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Phenolic compounds profile of macerates of different edible parts of carob tree (*Ceratonia siliqua* L.) using UPLC-ESI-Q-TOF-MS^E: Phytochemical screening and biological activities

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ABSTRACT

Locust bean pulp and gum extracts were prepared, and phytochemical tests based on color reactions and chromatographic analyzes were performed. A profile of seventy-six phenolic compounds was obtained by the ultra-high performance liquid chromatography with electrospray ionization and quadrupole time-of-flight mass spectrometry. The main groups of phenolic compounds identified in the both extracts of *Ceratonia siliqua* L., were flavonoids, tannins and phenolic acids.

Moreover, carob pulp and gum extracts were tested for their antimicrobial activity using disk diffusion tests which showed sensitivity of the different strains to the analyzed extracts at a concentration of 100 mg/mL. Additionally, the antioxidant activity of *Ceratonia siliqua* L. extracts was assessed by the 2,2-diphenyl-1-picrylhydrazyl acid test, which confirmed stronger antioxidant properties in the case of the pulp extract.

To sum up, carob pulp and gum extracts present promising alternatives to synthetic additives within the medicinal industry, serving as potential antioxidant agents and preservatives that combat bacterial contamination, thereby offering a more natural approach to enhancing product safety and efficacy.

1. Introduction

Phenolic compounds are the most important bioactive secondary metabolites found in plants and fruits with potential beneficial effects on human health. Their ingestion from fruits and vegetables could allow human body to strengthen its defenses against the oxidation process which threatens cells on a daily basis [1,2]. In addition, phenolic compounds have the advantage of a very great structural diversity possessing a wide range of biological activities: antioxidant, antimicrobial, anti-inflammatory, antitumoral, anticancer, anti-lipidemic, and neuroprotective activities [1,3–6].

Recently, due to the suspicion of toxicity of many synthetic antioxidants, researchers have focused on plant extracts rich in phenolic compounds, such as flavonoids and hydroxycinnamic acids, due to their multiple apparent biological effects, including scavenging of free radicals, metal chelation and inhibition of cell proliferation [1,7].

The carob tree (*Ceratonia siliqua* L.) is a plant that belongs to the Fabaceae (legume) family. The fruits of this plant are made up of elongated, straight or curved compressed pods, of a shiny dark brown color. Moreover, the main parts of carob are the pulp (90%) and the seeds (8–10%) consisting of bark, endosperm and germ [8,9]. This tree thrives in the semi-arid growing conditions of the Mediterranean region and has an annual worldwide production of over 315.000 tons of carob products [10].

The carob tree possesses considerable potential value for the medicinal industry, owing to its unique chemical components, therapeutic properties, and health benefits that stem from its constituents. It has been shown that plant contain a high content of bioactive compounds such as flavonoids, phenolic compounds, anthocyanins, phenolic acids, as well as nutritional compounds such as sugars, essential oils,

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carotenoids, vitamins and minerals [11,12]. Carob trees are traditionally used to obtain locust bean gum (LBG; thickener E410) from the seeds of the pod which is only 10% of the weight of the pod. The emergence of cheaper substitutes for LBG, such as guar or xanthan gum, has made carob cultivation more profitable in the European Union. Additionally, there is growing interest of carob tree because of its hardiness, its indifference to the nature of the soil, its high-quality wood, its ornamental and landscape value (especially for its seeds that are the subject of commercial transactions, which value far exceeds that of wood production). Thus, whole pods, pulp, seeds and gum are extensively traded [13]. The chemical composition of the different carob parts depends on the species, climatic and geographical conditions, harvesting and storage [14]. It should be highlighted, that it is very rich in carbohydrates (40–60%) in particular, sucrose (27–40%), fructose (3–8%) and glucose (3–5%), minerals, proteins, dietary fibers insoluble and tannic acid and is low in fat [15–17]. Due to their high content of bioactive phytochemicals, locust bean fruits are considered to be powerful antioxidants [18].

The aim of the present study was to determine the phenolic profile and other polar compounds of locust bean pulp and gum from Algeria using an ultra-high performance liquid chromatography with electrospray ionization and quadrupole time-of-flight mass spectrometry$^{elevated\ energy}$ (UPLC-ESI-Q-TOF-MS^{E}). To the best of our knowledge the number of studies on the composition of non-volatile compounds of carob pulp is minimal and there are no data in case of carob gum.

2. Materials and methods

2.1. Reagents

Methanol (> 99.9%, CAS 67–56-1); Ethanol (99.9%, CAS 64–17-5); Acetone (99.9%, CAS 67–64-1); Sodium carbonate (99.99%, CAS 497–19-8); Folin-Ciocalteu phenol reagent; Gallic acid (≥98.0%, CAS 149–91-7); Hydrochloric acid (HCl); Aluminum trichloride ($AlCl_3$); Sulfuric acid (H2SO4, 96%, CAS 7664–93); Sodium hydroxide (NaOH, CAS 1310-73-2);Acetic acid (≥ 99.7%, CAS 64–19-7); Phenol (≥99%, CAS 108–95-2); Ethyl ether (≥99.0%, CAS 60–29-7); Butanol (≥99%, CAS 71–36-3); 2,2-diphenyl-1-picrylhydrazyl (DPPH, CAS 1898-66-4) were obtained from Sigma Aldrich represented by Algerian Chemical Society.

2.2. Plant material

The plant material consisted of ripe carob pods collected in the region of Bejaia (Algeria) in August 2017. The specimens of collected samples were identified by the Vegetable Ecological Laboratory of the Algiers University, Algeria. The preparation of carob powder was as following. The pulp was dried at 40 °C in a ventilated oven, ground into a powder and sieved, then stored in the dark in glass vials for further analysis. While the preparation of carob gum was as follows: the endosperm of the carob bean was extracted by mechanical processing and crushed to give rise to a white powder.

2.3. Determination of dry matter

The sample was desiccated in an oven at temperatures of 100 °C to 105 °C, under atmospheric pressure until its mass was constant. The water content of the plant material is given by the following formula:

$$\text{Water content } (\%) = (P - P_1)/M \times 100\%$$

Where P is mass in g of the tested sample before drying; P_1 is mass in g of the tested sample after drying; M is mass of biological material.

From the water content, the dry matter content was determined according to the following formula:

$$\text{Dry matter content } (\%) = 100 - \text{water content } (\%)$$

2.4. Ash determination

The method consisted of weighing 2 g of powder in crucibles. Then, they were placed in a controlled muffle furnace and preheated to 600 °C during 6 h and 30 min (*AOAC 972.15*) [19]. The percentage of ash content was determined according to the following formula:

$$\%Ash = \frac{mass\ (g) crucible\ with\ ash\ after\ incineration – mass\ (g) empty\ crucible}{initial\ mass\ (g) of\ carob\ powder} \times 100$$

2.5. Total sugar content

2.5.1. Extraction

0.5 g of vegetable powder was extracted three times with 5 mL of 80% ethanol by boiling the closed tubes in a water bath at 95 °C for 10 min. After each extraction, the tubes were centrifuged at 2500 revolutions /10 min. The supernatants from the three extractions were filtered using Wattman paper and combined [20].

2.5.2. Dosage

The determination of total sugars was carried out by the method of [21]. Then, 1 mL of extract was placed in a tube and 1 mL of 5% phenol solution and 5 mL of 95% sulfuric acid were added. The tubes were stirred and then placed in a water bath at 100 °C for 5 min. Finally, the tubes were incubated at room temperature for 30 min in the dark. The absorbance was read at 490 nm and the sugar content was expressed as %.

2.6. Fiber content

The fiber content of the locust bean (pulp and gum) was determined according to the protocol described by De Pádua et al. [22] with some modifications. It consisted of the hydrolysis of 2 g of the powder in 100 mL of HCl (5%) for 30 min, the mixture was filtered and washed with hot water. Then, hydrolysis of the residue with NaOH (5%) under reflux for 30 min, followed by filtration and washing with water until the neutral pH, was performed. The residue was washed with ethanol and ethyl ether and dried at 100 °C for two hours. Fiber content was expressed as mass of residue.

2.7. Protein content

The total protein content was analyzed according to the method of (AOAC 976.062016) [23]. The sample (1 g) was mineralized with concentrated H_2SO_4 (15 mL) and anhydrous K_2SO_4 and $CuSO_4$ as catalysts. The process was run at 420 °C for 60 min. With this method, 40% NaOH was used to produce an alkaline distillation medium and 4% H_3BO_3 to collect the distilled ammonia. The titrations were carried out with a HCl (0.1 N) standard solution.

2.8. Quantitative determination of secondary metabolites

2.8.1. Preparation of extracts

The extraction of phenolic compounds was carried out by maceration according to the method of Oomah et al. [24]including methanol (80 and 60%) as extraction solvents.

To do this, 1 g of powder was macerated with 40 mL of each of the two solvents on a hot stirring plate for two hours at room temperature, protected from light. The macerates were filtered through filter paper and then stored at 4 °C in dark for subsequent analyzes. The yields obtained for the two extracts of the studied plant *Ceratonia siliqua* L, expressed as a percentage relative to the weight of the starting dry plant material were 45.2% for the pulp and 5% for the gum.

2.8.2. Determination of total phenolic compounds

The extract was analyzed by Folin-Ciocalteu method [25], adapted and optimized. For this purpose, 2.5 mL sample of water diluted Folin-Ciolcateu reagent (1/10) were added to the extract. The mixture was incubated for 2 min at room temperature, and 2 mL of sodium carbonate (75 g/L) was added. The mixture was incubated for 15 min at 50 °C and finally cooled in a water-ice bath. The specific absorbance at 760 nm was immediately measured. The concentrations were expressed as mg gallic acid equivalent (GAE) per g of dry weight (dw) according to a standard curve of gallic acid.

2.8.3. Determination of total flavonoids content

The content of total flavonoids (TF) was estimated by the $AlCl_3$ method [26]. Briefly, 1 mL of extract was added to 1 mL of 2% methanolic $AlCl_3$ $6H_2O$ incubated for 10 min at room temperature. The absorbance was then read at 415 nm (1 cm optical path). The results were expressed in mg quercetin equivalents (QE) per g dw. Quercetin was used as standard for the calibration curve.

