Food Chemistry 396 (2022) 133738

Contents lists available at ScienceDirect

Food Chemistry

journal homepage: www.elsevier.com/locate/foodchem

Mango 'criollo' by-products as a source of polyphenols with antioxidant capacity. Ultrasound assisted extraction evaluated by response surface methodology and HPLC-ESI-QTOF-MS/MS characterization

Gonzalo Adrián Ojeda [a,*], Sonia Cecilia Sgroppo [a], Concepción Sánchez-Moreno [b], Begoña de Ancos [b]

[a] Laboratorio de Tecnología Química y Bromatología, FaCENA, Universidad Nacional del Nordeste, Av. Libertad 5400, Corrientes, Argentina
[b] Institute of Food Science, Technology and Nutrition (ICTAN), Spanish National Research Council (CSIC), José Antonio Novais 10, Madrid, Spain

ARTICLE INFO

Keywords:
Polyphenols
Quercetin derivatives
Mangiferin
RSM
HPLC-MS/MS

Chemical compounds studied in this article:
Mangiferin (PubChem CID: 5281647)
Isomangiferin (PubChem CID: 5318597)
Ellagic acid (PubChem CID: 5281855)
Ethyl gallate (PubChem CID: 13250)
Quercitrin (PubChem CID: 5280459)
Isoquercitrin (PubChem CID: 5280804)
Penta-O-galloyl glucose (PubChem CID: 65238)
Quercetin-3-O-galactoside (PubChem CID: 5281643)

ABSTRACT

Ultrasound assisted extraction (UAE) was evaluated as a green procedure for the recovery of phenolic compounds with antioxidant capacity from underutilized mango 'criollo' (peel, pulp and seed). Magnetic stirred was performed as conventional extraction. Response surface methodology using a three-factor (% ethanol, amplitude and time) central composite design was used to maximize the extraction for total phenolic compounds (TPC), total flavonoids and antioxidant capacity. The operational conditions to maximize extraction were: peel, 46% ethanol/amplitude 60% (36 μm)/6.5 min; pulp, 25% ethanol/amplitude 75% (45 μm)/30 min; seed 49% ethanol/100% (60 μm) amplitude/20 min. The phenolic composition of the optimized extracts was characterized by HPLC-QTOF-MS/MS and 45 compounds were tentatively identified as xanthones (mangiferin), flavonoids (quercetin), ellagic acid, benzophenones (maclurin), gallate derivatives and gallotannins. UAE increased TPC extraction (33%); interestingly mangiferin extraction increased 53% in peel, similarly, ellagic acid increased up to 2.5 and 4.4 times in peel and seed extracts.

1. Introduction

Mango (*Mangifera indica*) is an important and widely cultivated fruit in tropical and subtropical regions, the global production in 2020 was 54.83 million tons (including mangosteens and guavas) (FAO, 2022). Mango is consumed in both, fresh and processed forms for its attractive sensory characteristics and nutritional value related to its high content of vitamins, sugars, protein and fibre (Maldonado-Celis et al., 2019; Quintana, Salas, & García-Zapateiro, 2021). In addition, mango fruit has a significant content of bioactive compounds related to health-promoting activities such as phenolic compounds and carotenoids (Anaya-Loyola et al., 2020; Ballesteros-Vivas et al., 2019; Torres-León et al., 2017b).

The mango processing industry produces large amounts of by-products, mainly peel and seed, that represent around 35–60% of the whole fruit (Jahurul et al., 2015; Serna-Cock, García-Gonzales, & Torres-León, 2016). Also, some varieties are not intensively cultivated due to various factors: limited local consumption, small size, or presence of unpleasant components, etc. (Alañón, Oliver-Simancas, Gómez-Caravaca, Arráez-Román, & Segura-Carretero, 2019). In this situation is mango 'criollo', a cultivar widely distributed in the northeast region of Argentina and other countries of South America. This cultivar is characterized by an intensely sweet flavour and aroma; however, its high fibre content and small size reduce its commercial value as fresh fruit.

Phenolic compounds and carotenoids are the most representative bioactive compounds present in mango pulp and peel (Masibo & Qian, 2008; Schieber, Berardini, & Carle, 2003). In seeds it has been reported the presence of polyphenols, dietary fibre and fatty acids with potential health benefits (Mercado-Mercado, Montalvo-González, González-Aguilar, Alvarez-Parrilla, & Sáyago-Ayerdi, 2018; Torres-León et al.,

* Corresponding author.
E-mail address: gaojeda@exa.unne.edu.ar (G.A. Ojeda).

https://doi.org/10.1016/j.foodchem.2022.133738
Received 15 December 2021; Received in revised form 11 July 2022; Accepted 15 July 2022
Available online 19 July 2022

2016; Torres-León, Rojas, Serna-Cock, Belmares-Cerda, & Aguilar, 2017a). Considering phenolic compounds present in mango products, mangiferin and its derivatives stand out due to its antioxidant, antiiflammatory, antimicrobial, antitumor, antidiabetic and inmunomodulatory effects, among others (Alañón et al., 2019; Jangra, Arora, Kisku, & Sharma, 2021; Kumar et al., 2021).

The precise chemical nature and the relative proportions of bioactive compounds can vary significantly depending on the variety, ripening stage, type of by-product and extraction methodology, circumstances that will modify the bioactivity of mango extracts (de Ancos et al., 2018; Dorta, González, Lobo, Sánchez-Moreno, & de Ancos, 2014; Palafox-Carlos, Yahia, & González-Aguilar, 2012).

In order to increase de sustainability of the whole food chain, it is necessary to implement environmentally friendly and sustainable procedures for waste management. On this basis, different green approaches can be used to extract phenolic compounds from mango by-products such as microwave assisted extraction (MAE), supercritical fluids assisted extraction (SFE) and ultrasound assisted extraction (UAE) among others (Chemat et al., 2017; Jirasuteeruk & Theerakulkait, 2019; Mercado-Mercado et al., 2018; Pal & Jadeja, 2020; Prado, Prado, Prado, & Meireles, 2013).

Compared to traditional solid–liquid extraction methods, UAE is considered a 'green' technology since it does not generate a large amount of effluents, minimizes solvent consumption and reduces considerably extraction time and temperature (Chemat et al., 2017; de Ancos et al., 2018; Liu et al., 2019; Quintana et al., 2021; Zou et al., 2014). The ultrasound waves cause a cavitation phenomenon which consists of a series of alternating compression and expansion waves near the solid matrix surface that causes the formation of air bubbles (Pingret, Fabiano-Tixier, & Chemat, 2012). The collapse of cavitation bubbles near the cell walls is expected to produce the formation of microscopic channels in the tissues together with cell disruption that facilitate solvent penetration and promotes the extraction of bioactive compounds. However, the intensity of the cavitation and the efficiency of the extraction not only depends on the parameters of the ultrasound process (power, amplitude, time) and the physical–chemical properties of the solvent, but it is also highly dependent on the nature of the matrix (Borrás-Enríquez, Reyes-Ventura, Villanueva-Rodríguez, & Moreno-Vilet, 2021). Thus, the process parameters need to be optimized to maximize recovery of phenolic compounds from each by-product and mango variety. Response surface methodology (RSM) is an effective technique to analyse interactions between factors and their relationships with the response variables, and for the optimization of extractive processes where multiple parameters can influence the results (Bezerra, Santelli, Oliveira, Villar, & Escaleira, 2008). Numerous examples are found in the literature of the use of RSM for the optimization of UAE of phenolic compounds from by-products of different commercial varieties of mango (Borrás-Enríquez et al., 2021; Jirasuteeruk & Theerakulkait, 2019; Martínez-Ramos et al., 2020; Quintana et al., 2021; Zou et al., 2014). However, to the best of our knowledge, mango 'criollo' by products has been scarcely studied and this work is the first report concerning its phenolic composition studied by HPLC-ESI-QTOF-MS/MS.

In order to extent the knowledge of underutilized mango varieties, the present work aims to evaluate the effect of UAE parameters such as solvent (% ethanol in water), sonication time and amplitude, on total phenolic compounds and flavonoids and on the individual phenolic compounds determined by HPLC-ESI-QTOF-MS/MS, of the underutilized Argentinean mango 'criollo' (peel, pulp and seed) and its antioxidant capacity. Experimental data were fitted to regression models to better represent the effects of the process parameters. The results of this study will help to increase interest in this underutilized mango variety in local communities in order to produce high value added products that promote economic development in the region.

2. Material and methods

2.1. Fruit material

Six kilograms (50 fruit) of fully ripe mango 'criollo' were harvested from trees in the city of Corrientes Argentina (-27.510501795690335, −58.82515496578836). The fruit were immediately washed with water and drained over paper. After this, the peel and seed were separated using a sharp knife and the remaining pulp was removed by gently scraping with its blunt edge. Three products were obtained: mango 'criollo peel (MCP), mango´criollo' pulp (MCPu) and mango 'criollo' seed (MCS). These products were freeze dried (48 h for peel and pulp and 72 h for seed) at −58 °C, 0.035 mBar using a lyophilizer Christ Alpha 1–4 LD (Osterode, Germany) and powdered using an industrial grinder Arcano FW 100 (Beijing, China) until 60 mesh size (diameter < 0.25 mm).The powdered dry samples were stored in well-sealed black PVC containers without headspace, at −20 °C until experiment (<30 days).

2.2. Chemical and reagents

Absolute ethanol and acetonitrile (HPLC-grade) were provided by Lab-Scan (Dublin, Ireland). Formic acid (98%) was obtained from Panreac Química (Barcelona, Spain). Folin Ciocalteau reagent, 2,2-diphenyl- 1-picrylhydrazyl (DPPH) and 2,2′-azinobis(3-ethylbenzothiazoline)- 6-sulphonate (ABTS) were purchased from Sigma Aldrich (St. Louis, MO, USA). Also, the following phenolic standards were supplied by Sigma Aldrich (St. Louis, MO, USA): gallic acid, quercetin, maclurin, mangiferin, quercitrin, quercetin-3-O-galactoside, quercetin-3-O-rhamnoside, ellagic acid and (-) epicatechin.

2.3. Experimental design

Extraction of phenolic compounds from MCP, MCPu and MCS in aqueous ethanol was carried out using RSM. A three factor and three level central composite design (CCD) consisting of 20 experimental runs including six replicates at the central point was employed for each section of the fruit, giving a total of 60 runs. The design variables were amplitude (X1, %), extraction time (X2, min) and % of ethanol in water (X3, %v/v) while response variables were: total phenolic content, total flavonoid content and total antioxidant capacity. The levels of the design variables were 20 to 100% for amplitude, 5 to 30 min for extraction time and 0 to 100% ethanol. The minimum and maximum levels (Table 1)

Table 1
Experimental conditions for the central composite design (CCD).

