

## Article

# Supercritical Fluid Extraction of Phenolic Compounds from Mango (*Mangifera indica* L.) Seed Kernels and Their Application as an Antioxidant in an Edible Oil

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**Citation:** Buelvas-Puello, L.M.; Franco-Arnedo, G.; Martínez-Correa, H.A.; Ballesteros-Vivas, D.; Sánchez-Camargo, A.d.P.; Miranda-Lasprilla, D.; Narváez-Cuenca, C.-E.; Parada-Alfonso, F. Supercritical Fluid Extraction of Phenolic Compounds from Mango (*Mangifera indica* L.) Seed Kernels and Their Application as an Antioxidant in an Edible Oil. *Molecules* **2021**, *26*, 7516. <https://doi.org/10.3390/molecules26247516>

Academic Editor: Antonio Zuorro

Received: 10 November 2021

Accepted: 8 December 2021

Published: 11 December 2021

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**Abstract:** Phenolic compounds from mango (*M. indica*) seed kernels (MSK) *var.* Sugar were obtained using supercritical CO<sub>2</sub> and EtOH as an extraction solvent. For this purpose, a central composite design was carried out to evaluate the effect of extraction pressure (11–21 MPa), temperature (40–60 °C), and co-solvent contribution (5–15% *w/w* EtOH) on (i) extraction yield, (ii) oxidative stability (OS) of sunflower edible oil (SEO) with added extract using the Rancimat method, (iii) total phenolics content, (iv) total flavonoids content, and (v) DPPH radical assay. The most influential variable of the supercritical fluid extraction (SFE) process was the concentration of the co-solvent. The best OS of SEO was reached with the extract obtained at 21.0 MPa, 60 °C and 15% EtOH. Under these conditions, the extract increased the OS of SEO by up to 6.1 ± 0.2 h (OS of SEO without antioxidant, Control, was 3.5 h). The composition of the extract influenced the oxidative stability of the sunflower edible oil. By SFE it was possible to obtain extracts from mango seed kernels (MSK) *var.* Sugar that transfer OS to the SEO. These promissory extracts could be applied to foods and other products.

**Keywords:** mango seed kernel; sunflower edible oil; oxidative stability; Rancimat method; phenolic compounds; supercritical fluid extraction

## 1. Introduction

Mango (*Mangifera indica* L.) is one of the most consumed fruits worldwide [1,2]. In Colombia, mango is among the most important permanent fruit crop, with a production of 325,000 t in 2019 [3]. More than 20 different cultivars have been described [4], with mango *variety* Sugar and *var.* Tommy Atkins as the most important ones for the Colombian agro-industry [5]. In fruit processing, the main by-products generated are epicarp (peel) and seed. These by-products represent around 35–60% of the fruit's total weight. The seed can reach up to 75,000 t/year, becoming a source of contamination without any sustainable disposal at present. This agricultural by-product, especially the mango seed kernels (MSK), is considered, however, an important source of biomolecules that could be exploited [1,6–10].

Nowadays, almost all processed foods include synthetic antioxidants. For instance, in the oil industry, butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA) or tert-butylhydroquinone (TBHQ) are the most commonly used [11,12]. Negative health effects, however, have been reported due to the consumption of synthetic antioxidants, which could be avoided by using natural antioxidants instead [13–15] such as those present in MSK. Recent work has described the presence of different families of phenolic compounds with interesting antioxidant properties [6]. Antioxidants extracted from natural sources might, therefore, be a good alternative to synthetic compounds.

Alternative extraction methods, such as supercritical fluid extraction (SFE), were explored to obtain enriched-biomolecules extracts with antioxidant properties. The use of supercritical CO<sub>2</sub> as an extraction solvent reduces not only the consumption of liquid solvents but also evaporation steps because it is gaseous under ambient conditions. In addition, it provides an inert environment during the extraction process that helps to prevent the degradation of compounds sensitive to oxidation and allows high selectivity [16,17].

On the basis of their chemical structure, the phenolic compounds found in MSK are of considerable polarity, which makes their extraction with supercritical CO<sub>2</sub> difficult. To increase the polarity of the extraction system small amounts of polar co-solvents, such as ethanol (EtOH), are used in combination with supercritical CO<sub>2</sub> [18–22]. Our previous works from guava seed studies have found that SFE using supercritical CO<sub>2</sub> with cosolvent (ethyl acetate or ethanol) led to better results in yield and extract quality (antioxidant activity), EtOH being the best co-solvent [23]. As a result an increase in the overall extraction yield and the compounds extraction efficiency, including mangiferin, gallic acid, and ellagic acid, present in mango fruit, might be expected [1,6,7,10,24]. To the best of our knowledge, the use of supercritical CO<sub>2</sub> with EtOH as co-solvent has not been used to extract biomolecules from MSK. Additionally, while the action mechanism of pure phenolic compounds on bulk oil and oil in water emulsion systems is well understood [25], studies of crude extracts are less well documented [12,26].

The main aim of this research was optimizing the production of an extract from MSK, using supercritical CO<sub>2</sub> and EtOH as co-solvent the best extract would transfer the major oxidative stability (OS) to sunflower edible oil (SEO). The supplementary aims of this research were (i) to evaluate the total phenolics content (TPC), the total flavonoids content (TFC), and the in vitro antioxidant activity by the DPPH method on such extracts, (ii) to characterize the extracts by means of reversed-phase (ultra high-performance liquid chromatography with diode array detector (RP-UHPLC-DAD)), and (iii) to evaluate the relationship between the TPC, TFC, DPPH, and composition of the extracts, and their antioxidant activity on a bulk sunflower oil system.

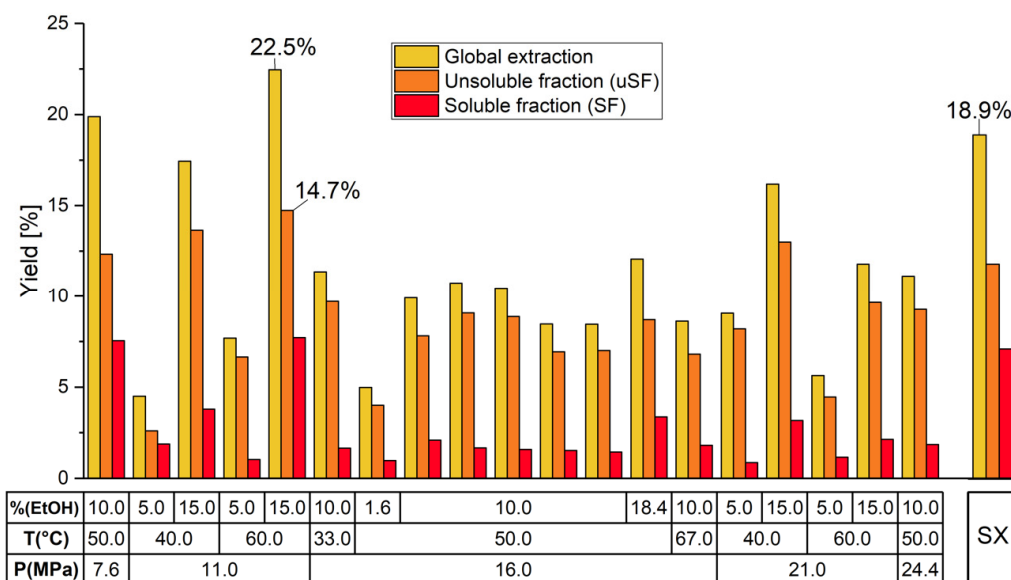
The OS was studied using the Rancimat method due to its high performance to evaluate the OS of the fats and oils, as well as, to assay the antioxidant activity of extracts and compounds [27]. In the same way, the DPPH method was selected to measure antioxidant activity because it was the most used method for the in vitro antioxidant activity evaluation [28]. This work proposes an application for important agro-industrial byproducts, the MSK var. sugar, which could be used as a source of antioxidant extract applied in the fats and oils industry, a topic which is framed in the guidelines of green chemistry.