2.8.4. Determination of condensed tannins

The method based on butanol / HCl dosage described by Nicholson and Vermerris [27] was followed with small modifications. 250 μL of each extract was mixed with 2.5 mL of an acidic solution of ferrous sulphate [77 mg of ferric ammonium sulphate: $Fe_2(SO_4)_3$ dissolved in 500 mL of (3: 2 n-butanol: HCl)]. After mixing and incubating at 95 °C for 50 min, absorbance at 530 nm was measured against a blank. Condensed tannins were calculated by using the following formula:

$$\text{Concentration of proanthocyanidins (mg/mL)} = \frac{\text{A550nm} \times \text{DF} \times \text{MW}}{\varepsilon \times l}$$

Where DF is the dilution factor, MW the molecular weight of the cyanidin (287 g/mol) and ε the molecular extinction coefficient (34,700 L / mol / cm). The condensed tannins were expressed as mg of cyanidin equivalent (CE)/ 100 g dw.

2.9. UPLC-ESI-Q-TOF-MS^E analysis

The UPLC analysis was performed using an Acquity unit with an ESI connected to a Xevo G2 QTOF (Time-of- flight mass spectrometer) from Waters (Milford, MA, USA). The chemicals were identified using an UPLC BEH C18 column with 1.7 μm particle size (2.1 × 100 mm) from Waters (Milford, MA, USA). The injection volume was 10 μL and the chromatography was performed at 0.4 mL min^{-1} column flow at 40 °C. MiliQ water with 0.1% formic acid (phase A) and methanol with 0.1% formic acid (phase B) were used as mobile phase. Chromatographic separation began at 98/2 phase A/phase B (1 min), then switched to 0/100 in 6 min and remained at 0/100 for 2 min. The electrospray probe (ESI) on positive ionization mode was designated. Three independent replicates were analyzed.

2.10. Antibacterial activity

The evaluation of the antibacterial capacity related to the locust bean pulp and gum extracts was studied with respect to six bacterial strains: *Staphylococcus aureus* (ATCC 6538), *Meticillin-resistant Staphylococcus aureus (MRSA*, ATCC 43300), *Bacillus cereus* (ATCC 6633), *Listeria innocua* (CLIP 74915), *Escherichia coli* (ATCC 25922), and *Salmonella sp* (Hospital strain). The antimicrobial activity was demonstrated by the diffusion method of the antibacterial compound on the agar medium. The bacterial strains were inoculated into Petri dishes containing agar as nutrient. After 18 h of incubation at 37 °C, microbial suspensions with an optical density of 0.5 Mc Farland were prepared. Whatman paper disks (d = 6 mm) were soaked with 20 μL of locust bean pulp and gum extracts. Then, they were placed on the surface of the dry Muller Hinton agar for incubation at 37 °C for 24 h. The inhibition halo (mm) was measured [28]. An extract was considered active when measuring a zone of inhibition around the disc with a diameter >6 mm without any bacterial growth was observed inside.

2.11. Antioxidant activity by DPPH method

DPPH free radical scavenging activity was determined by the method described by Brand-Williams et al. [29]. 100 μL samples of the extract solutions at different concentrations were added to 2 mL of DPPH solution and the mixtures were vigorously shaken and left to incubate for 20 min at room temperature in the dark. Absorbance was measured at 515 nm against a methanol blank without DPPH radical using a UV–Vis spectrophotometer.

The reduction from initial DPPH concentration by 50% or IC_{50} was calculated plotting the percentage of remaining DPPH against the extract concentration. All the measurements were done in triplicate. Percentage inhibition was calculated using the following formula:

$$\text{Inhibition (\%)} = [(A_B - A_S)/A_B] \times 100$$

Where A_B is the absorbance of the control reaction (containing all reagents except the test compound), and A_S is the absorbance of the tested compound.

2.12. Statistical analysis

All the measurements were performed in triplicate. The results are shown as the mean value of the individual measurements with the corresponding standard deviation (SD), using Microsoft Excel. The difference in means was considered significant at $p < 0.05$.

3. Results and discussion

3.1. Phytochemical screening of Ceratonia siliqua extracts

3.1.1. Dry matter (%)

According to the obtained results, the average dry matter content of the studied pulp and gum of *Ceratonia siliqua* L. was 79.26 ± 0.49 and 92.16 ± 0.65%, respectively. The content of gum dry matter is in agreement with the results reported by Simon [30]. The value found in the literature was 93.2 ± 0.2% for carob pulp. Furthermore, the dry matter content in the locust bean gum found by Mekhoukhe et al. [17]

Table 1
Chemical analysis of *Ceratonia siliqua* L. pulp and gum.

	Dry matter (%)	Ash (%)	Total sugars (%)	Fiber (%)	Protein (%)
C. siliqua pulp	89.26 ± 0.49	3.9 ± 0.4	63.6 ± 0.96	9.7 ± 0.35	5.8 ± 0.3
C. siliqua gum	92.16 ± 0.65	0.85 ± 0.06	22.43 ± 0.61	0.28 ± 0.02	6.53 ± 0.3

was 90.8 ± 0.12%.

3.1.2. Ash content

As shown in Table 1, the ash content found in both parts of *Ceratonia siliqua* L. was.

3.9 ± 0.4% and 0.85 ± 0.06% in the locust bean pulp and gum, respectively. Furthermore, it has been shown that there is a significant difference where the highest content was recorded in carob pulp. Moreover, [31] indicated that carob pulp is considered a good source of minerals, especially calcium, potassium, iron, magnesium and phosphorus.

3.1.3. Total sugar content

The average of the sugar content is 63.6 ± 0.96 and 22.43 ± 0.61% in the locust bean pulp and gum, respectively. The analysis of variance indicated a significant difference between the two parts of *Ceratonia siliqua* L., where the sugar content in the pulp is 3 times higher than that recorded in the gum.

The content of total sugars found in the pulp agrees with those found by other studies. Carbohydrate value of 20.85 ± 0.52% was found by Mekhoukhe et al. [17] in locust bean gum, but it is higher than the levels reported in some investigations [31,32].

According to the literature, the differences in content are attributed to many factors such as geographical origin, climatic conditions, diversity between varieties, harvesting and storage and technological factors [33].

3.1.4. Fiber content

The dosages of dietary fibers carried out on the locust bean pulp and gum gave contents of 9.7 ± 0.35 and 0.28 ± 0.02%, respectively. The analysis of variance indicated a highly significant difference (< 0.01) between the two samples.

Several studies have been carried out on carob fibers and have revealed that carob fibers exert a preventative role against heart disease, blood sugar levels and cancer [34,35]. Moreover, it has been shown that the ingestion of carob fibers reduces HDL and LDL cholesterol and triglyceride levels in the blood, thus contributing to the prevention and treatment of hyperlipidemia [36].

3.1.5. Protein content

Due to richness of carob in protein and their composition in amino acids, which constitute an important physiological characteristic, it could be used as food additive to enrich the protein content and to improve the biological activity of the food system [37].

The highest protein percentage was obtained in the locust bean gum samples with a value of 6.53 ± 0.3%. The protein content obtained in the case of carob pulp was 5.8 ± 0.3%. This result agreed with that observed by Youssef et al. [38] who found a content of 6.34%.

According to the literature, carob pulp contains 18 amino acids mainly represented by aspartic acid followed by alanine, glutamic acid, leucine, valine and arginine. On the other hand, the carob seed is rich in arginine, alanine and lysine, and moderate amounts of isoleucine and valine have been also identified [37].

3.1.6. Total phenolic content

The total phenolic contents measured by the Folin–Ciocalteu method (TPC) of the carob pulp and gum extracts are presented in Fig. 1. A significant difference ($p < 0.05$) was found between TPC of the both extracts, where the carob pulp extract recorded the highest content (13.8 ± 0.14 mg GAE/g dw).

A total phenolic amount recorded for the extracts investigated in the present study was lower than those found by Carbas et al. [39] where TPC was 17.7 ± 0.9 mg GAE/g dw. Although, the results are very different than those found in literature, not only depending on technological factors such as extraction and analysis methods, but also on geographical origin, climatic conditions, harvesting and storage.

3.1.7. Total flavonoid content (TFC)

The results presented in Fig. 1 reported that the TFC of locust bean pulp extract (3.54 ± 0.36 mg QE/g dw) is higher than the content found in gum extract (1.3 ± 0.04 mg QE/g dw). The results obtained in this work are slightly lower than those found by Rakib et al. [40], who reported flavonoid contents range from 5.54 to 5.92 mg/g DM of carob pod powder.

3.1.8. Condensed tannin contents

Condensed tannin contents vary between 5.52 ± 0.37 and 1.24 ± 0.02 mg ATE/g of dw respectively for the pulp and the gum of *Ceratonia*

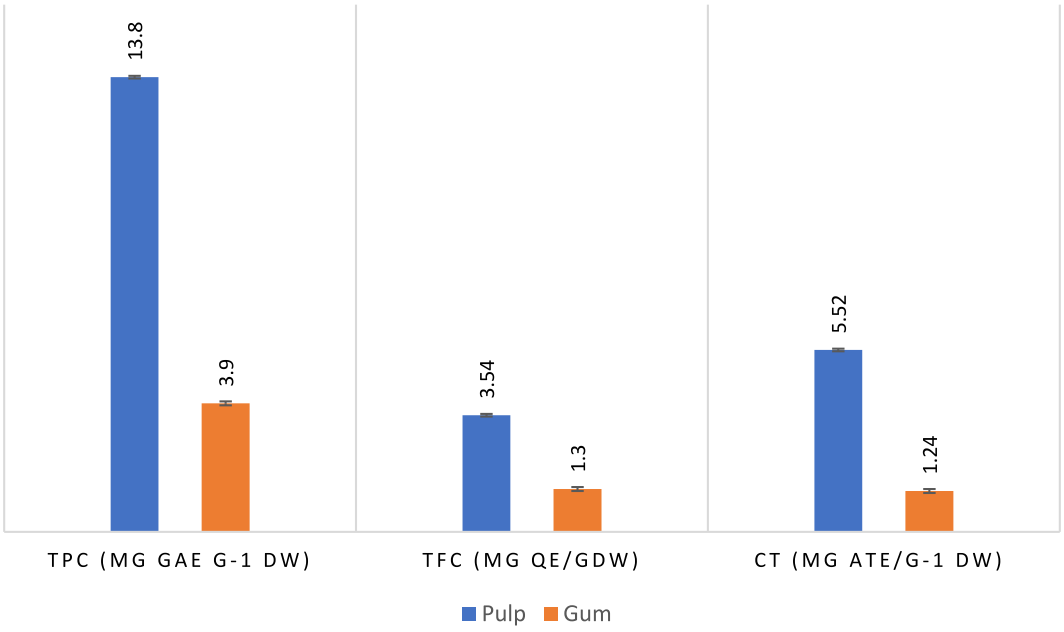

Fig. 1. Total phenolic content, flavonoids content and condensed tannin content in *Ceratonia siliqua* L. pulp and gum extracts.

