Available online at www.sciencedirect.com

Food and Bioproducts Processing

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

Sequential extraction of almond hull biomass with pulsed electric fields (PEF) and supercritical CO_2 for the recovery of lipids, carbohydrates and antioxidants

Manuel Salgado-Ramos[a], *Francisco J. Martí-Quijal*[b,*], *Alberto J. Huertas-Alonso*[a,c,1], *M. Prado Sánchez-Verdú*[a], *Giancarlo Cravotto*[d], *Andrés Moreno*[a,*], *Francisco J. Barba*[b]

[a] *Universidad de Castilla-la Mancha, Departamento de Química Inorgánica, Orgánica y Bioquímica, Facultad de Ciencias y Tecnologías Químicas, Avenida Camilo José Cela nº10, 13005 Ciudad Real, Spain*
[b] *Department of Preventive Medicine and Public Health, Food Science, Toxicology and Forensic Medicine. Faculty of Pharmacy. Universitat de València; Avenida Vicent Andrés Estellés s/n Burjassot, 46100 València, Spain*
[c] *Department of Materials and Environmental Chemistry, Stockholm University, SE-106 91 Stockholm, Sweden*
[d] *Dipartimento di Scienza e Tecnologia del Farmaco. University of Turin, Via Pietro Giuria 9, 10125 Turin Italy*

ARTICLE INFO

Article history:
Received 15 January 2023
Received in revised form 6 April 2023
Accepted 12 April 2023
Available online 20 April 2023

Keywords:
Waste valorisation
Sequential extraction process
Chemical composition
Bioactive compounds
Innovative extraction technologies

ABSTRACT

This work reports the first example of combined sequential extraction by pulsed electric fields (PEF) (3 kV/cm, 100 kJ/kg, 2 Hz, 100 ms) and supercritical (SC) fluid extraction (SFE) (15 MPa, 25 mL/min, 50°C, 60 min) with CO_2 (SC-CO_2) for the valorisation of almond hull (AH) biomass. PEF+SFE boosted the efficiency of the protocol up to 77% for total antioxidant capacity and 20% in terms of polyphenols recovery compared to the traditional soaking. Triple-TOF-LC-MS-MS analysis provided the phenolic profiles for the PEF and SC-CO_2 extracts, observing significant differences in the polyphenol profile according to the technology applied. Additionally, NMR analysis detected the presence of the carbohydrate soluble (mainly glucose, fructose and sucrose) and lipidic fractions, both selectively extracted by PEF or SC-CO_2, respectively. Finally, the post-extraction residual solid biomass was characterized by several techniques such as TGA, FT-IR and SEM. For the latter, the formation of surface pores after PEF and a high fibre compaction after SFE was observed. On the other hand, DTG curves allowed to firmly propose concurrent valorisation routes for this solid, in agreement with a zero-waste approach.

1. Introduction

Almond is one of the most valuable fruits worldwide due to the high nutritional value of its kernel, which is mainly composed of proteins and lipids, as well as others minor components such as fibres, minerals, and vitamins (Roncero et al., 2020). Almond production involves the generation of certain lignocellulosic wastes, all of them susceptible to be exploited (Kaur et al., 2020; Pasqualone et al., 2018). Among

* Corresponding authors.
E-mail addresses: francisco.j.marti@uv.es (F.J. Martí-Quijal), andres.moreno@uclm.es (A. Moreno).
[1] Present address: Department of Materials and Environmental Chemistry

https://doi.org/10.1016/j.fbp.2023.04.003

them, it should be noted that almond hull (AH) represents around 50% of the total almond fresh mass, being a well-known valuable source of bioactive compounds (BACs) (Garcia-Perez et al., 2021; Kahlaoui et al., 2019; Prgomet et al., 2017; Salgado-Ramos, et al. 2022a). Moreover, it is an interesting source of carbohydrates and lipids (Prgomet et al., 2017), with important applications in the food sector.

Regarding BACs, growing interest has been shown regarding polyphenols since they have demonstrated several health benefits in humans, such as reduced oxidative stress, as well as beneficial effects on autoimmune, neurodegenerative or cardiovascular diseases (Durazzo et al., 2019; Freyssin et al., 2020). Due to the several applications of polyphenols as food additives and nutraceuticals, they should be considered for a feasible exploitation of biomass as antioxidants sources.

Conventional extraction methods for polyphenols´ recovery from biomass require high amounts of organic solvents and are time consuming. Moreover, these methods can increase the extraction of unwanted compounds and promote the degradation of thermolabile ones. In this context, the application of process intensification technologies has been already reported (Mariatti et al., 2021; Tzima et al., 2021). These new protocols generally show higher efficiency and sustainability compared to traditional methods. Among them, microwave-assisted extraction (MAE) has been recently applied (Gunjević et al., 2021; Şahin et al., 2017), where the volumetric heating induced by microwaves can facilitate a higher recovery of polyphenols (and generally a higher extraction yield). Ultrasound-assisted extraction (UAE) has also demonstrated to enhance polyphenol recovery from AH (Kahlaoui et al., 2019) thanks to cavitation effects by sonication which induces cell wall disruption.

Furthermore, the application of pulsed electric fields to the matrix also leads to breaking of the cell due to the formation of pores or micropores in the structure, which can enhance further extraction of the polyphenols (Barba et al., 2016; Martí-Quijal et al., 2021; Salgado-Ramos et al. 2022a). This extraction technique requires shorter times and low energy consumption, since PEF usually takes microseconds, preventing the degradation of thermolabile polyphenols.

Polyphenols' extraction usually involves the recovery of sugars from the matrix owing to similar polarities. Among them, glucose, sucrose, fructose, and xylose are considered valuable compounds in the food sector due to their direct applications as additives. Moreover, they are also a useful source for the synthesis of fine chemicals, such as levulinic acid (LA), 5-hydroxymethylfurfural (5-HMF) or furfural (FF) (Mika et al., 2018), bio-based compounds with a wide range of applications in drugs, cosmetics, or flavours as well, among others.

Due to its ability to electroporate cell envelopes, PEF can be used as a pre-treatment to facilitate the extraction of biocompounds, followed by a subsequent traditional or novel extraction step. In this way, soaking (Martín-García et al., 2020) or UAE (Tzima et al., 2021) are commonly used for this combination. It is important to mention supercritical fluid extraction (SFE) as well, mainly as SC-CO_2. Solvents in SFE are employed at their critical pressure and temperature point to separate solutes from a solid matrix under pressurized conditions. Thus, under these conditions, solvents have intermediary properties between gases and liquids, leading to a higher diffusion coefficient and lower viscosity, thus enhancing penetration into the matrix (Al Khawli et al., 2019; Zhou et al., 2021). This fact, along with fibre compaction due to the high pressure in this system, facilitates the extraction of phenolics. CO_2 is usually employed as supercritical solvent due to several advantages in terms of availability, sustainability and price, safety as well as its excellent supercritical parameters (da Silva et al., 2016; Pimentel-Moral et al., 2019; Wrona et al., 2017). However, its low polarity makes it necessary for its utilization in combination with a polar co-solvent for a more efficient extraction of polyphenols. Ethanol is the most used doping solvent due to both green properties and the high solubility of phenolics. However, in some cases, the low flow of EtOH used leads to a low polarity in the system due to the high CO_2, thus impeding efficient recovery of anthocyanins or proanthocyanins (Pinelo et al., 2007). In contrast, other valuable compounds, such as lipids, can thereby be extracted from the matrix by SFE (Dienaitė et al., 2021; Talmaciu et al., 2016; Teixeira et al., 2021). These lipids have also demonstrated several benefits in humans, for instance, in healthy foods such as oil or dried nuts, and they can be useful for the obtention of biodiesel by transesterification with low-molecular weight alcohols as well (Carmona-Cabello et al., 2021), suggesting another route for valorisation.

Herein, to the best of our knowledge, the sequential process combination of PEF+SFE is reported for the first time in AH. This hybrid technique was shown to efficiently recover BACs and sugars. Moreover, the solid fraction after both PEF and PEF+SFE treatment was characterized by several techniques such as SEM, FT-IR or TGA, suggesting another valorisation pathway for AH and thus demonstrating a potential path to the desirable condition of *zero-waste*.

