

Review

Orange Peel Waste as a Source of Bioactive Compounds and Valuable Products: Insights Based on Chemical Composition and Biorefining

Mariana Ortiz-Sanchez ^{*}, Carlos Ariel Cardona Alzate  and Juan Camilo Solarte-Toro 

Departamento de Ingeniería Química, Instituto de Biotecnología y Agroindustria, Universidad Nacional de Colombia Sede Manizales, Manizales 170003, Colombia; ccardonaal@unal.edu.co (C.A.C.A.); jcsolartet@unal.edu.co (J.C.S.-T.)

* Correspondence: mortizs@unal.edu.co

Abstract: Few valorization pathways have been implemented as alternatives to reduce the orange peel waste (OPW) disposal in landfills. OPW can be a source of income or economic savings in juice production factories since this waste is a potential source of value-added products (e.g., bioactive compounds) and energy vectors (e.g., biogas). Valorization alternatives should be based on (i) orange peel chemical composition, (ii) market analysis, and (iii) availability. Nevertheless, few literature papers have highlighted the chemical composition change caused by the different juice production schemes as a potential opportunity to obtain different value-added products and biorefinery schemes. Thus, the aims of this review paper are related to (i) reviewing different orange fruit processing pathways, (ii) analyzing several OPW chemical compositions reported in the open literature, (iii) providing a summary of OPW extraction pathways for bioactive compounds production, and (iv) evaluating the effect of applying different extraction methods on bioactive compound extraction performance. This review includes a description of the OPW matrix, market insights, packaging, physicochemical characterization, processing technologies, and suggested biorefinery approaches. Finally, different extraction methods for obtaining bioactive compounds from OPW are compared. As a result, the supercritical fluid extraction process has the highest extraction performance and selectivity since this method extracted a high amount of hesperidin (8.18 g/kg OPW db.). In conclusion, OPW is a source of bioactive compounds and valuable products that can be introduced in juice-producing factories to increase product portfolio or economic savings by changing the energy matrix.

Keywords: bioactive compounds; biorefineries; chemical composition analysis; extraction technologies; orange peel waste valorization; orange processing



Citation: Ortiz-Sanchez, M.; Cardona Alzate, C.A.; Solarte-Toro, J.C. Orange Peel Waste as a Source of Bioactive Compounds and Valuable Products: Insights Based on Chemical Composition and Biorefining. *Biomass* **2024**, *4*, 107–131. <https://doi.org/10.3390/biomass4010006>

Academic Editors: Vassilis Athanasiadis, Theodoros G. Chatzimitakos, Dimitris P. Makris and Lasse Rosendahl

Received: 23 June 2023

Revised: 26 October 2023

Accepted: 2 January 2024

Published: 2 February 2024



Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Orange is one of the most popular citrus crops in the world. This fruit has several healthy compounds such as vitamin C, folic acid, antioxidants, flavonoids, and catechins [1,2]. The orange crop has been considered a versatile crop because this fruit can be produced in different soils and climatic conditions [3]. Several countries between 30°–35° north and south of Ecuador can produce oranges. *Citrus sinensis* (L.) Osbeck is the most important species of sweet orange in the world. Seminara et al. [3] reported four orange classifications according to the orange color. Hence, sweet oranges can be classified as common, navel, blood, and acidless. Common oranges are the most produced and consumed worldwide. Indeed, the common orange group can be subdivided into different types, such as Salustiana, Valencia Midnight, Valencia Barberina, Ovale, Valencia Late, Valencia Delta, and Ruby Valencia. All of these cultivars are suitable for industrial processing because these varieties have a high juice yield and low content of bittering compounds. However, Valencia oranges are the most used fruits as raw material for juice, jams, and pulp production due to the adaptability of this variety to different climatic conditions. The most important

orange exporters in the world are Spain, Egypt, Greece, Morocco, Netherlands, Italy, The United States of America (USA), Argentina, Brazil, Chile, Uruguay, Honduras, Mexico, Colombia, China, and Zimbabwe. Meanwhile, the most important countries for orange processing are the USA, Mexico, Brazil, China, Spain, Argentina, Greece, and Italy [4].

All orange varieties have a similar morphology. Nevertheless, this fruit has a different chemical composition and physical characteristics depending on the variety, rootstock, soil, fertilization, irrigation, age, maturity, and position in the tree [5,6]. Oranges' diameter ranges from 4 to 12 cm [7]. The fruit size depends on the variety, growing conditions, and maturation. This fruit comprises eight different tissues and the seed [7]. In general, the weight of oranges is 87% water and 13% compounds such as minerals, essential oils, fats, proteins, fibers, organic acids (e.g., formic acid and citric acid), pectin, glucosides, and pentosans [8]. These compounds are distributed in the eight tissues of the orange. On the other hand, oranges are consumed as a fresh product and juice. The edible fraction of the fruit involves the segments and juice sacs (pulp or rag). The edible fraction is about 31–51% of total fruit weight. Instead, the non-edible fraction is the cuticle, oil glands, flavedo, core, segment membranes, and albedo. The non-edible fraction corresponds to 49–69% of total fruit weight [7]. Moreover, the non-edible fraction is called orange peel waste (OPW) [9]. Figure 1 shows an outline of the morphology of an orange.

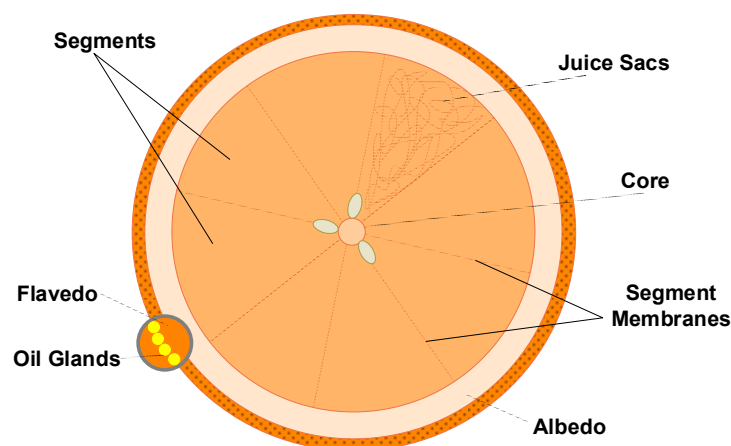


Figure 1. Orange fruit constituents.

Oranges have been used to produce several food products (e.g., juice) at the industrial level [10]. Thus, large amounts of OPW are produced worldwide without a specific treatment or valorization route (i.e., 24 million tons of OPW) [11]. Currently, OPW is disposed of in landfills producing large amounts of greenhouse gas emissions and leachates with a high chemical oxygen demand. Thus, innovative ways to use and valorize this waste have been studied to mitigate OPW environmental damage and promote the sustainability of the citrus value chain at regional, national, and worldwide levels. This statement is true since upgrading OPW to bio-based products reduces the environmental impact caused by the poor peel disposition and the replacement of oil-based products [12].

OPW has different chemical compositions depending on the juice extraction process (manual or industrial). Cellulose, hemicellulose, and pectin are the most important components. Several authors have reported different ways to upgrade and obtain different value-added products and extract bioactive compounds in stand-alone processes and biorefinery configurations [13–15]. Higher yields have been reported by applying different extraction methods such as solvent extraction, ultrasound-assisted extraction, microwave-assisted extraction, and supercritical fluids [16–19]. Nevertheless, few literature reports have analyzed the possible influence of the OPW chemical composition on obtaining high extraction yields. Moreover, few literature papers have highlighted the influence of the juice extraction method on the OPW chemical composition. On the other hand, a global summary related to the valorization possibilities of obtaining bioactive compounds, value-added

products, and energy vectors is required before proposing OPW upgrading pathways. For these reasons, the aims of this review paper are related to (i) reviewing different orange fruit processing pathways, (ii) analyzing several OPW chemical compositions reported in the open literature, (iii) providing a summary of OPW extraction pathways for bioactive compounds production, and (iv) evaluating the effect of applying different extraction methods on the bioactive compounds extraction performance. In addition, this review includes a description of the OPW matrix, market insights, packaging, physicochemical characterization, processing technologies, and suggested biorefinery approaches.

2. Orange Fruit Processing and OPW Origin

Oranges are commercialized as fresh fruit or juice [20]. Traditional orange marketing does not comply with technical standards in most producing areas [21]. Direct orange commercialization has a high participation of intermediaries in the orange value chain. Thus, the price per unit of orange increases until the final consumer. Traditional marketing has been denominated as primary processing, since oranges do not have a direct transformation [21]. On the other hand, juice production is the industrial commercialization way (so-called secondary processing) [22]. In this case, the industry directly purchases oranges from the producers (e.g., farmers or first-level organizations), decreasing the price per unit of the fruit. This orange commercialization pathway evidences more incomes for farmers since the traditional pathway dilutes the intermediaries' incomes. Moreover, juice production creates a specialized market with a greater demand for quality and size. Two modes are presented under this type of distribution [23]. The first mode is purchasing the fruit from the producer (industry only). The second mode is when the fruit producer also performs the processing (industrial orchard) [23]. The objective of the second mode is to maximize the crop proportion marketed as fresh fruit, processing only the fruit that cannot be sold due to external quality, fruit size, trade barriers, or excess production. In primary or secondary processing, fruit selection is needed. Then, the packing operations are an essential link in the citrus production, processing, and commercialization [24]. The stacked fruit for storage and transport is distributed according to weight. A standard packaged box corresponds to 90 lb (approximately 41 kg) [20]. Figure 2 presents the simplified flowchart of orange processing.

The orange processing industry generates different types of products and by-products. The most known orange-based products are juice, jellies, marmalades, and essential oils [25,26]. Since 1980, about 30% of the oranges grown worldwide have been processed [27]. Orange juice is considered the most significant product. After packing house operations (industrial orchard) or harvesting for industry, oranges are conveyed to the processing plant. In countries like the USA, Brazil, and China, the packing house operations are not considered because the processing plant is near the crop [24]. In contrast, countries such as Argentina and Colombia must include the packing and transport stages [10]. The next step is to deliver the oranges to the processing facility. Then, the fruits are washed (with 200 ppm of chlorine) and revised to identify low-quality fruits [21]. The juice extraction process is carried out after washing. This step is the "heart" of the juice production process. Orange juice is obtained by mechanical extraction. Juice extraction seeks to obtain as much juice as possible from the fruit, avoiding albedo and oil in the juice. These impurities can cause bitterness in the juice flavor and decrease product quality [22,28]. Thus, orange juice extraction is the key to defining product quality. Different equipment has been designed for producing orange juice, since the efficiency of the process means more income [28]. Essential oil extraction is mandatory, no matter the orange juice equipment. Nevertheless, some industries do not consider this step, adding fractions of essential oil to their products. Figure 3 shows the commercial schemes for extracting the juice and essential oil from oranges.

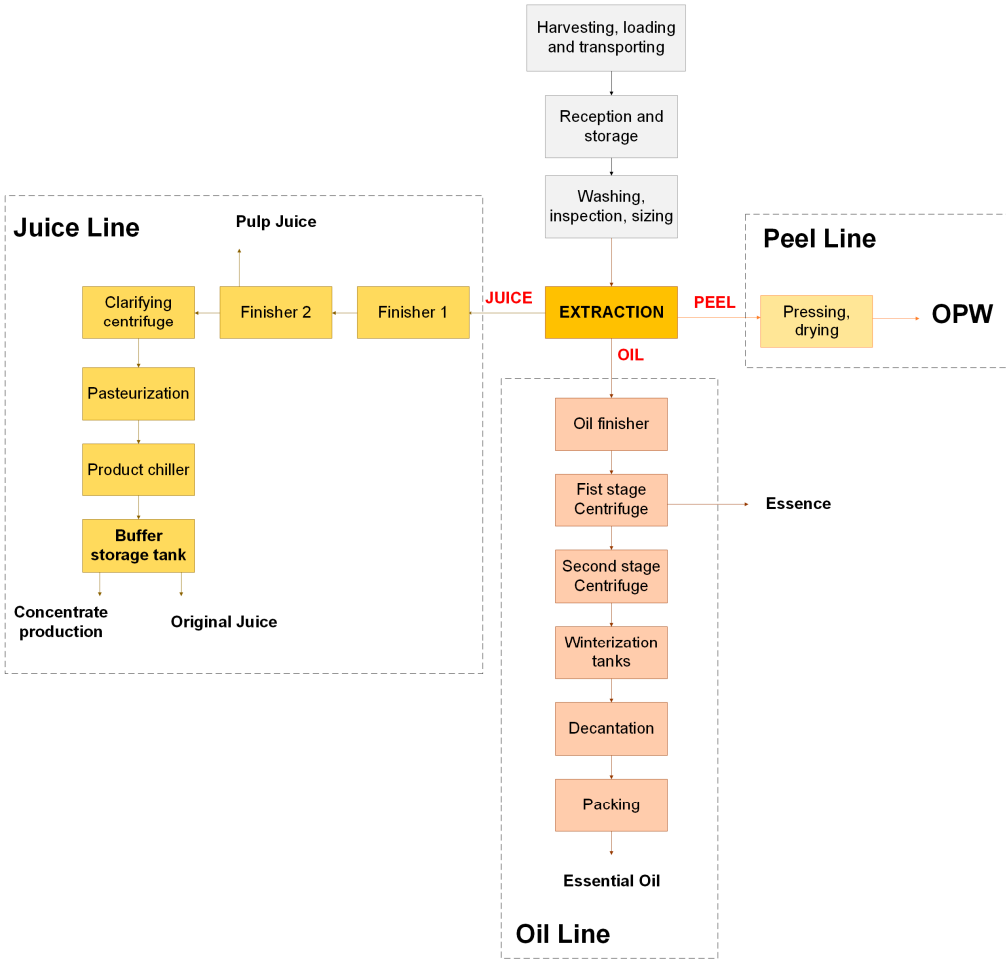


Figure 2. Simplified flowchart of orange processing.