Std order	Experiment	Amplitude (%)	Time (min)	Ethanol (%)
6	1	100	5.00	100
1	2	20	5.00	0
14	3	60	17.50	100
8	4	100	30.00	100
10	5	100	17.50	50
13	6	60	17.50	0
2	7	100	5.00	0
20	8	60	17.50	50
16	9	60	17.50	50
19	10	60	17.50	50
12	11	60	30.00	50
11	12	60	5.00	50
17	13	60	17.50	50
9	14	20	17.50	50
3	15	20	30.00	0
7	16	20	30.00	100
5	17	20	5.00	100
15	18	60	17.50	50
4	19	100	30.00	0
18	20	60	17.50	50

Std order: standard order of experiment.

given to each factor were chosen based on the results of other authors in obtaining extracts with high phenolic content from mango products (Dorta et al., 2014; Dorta, Lobo, & González, 2013; Martínez-Ramos et al., 2020). In all experiments, the lyophilized samples were placed in an adapted beaker and the solid-solvent ratio was maintained at 1:60, this proportion was chosen based on preliminary tests. The extraction process was carried out in ice bath with a solid tip of 19 mm (60 μm max amplitude range) connected to ultrasound generator equipment (Fisherbrand Model 505 Sonic Dismembrator − 500 W − 20 kHz Fisher Scientific™). After the extraction process, the extracts were filtered and concentrated at 40 °C by evaporation under reduced pressure in a rotator evaporator (Büchi model R111 Evaporator Lab) until obtaining 2–3 ml of extract which was poured into a volumetric flask and made up to 10 ml final volume. The extracts were referred as US-MCP (peel); US-MCPu (pulp); US-MCS (seed) and stored in falcon tubes at −20 °C until analysis.

2.4. Conventional extraction

Samples were extracted with ethanol 80% v/v and magnetic stirring (800 rpm) for 30 min at 25 °C, maintaining the solid:solvent ratio at 1:60 ratio, according to the methodology previously described (de Ancos et al., 2018; Dorta et al., 2014; Martínez-Ramos et al., 2020). Then, the extracts were filtered and concentrated as explained in section 2.3, named as EtOH-MPC, EtOH-MCPu, EtOH-MCS and stored at −20 °C until analysis.

2.5. Total phenolic content (TPC)

Total phenolic compounds were determined on the extracts following the methodology proposed by (Anaya-Loyola et al., 2020) with some modifications: 10 μL of properly diluted extract were added into 170 μL of distilled water and 20 μL of Folin-Ciocalteu reagent. Three minutes later, 40 μL of 20% Na_2CO_3 were added. The reaction mixture was left in dark and the absorbance at 760 nm was determined after 120 min in a microplate reader (BioTek Instruments Inc., Bad Friedrichshall, Germany). Results were expressed on a dry weight basis as mg gallic acid equivalents (GAE)/g dry weight (DW). Analysis was performed in triplicate (n = 3).

2.6. Total flavonoid content (TFC)

Total flavonoids were determined according to (Tomšik et al., 2016). Briefly, 10 μL of properly diluted extract, 90 μL of ethanol and 25 μL of 5% (w/v) of Na_2NO_2 were allowed to react for 5 min. Then 600 μL of 2% $AlCl_3$ were added and after 6 min, 500 μL of 1 M NaOH were finally added; after 10 min the absorbance was measured at 510 nm. The results were expressed mg of quercetin equivalents (QE)/g DW. Analysis was performed in triplicate (n = 3).

2.7. Antioxidant capacity (AOC)

The DPPH• solution was prepared following the methodology proposed by Floegel, Kim, Chung, Koo, & Chun, (2011). Briefly a 1 mM solution of DPPH in methanol was stirred for 40 min and absorbance of the solution was adjusted to 0.800 ± 0.020 at 517 nm. The ABTS•+ solution was prepared by mixing 7 mM ABTS solution and 2.45 mM potassium persulphate solution in equal volume left overnight in the dark at room temperature. This solution was then diluted with ethanol to obtain an absorbance of 0.700 ± 0.020 at 734 nm (Re et al., 1999).

Properly diluted extract was mixed with freshly prepared DPPH• or ABTS•+ solution and allowed to react for 30 min. Absorbance for each assay was determined using a microplate reader (BioTek Instruments Inc., Bad Friedrichshall, Germany). Results were expressed as μmol Trolox Equivalent Antioxidant Capacity (TEAC) (μmol of TEAC/g DW). Analysis was performed in triplicate (n = 3).

2.8. HPLC-DAD-ESI-QTOF-MS/MS

The separation, identification and quantification of phenolic compounds were achieved using an Agilent 1200 series high pressure liquid chromatography (HPLC) system coupled to mass quadrupole time-of-flight spectrometer with an electrospray ionization source (ESI) via Jet Stream Technology (Agilent G6530A Accurate Mass Q-TOF MS/MS) (Dorta et al., 2014). HPLC system was equipped with a quaternary pump and diode array detector (DAD) (Agilent Technologies, Santa Clara, CA, USA). Separation was carried out on a 4.6 × 250 mm id., 4.0 μm particle size, Poroshell C18 column (Agilent Technologies, Santa Clara, CA, USA). The mobile phase consisted of a linear gradient of 0.1% formic acid in Milli-Q-water (A) and 0.1% formic acid in acetonitrile (B) as follows: 0 min, 95% A; 5 min, 95% A; 10 min, 85% A; 20 min, 75% A; 30 min, 70% A; 60 min, 60% A; 65 min, 95% A; 70 min, 95%A. The flow rate was fixed at 0.7 ml/min and the injection volume was 20 μL. Runs were monitored at 360 nm, 320 nm, 280 nm and 255 nm.

To identify the phenolic compounds, total ion spectra were collected in the range *m/z*: 100–1300 in negative mode. Nitrogen was used as drying, collision and nebulizing gas. The drying gas temperature and flow rate were 225 °C and 10 L/min, respectively. The sheath gas temperature and flow rate were 300 °C and 10 L/min. The nebulizer gas pressure, skimmer voltage, octopole RF, and fragmentor voltage were, 45 psi, 65 V, 750 V and 125 V, respectively. The capillary voltage was set at 3 kV. The MS/MS collision energy was set at 15 eV (de Ancos et al., 2018; Dorta et al., 2014).

Data was acquired and analysed using a Masshunter Qualitative Analysis B.07.00 software and Masshunter Profinder B.08.00. The identification was possible by comparison with the mass spectral data generated by external standards, the data from databases (MassBank, Pubchem, Phenol explorer, ChemSpider) and a personal accurate mass database built using the information about mass data of the main phenolic compounds present in mango obtained from the literature.

Approximate quantification of phenolic compounds was performed in the QTOF in the MS1 mode using external calibration curves. Standard calibration curves of five points were made for each compound commercially available (gallic acid, ellagic acid, quercetin, epicatechin, mangiferin, quercetin-3-O-galactoside, quercetin-3-O-rhamnoside (quercitrin) and maclurin, in the range of 5 to 0.005 μg/mL and in the range of 50 to 5 μg/mL. When no commercial standard was available, the compounds were quantified using structurally related commercial standards (gallotannins and gallates as gallic acid; quercetin derivatives as quercetin-3-O-galactoside; xanthones as mangiferin and benzophenones as maclurin). It is necessary to consider that the use of structurally similar compounds to quantify phenolic compounds by HPLC/MS is not an accurate method of quantification but it is but it is widely used when commercial standards are not available. Analysis was performed in triplicate (n = 3). Results were statistically analyzed using analysis of variance (ANOVA). The differences among means were tested for statistical significance ($p < 0.05$) using a multiple-range least significant difference (LSD) test with Info Stat Statistical Software 2015 (Córdoba, Argentina).

2.9. Data analysis

Experimental data were fitted to second-order polynomial models using Design Expert (version 11.0) software and regression coefficients were obtained for each response variable in each section of the fruit. The generalized second-order polynomial model used in the response surface analysis was as follows:

$$y = \beta_0 + \sum_{i=1}^{3} \beta_i X_i + \sum_{i=1}^{3} \beta_{ii} {X_i}^2 + \sum \sum_{i<j=1}^{3} \beta_i X_i X_j$$

where β_0, β_i, β_{ii}, and β_{ij} are the regression coefficients for intercept, linear, quadratic and interaction terms, respectively, and X_i, and X_j are

the independent variables. The Design Expert software was used to generate response surfaces and contour plots while holding a variable constant in the second-order polynomial model.

2.10. Verification of the models

The conditions to obtain maximal extraction of phenolic compounds and maximal antioxidant capacity from mango products inside of the experimental region studied were obtained using numerical and graphical optimization. The adopted criterion for numerical optimization was to maximize phenolic, flavonoid and antioxidant capacity using the maximum importance in weight for each factor and maximum desirability (D). Graphical optimization was made setting the highest values for each response variable with a 25% tolerable variation. Extraction for each part of mango was performed in triplicate under these conditions and the response variables were evaluated. The experimental and predicted values were compared in order to determine the validity of the model.

3. Results and discussion

3.1. Analysis of RSM for response variables of CCD

3.1.1. Total phenolic content (TPC)

The predicted model for the UAE of TPC from US-MCP was mainly influenced by quadratics terms of amplitude, time and ethanol content. The model was significant ($p < 0.0001$), the R^2 predicted ($PredR^2$) was in reasonable agreement with the adjusted R^2 ($AdjR^2$), while the adequate precision (AdeqPrec = 16.313) indicated that the signal to noise ratio was adequate (Table 2). Fig. 1a shows TPC in US-MCP extracts as a function of amplitude and time, when ethanol content was fixed at 50%, the maximum values for TPC were obtained working at 60% of amplitude and variable time. Aqueous solutions of ethanol have been reported as an effective solvent to extract polyphenols from mango peel. Mixtures from 40 to 80% (v/v) ethanol: water have been studied as general solvents for phenolic compounds (Dorta et al., 2014; Martínez-Ramos et al., 2020). In our experiment mixtures with<30% or>80% of ethanol did not extract efficiently phenolic compounds. The effect of sonication time produced maximum TPC extraction at a low level (between 5 and 10 min) and in the maximum level of 30 min (Fig. 1a). These results could be a consequence of the degradation of complex compounds like lignin which could require longer times to become extractable (Liu et al., 2019). When the results are compared with the literature, large variability of the phenolic content in mango peel have been reported, this fact could be attributed to variations related to cultivar, ripening stages or extraction process conditions, however, the results are in the range compared with other studies (de Ancos et al., 2018; Martínez-Ramos et al., 2020).

The UAE of TPC from pulp adjusted to a quadratic model ($p < 0.0001$) with no significant lack of fit. This model was mainly affected by linear term amplitude ($p < 0.05$) and linear term of ethanol content ($p < 0.0001$). Meanwhile, the interaction terms were also significant (Table 2). These results indicate that the extraction procedure of TPC in MCPu is differently influenced by extraction conditions than MCP. The parameters $PredR^2$, $AdjR^2$ and AdeqPrec indicated that the model could predict the response variables. Fig. 1b shows that in order to achieve high extraction of phenolics, the conditions of UAE should be: amplitude between 60 and 80% and time between 25 and 30 min, when the ethanol content was fixed at 50%. However, the efficiency of extraction significantly increased when the ethanol content was reduced to 20–30%. Mango pulp has high content of soluble carbohydrates and dietary fibre such as pectin (Anaya-Loyola et al., 2020) which could modify the viscosity of the solution hence affecting efficiency of UAE; hence more time and amplitude are required when compared to peel extraction.