2. Materials and methods

2.1. Chemicals

Folin–Ciocalteu reagent, gallic acid (CAS No. 149–91–7), ABTS (2,2′-Azino-Bis-3- Ethylbenzothiazoline-6-Sulphonic Acid) (CAS No. 30931–67–0), potassium persulfate ($K_2S_2O_8$) (CAS No. 7727–21–1), 2,2′-Azobis(2-amidinopropane) dihydrochloride (AAPH) (CAS No. 2997–92–4), fluorescein (CAS No. 2321–07–5), 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid sodium salt (98 atom %D, CAS No. 24493–21–8) and trolox (6-hydroxy-2,5,7,8- tetramethylchroman-2-carboxylic acid) (CAS No. 53188–07–1) were purchased from Sigma–Aldrich (Steinheim, Baden-Württemberg, Germany). Methanol-d_4 (99.80 atom %D, CAS No. 811–98–3), sodium carbonate (Na_2CO_3) (CAS No. 497–19–8), sodium phosphate (Na_2HPO_4) (CAS No. 7778–77–0) and potassium phosphate (KH_2PO_4) were acquired from VWR (Saint-Prix, France). Maleic acid (CAS No. 110–123 16–7) was obtained from Fluka. Absolute ethanol (CAS No. 64–17–5) was purchased from Thermofisher (Waltham, Massachusetts, US), and ethanol 96° (CAS No. 64–17–5) was obtained from Guinama (La Pobla de Vallbona, Valencia, España).

2.2. Feedstock

Almond hull (AH) was collected at the beginning of the 2016–2017 harvest season in Los Yebenes (Toledo, Spain) and initially used without any treatment.

2.3. Pulsed electric fields (PEF)-assisted extraction

PEF pre-treatment was carried out in a PEF-Cellcrack III equipment (German Institute for Food Technology (DIL), ELEA, Germany), located at the Faculty of Pharmacy (University of Valencia, Valencia, Spain), under the same conditions as previously described (Salgado-Ramos et al. 2022a). Therefore, 20 g of raw AH and 200 mL of tap water were mixed in a 900 mL treatment chamber. Parameters for PEF-assisted extraction were: specific energy: 100 kJ/kg; field strength: 3 kV/cm; frequency: 2 Hz; pulse duration: 100 ms. After PEF treatment, the mixture PEF-treated AH + tap water was put in an Erlenmeyer flask along with 200 mL of EtOH 96%, and then stirred for 24 h at room temperature, according to reported works (Lapornik et al., 2005). Afterwards, the crude was filtered. The liquid fraction was stored at –20 °C and then analysed by TEAC, ORAC and TPC assays, as well as by NMR and HPLC-MS. The remaining solid fraction was first dried at a low temperature (60 °C) overnight and then blade milled in a Variable Speed Rotor Mill Fritsch Pulverisette 14 (Fritsch, Idar-Oberstein, Germany) for 1 min at 20 000 rpm to obtain a 1 mm particle size powder for further experiments.

In parallel, a conventional solid-liquid extraction with EtOH/H_2O 50% was performed, for the sake of comparison, without PEF treatment. Thus, the efficiency of PEF-assisted extraction was evaluated with respect to the traditional soaking. In this context, 10 g of raw AH and 100 mL of the above EtOH/H_2O solution were mixed, and the crude stirred for 24 h at room temperature. The workup after extraction was similar to described above, discarding in this case the solid fraction.

2.4. Supercritical fluid extraction (SFE)

The SFE was carried out using a supercritical extraction system (JASCO, Tokio, Japan) located at the Faculty of Pharmacy (University of Valencia, Valencia, Spain), composed of a main isocratic CO_2 pump (PU-4387), with a flow range ranging from 5 to 40 mL/min, adjustable in 0.01 mL/min increment, maximum pressure of 50 MPa and extraction system for pulses; a refrigerating recirculatory (JULABO FL 1201) for pump cooling, with a temperature range of –20–40 °C, flow range up to 23 L/min and cooling refrigeration capacity of 1.2 kW at 20°C; an isocratic organic modifier pump (PU-4086, HPLC), with a flow range from 0.001 to 10 mL/min, adjustable in 0.01 mL/min increments and max pressure of 70 MPa; a thermostatic oven for vessel reaction (CO-4065), with available temperature ranging from 4 to 90°C; a pressure regulator (BP-4340), and a supercritical extraction vessel of 25 mL (803559–25 mL).

For the experiments, 2.5 g of PEF-dried-treated AH were introduced into the 25 mL supercritical extraction glass. Absolute EtOH was employed as co-solvent. The rest of parameters were chosen based on work previously described by Talmaciu et al. (2016): pressure: 15 MPa; total flow: 25 mL/min (10% EtOH, 90% CO_2); temperature: 50°C; time: 60 min

After SFE, TEAC, ORAC and TPC assays, as well as NMR and HPLC-MS analysis were carried out with the collected liquid fraction. The remaining solid fraction was also dried at low temperature (60 °C) overnight and then blade milled for further experiments.

2.5. Antioxidants assays and phenolic compounds identification

The Total Antioxidant Capacity (TAC) (Trolox Equivalent Antioxidant Capacity (TEAC) and Oxygen Radical Absorbance Capacity (ORAC)) as well as total polyphenol content (TPC) were measured according to reported works (Salgado-Ramos et al. 2022a). Briefly, for TEAC, 25 mL of 7 mM ABTS solution was mixed with 440 µL of $K_2S_2O_8$ 140 mM. The mixture was stored in darkness for 12–16 h. Then, the solution was diluted with ethanol 96° until the absorbance was 0.700 ± 0.020 at 734 nm. Afterwards, 100 µL of antioxidant sample were added to 2 mL of the ABTS working solution, and then incubated for 3 min. The final absorbance measurement was carried out in triplicate at 734 nm. The antioxidant capacity was calculated as percentage of inhibition at 3 min and interpolated in a standard curve. Trolox was used as standard to prepare the calibration curve, and the results were thus expressed as µM Trolox Equivalents/g dry weight (µM TE/g DW). The absorbance measurements were performed in a Perkin-Elmer UV/Vis Lambda 2 spectrophotometer (Perkin-Elmer, Jügesheim, Germany).

On the other hand, ORAC assay measures the degradation of fluorescein by addition of the free radical generator 2,2-azobis(2-aminodinopropane) dihydrochloride (AAPH). Fluorescein, Trolox® and AAPH were dissolved in phosphate buffer solution (7.5 mM), up to a concentration of 78 nM, 100 µM and 221 mM, respectively. Then, 50 µL of fluorescein 78 nM, 50 µL of sample (antioxidant, blank (phosphate buffer) or standard (trolox 100 µM)) and 25 µL of AAPH 221 nM were placed in a 96 well plates. The plate was finally read in a Wallac 1420 VICTOR^3 plate reader (Perkin-Elmer, Jügesheim, Germany) at 37 °C. The measurements were recorded every 5 min until the fluorescence intensity of Trolox® 100 µM was less than 5% of the initial value. Area Under the Curve (AUC) was used for the determination of the antioxidant capacity. Results were expressed in µM TE/g DW as well.

The Folin-Ciocalteu assay, with some minor modifications based on the reported works (Salgado-Ramos et al. 2022a), was used to determine the total polyphenol content (TPC). Briefly, 100 µL of the aqueous antioxidant extract were mixed with 3 mL of Na_2CO_3 2% (w/v) solution. Then, 100 µL of Folin-Ciocalteu reagent were also added. After this last addition, the tube was vigorously shaken for a few seconds and then incubated for 1 h in darkness at room temperature. Afterwards the absorbance was measured at 765 nm by triplicate in a spectrophotometer. Gallic acid was used as standard. The results were expressed as mg Gallic Acid Equivalents/g dry weight (mg GAE/g DW).

The phenolic profile characterization and quantification was performed based on a previously described method (Roselló-Soto et al., 2019). Therefore, an Agilent 1260 Infinity (Agilent, Waldbronn, Germany) with a Waters C18 column 1.7 µm (2.1 × 50 mm) Acquity UPLC BEH.C18 (Waters, Cerdanyola del Vallès, Spain) was used for the separation of the main phenolic compounds in the samples, whereas a TripleTOF™ 5600 LC/MS/MS system (AB SCIEX, Foster City, CA, USA) was employed for the identification.

