

Review

Citrus Seed Waste and Circular Bioeconomy: Insights on Nutritional Profile, Health Benefits, and Application as Food Ingredient

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Abstract: *Citrus* fruits are widely grown, processed, and distributed in more than 140 countries, with annual global production exceeding 124.3 million metric tons. This substantial consumption generates significant organic waste, accounting for approximately 50–60% of the total fruit mass, primarily in the form of peel, pulp, and seeds. Often discarded or reused as animal feed, these wastes contribute to significant environmental pollution and economic losses. Therefore, the valorization of these by-products represents an important opportunity to mitigate these challenges and improve the sustainability of the *Citrus*-related industry. This review highlights *Citrus* seed waste concerning its invaluable bioactive compounds, including fatty acids, phenolic compounds, limonoids, dietary fibers, vitamins, and carotenoids. Chemical compositions of *Citrus* seed biowaste differ depending on a variety of factors, such as *Citrus* variety, fruit maturity, environmental conditions, waste storage conditions, and extraction methods. The extraction and purification of phytochemicals from *Citrus* seed biowaste are one of the major procedures for valorizing waste. The two types of effective extraction methods are traditional (conventional extraction) and innovative (green extraction). Furthermore, *Citrus* seeds have been demonstrated to exhibit several biological activities and health-promoting properties including antioxidative, anti-inflammatory, and anti-cancer activities. Therefore, these wastes are safe and beneficial compounds used in the production of functional foods, nutraceuticals, pharmaceuticals, and cosmetics. A conclusion can be reached by emphasizing the abundance of bioactive compounds in *Citrus* seed wastes, which makes them an excellent opportunity for increased environmental and economic utilization.



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1. Introduction

Citrus sp. or “citrics”, belonging to the Rutaceae family, are among the most important fruits produced worldwide [1–4]. *Citrus* species are believed to have originated from Southeast Asia, in Northeastern India, Myanmar, and China. The most commercialized *Citrus* species are sweet orange range (*Citrus sinensis* (L.) Osbeck), sour orange (*Citrus aurantium* L.), mandarin (*Citrus reticulata* Blanco), lemon (*Citrus limon* (L.) Osbeck), lime (*Citrus aurantifolia* (Christm.) Swingle), pomelo (*Citrus maxima* (Burm.) Merr.), and grapefruit (*Citrus paradisi* Macfad). Other relevant species with relatively minor commercial relevance include yuzu (*Citrus junos*), kumquat (*Citrus japonica*), bergamot (*Citrus bergamia*

Risso), or citron (*Citrus medica* L.) [1,5–7]. With an annual production estimated at 124.3 million tons, more than 140 countries of the world are *Citrus* producers, Asia being the first continent, followed by Africa [1,8]. *Citrus* fruits are a rich natural source of vitamin C (ascorbic acid), carotenoids with pro-vitamin A (namely β -cryptoxanthin), and vitamin B9 (folic acid), as well as being an excellent source of dietary fiber and antioxidants, namely phenolic compounds. More than 80% of the *Citrus* production is used in the manufacturing of processed items, with the main products being juice, marmalade, jam, and jellies [7,9,10]. The juice-processing industry generates around 10 million MT of waste, which represents 50% of the mass of fruits. These wastes are made up of 20 to 40% of seeds, 50 to 55% of peels, and wastewater [2]. However, *Citrus* wastes are considered a potential source of bio-ingredient intended for many applications. The processing of this fruit generates a huge quantity of waste rich in extractable bioactive compounds that have antimicrobial, antioxidant, and immunostimulant properties [11]. In this sense, extensive research has been conducted in the last decades on *Citrus* peels regarding the study and characterization of its bioactive compounds and properties, being the major waste derived from *Citrus* processing. On the other hand, *Citrus* seeds have received less attention, partly due to the processing. In fact, the seeds of *Citrus* fruits are usually discarded as waste because they are thought to be of no use [2,12]. Nevertheless, the *Citrus* seed waste antioxidant properties may be related to the diversity of its bioactive composition phytochemicals, such as essential oils (EOs), ascorbic acid, sugars, carotenoids, flavonoids, coumarins, limonoids, dietary fiber, polyphenols, phenolic acids, and trace elements [2,13]. Seeds are fundamentally composed of nitrogen-free extract, lipids, crude protein, and fiber [9]. Moreover, seeds have been found to have the highest concentration of limonoids, with a content of 10.1 g/kg, with limonin being the predominant compound at 5.3 g/kg, whereas flavonoids are typically present in quantities comparable to those found in juice, at 9.9 g/kg [14]. *Citrus* seeds' bioactive compounds are a source of natural ingredients that can be used in food industries for the formulation of nutraceuticals, functional foods, seed meals, antioxidant preservatives, and oils. They have also gained attention in pharmacological industries for developing, preventing, or treating against many non-communicative diseases and inflammation [15–17]. They also have a potential application in biodiesel, biosorbent development, cosmetics, and bio-food enhancement formulation [1,12]. For example, one study found that *C. reticulata* had a fatty acid profile of 67.4% unsaturated fatty acids (UFA) and 32% saturated fatty acids (SFA). The major components were palmitic acid (26.9%), oleic acid (25.5%), and linoleic acid (37.5%) [12]. Furthermore, *Citrus* seeds show a good nutritional composition. The macronutrient evaluation of dehulled and whole sweet orange seeds displayed a content of 54.2% fat, 28.5% carbohydrate, 5.5% crude fiber, 3.1% crude protein, and 2.5% ash [18]. Regarding the content of amino acids in *Citrus* seeds, 18 have been reported, with arginine, glutamic acid, and aspartic acid being the most abundant, comprising 14.41% to 19.33% of the total amino acids. The same study concluded that the total content of essential amino acids was comparable with the FAO/WHO standards, between 35.16 g/16 g N for orange seeds and 36.66 g/16 g N for *Citrus* seeds. Yet the levels of tryptophan are low, with values of 0.19 g for citron and 0.08 g for mandarin oranges [15]. The *Citrus* seeds' lipids present also very good properties and profiles. Their acid value is ranging between 0.5 and 2.2 mg KOH/g of oil., while their iodine and saponification values are, respectively, estimated in the following ranges: 99.9–110.0 and 180.90–198.90. The lipid characterization of *Citrus* seeds crude oil revealed the presence of different classes of oil such as free fatty acids, phospholipids, monoglycerides, diglycerides, triglycerides, and sterols. The *Citrus* seed oil is mainly composed of unsaturated fatty acids (between 33.2 and 38.4%), among which oleic and linoleic acid occupied the first place with a composition varying respectively between 22.3–26.0% and 2.6–9.6%. This oil is also a source of saturated fatty acids like stearic and palmitic acid. Thus, regarding the lipid profile of *Citrus* seed oil, it could be used for crude consumption in a salad, for cooking, or to produce margarine. On the other hand, its micronutrient composition shows that 100 g of the dried sample contains 160 mg of potassium, 136 mg of calcium, 7.5 mg of sodium, and 0.42 mg of iron [15,19].

The extraction yield of *Citrus* seeds oil and phytochemical compounds depends not only on the variety, origin, and growing conditions of *Citrus* trees, but also on sample-preparation conditions, particle size, the extraction method, the applied conditions, and the type and concentration of solvent. Although the bioactive compounds of the *Citrus* seed can be extracted by conventional methods like solvent extraction, distillation, and maceration, to both preserve the environment and the bioactive compounds of interest while obtaining the maximum of extractable compounds, novel and greener extraction methods are recommended [1,9,20]. For this purpose, innovative extraction methods like ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), pressurized liquid extraction (PLE), pulse electric field extraction (PEF), and supercritical fluid extraction (SFE) using CO₂ as solvent are suggested to obtain better recovery results, with each technique presenting their specific advantages but also some disadvantages [20–24].

Citrus seed waste is reported to contain bioactive compounds that may have significant cancer-preventive effects on skin and breast cancer [23,25]. In addition, this extract could help in the management of type I diabetes due to its lowering of blood glucose and lipid ability [1]. Also, the phenolic compounds of *Citrus* seeds have excellent antibacterial activity against targeted bacterial species, thus being a natural alternative source of ingredients for therapeutic purposes [26,27]. Likewise, with the resurgence of antibiotic resistance, natural *Citrus* seeds waste bioactive ingredients could therefore play an important role in the pharmaceutical industry to solve this serious global problem while also being a green processing technique with less harmful impact on the environment [28]. In food industries, the use of chemicals preservatives is subject to harmful effects on human health. So, for consumer safety, there is a growing demand for efficient food preservatives from natural sources [29]. Extracts from *Citrus* fruit seed waste contain numerous phytochemicals and bioactive compounds, making them valuable to the *Citrus* fruit industry and to manufacturers of food preservatives. These extracts can be incorporated into biodegradable films to reduce plastic pollution [4]. They may also serve as ingredients in functional foods or food additives. By valorizing *Citrus* seed waste, the food industry can capitalize on the health benefits of bioactive compounds and essential fatty acids to meet growing consumer interest in wellness and premium foods [9] *Citrus*. Thereby, in the present article, the nutritional and phytochemical composition of *Citrus* seeds are described, also reviewing conventional and innovative extraction techniques to obtain extracts of said phytochemicals, as well as discussing the potential industrial applications in relation to their composition and described biological properties.

2. Literature Search and Selection Methodology

The search methodology for literature compilation included a search strategy through PubMed, ScienceDirect, Scopus and Google Scholar on *Citrus* seed characterization and extraction methods. Keywords such as “*Citrus*”, “bioactive compounds”, and “extraction” (in various combinations) were chosen to filter the search. Inclusion criteria included “studies published in English”, “have been published during the past two decades (2004–2024)”, “publication type: article, review, or book chapter” or “include keywords: *Citrus*, bioactive compounds, extraction, yield, and biological properties”, among others. Findings in each study were sorted by species, extraction method, and operational conditions using a standardized data-extraction form. This review format is intended to compare conventional and advanced extraction techniques.

3. Bioactive Compounds of *Citrus* Seeds

There is potential for seeds to provide affordable and widely available bioactive compounds for use in food and pharmaceuticals (such as natural antioxidants). Consumption of seeds would also reduce the amount of waste generated by the agri-food industry on an annual basis [16]. This section reviews *Citrus* seeds based on their phytochemical composition.