The UAE of TPC from seeds fitted to a quadratic model, being the lack of fit not significant ($p = 0.9399$) and the $PredR^2$ and $AdjR^2$ in agreement, while the AdeqPrec indicated an adequate response (Table 2). Fig. 1c indicates that at a level of 50% of ethanol, high values of TPC were obtained in all the working space, being particularly high at amplitude levels close to 100% and operation time between 17.5 and 30 min. As observed for other sections of the fruit, seed matrix requires particular extraction conditions to maximize TPC extraction. Ethanol improves to a certain point the extraction of TPC; however, when ethanol content was higher than 60% the TPC did not present further increase. High starch and tannin content are characteristics of mango seed composition (Torres-León et al., 2016), the later could contribute to phenolic content. These results indicate that extraction of TPC is affected by different UAE terms depending on the fruit section. Amplitude and ethanol content had a significant impact in TPC extraction from MCPu and MCS, while this procedure in MCP was also influenced by time. The differential effect of extraction variables could be explained by factors related to the tissue characteristics e.g fibre, protein and fat content could affect differently the efficacy of the extraction procedure (Ballesteros-Vivas et al., 2019; López-Cobo et al., 2017) and factors related to the Follin Ciocalteau method e.g ascorbic acid present in pulp could also react, hence affecting data interpretation (Kim, Lee, Lee, & Lee, 2002). Nevertheless, these results indicate that in order to maximize TPC extraction from mango by-products an adequate selection of extraction variables should be performed to achieve adequate yield from each section of the fruit.

3.1.2. Total flavonoid content (TFC)

The results for TFC were in accordance with those found in TPC. The predicted models for US-MCP and US-MCS were significant ($p < 0.0001$) while the lack of fit was not significant. The models were mainly influenced by linear terms for amplitude and quadratic terms of ethanol content and amplitude (Table 2). Also, quadratic terms of time and ethanol content were significant in US-MCS. The $PredR^2$ and $AdjR^2$ were in agreement for both models; meanwhile, the AdeqPrec indicated that both models were adequate for discrimination of the response variable. Fig. 1d and 1f indicate that amplitude should be higher than 60% in order to enhance flavonoid extraction. Extraction time varied widely, being similar to the values found in the analysis for TPC. The efficiency of TFC extraction was particularly affected by solvent composition and amplitude. Flavonoids present in mango peel are mainly represented by mangiferin and quercetin-3-O-galactoside (Berardini, Carle, & Schieber, 2004; Schieber et al., 2003), both glycosylated compounds. Flavonoid glycosides are, in general, soluble in polar solvents; however, some of them are sparingly soluble in pure water. Ethanol is classified as a polar protic solvent, as it contains hydroxyl groups and is a hydrogen bond donor which favours preferential extraction of low molecular weight compounds, such as glycosylated and non-glycosylated phenolic compounds (Martínez-Ramos et al., 2020). The application of ultrasound could increase the solubility of flavonoids due to high efficiency of solvent/matrix mixture which enhances mass transfer.

The extraction of flavonoids in US-MCPu was influenced by linear terms of the three parameters; the quadratic terms for time and ethanol content were significant. The model resulted significant with $AdjR^2$ and $PredR^2$ in considerable agreement (Table 2). Fig. 1e analyzed at the same level as US-MCP and US-MCS, indicated a low extraction yield. However, working at ethanol concentration between 0 and 15%, amplitude between 80 and 100% and time > 25 min significantly increased extraction yield of flavonoids (data not shown). The characteristic properties of mango pulp are mainly related to its fibre content (Dorta et al., 2014); when dispersed in water, this fibre could affect the development of cavitation phenomena leading to low extraction efficiency. The fibre composition of peel, pulp and seed is different among varieties (Jahurul et al., 2015; Maldonado-Celis et al., 2019), and could have different water solubility and rheological properties. Therefore, in order to maximize bioactive extraction, solvent characteristics (% ethanol in water) and sonication parameters (time and amplitude) should be properly selected.

Table 2
Analysis of variance for response surface models showing linear, quadratic and interaction relations of each variable and coefficients for model prediction.

Factor/Term	Peel				Pulp				Seed			
	TPC	TFC	AOC-DPPH	AOC-ABTS	TPC	TFC	AOC-DPPH	AOC-ABTS	TPC	TFC	AOC-DPPH	AOC-ABTS
Intercept												
β_0	75.40	26.68	1367.56	1520.88	6.68	2.56	34.10	58.76	110.16	44.66	1322.65	1812.70
Linear												
β_1 (amplitude)	−0.11	1.69*	67.46	40.04	0.41*	0.69*	6.06*	2.36	9.69*	7.00*	75.05	150.07*
β_2 (time)	−2.24	0.49	42.92	54.53*	0.30	0.62*	4.22*	0.73	3.67	1.58	39.48	73.95
β_3 (ethanol)	−2.75	0.52	126.11	−20.78	−1.07**	−0.73*	−1.03	−2.19	−20.33**	−1.07	−200.95*	−116.89*
Interaction												
β_{12}	−0.67	1.20	28.98	36.78	−0.045*	0.11	1.44	1.48	3.41	0.99	73.26	85.63
β_{13}	1.79	0.90	13.29	51.43*	−0.37	−0.28	0.79	2.04	1.10	2.81	50.33	93.92
B_{23}	−1.26	0.67	15.29	−10.51	−0.34	−0.10	−1.54	1.15	2.83	1.89	76.61	50.24
Quadratic												
β_{11}	−26.07*	−3.23*	−356.15*	−110.59*	−0.84*	−0.30	−5.87*	−4.17	2.00	2.72	−43.17	22.36
β_{22}	11.09*	2.24	−175.55	−22.65	0.20	−0.63*	2.97	6.47*	−5.24	−5.49*	68.67	−120.19
β_{33}	−49.60**	−14.68**	−717.10*	−956.66**	−1.75**	0.93*	−11.93*	−20.41**	−53.85**	−22.17**	−722.32**	−941.36**
R^2	0.9724	0.9294	0.9206	0.9938	0.9373	0.7928	0.8808	0.7782	0.9683	0.9421	0.9105	0.9665
R^2 adjusted	0.9476	0.9106	0.8994	0.9882	0.9007	0.7188	0.8382	0.7521	0.9398	0.9154	0.8937	0.9363
Predicted R^2	0.8953	0.8599	0.8080	0.9793	0.8150	0.5197	0.7601	0.7051	0.9220	0.8510	0.8506	0.8901
Adeq precision	16.313	14.865	14.884	29.978	12.909	13.451	14.614	9.816	26.19	18.753	17.541	16.337
CV	17.2	13.18	25.29	6.00	8.68	21.56	14.56	11.22	10.16	12.62	13.84	10.78
p_m value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0002	<0.0001	0.0014	<0.0001	<0.0001	<0.0001	<0.0001
p_{lf} value	0.0618	0.1001	0.0404	0.1852	0.0745	0.4423	0.0536	0.0791	0.9399	0.4790	0.6082	0.8570

TPC: total phenolic content; TFC: total flavonoid content; AOC: antioxidant capacity; CV: coefficient of variation; p_m: p value for model; p_{lf}: p value for lack of fit.
*$p < 0.05$, **$p < 0.0001$ indicate the significance level for the analysed term.

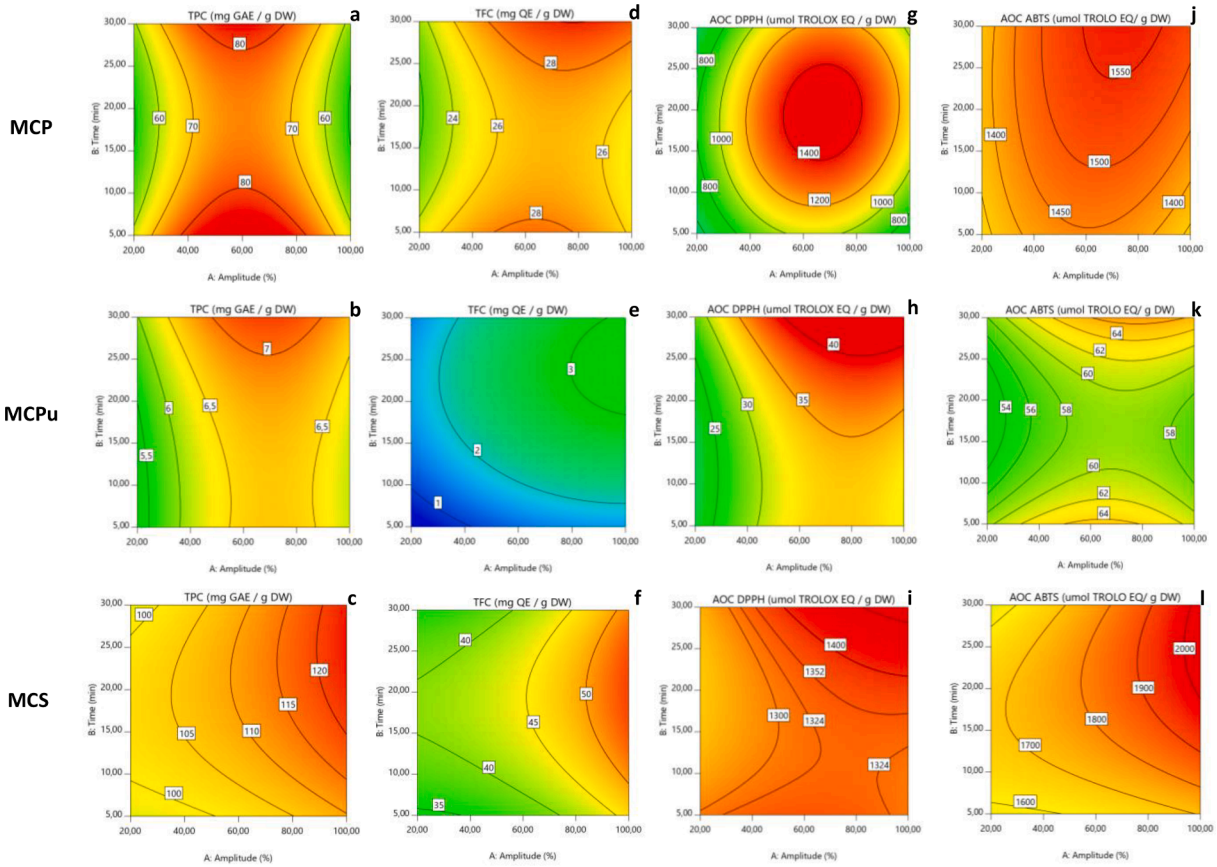

Fig. 1. Contour plots showing the effect of amplitude and time with 50% v/v of ethanol on TPC: total phenolic content (a,b,c); TFC: total flavonoid content (d,e,f), AOC: antioxidant capacity evaluated by DPPH (g,h,i) and ABTS (j,k,l). MCP: mango criollo peel; MCPu: mango criollo pulp; MCS: mango criollo seed.

The proposed model for flavonoids extraction in MCPu was differently influenced by the evaluated terms in comparison to the findings for MCP and MCS. The importance of selecting adequate extraction conditions, to ensure maximum yield from each fruit section, was once again highlighted. The different results for TFC could be a direct consequence of the variety of compounds present in each section of the fruit (Alañón et al., 2019); the effect of differential matrixes and the need of including particular conditions affecting the extraction of flavonoids from the pulp (Anaya-Loyola et al., 2020; Zou et al., 2014).