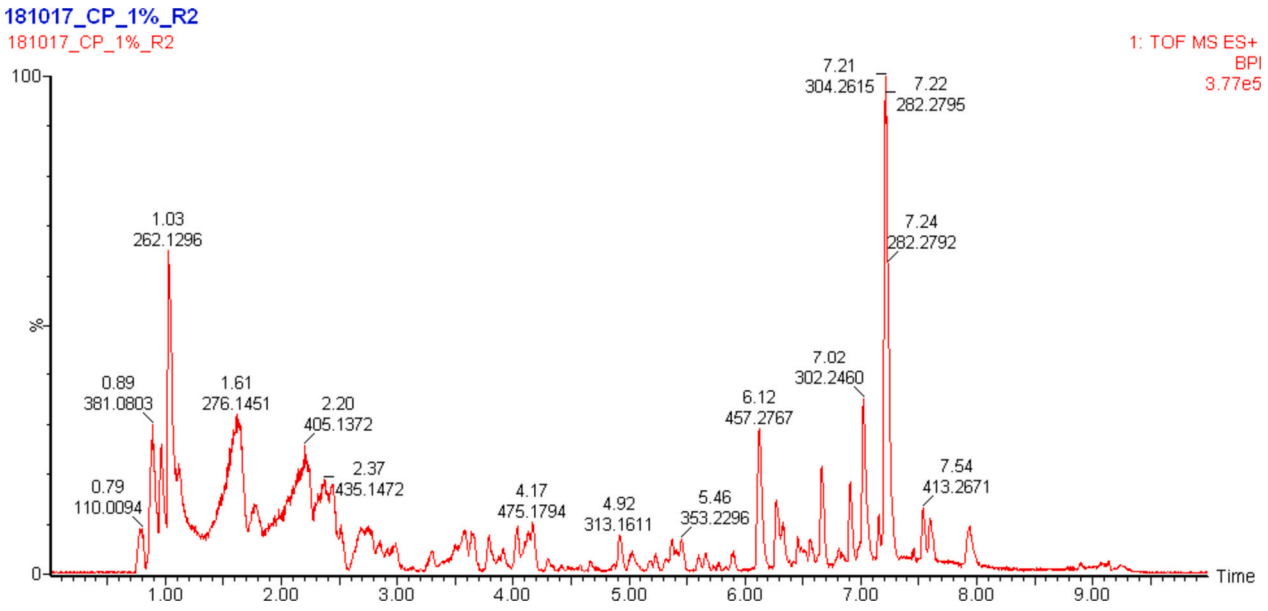

Fig. 2. UPLC-ESI-QTOF-MS^E chromatogram of *Ceratonia siliqua* L. pulp extract.

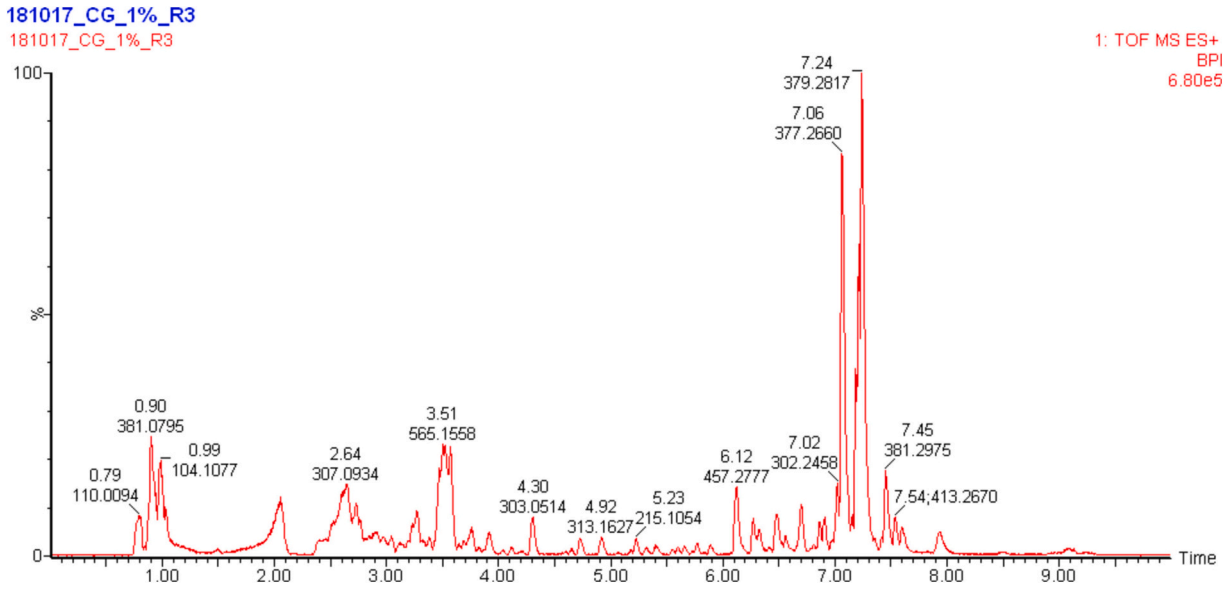

Fig. 3. UPLC-ESI-QTOF-MS^E chromatogram of *Ceratonia siliqua* L. gum extract.

siliqua L.. A significant difference was observed between the two samples and pulp extract manifested with the highest content with a value of 5.52 ± 0.37 mg EAT/g dw.

3.2. Characterization of chemical compounds by UPLC-ESI-Q-TOF-MS^E analysis

The obtained chromatograms of UPLC-ESI-QTOF-MS^E characterization of pulp and gum compounds are shown on Figs. 2 and 3.

The retention times detected precursor ions, and MS/MS fragment ions were determined and used for qualitative analysis. These parameters were given by the software MassLynx 4.1. The data obtained were compared with data from the literature. The ionization conditions were established in the mass spectrometer in order to enable the detection of the *m/z* value corresponding to the precursor ion [M + H] + .

Peak characteristics and tentative identities of compounds present in locust bean pulp and gum extract are presented in Table 2 according to their elution order (The elution time was chosen at 10 min because no analyte was eluted after this time). When a compound was present in both samples, the precursor ion was selected from the gum sample in case of compounds number 22, 24, 27, 41, 4, 46, 47, 48, 51, 53, 54,56, 60, 61, 66, 68, 70, 71. In case of rest of compounds presented in both samples the precursor ion was selected from the pulp sample. Moreover, MS2 spectrum of each compound have been added as supplementary material where CP and CG indicates pulp or gum sample, respectively and number indicates number of compound from Table 2. Spectrum of compounds from pulp and gum samples have been taken from second replicates.

Comparing the results of both samples, 76 different compounds were detected including 25 compounds in common (44 compounds were identified in the carob pulp extract and 57 compounds in the carob gum extract). To the best of our knowledge, no other publication covers such number of phenolic compounds in *Ceratonia siliqua* L pulp and gum extract. According to the literature, the number of studies is minimal on the composition of carob pulp and there are no data on the phenolic

Table 2
UPLC-ESI-Q-TOF-MS^E analysis of *Ceratonia siliqua* L. pulp and gum extracts [41,43,44,46–48,51,53–57,59,61,63–67].

No	RT (min)	[M+H]$^+$ (*m/z*)	MS/MS	Proposed compound	Samples		Literature
					pulp	gum	
1	2.30	479.0842	**121.0099**; 125.0604; **165.0574**; **171.0254**; **207.0610**; **315.0643**; 419.1497	Coumaroyl-*O*-galloyl-glucoside		•	[41]
2	2.43	233.1032	**92.5114**; **118.0876**; **146.0621**; **163.0389**; 167.0706	*p*-Coumaric acid prenyl ester	•		[42]
3	2.51	307.0932	**99.0432**; **127.0412**; **169.0515**; 188.0713; 205.0977; **210.1187**; **221.1026**; **227.1798**;	D-Gallocatechin		•	[43]
4	2.52	307.0919	**127.0443**; **141.0522**; 146.0610; **221.1778**; **263.4430**	Epigallocatechin		•	[44]
5	2.53	435.1484	188.0710; **302.1194**; **303,1462**; 432.1400;	Quercetin -3-*O*-α-L-abinopyranoside	•		[45]
6	2.73	419.1532	210.1148; 265.1437; **286.0629**; 416.1457	Kaempferol-3-*O*-arabinoside (Isomer 1)	•		[45]
7	2.76	295.1290	166.0866; 289.0828	Hydroxy-octadecatrienoic acid I		•	[46]
8	2.80	307.0922	**127.0388**; **141.9521**; 161.0594; **221.1013**; **263.0902**; 289.0818	Epigallocatechin	•		[44]
9	2.85	307.0932	**99.0418**; **127.0382**; **169.0611**; 178.1349; **210.1188**; **221.0956**; **227.0995**; 289.0832	D-Gallocatechin	•		[43]

