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Review

Advanced and Potential Methods for Extraction of Bioactive Compounds from Avocado Peel—A Review

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Abstract: Extraction techniques are continuously developed by the scientific community. Meanwhile, avocado peel is a by-product of avocado processing and a source of bioactive compounds. The purpose of this review was to summarize the use of advanced techniques for extracting bioactive compounds from avocado peel to help understand which techniques have and have not been applied to avocado peel. Three primary databases were used to collect the information, including Google Scholar, Scopus, and Web of Science, by using the keywords "avocado", "peel", and "extraction". Additional keywords related to the extraction technique were also used, including "Microwave-Assisted Extraction", "Ultrasound-Assisted Extraction", "Enzyme-Assisted Extraction", "Pressurized Liquid Extraction", "Supercritical Fluid Extraction", "Natural Deep Eutectic Solvents", "Three-phase partitioning (TPP)", "Pulsed-Electric Field", "High Voltage Electric Discharge Plasma", "Centrifugal Partition Extraction", and "Surfactant-Mediated Extraction". The results show that microwave-assisted extraction, ultrasound-assisted extraction, enzyme-assisted extraction, pressurized liquid extraction, supercritical fluid extraction, TPP, and natural deep eutectic solvent extraction have been used to retrieve bioactive compounds from avocado peel. Other techniques have not yet been applied for the extraction of bioactive compounds from avocado peel. This article is the first review discussing the advanced extraction technique for retrieving bioactive compounds from avocado peel. This article creates a paradigm for future studies.

Keywords: avocado peel; high voltage electric discharge plasma; natural deep eutectic solvent extraction; pulsed-electric field; three phase partitioning

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1. Introduction

The use of bioactive compounds extracted from various plants in the food and pharmaceutical industries has gained high interest recently. The incorporation of phenol-rich plants and extracts in food generally aims at improving its health-promoting properties [1,2]. Over the years, numerous methods have been developed to recover bioactive molecules from different agricultural products. An appropriate extraction method is essential for desorbing

compounds of interest from the plant matrix's active spots. This is because the extract's yield and quality are strongly linked to the effectiveness and selectivity of the extraction methods used [3,4].

Nowadays, scientists are making tremendous efforts to extract bioactive compounds from food by-products. In the context of sustainability and the circular economy, food by-products have been an emerging issue because 30–40% of the total food produced annually is wasted worldwide. About 40–50% of the food waste is from fruits, vegetables, and root crops [5]. The global consumption of fruit results in a vast quantity of solid waste, including peel, skin, and seeds. These materials still contain valuable, economically viable constituents.

Avocado (*Persea americana* Mill.) is a tropical fruit with economic significance in many countries [6]. Avocado has been used in several industries, including food and cosmetics. Thus, using avocado on an industrial scale brings a consequence in which the process generates a considerable number of by-products, such as peels and seeds. According to Figueroa et al. [7], the avocado peel is about 13% of the fruit weight. Avocado peel is a source of bioactive compounds. In their report, about 53 compounds were detected from the avocado peel, including phenolic content, and some of the compounds exhibited antioxidant activity. This implies that avocado peel is potentially further processed by appropriate extraction methods for retrieving its bioactive constituents.

Some established methods to obtain bioactive compounds from various plants include maceration, Soxhlet extraction, solvent–solvent extraction, and decoction. The aforementioned techniques are effective in retrieving bioactive compounds from avocado peels (Table in Section 4.7). The techniques, however, are considered traditional or conventional extraction methods because they are time-consuming and tedious and require large amounts of environmentally unfriendly organic solvents with low extraction yields. In recent decades, alternative environmentally friendly techniques have received more attention. Moreover, the advanced methods are faster, more selective, and automated, and they are able to preserve the quality of the extract. The advanced, so-called non-conventional methods include microwave-assisted extraction (MAE), ultrasound-assisted extraction (UAE), enzyme-assisted extraction, supercritical fluid extraction, and subcritical water extraction (SWE) for the quality of extracted molecules [8–11]. For this reason, developing a technique that aims to preserve the nature, quality, and quantity of molecules of interest and, thus, the success of the following steps is promising. This paper, therefore, discusses the advantages of the emerging techniques for extracting bioactive compounds from avocado peel. This paper also covers the advanced extraction techniques that have yet to be applied in avocado peel but may be interesting to conduct in future studies.

2. Method

To examine the research trend regarding the extraction of avocado peels, Google Scholar was used as the search engine. The search was limited to the last ten years, from 2014 onwards, by including patents and excluding citations. Three central databases were used to collect information for deeper discussion, including Google Scholar, Scopus, and Web of Science, by using the keywords "avocado", "peel", and "extraction". Additional keywords related to the extraction technique were also used, including "Microwave-Assisted Extraction", "Ultrasound-Assisted Extraction", "Enzyme-Assisted Extraction", "Pressurized Liquid Extraction", "Supercritical Fluid Extraction", "Natural Deep Eutectic Solvents", "Three-phase partitioning", "Pulsed-Electric Field", "High Voltage Electric Discharge Plasma", "Centrifugal Partition Extraction", and "Surfactant-Mediated Extraction". No specific duration was used to collect the information.

3. Research Trends in Extraction of Bioactive Compounds from Avocado Peel

Avocado is a source of nutrition and various bioactive compounds. The compounds may exhibit bioactivity, which may be beneficial for human health. The potential bioactivity of avocado lies not only in its flesh but also in its seeds and peels. Figure 1 illustrates the

potential bioactivity of avocado, including antioxidant, antimicrobial, anticancer, and anti-inflammatory activity. It is widely known that the bioactivity of each part is determined by its components inside the flesh, seed, peel, or extract [4].