3.1.3. Antioxidant capacity (AOC)

The results of AOC evaluated by DPPH and ABTS assays for US-MCP adjusted to quadratics models that were significant ($p < 0.0001$), in both cases the quadratics terms of amplitude and ethanol had a significant influence. The $AdjR^2$ and $PredR^2$ were in considerable agreement in both models (Table 2). Fig. 1g and 1j analyzed when ethanol content was 50% indicated that the maximum yields were obtained for amplitude values between 60 and 80%, and extraction times above 17.5 min. The contour plots indicated that the AOC evaluated in the same extract varies depending on the methodology and the extraction conditions. Although both radicals (ABTS•+ and DPPH•) could react with polyphenols, it has been informed a stronger correlation between TPC and ABTS results than with DPPH results (Floegel et al., 2011). The AOC of MCP extracts was significantly higher than the reported for Keitt (Dorta et al., 2013) and Tommy Atkins cultivars (Martínez-Ramos et al., 2020).

The proposed models for the AOC in US-MCPu were significant for AOC-DPPH and AOC-ABTS; both models had no significant lack of fit. The $AdjR^2$ and $PredR^2$ were slightly higher for AOC-DPPH model than for AOC-ABTS; however, in both, these values were acceptable for data interpretation (Table 2). Moreover, the AdeqPrec indicated that both models were adequate to evaluate the AOC as a response to the experimental variables. Fig. 1h indicated that the highest AOC-DPPD was obtained applying amplitude > 60% and operational times between 17.5 and 30 min. The AOC-ABTS increased when the time of the process was 30 min and amplitude between 60 and 80% (Fig. 1k). The antioxidant properties of mango pulp are mainly attributed to flavonoids, carotenoids, ascorbic acid and other compounds (Vithana, Singh, & Johnson, 2019). As observed for TPC and TFC, the AOC of pulp was significantly lower than peel, and these data agree with the results reported by Jahurul et al., (2015). The extraction conditions to maximize AOC in pulp also differ with those of peel and in general, longer extraction time is required. Although some studies reported that long extraction procedures might reduce AOC related to ascorbic acid or other labile compounds (Chemat et al., 2017; Liu et al., 2019), the extraction of antioxidant compounds present in MCPu could accept long procedures, which could be related to the dissipation effect of energy by insoluble fibre.

The AOC in US-MCS fit to quadratic models that were significant at a level of $p < 0.0001$, being lack of fit not significant for both AOC-DPPH and AOC-ABTS (Table 2). The models exhibited adequate regression parameters ($AdjR^2$, $PredR^2$ and AdeqPrec). Evaluating the AOC at a fixed level of ethanol of 50% indicated that this concentration was adequate to obtain high values of AOC evaluated by both methodologies. The process parameters to maximize these responses were time > 17.5 min and amplitude in the range of 60–100% (Fig. 1i and 1 L). Longer process time could imply that ultrasound might release some bound phenolic compounds attached to cell wall or starch macromolecules, hence increasing the AOC (Martínez-Ramos et al., 2020).

Both methodologies were able to adequately predict the results found in the different sections of the fruit; however the conditions to obtain maximal responses varied between the fruit section and methodology. The specificity of each radical to antioxidant compounds in the

assay condition could explain these differences. DPPH radical is generally considered to be less specific than ABTS. For instance, ABTS has shown to be more specific against phenolic compounds, as it is applicable to both hydrophilic and lipophilic antioxidant systems (Floegel et al., 2011). Particularly, it was reported that DPPH is more sensitive to the antioxidant effect of ascorbic acid when compared to ABTS (Kim et al., 2002), and this might explain the particular results for MCPu which has considerable high ascorbic acid content (Anaya-Loyola et al., 2020). Finally, the carotenoid content could also have a significant impact in the AOC of ethanol rich extracts (de Ancos et al., 2018; Mercado-Mercado et al., 2018; Quintana et al., 2021). The efficiency of the proposed models to predict the AOC could be influenced by the contribution and relative contents of the aforementioned compounds in the different sections of the fruit.

3.1.4. RSM optimization of UAE of TPC, TFC and AOC

Based on the experimental results and statistical analysis, numerical and graphical optimizations were conducted in order to establish the optimum level of the independent variables evaluated in this study with desirable values of response variables. Numerical optimization was evaluated using the desirability (D) function. The selected criteria for graphical optimization were selected to obtain results > 75% of the highest value of each response for each section of the fruit. A number of possible conditions were generated and the selection was based on maximum desirability (D) for numerical optimization and optimal operable conditions with graphical optimization. Fig. 2a shows the D

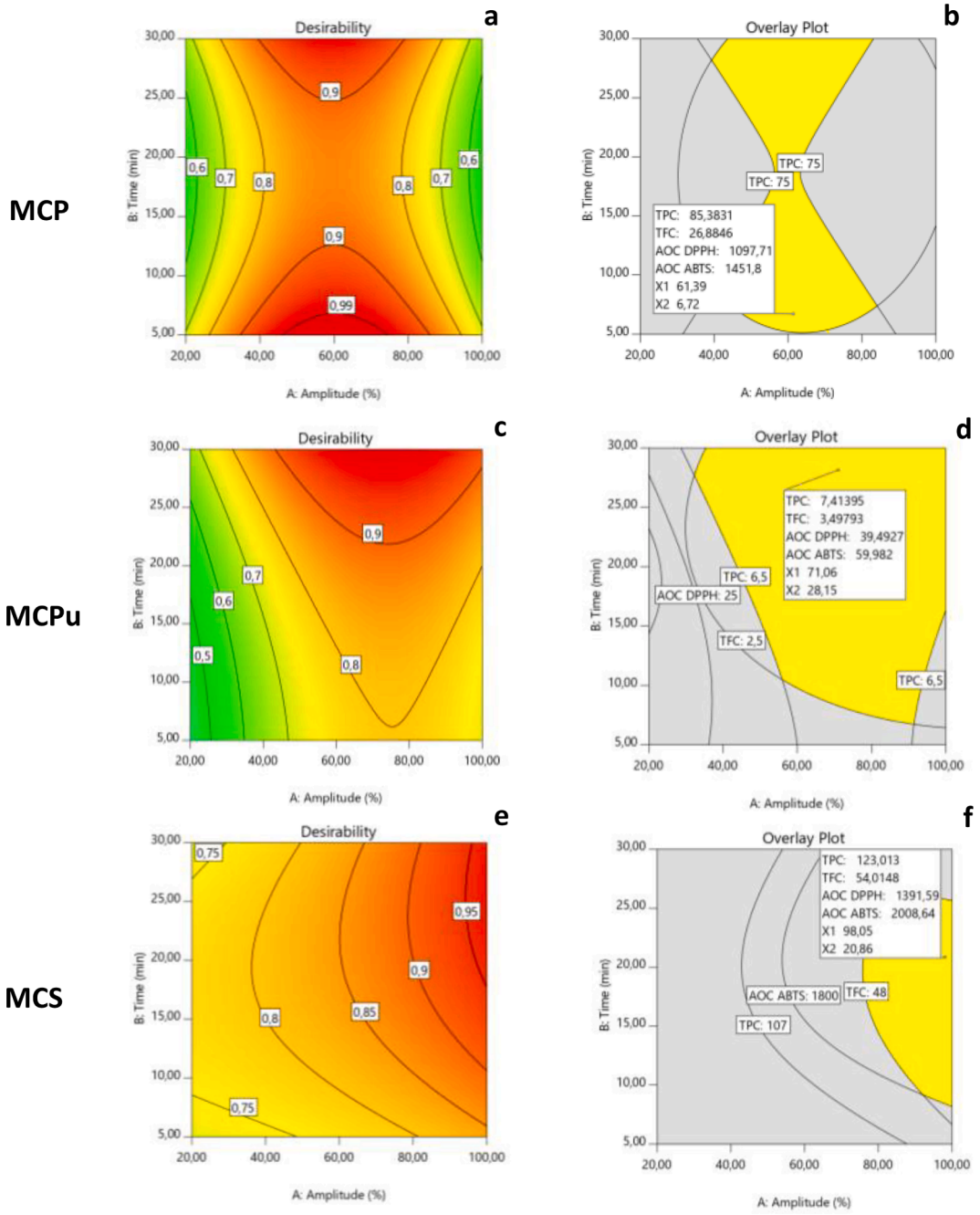

Fig. 2. Contour plots showing desirability (D) function for the numerical optimization (a,c,e) and graphical optimization where yellow shaded areas represent optimal operational conditions (b,d,f). MCP: mango criollo peel; MCPu: mango criollo pulp; MCS: mango criollo seed. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

values for one of the proposed solutions, while Fig. 2b shows also operational conditions where the responses were optimized. It can be seen that both, numerical and graphical optimization are in agreement with the proposed goals. The optimized conditions were time = 6.5 min, amplitude 60% and ethanol content 46%, with these parameters a new extraction procedure (OPT-MCP) was performed in order to validate the model.

Similarly, to US-MCP, the optimization of extraction process in US-MCPu was conducted adopting the same criteria for numerical and graphical optimization. Desirability values close to 1 (Fig. 2c) were obtained with ethanol content of 25%, amplitude of 75% and 30 min. Graphical optimization indicated that the working parameters were also suitable (Fig. 2d); a new extraction experiment was performed under these conditions (OPT-MCPu).

The optimization process in US-MCS was conducted following the same criteria previously mentioned. The selected solution indicated D > 0.930 when the operational conditions were time 20 min; amplitude 100% and ethanol content 49% (Fig. 2e). The graphical optimization (Fig. 2f) was in coincidence with the numerical optimization. Under these optimized conditions, a new experiment was conducted (OPT-MCS) for validation.

Our results showed that in order to maximize the extraction of phenolic compounds with antioxidant potential from different sections of mango fruit it is necessary to apply specific treatment conditions for each section of the fruit. Amplitude requirements for the different sections increased as follows peel < pulp < seed, also pulp and seed required longer extraction time than peel. Ethanol content in the extraction solvent was < 50% for all sections which could be associated to a cleaner procedure.

Other works (Martínez-Ramos et al., 2020; Mercado-Mercado et al., 2018) have reported that the efficiency of UAE varied with different solvents and the phenolic content with antioxidant activity of extracts were associated to a combination of different factors. These include temperature, particle size, cavitation phenomena, solvent viscosity, and dielectric constant, the solubility of compounds in the solvent, mass transfer phenomena or degradation of compounds.

3.1.5. Verification of the predicted optimal UAE conditions

Verification experiments performed at the predicted conditions derived from the optimization analysis indicated that experimental values were reasonably close to the predicted values confirming the validity and adequacy of the predicted models. Moreover, the verification experiments also proved that the predicted values of the response variables could be satisfactorily achieved within a 95% confidence interval of experimental values (Table S1).