10	2.96	511.1442	**171.1424**; 195.0666; 213.1132; 314.1611; 350.1826; **359.1369**; 467.0859	Unknown Gallotannin		•	[47]
11	3.04	727.2109	**287.0641**; 425.1425; 488.1164; **595.5740**	Kaempferol-3-*O*-rutinoside-7-*O*- pentoside		•	[46]
12	3.10	393.2096	**163.0739**; 125.9877; 209.1541	Glabrol	•	•	[45]
13	3.12	207.1395	**85.0284; 113.6460; 157.0086; 175.0062**; 189.1272	Shikimic acid derivative	•		[48]
14	3.26	619.0962	196.0965; 346.1868; 449.0730; 505.1910	bis[2-(4-Biphenylyl)-2-oxoethyl] dodecanedioate	•		[48]
15	3.27	595.1671	**355.1754; 385.1541;** 405.1724; **475.1479; 505.2128**	Apigenin-C-hexoside-C-hexoside		•	[49]
16	3.47	565.1556	**287.0906;** 302.0554; 355.1729; 481.2642	K 7-*O*-desoxyhexosyl-pentoside		•	[48]
17	3.57	465.1369	**153.0207**; **181.0835**; 261.1341; 273.0761; 301.1257;	Quercetin-3-glucoside	•		[50]

			302.1299; **303.0792**; 460.1705				
18	3.64	525.2889	**171.1307**; **193.0895**; **211.0972**; 219.0995; 301.0729; **315.1299**; **373.1068**; **507.2153**	Quinic acid derivative		•	[51]
19	3.65	475.1786	**171.9959**; 261.1340; **323.1178**; 364.1965; 463.1785	Trigallic acid	•		[51]
20	3.75	565.1556	260.0255; 319.0463; 355.1722; **373.1432**; **374.0781**; **555.2305**	Caffeoylglucaric acid derivative		•	[52]
21	3.79	463.1785	**163.1454**; **181.0835**; 261.1341; 273.0761; **286.0566**; **287.1393**; 301.1257; 460.1705; 475.1782; 599.1977	Kaempferol-3-*O*-glucuronide	•		[52]
22	3.81	475.1791	261.1340; **271.0649**;	Apigenin-7-*O*-(acetyl) glucoside	•	•	[53]

			273.0769; 301.1254; 435.1303				
23	3.83	535.1437	**137.1014** ; **181.0828** ; **193.1314** ; 229.1404 ; 273.1680 ; **355.1711**	Caffeic acid-*O*-hexoside derivative	•	•	[54]
24	3.91	147.0446	**51.9443; 65.0500; 77.2160; 91.7483; 103.0557; 119.0838**	Coumarin	•	•	[55]
25	3.94	319.0458	147.0449; 185.1160	Myricetin		•	[56]
26	4.14	395.2044	193.1594; 211.1705; 373.2216	Xanthone derivative		•	[57]
27	4.30	303.0507	**91.4092**; **126.9930**; **167.1517**; **275.0785**	7-*O*-Methyl aromadendrin	•	•	[58]
28	4.38	299.1105	249.1473; **256.0314; 271.0681; 284.1474**	4'-Methoxytectochrysin		•	[59]
29	4.42	331.2060	125.9862; **169.1158**; 291.1585	Vanillic acid-*O*-hexoside		•	[49]
30	4.33	505.1896	227.1247; **287.1258**; 303.0495; **401.1614**; 441.1524; **445.2100**	Luteolin 3'-(3''-acetylglucuronide)	•		[59]
31	4.43	433.2034	**121.1001**; **139.0036**; 245.0709;	Tyrosol-glucosyl-*O*-pentoside	•		[60]

			291.1555; **301.0984**; 331.2123			
32	4.44	331.2078	125.9872 ; 185.1176 ; **287.0537**	Carnosol	•	[49]
33	4.48	449.1079	**177.1741; 273.1752;** 293.1745; 301.1051	Naringenin-*O*-hexuronide	•	[49]
34	4.49	449.1073	233.0937; **287.0536;** 301.1049; 331.2096; 475.1911	Kaempferol-3-*O*-glucoside	•	[49]
35	4.57	277.1417	125.9869; **133.1175; 151.9529; 181.1280; 223.0914; 241.0690**	Unknown sugar	•	[61]
36	4.60	287.0551	**95.0824; 121.1002; 167.5509**; 277.1414	7-*O*-Methyl naringenin	•	[58]
37	4.65	483.1776	**231.2168;** 225.1120; **259.1061; 303.0517**; 317.0650; 469.2002	Galloyl-hexahydroxydiphenoyl (HHDP)-glucose	•	[47]
38	4.68	485.1992	**127.0395; 171.1459;** 203.1050; 293.1738	Digalloylglucose	•	[41]
39	4.73	491.2113	53.2227; 182.1182; 232.0958;	4”-*O*-Acetylquercitrin	•	[56]

			461.2021; 465.1740;				
40	4.73	941.4149	**171.1109**; 203.1044; 485.2010; 490.1849; **619.3463** ; 649.2856 ; **771.8959**	Pentagalloyl glucose		•	[41]
41	4.83	287.0562	**201.1241**; **203.0455**; **216.0623**; 225.1084; **231.1382**; 233.0950; **243.1045**; **245.1220**; **272.0538**	Sakuranetin or Isosakuranetin	•	•	[60]
42	4.91	313.1637	**137.1273** ; **151.1490** ; **181.0936**	trans-Caftaric acid or Caftaric acid	•	•	[62]
43	5.03	503.2111	84.9600 ; **91.2959** ; **231.1309** ; **270.1457** ; **297.1314**; **303.1604** ; **341.2039** ; 373.1845 ; 485.2016	Quercetin derivative	•		[63]
44	5.12	271.0615	125.9877 ; **150.0947** ;	Apigenin	•		[64]

			184.1483 ; 225.1096 ; **227.1228**				
45	5.14	461.2377	**165.1216** ; **175.0075** ; 223.0929 ; **297.1518** ; 307.0876 ; **339.1880** ; 355.1537	Coumaroylquinic acid derivative		•	[52]
46	5.32	425.1784	**151.0762;** **169.1233;** **195.1378;** **305.2056;** **313.2337**; 319.2244; 363.1931	Maclurin C-glucoside	•	•	[41]
47	5.38	353.2286	**173.0787** ; **191.1096** ; **192.0502** ; **193.0818** ; **215.1256** ; 350.9875	Cinnamic acid-3-*O*-acetylhexoside	•	•	[49]
48	5.66	451.1949	233.0946 ; 293.1336	Ferulic acid-*O*-hexoside derivative	•	•	[49]
49	5.73	437.1943	125.9862; 185.1165; **274.2784;** **287.1243;** **317.6177;** **347.2398;** 365.1047	Methoxyl mangiferin		•	[41]

50	5.83	541.2638	125.9875; **127.9807; 171.0074; 227.1456;** 230.2478; **333.2028; 379.2169**	Galloyl dihexoside derivative	•	[48]
51	5.89	509.2375	125.9859; 265.1806; **317.1742; 347.1794**; 365.1036	Syringetin-3-*O*-glucoside	• •	[49]
52	5.95	335.2187	**99.7165; 153.9504; 237.1093;** 289.1760; **317.2003**	Trihydroxyoctadecanoic acid sulphate	•	[65]
53	6.12	457.2783	**162.0748; 274.2141; 290.2791; 308.1920;** 237.1227; 337.2363	Caffeic acid derivative	• •	[49]
54	6.27	301.1417	**139.0372;** 149.0239; **181.0539; 241.1422**	p-Hydroxybenzoyl glucoside	• •	[62]
55	6.32	301.1416	**95.0872; 124.1193; 167.1432; 200.1277;** 240.2342; **258.0889; 286.3108**	Luteolin 7-methyl ether	• •	[58]
56	6.38	339.2500	125.9869; **165.0935; 193.0722;** 223.0934; 293.2094	Coumaroylquinic acid	• •	[66]

57	6.42	357.1471	**195.1106**; 235.2068; 295.1670	Ferulic acid-*O*-hexoside		•	[49]
58	6.46	317.2086	179.1438; 277, 2170; **289.2144**; **302.2225**; **303.1340**	Isorhamnetin	•		[59]
59	6.51	317.2089	**155.1033**; **163.1136**; **225.1854**; 254.1429; **271.6469**; 277.2173	Protocatechuic acid-*O*-hexoside	•		[49]
60	6.56	425.2142	**151.1006; 169.0458; 305.2061;** 319.2240; 363.1928	6-*O*-Galloyl arbutin	•	•	[41]
61	6.66	321.2405	**95.0911; 121.1054; 139.3092; 157.3731; 165.0910; 259.0498; 277.2127; 303.2260;** 319.2241	5-*O*-*p*-Coumaroylshikimic acid	•	•	[65]
62	6.70	319.2244	**275.0835**; 279.2324	(13:1) Anacardic acid		•	[51]
63	6.81	627.3351	228.2330; **303.2199; 316.1287**; 365.1054; 415.3023; **465.2848**	Dihexosylquercetin	•		[65]
64	6.96	351.2513	**126.4713; 191.1318;**	Ethyl 2,4-dihydroxy-3-(3,4,5-trihydroxybenzoyl)oxybenzoate		•	[41]

			199.1333; 276.2315; 341.2675				
65	7.00	629.3500	302.2455; **303.2410**; **321.2451**; 365.1054; 437.3445; 515.6150	Delphinidin-3-*O*-(6-p-coumaryl) glucoside	•		[62]
66	7.02	302.2449	**203.0504**; **231.1706**; 245.2253; 263.2373; 280.2630	Ellagic acid	•	•	[58]
67	7.07	377.2665	237.2220; 263.2376 ; **333.2438**	(17 :0)-Anacardic acid		•	[51]
68	7.22	282.2797	**149.1340**; 156.1394; **164.1537**; **234.1001**; 265.2535	p-Coumaric acid cinnamyl ester	•	•	[43]
69	7.24	379.2817	**109.0278**; **121.0962**; **127.0367**; **171.1310**; **227.2095**; 265.2534; 282.2799	Galloyl hexoside derivative		•	[48]
70	7.54	413.2657	**149.0226**; 163.0451; **251.0086**; **252.1334**; 332.2912; 365.1046	(Iso)pentyl dihexoside	•	•	[52]

71	7.60	481.2845	203.0539; 309.1999; **319.1942**; 413.2639	Petunidin-3-*O*-glucoside	•	•	[50]
72	7.69	365.1069	**115.0739** ; 125.9875 ; **163.1136 ;251.1597**	Unknown sugar	•	•	[52]
73	8.42	599.4242	125.9866 ; 203.0528 ; **359.2157** ; 365.1060 ; **389.3320 ; 419.4349 ; 479.3707**	Phloretin dihexoside		•	[46]
74	9.12	497.3959	**171.1493; 193.1598;** 280.6547; **345.0858;** 475.4202	3,5-Digalloylquinic acid		•	[41]
75	9.23	149.0030	107.0268; 121.0093; 141.9582	(E)-Cinnamic acid	•	•	[67]
76	9.75	127.0404	**110.0118**; 111.0432 ; 118.0859 ; 125.9854	Pyrogallol	•	•	[60]

The most intensive MS/MS fragments have been bolded and marked with blue color. Presence of compounds in each sample was marked with symbol '•'.

compounds of carob gum. The three quarters of all phytochemicals (compounds 1 → 16; 18 → 23; 26 → 28; 30 → 32; 35 → 37; 39; 41; 42; 45;46; 48; 49; 51;52; 54 → 56; 58 → 65; 67; 68; 70 → 74) corresponded to molecules first identified in carob pulp.

