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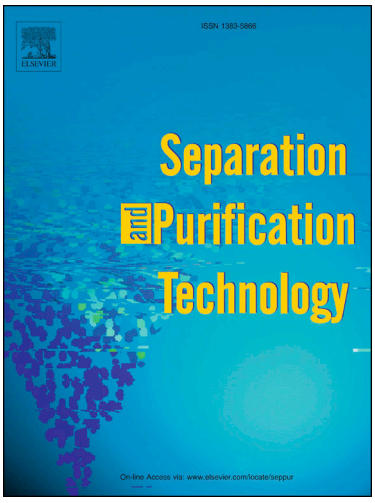

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USING BIOBASED SOLVENTS FOR THE EXTRACTION OF PHENOLIC COMPOUNDS FROM KIWIFRUIT INDUSTRY WASTE

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ABSTRACT

Valorization of wastes rich in valuable compounds is one of the most relevant topics in biorefinery and circular economy. Kiwifruit industry wastes are a potential source of bioactive compounds, such as phenolic compounds, which, in turn, exhibit many biological activities with potential health benefits. With the aim of developing a green approach for the valorization of kiwifruit waste, a study combining biobased solvents, and alternative extraction techniques for the recovery of phenolic compounds from by-products of kiwifruits (Actinidia deliciosa) 'Hayward' are presented. First, a pre-selection of the most suitable by-product for the recovery of phenolic compounds was done, being the peels the most promising. After, extractions using different biobased solvents mixtures with ethanol and/or water, was carried out. Gamma-valerolactone (GVL) mixtures yielded extracts with the highest phenolic compounds and antioxidant activity levels. The composition of GVL mixtures was optimized to GVL:ethanol in a ratio of 7:3 (wt/wt). Response surface methodology was used to optimize the operating conditions of different extraction techniques namely, conventional extraction and alternative techniques of ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE). MAE has shown to be the most promising technique to obtain an extract with high levels of phenolic compounds (TPC: 29.7 ± 0.6 mg GAE/g DW; epicatechin derivatives as the main constituents, achieving a total of 2.295 ± 0.005 mg/g DW) and the highest antioxidant activity (FRAP: 87 ± 4 mg TE/g DW, ABTS: 131 ± 1mg TE/g DW), in a shorter extraction time, as well as, when considering the estimated costs of the extraction processes. The results obtained showed the potential of using bio-based solvents (i.e. GVL) especially combined with alternative extraction techniques, to efficiently extract phenolic compounds from kiwifruit peels, paving the way for their use in the valorization of other waste rich in high-value compounds.

KEYWORDS: By-product, kiwi, solid-liquid extraction, phenolic compound, epicatechin, antioxidant activity.

INTRODUCTION

Worldwide food waste is a global problem that negatively impacts the economy, ecology, and society. According to the Food and Agriculture Organization (FAO), about a third of global food production, *i.e.*, more than 1.3 billion tons of food, are wasted [1]. Fruits, vegetables, roots and tubers have the highest wastage rates of any food staple, *ca.* of 40-50% [2]. Most of these wastes, especially fruits and vegetables, still contain many valuable components [3]. The recovery of phenolic compounds with high antioxidant activity from food waste has received significant attention. The widespread interest in phenolic compounds stems from their wide range of biological properties, *e.g.* anti-inflammatory, antioxidant and antimicrobial activities [4]. These properties make them interesting to be reused in new products, such as the preparation of cosmetics and nutraceutical formulations [5], contributing to the production of value-added products and, at the same time, to environmental sustainability by the valorization of natural resources.

Kiwifruit has been called the "king of fruits", since it is an excellent source of bioactive compounds, especially vitamin C and phenolic compounds (tannins, flavanols and phenolic acids). Kiwifruit is an edible berry native from China of the genus *Actinidia* and Actinidiaceae family. The cultivar *Actinidia deliciosa* 'Hayward' represents about half the kiwifruits produced in the world [6]. This species presents a hairy brown skin and is characterized by a bright green flesh, with a distinctive flavor and high nutritional level [7]. In 2020, global kiwifruit production reached 4.86 million tons [8], within the European Union reaching 923 thousand tons [9]. However, 5 to 20% of the produced fruits cannot be commercialized due to size or appearance reasons [10]. Beyond the kiwifruits that are rejected, the kiwifruit processing industry also generates a high number

of by-products, including seeds, peels, pomace, and pruning remains [11]. Thus, kiwifruit industry produces a considerable amount of residues, which represents the waste of an important source of valuable compounds, including phenolic compounds. The phenolic composition of kiwifruit varies with multiple factors including fruit species, horticultural practices, soil type, growing region, storage ripening conditions, and fruit maturity [4].

Currently, extraction of phenolic compounds from biomass, including kiwifruit, is commonly carried out with conventional techniques, including, maceration, soxhlet and conventional solid-liquid extraction (SLE). However, these techniques present several disadvantages, such as long extraction times and low extraction selectivity and yield [12,13]. New extraction techniques for the recovery of phenolic compounds from kiwifruits have also been proposed as alternatives, namely ultrasound-assisted extraction (UAE) [14], microwave-assisted extraction (MAE) [15] and high-pressure SLE (HP-SLE) [16,17]. For example, Carbone *et al.* [15] showed that MAE leads extracts with higher total phenolic content (TPC = 4.8 mg GAE/g DW) than conventional techniques (TPC < 2.0 mg GAE/g DW). Guthrie *et al.* [17] also showed that the alternative technique HP-SLE based on the use of subcritical water allows a more efficient extraction of phenolic antioxidants from kiwifruit peels (TPC: 51.2 mg GAE/g DW) than conventional SLE with a mixture of ethanol:water (5:5 wt/wt) and at the same pH (TPC = 26.2 mg GAE/g DW).

Volatile organic solvents (VOCs), such as acetone, for the extraction of phenolic compounds from kiwifruits are still the preferred choice [5]. However, solvents such as ionic liquids and eutectic solvents have emerged as promising alternatives to overcome some of the concerns associated with the use of VOCs in the extraction of bioactive compounds from biomass, either regarding their environmental footprint or when used

for the extraction of target compounds envisioned for human consumption [18,19]. In the same line, biobased solvents, sustainable solvents derived from renewable sources, such as alkanediols, dihydrolevoglucosenone (also known as cyrene) and gamma-valerolactone (GVL) and have been introduced as benign and less toxic solvents than volatile organic compounds, being thus an option in the extraction of bioactive compounds from natural sources [20]. Aqueous solutions of 1,2-ethanediol and 1,2-propanediol demonstrated high efficiency for the extraction of phenolic compounds (quercetin, coumaroylquinic acid, caffeoylquinic acid) from walnut leaves [21]. Despite their potential, biobased solvents have yet been scarcely investigated in the extraction of phenolic compounds from natural sources and have never been used to extract phenolic compounds from kiwifruit. Specifically, cyrene and GVL has not yet been used in biomass extraction processes, being crucial to test its efficiency. Thus, it is important to develop a sustainable and effective extraction process that can recover bioactive compounds that would otherwise be wasted, allowing the food waste to be valorized, fulfilling the sustainable development goals (SDG), and the development of a bioeconomy based on renewable resources.

In this work, biobased solvents combined with alternative extraction techniques were used to the extraction of phenolic compounds from peels of the kiwifruit cultivar *Actinidia deliciosa* 'Hayward'. Several ethanolic and aqueous solutions of biobased solvents (GVL and alkanediols) were evaluated and compared with common solvents. After the selection of the best solvent, experimental conditions for each extraction technique were optimized in order to compare the extraction efficiency of advanced techniques (UAE and MAE) with conventional extraction. Extraction conditions, namely, temperature/amplitude, extraction time and S/L ratio, were optimized by a response

surface methodology (RSM). Then, the identification of the main phenolic compounds of the optimized extracts was carried out. Finally, a simple economic study was carried out to understand which extraction technique is the most promising for extracting phenolic compounds from kiwifruit peels and to verify the advantage of using green chemistry tools on food waste valorization.

EXPERIMENTAL SECTION

Chemicals

The chemical compounds used in this work are summarized in Table 1 and the structures and the physicochemical of the solvents used in the extraction of the phenolic compounds from kiwifruit are presented in Figure S1 and Table S1, respectively. The water was double distilled, passed across a reverse osmosis system, and further treated with a Milli-Q plus 185 water purification device.

Table 1. List of substances used in this work, including the abbreviation, CAS number, purity and source.

Compound	Abbreviation	CAS number	Purity (wt%)	Source
[2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonate)]	ABTS	30931-67-0	98	Sigma
Acetic acid	---	64-19-7	≥99.7	Fisher Chemical
Acetone	Ace	67-64-1	100	Fisher Scientific
Acetonitrile	---	75-05-8	>99	Sigma
Caffeic acid	---	331-39-5	99	Acros

(+)-Catechin hydrate	---	225937-10-0	>98.0	Sigma
Cyrene	----	53716-82-8	99%	Sigma-Aldrich
1,2-Ethanediol or Ethylene glycol	ETG	107-21-1	99.5	Carlo Erba
Ethanol	EtOH	64-17-5	99.0	Fisher Scientific
(−)-Epicatechin	---	490-46-0	≥90	Sigma-Aldrich
Ferulic acid	---	537-98-4	99	TCI
Folin-Ciocalteu	---	n.a.	n.a.	Panreac
Formic acid	---	64-18-6	>98.0	Sigma
Gallic acid	GA	149-91-7	99.5	Merck
Hydrochloric acid	HCl	7647-01-0	37	Honeywell
1,6-hexanediol	HEX	629-11-8	97	Acros Organics
Iron (III) chloride hexahydrate	---	10025-77-1	99	Merck
Methanol	MeOH	67-56-1	99.8	Fisher Chemical
1,2-propanediol	PRO	57-55-6	99.5	Sigma-Aldrich
Potassium persulfate	---	7727-21-1	extra pure	Scharlau
Quercetin	---	117-39-5	> 95	Sigma-Aldrich
Sodium acetate	---	127-09-3	99	Prolabo (JMS)
Sodium carbonate	---	497-19-8	99	Vencilab
Sodium hydroxide	--	1310-73-2	98	Fisher
Syringic acid	---	530-57-4	>97	Acros Organics

2,4,6-Tris(2-pyridyl)-s-triazine	TPTZ	3682-35-7	>99	Sigma-Aldrich
Trolox	---	53188-07-1	97	Acros Organics
Gamma-valerolactone	GVL	108-29-2	98	Acros Organics

Biomass collection, selection and storage

Kiwifruit (*Actinidia deliciosa*) belonging to the 'Hayward' cultivar were purchased at a local producer from Vila Nova de Famalicão, Braga, Portugal. Kiwifruits were peeled and processed into juice and pulp. Whole kiwifruits (with peel) were also processed in a blender. Samples obtained (peels, pulp, juice and whole kiwifruit) were stored at -80 °C. Before extraction, samples were immersed in liquid nitrogen and grounded in a coffee grinder to obtain a powder. To select the kiwifruit part richest in phenolic compounds, soxhlet extraction for each type of sample (peels, pulp, juice, and whole kiwifruit) was performed for 6 h, using ethanol as the solvent and a solid:liquid ratio (S/L ratio), here defined as the mass of kiwifruit residue per mass of solvent, of 1:30. Then, the impact of the storage procedure on the total phenolic content of selected biomass was evaluated. In this study, biomass stored was used under three different conditions: (i) driy at room temperature and then stored at -10 °C; (ii) stored at -10 °C and (iii) stored at -80 °C. After a minimum of two weeks, the samples stored under the different conditions were analyzed.

The choice of biomass and storage conditions was made based on the TPC and antioxidant activity of an extract, measured by the ferric reductive antioxidant power (FRAP) and [2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonate)] (ABTS) methods, as described below. Notice that the combination of different methodologies (FRAP and

ABTS) to evaluate the antioxidant activity of the extracts is important, since the oxidizing agents can be affected differently by conditions such as the nature of the compounds present in the matrix, the pH of the solution, etc.

Selection of the best biobased solvent for the extraction of phenolic compounds

Extractions using different biobased solvents 1,2-ethanediol, 1,2-propanediol, 1,6-hexanediol, cyrene and GVL were performed. These solvents were applied pure and as binary mixtures by combining them with water or ethanol in the weight ratios 3:7 and 7:3. The extraction using 1,6-hexanediol was not performed, because this solvent is solid at room temperature. These were also used in ternary mixtures composed of biobased solvent, ethanol and water in the weight ratio of 4:4:2, respectively. All mixtures were prepared gravimetrically with an uncertainty of ± 10^{-4} g. The extraction of phenolic compounds from selected biomass was carried out in a Carousel Radleys Tech at constant stirring 500 rpm, 25 °C, S/L ratio of 1:20, during 60 min. The extraction of phenolic compounds using conventional solvents - water, acetone, methanol, ethanol, and a mixture of ethanol:water (weight ratios 3:7 and7:3) - without and with pH control at pH 2 (by adding HCl at 1 mol/L) were also performed for comparison purposes. After extraction, mixtures were centrifugated at 5000 rpm, 15 °C for 15 min. Supernatants were collected to separate the biomass from the extract. The supernatants were filtrated and stored at 4 °C until the analysis of the total phenolics and antioxidant capacity. All the experiments were executed protected from light since phenolic compounds are photosensitive. Each extraction was carried out in triplicate to determine the average content of phenolic compounds extracts and the respective standard deviation.

Phenolic compounds assays

The TPC of kiwifruit extracts was determined by the Folin-Ciocalteu method, according to the methodology proposed by Koşar *et al.* [22] with modification. The absorbance was measured at 760 nm in a microplate reader (UV-visible spectroscopy SYNERGY|HT microplate reader from BioTek). All analyses were carried out in triplicate and TPC was determined from a calibration curve previously established and by using gallic acid as the standard. The results were reported as mg GAE/g DW.

Antioxidant assays

The antioxidant capacity of the extract was evaluated by measuring FRAP and ABTS free radical scavenging activities. The FRAP assay of the extracts was carried out according to Benzie *et al.* [23] with few modifications. The extracts were diluted up to 100 times in water. The FRAP reagent prepared contained 300 mmol/L acetate buffer (pH 3.60), 10 mmol/L TPTZ in 40 mmol/L HCl, and 20 mmol/L $FeCl_3$, at a ratio of 10:1:1 (v/v/v). A volume of 10 µL of extract was mixed with 290 µL of FRAP reagent in a microplate, which was incubated for 30 min at 37 °C, in the absence of light. The absorbance was measured at 593 nm in a microplate reader. Trolox was used as standard to prepare the calibration curve to determine FRAP. Each experiment was repeated five times. The results were expressed in milligrams of trolox equivalent per gram of dry weight of biomass (mg TE/g DW).

The ABTS assay of the extracts was carried out according to Re *et al*. [24] with few modifications. Two stock solutions, 7 mmol/L ABTS solution and 2.45 mmol/L potassium persulfate solution, were mixed in a ratio of 1:1 (v/v), followed by the incubation for 16 h at 25 °C in the dark to react and produce the radical $ABTS^{\bullet}$. To study

the antioxidant activity, the ABTS• solution was diluted with distilled water to an absorbance of ≈ 0.70 at 734 nm. Kiwifruit extracts were diluted up to 100 times in water. Then, 280 µL of ABTS• and 20 µL of each extract sample were added to a microplate. Blank (20 µL of diluted solvent, 280 µL ABTS•) and control of each sample (20 µL of diluted extract, 280 µL of distilled water) were also prepared. The microplate was incubated in the dark for 30 min at 25 °C, and then the absorbance was recorded at 734 nm using a microplate reader. Each experiment was repeated five times. The antioxidant activity (AA%) of the samples was calculated using the following equation:

$$\mathrm{AA\%} = 100 - \left(\frac{Abs_{sample} - Abs_{control}}{Abs_{blank}}\right) \times 100 \qquad \text{(Eq. 1)}$$

where, Abs_{sample}, Abs_{blank} and $Abs_{control}$ are the sample, control and blank absorbance values, respectively. The results were reported in mg TE/g DW.

Mixture design

Experimental planning for mixtures optimization as extraction solvents is a valuable tool to study the synergistic or antagonistic effects of the components and, consequently to determine the optimum solvent composition [25]. The independent variables evaluated were water, GVL and ethanol from 0 to 100 wt% using fourteen different assays (Table S2). Extractions of phenolic compounds from selected biomass were carried out in a carousel under the conditions previously reported. Samples were centrifuged and the supernatant was collected, filtered and stored at 4 °C until the

determination of the response variables – TPC, FRAP and ABTS. All the experiments were carried out protected from light.

Response surface methodology (RSM)

The response surface methodology (RSM), such as the central composite design, is a multivariate statistical tool applied to optimize the extraction conditions of phenolic compounds from selected biomass. The relationship between the response and the independent variables was modelled according to this polynomial equation:

$$y = \beta_0 + \sum_{i=1}^{k} \beta_I X_I + \sum_{i=1}^{k} \beta_{ii} X_i^2 + \sum_{i<j}^{k} \beta_i \beta_j X_i X_j \qquad \text{(Eq. 2)}$$

where, β_0 represents the intercept or regression coefficient, β_i, β_{ii} and β_{ij} are the linear, quadratic and interaction coefficients, respectively, X_i and X_j are the independent variables, while k is the number of variables studied that can influence the response y. In this work, the independent variables were submitted to a factorial planning of 2^3 (3 variables, and 2 levels) to optimize the total phenolic content and antioxidant activity, using the optimized solvent composition previously determined by the design of mixture (GVL:ethanol, 7:3 wt/wt). The function responses measured were total phenolic content (by TPC) and antioxidant activity of the extracts (by FRAP and ABTS assays) to maximize the phenolic compounds content and the antioxidant activity of kiwifruit extracts. Twenty experiments were carried out and the conditions used are detailed in Table S3. The obtained results were statistically analyzed with a confidence level of 95%. The significance of the models, as well as the lack-of-fit, were evaluated by the analysis of variance (ANOVA). Coefficient of determination (R^2) and adequate precision

were used to estimate the adequacy of the polynomial equation to the response. The experimental design, statistical analysis and regression model were executed using the Statistic Software Version 10.

In this work, 3 factorial planning were executed, each one by applying different techniques of extraction. The first factorial planning was a conventional extraction, where the temperature (*T*), extraction time (*t*) and S/L ratio were optimized. The 2^3 factorial planning used is described in Table S4. The second factorial planning was an UAE carried out in an ultrasonic processor (Branson, Digital Sonifier 450) with a maximal power of 400 W. In this factorial plan, the amplitude (Amp), extraction time and S/L ratio were varied. Details are given in Table S5. Note that amplitude affects the amount of power applied during the experiment, where 100% of amplitude in this equipment corresponds to 400W. Thus, the higher the amplitude, the higher the power, and consequently the higher the energy input to the experiment. The third and last factorial planning corresponded to MAE done by a Monowave 300 microwave synthesis reactor from Anton Paar. The variables investigated in this methodology were temperature, extraction time and S/L ratio according to the experimental conditions evidenced in Table S6. After extraction, samples were centrifuged (conditions described above) and the supernatant filtered and stored at 4 °C until TPC and antioxidant activity assays (FRAP and ABTS) were determined. All the experiments were carried out protected from light.

Chemical characterization of the optimized extracts

High performance thin layer chromatography (HPTLC)

HPTLC analyses were performed using Merck (0.20 mm) silica gel 60 F254 (20 cm × 10 cm) glass HPTLC analytical plate using a Camag HPTLC system equipped with

an automatic TLC sampler (ATS 4), an automatic developing chamber ADC2 with humidity control and a visualizer controlled with WinCATS software.

All HPTLC analyses were carried out as previously reported by Do *et al*. [26] with a few modifications. HPTLC plates were developed from the lower edge of the plate until 70 mm. Before the development of the plates, the humidity was monitored within the development chamber and kept between 33 and 38 % of relative humidity, for 20 min. Then, the solvent was added and left for 20 min in order to reach saturation within the chamber. Visual check of the plate was carried out under 254 nm and 366 nm and white light to confirm the absence of impurities or contaminants. Each standard and sample solution were applied in triplicates on the same plate, bandwise. First track was applied to start at a distance of 15 mm from the edge of the plate. Each track was of 8 mm length, distance between each track was 2.6 mm and spraying speed was 50 nL/s. The plates were developed with a mixture of ethyl acetate:formic acid:acetic acid:water (100:11:11:26, v/v/v/v), a mobile phase often used for polyphenols analysis [27]. Plates were then dried for 5 min and recording of the developed plates was carried out under 254 nm and 366 nm and white light. The plate was finely cut into three identical plates using a glass cutter in order to be submitted to different derivatization.

Flavanols, further phenolics and tanning agents were visualized with the fast blue B salt derivatizing reagent as reported by Pedan *et al*. [28]. The derivatizing reagent led to the compounds develop a reddish color on a colorless background. To that end, a dried HPTLC plate was heated at 100 °C for 2 min on a TLC plate heater (CAMAG) and cooled down to room temperature for 1.5 min prior to derivatization. The derivatization solution was prepared by dissolving 140 mg fast blue B salt in a mixture of 140 mL methanol, 10 mL water, and 50 mL dichloromethane. Derivatization was done in the CAMAG TLC

Immersion Device III (vertical speed 5 cm/s, dwell time 0 s). After immersion, the plate was dried for 30 s with a stream of cold air using a hair dryer and documented under white light.

Visualization of flavanols, phenols and further natural compounds was done using NPA solution followed by a p-anisaldehyde derivatization as reported by Pedan *et al*. [28] with slight modifications. First, the plate was immersed (vertical speed 5 cm/s, dwell time 0 s) into a NPA solution (1 g of 2-aminoethyl diphenylborinate in 200 mL of ethyl acetate), dried for 1 min in a stream of warm air and documented under UV at 366 nm. Second, the same plate was immersed with a dwell time of 0 s and 5 cm/s, dipping into the anisaldehyde derivatization reagent (0.5 mL anisaldehyde, 10 mL acetic acid, 85 mL methanol, and 10 mL sulfuric acid), warmed at 100 °C for 5 min and documented under UV at 366 nm.

The post-chromatographic derivatization with DPPH was carried out as previously described [29]. The plate was immersed with a dwell time of 0 s and 5 cm/s, dipping into a DPPH solution (0.4 g of 2,2-diphenyl-1-picrylhydrazyl in 200 mL of methanol). After immersion, the plate was incubated in the dark for 30 min before documentation under white light. The antioxidants appeared whitish yellow on a violet background.

Ultra-high pressure liquid chromatography (UHPLC) analysis

The optimized kiwifruit extracts were firstly filtered using PTFE filters with 0.2 µm pore diameter for ultra-high performance liquid chromatography with diode array detection coupled to tandem mass spectrometry (UHPLC-DAD-MS^n) analysis. Extracts (20 µL) were injected in the UHPLC system equipped with an Accela 600 LC pump, an Accela autosampler (set at 16 ºC) and an Accela 80 Hz photo diode array detector (DAD).

The separation of extract components was developed in a Hypersil Gold RP C18 column (100 x 2.1 mm; 1.9 µm particle size), preceded by a C18 pre-column (2.1 mm i.d.), and both were kept at 40 ºC. The binary mobile phase included (A) water:acetonitrile (99:1, v/v) and (B) acetonitrile, both containing 0.1 % (v/v) formic acid. A gradient elution program was applied at a flow rate of 0.40 mL/min for 32 min, as follows: 1 % B kept from 0 to 1 min; 1-4 % B from 1 to 3 min; 4-27 % B from 3 to 17 min; 27-46 % B from 17 to 19 min and 46-100 % B from 19 to 22 min. Before the next run, the B percentage was reduced from 100 to 1 % for 4 min, and then kept at 1 % B for 4 min. The chromatograms were recorded at 280 nm, 325 nm and 370 nm, and the molecular absorption spectra between 210 and 600 nm.

The UHPLC system was coupled to a LCQ Fleet ion trap mass spectrometer equipped with an electrospray ionization (ESI) source. The ESI-MS was operated under the negative ionization mode with a spray voltage of 5 kV and capillary temperature of 320 ºC. The flow rate of nitrogen sheath and auxiliary gas were 40 and 5 (arbitrary units), respectively. The capillary and tube lens voltages were set at -44 and -225 V, respectively. Collision induced dissociation-MS^n experiments were executed on mass-selected precursor ions in the range of m/z 100-2000. The isolation width of precursor ions was 1.0 mass units. The scan time was 100 ms and the collision energy was 35 arbitrary units, using helium as collision gas. The data acquisition was carried out using Xcalibur® data system.