3.1. Essential Oils, Sterols, and Fatty Acids

The essential oils of *Citrus* fruits are volatile aromatic compounds formed by the combination of secondary metabolites [30]. *Citrus* seeds are considered reliable sources of essential oils based on their variety. It is estimated that *Citrus* seeds contain approximately 20–40% oil [13]. Oils produced from *Citrus* seeds have been identified by their composition of saturated fatty acids (32%) and unsaturated fatty acids (67%). In the seed oils of sweet orange and grapefruit, as well as those of mandarin, most of the acids are palmitic, oleic, and linoleic, with comparatively little stearic and linolenic acids [12,13,31,32]. The highest oil quantity among *Citrus* seed varieties was in lemon (78.9%), followed by sweet orange (51.8%), blood orange, bergamot, and bitter orange (26%). They also noted that linoleic acid was a remarkable fatty acid in all analyzed oil seeds [32]. The fatty acid profile of acid lime and sweet orange seed oils was evaluated [33]. Unsaturated fatty acids are abundant in these oils. Linoleic acid and oleic acids, with 36.69% and 22.54%, were the highest concentrations in acid lime and sweet orange, respectively. In another study, a high content of unsaturated acids in the 63.3–66.9% range was reported [34]. Also, the seed oils of four *Citrus* species, including grapefruit (*Citrus × paradisi*), mitha lemon, musami lime, and kinnow mandarin, were demonstrated as a potential source of unsaturated fatty acids, and their antioxidant activities were higher than sunflower, cottonseed, and groundnut [35]. Sterol ($C_{17}H_{28}O$) is composed of four rings that are steroid units. This compound is present in many fruit seeds and is much more stable than fatty acids. β -sitosterol is the most dominant sterol in grapefruit seed oil (81%), followed by campesterol, stigmasterol, and Δ -5-avenasterol [36,37]. The literature revealed that *Citrus* seeds, which are regarded as waste materials, can serve as a beneficent and innovative source of edible oils. Moreover, a wide range of antioxidant, anti-diabetic, insecticidal, antifungal, and antibacterial properties are produced by *Citrus* EOs, along with their pleasant aromas and flavors [38].

3.2. Phenolic Compounds

Phenolic acid is composed of a phenolic ring joined to a carboxylic ring, thus forming a C6–C1 molecular structure. The total phenolic content (TPC) of *Citrus* seeds varies widely among species, ranging from 1.2 mg gallic acid equivalents (GAE)/g dry weigh (DW) for lemon to 2.5 mg GAE/g DW for bitter orange [17]. *C. medica* L. seeds have a significantly higher TPC of 0.7136 mg GAE/g DW [39]. Sprouts can significantly increase the TPC, with sprouts showing values between 6.8 mg GAE/g DW for lemon and 11.2 mg GAE/g DW for blood sweet orange. Moreover, the internal waste parts of *Citrus* fruits, including seeds, show a TPC range of 16.2 to 19.2 mg GAE/g DW, indicating their potential as a source of valuable phenolic compounds [40]. Mandarins were found to have a TPC ranging from 0.07537 to 0.09136 mg GAE/g in a study examining the TPC of *Citrus* seeds. Oranges showed a wider variability with TPC ranging from 0.04663 to 0.08866 mg GAE/g DW, reflecting differences influenced by environmental factors. For lemons, a similar TPC range of 0.07716 to 0.09261 mg GAE/g DW was observed, with some reports indicating a total of 0.17283 to 0.19429 mg GAE/g DW [41]. Yet, another study established a range of TPC 14.51 mg of GAE/g for *Citrus limon* v. Eureka [27]. The TPC of *Citrus* seeds is influenced by the extraction methods. For example, oils extracted from *Citrus* seeds have different TPC depending on the extraction technique used, with values ranging from 0.682 to 0.932 mg GAE/g oil. The highest TPC was observed in sweet orange seed oil extracted by solvent extraction, which reached 0.932 mg GAE/g oil [33]. In a further study, the highest TPC was found in Kinnow mandarin with 158.2 mg GAE/g DW, followed by Orlando orange and Eureka lemon with 113 mg each. The optimization of post-harvest procedures is critical to increase phenolic recovery from seed biowaste and to overcome this variability [1]. Compared to other nutrient components of seeds, polyphenols contribute most to the *Citrus* seed's antioxidant activity. Some of their benefits include antioxidant, anticarcinogenic, and anti-inflammatory properties, and they are beneficial in treating cardiovascular disease, diabetes, and neurodegenerative disorders [42]. Phenolic acids (gallic acid and trans-ferulic acid) were significantly higher in the cold-pressed lemon

seed oils [43]. Other authors compared three different varieties of *Citrus* oil seeds. Lemon seed oil was found to have the highest total phenolic content level (82.02 mg GA/kg seed), followed by mandarin and orange (80.93 mg GA/kg seed and 78.43 mg GA/kg seed) [41]. In the *Citrus* genus, flavonoids are divided into three main groups: flavanones (naringin, naringenin, hesperidin, hesperetin), polymethoxylated flavones (nobiletin and tangeritin), and flavonol glycosides (rutin). These compounds in *Citrus* exhibit strong anti-inflammatory properties [44]. Much research has been conducted regarding the biological effects of grapefruit flavonoids, such as naringin on the components of the metabolic syndrome, including hyperglycemia, hypertension, insulin resistance, and obesity [45,46]. Naringin is a major flavonoid in grapefruit and sour orange, which contains a glucose moiety that provides it a bitter taste. Various *Citrus* species, including sweet orange, tangelo, lemon, and lime, possess low levels of naringin [44]. It is also possible to attribute the difference in naringin content to fruit maturity, as well as grapefruit varieties [45]. Moreover, grapefruit seed oil contains hesperidin/neohesperidin, which have several biological activities. It was also demonstrated that orange seeds are extremely rich in hesperidin (40 g/kg) [47]. In conclusion, the *Citrus* family contains a great deal of polyphenols Table 1.

Table 1. Concentration values (mg/kg) of phenolic acids and flavonoids content in three main groups of *Citrus* seeds.

Subclass	Seeds	Compound	Content	Ref.
Flavonoids	Orange	Narirutin	4704.7 ± 309.34	[47]
		Hesperidin	40,399.7 ± 1876.28	
		Eriocitrin	747.0 ± 35.07	
		Didimin	1584.3 ± 86.96	
		Apigenin7-(malonylpiosyl)-glucoside	36.0 ± 2.46	
	Grapefruit	Hesperidin	884.50 ± 17.50	[36]
		Neohesperidin	452.20 ± 63.60	
		Kaempferol	18.55 ± 2.14	
		Eriocitrin	94.70 ± 18.40	
		Rutin	443.0 ± 95.30	
		Naringin	1324.60 ± 76.60	
	Lemon	Naringenin	57.45 ± 9.90	[43]
		Hesperidin	907.39 ± 8.64	
		Eriocitrin	1051.60 ± 44.60	
Naringin		389.79 ± 0.98		
Neohesperidin		111.06 ± 3.45		
Naringenin		22.82 ± 0.98		
Rutin		76.80 ± 26.20		
Catechin	15.79 ± 1.15			
Phenolic acids	Orange	Caffeic acid	84.7 ± 3.38	[47]
		<i>p</i> -Hydroxybenzoic acid	153.6 ± 9.96	
	Grapefruit	Gallic	78.40 ± 12.20	[36]
		Syringic	7.23 ± 0.12	
		Rosmarinic	16.00 ± 0.17	
		tr-Ferulic	206.10 ± 34.00	
		tr-2-Hydrocinnamic	11.32 ± 0.55	
	Lemon	Gallic acid	93.42 ± 8.07	[43]
		tr-Ferulic acid	85.13 ± 2.68	
		Syringic acid	8.46 ± 0.09	
tr-2-Hydrocinnamic acid		10.99 ± 1.12		

3.3. Limonoids and Furanocoumarins

Among the natural products, limonoids are a unique family of triterpenoids whose backbones are highly oxygenated and present only in plants belonging to the Rutaceae and Meliaceae families [48]. These compounds are found in seeds in the form of aglycons and glucoside derivatives [45]. As limonoid glucosides are non-bitter, limonoid aglycons are responsible for the *Citrus*' bitter taste. Limonoids are abundant in various *Citrus* species seeds, such as lemon, mandarin, citron, and others [49,50]. According to animal and cell culture studies, *Citrus* limonoids inhibit the growth of cancer in various organs. Red Mexican grapefruit seed is a good source of limonoids, including nomilin, obacunone, deacetylnomilin, and, predominantly, limonin [51]. Limonin from sour orange seeds was investigated, isolating isolimonin and ichanexic acids [52]. They both have shown the capacity to act as growth inhibitors of human colon cancer cells [53]. In *Citrus*, furanocoumarins are secondary metabolites that are responsible for the plant's defensive ability against insects, pathogens, and other organisms. As a phenylpropanoid, furanocoumarin has a furan ring connected to a coumarin. Anticancer activity, antioxidative activity, anti-inflammatory activity, and bone health-promoting activity are some of the biological activities of this compound [54].

3.4. Vitamins and Minerals

Vitamins are organic compounds that are necessary for the appropriate performance of the body and are an essential component of our lives [55]. Vitamin E (tocopherols) is mainly found in *Citrus* seeds, which have been evaluated for their antioxidant properties. These properties prevent damage caused by lipid peroxidation to cell membranes [42]. Other authors reported that the total amount of tocopherols in Turkish *Citrus* seed oil ranged between 2.0 mg/100 g (*C. nobilis*) and 21.0 mg/100 g (*C. paradisi*) [56]. There were much higher levels of α - and γ -tocopherols in these seed oils [57]. α -tocopherols were an essential component with higher biological activity in the orange seeds (135.6 mg/kg). Regarding minerals, *Citrus* seeds are a sufficient origin of calcium, potassium, and sodium, as well as iron (75.9 mg/kg), copper (11.5 mg/kg), manganese (12.6 mg/kg), and zinc (19.4 mg/kg) [58].

3.5. Carotenoids

Carotenoids are naturally occurring pigments that are present in all *Citrus* tissues (mainly β -carotene, lycopene, lutein, phytoene, and β -cryptoxanthin). The carotenoid family is regarded as pro-vitamin A in medicine. They are responsible for stimulating the immune system and providing protection against degenerative disorders and cardiovascular disease [59]. Moreover, foods are often fortified with carotenoids due to their color properties, antioxidant properties, and biological functions [60]. Both β -carotene and lutein were reported at identical levels (2.3 ± 0.2 $\mu\text{g/g}$ oil). Lutein has also been shown to lower the risk of macular degeneration, which is the leading cause of blindness among the elderly [36]. The presence of total carotenoids in four different orange seed oils was studied. According to the results, the oil from Hamlin orange seeds contains a minor number of total carotenoids (11.64 mg/kg), while the oil from Perario orange seeds has the highest amounts: 26.69 mg/kg [57]. Various factors affect the total carotenoid content of seed oils, including the maturity stage of fruits, the extraction methods, and the storage conditions. Accordingly, the levels of carotenoids in *Citrus* seeds are much lower than those found in the peel. They range between 0.3 and 26.7 mg/kg and contribute to the yellow color of the oil [61].

3.6. Other Nutrients

In terms of nutritional composition, *Citrus* seeds offer a high level of protein (14%) [32]. In addition, various amino acids were found in *Citrus* seeds flour, including arginine, glutamic acid, aspartic acid, and leucine [58]. Due to the presence of these compounds, *Citrus* seeds are an interesting feedstock for cattle. In addition to this, *Citrus* seeds contain a

significant number of dietary fibers. Dietary fibers were extracted from lemon, orange, and grapefruit seeds when seeds have been defatted [62]. According to this study, *Citrus* seed dietary fibers are applied to design healthy food. Furthermore, they have interesting functional properties such as oil holding materials, so they might be suited for emulsification to improve the emulsion structure and prolong the stability of the food.