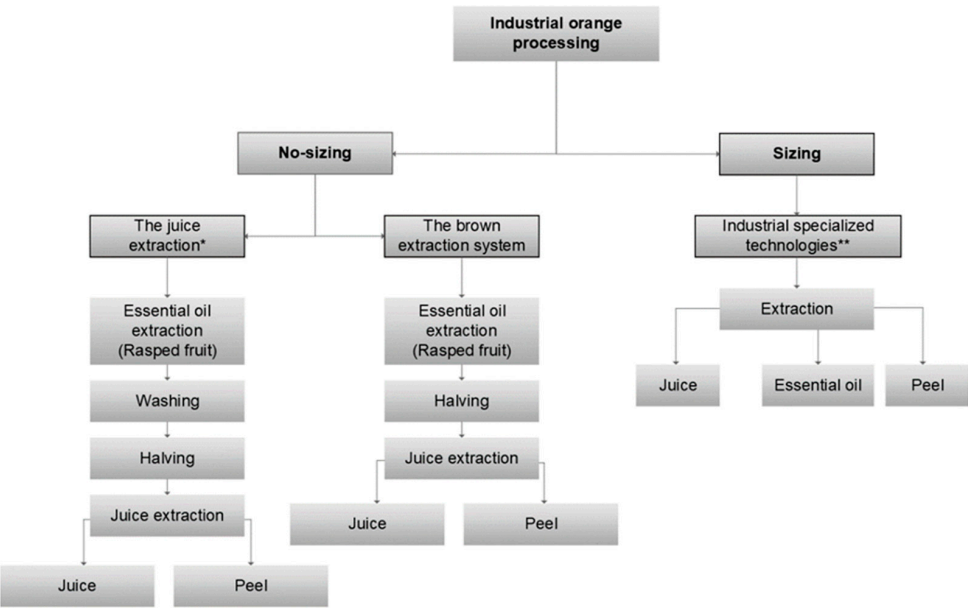


Figure 3. Commercial orange juice and essential oil extraction systems. * For example, the Fratellini Indelicato technology. ** For example, well-known in industry, the JBT (John Bean Technologies) FoodTech FMC (Food Machinery Corporation) system.

Orange juice extractors can be classified into different types. The rotative press extractor, the squeezer, and the reamer type are the most used extractors in orange processing plants [22,28]. Table 1 shows the advantages and disadvantages of these types of extraction equipment. Different outlet streams are obtained according to the extractor model. Each stream is upgraded (valorized or treated) in a specific processing line in the orange agro-industry (see Figure 3). These extractor models with oil removal produce a diluted oil stream. This stream must be sent to an equipment series to concentrate the oil [29].

Table 1. Extraction equipment: advantages and disadvantages [22,28].

| Feature | Rotative Press Extractor | Squeezer-Type Extractor | Reamer-Type Extractor |
|----------------|--|--|--|
| Outlet streams | Juice and peel. | Juice, oil emulsion, core (rag, seeds, and pulp), and peel. | Juice (pulp, seeds, and rag) and peel. |
| Advantages | The extractor has less investment and has greater capacity per unit. | The extractor provides excellent juice, oil, and peel separation. | The extractor gives higher quality pulp (longer and larger cell fragments). |
| Disadvantages | The extractor has the lowest yield and juice quality. | The extractor damages the peel and generates a diluted oil emulsion. | The extractor requires two separation steps to extract juice and oil from the fruit. |
| Capacity | 1500 L/h | 2500 L/h | 2500 L/h |

Three pathways for industrial orange processing have been elucidated based on the juice extraction model. The three industrial orange processing pathways involve some or all of the outlet streams presented in Figure 3. The first orange processing pathway has the lowest complexity at the industrial level (see Figure 4). The first processing pathway aims to produce only orange juice, leaving aside the possible upgrading of other compounds present in the fruit. The resulting juice in this process has essential oil traces, decreasing the juice quality. This processing line has been implemented in small-scale facilities, producing large amounts of OPW with a high concentration of essential oil, fiber, protein, and pectin [23].

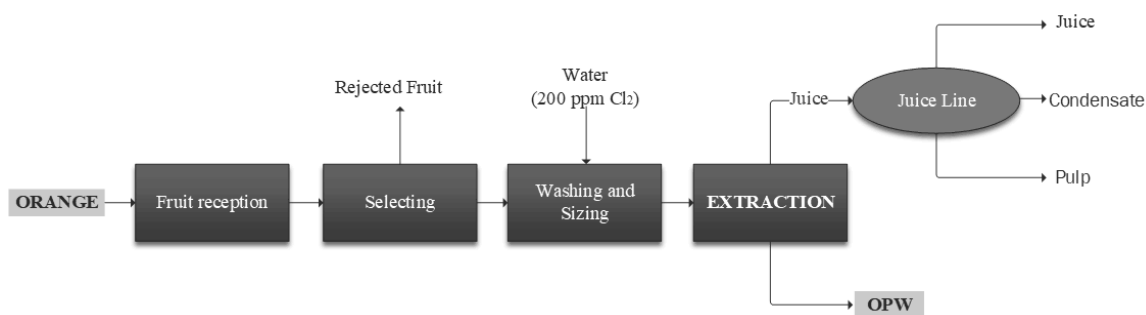


Figure 4. First pathway for industrial orange processing: low complexity—only orange juice production.

The second orange processing pathway involves an additional processing line compared to the first pathway. Thus, this pathway has a medium complexity level since orange juice and essential oil are produced simultaneously. The juice quality is better than in the case of the first pathway since essential oil traces are not present in the juice. The OPW produced in this process has a lower content of essential oil. Thus, lower yields will be obtained if some experiments are carried out. Nevertheless, this OPW can have a higher biogas production potential since limonene (the most important compound in essential oil) has been considered an inhibitor in this process. Figure 5 presents the block diagram of the second orange processing pathway [23].

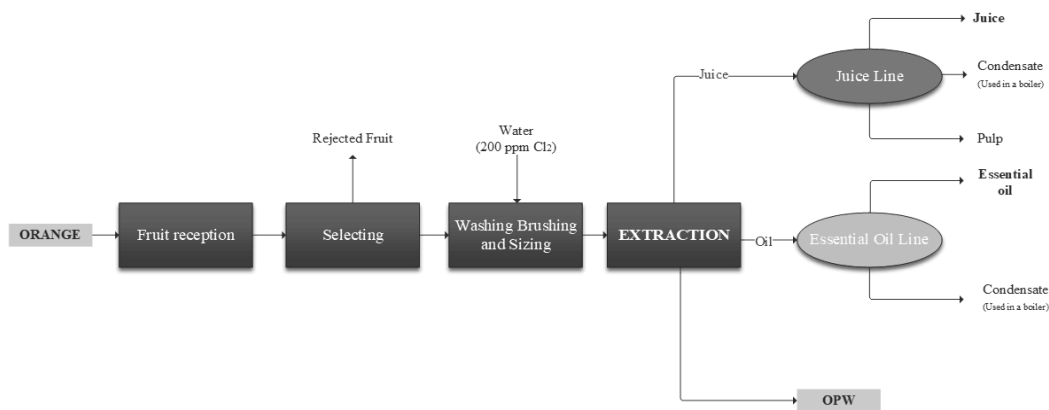


Figure 5. Second pathway for industrial orange processing: medium complexity—orange juice and essential oil production.

The third orange processing method involves three lines (i.e., orange juice, essential oil, and peel juice). This process configuration has been defined as the most sustainable orange processing configuration since oranges are used as much as possible. Nevertheless, this process configuration is common in large-scale processes since the capital and operational expenditures are the highest of the processing lines mentioned above. Figure 6 presents the block diagram of this industrial process [23].

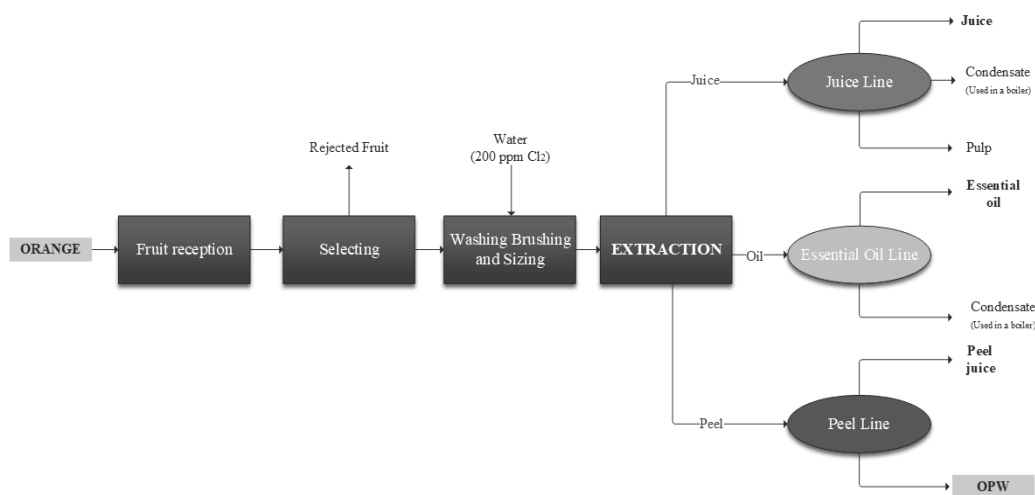


Figure 6. Third pathway for industrial orange processing: high complexity—orange juice, essential oil, and peel juice production.

The orange juice production line includes filtration, clarification, cooling, and juice concentration [30]. Orange juice comes out with 20–25% pulp. The first stage of the juice line consists of removing about 50% of the pulp. For this, the juice is pumped through a finisher, where solid particles are separated from the juice. On the other hand, the juice is clarified for finishing by removing seed fragments, filaments of the core material, and other undesirable high-density materials. Then, the juice must be pasteurized and cooled to 4 °C to minimize possible microbial activity. The juice can be labeled as original or concentrated. The original juice is fresh and has not been concentrated. The original juice is more popular than concentrated juice due to its image as a healthy and good flavor product [30]. The concentrated juice is diluted with water until reaching the required Brix degrees (°Bx) to be sold. Original juice is often more expensive than concentrated. After extraction, the juice is pasteurized. Finally, the final product is stored in refrigeration tanks [23].

The juice concentration stage is the most energy-demanding process in the orange processing system. Nevertheless, other alternatives for this process have been researched,

since the concentration stage decreases the antioxidant activity of the final product (i.e., degradation of ascorbic acid, anthocyanins, hydroxycinnamic acid, and flavonoids) [31,32]. For instance, juice concentration using membranes has been reported with relevant results [33]. Ultrafiltration has been used as a promising technology for removing impurities and concentrating the juice. This technology reduces the degradation of antioxidant compounds in juice by about 58% compared to thermal concentration [28]. Cryoconcentration is another alternative for the concentration of orange juice. This technique consists of juice cooling until reaching solid–liquid equilibria [28]. This step produces high-purity ice crystals. Then, water removal is carried out with the removal of the crystals [34]. Based on this concentration technique, the loss of aroma due to volatility or steam snatching is almost invisible. Despite the benefits in terms of quality, this technique has high investment costs, high energy consumption, and reaches a lower concentration (50 °Brix) [35].

On the other hand, the essential oil line comprises the separation and purification of the oil resulting from the extraction process (see, Figure 2) [36]. The resulting emulsion contains fruit substances—including peel, pulp particles, soluble pectin, and sugars. The essential oil extraction process comprises four steps (i.e., finishing, centrifugation, polishing, and traces removal). The first step is to pass the emulsion through a finisher unit to remove large shell pieces. The filtered emulsion contains approximately 0.5 to 2% of oil. The second step is to centrifuge the emulsion to concentrate the oil to 70 or 90% by weight. In this step, a three-phase centrifuge is used to obtain three streams (concentrated oil emulsion is the light phase, the heavy phase is the particulate matter, and the medium phase is water). The third step corresponds to polishing the oil in a second centrifuge. In this step, the oil is concentrated to more than 99% by weight. Finally, the oil goes through a winterization process. This process involves removing traces of wax dissolved in the oil. At temperatures of 1 °C or less, the waxes precipitate and sediment [37]. This step usually takes 30 days. Subsequently, the oil is decanted and packaged.

Finally, the orange peel processing line is upgraded to utilize the highest amount of the fruit. Then, most waste produced after orange processing is generated in this line. The most representative residue is known as OPW [38]. OPW is composed of the membrane residues resulting from juice extraction, seeds, and peel [39]. Different ways to upgrade OPW at the industrial level have been reported [40–42]. Some of the alternatives to take advantage of the side streams obtained are described.

Juice line waste: The pulp is the main waste obtained in this line. This residue is traded as “cells.” Usually, this subproduct is used in juice drinks to provide a natural appearance to the product [22].

Peel line waste: OPW is the most important waste produced in orange processing. Indeed, this residue is a problem in the citrus industry since the chemical composition is complex compared to other agro-industrial residues such as peels and seeds. The most important factor related to OPW complexity is the high moisture content (i.e., 80%), which encourages rotting and fungi issues in the plant (i.e., OPW is considered a source of cross-contamination). Therefore, OPW management is key in orange processing facilities beyond finding new valorization alternatives. One common way for OPW disposal is to sell this waste without further treatment to nearby farmers for directly feeding ruminants or silage [43,44]. However, stabilizing the peels by drying them is often necessary because there will not always be a constant demand for fresh pulp feed near the processing plant. Another alternative is to extract the pectin present in OPW. This allows us to obtain juice rich in gelling compounds with potential applications in the food and pharmaceutical industry.

