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Valorization of *Solanum melongena* L. crop by-products: Phenolic composition and *in vitro* antioxidant, antidiabetic, anti-inflammatory, cytotoxic, and antimicrobial properties

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ABSTRACT

This study explored the valorization of post-harvest eggplant aerial parts as a sustainable source of value-added ingredients by investigating their phenolic composition and *in vitro* bioactive properties. HPLC-DAD-ESI/MS^n analysis identified chlorogenic acid derivatives as the predominant phenolic compounds (53 % of the phenolic fraction), followed by *O*-glycosylated kaempferol and quercetin. The extract displayed antioxidant activity in physiologically relevant cell-based assays and significant α-glucosidase inhibitory capacity that far exceeded that of the standard drug acarbose. It also inhibited the formation of advanced glycation end-products (AGEs), suggesting its potential to mitigate diabetes-related complications. Furthermore, the extract showed a modest pancreatic lipase inhibitory effect and capacity to suppress interleukin 6 production. Selective cytotoxicity against human gastric and colon adenocarcinoma cell lines and strong antimicrobial activity against foodborne pathogens were observed. Given the growing demand for natural alternatives to synthetic drugs, these findings position eggplant crop biomass as a promising, sustainable source of active compounds with potential applications in food, nutraceutical, and pharmaceutical formulations for managing type 2 diabetes and other oxidative stress-mediated conditions. This study not only contributes to the valorization of agricultural waste but also expands the research on by-products of Solanaceae crops, offering a pathway for sustainable resource utilization.

1. Introduction

The exploration of agro-industrial by-products is gaining increasing attention from the scientific community and industry for being an available, cost-effective, and sustainable source of bioactive compounds with functional and health-promoting effects [1,2]. Multi-product biorefinery schemes have the potential to convert these renewable feedstocks into high-value products, including food ingredients, pharmaceuticals, nutrients, and enzymes [3]. This strategic zero-waste approach addresses waste management issues and protects the environment and ecosystems while contributing to the development of more sustainable production and consumption systems. Furthermore, it plays a crucial role in the transition towards sustainable development, aligning with global sustainability goals.

The Solanaceae family includes many popular food crops of high economic significance worldwide, such as tomato, pepper, potato, and

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eggplant, which have played an important role in human nutrition and health for centuries [4]. Despite extensive research, there are still new compounds being discovered from Solanaceae species, offering potential advantages for disease treatment, not only in pharmaceuticals but also as functional foods and food supplements that aid in daily health maintenance, particularly in combating oxidative stress [5]. Additionally, the often-overlooked and underutilized plant biomass (or by-products) from these crops presents a rich source of bioactive compounds and extracts, useful for both the food and pharmaceutical sectors [5,6].

Among the Solanaceae crops, eggplant (*Solanum melongena* L.) ranks the fifth most economically important after potato, tomato, pepper, and tobacco [7]. Eggplant is a versatile vegetable widely used in traditional and contemporary cuisines of many countries and is consumed cooked or processed in many ways. Although mainly produced in tropical and subtropical regions, this high-yielding and biomass-productive annual plant is well-adapted to hot and wet environments [8]. In 2022, the global eggplant production exceeded 59.31 million tons, harvested from over 1.8 million hectares [9]. Derived from this substantial production, a large amount of biomass (primarily leaves and stems) is generated and commonly left in the field after harvest. However, these agricultural residues or by-products could be valorized as a potential source of high-value-added compounds, thus generating revenue from otherwise worthless material, reducing waste accumulation and landfilling costs, and addressing social concerns.

Eggplant contains different classes of phytochemicals, including phenolic compounds, which are among the most studied bioactive constituents recoverable from plant by-products. These secondary metabolites are well known for their antioxidant activity and potential benefits in the management of oxidative stress-related diseases such as cancer, diabetes, and cardiovascular disease [10]. Notable examples include the anthocyanin nasunin (delphinidin-3-(*p*-coumaroylrutinoside)-5-glucoside), abundant in the fruit peel [11], and the glycosylated isorhamnetin derivative solanoflavone, found in the aerial parts of white eggplant [12]. These bioactive constituents may support the traditional uses of this species in folk medicine. For instance, eggplant stalks have been used in Korea for their therapeutic effects on burns and inflammatory conditions such as stomatitis, arthritis, and gastritis [13]. Meanwhile, in African countries, the leaves have been employed as a remedy for washing wounds and as an astringent for bladder hemorrhage and other bleeding disorders [14].

Diabetes mellitus is one of the most prevalent metabolic disorders worldwide, posing a significant public health challenge. Current pharmacological treatments rely primarily on synthetic drugs such as acarbose, an α-glucosidase inhibitor widely used for diabetes management [15]. However, consumers are increasingly demanding healthier products formulated with natural, clean-label ingredients, which are perceived as safer and more sustainable [16]. This trend aligns with the growing interest in functional foods and nutraceuticals, which go beyond basic nutrition to offer therapeutic benefits, particularly in the prevention and management of chronic diseases such as diabetes and obesity. In this context, bioactive extracts derived from underutilized agricultural by-products emerge as a promising avenue for developing innovative and sustainable solutions.

Despite the increasing research on bioactive compounds from Solanaceae species, the potential of eggplant crop by-products remains largely unexplored. Most investigations have focused primarily on eggplant fruits or leaves and stems harvested before the end of the fruit production cycle [2]. Therefore, the valorization of agricultural residues of eggplant crops stands as a forward-thinking approach, as this biomass can serve as a renewable source of high-value compounds for the formulation of functional ingredients, drugs, and other consumer goods. This study aimed to characterize the phenolic composition of eggplant crop by-products, specifically the plant aerial part (leaves and branches) at the end of the fruit production cycle, and to evaluate their *in vitro* antioxidant, anti-inflammatory, antimicrobial, cytotoxic, antidiabetic, and anti-obesity properties. By identifying alternative profitable applications for this underutilized biomass, the study may contribute to resource-use efficiency, sustainability, and the development of novel bio-based products. This research not only supports circular economy principles but also lays the groundwork for future advancements in the functional food and pharmaceutical industries.