4. Extraction of *Citrus* Seed's Phytochemicals

4.1. Traditional Extraction Methods

4.1.1. Solvent Extraction

The solvent extraction technique is an extraction technique that uses solvents, high temperatures, and long extraction times to obtain compounds. Thus, solvents are chosen considering the compounds of interest to be extracted, evaluating chemical properties such as polarity, affinity, and selectivity. For the *Citrus* seed compound extraction, the incubation of dried ground *Citrus* seeds in a solvent at a warm temperature is needed [1]. Considering the oil nature of *Citrus* seeds, non-polar solvents are commonly used, such as n-hexane, petroleum ether, and ethyl ether. However, methanol is also applied to obtain free phenolics such as flavones and glycosylated flavones. Moreover, alkaline hydrolysis is suitable for the bound phenolic recovery of phenolic acids and flavonols. For the total polyphenols and flavonoids extraction, ethanol was applied in grapefruit seeds and trifoliolate orange (*C. trifoliolata*), showing suitability for the limonoids recovery (limonin and nomilin). Furthermore, t-butyl methyl ether was also applied for the limonoid extraction from bitter orange [1]. By applying this methodology, a high oil yield and fatty acid extraction is achieved. Nevertheless, the phenolic extraction is limited [1]. Disadvantages of this technique include loss of volatile compounds, residues of toxic substances, and oxidation of fatty acids induced by high temperatures [23].

A study performed by Yilmaz et al. run a trial comparing the % yield of fatty acids, tocopherols, and sterols obtained with both solvent extraction and cold-press extraction applied in lemon seeds [63]. Results showed no significant differences between solvent and cold-press extraction techniques on fatty acids. Moreover, slightly differences were achieved regarding sterol content. Nevertheless, the alpha-tocopherol content was significantly higher when cold-press extraction was applied. Both characteristics and % of yield of two oil *Citrus* species seeds were compared applying conventional solvent extraction and supercritical fluid extraction using carbon dioxide (SFE-CO₂) [63]. Results in Table 2 showed significant differences between both extraction methodologies, being solvent extraction with hexane 95% the one with higher yield obtained. Nevertheless, the antioxidant activity of the oils extracted (measured by 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) assays) was slightly higher when SFE-CO₂ was applied in both operational conditions (200 bars, 45 °C = 36.82%; and 250 bars 60 °C = 36.25%) than when hexane was used as extraction solvent (32.82%).

Table 2. Compounds and yields obtained by traditional extraction techniques to *Citrus* seeds.

Matrix	Operational Conditions	Compounds	%Yield	Activity	Ref.
<i>Solvent extraction</i>					
<i>Citrus limon</i>	n-hexane, 3 h, 45 °C, 3 times	Fatty acids, sterols, tocopherols	71.3	-	[63]
<i>Citrus limon</i>	n-hexane, 8 h, 40 °C	Fatty acids	66.46	-	[64]
Dried orange			68.43	-	
<i>Citrus sinensis</i>	n-hexane, 3 h, 60 °C	Fatty acids	34.5	Antimicrobial, antioxidant, anti-parasite. Low cytotoxicity.	[65]

Table 2. Cont.

Matrix	Operational Conditions	Compounds	%Yield	Activity	Ref.
<i>Citrus aurantium</i>	Hexane, 60–70 °C, 4 h	Limonin/Isoobacunoic acid/Limonin glucoside	1.17/0.33/0.86	Anticancer and antifeedant against insect	[66]
<i>Citrus reticulata</i> var. Cleopatra		Nomilin/Isolimononic acid	0.59/0.006		
<i>Citrus reticulata</i> var. Nova		Nomilin/Isolimononic acid	0.35/0.33		
<i>Citrus paradisi</i> var. Rio		Limonin/Nomilin	6.17/0.42		
<i>Citrus ichangensis</i> and <i>Citrus reticulata</i>	Hexane 95%, 70 °C, 20 h	Limonene	5.1	-	[67]
<i>Citrus reticulata</i>	n-hexane, 60 °C, 6 h	Fatty acids (SFA/UFA/MUFA/PUFA)	27.20/71.87/26.48/45.59	-	[23]
<i>Citrus limon</i>			25.25/73.60/29.01/44.60	-	
<i>Citrus paradisi</i>			29.47/68.42/22.60/45.82	-	
<i>Citrus aurantifolia</i>	Acetone, 60–70 °C, 8 h	Limonin	0.005	-	[68]
		Limonin	0.02	-	
		Obacunne	2.86	Cytotoxic	[69]
	Ethyl acetate, 60–70 °C, 8 h	Limonin/Limonixic acid/Isolimonixic acid	3.91/2.11/10.61	Cytotoxic	[69]
	MeOH:H ₂ O, 60–70 °C, 8 h	Limonin glucoside	3.64	Cytotoxic	
EAE					
<i>Citrus limon</i>	<i>B. licheniformis</i> protease, 1:100 (w/w), 60 °C, 12 h	Fatty acids/sterols/tocopherols/protein	33.1/3.12/0.1/8.8	-	[70]
Cold press extraction					
<i>Citrus limon</i>	30 rpm, 10-mm exit die 40 °C	Fatty acids, sterols, tocopherols	36.8	-	[63]
<i>Citrus latifolia</i>	10 rpm, 10 kg/h, <40 °C	Fatty acids, sterols, tocopherols, phenolics	44.2	-	[71]

Abbreviations: EAE: enzyme assisted extraction; SFA: saturated fatty acids; UFA: unsaturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: poly-unsaturated fatty acids.

4.1.2. Enzyme-Assisted Extraction (EAE)

EAE is an extraction technique in which enzymes such as pectinases, cellulases, glucanases, or xylanases are used to degrade the cell wall so different compounds can be released [72]. The low solvent consumption, the short extraction time, and the milder conditions applied are the main advantages of this process. However, since cell walls are composed from different polymers, when hydrolysis is achieved, there can be released short chains of monomers and extract, affecting its turbidity and its organoleptic properties [73]. Unfortunately, to our knowledge, currently published works that study the parameters and yields of *Citrus* seeds in specific are very scarce. Nevertheless, a very recent study assessing protein and oil extraction from various seeds, including lemon seed, showed promising results. By submerging the seeds in *Bacillus licheniformis* protease for 12 h, the authors described a yield of extracted fat 62%, much higher than the 4 obtained by conventional solvent extraction [70]. However, the amount of bioactive phytochemicals present in the extracted oil was higher in the lemon seeds subjected to conventional solvent extraction (0.9%) than in the one extracted with protease (0.3%) [70]. It is worth noting that even if studies involving EAE and *Citrus* seeds are so very limited due to the lignocellulosic

composition of these seeds greater extraction yields and phytochemical concentrations are to be expected when using cellulose-degrading enzymes (Table 2).

4.1.3. Cold-Press Extraction

Cold-pressing extraction is an extraction technique applied for the extraction of edible oils from oily seeds, kernels, peels, and fruits [20]. This technique does not need solvent extraction and has a low energy cost. Moreover, oils obtained by cold-press extraction are characterized for a high polyunsaturated fatty acids recovery, although lower oil yields and fatty acids extraction is obtained comparing to solvent extraction, while the phenolic and volatiles content extraction is improved [1,74]. In fact, a study was run comparing cold-press extraction and solvent extraction, showing 71% of extraction yield when solvent extraction was applied versus 36% when cold-press extraction was applied Table 2. With cold-process extraction, high-quality oils are obtained since chemical contaminants are not present in the effluent. Moreover, the obtained oil is rich in bioactive compounds such as naringin, gallic, and syringic acids, as well as terpene volatiles such as b-pinene, b-myrcene, D-limonene, a-phellandrene, and b-cymene [1].

4.2. Innovative Extraction Methods

4.2.1. Ultrasound-Assisted Extraction (UAE)

UAE is an innovative extraction technique that uses sound waves between 20–100 MHz of frequency inducing cavitation and pressure variations through the extracting solvent. This force is transformed into mechanical energy, leading to the degradation of the cell wall and, consequently, improving the metabolites recovery into the extraction solvent [1]. Moreover, UAE is characterized for its selectivity, high efficiency, and low energy consumption, being suitable for the phenolic compounds' extraction such as phenolic acids and flavanone glycosides. Furthermore, the percentage of extracted yields obtained with UAE are better than those obtained with MAE [75]. UAE is the green extraction technique most used in plant materials and, especially, in *Citrus*-processing waste. As it is showed in Table 3, UAE has been applied in both lemon and mandarin seeds, showing suitable conditions for the flavonoid's recovery [76,77].

4.2.2. Microwave-Assisted Extraction (MAE)

MAE is an extraction technique that uses microwave radiation to heat solvents that are in contact with solid matrices, leading to a separation of the components present in the sample [75]. MAE successfully extracts phytochemicals present in plants by inducing molecular dipole rotation, allowing internal, rapid, and selective heating of the samples with higher recoveries [78]. Moreover, MAE is a cheap cost and cleanliness extraction methodology used for phenolic compounds' obtention. Its efficiency is high, while its energy consumption is low. Moreover, MAE requires low quantities of solvents, and it is rapid and easy to control [75].

Table 3. Compounds and yields obtained by innovative extraction techniques to *Citrus* seeds.

Matrix	Operational Conditions	Compounds	%Yield	Activity	Ref.
		<i>SFE-CO₂</i>			
<i>Citrus ichangensis</i> and <i>Citrus reticulata</i>	45 °C, 200 bars, 2 h, 27 g/min	Limonene	5.73	-	[67]
	60 °C, 250 bars, 2 h, 27 g/min		6.39	-	

Table 3. Cont.

Matrix	Operational Conditions	Compounds	%Yield	Activity	Ref.
<i>Citrus reticulata</i>	50 °C, 33 MPa, 2 h	Esters, flavonoids, phenols, aldehydes, and triterpenes	28.43/70.81/25.22/45.59	-	[23]
<i>Citrus limon</i>	40 °C, 300 bars, 8 h	Fatty acids (SFA/UFA/MUFA/PUFA)	25.74/73.90/28.80/45.10	Anticancer	
<i>Citrus × paradisi</i>			29.82/69.23/23.00/46.24	-	
<i>Citrus aurantifolia</i>	60.85 °C, 48.5 MPa, 2 h, 10 g/min	Limonin	11.64	Cytotoxic	[69]
	54.85 °C, 43.5 MPa, 2 h, 10 g/min		11.72		
UAE					
<i>Citrus limon</i>	EtOH, 1 h, 50 °C, 200 W	Flavonoids (epigallocatechin, caffeic acid, epicatechin, quercetin, and hesperidin)	-	-	[76]
<i>Citrus reticulata</i>	MeOH, 30 min, 320 W 40 kHz, 320 W	Limonin	0.11	-	[77]
<i>Citrus bergamia</i>	H ₂ O, 1 h, 25 °C, 59 kHz	Limonin/Nomilin/TPC/TFC	0.2/0.2/21.7/7.8	Antioxidant	[79]
PLE					
<i>Citrus sinensis</i>	H ₂ O, 180 °C, 10 min., 1002 kPa	Luteolin, diosmetin, quercetin, quercetin-3-O-xyloside, and rutin	-	Antidiabetic	[80]
MAE					
<i>Citrus bergamia</i>	EtOH:H ₂ O (50%), 800 W, 70 °C, 5 min	Limonin/Nomilin/TPC/TFC	0.2/0.2/19.4/5.5.	Antioxidant	[79]

Abbreviations: EAE: enzyme-assisted extraction; SFE-CO₂: supercritical fluid extraction using carbon dioxide; UAE: ultrasound-assisted extraction; PLE: pressurized liquid extraction; MAE: microwave-assisted extraction; SFA: saturated fatty acids; UFA: unsaturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids.