## 2. Results and Discussion

### 2.1. Extraction Yield

The yield results (soluble fraction-*SF* yield, insoluble fraction-*uSF* yield, and global extraction yield, *SF* + *uSF*) obtained under the SFE and the Soxhlet methods are shown in Figure 1. The highest overall and *SF* yields (22.5 and 7.7%, respectively), using the SFE technology, were obtained at 11.0 MPa, 60.0 °C and 15.0% EtOH. Under the Soxhlet (SX) method the overall yield reached 18.9% and the *SF* yield 7.1%. The maximum extraction yield for *uSF* under SFE (14.7%) was similar to those obtained by Jahurul et al. [29], which reported values of up to 13.5% of fat extracted by supercritical CO<sub>2</sub> from the kernel of six

mango varieties from Malaysia [30]. Our research shows that under the SX method the overall extraction yield was higher than those reported for the *var.* Kibangou (13.0%) [31] and the *var.* Kent (12.3%) [32], both extracted with petroleum ether from the mango seed kernel (MSK). Additionally, a research work using the SX extraction method and involving the kernel of 20 mango Colombian varieties reported a maximum overall extraction yield of 11.8% for the *var.* Rosa, using petroleum ether as solvent [33]. Furthermore, the highest overall extraction yield as obtained in the current research under SFE (22.5%) is far better than all those previously reported, using the SX extraction method. The higher extraction yield under SFE relative to that under Soxhlet may be due to the properties offered by the SFE technique. Changes in pressure and co-solvent cause an increase in density and polarity which is translated into an increase in the solubility of compounds, because of greater interaction between the extractant agent and the matrix [20]. Similarly, an increase in extraction temperature decreases the viscosity and facilitates the diffusion of compounds, thus allowing rapid exhaustion of the sample and increasing the yield.

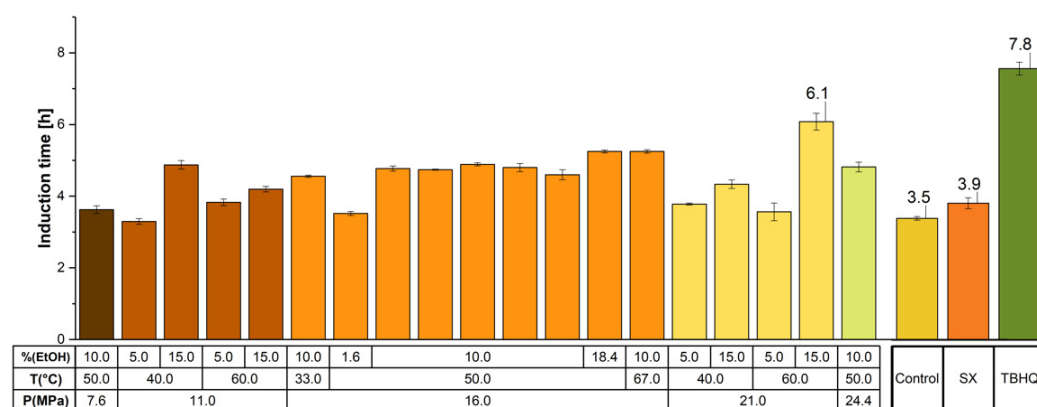


**Figure 1.** Extraction yield under the supercritical CO<sub>2</sub> + EtOH and Soxhlet (SX) extraction methods.

## 2.2. Oxidative Stability of Sunflower Edible Oil with Added Extracts

Figure 2 shows the results for sunflower edible oil (SEO) having added the extracts obtained under SFE and SX. It also shows the results for the OS of SEO with TBHQ, and those of the control without antioxidants. Most of the extracts (SFE and SX) increased the  $t_i$  with respect to the control (3.5 h), with TBHQ exhibiting the greatest  $t_i$  (7.8 h). The extract yielding the greatest  $t_i$  was obtained at 21.0 MPa, 60.0 °C, 15.0% EtOH (6.1 h), its protection factor (PF) was 1.7, equivalent to 78% of the effect generated by the TBHQ (PF 2.2).

To the best of our knowledge, there are no reports on the use of extracts obtained from MSK to protect edible oils from oxidation. Our results, however, can be compared with extracts from other biomasses. For instance, Asnaashari et al. [34] obtained extracts from *Rubus fruticosus* by conventional extraction using methanol and evaluated their antioxidant effect in SEO at 1000 mg Kg<sup>-1</sup>, 120 °C, and 20 L h<sup>-1</sup>. Under such conditions, the  $t_i$  and PF reached values of 10.8 h and 2.2, respectively. Promisingly, those values were higher than those obtained with 200 mg BHT Kg<sup>-1</sup> (9.8 h and PF 1.9). Another research, conducted by Upadhyay et al. [35], evaluated the effect of extracts obtained from *Rosmarinus officinalis*. They tested such extracts under the same Rancimat method conditions of this research and obtained a similar PF (1.6) to that given by the current research.



**Figure 2.** Oxidative stability of SEO as measured by the induction time (h) using the Rancimat method. SEO was added with SFE and Soxhlet extracts, and TBHQ as synthetic antioxidant, an SEO without antioxidants was included (Control).

### 2.3. Experimental Design on the Supercritical Fluid Extraction

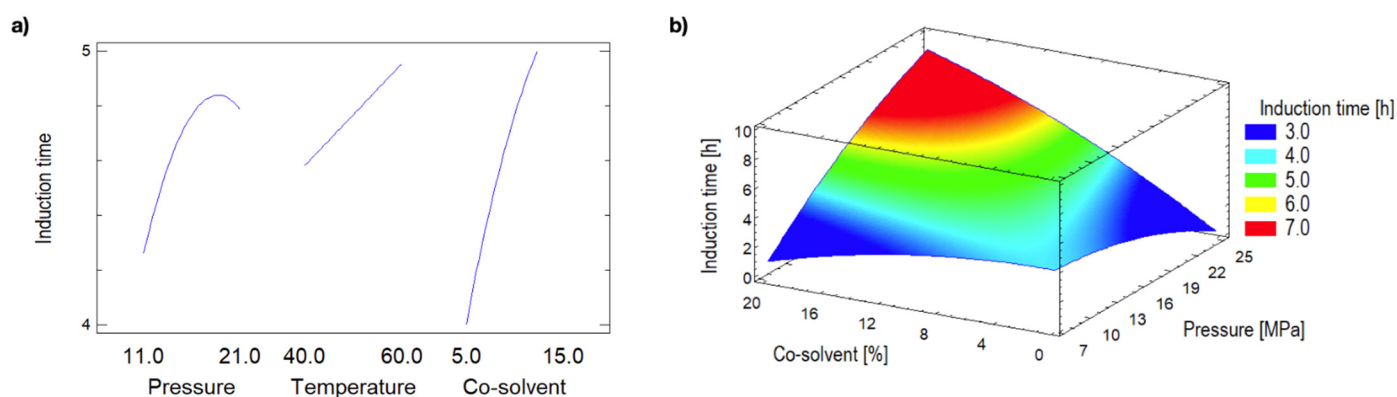
The experimental conditions (P, T, and %EtOH) are shown in Table 1.

The chosen variable main effects on the ability of the obtained extracts to increase the OS of the SEO as measured by the  $t_i$  are shown in Figure 3a. Although most of the variables together with their interactions had a statistically significant effect, it was observed that the variable that positively influenced the oxidative stability the most was the co-solvent factor, followed by pressure. Because EtOH is a polar solvent, the increase in its concentration in the extractant phase generates greater polarity in this phase, favoring the extraction of polar analytes, thus showing the modifying effect of the co-solvent.

**Table 1.** Central composite experimental design for the preparation of extracts from mango seed kernel employing supercritical fluid extraction (CO<sub>2</sub>-EtOH).

Experiment #	Pressure (MPa)	Temperature (°C)	Co-solvent (%)
1	11.0	60.0	15.0
2	16.0	50.0	10.0
3	7.6	50.0	10.0
4	24.4	50.0	10.0
5	16.0	50.0	18.4
6	16.0	33.0	10.0
7	21.0	40.0	5.0
8	16.0	50.0	10.0
9	11.0	40.0	5.0
10	21.0	60.0	15.0
11	11.0	40.0	15.0
12	21.0	60.0	5.0
13	16.0	50.0	10.0
14	16.0	67.0	10.0
15	16.0	50.0	10.0
16	11.0	60.0	5.0
17	21.0	40.0	15.0
18	16.0	50.0	1.6
19	16.0	50.0	10.0

Experiments are presented as they were performed, in a randomized order. Underlined values represent the central points of experimental design.



**Figure 3.** Main effects (a) and response surface predicted for the induction time of sunflower oil added with extracts obtained by supercritical fluid extraction at 67.0 °C (b).

