

Review

Technologies and Extraction Methods of Polyphenolic Compounds Derived from Pomegranate (*Punica granatum*) Peels. A Mini Review

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Abstract: The interest in using plant by-product extracts as functional ingredients is continuously rising due to environmental and financial prospects. The development of new technologies has led to the achievement of aqueous extracts with high bioactivity that is preferable due to organic solvents nonuse. Recently, widely applied and emerging technologies, such as Simple Stirring, Pressure-Applied Extraction, Enzymatic Extraction, Ultrasound-Assisted Extraction, Pulsed Electric Fields, High Hydrostatic Pressure, Ohmic Heating, Microwave Assistant Extraction and the use of “green” solvents such as the deep eutectic solvents, have been investigated in order to contribute to the minimization of disadvantages on the extraction of bioactive compounds. This review is focused on bioactive compounds derived from pomegranate (*Punica granatum*) peels and highlighted the most attractive extraction methods. It is believed that these findings could be a useful tool for the pomegranate juices industry to apply an effective and economically viable extraction process, transforming a by-product to a high added value functional product.



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1. Introduction

Modernization of lifestyle has led the human population to consume food with mis-doubt nutritional value-enhancing oxidative reactions, producing reactive oxygen species (ROS). This species mainly performed through enzymatic, and chemical reactions causing the rise of severe and various types of cancer, changes in protein–lipid and carbohydrate utilities, and other diseases related to food habits leading to reduction of life expectancy [1,2]. Thus, there is a growing awareness of consuming food containing natural bioactive ingredients, like antioxidants, to enhance and protect human health in the last years. Fruits and their wastes such as peels and seeds are essential food products containing substantial amounts of these bioactive ingredients. One such example is the pomegranate species (*Punica granatum* L.), also called “granular or seeded apple”, a well-known fruit with global consumption.

The pomegranate tree has been known for thousands of years and is considered to symbolize fertility, abundance, and good luck. Different peoples and cultures, including the Phoenicians, Greeks, Arabs, and Romans, have cultivated pomegranates for consumption as food and as medicine [3–6].

In recent years, the pomegranate tree has become increasingly popular, both economically and scientifically worldwide. Optimal growing conditions for pomegranate cultivation occur in climate conditions similar to the Mediterranean basin. Thus, pomegranate's commercial production is found mainly in Turkey, North Africa, Spain, Israel, and other Mediterranean countries, which were the main trading centers for pomegranate cultivation, followed by Asian countries and the countries of the former USSR. However, it is also cultivated in other regions such as the Middle East, the Americas (USA, Brazils, Chile, Mexico, and Argentina), and Australia [7–9].

This interest is motivated by the pleasant organoleptic properties of endocarp consumption and beneficial ingredients that make it a functional food. That is of great interest due to its association with potential health benefits, as it is rich in antioxidants, minerals, vitamins, and other useful ingredients for the prevention of certain diseases [10–12]. As the global pomegranate juice industry production increases, the quantities of pomegranate peels (PP) are also increasing [3]. This raises the question of finding alternative solutions, avoiding the use of harmful solvents, for the conversion of a fruit by-product into a functional ingredient with high antioxidant activity in order to be used as a natural additive in the food, pharmaceutical, cosmetic, and other industries.

2. Pomegranate Juice Production and Wastes

Pomegranate juice is obtained from the whole fruit, after the peeling process, with natural pressure and without chemicals. Therefore, the pomegranate fruits substances, such as anthocyanins, are transferred to the juice, which in turn retains the organoleptic properties of the fruit. Among pomegranate compounds, organic matter like immediately decomposing compounds (e.g., sugars, organic acids, and amino acids), and biodegradable polymers (proteins and hemicytarines), are the main ingredients of fruit juices.

Pomegranate juice wastes are the result of the fruits squeezing process. Due to the large amounts of wastes produced in the fruit juice industry every cultivation period, this industrial activity is of social [13], economic [14,15], and ecological importance [16,17].

Wastes, such as peels, leaves, and liquids like water used to clean surfaces, are among the main wastes produced during juicing processing and mainly discard without valorizations. Among these, the pomegranate peels (PP) amounted to 40–50% of the total weight of pomegranate wastes [18] can be used as a feedstock [19]. Two main by-product streams are produced during the juice production process after extraction of juice from fruit and separation of seeds from juice: PP and pomegranate seeds (PS) (Figure 1) [20].

