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Design of experiments for green and GRAS solvent extraction of phenolic compounds from food industry by-products - A systematic review

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ABSTRACT

Concerning the high impact of climatic change in the environment, the scientific community has focused on a circular economy perspective and the revalorization of waste generated by the food industry for bioactive uses. These applications are possible due to the presence of bioactive compounds in these food wastes. In this sense, phenolic compounds highlight for their positive health implications, as they possess potent activity to prevent diseases such as cancer, inflammation and obesity, among others. For this purpose, the optimized extraction of these target compounds from by-products with a novel green chemistry approach, by using environmentally clean and friendly extraction techniques, commonly known as green extractions, as well as those permitted in foods and safe for health (GRAS solvents) is commonly applied. Following this research line, a systematic review was conducted using different databases (Web of Science, PubMed and Scopus) following PRISMA guidelines to assess the optimization of different green and GRAS solvent extraction techniques from food by-products, the best extraction conditions, as well as the experimental design applied to obtained maximum amounts of the compounds of interest, considering the research published to date. Thus, 67 studies of 282 records identified met the inclusion criteria. A distinction has been made between the different technologies used in the extraction processes, paying special attention to the experimental designs applied and the optimized independent variables. Finally, a quantitative and qualitative comparison was made between the different matrices studied.

1. Introduction

During food processing, a high amount of wastes is usually collected at the point of production and burned or disposed of in landfills. As a result, the ecology and the ecosystem suffer numerous negative impacts. That is why sustainable food production and by-product revaluation have become crucial in the modern agricultural and food industries over the past years. At the same time, awareness of the relationship between nutrition enriched with bioactive compounds and the prevention of chronic diseases has increased [1]. Among these compounds, polyphenols are secondary plant metabolites and one of the scientific community's most extensively studied substances [2]. They have a large variety of biological properties, such as being anti-oxidative, anti-inflammatory, anti-obesogenic, anti-allergenic, anti-viral, anti-cancer, anti-thrombotic, anti-microbial, anti-mutagenic, vasodilatory and cardioprotective effects, among others [3–8].

In keeping with this objective of respecting the environment, the use of green extraction technologies that are also permitted for food use thanks to the use of GRAS solvents (generally recognized as safe) are becoming a habitual practice in current research [9–11]. Conventional extraction methods, including solid-liquid extraction (SLE) and liquid-liquid extraction (LLE), present limitations that have been attempted to be solved with the development of these advanced extraction techniques. Some of the advantages of green chemistry concerning extraction are the reduction of energy consumption, the use of alternative solvents, the decrease of extraction time, the maximization of yield and the production of high quality extracts [12,13].

In the last years, several research groups have worked on optimizing the extraction processes of by-products from the food industry by the Response Surface Methodology (RSM), as shown in Fig. 1 [10,14–17]. It is a set of mathematical techniques used in data processing in which a response of interest is influenced by several quantitative factors. The

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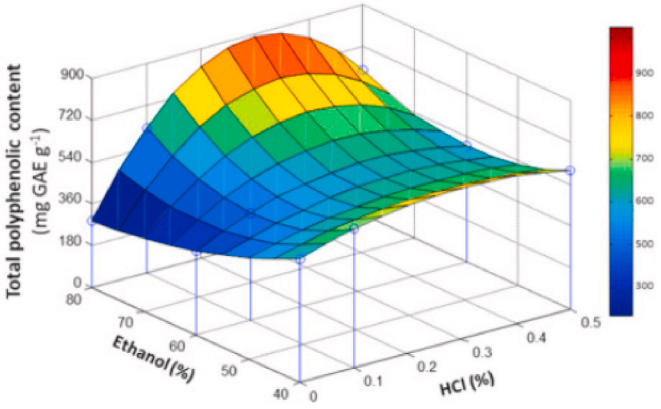

Fig. 1. Surface response depicting the extraction behaviour of total polyphenol content (mg GAE g^{-1} fresh weight) by UAE as a function of EtOH and HCl percentages for spinach residues [17].

purpose of these techniques is to design an experiment that provides specific values of the response variables and then to determine the mathematical model that best fits the obtained data. The ultimate goal is to establish the values of the independent factors that optimize the response variable. For this purpose, there are different types of designs for the optimization of the response variable, such as factorial design (FD), Box-Behnken Design (BBD) and Central Composite Design (CCD). FD consist of all combinations of the different levels of each experimental factor, while BBD is a three-level design that includes a subset of runs of a full three-level factorial. Lastly, CCD consists of a full factorial with points at the centre or a fractional FD with V resolution, to which star points used to model the curvature with respect to each factor are added.

The goal of this work is to describe, compare and discuss the application of design of experiments (DoE) for green and GRAS solvents extraction by advanced techniques aimed to recover bioactive compounds from food by-products and the phytochemical characterization of the obtained extracts by different analytical methodologies. For this purpose, a distinction has been made between the different extraction methodologies used for the recovery of these phytochemicals, concretely polyphenols. Thus, a special attention has been paid to the experimental designs applied and the optimized independent variables. Finally, the quantities extracted of the target compounds after the optimization were compared, in terms of theoretical or experimental values, for the different studied matrices. As far as we are concerned, a comparison of the research to date focused on the optimization of green extraction of phenolic compounds from food industry by-products taking into account the type of experimental design, the independent variables studied and the extraction optima for each technique, has not yet been performed. This literature review can be of great use to researchers in this field, providing a guide on the most commonly used extraction techniques, parameters and experimental designs applied for the different matrices used.

2. Materials and methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines 2020 [18]. The search for articles was conducted between September and December 2022. Journal articles were obtained from three electronic databases: PubMed, Web of Science and Scopus. The proposed objective was to identify all studies that would optimize the extraction of phenolic compounds from food by-products.

The search was made using a search equation by the combination of "green extraction" or "advanced extraction" or "PLE" or "MAE" or "SFE" or "UAE" or "SWE" and "phenolic compounds" or "polyphenols" or "phenolics" and "optimization" or "response surface methodology" or "RSM" and "waste" or "byproduct" or "by-product" or "peel" or "seed" or "leaves" and "HPLC". These terms were selected in order to search for overall studies focused on green and GRAS solvent extraction of phenolic compounds from food industry by-products. Moreover, a manual search of others articles referenced in revised papers was developed, considering the same eligibility criteria, and duplicate articles were removed. The search was not filtered by year of publication, including all articles to date. In the screening, the eligibility criteria applied were studies that included experimental data about the optimization by DoE, the use of advanced green extractions and GRAS solvents, the identification of the extracted compounds by analytical techniques and the revalorization of by-products as an extraction matrix. Review articles were excluded from the analysis and no language filter was applied. The study selection process is shown in Fig. 2.

3. Results and discussion

3.1. Extraction of bioactive compounds by design of experiments

Advanced extraction techniques employed in obtaining bioactive compounds from agri-food by-products are presented in this section, since these natural resources have been reported to be a good source of compounds with several properties that are beneficial for human health. Among these advanced methods, subcritical water extraction (SWE), microwave assisted extraction (MAE), supercritical fluid extraction (SFE), pressurized liquid extraction (PLE), and ultrasound assisted extraction (UAE) can be highlighted according to the inclusion criteria applied in this study.

In this sense, it is a usual practice to conduct numerous tests for the recovery of bioactive compounds in order to enhance the production of functional components, such as to get the highest yield possible during an extraction process. The results of these tests are typically evaluated based on a trial-and-error basis, with a high number of experiments that significantly affect the cost of this kind of procedures. Because DoE enables careful advance planning of the experiments with the goal of knowing the ideal conditions of a process using a limited number of tests, it has emerged as an effective alternative to these limitations.

Indeed, DoE provides a series of tests conducted to evaluate a system or process, leading to address the experimental conditions for optimizing the variable of interest in the base of the proper statistical analyses. RSM is widely used as DoE. This methodology includes the three elements of design, model, and optimization to explain the experimental designs. Design is referred to a mathematical model that enables a summary of how the response variables behaved under the tested experimental circumstances. This mathematical model may determine the linear, quadratic and interactions between independent variables after first or second order equations (Equations (1) and (2), respectively) [19].

$$Y = \beta_0 + \sum_{l=1}^{k} \beta_l X_l \tag{1}$$

$$Y = \beta_0 + \sum_{l=1}^{k} \beta_l X_l + \sum_{l=1}^{k} \beta_{ll} X_l^2 + \sum_{l=1<}^{k} \sum_{J=1}^{k} \beta_{lJ} X_l X_J \tag{2}$$

The response variable is represented by the letter Y; the constant coefficient 0 fixes the response at the experiment's centre; the letters i, ii, and ij are the regression coefficients for the linear, quadratic, and interaction factors, respectively; and the terms x_i and x_j, are the values of the independent variables [20]. In this sense, the first order design is employed when only the principal impacts of the components are assessed, but the second order design includes both an individual analysis of the factors and their interactions with their quadratic effects [19].

The second order models, which are more effective to optimize

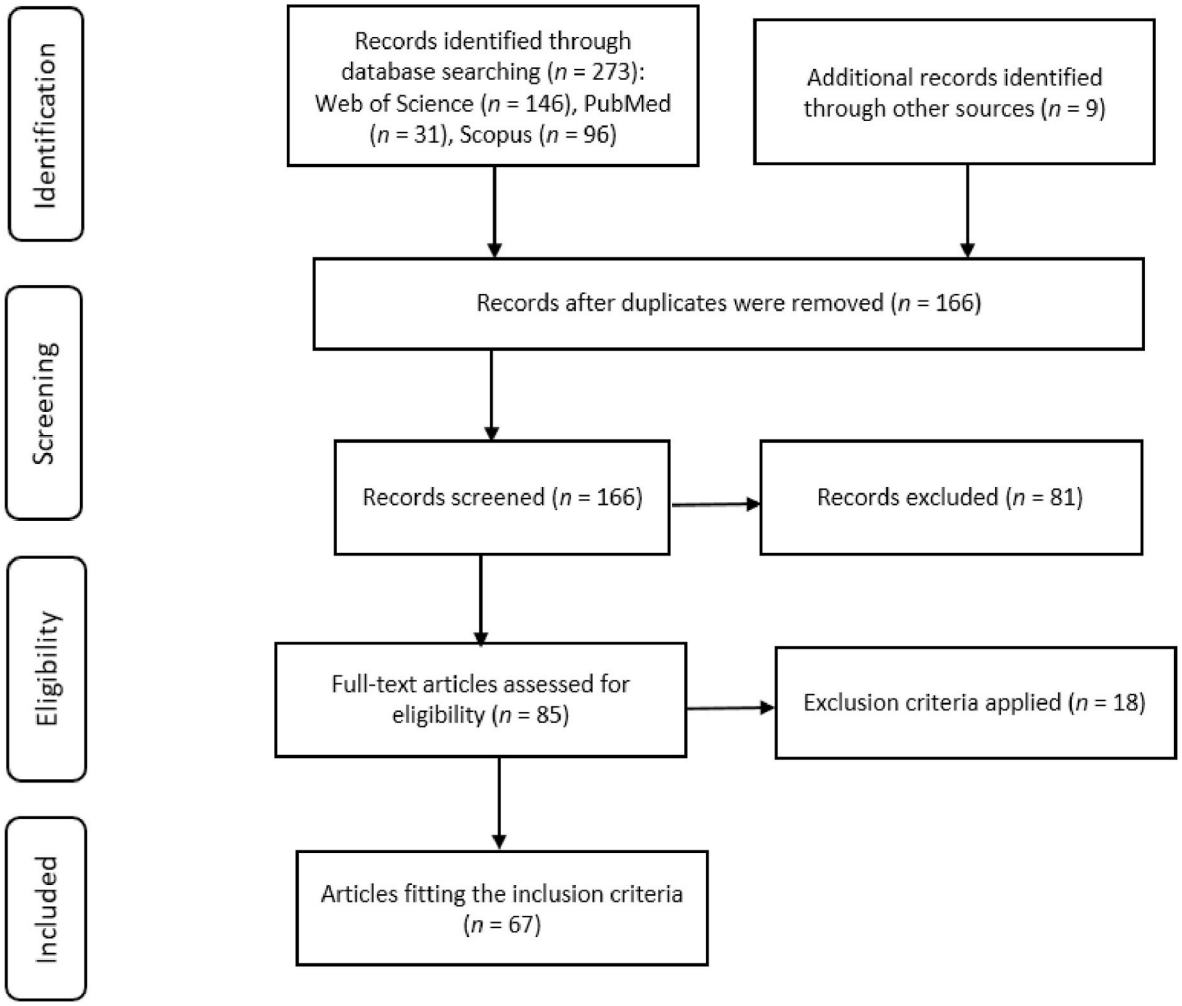

Fig. 2. Study selection process of the search for the systematic review.

complex processes, are the two primary types of mathematical models (Equations (1) and (2)) that are most frequently used in extraction techniques for the production of functional components from agri-food by-products. More information about the effects of factors, their interactions, and their quadratic effects is provided by this type of model, as well.

In order to estimate the curve produced on the response surface, the components must be taken into account in at least three levels (−1, 0, +1). In this regard, the BBD and CCD are the most popular experimental designs based on RSM. On the one hand, the BBD is employed whenever three or more variables are taken into account. A minimum of one of the factors is fixed at the middle range throughout each run because this type of design lacks experimental sites on the vertexes, preventing all factors from being simultaneously established at their maximum or lowest values [19].

The outcomes of this situation are helpful when performing under extreme circumstances is not possible, such as when the extraction solvent evaporates at a high temperature. On the other hand, because it does not involve these extreme circumstances, it is a rotatable or nearly rotational design. As a result, even if the level values are altered, the prediction of the behaviour of the evaluated answers will still hold true if the central circumstances are maintained.

The CCD, on the other hand, is widely utilized because of its high level of versatility. In fact, the experimental data early obtained in a FD may be used in a CCD performing only the axial points, so eliminating resource waste. Additionally, this design contains at least two replicates of the central points (0, 0, 0), just like the BBD, which enables to determine the reproducibility of the experiments. The axial points (−α, α) are the most distinctive parameters. These points guarantee the curvature of the response surface, go beyond the lowest and maximum limits of the factors, and allow for the creation of the ideal conditions. Contrary to the BBD, the orthogonal and rotatable properties can be attributed to a CCD that distinguishes between axial point estimates [19].

Therefore, each experimental element has five levels in the CCD. On the contrary, only three levels of each factor, a low level (−), central level (0), and high level (+), can be used in simpler designs like the 3-level FD. In this kind of designs, runs are produced at each combination of these three levels via three-level FD [19]. Fig. 3 displays a summary of the many designs that have been applied to optimize the recovery of phenolic compounds from agri-food by-products.