For HPLC separation, a mobile phase consisting of solvent A (water, 0.1% formic acid) and solvent B (methanol, 0.1% formic acid) was used as follows: 0–13 min 90% A; 13–15 min 100% (B); from 15 min, 90% A. Volume and flow rate were 5 µL and 0.4 mL/min, respectively.

MS data were obtained between 80 and 1200 *m/z* on negative mode, and the IDA acquisition method was carried out in the survey scan type (TOF-MS) using the dependent scan type (product ion). Parameters were: ion spray voltage (–4500 V); declustering potential (90 V); collision energy (–50 V); temperature with 25 psi curtain gas (400 °C); 50 psi for both ion source gas 1 (GC1) and ion source gas 2 (GS2).

The IDA MS/MS analysis was carried out with ion tolerance of 50 mDa, 25 V collision energy and activated dynamic background substraction. The software PeakView1.1 (AB SCIEX, Foster City, CA, USA) and its applications (XIC Manager and Formula Finder) were used for data acquisition and processing. For the quantification an external calibration curve using a representative polyphenol of each group of phenolic compounds potentially found in the samples was prepared, using the following phenolic compounds selected for each specific group: phenolic acids (gallic acid); flavonoids (flavones: apigenin; flavonols: kaempferol; flavanones: naringenin; flavanols: catechin); stilbenes (resveratrol); isoflavonoids (genistein); phenylethanoids (hydroxytyrosol).

2.6. NMR analyses

All crude reaction extracts were analysed by Nuclear Magnetic Resonance (NMR). The dried crude extracts were solubilized in MeOD (600 µL) and then passed through nylon syringe filters (13 mm diameter and 0.45 µm pore size). Samples were prepared in a 5 mm NMR tube. All samples were shaken to provide a homogeneous solution.

Regarding experiments, the ^{1}H NMR spectra were recorded on a Bruker AscendTM 500 spectrometer (Bruker Corporation, Billerica, MA, USA) operating at a frequency of 500.16 MHz for the ^{1}H nucleus. For soaking and PEF crude extracts, 50 µL of maleic acid 0.1 mol/L were added as internal standard for quantification. The following quantitative parameters were applied: acquisition time 2.723 min, 16 scans, 90° pulse (8 µs) and relaxation delay (D1) 5 s, to assure the complete relaxation of all nuclei. The temperature of the probe was adjusted to 25 °C. Chemical shifts were referred at 0 ppm with the addition to the tube of 10 µL of 3-(trimethylsilyl) propionic-2,2,3,3-d_4 acid sodium salt (TSP) solution (also for SFE experiments). The amount of sugars was calculated by quantitative NMR (qNMR) according to previous studies (Salgado-Ramos et al. 2022c).

2.7. Scanning electron microscopy (SEM)

SEM images were taken in a ZEISS Gemini500 high resolution scanning electron microscopy (HRSEM, ZEISS, Oberkochen, Germany), with an Oxford EDS 80 mm^2 detector operating from 3 pA to 20 nA for electrical current intensity and 0.02–30 kV for voltage, with a magnification range of 50–2.000.000 X.

2.8. Thermogravimetric (TGA) and Fourier-transformed infrared (FT-IR) analysis

Thermograms (TG) and differential thermogravimetric (DTG) analyses were measured on a thermogravimetric analyzer TA instruments Q50 (TA Instruments, New Castle, Delaware, USA) according to Salgado-Ramos et al. (2022a). The analysis was conducted by increasing the temperature from 25° to 800°C, at a heating rate of 10 °C/min, under inert atmosphere by using N_2.

FT-IR analyses were carried out in an IRAffinity-1S FT-IR instrument (Shimadzu, Kioto, Japan), equipped with a media work infrared lamp and DTGS Standard Detector. The pertinent samples were previously dried and placed onto the FT-IR crystal. The sample was analysed in transmittance mode with 45 scans per sample, with resolution of 4 cm^{-1}. The frequency range for each spectrum was from 4000 to 500 cm^{-1}.

2.9. Statistical analysis

Results for total antioxidant capacity (TAC) and polyphenols content (TPC) were statistically analysed using an ANOVA test, with a Tukey post-test, comparing control sample, PEF and PEF+SFE treatment (GraphPad Prism 8.0.2. software, San Diego, CA, USA). A value of $p < 0.05$ was considered significant. All results were expressed as mean ± standard deviation (SD) (n = 3).

3. Results and discussion

3.1. Recovery of bioactive phenolic compounds from AH via PEF+SFE

Pulsed electric fields (PEF) and supercritical fluid extraction (SFE) with CO_2 (SC-CO_2) were sequentially applied for the first time in almond hull (AH) for an efficient and sustainable valorisation of this matrix. The process is summarized in Fig. 1.

The significance of re-extracting PEF-treated AH with SC-CO_2 was due to some issues. For instance, the efficiency for BACs recovery could be significantly enhanced, thus intensifying this way for valorisation. Furthermore, it supposes the first application of this enabled protocol to this matrix, to the best of our knowledge, which leads to a distinguished improvement in the state-of-art for biomass upgrading and process intensification. Finally, other valorisation could be concurrently developed for AH, for instance, for the post-extraction residual solid remaining after treatment, in line with the zero-waste and circular economy concepts.

Therefore, PEF-assisted extraction experiments were carried out following our previous studies (Martí-Quijal et al., 2021; Salgado-Ramos et al. 2022a). For SFE, experimental conditions were selected according to the available literature (Talmaciu et al., 2016). In this regard, the liquid fractions I and II obtained after PEF and SFE processes (see Fig. 1) were analysed using different antioxidant assays to confirm the activity of these crudes. Results are summarized in Fig. 2.

As it can be depicted from Fig. 2, the combination PEF+SFE was overall noteworthy compared to the control (conventional EtOH/H_2O extraction). For instance, remarkable results were obtained by TEAC assay (Fig. 2a), with a total antioxidant capacity (TAC) of 88.20 µmol TE/g DW by soaking and 155.30 µmol TE/g DW by PEF application ($p < 0.001$). Furthermore, a similar trend was observed by TPC as well (Fig. 2c), with 25.83 mg GAE/g DW detected by soaking and 30.92 mg GAE/g DW by PEF ($p = 0.034$). However, in both cases the application of SFE (PEF+SFE) did not lead to any significant TAC and TPC improvement with respect to PEF itself ($p = 0.991$ and $p = 0.998$ respectively) (Fig. 2a, c). In this context, a value of 156 µmol TE/g DW was achieved for the former and 31.03 mg GAE/g DW for the latter, which suppose the same significance compared to soaking ($p < 0.001$ and $p < 0.05$, respectively).

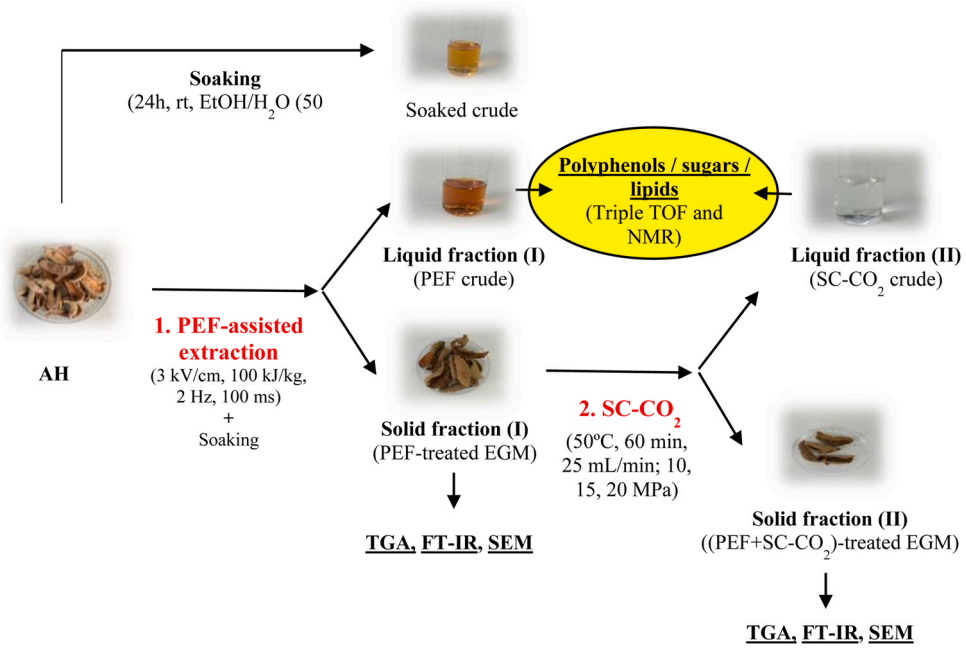

Fig. 1 – Sequential extraction of almond hull (AH) by combination of pulsed electric fields (PEF)-assisted extraction and supercritical fluid extraction (SFE) to recover polyphenols, sugars and lipids.