4.2.3. Pressurized-Liquid Extraction (PLE)

PLE is a green extraction technique that puts in contact low quantities of solvents (mL) with a solid matrix during low time (between 3–20 min) at high pressures (1500 psi) and moderate-to-high temperatures (40–200 °C). Operating at high-pressure conditions maintains liquid the solvent used above its boiling point and allows for the obtention of organic compounds from a complex solid matrix [22]. Both organic and aqueous solvents can be used in PLE. Moreover, the recovery and precision of PLE methodology have been compared to the standard EPA extraction [22]. PLE is also suitable for the extraction of anthocyanins, carotenoids, phenols, sterols, phospholipids, tocopherols, free fatty acids, and glycerides, since longer extractions at higher temperatures may degrade them [81]. Table 3 shows different extraction recoveries of grape seeds' lipidic compounds. Moreover, PLE has been applied in pomegranate for the obtention of both proteins and phenolic compounds, showing high extraction recovery yields.

4.2.4. High-Voltage Electric Discharge

High-voltage electric discharge (HVED) is an application of liquid-phase discharge technology in which mechanical disruption of the cell wall is achieved by using water as a solvent. This extraction method follows two steps: a pre-breakdown phase and a breakdown phase. In the pre-breakdown phase, there is a corona streamer discharge, while the breakdown phase consists in an arc discharge process. Weak waves and small bubbles

are generated. Moreover, there is a strong UV radiation formation and, consequently, active radicals appear [82]. Although there is no information about HVED applied in *Citrus* seeds, it has been used for the extraction of lignin from rapeseed straws and oil from sesame seeds. In fact, a study run by Boussetta et al. showed the positive effects of the arc treatment on the extraction of polyphenols from grape seeds [83]. HVED application for the *Citrus* seed extraction should be studied to obtain further information.

4.2.5. Pulsed Electric Field Extraction (PEF)

Pulsed electric field (PEF) is an extraction technique that provokes an electroporation of the cell membrane, allowing for the release of compounds without negative changes [73]. This non-thermal extraction process consists of introducing the food into a chamber with two electrodes, showing suitability for the grapes' polyphenol extraction [73]. Although there are no data available on the application of this technology on *Citrus* seeds, PEF was applied in *Citrus* juice [73,84]. In this way, a higher polyphenol extraction was obtained from orange, pomelo, and lemon skins, and a higher recovery of juice was achieved [73].

4.2.6. Supercritical Fluid-CO₂ Extraction

SCE is a rapid and efficient extraction technique to obtain triglycerides and polyphenols from different seeds since it works at low temperatures. The use of CO₂ in supercritical conditions leads to a physicochemical behavior between liquid and gas since it has liquid density but gas viscosity and diffusion coefficient. These properties allow for the penetration of CO₂ into the solid surface of plant parts, like seeds, improving the chemical extraction [1]. Moreover, SFE-CO₂ is characterized by its low toxicity, non-combustibility, and sample-processing automation [75]. SFE-CO₂ has been applied in different *Citrus* fruits for the recovery of both lipidic and flavonoid content (Table 3). Thus, SFE-CO₂ seems to be an interesting extraction methodology to be applied to different bioactive compounds present in *Citrus* fruits.

Overall, although traditional methods such as solvent extraction offer high yields, they also suffer limitations in terms of safety and quality. Innovative methods such as UAE, MAE, and SFE-CO₂ offer promising alternatives, especially when sustainability and efficiency are targeted. Nonetheless, the selection of the extraction method should depend on the specific application requirements, balancing efficiency, yield, and conservation of bioactive compounds. Eventually, a hybrid approach that integrates the strengths of multiple methods may provide the most desirable results for extracting high-value compounds from *Citrus* seeds. To refine extraction conditions and optimize methods for commercial applications, further research is essential.

5. Applications in Food Products and Nutraceuticals

5.1. Food Industry

5.1.1. Food Packaging

Citrus seed wastes cover a variety of bioactive components (e.g., polyphenols, limonoids, carotenoids, and tocopherols) with antioxidant and antimicrobial activities, as well as suitable compatibility with biopolymeric matrices that make them well-suited for formulating food packaging films [4,65]. This allows for the waste collected after the extraction of high-value components from *Citrus* fruits to be molded and turned into biodegradable packaging material, thus boosting the reuse of waste [85]. In this context, numerous investigations have been conducted on the development of packaging films from *Citrus* by-products [86]. A recent study evidenced that the incorporation of lemon peel extract-loaded nanogels in active food packaging films based on casein and basil seed gum enhanced the film properties; mechanical, thermal stability, hydrophobicity, water vapor permeability, biocompatibility, and water solubility, among others. Moreover, satisfactory results were also achieved in the evaluation of the antioxidant and antimicrobial activities of the films [87].

As in the previous example, lines of research in this field have focused mainly on the recovery of value-added products from *Citrus* pulp and peel. Seeds are underexploited de-

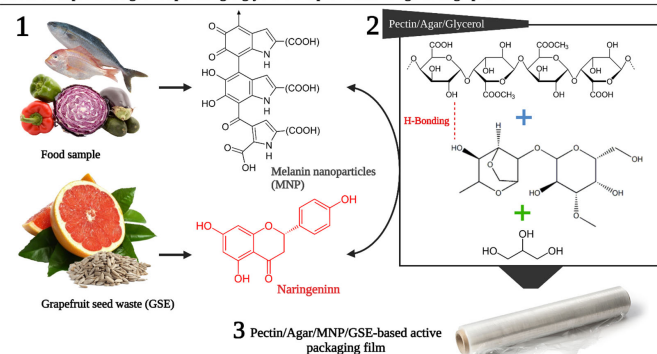
spite the value and potential reserve of their phytochemical composition. Moreover, scarce information is available about their recycling and valorization [1]. Nevertheless, certain *Citrus* fruits, such as mandarin, are especially rich in secondary compounds, contained mostly in the seeds, which are a source of antioxidants.

Ucak et al. analyzed the impact of gelatine films enriched with 2% lemon and sweet orange seed extracts on the quality of sea bass fillets during 15 days of chilled storage ($4 \pm ^\circ\text{C}$). Findings revealed that the inclusion of the seeds of both *Citrus* fruits made a significant sensory and microbiological contribution to their shelf life, as well as increasing the effectiveness of the packaging, resulting in a potent natural antioxidant additive, which could greatly enhance consumer acceptance [88].

Currently, grapefruit *Citrus* seed extracts (GSE) have been actively immobilized in different natural biopolymeric matrices to manufacture functional composite films and are commercially available [4,89]. Roy et al., 2021, prepared multifunctional pectin/agar composite films reinforced with melanin nanoparticles (MNP) and GSE. The pectin/agar/MNP/GSE composite film showed significant enhancement of physical and functional properties, as well as excellent antioxidant and antibacterial activity [89]. Roy et al., 2021, proved in the fabrication of a halochromic functional film based on carboxymethyl cellulose/agar by adding alizarin and GSE that the antioxidant and antimicrobial properties were strongly enhanced with the incorporation of GSE [90]. Oun et al. elaborated multifunctional carboxymethylcellulose (CMC) composite films by adding chitin nanocrystals from shrimp shell powder by acid hydrolysis. The results revealed that the addition of GSE reduced the strength and stiffness of the films by 10.4% and 30.3%, whereas the flexibility increased by 17.7%. Further, the films with GSE also exhibit strong antibacterial activity and UV barrier properties, so they are highly applicable as active food packaging materials [91].

As mentioned above, seed-based studies are not plentiful compared to those available on the *Citrus* peel. Nonetheless, those conducted with seeds have encouraging results. This may be because occasionally the direct use of *Citrus* seeds may lead to sensory issues in the product such as woody texture or astringent and bitter taste disorders resulting from metabolites such as limonin present in the seeds [88,92,93] (Figure 1).

A. An example of the generic pectin/agar/glycerol composite film design from grapefruit seed waste



B. Scheme of the biodiesel process for the production of biodiesel from citrus waste seeds

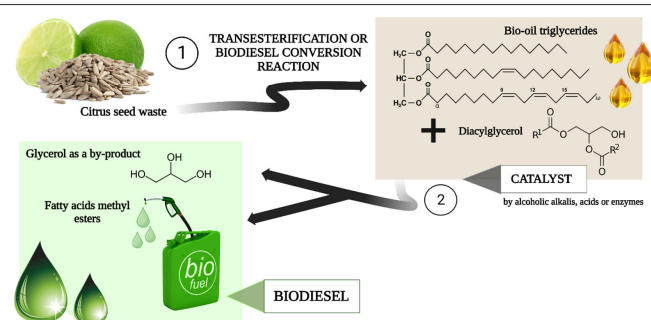


Figure 1. Examples of *Citrus* seeds waste applications in food and non-food industry. Created with BioRender.com.

5.1.2. Functional Foods

In the design of healthy foods as functional components, *Citrus* seeds could bring great results due to their composition rich in oil and unsaturated fatty acids, proteins, vitamins, tocopherols, phytosterols, carotenoids, and phenolics compounds, minerals, as well as flavonoids, and dietary fiber in the form of non-digestible carbohydrates [1,4,94,95]. *Citrus* seeds are also outstanding for their content of tetracyclic triterpenoid limonoids (limonin, nomilin, obacunone, and nomilinic acid) [92,96]. Yilmaz et al. used dietary fibers extracted from orange and grapefruit seeds in the production of cookies. Evaluation of the incorporation effects of the fibers showed beneficial impacts on dietary fiber contents and antioxidant and phenolic capacity mainly due to their composition in bioactive components. The highest content of flavonoids and phenolic acids reached 12.93 mg/g. Moreover, the samples used as controls showed no flavonoid content. So, these new cookies could be assigned as functional products with high dietary fiber content [93].