3.2. Phenolic profile evaluated by HPLC-ESI-QTOF-MS/MS

Once the optimal ultrasound extraction conditions had been identified in terms of maximum extraction of TPC, TFC and AOC; the composition of phenolic compounds of the UAE optimized extract of each mango section (OPT-MCP, OPT-MCPu and OPT-MCS) was studied in comparison with the results obtained with the conventional extraction using 80% ethanol and magnetic stirring (EtOH-MCP, EtOH-MCPu and EtOH-MCS). Although TPC increased up to 33% in the extracts obtained under optimized conditions; some individual phenolic compounds had higher increase rates (Table S2). The phenolic compounds were identified by HPLC-DAD and HPLC-ESI-QTOF-MS/MS on basis of their relative retention time, their UV–vis spectra, and mass spectra obtained using QTOF-MS together with information previously reported in the literature (Table 3). In this study, a total of 45 major phenolic compounds were tentatively identified in the three parts of mango analyzed (peel, pulp and seed). They can be classified in different families such as gallates and gallotannins, flavonoids (flavonols and flavanols), xanthones (mangiferin), benzophenone derivatives (maclurin) and ellagic acid derivatives. The results of the approximate quantification of the phenolic compounds in the three sections of mango are presented in Table S2.

Supplementary Fig. 1 (Fig. S1) shows the total ion chromatograms (TICs) of extracts obtained with conventional extraction (Fig. S1a, S1c and S1e) and those obtained with UAE under optimized conditions (Figs. S1b, d and f). The UAE seems to have minimal effects on the qualitative phenolic composition of mango peel (Figs. S1a and 1b) and seed (Figs. S1e and 1f); however significant quantitative variations were observed (Fig. 3 and Table S2). UAE had a significant impact on both, qualitative and quantitative parameters of phenolic profile in MCPu (Fig. S1c,d and Fig. 3b).

3.2.1. Gallates and gallotannins

Gallotannins are galloyl unit derivatives bounded to diverse groups, yielding gallic acid upon hydrolysis. Along with gallic acid and gallates, they represent an important group of phenolic compounds and have been reported in mango by-products (Ballesteros-Vivas et al., 2019; Dorta et al., 2014).

As many as 23 gallates (derived from gallic acid) were identified, listed in Table 3 as galloyl glucose (n° 1 and 2); theogallin (n° 3), gallic acid (n° 4), di-galloyl-glucose (n° 5), m-digallic acid (n° 8), methyl gallate (n° 10), cumaroyl galloyl glucose (n° 16), five isomers of tetra-O-galloyl-glucoside (peak n° 17 and 21 to 23), ethyl gallate (n° 25), methyl gallate ester (n° 29), penta-O-galloyl-glucoside (n° 30), three isomers of hexagalloyl hexose (n° 35, 37 and 39), m-digallic acid methyl ester (n° 40), two isomers of ethyl 2,4-dihydroxy-3-(3,4,5-trihydroxybenzoyl)-oxybenzoate (n° 42 and 43) and ethyl p-trigallate (n° 45).

The most abundant galloyl derivatives found in EtOH-MCP were n° 25 (9.237 ± 0.218 μg/g DW), n° 30 (8.946 ± 0.848 μg/g DW) and one isomer of n° 43 (9.255 ± 0.907 μg/g DW). The extraction of these compounds, and in general for all gallates, was significantly increased when the extracts were obtained with UAE. The extraction yield in OPT-MCP increased up to 4 times for compounds n° 30 (24.106 ± 1.835 μg/g DW) and n° 25 (36.160 ± 0.754 μg/g DW). Fig. 3a shows the relative concentrations of the different compounds evaluated in MCP extracts, it also shows how the extraction procedure under optimized conditions increased the extraction of gallates, this could be a direct consequence of solvent composition and ultrasound cavitation which could favour the release these compounds from its intracytoplasmatic localization or those attached to cell wall (Jirasuteeruk & Theerakulkait, 2019; Palafox-Carlos et al., 2012).

Gallic acid derivatives present in MCPu extracts were mainly compounds n° 1, 2, 21 and 25 (Table S2). The relative concentrations of some of these compounds increased significantly in the UAE optimized processes (Fig. 3b). A significant increase ($p < 0.05$) for compound n° 25 was found, the concentration value of 0.934 ± 0.045 μg/g DW in EtOH-MCPu increased to 8.817 ± 0.265 μg/g in OPT-MCPu. On the other hand, the concentration of compound n° 21 showed a decrease of 20% (Table S2). These results reveal the different effect that UAE had on the phenolic profile depending on the fruit section. Fig. 3b and Table S2 show that the phenolic compounds extracted and their relative abundance found in the MCPu depends on the extraction procedure, conventional (EtOH) and optimized UAE (OPT), and these results were significant different to those observed in peel and seed.

The profile and relative abundance of gallic acid derivatives isolated in MCS were particularly high for this section of the fruit. One of the major compounds was penta-O-galloyl-glucoside (n° 30) with a value of 49.325 ± 0.448 μg/g DW. Also, three hexagalloyl hexose isomers were found, in concentrations ranging 21 to 49 μg/g DW. Similarly, relatively high values of n° 43 (39.386 ± 1.841 μg/g DW) and n°25 (35.72 ± 1.554 μg/g DW) were found. The UAE significantly ($p < 0.05$) increase the concentrations of compounds n°30 and n°25 up to 50% and 25% for compound n°43, the other compounds had no significant changes with exception of one isomer of hexagalloyl-hexose (n° 39) that registered a significant ($p < 0.05$) decrease (Table S2).

The remarkable diversity of gallates and gallotannins is related to

Table 3
Identification of major phenolic compounds from mango by products by HPLC-DAD-ESI-QTOF-MS/MS.

Peak N°	Rt (min)	Proposed Compound	Molecular Formula	Family	*Fruit section	MI	$[M-H]^-$	Major fragment ions *m/z* (% base peak)
1	3.82	Galloyl glucose I	$C_{13}H_{16}O_{10}$	Gallotannin	MCP, MCPu, MCS	332.744	331.0687	169 (100), 331 (82), 151 (50), 123 (90)
2	6.38	Galloyl glucose II	$C_{13}H_{16}O_{10}$	Gallotannin	MCPu	332.0744	331.0687	169 (100), 211 (83), 123 (60), 59 (80)
3	8.41	5-Galloyl quinic acid (Theogallin)	$C_{14}H_{16}O_{10}$	Gallotannin	MCP, MCS	344.0744	343.0672	191 (100), 59 (10)
4	8.66	Gallic acid	$C_7H_6O_5$	Phenolic Acid	MCP, MCS	170.0215	169.0143	169 (10), 144 (45), 125 (100), 96 (33)
5	14.61	Di-galloyl-glucose	$C_{20}H_{20}O_{14}$	Gallotannin	MCP, MCPu, MCS	484.0853	483.0770	169 (100), 125 (3), 331 (8)
6	14.63	Maclurin-3-C-β-D-glucoside	$C_{19}H_{20}O_{11}$	Benzophenone	MCP, MCPu, MCS	424.1006	423.0935	303 (100), 233 (46), 209 (17), 333 (18), 193 (15)
7	16.45	Maclurin-3-C-(2-O-galloyl)-β-D-glucoside	$C_{26}H_{24}O_{15}$	Benzophenone	MCP, MCPu, MCS	576.1115	575.1049	575 (100), 423 (43), 303 (85), 285 (76), 169 (19)
8	17.31	m-Digallic acid	$C_{14}H_{10}O_9$	Gallate	MCPu, MCS	322.0325	321.0267	169 (100), 186 (84), 125 (42), 260 (30)
9	17.47	Catechin	$C_{15}H_{14}O_6$	Flavonoid	MCP, MCPu, MCS	290.0790	289.0729	109 (100), 123 (36), 175 (48), 205 (70)
10	17.72	Methyl gallate	$C_8H_8O_5$	Gallate	MCP, MCPu, MCS	184.0372	183.0301	124 (100), 78 (25)
11	18.17	Mangiferin	$C_{19}H_{18}O_{11}$	Xanthone	MCP, MCPu, MCS	422.0849	421.0777	301 (100), 331 (90), 259 (13), 421 (38)
12	18.93	Iriflophenone-3-C-(2-O-galloyl)-β-D-glucoside	$C_{26}H_{24}O_{14}$	Xanthone	MCP, MCS	560.1166	559.1094	287 (100), 269 (77), 470 (85), 169 (79)
13	18.97	Mangiferin-6́-O-gallate	$C_{26}H_{22}O_{15}$	Xanthone	MCP, MCPu, MCS	574.0959	573.0878	421 (100), 403 (30), 573 (57), 169 (18)
14	19.09	Maclurin-3-C-(2,3-di-O-galloyl)-β-D-glucoside	$C_{33}H_{28}O_{19}$	Benzophenone	MCP, MCS	728.1225	727.1157	727 (100), 575 (85), 405 (12), 303 (9)
15	19.09	Mangiferin-3-C-(2,3-di-O-galloyl)-β-D-glucoside	$C_{33}H_{26}O_{19}$	Xanthone	MCP	728.1225	727.1157	727 (100), 575 (85), 405 (12), 303 (9)
16	19.35	Cumaroyl galloyl glucose	$C_{22}H_{22}O_{12}$	Gallotannin	MCP, MCPu	478.1111	477.1051	163 (100), 313 (48), 477 (18), 169 (14)
17	20.08	Tetra-O-galloyl-glucoside I	$C_{34}H_{28}O_{22}$	Gallotannin	MCPu, MCS	788.1072	787.1005	787 (100), 635 (14), 617 (69), 169 (11)
18	20.94	Maclurin-3-C-(6́-p-hydroxybenzoyl-glucoside)	$C_{26}H_{24}O_{13}$	Benzophenone	MCP, MCPu, MCS	544.1217	543.1128	285 (100), 405 (6), 327 (10)
19	21.22	Isomangiferin-6́-O-gallate	$C_{26}H_{22}O_{15}$	Xanthone	MCP, MCPu, MCS	574.0959	573.0880	421 (100), 403 (27), 331 (13), 283 (20), 301 (7)
20	21.34	Quercetin-3-O-diglycoside	$C_{26}H_{28}O_{16}$	Flavonoid	MCP, MCPu	596.1377	595.1304	595 (100), 300 (17), 301 (5)
21	21.86	Tetra-O-galloyl-glucoside II	$C_{34}H_{28}O_{22}$	Gallotannin	MCP, MCPu, MCS	788.1072	787.1005	787 (100), 635 (9), 169 (4)
22	22.35	Tetra-O-galloyl-glucoside III	$C_{34}H_{28}O_{22}$	Gallotannin	MCS	788.1072	787.1005	787 (100), 635 (12), 169 (3)
23	22.54	Tetra-O-galloyl-glucoside IV	$C_{34}H_{28}O_{22}$	Gallotannin	MCPu, MCS	788.1072	787.1 005	787 (100), 617 (22), 170 (2), 146 (10)
24	22.7	Tetra-O-galloyl-glucoside V	$C_{34}H_{28}O_{22}$	Gallotannin	MCPu, MCS	788.1072	787.1005	787 (74), 617 (100), 618 (31), 635 (20)
25	23.04	Ethyl gallate	$C_9H_{10}O_5$	Gallate	MCP, MCPu, MCS	198.0528	197.0468	124 (100), 169 (22), 103 (11)
26	23.54	Ellagic acid	$C_{14}H_6O_6$	Phenolic acid	MCP, MCPu, MCS	302.0062	301.0021	301 (100), 229 (3)
27	23.65	Quercetin-3-O-galactoside	$C_{21}H_{20}O_{12}$	Flavonoid	MCP, MCPu	464.0955	463.0890	300 (100), 301 (82), 463 (85), 151 (3)
28	23.88	Quercetin-3-O-glucoside (isoquercitrin)	$C_{21}H_{20}O_{12}$	Flavonoid	MCP, MCPu	464.0955	463.0890	463 (41), 300 (69), 301 (100), 151 (4)
29	23.93	Methyl gallate ester	$C_{15}H_{12}O_9$	Gallate	MCS	336.0481	335.0418	183 (100), 216 (34), 168 (14), 96 (27)
30	24.35	Penta-O-galloyl-glucoside	$C_{41}H_{32}O_{26}$	Gallotannin	MCP, MCS	940.1182	939.1107	769 (100), 470 (31), 787 (33), 617 (16)
31	24.36	Valoneic acid dilactone	$C_{21}H_{10}O_{13}$	Tannin	MCP, MCPu, MCS	470.0121	469.0505	169 (100), 433 (19), 271 (78)
32	24.83	Quercetin pentoside I	$C_{20}H_{18}O_{11}$	Flavonoid	MCP, MCPu	434.0849	433.0783	301 (86), 433 (38), 30 (100)
33	25.33	Quercetin-3-O-rhamnoside (quercitrin) I	$C_{21}H_{20}O_{11}$	Flavonoid	MCP, MCPu	448.1006	447.0941	447 (100), 284 (77), 285 (23)
34	25.4	Quercetin pentoside II	$C_{20}H_{18}O_{11}$	Flavonoid	MCP, MCPu	434.0849	433.0783	301 (25), 433 (29), 30 (100), 178 (9)
35	25.83	Hexagalloyl hexose I	$C_{48}H_{36}O_{30}$	Gallotannin	MCS	1092.1290	1091.1200	770 (83), 879 (9), 498 (100), 169 (11), 279 (29)
36	25.95	Quercetin pentoside III	$C_{20}H_{18}O_{11}$	Flavonoid	MCP, MCPu	434.0849	433.0783	301 (100), 300 (60), 302 (26), 433 (35)
37	26.05	Hexagalloyl hexose II	$C_{48}H_{36}O_{30}$	Flavonoid	MCS	1092.129	1091.1200	433 (100), 787 (48), 839 (32), 16 (62)
38	26.11	Quercetin-3-O-rhamnoside (quercitrin) II	$C_{21}H_{20}O_{11}$	Flavonoid	MCP, MCPu	448.1006	447.0941	447 (92), 284 (100), 255 (24), 285 (29)
39	26.31	Hexagalloyl hexose III	$C_{48}H_{36}O_{30}$	Gallotannin	MCS	1092.1290	1091.1200	146 (100), 449 (60), 615 (64), 635 (54)