Evaluation of the economic viability of the extraction techniques

To better understand the economic viability of the three extraction techniques studied (conventional, UAE, and MAE), the following equation was used:

$$R = [C_{\text{pro}} \times €_{prod} - €_{biom}] - [V_{\text{BB}} \times €_{BB} \times r_{BB\,lost} \times \alpha + \beta] - \gamma \quad \text{(Eq. 3)}$$

This equation is based on the equation proposed by Passos *et al.* [30] with slight modifications. The equation proposed by Passos *et al.* [30] is a simplified model that relates the return (R) associated with the extraction of a particular value-added compound (phenolic compounds in this case) when alternative solvents (biobased solvents (BB), in this case) are used. Here the variable costs associated with energetic consumption (γ) was added to the equation. The variable C_{prod} is the concentration of the target compounds in the biomass (here, the value of total epicatechin derivatives extracted were considered), $€_{prod}$ is the price of the product per kg, and $€_{biom}$ is the cost associated with the biomass (which here was considered zero since the biomass used is a by-product). The extraction process cost is assumed to be proportional to the cost of BB lost per each kg of biomass treated. The variable V_{BB} is the volume of the BB needed to treat one kg of biomass, $€_{BB}$ is the price per kg, and $r_{BB\,lost}$ is the ratio of BB lost during the recycling approach, which is 100 % since in this study is not pretended to recycle the BB. Factors α and β represent the proportional costs of the process and nonproportional costs, respectively. With the application of this equation, it is possible to know which variables exhibit a significant impact on the return of a given process.

The main variables (*e.g.,* solid-liquid ratio that gives us the volume of solvent (V_{BB}) to treat a determined amount of biomass) for each extraction technique, including the energetic inputs used, are described in Table S7. The energy spent by each equipment during extraction was measured using an energy consumption meter, and it was considered that 1 kWh costs 0.15 € (electricity prices for companies in Portugal) [31]. All

the techniques have in common the BB concentration - GVL:EtOH (7:3 wt/wt) - and its price, which was considered 3.65 €/L (GVL = 5 kg/€, ethanol = 0.5 kg/€) taking into account that industrial reagents are acquired [32] and there is no recovery of the solvent (r_{BB} lost = 1). Furthermore, to keep this approach simple α and β have been considered one and zero respectively.

RESULTS AND DISCUSSION

Biomass collection, selection and storage

Kiwifruit peel, pulp and juice present different levels of phenolic compounds and antioxidant activity as mentioned above. Thus, the total phenolic content of the whole fruit and of different parts of kiwifruit, namely peel, pulp (including seeds) and juice, were studied individually, being the last used for comparison purposes. Polyphenols content (TPC) and antioxidant activity (FRAP and ABTS) were determined for each sample. Results obtained for TPC, FRAP and ABTS were found to follow the order: peels > whole fruit > pulp > juice (*cf.* Table S8 and Figure S2). Therefore, kiwifruit peels were identified and selected as the most promising kiwifruit residue to be used in the extraction of phenolic compounds, which is in agreement with literature results [33].All remaining experiments of this work were carried out by using kiwifruit peels.

The influence of different storage conditions (biomass dried at room temperature and stored at -10 ºC, fresh biomass stored at -10 ºC and -80 ºC) on the total phenolic content of peels was also investigated. The results obtained for TPC, FRAP and ABTS follow the order: fresh biomass stored at -80 ºC > fresh biomass stored at -10 ºC >> biomass dried and stored at -10 ºC. Results show that storing the fresh kiwifruit directly at -80 °C is the most efficient way to protect the total phenolic content and antioxidant

activity of kiwifruit peels (Table S9 and Figure S3). The decrease observed in TPC for the dried samples was also reported by other authors in the extraction of phenolic compounds from kiwifruit [34] or other fruits [35–38]. It is known that some phenolic compounds are quite sensitive to heat, i.e., they can be degraded or biotransformed at high temperatures, although we dried the kiwifruit peels at room temperature. On the other hand, drying at low temperatures does not completely inactivate oxidative and hydrolytic enzymes, resulting in the oxidation of phenolic substances, especially for long processes where a notable reduction of phenolic compounds can be observed [39]. In addition, a decrease in antioxidant activity was also observed for the dried samples, since a reduction in TPC, generally, results in a decrease in antioxidant activity, which is in agreement with the results obtained by Izli *et al.* [34]. Thus, the drying treatment may lead to the degradation of phenolic compounds and loss of antioxidant constituents from kiwifruit

Selection of the best biobased solvent for the extraction of phenolic compounds

Biobased solvents and their mixtures (biobased solvent + water, biobased solvent + ethanol and biobased solvent + ethanol + water) were investigated to evaluate their ability to extract phenolic compounds from kiwifruit peels. The biobased solvents chosen to extract phenolic compounds from kiwifruit were the following 1,2-ethanediol, 1,2-propanediol, 1,6-hexanediol, cryene and GVL. The choice of these solvents took into account two main aspects: i) to study biosolvents that had already been used in the extraction of biomass compounds such as alkanediols, especially 1,2-ethanediol, 1,2-propanediol [21], but usually more in the form of DES [40–43], while 1,6-hexanediol was used to try to understand the effect of increasing the chain length in the extraction of

phenolic compounds; ii) study new biosolvents that have not been explored in the extraction of value-added compounds from biomass, especially from food waste, such as cyrene and GVL, with these two solvents having the advantage of being applied as a green solvent in the pharmaceutical industry [44,45] or as food additive [46,47], respectively. Results are presented in Figure 1 (detailed experimental data are provided in Table S10). The antioxidant activity of the solvents used here was confirmed to be negligible. The only exception was the biobased solvent cyrene and their mixtures that showed to have antioxidant activity, perhaps due to the aromatic ring present in its structure. Thus, the extracts obtained with cyrene could not be quantified by any of the methods studied (TPC, FRAP and ABTS), and this solvent was not considered in the fowling steps. Moreover, the extraction using pure 1,6-hexanediol was not performed, because this solvent is solid at room temperature.

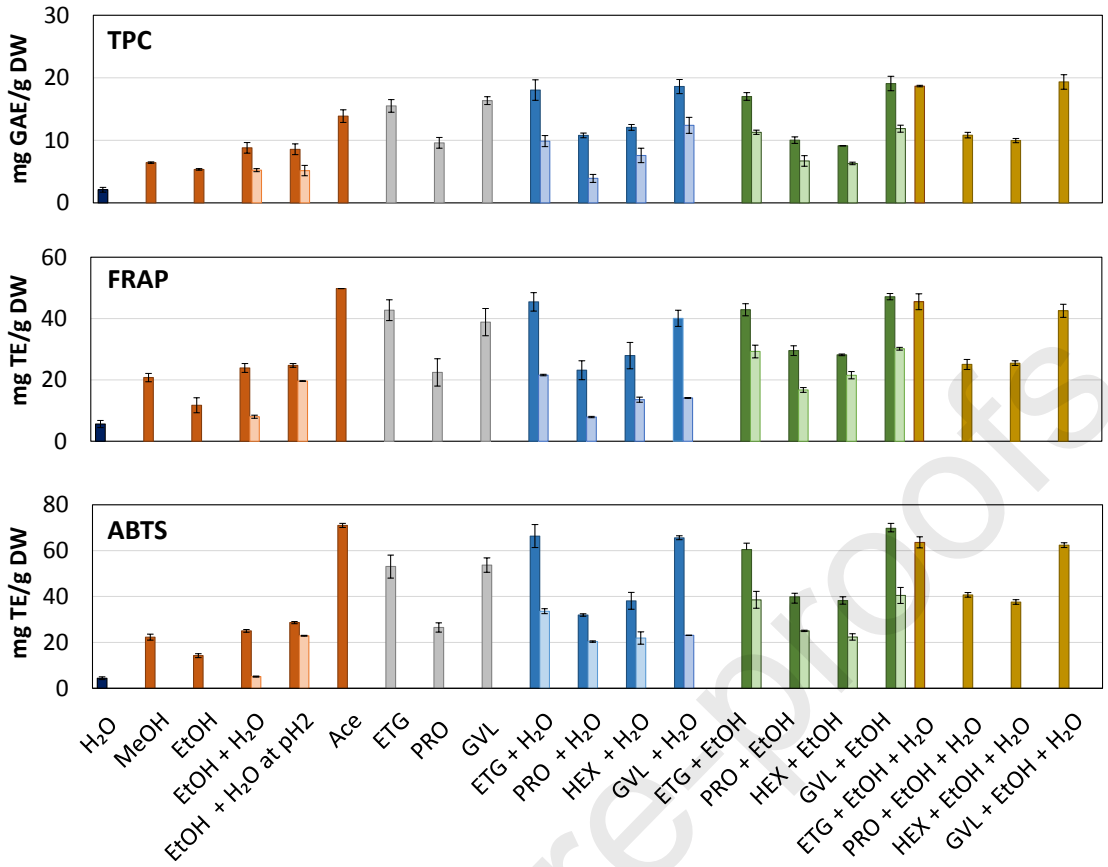

Figure 1. Evaluation of the total phenolic content (TPC) and the antioxidant activity (FRAP and ABTS) of kiwifruit peels extracts obtained by using conventional solvents (orange), biobased solvents (grey), binary mixtures of biobased solvents with water (blue) or ethanol (green) in a weight ratio of 3:7 (dark color) and 7:3 (light color), and ternary mixtures composed of biobased solvent, ethanol and water in a weight ratio of 4:4:2 (brown). Solvents nomenclature can be found in Table 1.

As shown in Figure 1, extracts obtained with biobased solvents and their mixtures present higher levels of total phenolic content and antioxidant activity than those obtained with conventional solvents. Binary and ternary mixtures composed of GVL and 1,2-ethanediol in weight ratios of 7:3 and 4:4:2 showed to be the best options for the

extraction of phenolic compounds, with GVL:ethanol in the ratio of 7:3 wt/wt leading to the highest extraction yield of TPC (19 ± 1) mg GAE/g DW and antioxidant properties: FRAP (47 ± 1) mg TE/g DW and ABTS (70 ± 2) mg TE/g DW. Considering mixtures based on alkanediols, the mixtures with 1,2-ethanediol lead to extracts with higher amounts of phenolic compounds and higher antioxidant activity than the others under study (1,2-propanediol and 1,6-hexanediol). These results can be explained by the effect of alkanediol alkyl chain length and, consequently, the polarity of the solvent. 1,2-Ethanediol presents a more polar structure in comparison to 1,2-propanediol and 1,6-hexanediol, since it has a shorter alkyl chain, which seems to facilitate the interaction between the phenolic compounds and the biobased solvent, as previously observed by Alañón *et al.* [42]. The authors analyzed the extraction of phenolic compounds from olive leafs using deep eutectic solvents (DES), demonstrating that choline chloride:1,2-ethanediol was the most effective DES due to its polarity and linear structure compared to choline chloride:1,2-propanediol or choline chloride:xylitol.

As seen in Figure 1, acetone was the only conventional solvent that presented better results than some biobased solvent mixtures. The high efficiency of acetone, when compared with other conventional solvents in the extraction of phenolic compounds, can be explained by the ability to act as a hydrogen bond acceptor strongly interacting with phenolic compounds by the formation of an *in situ* DES. This is in line with its facility to extract other strong antioxidant compounds, such as carotenoids, lutein, vitamin C and chlorophylls, as reported by Cassano *et al*. [48].

The influence of pH on the extraction of phenolic compounds appears to be negligible, as shown in Figure 1, Tables S10 and S11. For instance, ethanol:water (7:3 wt/wt) without pH control (pH ≈ 8) have values for TPC of (8.8 ± 0.9) mg GAE/g DW

and antioxidant activity according to FRAP and ABTS of (24 ± 1) mg TE/g DW and (25.0 ± 0.6) mg TE/g DW, respectively. These values are similar to those obtained with ethanol:water mixture (7:3 wt/wt) at pH 2, namely TPC = (8.6 ± 0.9) mg GAE/g DW and antioxydant activity using FRAP and ABTS of (24.7 ± 0.6) mg TE/g DW and (28.7 ± 0.5) mg TE/g DW, respectively. These results disagree somehow with experimental data previously reported by Aires *et al*. [49], reporting that ethanol:water (7:3 wt/wt) mixtures at pH 2 yield extracts from kiwifruit pomace with higher total phenolic content and antioxidant activities than those reported here. The differences observed between the results reported by Aires *et al*. [49] and this work can be ascribed to the different types of biomass under evaluation, since, as previously mentioned, each part of the kiwifruit has different levels and types of phenolic compounds [33], hence different solubilization properties in the extraction medium [50].

Optimization of the solvent composition

Considering the abovementioned results, binary and ternary mixtures composed of 1,2-ethanediol and GVL are the most promising solvents to obtain extracts with higher total phenolic content and antioxidant activity (*cf.* Figure 1). However, according to US Food and Drug Administration (FDA), 1,2-ethanediol belongs to Residual Solvents Class 2, implying its use is limited in pharmaceutical products due to an inherent toxicity [51]. On the other hand, GVL is present in fruits, and is frequently used as a food additive [47]. GVL and its mixtures have not been previously used to extract bioactive compounds from biomass so far, highlighting the novelty of this work. Based on its favorable properties, a ternary mixture design using GVL, ethanol and water was carried out in order to find the best solvent composition yielding an extract with high phenolic compounds content and

antioxidant activity. All analyses were carried out with a confidence level of 95% using the statistical model analysis variance (ANOVA) shown in the Supporting Information (Figures S4 and S5). The experimental and predicted results were very similar, supporting the adequability of the statistical model (all analyses present an $R^2 > 0.90$).

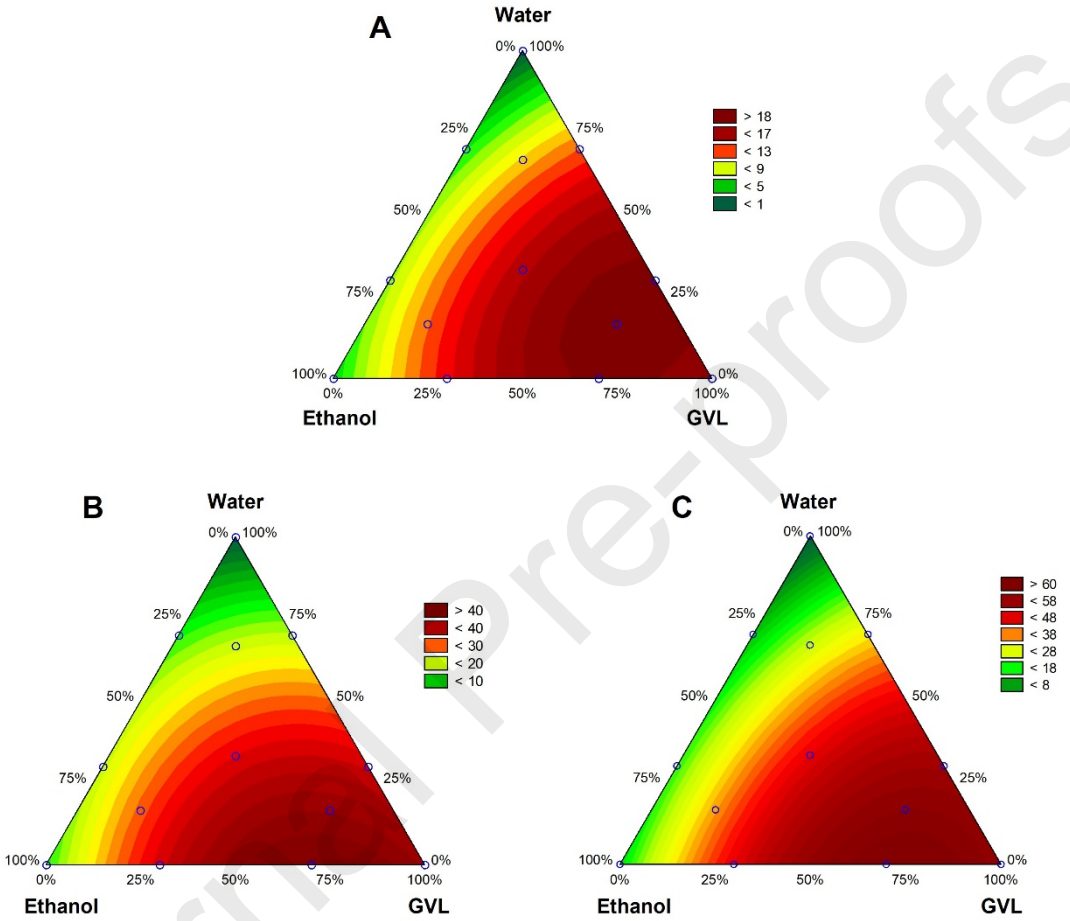

Figure 2. Response surface of (A) TPC (mg GAE/g DW), (B) FRAP (mg TE/g DW) and (C) ABTS (mg TE/g DW), as a function of the composition of the ternary mixture in weight percentage (GVL, ethanol and water).

Figure 2 presents the ternary diagrams of GVL, ethanol and water mixtures, and the corresponding TPC, FRAP, and ABTS values. All experimental data are detailed in Tables S12-S14. The isolated components GVL and ethanol, and the interaction between

GVL, ethanol and water, influenced the studied responses, as can be seen in Pareto Charts (Figures S5). According to Figure 2 and Figure S5, GVL was the most significant component, followed by ethanol. Moreover, the highest values for TPC, FRAP and ABTS are obtained with mixtures containing large amounts of GVL, typically above 70 wt%. Furthermore, a maximum value for TPC was found at a composition of approximately 55 wt%, 30 wt% and 15 wt% of GVL, ethanol and water, respectively. FRAP and ABTS were mostly influenced by GVL and ethanol, the highest values being found on the GVL/ethanol side of the ternary diagram. Therefore, in order to obtain the highest values for all three responses, namely TPC, FRAP and ABTS, the optimized mixture selected is a binary mixture of 70 wt% of GVL and 30 wt% of ethanol (*cf.* Figure S6). Using such a mixture, values for TPC, FRAP and ABTS were found to be (19 ± 1) mg GAE/g DW, (47 ± 1) mg TE/g DW and (70 ± 2) mg TE/g DW, respectively.

Optimization of extraction conditions

Univariate analysis for operational conditions optimization does not describe the interplay between variables and may not correspond to the overall optimal conditions. Therefore, a RSM was used in order to determine the relationship between the independent variables (S/L ratio, extraction time and temperature or amplitude) and the responses (TPC, FRAP and ABTS) and to optimize operating conditions. This methodology evaluates the dependence of the responses (TPC, FRAP and ABTS) on the independent variables that might influence the extraction. In this work, three 2^3 (3 variables and 2 levels) factorial plans were carried out, depending on the extraction technique used, namely conventional extraction, and two alternative techniques, the UAE

and MAE. All extractions were done by using the biobased solvent mixture previously optimized, that is, GVL:ethanol in the ratio of 7:3 (wt/wt)

Results obtained through the RSM with combined effects are depicted in Figures 3-5. Experimental conditions, TPC, FRAP and ABTS experimental results, and respective calculated values, as well as the statistical analysis, are provided in the Supporting Information. Variance analysis (ANOVA) was used in order to estimate the statistical significance of the variables and their interactions. For all response surfaces, and independently of the extraction technique evaluated, the equation of adjusted polynomial presented a R^2 value above 0.89, revealing no significant deviations between experimental and predicted responses, and demonstrating that established statistical models are suitable.

Conventional extraction

The effect of the three independent variables – S/L ratio, extraction time and temperature – on the extracts total phenolic content and antioxidant activity were obtained with conventional extraction. The results are presented in Figure 3 and Tables S15-S17 and Figures S7-S9.

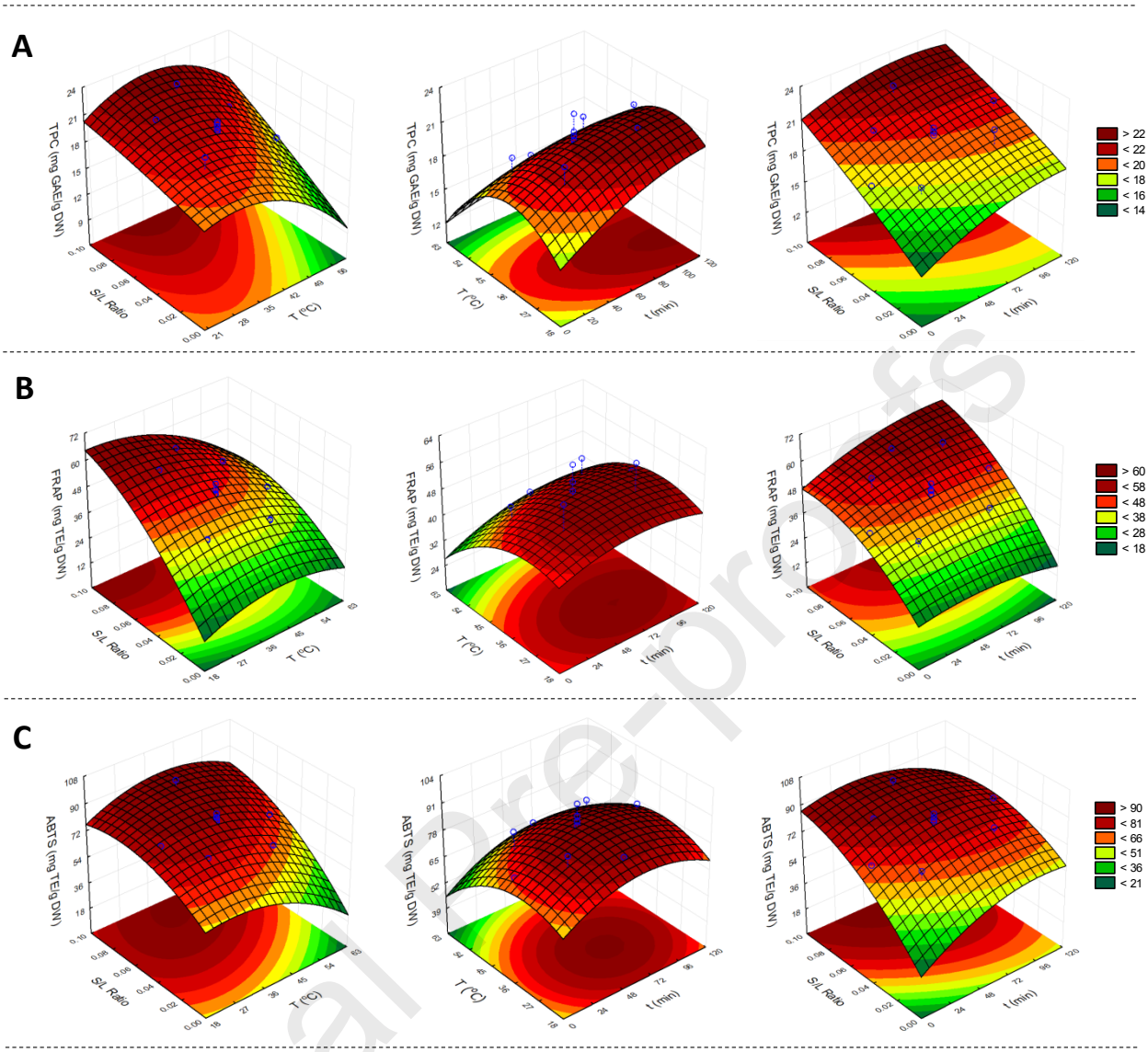

Figure 3. Response surface plot of (A) TPC, (B) FRAP and (C) ABTS assays, representing the influence of S/L ratio and temperature (left side); temperature and time (middle), and S/L ratio and time (right side), for the conventional extraction technique using a mixture of GVL:ethanol (7:3 wt/wt).

For the three response variables in study, namely TPC, FRAP and ABTS, S/L ratio was the most significant variable, followed by temperature and extraction time, as evidenced in the Pareto chart (Figure S8). The S/L ratio had a positive effect, *i.e.*, the total

phenolic content and antioxidant activity increased with the increase of this variable. The temperature and time of extraction had a positive impact on the total phenolic content and antioxidant activity of the obtained extracts up to a maximum at temperatures between 25 °C and 40 °C, and of time of extraction between 45 and 75 minutes. To obtain an extract with high total phenolic content and high antioxidant activity, a compromise between the different studied variable values was necessary in order to maximize the three responses. Best conditions identified here were T = 36 °C, S/L ratio = 1:12 and t = 60 min (Figure S9). Since the optimal S/L ratio was also the maximum value used in the experimental planning, temperature and time optimal conditions were evaluated at higher S/L ratio values (1:10 and 1:8). Results showed that an increase in S/L ratio above 1:12 had no positive effect on the extracts total phenolic content and antioxidant activities (*cf.* Table S18 and Figure S10), in agreement with the optimal extractions conditions determined within the experimental planning. At these conditions, the experimental results obtained were: TPC = (21.4 ± 0.5) mg GAE/g DW, FRAP = (61.3 ± 0.4) mg TE/g DW and ABTS = (92.0 ± 0.8) mg TE/g DW (for predicted results, see Figure S9). The experimental and predicted results were in good agreement, demonstrating the good predictive ability of these models.