The coefficients of the mathematical model that better described the  $t_i$  as a function of pressure, temperature, and co-solvent are shown in Table 2. Under such circumstances, the adjusted R-squared statistic indicates that the model explains 92.4% of the variability in the  $t_i$ . The lack-of-fit test ( $p = 0.06$ ) was also indicative of the adequacy of the mathematical model. According to the coefficients presented in Table 2, the optimum conditions predicted in the explored region correspond to 24.4 MPa, 67.0 °C and 18.4% EtOH, which was similar to the extract obtained at 21.0 MPa-60.0 °C-15.0% EtOH (See Table 1). Figure 3b shows the surface response obtained from the predicted induction time according to the mathematical model (Table 2). Such surface shows that increasing pressure and co-solvent percentage under SFE increases the induction time.

To explain how the composition of the extracts responds to the observed  $t_i$ , the TPC, TFC, DPPH, and individual phenolics in the extracts were studied and their contribution to the  $t_i$  was analyzed by mathematical models.

**Table 2.** Regression coefficients for the induction time ( $t_i$ ).

Coefficient	Estimate	p-Value
a	−8.8966	
b	0.8911	0.0008
c	0.1879	0.0028
d	1.3504	0.0000
e	−0.0097	0.0010
f	−0.0117	0.0050
g	−0.0737	0.0195
h	−0.0235	0.0664
i	−0.0074	0.0028
j	0.0016	0.0004
Lack of fit		0.0596
Adjusted R <sup>2</sup>		92.4%

Coefficients are given for the equation  $t[h] = a + bP + cT + dC + eP^2 + fPT + gPC + hTC + iC^2 + jPTC$ , where P is pressure, T is temperature, and C is %EtOH.

#### 2.4. Total Phenolics and Total Flavonoids Contents, and DPPH Radical Antioxidant Activity

The TPC, TFC, and DPPH in the SF obtained by SFE as well as in the SX extraction are shown in Figure 4a–c.

The greatest value for the TPC was obtained when extraction was made under the SX method (62.1 mg-eq GA g<sup>−1</sup> extract). The highest TPC value under SFE was obtained at 11.0 MPa, 60.0 °C, and 15.0% EtOH (57.3 mg-eq GA g<sup>−1</sup> extract). Under these SFE conditions, the TFC was also the highest (13.6 mg-eq Q g<sup>−1</sup> extract). The higher TPC under the SX extraction (relative to SFE) can be related to its high solvation power, typical of liquid solvents, and its high polarity, which is higher than that of supercritical CO<sub>2</sub>-EtOH [36].

This fact can also be observed taking into account the Hildebrand solubility parameters, where values of 26.2, 3.5, and 6.3 are reported for EtOH, supercritical CO<sub>2</sub>, and supercritical CO<sub>2</sub>-EtOH, respectively [37,38]. The results given by the current research were lower than those reported by Khammuang et al. for the kernel of mango *var.* Thai, which reported values of TPC and TFC of 118.1 mg-eq AG g<sup>-1</sup> extract and 110.1 mg-eq Q g<sup>-1</sup> extract, respectively, when the extraction was made by solid–liquid extraction using water [39]. Our results, however, were greater than those reported by Ballesteros for an SX methanolic extract of MSK *var.* Sugar with 16.2 mg-eq GA g<sup>-1</sup> extract and 2.0 mg-eq Q g<sup>-1</sup> extract [40]. TFC to TPC proportions obtained from MSK by SFE were 1:5 approximately, these values contrast with the same proportions obtained from MSK by PLE (they were 1:100 approximately), these results are in agreement with the high selectivity of SFE [8], PLE's obtained extract yields were better but lower selectivity than those obtained by SFE. On the other way, the differences observed between our results and those from elsewhere could be due to differences in the agroclimatic conditions of cultivation and the varieties of mango, among others [12].

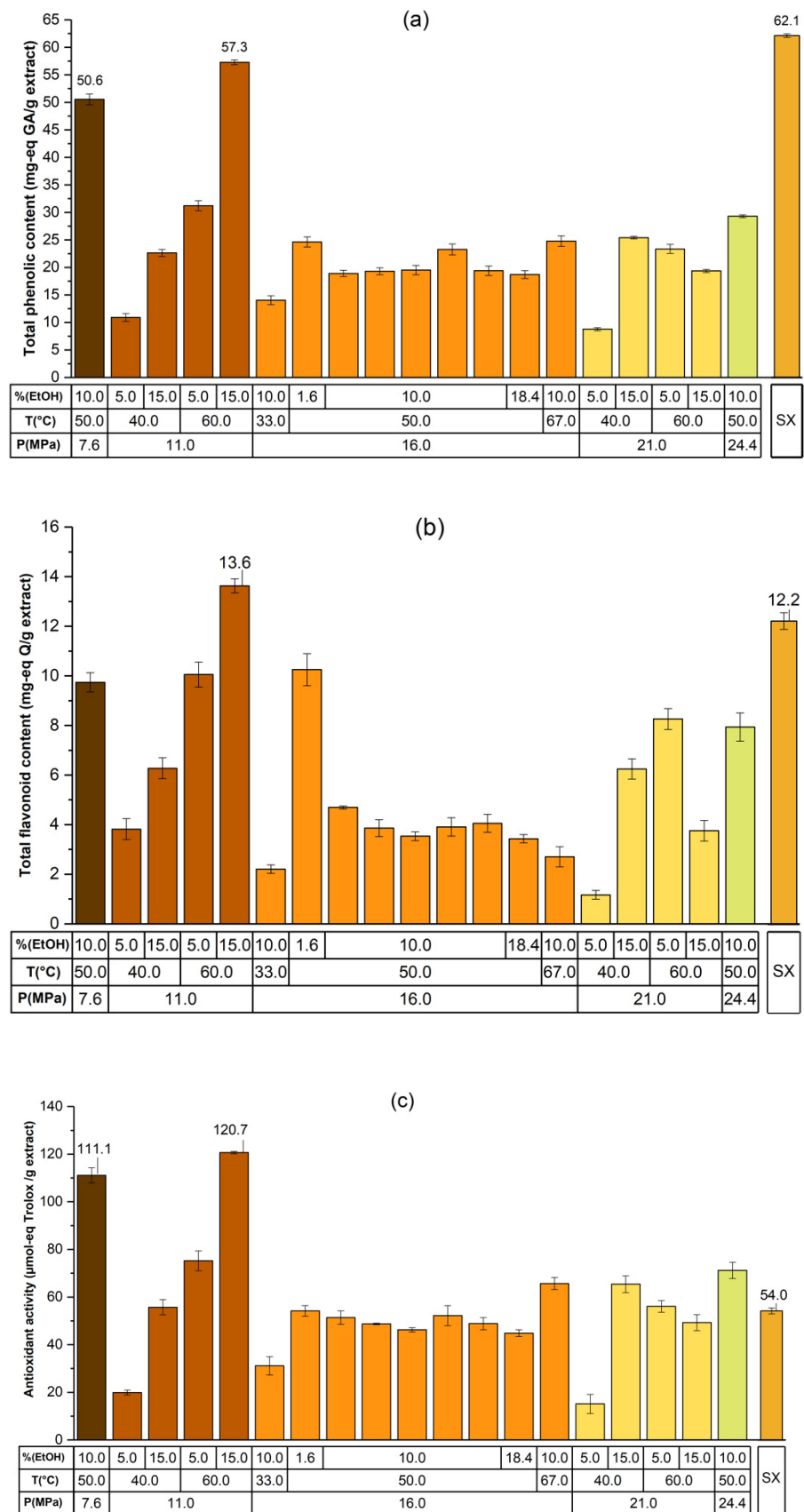
Under SFE, when measuring the DPPH radical scavenging activity, the most active extract was obtained at 11.0 MPa, 60.0 °C, and 15.0% EtOH (120.0 μmol-eq Trolox g<sup>-1</sup> extract), corresponding to 80.6% inhibition of DPPH radical. Meanwhile, the SX extract was less active showing an inhibition of 55.5%, which was equivalent to 54 μmol-eq trolox g<sup>-1</sup> extract. The best results obtained here were comparable to those obtained by El-Baroty et al., where they achieved similar inhibition activities for methanolic and aqueous extracts (up to 89% inhibition of DPPH radical) for the kernel of the mango *var.* Zebdeia [41,42]. The DPPH antioxidant activity of the most active extract referred to dry sample (0.931 mmol-eq trolox 100 g<sup>-1</sup> dry sample) was lower, however, than those reported by Dorta et al., who obtained values of 127.8 mmol-eq trolox 100 g<sup>-1</sup> dry sample for extracts from the kernel of the mango *var.* Keitt, using a microwave-assisted extraction technique [43].