Large amounts of disposal wastes from agricultural and industrial sectors that contain a high concentration of polyphenolic compounds can make them intractable due to their phytotoxic phenomena [21–23], particularly when they end up in water recipients with low water recirculation [24]. However, despite their environmental issues, some of the components contained in these wastes are of particular interest because of their possible use as natural preservatives. However, so far, no comprehensive solution has been proposed, but various techniques have been applied with technical or economical disadvantages.

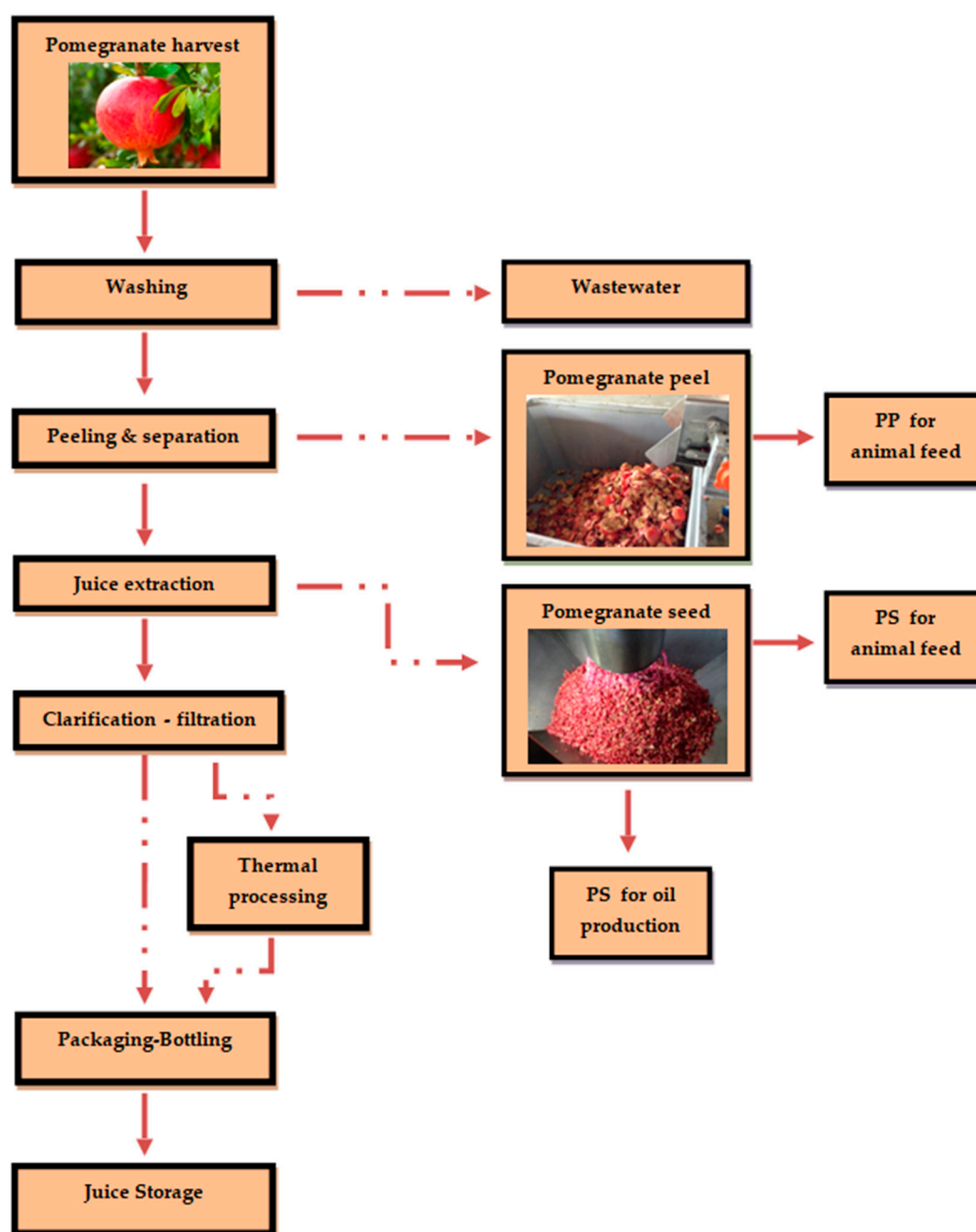


Figure 1. Schematic procedure of pomegranate juice and waste production.