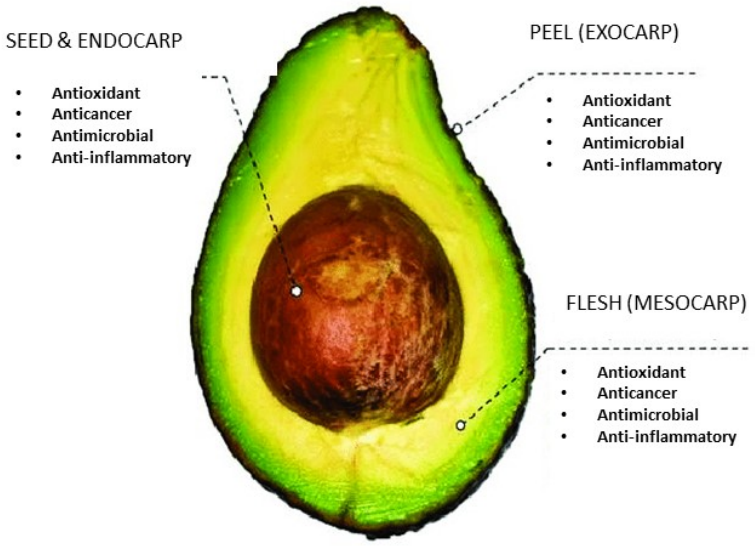

Figure 1. Illustration of avocado structure and its potential bioactivity. References: Alkhalaf et al. [12], Jimenez et al. [13], and Araujo et al. [14].

Flesh is the main product of avocado. However, nowadays, great attention is given to the bioactive compounds in the avocado's residue, including its peels, which are about 13% of the fruit's weight. As shown in Figure 2, the research trends regarding avocado peel extraction have increased significantly in the past ten years. In 2014, the publications on the topic of avocado peel extraction were about 811 articles, and in 2023, it increased to almost three times that, at 3080 publications. Various methods have been applied by scientists to extract bioactive compounds from avocado peels. It includes microwave-assisted extraction (MAE), ultrasound-assisted extraction (UAE), enzyme-assisted extraction (EAE), pressurized liquid extraction (PLE), supercritical fluid extraction (SFE), natural deep eutectic solvents (NaDESs) extraction, and three phase partitioning (TPP).

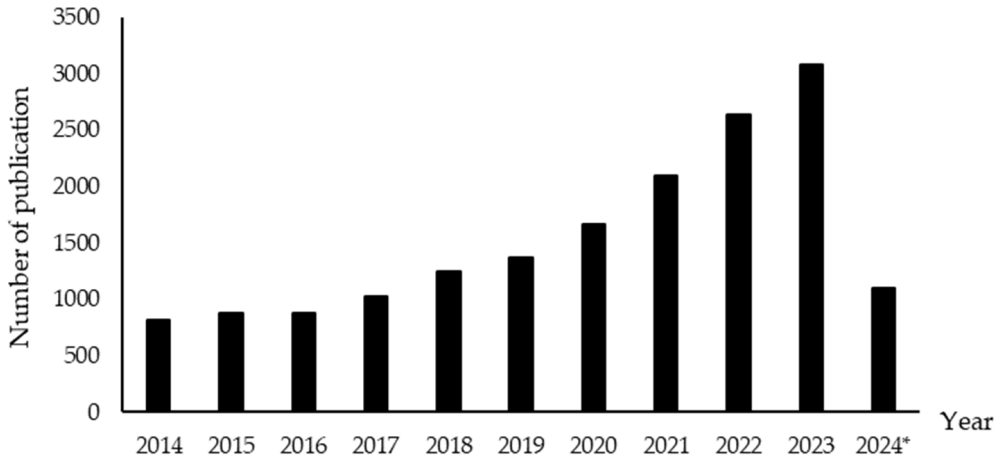

Figure 2. Number of publications regarding extraction of avocado peels. (*) Data up to May 2024.

4. Advanced Methods for Extraction of Bioactive Compounds from Avocado Peel

4.1. Microwave-Assisted Extraction (MAE)

Microwave-assisted extraction (MAE) is an improved maceration method for extracting bioactive compounds that use microwave energy. Typically, this method uses less

energy, less time, less water, and less cost. As in maceration, a separation step (filtration) is necessary to separate the matrix from the extraction medium at the end of the extraction [15]. It is important to note that microwave-generated temperatures can degrade heat-sensitive components. Even though the thermal deterioration of the compounds cannot be avoided, it is still lower than any traditional extraction method. However, microwave extraction is also limited by the higher investment cost than conventional extraction. According to Figueroa et al. [7], MAE has been successfully used to extract polyphenols from avocado peel. Temperature, duration, ethanol concentration, and solvent–sample ratio played significant roles in the yield of extractable phenols. The optimal MAE conditions were reported at the temperature of 130 °C, extraction time of 39 min, ethanol concentration of 36%, and solvent–sample ratio of 44 mL/g. The extract was reported to have contained 53 polar compounds. MAE extracted eight-fold higher phenols within similar conditions than conventional solid–liquid extraction. In addition, Araujo et al. [16] demonstrated that avocado peel extract contained procyanidins, catechin, and phenolic acids, exhibiting high antioxidant capacity. MAE can be conducted independently and be combined with another method, such as ultrasound-assisted extraction.