Oil line waste: This waste can be used to produce essences, which correspond to the volatile components recovered during the oil concentration process (see, Figure 2). This by-product can be obtained from the first centrifugation stage (aqueous phase). Water-soluble components such as essence aroma can be added to the concentrated product or juice [37].

The abovementioned orange juice production pathways are applied by different companies worldwide. Information to match a company with the current orange juice production line is difficult since primary data are required. Nevertheless, the most impor-

tant players related to the orange juice market are Astral Foods, Bar-S Foods, Campofrio Food Group, Cargill, and The Kraft Heinz Company, among others. These multinational companies are the leading orange juice producers today [20].

3. OPW Characterization and Potential Upgrading Routes

Several residues after orange fruit processing are produced. OPW is the most representative fraction [11]. This section presents an overview of the OPW chemical composition reported in the open literature. Chemical characterization refers to different compounds present in the matrix of the residue. The most important OPW components are pectin, cellulose, hemicellulose, lignin, protein, and fats. Nevertheless, components such as soluble sugars, terpenes, and phenolic compounds can be found [45]. Several ways for reporting the OPW composition have been published. For instance, Sanchez-Orozco [46] reported OPW characterization in terms of cellulose, hemicellulose, protein, and lignin, giving values of 11.93%, 14.46%, 5.97%, and 2.17% on a dry basis. Alvarez et al. [47] reported the cellulose, hemicellulose, pectin, and lignin mass fractions of OPW as 17.1%, 16.6%, 35.3%, and 28.7%, respectively. In the same way, different OPW chemical composition reports can be found in the open literature. Table 2 summarizes the OPW chemical compositions reported in the literature.

Table 2. OPW chemical characterization reported in the open literature (% wt., dry basis).

| Item | Sanchez-Orozco [46] | Álvarez et al. [47] | Mohsin et al. [48] | Ahmed et al. [49] | Rivas-Cantú et al. [37] ** | Ortiz-Sanchez et al. [41] |
|-----------------------|---------------------|---------------------|--------------------|-------------------|----------------------------|---------------------------|
| Cellulose | 11.93 | 17.10 | 34.53 | 17.52 | 33.98 | 30.17 |
| Hemicellulose | 14.46 | 16.60 | 11.38 | N.R. | 9.99 | 9.35 |
| Lignin | 2.17 | 28.70 * | 7.20 | 14.38 | 6.93 | 5.07 |
| Pectin | N.R. | 35.30 | 15.28 | 15.72 | 20.90 | 11.18 |
| Protein | 5.97 | N.R. | 7.80 | N.R. | 9.00 | 4.83 |
| Fat | N.R. | N.R. | 3.63 | 4.15 | 3.85 | 5.18 |
| Ash | N.R. | 2.30 | 2.81 | 16.59 | 2.46 | 3.61 |
| Total sugars | N.R. | N.R. | N.R. | 31.62 | 9.00 | N.R. |
| Flavonoids | N.R. | N.R. | N.R. | N.R. | 4.00 | N.R. |
| Total extractives *** | N.R. | N.R. | N.R. | N.R. | N.R. | 30.55 |

N.R. No reported value; * lignin + sugars + proteins. ** Values given as a review of the chemical characterizations given by other authors. *** Extractives in water and ethanol.

OPW chemical composition differs regarding the constituents and values (see Table 2). The chemical composition varies depending on factors such as orange variety, size, weather, soil properties, agrochemicals used, and ripening time. For instance, Citrus × Tangelo has higher juice yields than the Valencia variety. Thus, Citrus × Tangelo has a lower peel/pulp ratio. These aspects are related to the morphology of the fruit. On the other hand, the chemical characterization of OPW chemical composition varies depending on the agrochemicals used in the agronomic stage. This statement has been corroborated in other agronomic products such as cocoa, since the use of agrochemicals can increase the presence of heavy metals such as cadmium and lead. Finally, the lignocellulosic content can be increased based on the water supply to the orange plant. Indeed, low water levels produce oranges with a higher peel/pulp ratio [50].

Cellulose, hemicellulose, lignin, ash, protein, fat, sugars, flavonoids, and pectin are the most common fractions reported in the open literature. The chemical composition analysis is stated based on the aim of the study [51]. For instance, only pectin is characterized if the research objective is to valorize this fraction [52]. Proposals for the stand-alone valorization of OPW can use a partial chemical characterization. Nevertheless, a complete

chemical characterization is required for proposing OPW valorization processes based on the biorefinery concept since these facilities allow for the upgrading of almost a fraction of the raw material into a series of value-added products and energy vectors [53]. A complete chemical characterization refers to determining the mass fractions of different components as much as possible (e.g., bioactive compounds, essential oil, fats, pectin, cellulose, hemicellulose, lignin, proteins, ashes, minerals, fixed carbon, volatile matter, and moisture content). Chemical characterization allows us to elucidate the potential upgrading pathways and biorefinery schemes for the integral OPW processing. Indeed, the biorefinery concept has been applied to upgrade OPW at different levels [54,55].

OPW valorization has been guided toward several important high value-added compounds such as food-grade additives, D-limonene, dietary fibers, flavonoids, anthocyanins, carotenoids, and citric acid. Several OPW upgrading routes have been proposed based on the chemical composition. The OPW upgrading pathways are related to physical, thermochemical, biotechnological, and chemical processes. Physical upgrading has been applied to obtain essential oil, polyphenolic compounds, and terpenes by steam distillation and solvent extraction, respectively [56,57]. Thermochemical processing has been reported for producing energy vectors (e.g., biochar, ethanol, pellets, and butanol) and bioenergy [58–60]. Biotechnological upgrading refers to using microorganisms and enzymes to produce value-added products such as organic acids, alcohols, biogas, and ethers. The most common biotechnological pathways for upgrading OPW are related to the production of lactic acid [61], biogas [62], ethanol [14], mucic acid (i.e., galactaric acid) [40], docosahexaenoic acid [63], and sugars [52]. Finally, chemical routes have been applied to produce sulfonated carbon catalysts and polyurethane foams [64,65].

OPW valorization can also be classified depending on the technological readiness level (TRL) of the upgrading process. Indeed, the TRL of the production process is a key factor in elucidating those products with a high potential to be implemented at the industrial level. Applications with low TRL (i.e., 1–5) are addressed to obtain high value-added compounds through biotechnological and chemical pathways [48], for instance, fermentation products after pectin and cellulose hydrolysis. This statement is true when analyzing the research data related to the OPW conversion.

In contrast, high TRL (i.e., 6–9) applications are addressed to obtain products derived from thermochemical and physical processes such as combustion, torrefaction, pelletizing, and milling [66]. These mature upgrading processes are guided to produce pellets, animal feed, compost, and bioenergy [66–68]. These products can be produced at different scales, promoting rural bioeconomy trends or market alternatives at regional and national levels. In contrast, the scientific perspective requires more effort to scale up novel technologies and processes. Nevertheless, the high market value and bio-based plus can boost new market trends to replace oil-based products. Therefore, more efforts are necessary to decrease the gap between academics and the industry toward boosting a bioeconomy model based on the valorization of this agro-industrial waste to increase the product portfolio of the orange industry. Several alternatives for valorizing OPW are presented in Figure 7.

Different biorefinery schemes addressed to upgrade OPW are presented in Figure 8. OPW-based biorefineries have involved valorization technologies such as anaerobic digestion, simultaneous saccharification and fermentation, pyrolysis, combustion, pyrolysis, and pelletizing, among others. Several authors have proposed and studied different biorefinery configurations [67–69]. The integral OPW upgrading is a potential option to produce different value-added products. Nevertheless, technical, economic, environmental, and social assessments are necessary to define feasible biorefinery schemes for industrial analysis. The link between academics and the industry is the analysis of the abovementioned factors, since these analyses elucidate potential options and investment requirements.

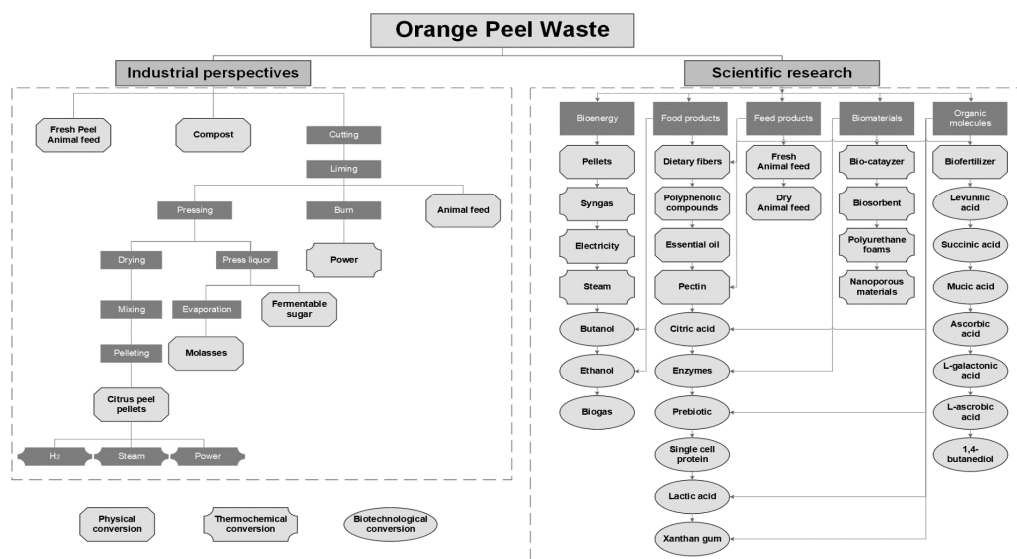


Figure 7. OPW-based products considering different perspectives: (i) academic research and (ii) industrial upgrading.

4. OPW as a Source of Bioactive Compounds

OPW has been considered a raw material for producing several products. Nevertheless, bioactive compound extraction has been one of the most studied areas [15,70]. OPW has been recognized as a potential source of antioxidants, phenolic compounds, and nutraceutical products [57]. Therefore, several extraction methods have been reported. This review paper focuses on the extraction of bioactive compounds using different technologies such as agitated solvent extraction, microwave-assisted extraction, ultrasound-assisted extraction, and supercritical fluid extraction [9,71]. Polyphenolic compounds are bioactive substances found in different plants, fruits, and vegetables. These compounds present antioxidant properties, sensory characteristics, and nutritional benefits. For these reasons, polyphenolic compounds are widely produced at the industrial level. These compounds can be applied in different sectors. For instance, polyphenolic compounds are used in cosmetics and paints, as coloring and flavoring in the food industry, as ingredients in nutraceuticals, as dietary supplements, as additives to antibiotics, and in anti-inflammatory and antiallergic medicines in the pharmaceutical industry. The polyphenolic compound market will increase in the next few years, which will increase the interest of different industries to produce them [72].

OPW is a source of polyphenolic compounds. Gallic acid, ferulic acid, and para-coumaric acid are the most important compounds present. These compounds can be extracted through different ways. Supercritical fluid extraction, conventional solvent extraction, microwave-assisted extraction, and the utilization of deep eutectic solvents are some of the ways reported in the open literature [73]. The methods, conditions, and typical yields are summarized in Table 3.

Table 3. Total polyphenolic compound (TPC) yields using different methods.

| Extraction Method | Conditions | Yield * | Ref. |
|--|---|----------------------|------|
| Agitated solvent | Ethanol: 80%; temperature: 35 °C | 15.80 mgGAE/g RM | [57] |
| Microwave-assisted | Power: 125 W; temperature: 35 °C | 23.40 mgGAE/g RM | [57] |
| Supercritical fluid | Temperature: 40–60 °C; pressure: 15–35 MPa | 18–21 mgGAE/g RM | [78] |
| Deep eutectic solvents | Choline chloride + glycerol or ethylene glycol, time: 100 min, and temperature: 30 °C | 1.28–2.91 mgGAE/g RM | [57] |
| Ultrasound-assisted + Pulse Electric field | Ethanol: 50%, time: 30 min, and temperature: 35 °C | 34.71 mgGAE/g RM | [16] |

* RM: raw material dry weight.