3. Phenolic Profile of Solid Waste of Pomegranate Juice Process

Various plant species are regularly exposed to environmental stress, including relatively high temperatures and ultraviolet radiation. Therefore, they need multiple compounds, such as antioxidants, to maintain their integrity by protecting lipids from oxidation, preventing the formation of flavors and aromas, and extending their shelf life [25,26]. Among antioxidant compounds, secondary metabolites such as phenolic compounds, which are derivatives of benzene with one or more hydroxyls in the phenolic ring, are essential due to their antioxidant properties. Depending on the carbon structure, these compounds are classified into phenolic acids, flavonoids, and lignans [27,28]. Extraction and application of these bioactive compounds exhibit functional properties that enhance human health [29–33] and play an essential role in organic plant production as plant promoters, fertilizers [34], and phytoprotective materials [35–38].

Pomegranate is known to be one of the richest fruit in phenolic compounds [39–41]. Studies have reported that the concentration of phenolics from PP was 10 times higher (249.4 mg/g) than that found in the pulp (24.4 mg/g) [37].

PP is one of the most valuable by-products of the food industry due to the high concentration in bioactive compounds [39] that possesses unique biological activities, antimicrobial properties [36], and protective effects against tumor and cardiovascular disorders [32].

As Figure 1 presents during the processing of pomegranate juice, large amounts of PP are collected as residue containing high concentrations of phenolic compounds. The major phytochemical component classes identified to date in PP are phenolic acids (ellagic and gallic acids), flavonoids (quercetin, cyaniding and complex substances), and hydrolysable tannins (punicalin and other complex substances) (Figure 2) [42].

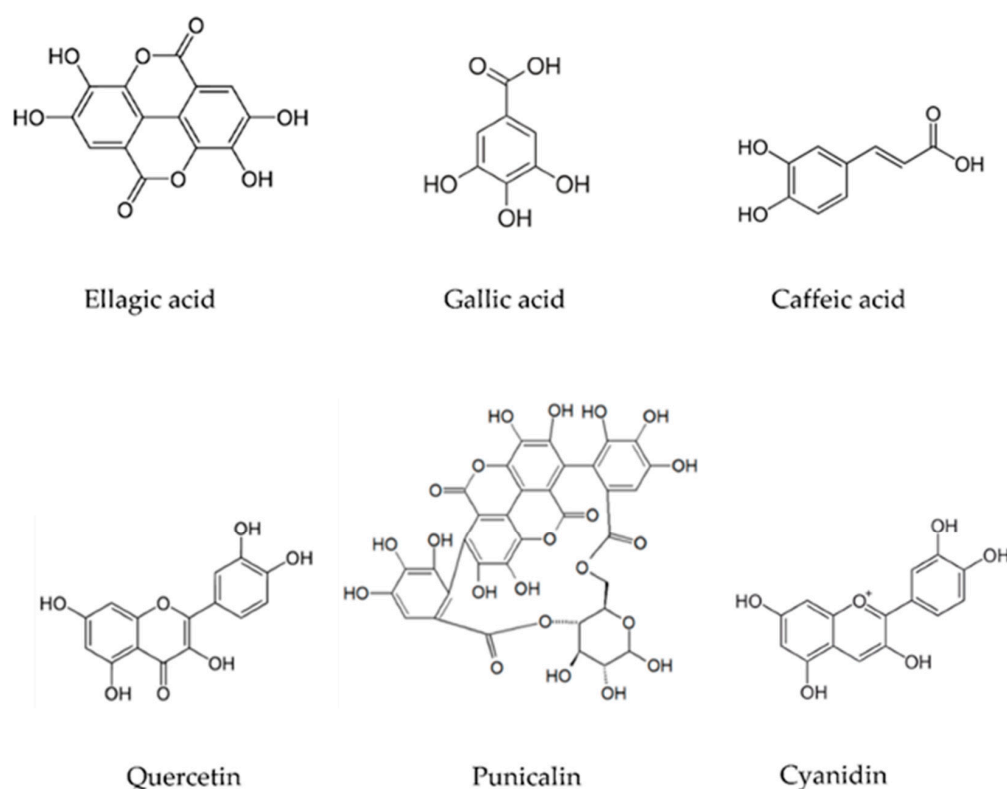


Figure 2. The structural formula of phenolic compounds in pomegranate peels (PP).