4.2. Ultrasound-Assisted Extraction (UAE)

Ultrasound-assisted extraction (UAE) is one of the most straightforward extraction techniques and an efficient method to extract metabolites from plants in shorter times than other extraction methods [17,18]. The main reasons why UAE is a favored extraction technique for extracting active compounds are its adaptability and the possibility of using less or no organic solvent, its nature as a physical extraction technique, its simplicity of operation, its extraction effectiveness, its capacity to preserve the biological activity of extracted substances, its reduced reliance on time, and its industrial application, among other things [19,20]. The type of plant material, extraction solvent, and microenvironmental extraction factors significantly impacted UAE outcomes. This means that the extraction technique must be optimized for each plant material and ultrasonic equipment employed to provide the optimum outcomes regarding extraction yields and biological activity preservation.

In the study of Hefzalrahman et al. [21], UAE was used to retrieve phenols from avocado peel. It was reported that the major polyphenolic compounds identified in the extracts were benzoic acid, vanillic acid, resveratrol, and syringic acid. The most effective conditions for recovering phenols from the avocado peel were reported to be a solid-to-solvent ratio of 1:20 (w/v), ultrasonic intensity of 20%, and duration of 30 min. This study concluded that the UAE was more efficient than enzyme-assisted extraction. As was well-stressed in the study of Rodríguez-Martínez et al. [22], the application of UAE resulted in avocado peel extract containing phenolic and flavonoid compounds, which presents high antioxidant activity and low cellular toxicity in normal cells, indicating that avocado peel extract is safe for human consumption.

UAE has been proven to retrieve bioactive compounds from avocado peel successfully. However, more studies are necessary to comprehend the effect of UAE on the extract composition and to understand the structure and functional changes before and after the extraction processes by comparing them with the controls. This can aid in determining the impact of chemicals on degradation and the amounts of certain compounds in extracts. In addition, to determine the process's safety for usage in foods and other applications, researchers must investigate the degradative effects of UAE on bioactive compounds and their intermediary products, as well as their biological impacts in vitro and in vivo. In this context, ion-based liquid, also called ion-based liquid ultrasound-assisted extraction (ILUAE), is now an emerging extraction technology that could replace conventional solvents in the UAE.

In recent years, IL-based extraction strategies have been employed to extract phenolic chemicals from plant sources [23,24]. Ionic liquids (ILs) are simple molten salts that are liquid at or near room temperature and include a relatively significant organic cation and an

inorganic anion. Ionic liquids provide potential advantages over ordinary organic solutions, such as a low melting point, a vast liquid temperature range, low vapor pressure, and extended, specialized solvent characteristics [25]. One of the advantages of this technology is the ability to optimize their properties for a specific application by changing the nature of the anion/cation pair; also, the speed of reactions, selectivity, and yield are frequently more incredible in ionic liquids. The non-volatility of ionic liquids is employed in many chemical processes because it prevents operators from being exposed to solvent vapors. At ambient temperatures, ionic liquids have no vapor pressure and are thus non-volatile, eliminating the hazards and pollution of solvent evaporation. Salts dissolve well in ionic liquids and are miscible with other solvents. The organic reaction product can be removed easily from the ionic liquids containing the catalysts. As a result, the catalyst can be extracted from the products and reused. Although an organic solvent is required for extraction, the catalyst and solvent are still recycled and environmentally friendly. Currently, no study has applied ILUAE to extract metabolites from the avocado peel. Therefore, a trajectory study in this area may be interesting.

4.3. Enzyme-Assisted Extraction (EAE)

The enzyme-assisted extraction (EAE) technique utilizes hydrolytic enzymes to deteriorate the structural integrity of cell walls, exposing intracellular components for increased extraction yield. Cellulase and pectinase enzymes are usually used as a pre-treatment step before solvent extraction. Cellulase breaks down the 1,4-d-glycosidic bonds in cellulose in plant cells' major cell walls. Pectinase, likewise, destroys pectic compounds and pectin in the middle lamella and primary cell walls [26]. The use of enzymes is an exciting alternative to environmentally damaging methods. One of the most valuable advantages of this technique is the possibility of reusing the enzymes, which makes the technique somewhat economical and facilitates the application of enzymes in medical analysis [27].

The enzymatic extraction of bioactive compounds has been used for a long time for some materials, but its use for extracting bioactive compounds from the avocado peel is scarcely reported. So far, Hefzalrahman et al. [21] reported that EAE was less effective than UAE. Therefore, it has to be improved or integrated with other techniques to boost efficiency, reduce processing time, and make the procedure competitive. Also, the most prevalent enzymes are unspecified enzymes like proteases, which might result in the extraction of other components [28]. EAE can be enhanced by combining it with other environmentally friendly approaches such as ultrasonic extraction, supercritical fluid extraction, ionic liquid extraction, three-phase partitioning, and microwaves.

4.4. Pressurized Liquid Extraction (PLE)

Pressurized liquid extraction (PLE) is also well-known as accelerated solvent extraction (ASE), pressurized hot solvent extraction (PHSE), high-pressure solvent extraction (HPSE), and high-pressure high-temperature solvent extraction (HPHTSE). This method is a constant high-pressure extraction that facilitates the improvement of cell permeability, intermolecular physical interactions, and penetration of the extraction solvent or solvents, thus improving the extraction efficiency.

PLE was first presented at the Pittcon Conference in 1995 by Dionex Corporation, and it is today a considerably more well-established technology. This approach has recently been integrated into the food field, which is a recent example. Figueroa et al. [29] demonstrated that PLE was successfully employed to extract phenols from avocado peel dominated by phenolic acid. It was reported that the most effective extraction conditions were at 200 °C with a solvent containing 1:1 v/v as ethanol/water ratio.