3.1.1. *Subcritical water extraction*

SWE technology is a successful process to recover bioactive compounds from food by-products in an environmentally friendly way. This technique applies water above the critical point as an extraction solvent using temperatures between 100 and 374 °C and pressures in the range from 10 to 60 bars that maintained water in its liquid state [21]. The combination of different temperature and pressure values provides changes in the water dielectric constant, which is modified to allow retrieving a wide range of chemical compounds with different polarity [22]. In addition to temperature and pressure applied to the process, other independent variables may be analysed to optimize the bioactive compounds recovery, such as the extraction time, particle size of the

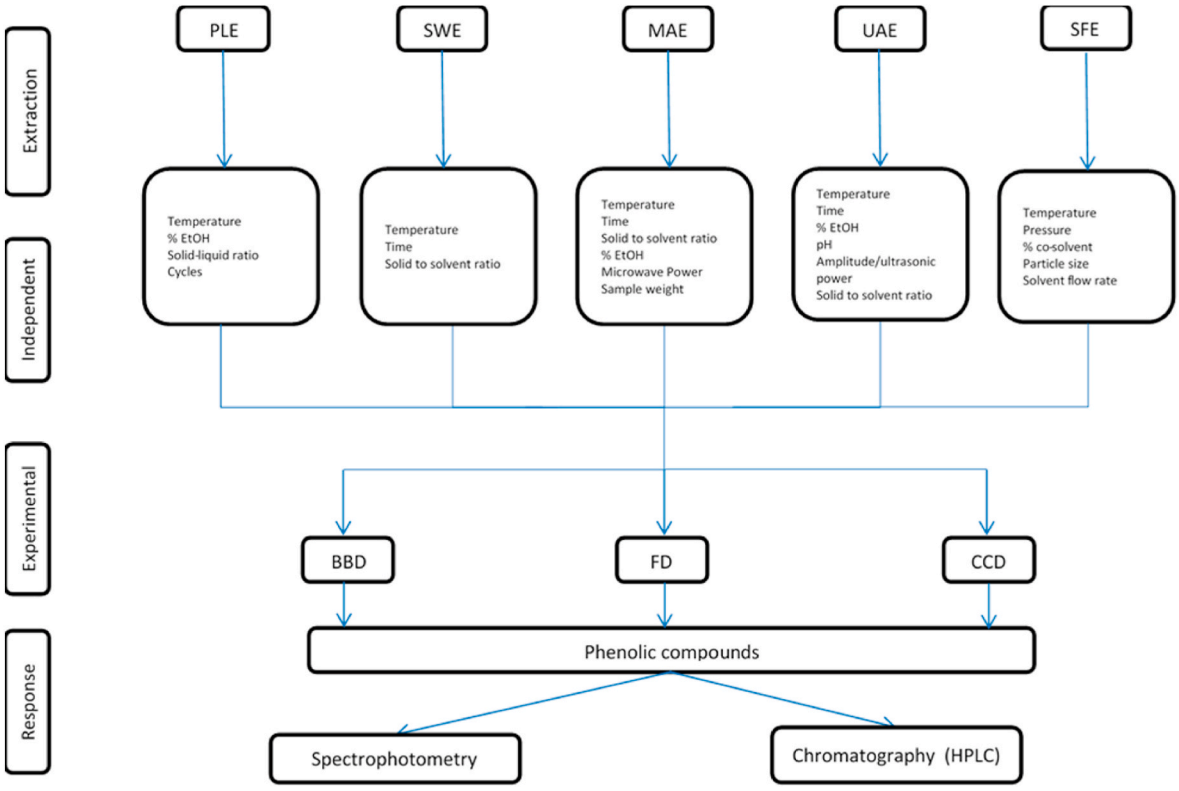

Fig. 3. Summary of different experimental designs, their independent variables to be optimized and the response variables for several extraction techniques. PLE: Pressurized Liquid Extraction, SWE: Subcritical Water Extraction, SFE: Supercritical Fluid Extraction, MAE: Microwave-assisted extraction, UAE: Ultrasound-Assisted Extraction, BBD: Box-Behnken Design, FD: factorial design, CCD: Composite Central Design, HPLC: High-performance liquid chromatography.

Table 1
Experimental designs, variables and optimums of the different matrices extracted by SWE.

By-products	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
Distillery stillage	Three-factor composite design	T, t and solid-to-solvent ratio	TPC: 140 °C, 30 min and 1:15 (w:v) TFC: 200 °C, 30 min and 1:15 (w:v)	TPC: 4.88 ± 0.16 mg GAE/g DM TFC: 1.24 ± 0.23 mg QUE/g DM	Identification: HPLC-DAD Stationary phase: Supelcosil C18 column (150 × 4.6 mm, 5 μm) Mobile phase: A: acidified acetonitrile (0.15% formic acid) B: acidified water (0.15% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu and aluminium chloride methods	[22]
Lotus seed epicarp	BBD	T, t, solvent-to-solid ratio and $NaHSO_3$ addition	160 °C, 15 min, 60 mL/g and 2% $NaHSO_3$	TPC: 89.14 mg GAE/g DW	Identification: HPLC-MS Stationary phase: Zorbax SB-C18 column (150 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[23]
Mandarin peel	BBD	T, t and solvent-to-solid ratio	Hesperidin: 153 °C, 15 min, 30 mL/g. Narirutin: 140 °C, 15 min, 29 mL/g. Rutin: 168 °C, 10 min, 30 mL/g Chlorogenic acid: 219 °C, 9 min, 30 mL/g	Hesperidin: 15.05 mg/g EMP Narirutin: 5.05 mg/g EMP Rutin: 3.79 mg/g EMP Chlorogenic acid: 68.76 mg/g EMP	Identification and quantification: HPLC-DAD Stationary phase: Cosmosil 5C18-MS-II column (250 × 4.6 mm, 5 μm). Mobile phase: A: acidified water (1% acetic acid) B: methanol	[24]

T: temperature; t: time; TPC: total phenolic content; TFC: total flavonoid content; EMP: exhausted mandarin peel; GAE: gallic acid equivalents; QUE: quercetin equivalents; DM: dry matter; DW: dry weight.

sample, the flow rate and the solvent to solid ratio.

Thus, due to its green nature, SWE was applied to recover phenolic compounds from different food by-products, as distillery stillage, lotus seed epicarp and mandarin peel (*Citrus unshiu* var. *Kuno*) [22–24]. Table 1 summarized the mentioned studies, detailing the experimental design, the experimental variables to be considered and their optimal values, together with experimental or predicted response variable for these conditions and the analytical technique and method employed for identification and quantitation purposes. Regarding the experimental design used, the potential of this technique to obtain enriched bioactive extract was evaluated using two different types of designs: CCD and BBD. Both of them optimized the extraction temperature (25–220 °C), extraction time (5–90 min) and solid-to-solvent ratio (1:5–1:50, w/v).

In the present research, the studies described below were divided according to whether the optimized response variables after applying the different experimental designs were the total phenolic content (TPC) determined spectrophotometrically or the content of these compounds of interest determined by chromatographic techniques.

Concerning the research that used different experimental designs to determine the total phenolic content and total flavonoid content (TFC) by spectrophotometry, it is worth mentioning the studies concerning to distillery stillage and lotus seed epicarp [22,23]. The polyphenol content was expressed as mg equivalent of gallic acid equivalent (GAE) per gram of dry matter (DM) or dry weight (DW) for TPC and mg equivalent of quercetin equivalent (QUE) per gram of dry matter in the case of TFC. The experimental designs applied in both studies were different, as shown in Table 1, as well as the experimental region studied since, for example, temperature and time ranges studied for distillery stillage (25–260 °C and 5–90 min) were much wider than for lotus seed epicarp (120–160 °C and 5–15 min). In the case of distillery stillage, the effects of the different values of the independent variables on the response ones were described and compared according to the experimental region. However, in this research the results obtained were not evaluated in terms of obtaining the optimal response value. This means that, despite applying experimental design, the optimal conditions for the extraction of TPC and TFC were selected from those experimental conditions of the experimental design. Thus, the best experimental results for TPC and TFC from distillery stillage were 30 min, 1:15 w/v and 140 °C or 200 °C, respectively. Researchers also evaluated and identified six phenolic acids in the obtained extracts by HPLC-DAD (high performance liquid chromatography coupled to diode-array detection). On the other hand, in lotus seed epicarp by-product, authors applied a BBD to optimize temperature, time, solvent-to-solid ratio and $NaHSO_3$ addition, obtaining a predicted value of 89.14 mg GAE/g DW. Between these two studies, both optimum temperatures and extraction times were very unequal (140 and 200 °C, and 15 and 30 min, respectively), so this shows that the type of plant matrix directly influences the extraction variables. For its part, proanthocyanidins and flavonoids were identified and quantified in the optimized lotus seed epicarp extracts. Comparing both studies, the results obtained for TPC of distillery stillage were much lower than the optimum value obtained for lotus seed epicarp [23], despite studying a larger experimental region.

On the other hand, only the research about mandarin peel [24] considered the individual content of bioactive compounds quantified by HPLC-DAD as the response variable of the extraction. The polyphenol content was expressed as mg compound (hesperidin, narirutin, rutin and chlorogenic acid) per gram of exhausted mandarin peel (EMP). This sample was submitted to a prior extraction with supercritical CO_2 with the aim of removing volatile and non-polar compounds. Applying a BBD, authors performed two optimizations taking into account the following experimental region: 130–220 °C, 5–15 min of extraction time and 10–30 mL/g of solvent-to-solid ratio. One of the optimizations was a multi-response maximising the content of three flavonoids and a phenolic acid, and minimising the content of an undesirable compound determined as hydroxymethylfurfural (HMF). This approach is pertinent, as some studies found in this review took into account the potential extraction of potentially hazardous non-target compounds. Achieving an extract rich in polyphenols while minimising the extraction of undesirable compounds makes more sense than achieving an extract very rich in polyphenols with a high presence of harmful compounds. Additionally, they also performed an individual optimization of each compound of interest without taking into account HMF. The main difference was reflected in the increase of temperature, since HMF is formed through Maillard reactions. That is why optimum conditions excluding the minimization of the content in 5-HMF used temperatures between 140 and 219 °C, while the optimum conditions for the extraction with the minimum content of 5-HMF were below 145 °C.

Therefore, this review reveals that the studies about extraction of bioactive compounds from by-products of the food industry by using SWE technology have focused on optimizing the same parameters (extraction temperature, time and solid/solvent ratio) as independent variables under the application of different experimental designs. Moreover, regarding the experimental design, it could be observed that the BBD was the most frequent in this case. As can be seen in Table 1, it should be highlighted that it is of vital importance to perform the optimization for each type of by-products for taking into account the matrix effect in each different sample. As can be observed, temperature plays a crucial role as it can enhance the extraction or degradation of the compounds of interest, making it an essential parameter to optimize. Moreover, extraction time is also a determining factor in the extraction of bioactive compounds, as choosing the right and optimum value can maximise extraction efficiency, while the solid/solvent ratio affects the rate of diffusion of target compounds from the extracted sample to the solvent. For this reason, all three parameters were significant in the performed extractions, except for the concentration of flavonoids from mandarin peel by-product, which was only influenced by the applied temperature and solvent/solid ratio.

Additionally, multi-response analysis has proven to be a very useful tool that allows modulating optimal conditions according to the interests of each study, such as maximising the recovery of the compounds of interest while minimising the extraction of other undesirable compounds. On the other hand, the compiled information has shown a tendency of most of the researches: there are many studies that consider certain experimental conditions included in the design as the optimal ones. Nevertheless, it should be considered that after conducting numerous experiments it is possible to find that the design does not fit correctly in the validation step. Therefore, in this case the optimization of variables is not possible and the experimental point of the design that showed the best result is considered as the optimal. Although it is not an ideal situation, is commonly accepted in the line of research. However, it should be noted that this fact could induce a bias in the study, since the best experimental conditions applied might not be in concordance with the real optimal extraction conditions.

In conclusion to this section, SWE extraction is an underused technique for the extraction of phenolic compounds by experimental designs from agri-food by-products. The reason could be that its use has gained more attention in recent years, and its background is limited compared to other techniques as UAE and MAE for the extraction of phenolic compounds. In addition, despite all the advantages mentioned above, SWE extraction requires specialized equipment to handle sub-critical conditions, which increases the costs and complexity of the process. Taking in mind that the ultimate goal of the research resides in the implementation of the revaluation of by-products in the industry, the disadvantages mentioned above may convert this extraction technique not the first choice at the industrial level. However, the use of water as an extraction solvent is an important step towards sustainability, ecology, profitability and circular economy in the recovery of phenolic compounds from by-products, so it is expected an increase in the use of this technology in the next years.

3.1.2. *Pressurized liquid extraction*

PLE is a faster, green and environmentally friendly method for the

recovery of bioactive compounds from food waste. In this technique, temperature and pressure improve the extraction of the compounds of interest from solid or semi-solid samples as SWE, since the increase in temperature and pressure favourably modifies the physical properties of the extraction solvents [25]. The different between SWE and PLE is the solvent used for the extraction, being pure water in the first technique and other kinds of GRAS solvents in the last one, commonly aqueous mixtures with ethanol (EtOH) for food purposes. PLE technique uses pressure around 110 bars and temperatures between room temperature up to 200 °C [19]. The most influential factors with effects in PLE extraction are temperature, extraction time, pressure, solvent composition and solid to solvent ratio.

Numerous research studies have applied PLE as a method of extracting bioactive compounds, such as olive leaves and pomace, wine lees and lees filters, avocado peel, apple pomace, spinach and orange residues and carao seed [14,15,17,26–30]. The revised studies have been included in Table 2 detailing the experimental design applied, the experimental parameters to be optimized, the optimum values and the response variables found for the optimum conditions, among others. The interaction between the variable factors was optimized through the development of different experimental designs, such as CCD, BBD and FD. In these studies, the most common considered variables were temperature (20–200 °C), percentage of EtOH in aqueous mixtures (0–100%), extraction time (3–22 min), solid-to-solvent ratio (0.2–0.8 g/mL) and number of cycles (1–3). The addition of hydrochloric acid to the extraction solvent to achieve an acidic environment was also studied in some cases.

Concerning the response variables to be optimized, some authors considered TPC and TFC determined by spectrophotometry as response variables obtaining different results depending on the plant matrix used for the PLE extraction. The polyphenol content was expressed as mg equivalents of the corresponding standard per gram of dry extract (DE), dry mass (DMS) or dry weight (DW). Likewise, other research considered the content of bioactive compounds obtained by HPLC as response variable of the PLE by-product extraction. In these cases, phenolic compounds contents were expressed as individual mass of the compound per gram of extract (E), DW or per kilogram of fresh weight (FW) of the by-product.

With respect to the studies that optimized by means of spectrophotometric techniques, the maximum content of TPC optimized for avocado peel [26] was 27.5 mg GAE/100 g DMS (obtained at 200 °C and 46% EtOH). This optimized value was much lower than that obtained for apple pomace (1487 mg GAE/100 g DW), for which 102 °C and 60% EtOH were shown to be the optimal conditions for the multi-response extraction of TPC, antioxidant capacity and individual phenolic compounds determined by HPLC-DAD [27]. In both cases, the experimental design applied was CCD and the authors studied a similar experimental region over temperature and percentage of EtOH (40–200 °C and 0–100% EtOH, respectively). In both studies, the results showed that temperature had a significant effect on polyphenol recovery. It should be noted that, in the case of apple pomace, the proposed optimal temperature was lower because the objective was to reduce the formation of undesirable compounds such as HMF, a product of degradation from Maillard reaction as previously mentioned. This makes the research especially valuable since, as mentioned in the previous section, few authors were concerned with obtaining the maximum extraction efficiency of target compounds while reducing the recovery of unwanted compounds. On the other hand, in both by-products, the optimum percentage of EtOH in water had intermediate values. Thus, the authors of the apple pomace research also studied the polyphenol contents by chromatographic techniques, obtaining very low contents of the monitored compounds compared to the TPC values obtained by spectrophotometric measures, as shown in Table 2. That could be explained by the presence of sugars co-extracted from the apple by-product with polyphenols at these experimental conditions. These substances also possess hydroxyl groups that could also react with the Folin-Ciocalteu reagent as polyphenols due to their reducing nature. For this reason, studies that include individual quantification of phenolic compounds with HPLC-DAD or MS (mass spectrometry) could be considered more revealing than the one which reported total content by spectrophotometric assays. This fact is supported by the limited selective of spectrophotometric assays compared to other analytical techniques. Finally, different phenolic compounds were identified by HPLC-MS in the optimized dried avocado peel extracts (concretely procyanidins, flavonoids, phenolic acids and catechins), being procyanidins the major phenolic compounds. For its part, phenolic compounds such as chlorogenic acid and phloretin glycoside were characterized in apple pomace also by chromatographic techniques.