The concentration of phenolics in PP varies between the pomegranate cultivars at different geographical conditions. Gallic, ellagic, caffeic, and p-coumaric acids were identified and quantified from PP of six Tunisian pomegranate ecotypes with mean concentrations of 123.79, 35.89, 20.56, and 4.48 mg/100 g, respectively [40].

It is also presented that a quantity of 1 g extract received by an enzymatic extraction from PP contains dietary fiber, lignin (200–410 mg), cellulose (165–208 mg), uronic acid (139–233 mg), and neutral sugars (glucose, rhamnose, fucose, mannose, xylose, galactose, and arabinose) (168–193 mg) [43].

4. Technologies and Extraction Methods Used for PP

Extraction is a process of separating and receiving a desired substance or a group of substances from a plant's raw material using solvent-based techniques, sorptive membrane—assisted and instrumental methods. It is a process in which a sense is transferred from a solid to a liquid phase. With extraction techniques, an isolation of a target substance from a mixture is completed by contacting a solvent that dissolves it selectively [43]. The initial mix can be a solid or liquid natural material. Depending on the raw material, a different extraction technique is applied. The disadvantages of low efficiency, high processing

time, high cost, and environmental considerations of the conventional extraction methods, such as Simple Stirring [44,45], lead to the investigation for new extraction processes. So far, several extraction methods, such as Pressure-Applied Extraction [46], Enzymatic Extraction [47], Ultrasound-Assisted Extraction [48] with the use of deep eutectic solvents [49,50], the cloud point extraction [51], and recently the Vacuum microwave aqueous assistant extraction have been presented for the extraction of PP and other agricultural wastes [52,53]. Furthermore emerging technologies, for example High Hydrostatic Pressure, Pulsed Electric Fields, and Ohmic Heating, Assistant Extraction have been investigated to contribute to the minimization of the extraction of bioactive compounds disadvantages [54,55].

Many studies have already been published about the methods that have been applied to extract PP ingredients. Most of them show the preparation stages of drying and grinding of the PP before the extraction, while one study presents the direct extraction of fresh PP in an industrial type extractor [52]. In general, the approaches studied include the simple stirring, pressure application, and extraction using ultrasound and microwaves assistance (Table 1) [44,56–59].

Table 1. Characteristic of various phenolic extraction techniques from PP.

Extraction Technique	Time (min)	Solvents	Total Phenolics	Flavonoids	Tannins	Reference
Simple stirring	60	Water, methanol, ethanol, ethyl acetate acetone	119–82.6 mg GAE/g DM			
	240		249.4 ± 17.2 mg GAE/g DM	59.1 ± 4.8 mg/g	10.9 ± 0.5 mg/g	[37,44,45]
	2		229mg TAE/g DM			[60]
Soxhlet	240	water ethyl acetate acetone, methanol, Water		165 mg CE/g DM 520 mg CE/g DM 462 mg CE/g DM 48 mg CE/g DM		[61]
Pressure	60	Water, methanol	45.65 mg GAE/g DM			[62,63]
		Water	264 mg TAE/g DM	13 mg CE/g	Hydrolyzable tannins 262 mg TAE/g) Condensed tannins 9.5 mg CE/g)	
UAE (continuous)	6	Water	148 mg GAE/g DM			
UAE (pulsed)	10	Water	145 mg GAE/g DM			
UAE		Water/ethanol	188.1 mg GAE/g DM	62.6 mg RE/g DM)	23.2 mg CE/g DM	[44,64–66]
		Water/ethanol ethyl-acetate	>200 mg GAE/g DM 138.5 mg GAE/g DM			
	10	Extraction yield increased in the following order of solvents: 70% methanol < 50% methanol < water < 70% ethanol < 50% Water	24.64 mg GAE/g DM. Ethanol varied from 202.8 to 214.5 mg GAE/g DM 146 mg GAE/g			[44,67,68]
MAE	1					[52]
VMAAE	10					
Enzyme-assisted supercritical fluid extraction	85		301.53 mg GAE/g			[69]
IRA	90	DES	152 mg/g DM			[70]

MAE: microwave assisted extraction, VMAAE: vacuum microwave aqueous assisted extraction, UAE: ultrasound assisted extraction, IRA: infrared assisted, GAE: gallic acid equivalents, CE: catechin equivalents, RE: rutin equivalents, TAE: tannic acid equivalents, DM: dry matter, DES: deep eutectic solvents.

