



*Review*

## **Bioactive compounds from plants and by-products: Novel extraction methods, applications, and limitations**

**Ahmed A. Zaky<sup>1,2</sup>, Muhammad Usman Akram<sup>3</sup>, Katarzyna Rybak<sup>1</sup>, Dorota Witrowa-Rajchert<sup>1</sup> and Malgorzata Nowacka<sup>1,\*</sup>**

<sup>1</sup> Department of Food Engineering and Process Management, Institute of Food Sciences, Warsaw University of Life Sciences-SGGW, Warsaw, 02-787, Poland

<sup>2</sup> Department of Food Technology, Food Industries and Nutrition Research Institute, National Research Centre, Dokki, Cairo, 12622, Egypt

<sup>3</sup> Department of Food and Human Nutritional Sciences, University of Manitoba, Winnipeg, Manitoba, R3T 2N2, Canada

\* **Correspondence:** Email: [malgorzata\\_nowacka@sggw.edu.pl](mailto:malgorzata_nowacka@sggw.edu.pl); Tel: +48225937579; Fax: +48225937576.

**Abstract:** In recent years, numerous articles documenting bioactive components derived from diverse food sources have been published. Plant-based bioactive substances hold significant prospects for use as dietary supplements and functional foods because of their potential advantages for human health as antimicrobial, anticancer, anti-inflammatory, and antioxidant agents. Utilizing plant by-products as raw materials can also lower production costs and lessen environmental impacts. Thus, this review covered the bioactive substances found in plants and their by-products. The health benefits of bioactive compounds obtained from plant origins were also highlighted in this review. Furthermore, we concentrated on both conventional extraction techniques (e.g., Soxhlet, heat reflux, and maceration) and innovative extraction strategies for bioactive substances, including pulsed electric field (PEF), pressurized liquid, microwave-assisted, ultrasonic-assisted, and subcritical fluid methods. Higher yields obtained by novel extraction methods were found to be of primary interest, considering immediate beneficial economic outcomes. The potential applications of those bioactive substances in the food industry have been studied. Additionally, this investigation handled concerns regarding the challenges and limitations related to bioactive compounds. It is anticipated that the information covered in this review will prove to be a useful resource for the plant food processing sector in suggesting a cost-effective and environmentally friendly extraction technique that would turn plant

wastes into a functional product with a high added value.

**Keywords:** plant sources; bioactive compounds; novel extraction technologies; applications; limitations

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## 1. Introduction

Large volumes of agro-industry raw materials are produced worldwide, mostly for the generation of energy and the consumption of humans and animals [1]. However, the agri-food business produces over 190 million tons of by-products yearly [2]. These by-products include leaves, seeds, pomaces, brans, skins, oilseed meals, and other co-products of the production process. It is vital to manage, recycle, or dispose of these by-products [3,4]. Nevertheless, most food by-products could be valued for profit based on their nature and amount [5]. On the other hand, food by-products could be used as raw materials to make crucial components for the functional foods industry, which is one of the most well-liked food trends [6]. They are plentiful in lipids, carbs, fiber, vitamins, and phenolics and can be employed in various applications [7,8]. Consequently, extracting valuable compounds from these by-products may contribute to the economy, environment, and sustainability of food worldwide [2].

Bioactive compounds from plants have benefits over those obtained from animal sources because they are plentiful, cholesterol-free, targeting vegetarian consumers, and inexpensive [9]. Researchers have been increasingly interested in bioactive compound recovery processes from plant-origin by-products, particularly in developed and developing nations [10,11].

Bioactive compound extraction techniques should be carefully chosen, especially for food and pharmaceutical applications, since they can obviously affect the functional, organoleptic, and nutritional properties of phytochemicals [12]. Using chemical techniques to recover natural products presents many concerns such as safety risks, high energy requirements, low product quality, environmental effects, and toxicological impacts [13]. The development of thorough and optimal methods is required for the improved recovery of bioactive compounds, particularly from plants where the cell wall can reduce the effectiveness of extraction.

Many cutting-edge methods have been created and improved to make bioactive compounds extraction more accessible and productive [14]. To obtain functional plant extracts, ultrasound, microwaves, pulsed electric fields, and others can be used as green and sustainable extraction techniques [15]. Here, we highlight bioactive compounds from diverse plant sources and their by-products in terms of extraction, health effects, and potential applications as well as challenges and limitations. In this investigation, suitable reports (in English) were gathered through the search of the PubMed database and Google (2000; up to date as of March 20, 2024). To find the relevant papers, we employed the keywords “bioactive compounds” combined with the terms “plant sources”, “agri-food by-products”, “extraction”, “bioactivities”, “health benefits”, “food applications”, and “limitations”. We set the titles, keywords, and abstracts of the reports compiled from the database. Full-text articles were collected if they were deemed suitable for objective evaluation.

## 2. Bioactive compounds generated from plants

Bioactive components or secondary metabolites are produced from the metabolism of plants,

which demonstrate promise as therapeutic agents, particularly in the area of antioxidation. Phenolics and carotenoids are thought to be the primary phytochemical or bioactive substances that can support improved human health [16]. Carotenoids are lipophilic substances found in abundance in most orange and yellow-colored fruits and vegetables [17]. These substances are highly valuable for usage in the food industry as colorings and nutritional additives that promote health [18]. Moreover, carotenoids are currently gaining a lot of attention since they may help lower the risk of chronic diseases because of their antioxidative activity [19]. Polyphenols, on the other hand, are natural antioxidants mostly found in food and medicinal plants, such as fruits, vegetables, grains, and spices. Polyphenols include categories such as anthocyanins, flavonoids, and phenolic acids. These compounds exhibit many biological characteristics, including anti-inflammatory, anti-aging, and anticancer effects [20] (Table 1).

Fruits, such as apples, kiwis, cherries, plums, and blueberries, are high in hydroxycinnamic acids, with values of 0.5–2 g/kg fresh weight. One of the most common phenolic acids is caffeic acid, which makes up between 75% and 100% of the hydroxycinnamic acids in some fruits [21]. Nonetheless, ferulic acid makes up 90% of the total polyphenol content (TPC) of wheat grains and is the most prevalent phenolic acid in cereal grains [20]. Also, fruit pulp and soluble cell wall fractions of bananas contain tannins and flavonoids including epicatechin, catechin, and gallic acid [22]. As documented by Singh et al. [23], salicylic, vanillic, p-coumaric, ferulic, sinapic, p-hydroxybenzoic, syringic, and gallic acids are the primary phenolic compounds in bananas. It is advised to consume fruits and vegetables since they are a great source of natural antioxidants like vitamins C and E [24]. As a rule, medicinal and food plants are rich in polyphenols, including lignans, stilbenes, flavonoids, and phenolic acids. Hydroxycinnamic acids are present in food plants in greater amounts than hydroxybenzoic acids [20]. According to Erlund [25], the best sources of catechins are tea and red wine. Usually, catechins are present as aglycones or esterified with gallic acid. Furthermore, the two primary flavones that occur in the human diet are luteolin and apigenin, which are mostly found in celery and red pepper. Edible plants like berries, plums, and eggplants are rich in anthocyanins, which account for their red or blue colors [25]. As reported by Toufektsian et al. [26], maize seed is a good source of anthocyanins, particularly cyanidin and pelargonidin. In the same context, Faria et al. [27] have identified delphinidin, cyanidin, petunidin, peonidin, and malvidin from blueberry. In general, pelargonidin, cyanidin, delphinidin, and malvidin are the most prevalent anthocyanidins. Legumes are the leading source of the isoflavonoids daidzein and genistein. The greatest dietary source of these substances is soybean and its products [28]. A polyphenol-rich lettuce, containing chlorogenic acid, cyanidin, and quercetin, was documented by Cheng et al [29]. On the other hand, pumpkins contain the most investigated carotenoids,  $\beta$ -carotene and lycopene, which have been linked to a variety of biological and pharmacological impacts [30]. Numerous plants, including apples, onions, and tea, contain quercetin, a flavonoid of the flavonol group [31]. Natural flavanone, naringenin, is mostly present in grapes and citrus fruits, and it has been shown to have the ability to preserve insulin signaling in the brain and regulate cognitive performance [32].