Despite that, it should be noted the significance of re-extracting PEF-treated AH (solid fraction (I), Fig. 1) with SC-CO_2, since an appreciable TAC and TPC were found in the liquid crude (II) (Fig. 1) by itself. Therefore, the scavenging activity detected by TAC was 0.70 µmol TE/g DW by TEAC and 45.42 µmol TE/g DW by ORAC, whereas 0.11 mg GAE/g DW were obtained for TPC.

Regarding the application of the advanced technologies to AH, no previous report was found to date in the available literature. However, some of these techniques were recently applied in other almond by-products or varieties, therefore it could be used as sake of comparison to these results. For instance, Moghaddam et al. (2020) reported the PEF-assisted extraction of antioxidant phenolic compounds from almond red leaves, with values for TPC of 241.40 mg GAE/g and 93.40% for DPPH radical inhibition. This notable difference compared to the results reported here might be related to the different composition and characteristics of almond by-products, i.e., red leaves and AH. Further, PEF-assisted extraction was combined with other intensified protocols, such as ultrasound-assisted extraction (UAE), as reported by Manzoor et al. (2019) for almond seeds. Herein, results for TPC are in line with those reported in this study, since values of 19.22 and 21.20 mg GAE/g were found for PEF and PEF+UAE, respectively, both significantly higher compared to the control (only 15.90 mg GAE/g) ($p < 0.05$). In addition, the antioxidant activity by DPPH assay was evaluated as well, showing the combination PEF+UAE a lower EC_{50} value (19.59) compared to PEF alone (21.96) and control (27.58). Finally, AH was potentially extracted with UAE as well, with no PEF previous step (Kahlaoui et. al. 2019). In this regard, a TPC up to 210.49 mg GAE/g DW was detected, 10 times higher compared to our PEF extracts. However, radical scavenging activity (RSA) showed a value of 199 µmol TE/g DW, similar to the 156 µmol TE/g DW detected by TEAC in this work.

On the other hand, by ORAC assay the results for soaking were noteworthy, with a higher TAC compared to PEF+SFE treatment, quite surprisingly (540.78 *vs.* 422.41 µmol TE/g DW, respectively). Maybe the high sensibility of ORAC with respect to other BACs different from polyphenols could explain this issue, since different compounds would be evaluated under TEAC or ORAC assays. However, as the opposite as occurred by TEAC and TPC, it should be noted that the application of SFE enhanced this TAC compared to PEF alone (from 376.99 to 422.41 µmol TE/g DW), since a lower significance with respect to control was found ($p = 0.004$ for PEF alone and $p = 0.018$ for PEF+SFE, Fig. 2b). However, no statistically significant differences were observed between them ($p = 0.354$). Additionally, it should be noted that the application of SFE involved the extraction of other BACs (mainly lipids), as will be discussed.

Overall, attending to the reported data for the scavenging activity, PEF+SFE boosted the efficiency up to 77% for TAC, concretely by TEAC assay, compared to the traditional soaking. Therefore, this fact suggests that this sequential combination could be useful for a distinguished polyphenols recovery from AH. Furthermore, this enhancement was also noteworthy for TPC, with a progress up to 20% by PEF+SFE with respect to the conventional extraction. Finally, it should be noted that an increase up to 38% was achieved after SFE application by ORAC assay, despite the lower activity detected compared to soaking. In any case, the significance of re-extracting PEF-treated AH with SFE was clearly demonstrated.

However, with the aim of enhancing this efficiency, for further studies the use of the sequential PEF + SC-CO_2 extraction with increased EtOH flow is recommended, since increasing the polarity might enhance the efficiency for polyphenols recovery. In parallel, and to the best of our knowledge, it could be interesting to directly apply SFE without PEF treatment as well. In that case, the aim is to observe whether SFE treatment would be efficient by itself, or it would be indeed necessary either to increase the EtOH flow or to apply PEF pre-treatment for a better recovery.

After evaluating the scavenging activity, LC-MS analysis provided valuable information about the phenolic profile for each liquid fraction, observing different kinds of polyphenols attending to the processing applied (PEF or SC-CO_2) (Table 1).

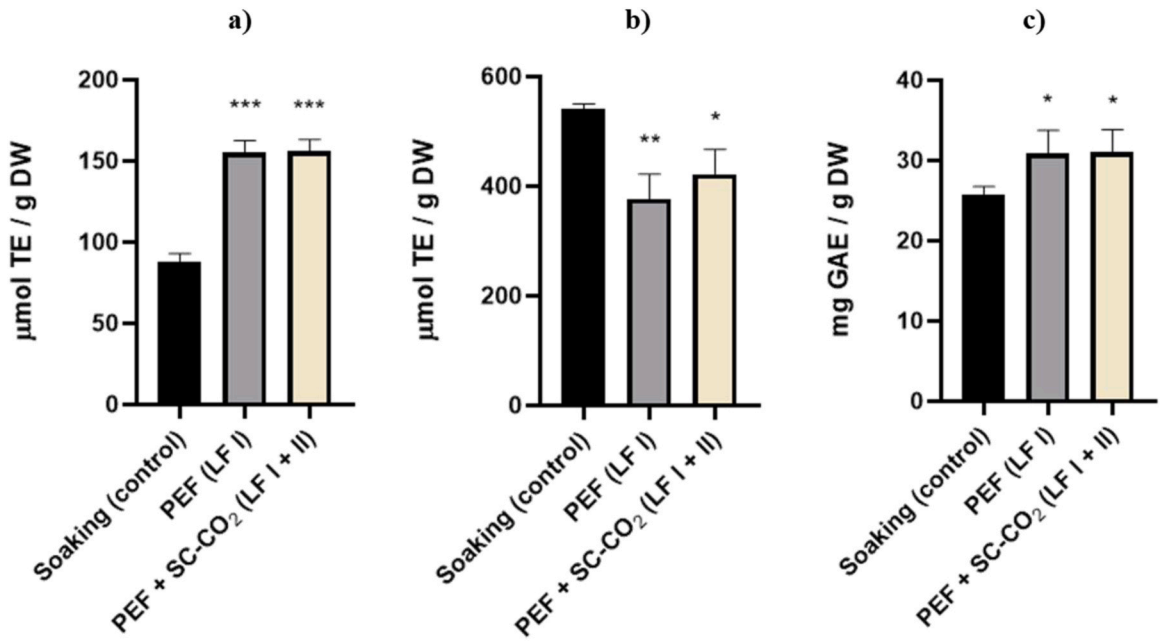

Fig. 2 – Radical scavenging activity by means of total antioxidant capacity (TEAC (a), ORAC (b)) and polyphenols content (TPC (c)) after pulsed electric field (PEF)-assisted extraction, PEF + SFE (supercritical fluid extraction), and soaking as control. Results are expressed as mean ± SD with n = 3. *=p < 0.05; **=p < 0.01; *** =p < 0.001 *vs.* Soaking (control). Abbreviations: LF: liquid fraction.