4.1. Extraction Technique with Simple Stirring

In the chemical analysis of plant samples for sample preparation and the recovery of bioactive compounds from plant tissues, extraction is an important stage [71]. Currently, there are numerous extraction techniques based on different physicochemical principles [72]. Among them, simple stirring is one of the most widely used and straightforward in extraction methods. Various factors like the method of extraction applied [61], the type and differences in a mixture of solvents used for the extraction [37], and the use of different

materials [73] affect efficient extraction of the compounds derived from plant tissues. Extraction of antioxidant compounds contained in fruits and their wastes is the first, and the more straight forward step, for their commercial-scale application. However, utilization of by-products such as PP in pomegranate juice industry has not been yet studied adequately. Thus, efficient methods for extraction of antioxidant compounds such as flavonoids, phenolics, proanthocyanidins, and their kinetic parameters embedded in the PP need to be evaluated in order to design and choose the most appropriate extract method. It has been found that fruit and particularly pomegranate antioxidant activity is typically higher in commercial juices extracted only due to the presence of seeds and peels during the squeezing process from whole pomegranates than in juices obtained from the arils. In particular, the peel has been reported to have relatively higher antioxidant activity than seed and pulp and may therefore be a rich source of natural antioxidants [45,60]. Solvents usually used for the extraction of pomegranate antioxidant compounds are methanol, ethanol, acetone, and water. However, generally, these solvents yield a significant co-extraction of concomitant substances and decrease the yield of target antioxidants [74]. Among these solvents, ethyl acetate may exhibit significant selectivity, while methanol and water may result in higher total extract yield. For example in a study completed by Pan et al. [44], PP (1 g) extracted using a magnetic stirrer with a stirring speed of 1200 rpm at 25 °C and using 50 mL of water for 60 min. The performance yield of the extraction was 11.9%. In another study, extraction by the same method at 40 °C yielded 8.26% when methanol was used for solvent, compared to 5.90% yield when water used as a solvent. Other solvents such as ethanol, acetone, and ethane ethyl ester yielded 1.55%, 0.37%, and 0.18%, respectively [45]. In another research study, Qu et al. [60] showed that water was an efficient “green” solvent for the extraction of antioxidants from pomegranate marc achieving high phenolic content (229 mg TAE/g) and DPPH scavenging activity (6.2 g/g) in 2 min extraction time.

4.2. Extraction by Applying Pressure

Pressure Liquid Extraction (PLE) is an extraction method that uses liquid solvents at high temperature and pressure, which increase the extraction efficiency. The advantages of using solvents at temperatures above their atmospheric boiling point are the increased solubility and the improved mass transfer properties [75]. This technique is also known as “pressurized liquid extraction” and “pressurized solvent extraction”. In the case where water is used as an extraction solvent, the technique is referred to as “pressurized hot water extraction” (PHWE), “subcritical water extraction” or “superheated water” [76]. According to Mendiola et al. [77], extraction at high temperatures has an advantage as it contributes to an increase in mass transfer rate and extraction efficiency because higher temperatures imply: (i) increase of solvents solubility to dissolve substances, (ii) increase in diffusion rates, (iii) more efficient breakdown of solute-uterine bonds, (iv) reduction of solvent viscosity, and (v) reduction of surface tension [78,79]. High pressure is usually applied at ranges from 4 to 20 Mpa. This pressure ensures that the solvent is kept in a liquid state at the applied temperature. High pressure has also been reported as a force for the solvent’s penetration into the matrix pores [78]. Pressurized water extraction was investigated for the extraction of polyphenols from PP in the study of Cam and Hisil [63]. They concluded that the most critical factors that affect the extraction results were the particle size, the extraction temperature, and the static time. Based on their study results, hydrolyzable tannins are the predominant polyphenols of PP corresponding to 262.7 mg/g of tannic acid equivalents. Additionally, punicalagin content was found to be 116.6 mg/g on dry matter basis [63]. In another study, Ranjbar et al. [62] used an instant controlled pressure drop process (ICPD) as a texturing pre-treatment for the enhancement of the extraction efficiency of phenolic compounds from PP. Their results presented that ICPD increases the extraction of phenolics and extracts antioxidant activity from 38.77 to 46.02 mg GAE/g dry material and from 62.10 to 74.12%, respectively [62].