2. Material and methods

2.1. Plant material and extract preparation

Eggplant (*S. melongena*) aerial parts at the end of the fruit production cycle were collected in October 2019 from a local farm in Bragança, Portugal. The plant material, consisting of leaves and branches, was freeze-dried, ground into a fine powder, and vacuum stored at −20 ºC until required for analysis. For solid-liquid extraction, 1 g of the plant sample was stirred with 30 mL of 80 % ethanol for 1 h at room temperature, followed by a re-extraction of the solid residue [17]. Then, ethanol was separated from the filtrates in a rotary evaporator with a water bath at 40 ºC and the aqueous phase was freeze-dried to obtain a dry extract.

2.2. Chemicals, biological materials, and equipment

The chemicals, standards, and biological materials used in the phytochemical and bioactivity analysis are detailed in Table A.1, and the equipment is listed in Table A.2.

2.3. Chromatographic analysis of profile compounds

The dry extract was reconstituted in 20 % ethanol to a concentration of 5 mg/mL, filtered through a 0.22-µm filter disk, and analyzed using an HPLC system equipped with a diode array detector (DAD) and a mass spectrometer with an electrospray interface. The equipment (described in Table A.2) and analytical conditions were followed as described by the authors [18]. Compound identification involved comparing their retention time and UV-Vis and mass spectra with those of commercial standards, and when not available, chromatographic data were compared with the literature. Compounds were quantified using calibration curves constructed with commercial standards (Table A.3), and the content of each compound was expressed in mg equivalents of its similar standard per gram of extract.

2.4. Bioactive properties evaluation

2.4.1. Antioxidant activity

The antioxidant activity was evaluated by measuring the extract's capability to inhibit oxidative hemolysis (OxHLIA) and the formation of thiobarbituric acid reactive substances (TBARS) *in vitro* [19]. These methods were chosen for their physiological relevance, as they measure the extract's ability to prevent lipid peroxidation in cell membranes, a major cause of cell damage.

TBARS assay: A porcine brain cell solution (1:2, *w/v*) prepared in ice-cold Tris–HCl buffer (20 mM, pH 7.4) was incubated with extract (0.0391–5 mg/mL), Trolox (3.125–100 µg/mL), or Tris–HCl buffer (negative control) plus $FeSO_4$ (10 µM) and ascorbic acid (0.1 mM) at 37 ºC for 1 h. The reaction was stopped using trichloroacetic acid (28 % *w/v*). Subsequently, thiobarbituric acid (TBA, 2 %, *w/v*) was added, and the mixture was heated at 80 ºC for 20 min. The absorbance was measured at 532 nm after centrifugation. The results were expressed as EC_{50} values (µg/mL).

OxHLIA assay: A sheep red blood cell solution (2.8 %, *v/v*) prepared in PBS (pH 7.4) was mixed with extract (13–400 µg/mL), Trolox (3.125–250 µg/mL), PBS (negative control), or distilled water (baseline). Following a 10-min pre-incubation at 37 ºC with shaking, the oxidant 2,2′-azobis(2-amidinopropane) dihydrochloride (160 mM) was

added, and the optical density ($OD_{690\ nm}$) was kinetically monitored over 400 min. Hemolytic curves for each extract concentration were fitted using nonlinear regression in GraphPad Prism® 8 at a 95 % confidence interval to determine the Ht_{50} values, i.e., the 50 % hemolysis time (min) graphically obtained from each hemolysis curve. These values were then correlated with extract concentrations to calculate the IC_{50} values (μg/mL) for time intervals (Δt) of 60, 120, and 180 min.

2.4.2. Antidiabetic activity

The antidiabetic activity of the extract was assessed based on its ability to inhibit yeast α-glucosidase and the formation of advanced glycation end products (AGEs).

α-Glucosidase inhibition assay. α-Glucosidase enzyme solution (1 U/mL) was mixed with the extract or the commercial inhibitor acarbose, along with potassium phosphate buffer (100 mM, pH 6.8), and incubated at 37 °C for 10 min. Subsequently, the substrate *p*-nitrophenyl glucopyranoside (PNPG, 3 mM) was added, and the 96-well plate was subjected to additional incubation. The yellow-colored *p*-nitrophenol released from PNPG was quantified at 405 nm [20]. The results were presented as IC_{50} values (μg/mL).

AGEs formation inhibition assay. A solution containing bovine serum albumin (BSA) and fructose was incubated with either the extract or the inhibitor aminoguanidine at 37 °C for 24 h in the dark and analyzed fluorometrically at an excitation wavelength of 355 nm and emission wavelength of 460 nm [20]. A blank control, containing only BSA and buffer, was prepared to serve as a reference for AGEs formation. Additionally, a blank for each sample was established by substituting the sugar with buffer to subtract intrinsic fluorescence from incubation with BSA. The results were expressed as IC_{50} values (μg/mL).

2.4.3. Anti-obesity capacity

The lipase inhibition assay was conducted according to the methodology described by Millán-Laleona et al. [20]. Briefly, a solution of porcine pancreatic lipase (2.5 mg/mL in 0.1 M PBS, pH 7.0) was mixed with the extract or the positive control orlistat, along with *p*-nitrophenyl butyrate (NPB, 10 mM), and incubated at 37 °C for 10 min. The absorbance was then measured at 405 nm. The results were presented as IC_{50} values (μg/mL).

2.4.4. Anti-inflammatory activity

The anti-inflammatory activity of the extract was evaluated through nitric oxide (NO) formation inhibition and Caco-2 monolayer immunomodulatory assays.

NO formation inhibition assay. The extract (6.25–400 μg/mL) was tested for its ability to inhibit NO production by lipopolysaccharide (LPS)-stimulated murine macrophages (RAW 264.7) by measuring the nitrite concentration in the culture medium using a Griess reagent system kit [21]. Dexamethasone (7.65–980 μg/mL) served as a positive control, while samples without extract or LPS served as negative controls. The results were presented as EC_{50} values (μg/mL).