(*continued on next page*)

Table 3 (*continued*)

Peak N°	Rt (min)	Proposed Compound	Molecular Formula	Family	*Fruit section	MI	$[M-H]^-$	Major fragment ions *m/z* (% base peak)
40	26.34	m-digallic acid methyl ester	$C_{15}H_{12}O_9$	Gallotannin	MCP, MCS	336.0481	335.0424	183 (100), 168 (11), 124 (10)
41	26.39	Quercetin-3-O-rhamnoside (quercitrin)	$C_{21}H_{20}O_{11}$	Flavonoid	MCP, MCPu	448.1006	447.0941	301 (100), 30 (90), 183 (10), 447 (39)
42	29.61	Ethyl 2,4-dihydroxy-3-(3,4,5-trihydroxybenzoyl)-oxybenzoate	$C_{16}H_{14}O_9$	Gallotannin	MCP,MCPu, MCS	350.0638	349.0577	197 (100), 124 (5)
43	31.95	Ethyl 2,4-dihydroxy-3-(3,4,5-trihydroxybenzoyl)-oxybenzoate	$C_{16}H_{14}O_9$	Gallotannin	MCP,MCPu, MCS	350.0638	349.0577	197 (100), 124 (6)
44	34.44	Rhamnetin hexoside	$C_{22}H_{22}O_{12}$	Flavonoid	MCP,MCPu	478.1111	477.1051	477 (100), 315 (98), 314 (78), 165 (12)
45	37.45	Ethyl p-trigallate	$C_{23}H_{18}O_{13}$	Gallotannin	MCP,MCPu, MCS	502.0747	501.0668	197 (100), 349 (29), 169 (4)

Rt: retention time; MI: monoisotopic mass.
*Fruit Section: section were the compound was identified, MCP: mango criollo peel, MCPu: mango criollo pulp, MCS: mango criollo seed.

metabolic changes due to maturation process, extraction procedure and fruit section (Alañón et al., 2019). The presence of multiple compounds and isomers has been previously reported (Ballesteros-Vivas et al., 2019; Berardini et al., 2004). To determine the precise chemical structure of some isomers requires other techniques like NMR.

This group of compounds, have been mentioned as major components of phenolic compounds found in mango seeds and peel of Tommy Atkins and Ataulfo cultivars (Berardini et al., 2004; Dorta et al., 2014; Jahurul et al., 2015). Penta-O-galloyl-glucoside (compound n° 30) was the major gallotannin present in peel and seed, characterized by an intense antioxidant potential and bioactive effects (Torres-León et al., 2017b). Moreover, gallotannins have important beneficial health effects related with their antioxidative, anti-mutagenic, anticancer, anti-inflammation and anti-diabetic properties (Anaya-Loyola et al., 2020). UAE with aqueous ethanol enhanced the extraction of these compounds from mango by-products.

3.2.2. Xanthone derivatives

Xanthones, comprise an important class of oxygenated heterocycles with high antioxidant potential (Masibo & Qian, 2008), and have been reported in bark, fruit, roots and leaves of *M. indica* L., and a few other medicinal plants (Anaya-Loyola et al., 2020; Dorta et al., 2014). Mangiferin is a xanthone present in significant levels in higher plants and different parts of mango fruit, such as the peel, stalks, leaves, barks, kernel, etc. (Ballesteros-Vivas et al., 2019; Jirasuteeruk & Theerakulkait, 2019; Zou et al., 2014).

Mangiferin (n° 11) and three derivatives mangiferin-6′-O-gallate (n°13), isomangiferin-6′-O-gallate (n°19) and mangiferin-3-C- (2,3-di -O-galloyl) -β-D-glucoside (n°15) were identified in the extracts (Table 3).

Along mangiferin, both mangiferin-6′-O-gallate and isomangiferin-6′-O-gallate were detected in EtOH-MCP with concentrations of 65.135 ± 1.880 μg/g DW; 4.053 ± 0.183 μg/g DW and 3.316 ± 0.768 μg/g DW, respectively, however, compound n°15 was not detected (Table S2). The contents of these compounds, including n°15, were significantly ($p < 0.05$) increased in the OPT-MCP samples (Fig. 3a and Table S2). These results indicate that the contents of distinctive compounds of mango products were significantly increased (up to 50%) with the UAE method under optimized conditions.

The presence of these compounds in pulp was lower than in peel, of those mentioned, only mangiferin was found in appreciable amounts in EtOH-MCPu (3.310 ± 0.198 μg/g DW), while compound n° 31 was not detected. The optimized extraction conditions failed to increase the extraction of mangiferin, indicating that conventional extraction would be sufficient to extract the majority of this compound from MCPu. This could indicate that mangiferin present in the pulp might be present as a free compound. A significant increase ($p < 0.05$) in the UAE of compounds n° 13 and n° 19 was observed, being 40 to 50% higher than conventional extraction (Table S2), although the values were significantly lower than those found in MCP, it is important to highlight the effect of the selected operating conditions to increase the extraction of mangiferin derivatives from MCPu.

Mangiferin was the main compound of this family found in MCS, registering a value of 35.136 ± 0.376 μg/g DW in EtOH-MCS; this content increased to 43.303 ± 0.558 μg/gDW in OPT-MCS. The presence of mangiferin-6′-O-gallate and isomangiferin-6′-O-gallate was also detected, and its values were significantly increased in the extracts prepared under optimized conditions (Table 3 and Fig. 3c).

Mangiferin and its derivatives have been reported in peel and seed extracts of Keitt, Gomera 3 and Tommy Atkins varieties (López-Cobo et al., 2017; Schieber et al., 2003). The results of this compound and the derivatives varies widely among cultivars, our results were in the range reported for Gomera 3 varieties (Dorta et al., 2014). The application of UAE extraction using green solvents provides an effective strategy to obtain higher yields of bioactive compounds. A great example of this is mangiferin which achieved extraction values 25 to 50% higher when compared to conventional extraction.

3.2.3. Benzophenones

The benzophenones are major intermediates in the biosynthetic pathway of xanthones and have been reported in mango fruit var. Tommy Atkins (Berardini et al., 2004).

The presence of the following maclurin derivatives was evaluated: maclurin-3-C-β-D-glucoside (n° 6), maclurin-3-C-(2-O-galoyl)-β-D-glucoside (n° 7), iriflophenone-3-C-(2-O-galloyl)-β-D-glucoside (n° 12), maclurin-3-C-(2,3-di-O-galloyl) -β-D-glucoside (n° 14) and maclurin-3-C-6′'-p-hydroxybenzoyl-glucoside (n° 18).

Compound n° 7 was the major derivative present in EtOH-MCP (9.420 ± 0.892 μg/g DW); its content was significantly increased in OPT-MCP samples (40.468 ± 1.143 μg/g DW). Also, the content of compounds n° 12 and n° 14 showed a significant ($p < 0.05$) increase up to 3.5 times the value obtained with conventional extraction (Table S2 and Fig. 3a).

The relative abundance of these derivatives in EtOH-MCPu and OPT-MCPu was significantly lower than those found in MCP (Table S2); these results also highlight the qualitative and quantitative diversity of phenolic compounds existing in different sections of the fruit.

Extracts of MCS, had contents of maclurin derivatives that were significant ($p < 0.05$) lower than those found in MCP and MCPu. All the evaluated compounds were found in MCS extracts, the most abundant were compound n° 14 (0.773 ± 0.016 μg/g DW) and n° 7 (0.535 ± 0.021 μg/g DW). The contents of these compounds increased by a factor of 2 in extracts obtained under optimized conditions (Table S2 and Fig. 3c).

Benzophenones were also reported in Tommy Atkins, Keitt, Sensation and Gomera 3 by-products (Berardini et al., 2004; Dorta et al., 2014). The relative values found in this work indicate that mango 'criollo' peel represents an interesting source of benzophenone derivatives, and in order to maximize its extraction, the peel should be selected rather than pulp or seed.