4.3. Ultrasound-Assisted Extraction (UAE)

The use of high-intensity ultrasounds for the food industry has been a very efficient tool for large-scale processes such as homogenization, emulsification, extraction, crystallization, dehydration, low-temperature pasteurization, depletion, enzyme deactivation and reduction of particle size [77]. The UAE method is used to improve the extraction performance of polysaccharides and oils from plant tissues, mainly through the phenomenon of “cavitation”. The effect of the ultrasound extraction method is that it accelerates more efficient compounds released from plant tissue due to cell wall destruction, enhancing mass transfer, and easier access of solvent to plant cell content [80,81]. In ultrasonic extraction, the sample is placed with a suitable organic solvent in the ultrasound device (Figure 3).

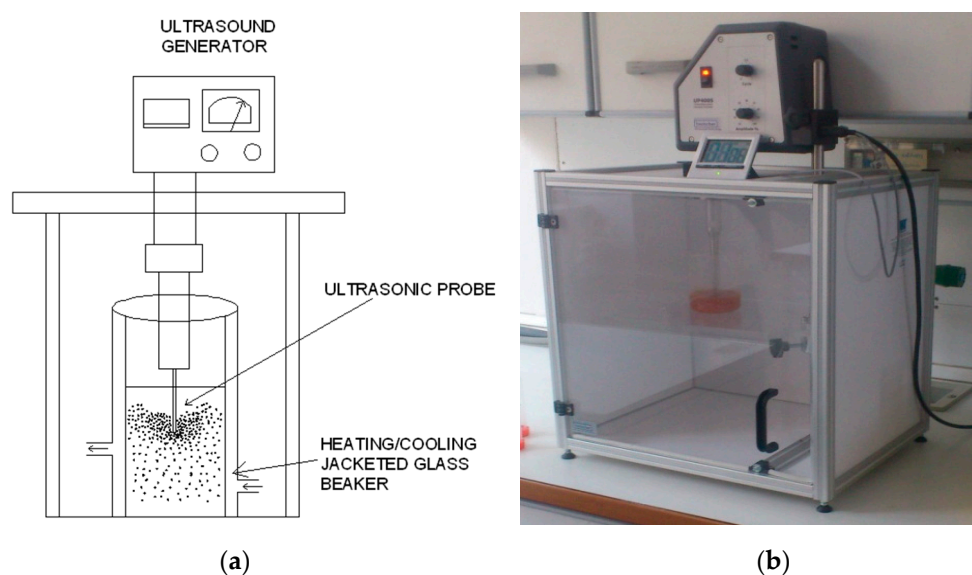


Figure 3. (a) Hardware of a typical ultrasound extractor and (b) ultrasound-assisted extraction.

Ultrasound propagation is characterized by a minimum frequency of 16 kHz and causes fluid to move due to compression and dilution. Regarding the use of ultrasound to extract phenolic from PP, Pan et al. [44] extracted phenolic components using a continuous (CUAE) and discontinuous pulsed ultrasound technique (PUAE). According to their findings, CUAE and PUAE raised the antioxidant yield by 24 percent and 22 percent, and lowered the extraction time by 90 and 87 percent, respectively, according to conventional extraction. Singh et al. [82] stated that the DPPH model system demonstrated 81 percent antioxidant activity at 50 ppm using a methanol extract of PP. However, in Kaderides et al. [66] study the received PP extracts from optimized MAE and UAE shown radical scavenging activity of 94.91 and 94.77%, respectively.

4.4. Microwave Assistant Extraction (MAE)

The application of microwaves (MW) is also used as a non-convenient extraction method. With microwaves, a significant reduction in extraction time is achieved compared to the classic methods (Soxhlet). Furthermore, MAE methods offer improved performance, low solvent consumption, and energy-saving combined with high automation [44,66,83–88]. Compared to Soxhlet extraction, this method contributes significantly to reduced volumes of samples and solvents. By conventional methods, heat is transferred from the heating plate to the heating tank and the solution. Unlike microwaves, heating starts with a sample since the container does not absorb microwave radiation (Figure 4). The MAE process is based on the formation of high-energy electromagnetic waves that can change the solvent’s molecular rotation and ionic mobility without altering the sample. These actions result from the friction produced by heat buildup and damage to the cellular structures leading to the rapid migration of all the active compounds from the solid-phase to the solvent-phase [89]. In other words, microwaves

produce energy absorbed by the molecules to be extracted and thus cause the solvent's polar molecules to rotate and ions to be transported, causing friction that destroys the plant tissues' cellular structures.