**Table 1.** Bioactive compounds from different sources of plant materials and their health benefits.

Source	Bioactive constituents	Health benefits	References
Kiwis	Hydroxycinnamic acids (caffeic acid)	Antioxidant activity	[21]
Plums	Coumaric acid	Antioxidant activity	[21]
Wheat grains	Caffeic acid	Antioxidant activity	[22]
Bananas	Phenolic acids (salicylic, vanillic, p-coumaric, ferulic, sinapic, p-hydroxybenzoic, syringic, and gallic acids)	Antioxidant activity	[23]
Tea and red wine	Catechin and their gallates	Antioxidant activity	[25]
Celery and red pepper	Flavones (luteolin and apigenin)	Antioxidant and anti-inflammatory activities	[25]
Maize seed	Anthocyanins (cyanidin and pelargonidin)	Lowering of cardiovascular disease	[26]
Blueberry	Anthocyanins (delphinidin, cyanidin, petunidin, peonidin, and malvidin)	Anticancer activity	[27]
Soybean	Isoflavonoids (daidzein and genistein)	Anticancer, antioxidant, and anti-helminthic activities	[28]
Lettuce	Polyphenols (chlorogenic acid, cyanidin, and quercetin)	Antidiabetic activity	[29]
Pumpkin	Carotenoids ( $\beta$ -carotene and lycopene)	Anticancer and immunomodulatory activities	[30]
Grapes and citrus fruits	Flavanone (naringenin)	Maintain insulin signaling in the brain	[32]
Berries	Anthocyanins (cyanidin and delphinidin)	Antidiabetic, antiatherogenic, and antioxidant activities	[33]
Black currants	Anthocyanins (cyanidin-3-glucoside; delphinidin-3-glucoside)	Antidiabetic activity	[34]
Hazelnut	Flavonoids (myricetin and syringetin and proanthocyanidins A and B)	Antibacterial, anti-inflammatory, and anti-tumor activities	[35]
Papaya peels	Phenolic acids (caffeic acid, p-coumaric acid, and ferulic acid); vitamin C	Antioxidant and anti-inflammatory activities	[36]
Mango peels	Polyphenols (gallic acid, chlorogenic acid, syringic acid, catechin, quercetin, and kaempferol)	Antioxidant, antimicrobial, and anti-inflammatory activities	[37]
Apple pomace	Flavonoids (quercetin, isorhamnetin, procyanidin catechin); phenolic compounds (chlorogenic acid, p-coumaroylquinic acid)	Antioxidant activity	[38]

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Source	Bioactive constituents	Health benefits	References
Tomato peels	Carotenoids (lycopene); polyphenols ( <i>p</i> -coumaric acid, chlorogenic acid, and quercetin)	Antioxidant and antimicrobial activities	[39]
Lemon seeds	Flavonoids (gallic acid, caffeic acid, epicatechin, vitexin, quercetin, and hesperidin)	Enhancement in oxidative damage	[40]
Beetroot	Polyphenols (betanin, betaxanthin, and betacyanin)	Antioxidant activity	[41]
Olive leaves	Phenolic compounds (rutin, tyrosol, luteolin, coumaric acid, ferulic acid, and quercetin)	Antioxidant and antimicrobial activities	[42]
Grape pomace	Flavonoids (quercetin, rutin, and epicatechin); phenolic acids (caffeic acid, gallic acid, and sinapic acid)	Antihypertensive, anti-atherosclerosis, and antioxidant activities	[43,44]
Potato peel	phenolic acids (caffeic acid, chlorogenic acid, gallic acid, isoferulic acid, and vanillic acid)	Antioxidant activity	[45]
Jujube peel	Flavonoids (rutin, quercetin)	Antioxidant, antimicrobial, and anti-melanogenesis	[46]
Pomegranate peel	Anthocyanins (cyanidin, delphinidin, and pelargonidin glycosides); flavonols (quercetin and kaempferol)	Anticancer, antioxidative and anti-inflammatory activities	[47]

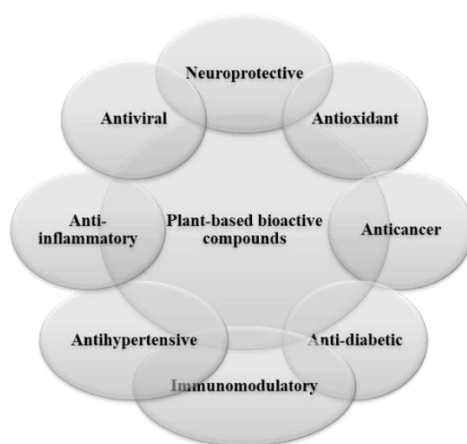
### 3. Bioactive compounds derived from plant by-products

Several investigations have concentrated on the assessment of various bioactive components in fruit and vegetable peels [48–51]. It is well known that the phenolic content of several fruit peels, such as papaya, passion fruit, and pomegranate, is almost twice as high as that of the seeds and pulp. It has been found that the mineral composition, vitamin C content, and antioxidant activity of papaya peels are higher than those of seeds, even with intra-varietal variations [36]. It was discovered that bemyricetin, quercetin, kaempferol, morin, apigenin, and luteolin are the primary flavonoid components present in papaya peels and leaves [36]. In the same respect, the mango peel has noticeably higher phenolic acids (gallic acid) and flavonoids (quercetin) than other fruit peels [37]. Similarly, Sultana et al. [52] discovered that the peels of most tropical fruits (mango, mangosteen, and dragon fruit) have substantially higher gallotannins and total phenolic content than the pulp. Antioxidant activity and phytochemical content of apples were evaluated by Wolfe et al. [53]. They found that the peels have a higher proportion of flavonoids and phenolic compounds than the flesh of the fruit. Citrus peels have a phenolic content of up to 5000 mg/g, which is more than the fruit's edible part [54]. Overall, the principal bioactive substances found in citrus fruits are classified as phenolics and terpenoids [55]. Similar to fruits, many reports have shown that vegetable peels have much more bioactives than the edible parts [36,56]. Vegetable processing, such as that of tomato and eggplant, results in waste in the form of 60%–40% of peels and seeds. Thus, the extraction of useful molecules like lycopene from tomato peels and high-quality proteins, pigments, fibers, carotenoids, and organic acids from other sources is the advised and efficient way to handle vegetable peel waste [36]. According to a different study by Guuntekin et al. [57], the extract of tomato stalks contained the greatest number of phenolic components (7.14%) when compared with other plants. In the same trend, lemon seeds were confirmed to own flavonoid compounds such as galocatechin, caffeic acid, epicatechin, vitexin, quercetin, and hesperidin [40]. As stated by Chhikara et al. [41] and Ravichandran et al. [58], root vegetable peels (beetroot, carrot) contain polyphenols (betagarin, betavulgarin, and cochliophilin A) and betalain (betacyanin and betaxanthin), which are beneficial antioxidants. According to Cartea et al. [59], the bioactive components found in cruciferous vegetables (broccoli, cauliflower) contain fiber, vitamin C, flavonoids (quercetin, kaempferol, and isorhamnetin), and phenolics (*p*-coumaric, sinapic, and ferulic acids). The efficient antioxidant action of potato peel extract prepared through lyophilization was demonstrated in a variety of *in vitro* systems [60]. The presence of phenolic and flavonoid compounds in discarded peels from the Cucurbitaceae family was found to reduce lipid peroxidation, according to Rajasree et al. [56]. Furthermore, olive leaves and by-products are excellent sources of bioactive substances such as rutin, tyrosol, hydroxytyrosol, and oleuropein [61]. Likewise, a study conducted by Talhaoui et al. [42] showed that a wide range of phenolic compounds including rutin, tyrosol, luteolin, quercetin, coumaric acid, ferulic acid, caffeic acid, and quercetin are present in olive leaves.

### 4. Health benefits of plant materials

Although plants have a variety of combinations of bioactive components that have therapeutic effects, they often include a single class of compounds that play common medicinal roles in human health. In this respect, the apple (*Malus domestica* L.) contains flavonoids such as epicatechin,

phloretin, and quercetin and phenolic acids such as chlorogenic and coumaroylquinic acids that are antioxidative polyphenols [62]. The flesh of the mandarin fruit is rich in nutritional content of antioxidants (e.g., ascorbic acid, carotenoids, and phenolic compounds), and has sugars, minerals, and volatile amino acids [63]. Furthermore, peels are a great source of polyphenols [64]. The majority of the health advantages linked to mandarin fruits stem from the antioxidative properties of their bioactive constituents. In addition, prickly pear fruit (*Opuntia* spp.) has high concentrations of polyphenols, betalains, ascorbic acid, minerals, and amino acids [65]. These compounds have been linked to benefits for health, including antioxidant, antiatherogenic, and antiulcerogenic properties, as well as the prevention of low-density lipoprotein peroxidation [66,67] (Figure 1). Similarly, antioxidants can be found in high levels in the extracts of berry fruits like blueberries (*Vaccinium* sp.), blackberries (*Rubus* sp.), strawberries (*Fragaria ananassa*), and grape berries (*Vitis* sp.) [68].