Furthermore, *Citrus* wastes are also characterized in terms of their content of complex polysaccharides and coloring material, which are used extensively by the soft drink industries as clouding agents [97]. But also, *Citrus* seeds have been used commercially to produce oil rich in unsaturated fatty acids (linolenic, palmitic, oleic, and stearic), so it is considered a healthy oil [94]. Antonella et al., 2019, screened the chemical composition and nutritional and biological attributes of SFE-CO₂-extracted oils extracted from waste mandarin, lemon, and grapefruit seeds. The results qualified the evaluated seed oils as a potential resource due to properties such as high content of essential fatty acids, radical scavenging activity, and significant inhibitory effects on fungal tyrosinase and on melanoma cell growth [23].

Polyphenols, carotenoids, and essential oils are recognized as the biologically most active compounds in *Citrus* wastes and are linked to the greatest health benefits, mainly attributed to their antioxidant activity [92]. Several studies have found that *Citrus* seed and leaf extracts contain high amounts of phenolic compounds, such as flavonoids [98]. For example, sour orange seeds have been found to contain limonoids and flavonoids as their main bioactive components. These flavonoids include flavanones such as hesperidin and naringin, compounds with direct health benefits due to their antioxidant, anticarcinogenic, anti-inflammatory, and cardiovascular-protective activities [99]. The phytochemical profile of *Citrus* fruits has led them to be considered worldwide as potent functional foods [100].

5.2. Non-Food Items

5.2.1. Cosmetic and Pharmaceutical Industry

Citrus fruits, apart from bioactive compounds, contain soluble sugar, starch, cellulose and hemicellulose fibers, ash, pectin, lignin, fat, and protein, which can be used in different fields of pharmaceuticals and nutraceuticals, food, beverage, and cosmetics [101]. For example, *Citrus* seed waste is being exploited in cosmetic applications, i.e., hair, nails, skin, antibacterial and antifungal soaps, and lotions in the cosmetic industry [1,92]. Albergamo et al. highlighted the presence of triterpenes in lemon seeds of triterpenes as minor bioactive compounds for exploitation in the pharmaceutical sector through the production of therapeutic steroids that serve as natural emulsifiers in diverse cosmetics [102]. Özcan et al. conducted a compositional study of seeds and seed oils of multiple *Citrus* fruits extracted by solvent extraction. The results showed that the total amounts of phenols and flavonoids in *Citrus* seeds ranged from 97.84 mg GAE/100 g to 814.84 mg GAE/100 g. Meanwhile, the antioxidant activity ranged from 53.27% to 74.21%. Also, it was found that the amounts of oleic and linoleic acid in *Citrus* seed oils ranged from 21.84% to 38.67%, and the most abundant minerals were phosphorus and iron [95].

The chemical composition of these by-products is a renewable, economical source, ideal to produce essential oils and *Citrus* hydrosols, as well as the presence of antioxidants such as vitamins C, B, and E or flavonoids such as quercetin, hesperidin, and rutin, which could act on the skin, delaying the aging factor and promoting skin health [86]. Antolani et al. developed a medicinal soap without synthetic additives showing potent bioactivities from the underutilized seeds of sweet oranges. The results showed a product that stands

out for excellent properties such as good solubility, foaming capacity, texture, color, low free caustic alkali content, antimicrobial activity, antioxidant potential, antiparasitic, and low cytotoxicity. In addition, also for its composition in linoleic acid (36%) and oleic acid (27%) and above all, for being a sustainable, environmentally conscious cosmeceutical that could turn *Citrus* seed residues into richness [65]. However, these applications are still scarce and barely exploited, the most crucial step for the development of natural cosmetics and pharmaceuticals should focus on the identification of the compounds of interest from the *Citrus* seed waste, together with research concerning the structure of the skin and the effects of the compounds on it [86].

5.2.2. Bio-Fuel Production

Manufacturing of biodiesel based on *Citrus* seed oil can be seen as an alternative for second-generation biodiesel production [103]. Sarno et al. conducted a proof of concept for the valorization of lemon seed waste oils in biodiesel with the aim of finding combinations that guarantee high biodiesel yields. The conversion of the lemon seed oil reached a value of 98.2% after 2 h at 15 V, 0.3% by weight of NaCl, and 20 °C [104]. Rozina et al. explored the potential of citron as a novel non-edible seed oil for biodiesel production using environmentally friendly copper oxide nanoparticles synthesized with aqueous extract of purslane (*Portulaca oleracea* L.) leaves. A 93% yield of methyl ester was obtained with optimal reaction conditions: 8:1 methanol to oil ratio in 120 min reaction time and 85 °C temperature [105].

Biodiesel production from *Citrus* seed residues could be efficiently employed for renewable energy generation, which would further support circular bioeconomy approaches [106].

5.2.3. Biosorbent Production

Although research is still limited, biosorbents derived from *Citrus* waste have been studied as a sustainable solution for removing toxic metals and pesticides from wastewater. This material, when modified through various physico-chemical treatments, has shown innovative solutions to waste management problems [107]. High surface area and the presence of functional groups, such as hydroxyl and carboxyl in adsorbent substrates, make them effective in adsorbing metal ions [108]. Activated carbon from *Citrus* waste is widely recognized as one of the most popular and effective biosorbents. Its cost-effectiveness and efficiency in removing contaminants make it a preferred choice for various adsorption applications [107]. Sudha et al. highlighted the effectiveness of activated carbon derived from sweet lime (*Citrus limettioides* Tanaka) peel and seed in removing Nickel (II) ions from aqueous solutions [109]. The ideal conditions for adsorption were a contact time of 4 h and a pH range of 4.0 to 7.0. Also, functional groups, including hydroxyl, carboxylic, and sulfonic acids, were effectively involved. Additionally, the adsorbents could be reused effectively for up to five cycles, making them a practical and cost-effective option for Nickel (II) ion removal in wastewater treatment, offering an alternative to more expensive materials such as ion-exchange resins and carbon nanotubes [109]. On the other hand, activated carbon derived from mandarin seeds successfully removed up to 100% of some carbamate pesticides after up to three absorption cycles. Even after three cycles, this activated carbon showed retention indexes close to 90% for carbaryl, methiocarb, or pirimicarb, whilst it did drop its retention capacity to ≈30% with others such as metolcarb or isoprocarb [110]. Therefore, even though there is ongoing research regarding *Citrus* seeds as biosorbent raw materials, peels have also been more extensively studied, and knowledge is still limited on their potential.

6. Conclusions

Recent decades have seen a significant increase in scientific interest in agricultural waste owing to its biological properties and its potential for economic growth. *Citrus* by-products are one of the most important sources of waste that are produced in large

quantities in various industries. Despite *Citrus* seeds' great value and high composition of phytochemicals, the concept of extracting and valorizing *Citrus* seeds is still fundamentally underdeveloped as compared with other parts of the plant. However, some research has focused on the recovery of bioactive compounds from *Citrus* seeds and several conventional, and innovative extraction methods have been developed. Because of their numerous health benefits, the extracted compounds find applications in food and non-food industries, serving as fortifying components for food products, as well as new formulations for cosmetic and pharmaceutical applications. Furthermore, it has been shown that *Citrus* seeds are effective as bioactive compounds and are used for anti-inflammatory, antioxidant, antibacterial, and antidiabetic properties. They also lower cholesterol levels and improve digestion. Moreover, as a promising healthy oil, preservative, and ingredient for food packaging, *Citrus* seed oil is used by the food industry.

The detailed comparison of extraction techniques, highlighting the advantages of innovative and environmentally friendly extraction methods, is one of the main contributions of this review. Techniques such as supercritical fluid extraction (SFE) and microwave-assisted extraction (MAE) have been found to improve yields and reduce the overall environmental impact compared to traditional methods. These innovations meet the growing demand for sustainable and cost-effective extraction processes.

To assist in the cost-effective and environmentally friendly valorization of *Citrus* seeds, innovative and green extraction strategies have been applied to various *Citrus* seeds, which have improved yields. There is a growing need for advanced technologies to enable the proper processing of generated *Citrus* by-products in the *Citrus* sector. In fact, it is possible to produce high-value products from recovered wastes in several fields. However, the scale-up of these technologies remains a challenge due to technical and economic barriers, such as high energy consumption and initial investment costs. It is still challenging to implement revaluation strategies due to technical (high energy consumption), economic (high investment), environmental, and social challenges. A comprehensive understanding of antioxidant molecules, mechanisms of action, extraction techniques, and correlations with other properties is required to accomplish this goal. Though it seems complex to revalorize strategies and reduce the environmental impact of waste, promising expectations are evident in the literature and successful examples can be found. Therefore, prospects indicate that *Citrus* seed waste can be further studied for a variety of applications, either as a source of biologically active compounds with potential benefits for health, or as a raw material for other applications. Nonetheless, it is evident that peels, as a major fraction of *Citrus*-derived waste, have been studied in more depth than seeds, and more research in this waste would be needed.