Ultrasound assisted extraction (UAE)

The influence of the ultrasound extraction technique on the total phenolic content and antioxidant activity was evaluated by considering the following variables: S/L ratio, extraction time and amplitude. The temperature was monitored during the extraction procedures and was found to vary in a similar range to that used in MAE, namely from 30 to 80 ºC. The influence of the three variables on the total phenolic content and

antioxidant activity when the extractions were performed by UAE is presented in Figure 4, while more details can be found in Tables S19-S21and Figures S11-S13.

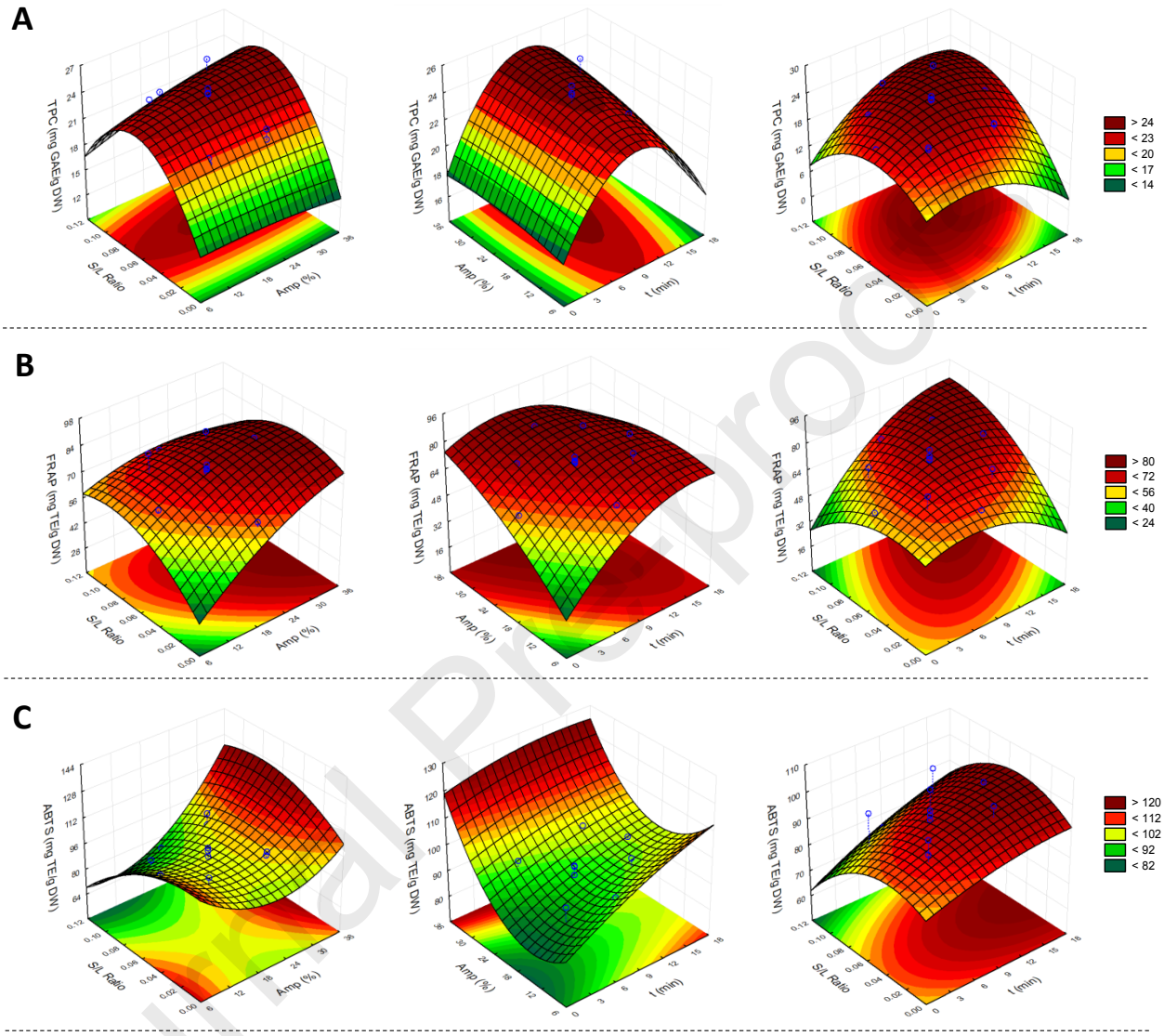

Figure 4. Response surface plots of (A) TPC, (B) FRAP and (C) ABTS assays, representing the influence of S/L ratio and amplitude (left side); amplitude and time (middle), and S/L ratio and time (right side), for the UAE technique, using a mixture of GVL:ethanol (7:3 wt/wt).

According to Pareto Charts (Figure S12) and data depicted in Figure 4, almost all variables and their interactions were significant, though to different extents, for the three responses under evaluation. Extraction time had a positive effect on all responses until a certain point with a region of maximum at extraction times between 10 and 12 min. Furthermore, this variable was the most significant for FRAP and ABTS, while presenting a slightly lower impact on TPC. Furthermore, the S/L ratio presented a similar behavior to the extraction time on the extracts' total phenolic content and antioxidant activity. Responses maximum values were observed at a S/L ratio between 1:17 and 1:12. On the other hand, ultrasound amplitude influenced mainly FRAP and ABTS. FRAP is maximum for amplitude values between 22% and 30%, while ABTS, despite the cell point observed in Figure 4C generally, can be said that increase with increasing amplitude.Aiming for a good compromise between the different extraction conditions, the following operating conditions for UAE were selected: Amp = 28%, S/L ratio = 1:13 and t = 12 min (*cf.* Figure S13). At these conditions the experimental results were: TPC = (24 ± 1) mg GAE/g DW, FRAP = (81 ± 4) mg TE/g DW and ABTS = (104 ± 2) mg TE/g DW (for predicted results, see Figure S13). As previously observed for conventional extraction, there is a good agreement between the experimental and predicted data for UAE, demonstrating the models good predictive capacity.

Microwave assisted extraction (MAE)

The last factorial planning was carried out for MAE. Variables evaluated were temperature, S/L ratio and extraction time. Results of the influence of each variable on total phenolic content (TPC) and antioxidant activity (FRAP and ABTS) for the extracts obtained using MAE are presented in Figure 5, Tables S22-S24 and Figures S14-S16.

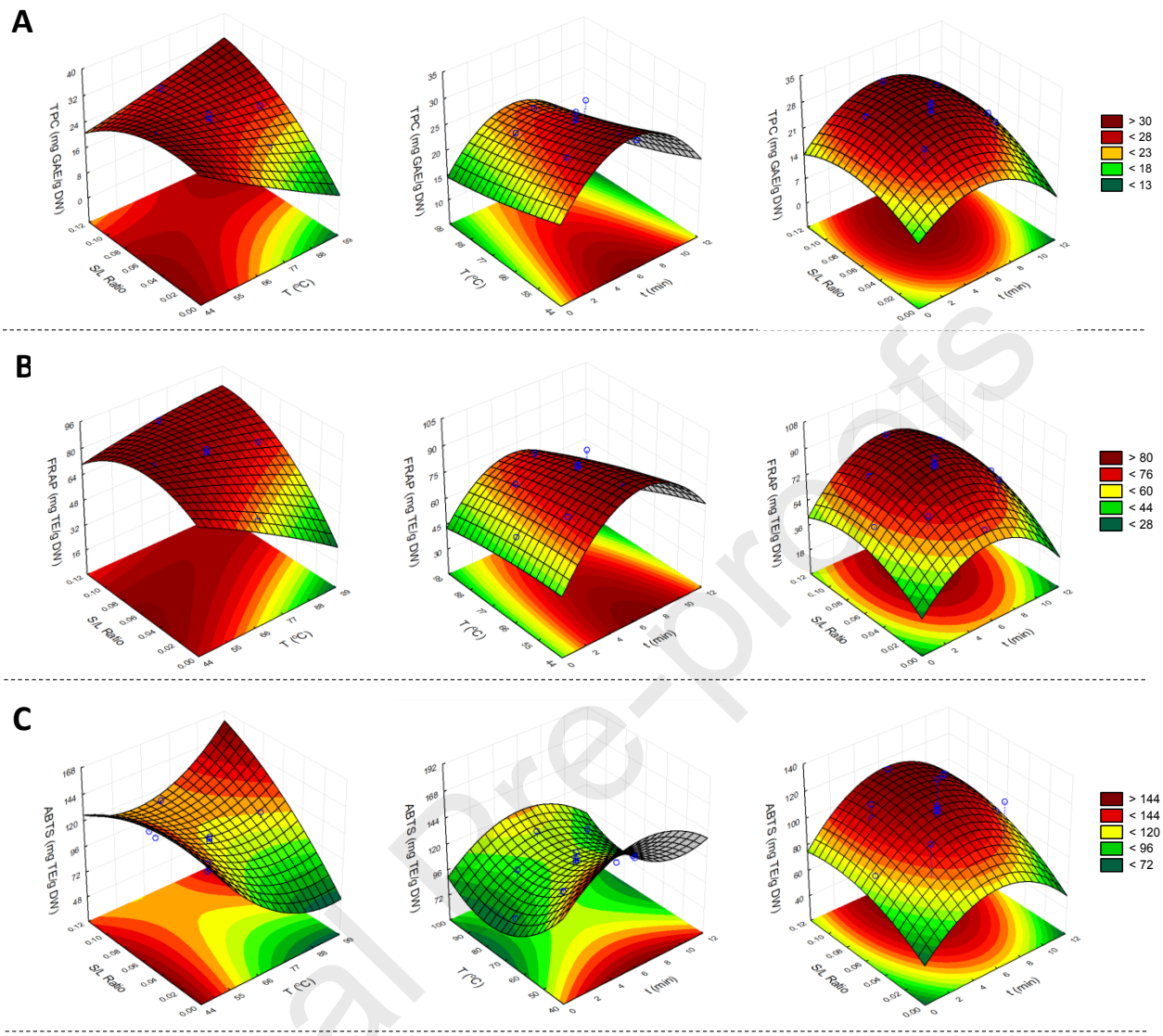

Figure 5. Response surface plots of (A) TPC, (B) FRAP and (C) ABTS assays, representing the influence of S/L ratio and temperature (left side); temperature and time (middle), and S/L ratio and time (right side), for the MAE technique, using a mixture of GVL:ethanol (7:3 wt/wt).

In general, all variables and their interactions were significant for the three responses under study, as can be seen in the Pareto Charts (Figure S15) and data depicted in Figure 5. Extraction time variable was the most significant for TPC and FRAP and the

second most significant for ABTS (temperature was the most significant). Still, it had a positive effect in all responses, leading to maximum values at extraction times between 5 and 7 min. Along the same line, maximum values for the responses were obtained at S/L ratios ranging from 1:20 to 1:14. Regarding temperature effect, a negative effect was observed. An increase in temperature led to a decrease in response variables, especially ABTS. Best results for total phenolic content and antioxidant activity were obtained at the lowest temperature evaluated here, namely 50 ºC. Note that temperatures below 50 ºC were not tested due to microwave equipment limitations.

The optimal conditions determined for MAE were T = 50 °C, S/L ratio = 1:16 and t = 6 min (*cf.* Figure S16). At this optimal point, the experimental values obtained were TPC = (29.7 ± 0.6) mg GAE/g DW, FRAP = (87 ± 4) mg TE/g DW and ABTS = (131 ± 1) mg TE/g DW. Results obtained with MAE were very promising, since this extraction technique allowed to obtain the extracts with the highest total phenolic content and antioxidant activity determined in this work. As previously observed for conventional extraction and UAE, there is here also a good agreement between the experimental and predicted data for MAE (Figure S16) revealing a good predictive ability of the models.

Chemical characterization of the optimized extracts

In order to characterize the main phenolic compounds present in the selected extracts (GVL:ethanol 7:3 wt/wt, ethanol:water 7:3 wt/wt and pure acetone), these were analyzed using HPTLC and UHPLC-DAD-MS^n.

The extracts were first analyzed using HPTLC to determine the chemical nature/family of the compounds responsible for the antioxidant activities. To that end, four detection reagents were used, namely DPPH for identifying antioxidant compounds,

natural product reagent A (NPA) solution for flavonoids and vegetable acids, fast blue B salt for phenolics and tanning agents, and p-anisaldehyde for sugars and terpenes [28, 29]. Results are reported in Figure S17. The fast blue B salt revealed the presence of three main compounds in the extracts, which may indicate that the antioxidants found in DPPH are polyphenolic compounds. In presence of NPA, one antioxidant appeared slightly orange and therefore was possibly a flavanol, while the other two components exhibited blue/cyan color, corresponding to polyphenols. Moreover, a red coloration was also observed in presence of NPA, characteristic of chlorophylls. Finally, in the presence of p-anisaldehyde, compounds exhibiting green and orange/brown colors were revealed, corresponding to sugars and tannins, respectively. In summary, this analysis revealed that the extracts are mainly composed of three types of compounds: chlorophylls, sugars and tannins.

The extracts were then analyzed by UHPLC-DAD-MS^n to determine the main phenolic compounds present in the extracts. It was possible to identify epicatechin, caffeic acid, and quercetin (Table S25-S26) derivatives as the main phenolic compounds, in agreement with the analysis by HPTLC reported above. In addition, these results also agree with other studies about the extraction of phenolic compounds from kiwifruit peels using organic solvents, that demonstrated that 'Hayward' kiwifruit peels are especially rich in flavonoids, such as epicatechin and catechin, and phenolic acids, *e.g.* p-coumaric acid, caffeic acid and protocatechuic acid [33]. Epicatechin derivatives are the major phenolic compounds extracted in all techniques/solvents, corresponding to more than 99% of the compounds extracted (Table S26 and Figure S18). Furthermore, considering the phenolic content, and antioxidant activity results, the best technique for the extraction of phenolic compounds was MAE. Concerning the solvents, the extract obtained with

acetone had a higher quantity of phenolic compounds (2520 μg/g) than the obtained with GVL:ethanol (2332 μg/g). However, differences in the extraction of each phenolic compound were observed among the various solvents used (Figures S19-21). For the epicatechin derivatives, the best solvent was acetone (2520 μg/g), followed by GVL:ethanol (2332 μg/g), and ethanol:water (1586 μg/g). On the other hand, for the caffeic acid derivatives, the best solvent was ethanol:water (43 μg/g), followed by acetone (26 μg/g), and GVL:ethanol (14 μg/g). In the case of quercetin glycosides, the type of solvent used did not influence the extraction process. Therefore, despite the best solvent being acetone when considering the overall yield of extracted compounds, the most selective one was a mixture composed of GVL and ethanol, leading to extracts rich in epicatechin derivatives. Moreover, from the extracts obtained using the solvent GVL:ethanol, that obtained by MAE was the one presenting the highest phenolic content.

Discussion

Finally, two analyses were done to assess the efficiency of different techniques evaluated in this work (conventional extraction, UAE and MAE) in the extraction of phenolic compounds from kiwifruit peels. First, extracts obtained under optimal conditions were compared in terms of total phenolic content (TPC) and antioxidant activity (FRAP and ABTS). Results are collected in Table 2. These extracts were obtained using the most efficient biobased solvent mixture, namely GVL:ethanol 7:3 wt/wt, and conventional solvents, namely ethanol:water 7:3 wt/wt and pure acetone for comparison purposes. Second, a study considering the energy costs of each technique and its efficiency in phenolic compounds extraction was carried out, in order to understand the

advantages and disadvantages of each extraction technique, and thus, choose the one best suiting the aim of this work (Table S7 and Figure S22).

From the results presented in Table 2, when acetone and the biobased solvent mixture are used, the amount of phenolic compounds and antioxidant activity of an extract are in the following order of extraction technique: MAE > UAE > conventional extraction. For ethanol:water mixture, UAE led to better results than MAE. MAE appeared as one of the most promising techniques evaluated here, since it allowed to obtain extracts with higher total phenolic content and higher antioxidant activity and allowed the use of a slightly lower S/L ratio when compared with the other two techniques. Comparing solvent efficiency under the optimal conditions of extraction, the following trend considering TPC, FRAP and ABTS results was observed: GVL:ethanol > acetone > ethanol:water. This trend appears to be independent of the extraction technique used. Although this result is not entirely in agreement with the results obtained by UHPLC-UV MS^n, where the extracts obtained with acetone showed higher phenolic content followed by GVL:ethanol and ethanol:water, it should be kept in mind that the GVL:ethanol mixture was the one that allowed obtaining more selective extracts.

Table 2. Total phenolic content and antioxidant activity of the extracts obtained using GVL:ethanol (7:3 wt/wt), acetone and ethanol:water (7:3 wt/wt) at the optimized extraction conditions with conventional extraction , UAE and MAE.*

		Variables				TPC	FRAP	ABTS
		Amp (%)	*t* (min)	S/L Ratio	*T* (°C)	(mg GAE/g DW)	(mg TE/g DW)	(mg TE/g DW)
GVL:ethanol (7:3 wt/wt)	**Conventional extraction**	---	60	1:12	36	21.4 $^{C, c}$ ± 0.5	61.3 ^{B,c} ± 0.4	92.0 ^{C,d} ± 0.8
	UAE	28	12	1:13	~51	24 $^{B, b}$ ± 1	81 ^{A,b} ± 4	104 ^{B,c} ± 2
	MAE	---	6	1:17	50	29.7 $^{A, a}$ ± 0.6	87 ^{A,a} ± 4	131 ^{A,a} ± 1
Acetone (pure)	**Conventional extraction**	---	60	1:12	36	19.3 $^{B, d}$ ± 0.8	59.7 ^{C,c} ± 0.8	83 ^{C,e} ± 2
	UAE	28	12	1:13	~51	24 $^{A, b}$ ± 2	78.4 ^{B,b} ± 0.9	95 ^{B,d} ± 1
	MAE	---	6	1:17	50	24.8 $^{A, b}$ ± 0.4	85.0 ^{A,a} ± 0.8	119 ^{A,b} ± 5
Ethanol:water (7:3 wt/wt)	**Conventional extraction**	---	60	1:12	36	12 $^{C, f,}$ ± 1	37 ^{C,e} ± 1	52 ^{C,g} ± 2
	UAE	28	12	1:13	~51	19.7 $^{A, d}$ ± 0.4	58 ^{B,c} ± 3	82 ^{A,e} ± 4
	MAE	---	6.0	1:17	50	17 $^{A, e}$ ± 1	49 ^{A,d} ± 2	69 ^{B,f} ± 2

*Results expressed as mean ± standard deviation. Different letters in the same column represent significant difference according to Fisher's LSD test ($p < 0.05$). Capital letters: significance of extraction techniques for each solvent in study. Lowercase letters: significance of all extraction techniques and solvents in study.

Finally, the equation suggested by Passos et al. [30] with slight modifications was used to better understand the economic viability of the three extraction techniques studied here. This equation is a simplified model that relates the return associated with the extraction of a particular value-added compound when alternative solvents are used as extraction solvents, which suffer a slight modification to account for the energetic costs (equation 3). Thus, this analysis aim is not to have a full-blown economic study, but a means to roughly compare each extraction technique using only the production costs.

Although MAE leads to an improved extraction yield in relation to UAE and conventional extraction techniques for phenolic compounds and antioxidant activity of kiwifruit peels extracts, this technique has a high energy consumption compared to the other techniques, especially in relation to conventional extraction (Table S7), being thus important to consider the energy costs of the processes. Moreover, recycling the biobased solvent is not proposed in the extraction process; instead, it is suggested to be present in the final formulation. We suggested that the obtained extracts might be used directly as a final product after the extraction process (possibly followed by a minor treatment for removal of part of the solvent) since GVL and ethanol are compounds authorized as food additives [52,53]. Thus, the main factors in the final product cost, in our case, are the energy consumption related to each technique, and the cost of the biobased solvent (GVL). Calculations were done considering that industrial reagents are acquired [32] and without the recovery of the biobased solvent, as explained in the experimental section. The results are displayed in Figure S22, which shows a linear relationship between the return and the production cost for all techniques.

Regarding the production cost for each technique, it is 6.2 €/kg_{prod}, 5.6 €/kg_{prod} and 5.3 €/kg_{prod}, for MAE, UAE and conventional extraction, respectively. As expected,

conventional extraction is the technique that allows a cheaper product since it is the one that spends less energy. Now looking for the return, for products with a lower price (<10 €$_{prod}$/Kg$_{prod}$) the best technique to use is conventional extraction since the return per kg of biomass is higher than the other techniques. Furthermore, and as unexpected, the high energy consumption of MAE did not have such a significant impact, showing that MAE is preferable to conventional extraction for products with a price higher than 10 €$_{prod}$/Kg$_{prod}$.

In summary, MAE technique is a good option when phenolic compounds are extracted, but the conventional technique is preferable for cheaper ones, while UAE is not recommended. In this study, since our extract is rich in epicatechin and its derivates, and the price of epicatechin at Sigma Aldrich is 126 €/g [54], the MAE is the preferable extraction technique.

CONCLUSION

This work reports alternative extraction techniques combined with biobased solvents and their mixtures to replace volatile organic solvents for the extraction of phenolic compounds from kiwifruit by-products. Kiwifruit peels were identified as the most promising kiwifruit by-product to obtain an extract rich in phenolic compounds. From the alternative solvents study, GVL mixtures with ethanol and/or water were the most efficient for obtaining extracts with high levels of phenolic compounds and antioxidant activity, especially GVL:ethanol in a ratio of 7:3 (wt/wt). To select the best extraction technique the extraction conditions (temperature/amplitude, extraction time and S/L ratio) for each extraction technique (conventional extraction, UAE and MAE) were optimized by RSM using the most efficient biobased solvent mixture. From the three

extraction techniques evaluated, MAE presented the best results, allowing to obtain an extract with the highest content of phenolic compounds (TPC: 29.7 ± 0.6 mg GAE/g DW) and antioxidant activity (FRAP: 87 ± 4 mg TE/g DW, ABTS: 131 ± 1mg TE/g DW), which were obtained at 50 °C with GVL:ethanol in a ratio of 7:3 (wt/wt), a solid–liquid ratio of 1:17, and for 6 min. Moreover, the biobased solvent mixture GVL:ethanol demonstrated higher efficiency than conventional solvents for any extraction technique, highlighting the advantages of biobased solvents. Finally, the extracts obtained at the optimized conditions were analyzed, presenting high levels of epicatechin (2.295 ± 0.005 mg/g DW), quercetin (0.023 ± 0.002 mg/g DW) and caffeic acid (0.013 ± 0.003 mg/g DW) derivates. Furthermore, estimated costs of the three extractions processes were provided, demonstrating that the MAE is also the preferable extraction technique to be used from an economic point of view, in specially for products with a price higher than 10 $€_{prod}/g_{prod}$. In summary, this work showed that alternative techniques and biobased solvents (especially food-grade ones) are great sustainable tools for extracting phenolic compounds from kiwifruit by-products.

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REFERENCES

[1] W. Jenkins, M.E. Tucker, J. Grim, Routledge Handbook of Religion and Ecology, Routledge, 2016. https://doi.org/10.4324/9781315764788.

[2] Worldwide food waste. http://www.unep.org/thinkeatsave/get-informed/worldwide-food-waste (accessed November 1, 2021).

[3] E. Ebikade, A. Athaley, B. Fisher, K. Yang, C. Wu, M.G. Ierapetritou, D.G. Vlachos, The Future is Garbage: Repurposing of Food Waste to an Integrated Biorefinery, ACS Sustain. Chem. Eng. 8 (2020) 8124–8136. https://doi.org/10.1021/acssuschemeng.9b07479.

[4] P. Latocha, The Nutritional and Health Benefits of Kiwiberry (Actinidia arguta) – a Review, Plant Foods Hum. Nutr. 72 (2017) 325–334. https://doi.org/10.1007/s11130-017-0637-y.