**Figure 1.** Health benefits of bioactive compounds from plant sources.

Generally, polyphenols and ascorbic acid have been demonstrated to have positive health effects on lung disorders, rheumatoid arthritis, cardiovascular disease, Parkinson's disease, and Alzheimer's [69,70] (Table 1). *Allium* species, which include garlic, onions, chives, and leeks, are significant vegetable examples since they are recognized for their organosulfur compounds while having large concentrations of flavonoids, steroidal saponins, and phytosterols [71]. Among their many health advantages are their immunomodulatory, antiviral, antidiabetic, antioxidant, anticarcinogenic, anti-inflammatory, and neuroprotective qualities [72,73]. In the same line, Montesano et al. [30] stated that pumpkin (*Cucurbita* sp.) contains significant amounts of bioactive compounds, which are high in terpenoids, particularly carotenoids, which boost immunity, reduce the risk of cancer and heart disease, and expand the prostate gland. As confirmed by some researchers, rosemary (*Rosmarinus officinalis* L.) has bioactive compounds linked to antifungal, antidepressant, antidiabetic, anti-inflammatory, and antithrombotic health benefits [74,75]. Extracts from medicinal and aromatic plants are accepted as safe [Generally Recognized As Safe (GRAS) classification], which means they can be utilized as a natural alternative to chemical additions [76]. Sage (*Salvia officinalis* L.), for example, has been shown to have high potential as an additive for food production [77] and to have anti-inflammatory, anticancer, antibacterial, and antiproliferative activities [77,78]. As reported by Wu et al. [79], oregano (*Origanum vulgare*) consumption has been linked to antimicrobial and antioxidant effects. The main constituents of thyme (*Thymus vulgaris* L.) include thymol, carvacrol, geraniol, and p-cymene [80], which also

have neuroprotective, respiratory, and antibacterial qualities [81]. Grape pomace, a by-product of winemaking that contains flavonoids, phenolic acids, and lignans among other polyphenolic antioxidants, is a valuable, economic source of bioactive compounds [44], with demonstrated therapeutic benefits in conditions such as hypertension, atherosclerosis, neurodegeneration, heart disease, and others [44]. Likewise, citrus by-products, which are rich in flavonoids and limonoids as well as essential oils, are also frequently left over after the manufacturing of citrus juice [82]. The antioxidant activity of citrus waste is mostly attributed to bioactive chemicals, whereas essential oils possess antibacterial, antimycotic, and antiviral properties [82]. Additionally, stevia is a great source of bioactive components like polyphenols, carotenoids, ascorbic acid, and chlorophylls. Its extracts are also rich in antioxidants, antimicrobials, hypotensive, anti-tumor, immunomodulatory, and anti-inflammatory qualities [83,84]. As reported by Bulotta et al. [85], olive leave extracts exhibit antiviral, anti-tumor, antioxidant, anticancer, antimicrobial, and cardiovascular health effects. In another study, Toufektsian et al. [26] assessed the cardioprotective benefits of anthocyanin-rich maize (20% seed diet) after feeding male Wistar rats for eight weeks. Anthocyanins may have cardioprotective properties, since a considerably ( $p < 0.01$ ) lower infarct size, coronary occlusion, and reperfusion was found in rats fed an anthocyanin-rich maize diet compared with rats fed an anthocyanin-free diet [26]. Using the human gastric cancer cell line, Afshari et al. [86] studied the anticancer effects of eggplant extract. The researchers found that, compared with a normal cell line, eggplant extract had a more harmful effect on human gastric cancer cells. Because of its strong antioxidant qualities and abundance of phenolic components, eggplant may be useful in the detoxification of free radicals. As a result, eggplants may be consumed as a dietary supplement to lower the risk of cancer [86]. Plant derivatives, including polyphenols, can restore harmful or unfavorable epigenetic alterations in cancer cells, hinder the growth of tumors, stop the spread of metastases, and make tumor cells more sensitive to radiation and chemotherapy [87]. As stated by Sharma [88], numerous cancer types can be prevented and treated with pomegranate wastes and by-product extracts. Similarly, pomegranate extract has been shown to suppress the development of cancerous prostate cells and trigger apoptosis through the suppression of NF- $\kappa$ B activity, according to Rettig et al. [89]. In the same line, anthocyanin-pyruvic acid adduct extracts and blueberry extracts were tested for their potential as anticancer agents using MDA-MB-231 and MCF7 breast cancer cell lines. It was verified that these extracts, which function as cell anti-invasive factors and inhibit the growth of cancer cells, exhibit promising anticancer potential in the studied breast cancer cell lines [90]. Moreover, it has been established that terpenoids and carotenoids derived from plants have anti-inflammatory and anticancer properties. They inhibit the activation of NF- $\kappa$ B signaling pathways, which play a major role in regulating the development of inflammatory and tumorous conditions [91]. On the other hand, black currants with high anthocyanin content can control hyperglycemia using CaCo-2 cells, according to Barik et al. [92]. These findings showed that anthocyanins in black currants mainly inhibit  $\alpha$ -glucosidase action to control postprandial hyperglycemia, while other phenolics affect salivary  $\alpha$ -amylase, sugar transporters, and glucose uptake, all of which may lessen the associated risk of developing type-2 diabetes. Likewise, using STZ-induced diabetic mice models, Yang et al. [93] investigated the potential of puerarin (isoflavones) to reduce glucose levels. After four weeks of treatment, they discovered that the puerarin group had improved blood insulin levels and a considerable drop in blood glucose (hypoglycemic effects). In a previous investigation by Anhê et al. [94], the authors found that a cranberry extract high in polyphenols reduces intestinal inflammation in mice. The results showed that supplementing with a polyphenol-rich cranberry extract for eight weeks dramatically increased the population of



*Akkermansia* spp., which was linked to decreases in visceral adiposity, intestinal inflammation, and weight gain, all of which were elevated by a high-fat/high-sucrose diet [94]. Due to their high phenolic content and dietary fiber level, whole-cereal grains have been associated with favorable changes in gut microbiota, according to Gong et al. [95]. It has been proposed that high-cereal diets, when processed properly, may improve and perhaps treat many metabolic diseases. On the other hand, in a dose-dependent manner, avocado seed extracts have demonstrated anti-inflammatory and antiproliferative properties against the colon cancer cell line HCT-116 and the liver cancer cell line HepG-2 [96]. As documented by Mirza et al. [97] and Donga et al. [98], mango peels are considered a great source of polyphenols, particularly protocatechuic acid and mangiferin, which have antimicrobial, anti-diabetic, anti-inflammatory, and anticarcinogenic effects. Several fruit and vegetable by-products have demonstrated antimicrobial efficacy against *L. monocytogenes*, including those derived from apple [99], cauliflower [100], elderberry [101], citrus [102] and pomegranate [103]. Likewise, other fruits and vegetables can serve as antimicrobial agents upon *S. aureus*, like co-products obtained from artichoke [104], banana [105], grape [106], orange [107], pomegranate [108], and tomato [109].

## 5. Extraction of bioactive compounds

Generally, bioactive compounds within plant materials are unevenly distributed, existing in both soluble and insoluble forms. Therefore, it is crucial to employ a suitable solvent system for the optimum extraction of bioactive compounds from food materials. The selection of solvents, such as water, alcohols (propanol, methanol, and ethanol), acetone, or ethyl acetate, either in their pure form or mixtures, has a significant impact on both the quantity and quality of the extracted components [110]. Moreover, the process of obtaining bioactive compounds from plant-based foods is greatly influenced by the appropriate combination of time and temperature treatments [111]. It has been observed that prolonged extraction and higher temperatures enhance the solubility of the analyte. Nevertheless, these conditions can also result in the undesired degradation of bioactive compounds [112].