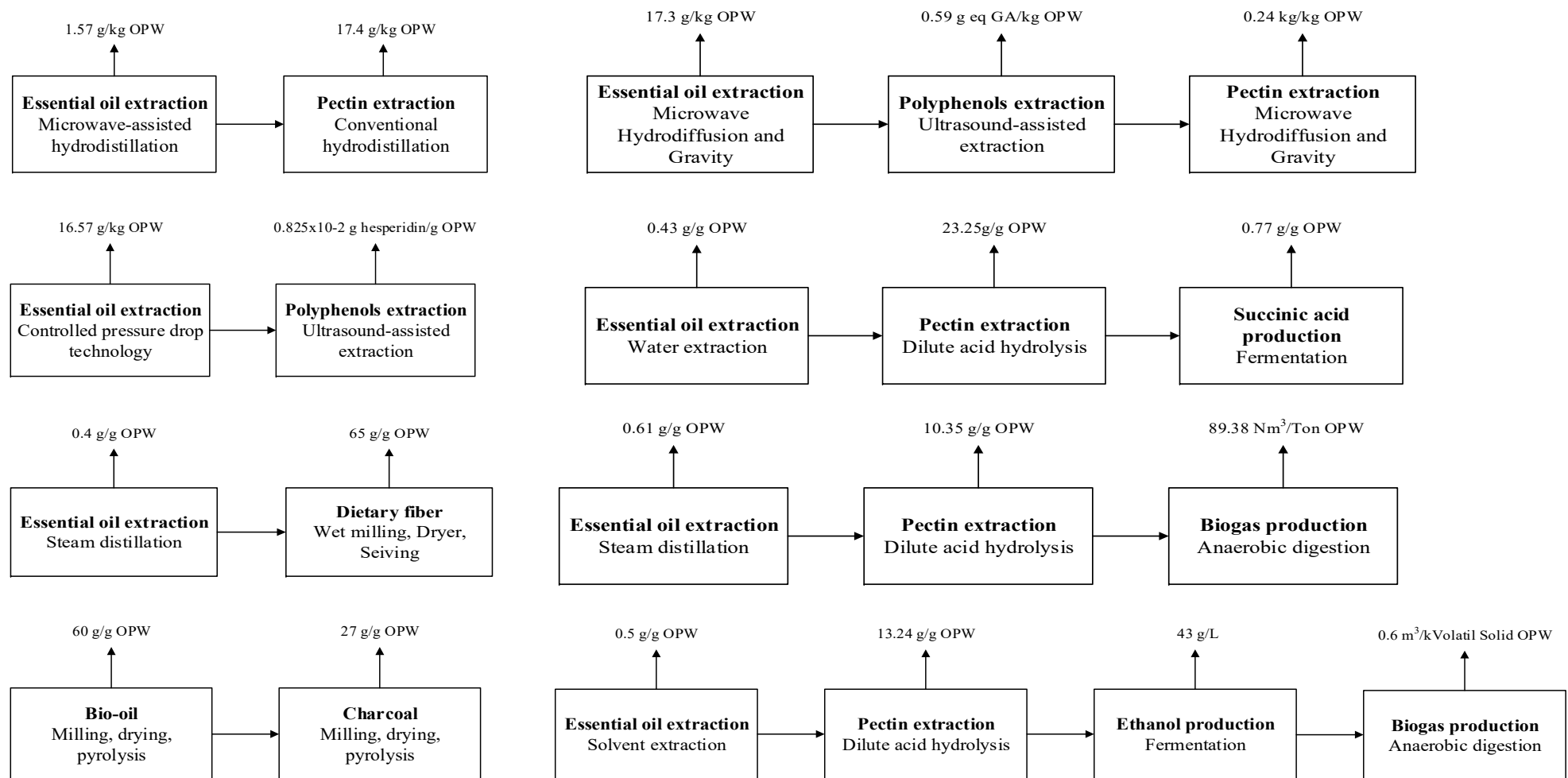


Figure 8. Experimental biorefineries for OPW valorization. The biorefineries have been proposed by several authors [41,55,67,68,74–77].

Solvents used for polyphenolic compound extraction are a key point for defining the final extract application. Indeed, solvents such as ethanol, acetic acid, water, or mixtures of both have been reported in the open literature as promising solvents, since these have been generally recognized as safe (GRAS) for use in the cosmetic and food industries [79]. New methods for extracting bioactive compounds have been reported in the open literature (e.g., deep eutectic solvents and pulse electric field). These novel extraction methodologies are addressed to improve extraction under lower conditions of temperature and solvent concentration. Nevertheless, these research efforts must be contextualized in a real process since the technological readiness level (TRL) of the new extraction methods is lower than seven (i.e., system prototype demonstration in a space environment). In addition, the economic and environmental performance of these extraction methods has not been reported widely in the open literature. Thus, this research area has been identified as a promising field for new developments.

OPW is considered an essential oil source. Essential oil is a terpenes combination produced by plants as secondary metabolites. Thus, these components are not needed for plant growth. The most important terpene produced in oranges is D-limonene. This compound can be found in higher quantities (i.e., concentrations higher than 90% %wt.) in OPW essential oil. Nevertheless, compounds such as camphene, α -pinene, and β -pinene can be extracted. Several methods for extracting essential oil have been researched. These methods are related to the dilation of the cell wall and the disruption of the OPW ligno-cellulosic matrix. The essential oil extraction methods are cold press, solvent extraction, steam distillation, supercritical fluids, and microwave-assisted extraction. The methods, conditions, and typical yields of essential oil extraction are summarized in Table 4.

Table 4. Common OPW essential oil extraction yields after using different methods.

| Extraction Method | Conditions | Yield | Ref. |
|---------------------------------------|--|------------|------|
| Soxhlet extraction | Solvent: hexane, temperature: 80 °C–100 °C, and time: 120–240 min. | 0.57–3.24% | [80] |
| Supercritical fluid extraction | Temperature: 40 °C, pressure: 20 MPa, and CO ₂ ratio: 5–75 kg/kg peel | 4–12% | [9] |
| Steam explosion | Pressure: 10 bar; time: 240 s | 1.34% | [81] |
| Hydrodistillation | N.R. | 1.2% | [82] |
| Steam distillation | Time: 45 min | 1.09% | [82] |
| Microwave-assisted steam distillation | Time: 35 min; power: 150 W. | 1.150% | [82] |

Finally, OPW can supply healthy properties to dietary supplements through phytochemicals such as vitamin C, folic acid, potassium, pectin, polyphenols, minerals, dietary fibers, essential oils, and carotenoids which present better antioxidant, disease-preventive properties than other parts of the fruit. In this sense, several health uses of orange peel can be cited: citrus flavonoids can replicate hepatic lipid metabolism, cure scurvy, and degenerative diseases [83,84]. The food and functional products industry has shifted its efforts to bio-based ingredients that can contribute to human health more than synthetic ingredients to establish a circular bioeconomy. OPW versatility encourages us to research the production of food products. Table 5 presents some studies conducted for OPW to obtain food products.

Table 5. Food products based on bioactive compound extraction from OPW.

| Product | Features and Uses | Technology and Complexity | Product Yield |
|------------------------|--|--|---|
| Polyphenolic compounds | These compounds present antioxidant properties, sensory characteristics, and nutritional benefits. In fact, these compounds can be applied in different sectors. For instance, polyphenolic compounds are used in cosmetics and paints, as coloring and flavoring in the food industry, as ingredients in nutraceuticals, as dietary supplements, as additives to antibiotics, and in anti-inflammatory and antiallergic medicines in the pharmaceutical industry [8]. The polyphenolic compound market will increase in the next few years, which will increase the interest of different industries to produce them. Modern studies show the use of OPW in various pharmaceutical/nutraceutical products [67]. | OPW is a source of polyphenolic compounds [68]. Indeed, hesperidin, narangin, gallic acid, ferulic acid, and para-coumaric acid are the most important compounds present in OPW [69]. These ones can be extracted through different methods. Supercritical fluid extraction, conventional solvent extraction, microwave-assisted extraction, and the utilization of deep eutectic solvents are some of the ways reported in the open literature to obtain polyphenolic compounds from orange peel [12]. | Solvent extraction [80]: Ethanol 80% <i>v/v</i> , 35 °C, 60 min, and 15.80 mgGAE/g. Microwave-assisted extraction [80]: 125 W, 35 °C, and 23.40 mgGAE/g. Supercritical fluid extraction [78]: 40–60 °C, 15–35 MPa, and 18–21 mgGAE/g. Deep eutectics solvents [57]: Choline chloride + glycerol or ethylene glycol, 100 min, 30 °C, and 1.28–2.91 mgGAE/g. |
| Essential oil | Essential oil is a combination of terpenes produced by plants as secondary metabolites. Thus, these components are not essential for plant growth. The most important terpene produced in the orange fruit is limonene. This compound can be found in higher quantities (i.e., concentrations higher than 90%) in the orange peel essential oil. Nevertheless, other compounds such as camphene, α -pinene, and β -pinene can be found. | These methods are related to the dilation of the cell wall as well as the disruption of the lignocellulosic matrix of the OPW. The physical methods used to remove essential oil are distillation (steam, steam/water, and water) and cold pressing, since cold pressing is the conventional method for the. However, essential oils have some disadvantages (the elevated temperatures and large time of the extraction). These shortcomings have boosted the use of new technologies such as supercritical fluid extraction, ultrasound extraction, subcritical water extraction, and microwave-assisted extraction. | Steam distillation [82]: 45 min and 1.095% <i>w/w</i> . Hydrodistillation [81]: 45 min and 1.2% <i>w/w</i> . Steam explosion [81]: 10 bar, 240 seg, and 1.34% <i>w/w</i> . Supercritical fluid extraction [9]: 40 °C, 20 MPa, CO ₂ ratio 5–75 kg/kg peel, and 1.34% <i>w/w</i> . Microwave-assisted steam distillation [82] 35 min, 150 W, and 1.150% <i>w/w</i> . |

5. Case Study: Bioactive Compound Extraction from OPW Using Different Methods

5.1. Raw Material Source and Conditioning

OPW from an orange juice factory (FLP Procesados) located in Colombia was used as the raw material for assessing the extraction performance of different methods. The orange juice company has a constant supply of 200 tons/month. The orange fruits are harvested from nearby fields (4°59'43.4" N 75°36'07.2" W). OPW is obtained by the industrial mechanical extraction of the fruit juice. The OPW samples were frozen at −4 °C for preservation after the extraction process. Then, the samples were dried in a convective oven at 40 °C until reaching a moisture content lower than 15%.

OPW samples were milled to a particle size of 0.4 mm (i.e., ASTM 40 Mesh). This was carried out in a knives mill (Gyratory mill SR200 Gusseisen, Retsch GmbH, Haan, Germany). The decrease in particle size guarantees the homogeneity of the sample and increases the transfer area in the extraction of polyphenolic compounds.

5.2. Extraction Methods

OPW has been used as a raw material for extracting bioactive compounds using several technologies such as agitated solvent extraction, ultrasound-assisted extraction, and Soxhlet extraction. All of the assays were conducted using 4 g of OPW. The solid to liquid ratio was 1:100.

5.2.1. Agitated Solvent Extraction (SLE)

Agitated solvent extraction was conducted using the conditions shown in Table 6 [41]. The OPW samples were mixed in an Erlenmeyer with the solvent. The extraction was carried out at room temperature (25 °C) in a shaker (Pro Digital Orbital Shaker SK-O330) at 200 rpm. The solvent was a mixture composed of 70% methanol, 28% water, and 2% acetic acid [10]. This mixture was selected since high hesperidin (an important flavone) extraction yields can be obtained [10]. After the extraction time (40 min), the mixture was vacuum filtered. The extract was stored in an amber bottle at 4 °C to avoid polyphenolic compound degradation. The solid was dried in a convective oven at 40 °C until it reached a constant weight.

Table 6. Extraction methods and conditions applied to OPW [41,51,85].

| Method | Temperature (°C) | S:L | Time (min) | Conditions |
|-----------|---------------------|-------|------------|------------------------|
| SLE | 25 | 1:100 | 40 | 200 rpm |
| UAE | 25 | 1:100 | 40 | 30 kHz; 100% amplitude |
| SE | Boiling temperature | 1:100 | 40 | N.A.* |
| SLE + UAE | 25 | 1:100 | 40 | 200 rpm |
| SFE | 70 | N.A. | 60 | 350 bar |

* N.A. Not Apply.

5.2.2. Ultrasound-Assisted Extraction (UAE)

The ultrasound-assisted extraction process (UAE) was carried out using the compact lab homogenizer UP-50H (Hielscher Ultrasound Technology) in a continuous pulse cycle. This equipment allows for the sonication of samples using a sonotrode. The amplitude was set to 100%. This value was kept constant in all assays. The extraction process was carried out with a probe working at 30 kHz. The provided power was 50 W. The operating conditions are shown in Table 6. These operating conditions were based on the results reported by Li et al. [83]. After the extraction time, the mixture was vacuum filtered. The extract was stored at −4 °C, and the solid was dried at 40 °C in a convective oven until it reached a constant weight [85].

5.2.3. Soxhlet Extraction (SE)

The sample was placed in a porous vessel (thimble). Then, milled OPW was placed into a Soxhlet apparatus working at constant reflux for 40 min. The extracts were stored in amber bottles at a temperature of 4 °C. The solid was dried at 40 °C in a convective oven until it reached a constant weight [86]. The Soxhlet extraction was conducted following the procedures described by the National Renewable Energy Laboratories (NREL) for extracting taxes, soluble sugars, and other polar components [87].

5.2.4. Agitated Solvent and Ultrasound-Assisted Extraction (SLE + UAE)

The extraction consisted of subjecting the mixture to a sound for 10 min (using the UP50H Ultrasound Processor Hielscher Ultrasound Technology), after which time the mixture was subjected to agitated solvent extraction for 30 min at room temperature. This extraction method was based on previous experiences related to the bioactive compound extraction from fruit wastes [41,51,85]. Then, the mixture was vacuum filtered. The extract

was stored at $-4\text{ }^{\circ}\text{C}$, and the solid was dried at $40\text{ }^{\circ}\text{C}$ in a convective oven until it reached a constant weight [85].

5.2.5. Supercritical Fluid Extraction (SFE)

The supercritical fluid extraction of bioactive compounds from OPW was conducted using lab-scale equipment (working volume 254 mL). The extraction conditions are presented in Table 6. The sample was introduced into the extraction tank. Carbon dioxide (CO_2) was used as the solvent. A solid to solvent (CO_2) ratio of 1:18 and a solid to co-solvent ratio (ethanol 10% + water 90%) of 1:5 were fixed. The extracts obtained were stored in amber containers at a temperature of $4\text{ }^{\circ}\text{C}$. Restrepo-Serna et al. [88] has described the used equipment in previous studies.

5.3. Quantification of Phenolic Compound Content, Total Antioxidant Capacity, and Hesperidin Content

The global yield after the extraction process was determined to elucidate the weight loss after the extractions. The total phenolic compound content (TPC), total antioxidant activity (TAA), and hesperidin content were determined for the OPW extracts resulting from the above-described experiments. TPC allows for the determination of any phenolic compound present in the extracts. TAA allows for the estimation of the antioxidant activity of the extracts by an inhibition method. Finally, the hesperidin content was determined via high-performance liquid chromatography (HPLC). These assays provide sufficient information for analyzing potential valorization pathways based on the extraction of the bioactive compounds.