The compounds identified in both extracts were classified into different families: flavonoids, condensed tannins, phenolic acids, organic acids, catechins and other polar compounds. Flavonoids are the most numerous groups of phenolic compounds found in the analyzed extracts.

D-gallocatechin and epigallocatechin were identified in both extracts. However, Quercetin arabinopyranoside, quercetin-3-glucoside and quercetin derivative were only identified in the pulp extract. . Another compound of the class of flavanones has been characterized as glabrol, which participates in the regulation of glucose and lipid metabolism [45].

Kaempferol-3-*O*-arabinoside and kaempferol-3-*O*-glucuronide were identified in the pulp extract while kaempferol rutinosidepentoside and kaempferol-3-*O*-glucoside were characterized in the gum extract. Each of these compounds showed the loss of different glycosides but had in common a characteristic aglycone fragment (*m/z* at 287) attributed to kaempferol [52]. Moreover, a flavone-like compound corresponding to apigenin has been identified in pulp extract. Nevertheless, other derivatives have been characterized as cosmoside (apigenin-7-*O*-glucoside) in both extracts of carob, while apigenin-C-hexoside-C-hexoside was found only in the gum extract [68]. Another flavone in the conjugated form of luteolin was identified in the pulp extract; luteolin-3′-acetyl-O-glucuronide which is considered among the main metabolites of human hepatic microsomes. Also, a methylated form of luteolin was detected in the pulp and gum extracts (luteolin-methyl-ether). Furthermore, myricetin and naringenin have been characterized in gum extract in two conjugated forms: glucuronide (naringenin-O-hexuronide) and methyl (methyl-naringenin); sakuranetin, a methoxy-flavanone; methyl-aromadendrin, an aglycone moiety of one of the flavonoid glycosides and syringetin 3-glucoside, a trihydroxyflavone were found in both extracts [58].

Two flavonols were identified only in the carob pulp extract, one in glycoside form: 4″-*o*-acetyl-quercitrin and the other is a monomethoxy-flavone: quercetin in which the hydroxy group in the 3′ position is replaced by a methoxy group: isorhamnetin [60].

Delphinidin-coumaryl-glucoside is an anthocyanin that been identified in the pulp extract [62]. Moreover, another anthocyanin compound which is petunidin substituted in position 3 by a beta-D-glucosyl residue has been characterized in both carob extracts [50].

Among the phenolic compounds, phenolic acids are linked to several health benefits. Due to their bioactive properties, they are extensively studied and there is evidence of their role in disease prevention.

Phenolic acids comprise one-third of the constituents among phenolic compounds, but they are found in more quantity in the flower, root, leafy, and stem vegetables than in fruits or vegetables [5].

In the present study, different subclasses of these compounds were characterized: hydroxycinnamic acids and hydroxybenzoic acids. Caftaric acid, caffeic acid and its derivatives were found in both samples. Caffeic acid-O-hexoside is a hydroxycinnamic acid and caffeic acid in which the phenolic hydroxy group has been converted to D-hexoside [49]. Similarly, ferulic acid was detected in two extracts in a glycolyzed form (ferulic acid-O-hexoside). Then, p-coumaric acid derivatives were represented in the carob extracts tested; p-coumaric acid prenyl ester and p-coumaric acid cinnamyl ester have been detected and identified only in carob pulp extract. Since, it belongs to the same class as caffeic acid, cross-reactivity may occur, so these natural constituents may also be potential allergens [42].

Moreover, ellagic acid, trigallic acid also called dihydroxybenzoic acid were identified in both samples, while vanillic acid in the glucoside form (vanillic acid-o-hexoside) was identified only in the gum extract and protocatechuic acid-O-hexoside in the pulp extract. Anacardic acid was also identified in locust bean gum. This compound is a hydroxybenzoic acid which is salicylic acid substituted with a pentadecyl group at position 6. It is a component with a wide range of bioactivities.

Other phenolic acids have been observed in locust bean pulp and gum: cinnamic acid, cinnamic acid acetylhexoside which is a hexoside of cinnamic acid where the hexoside is linked to the aromatic ring via an ether or acetal bond. Two other compounds belonging to the subclass of Cinnamic acids and derivatives have been characterized, these are coumaroylshikimic acid and coumaroylquinic acid. Also, three gallotannin have been found in the gum extract, hexahydroxydiphenoyl (HHDP)-glucose, digalloylglucose and pentagalloyl glucose resulting from the pentahydroxylated gallic acid ester of glucose, which is a phytogenic antineoplastic agent and an antibacterial agent.

Xanthones such as methoxyl mangiferin. a class of phenolic compounds with antioxidant properties and potential medicinal benefits, have been also characterized in locust bean gum.

Other compounds were identified, and among them maclurin C-glucoside which is a ketone, trihydroxyoctadecanoic acid sulfate (Phloionolic acid) which is a fatty acid, p-hydroxybenzoyl glucoside which is a benzoate ester. Sugars were also observed in both samples, especially locust bean gum, due to the carbohydrate richness of the carob extracts as reported in the chemical study previously discussed. Additionally, some terpenes were also characterized in the samples. These mainly included coumarin and carnosol.

Finally, pyrogallol was detected in both samples of *Ceratonia siliqua* L., this compound also called trihydroxybenzene or dihydroxyphenol can result from the heating of gallic acid.

3.3. Antibacterial capacity

The results reported in Table 3 show that the diameters of the inhibition zones caused by carob pulp and gum extracts at concentrations of 50 and 100 mg/mL are higher than that obtained with 20 mg/mL.

The pulp and gum extracts concentration of 20 mg/mL retard the growth of pathogenic bacteria; while higher concentration (>50 mg/mL) totally inhibit the bacterial growth strains tested except for *MRSA* in the case of gum extract and *Salmonella* in the case of pulp extract.

In terms of the inhibition zone diameter, the best antibacterial activity was determined for the strain *Listeria innocua* with 100 mg/mL in pulp (18.0 ± 1.0 mm) and gum (15.0 ± 0.5 mm) extracts. The second-best inhibition was obtained for *E. coli* with pulp extract (Φ = 17.0 ± 0.5 mm) and *Bacillus cereus* with gum extract (Φ = 12.0 ± 0.0 mm). Furthermore, inhibition diameters of 13.0 ± 1.0 mm and 09.0 ± 1.0 mm were recorded for *Staphylococcus aureus* strain with carob pulp and gum extracts, respectively, where the best antibacterial activity is attributed to the pulp extract.

The statistical study showed a significant difference ($p < 0.05$) between the antibacterial activity with all the strains studied of pulp and gum extracts using 20 and 100 mg/mL. However, no significant difference was observed between the 50 and 100 mg/mL with respect to the different strains.

Several researches and scientific works have been carried out over time on the antibacterial activity of phenolic compounds: Epigallocatechin has been shown to prevent the growth of different Gram-positive and Gram-negative bacteria responsible for food spoilage [69]. Moreover, a few coumarins have been evaluated for their in vitro antibacterial movement against *E. coli* and *S. aureus* pathogens and all have demonstrated moderate to excellent antibacterial action with MIC of 14_200 mg/mL [70]. Then, the mechanism of action of gallic and ferulic acids on *E. coli, P. aeruginosa, S. aureus* and L. *monocytogenes* has been demonstrated antimicrobial activity against the bacteria tested with an MIC of 500 μg/mL for *P. aeruginosa*, 1500 μg/mL for *E. coli*, 1750 μg/mL for *S. aureus* and 2000 μg/mL for L. *monocytogenes* with gallic acid; 100 μg/mL for *E. coli* and *P. aeruginosa*, 1100 μg/mL and 1250 μg/mL for *S. aureus* and *L. monocytogenes*, respectively, with ferulic acid [71] (Borges et al., 2013).

Besides, the wide range of bioactivities of shikimic acid and its derivatives indicate that a more detailed exploration of their potential for the prevention and treatment of certain diseases is warranted [72]. Furthermore, Wang et al. [73] demonstrated that myricetin inhibits the virulence of *S. aureus* by targeting Hla and negatively regulates the inflammatory response in host cells. According to Wang et al. [74], luteolin showed obvious antibacterial activity against *S. aureus*. The antibacterial mechanism of luteolin is that it could inhibit the activity of DNA topoisomerase I and II.

Other compounds have been reported in the literature showing antibacterial activity: quercetin against *S. aureus* [75], carnosol against *E. coli, P. aeruginosa, B. subtilis, and S. aureus* [76], and pyrogallol against 23 bacterial isolates including *B. cereus, B. subtilis, L. monocytogenes, S. aureus, C. michiganensis, E. coli, K. pneumoniae, S. anatum* and *P. aeruginosa* [77].

3.4. Antioxidant capacity

DPPH scavenging activity is usually presented as the concentration of the antioxidant providing 50% inhibition of DPPH in the test solution (IC_{50}).

Table 3
Diameters of inhibition halos of microbial growth for different extracts of *Ceratonia siliqua* L.