Caco-2 monolayer immunomodulatory assay. Human colon carcinoma epithelial cells (Caco-2) were cultured and seeded at 2.5×10^5 cells/well in 24-well plates, following the protocol by Machado et al. [22]. After incubation for 24 h, the culture media was replaced with media supplemented with extract at 1 μg/mL and further incubated for 24 h. Interleukin-1β (IL-1β) at 10 ng/mL was used as an inflammation control, while plain media served as a basal activity control. Supernatants were collected, centrifuged, and stored at −80 °C for further analysis. Interleukins 6 (IL-6) and 8 (IL-8) and tumor necrosis factor-alpha (TNF-α) were detected using ELISA kits. The protein content of samples was determined using the Pierce BCA Protein Assay Kit (Table A.2). Interleukin values were obtained in pg/ng of protein and expressed as a fold increase relative to the non-stimulated control (basal) activity.

2.4.5. Cytotoxic activity

The cytotoxic potential of the extract (6.25–400 μg/mL) was assessed on human Caco-2, gastric adenocarcinoma (AGS), breast adenocarcinoma (MCF-7), and non-small cell lung carcinoma (NCI-H460) cells, as well as on a non-tumor porcine liver primary cell culture (PLP2). The sulforhodamine B (SRB) assay, which relies on SRB dissociation under basic conditions and binding to basic amino acids in mildly acidic conditions, was employed [23], with ellipticine (0.38–12.3 μg/mL) used as the positive control and cells without extract served as negative controls. The results were presented as GI_{50} values (μg/mL).

2.4.6. Antimicrobial activity

The extract reconstituted in 30 % ethanol was tested against Gram-negative and Gram-positive bacteria and fungi described in Table A.1. Minimum inhibitory (MIC), bactericidal (MBC), and fungicidal (MFC) concentrations (mg/mL) were determined using the serial microdilution methods with *p*-iodonitrotetrazolium violet as the growth indicator [24]. Sodium benzoate and potassium metabisulfite were positive controls, while 30 % ethanol was used as the negative control.

2.5. Statistical analysis

The experiments were conducted in triplicate and the results were presented as mean ± standard deviation (SD), except for antimicrobial activity. The decimal place of the uncertain digit of the mean value was determined by rounding the SD value to one significant figure. Statistical tests were performed at a 5 % significance level using IBM SPSS Statistics software (22.0. Armonk, NY: IBM Corp.). Statistical differences between samples were assessed using a two-tailed paired Student's *t*-test.

3. Results and discussion

3.1. Phenolic composition

Data related to the identification of phenolic compounds in the hydroethanolic extract prepared from the eggplant aerial parts are presented in Table 1, namely retention time, λ_{max} in the UV–Vis region, pseudomolecular ion, and ions of major fragments in MS^2. Fifteen phenolic compounds were found, comprising five phenolic acids and ten *O*-glycosylated flavonoids. The chromatogram is depicted in Fig. A.1.

Compounds **1** and **2** showed the pseudomolecular ion $[M-H]^-$ at *m/z* 353, with fragment ions at *m/z* 191 (quinic acid fragment), *m/z* 179, and *m/z* 135, and a maximum UV-Vis absorbance at 321 nm. These compounds were tentatively identified as *cis*- and *trans*-3-*O*-caffeoylquinic acids based on retention time and fragment ions. However, compounds **3** and **4** only displayed fragment ions at *m/z* 191 for the same molecular ion, indicating that these compounds could also be tentatively identified as *cis*- and *trans*-5-*O*-caffeoylquinic acids, respectively. Compound **5** presented the $[M-H]^-$ ion at *m/z* 367, with a fragment ion also at *m/z* 191. In this case, the compound might be tentatively identified as feruloylquinic acid [25,26]. Compounds **6**, **7**, and **8** were tentatively identified as quercetin-*O*-dihexoside due to its pseudomolecular ion $[M-H]^-$ at *m/z* 625, fragment ions at *m/z* 301 (quercetin aglycone), *m/z* 271, *m/z* 299, and *m/z* 243 (two sugar moieties), and a maximum UV-Vis absorbance at 340 nm. In the case of compounds **9**, **10**, **12**, and **13**, the $[M-H]^-$ ions appeared at *m/z* 609, the main fragment ion at *m/z* 285 (kaempferol aglycone) after losing one sugar moiety, and the maximum UV-Vis absorbances at 339 nm, what suggested that these could be tentatively identified as kaempferol-*O*-dihexoside. Compound **11** showed its pseudomolecular ion $[M-H]^-$ at *m/z* 771, which lost three sugar moieties to yield the main fragment ion also at *m/z* 285, and the λ_{max} at 341 nm, indicating that it could be tentatively identified as kaempferol-*O*-dihexosyl-*O*-hexoside. For compound **14**, a pseudomolecular ion $[M-H]^-$ at *m/z* 447, with the main fragment ion at *m/z* 285, indicating a loss of a single sugar moiety, and λ_{max} at 328 nm, suggesting that this compound could be identified as kaempferol-*O*-hexoside. Compound **15** was identified as isorhamnetin-*O*-hexoside, based on the $[M-H]^-$ ion at *m/z* 477, and fragment ions at *m/z* 314, *m/z* 315, and *m/z*

Table 1
Phenolic compounds identified and quantified in the extract prepared from the eggplant aerial part at the end of the fruit production cycle. It presents the retention time (R*t*), wavelengths of maximum absorption in the UV–vis region (λ_{max}), and pseudomolecular and MS^2 fragment ions (with relative abundance in brackets).