Subcritical water above the standard boiling temperature of 100 °C, also called compressed hot water (CHW), is another solvent commonly used in PLE. This method is also well-known as accelerated water extraction (AWE). This extraction procedure is considered a green, non-toxic, and environmentally friendly technique involving subcritical water as the appropriate solvent for extracting solid and semi-solid samples. The use of water

in the subcritical region as a "green" solvent has attracted the interest of many scientists worldwide. It is a solid–liquid extraction technique in which organic or aqueous solvents are used to extract compounds from a solid or semi-solid material at high temperatures and pressures [30]. To the best of our knowledge, no study focuses on avocado peel extraction using subcritical water. In the study of Mazyan et al. [31], subcritical water extraction was used to extract phenols from avocado fruit flesh. The extraction duration employed in this study was 10–30 min, with the subcritical water conditions studied at 18 bar, 87 mL/min, and 105–140 °C. This condition may also apply to extracting bioactive compounds from the avocado peel.

PLE is regarded as a more environmentally friendly alternative to Soxhlet extraction. At the same time, the enhanced pressure keeps the solvent below its boiling point, allowing the sample to become more soluble and attain a higher diffusion rate. Solvents penetrate solid samples more efficiently at higher pressures and temperatures, thus reducing solvent usage [32]. Compared to traditional Soxhlet extraction, PLE achieved a considerable reduction in analysis time with improved recoveries for more pollutants, with no discrepancies in the data [33]. Thus, further exploration of this technique for extracting biological active compounds from avocado peel is still required.

4.5. Supercritical Fluid Extraction (SFE)

Supercritical fluid extraction (SFE) is also considered an environmentally friendly process. This is an efficient technique for extracting thermolabile compounds from a solid or liquid matrix, using supercritical CO_2 (SC-CO_2) as an extraction solvent. SFE obtained the most significant number of patents filed (7550 patents) for extracting compounds. Furthermore, SFE can operate at low temperatures without oxygen or light, which is critical for maintaining the purity and integrity of the extract prior to analysis. SFE has been used to extract alkaloids, phenolic chemicals, anthocyanins, flavonoids, carotenoids, saponins, and oils [34,35]. It may be applicable to the avocado peel as well.

Carbon dioxide is primarily capable of extracting non-polar molecules due to its polarity. To circumvent this problem, another solvent could be used in conjunction with CO_2 at deficient concentrations to improve the polarity of the supercritical fluid. Co-solvents have included ethanol or methanol and, more recently, ethyl lactate, vegetable oils, and ethyl acetate combined with less than 10% total CO_2 [35]. Using supercritical CO_2 has several advantages over traditional approaches. SC increased CO_2's diffusion coefficient and reduced viscosity, allowing it to quickly penetrate the pores of complex matrices, increasing extraction efficiency. Furthermore, because the depressurization process quickly separates CO_2, the extracts obtained via SFE are highly concentrated, leaving no trace of harmful organic solvents in the final product. Also, since CO_2 gas may be recycled, the disruption of cells by a quick depressurization treatment can be performed in the SFE equipment, which optimizes extraction by lowering the time and labor requirements [36]. Hitherto, PLE was compared to SFE to extract phytoactive compounds in buckwheat in a single case. The two types of extraction gave very similar results [36]. In the study of Restrepo-Serna et al. [37], SFE was used to retrieve bioactive compounds from avocado peels and seeds. Before extraction, the dried avocado peels and seeds are milled to a particle size of 0.4 mm. Then, the SFE was performed using CO_2 as a supercritical solvent with operating conditions of 80 °C and 250 bar for 30 min. Ethanol was presented as a co-solvent in a ratio of 1:1.5 S:L.

Thus, SFE is an alternative method for extracting valuable analytes from various matrices [38]. SFE is a selective and environmentally friendly technology primarily employed in large-scale industrial applications. However, it has also been examined as an unusual sample preparation technique because it decreases the usage of organic solvents while increasing yield [39,40]. Although various solvents can be used as supercritical fluids for extraction, carbon dioxide is the most popular due to its numerous advantages [41]. It is GRAS (Generally Recognized as Safe) for use in the food industry, inexpensive, and readily available; it enables the reuse of CO_2 generated in other industrial processes, thus meeting

some Green Chemistry principles. Its characteristics are essential because it enables the extraction of a solvent-free extract following depressurization, which is especially useful when the extract contains chemicals that are prone to degradation [34]. Carbon dioxide is widely known as an eco-friendly solvent, and several comprehensive reports have shown its benefits as a green solvent [41,42]. From the point of view of environmental analysis, CO_2 is the second green solvent, followed by water [43].

4.6. Natural Deep Eutectic Solvents (NaDESs) Extraction

Deep eutectic solvents (DESs) are an extraction method that increasingly uses solvents as a greener alternative to ionic liquids. DESs are solvents formed by mixing two or more compounds at an exact ratio corresponding to the eutectic point [44]. NaDES deserves special attention because of its characteristics, which make it very promising for future applications. Recently, NaDES has been identified as an ecological and green solvent that has attracted significant attention from the scientific community. NaDES has several beneficial physicochemical properties, including a liquid state across a wide temperature range, low volatility, chemical and thermal stability, nonflammability, and nontoxicity of constituent elements [45]. In addition, NaDES solvents are widely available in nature, easy to obtain, and renewable [46]. Furthermore, NaDES is made up of non-toxic ingredients that are found naturally in foods and can be employed directly in food compositions. The solvent purification phase is not required after the extraction process, and the extract can be used directly in food-grade applications, lowering production costs compared to the standard organic solvent extrication procedure [45]. Nevertheless, a disadvantage of NaDESs compared to standard organic or aqueous solvents is that NaDESs have relatively high viscosity. The high viscosity of NADESs would make extracting food extremely challenging. The difficulty, however, has been handled; it has been shown that adding water to NaDESs can reduce its viscosity [47]. This approach makes applying this technology in the industry more feasible. Rodríguez-Martínez et al. [48] reported that NaDES has been successfully used to extract bioactive phenolic compounds from avocado peels. From five selected DESs, it was found that the best extraction results were obtained with choline chloride-acetic acid and -lactic acid, the extraction efficiency of which was higher than that of ethanol. The avocado peel extract obtained by NaDES exhibited high antioxidant and antimicrobial activity, particularly against *Staphylococcus aureus*, *Streptococcus dysgalactiae*, *Escherichia coli*, and Pseudomonas putida.