5.3.1. Global Yield

The global yield was calculated as the ratio between the sample weights before and after extraction. This indicator helps to determine the best extraction method through weight loss. Nevertheless, the global yield does not provide specific information about the extracted compounds.

$$\text{Global Yield (\%)} = \left(\frac{\text{OD}_{\text{before}} - \text{OD}_{\text{after}}}{\text{OD}_{\text{before}}} \right) \times 100 \quad (1)$$

where OD before is the oven-dried sample before extraction and OD after is the oven-dried sample after extraction.

5.3.2. Total Polyphenol Content (TPC)

The total polyphenol content was measured with the Folin–Ciocalteu colorimetric method with modifications [85,89]. The method consists of mixing 150 μL of the extract with 2.4 mL of distilled water, 150 μL of Folin–Ciocalteu solution (1N), and 300 μL of sodium carbonate (20% *w/v*). The mixture was incubated for 2 h in the absence of light. Absorbance was read at 765 nm in a spectrophotometer of microplates (SpectraMax ABS Plus, Molecular Devices, LLC, San Jose, CA, USA) linked to the software SoftMax Pro v.7.0 [85]. A calibration curve was prepared at different dilutions of gallic acid from the stock solution. Distilled water was used as blank. The total polyphenol content is expressed in mg of gallic acid equivalent per 100 g of dry sample (mg GAE/100 g sample).

5.3.3. Total Antioxidant Activity (TAA)

The antioxidant activity was measured by the inhibition of the DPPH (2, 2-diphenyl-1-picryl-hydrazyl-hydrate) radical and the ABTS⁺ (2, 2'-azino-bis-(3-ethylbenzothiazoline-6-sulphonic acid) cation radical decolorization test. The DPPH radical inhibition assay was conducted according to the method described by Marinova et al. [90], Molyneux et al. [91], and Brand-Williams et al. [92]. The reaction was performed in a spectrophotometer of microplates (SpectraMax ABS Plus) by mixing 10 μL of OPW extract with 200 μL of DPPH solution at 60 μM . The mixtures were allowed to react for 1 h in the absence of light. The

samples were measured in a spectrophotometer of microplates (SpectraMax ABS Plus, Molecular Devices, LLC, San Jose, CA, USA) linked to the software SoftMax Pro v.7.0 at a wavelength of 517 nm [85]. The stock solution was prepared using ethanol. The radical inhibition was calculated using Equation (2). This equation has been reported everywhere [79]. A calibration curve was prepared with a standard solution of Trolox diluted in ethanol (100, 200, 250, 300, 350, 400, and 430 μM). Inhibition was reported considering the following units: μmol of Trolox/100 g of dry sample.

$$\text{Inhibition of absorbance } \lambda_{517} = \left(1 - \frac{A_f}{A_o}\right) \times 100 \quad (2)$$

The ABTS+ cation radical decolorization assay was determined based on the method described by Re et al. [93] and Ozgen et al. [94]. Dilutions of 1:150, 1:300, and 1:500 of the samples were prepared in ethanol. A total of 150 mL of extract was mixed with 3 mL of 60 μM solution of ABTS. This mixture was stirred and left in an ultrasound bath at room temperature for 20 min. Then, the samples were stored in the dark at 4 $^{\circ}\text{C}$ for 24 h. After this time, the solution was diluted with 20 mM of acetate buffer solution (pH 4.5) to an absorbance of 0.700 ± 0.01 at 734 nm. The mixture was left for 1 h in the absence of light. The samples were measured in a spectrophotometer of microplates (SpectraMax ABS Plus) linked to the software SoftMax Pro v.7.0 at a wavelength of 734 nm [85]. The inhibition percentage was calculated using Equation (2). The results were reported as μmol of Trolox/100 g of dry sample.

5.3.4. Hesperidin Quantification

Hesperidin quantification was performed via high-performance liquid chromatography (HPLC) with a UV-visible detector (LC-2010A HT—Shimadzu, Bogotá, Colombia). The chromatographic method reported by Adam [95] was used. The chromatographic separation was performed with a C18 column (150 mm, 4.6 mm, and 5 μm). An isocratic mobile phase condition was used. The mobile phase was composed of two solvents, 50% methanol (solvent A) and 50% water–phosphoric acid at a ratio of 99.9: 0.1 (solvent B). The flow rate, injection volume, column temperature, and absorbance were 0.9 mL/min, 20 μL , 30 $^{\circ}\text{C}$, and 280 nm. Hesperidin quantification was carried out using the standard internal method.

5.4. OPW Extracts: Results and Discussion of the Case Study

The case study was proposed to evaluate the best polyphenolic compound extraction method using an acidified methanol solution and ethanol. The acidification of the solution was carried out to dilate the cell membrane of raw materials [73]. Different authors report higher extraction yields of polyphenolic compounds with acidified solvents. For example, Bisognin et al. [96] reported an increase of about 13% in the TPC for *Ilex paraguariensis* leaf with a solution of methanol (70% *v/v*) and hydrochloric acid (1% *v/v*). Piovesana et al. [97] presented the use of acidified water as a better extraction solvent to obtain total phenolic acids, anthocyanins, flavonoids, and phenolic compounds compared to other studies using extraction with industrial organic solvents for *Hibiscus sabdariffa* L. Solvent acidification disrupts the lignocellulosic matrix of biomass. Thus, higher extraction yields can be achieved. Some phenolic compounds, flavonoids, and anthocyanins are covalently bound to the cell membrane layers of the raw material. The solvent acidification makes these layers more permeable (i.e., cellulose, hemicellulose, lignin, and pectin). Thus, the solvent can extract phenolic compounds more easily than without an acidified solvent. The addition of weak acids, such as citric acid, is recommended at pH between 3 and 4.8 to increase flavonoid extraction [98]. For this reason, this work studied the mixture of methanol, water, and acetic acid as a solvent in four (agitated solvent extraction, ultrasound-assisted extraction, Soxhlet extraction, and agitated solvent and ultrasound-assisted extraction) extraction methods. In the case of supercritical fluid extraction, the solvent used in the test

was carbon dioxide. To solubilize hesperidin, a mixture of ethanol–water was analyzed as a co-solvent. The overall extraction performance results are presented in Figure 9.

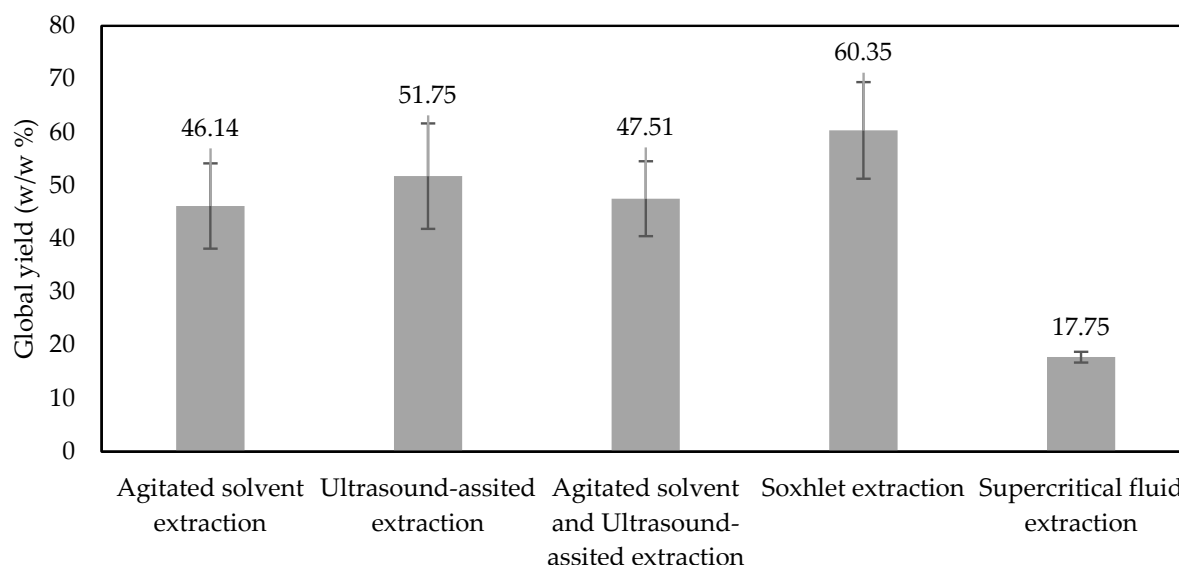


Figure 9. Global yield of different extraction methods applied to OPW.

Soxhlet extraction (SE) had the highest global performance with a value of 60.35%. Ultrasound-assisted extraction (UAE) was the method with the second highest extraction performance. On the other hand, SLE + UAE had a yield of 47.51%. Finally, agitated solvent extraction (SLE) and supercritical fluid extraction (SFE) had a yield of 46.14% and 17.75%, respectively. The global yield refers to the loss of mass suffered by the sample in the extraction time. Thus, higher yields are related to higher extraction performance. The SE global yield increased by 23.54% compared to the SLE process. The UAE global yield was lower (14.25%) than the SLE. On the other hand, the SLE + UAE process obtained a lower performance than the UAE process (8.2%). SFE had an extraction performance 3.4-fold higher than the SE method. The low overall performance in terms of loss of mass in the extraction with supercritical fluids is because by varying the conditions of temperature, pressure, and concentration of the co-solvent, the extraction becomes selective to a metabolite of interest [99].

SE was the best method for extracting compounds (see Figure 9). Nevertheless, the process temperature does not guarantee high-quality extracts, since several polyphenolic compounds can degrade at higher temperatures ($>50\text{ }^{\circ}\text{C}$) [100]. For this reason, a comparison not only in terms of global yield must be performed. A comparison between TPC, TAA (ABTS and DPPH), and value-added compound concentration (e.g., hesperidin) must be performed.

The results obtained are better than some studies reported in the literature. For example, Zia-ur-Rehman et al. [101] reported a global extraction yield of 11% for an ethanol extractor of dried and ground citrus peel. This result is lower than those presented. The same author reports a yield of 19.87% using methanol as a solvent. Goulas et al. [102] reported a global extraction yield with methanol (100%) of 70.2% by Soxhlet extraction for 30 min and a solid/liquid ratio of 1:0.26 w/v. This result is 14% higher than that obtained after OPW extraction. This difference could be attributed to the solid/liquid ratio applied in this case study. Goulas et al. [102] obtained more concentrated extracts, so the weight loss was higher. However, this result does not reflect higher concentrations of polyphenolic compounds (e.g., hesperidin). The extraction of flavonoids, glucosides, limonoids, and organic acids (e.g., ascorbic acid and citric acid) can be higher using methanol as the solvent. The TPC results are presented in Figure 10.

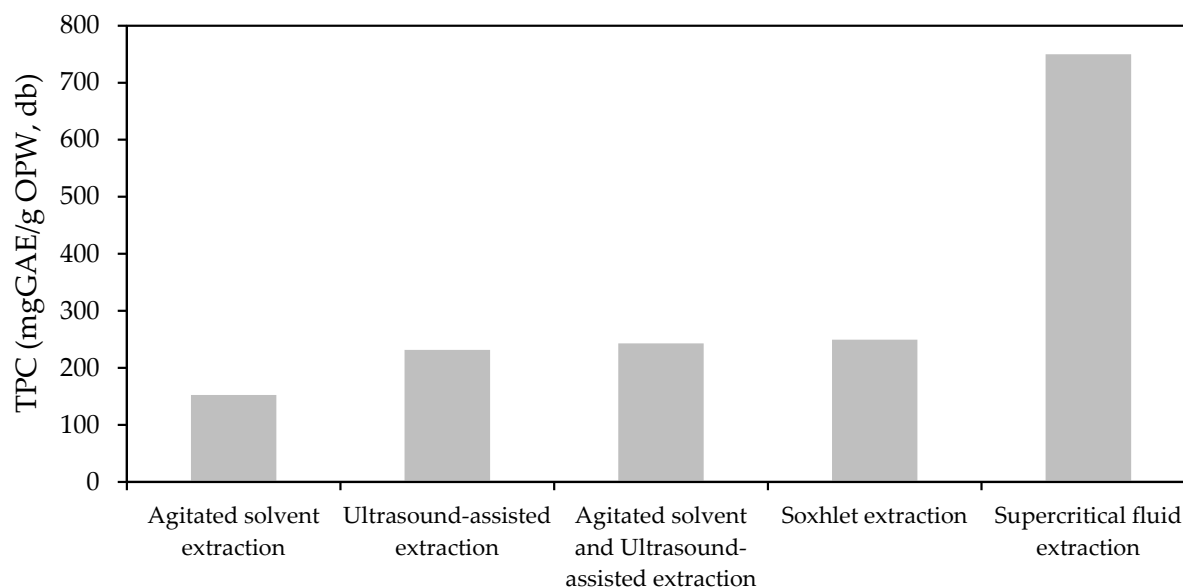
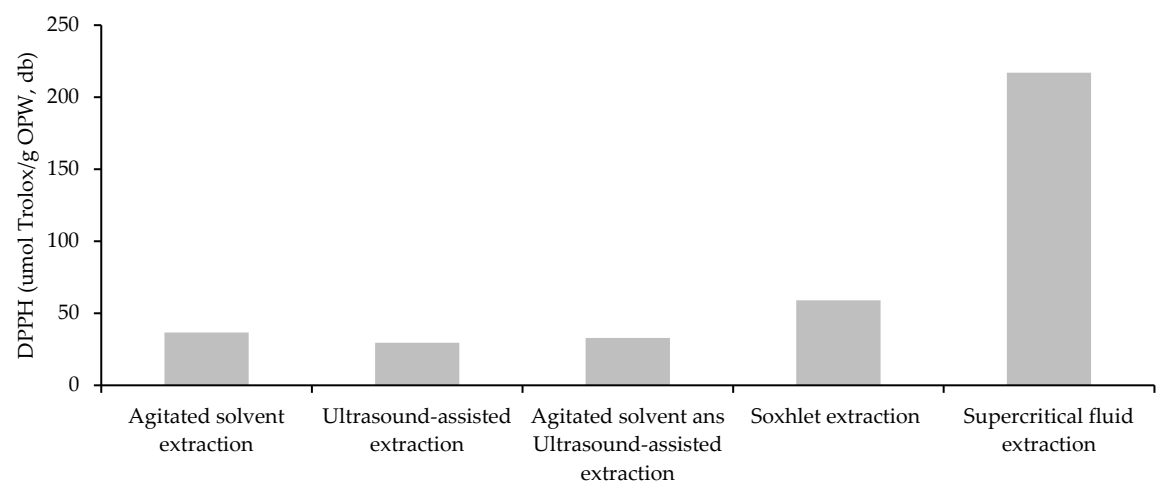


Figure 10. TPC content after OPW extraction by applying different methods.