On the other hand, as can be seen in Table 2, regarding the olive pomace study, the optimization of TPC, TFC and some individual phenolic compounds by HPLC-DAD-MS/MS analysis was performed individually and by multi-response [28]. Using the CCD design, the temperature (65–185 °C), the percentage of EtOH in aqueous mixtures (8–92%) and the solid-solvent ratio (0.2–0.8 g/mL) were studied. All the studied response variables presented 0.8 g/mL as the optimum solid-solvent ratio value. However, the highest optimum temperatures were found for maximum TPC, hydroxytyrosol and tyrosol contents, while the rest showed mean optimum temperature values. It is worth noting that the major compound found at optimum conditions (66.1 °C, 19.3% EtOH and 0.8 g/mL) was decarboxymethyl oleuropein aglycone dialdehyde (3,4-DHPEA-DEDA). For these compounds the optimum values of temperature and percentage of EtOH were very different from the optimum values for TPC, except for the solid-solvent ratio (183.9 °C, 84.7% EtOH, 0.8 g/mL). This may be due to their possible hydrolyzation to hydroxytyrosol and other phenolic compounds at high temperatures and also due to the % EtOH - temperature interaction. Therefore, a strong point of this research was to study separately the optimization of each response variable of interest, including both spectrophotometric and chromatographic quantifications. Indeed, phenolic compounds such as hydroxytyrosol, tyrosol, oleuropein and the previously mentioned 3, 4-DHPEA-DEDA were characterized in this by-product.

Moreover, extractions from wine lees, lees filters, olive pomace paste, and spinach and orange residues [17,29] conducted an individual characterization of phenolic compounds by HPLC-DAD. However, despite their individual characterization, their contents were simplified as the sum of all the chromatographic areas and quantified with gallic acid as standard. Therefore, the results were expressed in terms of TPC as mg GAE. Furthermore, in both studies, a FD and the same experimental region were applied for the response variables of temperature (80–120 °C), extraction time (5–15 min), number of cycles (1 or 2 cycles) and solvent composition (40–80% EtOH). Only in one of them, the addition of 0.1% HCl in the extraction solvent for an acidic medium was studied [17]. In the case of orange and spinach residues, the content of phenolic compounds was expressed per kilogram of FW of the by-product. The results highlighted that orange residues showed a higher content of compounds of interest. In this study, despite applying experimental designs, the optimal conditions obtained by RSM were not described, while the best experimental conditions from the design were chosen and applied as the optimum instead, as shown in Table 2. Thereby, both by-products presented the same “optimum” extraction temperature (80 °C) with a single extraction cycle, while the optimum time and percentage of EtOH were different. However, it is important to highlight that extraction time, temperature and solvent composition in the studied ranges were statistically non-significant in the PLE extraction from spinach residues. For its part, the application of different extraction cycles in the PLE from orange residues did not significantly improve the efficiency. In the case of wine lees, lees filters and olive pomace paste, as in the previous study, the best experimental conditions were chosen from the design experimental points (100 °C, 5 min, 50% EtOH and 1 extraction cycle). As mentioned in the previous section, describing experimental design conditions as optimal has been widely accepted by the scientific community.

Table 2
Experimental designs, variables and optimums of the different matrices extracted by PLE.

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
Avocado peel	Aqueous EtOH at different concentrations	CCD	T and % EtOH	200 °C and 46% EtOH	TPC: 27.5 mg GAE/ 100 g DMS	Identification: HPLC-DAD-MS Stationary phase: Zorbax Eclipse Plus C18 column (150 × 4.6 mm, 1.8 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[26]
Apple pomace	Aqueous EtOH at different concentrations	CCD	T and % EtOH	102 °C and 60% EtOH	TPC: 1487 mg GAE/ 100 g DW Chlorogenic acid: 550 μg chlorogenic acid/g DW Total flavonol level: 1205 μg rutin/g DW Phloretin glycoside: 826 μg phloridzin/g DW	Identification and quantification: HPLC-DAD Stationary phase: Zorbax SB-C18 column (150 × 4.6 mm, 5 μm) Mobile phase: A: sodium acetate with acetic acid B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[27]
Olive pomace	Aqueous EtOH at different concentrations	Circumscribed CD	T, % EtOH and solid-to- solvent ratio	TPC: 183.9 °C, 84.7% EtOH, 0.8 g/mL. TFC: 66.4 °C, 8% EtOH, 0.8 g/mL. Hydroxytyrosol: 183.9 °C, 90.0% EtOH and 0.8 g/mL Tyrosol: 183.9 °C, 92.0% EtOH and 0.8 g/mL Oleuropein: 66.4 °C, 92.0% EtOH and 0.8 g/mL 3,4-DHPEA-DEDA: 66.1 °C, 19.3% EtOH and 0.8 g/mL	TPC: 340 mg GAE/g DE TFC: 22 mg CATE/g DE Hydroxytyrosol: 9.5 mg/g DE Tyrosol: 5.3 mg/g DE Oleuropein: 13.8 mg/ g DE 3,4-DHPEA-DEDA: 52 mg/g DE	Identification and quantification: HPLC-DAD-MS/MS Stationary phase: C18 Mediterranean Sea column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (phosphoric acid) B: methanol Quantification: Spectrophotometry: Folin-Ciocalteu and aluminum chloride methods	[28]
Olive pomace paste, wine lees and lees filters	Aqueous EtOH at different concentrations	FD	T, t, % EtOH and number of extraction cycles	100 °C, 5 min, 50% EtOH and 1 cycle	NS	Identification: HPLC-DAD Stationary phase: Kinetex C18 column (100 × 4.6 mm, 2.6 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile	[29]
Spinach residues Orange residues	Aqueous EtOH at different concentrations and HCl	FD	T, t, % EtOH with 0.1 % HCl and number of extraction cycles	80 °C, 5 min, 40% EtOH with 0.1 % HCl and 1 cycle 80 °C, 15 min, 60% EtOH with 0.1% HCl and 1 cycle	TPC: 1000 ± 130 mg GAE/kg FW TPC: 3000 ± 70 mg GAE/kg FW	Identification: HPLC-DAD Stationary phase: Kinetex C18 column (100 × 4.6 mm, 2.6 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[17]
Carao seed	Aqueous EtOH at different concentrations	CCD	T, t and % EtOH	146.5 °C, 5 min and 54.8% EtOH	Yield: 25.7% o Total phenolics: 281 mg/g E	Identification and quantification: HPLC-MS Stationary phase: Zorbax Eclipse Plus C18 column (150 × 4.6 mm, 1.8 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile	[15]
Olive leaves	Aqueous EtOH at different concentrations	BBD	T, t and % EtOH	138 °C, 5 min and 100% EtOH	Yield: 42.2% Total phenolics: 144 mg/g DM	Identification and quantification: HPLC-MS Stationary phase: Poroshell 120 EC-C18 column (100 ×	[14]

(continued on next page)

Table 2 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
						4.6 mm, 2.7 μm) Mobile phase: A: acidified water (1% acetic acid) B: acetonitrile	
Olive leaves	Aqueous EtOH at different concentrations	CCD	T, % EtOH and extraction cycles	Yield: 190 °C, 100% EtOH and 3 cycles. Oleuropein content: 190 °C, 56% EtOH and 1 cycle	Yield: 46.64% ± 6.30% Oleuropein content: 26.1% ± 3.47%	Identification and quantification: HPLC-DAD Stationary phase: Poroshell 120 EC-C18 column (100 × 4.6 mm, 2.7 μm) Mobile phase: A: acidified water (1% acetic acid) B: methanol	[30]

T: temperature; t: time; TPC: total phenolic content; TFC: total flavonoid content; GAE: gallic acid equivalents; CATE: gatechin equivalents; DE: dry extract; DMS: dry mass; DW: dry weight; FW: fresh weight; DM: dry matter; 3,4-DHPEA-DEDA: decarboxymethyl oleuropein aglycone dialdehyde; NS: non specified.

To conclude, the studies that performed the extraction and identification of phenolic compounds by chromatographic methods include carao seed and olive leaves as starting material [14,15,30]. In these studies, the authors took into account both the extraction yield and the concentration of individual compounds recovered to perform the optimization, applying CCD or BBD designs. The experimental regions of the independent variables studied were similar (20–200 °C, 0–100% EtOH, 3–22 min). For carao seed, a multi-response optimization was evaluated to maximise both variables (extraction yield and total phenolic compounds), obtaining 25.7% of yield and 281 mg/g E for total polyphenols. Moreover, an analytical characterization by HPLC-MS allowed the identification and the quantification of phenolic compounds belonging to flavonoids and hydroxybenzoic acids families. Lastly, olive leaves research studied also the extraction yield and the total phenolic compounds present in the sample or the content of pure oleuropein in the dry extract. Only one of the studies applied a multi-response approach [14], which is a good option to improve the overall extraction process. However, the other one showed that the optimal extraction conditions for yield and oleuropein maximization were quite different in terms of the percentage of EtOH and the number of extraction cycles. In addition, it is reflected that compounds other than phenolics can be recovered during the extraction process. Moreover, each study applied different experimental designs (BBD or CCD), as can be seen in Table 2. For the extraction yield, in both cases, the optimum solvent extraction composition was 100% EtOH, while a clear difference was found between the optimal temperatures, a variable that prove to be significant in the extraction process. By comparing the optimums values for maximising the recovered compounds, large differences were observed between optimal temperatures (138 and 190 °C) and EtOH percentages (56 and 100%). This could be due to the different varieties of olive leaves used in each study (Koroneiki and Hojiblanca). In addition, simple phenols, secoiridoids, flavonoids and elenolic acids were identified by HPLC-MS or HPLC-DAD, among others minor substances.

As a conclusion, in the case of PLE for the recovery of food phytochemicals, the independent variables assessed had significant effects in most of the studies. However, it is important to note limitations observed in some of the studies reviewed. For example, a few investigations took into account only the influence of a limited number of experimental factors affecting the efficiency of PLE, concretely it were monitored the effects of temperature and extraction solvent composition. Thus, there were no data concerning the effect of the number of extraction cycles or extraction time, both independent variables that could possess a significant effect on the recovery of phenolic compounds from these by-products. In spite of each plant matrix has its particularities and, although for some of them the extraction cycles have proved to be non-significant, it is possible that for the extraction of others it may be relevant. Therefore, those studies that evaluated these independent variables were considered more complete and informative.

Furthermore, this review highlights that the most widely applied DoE for PLE extraction was CCD, while the most studied variables were temperature, time and solvent composition. Overall, the optimum temperature values found in these studies were medium-high (above 100 °C), which is in agreement with the fact that an increase in temperature facilitates the extraction of bioactive compounds from plant matrices. For its part, EtOH percentages varied similarly with medium-high trends. Nevertheless, the results for extraction time were more varied among different matrices, which could be attributed to their different composition and matrix effect. Thus, these results reveal the importance of studying each by-product individually, since the application of the optimum extraction conditions for a given matrix may not be the optimum for the extraction of a different one. In addition, as previously mentioned, in some cases different variables had non-significant effect on the extraction of the target compounds, as in the case of PLE from spinach and orange residues. Thus, it can be concluded that, depending on the plant matrix, the extraction of bioactive compounds will rely on the effect of some independent variables or others, not all of which are always significant in the recovery process. On the other hand, it should be mentioned that the phenolic content reported for the extracts in some of the studies may differ for the real concentration due to the analytical quantification carried out. In this sense, in some of the studies the phenolic compounds were identified by HPLC-DAD and MS and their concentration was determined using gallic acid as the standard. Thus, as the instrument response may vary from one compound to another due to chemical structure particularities, the best option for quantification is to use the commercial standard when available for each identified compound, or at least one standard representative for each phenolic sub-class. In this sense, gallic acid is a phenolic compound with a simple structure, which probable do not possess the same instrumental response as a more complex polyphenols, such as flavonoid glycosides.

In conclusion, this green extraction technique posses several advantages that can be enumerated. For example, PLE is a rapid, environmentally friendly and efficient technique that consumes little amount of solvent, concretely GRAS in the majority of application, while allows automation. However, its disadvantages should also be mentioned, such as the possible dilution of the analytes of interest when working with successive extraction cycles and the high cost of the equipment. In addition, as with SWE, the use of high pressures and its high instrumental costs may lead the food industry to prefer other extraction equipment for its implementation.

3.1.3. *Supercritical fluid extraction*

A supercritical fluid is obtained applying pressure and temperature above the critical point of the particular substance. These conditions

make the fluid behave as a hybrid between a liquid and a gas, both states being indistinguishable. Therefore, supercritical fluids have special and unique characteristics, such as viscosity and density [31]. The extraction capacity of the solvent used in this technique can be modified by changing the pressure or temperature, thereby the density of the fluid is changed, and consequently the solubility of the compounds of interest in the fluid could be enhanced, improving the selectivity of the extraction [32]. Supercritical Fluid Extraction (SFE) has several advantages over conventional extraction techniques. These include the extraction time, automation of the process and the possibility of using environmentally friendly solvent that can be easily removed from the extracted material by expansion at ambient pressure, being safe for the environmental. In this sense, carbon dioxide (CO_2) is the most commonly employed solvent in this extraction technique since it has been recognized as GRAS. In addition, it is cheap, volatile at ambient conditions and has low-moderate critical conditions (31.1 °C, 7.38 MPa). However, CO_2 has the disadvantage of being a non-polar solvent that can hardly extract polar compounds, such as polyphenols. To solve this problem the instruments have the option to pump another polar co-solvents, such as EtOH, mixed with CO_2, thus increasing the overall solvent polarity of the fluid phase during SFE extraction allowing the extraction of a wider range of compounds [32].

Thus, CO_2-SFE has been applied to recover phenolic compounds from different food waste, as orange pomace and waste-water, chokeberry pomace, papaya seed, carob kibbles, chestnut shells and mango leaves [33–39]. Table 3 details the extractive solvents, the experimental design and the optimal conditions, among other reported data. Regarding the experimental design used, the potential of this technique to obtain enriched polyphenol extract was evaluated using two different types of designs: CCD and FD. Both of them optimized the extraction temperature (35–70 °C) and extraction pressure (10–40 MPa) in most research. Only a few studies included the optimization of the co-solvent percentage (7–20%).

Concerning the studies that used experimental designs to determine TPC and TFC by spectrophotometry, the ones performed in orange pomace and waste-water, chokeberry pomace, papaya seed and carob kibbles were mentioned [33–36]. The phenolic compounds content found in these studies was expressed as mg equivalents of the corresponding standard per gram of DE, E, FW or L of the by-product, so it was not possible to compare the content between the studies because the results were expressed in different units.

The research focussed on orange pomace [33] applied a CCD to evaluate the extraction of this by-product using CO_2 with 6% EtOH as co-solvent. Although the highest experimental TPC was obtained at 40 °C and 35 MPa, no significant differences were found with respect to the TPC obtained at 60 °C and 25 MPa. Therefore, the authors, considering the lower energy consumption to pressurize the system, selected 60 °C and 25 MPa as the best SFE extraction parameters for orange pomace. This is a very positive aspect of the study, because if there is a possibility of reducing energy consumption, it is another way of being sustainable and respecting the environment. Flavonoids such as hesperetin were detected in orange pomace by HPLC-DAD. With regard to chokeberry pomace [34], a FD was applied to study the effect of temperature and the percentage of EtOH as co-solvent on the extraction of bioactive compounds. Pressure was not monitored during extraction but, since solvent density was held constant, the pressure should vary with temperature. This is a commonly accepted working mode with SFE, as it is another way of modifying and controlling the variables that affect the extraction process. In their case, the highest TPC recovered from the extraction was 3.42 ± 0.20 mg GAE/g FW at 68 °C with 10% EtOH as co-solvent, and three phenolic compounds (cyanidin hexose, cyanidin pentose and quercetin deoxyhexose-hexose) were identified by HPLC-MS.