Strains	Inhibition zone diameter (mm)						
	Pulp extract			Gum extract			Antibiotic
	20 mg/mL	*50 mg/mL*	*100 mg/mL*	*20 mg/mL*	*50 mg/mL*	*100 mg/mL*	
MRSA	06.0 ± 2.0	07.0 ± 0.5	07.0 ± 0.0	/	/	/	12
Staphylococcus aureus	10.0 ± 1.0	12.0 ± 0.0	13.0 ± 1.0	06.0 ± 1.0	08.0 ± 0.5	09.0 ± 1.0	22
Bacillus cereus	10.0 ± 0.0	14.0 ± 0.5	14.0 ± 0.0	09.0 ± 1.0	11.0 ± 0.5	12.0 ± 0.0	15
Listeria innocua	15.0 ± 2.0	18.0 ± 1.0	18.0 ± 1.0	13.0 ± 0.5	15.0 ± 0.0	15.0 ± 0.5	/
Salmonella sp	/	/	/	06.0 ± 1.0	07.0 ± 0.5	08.0 ± 0.0	/
Escherichia coli	11.0 ± 0.5	16.0 ± 1.0	17.0 ± 0.5	07.0 ± 0.0	10.0 ± 0.0	11.0 ± 0.5	25

The obtained results show that the tested extracts have an antiradical activity with an IC_{50} of 306.78 and 524.46 μg/mL for the pulp and gum extracts, respectively. High antioxidant activity is due to phenols, simple polyphenols and insoluble condensed tannins present in carob, which are considered to be efficient scavengers of reactive oxygen species. In addition, flavonoids are likely to react with most free radicals: hydroxyl radicals (OH·), superoxide anions ($O2^{-}$·) and peroxylipid radicals [78].

Most of the compounds identified in the two extracts exert antioxidant activity. The study of the antioxidant activities of luteolin, kaempferol, apigenin and quercetin showed that the four flavonols have the power to scavenge free radicals, the $IC_{50\ DPPH}$ values were 2.099, 5.318.1, 84, 10.5 and 3.028 μg/mL for luteolin, kaempferol and quercetin respectively; ABTS IC_{50} values were 0.59, 0.8506, 0.8243 and 0.5083 μg/mL for luteolin, kaempferol, apigenin, and quercetin, respectively [74]. According to Agraharam et al. [79], numerous studies indicated the antioxidant capacity of myricetin which included: lower O—H bond dissociation enthalpy which facilitates H abstraction; an enhanced ionization potential that hampers oxygen reduction by the antioxidant and sufficient solubility.

In addition, ellagic acid exhibited strong antioxidant activity with IC_{50} (0.309 mg/mL). Thus, it has been stated that there is a positive correlation between caffeic acid derivatives and antioxidant activity (radical cation scavenging activity (ABTS) and radical scavenging activity (DPPH)) [80]. Furthermore, Aalikhani et al. [81] demonstrated that coumarin is a powerful option to chelate iron ions and increase the activity of antioxidant enzymes.

4. Conclusion

The Algerian flora is very rich in medicinal plants with recognized benefits for human health. In this study, we tried to explore the potential of a local plant *Ceratonia siliqua* L. For this, we have taken advantage of the interesting properties of extracts from the pulp and gum of this plant.

Seventy-six different compounds have been detected in *Ceratonia siliqua* L. in both extracts (44 compounds have been identified in the carob pulp extract and 57 compounds in the carob gum extract). Flavonoids and phenolic acids are the main group of phenolic compounds found in the analyzed extracts.

The evaluation of the antibacterial activity demonstrated the inhibitory power of the pulp and gum extracts against a range of pathogenic bacteria. In addition, the sensitivity of the tested bacterial strains depend on the dose of the analyzed extracts. Moreover, both extracts have scavenging activity against DPPH free radicals, which makes these extracts good candidates for preventing diseases induced by oxidative stress.

Carob pulp and gum extracts have shown good antioxidant and antibacterial potential and an interesting source of TPC which deserves to be applied in the pharmaceutical and medicine industries.

Ethical standards

Ethics approval and consent to participate – not applicable.

Permissions

Consent for publication – not applicable.

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CRediT authorship contribution statement

Sabrina Djebari: Methodology, Validation, Investigation, Data curation. **Magdalena Wrona:** Conceptualization, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Supervision. **Cristina Nerín:** Conceptualization, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition. **Ouarda Djaoudene:** Conceptualization, Resources, Supervision, Project administration, Funding acquisition. **Sara Guemouni:** Conceptualization, Methodology, Validation, Investigation, Data curation. **Asma Boudria:** Conceptualization, Resources, Supervision, Project administration, Funding acquisition. **Khodir Madani:** Conceptualization, Resources, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

Authors disclose that they don't have any financial or non-financial interests that are directly or indirectly related to this work. Moreover, the authors have no other conflicts of interest to declare that are relevant to the content of this article.

Data availability

All data generated or analyzed during this study are included in this published article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fitote.2023.105696.

References

[1] Y. Wang, H. Du, M. Xie, G. Ma, W. Yang, Q. Hu, F. Pei, Characterization of the physical properties and biological activity of chitosan films grafted with gallic acid and caffeic acid: a comparison study, Food Packag. Shelf Life 22 (2019), https://doi.org/10.1016/j.fpsl.2019.100401.

[2] J. Pérez-Navarro, P.M. Izquierdo-Cañas, A. Mena-Morales, J. Martínez-Gascueña, J. L. Chacón-Vozmediano, E. García-Romero, I. Hermosín-Gutiérrez, S. Gómez-Alonso, Phenolic compounds profile of different berry parts from novel *Vitis vinifera* L. red grape genotypes and Tempranillo using HPLC-DAD-ESI-MS/MS: a varietal differentiation tool, Food Chem. 295 (2019), https://doi.org/10.1016/j.foodchem.2019.05.137.

[3] A. Abdel-Moneim, A.I. Yousef, S.M. Abd El-Twab, E.S. Abdel Reheim, M.B. Ashour, Gallic acid and p-coumaric acid attenuate type 2 diabetes-induced neurodegeneration in rats, Metab. Brain Dis. 32 (2017), https://doi.org/10.1007/s11011-017-0039-8.

[4] A. Durazzo, M. Lucarini, E.B. Souto, C. Cicala, E. Caiazzo, A.A. Izzo, E. Novellino, A. Santini, Polyphenols: a concise overview on the chemistry, occurrence, and human health, Phytother. Res. 33 (2019), https://doi.org/10.1002/ptr.6419.

[5] S.A. Heleno, A. Martins, M.J.R.P. Queiroz, I.C.F.R. Ferreira, Bioactivity of phenolic acids: metabolites versus parent compounds: a review, Food Chem. 173 (2015), https://doi.org/10.1016/j.foodchem.2014.10.057.

[6] M. Tajaldini, F. Samadi, A. Khosravi, A. Ghasemnejad, J. Asadi, Protective and anticancer effects of orange peel extract and naringin in doxorubicin treated esophageal cancer stem cell xenograft tumor mouse model, Biomed. Pharmacother. 121 (2020), https://doi.org/10.1016/j.biopha.2019.109594.

[7] D. Del Rio, A. Rodriguez-Mateos, J.P.E. Spencer, M. Tognolini, G. Borges, A. Crozier, Dietary (poly)phenolics in human health: structures, bioavailability, and evidence of protective effects against chronic diseases, Antioxid. Redox Signal. 18 (2013), https://doi.org/10.1089/ars.2012.4581.

[8] S. Ben Ayache, F.S. Reis, M. Inès Dias, C. Pereira, J. Glamočlija, M. Soković, E. Behija Saafi, I.C.F.R. Ferreira, L. Barros, L. Achour, Chemical characterization of carob seeds (*Ceratonia siliqua* L.) and use of different extraction techniques to promote its bioactivity, Food Chem. 351 (2021), https://doi.org/10.1016/j.foodchem.2021.129263.

[9] I.A.A.F. Adam, Wild Fruits: Composition, Nutritional Value and Products, 2019, https://doi.org/10.1007/978-3-030-31885-7.

[10] A. Baumel, P. Mirleau, J. Viruel, M.B.D. Kharrat, S. La Malfa, L. Ouahmane, K. Diadema, M. Moakhar, H. Sanguin, F. Médail, Assessment of plant species diversity associated with the carob tree (*Ceratonia siliqua*, fabaceae) at the mediterranean scale, Plant Ecol. Evol. 151 (2018), https://doi.org/10.5091/plecevo.2018.1423.

[11] M.E. Brassesco, T.R.S. Brandão, C.L.M. Silva, M. Pintado, Carob bean (*Ceratonia siliqua* L.): a new perspective for functional food, Trends Food Sci. Technol. 114 (2021), https://doi.org/10.1016/j.tifs.2021.05.037.

[12] S. Poyraz Engin, C. Mert, The effects of harvesting time on the physicochemical components of aronia berry, Turk. J. Agric. For. 44 (2020), https://doi.org/10.3906/tar-1903-130.

[13] J.I. López-Sánchez, D.A. Moreno, C. García-Viguera, D-pinitol, a highly valuable product from carob pods: health-promoting effects and metabolic pathways of this natural super-food ingredient and its derivatives, AIMS Agricult. Food 3 (2018), https://doi.org/10.3934/agrfood.2018.1.41.

[14] M.G. Bernardo-Gil, R. Roque, L.B. Roseiro, L.C. Duarte, F. Gírio, P. Esteves, Supercritical extraction of carob kibbles (*Ceratonia siliqua* L.), J. Supercrit. Fluids 59 (2011), https://doi.org/10.1016/j.supflu.2011.08.007.

[15] S.K. Choge, N.M. Pasiecznik, M. Harvey, J. Wright, S.Z. Awan, P.J.C. Harris, Prosopis pods as human food, with special reference to Kenya, in: Water SA, 2007, https://doi.org/10.4314/wsa.v33i3.180613.

[16] P. Felker, G. Takeoka, L. Dao, Pod mesocarp flour of North and South American species of leguminous tree prosopis (mesquite): composition and food applications, Food Rev. Int. 29 (2013), https://doi.org/10.1080/87559129.2012.692139.

[17] A. Mekhoukhe, H. Kicher, A. Ladjouzi, L. Medouni-Haroune, F. Brahmi, S. Medouni-Adrar, K. Madani, Antioxidant activity of carob seeds and chemical composition of their bean gum by- products, J. Complement Integr. Med. 16 (2019) 1–11, https://doi.org/10.1515/jcim-2017-0158.

[18] D. Santonocito, G. Granata, C. Geraci, A. Panico, E.A. Siciliano, G. Raciti, C. Puglia, Carob seeds: food waste or source of bioactive compounds? Pharmaceutics. 12 (2020) 1–12, https://doi.org/10.3390/pharmaceutics12111090.