The TPC content in the extracts allows us to elucidate the extraction efficiency better than the global yield. In the global yield, the loss of mass suffered by the samples is not directly related to the extraction of polyphenolic compounds. Conversely, other bioactive compounds present in OPW can be solubilized (e.g., soluble sugars). Indeed, OPW extracts can have a soluble sugar concentration between 29 and 44 g/100 g of sample [90]. The TPC content has a similar behavior to global yield. However, when comparing UAE with SE, the TPC content was 38.84% higher. In the SLE + UAE case, the TPC content was similar to SE (2.53% lower). Finally, the SFE provides a TPC content 3-fold higher than SE. This result reflects the high potential of SFE to obtain extracts rich in polyphenolic compounds. Saini et al. [91] reported a TPC content of 28.30 mg GAE/g of citric waste through ultrasound-assisted extraction with acetone and water as the solvents (1:3 *v/v*). The yield obtained in this case study by UAE was 8.18-fold higher than that reported by Saini et al. [91]. Moreover, the SLE + UAE process obtained a yield 8.59-fold higher than that reported by Saini et al. [91]. Goulas et al. [102] reported a TPC content of 108.5 mgGAE/g OPW through Soxhlet extraction. The TPC content was 2.3- and 7.0-fold higher than that reported by Goulas et al. [102]. Therefore, solvent acidification improves polyphenolic compound extraction. However, TPC analysis does not allow us to determine if SE is better for hesperidin extraction.

TAA was quantified in terms of DPPH and ABTS. The results of the OPW extractions are presented in Figure 11. Initially, the free radical scavenging activity of the extracts is analyzed by the DPPH scavenging assay. The SFE extracts had a higher antioxidant capacity compared to the other extracts. This behavior allows us to confirm that the hesperidin content in the supercritical fluid extraction was higher compared to the evaluated methods. Similar results were obtained using the ABTS method.

SFE had the highest hesperidin extraction yield (see Figure 12). The hesperidin concentration increased by 58%, compared to SLE. In addition, the hesperidin concentration was similar in the SLE and UAE processes (increases of 6.16%). Goulas et al. [102] reported a hesperidin content of OPW of 6.02 g/kg by SE. In this case study, a hesperidin content of 8.18 g/kg of OPW was obtained via SFE. This yield is higher than those reported in the open literature [102].



(a) DPPH results of the orange peel waste extracts.



(b) ABTS results of the orange peel waste extracts.

Figure 11. Antioxidant capacity of (a) DPPH and (b) ABTS after OPW bioactive compound extraction.

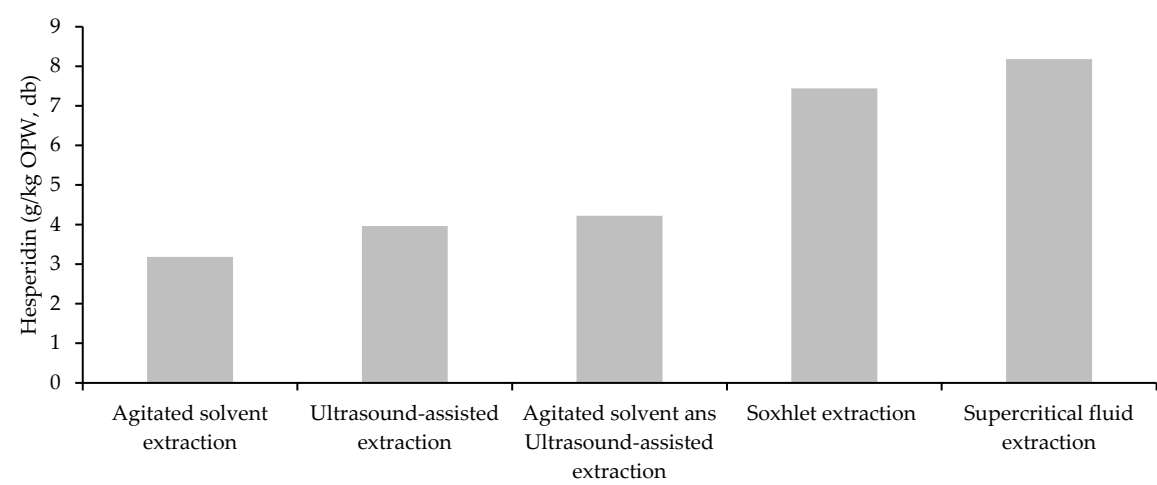


Figure 12. Hesperidin content in the OPW extracts.

6. Conclusions

Factors such as variety, agricultural practices, soil properties, and orange juice production methods influence OPW chemical composition. Specific applications based on OPW chemical composition and production context must be proposed. Thus, several OPW upgrading possibilities can be implemented at the industrial level. Nevertheless, more efforts should be made to bring academic proposals to the industrial sector, boosting the production of high value-added products such as essential oils, antioxidants, and organic acids. The gap between academics and the industry related to OPW valorization is attributed to the lack of a comprehensive analysis of OPW valorization pathways involving technical, economic, environmental, and social aspects based on a specific context (i.e., research based on industrial and market needs). Thus, more research efforts should be made on this topic.

OPW chemical composition is the basis for proposing different applications. Nevertheless, stand-alone applications must be evolved into a biorefinery system. This transition will increase the feasibility of OPW valorization schemes. Bioactive compound extraction is presented as a fundamental step when valorizing OPW, since these components have several applications at the industrial level. Exhausted OPW can be used as a source of bulk chemicals and bioenergy. The technological readiness level (TRL) must be considered when proposing valorization alternatives since higher innovative processes with a high TRL will be implemented faster than applications with a low development grade.

Supercritical fluid extraction is one of the most favorable methods to obtain bioactive or polyphenolic compounds at the technical level since high extraction yields and selectivity can be obtained. This statement is evidenced in the experimental results obtained in the case study. Nevertheless, the scale of the process should be analyzed based on economic aspects. The extraction of hesperidin with carbon dioxide under supercritical conditions yielded 58% more product than conventional stirred solvent extraction. Thus, this technology can be proposed as a potential alternative to valorize OPW. Bioactive compound extraction using methanol and acetic acid as the solvents was higher than the extraction yields reported in the open literature using other solvents (e.g., ethanol). Thus, the addition of a weak acid to the extraction process enhances the process. Ultrasound-assisted extraction was the second-best alternative to extract bioactive compounds. Nevertheless, more efforts are needed to scale up this technology.

7. Perspectives and Future Work

OPW is a raw material with high availability and the potential to be upgraded for different value-added products and energy vectors. Nevertheless, the gap between academics and the industry must be overcome to implement new valorization alternatives. Indeed, more studies focused on real OPW use as a raw material to give a solution for industries should be conducted. More contextualized valorization alternatives should be proposed based on regional and national market needs and technologies with a high TRL level. In contrast, research studies should present new upgrading alternatives to industrial stakeholders based on technical, economic, environmental, and social assessment. This fact will be the starting point to develop a bioeconomy based on the use of residual biomass.

On the other hand, integral OPW upgrading should be based on chemical composition analysis and physicochemical characteristics, since more reliable and feasible products can be proposed. Indeed, bioactive compounds will play an important role in OPW valorization, but structural polymers (i.e., pectin, cellulose, hemicellulose, and lignin) must be valorized toward sustainable production. Then, the chemical composition must be considered a key point when proposing valorization alternatives.

Finally, the assessment of different extraction methods should be addressed to optimize the extraction of bioactive compounds considering the origin and variety of the raw material.

Author Contributions: Conceptualization, J.C.S.-T., M.O.-S. and C.A.C.A.; formal analysis, C.A.C.A.; investigation, J.C.S.-T., M.O.-S. and C.A.C.A.; writing—original draft preparation, J.C.S.-T., M.O.-S. and C.A.C.A.; writing—review and editing, J.C.S.-T., M.O.-S. and C.A.C.A.; supervision, C.A.C.A.; funding acquisition, C.A.C.A. All authors have read and agreed to the published version of the manuscript.

Funding: This paper is the result of the research work developed through the research project “Repotenciación y adquisición de equipos para el laboratorio de Equilibrios Químicos y Cinéticas Enzimáticas para impulsar la línea de investigación dirigida a la extracción y análisis de compuestos bioactivos y nitrógeno” code 59387 of Vicerrectoría de Investigación y Docencia de la Facultad de Ingeniería y Arquitectura in Universidad Nacional de Colombia sede Manizales.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Tütem, E.; Başkan, K.S.; Karaman, Ş.; Apak, R. Citrus Fruits. In *Nutritional Composition and Antioxidant Properties of Fruits and Vegetables*; Jaiswal, A.K., Ed.; Academic Press: Cambridge, MA, USA, 2022; pp. 353–377, ISBN 978-0-12-812780-3.
2. Farag, M.A.; Abib, B.; Ayad, L.; Khattab, A.R. Sweet and Bitter Oranges: An Updated Comparative Review of Their Bioactives, Nutrition, Food Quality, Therapeutic Merits and Biowaste Valorization Practices. *Food Chem.* **2020**, *331*, 127306. [CrossRef] [PubMed]
3. Seminara, S.; Bennici, S.; Di Guardo, M.; Caruso, M.; Gentile, A.; La Malfa, S.; Distefano, G. Sweet Orange: Evolution, Characterization, Varieties, and Breeding Perspectives. *Agriculture* **2023**, *13*, 264. [CrossRef]
4. Food and Agriculture Organization of the United Nations. Available online: <https://www.fao.org/faostat/en/#data> (accessed on 3 December 2021).
5. Iglesias, D.J.; Cercós, M.; Colmenero-Flores, J.M.; Naranjo, M.A.; Ríos, G.; Carrera, E.; Ruiz-Rivero, O.; Lliso, I.; Morillon, R.; Tadeo, F.R.; et al. Physiology of Citrus Fruiting. *Braz. J. Plant Physiol.* **2007**, *19*, 333–362. [CrossRef]
6. Rapisarda, P.; Amenta, M.; Ballistreri, G.; Fabroni, S.; Timpanaro, N. Distribution, Antioxidant Capacity, Bioavailability and Biological Properties of Anthocyanin Pigments in Blood Oranges and Other Citrus Species. *Molecules* **2022**, *27*, 8675. [CrossRef] [PubMed]
7. Ladaniya, M. Fruit Morphology, Anatomy and Physiology. In *Citrus Fruits: Biology, Technology, and Evaluation*; Ladaniya, M., Ed.; Academic Press: Cambridge, MA, USA, 2022; pp. 145–171, ISBN 978-0-323-99306-7.
8. Ladaniya, M. Fruit Biochemistry. In *Citrus Fruits: Biology, Technology, and Evaluation*; Ladaniya, M., Ed.; Academic Press: Cambridge, MA, USA, 2022; pp. 173–247, ISBN 978-0-323-99306-7.
9. Siddiqui, S.A.; Pahmeyer, M.J.; Assadpour, E.; Jafari, S.M. Extraction and Purification of D-Limonene from Orange Peel Wastes: Recent Advances. *Ind. Crops Prod.* **2022**, *177*, 114484. [CrossRef]
10. Ortiz-Sanchez, M.; Omarini, A.B.; González-Aguirre, J.A.; Baglioni, M.; Zygadlo, J.A.; Breccia, J.; D’Souza, R.; Lemesoff, L.; Bodeain, M.; Cardona-Alzate, C.A.; et al. Valorization Routes of Citrus Waste in the Orange Value Chain through the Biorefinery Concept: The Argentina Case Study. *Chem. Eng. Process.-Process Intensif.* **2023**, *189*, 109407. [CrossRef]
11. Bouaita, R.; Derbal, K.; Panico, A.; Iasimone, F.; Pontoni, L.; Fabbicino, M.; Pirozzi, F. Methane Production from Anaerobic Co-Digestion of Orange Peel Waste and Organic Fraction of Municipal Solid Waste in Batch and Semi-Continuous Reactors. *Biomass Bioenergy* **2022**, *160*, 106421. [CrossRef]
12. Ortiz-Sanchez, M.; Cardona, C.A. Comparative Environmental Life Cycle Assessment of Orange Peel Waste in Present Productive Chains. *J. Clean. Prod.* **2021**, *322*, 128814. [CrossRef]
13. Wang, Z.; Zhong, T.; Mei, X.; Chen, X.; Chen, G.; Rao, S.; Zheng, X.; Yang, Z. Comparison of Different Drying Technologies for Brocade Orange (*Citrus sinensis*) Peels: Changes in Color, Phytochemical Profile, Volatile, and Biological Availability and Activity of Bioactive Compounds. *Food Chem.* **2023**, *425*, 136539. [CrossRef]
14. Espinosa, E.; Rincón, E.; Morcillo-Martín, R.; Rabasco-Vílchez, L.; Rodríguez, A. Orange Peel Waste Biorefinery in Multi-Component Cascade Approach: Polyphenolic Compounds and Nanocellulose for Food Packaging. *Ind. Crops Prod.* **2022**, *187*, 115413. [CrossRef]
15. Argun, M.E.; Argun, M.Ş.; Arslan, F.N.; Nas, B.; Ates, H.; Tongur, S.; Cakmakci, O. Recovery of Valuable Compounds from Orange Processing Wastes Using Supercritical Carbon Dioxide Extraction. *J. Clean. Prod.* **2022**, *375*, 134169. [CrossRef]
16. Athanasiadis, V.; Chatzimtakos, T.; Kotsou, K.; Palaiogiannis, D.; Bozinou, E.; Lalas, S.I. Optimization of the Extraction Parameters for the Isolation of Bioactive Compounds from Orange Peel Waste. *Sustainability* **2022**, *14*, 13926. [CrossRef]
17. Su, D.L.; Li, P.J.; Quek, S.Y.; Huang, Z.Q.; Yuan, Y.J.; Li, G.Y.; Shan, Y. Efficient Extraction and Characterization of Pectin from Orange Peel by a Combined Surfactant and Microwave Assisted Process. *Food Chem.* **2019**, *286*, 1–7. [CrossRef] [PubMed]