Solid-liquid extraction is a method of separation in which one or more components of a solid mixture are dissolved selectively in a liquid solvent. The process of removing precipitated solute from adsorbent material is usually referred to as leaching or elution [113]. Sequential extraction is another type of solid-liquid extraction that involves isolating compounds according to their differing polarities by performing multiple extractions on a solid sample aliquot using multiple solvents [114].

Liquid-liquid extraction, commonly referred to as partitioning or solvent extraction, is a method employed to separate constituents by utilizing their different solubilities in two incompatible liquids, usually polar (water) and nonpolar (organic) solvents [115]. On the other hand, the Folch and Bligh & Dyer method employs a two-step process, including solid-liquid and liquid-liquid extraction technologies. This technique efficiently transfers hydrophilic molecules into a phase that is rich in water, whereas hydrophobic lipids are gathered in a phase that is rich in organic solvent [116].

### 5.1. Conventional extraction techniques

Bioactive compounds are typically extracted from solid food materials using conventional techniques, including mainly Soxhlet extraction, heated reflux extraction, and maceration. The Soxhlet extraction technique was initially invented in 1879 by a German scientist (Frans Ritter von Soxhlet), being mainly used for the extraction of lipids [117]. The Soxhlet extraction is also important due to its

ability to compare the efficiency of various novel extraction protocols. In this context, the Soxhlet extraction method was used by Kodal and Aksu [118] to recover carotenoid pigments from orange peel. The authors stated that the greatest carotene pigment in the range of 4.5 mg carotene/g dry peel was obtained by treating frozen peel at 79 °C with ethanol at a liquid-to-solid ratio of 40:1. Nevertheless, because of lipid oxidation, it was discovered that the extract readily broke down into its terpene monomer units. Similarly, Caldas et al. [119] have extracted phenolics (catechin, rutin, and epicatechin) from grape peel using the Soxhlet technique. The heat reflux extraction method utilizes a reflux extractor as the reactor to enhance efficiency and optimize the mass transfer between the solvent and solute at an elevated temperature. This is achieved by allowing the heated solvent vapors to flow through the solute and ensuring consistent regeneration through the condenser [120]. Although these extraction methods are cheap and simple, they may jeopardize the integrity of heat-sensitive components. Therefore, maceration is usually employed to extract heat-labile components after reducing the size of solid samples. Romero-Cascales et al. [121] found that the maceration method with methanol at 25 °C produced the greatest amount of anthocyanin pigment (300 mg/g) from grape skin. Also, earlier research on the extraction of flavonoid components from different citrus peels by Sultana et al. [122] showed that the maceration process using methanol was the most effective in terms of yield and purity. Flavonoids (catechin) have also been isolated by maceration from the fruits of *Arbutus unedo* L. at an increased temperature of 79.6 °C in 3.7% diluted ethanol [123]. The maceration process typically involves extracting substances at room temperature for a prolonged period, while the Soxhlet and heated reflux extraction can be accomplished in a few hours at a temperature of 90 °C [124].

From the authors' point of view, conventional extraction methods have significant limitations despite their ease of use, cost-effectiveness, and ability to produce favorable outcomes in the extraction of bioactive compounds. These limitations include the requirement for extended extraction duration, the use of large volumes of potentially hazardous organic solvents, and the susceptibility to interference and deterioration from external factors including air, light, temperature, etc.

## 5.2. Novel extraction techniques

In addition to conventional extraction techniques, several novel approaches are commonly employed to increase the yield of extractable bioactive compounds, including ultrasound-assisted extraction, microwave-assisted extraction, infrared-assisted extraction, pulsed electric field extraction, pressurized liquid extraction, supercritical fluid extraction, subcritical fluid extraction, and enzyme-assisted extraction.

### 5.2.1. Ultrasound-assisted extraction (UAE)

Over the past few decades, a large amount of research has focused on the potential of UAE as a low-impact, environmentally friendly, and economically feasible alternative to conventional extraction methods. Ultrasound waves within the frequency range of 20 kHz to 100 MHz have been widely used to improve the processing of food due to their ability to pass through any medium, causing expansion and compression and inducing cavitation or bubble formation. The collapse of these bubble-like structures causes microturbulence, significant extractant agitation, and sample particle collisions between extractant particles. The utilization of an ultrasound-assisted technique to extract chlorogenic acid from artichoke leaves (*Cynara scolymus* L.) in 15 min at room temperature with 80% methanol

demonstrated a substantial increase in yield of up to 50% when compared with maceration [112]. According to Altemimi et al. [125], this process has been demonstrated to accelerate the breakdown of cell tissue and boost the rate at which lutein and  $\beta$ -carotene are extracted from spinach. To extract phenolic compounds from purple eggplant peel, Ferarsa et al. [126] performed UAE and found that the ideal conditions for maximum carotenoid yield were 60 °C for 60 min at pH 2.0. Besides, the best conditions for gallic acid extraction from goji berry peels by UAE, which have strong antibacterial properties, were found to be 55 °C for 25 min at 220 W/cm<sup>2</sup>, according to Skenderidis et al. [127]. The recovery of flavonoids (neohesperidin, tangeritin, hesperidin, and diosmin) from citrus peel was shown to be effectively achieved with the use of UAE, as reported by Londoño-Londoño et al. [128]. Similarly, Zhu et al. [129] also discovered a great enhancement in polyphenols, mainly flavonoids (rutin, quercetin 3- $\beta$ -D-glucoside, and kaempferol-3-O-rutinosid) from jujube peels employing UAE treatment. Recently, Sulejmanović et al. [130] studied the impact of UAE to maximize the use and recovery of phenolic compounds from ginger herbal dust. It was discovered that the extract exhibited elevated levels of TPC, 6-gingerol (44.57 mg/gDE), 8-gingerol (8.62 mg/gDE), and 6-shogaol (6.92 mg/gDE). According to a similar investigation by Raj and Dash [131], the UAE is superior to other methods for the extraction of flavonoid (betacyanin) from dragon fruit peel. Likewise, diverse functional molecules, such as lycopene from tomatoes [132], quercetin from onion wastes [133], carotenoids from pomegranate wastes [134], and anthocyanins from plum and grape peels [135] have been effectively recovered using UAE.

From the experience of the authors, using the ultrasonic technique might be considered a cost-effective substitute for increasing the extraction of bioactive chemicals from plant sources.

### 5.2.2. Infrared-assisted extraction

Infrared radiation is subdivided into near, mid, and far wavelengths, ranging from 0.78–1000  $\mu$ m; their ability to penetrate decreases as the energy level increases. Infrared radiation induces vibrations of the atoms or molecules in the plant material, leading to the generation of thermal energy. This leads to an elevation in the temperature, causing the liquid to evaporate and break the structure of the material to promote the extraction of specific target molecules.

Far-infrared extraction technology is commonly utilized, since water and most organic molecules absorb at wavelengths higher than 2.5  $\mu$ m. Infrared-assisted extraction has been used to create a quick, easy, and affordable way to extract quercitrin, iso-quercitrin, and rutin from *Magnolia officinalis* leaves [136]. The benefits include simplicity, high concentrations of key flavonoid components, and high extraction yield. In another study, Wang et al. [137] introduced a novel, easy, and rapid method of infrared-assisted self-enzymolysis extraction for obtaining total flavonoid aglycones, particularly oroxylin A, wogonin, and baicalein from *Scutellariae radix* with improved efficiency. El Kantar et al. [138] utilized infrared-assisted extraction as a preliminary step to extract polyphenols from fresh orange peel. Their study has shown that this technique significantly increased the yield of obtained polyphenols with reduced extraction time. In a study by Cheaib et al. [139], the effectiveness of several methods was examined in terms of polyphenol yield and bioactivity from apricot pomace, including ultrasounds, microwaves, and infrared. Infrared was the most successful technique with the greatest polyphenol (10 mg GAE/g DM), flavonoid (6 mg CE/g DM), and tannin (3.6 mg/L) yields. In addition, compared with other methods, infrared extracts exhibited the highest levels of epicatechin, catechin, and rutin. In comparison to solid-liquid ones, the infrared extraction of polyphenols from *Salviae miltiorrhizae*

(danshen) demonstrated an improvement in antioxidant capacity from 47% to 79% and an increase from 0.12 to 0.19 mM after 30 min, according to Chen et al. [140]. They also separated eight polyphenol compounds from danshen, particularly danshensu, protocatechuic acid, protocatechuic aldehyde, salvianolic acid B, dihydrotanshinone, cryptotanshinone, tanshinone I, and tanshinone IIA. Similarly, Abi-Khattar et al. [141] used an infrared-assisted extraction strategy to obtain polyphenols (oleuropein and hydroxytyrosol) from olive leaves. The TPC was improved by more than 30% using infrared as compared with the water bath method, which needed 27% more ethanol consumption.