Peak	R*t* (min)	λ_{max} (nm)	$[M-H]^-$ (*m/z*)	MS^2 (*m/z*)	Tentative identification	Content (mg/g extract)
1 [A]	6.27	325	353	191(100), 179(8), 135(<5)	*cis*−3-*O*-Caffeoylquinic acid	6.8 ± 0.2
2 [A]	7.34	325	353	191(100), 179(15), 135(<5)	*trans*−3-*O*-Caffeoylquinic acid	1.18 ± 0.03
3 [A]	8.02	325	353	191(100)	*cis*−5-*O*-Caffeoylquinic acid	1.78 ± 0.05
4 [A]	8.86	325	353	191(100)	*trans*−5-*O*-Caffeoylquinic acid	1.60 ± 0.04
5 [B]	11.89	322	367	191(100), 193(5), 173(6), 134(<5)	5-*O*-Feruloylquinic acid	0.187 ± 0.005
6 [C]	12.76	340	625	301(100), 271(100), 299(16), 243(5)	Quercetin-*O*-dihexoside	1.29 ± 0.01
7 [C]	13.96	340	625	301(100), 271(100), 299(10), 243(2)	Quercetin-*O*-dihexoside	0.94 ± 0.01
8 [C]	14.65	340	625	301(100), 271(100), 299(14), 243(3)	Quercetin-*O*-dihexoside	1.00 ± 0.01
9 [C]	15.06	339	609	285(100)	Kaempferol-*O*-dihexoside	1.16 ± 0.01
10 [C]	15.57	339	609	285(100)	Kaempferol-*O*-dihexoside	1.00 ± 0.01
11 [C]	16.06	341	771	285(100)	Kaempferol-*O*-dihexosyl-*O*-hexoside	0.95 ± 0.01
12 [C]	16.98	339	609	285(100)	Kaempferol-*O*-dihexoside	0.94 ± 0.02
13 [C]	17.75	340	609	285(100)	Kaempferol-*O*-dihexoside	0.94 ± 0.02
14 [C]	20.98	328	447	285(100)	Kaempferol-*O*-hexoside	0.93 ± 0.01
15 [C]	21.84	332	477	314(100), 315(29), 357(15)	Isorhamnetin-*O*-hexoside	0.95 ± 0.01
					Σ Phenolic acids	11.3 ± 0.3
					Σ Flavonoids	10.1 ± 0.1
					Σ Phenolic compounds	21.4 ± 0.3

Phenolic acids were tentatively identified based on Clifford et al. (2006, 2003), whereas flavonoids were tentatively identified with MS/DAD data. Standards used in quantification: [A] chlorogenic acid; [B] ferulic acid; [C] quercetin-3-*O*-glucoside (Table A.3). The quantitative results are presented as mean ± standard deviation.

357. The presence of the aglycone (*m/z* 315) in the MS^3 product ion analysis allowed the unambiguous differentiation of rhamnetin and isorhamnetin.

In quantitative terms, *cis*-3-*O*-caffeoylquinic acid emerged as the most abundant (~32 %) phenolic compound in the hydroethanolic extract of eggplant aerial parts, with a concentration of 6.8 mg/g extract (Table 1). Collectively, the *cis*- and *trans*- forms of 3-*O*-caffeoylquinic acid and 5-*O*-caffeoylquinic acid accounted for 50 % of the quantified compounds. Additionally, kaempferol-*O*-dihexoside and quercetin-*O*-dihexoside were the predominant flavonoids, quantified at 4.04 mg/g and 3.23 mg/g extract, respectively.

Chlorogenic acid (5-caffeoylquinic acid) was previously identified in an eggplant leaf hydromethanolic extract, along with caffeic acid, cryptochlorogenic acid (4-*O*-caffeoylquinic acid), panasenoside (a known α-glucosidase inhibitor), and (6 R,7*E*,9 R)-4,7-megastigmadien-3-one-9-β-D-glucopyranoside [27]. Additionally, 5-*O*-caffeoylquinic acid has been reported as the most abundant phenolic compound in eggplant fruit pulp [2]. A previous study also found a higher total phenolic content in eggplant leaf extract compared to the fruit, stem, or root extracts [28]. This can be explained by the fact that phenolic compounds are generally located mainly in the plant's dermal tissues rather than in the edible portions, due to their protective functions.

When compared to tomato (*Solanum lycopersicum* L.) aerial parts, which contain up to 3.37 mg/g extract of phenolic acids and up to 20.99 mg/g extract of flavonoids (mainly quercetin-3-*O*-rutinoside), eggplant aerial parts had 3.35 times more phenolic acids but approximately half the flavonoids content [17]. In contrast, bell pepper (*Capsicum annuum* L.) plants at the end of the fruit production cycle contain 41.3–50.0 mg/g of phenolic compounds, with flavonoids (mainly *O*-glycosylated luteolin derivatives) as the predominant compounds (75.6–77.7 %), followed by phenolic acids. Therefore, eggplant aerial parts contain 2.3 fewer phenolic compounds than bell pepper aerial parts [5]. Nonetheless, these are noteworthy by-products as a sustainable source of high-value compounds.

3.2. Bioactive properties

3.2.1. Antioxidant activity

Previous studies have attributed antioxidant properties to eggplant leaf extracts, highlighting their capacity to scavenge DPPH free radicals and $ABTS^{\bullet+}$ radical cations *in vitro* [29–31]. Notably, eggplant leaf extract has demonstrated greater scavenging activity compared to root, stem, and fruit extracts [28]. However, these chemical assays have been criticized for not accurately representing *in vivo* systems. Indeed, these radicals are not found in the human body and exhibit high steric hindrance around their nitrogen-cantered atom, making them poor models for biologically relevant highly reactive radicals such as hydroxyl ($OH^{\bullet}$) and peroxyl ($LOO^{\bullet}$) radicals [28].

To the best of the authors' knowledge, no studies have investigated the antioxidant activity of eggplant leaf extracts using living cells as oxidizable targets or physiologically relevant free radicals. Therefore, this study assessed the *in vitro* antioxidant activity through TBARS formation inhibition and oxidative hemolysis inhibition assays, which measure the extent of hydroxyl radical-induced lipid peroxidation of polyunsaturated fatty acid moieties in porcine brain tissue cell membranes [19] and peroxyl radical-induced membrane damage in sheep erythrocytes [32], respectively. Although involving a different mechanism of action, both assays rely on lipid oxidation, and the results obtained reflect biologically relevant radical-scavenging activity and microlocalization of antioxidants. Specifically, the TBARS assay establishes the extract concentration needed to prevent the formation of malondialdehyde (MDA), a highly reactive end-product, by donating H atoms to the free radicals. In contrast, the OxHLIA assay defines the extract concentration needed to retard oxidative hemolysis by eliminating the free radicals generated in the system over time.