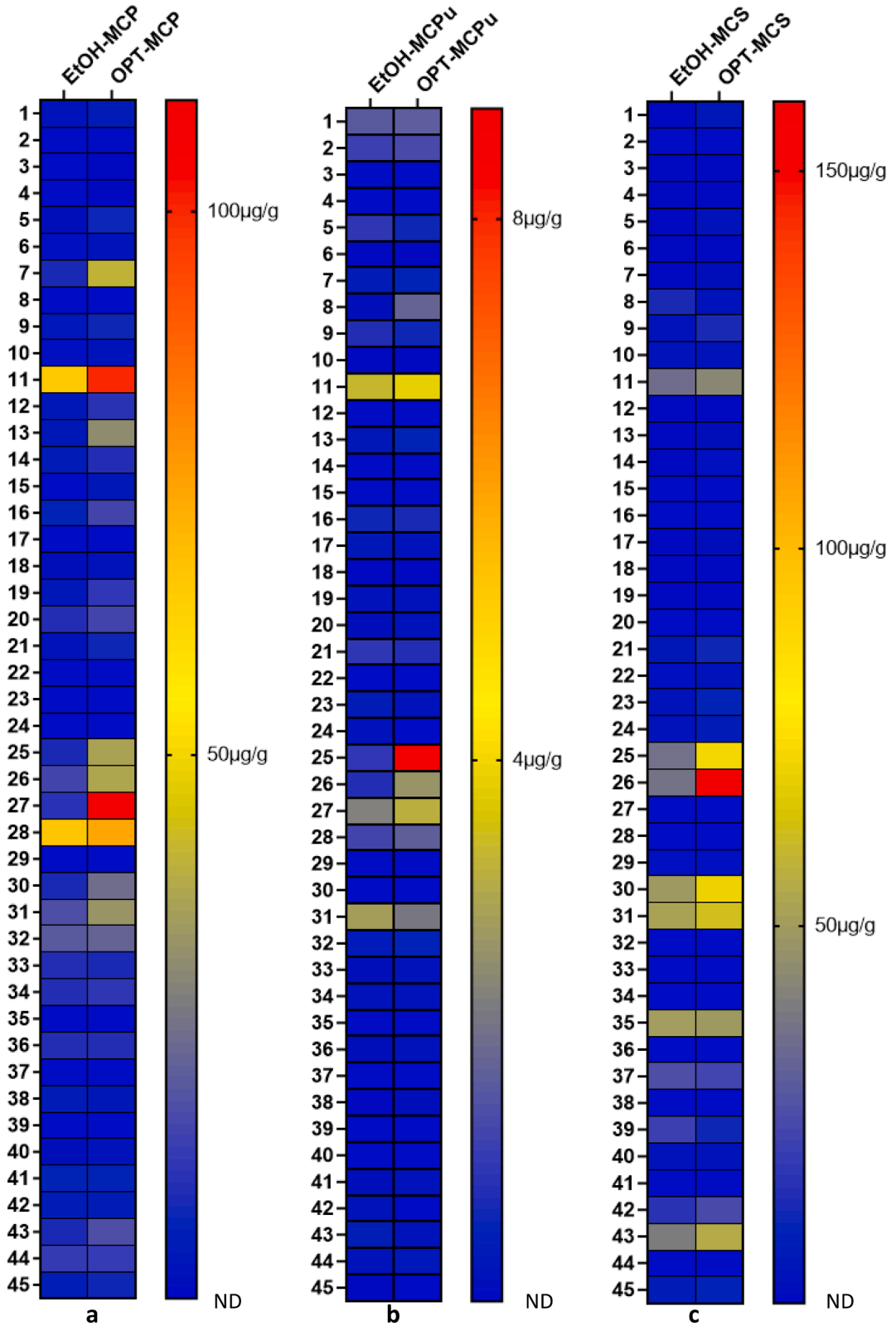

Fig. 3. Heatmap showing the relative concentration of the 45 phenolic compounds tentatively identified in different sections of mango criollo using conventional extraction (EtOH) or ultrasound assisted extraction under optimized conditions (OPT) for MCP: mango criollo peel (a); MCPu: mango criollo pulp (b) and MCS: mango criollo seed (c). ND: not detected.

3.2.4. Flavonoid derivatives

Flavonoids are phenolic compounds that constitute an interesting group of compounds due to their beneficial health related properties (Anaya-Loyola et al., 2020; Jahurul et al., 2015).

The examination of the MS chromatograms of peel, pulp and seeds identified peaks 20, 27, 28, 32, 33, 34, 36, 38 and 41 as quercetin derivatives. Peak 9 was identified as catechin while peak 44 was identified as a rhamnetin derivative (Table 3).

Compound n° 27 (quercetin-3-O-galactoside) was the most abundant flavonoid in EtOH-MCP (100.5940 ± 1.5745 μg/g DW) and the extraction under UAE optimized conditions induced a slight decrease ($p > 0.05$) in the extraction of this compound (Table S2). This compound was also the most abundant in EtOH-MCPu and its content increased 10% in OPT-MCPu ($p < 0.05$). The presence of quercetin-3-O-galactoside was previously reported in mango by-products (Dorta et al., 2014; Schieber et al., 2003). Surprisingly no quercetin or rhamnetin derivatives were detected in MCS extracts. Catechin (n° 9) content was particularly high in ETOH-MCP and UAE increased its yield by a 2.5 factor (Table S2). Moreover, catechin extraction was also significantly ($p < 0.05$) increased in OPT-MCS, however, no significant changes were observed in OPT-MCPu.

Rhamnetin hexoside was detected in peel and pulp, being the peel content significantly higher ($p < 0.05$) than pulp; the extraction under optimized conditions did not have a significant effect on its yield (Table S2).

Quercetin derivatives are of particular interest due to their proven health benefits (Ballesteros-Vivas et al., 2019; Jahurul et al., 2015), our results indicate that MCP is a good source of quercetin derivatives and that UAE did not affect its relative concentration. Catechin has also been related to beneficial effects on health, mainly because of its antioxidant potential (Masibo & Qian, 2008).

These results are of particular interest when mango by-products are used as sources of bioactive compounds since they indicate the importance of selecting an adequate approach for extraction considering qualitative and quantitative diversity of flavonoids.

3.2.5. Ellagic acid and derivatives

Ellagic acid possesses antioxidant, antimutagenic, and anticancer properties and has been widely reported in fruits and vegetables, including mango fruit (Anaya-Loyola et al., 2020; de Ancos et al., 2018).

Ellagic acid (n° 26) and valoneic acid dilactone (n° 31) were detected in all the evaluated sections of mango 'criollo'.

A concentration of 15.995 ± 0.815 μg/g DW for ellagic acid and 17.322 ± 0.876 μg/g DW for valoneic acid dilactone were found in EtOH-MCP extracts, both compounds presented a two fold increase ($p < 0.05$) in the samples obtained under optimized conditions (Fig. 3a and Table S2).

In the extracts obtained from MCPu, the dilactone concentration was higher than ellagic acid, while the ellagic acid concentration increased by a factor of 10 in OPT-MCPu samples, the dilactone concentration did not change significantly ($p > 0.05$) (Table S2 and Fig. 3b).

In MCS extracts obtained by conventional methodology (EtOH-MCS), the valoneic acid dilactone content was higher than the content of ellagic acid (Table S2). However, ellagic acid extraction increased by a factor of 4.4 in OPT-MCS samples (Fig. 3c), while the content of dilactone only increased by a factor of 1.2.

These results indicate that UAE represents a valid strategy for recovering of ellagic acid from mango by-products, particularly from mango seed and peel. The application of UAE proved to significantly increase the extraction of ellagic acid from mango peel and seed. Considering the yields of both sections they could be used as an interesting source of this compound.

4. Conclusion

Although mango 'criollo' is not commercially exploited, its by-products are a good and non-expensive sources of phenolic compounds that can be used as food additives by food industry.

Each section of the fruit exhibited different UAE conditions to maximize phenolic and antioxidants yield. Mango peel required 6.5 min, 60% of amplitude and 46% of ethanol in the solvent. The pulp required 30 min, amplitude of 75% and ethanol content of 25% and the seed required 20 min, 100% amplitude and 49% ethanol. These results proved that the use of experimental design is a key step in order to maximize the extraction procedure in different fruit sections. The UAE increased up to 33% the extraction yield of phenolic compounds.

The qualitative and quantitative phenolic compound profile was different and characteristic of each section of the fruit, and the UAE had differential effects. The extraction of highly recognized bioactive compounds like mangiferin, ellagic acid and quercetin derivatives was improved with UAE in different sections of the fruit. Under optimized conditions, mangiferin extraction increased up to 53% in peel extracts. Similarly, ellagic acid extraction under optimized conditions increased up to 80% in peel extracts while optimized seed extracts had ellagic acid contents 4.4 times higher than conventional extraction. Although UAE in pulp also increased extraction of phenolic compounds, the absolute values were significantly lower than those obtained for peel and seed.

Knowing the impact of the extraction procedure on individual compounds is of particular interest since it provides an objective criterion to design and select optimal extraction conditions depending on the target compound or chemical family of interest.

CRediT authorship contribution statement

Gonzalo Adrián Ojeda: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft. **Sonia Cecilia Sgroppo:** Data curation, Supervision. **Concepción Sánchez-Moreno:** Project administration, Funding acquisition, Resources. **Begoña de Ancos:** Project administration, Funding acquisition, Resources, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Gonzalo Ojeda reports travel was provided by Carolina Foundation. Gonzalo Ojeda reports travel was provided by Argentina Ministry of Education Culture Science and Technology. Begoña de Ancos reports financial support was provided by Spanish State Agency of Research.

Data availability

Data will be made available on request.

Acknowledgements

This study has been funded by the Spanish State Agency of Research (PID2019-107980RB-100/AEI/10.13039/501100011033). The authors are grateful to the Analysis Service Unit facilities of ICTAN for the analysis of chromatography and mass spectrometry and to the graduate Lucía Gimenez for her technical support. Dr. Ojeda thanks the Carolina Foundation and the Ministry of Education of Argentina for the grant received.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.foodchem.2022.133738.