[5] V. Sanz, L. López-Hortas, M.D. Torres, H. Domínguez, Trends in kiwifruit and byproducts valorization, Trends Food Sci. Technol. 107 (2021) 401–414. https://doi.org/10.1016/j.tifs.2020.11.010.

[6] A.R. Ferguson, A.G. Seal, Kiwifruit, in: Temp. Fruit Crop Breed., Springer Netherlands, Dordrecht, 2008: pp. 235–264. https://doi.org/10.1007/978-1-4020-6907-9_8.

[7] Y.J. Lim, C.-S. Oh, Y.-D. Park, S.H. Eom, D.-O. Kim, U.-J. Kim, Y.-S. Cho, Physiological components of kiwifruits with in vitro antioxidant and acetylcholinesterase inhibitory activities, Food Sci. Biotechnol. 23 (2014) 943–949. https://doi.org/10.1007/s10068-014-0127-z.

[8] Kiwi production worldwide from 2000 to 2020. https://www.statista.com/statistics/577896/world-kiwi-production/ (accessed May 4, 2022).

[9] Production Statistics - Crops, Crops Processed.

https://pt.knoema.com//FAOPRDSC2020/production-statistics-crops-crops-processed?tsId=1477610 (accessed November 1, 2021).

[10] M. Gómez-López, M. García-Quiroga, E. Arbones-Maciñeira, M.L. Vázquez-Odériz, M.A. Romero-Rodríguez, Comparison of different peeling systems for kiwifruit (Actinidia deliciosa , cv Hayward), Int. J. Food Sci. Technol. 49 (2014) 107–113. https://doi.org/10.1111/ijfs.12281.

[11] W. SM, A. M, M. SA, G. I, M. FA, W. SA, A Review of Production and Processing of Kiwifruit, J. Food Process. Technol. 8 (2017). https://doi.org/10.4172/2157-7110.1000699.

[12] M.. Luque de Castro, L.. García-Ayuso, Soxhlet extraction of solid materials: an outdated technique with a promising innovative future, Anal. Chim. Acta. 369 (1998) 1–10. https://doi.org/10.1016/S0003-2670(98)00233-5.

[13] L. Wang, C.L. Weller, Recent advances in extraction of nutraceuticals from plants, Trends Food Sci. Technol. 17 (2006) 300–312. https://doi.org/10.1016/j.tifs.2005.12.004.

[14] M. Giordano, J. Pinela, M.I. Dias, R.C. Calhelha, D. Stojković, M. Soković, D. Tavares, A.L. Cánepa, I.C.F.R. Ferreira, C. Caleja, L. Barros, Ultrasound-Assisted Extraction of Flavonoids from Kiwi Peel: Process Optimization and Bioactivity Assessment, Appl. Sci. 11 (2021) 6416. https://doi.org/10.3390/app11146416.

[15] K. Carbone, T. Amoriello, R. Iadecola, Exploitation of Kiwi Juice Pomace for the Recovery of Natural Antioxidants through Microwave-Assisted Extraction, Agriculture. 10 (2020) 435. https://doi.org/10.3390/agriculture10100435.

[16] H. Kheirkhah, S. Baroutian, S.Y. Quek, Evaluation of bioactive compounds extracted from Hayward kiwifruit pomace by subcritical water extraction, Food Bioprod. Process. 115 (2019) 143–153. https://doi.org/10.1016/j.fbp.2019.03.007.

[17] F. Guthrie, Y. Wang, N. Neeve, S.Y. Quek, K. Mohammadi, S. Baroutian, Recovery of phenolic antioxidants from green kiwifruit peel using subcritical water extraction, Food Bioprod. Process. 122 (2020) 136–144.

https://doi.org/10.1016/j.fbp.2020.05.002.

[18] J.P. Wojeicchowski, A.M. Ferreira, D.O. Abranches, M.R. Mafra, J.A.P. Coutinho, Using COSMO-RS in the Design of Deep Eutectic Solvents for the Extraction of Antioxidants from Rosemary, ACS Sustain. Chem. Eng. 8 (2020) 12132–12141. https://doi.org/10.1021/acssuschemeng.0c03553.

[19] S.P.M. Ventura, F.A. E Silva, M. V. Quental, D. Mondal, M.G. Freire, J.A.P. Coutinho, Ionic-Liquid-Mediated Extraction and Separation Processes for Bioactive Compounds: Past, Present, and Future Trends, Chem. Rev. 117 (2017) 6984–7052. https://doi.org/10.1021/acs.chemrev.6b00550.

[20] C.J. Clarke, W.-C. Tu, O. Levers, A. Bröhl, J.P. Hallett, Green and Sustainable Solvents in Chemical Processes, Chem. Rev. 118 (2018) 747–800. https://doi.org/10.1021/acs.chemrev.7b00571.

[21] V. Vieira, R.C. Calhelha, L. Barros, J.A.P. Coutinho, I. C. F. R. Ferreira, O. Ferreira, Insights on the Extraction Performance of Alkanediols and Glycerol: Using Juglans regia L. Leaves as a Source of Bioactive Compounds, Molecules. 25 (2020) 2497. https://doi.org/10.3390/molecules25112497.

[22] M. Koşar, H.J.D. Dorman, R. Hiltunen, Effect of an acid treatment on the phytochemical and antioxidant characteristics of extracts from selected Lamiaceae species, Food Chem. 91 (2005) 525–533. https://doi.org/10.1016/j.foodchem.2004.06.029.

[23] I.F.F. Benzie, J.J. Strain, The Ferric Reducing Ability of Plasma (FRAP) as a Measure of "Antioxidant Power": The FRAP Assay, Anal. Biochem. 239 (1996) 70–76. https://doi.org/10.1006/abio.1996.0292.

[24] R. Re, N. Pellegrini, A. Proteggente, A. Pannala, M. Yang, C. Rice-Evans, Antioxidant activity applying an improved ABTS radical cation decolorization assay, Free Radic. Biol. Med. 26 (1999) 1231–1237. https://doi.org/10.1016/S0891-5849(98)00315-3.

[25] C.L. Handa, F.S. de Lima, M.F.G. Guelfi, S.R. Georgetti, E.I. Ida, Multi-response

optimisation of the extraction solvent system for phenolics and antioxidant activities from fermented soy flour using a simplex-centroid design, Food Chem. 197 (2016) 175–184. https://doi.org/10.1016/j.foodchem.2015.10.124.

[26] T.K.T. Do, F. Hadji-Minaglou, S. Antoniotti, X. Fernandez, Secondary metabolites isolation in natural products chemistry: Comparison of two semipreparative chromatographic techniques (high pressure liquid chromatography and high performance thin-layer chromatography), J. Chromatogr. A. 1325 (2014) 256–260. https://doi.org/10.1016/j.chroma.2013.11.046.

[27] R.S. Shivatare, D.H. Nagore, S.U. Nipanikar, "HPTLC" an important tool in standardization of herbal medical product: A review, J. Sci. Innov. Res. 2 (2013) 1086–1096. www.jsirjournal.com.

[28] V. Pedan, C. Weber, T. Do, N. Fischer, E. Reich, S. Rohn, HPTLC fingerprint profile analysis of cocoa proanthocyanidins depending on origin and genotype, Food Chem. 267 (2018) 277–287. https://doi.org/https://doi.org/10.1016/j.foodchem.2017.08.109.

[29] N. Sethiya, M. Mohan Maruga Raja, S. Mishra, Antioxidant markers based TLC-DPPH differentiation on four commercialized botanical sources of *Shankhpushpi* (A Medhya Rasayana): A preliminary assessment, J. Adv. Pharm. Technol. Res. 4 (2013) 25–30. https://doi.org/10.4103/2231-4040.107497.

[30] H. Passos, M.G. Freire, J.A.P. Coutinho, Ionic liquid solutions as extractive solvents for value-added compounds from biomass, Green Chem. 16 (2014) 4786–4815. https://doi.org/10.1039/C4GC00236A.

[31] Global Petrol Prices, Portugal electricity prices. https://www.globalpetrolprices.com/Portugal/electricity_prices/ (accessed September 9, 2022).

[32] Alibaba. https://www.alibaba.com (accessed November 23, 2021).

[33] Y. Wang, L. Li, H. Liu, T. Zhao, C. Meng, Z. Liu, X. Liu, Bioactive compounds and in vitro antioxidant activities of peel, flesh and seed powder of kiwi fruit, Int.

J. Food Sci. Technol. 53 (2018) 2239–2245. https://doi.org/10.1111/ijfs.13812.

[34] N. Izli, G. Izli, O. Taskin, Drying kinetics, colour, total phenolic content and antioxidant capacity properties of kiwi dried by different methods, J. Food Meas. Charact. 11 (2017) 64–74. https://doi.org/10.1007/s11694-016-9372-6.

[35] Y. Maghsoudlou, M. Asghari Ghajari, S. Tavasoli, Effects of heat treatment on the phenolic compounds and antioxidant capacity of quince fruit and its tisane's sensory properties, J. Food Sci. Technol. 56 (2019) 2365–2372. https://doi.org/10.1007/s13197-019-03644-6.

[36] A. Wojdyło, A. Figiel, J. Oszmiański, Effect of Drying Methods with the Application of Vacuum Microwaves on the Bioactive Compounds, Color, and Antioxidant Activity of Strawberry Fruits, J. Agric. Food Chem. 57 (2009) 1337–1343. https://doi.org/10.1021/jf802507j.

[37] J. López, E. Uribe, A. Vega-Gálvez, M. Miranda, J. Vergara, E. Gonzalez, K. Di Scala, Effect of Air Temperature on Drying Kinetics, Vitamin C, Antioxidant Activity, Total Phenolic Content, Non-enzymatic Browning and Firmness of Blueberries Variety O´Neil, Food Bioprocess Technol. 3 (2010) 772–777. https://doi.org/10.1007/s11947-009-0306-8.

[38] S. Kayacan, O. Sagdic, I. Doymaz, S. Karasu, The effect of different drying methods on total bioactive properties, individual phenolic compounds, rehydration ability, color, and microstructural characteristics of Asian pear, J. Food Process. Preserv. 46 (2022) e16682. https://doi.org/10.1111/jfpp.16682.

[39] A. Orphanides, V. Goulas, V. Gekas, Effect of drying method on the phenolic content and antioxidant capacity of spearmint, Czech J. Food Sci. 31 (2013) 509–513. https://doi.org/10.17221/526/2012-CJFS.

[40] S. Şahin, A.G. Pekel, İ. Toprakçı, Sonication-assisted extraction of Hibiscus sabdariffa for the polyphenols recovery: application of a specially designed deep eutectic solvent, Biomass Convers. Biorefinery. (2020). https://doi.org/10.1007/s13399-020-00837-4.

[41] X.-L. Qi, X. Peng, Y.-Y. Huang, L. Li, Z.-F. Wei, Y.-G. Zu, Y.-J. Fu, Green and efficient extraction of bioactive flavonoids from Equisetum palustre L. by deep eutectic solvents-based negative pressure cavitation method combined with macroporous resin enrichment, Ind. Crops Prod. 70 (2015) 142–148. https://doi.org/10.1016/j.indcrop.2015.03.026.

[42] M.E. Alañón, M. Ivanović, A.M. Gómez-Caravaca, D. Arráez-Román, A. Segura-Carretero, Choline chloride derivative-based deep eutectic liquids as novel green alternative solvents for extraction of phenolic compounds from olive leaf, Arab. J. Chem. 13 (2020) 1685–1701. https://doi.org/10.1016/j.arabjc.2018.01.003.

[43] M. Ivanović, M. Islamčević Razboršek, M. Kolar, Innovative Extraction Techniques Using Deep Eutectic Solvents and Analytical Methods for the Isolation and Characterization of Natural Bioactive Compounds from Plant Material, Plants. 9 (2020) 1428. https://doi.org/10.3390/plants9111428.

[44] I.C. Adaka, P.F. Uzor, Cyrene as a green solvent in the pharmaceutical industry, in: Inamuddin, R. Boddula, M.I. Ahamed, A.M.B.T.-G.S.P. for C. and E.E. and S. Asiri (Eds.), Green Sustain. Process Chem. Environ. Eng. Sci., Elsevier, 2021: pp. 243–248. https://doi.org/10.1016/B978-0-12-821885-3.00001-3.

[45] J.E. Camp, S.B. Nyamini, F.J. Scott, Cyrene™ is a green alternative to DMSO as a solvent for antibacterial drug discovery against ESKAPE pathogens, RSC Med. Chem. 11 (2020) 111–117. https://doi.org/10.1039/C9MD00341J.

[46] I.T. Horváth, H. Mehdi, V. Fábos, L. Boda, L.T. Mika, γ-Valerolactone—a sustainable liquid for energy and carbon-based chemicals, Green Chem. 10 (2008) 238–242. https://doi.org/10.1039/B712863K.

[47] I.T. Horváth, Solvents from nature, Green Chem. 10 (2008) 1024–1028. https://doi.org/10.1039/B812804A.

[48] A. Cassano, L. Donato, C. Conidi, E. Drioli, Recovery of bioactive compounds in kiwifruit juice by ultrafiltration, Innov. Food Sci. Emerg. Technol. 9 (2008) 556–562. https://doi.org/10.1016/j.ifset.2008.03.004.

[49] A. Aires, R. Carvalho, Kiwi fruit residues from industry processing: study for a maximum phenolic recovery yield, J. Food Sci. Technol. 57 (2020) 4265–4276. https://doi.org/10.1007/s13197-020-04466-7.

[50] C.M. Galanakis, V. Goulas, S. Tsakona, G.A. Manganaris, V. Gekas, A Knowledge Base for The Recovery of Natural Phenols with Different Solvents, Int. J. Food Prop. 16 (2013) 382–396. https://doi.org/10.1080/10942912.2010.522750.

[51] International Council for Harmonisation, Guidance for Industry Q3C, U.S. Dep. Heal. Hum. Serv. Food Drug Adm. 9765 (2017) 1–8. http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htmorhttps://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm%0Ahttp://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInforma.

[52] W.H. Organization, Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives - gamma-VALEROLACTONE. https://inchem.org/documents/jecfa/jeceval/jec_2378.htm (accessed May 4, 2022).

[53] Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives - ETHANOL. https://inchem.org/documents/jecfa/jeceval/jec_706.htm (accessed May 4, 2022).

[54] Merck, Sigma-Aldrich: (−)-Epicatechin. https://www.sigmaaldrich.com/PT/en/product/sigma/e1753 (accessed May 4, 2022).

Supporting Information

USING BIOBASED SOLVENTS FOR THE EXTRACTION OF PHENOLIC COMPOUNDS FROM KIWIFRUIT INDUSTRY WASTE

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Tables

Table S3. Main physicochemical properties of the evaluated solvents.

Solvent	Molecular weight (mol/g)	Boiling Temperature (°C)	Melting Temperature (°C)	Relative density (g/mL)
H_2O	18.02	100	0	0.995*
MeOH	32.04	65	-98	0.791*
EtOH	46.07	78	-144	0.790*
Acetone	58.08	56	-94	0.791*
ETG	62.07	196-198	-13	1.113*
PRO	76.09	187	-60	1.036*
HEX	118.17	250	38-42	0.960**
GVL	100.12	207-208	-31	1.05*

* at 25 °C; ** at 20 °C

Table S4. Mixture design for optimization of the solvent composition.

Run	Coded variables		
	X_1	X_2	X_3
1	0.00	0.67	0.33
2	0.00	0.00	1.00
3	0.33	0.33	0.33
4	0.00	1.00	0.00
5	0.17	0.67	0.17
6	1.00	0.00	0.00
7	0.33	0.67	0.00
8	0.67	0.00	0.33
9	0.00	0.33	0.67
10	0.33	0.33	0.33
11	0.67	0.33	0.00
12	0.17	0.17	0.67
13	0.67	0.17	0.17
14	0.33	0.00	0.67

Table S5. Factorial planning (2^3) for the optimization of operating conditions by response surface methodology (RSM).

Run	Coded variables		
	X_1	X_2	X_3
1	-1	-1	-1
2	1	-1	-1
3	-1	1	-1
4	1	1	-1
5	-1	-1	1
6	1	-1	1
7	-1	1	1
8	1	1	1
9	-1.68	0	0
10	1.68	0	0
11	0	-1.68	0
12	0	1.68	0
13	0	0	-1.68
14	0	0	1.68
15	0	0	0
16	0	0	0
17	0	0	0
18	0	0	0
19	0	0	0
20	0	0	0

Table S6. Coded levels of independent variables used in the factorial planning for the optimization of operating conditions by carousel extraction (CE).

Independent variables	Axial -1.682	Factorial -1	Central 0	Factorial 1	Axial 1.68
Temperature (T, ºC) - X1	23	30	40	50	57
Time (t, min) - X2	9.5	30.0	60.0	90.0	110.4
Solid-liquid ratio (S/L ratio) - X3	0.016	0.030	0.050	0.070	0.084

Table S7. Coded levels of independent variables used in the factorial planning for the optimization of operating conditions by ultrasound-assisted extraction (UAE).

Independent variables	Axial -1.682	Factorial -1	Central 0	Factorial 1	Axial 1.68
Amplitude (Amp, %) - X1	10	14	20	26	30
t (min) - X2	1.3	4.0	8.0	12.0	14.7
S/L ratio - X3	0.010	0.030	0.060	0.090	0.110

Table S8. Coded levels of independent variables used in the factorial planning for the optimization of operating conditions by microwave-assisted extraction (MAE).

Independent variables	Axial -1.682	Factorial -1	Central 0	Factorial 1	Axial 1.68
T (ºC) - X1	50	58	70	82	90
t (min) - X2	1.0	3.0	6.0	9.0	11.0
S/L ratio - X3	0.010	0.030	0.060	0.090	0.110

Table S9. Optimal extraction conditions for each technique (Conventional extraction, UAE and MAE) and the respective value of the consumed energy.

	Amp (%)	T (min)	S/L Ratio	T (°C)	Consumed energy /Kg biomass (J/kg)
Conventional extraction	---	60	0.084	36	$1.36x10^7$
UAE	28	12	0.077	~51	$1.13x10^7$
MAE	---	6	0.06	50	$5.00x10^7$

Table S10. Total phenolic content (TPC) and antioxidant activity (FRAP and ABTS) levels of the extracts obtained using different kiwifruit parts (peel, pulp, juice and whole fruit) by soxhlet extraction with ethanol.

	Juice	Peel	Pulp	Whole Kiwifruit
TPC (mg GAE/g DW)	7 ± 1	8.3 ± 0.2	2.05 ± 0.01	7 ± 1
FRAP (mg TE/g DW)	10.4 ± 0.3	16.7 ± 0.5	5 ± 1	11.1 ± 0.4
ABTS (mg TE/g DW)	7.1 ± 0.1	19.9 ± 0.3	3.6 ± 0.1	10.8 ± 0.4

Table S11. Phenolic content (TPC) and antioxidant activity (FRAP and ABTS) values of the extracts obtained from kiwifruit peels storage at different conditions, using EtOH:H_2O (7:3, wt/wt) in CE.

	biomass dry and stored at -10 ºC	biomass directly stored at -10 ºC	biomass directly stored at -80 ºC
TPC (mg GAE /g DW)	0.8 ± 0.3	3.33 ± 0.06	8.8 ± 0.8
FRAP	1.3 ± 0.1	20 ± 2	24 ± 1

(mg TE/g DW)			
ABTS (mg TE/g DW)	1.6 ± 0.2	19.8 ± 0.6	25.0 ± 0.6

Table S12. Evaluation of TPC, FRAP and ABTS of the kiwifruit peels extracts using conventional solvents, binary mixtures of biobased solvents with water or ethanol in the weight ratios of 3:7 and 7:3, and ternary mixtures composed of biobased solvent, ethanol and water in the weight ratio of 4:4:2. Fixed extraction conditions: solid-liquid ratio of 0.05, 60 min and at 25 °C, by CE.

Extraction solvent	TPC (mg GAE/g DW)	FRAP (mg TE/g DW)	ABTS (mg TE/g DW)
H_2O	2.1 ± 0.4	6 ± 1	4.4 ± 0.6
MeOH	6.4 ± 0.1	21 ± 1	22 ± 1
EtOH	5.4 ± 0.1	12 ± 2	14.3 ± 0.9
EtOH:H_2O (7:3)	8.8 ± 0.9	24 ± 1	25.0 ± 0.6
EtOH:H_2O (3:7)	5.2 ± 0.2	8.0 ± 0.5	5.1 ± 0.2
EtOH:H_2O at pH2 (7:3)	8.6 ± 0.9	24.7 ± 0.6	28.7 ± 0.5
EtOH:H_2O at pH2 (3:7)	5.2 ± 0.8	19.59 ± 0.06	22.9 ± 0.2
Acetone	14 ± 1	43 ± 2	55.1 ± 0.9
ETG	16 ± 1	43 ± 3	53 ± 5
PRO	9.6 ± 0.9	22 ± 4	267 ± 2
GVL	16.4 ± 0.6	3 ± 4	53 ± 3
ETG:H_2O (7:3)	18 ± 2	45 ± 3	66 ± 5
ETG:H_2O (3:7)	9.9 ± 0.9	21.6 ± 0.3	34 ± 1
PRO:H_2O (7:3)	10.8 ± 0.4	23 ± 3	31.9 ± 0.5
PRO:H_2O (3:7)	3.9 ± 0.6	7.8 ± 0.2	20.4 ± 0.3
HEX:H_2O (7:3)	12.1 ± 0.5	28 ± 4	38 ± 4
HEX:H_2O (3:7)	8 ± 1	13.6 ± 0.8	22 ± 3
GVL:H_2O (7:3)	19 ± 1	40 ± 3	65.6 ± 0.9
GVL:H_2O (3:7)	12 ± 1	14.1 ± 0.1	23 ± 1
ETG:EtOH (7:3)	17.0 ± 0.6	43 ± 2	60 ± 3
ETG:EtOH (3:7)	11.3 ± 0.4	29 ± 2	39 ± 4
PRO:EtOH (7:3)	10.0 ± 0.5	30 ± 2	40 ± 2
PRO:EtOH (3:7)	6.7 ± 0.9	16.7 ± 0.8	25.0 ± 0.3

HEX:EtOH (7:3)	9.12 ± 0.01	28.2 ± 0.3	38 ± 2
HEX:EtOH (3:7)	6.3 ± 0.2	22 ± 1	22 ± 1
GVL:EtOH (7:3)	19 ± 1	47 ± 1	70 ± 2
GVL:EtOH (3:7)	11.9 ± 0.6	30.2 ± 0.4	40 ± 3
ETG:EtOH:H_2O (4:4:2)	18.7 ± 0.1	45 ± 3	64 ± 2
PRO:EtOH:H_2O (4:4:2)	10.8 ± 0.5	25 ± 2	41 ± 1
HEX:EtOH:H_2O (4:4:2)	10.0 ± 0.3	25.5 ± 0.7	38 ± 1
GVL:EtOH:H_2O (4:4:2)	19 ± 1	43 ± 2	62 ± 1

Table S13. Initial pH of all mixtures used in the biobased solvent screening for the extraction of phenolic compounds.

Extraction solvent (ratio weight)	**pH**
EtOH:H_2O (7:3)	8.08±0.01
EtOH:H_2O (3:7)	7.02±0.01
GVL:H_2O (7:3)	3.62±0.01
GVL:H_2O (3:7)	2.81±0.02
ETG:H_2O (7:3)	5.93±0.01
ETG:H_2O (3:7)	5.29±0.03
PRO:H_2O (7:3)	6.06±0.03
PRO:H_2O (3:7)	6.01±0.01
HEX:H_2O (7:3)	6.20±0.01
HEX:H_2O (3:7)	5.27±0.01
GVL:EtOH:H_2O (4:4:2)	5.52±0.01
ETG:EtOH:H_2O (4:4:2)	5.52±0.01

PRO:EtOH:H_2O (4:4:2)	7.38±0.02
HEX:EtOH:H_2O (4:4:2)	6.90±0.01

Table S14. TPC of the extracts obtained with mixtures composed of gamma-valerolactone, ethanol and water during the optimization of the solvent composition. Model: $R^2 = 0.93$ and $R^2_{adj} = 0.88$.