### 2.5. Identification and Quantification of Phenolic Compounds in the Extracts

The analysis of the extract obtained under SFE with the highest t<sub>i</sub> (experiment #10 in Table 1) gave a chromatogram dominated by ellagic acid (compound 2), followed by gallic acid (compound 1), and other unknown compounds (Figure 5). Although compounds 3–8 were found in low abundance in experiment #10, these were abundant in other extracts obtained under the SFE and the SX extraction methods (Supplementary Table S1). Gallic acid together with ellagic acid were previously reported in the varieties of mango: Keitt, Osteen, Sensation, and Gomera [6,7,40]. The quantification of compounds revealed a variation for gallic acid (compound 1) contents from 8.4 to 59.9 mg gallic acid g<sup>-1</sup> extract and for ellagic acid (compound 2) from 7.1 to 178.0 mg ellagic acid g<sup>-1</sup> extract. The extract that generated the greatest OS to SEO (SFE experiment 10) content 59.9 mg gallic acid g<sup>-1</sup> extract and 163.8 mg ellagic acid g<sup>-1</sup> extract.

### 2.6. Correlations among Variables

Evaluation of Pearson correlation coefficients revealed that TPC, TFC, and DPPH radical scavenging activity were positively correlated among them ( $p < 0.0001$ ). The correlation study between the concentration of each individual phenolic compound with the values of TPC, TFC, and DPPH was made. When doing so, compounds 3–7 were positively correlated with TPC ( $p$ -values ranging from 0.00001 to 0.0020), compounds 1, 3–5, and 7 were positively correlated with TFC ( $p$ -values ranging from 0.00001 to 0.0200), and DPPH was positively correlated with compounds 3–7 ( $p$ -values ranging from 0.00001 to 0.0100). The lack of any correlation between gallic acid and DPPH could be due to its low radical scavenging activity [44]. Despite ellagic acid having been shown to exhibit good DPPH antioxidant activity as compared to quercetin, chlorogenic acid or gallic acid [44] when tested in a pure form, no statistical correlation between DPPH and the concentration of ellagic acid was found in the current research. These results suggest that compounds 3–7 have stronger radical scavenging activity than either gallic acid or ellagic acid.



**Figure 4.** Total phenolics content (a), total flavonoids content (b), and antioxidant activity (c) as measured by the radical scavenging method from supercritical fluid and Soxhlet extracts.

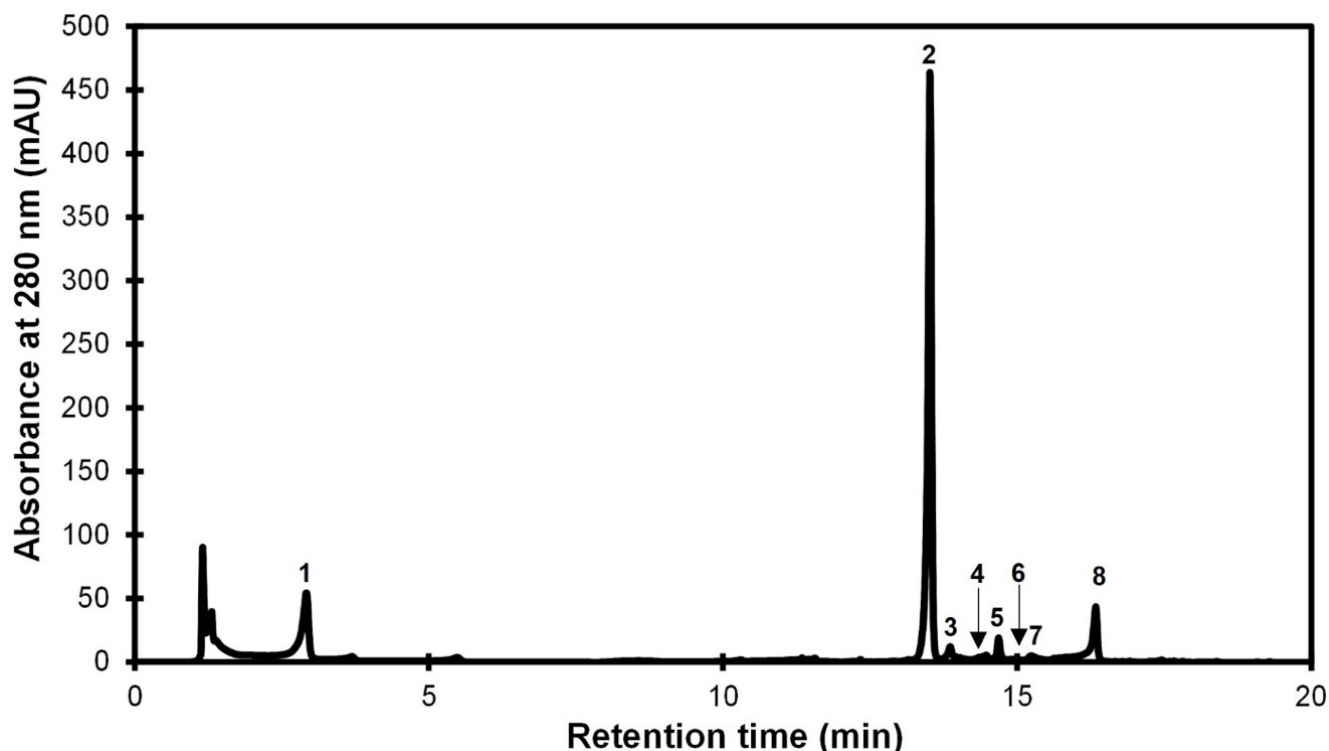


Figure 5. RP-UHPLC analysis of the extract obtained by supercritical fluid extraction at 21.0 MPa, 60.0 °C, and 15.0% EtOH.

### 2.7. Induction Time and the Composition of the Extract

To evaluate if the composition of the extract (obtained under SFE or SX extraction) was responsible for the induction time observed when extracts were added to an SEO, different mathematical approaches were tested. The response variable  $t_i$  was not correlated to TPC, TFC, and DPPH when these three were evaluated as independent variables in linear or quadratic mathematical models with backward stepwise elimination. In those scenarios, despite the low values for the absolute standard deviation, the mathematical models did not represent well the variation observed in the  $t_i$  as judged by the low value for the adjusted  $R^2$ . The adjusted  $R^2$  and absolute standard deviation values reached 33.1 and 8.9% for the linear mathematical model with stepwise backward elimination and 61.0 and 6.6% for the quadratic model with stepwise backward elimination. That is to say that the extracts with the highest TPC, TFC, and DPPH values were not those that protected the SEO from lipid oxidation. Therefore, the reducing power (as measured by the TPC) and radical scavenging activity (accessed by the DPPH method) of the extracts did not explain their behavior in the edible oil.

In a previous work of our research group, a protection effect of a crude extract from *Rubus glaucus* waste against lipidic oxidation in an edible oil emulsion was found [12]. This protecting effect was partially related to the TPC and the partition coefficient. This last parameter is characteristic of each individual phenolic compound. In the current research, a clear relationship was not found between the values of TPC, TFC or DPPH. To understand how a crude extract can protect bulk oil against lipid oxidation, the concentration effect of each individual compound present in the crude extract was studied. On the basis of the coefficients shown in Table 3, mathematical modeling indicated that gallic acid (compound 1), together with compounds 3 and 8 were those that contributed the most to the control of lipid oxidation in the SEO. In contrast, the presence of compound 5 negatively affected the behavior of the extracts.



**Table 3.** Linear mathematical model, after stepwise backward elimination, to evaluate how the composition of the extract can explain the observed induction time.

Parameter	Estimate	Standard Error	T Statistic	p-Value
Constant	2.9324	0.2885	10.1628	0.0000
Peak 1	0.0315	0.0066	4.7662	0.0002
Peak 3	0.0342	0.0104	3.3071	0.0048
Peak 5	−0.0146	0.0037	3.9829	0.0012
Peak 8	0.0328	0.0119	2.7599	0.0146

Adjusted R<sup>2</sup>: 89.3%. Absolute standard deviation: 4.6%.