4.7. Three-Phase Partitioning (TPP)

Three-phase partitioning (TPP) is a simple and effective one-step technique for separating, purifying, and concentrating biomolecules such as enzymes, lipids, polysaccharides, and other biomolecules from complicated mixtures. This technique is also scalable and fast and considered an economical and efficient process for separations. In the TPP method, a solvent, such as t-butanol, is mixed with an aqueous anti-chaotropic salt, ammonium sulfate, at ambient temperature to generate two phases: the aqueous layer and the organic layer. It has been used to extract a wide range of biomolecules, most of which are proteins [49,50].

The application of TPP has developed as a more ecologically friendly alternative to hexane extraction, allowing for the separation of important biological components. As a result, searching for new suitable salts and solvents that would allow for more appealing and cost-effective phase systems appears promising and potentially expands the scope of this technique's uses [51]. Indeed, the TPP technique is still a relatively new method for biomolecule recovery. It has yet to be widely used to extract compounds from avocado peel. Jiménez-Velázquez and his co-workers [52] extracted the avocado peels using polyethylene glycol with 24.9–14.5% sodium nitrate and 12.2–15.5% magnesium sulfate. They found that the recovery was more than 82% of flavonoids, phenols, and condensable tannin from the avocado peel.

The possibility of incorporating external approaches into TPP, such as ultrasound high pressure and even microwaves, to improve the separation process is very promising and may be interesting for future research. Optimization steps can also be established and recommended to assess the effect of various process parameters on the recovery yield and purity of the extraction of compounds. This would bolster TPP's advantages in biomolecule separation and purification in the future. A summary of TPP extraction, as well as other techniques that have been used to extract bioactive compounds from avocado peels, is shown in Table 1.

Table 1. Various extraction methods for retrieving bioactive compounds from avocado peels.

Extraction Method	Important Finding	Ref.
Maceration	The extract contained 48 compounds, where the major components were flavonoids and procyanidins. The extract inhibited platelet aggregation (at 1, 0.75, and 0.5 mg/mL) and reduced enzymatic inhibition, especially inhibition of xanthine oxidase, hyaluronidase, and acetylcholinesterase.	[53]
	Avocado peel methanolic extract contained phenolic compounds (21.833 ± 0.118 mg/100 g extract), flavonoids (2.607 ± 0.111 mg/100 g extract), tannins (38.357 ± 0.202 mg/100 g extract), saponins (8.874% ± 0.031%), and alkaloids (9.95 ± 0.035 mg CE/g extract) that contributed to its antioxidant activities. Its IC_{50} was 185.891 ± 1.598 ppm.	[54]
	The ethanolic extract inhibited the growth of *Staphylococcus*. A longer extraction time (1.5, 3, and 4 h) showed a higher antioxidant and antibacterial activity.	[55]
	The optimal maceration of avocado peel was obtained with 40% ethanol, 49.3 °C, solvent/feed ratio of 14.3 mL/g, and 60 min process. The optimal extract showed the highest total phenolic content (44.24 mg GAE/g peel dw), total flavonoid content (786.08 mg QE/g peel dw), antioxidant capacity against DPPH (564.82 µmTE/g peel dw), FRAP (1006.21 82 µmTE/g peel dw), and ABTS (804.40 82 µmTE/g peel dw).	[56]
	The total polyphenolic content of avocado peel, pulp, and seed ethanolic extract was 200, 245, and 424 mg GAE/100 g DW, respectively. The total flavonoid contents of avocado peel, pulp, and seed ethanolic extract were 36.06, 36.98, and 32.54 mg RE/100 g DW, respectively. The radical scavenging activity of avocado peel, pulp, and seed extract was 4.90, 3.24, and 3.63 µg/mL, respectively.	[57]
	The extract contained the phenolic compound (59.55 GAE mg/gram extract), flavonoid (2.96 QE mg/gram extract), and tannin (22.63 TAE mg/gram extract). The extract significantly changed hydration levels, collagen, and skin elasticity with 2 times application per day for 4 weeks in male rats (in vivo).	[58]
	The avocado peel extract contained phenolics compounds (309.95 ± 25.33 mmol GA/100 g of extract), flavonoids (12.54 ± 0.52 mmol Cat.eq/100 g of extract), and anthocyanins (622.37 ± 17.26 mmol Cyanidin-3-glucoside eq./100 g of extract). The extract showed an antiproliferative effect mediated by apoptosis, oxidative stress reduction, and antiproliferative effect.	[59]
	The extracts showed a high content of Ca, Mg, Fe, Zn, ω-6 linoleic acid, and flavonoids. The extract showed acetylcholinesterase inhibition with no significant difference with eserine control.	[60]
	The wet grinding plus maceration showed the highest value of total phenols (2143.1 mg GAE/100 g dry weight), chlorogenic acid (244.3 mg/100 g dry matter), and epicatechin (181.7 mg/100 g dry matter). The wet grinding plus maceration method used accessible technology and more environment-friendly solvent than others.	[61]