On the other hand, results obtained for papaya seeds [35] showed that 50 °C and 20 MPa were the best experimental conditions to obtain the largest TPC from this by-product using FD as experimental design. The authors compared the TPC concentrations obtained under optimal conditions according to the different extraction solvents used: neat CO_2 and CO_2 with different percentages of EtOH as co-solvent (2, 5 and 8% EtOH), being 8% the best co-solvent percentage for the extraction of the compounds of interest. This result can be explained by the fact that phenolic compounds are polar and the polarity of the solvent (CO_2) increases with the addition of a polar co-solvent (EtOH), improving the extraction of the analytes. HPLC-MS analysis showed that papaya seeds contained phenolic acids and flavonoids. Furthermore, it should be noted that the study on carob kibbles [36] was the only one that studied other independent variables in addition to temperature, pressure and co-solvent percentage, which is remarkable. Moreover, the used co-solvent was different from the one mentioned above, as in this case, the authors increased the CO_2 polarity with a mixture of EtOH and water. This is interesting because the inclusion of water as co-solvent is in line with the ultimate goal of green and environmentally friendly chemistry. Despite the application of a CCD, the exact TPC content obtained under the best experimental extraction conditions was not specified. The characterization of major phenolic compounds present in the optimized extracts was performed by HPLC-DAD, and phenolic acids such as coumaric, ferulic and caffeic acids were revealed as the main phenolic compounds present in this matrix.

Finally, research about orange pomace and waste-water [37] applied a CCD to obtain the largest TPC and TFC per litre of sample. For this purpose, an optimization study was carried out using RSM in terms of temperature and pressure, and the optimum experimental conditions were found to be 60 °C and 28.7 MPa. This research was the only one that used pure water as co-solvent to enhance the extraction efficiency, which is a very good choice from an environmentally point of view. On the optimized extract, the authors characterized by HPLC-DAD the phenolic compounds present, such as hesperetin-7-O-rutinoside, quercetagetin, peonidin, apigenin-7-O-glucoside and cyanidin. In the research on chestnut shells [38], the optimization of the extraction was performed by applying a CCD, based on the antioxidant activity of the extracts. Phenolic compounds were characterized by HPLC-DAD on the optimized extract, being ellagic acid the most abundant. After graphing a response surface plot, authors concluded that the optimal conditions were 60 °C, 35 MPa and 15% of EtOH as co-solvent.

Finally, only a study conducted in mango leaves [39] considered the individual content of phenolic compounds determined by HPLC-DAD as response variable. In this research, temperature and pressure were studied as independent variables of a FD, using CO_2 with 20% EtOH as solvent extraction from different mango cultivars. It should be highlighted the study of phytochemicals in different cultivars in order to know the variation in the content of each compound. The best experimental condition was 55 °C at 10 MPa, and the contents of mangiferin and quercetin 3-β-d-glucoside were determined in the extracts.

As a conclusion, this review reveals that the research about extraction of phenolic compounds from by-products by SFE technology have focused on optimizing certain common parameters, such as extraction temperature, pressure and co-solvent percentage as independent variables under the application of different experimental designs. CCD was the most frequent in this case. On the other hand, Table 3 shows that the study of temperature and pressure were the essential independent variables in this type of extraction, since all the research studies took into account these parameters. This is explained by the fact that these are variables that directly affect the solvent and co-solvent, modifying the ability to dissolve the analytes of interest. Therefore, in this line, monitoring the effect of different percentages of polar co-solvent could greatly enrich the studies due to its high influence in the recovery of polar compounds. In addition, most of the independent variables studied, such as temperature and pressure, had significant effects on the extraction process with a few exceptions. For example, pressure was not statistically significant in the case of papaya seed and chestnut shells.

In conclusion to this section, SFE technique includes advantages such as the speed of the extraction process (30 min or less), the protection of

Table 3
Experimental designs, variables and optimums of the different matrices extracted by SFE.

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
Orange pomace	CO_2 with 6% EtOH	CCD	T and P	60 °C and 25 MPa	TPC: 21.2 ± 0.8 mg GAE/g DE	Identification: HPLC-DAD Stationary phase: Waters C18 column (150 × 4.6 mm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified methanol (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	[33]
Chokeberry pomace	CO_2 with EtOH	FD	T and % co-solvent	68 °C and 10% EtOH	TPC: 3.42 ± 0.20 mg GAE/g FW	Identification: HPLC-MS Stationary phase: RESTEK Roc C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified methanol (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	[34]
Papaya seed	Neat CO_2 and CO_2 with EtOH	FD	T, P and solvent composition	50 °C, 20 MPa, CO_2 with 8% EtOH	TPC: 15.34 mg GAE/g E	Identification: HPLC-MS Stationary phase: Bischoff ProntoSIL 300-5-C-18 column (150 × 4 mm, 5 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[35]
Carob kibbles	CO_2 with EtOH:H_2O (80:20, v/v)	CCD	T, P, % co-solvent, particle size and flow rate of CO_2	40 °C, 22 MPa, 12.4% EtOH:H_2O, 0.27 mm and 0.29 kg/h CO_2	TPC: NS	Identification: HPLC-DAD Stationary phase: Bischoff ProntoSIL 300-5-C-18 column (150 × 4 mm, 5 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[36]
Orange pomace and waste-water	CO_2 with H_2O	CCD	T and P	60 °C and 28.7 MPa	TPC: 851 mg GAE/L TFC: 585 mg QUE/L Hesperetin-7-O-rutinoside (26.9%), Quercetagetin (7.2%), Peonidin (6.1%), Apigenin-7-O-glucoside (5.4%), Cyanidin (3.4%)	Identification and quantification: HPLC-DAD Stationary phase: Waters Nova-Pak C18 column (300 × 3.9 mm; 4.0 μm) Mobile phase: A: acidified water (0.5% acetic acid) B: methanol Quantification: Spectrophotometry: Folin-Ciocalteu, sodium nitrite and aluminium chloride methods	[37]
Chestnut shells	CO_2 with EtOH	CCD	T, P and % co-solvent	60 °C, 35 MPa and 15% EtOH	Ellagic acid: 1.23 ± 0.06 mg/g DW Caffeic acid derivative: 0.31 ± 0.06 mg/g DW Catechin/epicatechin: 0.32 ± 0.06 mg/g DW Epigallocatechin: 0.44 ± 0.06 mg/g DW	Identification and quantification: HPLC-DAD Stationary phase: Tosohas amide 80 column (150 × 2.1 mm, 3.5 μm). Mobile phase: A: acidified water (1% formic acid) B: acetonitrile	[38]
Mango leaves	CO_2 with 20% EtOH	FD	T and P	55 °C and 10 MPa	Kent cultivar: Magniferin: 7.25 ± 0.01 g/100 g E Quercetin 3-β-d-glucoside: 1.37 ± 0.02 g/	Identification and quantification: HPLC-DAD Stationary phase: Thermo Electron Corporation C18	[39]

(*continued on next page*)

Table 3 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
					100 g E Osteen cultivar: Magniferin: 2.83 ± 0.01 g/100 g E Quercetin 3-β-d-glucoside: 3.55 ± 0.05 g/100 g E	column (250 × 4.6 mm; 5.0 μm) Mobile phase: A: acidified water (2% acetic acid) B: methanol	

T: temperature; P: pressure; MPa: megapascal; TPC: total phenolic content; TFC: total flavonoid content; GAE: gallic acid equivalents; QUE: quercetin equivalents; DE: dry extract; E: extract; DW: dry weight; FW: fresh weight; NS: non specified.

the more labile compounds, the possibility of coupling the extraction process with the chromatographic analysis, the avoidance of potential degradation of the compounds of interest (since they are not in contact with atmospheric oxygen) and the instantaneous removal of CO_2 at atmospheric conditions obtaining extracts free of solvent [40]. However, the recoveries for some phenolic compounds, such as phenolic acids, are not entirely satisfactory due to their high polarity [41]. This is because the addition of the co-solvent is not sufficient for their complete extraction. Therefore, although this extraction method can be applied on an industrial scale, more research is needed to increase the extraction yield of phenolic compounds by SFE from food wastes [42].

3.1.4. Microwave-assisted extraction

Microwaves consist of a combination of electric and magnetic fields that produce localized heating and cause the destruction of the plant matrix, which facilitates the diffusion of the solvent through the sample. As a result, the disruption of the hydrogen bonds present in the sample is increased, allowing the compounds of interest to dissolve in the extraction solvent [43]. For this purpose, microwave power between 300 MHz and 300 GHz are generally used [44]. In this research topic, MAE technique has been applied for the extraction of various phytochemicals of different natures, including phenolic compounds, providing good extraction performance of compounds of interest in less time and consuming fewer solvents compared to conventional methods [45]. In this technique, the most influential variables with effects in MAE extraction are temperature, extraction time, microwave power, solvent composition, heat capacity and solvent-to-sample ratio.

The results of the literature search have been depicted in Table 4, including the same information previously mentioned for other extraction techniques. As can be observed, with the aim of optimizing the variables that affect the MAE extraction of bioactive compounds from by-products of the food industry, researchers have applied different experimental designs (BBD, CCD and FD). The independent variables optimized by almost all of these studies were the extraction temperature (40−150 °C), extraction time (1−47 min or 20−90 s), solvent composition (acetone, NADES or aqueous EtOH with/without HCl), sample-to-solvent ratio (0.05–0.2 g/mL) and microwave power (80−700 Watt, W), among others. It is important to note that many of the studies did not optimize the microwave power, but they studied the effect of temperature, which it directly linked to it.

Concerning the studies that did not optimize the microwave power of the MAE technique but used experimental designs to determine TPC and TFC by spectrophotometry, the ones performed in tomato seeds, avocado peel and seed, Russian olive leaves and flowers, and mulberry leaves were considered [46–50]. The polyphenol contents were expressed as mg equivalents of the corresponding standard per gram of DM or DW. The studies focussed on avocado by-products (peel and seed) [46,47] applied two different experimental designs (CCD and BBD) to evaluate the extraction of both by-products with different extraction solvents (70% acetone and different percentages of EtOH in water). The investigation of different extraction solvents and comparing their results enriched the study. Although it could be convenient to study other percentages of acetone, the authors relied on a previous study on avocado extraction that present this solvent composition as optimum. Both designs studied the same independent variables in similar experimental regions. The obtained results showed no statistical difference between the different experimental conditions for TPC. However, for the antioxidant activity determined by DPPH (2,2′-diphenyl-1-picrylhydrazyl) assay, a statistical difference was observed. Therefore, the authors estimated the optimum extraction conditions for the recovery of bioactive compounds (66.37 °C during 0.97 min with 42.58% EtOH) based on a high antioxidant activity. Thus, avocado peel was found to be richer in bioactive compounds with high antioxidant activity than its seed extracted at this optimum experimental values. Finally, authors investigated the bioactive compounds contained in avocado by-products by HPLC-MS, being procyanidins, catechin and phenolic acids the major polyphenols found in these samples.

On the other hand, results obtained for tomato seeds [48], mulberry leaves [49] and Russian olive leaves and flowers [50] showed that the last one was the by-product with the highest TPC content (51.47 mg GAE/g DW), whereas tomato seed was the lowest (1.52 ± 0.21 mg GAE/g DM). On the other hand, Russian olive and mulberry leaves showed intermediate TPC concentrations. The investigations applied different experimental designs (BBD, FD and CCD) and coincided on few independent variables studied. Of these three studies, those on olive by-products were the only ones that used citric acid to enhance the extraction of target compounds, which appears to be a good choice as they achieved the highest TPC values. Citric acid is a harmless organic acid that is used to improve the extraction of phenolic compounds since, by reducing the pH of the medium, it creates a more favourable environment for the release of polyphenols from the samples, enhancing their extraction and improving their solubility. On the other hand, temperature was evaluated by all studies, and for all these samples it was found to be a parameter that significantly affected the extraction of phenolic compounds. The experimental regions studied of this variable for mulberry and Russian olive were very similar (66–134 °C and 60–110 °C, respectively), while the experimental region for tomato was lower (40–80 °C). Finally, it should be noted that the study on Russian olive leaves and flowers performed a multi-response to also optimize the extraction yield and TFC, with flowers showing the highest recoveries. The characterization of major phenolic compounds present in the optimized extracts was performed by HPLC-DAD, and flavonoids and phenolic acids were revealed as the main phenolic compounds present in these matrices.

Besides, related to research which optimized the microwave power and considered TPC, TFC or total anthocyanin content (TAC) by spectrophotometry as response variables, numerous waste products can be named: avocado seed, sour cherry, mango and pomegranate peels, grapevine and strawberry leaves, wine lees and okra stems [51–58]. In these studies, the phenolic compounds contents were expressed as mg equivalents of the standard per gram of DW, FW or E.

With regard to the by-products which expressed the analyte contents as mg of standard per gram of extract, investigations about evaluating okra stems [51], wine lees [52] and grapevine leaves [53] as sources of

Table 4
Experimental designs, variables and optimums of the different matrices extracted by MAE.