18. Senit, J.J.; Velasco, D.; Gomez Manrique, A.; Sanchez-Barba, M.; Toledo, J.M.; Santos, V.E.; Garcia-Ochoa, F.; Yustos, P.; Ladero, M. Orange Peel Waste Upstream Integrated Processing to Terpenes, Phenolics, Pectin and Monosaccharides: Optimization Approaches. *Ind. Crops Prod.* **2019**, *134*, 370–381. [\[CrossRef\]](#)
19. Lachos-Perez, D.; Baseggio, A.M.; Mayanga-Torres, P.C.; Maróstica, M.R.; Rostagno, M.A.; Martínez, J.; Forster-Carneiro, T. Subcritical Water Extraction of Flavanones from Defatted Orange Peel. *J. Supercrit. Fluids* **2018**, *138*, 7–16. [\[CrossRef\]](#)
20. Data Bridge Market Research. *Global Orange Juices Market—Industry Trends and Forecast to 2028*; Data Bridge Market Research: Pune, India, 2021.
21. Ladaniya, M. Growth, Maturity, Grade Standards, and Physico-Mechanical Characteristics of Fruit. In *Citrus Fruit Biology, Technology and Evaluation*; Ladaniya, M., Ed.; Academic Press: Cambridge, MA, USA, 2022; pp. 191–213, ISBN 978-0-12-374130-1.
22. Mushtaq, M. Extraction of Fruit Juice: An Overview. In *Fruit Juices Extraction, Composition, Quality and Analysis*; Rajauria, G., Tiwari, B.K., Eds.; Academic Press: Cambridge, MA, USA, 2018; pp. 131–159, ISBN 978-0-12-802230-6.
23. Berk, Z. Production of Single-Strength Citrus Juices. In *Citrus Fruit Processing*; Academic Press: Boca Raton, FL, USA, 2016; pp. 127–185, ISBN 9780128031339.
24. Ladaniya, M. Packaging. In *Citrus Fruit Biology, Technology and Evaluation*; Ladaniya, M., Ed.; Academic Press: Cambridge, MA, USA, 2022; pp. 287–317, ISBN 978-0-323-99306-7.
25. Kassem, H.S.; Alotaibi, B.A.; Aldosari, F.O.; Herab, A.; Ghazy, R. Factors Influencing Smallholder Orange Farmers for Compliance with GobaLAP Standards. *Saudi J. Biol. Sci.* **2021**, *28*, 1365–1373. [\[CrossRef\]](#) [\[PubMed\]](#)
26. Bonales-Revuelta, J.; Musule, R.; Navarro-Pineda, F.S.; García, C.A. Evaluating the Environmental Performance of Orange Production in Veracruz, Mexico: A Life Cycle Assessment Approach. *J. Clean. Prod.* **2022**, *343*, 131002. [\[CrossRef\]](#)
27. Food and Agriculture Organization of the United Nations—FAO. *Citrus Fruit: Fresh and Processed. Statistical Bulletin 2020*; FAO: Rome, Italy, 2021.
28. Mushtaq, M.; Akram, S.; Adnan, A. Novel Extraction Technologies. In *Fruit Juices: Extraction, Composition, Quality and Analysis*; Rajauria, G., Tiwari, B.K., Eds.; Academic Press: Cambridge, MA, USA, 2018; pp. 161–181, ISBN 978-0-12-802230-6.
29. Zema, D.A.; Calabrò, P.S.; Folino, A.; Tamburino, V.; Zappia, G.; Zimbone, S.M. Valorisation of Citrus Processing Waste: A Review. *Waste Manag.* **2018**, *80*, 252–273. [\[CrossRef\]](#)
30. Ringblom, U. *The Orange Book*, 1st ed.; Tetra Pak Processing Systems AB: Lund, Sweden, 2004; pp. 1–13, ISBN 91-3428-4.
31. Galaverna, G.; Di Silvestro, G.; Cassano, A.; Sforza, S.; Dossena, A.; Drioli, E.; Marchelli, R. A New Integrated Membrane Process for the Production of Concentrated Blood Orange Juice: Effect on Bioactive Compounds and Antioxidant Activity. *Food Chem.* **2008**, *106*, 1021–1030. [\[CrossRef\]](#)
32. Lanza, C.M. Citrus Fruit: Processed and Derived Products of Oranges. In *Encyclopedia of Food Sciences and Nutrition*; Elsevier: Amsterdam, The Netherlands, 2003; pp. 1346–1354.
33. Adnan, A.; Mushtaq, M.; Islam, T. ul Fruit Juice Concentrates. In *Fruit Juices: Extraction, Composition, Quality and Analysis*; Elsevier Inc.: Amsterdam, The Netherlands, 2018; pp. 217–240, ISBN 9780128024911.
34. Aider, M.; de Halleux, D. Cryoconcentration Technology in the Bio-Food Industry: Principles and Applications. *LWT—Food Sci. Technol.* **2009**, *42*, 679–685. [\[CrossRef\]](#)
35. Jariel, O.; Reynes, M.; Courel, M.; Durand, N.; Dornier, M.; Deblay, P. Comparison of Some Fruit Juice Concentration Techniques. *Fruits* **1996**, *51*, 437–450.
36. Adetunji, C.O.; Sharifi-Rad, J. *Applications of Essential Oils in the Food Industry*, 1st ed.; Adetunji, C.O., Sharifi-Rad, J., Eds.; Academic Press: Cambridge, MA, USA, 2023; ISBN 9780323983402.
37. Kaur, G.; Kaur, K.; Saluja, P. Citrus Essential Oil (Grapefruit, Orange, Lemon). In *Essential Oils Extraction, Characterization and Applications*; Ahmad Nayik, G., Ansari, M., Eds.; Academic Press: Cambridge, MA, USA, 2023; pp. 179–215, ISBN 978-0-323-91740-7.
38. Cypriano, D.Z.; da Silva, L.L.; Tasic, L. High Value-Added Products from the Orange Juice Industry Waste. *Waste Manag.* **2018**, *79*, 71–78. [\[CrossRef\]](#) [\[PubMed\]](#)
39. Paone, E.; Komilis, D. Strategies for the Sustainable Management of Orange Peel Waste through Anaerobic Digestion. *J. Environ. Manag.* **2018**, *212*, 462–468. [\[CrossRef\]](#)
40. Ortiz-Sanchez, M.; Solarte-Toro, J.-C.; González-Aguirre, J.-A.; Peltonen, K.E.; Richard, P.; Cardona Alzate, C.A. Pre-Feasibility Analysis of the Production of Mucic Acid from Orange Peel Waste under the Biorefinery Concept. *Biochem. Eng. J.* **2020**, *161*, 107680. [\[CrossRef\]](#)
41. Ortiz-Sanchez, M.; Solarte-Toro, J.C.; Orrego-Alzate, C.E.; Acosta-Medina, C.D.; Cardona-Alzate, C.A. Integral Use of Orange Peel Waste through the Biorefinery Concept: An Experimental, Technical, Energy, and Economic Assessment. *Biomass Convers. Biorefin.* **2020**, *11*, 645–659. [\[CrossRef\]](#)
42. Bassani, A.; Montes, S.; Jubete, E.; Palenzuela, J.; Sanjuán, A.P.; Spigno, G. Incorporation of Waste Orange Peels Extracts into PLA Films. *Chem. Eng. Trans.* **2019**, *74*, 1063–1068. [\[CrossRef\]](#)
43. Zhou, Y.M.; Chen, Y.P.; Guo, J.S.; Shen, Y.; Yan, P.; Yang, J.X. Recycling of Orange Waste for Single Cell Protein Production and the Synergistic and Antagonistic Effects on Production Quality. *J. Clean. Prod.* **2019**, *213*, 384–392. [\[CrossRef\]](#)

44. Majekodunmi, B.; Abioja, M.; Adekunle, E.; Logunleko, S.M.; Daramola, J. Productive Performance Response of Broiler Chickens to Water Supplementation with Sweet Orange Peel Powder in a Hot Humid Environment. *Anim.—Sci. Proc.* **2022**, *13*, 20–21. [\[CrossRef\]](#)
45. Mohsin, A.; Hussain, M.H.; Zaman, W.Q.; Mohsin, M.Z.; Zhang, J.; Liu, Z.; Tian, X.; Salim-ur-Rehman, X.; Khan, I.M.; Niazi, S.; et al. Advances in Sustainable Approaches Utilizing Orange Peel Waste to Produce Highly Value-Added Bioproducts. *Crit. Rev. Biotechnol.* **2021**, *42*, 1284–1303. [\[CrossRef\]](#)
46. Orozco, R.S.; Hernández, P.B.; Morales, G.R.; Núñez, F.U.; Villafuerte, J.O.; Lugo, V.L.; Ramírez, N.F.; Díaz, C.E.B.; Vázquez, P.C. Characterization of Lignocellulosic Fruit Waste as an Alternative Feedstock for Bioethanol Production. *BioResources* **2014**, *9*, 1873–1885.
47. Alvarez, J.; Hooshdaran, B.; Cortazar, M.; Amutio, M.; Lopez, G.; Freire, F.B.; Haghshenasfard, M.; Hossein, S.; Olazar, M. Valorization of Citrus Wastes by Fast Pyrolysis in a Conical Spouted Bed Reactor. *Fuel* **2018**, *224*, 111–120. [\[CrossRef\]](#)
48. Mohsin, A.; Zhang, K.; Hu, J.; Salim-ur-Rehman; Tariq, M.; Zaman, W.Q.; Khan, I.M.; Zhuang, Y.; Guo, M. Optimized Biosynthesis of Xanthan via Effective Valorization of Orange Peels Using Response Surface Methodology: A Kinetic Model Approach. *Carbohydr. Polym.* **2018**, *181*, 793–800. [\[CrossRef\]](#) [\[PubMed\]](#)
49. Ahmed, I.; Zia, M.A.; Hussain, M.A.; Akram, Z.; Naveed, M.T.; Nowrouzi, A. Bioprocessing of Citrus Waste Peel for Induced Pectinase Production by *Aspergillus Niger*; Its Purification and Characterization. *J. Radiat. Res. Appl. Sci.* **2016**, *9*, 148–154. [\[CrossRef\]](#)
50. Borges, C.V.; Amorim, E.P.; Leonel, M.; Gomez, H.A.G.; dos Santos, T.P.R.; Ledo, C.A.D.S.; Belin, M.A.F.; de Almeida, S.L.; Minatel, I.O.; Lima, G.P.P. Post-Harvest Physicochemical Profile and Bioactive Compounds of 19 Bananas and Plantains Genotypes. *Bragantia* **2019**, *78*, 284–296. [\[CrossRef\]](#)
51. Ortiz-Sanchez, M.; Solarte-Toro, J.C.; Cardona Alzate, C.A. A Comprehensive Approach for Biorefineries Design Based on Experimental Data, Conceptual and Optimization Methodologies: The Orange Peel Waste Case. *Bioresour. Technol.* **2021**, *325*, 124682. [\[CrossRef\]](#)
52. Kuo, C.H.; Huang, C.Y.; Shieh, C.J.; Wang, H.M.D.; Tseng, C.Y. Hydrolysis of Orange Peel with Cellulase and Pectinase to Produce Bacterial Cellulose Using *Gluconacetobacter xylinus*. *Waste Biomass Valorization* **2017**, *10*, 85–93. [\[CrossRef\]](#)
53. Rivas-Cantu, R.C.; Jones, K.D.; Mills, P.L. A Citrus Waste-Based Biorefinery as a Source of Renewable Energy: Technical Advances and Analysis of Engineering Challenges. *Waste Manag. Res.* **2013**, *31*, 413–420. [\[CrossRef\]](#)
54. Patsalou, M.; Samanides, C.G.; Protopapa, E.; Stavrinou, S.; Vyrides, I.; Koutinas, M. A Citrus Peel Waste Biorefinery for Ethanol and Methane Production. *Molecules* **2019**, *24*, 2451. [\[CrossRef\]](#)
55. Patsalou, M.; Menikea, K.K.; Makri, E.; Vasquez, M.I.; Drouza, C.; Koutinas, M. Development of a Citrus Peel-Based Biorefinery Strategy for the Production of Succinic Acid. *J. Clean. Prod.* **2017**, *166*, 706–716. [\[CrossRef\]](#)
56. Ozturk, B.; Winterburn, J.; Gonzalez-Miquel, M. Orange Peel Waste Valorisation through Limonene Extraction Using Bio-Based Solvents. *Biochem. Eng. J.* **2019**, *151*, 107298. [\[CrossRef\]](#)
57. Ozturk, B.; Parkinson, C.; Gonzalez-Miquel, M. Extraction of Polyphenolic Antioxidants from Orange Peel Waste Using Deep Eutectic Solvents. *Sep. Purif. Technol.* **2018**, *206*, 1–13. [\[CrossRef\]](#)
58. Pandiarajan, A.; Kamaraj, R.; Vasudevan, S.; Vasudevan, S. OPAC (Orange Peel Activated Carbon) Derived from Waste Orange Peel for the Adsorption of Chlorophenoxyacetic Acid Herbicides from Water: Adsorption Isotherm, Kinetic Modelling and Thermodynamic Studies. *Bioresour. Technol.* **2018**, *261*, 329–341. [\[CrossRef\]](#) [\[PubMed\]](#)
59. Martín, M.A.; Fernández, R.; Gutiérrez, M.C.; Siles, J.A. Thermophilic Anaerobic Digestion of Pre-Treated Orange Peel: Modelling of Methane Production. *Process Saf. Environ. Prot.* **2018**, *117*, 245–253. [\[CrossRef\]](#)
60. Arenas, C.N.; Navarro, M.V.; Martínez, J.D. Pyrolysis Kinetics of Biomass Wastes Using Isoconversional Methods and the Distributed Activation Energy Model. *Bioresour. Technol.* **2019**, *288*, 121485. [\[CrossRef\]](#) [\[PubMed\]](#)
61. de la Torre, I.; Acedos, M.G.; Ladero, M.; Santos, V.E. On the Use of Resting *L. Delbrueckii* Spp. *Delbrueckii* Cells for D-Lactic Acid Production from Orange Peel Wastes Hydrolysates. *Biochem. Eng. J.* **2019**, *145*, 162–169. [\[CrossRef\]](#)
62. Calabrò, P.S.; Panzera, M.F. Anaerobic Digestion of Ensiled Orange Peel Waste: Preliminary Batch Results. *Therm. Sci. Eng. Prog.* **2018**, *6*, 355–360. [\[CrossRef\]](#)
63. Park, W.K.; Moon, M.; Shin, S.E.; Cho, J.M.; Suh, W.I.; Chang, Y.K.; Lee, B. Economical DHA (Docosahexaenoic Acid) Production from *Aurantiochytrium* Sp. KRS101 Using Orange Peel Extract and Low Cost Nitrogen Sources. *Algal Res.* **2018**, *29*, 71–79. [\[CrossRef\]](#)
64. Lathiya, D.R.; Bhatt, D.V.; Maheria, K.C. Synthesis of Sulfonated Carbon Catalyst from Waste Orange Peel for Cost Effective Biodiesel Production. *Bioresour. Technol. Rep.* **2018**, *2*, 69–76. [\[CrossRef\]](#)
65. Domingos, I.; Ferreira, J.; Cruz-Lopes, L.; Esteves, B. Polyurethane Foams from Liquefied Orange Peel Wastes. *Food Bioprod. Process.* **2019**, *115*, 223–229. [\[CrossRef\]](#)
66. Teigiserova, D.A.; Hamelin, L.; Tiruta-Barna, L.; Ahmadi, A.; Thomsen, M. Circular bioeconomy: Life cycle assessment of scaled-up cascading production from orange peel waste under the current and future electricity mixes. *Sci. Total Environ.* **2022**, *812*, 152574. [\[CrossRef\]](#)
67. González-Rivera, J.; Spepi, A.; Ferrari, C.; Duce, C.; Longo, I.; Falconieri, D.; Piras, A.; Tiné, M.R. Novel Configurations for a Citrus Waste Based Biorefinery: From Solventless to Simultaneous Ultrasound and Microwave Assisted Extraction. *Green Chem.* **2016**, *18*, 6482–6492. [\[CrossRef\]](#)

68. Ángel Siles López, J.; Li, Q.; Thompson, I.P. Biorefinery of Waste Orange Peel. *Crit. Rev. Biotechnol.* **2010**, *30*, 63–69. [CrossRef] [PubMed]
69. Luengo, E.; Álvarez, I.; Raso, J. Improving the pressing extraction of polyphenols of orange peel by pulsed electric fields. *Innov Food Sci Emerg Technol.* **2013**, *17*, 79–84. [CrossRef]
70. Pathak, P.D.; Mandavgane, S.A.; Kulkarni, B.D. Fruit Peel Waste: Characterization and Its Potential Uses. *Curr. Sci.* **2017**, *113*, 444–454. [CrossRef]
71. M'hiri, N.; Ioannou, I.; Mihoubi Boudhrioua, N.; Ghoul, M. Effect of Different Operating Conditions on the Extraction of Phenolic Compounds in Orange Peel. *Food Bioprod. Process.* **2015**, *96*, 161–170. [CrossRef]
72. Markets and Markets Foods Antioxidant Market. Available online: <https://www.marketsandmarkets.com/Market-Reports/food-antioxidants-market-91651246.html#:~:text=The%20food%20antioxidants%20market%20is,the%20creation%20of%20free%20radicals> (accessed on 5 September 2023).
73. García-Nicolás, M.; Ledesma-Escobar, C.A.; Priego-Capote, F. Spatial Distribution and Antioxidant Activity of Extracts from Citrus Fruits. *Antioxidants* **2023**, *12*, 781. [CrossRef]
74. Boukroufa, M.; Boutekedjiret, C.; Petigny, L.; Rakotomanomana, N.; Chemat, F. Bio-Refinery of Orange Peels Waste: A New Concept Based on Integrated Green and Solvent Free Extraction Processes Using Ultrasound and Microwave Techniques to Obtain Essential Oil, Polyphenols and Pectin. *Ultrason. Sonochem.* **2015**, *24*, 72–79. [CrossRef]
75. Allaf, T.; Tomao, V.; Ruiz, K.; Chemat, F. Instant Controlled Pressure Drop Technology and Ultrasound Assisted Extraction for Sequential Extraction of Essential Oil and Antioxidants. *Ultrason. Sonochem.* **2013**, *20*, 239–246. [CrossRef]
76. Bizzo, H.R.; Ana Maria, C.H.; Rezende, C.M. Oleos Essenciais No Brasil: Aspectos Gerais, Desenvolvimento e Perspectivas. *Quim. Nova* **2009**, *32*, 588–594. [CrossRef]
77. Rezzadori, K.; Benedetti, S.; Amante, E.R. Proposals for the Residues Recovery: Orange Waste as Raw Material for New Products. *Food Bioprod. Process.* **2012**, *90*, 606–614. [CrossRef]
78. Espinosa-Pardo, F.A.; Nakajima, V.M.; Macedo, G.A.; Macedo, J.A.; Martínez, J. Extraction of Phenolic Compounds from Dry and Fermented Orange Pomace Using Supercritical CO₂ and Cosolvents. *Food Bioprod. Process.* **2017**, *101*, 1–10. [CrossRef]
79. Figueroa, J.G.; Borrás-Linares, I.; Del Pino-García, R.; Curiel, J.A.; Lozano-Sánchez, J.; Segura-Carretero, A. Functional Ingredient from Avocado Peel: Microwave-Assisted Extraction, Characterization and Potential Applications for the Food Industry. *Food Chem.* **2021**, *352*, 129300. [CrossRef]
80. Fakayode, O.A.; Abobi, K.E. Optimization of Oil and Pectin Extraction from Orange (*Citrus sinensis*) Peels: A Response Surface Approach. *J. Anal. Sci. Technol.* **2018**, *9*, 20. [CrossRef]
81. Golmohammadi, M.; Borghei, A.; Zenouzi, A. Optimization of Essential Oil Extraction from Orange Peels Using Steam Explosion. *Heliyon* **2018**, *4*, e00893. [CrossRef] [PubMed]
82. Farhat, A.; Fabiano-Tixier, A.; El, M.; Maingonnat, J. Microwave Steam Diffusion for Extraction of Essential Oil from Orange Peel: Kinetic Data, Extract's Global Yield and Mechanism. *Food Chem.* **2011**, *125*, 255–261. [CrossRef]
83. Li, Q.; Putra, N.R.; Rizkiyah, D.N.; Abdul Aziz, A.H.; Irianto, I.; Qomariyah, L. Orange Pomace and Peel Extraction Processes towards Sustainable Utilization: A Short Review. *Molecules* **2023**, *28*, 3550. [CrossRef]
84. Leo, C.H.; Foo, S.Y.; Tan, J.C.W.; Tan, U.X.; Chua, C.K.; Ong, E.S. Green Extraction of Orange Peel Waste Reduces TNF α -Induced Vascular Inflammation and Endothelial Dysfunction. *Antioxidants* **2022**, *11*, 1768. [CrossRef]
85. Garcia-Vallejo, M.C.; Solarte-Toro, J.C.; Ortiz-Sanchez, M.; Chamorro-Anaya, L.; Chamorro-Anaya, L.; Peroza-Piñeres, P.; Pérez-Cordero, A.; Cardona Alzate, C.A. Exploring the Production of Antioxidants and Biogas from Avocado (*Persea Americana* Var. *Americana*) Residues as an Alternative for Developing Rural Bioeconomies. *Sustain. Chem. Pharm.* **2023**, *33*, 101089. [CrossRef]
86. Battista, F.; Remelli, G.; Zanzoni, S.; Bolzonella, D. Valorization of Residual Orange Peels: Limonene Recovery, Volatile Fatty Acids, and Biogas Production. *ACS Sustain. Chem. Eng.* **2020**, *8*, 6834–6843. [CrossRef]
87. Sluiter, A.; Hames, B.; Ruiz, R.; Scarlata, C.; Sluiter, J.; Templeton, D. *Determination of Extractives in Biomass: Laboratory Analytical Procedure (LAP)*; NREL/TP-510-42619; Cole Boulevard: Golden, CO, USA, 2008.
88. Restrepo-Serna, D.L.; Solarte-Toro, J.C.; Cardona-Alzate, C.A. A Biorefinery Approach for an Integral Valorisation of Avocado Peel and Seeds Through Supercritical Fluids. *Waste Biomass Valorization* **2022**, *13*, 3973–3988. [CrossRef]
89. Rover, M.R.; Brown, R.C. Quantification of Total Phenols in Bio-Oil Using the Folin-Ciocalteu Method. *J. Anal. Appl. Pyrolysis* **2013**, *104*, 366–371. [CrossRef]
90. Marinova, G.; Batchvarov, V. Evaluation of the Methods for Determination of the Free Radical Scavenging Activity by DPPH. *Bulg. J. Agric. Sci.* **2011**, *17*, 11–24. [CrossRef]
91. Molyneux, P. The Use of the Stable Free Radical Diphenylpicryl-Hydrazyl (DPPH) for Estimating Anti-Oxidant Activity. *Songklanakarin J. Sci. Technol.* **2004**, *26*, 211–219.
92. Brand-Williams, W.; Cuvelier, M.; Berset, C. Use of a Free Radical Method to Evaluate Antioxidant Activity. *LWT—Food Sci. Technol.* **1995**, *28*, 25–30. [CrossRef]
93. Re, R.; Pellegrini, N.; Proteggente, A.; Pannala, A.; Yang, M.; Rice-Evans, C. Antioxidant Activity Applying an Improved ABTS Radical Cation Decolorization Assay. *Free Radic. Biol. Med.* **1999**, *26*, 1231–1237. [CrossRef] [PubMed]

94. Ozgen, M.; Reese, R.N.; Tulio, A.; Scheerens, J.; Miller, R. Modified 2,2-Azino-Bis-3-Ethylbenzothiazoline-6-Sulfonic Acid (ABTS) Method to Measure Antioxidant Capacity of Selected Small Fruits and Comparison to Ferric Reducing Antioxidant Power (FRAP) and 2,2'-Diphenyl-1-Picrylhydrazyl (DPPH) Methods. *J. Agric. Food Chem.* **2006**, *54*, 1151–1157. [[CrossRef](#)] [[PubMed](#)]
95. Adham, A.N. Qualitative and Quantitative Estimation of Hesperidin in Peel and Juice of Citrus Fruits by RP-HPLC Method Growing in Kurdistan Region/Iraq. *Int. J. Pharm. Sci. Rev. Res.* **2015**, *46*, 220–224.
96. Bisognin, D.A.; da Luz, L.V.; Lencina, K.H.; dos Santos, C.O.; Sautter, C.K. Contents of Total Phenolics and Flavonoids in and Antioxidant Activity of Ilex Paraguariensis Leaves. *Pesqui. Agropecuária Bras.* **2019**, *54*, e00856. [[CrossRef](#)]
97. Piovesana, A.; Noreña, C.P.Z. Study of Acidified Aqueous Extraction of Phenolic Compounds from Hibiscus Sabdariffa L. Calyces. *Open Food Sci. J.* **2019**, *11*, 25–34. [[CrossRef](#)]
98. Zimmermann, B.F.; Gleichenhagen, M. The Effect of Ascorbic Acid, Citric Acid and Low PH on the Extraction of Green Tea: How to Get Most out of It. *Food Chem.* **2011**, *124*, 1543–1548. [[CrossRef](#)]
99. De Melo, M.M.R.; Barbosa, H.M.A.; Passos, C.P.; Silva, C.M. Supercritical Fluid Extraction of Spent Coffee Grounds: Measurement of Extraction Curves, Oil Characterization and Economic Analysis. *J. Supercrit. Fluids* **2014**, *86*, 150–159. [[CrossRef](#)]
100. Skenderidis, P.; Leontopoulos, S.; Petrotos, K.; Giavasis, I. Vacuum Microwave-Assisted Aqueous Extraction of Polyphenolic Compounds from Avocado (Persea Americana) Solid Waste. *Sustainability* **2021**, *13*, 2166. [[CrossRef](#)]
101. Zia-ur-Rehman. Citrus Peel Extract—A Natural Source of Antioxidant. *Food Chem.* **2006**, *99*, 450–454. [[CrossRef](#)]
102. Goulas, V.; Manganaris, G.A. Exploring the Phytochemical Content and the Antioxidant Potential of Citrus Fruits Grown in Cyprus. *Food Chem.* **2012**, *131*, 39–47. [[CrossRef](#)]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.