Regarding PEF crudes, the recovery of 5-caffeoylquinic acid (or chlorogenic acid) was noticeable, since according to Prgomet et. al., 2017, this structure appears as the most abundant phenolic acid in the AH extracts. Further, it can be observed some flavanols (catechin (Sang et al., 2002) and epicatechin), both useful as anti-obesity agents (Akhlaghi et al., 2018), as well as flavonoids (3-hydroxyphloretin), which showed several benefits against ovarian cancer (Mohammadi et al., 2016). Moreover, other glycosylated, as kaempferol 3,7-O-diglucoside, were detected. The presence of these structures also agrees with Prgomet et al., 2017 for AH. However, this glycosylation can sometimes hinder the scavenging activity of the polyphenols (Cyboran-Mikołajczyk et al., 2019), mainly due to the lower proportion of hydroxyl groups (OH) present in aromatic polyphenols rings, which are involved in the inhibition mechanism of free radicals.

For SFE extracts, the presence of non-polar aglycones as ishoramnetin or kaempferol, useful in reducing the risk for type 2 diabetes (Rienks et al., 2018), should be noted. It can be explained by the low polarity of CO_2, in contrast to the high-polar system applied to PEF-assisted extraction ($EtOH/H_2O$). This fact is noteworthy, since this difference in terms of polarity supposes a selective recovery of polyphenols depending on the technology applied (PEF or SC-CO_2 extraction), thus affecting the phenolic profile obtained for both crudes. Therefore, despite the moderate amount detected in SFE crudes (2.46–5.87 mg/L), which agrees with the TAC and TPC previously reported (see Fig. 2), the presence of widely different kind of structures potentiates the protocol developed. Finally, other structures as luteolin, nepetin or scutellarin, were also detected by SC-CO_2 extraction (Table 1).

3.2. *Simultaneous extraction of carbohydrates and lipids by PEF and SC-CO_2*

Furthermore, liquid fractions I and II were also analysed by NMR. The ^{1}H NMR spectrum for PEF and soaking shows the presence of other primary metabolites as sugars (Fig. 3a), selectively extracted with this technique, and with high presence in AH (Holtman et al., 2015; Salgado-Ramos et al. 2022a). Among these sugars, mostly glucose and sucrose, as well as others such as fructose, all of them characterized in previous studies (Salgado-Ramos et al. 2022a). These sugars have direct application in the food sector as additives, and they could be useful for the obtention of other valuable chemicals as well, such as LA or 5-HMF.

In addition, quantitative NMR (qNMR) allowed us to know the amount of glucose and sucrose in each crude (Table S1). In that case, the slightly low amount of these sugars in PEF crudes could be related to the higher glycosylation in polyphenols structure compared to soaking. Despite that, PEF extraction appears more useful for polyphenols recovery from AH, according to antioxidant assays, whereas freely accessible sugars could be more efficiently extracted by soaking, with no significant difference in comparison with PEF.

Apart from that, in this ^{1}H NMR spectrum, it is indeed possible to observe both the signals related to the aromatic rings of polyphenols (8–6 ppm) and methoxy groups (3.5–4 ppm), thus corroborating the antioxidant activity previously showed.

By contrast, ^{1}H NMR spectrum for liquid fraction II (PEF + SFE) mainly showed the presence of lipids (Fig. 3b), also considered as BACs. This seems logical attending to the low polarity system applied to SFE, as mentioned. Therefore, SC-CO_2 extraction allowed not only to recover the remaining polyphenols in the solid fraction I (see Fig. 1), but also the lipidic fraction which could not be extracted by PEF. Once again, this profile was assigned according to our previous studies (Lucas-Torres et al., 2014). Lipids are useful, as mentioned, for the obtention of biodiesel by transesterification with low-molecular weight alcohols, and they can be considered as BACs as well, since they are present in several healthy foods such as oil or dried nuts.

Table 1 – Phenolic profile by LC-MS for the antioxidant liquid fractions obtained by pulsed electric fields (PEF)-assisted extraction and supercritical fluid extraction (SFE) from almond hull (AH) biomass.

	Compound	Formula	Intensity	RT[a] (min)	mg/L
PEF	3-hydroxyphloretin	$C_{15}H_{14}O_6$	1 230 536	5.72	230.20
	(±)-Catechin	$C_{15}H_{14}O_6$	1 230 536	5.72	230.20
	(±)-Epicatechin	$C_{15}H_{14}O_6$	1 230 536	5.72	230.20
	5-caffeoylquinic acid	$C_{16}H_{18}O_9$	312 984	11.49	58.55
	Kaempferol 3,7-O-diglucoside	$C_{27}H_{30}O_{16}$	908 977	10.05	170.05
SFE	Kaempferol	$C_{15}H_{10}O_6$	13 087	14.03	2.46
	Luteolin	$C_{15}H_{10}O_6$	13 087	14.03	2.46
	Scutellarein	$C_{15}H_{10}O_6$	13 087	14.03	2.46
	Nepetin	$C_{16}H_{12}O_7$	31 290	14.14	5.87
	Isorhamnetin	$C_{16}H_{12}O_7$	31 290	14.14	5.87

a. Retention time.

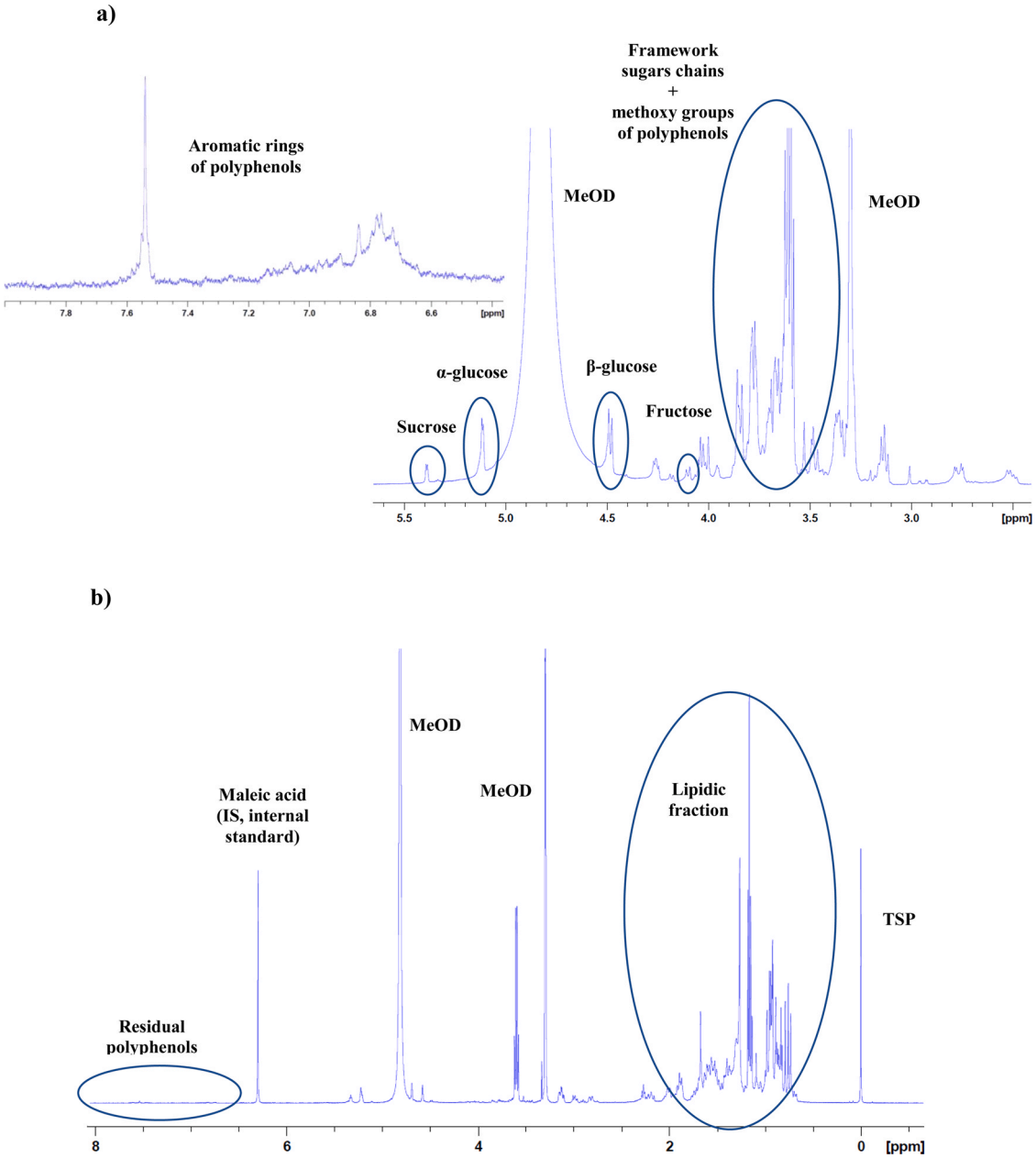

Fig. 3 – ^{1}H NMR spectra (MeOD, 500 MHz) for the liquid fractions obtained after soaking or pulsed electric field (PEF)-assisted extraction (a) and after supercritical fluid extraction (SFE) from PEF-treated almond hull (AH) biomass.

