 bond conjugated with a 4-carbonyl group; on the other hand, a decrease in their inhibitory effect can be related to the glycosylation of flavonoids (conjugation site and sugar class), as well as methylation and methoxylation, in addition some galloylated catechins, catechol-type catechins also have a better inhibitory effect than other types of catechins [74]. In general, the strongest inhibitory activity was observed in leaf extracts for both α -amylase and α -glucosidase, even though fruits exhibited a high total phenolic content. This suggests that the composition and diversity of secondary metabolites play a more relevant role. In particular, the flavonoids and chlorogenic acid, as well as other bioactive compounds present in the leaf extracts, could contribute more effectively to enzyme inhibition. In this context, these results suggest that *P. edulis* contains secondary metabolites of interest that may interact with the enzymes α -amylase and α -glucosidase. Considering the overall enzyme inhibition results, the observed inhibitory effects and IC_{50} values should be interpreted with caution, as they correspond to the in vitro inhibitory activity of crude extracts and do not directly represent bioavailable concentrations with an in vivo effect.

Molecular docking analysis provided structural information on potential ligand enzyme interaction sites and binding behavior, contributing to the interpretation of experimental inhibition results. The docking results suggest distinct interaction patterns between the evaluated phenolic acids and both digestive enzymes. The results demonstrate that chlorogenic acid had the best binding energy with the enzyme α -glucosidase ($-7.9 \text{ kcal}\cdot\text{mol}^{-1}$) and with α -amylase ($-8.5 \text{ kcal}\cdot\text{mol}^{-1}$). When analyzing the interaction profiles of chlorogenic, quinic, and ferulic acids, it was observed that chlorogenic acid interacts with Pro825 and Glu748, and also interacts with Ile823 and Arg854, as does quinic acid. These interactions could be related to the greater allosteric affinity observed. Previous scientific studies have demonstrated interactions between phenolic acids and digestive enzymes. For example, Zheng, et al. [75] studied the mechanism of ferulic acid inhibition against α -amylase and α -glucosidase; they demonstrated the modification of their structures due to their binding. In addition, FT-IR showed that the main interactions are carried out in a non-covalent manner. As observed in our study, the binding energies were found

to have similar values for both enzymes (−5.3 and −5.7 kcal/mol), and the interactions were through hydrogen bonds. Molecular docking of different phenolic acids and flavonoids with α -amylase identified in *Ferula tunetana* showed that ferulic acid (−6.8 kcal/mol) and chlorogenic acid (−7.6 kcal/mol) presented some of the best affinity energy values, surpassing gallic, p-hydroxybenzoic, caffeic, vanillic, syringic, and p-coumaric acids, highlighting that the interactions were established through hydrogen bonds [76]. Likewise, in a study of *Artemisia argyi*, it has been reported that chlorogenic acid (−7.36 kcal/mol) has good affinity to α -glucosidase (PDB: 7KBR) through the interaction with the active site with amino acid residues Asp451, Asp564, His700, Phe571, Trp525, and Ile452, with hydrogen bond, Pi-Pi stacked, Pi-alkyl, and Pi-anion interactions [77]. Similarly, in a study of *Smilax aristolochiifolia* root extract, chlorogenic acid was identified as one of the major compounds and was shown to inhibit α -amylase through a non-competitive mechanism, with a binding energy of −5.97 kcal/mol, while exhibiting lower affinity toward α -glucosidase (−3.75 kcal/mol)[78].

In another study on *Pistacia atlantica* Desf., a medicinal plant used for its potential antidiabetic use, some compounds of interest were identified, including quinic acid. The molecular docking results were consistent with our research concerning the binding energy with α -glucosidase (−6.6 kcal/mol) and α -amylase (−5.5 kcal/mol). In the case of α -glucosidase, quinic acid presented five interactions through hydrogen bonds (Lys156, Asp233, Asn235, His423, and Glu429), but also showed hydrophobic interactions with Ser236, Phe314, Asn317, and Ile419. In α -amylase, hydrogen bond interactions of amino acid residues His101 and Glu233 were consistent with our results, but hydrophobic interactions with Tyr62, Leu162, Ala198, Ile235, His299, and Asp300 were also reported [79]. Furthermore, quinic acid has been described as acting as a non-competitive inhibitor of α -glucosidase, showing greater efficacy than other common organic acids such as citric, malic, and gallic acids [80]. In this context, the analyzed phenolic acids have demonstrated the ability to form both amylase and glucosidase interactions with an adequate affinity energy (values < −5 kcal/mol) [25], demonstrating a possible inhibitory effect. The main form of interaction of phenolic acids is hydrogen bonds [81]. Overall, the results obtained from this analysis demonstrate that the main phenolic acids present in *P. edulis*, such as quinic (Arg197 and Glu233) and chlorogenic (Glu233) acids, interact with amino acids that play a catalytic role in enzymes of therapeutic interest, in addition to interesting binding energy values at allosteric sites. In this context, the molecular docking results support the potential contribution of major phenolic acids to the enzyme inhibitory activity observed in vitro. These results could partially explain the potential contribution of the main phenolic acids in *P. edulis* extracts to the observed enzyme inhibitory activity; however, when considering the inhibitory responses observed among the different plant parts, the strongest activity was detected in leaf extracts, which are characterized by a higher chlorogenic acid content. The overall inhibitory effect of the crude extract cannot be attributed exclusively to individual phenolic acids, since other classes of metabolites, including flavonoid compounds that are also more abundant in leaves, as well as additional bioactive components and possible synergistic interactions, may contribute to the observed effect.

5. Conclusions

Overall, this research confirms that *P. edulis* possesses a diverse and interesting phytochemical profile, distributed throughout its leaves, fruits, and stems. The fruit presented the highest levels of total phenolic compounds, while the leaves had the highest flavonoid content. The antioxidant capacity varied depending on the plant part analyzed. Furthermore, six major bioactive acids were tentatively identified (ferulic, chlorogenic, caffeic, p-coumaric, quinic, and gallic acids), with ferulic, chlorogenic, and quinic being the most abundant. These compounds exhibited potential interactions at the active and allosteric

sites of α -glucosidase and α -amylase, suggesting that they could participate in both competitive and non-competitive inhibition. However, their inhibition concentrations may be relatively high compared to those of other species. This study provides an integrative biochemical insight into the relationship between the phenolic composition of *P. edulis* and its potential enzyme-inhibitory activity. These findings provide preliminary scientific support for the study of the traditional pharmacological use of *P. edulis* and highlight the need for further research, including studies in other parts of the plant, as well as the isolation and characterization of additional bioactive compounds, particularly flavonoids and other metabolite classes, which could contribute in a complementary manner to the therapeutic effects attributed to this species. Because the present work was conducted exclusively in vitro, these observations should be considered exploratory, and future studies addressing the in vivo efficacy and bioavailability of *P. edulis* extracts will be essential to validate their potential applications.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/metabo16020146/s1>, Figure S1. Total ion current (TIC) UPLC-qTOF-MS/MS chromatograms from independent analytical runs of *Parmentiera edulis* extracts: (a) fruit, (b) leaf, and (c) stem.; Figure S2. Representative MS/MS spectra of selected compounds identified in *Parmentiera edulis*: (a) quinic acid, (b) ferulic acid. Spectra are dominated by the precursor ion signal under the experimental conditions; Figure S3. Calibration curves of phenolic acids used for quantification by UPLC-qTOF-MS/MS.

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