The antioxidant activity results of the eggplant aerial parts extract and the positive control, Trolox, are summarized in Table 2. For the TBARS assay, data are expressed as EC_{50} values, translating the extract concentration required to achieve 50 % antioxidant activity. For the OxHLIA assay, data are presented as IC_{50} values, representing the concentration needed to protect 50 % of the erythrocytes from oxidative hemolysis for a given time. In both assays, lower EC_{50} or IC_{50} values signify greater antioxidant activity. The extract showed significant antioxidant potential, inhibiting MDA formation with an EC_{50} value of 97 μg/mL and oxidative hemolysis with IC_{50} values of 25.3, 49, and 73 μg/mL for 60, 120, and 180 min, respectively. Although statistically different ($p < 0.05$), the results obtained with the extract are comparable to those of Trolox, the water-soluble α-tocopherol analog used as the positive control.

3.2.2. Antidiabetic activity

The rising prevalence of diabetes mellitus presents a significant and challenging public health issue. Despite the increasing availability of newer antidiabetic agents for managing hyperglycemia, current treatment approaches remain far from optimal, underscoring the need for further advancements in the field. Among the therapeutic options,

Table 2
Bioactive properties of the extract of eggplant aerial parts at the end of the production cycle and positive controls.

		Extract	Positive control
TBARS formation inhibition			Trolox
EC_{50} values (μg/mL)		97 ± 2	5.4 ± 0.3
Oxidative hemolysis inhibition			Trolox
IC_{50} values (μg/mL)	Δ*t* 60 min	25.3 ± 0.6	19.6 ± 0.7
	Δ*t* 120 min	49 ± 1	41 ± 1
	Δ*t* 180 min	73 ± 1	63 ± 1
α-Glucosidase inhibition			Acarbose
IC_{50} values (μg/mL)		8.06 ± 2.31	285.65 ± 117.62
AGEs formation inhibition			Aminoguanidine
IC_{50} values (μg/mL)		1.24 ± 0.15	81.92 ± 24.06
Lipase inhibition			Orlistat
IC_{50} values (μg/mL)		3917 ± 629.63	27.68 ± 15.31
NO production inhibition			Dexamethasone
EC_{50} values (μg/mL)		> 400	6 ± 1
Cell growth inhibition			Ellipticine
GI_{50} values (μg/mL)	AGS	16.7 ± 0.4	1.23 ± 0.03
	CaCo−2	11.5 ± 0.3	1.21 ± 0.02
	MCF−7	> 400	1.02 ± 0.02
	NCI-H460	> 400	1.02 ± 0.01
	PLP2	> 400	2.3 ± 0.2

AGS – gastric adenocarcinoma; Caco-2 – colorectal adenocarcinoma; MCF-7 – breast adenocarcinoma; NCI-H460 – non-small cell lung carcinoma; PLP2 – porcine liver primary cell culture. The results are presented as mean ± standard deviation. In each line, there are statistically significant differences ($p < 0.05$) between extract and positive control according to a Student's *t*-test.

α-glucosidase inhibitors stand out as particularly valuable, especially for individuals consuming high-carbohydrate diets. These inhibitors function by competitive inhibition of the α-glucosidase enzyme located at the brush border of the small intestines, thereby delaying the digestion of complex carbohydrates and the subsequent absorption of glucose [33]. While various α-glucosidase inhibitor drugs are currently in use, such as acarbose, these can cause abdominal distention, flatulence, meteorism, and diarrhea [34]. Therefore, there is a growing interest in exploring natural products with this inhibitory action from plant materials, which could have a strong α-glucosidase inhibitory activity and a lower α-amylase inhibitory effect, thus presenting minimal side effects [35].

In this study, the crude extract prepared from eggplant aerial parts demonstrated a very promising α-glucosidase inhibitory capacity, exhibiting an IC_{50} value 47.5 times lower than that of acarbose, the competitive inhibitor used as positive control. Specifically, the IC_{50} value of the extract was determined to be 8.06 μg/mL, compared to 285.65 μg/mL for acarbose (Table 2, Fig. 1A). This result indicates that the extract's enzyme inhibition potential is exceptionally strong, suggesting its potential utility as a functional ingredient in different food matrices and therapeutic agents for managing type 2 diabetes by controlling glucose absorption.

A previous study found that phenolic-enriched extracts from eggplant fruit demonstrated moderate DPPH free radical scavenging activity and strong α-glucosidase inhibitory capacity, suggesting their potential for managing glucose-induced hyperglycemia [34]. Chlorogenic acids, known to inhibit α-glucosidase, were already identified as key contributors to this effect [36]. Additionally, in an *in vivo* trial using alloxan-induced diabetic rats, a methanolic extract from eggplant leaves was shown to reduce glucose levels, as well as urea, protein, and total cholesterol levels, with prolonged treatment [37]. However, further research is needed to fully understand the inhibitory potential of eggplant aerial parts, particularly their extracts and phytochemicals.

Glucose and other reducing sugars are crucial nutrients for sustaining life. However, within living organisms, sugars like fructose and glucose can undergo non-enzymatic binding to proteins, altering their structure and function in a process known as glycation. This process leads to the formation and accumulation of AGEs. The interaction between AGEs and their receptors, particularly the receptor for AGEs (RAGE), can result in the degradation of functional proteins and tissue damage. The accumulation of AGEs also plays a significant role in the onset and progression of diabetes-related complications [38]. While certain drugs, such as guanidines (with aminoguanidine being the most studied and widely used), telmisartan, and kremezin, are employed to mitigate the accumulation of AGEs, little is known about the potential of plant extracts to inhibit glycation [39].

In this work, the extract from eggplant aerial parts was found to be about 31 times more potent than aminoguanidine, with an IC_{50} value of 1.24 μg/mL, compared to 81.92 μg/mL for aminoguanidine (Table 2, Fig. 1B). This result, along with the observed α-glucosidase inhibition activity, indicates that this plant extract possesses a significant antidiabetic potential and could be revolutionary in the food and pharmaceutical industries as a sustainable, functional ingredient to improve the quality of life in patients with diabetes mellitus.