From the authors' viewpoint and compared with other traditional extraction techniques, infrared-assisted extraction is quick, cheap, effective, and environmentally friendly, as radiation heat spreads within the sample uniformly to improve heat efficiency and reduce energy waste.

### 5.2.3. Microwave-assisted extraction (MAE)

Microwave-assisted extraction is also an effective green technology that has evolved to be one of the main methods of extracting bioactive components from complex herbal formulations [142]. Microwaves, as electromagnetic waves having a frequency ranging from 300 MHz to 300 GHz, are responsible for heating the substances by means of the combination of ionic conduction and dipole movement [143]. Solvents, such as water, possessing a high dielectric constant, can absorb and release microwave energy, consequently raising the temperature needed for an enhanced rate of extraction. A novel approach for extracting and purifying alkaloids from *Sophora flavescens* Ait. utilizing focused microwave-assisted aqueous extraction in conjunction with inverse micellar extraction was proposed by Zhang et al. [144]. Similarly, different natural deep eutectic solvents combined with MAE were used to extract bioactive components such as iridoids, phenylpropanoids, and flavonoids from *Lippia citriodora* compared with conventional methanol [145]. In another study by Simsek et al. [146], phenolic components (syringic, vanillic, epicatechin, gentisic, and quercetin) were isolated from sour cherry pomace by using MAE. According to Asghari's [147] research, MAE is a quicker and simpler technique than conventional extraction processes for removing bioactive components (tannin and cinnamaldehyde) from a range of medicinal Asian plants (*C. mukul*, *Q. infectoria*, and *C. verum* J.S. Presl). Condensed tannins and polyphenols have been effectively extracted from grape wastes using optimized MAE [148]. Pure extracts of the polyphenolic pigment betalain were obtained from the peel of *Opuntia ficus-indica* fruits by Ciriminna et al. [149] using MAE (1 h at 70 °C). Liazid et al. [150] utilized MAE to extract anthocyanin pigment from grape peels and found that the anthocyanin extract exhibited greater stability at a temperature of 100 °C. However, above this temperature, the extract yield and stability declined, suggesting a breakdown of the molecule. Likewise, Torres-León et al. [151] demonstrated that MAE could extract a high concentration of bioactive substances from mango seeds at optimum conditions of a solid-to-solvent ratio of 1/60 g/mL. The study also stated that ethyl gallate, pent-O-galloyl-glucoside (PGG), and hamnetin-3-[6-2-butenoil-hexoside] were the main antioxidants present in mango seeds. In addition, Araújo et al. [152] demonstrated that acetone (72.18 °C and 19.01 min) and ethanol (71.64 °C and 14.69 min), two different solvents, could be used to extract the largest amount of bioactive substances (e.g., procyanidins dimer B, catechin, and epicatechin) from avocado seeds employing MAE.

Along with this, solvent-free microwave extraction can also be performed by using the residual water of plant material, thus minimizing the additional hydrolysis reactions. Solvent-free extraction of oxygenated compounds from cardamom oil (*Elletaria cardamomum* L.) was performed and optimized

by Lucchesi et al. [153]. In another work, a direct irradiation-based MAE was performed by Michel et al. [154] to isolate the polar antioxidant components from sea berries (*Hippophae rhamnoides*) using residual water contents. In comparison to the conventional Soxhlet extraction, a quick method of extracting the two main capsaicinoids from habanero peppers using ultrasound, near-infrared, or microwave radiation-based novel extraction techniques resulted in higher overall yields and a higher ratio of capsaicin to dihydrocapsaicin [155].

From the authors' experience, MAE has been considered a valuable alternative to conventional methods for the extraction of numerous biologically active compounds from raw plants and by-products. The main advantages of MAE are (1) higher extraction yield and (2) shorter extraction times.

#### 5.2.4. Pulsed electric field extraction (PEF)

Pulse electric field is an innovative technology that can be considered green and environmentally safe and does not require any thermal energy. It is applied by passing food for a short time in between two electrodes containing a high-voltage electric field. The electric pulses with 20 to 1000  $\mu$ s intervals with high electric field strength are generally employed for improved preservation of food quality [156]. The strength of the electric field is a critical factor in determining the level of extraction, as it directly influences the physical characteristics of the molecule being targeted, including solubility, diffusivity, viscosity, and surface tension [157].

The PEF treatment is an ideal nonthermal method for extracting phenols and flavonoids from onions while minimizing any notable degradation in quality. Its application causes irreversible structural changes in the cell membrane by inducing cellular tissue disintegration, which increases the mass transfer rate and membrane permeability [158,159]. In the same trend, Yu et al. [160,161] demonstrated that the PEF method helped the extraction of polyphenols and proteins from rapeseed stems and leaves, resulting in higher polyphenol purity. As reported by Medina-Meza and Barbosa-Canovas [135], the use of PEF also increased the recovery of anthocyanins, flavonoids, and phenols from plum and grape peels. In another study, the phenolic compounds were extracted from apple peels by subjecting them to a pulsed electric field with varying electric intensities and times [162]. According to its findings, the intensity of the electric field and the cell integration index affected the extraction process. Parniakov et al. [163] also documented that PEF was used to extract bioactive components from papaya seeds. Additionally, Koubaa et al. [164] discovered that the application of PEF resulted in a noticeably greater extraction yield of red colorants (isobetanin and betanin) found in pear peel. Comparably, Luengo et al. [165] declared that the polyphenols and flavonoid components (naringin and hesperin) in orange peel could be effectively extracted using an electric-field treatment with an intensity of 7 kV/cm and a pulse rate of 20 in 60 ms. As stated by Corrales et al. [166], anthocyanins from grape by-products are typically extracted using an industrial batch PEF process.

#### 5.2.5. Pressurized liquid extraction

In pressurized liquid extraction, the extraction of bioactive phytochemicals typically requires a pressure ranging from 100 to 1000 MPa. This pressure is usually applied to increase the temperature of the solvent beyond its boiling point, causing a decrease in its viscosity and an increase in its penetration and solubility to improve the efficiency of extraction as compared with conventional methods. The temperature is often regarded as the principal regulating factor in pressurized liquid

extraction, as it has the potential to either positively or adversely influence the selective extraction of molecules based on their chemical composition. The increase in temperature can also improve the extraction efficiency by enhancing the solvent diffusivity in the food matrix. In a study, Gómez-Mejía et al. [167] reported improved extraction yield of bioactive polyphenols (t-ferulic acid, p-coumaric acid, rutin, and hesperidin) from citrus peel waste with pressurized liquid extraction at a temperature of 90 °C. This phenomenon was also observed by Benito-Román et al. [168] while optimizing the extraction of phenols and  $\beta$ -glucans from waxy barley at elevated temperatures (135–175 °C). Nevertheless, temperature had a positive influence on the yield of total phenolics while negatively influencing the glucan yield. According to Markom et al. [169], a pressurized liquid extraction was used to extract the tannins from *Phyllanthus niruri* at 100 °C and 107 Pa. The pressurized liquid extraction produced the highest total yield of tannin and corilagin in the shortest time when compared with the Soxhlet method. In an additional investigation by Mohd et al. [170], hydrolysable tannins from *Phyllanthus tenellus* Roxb. were separated by pressurized liquid extraction.

#### 5.2.6. Supercritical fluid extraction (SFE)

A fluid is referred to its critical state when it is subjected to pressure and heat beyond its critical pressure and temperature levels. Supercritical fluid extraction is widely recognized as an ecologically sustainable technique owing to its application of a renewable solvent such as carbon dioxide, non-toxic and suitable for usage in the supercritical state. The primary benefit of using a solvent in the supercritical phase is that the fluid displays characteristics of both a gas and a liquid. CO<sub>2</sub> is nonpolar; therefore, mixing a minimal amount of polar solvent can considerably increase the overall yield of extraction [171].