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
Avocado peel	Acetone:water (70:30, v/v)	CCD	T and t	74.48 °C and 14.32 min	AC: 188.31 mg TE/g DM	Identification: HPLC-MS	[47]
	Aqueous EtOH at different concentrations	BBD	T, t and % EtOH	66.37 °C, 0.97 min and 42.58% EtOH	AC: 189.06 mg TE/g DM	Stationary phase: Denali C18 column (150 × 2.1 mm, 3 μm) Mobile phase: A: acidified water (0.2% formic acid) B: acetonitrile Quantification: Spectrophotometry: DPPH method	
Avocado seeds	Acetone:water (70:30, v/v)	CCD	T and t	72.18 °C and 19.01 min	AC: 131.17 mg TE/g DM	Identification: HPLC-MS	[46]
	Aqueous EtOH at different concentrations	BBD	T, t and % EtOH	71.64 °C, 14.69 min and 58.51% EtOH	AC: 126.30 mg TE/g DM	Stationary phase: Denali C18 column (150 × 2.1 mm, 3 μm) Mobile phase: A: acidified water (0.2% formic acid) B: acetonitrile Quantification: Spectrophotometry: DPPH method	
Tomato seed	Aqueous EtOH at different concentrations	BBD	T, t, % EtOH and solvent volume	80 °C, 15 min, 63% EtOH and 80 mL	TPC: 1.52 ± 0.21 mg GAE/g DM	Identification: HPLC-DAD-MS Stationary phase: HALO C18 column (100 × 4.6 mm, 2.7 μm) Mobile phase: A: acidified water (0.1% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[48]
Mulberry leaves	Aqueous EtOH at different concentrations	FD	T, t and sample weight	121.8 °C, 28.3 min and 0.414 g	TPC: 18.7 mg GAE/g DM	Identification: HPLC-DAD Stationary phase: Phenomenex Gemini C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% formic acid) B: methanol Quantification: Spectrophotometry: Folin-Ciocalteu method	[49]
Russian olive leaves	Aqueous EtOH at different concentrations with citric acid	CCD	T, % EtOH, solid-to-solvent ratio and citric acid concentration	97.4 °C, 59.8% EtOH, 7.5 (w/v) and 2 M	Yield: 33.71 % TPC: 37.91 mg GAE/g DW TFC: 512.91 mg QUE/g DW	Identification: HPLC-MS Stationary phase: Discovery C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.17% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu and aluminium chloride methods	[50]
Russian olive flowers				97.5 °C, 66.6% EtOH, 7.5 (w/v) and 2 M	Yield: 39.74% TPC: 51.47 mg GAE/g DW TFC: 2786.17 mg QUE/g DW		
Okra stem	EtOH:water (50:50, v/v)	CCD	t and MP	7.36 min and 170.08 W	TPC: 69.99 mg GAE/g E	Identification: HPLC-DAD Stationary phase: C18 column (150 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (formic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[51]
Grapevine leaves	Aqueous EtOH at different concentrations	BBD	t, % EtOH, MP and solvent-to-solid ratio	47 s, 34% EtOH, 474 W, and 40:1 mL:g	TPC: 52 mg GAE/g E	Identification: HPLC-DAD-MS Stationary phase: Zorbax SB-C18 column (100 × 2.1 mm,	[53]

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Table 4 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
						1.8 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified acetonitrile (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	
Wine lees	Aqueous EtOH and HCl at different concentrations	FD + CCD	t, % EtOH. % HCl and MP	17 min, 75% EtOH, 1 % HCl and 200 W	TPC: 53.2 mg GAE/100 mg E	Identification: HPLC-DAD Stationary phase: Nova-pack C18 column (250 × 3.9 mm) Mobile phase: A: acidified water (10% formic acid) B: acidified acetonitrile (10% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	[52]
Avocado seeds	Aqueous EtOH at different concentrations	Face CCD	t, % EtOH and MP	4.8 min, 58.3% EtOH and 400 W	TPC: 83.90 mg GAE/g DW TFC: 21.84 mg QUE/g DW	Identification: HPLC-DAD Stationary phase: Luna C18 column (150 × 4.6 mm, 3 μm) Mobile phase: A: acidified acetonitrile (1% acetic acid) B: acidified water (1% acetic acid) Quantification: Spectrophotometry: Folin-Ciocalteu and aluminium chloride methods	[55]
Strawberry leaves	Aqueous EtOH at different concentrations	BBD	t, % EtOH, MP and solvent-to-solid ratio	40 s, 51.1% EtOH, 300 W and 61.6 mL/g	TPC: 85.75 mg GAE/g DW	Identification: HPLC-DAD Stationary phase: Ultimate XB-C18 ODS column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (2% acetic acid) B: 73% water, 25% acetonitrile, and 2% acetic acid Quantification: Spectrophotometry: Folin-Ciocalteu method	[56]
Mango peel	NADES (lactic acid/sodium acetate)	BBD	t, MP and solvent-to-solid ratio	19.66 min, 436.45 W and 59.82 mL/g	TPC: 56.17 mg GAE/g DW	Identification: HPLC-DAD Stationary phase: C18 column (dimensions not detailed) Mobile phase: A: acetonitrile (45%) and water (55%) B: acidified water (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	[54]
Pomegranate peel	EtOH:water (50:50, v/v)	CCD	MP and solvent-to-solid ratio	600 W and 60 mL/g	TPC: 202.8 mg GAE/g DW	Identification: HPLC-DAD Stationary phase: C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (5% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[57]
Sour cherry peel	Aqueous EtOH at different concentrations	Face CCD	t, % EtOH and MP	90 s, 80% EtOH and 500 W	TPC: 44.15 mg GAE/g FW TAC: 12.47 mg C-3-GE/g FW	Identification: HPLC-DAD Stationary phase: Agilent Eclipse Plus C18 RRHD 18 column (50 × 3 mm, 1.8 μm) Mobile phase: A: acidified	[58]

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Table 4 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
						water (0.1% formic acid) B: acidified acetonitrile (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu and pH differential methods	
Olive pomace paste, wine lees and lees filters	EtOH and Milli-Q water	FD	T, t and % EtOH	90 °C, 5 min and 50% EtOH	NS	Identification: HPLC-DAD Stationary phase: Kinetex C18 column (100 × 4.6 mm, 2.6 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile	[29]
Spinach residues Orange residues	Aqueous EtOH at different concentrations and HCl	FD	T, t, and % EtOH with 0.1 % HCl	90 °C, 5 min, 60% EtOH with 0.1 % HCl 120 °C, 15 min, 60% EtOH with 0.1% HCl	TPC: 950 ± 7 mg GAE/kg FW TPC: 2000 ± 130 mg GAE/kg FW	Identification: HPLC-DAD Stationary phase: Kinetex C18 column (100 × 4.6 mm, 2.6 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[17]
Olive leaves	NADES choline chloride-ethylene glycol	BBD	T, t and % water in NADES	79.79 °C, 19,86 min and 50,19% water Total phenolics: 79.98 °C, 15.28 min and 48.63% water Oleuropein: 79.64 °C, 16.69 min and 43.34% water	TPC: 32,67 mg GAE/g DW Total phenolics: 28.52 mg/g DW Oleuropein: 10.58 mg/g DW	Identification and quantification: HPLC-DAD-MS Stationary phase: Poroshell 120 EC-C18 column (100 × 4.6 mm, 2.7 μm) Mobile phase: A: acidified water (1% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[59]
Olive leaves	Aqueous EtOH at different concentrations	BBD	T, t and % EtOH	123 °C, 23 min and 100% EtOH	Total phenolics: 75.60 mg/g DM	Identification and quantification: HPLC-MS Stationary phase: Poroshell 120 EC-C18 column (100 × 4.6 mm, 2.7 μm) Mobile phase: A: acidified water (1% acetic acid) B: acetonitrile	[60]
Eugenia uniflora L. leaves	NADES choline chloride:lactic acid 1:3 (mol/mol) solubilized in 20% of H_2O	CCD	T, t and solid-to-solvent ratio	39 °C, 47 min and 0.05:1 (wt/wt)	NQ	Identification: HPLC-DAD Stationary phase: XSelect column (150 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (1% acetic acid) B: Bioethanol 95°GL	[62]
Grape peel	Water/EtOH/ phosphoric acid (70:30:1, v/v/v)	FD	t and solid-to-solvent ratio	10.5 min and 0.05 g/mL	Peonidin-3-O-glucoside: 38.25 mg/g 100 FW Catechin: 7.40 mg/g 100 FW Procyanidin B1: 6.33 mg/g 100 FW	Identification and quantification: HPLC-DAD-MS/MS Stationary phase: Luna C18 column (150 × 2 mm, 5 μm) Mobile phase: A: acidified water (1% formic acid) B: acetonitrile	[61]

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Table 4 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
Red onion scales wastes	Water:EtOH (50:50, v/v)	FD	t, solid-to-solvent ratio and MP	NS	Quercetin: 27.20 ± 1.55 mg/g DW	Identification and quantification: HPLC-DAD Stationary phase: HC-C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% orthophosphoric acid) B: acetonitrile	[63]

T: temperature; t: time; MP: microwave power; TPC: total phenolic content; TFC: total flavonoid content; TAC: total anthocyanin content; AC: antioxidant capacity; DPPH: 2,2′-diphenyl-1-picrylhydrazyl; TE: trolox equivalents; GAE: gallic acid equivalents; QUE: quercetin equivalents; C-3-GE: cyanidin-3-glucoside equivalents; DM: dry matter; DW: dry weight; FW: fresh weight; DE: dry extract; NS: non specified; NQ: non quantified.

phenolic compounds optimized the extraction parameters after applying different experimental designs for the study of the independent variables, as shown in Table 4. Investigations agreed in optimizing time and microwave power for all these studies. While both variables were found to be significant for okra stem phenolic extraction (determined as TPC), only microwave power was significant for grapevine leaves. On the other hand, only the percentage of EtOH was significant in wine lees extraction. The experimental regions applied for both time and microwave power were very different. Thus, in okra stem and wine lees the applied microwave power was below 200 W and time was studied in term of minutes, while in grapevine leaves the applied microwave power was above 300 W and time was studied in seconds. As a result, wine lees were richer in TPC per gram of extract than okra stem and grapevine leaves. It is noteworthy that the by-product with the highest TPC, once again, used an acidic solvent in the extraction. In this case, hydrochloric acid was used. While it is true that this acid is corrosive, it may have indirect applications in the production of certain food ingredients or in specific processes. However, if the objective is to applied a green chemistry approach with innocuous reagents, when possible, it would be more convenient to use other less harmful acids. Furthermore, in the one hand, flavonoids and phenolic acids were identified by HPLC-DAD in wine lees; on the other hand flavonoids, phenolic acids and stilbenes were characterized in grapevine leaves; and finally flavonols, catechins and hydroxycinnamic acid derivatives were detected in okra stems.

In contrast, among the studies that expressed the TPC as mg GAE per gram of DW, the optimized value for a higher TPC extraction from mango peel [54] was much lower than those obtained for avocado seeds [55] and strawberry leaves [56]. For its part, pomegranate peel [57] was found to be the by-product with the highest TPC (202.8 mg GAE/g DW). While for the mango peel study the authors applied a BBD, CCD was chosen as the experimental design to evaluate pomegranate peel. Both investigations studied the solvent-to-solid ratio and microwave power in similar experimental regions, and in both cases the solvent-to-solid ratio had significant effects on TPC extraction. Moreover, the optimum TPC for avocado seed and strawberry leaves were very similar, as shown in Table 4, although different experimental designs were applied to each by-product (CCD and BBD, respectively). Regarding avocado seed, it was also possible to optimize the extraction of TFC by means of multi-response approach. Despite the two studies coincided in studying the same independent variables (except for the solid-to-solvent ratio), the experimental ranges applied were very different. An example of this fact could be observed for time, a variable with significant effects that was studied in seconds or minutes, depending on the research. On the other hand, despite being the by-product with the lowest TPC recovery, it should be noted that the extraction on mango peel was the only one to use NADES as an extraction solvent. This fact can be considered particularly relevant and accurate according to current GRAS extraction trend. Finally, considering HPLC-DAD analysis, the major phenolic compounds characterized in avocado seeds and strawberry leaves were flavonoids such like rutin, and phenolic acids as syringic and sinapic acids, respectively. On the other hand, mangiferin and punicalagin were the major polyphenols detected in mango and pomegranate peels, respectively.

Lastly, another study that optimized by means of multi-response strategy, taking into account TPC and TAC, was focused on sour cherry peel [58]. In this case, the optimum content values were expressed per gram of FW, and the experimental values of response variables obtained by applying the optimal conditions of the independent variables (90 s, 80% EtOH and 500 W) were similar to the theoretical ones. Additionally, it was observed that cyanidin-3-glucoside was identified as the major anthocyanin in sour cherry peel samples.

With respect to the research mentioned above, an important difference should be considered between those studies that kept the microwave parameters constant and those studies that optimized these extraction parameters: the former studied temperature as an independent variable while the latter did not. In this sense, it should be mentioned that, despite temperature has proven to be an influencing parameter in extraction efficiency, in this extraction technique temperature is directly linked to microwave power. Therefore, when microwaves are applied, the extraction solvent is heated, and its molecules begin to move faster due to the temperature increase, facilitating the release and transfer of the compounds of interest. Therefore, the increase in microwave power induces an increase in temperature, and consequently for their study only one of them could be included as independent variable.

A few other studies considered the individual content of bioactive compounds determined by HPLC-DAD or others analytical platforms as response variable, while the microwave power was not optimized: by-products such as wine lees and lees filters, olive pomace paste, *Eugenia uniflora* L. leaves, olive leaves, grape peel, and orange and spinach residues was reported [17,29,59–62]. The phenolic content was expressed as mg or mg equivalents of the corresponding standard per gram of FW, DM or DW. In studies on wine lees, lees filters, olive pomace paste, and spinach and orange residues [17,29], the FD was applied. Independent variables such as temperature, time and solvent composition were evaluated. The same experimental region was evaluated for the independent variables of temperature (60–120 °C) and extraction time (5–15 min), but this was not the case for EtOH percentage. Only for spinach and orange residues the addition of 0.1% HCl for an acidic solvent was studied and, as mentioned above, this is an acceptable practice to improve the recovery since the amount of this acid added is minimal. Again, the addition of an acid was shown to improve the extraction of phenolic compounds, so this could be considered a novel strength of the research. On the other hand, HPLC-DAD analyses were carried out considering the total chromatographic area for all the detected compounds for the quantification of total polyphenols with gallic acid as standard, as mentioned in the previous section about PLE extraction. Orange residues were found to be richer in TPC than spinach

samples, applying higher extraction temperatures (120 °C) and longer extraction time (15 min) with the same percentage of EtOH in the solvent (60%). As in the previous section, in these studies the optimum TPC contents obtained for olive pomace, wine lees and lees filters were not indicated. It is important to remark that despite of this strategy, the optimized conditions were not described, but rather the best experimental conditions were chosen from the experimental design points.

While one of the researches about olive leaves [59] used NADES based on choline chloride as extraction solvent, the other one [60] used different percentages of EtOH in mixtures with water. Both studies applied a BBD for the study of the independent variables, both focusing on the study of temperature and extraction time. The experimental region studied for temperature, a significant variable for the extraction, was very similar in both cases. Although both by-products were olive leaves of the Hojiblanca variety, the optimum temperatures found were very different, on the opposite that the optimum values found for the extraction time, which were similar. Likewise, there was a large difference between the phenolic compounds recovered between both leaf samples, as can be seen in Table 4. This comparison showed that, although there is a clear current trend in the study of NADES as extraction solvents, there may be matrices in which EtOH-water mixtures are more effective. Another interesting possible research line would be the study of the use of EtOH-water mixtures with the addition of an acid, since their inclusion in the extraction seems to have positive effects on the recovery of phenolic compounds. Simple phenols and derivatives, flavonoids and secoiridoids were identified and quantified, and as expected, oleuropein was the most abundant compound present in the olive leaves.

On the other hand, a study concerning grape peel [61] applied a FD with time and solid-to-solvent ratio as independent variables. Authors developed a multi-response optimization of the content of the major 17 phenolic compounds, which highlights the value of the research, since few studies included it. Results were expressed as mg of the compounds per gram of FW, being flavonoids the main polyphenols detected in this by-product. Lastly, a study about *Eugenia uniflora* L. leaves [62] applied a CCD using NADES based on choline chloride as extraction solvent. The response variable was the total peak area of the chromatograms obtained by HPLC-DAD.

Finally, only one of the revised studies that determined the individual phenolic content of onion scales wastes by HPLC-DAD optimized microwave power, despite the optimum values were not detailed in the manuscript [63]. In this case, a FD was applied and, in addition to optimizing the microwave power, the influence of extraction time and solid-to-solvent ratio were also assayed. In this case, the results were expressed as mg QUE/g DW.

Concerning these studies based on the extraction of bioactive compounds by MAE, the application of CCD and BBD as DoE was very similar in this case. Moreover, it could be observed that several experimental variables were optimized to achieve the highest phytochemical recovery, being the most frequent time, solvent composition and temperature or microwave power. As mentioned above, although many of the studies did not consider the effect of microwave power, the effect of temperature was monitored, so an adequate study of the extraction technique was developed. The reason is that temperature and microwave power are directly proportional, so both parameters were not selected for their study at the same investigation. Results put into light that most of the independent variables had significant effects on the response variable, with a few exceptions. For example, sample-to-solvent ratio was not always significant in the extraction of different polyphenols from grape peel. Moreover, no significant improvement was observed by changing the extraction time from olive pomace, spinach residues and lees filters. However, as noted in the previous section on PLE extraction, some of the investigations studied the effect of only a few independent variables. In this sense, it should be note that studying a higher number of independent variables would reduce the risk of bias, thus being sure whether its effect on extraction was significant or not.