A study by Yoshika Ishioka et al. [38] examined 187 plant matrices for their anti-glycation properties, including eggplant fruit peel, which was found to be 3.5 times less potent than aminoguanidine. Despite this, it ranked among this study's top 10 more potent matrices. Additionally, an *in vivo* study reported that African eggplant (*Solanum macrocarpon* L.) leaf extract exhibits antidiabetic activity in alloxan-induced diabetic adult male albino rats [40]. Compounds such as chlorogenic acids, quercetin, and kaempferol derivatives have been recognized for their antidiabetic effects [36,41–43]. Furthermore, isorhamnetin derivatives have been highlighted as promising agents in antidiabetic therapy, with actions including reducing insulin resistance, enhancing glucose uptake by skeletal muscle, improving lipid profile, and mitigating oxidative stress and inflammation [44,45].

The use of plant extracts as therapeutic agents offers several advantages over synthetic drugs due to their multi-target mechanisms. Unlike individual compounds, plant extracts contain a diverse array of bioactive molecules, such as phenolic acids and flavonoids, which can act synergistically to enhance efficacy while potentially minimizing adverse effects associated with high doses of single compounds [15,46]. This multi-target approach can be particularly beneficial for managing complex metabolic disorders such as diabetes, where oxidative stress, inflammation, and enzyme regulation are interconnected [15,46]. Moreover, plant-derived extracts, especially those from agro-industrial by-products, support sustainable development by promoting waste valorization and reducing the environmental footprint of synthetic drug production. In this context, the findings of this study highlight the potential of post-harvest eggplant aerial parts as a renewable source of active compounds with *in vitro* antioxidant, anti-inflammatory, and antidiabetic properties, reinforcing the role of natural extracts in functional food, nutraceutical, and pharmaceutical applications, providing sustainable and effective alternatives for health management.

3.2.3. *Anti-obesity potential*

Pancreatic lipase is the main enzyme responsible for the digestion and absorption of triglycerides. Inhibition of pancreatic lipase is one of the most extensively studied approaches for assessing the potential of natural products to reduce the absorption of dietary fat. The reduction of energy intake from dietary fat through the inhibition of this enzyme stands as a strategy for the prevention and treatment of obesity [47]. Today, orlistat is among the most commonly used drugs for lipase inhibition; however, consumer interest is growing in more effective and natural products. As a result, research on natural extracts as lipase inhibitors has become increasingly important.

In this study, eggplant leaf extract exhibited an IC_{50} value of 3917 μg/mL, making it 100 times less potent than the reference drug orlistat (Table 2, Fig. 1C). Despite its lower activity, this result is promising given its natural origin, and it may serve as an adjuvant to enhance the lipase inhibitory effect when combined with certain drugs or other extracts. Furthermore, the extract can be purified to increase the concentration of natural compounds involved in lipase inhibition.

Chlorogenic acids have been found to enhance lipid metabolism,

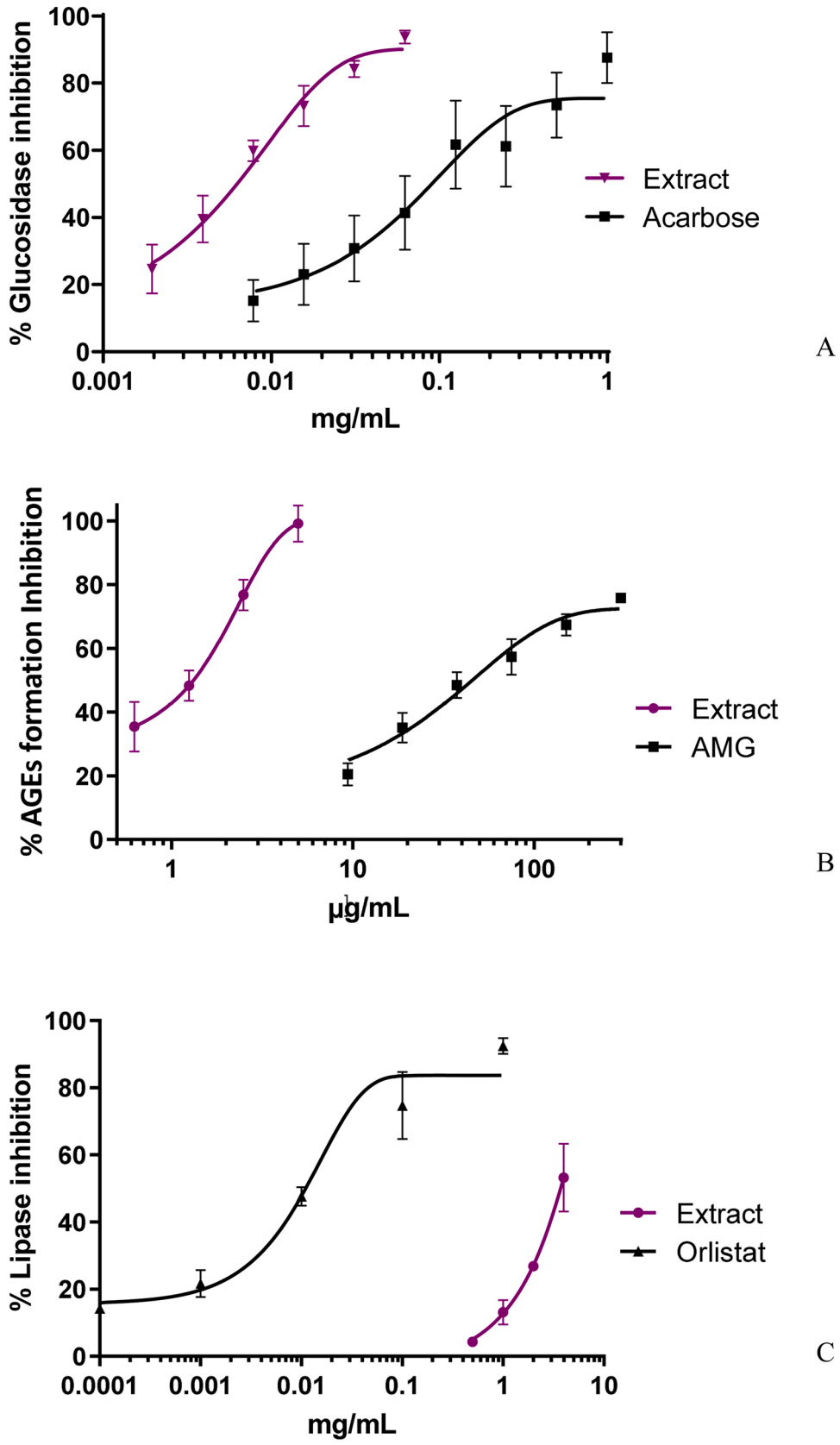

Fig. 1. Inhibitory capacity of eggplant aerial part extract and positive controls on (A) α-glucosidase activity, (B) AGEs formation, and (C) lipase activity.