[19] AOAC, Official methods of analysis of the AOAC, 15th ed., 1990. Arlington, VA.

[20] P.S. Chow, S.M. Landhäusser, A method for routine measurements of total sugar and starch content in woody plant tissues, Tree Physiol. 24 (2004), https://doi.org/10.1093/treephys/24.10.1129.

[21] M. Dubois, K.A. Gilles, J.K. Hamilton, P.A. Rebers, F. Smith, Colorimetric method for determination of sugars and related substances, Anal. Chem. 28 (1956), https://doi.org/10.1021/ac60111a017.

[22] M. De Pádua, P.S. Growoski Fontoura, A.L. Mathias, Chemical composition of Ulvaria oxysperma (Kützing) bliding, *Ulva lactuca* (Linnaeus) and Ulva fascita (Delile), Braz. Arch. Biol. Technol. 47 (2004), https://doi.org/10.1590/s1516-89132004000100007.

[23] AOAC, AOAC official method 2001.11 protein (crude), in animal feed, foorage (plant tissue). Grain, and oilseeds block disgestion method using copper catalyst and steam distilation into boric acid, J. Frankl. Inst. 219 (2001).

[24] B.D. Oomah, A. Corbé, P. Balasubramanian, Antioxidant and anti-inflammatory activities of bean (*Phaseolus vulgaris* L.) hulls, J. Agric. Food Chem. 58 (2010), https://doi.org/10.1021/jf1011193.

[25] N. Turkmen, F. Sari, Y.S. Velioglu, Effects of extraction solvents on concentration and antioxidant activity of black and black mate tea polyphenols determined by ferrous tartrate and Folin-Ciocalteu methods, Food Chem. (2006), https://doi.org/10.1016/j.foodchem.2005.08.034.

[26] C. Quettier-Deleu, B. Gressier, J. Vasseur, T. Dine, C. Brunet, M. Luyckx, M. Cazin, J.C. Cazin, F. Bailleul, F. Trotin, Phenolic compounds and antioxidant activities of buckwheat (*Fagopyrum esculentum* Moench) hulls and flour, J. Ethnopharmacol. 72 (2000), https://doi.org/10.1016/S0378-8741(00)00196-3.

[27] W. Vermerris, R. Nicholson, Phenolic compounds and their effects on human health, in: Phenolic Compound Biochemistry, 2006, https://doi.org/10.1007/978-1-4020-5164-7_7.

[28] R. Nalubega, J. David Kaba, D. Olila, J. Kateregga, Antibacterial activity and phytochemical screening of eleven plants used as poultry ethnomedicines in Southern Uganda, Agric. J. 6 (2011) 303–309, https://doi.org/10.3923/aj.2011.303.309.

[29] W. Brand-Williams, M.E. Cuvelier, C. Berset, Use of a free radical method to evaluate antioxidant activity, LWT Food Sci. Technol. 28 (1995) 25–30, https://doi.org/10.1016/S0023-6438(95)80008-5.

[30] M. Simon, Production enzymatique d'oligosaccharides à partir de gomme de caroube, Faculté universitaire des Sciences agronomiques de Gembloux, Belgique, 2010.

[31] G. Salih, A. Jilal, Utilisation alimentaire de la pulpe de caroube: Formulation et test consommateur 8, Revue Marocaine Des Sciences Agronomiques et Vétérinaires, 2020.

[32] R. Mahtout, V.M. Ortiz-Martínez, M.J. Salar-García, I. Gracia, F.J. Hernández-Fernández, A.P. de los Ríos, F. Zaidia, S. Sanchez-Segado, L.J. Lozano-Blanco, Algerian carob tree products: a comprehensive valorization analysis and future prospects, Sustainability (Switzerland) 10 (2018), https://doi.org/10.3390/su10010090.

[33] M. Papagiannopoulos, H.R. Wollseifen, A. Mellenthin, B. Haber, R. Galensa, Identification and quantification of polyphenols in carob fruits (*Ceratonia siliqua* L.) and derived products by HPLC-UV-ESI/MSn, J. Agric. Food Chem. 52 (2004), https://doi.org/10.1021/jf030660y.

[34] V. Goulas, E. Georgiou, Utilization of carob fruit as sources of phenolic compounds with antioxidant potential: extraction optimization and application in food models, Foods. 9 (2020), https://doi.org/10.3390/foods9010020.

[35] S. Gruendel, A.L. Garcia, B. Otto, C. Mueller, J. Steiniger, M.O. Weickert, M. Speth, N. Katz, C. Koebnick, Carob pulp preparation rich in insoluble dietary fiber and polyphenols enhances lipid oxidation and lowers postprandial acylated ghrelin in humans, J. Nutr. 136 (2006), https://doi.org/10.1093/jn/136.6.1533.

[36] B. Ruiz-Roso, J.C. Quintela, E. de la Fuente, J. Haya, L. Pérez-Olleros, Insoluble carob fiber rich in polyphenols lowers total and ldl cholesterol in hypercholesterolemic sujects, Plant Foods Hum. Nutr. 65 (2010), https://doi.org/10.1007/s11130-009-0153-9.

[37] H. Fidan, S. Stankov, N. Petkova, Z. Petkova, A. Iliev, M. Stoyanova, T. Ivanova, N. Zhelyazkov, S. Ibrahim, A. Stoyanova, S. Ercisli, Evaluation of chemical composition, antioxidant potential and functional properties of carob (Ceratonia siliqua L.) seeds, J. Food Sci. Technol. 57 (2020) 2404–2413, https://doi.org/10.1007/s13197-020-04274-z.

[38] M.K.E. Youssef, M.M. El-Manfaloty, H.M. Ali, Assessment of proximate chemical composition, nutritional status, fatty acid composition and phenolic compounds of carob (*Ceratonia siliqua* L.), Food Public Health 3 (2013).

[39] B. Carbas, M.V. Salinas, C. Serrano, J.A. Passarinho, M.C. Puppo, C.P. Ricardo, C. Brites, Chemical composition and antioxidant activity of commercial flours from *Ceratonia siliqua* and Prosopis spp, J. Food Measur. Character. 13 (2019), https://doi.org/10.1007/s11694-018-9945-7.

[40] E.M. Rakib, H. Chicha, S. Abouricha, M. Alaoui, Determination of phenolic composition of carob pods grown in different regions of Morocco, J. Nat. Prod. 3 (2010).

[41] A.M. Gómez-Caravaca, A. López-Cobo, V. Verardo, A. Segura-Carretero, A. Fernández-Gutiérrez, HPLC-DAD-q-TOF-MS as a powerful platform for the determination of phenolic and other polar compounds in the edible part of mango and its by-products (peel, seed, and seed husk), Electrophoresis. 37 (2016), https://doi.org/10.1002/elps.201500439.

[42] L. Saftić, Ž. Peršurić, S. Kraljević Pavelić, LC–QQQ and LC–QTOF MS methods for comprehensive detection of potential allergens in various propolis extracts, Eur. Food Res. Technol. 245 (2019), https://doi.org/10.1007/s00217-019-03308-x.

[43] M.B. Hossain, D.K. Rai, N.P. Brunton, A.B. Martin-Diana, A.C. Barry-Ryan, Characterization of phenolic composition in lamiaceae spices by LC-ESI-MS/MS, J. Agric. Food Chem. 58 (2010), https://doi.org/10.1021/jf102042g.

[44] C. Wu, H. Xu, J. Héritier, W. Andlauer, Determination of catechins and flavonol glycosides in Chinese tea varieties, Food Chem. 132 (2012), https://doi.org/10.1016/j.foodchem.2011.10.045.

[45] C. Rodríguez-Pérez, R. Quirantes-Piné, N. Ouchemoukh, K. Madani, A. Segura Carretero, A. Fernández-Gutiérrez, A metabolite-profiling approach allows the identification of new compounds from Pistacia lentiscus leaves, J. Pharm. Biomed. Anal. 77 (2013) 167–174, https://doi.org/10.1016/j.jpba.2013.01.026.

[46] M. Gómez-Romero, A. Segura-Carretero, A. Fernández-Gutiérrez, Metabolite profiling and quantification of phenolic compounds in methanol extracts of tomato fruit, Phytochemistry. 71 (2010) 1848–1864, https://doi.org/10.1016/j.phytochem.2010.08.002.

[47] M.J. Simirgiotis, J. Bórquez, G. Schmeda-Hirschmann, Antioxidant capacity, polyphenolic content and tandem HPLC-DAD-ESI/MS profiling of phenolic compounds from the South American berries *Luma apiculata* and L. chequén, Food Chem. 139 (2013), https://doi.org/10.1016/j.foodchem.2013.01.089.

[48] A. Alberti-Dér, LC-ESI-MS/MS methods in profiling of flavonoid glycosides and phenolic acids in traditional medicinal plants: *Sempervivum tectorum* L. and *Corylus avellana* L, Semmelweis University, 2013.

[49] A. Vallverdú-Queralt, J. Regueiro, M. Martínez-Huélamo, J.F. Rinaldi Alvarenga, L. N. Leal, R.M. Lamuela-Raventos, A comprehensive study on the phenolic profile of widely used culinary herbs and spices: rosemary, thyme, oregano, cinnamon, cumin and bay, Food Chem. 154 (2014) 299–307, https://doi.org/10.1016/j.foodchem.2013.12.106.

[50] V. Gavrilova, M. Kajdžanoska, V. Gjamovski, M. Stefova, Separation, characterization and quantification of phenolic compounds in blueberries and red and black currants by HPLC-DAD-ESI-MSn, J. Agric. Food Chem. 59 (2011), https://doi.org/10.1021/jf104565y.

[51] S. Erşan, Ö. Güçlü Üstündağ, R. Carle, R.M. Schweiggert, Identification of phenolic compounds in red and green pistachio (*Pistacia vera* l.) hulls (exo- and mesocarp) by HPLC-DAD-ESI-(HR)-MSn, J. Agric. Food Chem. 64 (2016), https://doi.org/10.1021/acs.jafc.6b01745.