Finally, it should be highlighted the research on avocado peel and seed, in which different DoE, solvents and independent experimental extraction variables were studied on the same matrices. The obtained results showed that the optimum recovery conditions for the compounds of interest were very similar between those matrices. Despite these results, it should be mentioned that this fact is unusual, and as previously mentioned for other green techniques, the optimal extraction conditions varied significantly depending on the studied by-product, as expected, due to the matrix effect. Lastly, these studies put into light that, thanks to the optimization through DoE, the maximum recovery of phenolic compounds can be achieved for very different matrices. In general, the optimum values found in these studies ranged from low temperatures around 40 °C to medium-high temperatures around 123 °C or lower microwave power ratings from 170.08 W up to 500 W.

To conclude this section dedicated to MAE extraction, a notable advantage of this technique is its applicability in the rapid extraction of substances of various nature, including thermally unstable analytes [64]. In addition, higher extraction rates are obtained with intermediate volumes of extraction solvent and extraction time is significantly reduced. However, different considerations must be taken into account before applying MAE. For example, the polarity of the extraction solvent seems to be very important, as those with high dielectric constants absorb more microwave energy. Furthermore, it is important to control the volumes of solvent used in the extraction, as larger volumes require higher microwave energies. This could excessively increase the heating of the solvent and/or sample, thus increasing the risk of thermal degradation and energy consumption [64]. On the other hand, microwave extraction may be an interesting option to be applied at an industrial scale in the food industry. Although large-scale implementation means a significant investment in equipment acquisition, the speed and efficiency of microwaves for the extraction of target compounds could be beneficial in terms of time and resources.

3.1.5. Ultrasound-assisted extraction (UAE)

In recent years, the use of ultrasound-assisted extraction (UAE) for the recovery of polyphenols from natural sources has been increasing. UAE guarantees faster and better extraction of phenolic compounds with minimised degradation of compounds in comparison to other extraction techniques [65]. Furthermore, it meets the requirements of clean technique coupled with high extraction efficiency, good yield and high purity of obtained extracts. The potential of this technique resides in the vibrations of the applied ultrasound waves, which cause disruption or breakdown of the cell walls of the plant material and enhance mass transfer across cell membranes. This action of ultrasound waves increases the penetration of the solvent in the sample matrix and their access to analytes [44]. The range of ultrasound frequency generally used in these extraction processes is between 20 and 2000 kHz, aimed at increasing the permeability of the cell wall and producing a cavitation phenomenon [45]. Several factors such as solvent composition, solvent-sample ratio, number of ultrasound cycles, duration of phase contact, solvent pH and temperature can affect the extraction efficiency. Solvent selection and temperature have shown to be the most important factors influencing the efficiency of this type of extraction. With the aim of optimizing the variables that affect the UAE of bioactive compounds from food industry wastes, as can be observed in Table 5, authors have applied different experimental designs in their research: BBD, CCD and FD. The extraction temperature (20−93 °C), time (1−90 min), solvent composition (acetone, NADES, water and EtOH with or without HCl, among others), sample-to-solvent ratio (1:10–1:70 w/v), amplitude (0–100%) and ultrasound power (29–500 W) were the independent variables optimized by most studies.

As for previous techniques, several researchers studied TPC, TFC, TAC by spectrophotometry as response variables, obtaining different results for the optimization of the UAE of bioactive compounds. These studies were divided into those that optimized the extraction conditions without modifying the ultrasound parameters, and those in which the

Table 5
Experimental designs, variables and optimums of the different matrices extracted by UAE.

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
Okra stem	EtOH:water (50:50, v/v)	CCD	T and t	26.11 °C and 33.71 min	TPC: 61.55 mg GAE/g E	Identification: HPLC-DAD Stationary phase: C18 column (150 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (formic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[51]
Banana bract	Aqueous EtOH at different concentrations	CCD	T, % EtOH and solvent-to-solid ratio	49.4 °C, 54% EtOH and 15:0.5 v:v	TAC: 57.29 mg C-3-GE/100 g E	Identification: HPLC-DAD Stationary phase: C18 hypersil ODS column (200 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (10% formic acid) B: 50% methanol, 40% water and 10% formic acid. Quantification: Spectrophotometry: pH differential method	[68]
Hemerocallis fulva leaves	Aqueous EtOH at different concentrations	BBD	T, % EtOH, solvent-to-sample ratio	61.7 °C, 70.6% EtOH and 43.9:1 mL/g	TFC: 23.135 mg RE/g E	Identification: HPLC-DAD Stationary phase: Agilent Eclipse Plus C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile Quantification: Spectrophotometry: aluminium nitrate method	[67]
Plum peel	Aqueous EtOH at different concentrations with HCl	BBD	T, t and % EtOH	49 °C, 37 min and 68% EtOH	TPC: 6.22 ± 0.76 mg GAE/g E TAC: 5.42 ± 0.61 mg C-3-GE/g E	Identification: HPLC-DAD Stationary phase: CLC-ODS C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (6% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu and pH differential methods	[66]
Sugar beet molasses	Aqueous EtOH and HCl at different concentrations	CCD	T, t, % EtOH and HCl	TPC: 43 °C, 73 min, 57% EtOH and 1.55 mol/L HCl TAC: 41 °C, 68 min, 61% EtOH and 1.72 mol/L HCl	TPC: 17.36 mg GAE/g DW TAC: 31.81 mg C-3-GE/100 g DW	Identification: HPLC-DAD-MS/MS Stationary phase: Agilent C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (1% acetic acid) B: methanol Quantification: Spectrophotometry: Folin-Ciocalteu method	[74]
Apricot pomace	EtOH:water (50:50, v/v)	CCD	T and t	50 °C and 90 min	TPC: 1.210 mg GAE/g DM TFC: 1.032 mg CATE/g DM	Identification: HPLC-DAD Stationary phase: Inter-sil ODS C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% acetic acid) B: acidified acetonitrile (0.1% acetic acid) Quantification: Spectrophotometry: Folin-Ciocalteu and aluminium chloride methods	[70]
Pomegranate peel	Water with β-Cyclodextrin	BBD	T, t and % β-CD	55.7 °C, 15.38 min and 1.8%	TPC: 158.10 mg GAE/g DW TFC: 82.30 mg QUE/g DW	Identification: HPLC-DAD Stationary phase: Eurospherium C18 column (250 × 4.6 mm, 5 μm)	[69]

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Table 5 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
					TAC: 0.52 mg C-3-GE/g DW	Mobile phase: A: acidified water (1% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu, aluminium chloride and pH differential methods	
Jabuticaba peel	Aqueous EtOH at different concentrations	CCD	t, % EtOH and pH	10 min, 46% EtOH and pH 1	TPC: 92.8 mg GAE/g DW TAC: 4.8 mg C-3-GE/g DW Cyanidin-3-O-glucoside: 4.9 mg/g DW Ellagic acid: 7.8 mg/g DW	Identification and quantification: HPLC-DAD Stationary phase: Symmetry C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified acetonitrile (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu and pH differential methods	[71]
Apple peel	Aqueous EtOH at different concentrations	BBD	T, t and % EtOH	29 °C, 32 min and 56% EtOH	TPC: 35.08 ± 0.26 mg GAE/g DW	Identification: HPLC-MS/MS Stationary phase: ACQUITY C18 column (100 × 2.1 mm, 1.7 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified acetonitrile (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	[72]
Mango peel	Aqueous EtOH at different concentrations	BBD	T, t and % EtOH	51 °C, 71 min and 50% EtOH	TPC: 19.37 mg GAE/g DW Mangiferin: 1.22 mg GAE/g DW	Identification and quantification: HPLC-MS Stationary phase: C18 column (150 × 3 mm, 3 μm) Mobile phase: A: acidified water (0.1% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[73]
Brewers' spent grain	Aqueous EtOH at different concentrations	BBD	T, t and % EtOH	80 °C, 50 min and 65% EtOH	TPC: 4.11 mg GAE/g DW	Identification: HPLC-DAD Stationary phase: Dionex Acclaim 120 C^{18} column (250 × 4.6 mm, 5 μm) Mobile phase: A: 50 mM ammonium dihydrogen phosphate with orthophosphoric acid B: 20% solvent A and 80% acetonitrile C: 0.2 M orthophosphoric acid with NaOH Quantification: Spectrophotometry: Folin-Ciocalteu method	[16]
Almond hulls	Aqueous EtOH at different concentrations	BBD	t, % EtOH and solid-to-solvent ratio	13 min, 51.2% EtOH and 2 g/100 mL	TPC: 6.81 mg GAE/g DW	Identification: HPLC-DAD Stationary phase: Kinetex Phenyl-Hexyl C18 column (150 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% formic acid) B: methanol Quantification: Spectrophotometry: Folin-Ciocalteu method	[75]
Barley malt rootlets	NADES based on choline chloride and malic acid	BBD	T, t, solid-to-solvent ratio and % water added to NADES	80 °C, 43 min, 1:21 (w/v) and 29% of water in NADES	TPC: 8.16 mg GAE/g FW	Identification: HPLC-DAD-MS Stationary phase: Ascentis C18 column (150 × 4.6 mm, 2.7 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified methanol (0.1%	[76]

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Table 5 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
						formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	
Hazelnut skin	NADES based on choline chloride and betaine	ND	T, solid-to-solvent ratio and % water added to NADES	80 °C, 1:25 g/mL and 35% of water in NADES	TPC: 16.96 g GAE/100 g FW	Identification: HPLC-DAD-MS Stationary phase: Core Shell C18 column (150 × 4.6 mm, 2.7 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified acetonitrile (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	[77]
Elaeis guineensis leaves	Aqueous EtOH at different concentrations	BBD	t, % EtOH, solvent-to-solid ratio and A	30 min, 50% EtOH, 25 mL/g and 60% amplitude	TPC: 209.70 mg GAE/g E	Identification: HPLC-DAD Stationary phase: Agilent C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[78]
Psidium guajava leaves	Distilled water	BBD	T, t and UP	72.69 °C, 35.15 min and 407.41 W	Flavonoids extraction rate: 5.12%	Identification: HPLC-DAD Stationary phase: Agilent 5 TC-C18 column (150 × 4.6 mm) Mobile phase: A: acidified water (0.4% formic acid) B: methanol Quantification: Spectrophotometry: Folin-Ciocalteu and aluminium chloride methods	[79]
Mango 'criollo' peel	Aqueous EtOH at different concentrations	CCD	T, % EtOH and A	6.5 min, 46% EtOH and 60% amplitude	TPC: 86.1 mg GAE/g DW TFC: 26.8 mg QUE/g DW	Identification: HPLC-MS/MS Stationary phase: Poroshell C18 column (250 × 4.6 mm, 4 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified acetonitrile (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu and aluminium chloride methods	[82]
Mango 'criollo' seed				20 min, 49% EtOH and 100% amplitude	TPC: 124.2 mg GAE/g DW TFC: 53.8 mg QUE/g DW		
Chayote leaves	EtOH:water (50:50, v/v)	BBD	T, t and A	50 °C, 30 min and 60% amplitude	TPC: 5.09 mg GAE/g DW	Identification: HPLC-DAD Stationary phase: C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: methanol B: acidified water (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	[81]
Psidium cattleianum leaves	Acetone:water (80:20, v/v)	BBD	t, A and pulse cycle	4 min, 100% amplitude and 0.6 s	TPC: 155.31 mg GAE/g DM	Identification: HPLC-DAD Stationary phase: C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (2% acetic acid) B: 10% acidified water (0.5% acetic acid) with 90% methanol Quantification: Spectrophotometry: Folin-Ciocalteu method	[83]
Kiwi leaves	Acetone	CCD	T, t, solid-to-solvent ratio and A	70 °C, 15 min, 30 mL/g and 40% amplitude	PAC: 119.55 mg PC/g DW	Identification: HPLC-MS/MS Stationary phase: Agilent Zorbax Extend C18 column (250 × 4.6 mm, 5 μm)	[84]

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Table 5 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
						Mobile phase: A: acidified water (7% formic acid) B: acetonitrile Quantification: Spectrophotometry: vanillin method	
Olive pomace	Milli-Q water	BBD	t, sample-to-solvent ratio and UP	75 min, 2 g/100 mL and 250 W	TPC: 22.02 ± 2.66 mg GAE/g DW	Identification: HPLC-DAD Stationary phase: Synergi Fusion-RP 80A C18 column (250 × 4.6 mm, 4 μm) Mobile phase: A: acidified water (0.1% orthophosphoric acid) B: methanol Quantification: Spectrophotometry: Folin-Ciocalteu method	[85]
Java plum pomace	Aqueous EtOH at different concentrations with HCl	BBD	T, t, % EtOH and UP	37.6 °C, 47.5 min, 70% EtOH and 366.25 W	TPC: 2266.36 mg GAE/100 g DW TFC: 1668.43 mg QUE/100 g DW TAC: 649.47 mg C-3-GE/100 g DW	Identification: HPLC-DAD Stationary phase: X-Bridge C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified acetonitrile (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu, aluminium chloride and pH differential methods	[87]
Blueberry pomace	EtOH and citric acid	BBD	T, t and UP	40 °C, 40 min and 400 W	TAC: 108.23 mg C-3-GE/100 g DW	Identification: HPLC-MS Stationary phase: C18 column (100 × 2.1 mm, 1.8 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile Quantification: Spectrophotometry: pH differential method	[86]
Pineapple peel	Aqueous EtOH at different concentrations	BBD	t, % EtOH, solvent-to-solid ratio and A	5 min, 50% EtOH, 35:1 mL/g and 65% amplitude	TPC: 686.31 mg GAE/g DW	Identification: HPLC-DAD Stationary phase: Supelco Ascentis C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (0.1% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[80]
Orange peel	EtOH:water (50:50, v/v)	BBD	t, solvent-to-solid ratio and A	35 min, 40 mL/g and 70,89% amplitude	TPC: 1602.67 mg GAE/100 g DW TFC: 106.191 mg QUE/100 g DW	Identification: HPLC-DAD Stationary phase: Supelco C18 column (dimensions not detailed) Mobile phase: A: acidified water (0.1% formic acid) B: acidified acetonitrile (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	[88]
Tomato seed	Aqueous EtOH at different concentrations	BBD	t, solvent composition and A	15 min, 61% EtOH and 85% amplitude	TPC: 1.53 ± 0.07 mg GAE/g FW	Identification: HPLC-DAD-MS Stationary phase: HALO C18 column (100 × 4.6 mm, 2.7 μm) Mobile phase: A: acidified water (0.1% acetic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[48]
Olive pomace paste, wine lees and lees filters	EtOH, HCl and Milli-Q water	FD	% EtOH and % HCl	50% EtOH and 0% HCl	NS	Identification: HPLC-DAD Stationary phase: Kinetex C18	[29]