The amount of monoterpene content shows a direct relationship with pressure, which can be explained by an increase in density. Similarly, elevating the temperature leads to a rise in the vapor pressure of the analytes, facilitating the sequential extraction of compounds with varying densities. On the other hand, Montañés et al. [172] investigated tocopherol extraction from apple seed oil using supercritical carbon dioxide, finding that increased pressure improved extraction yield, while higher temperatures decreased tocopherol content. The impact of temperature and pressure on the recovery of monoterpenes from the sage herbal dust was investigated by Pavlić et al. [173] using SFE. Kitryté et al. [174] optimized parameters such as temperature, pressure, and time duration for supercritical carbon dioxide extraction to isolate the non-polar fraction of elderberry pomace. Also, subcritical water extraction is an effective method for recovering phenolic substances from potato peels (gallic acid, chlorogenic acid, caffeic acid, protocatechuic acid, syringic acid, p-hydroxyl benzoic acid, ferulic acid, and coumaric acid) and pomegranate wastes, as well as antioxidants from winery by-products [175–177]. As reported by Jiao and Kermanshahi [178], anthocyanins were recovered successfully from haskap berries using subcritical CO<sub>2</sub> under the following conditions: 45 MPa, 65 °C, 15–20 min. The phenolic component punicic acid was extracted from pomegranate seeds using SFE at 60 °C and 320 bars, according to Natolino and Da Porto [179]. In the same regard, various studies discovered that supercritical extraction using CO<sub>2</sub> was effective in extracting phenolic compounds, including terpene,  $\gamma$ -element, germacrene from Brazilian cherries and ellagitannins, and flavanols from strawberry seeds [180,181]. In terms of extraction yields and duration, SFE with CO<sub>2</sub> was generally less efficient than novel pressurized liquid extraction and ultrasonic-assisted extraction but more efficient than conventional Soxhlet and solid-liquid extraction.

### 5.2.7. Subcritical fluid extraction

Subcritical fluid extraction is an innovative method that employs a selected extraction solvent at a temperature exceeding its boiling point but below its critical temperature, with the pressure carefully adjusted to keep the solvent in a liquid state during the process. This is performed at a lower temperature and pressure than in supercritical fluid extraction, making this technique safe and effective without degrading the heat-labile components of the food materials [182].

It is much more advantageous to extract economically important phenolic compounds from food products using water rather than organic solvents. In a study by Abdelmoez et al. [183], water-based subcritical extraction has been employed for the extraction of bioactive phenolic compounds from wheat straw, revealing the optimal conditions for hydrolysis as 30 min of hydrolysis time at 190 °C, 180–355 µm particle size, and a water to wheat-straw ratio of 6:1. Subcritical water extraction was found to be a highly effective alternative to conventional solvent extraction utilizing ethanol for the extraction of bioactive components from onion peel [184]. According to Rodrigues et al. [185], the papaya seed extracts might be isolated using subcritical water extraction in 5 min at 150 °C. The main components of phenolic classes were discovered to be ferulic, mandelic, and vanillic acids, which are substantially greater than with the Soxhlet extraction at 40 °C for 6 h. Another work revealed that tocopherols, strong antioxidants utilized in chemical and pharmaceutical applications, are present in sweet passion fruit seed oil. A considerably higher yield was obtained from oil extracted using subcritical propane extraction at 60 °C and 6 MPa pressure than from Soxhlet procedure at 65 °C for 4 h utilizing n-hexane solvent [186]. Similar research on the extraction of polyphenols from grape pomace using subcritical water extraction in semi-continuous mode shows that heating water to 80–120 °C and under 100 MPa of pressure yields in total 44.3–77 mg/g of polyphenol and 44–124 mg/g from pomace [187].

### 5.2.8. Enzyme-assisted extraction

Another innovative approach is enzyme-assisted extraction, which involves the use of enzymes in the extraction medium to enhance the recovery of target molecules. This technique is gaining popularity over solvent extraction due to its enhanced safety, environmental tolerance, and performance.

The primary constituents of the plant cell wall are cellulose, hemicellulose, and pectin, which are the primary constraints to the extraction of bioactive phytochemicals. Application of various enzymes such as  $\alpha$ -amylase, cellulase, hemicellulase, or pectinase promotes the efficiency and yield of extraction by dissolving the main components of the cell wall, ultimately improving the interaction between target compounds and solvents [188]. Deng et al. [189] optimized the efficiency of the enzyme-assisted aqueous extraction for an improved yield of peanut oil by preheating the peanuts using short-wave infrared radiation. In another study, it was observed that applying the glycosidase enzyme to the freeze-dried tomato material before CO<sub>2</sub>-based supercritical extraction can increase the amount of lycopene by three-fold [190]. Boulila et al. [191] stated that the yield of essential oil extraction from bay leaves can be increased by employing the cellulase, hemicellulase, xylanase, and ternary mixture of them. Other researchers were also able to extract more curcumin from turmeric by utilizing a combination of  $\alpha$ -amylase and amyloglucosidase enzymes [192]. In another study, Xu et al. [193] compared the extraction of polysaccharides from grape peels using ethanol as a solvent and a mixture of enzymes such as cellulase, pectinase, and  $\beta$ -glucosidase. According to this study, a

larger yield of pectin containing phenolic compounds like anthocyanin was obtained with a shorter extraction time using enzyme-assisted extraction as opposed to solvent extraction. Likewise, Vasco-Correa and Zapata [194] found that the proto-pectinase enzyme yields a higher amount of pectin from passion fruit peels than traditional chemical extraction. Moreover, enzymes including cellulase, hemicellulase, and pectinase can be used to extract vinegar from pineapple peels, which is employed in the manufacturing of sugar [195].

While these innovative techniques possess the capability to enhance extraction yields, they also result in the excessive disruption of bonding forces within the targeted bioactive compounds [196,197]. The combination of conventional and novel extraction techniques is also another trend being applied in modern research. Both conventional and novel extraction techniques are compared in Table 2, along with their advantages and disadvantages in Table 3.

## 6. Economical cost evaluations

An economic comparison of traditional extraction methods and modern extraction approaches is necessary. However, there are very few reports that have addressed this point. For example, the economic costs of ethanol extraction and subcritical water extraction of bioactive kanuka leaves were studied by Essien et al. [202]. The outcomes showed that the costs of manufacturing and unit production for subcritical water extraction were NZ\$ 4.49 million and NZ\$ 2.14/kg, whereas the costs for ethanol extraction were NZ\$ 4.7 million and NZ\$ 5.57/kg, respectively. In the same respect, Lopeda-Correa et al. [203] assessed the economic costs of using the Soxhlet technique versus the UAE when separating polyphenols from *Adenaria floribunda* stems. Manufacturing costs for the UAE are US\$ 3.86/flask, and less than US\$ 5.8/flask for the Soxhlet process. It is identifiable that new extraction processes are more cost-effective than traditional techniques.

**Table 2.** Application of conventional and novel technologies for the extraction of bioactive compounds from plant sources.

Extraction techniques	Source	Extracted compound	References
Conventional techniques			
Soxhlet extraction	Orange peel	Carotene pigment	[118]
	Grape peel	Catechin, rutin, and epicatechin	[119]
Maceration	Grape skin	Anthocyanin pigment	[121]
	Kinnow peels	Flavonoids (glycosides)	[198]
	<i>Arbutus unedo</i> L. Fruits	Flavonoid (catechin)	[123]
Novel techniques			
Ultrasound-assisted extraction	Artichoke leaves	Chlorogenic acid	[112]
	Spinach	Lutein and $\beta$ -carotene	[125]
	Purple eggplant peel	Carotenoid	[126]
	Goji berry peels	Gallic acid	[127]
	Citrus peel	Neohesperidin, tangeritin, hesperidin, and diosmin	[128]