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References

1. Zayed, A.; Badawy, M.T.; Farag, M.A. Valorization and extraction optimization of Citrus seeds for food and functional food applications. *Food Chem.* **2021**, *355*, 129609. [[CrossRef](#)] [[PubMed](#)]
2. Maqbool, Z.; Khalid, W.; Atiq, H.T.; Koraqi, H.; Javaid, Z.; Alhag, S.K.; Al-Shuraym, L.A.; Bader, D.M.D.; Almarzuq, M.; Afifi, M.; et al. Citrus Waste as Source of Bioactive Compounds: Extraction and Utilization in Health and Food Industry. *Molecules* **2023**, *28*, 1636. [[CrossRef](#)] [[PubMed](#)]
3. Savita; Pati, P.K.; Nagpal, A.K. Rough Lemon (*Citrus Jambhiri Lush.*). In *Forestry Sciences*; Springer International Publishing: Cham, Switzerland, 2018; pp. 199–208, ISBN 9783319790879.
4. Yun, D.; Liu, J. Recent advances on the development of food packaging films based on citrus processing wastes: A review. *J. Agric. Food Res.* **2022**, *9*, 100316. [[CrossRef](#)]
5. Porat, R.; Deterre, S.; Giampaoli, P.; Plotto, A. The flavor of citrus fruit. In *Biotechnology in Flavor Production*; John Wiley & Sons: Hoboken, NJ, USA, 2016; pp. 1–31.
6. Liu, S.; Lou, Y.; Li, Y.; Zhang, J.; Li, P.; Yang, B.; Gu, Q. Review of phytochemical and nutritional characteristics and food applications of *Citrus L.* fruits. *Front. Nutr.* **2022**, *9*, 968604. [[CrossRef](#)] [[PubMed](#)]
7. Sharma, K.; Mahato, N.; Cho, M.H.; Lee, Y.R. Converting citrus wastes into value-added products: Economic and environmentally friendly approaches. *Nutrition* **2017**, *34*, 29–46. [[CrossRef](#)] [[PubMed](#)]
8. Richa, R.; Kohli, D.; Vishwakarma, D.; Mishra, A.; Kabdal, B.; Kothakota, A.; Richa, S.; Sirohi, R.; Kumar, R.; Naik, B. Citrus fruit: Classification, value addition, nutritional and medicinal values, and relation with pandemic and hidden hunger. *J. Agric. Food Res.* **2023**, *14*, 100718. [[CrossRef](#)]
9. Andrade, M.A.; Barbosa, C.H.; Shah, M.A.; Ahmad, N.; Vilarinho, F.; Khwaldia, K.; Silva, A.S.; Ramos, F. Citrus By-Products: Valuable Source of Bioactive Compounds for Food Applications. *Antioxidants* **2023**, *12*, 38. [[CrossRef](#)]
10. Ben Rejeb, I.; Dhen, N.; Kassebi, S.; Gargouri, M. Quality Evaluation and Functional Properties of Reduced Sugar Jellies Formulated from Citrus Fruits. *J. Chem.* **2020**, *2020*, 1–8. [[CrossRef](#)]
11. Mahato, N.; Sinha, M.; Sharma, K.; Koteswararao, R.; Cho, M.H. Modern extraction and purification techniques for obtaining high purity food-grade bioactive compounds and value-added co-products from citrus wastes. *Foods* **2019**, *8*, 523. [[CrossRef](#)]
12. Rashid, U.; Ibrahim, M.; Yasin, S.; Yunus, R.; Taufiq-Yap, Y.H.; Knothe, G. Biodiesel from *Citrus reticulata* (mandarin orange) seed oil, a potential non-food feedstock. *Ind. Crops Prod.* **2013**, *45*, 355–359. [[CrossRef](#)]
13. Suri, S.; Singh, A.; Nema, P.K. Current applications of citrus fruit processing waste: A scientific outlook. *Appl. Food Res.* **2022**, *2*, 100050. [[CrossRef](#)]
14. Russo, M.; Bonaccorsi, I.L.; Arigò, A.; Cacciola, F.; De Gara, L.; Dugo, P.; Mondello, L. Blood orange (*Citrus sinensis*) as a rich source of nutraceuticals: Investigation of bioactive compounds in different parts of the fruit by HPLC-PDA/MS. *Nat. Prod. Res.* **2021**, *35*, 4606–4610. [[CrossRef](#)]
15. El-Adawy, T.A.; Rahma, E.H.; El-Bedawy, A.A.; Gafar, A.M. Properties of some citrus seeds. Part 3. Evaluation as a new source of protein and oil. *Food/Nahrung* **1999**, *43*, 385–391. [[CrossRef](#)]
16. Allaqaband, S.; Dar, A.H.; Patel, U.; Kumar, N.; Nayik, G.A.; Khan, S.A.; Ansari, M.J.; Alabdallah, N.M.; Kumar, P.; Pandey, V.K.; et al. Utilization of Fruit Seed-Based Bioactive Compounds for Formulating the Nutraceuticals and Functional Food: A Review. *Front. Nutr.* **2022**, *9*, 902554. [[CrossRef](#)] [[PubMed](#)]
17. Falcinelli, B.; Famiani, F.; Paoletti, A.; D’egidio, S.; Stagnari, F.; Galieni, A.; Benincasa, P. Phenolic compounds and antioxidant activity of sprouts from seeds of *Citrus* species. *Agriculture* **2020**, *10*, 33. [[CrossRef](#)]
18. Akpata, M.I.; Akubor, P.I. Chemical composition and selected functional properties of sweet orange (*Citrus sinensis*) seed flour. *Plant Foods Hum. Nutr.* **1999**, *54*, 353–362. [[CrossRef](#)]
19. Rahman, M.M.; Jahan, F.I.; Mim, S.A. A brief phytochemical investigation and pharmacological uses of citrus seed—A review. *Pharmacologyonline* **2019**, *1*, 94–103.
20. Putnik, P.; Bursać Kovačević, D.; Režek Jambak, A.; Barba, F.J.; Cravotto, G.; Binello, A.; Lorenzo, J.M.; Shpigelman, A. Innovative “green” and novel strategies for the extraction of bioactive added value compounds from citrus wastes—A review. *Molecules* **2017**, *22*, 680. [[CrossRef](#)]
21. Chan, C.H.; Yusoff, R.; Ngoh, G.C.; Kung, F.W.L. Microwave-assisted extractions of active ingredients from plants. *J. Chromatogr. A* **2011**, *1218*, 6213–6225. [[CrossRef](#)]
22. Freitas, L.D.S.; Dariva, C.; Jacques, R.A.; Caramão, E.B. Effect of experimental parameters in the pressurized liquid extraction of brazilian grape seed oil. *Sep. Purif. Technol.* **2013**, *116*, 313–318. [[CrossRef](#)]
23. Rosa, A.; Era, B.; Masala, C.; Nieddu, M.; Scano, P.; Fais, A.; Porcedda, S.; Piras, A. Supercritical CO₂ Extraction of Waste Citrus Seeds: Chemical Composition, Nutritional and Biological Properties of Edible Fixed Oils. *Eur. J. Lipid Sci. Technol.* **2019**, *121*, 1800502. [[CrossRef](#)]
24. El Kantar, S.; Boussetta, N.; Lebovka, N.; Foucart, F.; Rajha, H.N.; Maroun, R.G.; Louka, N.; Vorobiev, E. Pulsed electric field treatment of citrus fruits: Improvement of juice and polyphenols extraction. *Innov. Food Sci. Emerg. Technol.* **2018**, *46*, 153–161. [[CrossRef](#)]
25. Madureira, M.B.; Concato, V.M.; Cruz, E.M.S.; Bitencourt de Morais, J.M.; Inoue, F.S.R.; Concimo Santos, N.; Gonçalves, M.D.; Cremer de Souza, M.; Basso Scandola, T.; Fontana Mezoni, M.; et al. Naringenin and Hesperidin as Promising Alternatives for Prevention and Co-Adjuvant Therapy for Breast Cancer. *Antioxidants* **2023**, *12*, 586. [[CrossRef](#)] [[PubMed](#)]

26. Sakthivel, S.; Dhanapal, A.R.; Paulraj, L.P.; Gurusamy, A.; Venkidasamy, B.; Thiruvengadam, M.; Govindasamy, R.; Shariati, M.A.; Bouyahya, A.; Zengin, G.; et al. Antibacterial activity of seed aqueous extract of *Citrus limon* (L.) mediated synthesis ZnO NPs: An impact on Zebrafish (*Danio rerio*) caudal fin development. *Heliyon* **2022**, *8*, e10406. [[CrossRef](#)]
27. Halima-Mansour, S.; Allem, R. Evaluation of antimicrobial activity of Algerian Lemon (*Citrus limon* v. Eureka) peels and juice extracts. *Der Pharm. Lett.* **2016**, *8*, 197–204.
28. Muteeb, G.; Rehman, M.T.; Shahwan, M.; Aatif, M. Origin of Antibiotics and Antibiotic Resistance, and Their Impacts on Drug Development: A Narrative Review. *Pharmaceuticals* **2023**, *16*, 1615. [[CrossRef](#)]
29. Novais, C.; Molina, A.K.; Abreu, R.M.V.; Santo-Buelga, C.; Ferreira, I.C.F.R.; Pereira, C.; Barros, L. Natural Food Colorants and Preservatives: A Review, a Demand, and a Challenge. *J. Agric. Food Chem.* **2022**, *70*, 2789–2805. [[CrossRef](#)]
30. Bora, H.; Kamle, M.; Mahato, D.K.; Tiwari, P.; Kumar, P. Citrus Essential Oils (CEOs) and Their Applications in Food: An Overview. *Plants* **2020**, *9*, 357. [[CrossRef](#)]
31. Juhaimi, F.A.L.; Matthäus, B.; Özcan, M.M.; Ghafoor, K. The physico-chemical properties of some citrus seeds and seed oils. *Z. Naturforsch.—Sect. C J. Biosci.* **2016**, *71*, 79–85. [[CrossRef](#)]
32. Tounsi, M.S.; Dhifi, W.; Marzouk, B. Lipid evaluation of some Tunisian Citrus seeds. *J. Food Lipids* **2004**, *11*, 242–250. [[CrossRef](#)]
33. Garrido, G.; Chou, W.H.; Vega, C.; Goity, L.; Valdés, M. Influence of extraction methods on fatty acid composition, total phenolic content and antioxidant capacity of Citrus seed oils from the Atacama Desert, Chile. *J. Pharm. Pharmacogn. Res.* **2019**, *7*, 389–407. [[CrossRef](#)]
34. Adeyeye, E.I.; Adesina, A.J. Citrus Seeds Oils as Sources of Quality Edible Oils. *Int. J. Curr. Microbiol. Appl. Sci.* **2015**, *4*, 537–554.
35. Anwar, F.; Naseer, R.; Bhangar, M.I.; Ashraf, S.; Talpur, F.N.; Aladedunye, F.A. Physico-chemical characteristics of citrus seeds and seed oils from Pakistan. *JAOCS J. Am. Oil Chem. Soc.* **2008**, *85*, 321–330. [[CrossRef](#)]
36. Yilmaz, E.; Aydeniz, B.; Selçuk, G. Valorization of Grapefruit Seeds: Cold Press Oil Production. *Waste Biomass Valorization* **2019**, *10*, 2713–2724. [[CrossRef](#)]
37. Reynoso-Camacho, R.; Rodríguez-Villanueva, L.D.; Sotelo-González, A.M.; Ramos-Gómez, M.; Pérez-Ramírez, I.F. Citrus decoction by-product represents a rich source of carotenoid, phytosterol, extractable and non-extractable polyphenols. *Food Chem.* **2021**, *350*, 129239. [[CrossRef](#)] [[PubMed](#)]
38. Medeleanu, M.L.; Fărcaș, A.C.; Coman, C.; Leopold, L.; Diaconeasa, Z.; Socaci, S.A. Citrus essential oils–Based nano-emulsions: Functional properties and potential applications. *Food Chem. X* **2023**, *20*, 100960. [[CrossRef](#)] [[PubMed](#)]
39. Mateus, A.R.S.; Teixeira, J.D.; Barros, S.C.; Almeida, C.; Silva, S.; Sanches-Silva, A. Unlocking the Potential of *Citrus medica* L.: Antioxidant Capacity and Phenolic Profile across Peel, Pulp, and Seeds. *Molecules* **2024**, *29*, 3533. [[CrossRef](#)]
40. Sir Elkhatim, K.A.; Elagib, R.A.A.; Hassan, A.B. Content of phenolic compounds and vitamin C and antioxidant activity in wasted parts of Sudanese citrus fruits. *Food Sci. Nutr.* **2018**, *6*, 1214–1219. [[CrossRef](#)]
41. İnan, Ö.; Özcan, M.M.; Aljuhaimi, F. Effect of location and Citrus species on total phenolic, antioxidant, and radical scavenging activities of some Citrus seed and oils. *J. Food Process. Preserv.* **2018**, *42*, e13555. [[CrossRef](#)]
42. Zou, Z.; Xi, W.; Hu, Y.; Nie, C.; Zhou, Z. Antioxidant activity of Citrus fruits. *Food Chem.* **2016**, *196*, 885–896. [[CrossRef](#)]
43. Guneser, B.A.; Yilmaz, E. Bioactives, Aromatics and Sensory Properties of Cold-Pressed and Hexane-Extracted Lemon (*Citrus limon* L.) Seed Oils. *JAOCS J. Am. Oil Chem. Soc.* **2017**, *94*, 723–731. [[CrossRef](#)]
44. Khan, M.K.; Zill-E-Huma; Dangles, O. A comprehensive review on flavanones, the major citrus polyphenols. *J. Food Compos. Anal.* **2014**, *33*, 85–104. [[CrossRef](#)]
45. Khalil, M.N.A.; Farghal, H.H.; Farag, M.A.; Khalil, M.N.A.; Farghal, H.H.; Farag, M.A. Outgoing and potential trends of composition, health benefits, juice production and waste management of the multi-faceted Grapefruit *Citrus X paradisi*: A comprehensive review for maximizing its value. *Crit. Rev. Food Sci. Nutr.* **2022**, *62*, 935–956. [[CrossRef](#)] [[PubMed](#)]
46. Alam, M.A.; Subhan, N.; Rahman, M.M.; Uddin, S.J.; Reza, H.M.; Sarker, S.D. Effect of Citrus Flavonoids, Naringin and Naringenin, on Metabolic Syndrome and Their Mechanisms of Action. *Adv. Nutr.* **2014**, *5*, 404–417. [[CrossRef](#)] [[PubMed](#)]
47. Russo, M.; Bonaccorsi, I.; Inferrera, V.; Dugo, P.; Mondello, L. Underestimated sources of flavonoids, limonoids and dietary fiber: Availability in orange's by-products. *J. Funct. Foods* **2015**, *12*, 150–157. [[CrossRef](#)]
48. Shi, Y.-S.; Zhang, Y.; Li, H.-T.; Wu, C.-H.; El-Seedi, H.R.; Ye, W.-K.; Wang, Z.-W.; Li, C.-B.; Zhang, X.-F.; Kai, G.-Y. Limonoids from Citrus: Chemistry, anti-tumor potential, and other bioactivities. *J. Funct. Foods* **2020**, *75*, 104213. [[CrossRef](#)]
49. Nakagawa, H.; Duan, H.; Takaishi, Y. Limonoids from *Citrus sudachi*. *Chem. Pharm. Bull.* **2001**, *49*, 649–651. [[CrossRef](#)]
50. Khalil, A.T.; Maatooq, G.T.; El Sayed, K.A. Limonoids from *Citrus reticulata*. *Z. Naturforsch.—Sect. C J. Biosci.* **2003**, *58*, 165–170. [[CrossRef](#)]
51. Mandadi, K.K.; Jayaprakasha, G.K.; Bhat, N.K.; Patil, B.S. Red Mexican Grapefruit: A Novel Source for Bioactive Limonoids and their Antioxidant Activity. *Z. Naturforsch. C J. Biosci.* **2007**, *62*, 179–188. [[CrossRef](#)]
52. Dandekar, D.V.; Jayaprakasha, G.K.; Patil, B.S. Hydrotropic extraction of bioactive limonin from sour orange (*Citrus aurantium* L.) seeds. *Food Chem.* **2008**, *109*, 515–520. [[CrossRef](#)]
53. Jayaprakasha, G.K.; Mandadi, K.K.; Poulouse, S.M.; Jadegoud, Y.; Nagana Gowda, G.A.; Patil, B.S. Novel triterpenoid from *Citrus aurantium* L. possesses chemopreventive properties against human colon cancer cells. *Bioorg. Med. Chem.* **2008**, *16*, 5939–5951. [[CrossRef](#)] [[PubMed](#)]
54. Chidambara Murthy, K.N.; Jayaprakasha, G.K.; Safe, S.; Patil, B.S. Citrus limonoids induce apoptosis and inhibit the proliferation of pancreatic cancer cells. *Food Funct.* **2021**, *12*, 1111–1120. [[CrossRef](#)] [[PubMed](#)]