### 3. Material and Methods

#### 3.1. Chemicals and Reagents

For SFE, CO<sub>2</sub> (purity 99.9%, *v/v*) and EtOH 96% (*v/v*) were purchased from Linde S.A. (Bogotá, Colombia) and from Empresa de Licores de Cundinamarca (Bogotá, Colombia), respectively. Folin–Ciocalteu reagent and pure grade gallic acid were obtained from Merck (Darmstadt, Germany); anhydrous sodium carbonate was from JT Baker; 2,2 diphenyl-1-picrylhydrazyl (DPPH), Trolox, quercetin, and ellagic acid were from Sigma Aldrich Corp (St. Louis, MO, USA); absolute ethanol was from Panreac (Barcelona, Spain); and the tertiary butylhydroquinone (TBHQ) was from TCI (Tokyo, Japan). Solvents used for the UHPLC-DAD were of HPLC grade, from J. T. Baker (Ecatepec, México). Ultrapure water was produced using a Milli-Q system (Billerica, MA, USA).

#### 3.2. Oil Sample

The refined, bleached, and deodorized sunflower edible oil (SEO), without antioxidants, was supplied by Team Foods (Bogotá, Colombia).

#### 3.3. Sample Treatment

Mango (*Mangifera indica* L.) seeds *var.* Sugar were obtained from a batch of a local agro-industrial processor (Pulpas Oni S.A.S., Bogotá, Colombia). The residual pulp was manually separated and the kernel was separated from the endocarp. Two kilograms of mango seed kernel (MSK) were vacuum-dried (150 mbar) in an oven (VWR Scientific 1410 Vacuum Oven, Cornelius, OR, USA), ground using a grain mill (Corona-Universal, Bogotá, Colombia), and sieved to a particle size lower than 0.30 mm. The ground MSK was stored at room temperature in dark place until use.

#### 3.4. Soxhlet Extraction

For the purpose of comparing SFE with a conventional extraction method, Soxhlet (SX) extraction was used. A solute to solvent ratio of 1.0 g: 25.0 mL, with 96% (*v/v*) EtOH by reflux of 8 h was used. To reduce the temperature of extraction ( $T = 45\text{ }^{\circ}\text{C}$ ) and therefore to avoid degradation of thermosensitive analytes, a vacuum system (150 mbar) was used. After SX extraction was completed, the lipid fraction was separated from the whole extract, by means of a winterization process. The whole extract was frozen and centrifuged at  $-20\text{ }^{\circ}\text{C}$ . (Hettich Universal 320R, Tuttlingen, Baden-Württemberg, Germany). Immediately after, the two immiscible phases were filtrated and two fractions were obtained: The solid retained on the filter, called non-soluble fraction (*uSF*), and the filtrated liquid, referred to as soluble fraction (*SF*). The remaining solvent in *uSF* and *SF* was removed using a rotary evaporator (Buchi Rotavapor<sup>®</sup> R-300, Flawil, Switzerland). The yields in each fraction (*uSF* and *SF*), as well as the overall yield (adding up the *uSF* and the *SF*), were evaluated by a gravimetric method. The *SF* under SX extraction was stored in dark place at  $-20\text{ }^{\circ}\text{C}$  until use. This fraction was evaluated as a potential inhibitor of lipid oxidation when added to an SEO. Moreover, it was characterized measuring the total phenolic content (TPC), total flavonoid content (TFC), and the radical scavenging activity (DPPH assay). SX extraction was performed in triplicate.

### 3.5. Extraction with Supercritical CO<sub>2</sub> and EtOH as Co-Solvent

A schematic diagram of the equipment used for SFE is shown in Figure S1. Extractions were performed in a home-built experimental unit (at the High-Pressure Laboratory, Universidad Nacional de Colombia, Colombia). The equipment used comprised a 5 mL extraction cell (316L), covered with an electric heat jacket connected to a PID temperature controller. CO<sub>2</sub> was pressurized through a diaphragm pump (Nova-Swiss 554-2121, Etfretikon, Switzerland), connected to a frequency regulator. EtOH (96%, *v/v*) was pumped according to the experimental design by using an HPLC pump (Beckman 140A model, Indianapolis, IN, USA). The connection pipes were of 316 stainless steel with a diameter of 1/8". Each extraction was performed for 3 h at a flow of 10 g CO<sub>2</sub> min<sup>-1</sup>. The system for the separation of CO<sub>2</sub> and extract consisted of a back-pressure regulator (BPR, Pressure Tech LF540, Houston, TX, USA) and a separator, in which a depressurization was carried out at 5 MPa and 50 °C to avoid the formation of dry ice due to a high-pressure drop. Finally, the extract was accumulated in a vessel collector at laboratory conditions. For the SFE strategy, the extraction cell was filled with approximately 5.0 g of dry sample and experimental conditions were set for the extraction. Extraction was carried out in a semi-continuous mode. Similar to the Soxhlet extraction, two fractions were obtained and separated (*μSF* and *SF*). Once each fraction was obtained and yield measured, the *SF* was stored in a dark place at -20 °C until use.

A factorial central composite experimental design 2<sup>3</sup> (with five replicates in the central point) was undertaken to observe the effect of (a) extraction pressure (11.0–21.0 MPa), (b) temperature (40.0–60.0 °C), and (c) composition of EtOH (96% *v/v*) in the solvent mixture (5.0–15.0%) on the induction time (*t<sub>i</sub>*)—the response variable—when the obtained *SF* extracts were added to a bulk oil system. Likewise, the yield (yield of the *SF*, *μSF*, and the overall yield) and TPC, TFC, and DPPH of the *SF* were evaluated (by triplicate) to explain the behavior of the induction time. The experimental conditions are shown in a randomized order in Table 1.

### 3.6. Inhibition of Lipid Oxidation of Sunflower Oil by the Rancimat Method

An accelerated oxidation test using an antioxidant-free SEO was assayed by the Rancimat method. Three grams of SEO added with extract or TBHQ were taken into a reaction vessel. The *SF* of extracts were tested at a concentration of 1000 mg Kg<sup>-1</sup> at an airflow of 20 L h<sup>-1</sup> and 120 °C. The *t<sub>i</sub>* of the extracts was compared with the one obtained with a control (SEO without antioxidants). For the sake of comparison, the *t<sub>i</sub>* with TBHQ (200 mg Kg<sup>-1</sup>) was also tested. Concentration of TBHQ was selected according to the Alimentary Codex [45,46]. The results were expressed as *t<sub>i</sub>* and protection factor (PF), where *t<sub>i</sub>*<sub>antioxidant</sub> and *t<sub>i</sub>*<sub>control</sub> were induction time for SEO with extract or TBHQ and without extract, respectively (Equation (1)).

$$PF = \frac{t_{i \text{ antioxidant}}}{t_{i \text{ control}}} \quad (1)$$

### 3.7. Total Phenolic Content

The total phenolic content (TPC) in the obtained extracts was measured, using the Folin–Ciocalteu reagent and followed with some modifications to the methodology reported by Carrillo et al. [47]. For the determination, 100 μL of extract solution (10 mg mL<sup>-1</sup>) was mixed with 100 μL Folin–Ciocalteu reagent, shaken and left to stand for 5 min in a dark place. Then, 300 μL of aqueous Na<sub>2</sub>CO<sub>3</sub> (20%, *w/v*) was added, shaken, and left to stand for 90 min in a dark place while it reacted. The absorbance of the blue-colored solution was measured as 765 nm in a UV-Vis spectrophotometer (Thermo-Scientific Genesys 10 UV-Vis, Waltham, MA, USA). Gallic acid (GA) was used to build a standard curve (20–140 mg GA L<sup>-1</sup>, R<sup>2</sup> = 99.71%) for the determination. The TPC was expressed in milligrams of GA equivalents per g of extract (mg-eq GA g<sup>-1</sup> extract).

### 3.8. Total Flavonoid Content

Total flavonoid content (TFC) was determined using the aluminum chloride assay through colorimetry, as described by Chang et al. [48]. Each extract solution (500  $\mu\text{L}$  at 20  $\text{mg mL}^{-1}$ ) was mixed with 1500  $\mu\text{L}$  of 100% *v/v* EtOH, 100  $\mu\text{L}$  of 10% *w/w* aluminum chloride, 100  $\mu\text{L}$  of 1 M sodium acetate, and 2800  $\mu\text{L}$  of water. The mixture was stirred and incubated at room temperature for 30 min. After such reaction time, the absorbance was measured at 415 nm in a spectrophotometer Thermo-Scientific Genesys 10 UV-Vis (Waltham, MA, USA). The TFC results were expressed as mg of quercetin (Q) equivalents per g of extract ( $\text{mg-eq Q g}^{-1}$  extract), by using a Q calibration line (20–160  $\text{mg Q L}^{-1}$ ,  $R^2 = 99.65\%$ ).