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Table 5 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
						column (100 × 4.6 mm, 2.6 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile	
Spinach residues Orange residues	Aqueous EtOH at different concentrations and HCl	FD	% EtOH and % HCl	80% EtOH and 0.1% HCl 60% EtOH and 0.1% HCl	TPC: 820 ± 20 mg GAE/kg FW TPC: 400 ± 100 mg GAE/kg FW	Identification: HPLC-DAD Stationary phase: Kinetex C18 column (100 × 4.6 mm, 2.6 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acetonitrile Quantification: Spectrophotometry: Folin-Ciocalteu method	[17]
Grape peel	Water/EtOH/ phosphoric acid (70:30:1, v/v/v).	FD	t and sample-to-solvent ratio	21 min and 0.07 g/mL	Peonidin-3-O-glucoside: 59.04 mg/g 100 FW Procyanidin B1: 9.49 mg/g 100 FW Catechin: 10.80 mg/g 100 FW	Identification and quantification: HPLC-DAD-MS/MS Stationary phase: Luna C18 column (150 × 2 mm, 5 μm) Mobile phase: A: acidified water (1% formic acid) B: acetonitrile	[61]
Red orange peel	EtOH:water (70:30, v/v)	CCD	T, t and solid-to-solvent ratio	50 °C, 40 min and 1:20 g/mL	Tangeretin: 2.6 mg/g FW Nobiletin: 6.4 mg/g FW	Identification and quantification: HPLC-DAD-MS/MS Stationary phase: C18 column (150 × 4.6 mm) Mobile phase: A: water B: acetonitrile	[91]
Pomegranate husk	Aqueous EtOH at different concentrations	CCD	T, t, % EtOH and solid-to-solvent ratio	93.60 °C, 55.23 min 75.23% EtOH and 3.27 g/mL	Ellagic acid: 33.5 mg/g FW	Identification and quantification: HPLC-DAD Stationary phase: Denali C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: acidified water (3% acetic acid) B: acetonitrile	[92]
Eugenia uniflora L. leaves	Aqueous EtOH at different concentrations	BBD	T, t and % EtOH	59 °C, 22 min and 44% EtOH	Ellagic acid: 26.0 μg/mL	Identification and quantification: HPLC-DAD Stationary phase: Supelco C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: water B: acetonitrile	[93]
Crataegus pinnatifida leaves	Aqueous EtOH at different concentrations	BBD	T, t, % EtOH and solvent-to-solid ratio	41 °C, 31 min, 39% EtOH and 15 mL/g	Total phenolics: 6.876 mg/g DW	Identification and quantification: HPLC-DAD Stationary phase: Waters C18 column (250 × 4.6 mm, 5 μm) Mobile phase: A: water B: acetonitrile	[89]
Seed coat of red sword bean	Aqueous EtOH at different concentrations	CCD	t, % EtOH and solvent-to-solid ratio	18.4 min, 60.2% EtOH and 29.3 mL/g	TPC: 59.62 ± 2.77 mg GAE/g DW TFC: 4.46 ± 0.15 mg CE/g DW Digalloyl hexoside: 15.30 ± 0.98 mg/g DW Methyl gallate: 8.85 ± 0.51 mg/g DW Gallic acid: 8.76 ± 0.36 mg/g DW Trigalloyl hexoside: 4.27 ± 0.21 mg/g DW Digallic acid: 2.89 ± 0.13 mg/g DW	Identification and quantification: HPLC-DAD-MS/MS Stationary phase: Symmetry Shield RP18 column (150 × 2.1 mm, 3.5 μm) Mobile phase: A: acidified water (0.1% formic acid) B: acidified methanol (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu and aluminium chloride methods	[90]
Red onion scales wastes	Glycerol with EtOH and HCl	FD	t, solid-to-solvent ratio, mL EtOH and mL HCl	NS	Quercetin: 16.55 ± 0.81 mg/g DW	Identification and quantification: HPLC-DAD Stationary phase: HC-C18 column (250 × 4.6 mm, 5 μm) Mobile phase: THF-acetonitrile-water-phosphoric acid (175:31:794:0.385, v/v/v/v)	[63]

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Table 5 (*continued*)

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
Feijoa sellowiana leaves	EtOH	BBD	T, duty cycle and UI	46 °C, 89% and 1569.10 W/cm^2	UAE: Gallic acid: 102.12 ± 0.11 mg/g E Catechin: 41.11 ± 0.10 mg/g E Rutin: 13.15 ± 0.09 mg/g Ferulic acid: 60.10 ± 0.11 mg/g E Quercetin: 29.27 ± 0.11 mg/g E Apigenin: 40.53 ± 0.07 mg/g E PLS- UAE: Gallic acid: 123.15 ± 0.11 mg/g E Catechin: 56.10 ± 0.05 mg/g E Rutin: 37.13 ± 0.10 mg/g E Ferulic acid: 69.33 ± 0.11 mg/g E Quercetin: 40.60 ± 0.10 mg/g E Apigenin: 46.30 ± 0.10 mg/g E	Identification and quantification: HPLC-DAD Stationary phase: Eclipse RP- C18 column (250 × 4.6 mm × 5 μm) Mobile phase: A: trifluoroacetic acid, 2.5 pH in deionized water B: methanol	[96]
Psidium guajava L. leaves	Aqueous EtOH at different concentrations	BBD	t, % EtOH and UP	SPC: 41 min, 62% EtOH and 235 W Flavonols: 38 min, 62% EtOH and 235 W Flavan-3-ols: 37 min, 63% EtOH and 228 W	SPC: 51 mg/g DW Flavonols: 13 mg/g DW Flavan-3-ols: 7 mg/g DW	Identification and quantification: HPLC-MS Stationary phase: Poroshell 120 SB C18 column (100 × 3 mm, 2.7 μm) Mobile phase: A: acidified water (1% acetic acid) B: acetonitrile	[94]
Olive leaves	Aqueous EtOH at different concentrations	BBD	t, % EtOH and UP	8 min, 55% EtOH and 151 W	Total phenolics: 36 ± 5 mg/g DM Oleuropein: 23 ± 2 mg/g DM Hydroxytyrosol: 0.8 ± 0.3 mg/g DM	Identification and quantification: HPLC-MS Stationary phase: Poroshell 120 EC C18 column (100 × 4.6 mm, 2.7 μm) Mobile phase: Not detailed	[95]
Kiwi peel	Aqueous EtOH at different concentrations	CCD	t, % EtOH and UP	14.8 min, 68.4% EtOH and 94.4 W	Yield: 46 ± 1% Total flavonoids: 1.49 ± 0.03 mg/g DW	Identification and quantification: HPLC-DAD-MS/MS Stationary phase: Waters Spherisorb S3 ODS-2 column (150 × 4.6 mm, 3 μm) Mobile phase: Not detailed	[97]

T: temperature; t: time; A: amplitude; UP: ultrasound power; UI: ultrasonic intensity; PLS: pre-leaching stage; TPC: total phenolic content; TFC: total flavonoid content; TAC: total anthocyanin content; GAE: gallic acid equivalents; CATE: catechin equivalents; CE: catechin equivalents; QUE: quercetin equivalents; C-3-GE: cyanidin-3-glucoside equivalents; RE: rutin equivalents; PAC: proanthocyanidin content; PC: procyanidin equivalent; DM: dry matter; DW: dry weight; E: extract; FW: fresh weight; SPC: sum of phenolic compounds; NQ: non quantified; NS: non specified.

ultrasound conditions were an additional parameter to be optimized.

With regard to studies that did not optimize the characteristic parameters of UAE technique, we can list bibliography concerning to brewers' spent grain, plum, pomegranate, apple, mango and jabuticaba peels, barley malt rootlets, apricot pomace, hazelnut skin, okra stem, almond hulls, banana bract, sugar beet molasses, and *Hemerocallis fulva* leaves [16,51,66–77]. In these studies, the phenolic compounds contents were expressed as mg of standard per gram of E, DW, DM or FM.

With regard to bioactive contents per extract, the optimum content of TPC quantified in okra stems [51] was the most abundant (TPC: 61.55 mg GAE/g E) while the TPC of plum peel was the scarcest (6.22 mg GAE/g E) [66]. Whereas the first study applied a CCD and optimized TPC, the second applied a BBD using TPC and TAC as multi-response variables. The studied experimental regions were very unequal, as the okra stems research studied a wider range of temperature and time. Moreover, the major phenolic compounds identified in okra stems were flavonols, catechins and hydroxycinnamic acid derivatives, while in plum peel were phenolic acids and flavonoids also. On the other hand, the TPC results obtained for *Hemerocallis fulva* leaves were between those mentioned above, and the researchers applied a BBD to study the effects of temperature (50–70 °C), percentage of EtOH (60–80%) and solvent-to-solid ratio (35–45 mL/g) [67]. Five different flavonoids were identified in *Hemerocallis fulva* leaves by advanced analytical techniques. To conclude this section, it is worth mentioning that the TAC of plum peel [66] was nine times fewer than that reported for banana bract [68]. Again, both studies applied different experimental designs (BBD and CCD, respectively) and the studied ranges of temperature and percentage of EtOH were similar in both studies (35–60 °C and 40–90 % EtOH). In this case, the optimum values of the independent variables were very similar, with medium temperature and percentages of EtOH in aqueous mixtures. However, in these investigations the authors decided to optimized different independent variables, concretely extraction time for plum peel and solid-to-solvent ratio in banana bract extraction. By last, the extract obtained from banana bract was characterized showing

the presence of different anthocyanins, for example, cyanidin-3-O-glucoside and peonidin-3-O-glucoside.

Continuing with those studies that expressed their results as mg of standard per gram of DW or DM, the study on pomegranate peel stood out for being the one that managed to report the highest TPC, TFC and TAC (158.10 mg GAE/g DW, 82.30 mg QUE/g DW and 0.52 mg C-3-GE/g DW, respectively) after multi-response optimization [69]. On the other hand, apricot pomace was found to have the lowest TPC and TFC of this group (TPC: 1.210 mg GAE/g DM and TFC: 1.032 mg CATE/g DM, respectively), also after a multi-response optimization [70], as can be seen in Table 5. Despite the two studies coincided in performing a multi-response approach, they applied different experimental designs (BBD and CCD, respectively). The optimized variables in common were temperature and extraction time, being the first a significant parameter in both studies. It should be noted that the experimental range of temperature in both studies was very similar (30–70 °C). Moreover, regarding the individual characterization, phenolic acids and flavonoids were the main polyphenols detected in apricot pomace and pomegranate peel.

The rest of the by-products obtained an intermediate TPC content between the two previously mentioned researches. Jabuticaba peel [71], apple peel [72], mango peel [73], sugar beet molasses [74], almond hulls [75] and brewers' spent grain [16] can be ranked from the highest to the lowest TPC content, as can be seen in Table 5. Most of them applied BBD as experimental design, except for jabuticaba peel and sugar beet molasses, which applied CCD. Likewise, most of these studies optimized the same independent variables, temperature, time and percentage of EtOH. In the case of peels, the experimental regions studied were very unequal, since apple peel study fixed the maximum extraction time in 52 min whereas for mango peel was up to 120 min, for example. The same was observed for the EtOH-aqueous mixture composition, since jabuticaba peel only tested up to 47% EtOH in water. In addition, it should be noted that the studies on jabuticaba and mango peel performed a multi-response optimization, taking into account the contents of specific compounds of interest quantified by chromatographic techniques, such as HPLC-DAD. In the first study, the TPC, TAC, and the individual concentrations of cyanidin-3-O-glucoside and ellagic acids were maximized, whereas for mango peel the TPC and mangiferin content were the considered variables for multi-response optimization. Moreover, regarding the individual characterization, ellagic acid and cyanidin-3-O-glucoside were the bioactive compounds identified in jabuticaba peel, while flavonoids, phenolic acids and xanthones were detected in the rest of the by-products.

In terms of TAC, jabuticaba peel [71] showed the highest content (4.8 mg C-3-GE/g DW) in contrast to sugar beet molasses [74], with the lowest concentration (31.81 mg C-3-GE/100 g DW). Both studies applied a CCD as experimental design, coinciding in some of the optimized variables, such as time and EtOH percentage. In this case, a large difference between the assayed experimental regions of EtOH composition was found, as the jabuticaba peel study used up to 47% of alcohol and the sugar beet molasses had a minimum percentage of 50%. Lastly, pomegranate peel [69] obtained an intermediate TAC between the above-mentioned by-products. Finally, to conclude this group of by-products, a mention should be made of barley malt rootlets [76] and hazelnut skins [77]. In both cases, NADES based on choline chloride were used to carry out the extraction, and the same independent variables were studied, with the exception of time. The use of NADES as extraction solvents in this research line provides novelty, since most of the studies included in this review used aqueous EtOH mixtures. However, NADES promise to be a valuable extraction tool that should be further investigated to get insight in the potential as extract solvent for phytochemicals recovery. In addition, the experimental region of the examined variables was quite similar, with medium-low percentages of water in NADES and temperatures below 80 °C. However, the type of experimental design applied was not specified for hazelnut skins, whereas in the case of barley malt rootlets, a BBD was applied. According to the obtained optimized results, barley malt rootlets showed higher TPC than hazelnut skins, with very similar optimum extraction conditions, in terms of temperature (80 °C) and percentage of NADES in water (29% and 35%, respectively). In addition, flavonoids and phenolic acids were identified in both samples by HPLC-DAD.

With respect to the aforementioned studies, several advantages could be listed due to the fact of applying constant conditions of the ultrasound parameters, such as easy operation and lower acquisition costs of the extraction equipment (ultrasound bath). However, this operation mode would present the disadvantage of not being able to take advantage of the potential of the technique itself, since neither the amplitude nor the power of the ultrasound can be modified, so the extraction efficiency could be reduced.

Nevertheless, these articles examined a wide range of independent variables directly connected with the extraction process that could affect the process efficiency. For instance, as mentioned earlier, solvent composition has proven to be one of the most important factors influencing the effectiveness of this type of extraction. This fact was demonstrated in the extraction of plum peel, where the composition of hydro-ethanolic mixtures was a variable with significant effects in the bioactive recovery. Additionally, the temperature was another crucial variable for UAE, as this experimental parameter is well-known for its ability to modulate extractions. However, it is important to note that it is possible that some studies carry out preliminary optimization assays that put into light that there is no significant effect of some experimental variables, which would justify not including them in the optimization study.

On the other hand, research on mango peel and seed, tomato seed, chayote, kiwi, *Psidium cattleianum, Elaeis guineensis* and *Psidium guajava* leaves, pineapple and orange peels, olive, java plum and blueberry pomaces optimized the UAE parameters directly connected to ultrasounds waves [48,78–88]. In these studies, the phenolics contents were mostly expressed as mg of standard per gram of DW, DM, FW or E. *Elaeis guineensis* [78] and *Psidium guajava* leaves [79] were studied as potential sources for the extraction of bioactive compounds by UAE. While the first research used aqueous EtOH at different concentrations as extraction solvent, the latter opted for pure distilled water. This was quite novel considering the general trend of using EtOH as solvent, as well as open the way to the ultimate exponent of environmentally friendly and sustainable extraction. Both studies applied the same experimental design (BBD) but optimized different extraction parameters, agreeing only in the optimization of extraction time, being the optimum very similar (30 and 35 min, respectively). In the case of *Elaeis guineensis* leaves, despite applying a RSM, no theoretical optimization was performed, but the best applied extraction condition was selected as the optimal one, obtaining a TPC of 209.70 mg GAE/g E. On the other hand, results from *Psidium guajava* leaves were expressed as flavonoids extraction rate, measured spectrophotometrically using rutin as standard. Therefore, the obtained results were expressed in different units and could not be compared. Additionally, phenolic acids and flavonoids were identified in these by-products.

With regard to the by-products which expressed the contents as mg of standard per gram of DW or DM, pineapple peel [80] showed the highest TPC content (686.31 mg GAE/g DW), while chayote leaves [81] was the by-product with the lowest TPC content (5.09 mg GAE/g DW). Both studies applied a BBD to study the effect of the different independent variables, being only in common the study of time and amplitude. On the other hand, in both cases, time was significant and wide time ranges were studied. The rest of the by-products described in this section obtained TPC values in between those mentioned above.

Many studies agreed on the type of the by-product or the matrix described and, by expressing the results in the same units, comparison between them at a higher level of detail was possible. Thus, research on the extraction of phenolic compounds from mango waste (peel and seed) [82] optimized TPC and TFC by multi-response approach, applying in both cases a CCD. The same independent variables were studied for

these by-products, under the same experimental regions (20–100% amplitude, 5–30 min and 0–100% EtOH). As a result, seed was shown to be more abundant than peel in TPC and TFC contents. In these studies, a total of 45 phenolic compounds were characterized by HPLC-MS in the optimized extracts. Among them, flavonoids, xanthones (specially mangiferin) and gallotannins were found.