3.3. *Analysis of the remaining solid fraction after processing: influence of the technology and zero-waste assessment*

Finally, solid fractions I and II (see Fig. 1) were evaluated by several techniques. Firstly, the influence of the technology can be evaluated by SEM analysis, with different morphology attending to the processing applied (Fig. S1).

Many changes in the initial matrix are usually induced by the extraction process, normally converting the raw material into products with reduced particle size (Teixeira et al., 2021). These changes could be largely caused by several chemical and physical processes, such as diffusivity, density or viscosity variations, among others (Osorio-Tobón, 2020). Therefore, a high number of reactions that take place by applying intensification technologies involved sequential mechanisms responsible for changing the physical structure of samples, thus facilitating the recovery of the metabolites (Khadhraoui et al., 2018).

For instance, PEF treatment clearly leads to cell damage (Fig. S1b) when comparing to the untreated biomass (Fig. S1a), in agreement with the literature (Koubaa et al., 2016; Loginova et al., 2011). This cell damage involves the formation of pores (Fig. S1e, 20.00 K X magnification), thus facilitating the extraction of the primary metabolites. By contrast, after SFE, fibres presented in AH become compacted due to the high pressures employed (Fig. S1c) (Mesquita et al., 2021). Therefore, sequential combination of PEF + SFE together leads to a high compaction by SFE, and the cell damage or breakage previously induced by PEF (Fig. S1f, 100 X magnification). It should be noted that most of the pores from PEF treatment could become excessively close due to these high pressures employed in SFE, which can explain the smooth surface in fibres after this treatment, similar to fibres in untreated AH (Figs. S1, 2 K X magnification).

In addition, thermogravimetric (TGA) and Fourier transformed infrared (FT-IR) analyses were carried out. For the former, differential thermogravimetric (DTG) curves provided information about AH composition, once again with valuable difference between solids after PEF and SFE compared to the untreated AH (Fig. S2).

DTG curves allow to relate each peak of this curve to one compound present in biomass. The assignment was carried out attending to the literature and previous studies in our research group with AH and other biomass (Lucas-Torres et al., 2016; Salgado-Ramos et al. 2022a).

Thus, as depicted from Fig. S2a, the decomposition peak around 200°C is related to freely accessible, high-polar compounds presented in biomass, mainly sugars and/or polyphenols, both efficiently extracted after PEF treatment (as observed in Figs. 2 and 3). Therefore, a low amount in the PEF-treated AH (black DTG curve in Fig. S2a) compared to the untreated biomass (blue DTG in Fig. s2a) was observed. For SFE, by contrast, despite the scavenging activity showed by the liquid extracts, a selective recovery of the lipidic fraction was mainly carried out. Therefore, any remarkable difference between solid fraction I and II was observed (red DTG curve in Fig. S2a).

Overall, this DTG analysis supports that the proportion of fibres in solid fractions I and II is higher compared to the untreated biomass (Fig. S2a). Therefore, the cellulose, hemicellulose and lignin presented in the remaining AH could be more prone to its further transformation into other valuable compounds. This concurrently suggest other valorisation pathway for AH, in line with a zero-waste approach. For instance, cellulose and hemicellulose are useful for the development of levulinic acid or furfural, respectively, distinguished bio-based compounds as platform chemicals or with high-industrial application (Mika et al., 2018). Moreover, lignin could be a good source of antioxidants (Salgado-Ramos, et al. 2022b), and valuable feedstock towards widely industrial-applied bioaromatics (vanillin or syringaldehyde), or biofuel precursors as long-chain fatty acids (Salgado-Ramos et al. 2022c).

Finally, FT-IR analysis was also carried out (Fig. S2b). Briefly, a decrease in band intensity for O-H (broad), C-O and C═O linkages, which are predominantly in both polyphenols and sugars, was observed. Moreover, the aromaticity, supported by region between 1600 and 1000 cm^{-1}, was considerably lower, once again supporting the efficiency of PEF + SFE for polyphenols recovery, and thus corroborating the antioxidant activity showed by the analysed liquid fractions (Fig. 2).

In summary, the enabling combination PEF+SC-CO_2 demonstrated to be useful for an in-depth valorisation of AH, not only for recovering bioactive phenolic compounds, but also for the simultaneous extraction of carbohydrates (PEF) and lipids (SC-CO_2) that carried out. In addition, the post-extraction solid demonstrated a wide potential for the development of fine chemicals. In this line, a zero-waste status for the total exploitation of biomass could be achieve, in agreement with a life-cycle economy.

4. Conclusions

Aiming to recover polyphenols, sugars and lipids from AH, a sequential extraction process based on PEF + SFE with CO_2 (PEF+SC-CO_2) was developed for the first time, to the best of our knowledge. With this regard, PEF+SFE boosted the efficiency in terms of total antioxidant capacity (TAC) by TEAC assay up to 77% with respect to the traditional soaking. Furthermore, this enhancement was also remarkable for TPC, with a progress up to 20% by PEF+SFE compared to the conventional extraction. LC-MS analysis provided the phenolic profiles of the crudes, with significant differences attending to the technology applied. Additionally, NMR analysis detected the presence of the carbohydrate soluble and lipidic fractions, both selectively extracted by PEF or SC-CO_2, respectively. Finally, the post-extraction remaining solid fractions after both PEF and PEF+SFE treatments were evaluated by SEM, TGA and FT-IR. SEM analysis showed the formation of surface pores after PEF and fibres compaction after SFE, whereas DTG curves suggested other concurrent valorisation ways for these AH fractions, in line with a zero-waste approach.

Funding

This study forms part of the AGROALNEXT programme (AGROALNEXT/2022/060 - Desarrollo y optimización de procesos innovadores y sostenibles de extracción de aceite y proteínas a partir de microalgas, insectos, residuos y subproductos agroalimentarios: Evaluación de propiedades biológicas (EXTRAOLIOPRO)) and was supported by MCIN with funding from European Union NextGenerationEU (PRTR-C17. I1) and the Generalitat Valenciana. Authors would like to acknowledge Generalitat Valenciana (Spain) for the financial support (IDIFEDER/2018/046—Procesos

innovadores de extracción y conservación: pulsos eléctricos y fluidos supercríticos) through the European Union ERDF funds (European Regional Development Fund). The research was also funded by Consejería de Educación, Cultura y Deporte of Junta de Comunidades de Castilla-la Mancha (Spain) and Ministerio de Ciencia, Innovación y Universidades (projects SBPLY/17/180501/000522-"Valorización energética de residuos agroindustriales: obtención de precursores de biocombustibles y evaluación de los efectos de sus emisiones en la contaminación atmosférica" and "RTI2018–099503–8-I00-Formación, caracterización y reactividad química de aerosoles en la atmósfera", respectively), both co-financed by the Fondo Europeo de Desarrollo Regional (FEDER). This research was funded by the University of Valencia through the project OTR2022–23064INVES, supported by the University of Vigo. M. Salgado-Ramos, A. Moreno, M.P. Sánchez-Verdú, F.J. Barba and F.J. Martí-Quijal are members of the CYTED network "P320RT0186 - Aprovechamiento sostenible de recursos biomásicos vegetales iberoamericanos en cosmética (BIOLATES)"; F. J. Martí-Quijal would like to acknowledge the pre-PhD scholarship programme of University of Valencia "Atracció de Talent". M. Salgado- Ramos and A.J. Huertas-Alonso would like to express their gratitude to Junta de Comunidades de Castilla-la Mancha (Spain) for their pre- PhD fellowship.