Figure 4. (a) Lab scale and (b) industrial scale of microwave-assisted extractors.

This phenomenon allows polyphenolic compounds to escape from the damaged plant cells to the solvent, facilitating extraction. An advantage of the microwave extraction method is the solvent absence [90].

4.5. Comparison of UAE, MAE and Conventional Extraction Methods

The cost-effective extraction of PP polyphenols using convenient extraction methods has been documented by several authors. In their research, Negi et al. [61] with the use of various solvents examined the antioxidant and antimutagenic potential of PP derived from the Ganesha variety using the Soxhlet process. They reported that they achieved, after a 4 h extraction, an improvement in extracted yield of 4.8% with the use of water as a “green” solvent. In addition, the extraction performance, expressed as the total phenolic content of extracts, exceeded 119 and 82.6 mg GAE/g dry matter under continuous stirring for 1 h and 4 h of extraction, respectively [45,91].

Latest reports have discussed the use of energy-efficient systems that are known to be UAE and MAE techniques. However, these methods are increasingly used as alternatives to conventional extraction methods in the production of natural resources. Pan et al. [44] recorded that aqueous UAE resulted in 14.8% and 14.5% polyphenol yields after 6 min and 8 min PP extractions, using constant and pulse UAE, respectively. Kaderides et al. [68] analyzed the UAE and MAE extraction of PP in a comparative way and concluded that MAE was a more effective method of extraction that produced 199.4 mg of GAE/g of dry PP after 4 min of extraction. Finally, Skenderidis et al. [52] presented a vacuum microwave-assisted aqueous extraction (VMAAE) in an industrial type extractor achieving a high TPC of 137.97 mg GAE/g, after a 10 min extraction.

4.6. Pulsed Electric Fields (PEF) and High Voltage Electrical Discharge (HVED) Assisted Extraction

The extraction with use of PEF is based on the membrane electroporation creation, which can lead to a substantial acceleration of mass transfer processes [92]. On the other side, as can be seen in Figure 5, HVED produced directly in water (electrohydraulic discharge) initiates both chemical reactions and physical processes. It directly transmits energy into a plasma channel created by a high-current/high voltage electrical discharge between two submerged electrodes into an aqueous solution [93]. Both techniques have been tested and demonstrated their ability to significantly increase the extraction yield of polyphenolic compounds from plant by-products [92–94].

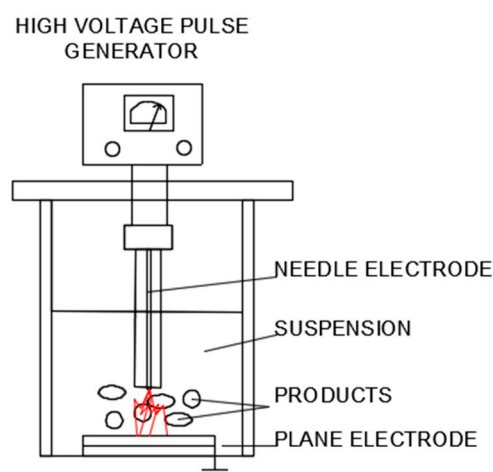


Figure 5. Draw of batch High Voltage Electrical Discharge (HVED) extraction device.

Recently, in the study of Rajha et al. [59] the efficacy of the PEF and HVED assisted extractions of polyphenols from PP have been examined. Results from this study indicated that HVED is more effective for polyphenols recovery by ≈ 3 and ≈ 1.3 times compared to UAE and PEF methods. Furthermore, they presented that the PEF method, selectively extracted and enhanced the recovery of ellagic acid ($\approx 740 \mu\text{g/g DM}$), whereas HVED ($\approx 345 \mu\text{g/g DM}$) intensified gallic acid extraction compared to UAE, IR, HVED and conventional extraction in a water bath.