### 3.9. DPPH Radical Scavenging Antioxidant Activity

Radical scavenging activity of the extracts was evaluated by the DPPH assay, following with certain modifications the procedure described by Carrillo et al. [47]. The test was carried out using 950  $\mu\text{L}$  of a 100  $\mu\text{M}$  DPPH solution prepared in EtOH, and it was mixed with 50  $\mu\text{L}$  of either extract (at 10  $\text{mg extract mL}^{-1}$ ) or standard (Trolox) in EtOH. As a negative control, the same amount of DPPH and 50  $\mu\text{L}$  of EtOH were used. The mixtures were shaken and left to react at room temperature in a dark place for 60 min. The absorbance was registered at 517 nm in a spectrophotometer (Thermo-Scientific Genesys 10 UV-Vis, Waltham, MA, USA). The results were expressed as a percentage of inhibition of DPPH radical (Equation (2)) and as TEAC values ( $\mu\text{mol Trolox g}^{-1}$  extract). TEAC values were calculated by means of a calibration curve using different concentrations of the standard Trolox (125–3000  $\mu\text{M}$ ,  $R^2 = 99.15\%$ ).

$$\%Inhibition = \frac{(A_o - A_f)}{A_o} \times 100 \quad (2)$$

where  $A_o$  refers to the absorbance at  $t = 0$  and  $A_f$  refers to the absorbance after 30 min of reaction.

### 3.10. Evaluation of Phenolic Compounds by RP-UHPLC-DAD

Extracts obtained by the SX and SFE methods as described in Sections 2.4 and 2.5 were analyzed by RP-UHPLC-DAD. Chromatographic conditions were those described by Cuellar et al. [49]. Extracts were injected at a concentration of 1.0  $\text{mg L}^{-1}$ . Authentic standards of gallic acid, ellagic acid, mangiferin, (+)-catechin, and (–)-epicatechin were injected under the same conditions the extracts were analyzed. Tentative identification was based on the comparison of retention time and UV-Vis spectra against the authentic standards. The compounds were quantified by the external standard method. Gallic and ellagic acids were quantified with authentic standards (six data points, ranging from 1.0 to 100.0  $\text{mg L}^{-1}$ ,  $R^2 = 99.80$  and  $99.91\%$  for gallic and ellagic acids, respectively), other compounds were quantified as ellagic acid equivalents. The results were expressed as mg either gallic or ellagic acid  $\text{g}^{-1}$  extract. No correction for different molecular weights or for different molar extinction coefficients was applied to the compounds different from gallic acid or ellagic acid.

### 3.11. Statistical Analysis

Values for  $t_i$ , TPC, TFC, DPPH, and the concentration of each individual phenolic compound were expressed as an average  $\pm$  SD (standard deviation), with three replicates. Normality of the dataset was tested by the Kolmogorov–Smirnov test. Correlation among the response variables was evaluated by Pearson's correlation coefficient ( $p < 0.05$ ). For the results of SFE assays, an analysis of variance (ANOVA) was carried out ( $p < 0.05$ ). A second-degree mathematical model was tested to evaluate how the  $t_i$  was correlated with the factors pressure, temperature, and %EtOH. The lack of fit and the adjusted coefficient of determination ( $R^2$ ) were calculated to assess the adequacy of

the mathematical model. Stepwise backward elimination was used to eliminate those regression coefficients without statistical significance. Those with statistical significance ( $p < 0.05$ ) were kept. The mathematical model in the SFE was represented by a surface response.

Linear and quadratic mathematical models were tested to evaluate if the TPC, TFC, and DPPH were responsible for the  $t_i$  when each extract was used to protect an edible oil. Similarly, linear and quadratic models were used to evaluate if the concentration of the individual phenolics in the extracts was responsible for the observed  $t_i$ . The adjusted  $R^2$  and the absolute average deviation were calculated to estimate the adequacy of each mathematical model under study. Stepwise backward elimination was used to eliminate those regression coefficients without statistical significance; those with statistical significance were kept ( $p < 0.05$ ).

All statistical analyses were performed with Statgraphics® Centurion XVI software (Manugistics, Inc., Rockville, MD, USA).

#### 4. Conclusions

Supercritical fluid extraction (SFE) was found to be a suitable extraction method to obtain extracts from the mango seed kernel (MSK), which showed antioxidant activity and modified the oxidative stability of antioxidant-free sunflower edible oil (SEO). SC-CO<sub>2</sub> + EtOH allowed for obtaining extraction yields, TPC and TFC equal to or greater than those obtained by the Soxhlet (SX) extraction. The extract that showed the highest protection against oxidation of SEO ( $t_i = 6.1$  h) was obtained at 21.0 MPa, 60.0 °C and 15.0% EtOH, with a total yield of 11.8%, TPC 19.4 mg-eq AG g<sup>-1</sup> extract, TFC 3.8 mg-eq Q g<sup>-1</sup> extract, and percentage of inhibition of DPPH radical of 36.0%. Gallic acid and ellagic acid were found in the extract. The composition of the extract was found to influence the stability of the SEO. Finally, it can be concluded that it is possible to obtain extracts from Colombian MSK *var.* Sugar with antioxidant activity comparable to that of commercial antioxidants (TBHQ).

The set of results obtained provides the basis for proposing the use of mango seed *var.* Sugar—an important agro-industrial by-product in the fats and oils industry. The MSK could be a source of antioxidant extracts applied as additives in edible oils. This work is framed within the guidelines of green chemistry and it was proposed by other authors as a feasible way to deal with large amounts of agro-industrial residues. Lavecchia and Zuurro obtained flavonoid-rich extracts from the olive pomace by a classic extraction technique [50]; Lima et al. obtained promissory ingredients for functional foods by processing guava waste under ultrasound extraction [51]; Dominguez et al. proposed further research into some Passiflora species peels so as to obtain antioxidant extracts rich in phenols under pressurized liquid extraction [52]. Indeed, our work and that of other authors are contributing to new research topics in Green Foodomics [53].

**Supplementary Materials:** The following are available online, Figure S1: Schematic diagram of the equipment employed for SFE (home-build experimental unit), Table S1: Retention time, UV-Vis spectra, and quantification of compounds by supercritical extraction as well as by Soxhlet extraction.

**Author Contributions:** Conceptualization, A.d.P.S.-C., C.-E.N.-C. and F.P.-A.; experimental work, L.M.B.-P., G.F.-A. and D.B.-V.; writing—original draft preparation, L.M.B.-P., H.A.M.-C., D.B.-V., A.d.P.S.-C. and D.M.-L.; writing—review and editing, L.M.B.-P., A.d.P.S.-C., C.-E.N.-C. and F.P.-A.; funding acquisition, D.M.-L., C.-E.N.-C. and F.P.-A. All authors have read and agreed to the published version of the manuscript.

**Funding:** The authors thanks to the Special Agreement on Derivative Cooperation 2. “Corredor Tecnológico Agroindustrial (CTA) INVESTIGACIÓN, DESARROLLO Y TRANSFERENCIA TECNOLÓGICA EN EL SECTOR AGROPECUARIO Y AGROINDUSTRIAL CON EL FIN DE MEJORAR TODO EL DEPARTAMENTO, CUNDINAMARCA, CENTRO ORIENTE” with funding from Sistema General de Regalías, Secretaría de Ciencia, Tecnología del Departamento de Cundinamarca, Secretaría de Desarrollo Económico de Bogotá, Universidad Nacional de Colombia and Corporación Colom-

biana de Investigación Agropecuaria—AGROSAVIA. The authors also express their gratitude to the Universidad Nacional de Colombia for the support to the project “Obtaining functional compounds from Mango *var.* Sugar (*Mangifera indica* L.) using emerging strategies of extraction” through national call for projects for strengthening of the investigation, creation, and innovation of Universidad Nacional de Colombia 2016–2018 (code 37767; QUIPU 201010027080). A.D.P.S.-C. thanks to Ministerio de Ciencia, Tecnología e Innovación for her postdoctoral fellowship (784-2017). Finally, L.M.B.-P. thanks to the Fundación Juan Pablo Gutierrez Caceres for the fellowship and the Departamento Administrativo de Ciencia, Tecnología e Innovación -Colciencias-, Convocatoria Nacional Jóvenes Investigadores e Innovadores por la Paz 2017.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Data are presented in the paper and available from the authors.

**Acknowledgments:** The authors give thanks to the Team Foods company (Bogotá, Colombia) who supplied the free-antioxidants sunflower edible oil (SEO) and Alexander J. Campbell who reviewed the text in English.