Moreover, for the studies focused on leaves, it is worth mentioning chayote [81], *Psidium cattleianum* [83] and kiwi leaves [84]. While the first two applied BBD as the experimental design, the authors of the kiwi leaves research applied a CCD. *Psidium cattleianum* leaves obtained the highest TPC, while chayote was the poorest leaf in compounds of interest, as can be seen in Table 5. Nevertheless, the independent variables and experimental region examined were very diverse, making it difficult to compare these studies. For example, time was significant in the extraction of chayote and *Psidium cattleianum* leaves, but they studied a very different range (30–80 min and 2–6 min, respectively). However, more similarity could be observed between the experimental temperatures applied for chayote and kiwi leaves, with medium-low extraction temperatures. In regards to the characterization, *Psidium cattleianum* leaves were analysed by HPLC-DAD, and 9 phenolic compounds were identified, mainly phenolic acids and flavonoids. For their part, phenolic acids, flavonoids and procyanidins were the main bioactive compounds in chayote and kiwi leaves.

On the other hand, studies focused on pomaces obtained from olive [85], blueberry [86] and java plum [87] applied BBD as experimental design for the research, and the latest study applied a multi-response to optimize TPC, TFC and TAC at the same time. Research on java plum and blueberry studied the addition of acids to the solvent to improve extraction. Apparently, as other studies mentioned before, good results were obtained with acidic environment. However, olive and java plum pomace obtained very similar optimal TPC values, and the first study did not add any acid for the extraction. This could be due to the matrix effect and its interaction with the analytes of interest. On the other hand, it could be clearly observed that java plum pomace obtained 6 times more TAC than blueberry pomace, as shown in Table 5. The effect of ultrasound power was shown to be significant in the extraction of TPC from olive pomace, and the studied experimental region (150–250 W) was very different from that studied in java plum pomace (200–400 W). However, temperature had a significant effect on this java plum by-product extraction and was not studied in olive pomace. Regarding anthocyanin extraction, in both by-products, the experimental regions of the variables under study were similar. Phenolic acids, flavonoids and anthocyanins were the main phenolics identified in these matrices.

Additionally, orange peel [88] and pineapple peel [80] studies also applied the BBD to investigate how the independent variables affected the response variables. In particular, the orange peel study performed a multi-response to optimize TPC and TFC. Both studies were concordant concerning the variables under study (time, solvent-to-solid ratio and amplitude). The experimental regions studied for the variables time and solvent-to-solid ratio were very different, as the study on pineapple peel applied wider study ranges. As for the optimal conditions, the extraction times were very unequal, while the solvent-to-solid ratio and the percentage of amplitude showed similar values, as can be seen in Table 5. Pineapple peel was shown to have the highest TPC content, while flavonoids and phenolic acids were the main phenolic compounds detected by HPLC-DAD in these by-products.

Finally, a study on tomato seed [48] applied a BBD to optimize the extraction of total polyphenols expressing the TPC in mg GAE/g FW, so it could not be compared to any other study. Phenolic acids and flavonoids were the main phenolic compounds identified in this matrix.

Regarding the studies that modified the UAE parameters in their research, it could be noted that they developed an optimization of the parameters that are directly linked to ultrasound extraction technique. This consideration has the advantage of being able to get the most out of the extraction technique although, at the same time, this implies higher equipment acquisition costs (ultrasonic probe) and a higher degree of difficulty of the process with respect to the other modality of UAE (without controlling ultrasound parameters). On the other hand, as occurred with the ultrasonic bath studies, extensive research was found with a very complete study on the independent variables that can affect the extraction process, while others studied a more limited numbers of independent variables. The study of temperature and solvent composition are fundamental, since they have shown to be influential parameters in UAE extraction depending on the plant matrix used. However, as mentioned above, the absence of these variables in the optimization could be justified if preliminary studies show that they are not significant variables in that particular extraction process.

In addition, some research has focused on the detailed study of the individual phenolic compounds found in the extracts, carrying out an identification and quantification of individual bioactive compounds by advanced chromatographic methodologies. As previously described for spectrophotometric determinations, research studies were divided between those which optimize the UAE parameters in the extraction process and those that did not.

With respect to those studies that did not take into account amplitude or ultrasonic power for the optimization of the independent variables, *Crataegus pinnatifida* and *Eugenia uniflora* L. leaves, seed coat of red sword bean, red onion scales wastes, pomegranate husk, red orange and grape peels, olive pomace, wine lees and lees filters, spinach and orange residues should be mentioned [17,29,61,63,89–93]. In these studies, the phenolics contents were expressed as quantity of compound (mg or μg) per gram of DW, FW or mL. In the case of *Crataegus pinnatifida* leaves [89], seed coat of red sword bean [90], and red onion scales wastes [63], optimization was carried out using different experimental designs (CCD and FD, respectively). Despite these research papers are in agreement with the study of some independent variables, the experimental regions used were very diverse. The results showed that the phenolic compound content of seed coat of red sword bean was higher than the quercetin content of the onion by-products (16.55 ± 0.81 mg/g DW) and the TPC of *Crataegus pinnatifida* leaves (6.876 mg/g DW). Moreover, phenolic acids and flavonoids were characterized in *Crataegus pinnatifida* leaves by HPLC-DAD.

Research on the extraction of bioactive compounds from wine lees, lees filters, olive pomace paste, and orange and spinach wastes [17,29] were only focused on an independent variable, the solvent composition, which varied in the percentages of EtOH and HCl in aqueous mixtures. Both investigations studied by a FD the same experimental region of the two independent variables (40–80% EtOH and 0–0.5% HCl), being significant alcohol concentration for lees and orange waste, and both of these variables for spinach by-product. The chromatographic areas of the different compounds detected were summed and quantified as gallic acid equivalent. Despite applying experimental designs, the optimal conditions for the UAE extraction were not described, so the authors chose the best experimental UAE conditions from the design runs for the characterization of all by-products. In this regard, hydroxytyrosol, oleuropein and different phenolic acids and flavonoids were components confirmed in different by-products UAE extracts by HPLC-DAD. The results showed that spinach residues obtained higher TPC than orange wastes (820 ± 20 mg GAE/kg FW and 400 ± 100 mg GAE/kg FW, respectively), with extraction conditions only in agreement regarding the optimal percentage of HCl (0.1%). Another study that showed low contents of specific polyphenols was developed in grape peel [61]. This research, like the previous one, applied a FD, but the studied independent variables were different. Likewise, when comparing the results of orange wastes [17] with another study on orange peel [91], it could be observed that the latter showed higher contents of specific phenolic compounds (tangeretin and nobiletin) obtained by multi-response, as can be seen in Table 4. This research on orange peel applied a CCD to study the effect of temperature, time and solid-to-solvent ratio, as another research did on pomegranate husk [92]. Despite in these studies the same independent variables were optimized, the experimental regions studied were different since, in the case of orange peel,

temperatures were not as high and time was not as short as in pomegranate husk. Furthermore, the ellagic acid content of pomegranate husk was much higher than the tangeretin and nobiletin contents of orange peel. Another research that studied the ellagic acid content in *Eugenia uniflora* L. leaves determined by HPLC-DAD [93] applied a BBD, but their contents could not be compared as they were expressed in different units. As before, despite studying the same variables as pomegranate husk, the experimental regions studied were different.

Finally, it is worth mentioning those studies that optimized the extraction parameters of the UAE technique and identified and quantified the individual compounds by HPLC coupled to DAD or MS detectors: kiwi peel, *Psidium guajava* L., *Feijoa sellowiana* and olive leaves [94–97]. The phenolic compounds contents were expressed as mg of compound per gram of E, DW or DM.

Studies performed in *Psidium guajava* L. leaves [94] and olive leaves [95] applied a BBD to evaluate the effect of the independent variables on the response variables. Both of them optimized time, EtOH percentage and ultrasound power, but only the percentage of alcohol was studied in a similar experimental region in both investigations. According to the results shown in Table 4, it can be stated that *Psidium guajava* L. leaves was richer in bioactive compounds. However, it should be noted that in the case of the optimization of guajava leaves, no multi-response was considered taking into account the other response variables. Regarding the optimum conditions, both extraction time and ultrasound power were very different between the two studies, however, the percentage of EtOH was similar (55–62%). For their part, the authors who studied the olive leaves obtained the same optimal conditions for all responses (hydroxytyrosol and oleuropein concentrations, as well as TPC), suggesting a positive correlation between them. Different flavonoids, as well as other phenolic compounds, were identified in these by-products. In relation to *Feijoa sellowiana* leaves [96], the extraction process was optimized using a BBD. As can be seen in Table 5, the authors compared the content of various phenolic compounds obtained using the optimal extraction conditions applying UAE or pre-leaching stage UAE (PLS-UAE), concluding that the soaking of the dried leaves in the same solvent used for UAE extraction improved the process. With regard to kiwi peel [97], which was studied under a CCD, the optimal flavonoid content obtained by multi-response was much lower than for flavonols and flavan-3-ols from *Psidium guajava* L. leaves.

To conclude, with regard to the extraction of bioactive compounds by UAE, as previously detailed, several independent variables were studied with the aim to maximise the polyphenols recovery. Of them, the most frequently monitored variables in the studies were the extraction temperature, time, solvent composition and solid-to-solvent ratio, mostly studied under a BBD. It is worth noting the large amount of research that did not considered the specific parameters of the ultrasound equipment for the extractions. This fact could be explained by the use of non-specific ultrasonic baths used for extraction with no possible control of ultrasound power. It is true that this type of extraction technique increases the recovery of analytes of interest compared to conventional extraction techniques thanks to the ultrasounds applied. However, when comparing the ultrasonic bath with the ultrasonic probe with control of ultrasound waves, the latter is more efficient and powerful due to the limitations of the ultrasonic bath. Thus, the main drawback of the ultrasonic bath is based on the weak, uncontrolled and non-uniform ultrasonic irradiation that it performs, which result in a low repeatability of the extraction step. However, despite these limitations, it also has several advantages, such as its simplicity and low cost. For these reasons, the ultrasonic bath is one of the most commonly used extraction techniques in laboratories, as evidenced by the present compilation of studies. Therefore, although it is true that studies working with ultrasound baths have limitations, their good results make this technique a very widespread methodology in the context of extraction.

On the other hand, this review showed the significant effect of the independent variables on the response ones, with a few exceptions. For instance, EtOH concentration was the only variable with significant effects on the response variables in the plum peel study, whereas time had no significant effect on the TPC and TFC extraction from pomegranate peel. It should also be emphasized that the majority of the studies performed a multi-response optimization with the aim of improving the recoveries of different target variables (TPC, TFC, TAC, yield and total phenolic compounds determined by different analytical platforms), such as pomegranate peel, java plum pomace and kiwi peel, which highlights the great effort of the authors. This fact endows these studies with high quality and leads the research to a very enriching horizon. It can be concluded that this extraction technique was the most commonly used by several research groups to carry out their studies, and this may be due to the lower investment needed to acquire an ultrasonic instrument, its simplicity and the lower operational costs reported [98,99]. However, one of its main drawbacks is the need of a sample treatment after the extraction, mainly with filtration steps, which are translated in longer and laborious processes. In addition, more specifically with respect to the ultrasonic bath, an important disadvantage to consider is the impossibility to control the extraction temperature in the bath, which could cause phytochemicals degradation.

Finally, UAE was compared with enzyme assisted extraction (EAE) in a study that applied both extraction techniques on orange peel for recovering polyphenols [88]. UAE was optimized by BBD as it was described above. With the aim of optimizing the EAE extraction, authors also applied a BBD with different independent variables to be optimized: extraction time (4–6 h), solvent-to-solid ratio (20–40 mL/g) and enzyme concentration (0.7–0.9%), as shown in Table 6. In this case, the selected enzyme used for enzymatic extraction was Viscozyme L. (from *Aspergillus aculeatus*). The results showed a recovery of 3311.61 mg GAE/100 g DW of TPC and 258.85 mg QE/100 g DE for TFC, and all the studied variables had significant effects. The EAE is a new emerging technology applied in the food industry, which has numerous advantages over

Table 6
Experimental designs, variables and optimums of the different matrices extracted by EAE.

By-products	Extractive solvents	Experimental design	Experimental variables	Optimal conditions	Optimal predicted or experimental response variable	Analytical Technique/Method	Reference
Orange peel	EtOH:water (70:30, v/v)	BBD	t, solvent-to-solid ratio and enzyme concentration	4.87 h, 30.94 mL/g and 0.84% enzyme	TPC: 3311.61 mg GAE/100 g DW TFC: 258.85 mg QUE/100 g DW	Identification: HPLC-DAD Stationary phase: Supelco C18 column (dimensions not detailed) Mobile phase: A: acidified water (0.1% formic acid) B: acidified acetonitrile (0.1% formic acid) Quantification: Spectrophotometry: Folin-Ciocalteu method	[88]

t: time; TPC: total phenolic content; TFC: total flavonoid content; GAE: gallic acid equivalents; QUE: quercetin equivalents; DW: dry weight.

conventional extraction. In summary, it offers high efficiency and reproducibility, high extraction yield, lower energy requirements and simplified manipulation at shorter extraction times [88,100]. In addition, it is also a process that presents the advantage of being environmentally friendly [101]. The substantiation behind this technique is that the catalytic power of the enzymes enhances the degradation of the cell wall, allowing a greater release of bioactive compounds to the solvent [101]. Therefore, this could be a good alternative for the extraction of phenolic compounds from food industry by-products.

4. Conclusion

Through this systematic review, different techniques applied for optimized green extraction of phenolic compounds from different food by-products found in the scientific literature to date was exposed. Phenolic compounds have become interesting bioactive compounds with positive health implications, so their recovery from food wastes could be of interest for their use for health benefits purposes. In this sense, following a circular economy perspective, numerous research projects have focused on the optimization of different extraction processes for the recovery of these compounds from wastes generated by the food industry, an under exploited and cheap resource. The different vegetable matrices used as potential sources of these phytochemicals, the green extraction techniques, the extractive GRAS solvents used, the experimental designs applied with the independent variables optimized, the optimal conditions established as well as the optimal predicted or experimental response variables were collected and summarized by the present work from recent bibliography. The objectives were to present the most used extraction techniques and the experimental designs applied to achieve high recovery of polyphenols from these waste sources, as well as to compare the values of the optimized experimental variables and the recovery results obtained in these studies. Likewise, an important point of this research was to gather information on the analytical technique used to determine the response variable of these studies. Based on the aforementioned aspects and the studied results, the use of experimental designs to improve the performance of different extraction techniques and methods has become a widely used tool in current research. It can be concluded that, among them, FD, CCD and BBD have proven to be the most preferred options for researchers to improve the recovery of phenolic compounds from food wastes by different extraction technologies. The continuation of the study in this line of research opens up many possibilities to achieve the ultimate goal of being more efficient, economical, sustainable and less harmful to the environment in a world that is increasingly aware of protecting the environment and promoting health and well-being.

CRediT authorship contribution statement

Lucía López-Salas: Investigation, Methodology, Writing – original draft. **Xavier Expósito-Almellón:** Investigation, Methodology, Writing – original draft. **Isabel Borrás-Linares:** Conceptualization, Investigation, Supervision, Writing – review & editing. **Jesús Lozano-Sánchez:** Conceptualization, Funding acquisition, Investigation, Project administration, Supervision, Writing – review & editing. **Antonio Segura-Carretero:** Conceptualization, Supervision.

Declaration of competing interest

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

Data availability

No data was used for the research described in the article.

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