References

Alañón, M. E., Oliver-Simancas, R., Gómez-Caravaca, A. M., Arráez-Román, D., & Segura-Carretero, A. (2019). Evolution of bioactive compounds of three mango cultivars (Mangifera indica L.) at different maturation stages analyzed by HPLC-DAD-q-TOF-MS. *Food Research International, 125*(June), Article 108526. https://doi.org/10.1016/j.foodres.2019.108526

Anaya-Loyola, M. A., García-Marín, G., García-Gutiérrez, D. G., Castaño-Tostado, E., Reynoso-Camacho, R., López-Ramos, J. E., … Pérez-Ramírez, I. F. (2020). A mango (Mangifera indica L.) juice by-product reduces gastrointestinal and upper respiratory tract infection symptoms in children. *Food Research International, 136*(February), Article 109492. https://doi.org/10.1016/j.foodres.2020.109492

Ballesteros-Vivas, D., Álvarez-Rivera, G., Morantes, S. J., Sánchez-Camargo, A. del P., Ibáñez, E., Parada-Alfonso, F., & Cifuentes, A. (2019). An integrated approach for the valorization of mango seed kernel: Efficient extraction solvent selection, phytochemical profiling and antiproliferative activity assessment. *Food Research International, 126*(August). https://doi.org/10.1016/j.foodres.2019.108616

Berardini, N., Carle, R., & Schieber, A. (2004). Characterization of gallotannins and benzophenone derivatives from mango (Mangifera indica L. cv. 'Tommy Atkins') peels, pulp and kernels by high-performance liquid chromatography/electrospray ionization mass spectrometry. *Rapid Communications in Mass Spectrometry, 18*(19), 2208–2216. https://doi.org/10.1002/rcm.1611

Bezerra, M. A., Santelli, R. E., Oliveira, E. P., Villar, L. S., & Escaleira, L. A. (2008). Response surface methodology (RSM) as a tool for optimization in analytical chemistry. *Talanta, 76*(5), 965–977. https://doi.org/10.1016/j.talanta.2008.05.019

Borrás-Enríquez, A. J., Reyes-Ventura, E., Villanueva-Rodríguez, S. J., & Moreno-Vilet, L. (2021). Effect of ultrasound-assisted extraction parameters on total polyphenols and its antioxidant activity from mango residues (Mangifera indica L. var. manililla). *Separations, 8*(7). https://doi.org/10.3390/separations8070094

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

de Ancos, B., Sánchez-Moreno, C., Zacarías, L., Rodrigo, M. J., Sáyago Ayerdí, S., Blancas Benítez, F. J., … González-Aguilar, G. A. (2018). Effects of two different drying methods (freeze-drying and hot air-drying) on the phenolic and carotenoid profile of 'Ataulfo' mango by-products. *Journal of Food Measurement and Characterization, 12*(3), 2145–2157. https://doi.org/10.1007/s11694-018-9830-4

Dorta, E., González, M., Lobo, M. G., Sánchez-Moreno, C., & de Ancos, B. (2014). Screening of phenolic compounds in by-product extracts from mangoes (Mangifera indica L.) by HPLC-ESI-QTOF-MS and multivariate analysis for use as a food ingredient. *Food Research International, 57*, 51–60. https://doi.org/10.1016/j.foodres.2014.01.012

Dorta, E., Lobo, M. G., & González, M. (2013). Improving the Efficiency of Antioxidant Extraction from Mango Peel by Using Microwave-assisted Extraction. *Plant Foods for Human Nutrition, 68*(2), 190–199. https://doi.org/10.1007/s11130-013-0350-4

Floegel, A., Kim, D. O., Chung, S. J., Koo, S. I., & Chun, O. K. (2011). Comparison of ABTS/DPPH assays to measure antioxidant capacity in popular antioxidant-rich US foods. *Journal of Food Composition and Analysis, 24*(7), 1043–1048. https://doi.org/10.1016/j.jfca.2011.01.008

Jahurul, M. H. A., Zaidul, I. S. M., Ghafoor, K., Al-Juhaimi, F. Y., Nyam, K. L., Norulaini, N. A. N., … Mohd Omar, A. K. (2015). Mango (Mangifera indica L.) by-products and their valuable components: A review. *Food Chemistry, 183*, 173–180. https://doi.org/10.1016/j.foodchem.2015.03.046

Jangra, A., Arora, M. K., Kisku, A., & Sharma, S. (2021). The multifaceted role of mangiferin in health and diseases: A review. *Advances in Traditional Medicine, 21*(4), 619–643. https://doi.org/10.1007/s13596-020-00471-5

Jirasuteeruk, C., & Theerakulkait, C. (2019). Ultrasound-assisted extraction of phenolic compounds from mango (Mangifera indica cv. Chok Anan) peel and its inhibitory effect on enzymatic browning of potato puree. *Food Technology and Biotechnology, 57*(3), 350–357. https://doi.org/10.17113/ftb.57.03.19.5728

Kim, D. O., Lee, K. W., Lee, H. J., & Lee, C. Y. (2002). Vitamin C equivalent antioxidant capacity (VCEAC) of phenolic phytochemicals. *Journal of Agricultural and Food Chemistry, 50*(13), 3713–3717. https://doi.org/10.1021/jf020071c

Kumar, M., Saurabh, V., Tomar, M., Hasan, M., Changan, S., Sasi, M., … Mekhemar, M. (2021). Mango (Mangifera indica l.) leaves: Nutritional composition, phytochemical profile, and health-promoting bioactivities. *Antioxidants, 10*(2), 1–23. https://doi.org/10.3390/antiox10020299

Liu, Y., Chen, S., Pu, Y., Muhammad, A. I., Hang, M., Liu, D., & Ye, T. (2019). Ultrasound-assisted thawing of mango pulp: Effect on thawing rate, sensory, and nutritional properties. *Food Chemistry, 286*, 576–583. https://doi.org/10.1016/j.foodchem.2019.02.059

López-Cobo, A., Verardo, V., Diaz-de-Cerio, E., Segura-Carretero, A., Fernández-Gutiérrez, A., & Gómez-Caravaca, A. M. (2017). Use of HPLC- and GC-QTOF to determine hydrophilic and lipophilic phenols in mango fruit (Mangifera indica L.) and its by-products. *Food Research International, 100*, 423–434. https://doi.org/10.1016/j.foodres.2017.02.008

Maldonado-Celis, M. E., Yahia, E. M., Bedoya, R., Landázuri, P., Loango, N., Aguillón, J., … Guerrero Ospina, J. C. (2019). Chemical Composition of Mango (Mangifera indica L.) Fruit: Nutritional and Phytochemical Compounds. *Frontiers. Plant Science, 10*(October), 1–21. https://doi.org/10.3389/fpls.2019.01073

Martínez-Ramos, T., Benedito-Fort, J., Watson, N. J., Ruiz-López, I. I., Che-Galicia, G., & Corona-Jiménez, E. (2020). Effect of solvent composition and its interaction with ultrasonic energy on the ultrasound-assisted extraction of phenolic compounds from Mango peels (Mangifera indica L.). *Food and Bioproducts Processing, 122*, 41–54. https://doi.org/10.1016/j.fbp.2020.03.011

Masibo, M., & Qian, H. (2008). Major mango polyphenols and their potential significance to human health. *Comprehensive Reviews in Food Science and Food Safety, 7*(4), 309–319. https://doi.org/10.1111/j.1541-4337.2008.00047.x

Mercado-Mercado, G., Montalvo-González, E., González-Aguilar, G. A., Alvarez-Parrilla, E., & Sáyago-Ayerdi, S. G. (2018). Ultrasound-assisted extraction of carotenoids from mango (Mangifera indica L. 'Ataulfo') by-products on in vitro bioaccessibility. Food. *Bioscience, 21*, 125–131. https://doi.org/10.1016/j.fbio.2017.12.012

Pal, C. B. T., & Jadeja, G. C. (2020). Microwave-assisted extraction for recovery of polyphenolic antioxidants from ripe mango (Mangifera indica L.) peel using lactic acid/sodium acetate deep eutectic mixtures. *Food Science and Technology International, 26*(1), 78–92. https://doi.org/10.1177/1082013219870010

Palafox-Carlos, H., Yahia, E. M., & González-Aguilar, G. A. (2012). Identification and quantification of major phenolic compounds from mango (Mangifera indica, cv. Ataulfo) fruit by HPLC-DAD-MS/MS-ESI and their individual contribution to the antioxidant activity during ripening. *Food Chemistry, 135*(1), 105–111. https://doi.org/10.1016/j.foodchem.2012.04.103

Pingret, D., Fabiano-Tixier, A. S., & Chemat, F. (2012). Accelerated methods for sample preparation in food. In *Comprehensive Sampling and Sample Preparation* (Vol. 4). https://doi.org/10.1016/B978-0-12-381373-2.00143-5.

Prado, I. M., Prado, G. H. C., Prado, J. M., & Meireles, M. A. A. (2013). Supercritical CO2 and low-pressure solvent extraction of mango (Mangifera indica) leaves: Global yield, extraction kinetics, chemical composition and cost of manufacturing. *Food and Bioproducts Processing, 91*(4), 656–664. https://doi.org/10.1016/j.fbp.2013.05.007

Quintana, S. E., Salas, S., & García-Zapateiro, L. A. (2021). Bioactive compounds of mango (Mangifera indica): A review of extraction technologies and chemical constituents. *Journal of the Science of Food and Agriculture, 101*(15), 6186–6192. https://doi.org/10.1002/jsfa.11455

Re, R., Nicoletta, P., Anna, P., Ananth, P., Min, Y., & Catherine, R.-E. (1999). Antioxidant activity applying an improved ABTS radical cation decolorization assay. *Free Radical Biology and Medicine*, *26*((9-10)), 1231–1237. Retrieved from https://doi.org/10.1016/S0891-5849(98)00315-3.

Schieber, A., Berardini, N., & Carle, R. (2003). Identification of flavonol and xanthone glycosides from mango (Mangifera indica L. cv. "Tommy Atkins") peels by high-performance liquid chromatography-electrospray ionization mass spectrometry. *Journal of Agricultural and Food Chemistry, 51*(17), 5006–5011. https://doi.org/10.1021/jf030218f

Serna-Cock, L., García-Gonzales, E., & Torres-León, C. (2016). Agro-industrial potential of the mango peel based on its nutritional and functional properties. *Food Reviews International, 32*(4), 364–376. https://doi.org/10.1080/87559129.2015.1094815

Tomšik, A., Pavlić, B., Vladić, J., Ramić, M., Brindza, J., & Vidović, S. (2016). Optimization of ultrasound-assisted extraction of bioactive compounds from wild garlic (Allium ursinum L.). *Ultrasonics Sonochemistry, 29*, 502–511. https://doi.org/10.1016/j.ultsonch.2015.11.005

Torres-León, C., Rojas, R., Contreras-Esquivel, J. C., Serna-Cock, L., Belmares-Cerda, R. E., & Aguilar, C. N. (2016). Mango seed: Functional and nutritional properties. *Trends in Food Science and Technology, 55*, 109–117. https://doi.org/10.1016/j.tifs.2016.06.009

Torres-León, C., Rojas, R., Serna-Cock, L., Belmares-Cerda, R., & Aguilar, C. N. (2017). Extraction of antioxidants from mango seed kernel: Optimization assisted by microwave. *Food and Bioproducts Processing, 105*, 188–196. https://doi.org/10.1016/j.fbp.2017.07.005

Torres-León, C., Ventura-Sobrevilla, J., Serna-Cock, L., Ascacio-Valdés, J. A., Contreras-Esquivel, J., & Aguilar, C. N. (2017). Pentagalloylglucose (PGG): A valuable phenolic compound with functional properties. *Journal of Functional Foods, 37*, 176–189. https://doi.org/10.1016/j.jff.2017.07.045

Vithana, M. D. K., Singh, Z., & Johnson, S. K. (2019). Regulation of the levels of health promoting compounds: Lupeol, mangiferin and phenolic acids in the pulp and peel of mango fruit: A review. *Journal of the Science of Food and Agriculture, 99*(8), 3740–3751. https://doi.org/10.1002/jsfa.9628

Zou, T. B., Xia, E. Q., He, T. P., Huang, M. Y., Jia, Q., & Li, H. W. (2014). Ultrasound-assisted extraction of mangiferin from mango (Mangifera indica L.) leaves using response surface methodology. *Molecules, 19*(2), 1411–1421. https://doi.org/10.3390/molecules19021411