Real variables			TPC		
EtOH	GVL	H_2O	Experimental (mg GAE/g DW)	Predicted (mg GAE/g DW)	Relative deviation (%)
0.00	0.67	0.33	18.61	18.45	0.87
0.00	0.00	1.00	2.09	0.64	24.82
0.33	0.33	0.33	17.92	15.67	14.33
0.00	1.00	0.00	16.35	16.76	2.48
0.17	0.67	0.17	18.27	18.75	2.54
1.00	0.00	0.00	5.35	5.20	2.82
0.33	0.67	0.00	19.09	18.28	4.43
0.67	0.00	0.33	8.81	7.70	14.39
0.00	0.33	0.67	12.40	12.00	3.32
0.33	0.33	0.33	16.98	15.67	8.34
0.67	0.33	0.00	11.88	13.66	13.02
0.17	0.17	0.67	6.17	10.25	29.78
0.67	0.17	0.17	11.69	11.91	1.91
0.33	0.00	0.67	5.23	5.88	11.01

Table S15. Antioxidant activity evaluated with FRAP assay of the extracts obtained during the optimization of the solvent composition composed of gamma-valerolactone, ethanol and water. Model: $R^2 = 0.90$ and $R^2_{adj} = 0.84$.

Real variables			FRAP		
EtOH	GVL	H_2O	Experimental (mg TE/g DW)	Predicted (mg TE/g DW)	Relative deviation (%)
0.00	0.67	0.33	40.07	35.55	12.71
0.00	0.00	1.00	5.58	-1.04	-34.57
0.33	0.33	0.33	35.46	33.98	4.35
0.00	1.00	0.00	38.81	41.60	6.71
0.17	0.67	0.17	43.27	41.77	3.59
1.00	0.00	0.00	11.70	13.17	11.18
0.33	0.67	0.00	47.13	46.47	1.42
0.67	0.00	0.33	23.90	19.14	24.86
0.00	0.33	0.67	14.12	18.50	23.69
0.33	0.33	0.33	37.26	33.98	9.64
0.67	0.33	0.00	30.18	35.10	14.01
0.17	0.17	0.67	11.77	19.19	28.69
0.67	0.17	0.17	32.58	28.94	12.60
0.33	0.00	0.67	7.98	13.45	40.69

Table S16. Antioxidant activity evaluated with ABTS assay of the extracts obtained during the optimization of the solvent composition composed of gamma-valerolactone, ethanol and water. Model: $R^2 = 0.92$ and $R^2_{adj} = 0.86$.

Real variables			ABTS		
EtOH	GVL	H_2O	Experimental (mg TE/g DW)	Predicted (mg TE/g DW)	Relative deviation (%)
0.00	0.67	0.33	65.61	55.65	17.91
0.00	0.00	1.00	4.37	-3.19	-37.18
0.33	0.33	0.33	52.58	46.14	13.94
0.00	1.00	0.00	53.67	58.51	8.28
0.17	0.67	0.17	54.59	60.16	9.26
1.00	0.00	0.00	14.25	14.48	1.60
0.33	0.67	0.00	69.77	63.81	9.33
0.67	0.00	0.33	25.04	18.26	37.10
0.00	0.33	0.67	23.10	30.97	25.41
0.33	0.33	0.33	48.60	46.14	5.33
0.67	0.33	0.00	40.47	46.20	12.39
0.17	0.17	0.67	18.80	25.57	26.46
0.67	0.17	0.17	33.47	35.54	5.82
0.33	0.00	0.67	5.13	11.19	54.20

Table S17. TPC of the extracts obtained by conventional extraction during the optimization of extractions conditions. Model: $R^2 = 0.93$ and $R^2_{adj} = 0.87$.

Real variables			TPC		
T (°C)	t (min)	S/L ratio	Experimental (mg GAE/g DW)	Predicted (mg GAE/g DW)	Relative deviation (%)
30	30.0	0.030	18.19	18.07	0.62
50	30.0	0.030	16.12	15.71	2.64
30	90.0	0.030	20.54	20.12	2.10
50	90.0	0.030	16.14	16.74	3.58
30	30.0	0.070	20.61	20.13	2.37
50	30.0	0.070	18.40	18.94	2.88
30	90.0	0.070	21.23	21.77	2.46
50	90.0	0.070	19.34	19.57	1.20
23	60.0	0.050	19.24	19.58	1.74
57	60.0	0.050	16.26	15.75	3.28
40	9.5	0.050	17.86	18.19	1.82
40	110.4	0.050	20.95	20.44	2.48
40	60.0	0.016	17.51	17.78	1.49
40	60.0	0.084	22.37	21.93	1.98
40	60.0	0.050	19.75	20.00	1.26
40	60.0	0.050	20.41	20.00	2.07
40	60.0	0.050	19.54	20.00	2.28
40	60.0	0.050	20.79	20.00	3.94
40	60.0	0.050	20.06	20.00	0.30
40	60.0	0.050	19.42	20.00	2.91

Table S18. Antioxidant activity evaluated with FRAP assay of the extracts obtained by conventional extraction during the optimization of extractions conditions. Model: R^2 = 0.95 and R^2_{adj} = 0.90.

Real variables			FRAP		
T (°C)	t (min)	S/L ratio	Experimental (mg TE/g DW)	Predicted (mg TE/g DW)	Relative deviation (%)
30	30.0	0.030	40.53	38.84	4.37
50	30.0	0.030	36.10	35.33	2.18
30	90.0	0.030	40.88	39.05	4.68
50	90.0	0.030	36.92	37.10	0.51
30	30.0	0.070	55.29	54.02	2.36
50	30.0	0.070	44.58	45.32	1.64
30	90.0	0.070	58.24	57.92	0.54
50	90.0	0.070	50.17	50.78	1.20
23	60.0	0.050	46.35	48.86	5.15
57	60.0	0.050	40.91	39.93	2.46
40	9.5	0.050	42.11	43.38	2.91
40	110.4	0.050	47.87	48.15	0.57
40	60.0	0.016	30.64	32.53	5.81
40	60.0	0.084	57.45	57.06	0.68
40	60.0	0.050	47.44	48.54	2.25
40	60.0	0.050	49.47	48.54	1.92
40	60.0	0.050	45.53	48.54	6.19
40	60.0	0.050	49.64	48.54	2.28
40	60.0	0.050	52.40	48.54	7.95
40	60.0	0.050	46.97	48.54	3.23

Table S19. Antioxidant activity evaluated with ABTS assay of the extracts obtained by conventional extraction during the optimization of extractions conditions. Model: $R^2 = 0.94$ and $R^2_{adj} = 0.88$.

Real variables			ABTS		
T (°C)	t (min)	S/L ratio	Experimental (mg TE/g DW)	Predicted (mg TE/g DW)	Relative deviation (%)
30	30.0	0.030	71.31	70.62	0.98
50	30.0	0.030	60.92	59.65	2.14
30	90.0	0.030	78.39	77.94	0.58
50	90.0	0.030	67.92	68.62	1.02
30	30.0	0.070	85.46	85.98	0.61
50	30.0	0.070	79.99	81.66	2.05
30	90.0	0.070	82.58	85.08	2.94
50	90.0	0.070	80.49	82.41	2.33
23	60.0	0.050	82.50	81.98	0.64
57	60.0	0.050	71.74	70.53	1.71
40	9.5	0.050	72.07	72.52	0.62
40	110.4	0.050	81.50	79.32	2.75
40	60.0	0.016	64.46	66.07	2.43
40	60.0	0.084	94.15	90.85	3.63
40	60.0	0.050	82.59	83.75	1.39
40	60.0	0.050	82.62	83.75	1.35
40	60.0	0.050	79.25	83.75	5.37
40	60.0	0.050	85.64	83.75	2.25
40	60.0	0.050	88.39	83.75	5.54
40	60.0	0.050	83.75	83.75	0.00

Table S20. TPC, FRAP and ABTS results obtained using the optimal conventional extraction conditions (36 ºC, 60 min) and applying different values of solid-liquid ratio (S/L ratio).

S/L Ratio	TPC (mg GAE/g DW)	FRAP (mg TE/g DW)	ABTS (mg TE/g DW)
1:12	21 ± 3	61 ± 5	99.5 ± 0.8
1:10	21 ± 3	56 ± 6	91 ± 7
1:8	22 ± 2	56 ± 2	93 ± 4

Table S21. TPC of the extracts obtained by UAE during the optimization of extractions conditions factorial planning. Model: $R^2 = 0.89$ and $R^2_{adj} = 0.79$.

Real variables			TPC		
Amp (%)	t (min)	S/L ratio	Experimental (mg GAE/g DW)	Predicted (mg GAE/g DW)	Relative deviation (%)
14	4.0	0.030	21.08	20.40	3.34
26	4.0	0.030	21.45	20.30	5.67
14	12.0	0.030	20.43	19.18	6.51
26	12.0	0.030	20.28	19.52	3.89
14	4.0	0.090	19.71	19.60	0.55
26	4.0	0.090	20.23	20.61	1.86
14	12.0	0.090	23.43	23.71	1.20
26	12.0	0.090	25.35	25.16	0.74
10	8.0	0.060	22.79	23.43	2.71
30	8.0	0.060	23.94	24.56	2.49
20	1.3	0.060	18.99	19.50	2.60
20	14.7	0.060	21.59	22.31	3.22
20	8.0	0.010	15.02	16.91	11.17
20	8.0	0.110	21.58	20.94	3.06
20	8.0	0.060	23.17	24.18	4.18
20	8.0	0.060	24.83	24.18	2.69
20	8.0	0.060	23.40	24.18	3.25
20	8.0	0.060	23.86	24.18	1.31
20	8.0	0.060	24.70	24.18	2.13
20	8.0	0.060	25.38	24.18	4.97

Table S22. Antioxidant activity evaluated with FRAP assay of the extracts obtained by UAE during the optimization of extractions conditions. Model: R^2 = 0.98 and R^2_{adj} = 0.96.

Real variables			FRAP		
Amp (%)	t (min)	S/L ratio	Experimental (mg TE/g DW)	Predicted (mg TE/g DW)	Relative deviation (%)
14	4.0	0.030	56.37	55.80	1.03
26	4.0	0.030	73.82	75.52	2.26
14	12.0	0.030	60.75	63.32	4.05
26	12.0	0.030	73.24	72.46	1.08
14	4.0	0.090	53.23	54.79	2.85
26	4.0	0.090	68.32	66.53	2.68
14	12.0	0.090	80.93	80.01	1.15
26	12.0	0.090	79.82	81.18	1.67
10	8.0	0.060	65.48	64.28	1.87
30	8.0	0.060	81.61	81.69	0.10
20	1.3	0.060	58.58	58.42	0.28
20	14.7	0.060	78.01	77.07	1.22
20	8.0	0.010	65.00	63.63	2.16
20	8.0	0.110	69.80	70.05	0.36
20	8.0	0.060	74.88	75.94	1.39
20	8.0	0.060	78.09	75.94	2.84
20	8.0	0.060	76.39	75.94	0.59
20	8.0	0.060	74.50	75.94	1.89
20	8.0	0.060	76.05	75.94	0.15
20	8.0	0.060	75.48	75.94	0.60

Table S23. Antioxidant activity evaluated with ABTS assay of the extracts obtained by UAE during the optimization of extractions conditions. Model: R^2 = 0.91 and R^2_{adj} = 0.83.

Real variables	ABTS

Amp (%)	t (min)	S/L ratio	Experimental (mg TE/g DW)	Predicted (mg TE/g DW)	Relative deviation (%)
14	4.0	0.030	92.87	91.59	1.39
26	4.0	0.030	98.26	94.70	3.75
14	12.0	0.030	100.14	99.54	0.60
26	12.0	0.030	100.08	99.27	0.82
14	4.0	0.090	78.66	77.21	1.89
26	4.0	0.090	93.88	92.21	1.81
14	12.0	0.090	86.85	88.14	1.46
26	12.0	0.090	100.76	99.76	1.00
10	8.0	0.060	95.17	95.31	0.14
30	8.0	0.060	104.46	107.59	2.91
20	1.3	0.060	81.71	85.34	4.26
20	14.7	0.060	98.80	98.37	0.44
20	8.0	0.010	88.31	90.96	2.92
20	8.0	0.110	78.77	79.38	0.77
20	8.0	0.060	90.29	93.25	3.17
20	8.0	0.060	91.49	93.25	1.90
20	8.0	0.060	93.22	93.25	0.04
20	8.0	0.060	91.79	93.25	1.58
20	8.0	0.060	96.73	93.25	3.73
20	8.0	0.060	96.68	93.25	3.67

Table S24. TPC of the extracts obtained by MAE during the optimization of extractions conditions. Model: $R^2 = 0.93$ and $R^2_{adj} = 0.87$.

Real variables			TPC		
T (°C)	t (min)	S/L ratio	Experimental (mg GAE/g DW)	Predicted (mg GAE/g DW)	Relative deviation (%)
58	3.0	0.030	26.44	25.89	2.13
82	3.0	0.030	20.16	18.67	7.99
58	9.0	0.030	25.25	24.42	3.40
82	9.0	0.030	16.16	16.73	3.40
58	3.0	0.090	25.05	24.23	3.36
82	3.0	0.090	24.80	25.39	2.32
58	9.0	0.090	23.72	24.98	5.02
82	9.0	0.090	25.35	25.66	1.21
50	6.0	0.060	29.55	30.00	1.50
90	6.0	0.060	24.59	24.50	0.39
70	1.0	0.060	18.99	20.22	6.10
70	11.0	0.060	20.14	19.24	4.68
70	6.0	0.010	19.09	20.34	6.16
70	6.0	0.110	27.38	26.47	3.45
70	6.0	0.060	26.67	26.92	0.93
70	6.0	0.060	28.91	26.92	7.41
70	6.0	0.060	26.00	26.92	3.42
70	6.0	0.060	27.45	26.92	1.98
70	6.0	0.060	26.27	26.92	2.42
70	6.0	0.060	26.28	26.92	2.36

Table S25. Antioxidant activity evaluated with FRAP assay of the extracts obtained by MAE during the optimization of extractions conditions. Model: R^2 = 0.98 and R^2_{adj} = 0.97.

Real variables			FRAP		
T (°C)	t (min)	S/L ratio	Experimental (mg TE/g DW)	Predicted (mg TE/g DW)	Relative deviation (%)
58	3.0	0.030	71.59	71.34	0.35
82	3.0	0.030	59.39	58.20	2.04
58	9.0	0.030	75.08	73.39	2.30
82	9.0	0.030	54.34	55.02	1.23
58	3.0	0.090	73.67	73.38	0.39
82	3.0	0.090	72.79	74.88	2.79
58	9.0	0.090	77.70	79.28	2.00
82	9.0	0.090	74.89	75.54	0.86
50	6.0	0.060	87.63	88.20	0.65
90	6.0	0.060	75.15	74.02	1.53
70	1.0	0.060	58.42	58.39	0.04
70	11.0	0.060	61.26	60.72	0.88
70	6.0	0.010	60.68	62.33	2.64
70	6.0	0.110	83.53	81.32	2.72
70	6.0	0.060	81.54	82.24	0.86
70	6.0	0.060	82.78	82.24	0.65
70	6.0	0.060	84.26	82.24	2.46
70	6.0	0.060	82.81	82.24	0.69
70	6.0	0.060	81.71	82.24	0.64
70	6.0	0.060	80.23	82.24	2.44

Table S26. Antioxidant activity evaluated with ABTS assay of the extracts obtained by MAE during the optimization of extractions conditions. Model: $R^2 = 0.94$ and $R^2_{adj} = 0.89$.

Real variables			ABTS		
T (°C)	t (min)	S/L ratio	Experimental (mg TE/g DW)	Predicted (mg TE/g DW)	Relative deviation (%)
58	3.0	0.030	111.88	110.04	1.67
82	3.0	0.030	83.45	79.99	4.33
58	9.0	0.030	119.04	112.56	5.76
82	9.0	0.030	78.35	80.93	3.19
58	3.0	0.090	112.86	109.53	3.03
82	3.0	0.090	102.51	108.24	5.30
58	9.0	0.090	113.10	115.82	2.35
82	9.0	0.090	111.85	112.95	0.97
50	6.0	0.060	133.32	138.27	3.58
90	6.0	0.060	114.47	110.57	3.53
70	1.0	0.060	82.41	83.77	1.62
70	11.0	0.060	90.21	89.90	0.35
70	6.0	0.010	82.62	87.72	5.82
70	6.0	0.110	118.29	114.22	3.56
70	6.0	0.060	106.92	109.22	2.11
70	6.0	0.060	112.50	109.22	3.00
70	6.0	0.060	111.14	109.22	1.76
70	6.0	0.060	110.47	109.22	1.15
70	6.0	0.060	108.33	109.22	0.81
70	6.0	0.060	106.13	109.22	2.83

Table S27. UHPLC-DAD-MS^n data of compounds identified in kiwifruit peel extracts.

Peak	Rt (min)	Λmax (nm)	[M−H]$^-$ (*m/z*)	MS^n (*m/z*)	Identification
1	6.74	322	297	179 (30), 135(100)	Caffeic acid derivative
2	7.56	313	341	179 (100), 135(15)	Caffeic acid hexoside
3	8.90	280	865	739(100),713(60), 577(40), 425(35)	B-type (epi)catechin trimer
4	9.10	280	577	559 (15), 533 (10), 451(40),425(100),407(20),289(15), 245 (10)	B-type (epi)catechin dimer
5	9.16	335	369	207(100), 191(40)	Dimethyl caffeic acid hexoside
6	9.22	280	1153	575(100)	B-type (epi)catechin tetramer
7	9.45	280	289	245(100), 205(20), 203(20), 161(40)	Epicatechin
8	9.54	281	1153	863(100)	B-type (epi)catechin tetramer
9	10.50	280	865	847(95), 821 (30), 739(80),713(75),695(50),577(100), 575(85), 413(55), 287(20)	B-type (epi)catechin trimer

10	10.95	281	1153	865(100), 863(40), 575(50)	B-type (epi)catechin tetramer
11	11.19	280	1441	863(100)	B-type (epi)catechin pentamer
12	11.50	280	865	847(100), 739(60),713(30), 575(70)	B-type (epi)catechin trimer
13	11.83	319	411	207 (100)	Acetyl-dimethyl caffeic acid hexoside
14	12.57	368	609	591 (40), 565(20), 463(15), 301(70), 300(100), 271(40)	Quercetin-3-O-rutinoside
15	12.81	365	463	301(100)	Quercetin-3-O-glucoside
16	12.92	280	865	847(20), 739(60),713(100), 575(50)	B-type (epi)catechin trimer

m/z: relative intensity.

Table S28. Abundance of phenolic compounds detected in kiwifruit peel extracts.

No.	Compound	Λ (nm)	C (µg/g DW)								
			Acetone pure			EtOH: H2O (7:3 wt/wt)			GVL:EtOH (7:3 wt/wt)		
			CE	UAE	MAE	CE	UAE	MAE	CE	UAE	MAE
1	Caffeic acid derivative	325	2.21	1.62	3.87	2.51	0.58	tr	tr	0.07	0.43
2	Caffeic acid hexoside	325	tr	tr	tr	tr	tr	0.10	tr	tr	tr
3	B-type (epi)catechin trimer	280	476.53	356.34	655.72	370.25	205.29	113.46	474.95	469.44	571.34
4	B-type (epi)catechin dimer	280	67.76	67.38	87.94	88.72	80.60	29.42	53.27	55.32	59.96
5	Dimethyl caffeic acid hexoside	325	14.18	24.36	21.53	34.51	29.36	40.97	10.91	12.64	13.04
6	B-type (epi)catechin tetramer	280	103.50	74.19	125.93	56.47	28.87	29.36	112.79	104.33	136.97
7	Epicatechin	280	178.90	141.44	284.32	201.77	126.41	62.55	146.66	161.30	205.76
8	B-type (epi)catechin tetramer	280	105.77	79.13	113.95	64.37	43.31	31.14	114.35	107.39	130.19
9	B-type (epi)catechin trimer	280	340.83	232.12	406.53	259.89	148.72	84.69	294.43	299.19	373.13
10	B-type (epi)catechin tetramer	280	204.31	156.64	272.38	175.98	93.07	63.78	213.94	217.64	268.25
11	B-type (epi)catechin pentamer	280	176.87	101.75	226.04	125.78	67.50	50.71	189.92	176.26	215.34
12	B-type (epi)catechin trimer	280	181.60	131.87	221.13	128.32	78.33	46.60	187.53	193.71	244.33
13	Acetyl-dimethyl caffeic acid hexoside	325	tr	0.15	0.50	1.50	1.47	1.78	tr	tr	tr
14	Quercetin-3-O-rutinoside	370	9.17	10.22	12.48	9.75	10.83	11.00	8.96	10.09	11.80
15	Quercetin-3-O-glucoside	370	8.71	9.39	11.39	8.94	9.53	10.73	8.66	9.35	11.20
16	B-type (epi)catechin trimer	280	55.36	57.97	76.15	57.35	49.27	32.67	54.54	76.32	90.18
	Sum		1925.71	444.57	2519.86	1586.11	973.14	608.96	1870.91	1893.05	2331.92

Tr: <LOQ.

Figures

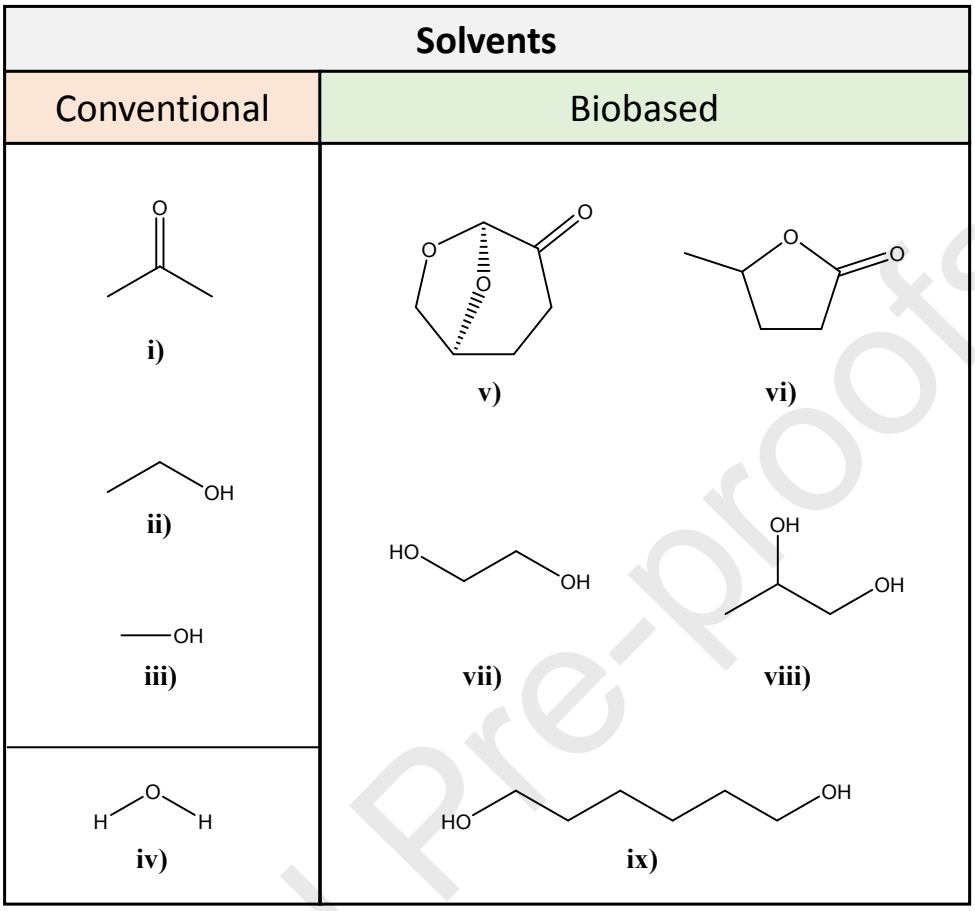


Figure S6. Chemical structure of the solvents used in the study: (i) acetone (Ace); (ii) ethanol (EtOH); (iii) methanol (MeOH); (iv) water (H_2O); (v) cyrene (CYR); (vi) gamma-valerolactone (GVL); (vii) 1,2-ethanediol (ETG); (viii) 1,2-propanediol (PRO) and (ix) 1,6-hexanediol (HEX).