55. Barker, T. Vitamins and Human Health: Systematic Reviews and Original Research. *Nutrients* **2023**, *15*, 2888. [[CrossRef](#)] [[PubMed](#)]
56. Matthaus, B.; Özcan, M.M. Chemical evaluation of citrus seeds, an agro-industrial waste, as a new potential source of vegetable oils. *Grasas y Aceites* **2012**, *63*, 313–320. [[CrossRef](#)]
57. Jorge, N.; Da Silva, A.C.; Aranha, C.P.M. Antioxidant activity of oils extracted from orange (*Citrus sinensis*) seeds. *Int. News Fats Oils Relat. Mater.* **2017**, *28*, 23–26. [[CrossRef](#)]
58. Ramadan, M.F.; Farag, M.A. Mediterranean Fruits Bio-wastes: Chemistry, Functionality and Technological Applications. In *Mediterranean Fruits Bio-Wastes: Chemistry, Functionality and Technological Applications*; Ramadan, M.F., Farag, M.A., Eds.; Springer: Cham, Switzerland, 2022; pp. 1–855, ISBN 9783030844363.
59. Saini, R.K.; Ranjit, A.; Sharma, K.; Prasad, P.; Shang, X.; Gowda, K.G.M.; Keum, Y.S. Bioactive Compounds of Citrus Fruits: A Review of Composition and Health Benefits of Carotenoids, Flavonoids, Limonoids, and Terpenes. *Antioxidants* **2022**, *11*, 239. [[CrossRef](#)]
60. Cheng, S.-H.; Khoo, H.E.; Kong, K.W.; Prasad, K.N.; Galanakis, C.M. Extraction of carotenoids and applications. In *Carotenoids: Properties, Processing and Applications*; Academic Press: Cambridge, MA, USA, 2020; pp. 259–288, ISBN 9780128170670.
61. Ordoudi, S.A.; Bakirtzi, C.; Tsimidou, M.Z. The Potential of Tree Fruit Stone and Seed Wastes in Greece as Sources of Bioactive Ingredients. *Recycling* **2018**, *3*, 9. [[CrossRef](#)]
62. Karaman, E.; Emin, Y.; Tuncel, N.B. Physicochemical, microstructural and functional characterization of dietary fibers extracted from lemon, orange and grapefruit seeds press meals. *Bioact. Carbohydrates Diet. Fibre* **2017**, *11*, 9–17. [[CrossRef](#)]
63. Yilmaz, E.; Güneşer, B.A. Cold pressed versus solvent extracted lemon (*Citrus limon* L.) seed oils: Yield and properties. *J. Food Sci. Technol.* **2017**, *54*, 1891–1900. [[CrossRef](#)]
64. Reazai, M.; Mohammadpourfard, I.; Nazmara, S.; Jahanbakhsh, M.; Shiri, L. Physicochemical Characteristics of Citrus Seed Oils from Kerman, Iran. *J. Lipids* **2014**, *2014*, 174954. [[CrossRef](#)]
65. Atolani, O.; Adamu, N.; Oguntoye, O.S.; Zubair, M.F.; Fabiyi, O.A.; Oyegoke, R.A.; Adeyemi, O.S.; Areh, E.T.; Tarigha, D.E.; Kambizi, L.; et al. Chemical characterization, antioxidant, cytotoxicity, Anti-*Toxoplasma gondii* and antimicrobial potentials of the *Citrus sinensis* seed oil for sustainable cosmeceutical production. *Heliyon* **2020**, *6*, e03399. [[CrossRef](#)] [[PubMed](#)]
66. Vikram, A.; Jayaprakasha, G.K.; Patil, B.S. Simultaneous determination of citrus limonoid aglycones and glucosides by high performance liquid chromatography. *Anal. Chim. Acta* **2007**, *590*, 180–186. [[CrossRef](#)]
67. Ndayishimiye, J.; Tilahun Getachew, A.; Soo Chun, B. Comparison of Characteristics of Oils Extracted from a Mixture of Citrus Seeds and Peels Using Hexane and Supercritical Carbon Dioxide. *Waste Biomass Valorization* **2017**, *8*, 1205–1217. [[CrossRef](#)]
68. Castillo-Herrera, G.A.; Fariás-Álvarez, L.J.; García-Fajardo, J.A.; Delgado-Saucedo, J.I.; Puebla-Pérez, A.M.; Lugo-Cervantes, E. Bioactive extracts of *Citrus aurantifolia* swingle seeds obtained by supercritical CO₂ and organic solvents comparing its cytotoxic activity against L5178Y leukemia lymphoblasts. *J. Supercrit. Fluids* **2015**, *101*, 81–86. [[CrossRef](#)]
69. Patil, J.R.; Jayaprakasha, G.K.; Murthy, K.N.C.; Chetti, M.B.; Patil, B.S. Characterization of *Citrus aurantifolia* bioactive compounds and their inhibition of human pancreatic cancer cells through apoptosis. *Microchem. J.* **2010**, *94*, 108–117. [[CrossRef](#)]
70. Lolli, V.; Viscusi, P.; Bonzanini, F.; Conte, A.; Fuso, A.; Larocca, S.; Leni, G.; Caligiani, A. Oil and protein extraction from fruit seed and kernel by-products using a one pot enzymatic-assisted mild extraction. *Food Chem. X* **2023**, *19*, 100819. [[CrossRef](#)]
71. Fathollahi, I.; Farmani, J.; Kasaii, M.R.; Hamishehkar, H. Some physical properties of Persian lime (*Citrus latifolia*) seeds and physicochemical properties of the seed oil as affected by solvent extraction and cold pressing methods. *J. Food Meas. Charact.* **2021**, *15*, 1169–1178. [[CrossRef](#)]
72. Iqbal, A.; Schulz, P.; Rizvi, S.S.H. Valorization of bioactive compounds in fruit pomace from agro-fruit industries: Present Insights and future challenges. *Food Biosci.* **2021**, *44*, 101384. [[CrossRef](#)]
73. Rafińska, K.; Wrona, O.; Krakowska-Sieprawska, A.; Walczak-Skierska, J.; Kielbasa, A.; Rafiński, Z.; Pomastowski, P.; Kolankowski, M.; Buszewski, B. Enzyme-assisted extraction of plant material—New functional aspects of the process on an example of *Medicago sativa* L. *Ind. Crops Prod.* **2022**, *187*, 115424. [[CrossRef](#)]
74. Aydeniz-Guneser, B. Cold pressed orange (*Citrus sinensis*) oil. In *Cold Pressed Oils: Green Technology, Bioactive Compounds, Functionality, and Applications*; Academic Press: Cambridge, MA, USA, 2020; pp. 129–146, ISBN 9780128181881.
75. Shorbagi, M.; Fayek, N.M.; Shao, P.; Farag, M.A. *Citrus reticulata* Blanco (the common mandarin) fruit: An updated review of its bioactive, extraction types, food quality, therapeutic merits, and bio-waste valorization practices to maximize its economic value. *Food Biosci.* **2022**, *47*, 101699. [[CrossRef](#)]
76. Yang, M.; Sun, F.; Zhou, Y.; He, M.; Yao, P.; Peng, Y.; Luo, F.; Liu, F. Preventive effect of lemon seed flavonoids on carbon tetrachloride-induced liver injury in mice. *RSC Adv.* **2020**, *10*, 12800–12809. [[CrossRef](#)] [[PubMed](#)]
77. Zheng, G.D.; Yang, X.J.; Chen, B.Z.; Chao, Y.X.; Hu, P.J.; Cai, Y.; Wu, B.; Wei, M.Y. Identification and determination of chemical constituents of *Citrus reticulata* semen through ultra high performance liquid chromatography combined with Q Exactive Orbitrap tandem mass spectrometry. *J. Sep. Sci.* **2020**, *43*, 438–451. [[CrossRef](#)] [[PubMed](#)]
78. Silva, G.C.; Rodrigues, R.A.F.; Bottoli, C.B.G. Passion fruit seed extract enriched in piceatannol obtained by microwave-assisted extraction. *Sustain. Chem. Pharm.* **2021**, *22*, 100472. [[CrossRef](#)]
79. Gattuso, A.; Piscopo, A.; Romeo, R.; De Bruno, A.; Poiana, M. Recovery of Bioactive Compounds from Calabrian Bergamot Citrus Waste: Selection of Best Green Extraction. *Agriculture* **2023**, *13*, 1095. [[CrossRef](#)]