**Conflicts of Interest:** Authors declare there are no conflict of interest.

**Sample Availability:** Samples of the compounds are available from the authors.

## References

1. Torres-León, C.; Rojas, R.; Contreras-Esquivel, J.C.; Serna-Cock, L.; Belmares-Cerda, R.E.; Aguilar, C.N. Mango seed: Functional and nutritional properties. *Trends Food Sci. Technol.* **2016**, *55*, 109–117. [CrossRef]
2. FAO Statistical Database Food and Cultural Organization. Available online: <http://faostat3.fao.org/home/E>. (accessed on 6 June 2015).
3. Departamento Administrativo Nacional de Encuesta Boletín técnico-Encuesta Nacional Agropecuaria. 2020. Available online: <https://www.agronet.gov.co/estadistica/Paginas/home.aspx?cod=1> (accessed on 9 September 2021).
4. García Lozano, J.; Floriano, J.A.; Corredor, J.P.; Bernal, J.; Vásquez, L.A.; Sandoval, A.P.; Forero Longas, F.; Gómez Barros, G. *Descripción de las Variedades de Mango Criollo Colombiano*, 1st ed.; CORPOICA: Bogotá, Colombia, 2010; 72p.
5. Castro-Vargas, H.; Ballesteros Vivas, D.; Ortega Barbosa, J.; Morantes Medina, S.; Aristizabal Gutiérrez, F.; Parada-Alfonso, F. Bioactive Phenolic Compounds from the Agroindustrial Waste of Colombian Mango Cultivars ‘Sugar Mango’ and ‘Tommy Atkins’—An Alternative for Their Use and Valorization. *Antioxidants* **2019**, *8*, 41. [CrossRef] [PubMed]
6. López-Cobo, A.; Verardo, V.; Diaz-de-Cerio, E.; Segura-Carretero, A.; Fernández-Gutiérrez, A.; Gómez-Caravaca, A.M. Use of HPLC- and GC-QTOF to determine hydrophilic and lipophilic phenols in mango fruit (*Mangifera indica* L.) and its by-products. *Food Res. Int.* **2017**, *100*, 423–434. [CrossRef] [PubMed]
7. Dorta, E.; González, M.; Lobo, M.G.; Sánchez-Moreno, C.; de Ancos, B. 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 Res. Int.* **2014**, *57*, 51–60. [CrossRef]
8. Ballesteros-Vivas, D.; Álvarez-Rivera, G.; Morantes, S.J.; del Pilar Sánchez-Camargo, A.; Ibáñez, E.; Parada-Alfonso, F.; Cifuentes, A. An integrated approach for the valorization of mango seed kernel: Efficient extraction solvent selection, phytochemical profiling and antiproliferative activity assessment. *Food Res. Int.* **2019**, *126*, 108616. [CrossRef] [PubMed]
9. Ballesteros-Vivas, D.; Alvarez-Rivera, G.; Ocampo, A.F.; Morantes, S.J.; Camargo, A.D.; Cifuentes, A.; Parada-Alfonso, F.; Ibanez, E. Supercritical antisolvent fractionation as a tool for enhancing antiproliferative activity of mango seed kernel extracts against colon cancer cells. *J. Supercrit. Fluids* **2019**, *152*, 104563. [CrossRef]
10. Alañón, M.E.; Pimentel-Moral, S.; Arráez-Román, D.; Segura-Carretero, A. HPLC-DAD-Q-ToF-MS profiling of phenolic compounds from mango (*Mangifera indica* L.) seed kernel of different cultivars and maturation stages as a preliminary approach to determine functional and nutraceutical value. *Food Chem.* **2021**, *337*, 127764. [CrossRef]
11. Segovia, F.J.; Corral-Pérez, J.J.; Almajano, M.P. Avocado seed: Modeling extraction of bioactive compounds. *Ind. Crops Prod.* **2016**, *85*, 213–220. [CrossRef]
12. Ospina, M.; Montaña-Oviedo, K.; Díaz-Duque, Á.; Toloza-Daza, H.; Narváez-Cuenca, C.E. Utilization of fruit pomace, overripe fruit, and bush pruning residues from Andes berry (*Rubus glaucus* Benth) as antioxidants in an oil in water emulsion. *Food Chem.* **2019**, *281*, 114–123. [CrossRef] [PubMed]
13. Castro-Vargas, H.I.; Baumann, W.; Parada-Alfonso, F. Valorization of agroindustrial wastes: Identification by LC-MS and NMR of benzylglucosinolate from papaya (*Carica papaya* L.) seeds, a protective agent against lipid oxidation in edible oils. *Electrophoresis* **2016**, 1–8. [CrossRef]