Table 1. *Cont.*

Extraction Method	Important Finding	Ref.
Microwave-assisted extraction	The extract showed high matrix metalloproteinases inhibitory capacity and antioxidant activity. The total phenolic content of the extract was 18.1–68.8 mg GAE/g peel DE, which was affected by time, temperature, and solvents during extraction.	[7]
	The highest antioxidant capacity was obtained by 74.48 °C–4.13 min and 66.37 °C–0.97 min extractions with 42.58% ethanol. The extract showed a high polyphenolic content (3.79.28 ± 19.35 mg GAE/g dry extract) and high antioxidant activity measured by DPPH, ABTS, and ORAC assay.	[16]
Vacuum microwave-assisted aqueous extraction	The optimal extractions were temperature of 79.64 and 78.11 °C, time of 11.89 and 11.75 min, ratio of water and avocado peel 16.45 and 10.02%, and microwave power of 5708.04 and 5699.10 W. The conditions showed the highest TPC (0.352 gallic acid equivalent-GAE/g fresh avocado peel/min) and DPPH radical scavenging activity (0.104 L/min).	[62]
Vacuum microwave-assisted aqueous extraction	- The avocado peel extract contained flavonoids that exhibited antioxidant, antimicrobial, and antifungal activity.	[63]
Ultrasound-assisted extraction	The extract by Sonotrode extraction had higher flavan-3-ols recovery (54%) and antioxidant activity (62–76%) than ultrasound bath extraction. Sonotrode extraction was an alternative to non-thermal, low-time-consuming, and scalable methods for extracting the bioactive compounds as functional ingredients.	[64]
	The extract with acetone–water solvent showed higher total phenolic content (208.5 ± 19.8 mg GAE/g DE) than the extract with ethanol (183.4 ± 6.0 mg GAE/g DE) and ethanol–water solvent (192.6 ± 11.1 mg GAE/g DE).	[65]
	The optimal extraction obtained by response surface methodology was 50.9 °C of temperature, 49.5% of ethanol/water, and 61.8 min. The extract contained 124.050–125.187 mg GAE/g of phenolic content.	[66]
	The ethanol concentration higher than 40% decreased phenolic content. The optimized extract was obtained with 38.46% of ethanol, 44.06 min, and 50 °C. The extract contained high phenolic and flavonoid compounds. It influenced the metabolic activity of normal and cancer cells, but the extract had positive effects on metabolic activity and inhibited cancer (Caco-2, A549, and HeLa) cells. The extract showed low cellular toxicity in normal cells but negatively affected cancer cells, particularly HeLa cells.	[22]
	The avocado peel extract had higher phenolic content and antioxidant activity but lower IC_{50} value (59 ppm) than cocoa bean, coconut, and cactus pear extract. The avocado peel extract showed inhibitory activity against *Staphylococcus aureus*, *Shigella dysenteriae*, and *Candida albicans*.	[67]
Ultrasound–microwave combined extraction	The avocado extract had higher phenolic compounds and antioxidant activity than the aqueous fraction and the acid-microwave hydrolyzed fraction. The extract inhibited growth of *Pseudomonas aeruginosa* and *Bacillus cereus*, *Staphylococcus aureus*, *Salmonella* spp., and *Salmonella* spp.	[68]
Ultrasound-assisted deep eutectic solvent extraction	The optimal extraction conditions were a matrix/solvent ratio of 1:30 (*w*/*v*), an extraction time of 15 min, and a temperature of 25 °C. The phenolic compounds of 8.29 ± 0.07 g GAE/100 g of dry avocado peel were extracted by the optimal extraction above.	[69]
Ultrasound-assisted extraction and enzyme-assisted extraction	The major polyphenolic compounds of the extract were benzoic acid, vanillic acid, syringic acid, and resveratrol. The ultrasound-assisted extraction yielded phenolic extraction equal to that of enzyme-assisted extraction. The extract of ultrasound-assisted extraction showed a solid-to-solvent ratio of 1:20 (*w*/*v*), 20% ultrasonic intensity, 30 min showed the highest polyphenols (35.4 mg GAE/g of dried peel).	[21]