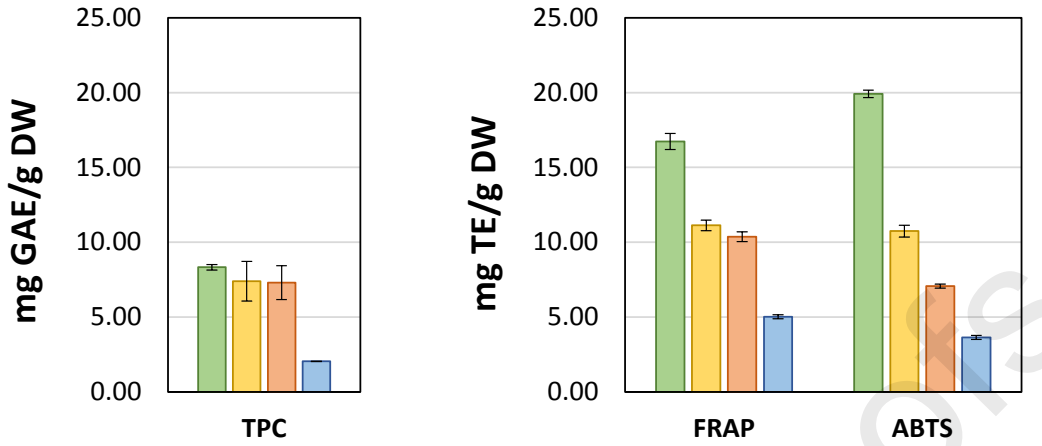


Figure S7. Phenolic content (TPC) and antioxidant activity (FRAP and ABTS) of all kiwifruit parts: peel (green), whole kiwifruit (yellow), juice (red) and pulp (blue) obtained by soxhlet extraction.

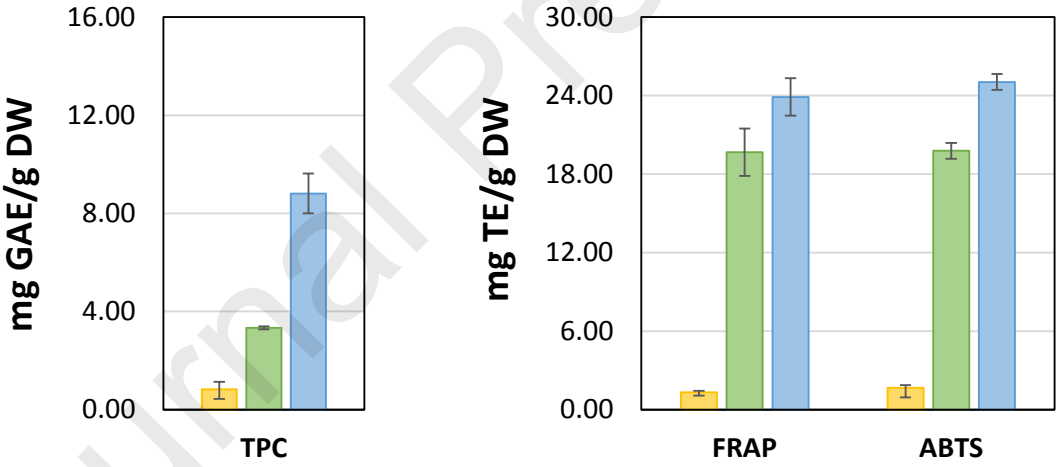


Figure S8. Phenolic content (TPC) and antioxidant activity (FRAP and ABTS) values from extracts from kiwifruit peels storage at different conditions: biomass dry and stored at -10 ºC (yellow), biomass directly stored at -10 ºC (green) and biomass directly stored at -80 ºC (blue), using EtOH:H_2O (7:3, wt/wt) in CE.

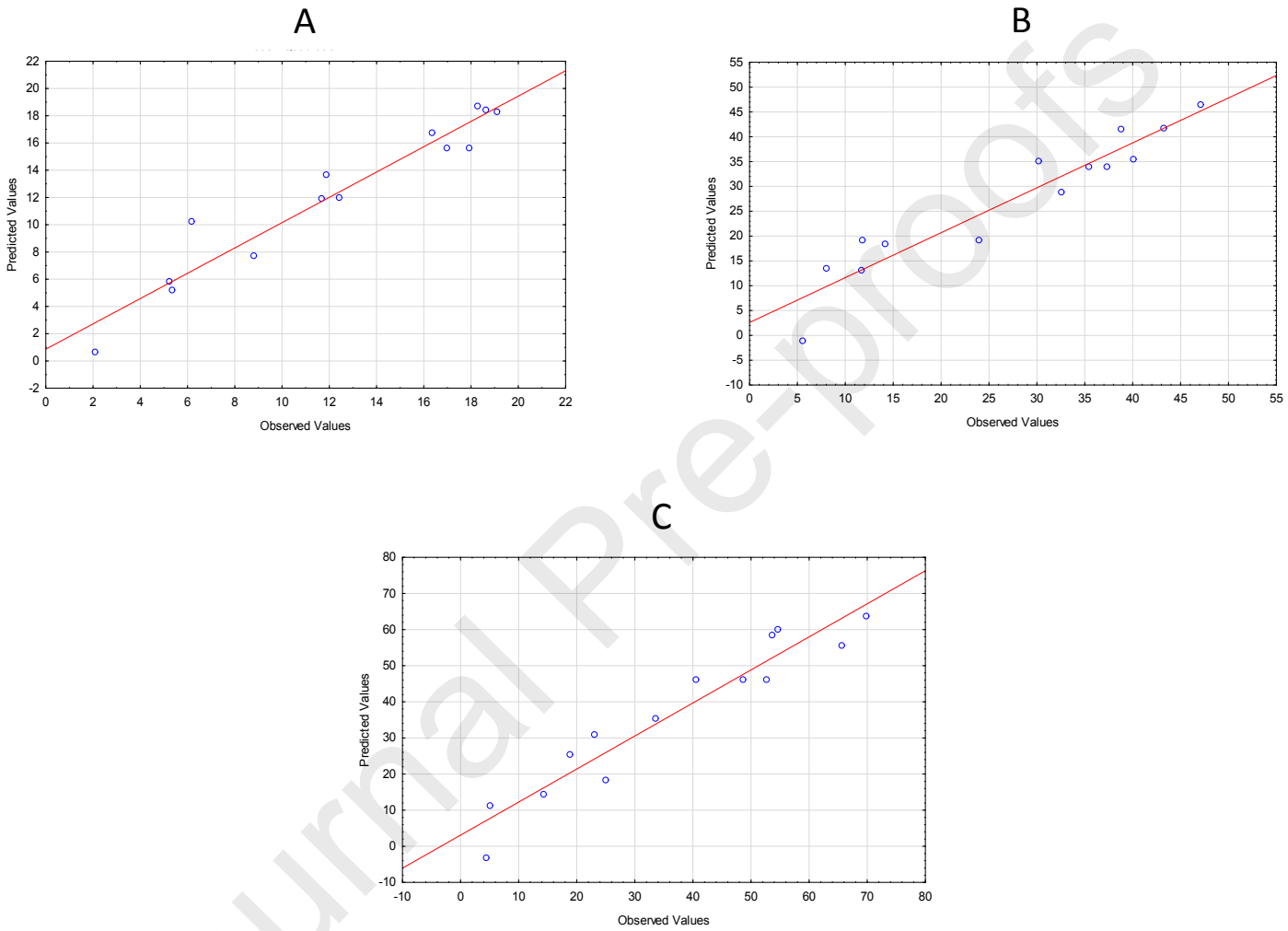


Figure S9. Predict *vs.* observed values of (A) TPC, (B) FRAP and (C) ABTS from mixture design.

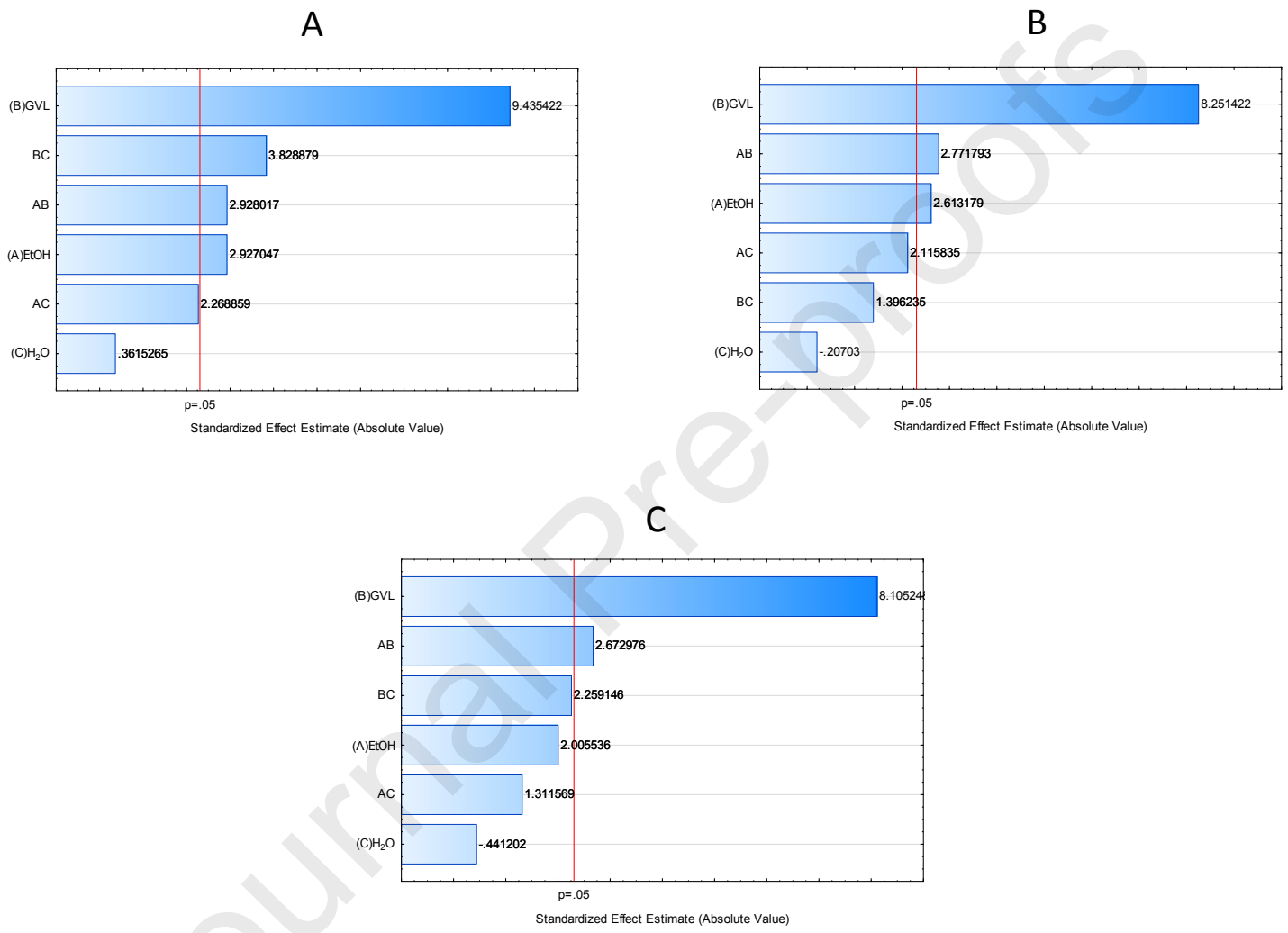


Figure S10. Pareto charts for the standardized main effects in the mixture design for (A) TPC, (B) FRAP and (C) ABTS. The vertical line indicates the statistical significance of the effects (95% of confidence).

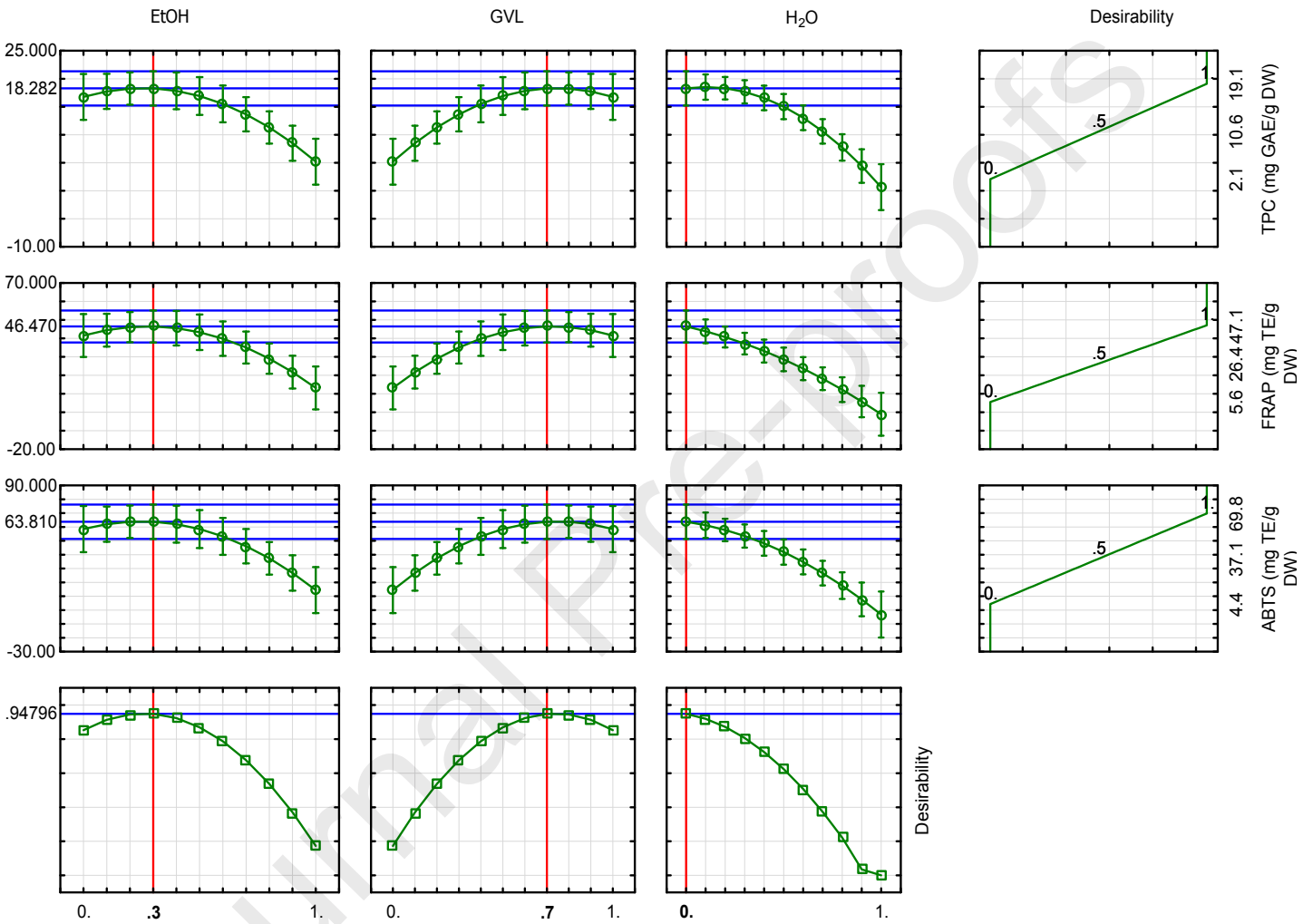


Figure S11. Profiles for predicted values and desirability function for the TPC, FRAP and ABTS from mixture design. Red lines indicate optimized values for each component.

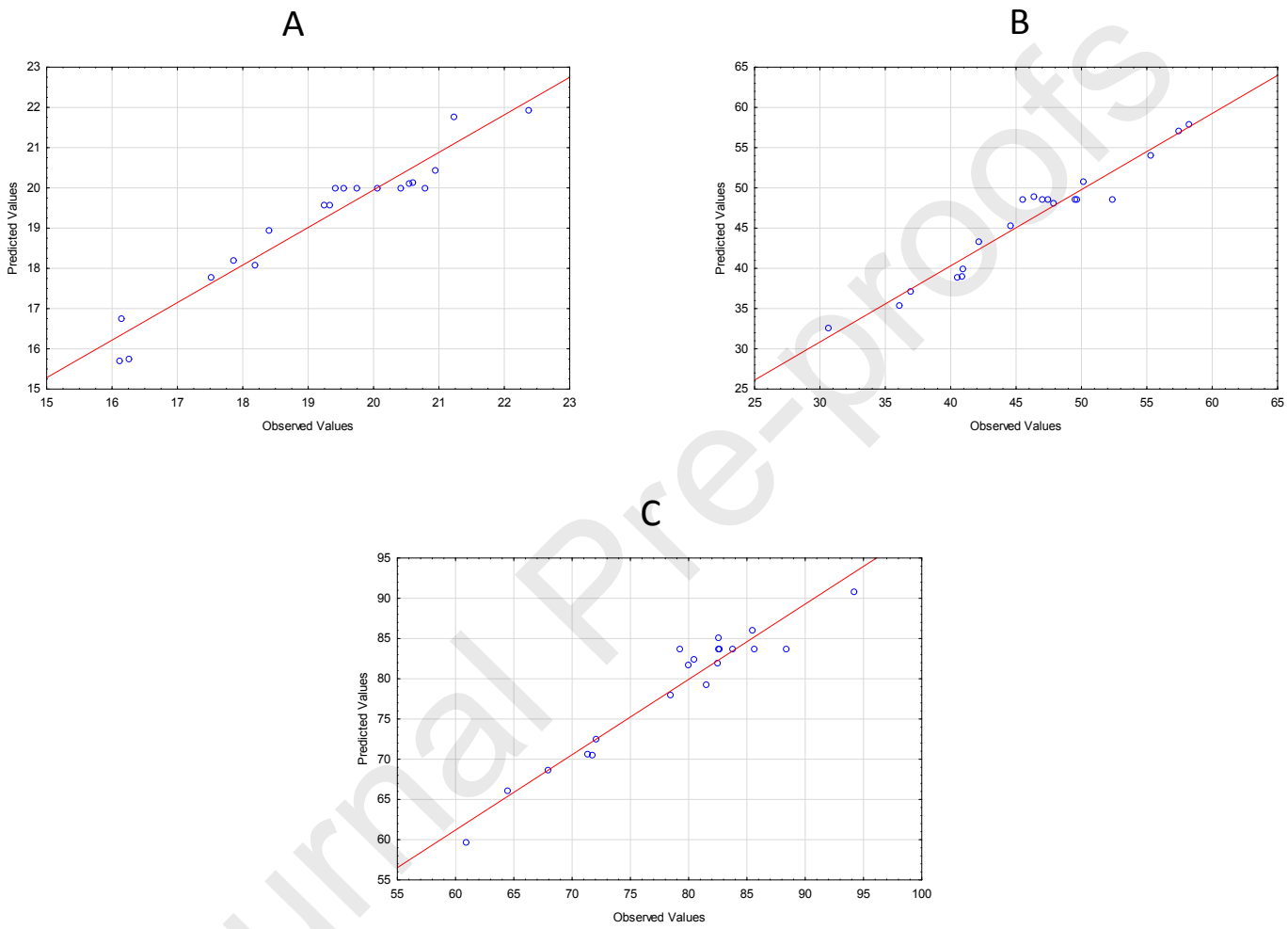


Figure S12. Predict *vs.* observed values of (A) TPC, (B) FRAP and (C) ABTS for the extracts obtained by conventional extraction from the factorial planning.

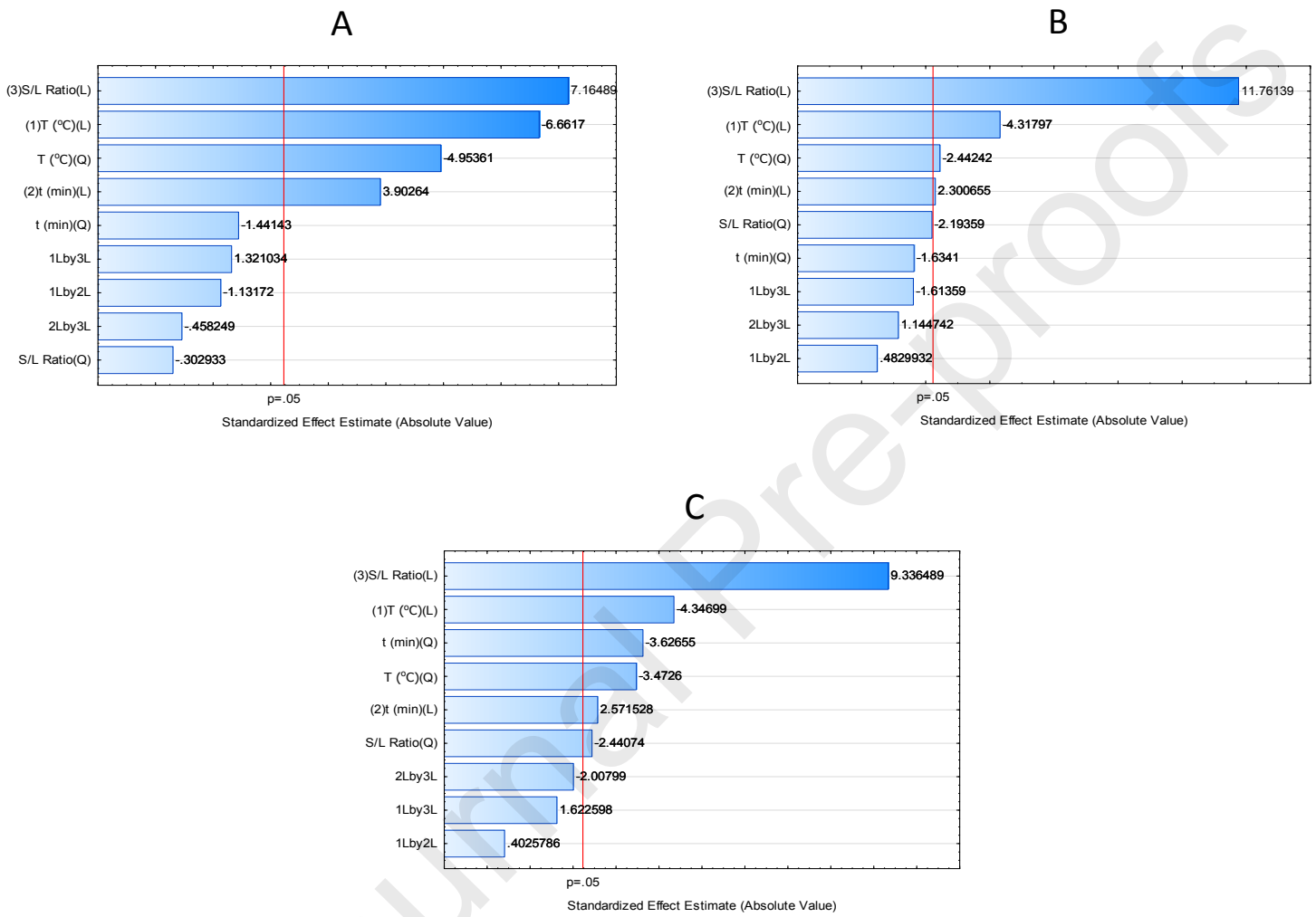


Figure S13. Pareto charts for the standardized main effects in the factorial planning for (A) TPC, (B) FRAP and (C) ABTS, for the extracts obtained by conventional extraction. The vertical line indicates the statistical significance of the effects (95% of confidence).