[52] V. Spínola, J. Pinto, P.C. Castilho, Identification and quantification of phenolic compounds of selected fruits from Madeira Island by HPLC-DAD-ESI-MSn and screening for their antioxidant activity, Food Chem. 173 (2015), https://doi.org/10.1016/j.foodchem.2014.09.163.

[53] I.M. Abu-Reidah, D. Arraez-Roman, A. Segura-Carretero, A. Fernandez-Gutierrez, Extensive characterisation of bioactive phenolic constituents from globe artichoke (*Cynara scolymus* L.) by HPLC-DAD-ESI-QTOF-MS, Food Chem. 141 (2013), https://doi.org/10.1016/j.foodchem.2013.04.066.

[54] S. Gouveia, P.C. Castilho, Antioxidant potential of *Artemisia argentea* L'Hér alcoholic extract and its relation with the phenolic composition, Food Res. Int. 44 (2011), https://doi.org/10.1016/j.foodres.2011.04.040.

[55] C. Sun, Y. Wang, S. Sun, X. Chen, X. Shi, H. Fang, Y. Zhang, Z. Fang, Fragmentation pathways of protonated coumarin by ESI-QE-Orbitrap-MS/MS coupled with DFT calculations, J. Mass Spectrom. 55 (2020), https://doi.org/10.1002/jms.4496.

[56] I. Borrás-Linares, S. Fernández-Arroyo, D. Arráez-Roman, P.A. Palmeros-Suárez, R. Del Val-Díaz, I. Andrade-Gonzáles, A. Fernández-Gutiérrez, J.F. Gómez-Leyva, A. Segura-Carretero, Characterization of phenolic compounds, anthocyanidin, antioxidant and antimicrobial activity of 25 varieties of Mexican Roselle (*Hibiscus sabdariffa*), Ind. Crop. Prod. 69 (2015), https://doi.org/10.1016/j.indcrop.2015.02.053.

[57] O. Tusevski, J. Petreska Stanoeva, M. Stefova, S.G. Simic, Phenolic profile of dark-grown and photoperiod-exposed *hypericum perforatum* L. hairy root cultures, Sci. World J. 2013 (2013), https://doi.org/10.1155/2013/602752.
[58] M.P. Rubinho, P.L.N. de Carvalho, A.L.L.E. Reis, S.M. de Alencar, A.L.T.G. Ruiz, J. E. de Carvalho, M. Ikegaki, A comprehensive characterization of polyphenols by LC-ESI–QTOF-MS from *Melipona quadrifasciata anthidioides* geopropolis and their antibacterial, antioxidant and antiproliferative effects, Nat. Prod. Res. 34 (2020), https://doi.org/10.1080/14786419.2019.1607851.
[59] P. Mena, M. Cirlini, M. Tassotti, K.A. Herrlinger, C. Dall'Asta, D. Del Rio, Phytochemical profiling of flavonoids, phenolic acids, terpenoids, and volatile fraction of a rosemary (*Rosmarinus officinalis* L.) extract, Molecules. 21 (2016), https://doi.org/10.3390/molecules21111576.
[60] J.G. Figueroa, I. Borrás-Linares, J. Lozano-Sánchez, A. Segura-Carretero, Comprehensive characterization of phenolic and other polar compounds in the seed and seed coat of avocado by HPLC-DAD-ESI-QTOF-MS, Food Res. Int. 105 (2018) 752–763, https://doi.org/10.1016/j.foodres.2017.11.082.
[61] E.J. Llorent-Martínez, V. Spínola, P.C. Castilho, Phenolic profiles of Lauraceae plant species endemic to Laurisilva forest: a chemotaxonomic survey, Ind. Crop. Prod. 107 (2017), https://doi.org/10.1016/j.indcrop.2017.05.023.
[62] R. Perestrelo, Y. Lu, S.A.O. Santos, A.J.D. Silvestre, C.P. Neto, J.S. Câmara, S. M. Rocha, Phenolic profile of Sercial and Tinta Negra *Vitis vinifera* L. grape skins by HPLC-DAD-ESI-MS n: novel phenolic compounds in *Vitis vinifera* L. grape, Food Chem. 135 (2012), https://doi.org/10.1016/j.foodchem.2012.04.102.
[63] N. Nabet, B. Gilbert-López, K. Madani, M. Herrero, E. Ibáñez, J.A. Mendiola, Optimization of microwave-assisted extraction recovery of bioactive compounds from Origanum glandulosum and Thymus fontanesii, Ind. Crop. Prod. 129 (2019), https://doi.org/10.1016/j.indcrop.2018.12.032.
[64] C. Olate-Gallegos, A. Barriga, C. Vergara, C. Fredes, P. García, B. Giménez, P. Robert, Identification of polyphenols from Chilean brown seaweeds extracts by LC-DAD-ESI-MS/MS, J. Aquat. Food Prod. Technol. 28 (2019), https://doi.org/10.1080/10498850.2019.1594483.
[65] R. Ben Said, A.I. Hamed, U.A. Mahalel, A.S. Al-Ayed, M. Kowalczyk, J. Moldoch, W. Oleszek, A. Stochmal, Tentative characterization of polyphenolic compounds in the male flowers of *Phoenix dactylifera* by liquid chromatography coupled with mass spectrometry and DFT, Int. J. Mol. Sci. 18 (2017), https://doi.org/10.3390/ijms18030512.
[66] R.F. Guerrero, M.C. García-Parrilla, B. Puertas, E. Cantos-Villar, Wine, resveratrol and health: a review, Nat. Prod. Commun. 4 (2009), https://doi.org/10.1177/1934578x0900400503.
[67] Y. Liang, Y. Li, A. Sun, X. Liu, Chemical compound identification and antibacterial activity evaluation of cinnamon extracts obtained by subcritical n-butane and ethanol extraction, Food Sci. Nutr. 7 (2019) 2186–2193, https://doi.org/10.1002/fsn3.1065.
[68] I.M. Abu-Reidah, M.S. Ali-Shtayeh, R.M. Jamous, D. Arráez-Román, A. Segura-Carretero, HPLC-DAD-ESI-MS/MS screening of bioactive components from *Rhus coriaria* L. (Sumac) fruits, Food Chem. 166 (2015), https://doi.org/10.1016/j.foodchem.2014.06.011.
[69] M. Nikoo, J.M. Regenstein, H. Ahmadi Gavlighi, Antioxidant and antimicrobial activities of (−)-Epigallocatechin-3-gallate (EGCG) and its potential to preserve the quality and safety of foods, Compr. Rev. Food Sci. Food Saf. 17 (2018), https://doi.org/10.1111/1541-4337.12346.
[70] H.L. Qin, Z.W. Zhang, L. Ravindar, K.P. Rakesh, Antibacterial activities with the structure-activity relationship of coumarin derivatives, Eur. J. Med. Chem. 207 (2020), https://doi.org/10.1016/j.ejmech.2020.112832.
[71] A. Borges, C. Ferreira, M.J. Saavedra, M. Simões, Antibacterial activity and mode of action of ferulic and gallic acids against pathogenic bacteria, Microb. Drug Resist. 19 (2013), https://doi.org/10.1089/mdr.2012.0244.
[72] G.R. Gandhi, A.B.S. Vasconcelos, P.J. Antony, M.M. Montalvao, M.N.F. de Franca, V.E. Hillary, S.A. Ceasar, D. Liu, Natural sources, biosynthesis, biological functions, and molecular mechanisms of shikimic acid and its derivatives, Asian Pac. J. Trop. Biomed. 13 (2023), https://doi.org/10.4103/2221-1691.374230.
[73] T. Wang, P. Zhang, H. Lv, X. Deng, J. Wang, A natural dietary flavone myricetin as an α-hemolysin inhibitor for controlling *Staphylococcus aureus* infection, Front. Cell. Infect. Microbiol. 10 (2020), https://doi.org/10.3389/fcimb.2020.00330.
[74] C. Tian, X. Liu, Y. Chang, R. Wang, T. Lv, C. Cui, M. Liu, Investigation of the anti-inflammatory and antioxidant activities of luteolin, kaempferol, apigenin and quercetin, S. Afr. J. Bot. 137 (2021), https://doi.org/10.1016/j.sajb.2020.10.022.
[75] S.A.N. Aljadaan, R.S. Elias, R.A. Al-Anssari, Investigation of the antioxidant and antibacterial activity of novel quercetin derivatives, Biointerface Res. Appl. Chem. 10 (2020), https://doi.org/10.33263/BRIAC106.73297336.
[76] V. Pavić, M. Jakovljević, M. Molnar, S. Jokić, Extraction of carnosic acid and carnosol from sage (*Salvia officinalis* l.) leaves by supercritical fluid extraction and their antioxidant and antibacterial activity, Plants. 8 (2019), https://doi.org/10.3390/plants8010016.
[77] S. Chaturvedi, P. Gupta, Plant secondary metabolites for preferential targeting among various stressors of metabolic syndrome, in: Studies in Natural Products Chemistry, 2021, https://doi.org/10.1016/B978-0-323-91095-8.00012-X.
[78] R.W. Owen, R. Haubner, W.E. Hull, G. Erben, B. Spiegelhalder, H. Bartsch, B. Haber, Isolation and structure elucidation of the major individual polyphenols in carob fibre, Food Chem. Toxicol. 41 (2003) 1727–1738, https://doi.org/10.1016/S0278-6915(03)00200-X.
[79] G. Agraharam, A. Girigoswami, K. Girigoswami, Myricetin: a multifunctional flavonol in biomedicine, Curr. Pharmacol. Rep. 8 (2022), https://doi.org/10.1007/s40495-021-00269-2.
[80] J.Y. An, L.T. Wang, M.J. Lv, J.D. Wang, Z.H. Cai, Y.Q. Wang, S. Zhang, Q. Yang, Y. J. Fu, An efficiency strategy for extraction and recovery of ellagic acid from waste chestnut shell and its biological activity evaluation, Microchem. J. 160 (2021), https://doi.org/10.1016/j.microc.2020.105616.
[81] M. Aalikhani, Y. Safdari, M. Jahanshahi, M. Alikhani, M. Khalili, Comparison between hesperidin, coumarin, and deferoxamine iron chelation and antioxidant activity against excessive iron in the iron overloaded mice, Front. Neurosci. 15 (2022), https://doi.org/10.3389/fnins.2021.811080.