14. Ramful, D.; Aumjaud, B.; Neergheen, V.S.; Soobrattee, M.A.; Googoolye, K.; Aruoma, O.I.; Bahorun, T. Polyphenolic content and antioxidant activity of *Eugenia pollicina* leaf extract in vitro and in model emulsion systems. *Food Res. Int.* **2011**, *44*, 1190–1196. [[CrossRef](#)]
15. Rössing, D.; Kahl, R.; Hildebrandt, A.G. Effect of synthetic antioxidants on hydrogen peroxide formation, oxyferro cytochrome P-450 concentration and oxygen consumption in liver microsomes. *Toxicology* **1985**, *34*, 67–77. [[CrossRef](#)]
16. Co, M.; Turner, C. Conventional Separation Approaches. In *Biorefinery Co-Products: Phytochemicals, Primary Metabolites and Value-Added Biomass Processing*; John Wiley & Sons, Ltd.: Ghent, Belgium, 2012; p. 273.
17. Herrero, M.; Cifuentes, A.; Ibañez, E. Sub- and supercritical fluid extraction of functional ingredients from different natural sources: Plants, food-by-products, algae and microalgae—A review. *Food Chem.* **2006**, *98*, 136–148. [[CrossRef](#)]
18. Corzzini, S.C.S.; Barros, H.D.F.Q.; Grimaldi, R.; Cabral, F.A. Extraction of edible avocado oil using supercritical CO<sub>2</sub> and a CO<sub>2</sub>/ethanol mixture as solvents. *J. Food Eng.* **2017**, *194*, 40–45. [[CrossRef](#)]
19. Azmir, J.; Zaidul, I.S.M.; Rahman, M.M.; Sharif, K.M.; Mohamed, A.; Sahena, F.; Jahurul, M.H.A.; Ghafoor, K.; Norulaini, N.A.N.; Omar, A.K.M. Techniques for extraction of bioactive compounds from plant materials: A review. *J. Food Eng.* **2013**, *117*, 426–436. [[CrossRef](#)]
20. Ghoreishi, S.M.; Heidari, E. Extraction of epigallocatechin gallate from green tea via modified supercritical CO<sub>2</sub>: Experimental, modeling and optimization. *J. Supercrit. Fluids* **2012**, *72*, 36–45. [[CrossRef](#)]
21. Herrero, M.; Mendiola, J.A.; Cifuentes, A.; Ibañez, E. Supercritical fluid extraction: Recent advances and applications. *J. Chromatogr. A* **2010**, *1217*, 2495–2511. [[CrossRef](#)] [[PubMed](#)]
22. Franco-Arnedo, G.; Buelvas-Puello, L.M.; Miranda-Lasprilla, D.; Martínez-Correa, H.A.; Parada-Alfonso, F. Obtaining antioxidant extracts from tangerine (*C. reticulata* var. *Arrayana*) peels by modified supercritical CO<sub>2</sub> and their use as protective agent against the lipid oxidation of a mayonnaise. *J. Supercrit. Fluids* **2020**, *165*, 104957. [[CrossRef](#)]
23. Castro-Vargas, H.I.; Rodríguez-Varela, L.I.; Ferreira, S.R.S.; Parada-Alfonso, F. Extraction of phenolic fraction from guava seeds (*Psidium guajava* L.) using supercritical carbon dioxide and co-solvents. *J. Supercrit. Fluids* **2010**, *51*, 319–324. [[CrossRef](#)]
24. Fernández-Ponce, M.T.; Casas, L.; Mantell, C.; De La Ossa, E.M. Use of high pressure techniques to produce *Mangifera indica* L. leaf extracts enriched in potent antioxidant phenolic compounds. *Innov. Food Sci. Emerg. Technol.* **2015**, *29*, 94–106. [[CrossRef](#)]
25. Waraho, T.; McClements, D.J.; Decker, E.A. Mechanisms of lipid oxidation in food dispersions. *Trends Food Sci. Technol.* **2011**, *22*, 3–13. [[CrossRef](#)]
26. Frankel, E.N.; Huang, S.W.; Aeschbach, R.; Prior, E. Antioxidant activity of a rosemary extract and its constituents, carnosic acid, carnosol, and rosmarinic acid, in bulk oil and oil-in-water emulsion. *J. Agric. Food Chem.* **1996**, *44*, 131–135. [[CrossRef](#)]
27. Läubli, M.W.; Bruttel, P.A. Determination of the oxidative stability of fats and oils: Comparison between the active oxygen method (AOCS Cd 12-57) and the Rancimat method. *J. Amer. Oil Chem. Soc.* **1986**, *63*, 792–795. [[CrossRef](#)]
28. Nur Alam, M.; Jahan Bristi, N.; Rafiquzzaman, M. Review on in vivo and in vitro methods evaluation of antioxidant activity. *Saudi Pharm. J.* **2013**, *21*, 143–152. [[CrossRef](#)]
29. Jahurul, M.H.A.; Zaidul, I.S.M.; Norulaini, N.N.A.; Sahena, F.; Jaffri, J.M.; Omar, A.K.M. Supercritical carbon dioxide extraction and studies of mango seed kernel for cocoa butter analogy fats. *Cyta-J. Food* **2014**, *12*, 97–103. [[CrossRef](#)]
30. Jahurul, M.H.A.; Zaidul, I.S.M.; Ghafoor, K.; Al-Juhaimi, F.Y.; Nyam, K.L.; Norulaini, N.A.N.; Sahena, F.; Mohd Omar, A.K. Mango (*Mangifera indica* L.) by-products and their valuable components: A review. *Food Chem.* **2015**, *183*, 173–180. [[CrossRef](#)] [[PubMed](#)]
31. Nzikou, J.; Kimbonguila, A.; Matos, L.; Loumouamou, B.; Pambou-Tobi, N.; Ndangui, C.; Abena, A.; Silou, T.; Scher, J.; Desobry, S. Extraction and Characteristics of Seed Kernel Oil from Mango (*Mangifera indica*). *Res. J. Environ. Earth Sci.* **2010**, *2*, 31–35.
32. Mutua, J.K.J.K.; Imathiu, S.; Owino, W. Evaluation of the proximate composition, antioxidant potential, and antimicrobial activity of mango seed kernel extracts. *Food Sci. Nutr.* **2016**, *5*, 1–9. [[CrossRef](#)]
33. López Hernández, M.D.P. *Evaluación del Rendimiento de Extracción y Caracterización de la Grasa de Semilla de 20 Acciones de Mango del Banco de Germoplasma y Materiales Nativos*; Agroindustrial Engineering, Universidad del Tolima: Ibagué, Colombia, 2013.
34. Asnaashari, M.; Tajik, R.; Khodaparast, M.H.H. Antioxidant activity of raspberry (*Rubus fruticosus*) leaves extract and its effect on oxidative stability of sunflower oil. *J. Food Sci. Technol.* **2015**, *52*, 5180–5187. [[CrossRef](#)]
35. Upadhyay, R.; Mishra, H.N. Multivariate Analysis for Kinetic Modeling of Oxidative Stability and Shelf Life Estimation of Sunflower Oil Blended with Sage (*Salvia officinalis*) Extract Under Rancimat Conditions. *Food Bioprocess Technol.* **2015**, *8*, 801–810. [[CrossRef](#)]
36. Mendiola, J.A.; Herrero, M.; Castro-Puyana, M.; Ibañez, E. Supercritical Fluid Extraction. In *Natural Product Extraction: Principles and Applications*; Rostagno, M.A., Prado, J.M., Eds.; Green Chemistry Series; Royal Society of Chemistry: Cambridge, UK, 2013; pp. 113–156.
37. Barton, A.F.M. *CRC Handbook of Solubility Parameters and Other Cohesion Parameters*, 2nd ed.; CRC, Ed.: Boca Raton, FL, USA, 2017; p. 14.
38. De Melo, M.M.R.; Silvestre, A.J.D.; Silva, C.M. Supercritical fluid extraction of vegetable matrices: Applications, trends and future perspectives of a convincing green technology. *J. Supercrit. Fluids* **2014**, *92*, 115–176. [[CrossRef](#)]
39. Khammuang, S.; Sarnthima, R. Antioxidant and antibacterial activities of selected varieties of Thai mango seed extract. *Pak. J. Pharm. Sci.* **2011**, *24*, 37–42.

40. Ballesteros Vivas, D. Estudio Comparativo Sobre la Obtención de Extractos con Actividad Citotóxica a Partir de Residuos Frutícolas. Master's Thesis, Universidad Nacional de Colombia, Bogotá, Colombia, 2015.
41. El-Baroty, G.S.; Khalil, M.F.; Mostafa, S.H.A. Natural antioxidant ingredient from by-products of fruits. *Am. J. Agric. Biol. Sci.* **2014**, *9*, 311–320. [[CrossRef](#)]
42. Sogi, D.S.; Siddiq, M.; Dolan, K.D. Total phenolics, carotenoids and antioxidant properties of Tommy Atkin mango cubes as affected by drying techniques. *LWT Food Sci. Technol.* **2015**, *62*, 564–568. [[CrossRef](#)]
43. Dorta, E.; Lobo, M.G.; González, M. Optimization of Factors Affecting Extraction of Antioxidants from Mango Seed. *Food Bioprocess Technol.* **2013**, *6*, 1067–1081. [[CrossRef](#)]
44. Chaillou, L.L.; Nazareno, M.A. New method to determine antioxidant activity of polyphenols. *J. Agric. Food Chem.* **2006**, *54*, 8397–8402. [[CrossRef](#)] [[PubMed](#)]
45. FAO Norma General Del Codex Para Los Aditivos Alimentarios Codex Stan 192-1995. Available online: [https://www.fao.org/gsaonline/docs/CXS\\_192s.pdf](https://www.fao.org/gsaonline/docs/CXS_192s.pdf) (accessed on 6 June 2017).
46. Ministerio de Salud Resolucion 4124 de 1991. Available online: [https://www.invima.gov.co/images/stories/resoluciones/resolucion\\_4124\\_1991.pdf](https://www.invima.gov.co/images/stories/resoluciones/resolucion_4124_1991.pdf) (accessed on 8 November 2021).
47. Carrillo, L.C.; Londoño-Londoño, J.; Gil, A. Comparison of polyphenol, methylxanthines and antioxidant activity in Theobroma cacao beans from different cocoa-growing areas in Colombia. *Food Res. Int.* **2013**, *60*, 273–280. [[CrossRef](#)]
48. Chang, C.C.; Yang, M.H.; Wen, H.M.; Chern, J.C. Estimation of total flavonoid content in propolis by two complementary colometric methods. *J. Food Drug Anal.* **2002**, *10*, 178–182. [[CrossRef](#)]
49. Cuéllar-Cepeda, F.A.; Parra-Galindo, M.A.; Urquijo, J.; Restrepo-Sánchez, L.P.; Mosquera-Vásquez, T.; Narváez-Cuenca, C.E. Influence of genotype, agro-climatic conditions, cooking method, and their interactions on individual carotenoids and hydroxycinnamic acids contents in tubers of diploid potatoes. *Food Chem.* **2019**, *288*, 127–138. [[CrossRef](#)] [[PubMed](#)]
50. Lavecchia, R.; Zuorro, A. Recovery of flavonoids from three-phase olive pomace by aqueous ethanol extraction. *ARPN J. Eng. Appl. Sci.* **2016**, *11*, 13802–13809.
51. Lima, R.D.S.; Ferreira, S.R.S.; Vitali, L.; Block, J.M. May the superfruit red guava and its processing waste be a potential ingredient in functional foods? *Food Res. Int.* **2019**, *115*, 451–459. [[CrossRef](#)] [[PubMed](#)]
52. Domínguez-Rodríguez, G.; García, M.C.; Plaza, M.; Marina, M.L. Revalorization of *Passiflora* species peels as a sustainable source of antioxidant phenolic compounds. *Sci. Total Environ.* **2019**, *696*, 134030. [[CrossRef](#)]
53. Gilbert-López, B.; Mendiola, J.A.; Ibáñez, E. Green Foodomics. Towards a cleaner scientific discipline. *TrAC-Trends Anal. Chem.* **2017**, *96*, 31–41. [[CrossRef](#)]