4.7. Non Conventional Extraction Solvents Used on PP

The emerged green method of Supercritical fluid extraction (SFE) that uses supercritical carbon dioxide (SC-CO_2) is believed to be an alternative method for extraction and separation of high value natural products containing phytochemicals. The recovery of relatively pure and clean extracts, especially useful for functional foods and nutraceutical/pharmaceutical products lead to the superiority of this technique [95]. As far as plant phenolic extraction is concerned, these compounds are not fully soluble in SC-CO_2 because they are polar in nature. Thus, various enzyme formulations are tested and optimized for the maximum liberation of polyphenols. The extraction of polyphenols from the hydrolyzed plant material is subsequently accomplished by SC-CO_2 and a polar solvent [96]. Enzyme-Assisted Supercritical Fluid Extraction (EASCFE) of PP has been reported to double the recovery of crude extracts, increase extracts polyphenols concentration, and improve the ability of radical scavenging (RSC). In addition, the trolox equivalent antioxidant potential (TEAC) and the inhibition of linoleic acid peroxidation may be enhanced [69].

Deep Eutectic Solvents (DES) have also been presented as an alternative “green” extraction solvent. Because they are not only eco-friendly, non-toxic, and biodegradable organic compounds, but also have a low cost and are simple to manufacture in the laboratories. It was first reported two decades ago that a mixture of choline chloride and zinc chloride can be in liquid form below 100°C [97]. In the year of 2003, the same research team developed a combination of ChCl with a hydrogen-bond donor (urea) designating it as DES [98] and one year after they reported that formed a mixture of ChCl with different carboxylic acids (oxalic, malonic, and succinic acids) [99]. New DES that combine a carbohydrate (or a reduced derivative as is the case for sorbitol and mannitol), a urea derivative ($\text{N,N'$ -dimethylurea), and a chloride salt (ammonium chloride) are also a significant class that has been thoroughly examined [100]. The melting point of the DES is usually smaller than the melting points of any of its starting elements. The probability of getting, by merely modifying one or both components, a vast number of eutectic mixtures with different chemical properties is one of the enticing features of these novel solvents. The efficacy of Infrared (IR) assisted extraction of PP polyphenols using DES examined against solid-liquid (SL) and ultrasound (UAE). Results indicated that the highest concentration of

polyphenols (152 mg/g DM) was obtained with the IR combined with the deep eutectic solvent. The extraction with the use of the combinations of DES and IR technique gave the highest antioxidant and antiradical activities [70].

Recently, the extraction of bioactive substances from PP with the use of the PLE and DES methodologies was presented in a study. The results of this survey indicate that PLE achieves extracts with higher antioxidant activity based on the higher concentration of polyphenols in the extracts [49].

5. Conclusions

Wastes of the food industry are a constant threat to the environment and a severe operational issue for food industries. In this overview, the extraction technologies for the production of bioactive compounds from PP have been highlighted. The efficacy of the extraction is highly dependent on the solvents, the design equipment, and the extraction method developed. New non-convenient green extraction methodologies have been proved as a promising technique for the extraction of PP polyphenols, as presented in this study. Conventional PP extraction methods (such as simple stirring, decoction, and maceration) are characterized by low disruption ability of the cell walls and, consequently, low diffusion of the solvents used for the extraction of PP. Non-conventional extraction methods involving the use of ultrasound and electrically pulsed fields, as well as the use of microwaves, achieve larger scale cell wall rupture leading to increased extraction efficiency, while the simultaneous use of a vacuum enhances protection against thermal degradation and oxidation of sensitive bioactive components, such as polyphenols. The choice of the appropriate solvent is crucial for the performance of PPs extraction. Finding new, inexpensive, non-toxic solvents that are easy to recycle and have no effect on the environment is a field of research in which DES in combination with non-conventional extraction methods may lead to improved extraction performance. Nevertheless, despite the increased research studies focusing on a wide range of methods applied, further research studies are still needed in order to adapt the examined extraction methods of bioactive compounds derived from PP in industrial scale. Most of the reports, however, are focused on laboratory-scale reactors that may not be efficient for commercial-scale operation. Furthermore, no clarification was given as to the field parameters induced by the treatment of the extraction methodology in the mechanism and industrial data supporting the treatment methodology. Further research may be directed in terms of the development of novel green extraction techniques in industrial type extractors.

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