thus presenting potential as anti-obesity agents [48]. Similarly, quercetin has been linked to anti-obesity effects [42]. Kaempferol derivatives are also being investigated for their potential as agents against obesity [49]. However, the anti-obesity effects of isorhamnetin remain somewhat controversial, with some studies providing conflicting evidence [45,50]. In an *in vivo* study, eggplant leaf hot water extracts significantly reduced glucose levels in alloxan-induced diabetic rats. These effects were comparable to those of glibenclamide (10 mg/kg), a second-generation sulfonylurea antidiabetic agent known for its hypoglycemic properties [37].

3.2.4. Anti-inflammatory potential

NO plays a complex role in inflammation and has a bidirectional relationship with pro-inflammatory cytokines such as IL-6, IL-8, and TNF-α. The studied plant extract did not inhibit the NO production by LPS-stimulated macrophages at concentrations up to 400 μg/mL (Table 2). Additionally, neither IL-8 nor TNF-α production was detected under the assayed conditions, regardless of the presence or absence of the inflammatory stimuli. This result was unexpected, as previous studies conducted under similar conditions reported the production of these metabolites [22,51]. The absence of their production suggests that the plant extract may specifically target pathways upstream of TNF-α and IL-8, suppressing their production. This may indicate that the extract has a unique or context-dependent anti-inflammatory mechanism, potentially offering high pharmacological value. Additionally, TNF-α-blocking agents are commonly used to treat inflammatory conditions like rheumatoid arthritis and Crohn's disease [52].

On the other hand, data for IL-6 showed that the extract alone did not induce its production, as no IL-6 was detected in the presence of the extract, indicating a strong suppression. This data was corroborated by the results obtained in the presence of the inflammatory stimuli, as the presence of the eggplant aerial parts extract led to a 1-fold reduction in IL-6 expression relative to the inflammatory control. Given that IL-6 is involved in both pro- and anti-inflammatory responses and plays a key role in chronic inflammation and epithelial cell function [53], this reduction indicates that the plant extract effectively suppresses this inflammatory marker. The findings suggest that the extract might interfere with signaling pathways responsible for IL-6 production, potentially inhibiting nuclear factor kappa B (NF-κB) or other transcription factors involved in cytokine expression [54].

The anti-inflammatory activity of an aqueous eggplant leaf extract was previously demonstrated in Wistar albino rats, which did not experience any adverse effects or mortality when administrated at a dose of 2 g/kg [55]. The anti-inflammatory effects of eggplant stalk were also studied in RAW 264.7 cells, where hexane and dichloromethane fractions significantly reduced TNF-α, IL-6, and IL-1β production at concentrations that caused no cytotoxicity [13]. However, these extracts contained low phenolic levels, suggesting that other compounds may be responsible for the observed effects. Additionally, some lignanamides isolated from the eggplant roots have been reported to inhibit NO production in LPS-stimulated RAW 264.7 cells [56]. Further studies are needed to characterize the mechanisms underlying the anti-inflammatory effects and to identify the bioactive components involved.

3.2.5. Cytotoxic activity

Plants exhibit diverse chemical profiles and bioactivities, making the discovery of new plant-based antitumor agents particularly challenging. Ideally, these agents should selectively target tumor cells while sparing non-tumor cells from toxicity. Current antitumor drugs are known for their aggressive impact on the human body, underscoring the potential of natural extracts and compounds in chemotherapy and chemoprevention. In this study, the eggplant aerial parts extract showed no cytotoxicity toward porcine liver primary cells (PLP2) at the maximal concentration tested (IC_{50} > 400 μg/mL). However, it exhibited significant cytotoxicity against human gastric (AGS) and colon (CaCo-2) adenocarcinoma cell lines, with IC_{50} values of 16.7 and 11.5 μg/mL, respectively (Table 2). Although these values are approximately 10 times higher than those of ellipticine, they are promising for a natural plant extract. These findings suggest that eggplant aerial parts extract could be further explored as a potential source for developing new bio-based medicines, offering a less aggressive alternative to the drugs currently used to treat these digestive system cancers.

3.2.6. Antimicrobial activity

Phenolic compound-enriched extracts with antimicrobial activity have attracted growing research interest in recent years, as these bioactive ingredients could potentially replace or serve as alternatives to certain artificial food preservatives. As shown in Table 3, the studied plant extract demonstrated superior inhibitory (MIC ≤ 1.54 mg/mL) and bactericidal (MBC ≤ 3.08 mg/mL) effects against *Staphylococcus aureus*, *Listeria monocytogenes*, *Salmonella enterica* subsp. *enterica* serovar Typhimurium, and *Enterobacter cloacae* compared to sodium benzoate (E 211), a widely used artificial preservative in processed foods and beverages. Additionally, the extract outperformed potassium metabisulfite (E 224) in inhibiting growth of *Bacillus cereus*. The extract also showed effectiveness against fungal species, namely *Aspergillus versicolor*, *Penicillium funiculosum*, *P. verrucosum* var. *cyclopium*, and *Trichoderma viride*. Since these bacterial and fungal strains are associated with food contaminations, incorporating the studied extract into food products could potentially reduce or eliminate the need for artificial preservatives, in line with contemporary consumer expectations.