80. Shakthi Deve, A.; Sathish Kumar, T.; Kumaresan, K.; Rapheal, V.S. Extraction process optimization of polyphenols from Indian *Citrus sinensis*—As novel antiglycative agents in the management of diabetes mellitus. *J. Diabetes Metab. Disord.* **2014**, *13*, 11. [[CrossRef](#)]
81. dos Santos Freitas, L.; Jacques, R.A.; Richter, M.F.; da Silva, A.L.; Caramão, E.B. Pressurized liquid extraction of vitamin E from Brazilian grape seed oil. *J. Chromatogr. A* **2008**, *1200*, 80–83. [[CrossRef](#)]
82. Li, Z.; Fan, Y.; Xi, J. Recent advances in high voltage electric discharge extraction of bioactive ingredients from plant materials. *Food Chem.* **2019**, *277*, 246–260. [[CrossRef](#)]
83. Boussetta, N.; Lesaint, O.; Vorobiev, E. A study of mechanisms involved during the extraction of polyphenols from grape seeds by pulsed electrical discharges. *Innov. Food Sci. Emerg. Technol.* **2013**, *19*, 124–132. [[CrossRef](#)]
84. Cserhalmi, Z.; Sass-Kiss, Á.; Tóth-Markus, M.; Lechner, N. Study of pulsed electric field treated citrus juices. *Innov. Food Sci. Emerg. Technol.* **2006**, *7*, 49–54. [[CrossRef](#)]
85. Chavan, P.; Singh, A.K.; Kaur, G. Recent progress in the utilization of industrial waste and by-products of citrus fruits: A review. *J. Food Process Eng.* **2018**, *41*, e12895. [[CrossRef](#)]
86. Panwar, D.; Saini, A.; Panesar, P.S.; Chopra, H.K. Unraveling the scientific perspectives of citrus by-products utilization: Progress towards circular economy. *Trends Food Sci. Technol.* **2021**, *111*, 549–562. [[CrossRef](#)]
87. Mortazavi Moghadam, F.A.; Khoshkalampour, A.; Mortazavi Moghadam, F.A.; PourvatanDoust, S.; Naeijian, F.; Ghorbani, M. Preparation and physicochemical evaluation of casein/basil seed gum film integrated with guar gum/gelatin based nanogel containing lemon peel essential oil for active food packaging application. *Int. J. Biol. Macromol.* **2022**, *224*, 786–796. [[CrossRef](#)] [[PubMed](#)]
88. Ucak, I.; Abuibaid, A.K.M.; Aldawoud, T.M.S.; Galanakis, C.M.; Montesano, D. Antioxidant and antimicrobial effects of gelatin films incorporated with citrus seed extract on the shelf life of sea bass (*Dicentrarchus labrax*) fillets. *J. Food Process. Preserv.* **2021**, *45*, e15304. [[CrossRef](#)]
89. Roy, S.; Rhim, J.W. Fabrication of pectin/agar blended functional film: Effect of reinforcement of melanin nanoparticles and grapefruit seed extract. *Food Hydrocoll.* **2021**, *118*, 106823. [[CrossRef](#)]
90. Roy, S.; Rhim, J.W. Fabrication of Carboxymethyl Cellulose / Agar-Based Functional Films Hybridized with Alizarin and Grapefruit Seed Extract. *ACS Appl. Bio Mater.* **2021**, *4*, 4470–4478. [[CrossRef](#)]
91. Oun, A.A.; Rhim, J.W. Preparation of multifunctional carboxymethyl cellulose-based films incorporated with chitin nanocrystal and grapefruit seed extract. *Int. J. Biol. Macromol.* **2020**, *152*, 1038–1046. [[CrossRef](#)]
92. Mahato, N.; Sharma, K.; Sinha, M.; Cho, M.H. Citrus waste derived nutra-/pharmaceuticals for health benefits: Current trends and future perspectives. *J. Funct. Foods* **2018**, *40*, 307–316. [[CrossRef](#)]
93. Yilmaz, E.; Karaman, E. Functional crackers: Incorporation of the dietary fibers extracted from citrus seeds. *J. Food Sci. Technol.* **2017**, *54*, 3208–3217. [[CrossRef](#)]
94. Kumar, V.; Kaur, R.; Aggarwal, P.; Singh, G. Underutilized citrus species: An insight of their nutraceutical potential and importance for the development of functional food. *Sci. Hort.* **2022**, *296*, 110909. [[CrossRef](#)]
95. Özcan, M.M.; Öztürk, Ö.; Lemiasheuski, V. Quality Properties, Fatty Acid Composition, and Mineral Contents of Some Citrus Seeds and Oils Extracted by Solvent Extraction. *Erwerbs-Obstbau* **2023**, *65*, 127–132. [[CrossRef](#)]
96. Fernández-Fernández, A.M.; Dellacassa, E.; Medrano-Fernandez, A.; Castillo, M.D. Citrus Waste Recovery for Sustainable Nutrition and Health. In *Food Wastes and By-Products*; Campos-Vega, R., Dave Oomah, B., Vergara-Castaneda, H.A., Eds.; Wiley: Hoboken, NJ, USA, 2020; pp. 193–222, ISBN 9781119534105.
97. Rao, M.J.; Wu, S.; Duan, M.; Wang, L. Antioxidant metabolites in primitive, wild, and cultivated citrus and their role in stress tolerance. *Molecules* **2021**, *26*, 5801. [[CrossRef](#)] [[PubMed](#)]
98. Addi, M.; Elbouzidi, A.; Abid, M.; Tungmunnithum, D.; Elamrani, A.; Hano, C. An Overview of Bioactive Flavonoids from Citrus Fruits. *Appl. Sci.* **2022**, *12*, 29. [[CrossRef](#)]
99. Abou Baker, D.H.; Ibrahim, B.M.M.; Hassan, N.S.; Yousuf, A.F.; Gengaihi, S. El Exploiting *Citrus aurantium* seeds and their secondary metabolites in the management of Alzheimer disease. *Toxicol. Rep.* **2020**, *7*, 723–729. [[CrossRef](#)] [[PubMed](#)]
100. Smeriglio, A.; Denaro, M.; Di Gristina, E.; Mastracci, L.; Grillo, F.; Cornara, L.; Trombetta, D. Pharmacognostic approach to evaluate the micromorphological, phytochemical and biological features of *Citrus lumia* seeds. *Food Chem.* **2022**, *375*, 131855. [[CrossRef](#)]
101. Dubey, P.; Tripathi, G.; Mir, S.S.; Yousuf, O. Current scenario and global perspectives of citrus fruit waste as a valuable resource for the development of food packaging film. *Trends Food Sci. Technol.* **2023**, *141*, 104190. [[CrossRef](#)]
102. Albergamo, A.; Costa, R.; Dugo, G. Cold pressed lemon (*Citrus limon*) seed oil. In *Cold Pressed Oils: Green Technology, Bioactive Compounds, Functionality, and Applications*; Ramadan, M.F., Ed.; Elsevier Inc.: Zagazig, Egypt, 2020; pp. 159–180, ISBN 9780128181881.
103. Singh, G.; Jeyaseelan, C.; Bandyopadhyay, K.K.; Paul, D. Comparative analysis of biodiesel produced by acidic transesterification of lipid extracted from oleaginous yeast *Rhodospiridium toruloides*. *3 Biotech* **2018**, *8*, 434. [[CrossRef](#)]
104. Sarno, M.; Ponticorvo, E. A new nanohybrid for electrocatalytic biodiesel production from waste Amalfi coast lemon seed oil. *Fuel* **2020**, *267*, 117178. [[CrossRef](#)]
105. Rozina; Chia, S.R.; Ahmad, M.; Sultana, S.; Zafar, M.; Asif, S.; Bokhari, A.; Nomanbhay, S.; Mubashir, M.; Khoo, K.S.; et al. Green synthesis of biodiesel from *Citrus medica* seed oil using green nanoparticles of copper oxide. *Fuel* **2022**, *323*, 124285. [[CrossRef](#)]

106. Rozina; Ahmad, M.; Zafar, M. Conversion of waste seed oil of *Citrus aurantium* into methyl ester via green and recyclable nanoparticles of zirconium oxide in the context of circular bioeconomy approach. *Waste Manag.* **2021**, *136*, 310–320. [[CrossRef](#)]
107. Mahato, N.; Sharma, K.; Sinha, M.; Baral, E.R.; Koteswararao, R.; Dhyani, A.; Hwan Cho, M.; Cho, S. Bio-sorbents, industrially important chemicals and novel materials from citrus processing waste as a sustainable and renewable bioresource: A review. *J. Adv. Res.* **2020**, *23*, 61–82. [[CrossRef](#)]
108. Mahato, N.; Agarwal, P.; Mohapatra, D.; Sinha, M.; Dhyani, A.; Pathak, B.; Tripathi, M.K.; Angaiah, S. Biotransformation of Citrus Waste-II: Bio-Sorbent Materials for Removal of Dyes, Heavy Metals and Toxic Chemicals from Polluted Water. *Processes* **2021**, *9*, 1544. [[CrossRef](#)]
109. Sudha, R.; Srinivasan, K.; Premkumar, P. Removal of nickel(II) from aqueous solution using *Citrus limettioides* peel and seed carbon. *Ecotoxicol. Environ. Saf.* **2015**, *117*, 115–123. [[CrossRef](#)] [[PubMed](#)]
110. Wang, Y.; Wang, S.; Xie, T.; Cao, J. Activated carbon derived from waste tangerine seed for the high-performance adsorption of carbamate pesticides from water and plant. *Bioresour. Technol.* **2020**, *316*, 123929. [[CrossRef](#)] [[PubMed](#)]

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