*Continued on next page*



Extraction techniques	Source	Extracted compound	References
Novel techniques			
Ultrasound-assisted extraction	Jujube peels	Rutin, quercetin 3- $\beta$ -D-glucoside, and kaempferol-3-O-rutinosid	[129]
	Ginger herbal dust	6-gingerol, 8-gingerol, and 6-shogaol	[130]
	Dragon peel	Betacyanin	[131]
	Tomatoes	Lycopene	[132]
	Onion wastes	Quercetin	[133]
	Plum and grape peels	Anthocyanins	[135]
Infrared-assisted extraction	<i>Magnolia officinalis</i> leaves	Quercitrin, iso-quercitrin, and rutin	[136]
	<i>Scutellariae Radix</i>	Oroxylin A, wogonin, and baicalein	[137]
	Orange peels	Polyphenols	[138]
	Apricot pomace	Epicatechin, catechin, and rutin	[139]
	<i>Salviae miltiorrhizae</i> (danshen)	Danshensu, protocatechuic acid, protocatechuic aldehyde, salvianolic acid B, dihydrotanshinone, cryptotanshinone, tanshinone I, and tanshinone IIA	[140]
	Olive leaves	Oleuropein and hydroxytyrosol	[141]
Microwave-assisted extraction	<i>Lippia citriodora</i>	Iridoids, phenylpropanoids, and flavonoids	[145]
	Sour cherry pomace	Syringic, vanillic, epicatechin, gentisic, and quercetin	[146]
	Asian plants ( <i>C. mukul</i> , <i>Q. infectoria</i> , and <i>C. verum</i> J. S. Presl)	Tannin and cinnamaldehyde	[147]
	Grape waste	Tannins and polyphenols	[148]
	<i>Opuntia ficus-indica</i>	Betalain	[149]
	Grape peels	Anthocyanin	[150]
	Mango seeds	Ethyl gallate, pent-O-galloyl-glucoside (PGG), and hamnetin-3-[6-2-butenoil-hexoside]	[151]
	Avocado seeds	Procyanidins dimer B, catechin, and epicatechin	[152]
Pulsed electric field extraction	Rapeseed stems	Polyphenols and proteins	[160]
	Plum and grape peels	Anthocyanins, flavonoids, and phenols	[135]
	Apple peels	Total phenolic acids	[162]
	Papaya seeds	Total phenolic acids, proteins, carbohydrates, and isothiocyanates	[163]

Continued on next page

Extraction techniques	Source	Extracted compound	References
<b>Novel techniques</b>			
Pulsed electric field extraction	Pear peel	Isobetanin and betanin	[164]
	Orange peel	Naringin and hesperin	[165]
	Grape by-products	Anthocyanins	[166]
Pressurized liquid extraction	Citrus peel waste	t-ferulic acid, p-coumaric acid, rutin, and hesperidin	[167]
	Waxy barley	Phenols and $\beta$ -glucans	[168]
	<i>Phyllanthus niruri</i>	Tannin and corilagin	[169]
	<i>Phyllanthus tenellus</i>	Hydrolysable tannins	[170]
Supercritical fluid extraction	Apple seed oil	Tocopherol	[172]
	Sage herbal dust	Monoterpenes	[173]
	Elderberry pomace	Total phenolic acids	[174]
	Pomegranate seed	Total phenolic acids	[175]
	Potato peels	Gallic acid, chlorogenic acid, caffeic acid, protocatechuic acid, syringic acid, p-hydroxyl benzoic acid, ferulic acid, and coumaric acid	[176]
	Winery by-products	Total polyphenols and flavonoids	[177]
	Haskap berries pulp	Anthocyanins	[178]
	Pomegranate seeds	Punicic acid	[179]
	Brazilian cherries	Terpene, $\gamma$ -element, and germacrene	[180]
	Strawberry seeds	Ellagitannins and flavanols	[181]
Subcritical fluid extraction	Wheat straw	Phenolic compounds	[183]
	Papaya seeds	Ferulic, mandelic, and vanillic acids	[185]
	Sweet passion fruit seeds	Tocopherols	[186]
	Grape pomace	Polyphenols	[187]
Enzyme-assisted extraction	Tomato	Lycopene	[190]
	Bay leaves	Essential oil	[191]
	Turmeric	Curcumin	[192]
	Grape peels	Pectin	[193]
	Passion fruit peels	Pectin	[194]
	Pineapple peels	Vinegar	[195]

**Table 3.** Advantages and disadvantages of conventional and novel extraction techniques.

Extraction techniques	Advantages	Disadvantages	References
<b>Conventional techniques</b>			
Soxhlet extraction	Simple and reproducible	High temperature Large solvent consumption	[15,199]
Heated reflux extraction	High efficiency Low solvent usage	Thermal degradation	[120]
Maceration	Extraction of heat labile compounds	Large organic waste Long duration of extraction	[188]
<b>Novel techniques</b>			
Ultrasound-assisted extraction	High yield in short duration Easy to utilize at pilot, industrial, and laboratory scales	Energy consumption Swelling of plant material	[14,200]
Microwave-assisted extraction	Rapid and efficient High extraction yield	Need of solvent with ability to absorb microwave radiation Lower selectivity	[15,199]
Infrared-assisted extraction	Environmentally friendly Energy efficient Uniform heating	Limited penetration	[189]
Pulsed electric field extraction	Non-thermal process Short processing time Extraction of thermolabile components	Equipment cost Need of conductivity	[158,201]
Pressurized liquid extraction	Increased rate of extraction Low solvent consumption	High cost	[167]
Supercritical fluid extraction	High efficiency Rapid extraction	High equipment cost	[15,199]
Subcritical fluid extraction	Cost-effective processing	Accelerated hydrolysis of compounds Hard-to-clean equipment	[15,184]
Enzyme-assisted extraction	Environmentally friendly Improved food safety	Sensitive to external factors like temperature, pH, etc.	[188,189]

## 7. Food applications

The utilization of plants and their by-products to gain bioactive compounds is encouraged by the growing need for foods that are healthy and sustainable [204]. Bioactive compounds are used in food in a variety of ways, including as texture modifiers, antioxidants, antimicrobials, natural dyes, and enhancing ingredients [205]. Numerous research studies document the incorporation of bioactive compounds derived from by-products into diverse food models. These compounds are utilized as agents to enhance the nutritious and functional value of food products, including yogurt [206], dry frozen fish [207], bread [208], petit Suisse cheese [209], beef patties [210], and cured sausage [211].

Overall, by-product extracts are commonly employed in food applications, and their antioxidant capacity has been primarily linked to the amount of total phenolic compounds they contain, which may be found by using several techniques [206,210,211]. In this context, pomegranate peel extract (1000 mg/100 g) was added to beef meatballs by Turgut et al. [212]. Following an 8-day storage period at 4 °C, the 1% extract and artificial antioxidant (BHT) samples showed 53% and 50% reduction in thiobarbituric acid-reactive substances (TBARS), a marker of secondary lipid oxidation products, compared with the control. According to Choe et al. [213], persimmon peel extract was used to reinforce ground pork meat. Meats enriched with extract (200 mg/100 g) and BHT had reduced levels of primary lipid oxidation products, as measured by peroxide values (PV) and conjugated dienes (CD), following a 12-day storage period at 3 °C. In comparison with the ground pork without antioxidants, the PV lowering was 43% and 34%, respectively, and the extract group was the most successful in postponing CD production. In another work, Ergezer and Serdaroglu [214] investigated the effects of incorporating BHT and extract produced from artichoke by-products into beef patties. The addition of the extract (27 mg/100 g) significantly reduced lipid and protein oxidation during storage compared with BHT treatment. By the end of storage, these samples demonstrated a 42% and 114% boost to TPC and scavenging capacity against the DPPH radical, respectively, compared with the control, whereas these values stood at 4% and 9% for BHT samples. The authors assigned these results to the TPC and antioxidant abilities of artichoke by-products. On the other hand, lamb patties were enhanced with grape, olive, tomato, and pomegranate pomace extract by Andrés et al. [215]. All meats enriched with plant extracts had between 10% and 21% lower mesophilic microbe microbiological counts after seven days in chilled storage as compared with the control group. Additionally, pomegranate peel-enhanced beef sausages and shrimp immersed in a solution having this coproduct exhibited comparable microbiological findings [216,217]. As mentioned by Nishad et al. [218], meatballs treated with nutmeg and citrus peel extracts (100 mg/100 g) retarded lipid and protein oxidation as well as enhanced sensory evaluations for color, odor, taste, and overall acceptability after storage when compared with control samples. In a different study, the addition of 2.5 g/100 g and 2 g/100 g of apple and banana peels, respectively, were sufficient to improve the sensory properties of chicken meat wafers [219]. According to Abid et al. [220], tomato pomace extracts were added to butter. Supplemented butter (40 mg/100 g) showed the lowest PV during storage, probably as a result of the extract's high lycopene and phenolic content. As reported by Bertolino et al. [221], the addition of skin hazelnuts powder to yoghurt increased the yoghurt's DPPH capability and TPC (3000 mg/100 g) by 96% and 31%, respectively, as compared with the control. On the other hand, probiotic development was increased when yoghurts containing powdered pineapple peel were stored at 4 °C [222]. Compared with the non-fortified juice, reinforced fresh orange juice with a banana peel extract (500 mg/100 mL) displayed growth of approximately 21% and 150% for DPPH and FRAP tests, respectively [223]. In a recent study by Zaky et al. [224], different concentrations (3%, 6%, and 9%) of sunflower meal protein isolate (SMPI) rich in active components were added to pasta. The results showed that the nutritional value of pasta was improved, and the samples were acceptable to consumers, especially those enriched with 3% and 6% SMPI. According to Kampuse et al. [225], adding pumpkin pomace powder (5.5 g/100 g dough) to wheat bread increased the quantity of carotenoids by a factor of 13. In general, many other plant-based sources have demonstrated their ability to increase the TPC and antioxidant efficacy in bakery products including grape pomace [226,227], plantain peel [228], mango peel [229], potato peel [45], raspberry and cranberry pomaces [230], beetroot pomace [231], apple pomace [232], and rosehip, blackcurrant, and elderberry pomaces [233]. Several studies on the incorporation of bioactive ingredients into food products are displayed in Table 4.