A previous study attributed antibacterial properties to young leaves from eggplant cv. Mirval grown in Tunisia, specifically against *S. aureus* and *Candida albicans*, with MIC values of 0.2 mg/mL and 0.8 mg/mL and MBC values of 0.2 mg/mL and 3.1 mg/mL, respectively [14]. The authors also found a correlation between antimicrobial activity and phenolic content. Additionally, the antifungal activity of eggplant leaf extracts, obtained using petroleum ether, chloroform, methanol, and water, was evaluated against human pathogenic dermatophytes

Table 3
Antimicrobial activity of the extract of eggplant aerial parts at the end of the fruit production cycle and positive controls.

Microorganisms	Extract		Positive controls			
			E 211		E 224	
Bacteria	MIC (mg/mL)	MBC (mg/mL)	MIC (mg/mL)	MBC (mg/mL)	MIC (mg/mL)	MBC (mg/mL)
Staphylococcus aureus	1.54	3.08	4.00	4.00	1.00	1.00
Bacillus cereus	0.77	1.54	0.50	0.50	2.00	4.00
Listeria monocytogenes	0.77	1.54	1.00	2.00	0.50	1.00
Salmonella enterica subsp. *enterica* serovar Typhimurium	0.77	1.54	1.00	2.00	1.00	1.00
Escherichia coli	1.54	3.07	1.00	2.00	0.50	1.00
Enterobacter cloacae	0.77	1.54	2.00	4.00	0.50	0.50
Fungi	MIC (mg/mL)	MFC (mg/mL)	MIC (mg/mL)	MFC (mg/mL)	MIC (mg/mL)	MFC (mg/mL)
Aspergillus fumigatus	1.54	3.08	1.00	2.00	1.00	1.00
Aspergillus versicolor	0.77	1.54	2.00	4.00	1.00	1.00
Aspergillus niger	1.54	3.08	1.00	2.00	1.00	1.00
Penicillium funiculosum	0.77	1.54	1.00	2.00	0.50	0.50
Penicillium verrucosum var. *cyclopium*	0.77	1.54	2.00	4.00	1.00	1.00
Trichoderma viride	0.77	1.54	1.00	2.00	0.50	0.50

E 211 – sodium benzoate (food additive); E 224 – potassium metabisulfite (food additive); MIC - minimum inhibitory concentration; MBC - minimum bactericidal concentration; MFC - minimum fungicidal concentration. The negative control showed no influence on microbial growth at the highest tested concentration.

(*Trichophyton mentagrophytes*, *T. rubrum* and *T. tonsurans*) and opportunistic fungi (*Candida albicans* and *Trichosporon beigelii*) [57]. All extracts, except the aqueous one, demonstrated antifungal properties in agar well diffusion tests, with the chloroform extract showing the highest efficacy against the tested pathogens.

4. Conclusion

The hydroethanolic extract prepared from eggplant aerial parts (leaves and branches) revealed a rich profile of phenolic compounds, particularly caffeoylquinic acids and *O*-glycosylated quercetin and kaempferol, which may contribute to its bioactive properties. The extract showed strong antioxidant, antidiabetic, and antimicrobial activities, as well as promising cytotoxic effects against human gastric (AGS) and colon (CaCo-2) adenocarcinoma cells, along with anti-inflammatory potential by reducing IL-6 expression. Thus, the extract's ability to manage glucose absorption and enhance cellular antioxidant protection *in vitro* suggested its potential role in preventing oxidative stress-related diabetic complications. These findings highlight the potential of eggplant crop by-products as a sustainable and cost-effective source of bioactive compounds for the development of functional foods, therapeutic agents, and natural food preservatives. The incorporation of this bioactive extract into food matrices, such as dairy products (e.g., yogurt, cheese) and beverages (e.g., functional drinks, smoothies), could enhance their health benefits while simultaneously contributing to their preservation. For instance, the antioxidant and antimicrobial properties of the extract could help reduce the need for synthetic additives, aligning with the growing consumer demand for clean-label products.

Proposals for future research

Despite the promising bioactive properties observed in the extract from eggplant aerial parts, this study presents some limitations that open avenues for future research. First, while *in vitro* bioactivity assays provide valuable insights, they do not fully capture the complexity of metabolic interactions *in vivo*. Therefore, future studies should incorporate animal models or clinical trials to validate these findings under physiological conditions. Second, it will be crucial to develop more efficient and sustainable extraction methods on a larger scale to maximize the recovery of bioactive compounds, enhance their bioactivity, and reduce solvent consumption, making the process both more efficient and environmentally sustainable. Finally, although this study highlights the potential of the extract for applications in food, nutraceutical, and pharmaceutical formulations, further research is needed to assess its impact when incorporated into different matrices, including its influence on sensory characteristics in real food products. Additionally, studies should evaluate the stability, bioaccessibility, and bioavailability of the bioactive compounds. Addressing these aspects in future research will be essential to fully explore the potential of this underutilized biomass in the food and health industries.

CRediT authorship contribution statement

NÚÑEZ Sonia: Writing – review & editing, Investigation, Formal analysis. **CALHELHA Ricardo C.:** Writing – review & editing, Validation, Investigation. **COSTA Eduardo M.:** Writing – review & editing, Investigation, Formal analysis. **MACHADO Manuela:** Writing – review & editing, Investigation, Formal analysis. **PINTADO Manuela:** Writing – review & editing, Validation, Resources. **SOKOVIĆ Marina:** Writing – review & editing, Validation, Resources. **LÓPEZ Víctor:** Writing – review & editing, Validation, Resources, Investigation, Formal analysis. **BARROS Lillian:** Writing – review & editing, Validation, Resources. **Pinela José:** Writing – original draft, Validation, Supervision, Conceptualization. **AÑIBARRO-ORTEGA Mikel:** Writing – original draft, Validation, Investigation, Formal analysis, Conceptualization. **DIAS Maria Inês:** Writing – review & editing, Validation, Investigation. **PETROVIĆ Jovana:** Writing – review & editing, Investigation, Formal analysis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.procbio.2025.04.002.

Data availability

No data was used for the research described in the article.

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