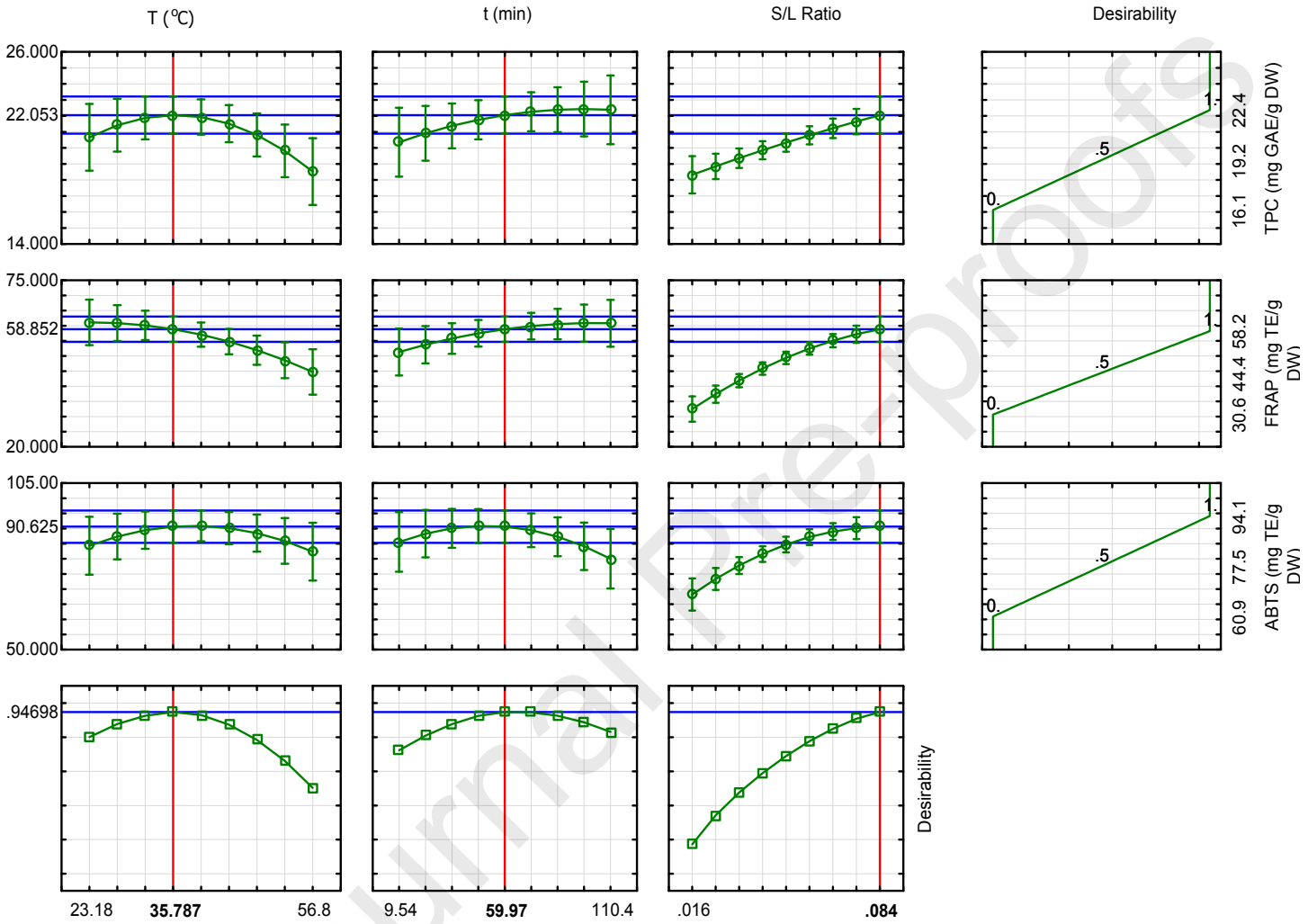


Figure S14. Profiles for predicted values and desirability function for the TPC, FRAP and ABTS for the extracts obtained by conventional extraction from the factorial planning. Red lines indicate optimized values for each variable.

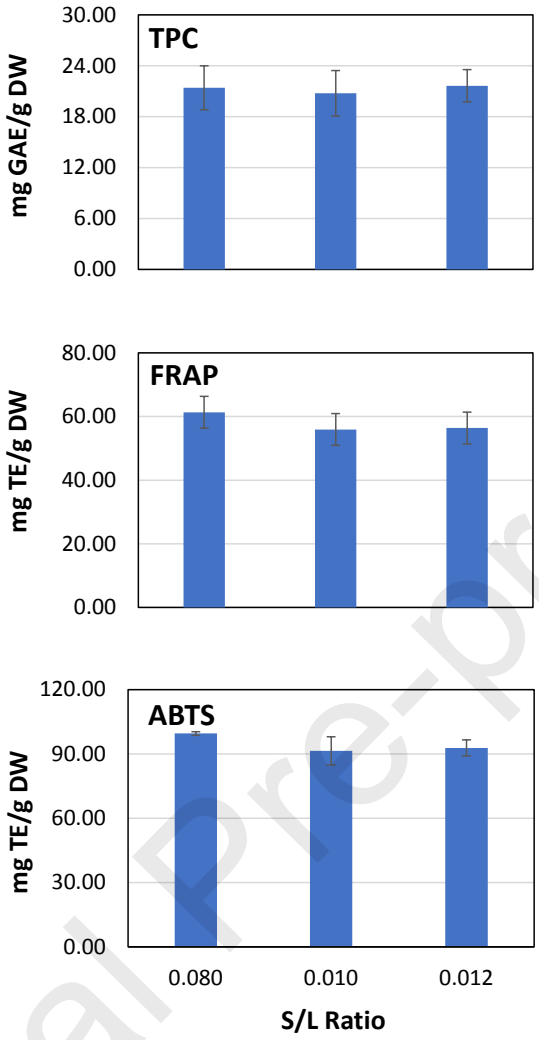


Figure S15. Levels of TPC, FRAP and ABTS obtained using the optimal conventional extraction conditions (36 ºC, 60 min) and applying different values of solid-liquid ratio (S/L Ratio).

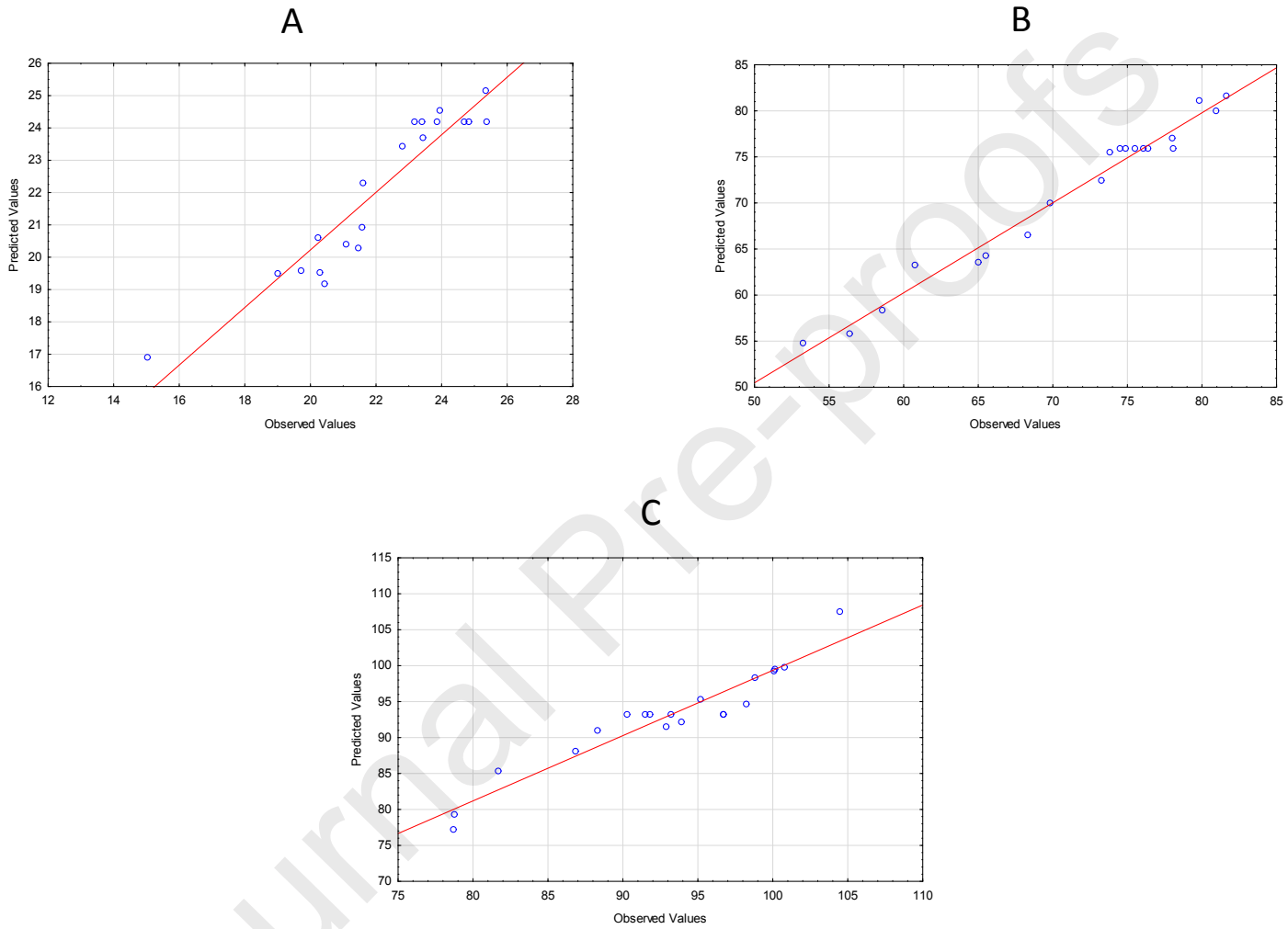


Figure S16. Predict *vs*. observed values of (A) TPC, (B) FRAP and (C) ABTS for the extracts obtained by UAE from the factorial planning.

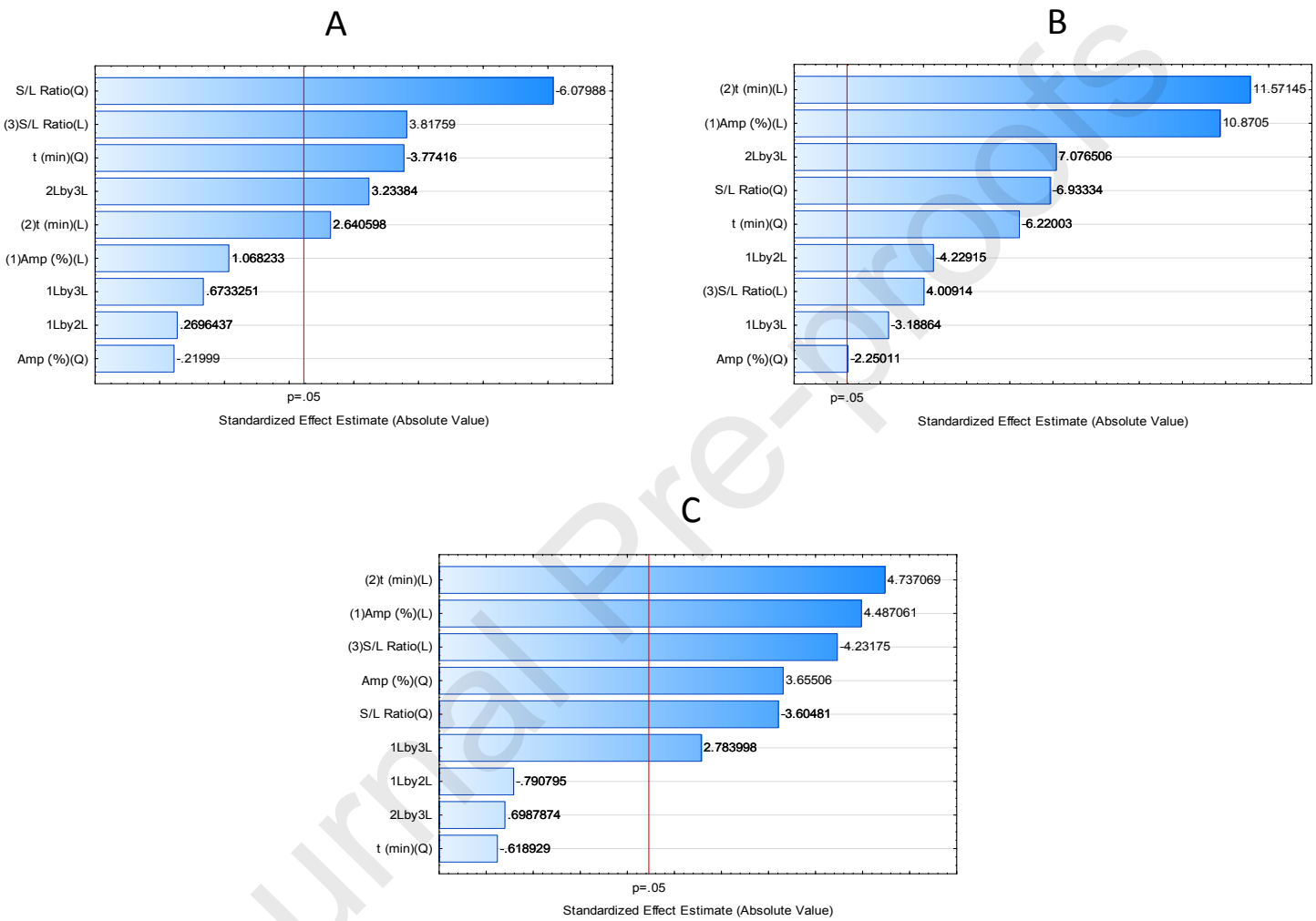


Figure S17. Pareto charts for the standardized main effects in the factorial planning for (A) TPC, (B) FRAP and (C) ABTS, for the extracts obtained by UAE. The vertical line indicates the statistical significance of the effects (95% of confidence).

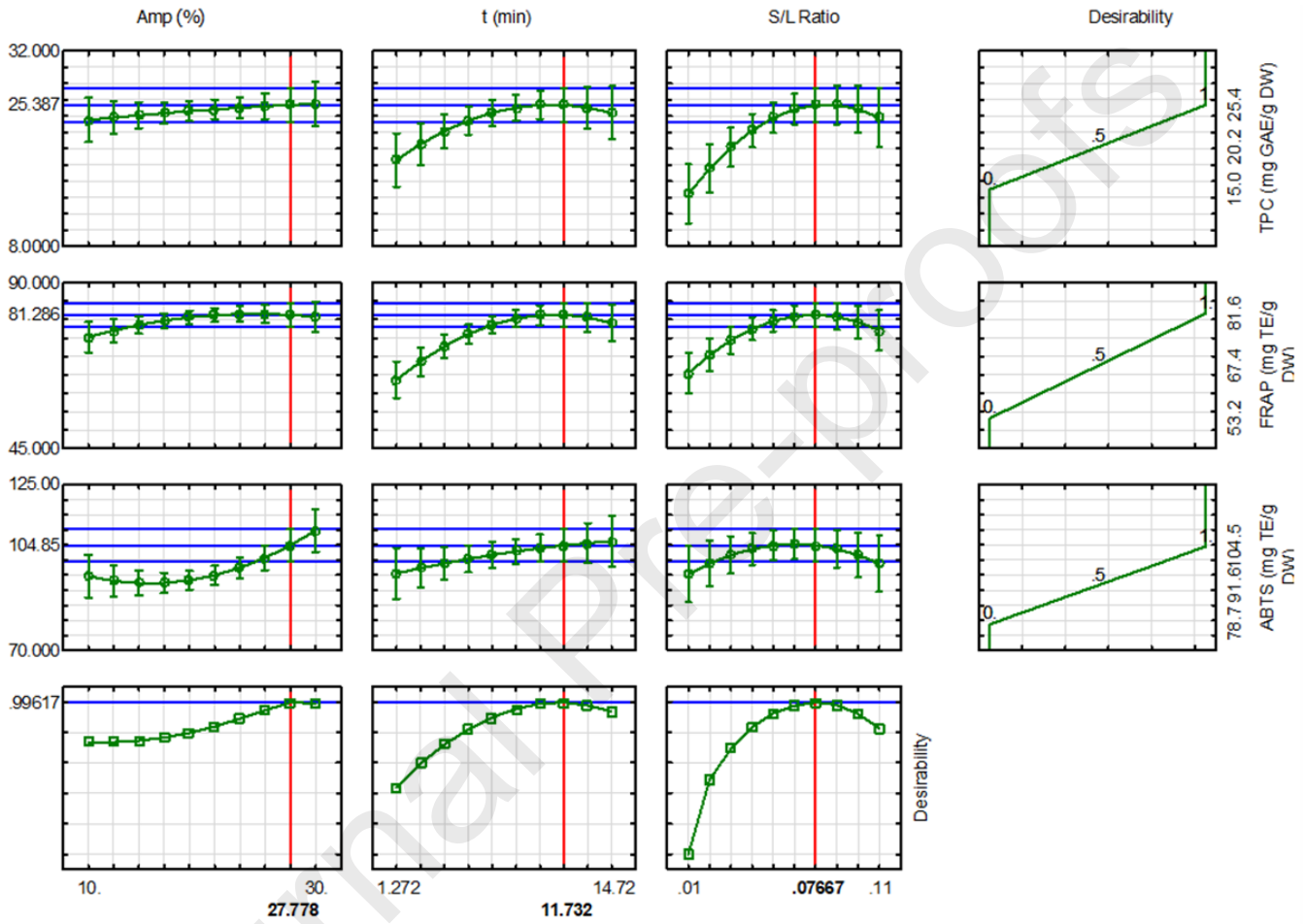


Figure S18. Profiles for predicted values and desirability function for the TPC, FRAP and ABTS for the extracts obtained by UAE from the factorial planning. Red lines indicate optimized values for each variable.

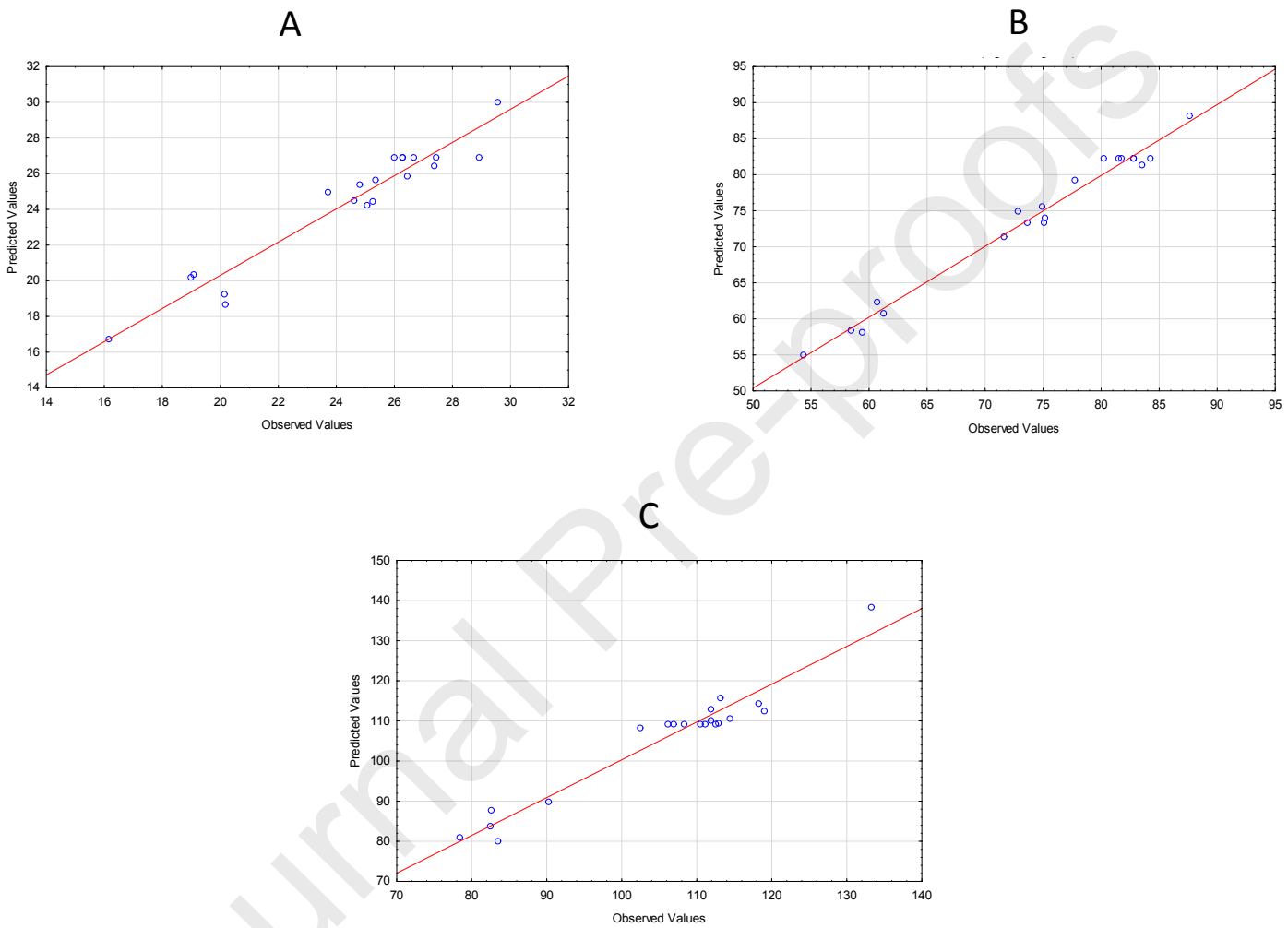


Figure S19. Predict *vs*. observed values of (A) TPC, (B) FRAP and (C) ABTS for the extracts obtained by MAE from the factorial planning.

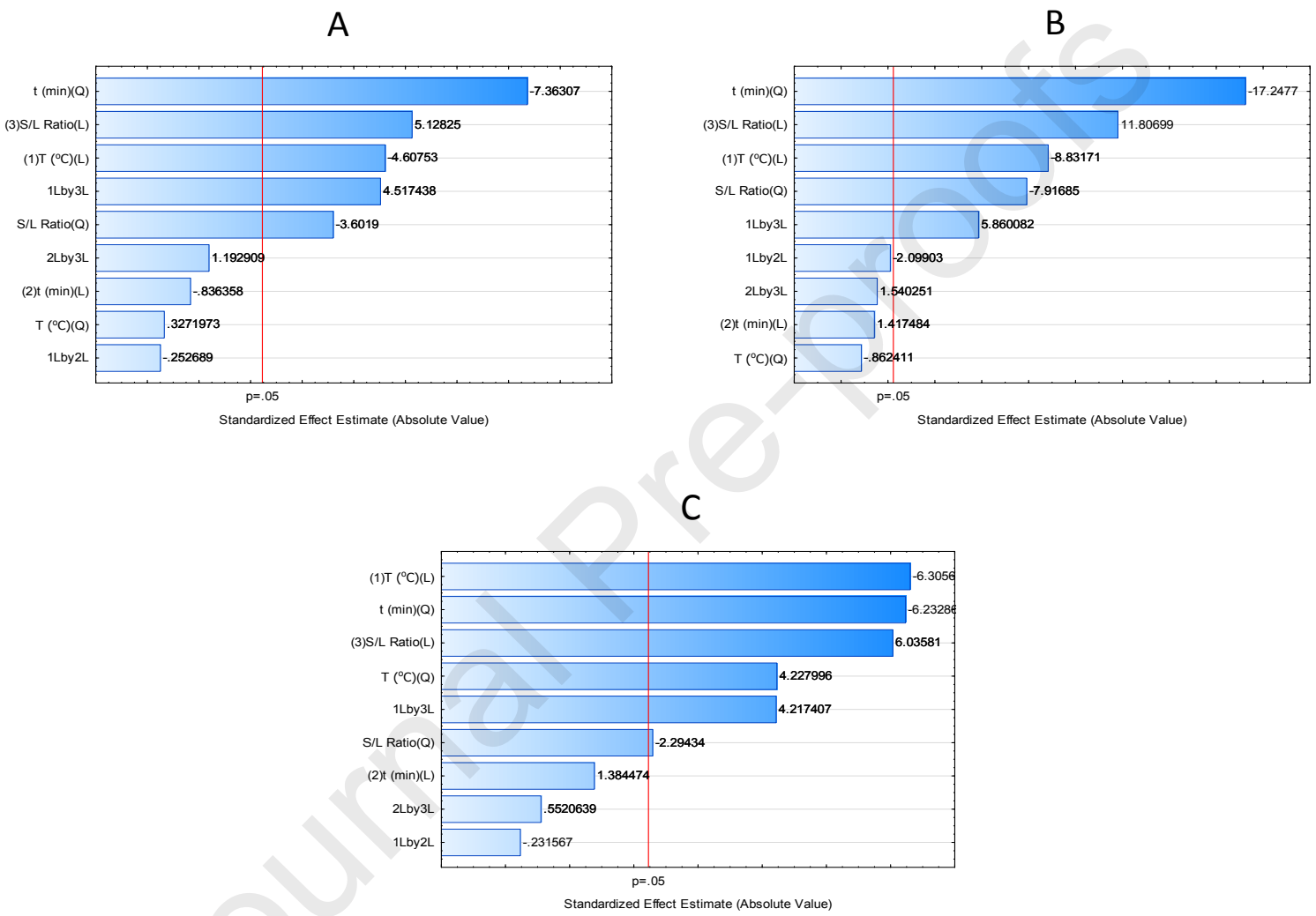


Figure S20. Pareto charts for the standardized main effects in the factorial planning for (A) TPC, (B) FRAP and (C) ABTS, for the extracts obtained by MAE. The vertical line indicates the statistical significance of the effects (95% of confidence).