Table 1. *Cont.*

Extraction Method	Important Finding	Ref.
Enzymatic-assisted extraction	The avocado peel extract treated by peptidase showed higher total phenolics (45.46 mg GAE/g DW) and antioxidant activities (FRAP: 1547.00 µmolTE/g, DPPH: 243.93 µmolTE/g, ABTS assay: 211.96 µmolTE/g) than the methanolic extract.	[70]
	Total phenolic content (TPC) of avocado peel (296.5–515.1 mg/100 g DM) between TPC of avocado pulp (38.0–41.0 mg/100 g DM) and TPC of avocado seed (395.3–663.93 mg/100 g DM). The antioxidant capacity of avocado peel extract (ABTS: 6.407–20.96 mmol TE/g, DPPH: 9.341–22.85 µmol TE/g) was lower than avocado seed extract (ABTS: 14.70–24.54 mmol TE/g, DPPH: 24.78–52.08 µmol TE/g), but higher than avocado pulp (ABTS: 3.587–5.748 mmol TE/g, DPPH: 0.635–0.962 µmol TE/g) and avocado oil (ABTS: 0.320–0.561 mmol TE/g, DPPH: 0.040–0.351 µmol TE/g).	[71]
Natural deep eutectic solvent (NaDES) extraction	The best solvents used were choline chloride-acetic acid and -lactic acid., The deep eutectic solvents were more efficient than ethanol. The extract contained higher phenolics (92.03 ± 2.11 mg GAE/g DAP) and flavonoid content (186.01 ± 3.27 mg RE/g DAP) than conventional extract with ethanol.	[48]
Pressurized liquid extraction	The extraction with pure water (without ethanol) at 100 bar and 40 °C obtained a high extraction yield (26.8 ± 0.9%), antioxidant capacity (ABTS: 3350 ± 179 µmol TE/g dry extract, ORAC: 0.14 ± 0.01 µg/mL), total phenol content (505 ± 25 mg GAE/g dry extract), and acetylcholinesterase inhibition (33.6 ± 2.9 µg/mL).	[72]
	The total phenolic content of avocado peel extract was 158.8 ± 25.9 mg GAE/g DE—higher than the phenolic content of avocado seed tegument extract (9.5 ± 0.16 mg GAE/g DE) but lower than avocado seed extract (11.9 ± 0.05 mg GAE/g DE). The antioxidant capacity of avocado peel extract was 1329.4 ± 492.1 µmol TE/g DE of DPPH, 829.8 ± 445.4 µmol TE/g DE of ABTS, and 3215.1 ± 668.4 µmol Fe^{2+}/g DE of FRAP.	[65]
Supercritical fluid extraction	Avocado peel extract contained phenolic acid, flavonoid, quercetin, and catechin. The production cost is 5.52 USD/kg for stand-alone extraction processes, with profit margins of 21.14%.	[37]
	The supercritical fluids extraction increased 14.20–17.14% extraction yield but decreased catechins concentration on Lorena variety. The optimal conditions during supercritical fluids extraction were 60 C, 0.2 mg avocado peel every liter of solvent, 30 kHz, and 60 min. The minimum extraction cost was 8.21 USD/kg of avocado peel extract.	[73]
Aqueous two-phase extraction	The extraction based on polyethylene glycol with 24.9–14.5% sodium nitrate and 12.2–15.5% magnesium sulfate recovered more than 82% flavonoids, phenols, and condensable tannin from the avocado peel.	[52]
Hydrothermal treatment	This extraction was due to increased oligosaccharides and polyphenolics recovery. The optimal extraction obtained by 150 °C with the highest oligosaccharide recovery (14.3 g oligosaccharides/100 g avocado peel) and antioxidant phenolics recovery (3.48 g gallic acid equivalents/100 g AP and 10.80 g Trolox equivalents/100 g avocado peel measured with $ABTS^{\bullet+}$ assay).	[74]
Combination of maceration and hydrothermal carbonization	The extract was divided into ethanolic extract, liquid phases, and heavy bio-oils. Ethanolic extract had the highest proanthocyanidins content. The liquid phases were high in total phenols, flavonoids, and hydroxynamic acids. Heavy bio-oils inhibited tyrosinase and elastase activities significantly.	[75]

5. Potential Techniques for Extraction of Bioactive Compounds from Avocado Peel

Aside from the above-mentioned extraction techniques, there are some other modern extraction methods, including (a) pulsed-electric field extraction (PEF); (b) high voltage electric discharge plasma (HVED); (c) centrifugal partition extraction (CPE); and (d) surfactant-mediated extraction (SME). To the best of our knowledge, the methods have yet to be applied to extracting the valuable compounds of avocado peels. Considering the

characteristics of the process, these techniques could be developed for extracting biological compounds from avocado peel.

5.1. Pulsed-Electric Field Extraction (PEF)

PEF is a non-thermal approach in which the electric potential divides molecules in the cell membrane based on their charge due to the dipole nature of membrane molecules. PEF has increased cell membrane permeability and improved intracellular chemical release from plant tissue [76]. In this technique, materials are treated with PEF electrodes that have brief(s) and high voltage pulses (kV/cm) surrounding them [77,78]. Plant tissue cell membranes are damaged by PEF treatment at a modest electric field (500 and 1000 V/cm; for 104–102 s) with little temperature increase [79].

PEFs can be employed for industrial purposes due to various advantages, including a shorter extraction time, higher yield, and low process temperature [80,81]. In previous decades, the pulsed electric field (PEF) treatment has been acknowledged as effective in improving pressing, extraction, drying, and diffusion processes [77]. PEF destroys the cellular membrane structure to improve mass transfer during extraction, resulting in faster extraction. As a result, PEF can help to prevent heat-sensitive chemicals from degrading. However, the study focusing on extracting avocado peel using PEF still needs to be discovered. Thus, in-depth research on the application of this technique for extracting valuable compounds from the avocado peel is required.

So far, there are some examples of successful PEF extraction. An earlier report presented that PEF was successfully employed to extract quercetin and ellagic acid from fresh *Emblica officinalis* juice at 18 to 24 kV/cm with a pulsed time duration of 300 to 1000 s. The best field strength was shown at 22 kV/cm, which resulted in a disintegration index of 0.79 in 500 s. PEF samples demonstrated a nine-fold increase in quercetin and ellagic acid content compared to thermally treated juice [82]. Another study looked at the effects of PEF on the extraction efficiency of fresh spearmint (*Mentha* × spicata L.) leaves [83] and found that the conditions that resulted in the maximum disintegration (0.860.02) were 99 pulses, 3 kV/cm field strength, and 4,102,239 J/kg specific energy input PEF extraction of total phenolic content (TPC), antioxidant capacity (AC), and antioxidant activity (AA), was also comparable to heat and microwave pre-treatments, with much higher AA value than freezing/thawing, according to the same study's findings. In addition, compared to untreated samples, the product kept a better color, had a deeper flavor, and had a higher rehydration capacity [84]. PEF also effectively extracts anthocyanin monoglucosides from grape by-products [85]. PEF can also be used as a pre-treatment technique on plant materials before traditional extraction to reduce extraction effort [86]. Before the maceration process, a PEF treatment on the grape skin can shorten the maceration time and improve the stability of bioactive compounds (anthocyanin and polyphenols) during vinification [87]. Another example showed that using PEF to permeabilize Merlot skin resulted in greater extraction of anthocyanins and polyphenols [88].