CRediT authorship contribution statement

Manuel Salgado-Ramos: Methodology, Formal analysis, Writing – original draught preparation, Writing – review & editing. **Francisco J. Martí-Quijal:** Methodology, Formal analysis, Writing – original draught preparation, Writing – review & editing. **Alberto J. Huertas-Alonso:** Methodology, Formal analysis, Writing – review & editing. **M. Prado Sánchez-Verdú:** Conceptualization, Resources, Writing – review & editing, Supervision, Funding acquisition. **Giancarlo Cravotto:** Conceptualization, Writing – review & editing. **Andrés Moreno:** Conceptualization, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition. **Francisco J. Barba**: Conceptualization, Resources, Supervision, Project administration, Funding acquisition, Writing – review & editing.

Declaration of Competing Interest

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

Acknowledgements

The authors are grateful for the technical support from the mass spectrometry group in the Central Service for Experimental Research (SCSIE) at the Universitat de València for their help in the analysis of the triple TOF-LC-MS-MS data.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.fbp.2023.04.003.

References

Akhlaghi, M., Ghobadi, S., Mohammad Hosseini, M., Gholami, Z., Ghobadi, F., 2018. Flavanols are potential anti-obesity agents a systematic review and meta-analysis of controlled clinical trials. Nutr. Metab. Cardiovas. Dis. 28 (7), 675–690 https://doi.org/10.1016/j.numecd.2018.04.001.

Barba, F.J., Zhu, Z., Koubaa, M., Sant'Ana, A.S., Orlien, V., 2016. Green alternative methods for the extraction of antioxidant bioactive compounds from winery wastes and by-products: a review. Trends Food Sci. Technol. 49, 96–109. https://doi.org/10.1016/j.tifs.2016.01.006

Carmona-Cabello, M., García, I.L., Papadaki, A., Tsouko, E., Koutinas, A., Dorado, M.P., 2021. Biodiesel production using microbial lipids derived from food waste discarded by catering services. Biores. Technol. 323, 124597. https://doi.org/10.1016/j.biortech.2020.124597

Cyboran-Mikołajczyk, S., Solarska-Ściuk, K., Mieszała, K., Glatzel-Plucińska, N., Matczak, K., Kleszczyńska, H., 2019. The impact of O-glycosylation on cyanidin interaction with RBCs and HMEC-1 cells-structure–activity relationships. Int. J. Mol. Sci. 20 (8), 1928. https://doi.org/10.3390/ijms20081928

da Silva, R.P.F.F., Rocha-Santos, T.A.P., Duarte, A.C., 2016. Supercritical fluid extraction of bioactive compounds. TrAC Trends Anal. Chem. 76, 40–51. https://doi.org/10.1016/j.trac.2015.11.013

Dienaitė, L., Baranauskienė, R., Rimantas Venskutonis, P., 2021. Lipophilic extracts isolated from European cranberry bush (*Viburnum opulus*) and sea buckthorn (*Hippophae rhamnoides*) berry pomace by supercritical CO_2 – promising bioactive ingredients for foods and nutraceuticals. Food Chem. 348, 129047. https://doi.org/10.1016/j.foodchem.2021.129047

Durazzo, A., Lucarini, M., Souto, E.B., Cicala, C., Caiazzo, E., Izzo, A.A., Novellino, E., Santini, A., 2019. Polyphenols: a concise overview on the chemistry occurrence and human health. Phytother. Res. 33 (9), 2221–2243. https://doi.org/10.1002/ptr.6419

Freyssin, A., Page, G., Fauconneau, B., Rioux Bilan, A., 2020. Natural stilbenes effects in animal models of Alzheimer's disease. Neural Regen. Res. 15 (5), 843. https://doi.org/10.4103/1673-5374.268970

Garcia-Perez, P., Xiao, J., Munekata, P.E.S., Lorenzo, J.M., Barba, F.J., Rajoka, M.S.R., Barros, L., Mascoloti Sprea, R., Amaral, J.S., Prieto, M.A., Simal-Gandara, J., 2021. Revalorization of almond by-products for the design of novel functional foods: an updated review. Foods 10 (8), 1823. https://doi.org/10.3390/foods10081823

Gunjević, V., Grillo, G., Carnaroglio, D., Binello, A., Barge, A., Cravotto, G., 2021. Selective recovery of terpenes polyphenols and cannabinoids from *Cannabis sativa L.* inflorescences under microwaves. Ind. Crops Prod. 162, 113247. https://doi.org/10.1016/j.indcrop.2021.113247

Holtman, K.M., Offeman, R.D., Franqui-Villanueva, D., Bayati, A.K., Orts, W.J., 2015. Countercurrent extraction of soluble sugars from almond hulls and assessment of the bioenergy potential. J. Agric. Food Chem. 63 (9), 2490–2498. https://doi.org/10.1021/jf5048332

Kahlaoui, M., Borotto Dalla Vecchia, S., Giovine, F., ben Haj Kbaier, H., Bouzouita, N., Barbosa Pereira, L., Zeppa, G., 2019. Characterization of polyphenolic compounds extracted from different varieties of almond hulls (*Prunus dulcis L.*). Antioxidants 8 (12), 647. https://doi.org/10.3390/antiox8120647

Kaur, M., Kumar, M., Sachdeva, S., Puri, S.K., 2020. An efficient multiphase bioprocess for enhancing the renewable energy production from almond shells. Energy Convers. Manag. 203, 112235. https://doi.org/10.1016/j.enconman.2019.112235

Khadhraoui, B., Turk, M., Fabiano-Tixier, A.S., Petitcolas, E., Robinet, P., Imbert, R., Maâtaoui, M. el, Chemat, F., 2018. Histo-cytochemistry and scanning electron microscopy for studying spatial and temporal extraction of metabolites induced by ultrasound Towards chain detexturation mechanism. Ultrason. Sonochem. 42, 482–492. https://doi.org/10.1016/j.ultsonch.2017.11.029

(al)Khawli, F., Pateiro, M., Domínguez, R., Lorenzo, J.M., Gullón, P., Kousoulaki, K., Ferrer, E., Berrada, H., Barba, F.J., 2019. Innovative green technologies of intensification for valorization of seafood and their by-Products. Mar. Drugs 17 (12), 689. https://doi.org/10.3390/md17120689

Koubaa, M., Barba, F.J., Grimi, N., Mhemdi, H., Koubaa, W., Boussetta, N., Vorobiev, E., 2016. Recovery of colorants from red prickly pear peels and pulps enhanced by pulsed electric field and ultrasound. Innov. Food Sci. Emerg. Technol. 37, 336–344. https://doi.org/10.1016/j.ifset.2016.04.015

Lapornik, B., Prošek, M., Wondra, A.G., 2005. Comparison of extracts prepared from plant by-products using different solvents and extraction time. J. Food Eng. 71 (2), 214–222. https://doi.org/10.1016/j.jfoodeng.2004.10.036

Loginova, K.V., Lebovka, N.I., Vorobiev, E., 2011. Pulsed electric field assisted aqueous extraction of colorants from red beet. J. Food Eng. 106 (2), 127–133. https://doi.org/10.1016/j.jfoodeng.2011.04.019

Lucas-Torres, C., Pérez, Á., Cabañas, B., Moreno, A., 2014. Study by ^{31}P NMR spectroscopy of the triacylglycerol degradation processes in olive oil with different heat-transfer mechanisms. Food Chem. 165, 21–28. https://doi.org/10.1016/j.foodchem.2014.05.092

Lucas-Torres, C., Lorente, A., Cabañas, B., Moreno, A., 2016. Microwave heating for the catalytic conversion of melon rind waste into biofuel precursors. J. Clean. Prod. 138, 59–69. https://doi.org/10.1016/j.jclepro.2016.03.122

Manzoor, M.F., Zeng, X.-A., Rahaman, A., Siddeeg, A., Aadil, R.M., Ahmed, Z., Li, J., Niu, D., 2019. Combined impact of pulsed electric field and ultrasound on bioactive compounds and FT-IR analysis of almond extract. J. Food Sci. Technol. 56, 2355–2364. https://doi.org/10.1007/s13197-019-03627-7

Mariatti, F., Gunjević, V., Boffa, L., Cravotto, G., 2021. Process intensification technologies for the recovery of valuable compounds from cocoa by-products. Innov. Food Sci. Emerg. Technol. 68, 102601. https://doi.org/10.1016/j.ifset.2021.102601