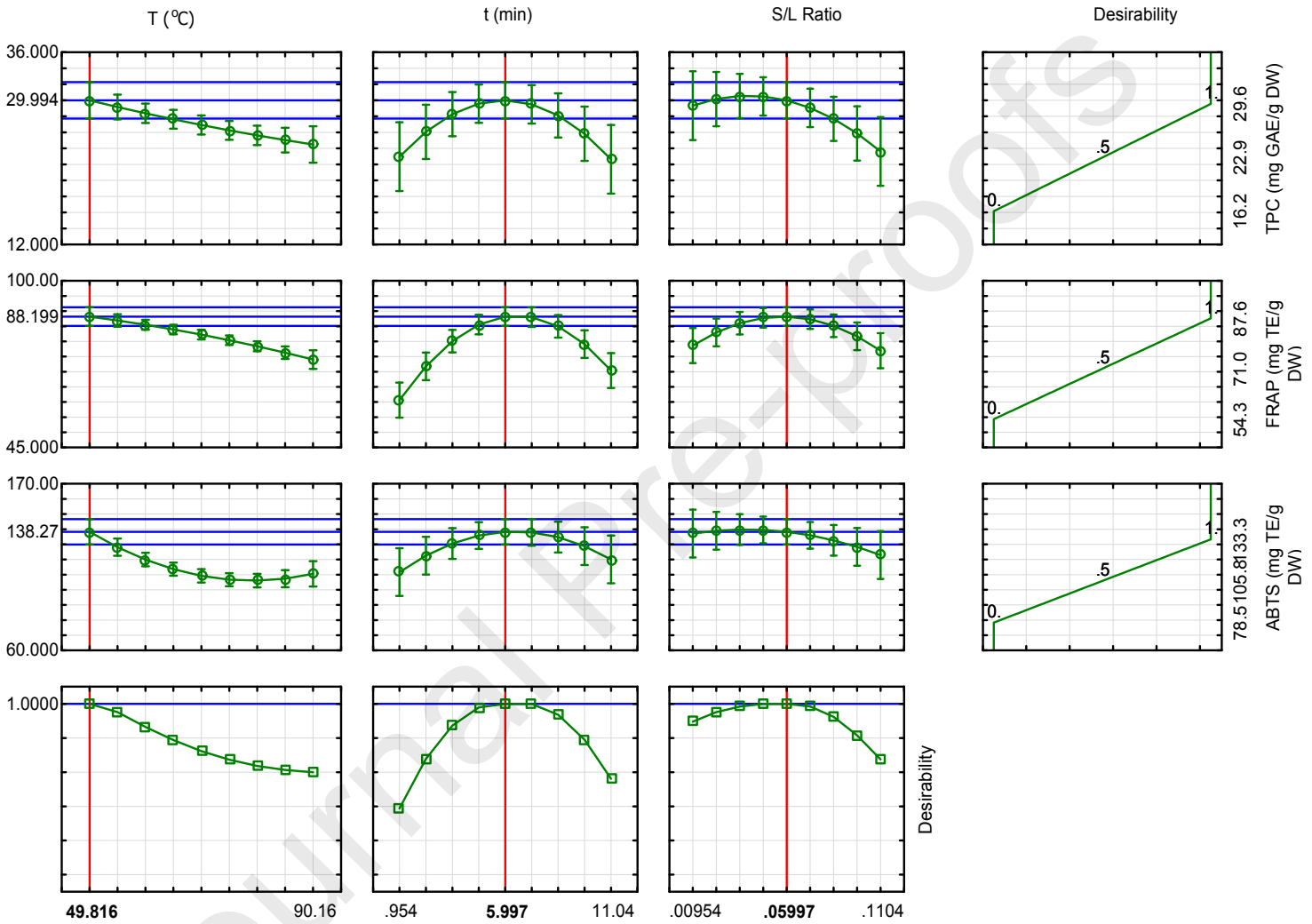
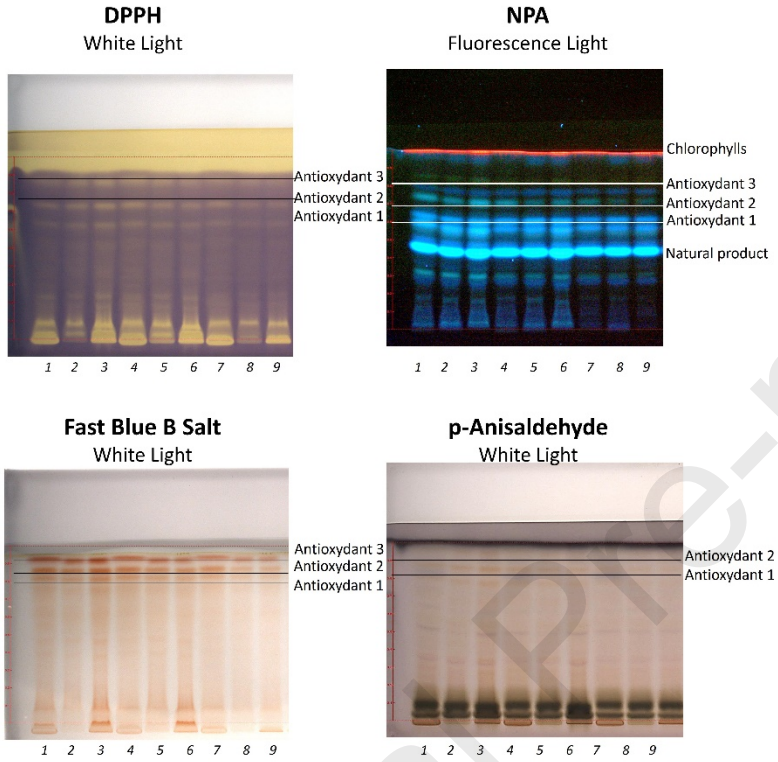


Figure S21. Profiles for predicted values and desirability function for the TPC, FRAP and ABTS for the extracts obtained by MAE from the factorial planning. Red lines indicate optimized values for each variable.



Track	Extraction Solvent – Extraction Technique
1	GVL:EtOH (7:3 wt/wt) - CE
2	EtOH:H_2O (7:3 wt/wt) - CE
3	Ace - CE
4	GVL:EtOH (7:3 wt/wt) - UAE
5	EtOH:H_2O (7:3 wt/wt) - UAE
6	Ace - UAE
7	GVL:EtOH (7:3 wt/wt) - MAE
8	EtOH:H_2O (7:3 wt/wt) - MAE
9	Ace - MAE

Figure S22. HPTLC profiling of kiwifruit peels extracts.

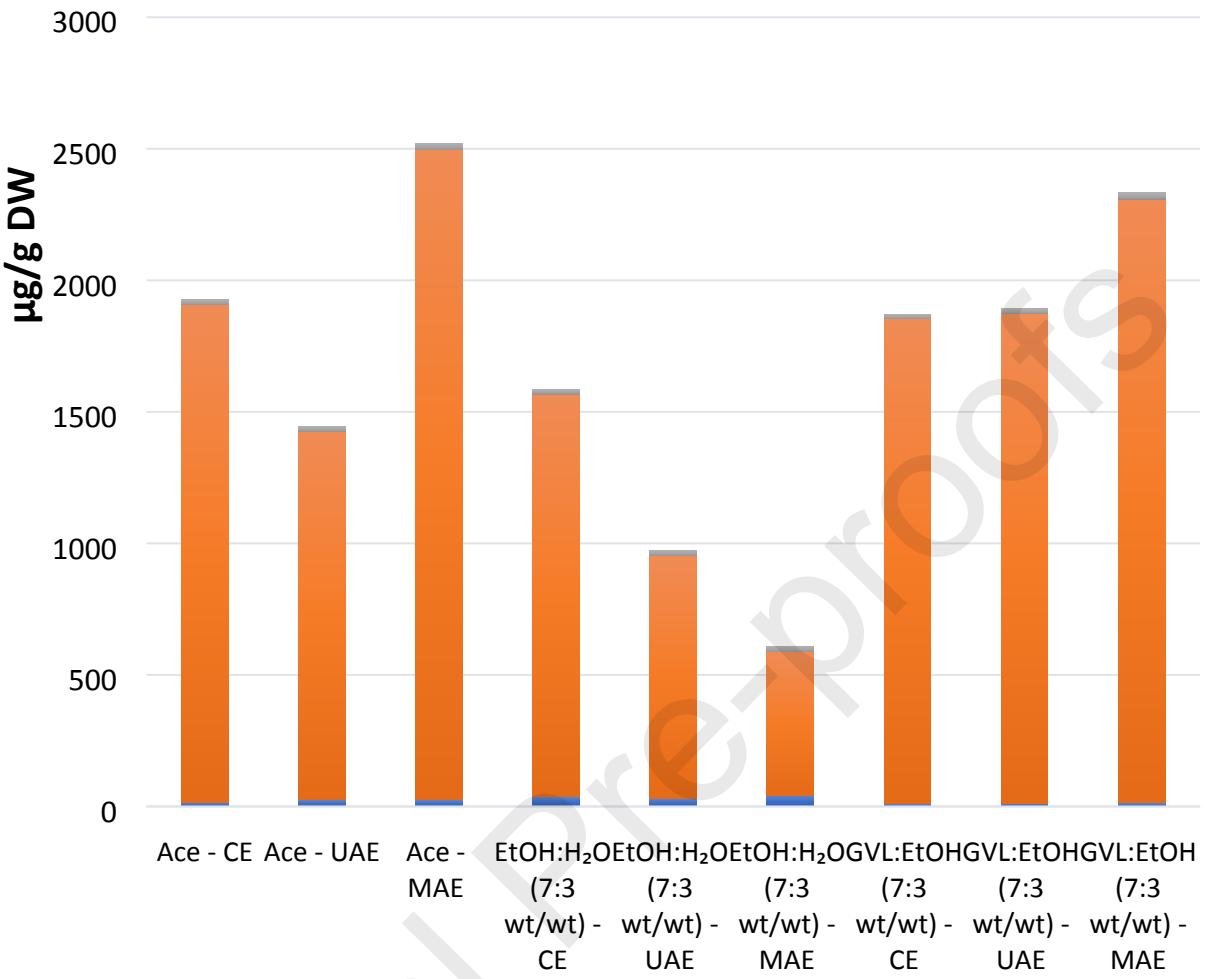


Figure S23. Extraction efficiency of caffeic acid derivatives (blue), epicatechin derivatives (orange) and quercetin glycosydes (grey) from kiwifruit peel in each solvent (pure acetone, EtOH:H_2O at 7:3 wt/wt, and GVL:EtOH at 7:3 wt/wt) and each technique (CE, UAE and MAE).

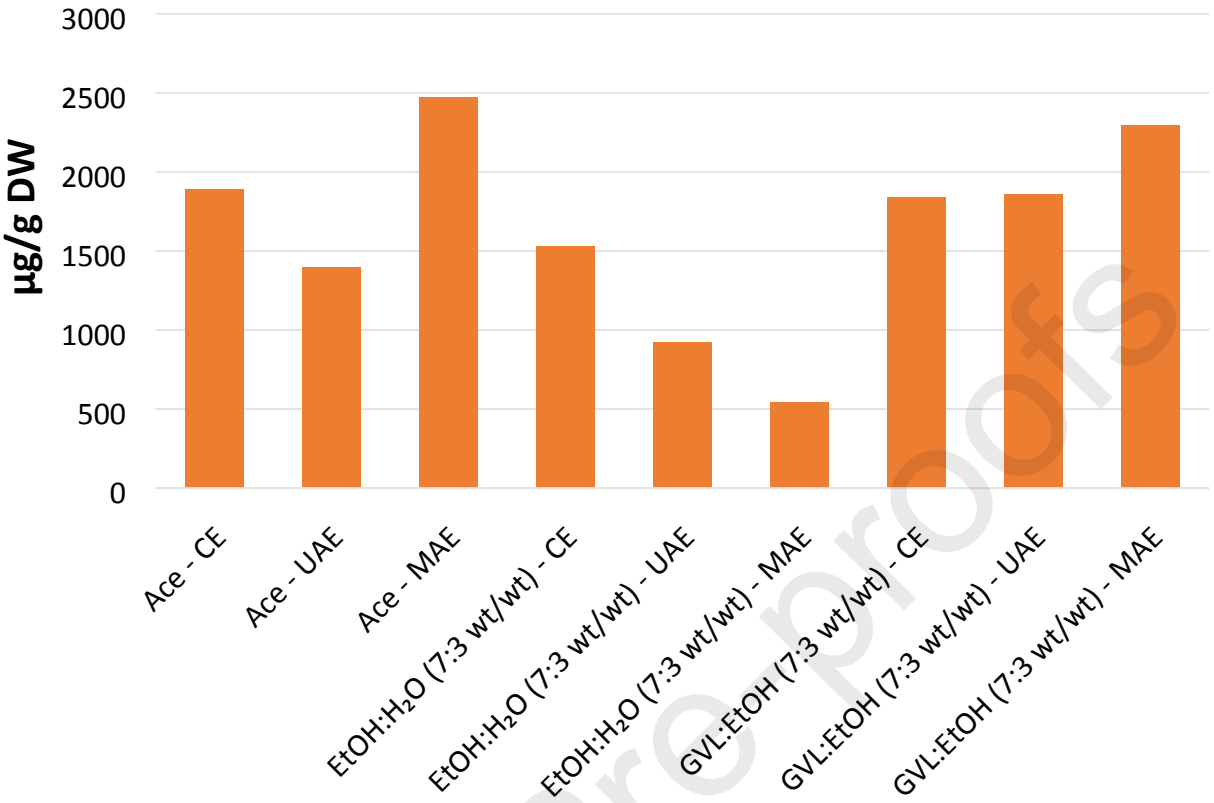


Figure S24. Extraction efficiency of epicatechin derivatives from kiwifruit peels in each solvent (pure acetone, EtOH:H_2O at 7:3 wt/wt, and GVL:EtOH at 7:3 wt/wt) in each technique (CE, UAE and MAE).

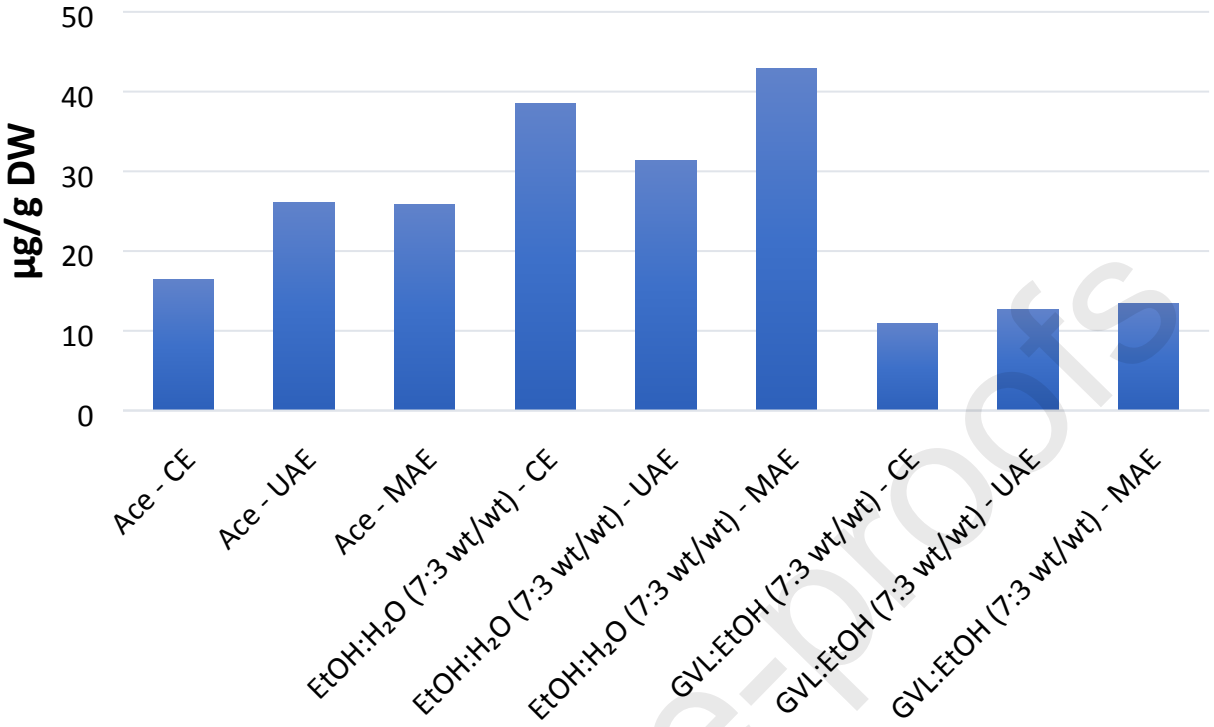


Figure S25. Extraction efficiency of caffeic acid derivatives from each solvent (pure acetone, EtOH:H_2O at 7:3 wt/wt, and GVL:EtOH at 7:3 wt/wt) in each technique (CE, UAE and MAE).

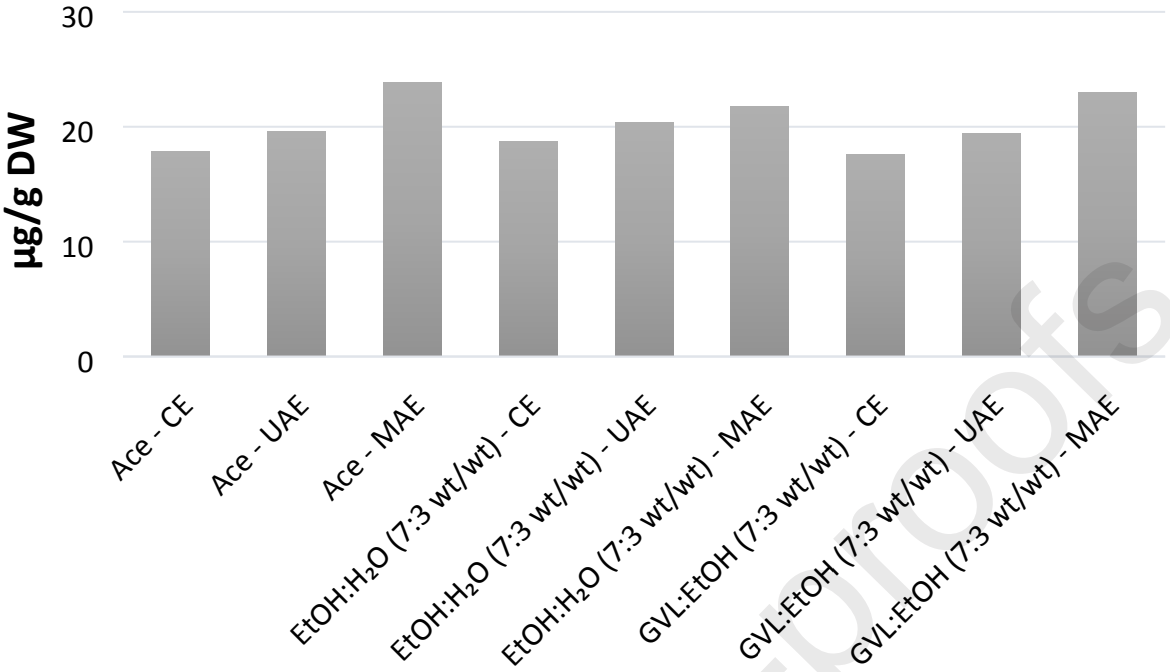


Figure S26. Extraction efficiency of quercetin glycosides from kiwifruit peels in each solvent (pure acetone, EtOH:H_2O at 7:3 wt/wt, and GVL:EtOH at 7:3 wt/wt) in each technique (CE, UAE and MAE).

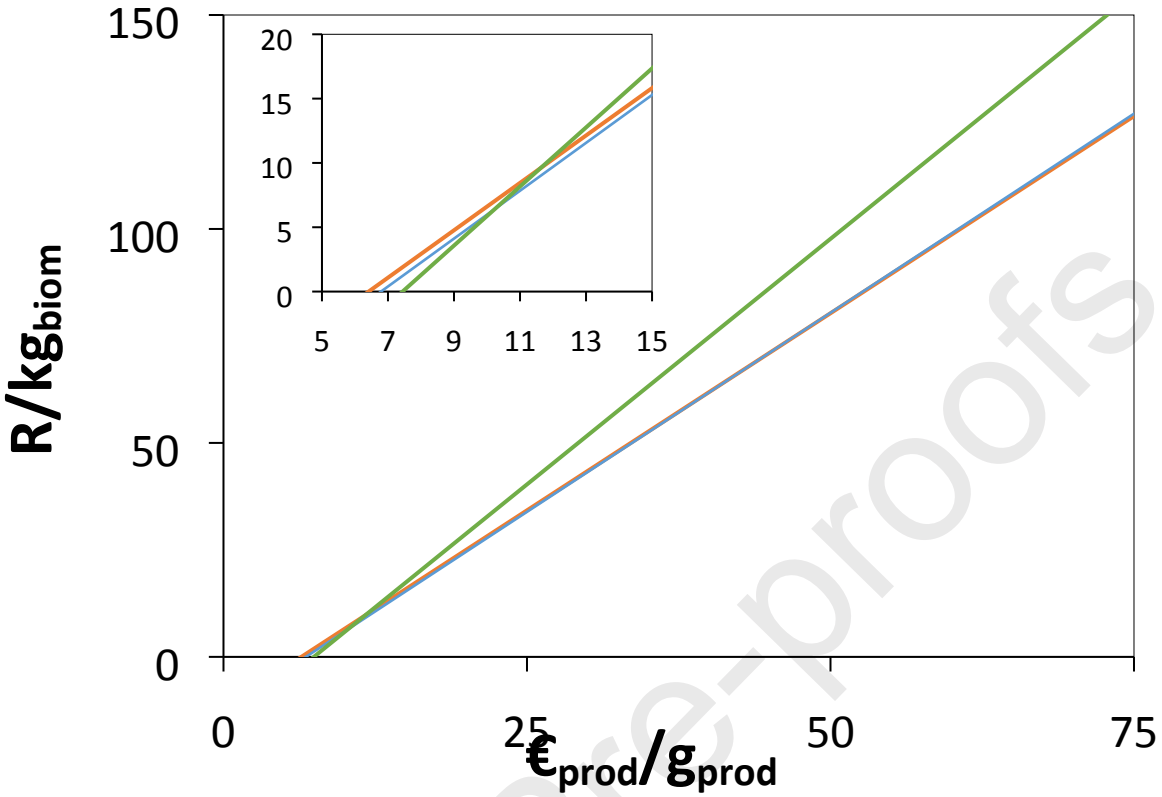
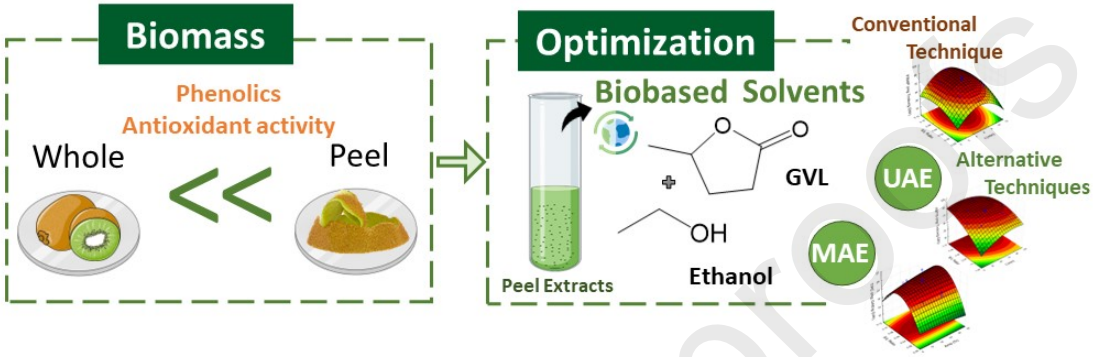


Figure S27. Return (R) obtained *per* each kilogram of treated biomass as a function of derivates of epicatechin cost ($€_{prod}/g_{prod}$) for each studied technique – conventional extraction (orange), UAE (blue), MAE (green).



- Production of extracts with high phenolic content and antioxidant activity from kiwi peels.
- Optimization of biobased solvent mixtures composition and operating extraction conditions.
- Mixtures of gamma-valerolactone and ethanol were the most promising solvents.
- UAE was the best technique considering its efficiency and extraction process costs.

Declaration of interests

☒ 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.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: