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Review

From Citrus Waste to Valuable Resources: A Biorefinery Approach

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Abstract: Typically, citrus waste is composted on land by producers or used as livestock feed. However, the biorefinery approach offers a sustainable and economically viable solution for managing and valorizing these agricultural residues. This review examines research from the period 2014 to 2024. Citrus waste can be utilized initially by extracting the present phytochemicals and subsequently by producing value-added products using it as a raw material. The phytochemicals reported as extracted include essential oils (primarily limonene), pectin, polyphenolic components, micro- and nano-cellulose, proteins, and enzymes, among others. The components produced from the waste include bioethanol, biogas, volatile acids, biodiesel, microbial enzymes, and levulinic acid, among others. The review indicates that citrus waste has technical, economic, and environmental potential for utilization at the laboratory scale and, in some cases, at the pilot scale. However, research on refining pathways, optimization, and scalability must continue to be an active field of investigation.

Keywords: citrus waste; biorefinery; phytochemicals; biofuels; bioactive compounds; enzymes

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1. Introduction

The production of citrus fruits worldwide includes products such as oranges, limes, lemons, grapefruits, and tangerines. Globally, orange production reached a total of approximately 143.8 million tons in 2019. In Mexico, production reached 8.4 million tons that year, with about 10.7% used for processing [1]. However, even though the amount of processed citrus represents a small percentage of the total produced, it is important to note that all production eventually becomes waste, whether consumed as fruit or as a processed product, since peel, bagasse, and seeds are discarded as trash. In the specific case of processing, it is estimated that peels constitute around 50–70% *w*/*w* of the waste, which constitutes approximately ten million tons annually worldwide [2].

The handling of waste from the citrus industry mainly involves feeding livestock or disposal in landfills; however, these procedures create environmental problems. Therefore, to reduce costs and environmental impact, new ways of processing this waste have been evaluated to make the most of all its organic compounds, with biorefinery being one of those options [2].

In recent years, several studies have been conducted to carry out the citrus waste valorization with this biorefinery approach. Citrus waste, such as orange residues (which is the most studied by-product) corresponds to approximately 43% of the total fruit mass, from these wastes consist of around 37% of bagasse, 35% of peel, 14% of fruit, and 13% pulp [3]. Because disposal of these residues becomes a problem for industries the implementation of different strategies for its valorization is crucial. Thus, biorefinery systems, have emerged as promising strategies for obtaining several products after a sequential complete valorization of citrus by-products such as essential oils, pectin, volatile fatty acids, biogas, and ethanol, among others (Figure 1) [4–6].

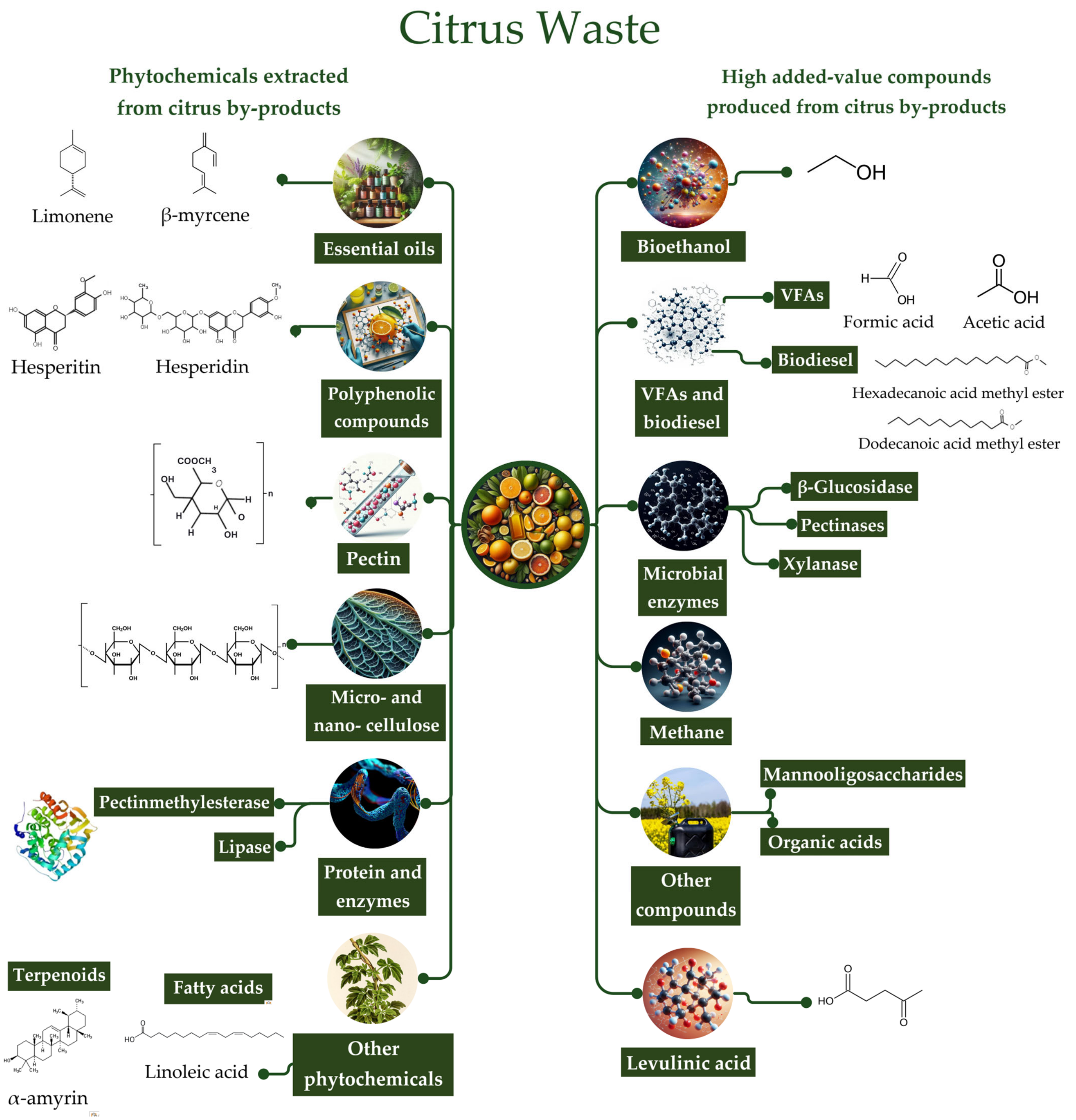

Figure 1. Phytochemicals and added-value compounds extracted or produced from citrus by-products. Illustrations were obtained using Microsoft AI image generator v10.

In addition, new environmental trends demand the minimization of wastes through the recuperation or production of high-value-added compounds by a cascade biorefinery model. This model consists of sequential processing through unit operations for the valorization of organic waste to obtain various value-added products, bioproducts, and biofuels [4,7]. For this purpose, physicochemical and biotechnological approaches have been applied as described below. Usually, physicochemical techniques are based on solvent extraction methods and involve the use of conventional methodologies (e.g., homogenization, Soxhlet extraction) as well as non-conventional extraction methods (e.g., microwave- and ultrasound-assisted extraction, supercritical fluid extraction) for the recovery of phytochemicals present in citrus waste. Meanwhile, biotechnological techniques are based on biochemical processes and mainly involve the use of enzyme technology and fermentation technology to produce bioproducts and biofuels. These techniques are typically employed separately or sequentially depending on the specific objectives, often within a biorefinery framework.

Ortiz-Sanchez et al. (2021a) [8] proposed a comprehensive methodology composed of eight relevant steps such as: (i) defining the main processes and preliminary biorefinery configuration; (ii) complete chemical characterization; (iii) know-how experience, hierarchical and sequencing concepts; (iv) analytical and experimental procedures; (v) design and simulation of the early unit processes involved in the biorefinery; (vi) estimation of capital and operational expenditures of early-unit processes; (vii) defining the optimization objective; and (viii) mathematical modeling and solving of the superstructure, which were design for a ease biorefinery implementation. Then, the study of biorefineries should be continuous due to the changes in raw materials produced by the industries and the technological advances [9]. This methodology can be relevant for further studies as it provides a structured approach to fully utilize agroindustrial residues, including citrus waste, addressing both environmental and economic challenges associated with waste management. By offering a structured guide for converting waste into valuable products and renewable energy, this proposed methodology promotes a circular economy and sustainable development.

In this sense, this review summarizes recent knowledge and interesting information on the phytochemicals and added-value compounds that can be extracted and produced from citrus by-products, based on several studies applying a biorefinery approach.

2. Methodology

According to Guarín-Manrique et al. [10], the Scopus database is a robust document management source, notable for its global reach and the multidisciplinary of the fields it encompasses. Furthermore, it includes renowned publishers such as Elsevier, Wiley, the Multidisciplinary Digital Publishing Institute (MDPI), Springer, among others. Moreover, this database is distinguished for containing high-quality documents, which undergo rigorous review and validation by experts. This ensures for comprehensive analysis of topics such as citrus waste valorization using a biorefinery approach. In this sense, the keywords "citrus waste biorefinery" were used to search for recent information in this field in the Scopus database. In order to review the most recent studies, articles published between 2014 to 2024 were included in this analysis. However, other documents (e.g., reviews, book chapters, and conference papers) related to citrus waste valorization were excluded from the review. In addition, studies that did not provide relevant information for the preparation of this review were also excluded. Finally, another few studies were used to clarify and propose ideas.

3. Search Results

Based on the methodology used for this study, one hundred and fourteen documents were identified in the Scopus database (www.scopus.com accessed on 29 June of 2024) using the keywords "citrus waste biorefinery", which were published between 2005 and 2024 (Figure 2). It can be observed that the valorization of citrus wastes through a biorefinery approach has been a topic under constant study in the last twelve years, with a notable rise in publications in the last six years.

After narrowing the search to the period from 2014 to 2024, the obtained results included: sixty-three research articles, twenty-seven review articles, seven book chapters, three conference papers, and one book. In this context, the distribution of research articles published among various publishers was as follows: Elsevier (34) > Springer (12) > miscellaneous publishers (6) > American Chemical Society (4) > MDPI (3) > the Italian Association of Chemical Engineering (2) = Wiley (2). Notably, the journals "Biomass Conversion and Biorefinery" from Springer, "Bioresource Technology", and "Waste Management" from Elsevier featured the most publications with totals of seven, five, and five articles, respectively. Furthermore, according to the methodology previously described, fifty-eight experimental papers related to citrus waste biorefinery were used to construct this review.

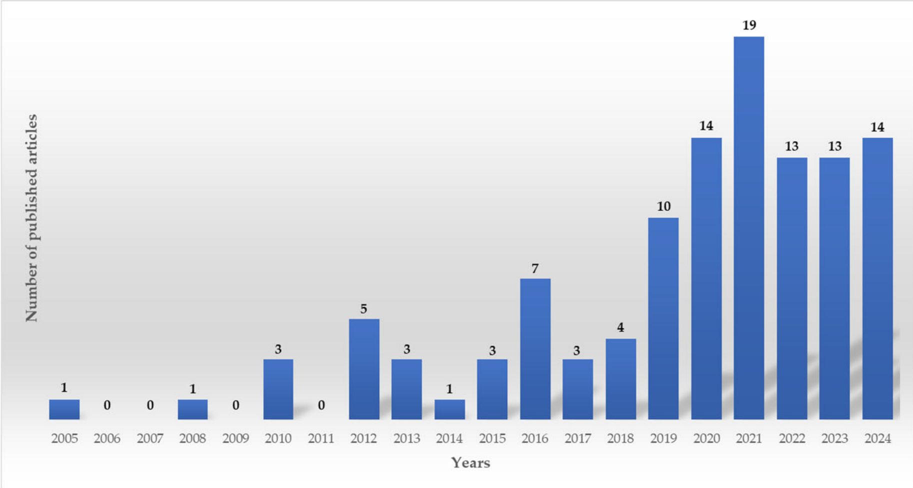

Figure 2. Number of papers resulting from the search using the keywords "citrus waste biorefinery" in the Scopus database.

4. Chemical Composition of Citrus Wastes

Biorefinery systems can integrate different extraction and/or conversion pathways, such as solid/liquid extraction, distillation, biotechnological, and thermochemical processes, among others. The implementation of these pathways depends on the chemical composition of the feedstock and the desired product [9]. In this context, the physicochemical characterization of citrus waste underscores its suitability for the extraction, synthesis, or production of several compounds and materials into a "cascade biorefinery" model for the industry.

The chemical composition of various citrus wastes studied in recent years is summarized in Table 1. The reported moisture content ranges from 7.41 to 81%. In the valorization of citrus waste using a biorefinery approach, moisture content is a crucial parameter. Low moisture content decreases the weight of the waste making transport to the plant more efficient in terms of environmental burdens [11]. On the other hand, high moisture content decreases the calorific value of this plant material [9], theoretically resulting in less energy being obtained. Regarding ash content, this is associated with the inorganic non-volatile compounds such as alkaline carbonates and oxides (e.g., $K_2Ca(CO_3)_2$, K_2CO_3, $CaCO_2$, CaO, MgO) [12,13]. Citrus wastes exhibit ash content values ranging from 1 to 6.58%. This could be related to the ash content in pectin obtained from these by-products, as it can affect the gelling properties of this biopolymer since the hardness and cohesiveness of gels are inversely proportional to ash concentration [14,15]. Additionally, ashes from citrus wastes (tangerine peels) have been identified as a promising alternative for biodiesel production via alkaline transesterification [13].

Table 1. Chemical composition of citrus wastes.

Citrus Waste	Moisture (%)	Ash (%)	Non-Polar Solvent Extractables (%)	Polar Solvent Extractables	Cellulose/Glucan (%)	Hemicellulose (%)	Lignin (%)	Fat	Protein	Free Sugars	References
Citrus by-products	–	6.58 ± 0.11	–	25.04 ± 2.14	11.94 ± 0.16	6.50 ± 0.09 **	21.58 ± 1.45	2.08 ± 0.19	6.56 ± 0.31	–	[16]
Citrus pulp	–	1.7	3.9	–	16.2	13.8	1	–	7.9	41	[17]
Distilled kinnow peels	–	–	–	–	13 ± 0.8	8.3 ± 0.8	3.6 ± 0.4	–	–	–	
Distilled mosambi peels	–	–	–	–	21.2 ± 1.1	12.5 ± 0.6	5.1 ± 0.5	–	–	–	[18]
Distilled orange peels	–	–	–	–	24.6 ± 0.9	13.4 ± 0.7	6.5 ± 0.4	–	–	–	
Finisher pulp	–	2.81 ± 0.03	1.1 ± 0.1	56 ± 1	8 ± 0.9	5.74 ± 0.08	1.2 ± 0.5	–	–	–	[19]
Lemon Myrtle	7.41	4.88	–	–	–	–	–	–	–	–	[20]
Orange peel	8.71 ± 0.0	3.99 ± 0.04	3.79 ± 1.04	17.15 ± 1.73	34.22 ± 4.68	6.32	16.8	–	6.85	–	[21]
Orange peel	–	2.3–3.1 *	–	–	55.4–67.1 *	* 0.3–2.5 **	8.5–25.4 *	–	–	–	[22]
Orange peel	–	4.3	–	–	25.3	5.3	5.4	2.1	5.2	31.3	[23]
Orange peel	–	4.4 ± 0.1	4.1 ± 0.2	43.8 ± 0.7	8.8 ± 0.1	7.6 ± 0.4	2.4	–	–	–	[19]
Orange peel waste	14.28	–	–		9.32	32.7	13.68	–	–	–	[24]
Orange peel waste	–	–	–	–	20.45 ± 0.45	26 ± 2.82	2.75	12.02 ± 0.23	8.11 ± 0.13	–	[25]
Orange peel waste	79.1 ± 0.01	3.3 ± 0.20	–	–	9.2 ± 0.21	5.4 ± 0.19	1.2 ± 0.5	–	6.6 ± 0.30	50 ± 2.01	[26]
Orange peel waste	77.38 ± 0.36	2.1 ± 0.20	–	26.56	23.88 ± 0.50	14.15 ± 2.01	5.1 ± 2.44	4.6 ± 1.91	4.96 ± 0.20	–	[8]
Orange peel waste	78.53 ± 0.15	3.61 ± 0.20	–	–	30.17 ± 0.50	9.35 ± 4.36	5.07 ± 2.14	5.18 ± 1.91	4.68 ± 0.20	–	[27]
Orange peel waste	80	4.5	–	–	21.3	4.8	0.5	–	–	–	[28]
Orange peel waste	–	2.53 ± 0.19	–	27.61	28.78 ± 4.61	14.89 ± 4.45	4.62 ± 1.25	4.72 ± 0.10	–	–	[9]
Orange pomace	–	3.12 ± 0.01	3.6 ± 0.4	39 ± 4	13 ± 2	8.6 ± 0.4	2.62	–	–	–	[19]
Orange pulp	–	1.7–4 *	–	–	49.4–60.9 *	* 0.3–3.2 **	2.7–26.3 *	–	–	–	[22]
Orange wastes	81 ± 1.9	1	–	–	39 ± 2.4 ***	14.8 ± 0.2	1.2	2.3 ± 0.1	3.2 ± 0.1	50 ± 4.3	[29]
Undistilled kinnow peels	–	–	–	–	13.8 ± 0.9	8.4 ± 1.6	3.8 ± 0.3	–	–	–	
Undistilled mosambi peels	–	–	–	–	21.6 ± 1.1	12.9 ± 0.8	5.2 ± 0.5	–	–	–	[18]
Undistilled orange peels	–	–	–	–	24.6 ± 1.3	13.7 ± 0.7	6.8 ± 0.3	–	–	–	

* depending on the dilute acid treatment. ** reported as xylan content. *** cellulose + starch.

Polar solvent extractives from orange wastes are likely composed mainly of polyphenolic compounds (discussed below), amino acids, organic acids, and vitamins. In contrast, non-polar solvents are probably rich in terpenes such as limonene, the main component of citrus essential oils, and carotenoids [19,21]. In addition, due to its chemical composition (Table 1), citrus wastes are a valuable source of high-added valuable compounds that can be obtained via the biorefinery concept. In this context, the main structural components of citrus wastes consist of cellulose, hemicellulose, and lignin. According to the literature these components ranged from 8 to 55.4%, 0.3 to 26%, and 0.5 to 21.58%, respectively depending on the study. Pectin and protein are other important constituents, which are discussed in the subsections below.

Considering the concentration of the polysaccharides, this point is particularly significant during dark fermentation for volatile fatty acids (VFAs) production. High concentrations of organic matter concentrations and short fermentation times can favor the glycolytic pathway, allowing for VFA production, while inhibiting the methanogens [4]. Similarly, Giannakis et al. [23], reported that orange peels reach 31.3% of free sugars, a concentration that could be increased by ultrasound-assisted dilute acid hydrolysis [28]. In addition, other eco-friendly techniques such as semi-continuous subcritical hydrolysis have been applied using water under subcritical conditions to release fermentable sugars from citrus wastes [30].

Furthermore, these sugars can be utilized during fermentation by various yeast (e.g., *Pichia kudriavzevii*, *Kluyveromyces marxianus*, and *Saccharomyces cerevisiae*) for ethanol production [5,31], as well as for producing other valuable chemical compounds such as succinic acid, lactic acid, and biocombustibles [27].

The processing of citrus residues into high-value compounds within the biorefinery concept supports the circular economy [12]. Furthermore, since citrus wastes are rich in cellulose, they can be processed to obtain micro- and nano-cellulose for different applications as detailed below.

5. Phytochemicals Extracted from Citrus Wastes

The efficient valorization of citrus byproducts through a biorefinery approach involves the removal of polar and non-polar extractable compounds from citrus wastes, offering several advantages for the subsequent processing of solid waste [7,32]. Additionally, this process yields high-quantity and high-quality added-value phytochemicals for further applications. Utilizing agro-industrial by-products has been established as a sustainable practice for obtaining various native compounds from these residues, thereby addressing waste disposal problems by adding value to these wastes [3]. In this section, the recovery of several phytochemicals found in citrus by-products is presented.

5.1. Extraction of Essential Oil

Essential oils constitute an important bioactive fraction from diverse plant materials, including citrus wastes, and represent high added-value commodities due to various biological properties and aroma. Essential oils derived from citrus materials are among the most widely applied worldwide [33,34].

From the reviewed literature, different methodologies have been applied for obtaining essential oils from citrus wastes. The most commonly used methods include hydro-distillation, steam-distillation, and cold pressing [8,11,14,35], with cold pressing being the extraction technique that results in the lowest environmental impact [11]. Moreover, other traditional methodologies using non-polar solvents as extraction agents have also been utilized for essential oil recovery from citrus wastes. Due to its high positive Kow (water-octanol partition coefficient) and low polar index, the use of *n*-hexane as an extraction agent has been validated by several studies [4,6,28]. Moreover, as reported by González-Rivera et al. [36], essential oils can be obtained from citrus waste using alternative extraction methods such as microwave-assisted hydro-distillation (MWHD), ultrasound coaxial MW-assisted hydro-distillation (US-MWHD), and coaxial solventless MW-assisted extraction (SMWAE).

On the other hand, several citrus wastes including clementine, lemon, lime, orange, and citrus pruning leftovers, have been investigated for essential oil extraction using a biorefinery approach. Among these materials, orange waste has emerged as the most studied in recent years. This presents an opportunity for developing innovative research in this area for other understudied citrus materials. Different yields and chemical compositions have been reported for essential oils extracted from citrus wastes. In this context, yields can range from 0.12 to 4.19%. Kundu et al. [31] reported the highest yield (4.19 ± 0.11%) of essential oil recovery from Assam lemon peels. This high yield could be attributed to the prior enzymatic pretreatment at pH 4.5 for 12 h using fungal cellulose before the distillation process was applied to this by-product. Thus, this enzymatic pretreatment could potentially increase the essential oils yields for other citrus wastes. However, a deeper investigation in this regard is needed.

On the other hand, both yield and chemical composition of essential oils from citrus wastes, not only depend on the source, environmental, and geographical conditions but also on ripeness, storage process, and extraction techniques employed for extraction should also be considered [4,6,11,14,28,31,33,37]. Regarding chemical composition, it has been reported that citrus waste essential oils are mainly composed of monoterpenes, sesquiterpenes, and their oxygenated derivatives. The yields and the names of the main three components identified in the essential oils for each study (if provided) are presented in Table 2. It can be observed that limonene is the most abundant compound found in citrus wastes, representing up to 96% of all the components depending on the aforementioned factors. Although this high percentage is promising, low yields in the recovery of this compound have highlighted the need to enhance extraction techniques from citrus residues using mathematical tools and models for this purpose [38,39].

Table 2. Yields, main chemical components, and extraction methods of essential oils from citrus wastes.

Citrus By-Product	Essential Oil Yield (%)	Main Components	Percentage of Main Components	Extraction Methods	References
Assam lemon	4.19 ± 0.11	Limonene β-bisabolene Minor components (i.e., α-pinene, among others)	94.47 1.26 0.1–0.9	Distillation	[31]
C. aurantium pruning leftovers	0.66	Linalyl acetate Linalool β-fenchyl alcohol β-pinene β-ocimene	33.23 26.3 7.7 6.14 4.7	Hydro-distillation	[34]
C. limon pruning leftovers	0.85	Limonene (E)-citral β-pinene Sabinene Neryl acetate	25.52 15.55 11.21 8.42 8.81	Hydro-distillation	
C. reticulata pruning leftovers	1.5	Methyl N-methyl anthranilate γ-terpinolene Limonene *p*-cymene β-pinene	78.34 12.91 4.36 2.24 1.29	Hydro-distillation	
Citrus household kitchen residues	0.24	Limonene β-myrcene Linalool	94.41 ± 0.2 1.32 ± 0.04 1.30 ± 0.04	Distillation	[33]

Table 2. *Cont.*

Citrus By-Product	Essential Oil Yield (%)	Main Components	Percentage of Main Components	Extraction Methods	References
Citrus peel wastes	0.43	Limonene	–	Distillation	[40]
Citrus wax	–	Limonene	4	–	[12]
Flavedo orange peels	0.42	α-pinene β-myrcene Linalool	80–85 – –	Steam distillation	[14]
Ground mandora residues	0.43	Limonene β-myrcene Decanol	96.36 ± 0.09 1.35 ± 0.02 0.58 ± 0.01	Distillation	[33]
Non-ground mandora residues	0.19	Limonene β-myrcene α-pinene	96.70 ± 0.02 1.53 ± 0.02 0.34 ± 0.01	Distillation	
Orange flavedo	0.7 ± 0.01	–	–	Steam distillation	[26]
Orange juice waste	–	Limonene linalyl acetate α-pinene	89.65 4.51 1.4	Solid/liquid (hexane) extraction	[38]
Orange peel	1.03 ± 0.015	Limonene Myrcene	95.96 1.7	Solar hydro-distillation	[41]
Orange peel	1.05 ± 0.011	Limonene Myrcene	95.24 1.73	Conventional steam hydro-distillation	
Orange peel	1.16 ± 0.01	Limonene Valencene	95.2 0.2	Coaxial solventless MW-assisted extraction	[36]
Orange peel	1.17	Limonene	91.62	distillation	[9]
Orange peel	1.2 *	–	–	Solid/liquid (hexane) extraction	[6]
Orange peel	1.31	Limonene	–	Solid/liquid (hexane) extraction	[4]
Orange peel	1.53 ± 0.04	Limonene Valencene	95 0.4	Ultrasound coaxial MW-assisted hydro-distillation	[36]
Orange peel	1.55 ± 0.05	Limonene Valencene	94.4 0.3	Hydro-distillation	
Orange peel	1.57 ± 0.04	Limonene Valencene	94.7 0.3	Microwave-assisted hydro-distillation	
Orange peel waste	0.12 *	–	–	Solid/liquid (hexane) extraction	[28]
Orange peel waste	0.66 ± 0.05	Limonene β-myrcene γ-terpinolene Linalool	88.39 ± 1.33 2.28 ± 0.37 4.96 ± 0.83 3.51 ± 0.64	Steam distillation	[8]
Orange peel waste	0.84 ± 0.01	Limonene γ-terpinolene Linalool	88.39 4.96 3.51	Steam distillation	[27]

Table 2. *Cont.*

Citrus By-Product	Essential Oil Yield (%)	Main Components	Percentage of Main Components	Extraction Methods	References
Orange peel waste	1.14 ± 0.11	Limonene β-myrcene γ-terpinolene Linalool	91.27 ± 1.26 1.82 ± 0.19 2.76 ± 0.75 2.23 ± 0.35	Steam distillation	[8]
Ripe kaffir lime peels	–	Limonene β-pinene β-citronellol	24.62 16.71 8	Hydro-distillation	[35]
Unripe kaffir lime peels	–	β-pinene β-citronellol 4-terpineol	23.67 13.96 11.92	Hydro-distillation	
Waste lemon peel	≈0.05	Limonene	–	Microwave-assisted hydro-distillation	[37]

* under optimized conditions.

Recently, non-toxic green solvents such as natural deep eutectic solvents (NADESs), composed of hydrogen networking between a hydrogen acceptor (e.g., choline chloride) and a hydrogen bond donor (e.g., sugars or amino acids) [15], have shown to be suitable for extracting limonene from citrus waste (orange peels) using a biorefinery approach. This study reported a promising method for obtaining higher purity limonene using NADESs compared to hexane [42]. Thus, the combination of mathematical tools and NADESs could be a favorable strategy within a biorefinery system, aiming to reduce the environmental burdens derived from its implementation, mainly in the purification stage [11]. However, this suggestion needs to be validated by future investigations. Furthermore, limonene, a cycle monoterpene, has several functional properties, acting as a flavoring and antimicrobial agent, as well as having important applications in the food, cosmetic and pharmaceutical industries [4,6,34,35,38]. Therefore, considering that approximately 40.5 kg of limonene can be obtained from a ton of citrus wax (a residue from essential oil processing) [12], citrus waste essential oils and wax can be considered promising commodities for various industrial fields.

5.2. Extraction of Polyphenolic Compounds

Polyphenolic compounds are secondary metabolites with several bioactive properties found in plants, they have diverse applications across various industries. The extraction of phenolic-rich fractions from both pre- and post-essential oil extraction materials typically involves the use of polar solvents, including ethanol, methanol, water, and their combinations. Ethanol is particularly suitable for extracting these bioactive compounds from citrus wastes (such as orange peels) due to its ability to increase cell permeability by affecting the phospholipid bilayer, which enhances the solvent penetration and the extraction of phenolic compounds [7,18,21]. Moreover, various traditional and emerging technologies, such as maceration, Soxhlet, homogenization, subcritical water processing, supercritical fluid (CO_2), and ultrasonic-assisted extraction, have been reported in combination with these solvents for this purpose. Subsequently, the Folin–Ciocalteu method is commonly employed for quantification, while more specialized techniques such as Fourier transform infrared spectroscopy (FRIR), gas chromatography, and liquid chromatography have been employed to characterize these bioactive compounds [7,8,18,20,21,43].

In biorefinery systems, it has been reported that after the recovery of essential oils, solid citrus wastes still contain a phenolic-rich fraction, which can comprise more than 80% of polyphenolic compounds present in these plant materials [18]. In addition, total phenolic content (TPC) has been analyzed in essential oils from citrus wastes due to the removal of a fraction of these compounds during the extraction process [26,35]. Furthermore, it has recently been demonstrated that post-hydro-distillation wastewater contains significant amounts of polyphenolic compounds and flavonoids in various citrus pruning waste materials [34,44]. Similarly, in a previous study using a biorefinery approach conducted by García-Cruz et al. [12], polyphenolic compounds, among other phytochemicals, were identified in citrus wax waste. Since this residue is generated during the purification process of citrus essential oil, this study represents an important step towards establishing a circular economy for the valorization of this by-product.

In this context, the values of TPC reported in each study are shown in Table 3. The study conducted by Lamine et al. [34], reported the maximum TPC for citrus solid wastes, which were obtained from *C. limon*, *C. reticulata*, and *C. aurantium*, achieving values of 25.5 ± 0.5, 340 ± 0.95, and 350 ± 0.85 GAE per gram of citrus pruning wastes, respectively. Moreover, Sarkar et al. [18] reported TPC values of 132, 118.7, and 95.4 GAE per gram of undistilled kinnow, orange and, mosambi peels, respectively.

Table 3. Yields, main chemical components, and extraction methods of polyphenolic compounds from citrus wastes.

Citrus By-Product	Total Polyphenolic Content (GAE/g)	Main Components	Predominance (%) or Concentration	Extraction Method	References
C. aurantium post-hydrodistillation wastewater	26.30 ± 0.15	Hesperetin Benzoic acid	0.66 mg/g 0.08 mg/g	–	[34]
C. aurantium pruning leftovers	350 ± 0.85	Flavonoids	30.10 ± 0.45 **	Homogenization	
C. limon post-hydrodistillation wastewater	45.79 ± 0.34	4-coumaric acid Ferulic acid Sinapinic acid Isovanillic acid	2.83 mg/g 1.15 mg/g 0.51 mg/g 0.28 mg/g	–	
C. limon pruning leftovers	25.5 ± 0.5	Flavonoids	38.20 ± 0.80 **	Homogenization	
C. reticulata post-hydrodistillation wastewater	13.45 ± 0.45	Ferulic acid Caffeic acid Benzoic acid Protocatechoic acid	1.83 mg/g 0.71 mg/g 0.61 mg/g	–	
C. reticulata pruning leftovers	340 ± 0.95	Flavonoids	45.50 ± 0.09 **	Homogenization	
Citrus fruit processing wastes	–	Hesperitin Naringenin Nobiletin 3,5,6,7,3′,4′-hexamethoxyflavone 3,5,6,7,4′-pentamethoxyflavone	8.11 mg/g 5.76 mg/g 3.25 mg/g 3.0 mg/g 2.73 mg/g	Homogenization	[43]
Citrus paradisi L. peel	–	Neohesperidin Neoeritrocin Narirutin Naringin Hesperidin Tangeritin	0.03–0.09 mg/g # 0.03–0.16 mg/g # 0.28–0.70 mg/g # 18–28 mg/g # 0.23–0.74 mg/g # 0.09–0.07 mg/g #	Conventional solid-liquid extraction	[45]
Citrus paradisi L. peel	–	Neohesperidin Neoeritrocin Narirutin Naringin Hesperidin Tangeritin	0.04–0.16 mg/g # 0.05–0.18 mg/g # 0.42–0.98 mg/g # 24–33 mg/g # 0.72–1.14 mg/g # 0.01–0.02 mg/g #	Ultrasound assisted extraction	

Table 3. *Cont.*

Citrus By-Product	Total Polyphenolic Content (GAE/g)	Main Components	Predominance (%) or Concentration	Extraction Method	References
Citrus wax	–	3,7-dimethylquercetin 5,6-dihydroxy-7,8,3′,4′-tetramethoxyflavone 5-5′-dehydrodiferulic acid Tangeretin	1.05% 0.89% 0.58% 0.39%	–	[12]
Distilled kinnow peels	98.7	Flavonoids	32.8 **	Ultrasonic-assisted extraction	[18]
Distilled mosambi peels	78.1	Flavonoids	22.9 **	Ultrasonic-assisted extraction	
Distilled orange peels	97	Flavonoids	32.6 **	Ultrasonic-assisted extraction	
Kinnow peels	25.96–41.24 $	–	–	–	[15]
Lemon myrtle oil	–	Catechol *p*-cresol Gayacol Syringol	21.67% 4.17% 2.77% 2.69%	Pyrolisis	[20]
Mandarin waste	0.015	Rutin Catechin hydrate *p*-coumaric acid Isorhamnetin 3-O-rutoside Gallic acid	12 mg/g 6.56 mg/g 6.12 mg/g 5.29 mg/g 4.8 mg/g	Maceration	[46]
Orange peel waste	–	Hesperidin	3.50%	–	[25]
Orange peel waste	9–11	–	–	Ultrasonic-assisted extraction	[7]
Orange peels	–	Hesperidin Apigenin Naringenin	4.42–7.88 mg/g Φ 0.97–0.48 mg/g Φ 0–0.675 mg/g Φ	Homogenization	[9]
Orange peels	1.96–9.4 ± 0.35	Flavonoids Hesperidin Naruritin	0.12–3.70 ** @ 0.08–1.21 mg/g @ 0.08–0.24 mg/g @	Conventional steam hydro-distillation	[41]
Orange peels	2.13–9.7 ± 0.37	Flavonoids Hesperidin Naruritin	0.14–3.81 ** @ 0.1–1.9 mg/g @ 0.08–0.26 mg/g @	Solar hydro-distillation	
Orange peels	3.009 ± 0.245	–	–	Fermentation	[47]
Orange peels	3.4 ± 0.73–5.53 ± 0.43 ***	Hesperidin Narirutin	9.82–22.9 0.99–22.99 mg/g	Sequential subcritical water process	[21]
Orange peels	5.5–6.0 *	Quinic acid Hesperidin Hesperetin	72.50% 14.50% 4.90%	Ultrasonic-assisted extraction	[26]
Oranges waste	67–79 mM GAE ^ 2.17–2.47 mM GAE ^	Tannins Other phenolics	– –	High pressure	[32]
Ripe kaffir lime peel oil	15.76 ± 1.74	–	–	Hydro-distillation	[35]
Sour orange waste	0.021	Luteolin 7-O glucoside Ferulic acid Kaempferol 3-rutinoside-7-galactoside Myrcetin Isorhamnetin	8.58 mg/g 7.5 mg/g 5.11 mg/g 4.53 mg/g 3.54 mg/g	Maceration	[46]
Sweet orange waste	0.0423	Myrcetin Sinapic acid Apigenin Ferulic acid Amentoflavone	9.5 mg/g 7.64 mg/g 6.28 mg/g 3.75 mg/g 2.67 mg/g	Maceration	

Table 3. *Cont.*

Citrus By-Product	Total Polyphenolic Content (GAE/g)	Main Components	Predominance (%) or Concentration	Extraction Method	References
Undistilled kinnow peels	132	Flavonoids	47.4 **	Ultrasonic-assisted extraction	[18]
Undistilled mosambi peels	95.4	Flavonoids	34.1 **	Ultrasonic-assisted extraction	
Undistilled orange peels	12.48 ± 0.14	Flavonoids Hesperidin Naruritin	4.84 ± 0.026 ** $2.44 \pm 1.4\ 10^{-3}$ mg/g $0.041 \pm 6.4\ 10^{-4}$ mg/g	–	[41]
Undistilled orange peels	118.7	Flavonoids	41.7 **	Ultrasonic-assisted extraction	[18]
Unripe kaffir lime peel oil	16.17 ± 1.81	–	–	Hydro-distillation	[35]

* depending on the solid/liquid ratio. ** mg of QE/g of dry extract. *** depending on the treatment. $ depending on the NADE used for extraction expressed in grams of pectin. ^ Analyzed in the Hydrothermal pretreatment liquors. $^{\Phi}$ depending on the scenario evaluated. # depending on the experimental run. @ depending on the phase.

Ortiz-Sanchez et al. [8] noted the potential to obtain more than 11 g of polyphenolic compounds (expressed as hesperidin, identified as the most abundant polyphenolic compound present in orange peel wastes) per kilogram of this byproduct during a biorefinery process. According to Cho et al. [48], these yields could be improved by removing the essential oil and applying an enzymatic pretreatment using cellulases and pectinases. Similarly, a previous report disclosed the possibility of obtaining significant quantities of various flavonoids per kilogram of citrus fruit processing wastes through a simple, fast, and green method. These included 8.11 g of hesperitin, 5.76 g of naringenin, 3.25 g of nobiletin, 3.0 g of 3,5,6,7,3′,4′-hexamethoxyflavone and 2.73 g of 3,5,6,7,4′-pentamethoxyflavone [43]. This is in agreement with a more recent study aiming at promising a sustainable bioeconomy and agriculture, conducted by Lamine et al. [46], who reported high quantities of polymethoxy flavones and O-glycosylpolymethoxylated flavonoids in extracts from sweet orange, sour orange and mandarin residues. These bioactive compounds, obtained through a simple method (hydro-alcoholic homogenization), have been demonstrated to be effective as antimicrobial agents against Gram-positive and Gram-negative bacteria.

Since the industry is still immature and primarily influenced by costs associated with the implementation of biorefinery processes [42], the application of these simple methodologies could be advantageous for citrus waste valorization saving costs in its processing. Furthermore, NADESs have also been demonstrated to be suitable for polyphenolic extraction in a biorefinery system for citrus waste (orange peels) valorization obtaining higher or similar yields of these bioactive compounds with NADESs than those obtained with conventional solvent (acidified ethanol) [42].

Furthermore, catechol has been reported to increase approximately 1.5-fold in the bio-oil obtained after lemon myrtle pyrolysis when the process temperature increases from 350 to 550 °C. However, other lignin-derived phenolics, such as p-cresol and syringol decreased by degradation during this process [20]. Similarly, important amounts of polyphenolic compounds have been detected in pectin extracted from kinnow peels which could be an advantage for further application in functional food systems [15]. In the same vein, a study on a multi-product cascade biorefinery approach by Espinosa et al. [7], demonstrated that the incorporation of 5% of polyphenolic-rich extract from orange peel waste into poly(vinyl alcohol)(PAV)-based films can decrease their water vapor permeability. This is due to the formation of hydrogen bonds and hydrophobic interactions with PVA, reducing the number of free OH groups available to interact with water molecules. Moreover, a recent study by Santos et al. [19] confirmed further functionalization (by antioxidant capacity) of bioplastics formulated from different orange wastes by the presence of phenolic compounds, indicating their potential applicability as active packaging materials for oxidizable products.

Although it is evident that citrus wastes are rich sources of polyphenolic compounds with functional properties, most of the reviewed studies have focused solely on the extraction and quantification of these compounds from a polyphenolic-rich crude extract. Consequently, the recovery of polyphenolic compounds in their purified form (as a solid powder), as reported by Bautista-Hernández et al. [49], may be more suitable for the biorefinery concept of this plant material, as it could enhance the stability of these compounds for future applications. This suggests the potential for developing further studies in this area.

On the other hand, it has been reported that removing polyphenolic compounds is a crucial step prior to the production of ABE (acetone–butanol–ethanol) fermentation metabolites (i.e., butanol, acetone, ethanol, butyric acid, and acetic acid), and biohydrogen during a biorefinery process for the valorization of orange waste. This removal process improves the enzymatic hydrolysis of citrus wastes, facilitating subsequent fermentation [32]. This effect was recently confirmed by Ortiz-Sanchez et al. [9], who reported that the extraction of bioactive compounds (polyphenolic compounds) enhances enzymatic digestion, leading to a 205.26% increase in glucose production for anaerobic digestion. Additionally, this process was reported to increase biogas (methane) production in a sustainability analysis of orange peel biorefineries. Therefore, the removal of polyphenolic compounds not only allows the recovery of bioactive compounds for further application but also aids in the bioconversion of citrus waste metabolites (e.g., sugars) into biofuels.

5.3. Pectin Extraction

Pectin is a heteropolysaccharide predominantly found in the cell walls of plants, playing a crucial role in providing structural integrity to plant tissue. It is located within the primary cell wall and middle lamella, associated with cellulose and lignin [15,37,50]. This carbohydrate has numerous applications in the food industry due to its technological properties acting as a prebiotic, gelling, stabilizing, thickening, and emulsifying agent in food applications [15,26]. Usually, pectin is isolated from citrus wastes after juicing and essential oil extraction by acidic-assisted hydrolysis as shown in Table 4. However, it has been observed that during the distillation process for essential oil recovery, a loss in pectin content (up to 35%) can take place due to the solubility of this biopolymer during this process [18,51].

Table 4. Yields and extraction methods of pectin from citrus waste.

Citrus Waste	Yield (%)	Extraction Method	References
Assam lemon	12.67 ± 0.46	Enzymatic hydrolysis	[31]
Citrus peel wastes	30.5	Sulfuric acid hydrolysis	[51]
Citrus peel wastes	23.25	Dilute-acid hydrolysis	[40]
Citrus pulp	14.4	–	[17]
Distilled innow peels	11.6 ± 0.5	HCl acid hydrolysis	[18]
Distilled mosambi peels	14.9 ± 0.3		
Distilled orange peels	15.3 ± 0.6		
Finisher pulp	17.1 ± 0.6	Citric acid hydrolysis	[19]
Kinnow peels	16.93–35.66 **	Natural deep eutectic solvents	[15]
Orange albedo	19.36 ± 0.44	HCl acid hydrolysis	[14]
Orange peel	<1–24.7 ^	Sulfuric acid hydolisis	[22]
Orange peel	1.9	Fermentation	[47]

Table 4. *Cont.*

Citrus Waste	Yield (%)	Extraction Method	References
Orange peel	14.2 ± 1.3	Ultrasound coaxial MW-assisted hydro-distillation	[36]
Orange peel	15.7 ± 2.5	Coaxial solventless MW-assisted extraction	
Orange peel	15.9 ± 3.0	Microwave-assisted hydro-distillation	
Orange peel	17.4 ± 3.3	Hydro-distillation	
Orange peel	3.05	HCl acid hydrolysis	[52]
Orange peel	5	Microwave-assisted extraction	
Orange peel	0.47–8.26 #	Solar hydro-distillation	[41]
Orange peel	0.51–7.69 #	Conventional steam hydro-distillation	
Orange peel	19.62 ± 3.24	Subcritical water extraction	[21]
Orange peel	23.9 ± 0.3	Citric acid hydrolysis	[19]
Orange peel residues	17.6	HCl acid hydrolysis	[23]
Orange peel residues	≈19	Citric acid hydrolysis	
Orange peel residues	≈44	Sulfuric acid hydrolysis	
Orange peel residues	46.7	Oxalic acid hydrolysis	
Orange peel waste	15.85 ± 0.6	Citric acid hydrolysis	[53]
Orange peel waste	10.35	Citric acid hydrolysis	[27]
Orange peel waste (dry)	2.24	Citric acid hydrolysis	[8]
Orange peel waste (wet)	14.6		
Orange peels	NI	Sulfuric acid hydrolysis	[5]
Orange pomace	25.2 ± 0.6	Citric acid hydrolysis	[19]
Orange pulp	<1–23.7 ^	Sulfuric acid hydrolysis	[22]
Orange residues	43 (lab-scale)	sulfuric UADAH	[28]
Orange residues	45 (pilot-scale)		
Orange wastes	6–42 ***	Citric acid hydrolysis	[29]
Orange peel waste	≈8–22 *	HCl hydrolysis	[26]
Orange peel waste	≈19–32.6 *	Citric acid hydrolysis	
Undistilled orange peels	12.08 ± 0.7	–	[41]
Undistilled kinnow peels	17.8 ± 0.6	HCl acid hydrolysis	[18]
Undistilled mosambi peels	20.9 ± 0.4		
Undistilled orange peels	23.3 ± 0.8		
Waste lemon peel	15	Microwave-assisted hydro-distillation	[37]

* depending on the solid:liquid ratio. *** depending on the experimental run. # depending on the phase. ** depending on the NADESs used. ^ depending on the temperature and extraction time.

Strong acids such as sulfuric and hydrochloric acids are the most commonly mineral acids used for pectin extraction due to their ability to efficiently disrupt this polysaccharide [27]. However, their corrosive nature can raise environmental concerns [5,14]. In this context, some organic acids, such as citric and oxalic acids, have been successfully used for this purpose [23,26]. Concerning pectin yields, the reviewed literature indicates that they ranged from 2.24 to 46.7%, depending on extraction process parameters and source

(Table 4). Recently, Giannakis et al. [23], reported the highest values of pectin recovery from citrus wastes (orange peels), achieving 46.7% of this biopolymer using oxalic acid as an extracting agent. Similarly, in a previous study, Karanicola et al. [28] reported similar values of pectin recovery, reaching 43 and 45% of this polysaccharide. These results were attained under optimal conditions of ultrasound-assisted dilute acid hydrolysis (1.21% H_2SO_4, 5.75% solid loading, and 34.2 min process duration) using orange residues in lab- and pilot-scale systems, respectively. These findings are consistent with those reported by Giannakis et al. [23], who indicated that oxalic acid extracted similar amounts of pectin than sulfuric acid.

Furthermore, another organic acid, citric acid, has been demonstrated to be a better extracting agent to obtain higher amounts of pectin than mineral hydrochloric acid, extracting more than 32% of this hydrocolloid from dried orange peel waste at a solid/liquid ratio of 1:50 (*w*/*v*). This may be due to the easy access of the citric acid into the by-product [8,26]. These results were consistent with the study conducted by Giannakis et al. [23], who reported higher pectin yields using citric acid as an extracting agent compared to hydrochloric acid. Furthermore, other acid-free strategies such as microwave-assisted extraction have been implemented, allowing increases in pectin extraction yield by up to a factor of 1.64 compared to hydrochloric acid [23]. Furthermore, another study has reported lower extraction yields of pectin from orange peel waste using this organic acid as the extracting agent compared to those reported in the literature for mineral hydrolysis-assisted extraction. This difference was attributed to the specific conditions applied during the extraction process [27]. Moreover, a pectin with higher purity and lower degree of esterification can be obtained using hydrochloric acid [23,26]. Therefore, not only the source and extraction process parameters but also the physicochemical characteristics of the desired final product should be considered. Purification is primarily responsible for the highest environmental loads in different scenarios of citrus waste valorization from a biorefinery approach due to the energy required at this stage [11].

Recently NADESs, have also demonstrated suitability for pectin extraction in a biorefinery system of citrus waste (kinnow peels) valorization. In a study by Santra et al. [15], five carbohydrate- and acid-based NADESs were evaluated for pectin extraction. They found that the highest pectin yields were obtained using choline chloride–maltose (35.66 ± 2.23%) and choline chloride–acetic acid (33.73 ± 0.86%) as extracting solvents. In this context, the use of organic acids (citric and oxalic acids) and NADESs as pectin extracting agents could improve the process economics into a biorefinery approach for valorizing citrus waste with minimal or no environmental impact.

Temperature and extraction time on the pectin extraction yields are also important factors influencing pectin extraction yields. It has been reported that extraction processes at temperatures over 100 °C result in lower yields than those conducted at 94 °C, while an increase in extraction time also produces a similar effect. This reduction is attributed to the degradation of pectin at high temperatures (140 and 180 °C), as confirmed by FTIR assay [22]. In fact, pectin recovered from orange wastes has exhibited similar or better physicochemical and functional properties for food applications compared to commercial pectin [14,15,51]. This suggests that this pectin obtained through "cascade extractions" using a biorefinery approach to citrus wastes has the potential to be scaled up to an industrial level.

5.4. Micro- and Nano-Cellulose

After the removal of the aforementioned phytochemicals and prior to the implementation of fermentation processes, citrus wastes, being rich in cellulose, can be utilized for the recovery of microcrystalline and nano-cellulose for various applications. In this context, a study conducted by Espinosa et al. [7] implemented an economical and eco-friendly high-pressure homogenization treatment to isolate cellulose nanofibers from orange peel waste after cellulosic pulp production. They obtained higher yields of nanofibers compared to other agricultural residues, with the advantage of not requiring pretreatment. The obtained material exhibited favorable characteristics including low lignin content and high surface area, making it suitable for further application as a reinforcing agent in poly(vinyl alcohol)-based films for food packaging. Additionally, Sohni et al. [54] demonstrated that the removal of non-cellulosic constituents from orange peel waste led to microcrystalline cellulose with improved functional properties, such as holding capacity and potentially superior tensile strength when compared to untreated by-products. These recent studies provide a baseline for innovative research on the recovery and application of microcrystalline and nano-cellulose as reinforcing agents for packaging materials and food stabilizers. Furthermore, in an earlier study, Thulasisingh et al. [24] reported that due to their lack of toxicity, cellulose nanocrystals derived from citrus wastes could serve as potential drug carrier agents in the pharmaceutical industry.

5.5. Protein and Enzymes

The protein content in citrus waste ranged from 3.2 to 8.11% (Table 1). This includes membrane proteins resulting from membrane disruption, as well as other soluble non-membrane proteins such as hydrolytic enzymes such as lipases and pectinmethylesterase (PME). In this context, Okino-Delgado et al. [3] reported the potential to obtain native lipases from citrus byproducts, specifically orange waste, by incorporating the biorefinery concept into the juice industry. These lipases exhibited activity within a pH range of 6.0 to 8.0 and a temperature range of 30 to 80 °C, depending on the source variety (Natal, Hamlin, and Valencia) and type of residue used (peel, fruit, bagasse, and pulp). Such lipase potentiality can be used for application in areas such as bioremediation and biodiesel production. Likewise, a more recent study conducted by Panić et al. [42], disclosed the potential use of orange peels as a source of extracts presenting PME activity, which can be obtained with two cholinium-based NADESs with polyalcohol as a hydrogen donator (i.e., ChEg, choline chloride:ethylene glycol and ChGly, choline chloride:glycerol). Although lower volumetric activities of PME were recorded for ChEg and ChGly, ranging from 0.00023 to 0.00026 mL·min^{-1} (depending on the ratio used) compared to those obtained with phosphate buffer (0.00085 mL·min^{-1}), PME activity was more stable over time (30 days) in the extracts obtained with NADESs than those obtained with the buffer. Thus, NADESs, which have been demonstrated to be suitable solvents for the chemical extraction of different compounds such as polyphenols, pectin, and enzymes, seem to be more appropriate for a biorefinery approach due to the availability, low cost, biodegradability, and biocompatibility of their components.

5.6. Other Phytochemicals

In recent comprehensive research, Lamine et al. [34] applied a circular bioeconomy approach and reported the identification of various bioactive compounds using GC–TOF-MS-based metabolite profiling extracted from three different citrus pruning leftovers wastes, including *C. limon*, *C. reticulata*, and *C. aurantium*. The authors explored the possibility of obtaining amino acids (e.g., alanine and proline), organic acids (e.g., succinic and quinic acids), fatty acids (α-linolenic acid and palmitic acid), sterols (e.g., β-Sitosterol), tocopherols (α-tocopherol), and terpenoids (e.g., α-amyrin) from a water/chloroform/methanol (1 mL; 1:1:2.5 $v/v/v$) mixture extract of these residues. However, the recovery and application of these compounds remain unstudied, presenting an opportunity for innovative investigation in this field. Other compounds such as organic acids, alcohol terpenes, esters, and carbonyl compounds have been identified in a citrus waste brewing biocatalyst [55].

6. Added-Value Compounds Produced from Citrus Wastes

Essential oil, polyphenolic compounds, and sometimes pectin are removed from citrus waste to facilitate the production of other valuable compounds through different biotechnological processes, which can produce a wide range of marketable commodities and are important steps in biorefinery systems [9]. In this section, the production of added-value compounds from citrus by-products obtained through biotechnological strategies is reviewed. Additionally, some chemical synthesis reactions that have been conducted to obtain bioactive compounds from these residues also are incorporated.

6.1. Bioethanol Production

Bioethanol has gained popularity as a potential substitute for gasoline over the last few decades. It is produced through the fermentation of sugars by the action of yeast. Since citrus by-products are cellulose-rich materials, pretreatment is necessary to break down long chains into fermentable sugars. In this context, in the study conducted by Kammoun et al. [56], the authors estimated an ethanol production of 0.20 $MT{\cdot}y^{-1}$ from orange peel, which is only lower than the production from wheat straw among the agricultural residues analyzed in their work. These findings were corroborated by Sarkar et al. [18], who reported lower ethanol production from fresh materials (2.0–2.7 $g{\cdot}L^{-1}$) compared to distillated by-products (3.9–7.9 $g{\cdot}L^{-1}$). Since the previous extraction of polyphenolic compounds did not statistically change the proportion of cellulose compared to fresh material, this difference might be attributed to the inhibition of limonene and phenolic compounds. The ethanol yield of distillated orange peels (7.89 $g{\cdot}L^{-1}$) was 2.5 times greater than the fresh peels, due to limonene removal during distillation.

Due to the antimicrobial properties of limonene, the removal of essential oil must be performed prior to fermentation [5,18]. Several pretreatments have been reported, being acid hydrolysis the most common. After pretreatment, the fermentation step takes place. There are important differences in the fermentation process, such as the microorganisms used, the type of fermentation, and the temperature range. A summary of the principal factors is shown in Table 5. It can be observed that the most commonly reported microorganism for bioethanol production is *Saccharomyces cerevisiae*. However, Patsalou et al. [5] evaluated the bioethanol production with three yeast strains using orange peel wastes obtained after a dilute acid hydrolysis (5% of H_2SO_4) at different thermal conditions (108, 116, 125 °C). They found that the thermotolerant strain of *P. kudriavzevii* performed the best ethanol production, achieving production of 5.8 $g{\cdot}L^{-1}$ using the waste obtained from the pretreatment of 116 °C for 10 min. Furthermore, the authors noted that incorporating an enzymatic pretreatment stage enhanced ethanol production from 0.32 g $ETOH{\cdot}gTSC^{-1}$ (total sugar consumed) to 0.42 g $ETOH{\cdot}gTSC^{-1}$, yielding 9.2 $g{\cdot}L^{-1}$. Recycling process water led to a three-fold increase in ethanol concentration, reaching 30.7 $g{\cdot}L^{-1}$. On the other hand, Vaez et al. [22] analyzed ethanol production within a zero-waste biorefinery scheme. Their most significant contribution is the elimination of enzyme hydrolysis in the pretreatment process, making it more cost-effective. They focus on identifying the optimal conditions for producing different products, concluding that the best pretreatment conditions for pectin production do not coincide with those optimal for ethanol and biogas production.

Table 5. Ethanol production from citrus wastes.

Citrus Waste	Pretreatment	Microorganism	Fermentation Type	Temperature Range (°C)	Yield	References
Assam lemon waste	Enzyme hydrolysis	*Saccharomyces cerevisiae* and *Pichia kudriavzevii*	Partial simultaneous saccharification and co-fermentation	35	12.16 (%)	[31]
Citrus peel waste	Acid and enzyme hydrolysis	*Pichia kudriavzevii*	Batch	42	30.7 $g{\cdot}L^{-1}$	[5]
Citrus peel waste	-	*Saccharomyces cerevisiae*	Batch	37	63 $g{\cdot}L^{-1}$	[51]

Table 5. *Cont.*

Citrus Waste	Pretreatment	Microorganism	Fermentation Type	Temperature Range (°C)	Yield	References
Clementine peel waste	Ultrasound-assisted extraction	*Saccharomyces cerevisiae*	Simultaneous saccharification and sermentation	37	1.97 g·L^{-1}	[39]
Clementine peel waste	Ultrasound-assisted extraction	*Saccharomyces cerevisiae*	Sequential hydrolysis and fermentation	37	1.39 g·L^{-1}	
Kinnow peels	Hydro-distillation	*Saccharomyces cerevisiae*	Batch	30	5.08 g·L^{-1}	[18]
Mosambi peels				30	7.16 g·L^{-1}	
Orange peel				30	7.89 g·L^{-1}	
Orange peel	Dilute acid	*Saccharomyces cerevisiae*	Batch	32	81.5 (%)	[22]
Orange pulp	Dilute acid	*Saccharomyces cerevisiae*	Batch	32	82.9 (%)	
Orange waste	Hydrothermal	*Clostridium acetobutylicum*	Batch	37	42.3 (g·kg^{-1})	[32]

Several factors can affect the extraction processes of the different biomolecules aforementioned, as well as the bioethanol production. For example, moisture and solid-liquid ratio can significantly affect the recovery of pectin from orange peels [8,28]. In this context, Karanicola et al. [28], have expressed the importance of applying a system engineering approach to optimize process productivity in a biorefinery approach. Thus, diverse mathematical and modeling tools have been applied to evaluate the recovery and production of the added-value compounds from citrus wastes. In this line, studies focused on the optimization of ethanol production. Kyriakou et al. [51] developed a method to enhance ethanol production through fermentation with *S. cerevisiae* utilizing a biochar-based biocatalyst (BBB). Their results indicated that the BBB could be successfully employed for at least three consecutive batches with equivalent performance, demonstrating its durability. In terms of ethanol production, two of the three BBB batches achieved better sugar conversions, reaching up to 80% within 13 h, compared to free cell fermentation. Furthermore, Kundu et al. [31] reported the valorization of Assam lemon by-products through a biorefinery system. They extracted essential oils and pectin, and the remaining biomass was subjected to a partial simultaneous saccharification and co-fermentation process for ethanol production. This type of processing overcomes the limitations of separate hydrolysis and saccharification. They achieved a yield of 12.16% (*v*/*v*) using a solid loading of 30% (*w*/*v*) at temperature of 35 °C with a fermentation time of 24 h.

Several studies offer valuable insights into the utilization of citrus wastes for more sustainable bioethanol production. Saadatinavaz et al. [32] provide a broad perspective on biorefinery, highlighting the importance of optimizing pretreatment, detoxification, and the potential for co-producing multiple biofuels. This comprehensive strategy holds promise for the sustainable valorization of orange waste and other agricultural by-products, contributing to more sustainable biofuel production. In this sense, Machin-Ferrero et al. [57] perform a life cycle assessment within a circular economy context for a zero-waste refinery concept. They found that implementing circular economy strategies and adding value to waste can sometimes be counterproductive to environmental goals if not designed and implemented strategically. In addition, studying the life cycle of citrus residues allows for the evaluation of environmental impacts based on the multiple extractions to improve energy efficiency. This should be considered an important step in the implementation of a biorefinery system for citrus waste valorization [58,59].

Therefore, an effective implementation of the biorefinery concept with ethanol production should consider different operational conditions, such as microorganism strain, retention time, and temperature range. In addition, an environmental impact analysis is necessary to ensure the adoption of the best practices. Furthermore, it is recommended to evaluate this process in terms of economic and practical viability, as citrus are seasonal products.

6.2. Biomethane Production

Biomethane production through anaerobic digestion supports the concept of a zero-waste biorefinery, as all non-valorized materials can be converted into biogas and subsequently into energy. Anaerobic digestion relies on a consortium of microorganisms, which are known to be inhibited by the presence of limonene. Consequently, the presence of limonene poses a significant challenge to the anaerobic digestion of citrus waste. Several studies have analyzed the effect of limonene on the digestion of orange peels [4,5,27,60]. These studies found that the prior removal of essential oils improves biogas production, as well as methane concentrations and yield. Conversely, the removal of cellulose has a negative impact on methane production [8].

It is important to note that, while numerous studies have analyzed ethanol and methane production, only Saadatinavaz et al. [32] have examined these processes sequentially. The authors reported that the biogas obtained after the anaerobic fermentation consisted of between 60 and 70% methane, depending on the experiment conducted. The highest yield of methane production (162 NmL·g^{-1} volatile solids) was recorded after 45 days of anaerobic digestion of orange waste obtained from enzymatic hydrolysis pretreated residues (hydrothermal pretreatment) at 100 °C for 30 min. However, higher yields of this biogas (194 NmL·g^{-1} volatile solids) were obtained from the untreated residues, which was attributed to the removal of hemicellulosic sugars and other biodegradable materials during the pretreatment and enzymatic hydrolysis processes. Furthermore, Ortiz-Sanchez et al. [8] proposed an approach based on experimental data, simulation, and optimization to identify the best biorefinery configuration including a superstructure for methane production. The authors reported that the results of the proposed methodology highlighted the importance of contextualizing the possibilities for upgrading biomass, as most processes and products described in the literature do not consider the specific context of the facility.

Another crucial aspect of the zero-waste biorefinery concept is the environmental impact and optimal residue management. In this context, Battista et al. [4] analyzed the pyramidal hierarchy of residue management. They implemented the optimization of essential oil from orange peels, in order to reduce the energetic and environmental impact associated with the use of *n*-hexane as an extracting solvent. Additionally, they demonstrated that limonene did not affect the final yields of methane production, which is a relevant finding for reducing environmental burdens during citrus waste valorization. However, the removal of limonene favored a quicker hydrolysis and conversion into methane of both sugars and other carbohydrates. Moreover, Joglekar et al. [61] conducted a life cycle assessment (LCA) of citrus waste biorefinery and identified hydrolysis and flashing as the most significant contributors to the global warming potential of the biorefinery configuration. Additional studies have examined the environmental impact of methane production using life cycle analysis and circular economy approaches [57,62]. From these analyses, it was found that agrochemicals make up 60% of the eleven categories examined, and implementing circular economy principles does not necessarily lead to better environmental outcomes. Furthermore, it can be concluded that processing orange and lemon peels in a biorefinery with anaerobic digestion is a better environmental option than the current practice of disposing of residues on land.

6.3. Production of Volatile Fatty Acids and Biodiesel

Volatile fatty acids (VFAs) are carboxylic acids of 2–6 carbon atoms that have been adopted for various applications in the food and farming industries. Recently, citrus wastes have been explored as a substrate for VFA production using a biorefinery approach. Battista et al. [4] reported that up to 35% of total VFAs can be obtained per gram of the total solids from orange peels at a total solids concentration of 15% (obtained after the extraction of the essential oils) and after 5 days of fermentation. They found that the yields of different VFAs such as acetic, propionic, butyric, and caproic acids, ranged from 20%, 4%, 14%, and 0% to 79%, 15%, 72%, and 1%, respectively, depending on the total solid (10 or 15%) and the fermentation time (3, 5 or 7 days). Earlier, Rizzioli et al. [6] investigated the valorization of orange peels at the laboratory scale. The authors reported the potential of this by-product to recover VFAs (acetic and formic acids), achieving yields up to 43% of total VFAs per gram of the total solids of orange peels. This yield was higher than those reported in the previously mentioned study, and this effect was attributed to the operation conditions, specifically continuous agitation, which improved heat and mass transfer in the reactor used. Additionally, this process was more efficient, as it used lower solids (10%) and shorter fermentation time (5 days), making it more suitable for a biorefinery system.

On the other hand, biodiesel is defined as mono-alkyl esters of vegetable oils or animal fats resulting from the transesterification process of these oils and fats [12]. In this sense, as aforementioned, citrus wax can serve as a source of polyphenolic compounds, but it can also be considered a raw material for producing fatty acid methyl esters (FAMEs). In their study, García-Cruz et al. [12], reported the possibility of obtaining FAMEs through the acid transesterification of citrus wax, yielding these compounds at a rate of 3.03%. Among them, hexadecanoic acid methyl ester constitutes 0.32% of the biodiesel obtained from this by-product. Moreover, investigation into bio-oil production via pyrolysis of solid waste residues from Lemon Myrtle resulted in the production of esters such as dodecanoic acid methyl, indicating the potential of this by-product for biodiesel production [20]. Furthermore, the utilization of orange peel residues in combination with spent coffee grounds has also been evaluated after the enzymatic hydrolysis for the production of microbial oil, which could potentially be used for biodiesel production [23]. While the potential for utilizing citrus wastes for biodiesel production has been disclosed, the research conducted so far has been only at a basic level. Therefore, deeper knowledge of this field is necessary.

6.4. Production of Microbial Enzymes

Microbial enzymes play an important role in various industrial sectors; therefore, the exploration of agroindustrial residues for their production has gained attention as a means of saving production costs. In this context, in their exploratory study, Lima et al. [16] investigated the co-production of a red colorant and different enzymes (endo-glucanase, β-glucosidase, and xylanase) under a submerged cultivation system using citrus by-product without pectin at two concentrations (56.12 and 28.0 $g \cdot L^{-1}$) and times (168 and 336 h) with the supplementation of monosodium glutamate, glucose and a salt mixture. The authors informed that different levels of enzymatic activities were recorded ranging from 0.04 to 0.20 $U \cdot min^{-1}$ for endo-glucanase, from 0.042 to 2.811 $U \cdot min^{-1}$ for β-glucosidase, and from 0.155 to 0.868 $U.min^{-1}$ for xylanase from filamentous fungi *Talaromyces amestolkiae*. These levels varied according to the experiment conducted, being the β-glucosidase which presented the highest activity (2.8 $U \cdot min^{-1}$). This could be related to the better accessibility to the cellulose and low viscosity of the cultivation medium, which could improve enzyme production. This finding aligns with the study conducted by Sohni et al. [54], which demonstrated that the removal of non-cellulosic constituents (pectin) from citrus wastes enhances the recovery and production of other compounds with added value for the industry within a biorefinery framework. The study of microbial polysaccharide hydrolases remains relevant as they facilitate the conversion of indigestible carbohydrates into digestible substances. In this context, citrus waste has also been explored as a reservoir of pectolytic bacteria with successful results [63]. In addition, fungal pectinases have been successfully produced by solid-state fermentation on a pilot scale using a mixture of citrus waste and sugarcane bagasse [17]. Considering that microbial pectinase accounts for 25% of global food and industrial enzyme sales, this could be an efficient step towards biorefinery integration [63].

6.5. Production of Levulinic Acid

In terms of compound synthesis, citrus waste has been explored for obtaining different compounds for industrial applications. In this context, levulinic acid is primarily derived from sugars such as fructose and glucose through dehydration processes. Citrus waste, being rich in cellulose, has also been investigated for levulinic acid production via acidic-catalyzed hydrothermal conversion. Cellulose can undergo depolymerization and dehydration to produce furanic intermediates such as 5-hydroxymethyl-2-furaldehyde (5-HMF) and furfural. Subsequent rehydration of 5-HMF leads to the production of levulinic and formic acids in equimolar amounts [64,65]. Therefore, citrus waste holds potential as a feedstock for this process in a biorefinery system. Licursi et al. [64] reported a maximum yield of 22% for the production of levulinic acid from exhausted lemon peels (a by-product of the "Limoncello" liqueur production). This yield was higher than that obtained from other agricultural wastes, such as coffee silverskins. This yield was achieved after a preliminary hydrolysis pretreatment of 2 h using a solid/liquid ratio of 5% and 3.36% HCl at 120 °C. As previously mentioned, the application of mathematical tools can enhance the extraction and production of desired compounds. In this regard, a recent study conducted by Jeong [65] investigated the optimization of levulinic acid production from orange peel waste. The authors reported levulinic acid yields ranging from 14.34 ± 0.21 to 18.18 ± 0.20%, depending on the experimental design run. They concluded that under optimized conditions of acidic-catalyzed hydrothermal conversion (10% of dry biomass, 0.3% of H_2SO_4, at 185 °C for 30 min), a yield of 17.13 g of levulinic acid can be achieved, translating to 46.93 kg of levulinic acid from 1 ton of fresh orange peel waste. Given that levulinic acid is a versatile compound with multiple applications across various industries, including chemistry to energy and agriculture, its production from citrus waste could be highly profitable within a biorefinery framework.

6.6. Other Added-Value Compounds

As with levulinic acid, citrus waste can be utilized for the synthesis of other bioactive molecules and isomers [25,42]. For example, in a recent study, Baglioni et al. [25] demonstrated the possibility of using orange peel waste as a sugar donator in the synthesis of 4-methylumbellipheryl rutinoside and glyceryl rutinoside through biosynthesis. This process involved the fungal diglycosidase α-rhamnosyl-β-glucosidase I from *Acremonium* sp., highlighting the advanced potential in valorizing this citrus by-product. In the same way, the potential of the citrus waste (orange peel) for producing mannooligosaccharides (MOS) through a hydrolytic-based process has been disclosed. Zhou et al. [66] reported the production of 17.1 $g{\cdot}L^{-1}$ of MOS through the action of a β-mannanase expressed in the recombinant strain of *Trichosporonoides oedocephalis*. Since these compounds can act as probiotic and antioxidant agents in humans and animals, this study is relevant for biorefinery systems. In another study involving the production of added-valued compounds from citrus wastes, Santra et al. [15] investigated the production of lactic acid using a secondary waste product of kinnow fruit peels (kinnow pectin effluent, KPE), which resulted from the NADESs-based pectin extraction, within the framework of the circular economy concept. They reported that higher yields of lactic acid were obtained with the KPE obtained from the pectin isolation NADESs formulated with carbohydrates compared to those obtained from KPE using NADESs-based acids. Since the integral biorefinery approach of citrus waste valorization is expected to reduce the environmental burdens, there is a need to explore the exploitation of other secondary wastes for the recovery and production of additional high-value commodities within a biorefinery system. Moreover, Patsalou et al. [33,40] explored the production of other organic acids through a biorefinery conversion of citrus waste (mandora residues) hydrolysates into succinic acid using *Actinobacillus succinogenes*. It was demonstrated that after the extraction of the essential oil and pectin, hydrolysates of mandora residues can be fermented by *A. succinogenes* to obtain up to 10 kg of succinic acid representing an attractive alternative for citrus waste valorization.

7. Concluding Remarks and Future Trends

Citrus waste can be processed within a biorefinery framework. A classification was conducted between compounds reported as extracted and the value-added products produced from citrus waste. The studies reviewed in this paper have demonstrated the technical, sustainable, and economic feasibility of managing these wastes in a biorefinery. Some of them analyze different variables to achieve better yields of various components. The primary focus of the reviewed research encompasses laboratory studies thus far. However, further research is necessary to ensure the scalability of the process, given the challenge of the seasonal availability of the waste. Moreover, the sequence of citrus waste refinement needs further investigation. A relevant aspect, the extraction of essential oils should precede the production of value-added components, but optimal refining pathways need to be explored. Additionally, mathematical modeling and process simulation are seen as tools to advance and realize the findings of the reviewed research. Therefore, although technical feasibility has been demonstrated at the laboratory level, greater efforts by the scientific community are needed to propose viable industrial-scale biorefinery schemes.

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