5.2. High Voltage Electric Discharge Plasma (HVED)

Another new technology, high voltage electric discharge plasma (HVED), is a unique and exciting alternative to extraction technology. HVED is a general term for pulsed mode plasma systems. However, it is most commonly called "corona discharge" since it resembles a crown around the cathode wire when utilizing a pulsed DC power supply. This technology, which uses pulsed rapid discharge voltages (electric field intensity ranging from 20 to 80 kV/cm), is based on the mechanism of electrical breakdown in liquid, which causes physical and chemical processes that affect both cell walls and membranes while also releasing intracellular components [89]. Moreover, during the photonic dissociation of water, HVED forms heat and confines plasma, which emits UV light and -OH radicals. HVED will produce shockwaves and pyrolysis due to electrohydraulic cavitation at the same time [90,91].

Recent research verified HVED as a practical extraction approach with a considerable improvement in yield due to sample cell disturbances and improved mass transfer during electrical breakdown [92]. Another study discovered that HVED is a pre-treatment strategy that improves pectin recovery from sugar beet pulp without changing the structure or chemical makeup of the pectin [93].

The application of HVED for extracting bioactive compounds from avocado peel has not yet been carried out up till now. However, the extraction of proteins and polyphenols from olive pits has been successfully conducted, and it was proven that HVED was faster than UAE or PEF [94]. This method preserved more proteins and polyphenols during processing [95]. PEF and HVED, as well as other electrically assisted extractions, are less thermally damaging and are more effective for particular compound extraction. Extracts can be obtained in less time and at lower temperatures [96,97]. Thus, this technique may potentially extract bioactive compounds from the avocado peel.

5.3. Centrifugal Partition Extraction (CPE)

Centrifugal Partition Extraction (CPE) is a centrifugal-field-based multi-stage liquid–liquid extraction process. The partition coefficients between the two liquid phases are used to extract the specified components [98]. CPE is derived from centrifugal partition chromatography (CPC) with a column design characterized by fewer cells of larger volume. The purification of phenolic chemicals from marine resources is the most common application of this approach [99,100]. CPE was employed to recover bioactive phenolic compounds from the brown seaweed *Sargassum muticum*. It was shown that the total phenolic content of the CPE extract was higher than that of the PLE and SFE extracts. The total phenolic compound content in CPE was double that of PLE, which had the second-highest concentration [101]. Still, more research is needed to investigate alternate methodologies, improve operating conditions, and apply them to different agricultural products, including avocado peel.

There are various advantages to CPE and CPC. The essential advantage is that, unlike HPLC, this separation technique does not necessitate changing the chromatographic column between analyses. Furthermore, no silica must be used or recycled because the stationary phase is a liquid. In most cases, only a tiny amount of the stationary phase is needed for extraction. All of these benefits result in a reduction in the expenses associated with extractions. CPC, on the other hand, is a technique known as “soft separation”. Indeed, there is no irreversible adsorption, resulting in a 90% recovery rate. The molecules to be removed are also subjected to minimal or no denaturation. These compounds have a purity percentage of >99%. The CPC, on the other hand, has some limitations. It has a low efficiency in terms of theoretical plate height, which is one of its drawbacks. Furthermore, its extractions can only reach the milligram mass level of an analyte, whereas other separation techniques can reach the microgram level. A robust seal is also required for the CPC to function correctly [102].

5.4. Surfactant-Mediated Extraction (SME)

Surfactant-Mediated Extraction (SME), which uses surfactants to remove phenolic chemicals, is also a promising new method [103]. Surfactants can produce monomolecular layers on a liquid’s surface, lowering the interfacial tension between two liquids and allowing them to mix. SMEs may be able to isolate molecules with a wide range of polarities and complex chemical structures. SME was compared to EAE and PLE to isolate total phenolic compounds and phlorotannins from the brown seaweed *Lobophora variegata* by Gümüş Yilmaz et al. [104]. It was shown that SME produced more total phenolics and phlorotannins than EAE and PLE. However, until now, no study has focused on the use of SMEs for extracting bioactive compounds from avocado peel.

6. Conclusions and Outlook

To sum up, bioactive compounds shall be produced sustainably. Advanced techniques have been applied to extract bioactive compounds of avocado peels to improve efficiency

and thus minimize the extraction process's negative impact on the environment. Advanced techniques are more efficient in terms of extraction yield than traditional methods. For extracting bioactive compounds from the avocado peel, there are some advanced methods that have been applied, including (a) microwave-assisted extraction (MAE), (b) ultrasound-assisted extraction (UAE), (c) enzyme-assisted extraction (EAE), (d) pressurized liquid extraction (PLE), (e) supercritical fluid extraction (SFE), (f) natural deep eutectic solvents (NaDESs) extraction, and (g) three-phase partitioning (TPP). On the other hand, some other advanced methods have been applied to extract bioactive compounds from the avocado peel, including (a) pulsed-electric field extraction (PEF), (b) high voltage electric discharge plasma (HVED), (c) centrifugal partition extraction (CPE), and (d) surfactant-mediated extraction (SME). An in-depth investigation of each extraction technique may be fascinating for future studies. The yield may increase even more by using a mix of these strategies. A combination of at least two new technologies may be used to increase the extractability of compounds. Moreover, this review clearly shows that some new technologies still need to be implemented to extract compounds from the avocado peel. Therefore, exploration in this area may be interesting for future research. However, researchers working in this field should consider integrating such necessary information to understand the impact of each new extraction process on the yield and quality of compounds in the avocado peel. Furthermore, researchers must investigate the degrading effects of each new technique on phytochemical compounds, their metabolites intermediates, and their biological implications in vitro and in vivo.

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