**Table 4.** Application of bioactive compounds obtained from plant sources in the food industry.

Source	Product	Function	References
Camu-camu ( <i>Myrciaria dubia</i> ) seed	Yogurt	Increasing antioxidant activity	[206]
Pomegranate and grape seeds	Minced fish muscle	Controlling lipid oxidation	[207]
Grape seed	Bread	Increasing antioxidant activity Acceptable color change	[208]
Grape seed	Petit Suisse cheese	Increasing antioxidant activity 73% sensory acceptance	[209]
Hull, bur, and leaf chestnut	Beef patties	Reducing lipid oxidation; it did not impact sensory acceptance	[210]
Grape seed	Dry cured sausage “chorizo”	Decreasing lipid oxidation Improving the sensory quality	[211]
Pomegranate peel	Beef meatballs	Inhibiting lipid and protein oxidation	[212]
Persimmon peel	Ground pork meat	Reducing lipid and protein oxidation	[213]
Artichoke by-products	Beef patties	Lowering lipid and protein oxidation	[214]
Grape, olive, tomato, and pomegranate pomace	Lamb patties	Lowering mesophilic microbe microbiological counts	[215]
Pomegranate peel	Beef sausages and white shrimp	Increasing antimicrobial activity	[216,217]
Nutmeg and citrus peel	Meatballs	Retarding lipid and protein oxidation Enhancing sensory evaluations	[218]
Apple and banana peels	Chicken meat wafers	Improving the sensory properties	[219]
Tomato pomace	Butter	Decreasing lipid oxidation	[220]
Hazelnut skins	Yogurt	Increasing antioxidant activity	[221]
Pineapple peel	Yogurt	Enhancing probiotic viability	[222]
Banana peel	Fresh orange juice	Increasing antioxidant activity Enhancing sensory evaluations	[223]
Sunflower meal protein isolate	Pasta	Enhancing nutritional value	[224]
Pumpkin pomace	Wheat bread	Increasing carotenoid content Enhancing sensory evaluations	[225]
Grape pomace	Bread	Increasing antioxidant activity Improving the sensory properties	[226]
Grape pomace	Biscuits	Reducing lipid peroxidation	[227]
Nendran peel	Cookies	Increasing antioxidant dietary fiber	[228]
Mango peel	Biscuits	Inhibiting lipid peroxidation	[229]
Potato peel	Biscuits	Reducing lipid peroxidation	[45]
Red beetroot pomace	Biscuits	Enhancing nutritional characteristics Increasing antioxidant activity	[231]
Apple pomace	Rice-based cracker	Increasing antioxidant activity Enhancing sensory attributes	[232]
Rosehip, blackcurrant, and elderberry pomaces	Cookies	Boosting antioxidant activity Enhancing sensory attributes	[233]

## 8. Challenges and limitations

Global food markets are witnessing an increase in the production of food; to meet industry demands, extraction processes must be improved to provide high-grade extracts that can be utilized as raw materials. Although the primary method for getting bioactive compounds is still conventional extraction, this technique is not in line with "green" and sustainable manufacturing because it frequently involves significant costs and the disposal of hazardous chemicals and energy. Furthermore, this thermal method works by harming bioactive molecules that are thermally unstable and should be generated in the first place. However, innovative solutions are frequently quicker, more selective, environmentally friendly, and sensitive to temperature, but still lack adequate testing for use in industry [234]. Numerous other arguments characterize them as costly and unsuitable for industrial use because of the high cost of industrial equipment, which for certain technologies is still in the prototype stage or needs to be specially designed for each application. In general, greater industrial production and application solutions are anticipated in the future for the food-manufacturing sector.

On the other hand, there is a sharp rise in demand for nutrient-rich food and the food industry as a result of consumers' growing consciousness of their physical health and willingness to pay for nutritious meals, especially those of plant origin. Nowadays, a wide range of plant extracts are easily accessible for use in the food processing industry. Before being employed, the bioactive components or active substances from plant extracts are purified or concentrated. Those plant extracts' purified forms are now easily found on the market as premium goods, dietary supplements, and nutraceuticals. These present several health benefits, including lowering LDLs and blood pressure, managing atherosclerosis, boosting memory, minimizing oxidative stress, and having anticancer action [235]. Commercial grape seed extracts with the trade name ORAC-15 M (80% polyphenols and 15,000 oxygen radical absorption capacity) were prepared by Natural Products Insiders Inc. in California, USA, and were suggested for use in reducing the body's oxidative stress. Applied Food Science Inc. also offers a broad variety of commercial plant extract preparations, including green coffee extract (GCE-50% chlorogenic acids from raw coffee beans), organic ginger powder (PureGinger with 2% gingerol), cascara fruit extract (CoffeeNectar from coffee cherry), green tea (Purtea) caffeine, and so on [236].

Due to their high phenolic content, plant extracts have an increased chance of causing bitterness or aftertaste as well as a darker color in the final product at greater inclusion or concentration levels. It is always preferable to investigate and utilize plant extracts because of their higher antioxidant capacity with the lowest impact on the sensory characteristics of food products [237]. However, there is still a long way to go before plant-based antioxidant extracts become widely used. The dearth of human clinical trials and animal model studies has impeded the advancement of bioavailability evaluation and its subsequent market applicability. Therefore, further investigation into the potential effects of plant extracts *in vivo* is required. Generally, ensuring plant extract safety, including the lack of toxicity, cytotoxicity, and allergenicity, is crucial [14]. To safeguard consumers from misleading products, strict and precise laws are needed.

## 9. Conclusions and future prospects

The advantages and functions of bioactive compounds derived from plants and their waste products were highlighted in this review. Owing to their biological activities, such as antioxidant,

antimicrobial, antiviral, antidiabetic, and anti-inflammatory attributes, these compounds have gained much attention due to their beneficial impacts on human health. The extraction of bioactive compounds using conventional and environmentally friendly extraction techniques was also covered. The selection of the extraction procedure is essential as it impacts the dependability and caliber of the analytical tasks that follow. The primary goals of extraction are to maximize the yields of bioactive substances while maintaining biological activity and achieving economic viability, environmental friendliness, and shorter extraction times. Reports indicate that green extraction strategies are becoming a more effective and efficient approach for extracting bioactive substances than conventional techniques. Conventional extraction methods exhibit several drawbacks, including extended extraction times, increased solvent requirements, potential damage to bioactivity, and reduced yield. On the contrary, novel methods have various benefits such as shorter extraction times, lower solvent demands, maintenance of biological activity, higher yields, and lower energy use. As food additives, plant-based bioactive components can be added to fatty products to improve oxidative stability and extend shelf life. Overall, the usage of plant food by-products as raw materials can aid in decreasing the production cost and contribute to recycling waste as well as creating a more environmentally friendly atmosphere. More investigation is needed into the stability of bioactive compounds and their regulatory factors, in addition to the confirmation of possible bioactivity. To find out which doses are safe, their dosage-response relationship, bioavailability, and whether they may be consumed with food, preclinical and clinical research is also necessary.

### Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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### Conflict of interest

The authors declare no conflict of interest.

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