Martín-García, B., Tylewicz, U., Verardo, V., Pasini, F., Gómez-Caravaca, A.M., Caboni, M.F., Dalla Rosa, M., 2020. Pulsed electric field (PEF) as pre-treatment to improve the phenolic compounds recovery from brewers' spent grains. Innov. Food Sci. Emerg. Technol. 64, 102402. https://doi.org/10.1016/j.ifset.2020.102402

Martí-Quijal, F.J., Ramon-Mascarell, F., Pallarés, N., Ferrer, E., Berrada, H., Phimolsiripol, Y., Barba, F.J., 2021. Extraction of antioxidant compounds and pigments from spirulina (*Arthrospira platensis*) assisted by pulsed electric fields and the binary mixture of organic solvents and water. Appl. Sci. 11 (16), 7629. https://doi.org/10.3390/app11167629

Mesquita, P.C., Rodrigues, L.G.G., Mazzutti, S., da Silva, M., Vitali, L., Lanza, M., 2021. Intensified green-based extraction process as a circular economy approach to recover bioactive compounds from soursop seeds (Annona muricata L.). Food Chem. 12, 100164. https://doi.org/10.1016/j.fochx.2021.100164

Mika, L.T., Cséfalvay, E., Németh, Á., 2018. Catalytic conversion of carbohydrates to initial platform chemicals: chemistry and sustainability. Chem. Rev. 118 (2), 505–613. https://doi.org/10.1021/acs.chemrev.7b00395

Moghaddam, Tayebeh Nakhaei, Elhamirad, Amir Hossein, Saeidi Asl, M.R., Shahidi Noghabi, M., 2020. Pulsed electric field-assisted extraction of phenolic antioxidants from tropical almond red leaves. Chem. Pap. 3957–3961. https://doi.org/10.1007/s11696-020-01153-x

Mohammadi, V., Dehghani, S., Larijani, B., Azadbakht, L., 2016. Ovarian cancer risk and nonisoflavone flavonoids intake: a systematic review of epidemiological studies. J. Res. Med. Sci. 21 (1), 123. https://doi.org/10.4103/1735-1995.196605

Osorio-Tobón, J.F., 2020. Recent advances and comparisons of conventional and alternative extraction techniques of phenolic compounds. J. Food Sci. Technol. 57 (12), 4299–4315. https://doi.org/10.1007/s13197-020-04433-2

Pasqualone, A., Laddomada, B., Spina, A., Todaro, A., Guzmàn, C., Summo, C., Mita, G., Giannone, V., 2018. Almond by-products: extraction and characterization of phenolic compounds and evaluation of their potential use in composite dough with wheat flour. LWT Food Sci. Technol. 89, 299–306. https://doi.org/10.1016/j.lwt.2017.10.066

Pimentel-Moral, S., Borrás-Linares, I., Lozano-Sánchez, J., Arráez-Román, D., Martínez-Férez, A., Segura-Carretero, A., 2019. Supercritical CO_2 extraction of bioactive compounds from *Hibiscus sabdariffa*. J. Supercrit. Fluids 147, 213–221. https://doi.org/10.1016/j.supflu.2018.11.005

Pinelo, M., Ruiz-Rodríguez, A., Sineiro, J., Señoráns, F.J., Reglero, G., Núñez, M.J., 2007. Supercritical fluid and solid-liquid extraction of phenolic antioxidants from grape pomace: a comparative study. Eur. Food Res. Technol. 226 (1–2), 199–205. https://doi.org/10.1007/s00217-006-0526-3

Prgomet, I., Gonçalves, B., Domínguez-Perles, R., Pascual-Seva, N., Barros, A., 2017. Valorization challenges to almond residues: phytochemical composition and functional application. Molecules 22 (10), 1774. https://doi.org/10.3390/molecules22101774

Rienks, J., Barbaresko, J., Oluwagbemigun, K., Schmid, M., Nöthlings, U., 2018. Polyphenol exposure and risk of type 2 diabetes: dose-response meta-analyses and systematic review of prospective cohort studies. Am. J. Clin. Nutr. 108 (1), 49–61. https://doi.org/10.1093/ajcn/nqy083

Roncero, J.M., Álvarez-Ortí, M., Pardo-Giménez, A., Rabadán, A., Pardo, J.E., 2020. Review about non-lipid components and minor fat-soluble bioactive compounds of almond kernel. Foods 9 (11), 1646. https://doi.org/10.3390/foods9111646

Roselló-Soto, E., Martí-Quijal, F., Cilla, A., Munekata, P., Lorenzo, J., Remize, F., Barba, F., 2019. Influence of temperature solvent and pH on the selective extraction of phenolic compounds from tiger nuts by-products: Triple-TOF-LC-MS-MS characterization. Molecules 24 (4), 797. https://doi.org/10.3390/molecules24040797

Şahin, S., Samli, R., Tan, A.S.B., Barba, F.J., Chemat, F., Cravotto, G., Lorenzo, J.M., 2017. Solvent-free microwave-assisted extraction of polyphenols from olive tree leaves: antioxidant and antimicrobial properties. Molecules 22 (7), 1056. https://doi.org/10.3390/molecules22071056

Salgado-Ramos, M., Martí-Quijal, F.J., Huertas-Alonso, A.J., Sánchez-Verdú, M.P., Barba, F.J., Moreno, A., 2022a. Almond hull biomass: preliminary characterization and development of two alternative valorization routes by applying innovative and sustainable technologies. Ind. Crops Prod. 179, 114697. https://doi.org/10.1016/j.indcrop.2022.114697

Salgado-Ramos, M., Tabasso, S., Calcio Gaudino, E., Moreno, A., Mariatti, F., Cravotto, G., 2022b. An innovative green cascade protocol for grape stalk valorization with process intensification technologies. Appl. Sci. 12 (15), 7417. https://doi.org/10.3390/app12157417

Salgado-Ramos, M., Mariatti, F., Tabasso, S., Sánchez-Verdú, M.P., Moreno, A., Cravotto, G., 2022c. Sustainable and non-conventional protocols for the three-way valorisation of lignin from grape stalks. Chem. Eng. Process. Process. Intensif. 178, 109027. https://doi.org/10.1016/j.cep.2022.109027

Sang, S., Lapsley, K., Rosen, R.T., Ho, C.T., 2002. New prenylated benzoic acid and other constituents from almond hulls (*Prunus amygdalus Batsch*). J. Agric. Food Chem. 50, 607–609. https://doi.org/10.1021/jf0110194

Talmaciu, A.I., Ravber, M., Volf, I., Knez, Ž., Popa, V.I., 2016. Isolation of bioactive compounds from spruce bark waste using sub- and supercritical fluids. J. Supercrit. Fluids 117, 243–251. https://doi.org/10.1016/j.supflu.2016.07.001

Teixeira, G.L., Maciel, L.G., Mazzutti, S., Barbi, R.C.T., Ribani, R.H., Ferreira, S.R.S., Block, J.M., 2021. Sequential green extractions based on supercritical carbon dioxide and pressurized ethanol for the recovery of lipids and phenolics from *Pachira aquatica* seeds. J. Clean. Prod. 306, 127223. https://doi.org/10.1016/j.jclepro.2021.127223

Tzima, K., Brunton, N.P., Lyng, J.G., Frontuto, D., Rai, D.K., 2021. The effect of pulsed electric field as a pre-treatment step in ultrasound assisted extraction of phenolic compounds from fresh rosemary and thyme by-products. Innov. Food Sci.

Emerg. Technol. 69, 102644. https://doi.org/10.1016/j.ifset.2021.102644

Wrona, O., Rafińska, K., Możeński, C., Buszewski, B., 2017. Supercritical fluid extraction of bioactive compounds from plant materials. J. AOAC Int. 100 (6), 1624–1635. https://doi.org/10.5740/jaoacint.17-0232

Zhou, J., Gullón, B., Wang, M., Gullón, P., Lorenzo, J.M., Barba, F.J., 2021. The application of supercritical fluids technology to recover healthy valuable compounds from marine and agricultural food processing by-products: a Review. Processes 9 (2), 357. https://doi.org/10.3390/pr9020357