



From Bin to Benefit: Sustainable Valorization of Grapefruit (*Citrus paradisi*) Byproducts Towards the Circular Economy

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Abstract

Purpose of Review This study aims to communicate updated information on the recent innovations in grapefruit byproduct valorization.

Recent Finding Grapefruit is an important fruit of the citrus genus which has commercial importance and its processing generates waste in bulk, mainly in the form of peels, seeds, and pomace, which only leads to a strenuous waste stream that ends up in landfills causing environmental issues if overlooked. However, grapefruit byproducts are rich in high-value compounds including dietary fiber, polyphenols, pectin, and essential oil, which therefore could be valorized for different applications in the food sector and other realms as well. In line with the United Nations Sustainable Development Goals (UN-SDGs) to ensure sustainable consumption and production patterns, the valorization of these byproducts in the most efficient and environment-friendly manner is of great importance for the future.

Summary The valorization of grapefruit byproducts can be addressed through environmentally friendly extraction procedures that allow recovery of target high-value compounds and open new vistas for their applications. Overall, this work describes an updated tapestry of reports about the characteristics and compositions of grapefruit byproducts. In parallel, it offers an updated vision of high-value compounds and the various extraction techniques used for their extraction have been discussed. Comprehensively, the current review summarizes the latest advancements in the application of high-value compounds from grapefruit waste in the numerous areas of the food, pharma, and cosmetics realm, along with the utilization for development of environmentally sustainable materials, fostering a sustainable economy.

Keywords Grapefruit · Waste management · Bioactive compounds · Extraction technologies · Food applications

Introduction

Grapefruit (*Citrus paradisi*) is a commercially important cultivar of the citrus family that encompasses a myriad of bioactive chemicals. Originating in Barbados in the eighteenth century, it is reported to be an accidental cross between the sweet orange (*C. sinensis*) and the pomelo (*C. maxima*). It is widely distributed throughout the world's subtropical and tropical regions [1–3]. During the marketing year 2022/2023, global grapefruit production amounted

to about 6.81 million metric tons [4], with China ranking top among the producers followed by Mexico, South Africa, and the U.S. The grapefruit market is flourishing due to its rich nutrients and health-promoting properties [5]. Grapefruit varieties include Marsh Seedless, Duncan, Red Blush, Flame, Foster, Star Ruby, Thompson, and White Marsh [6]. Mainly consumed in the form of juice and segments, grapefruit can be transformed into various confectionery items. However, growing recognition and increased grapefruit production also draw attention to the wastes and byproducts generated from its processing. These byproducts mainly include peels, seeds, and pomace, and account for more than 50% of the total fruit weight like other citrus fruits [7]. Improper disposal of this organic waste, therefore, can invoke the release of greenhouse gases like methane and volatile compounds during decomposition in landfills which contributes to climate change [8]. Therefore, eco-friendly valorization of grapefruit processing waste is crucial.

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Grapefruit byproduct Valorization Towards the Circular Economy

To promote sustainable development, the United Nations Assembly adopted the "2030 Agenda" in 2015, outlining 17 major goals, also known as the Sustainable Development Goals, or SDGs [9]. The conversion of food wastes and byproducts into valuable products presents a significant potential and overall opportunity to support sustainable development, adhering to the circular economy approach, upon which the futurologists and policymakers stress to implement. Opposite to the conventional "cradle-to-grave" or "take-make-waste" approach, the circular economy follows a "cradle-to-cradle" approach [10, 11]. Deemed as the blueprint for a sustainable future, the circular economy is a closed-loop system and is generally opposite to the linear economy that makes waste. Governments and the food industries are implementing policies to reduce food waste, with studies highlighting the potential of transforming byproducts into value-added products to contribute to meeting the 'zero waste' target. Henceforth, adequate waste management in the most systematic and eco-friendly manner is of great interest for the future. By efficiently utilizing grapefruit byproducts, we can adopt a sustainable consumption and production pattern that aligns with the Sustainable Development Goals (SDGs), in particular SDG 12 (responsible consumption and reproduction) [12, 13]. This article provides an updated overview of grapefruit byproducts as natural resources of bioactive compounds, and their extraction methods, alongside valorization strategies for their comprehensive and effective utilization in food, pharma, and cosmetic industries to promote sustainability (Fig. 1).

Grapefruit Processing byproducts

Peels

Grapefruit peels are important byproducts accounting for around 35.0–41.0% of the total fruit [14]. Proximate analysis for crude protein, fat, ash, crude fiber, and carbohydrate, reports around 9.27–10.71%, 6.13–6.64%, 3–3.97%, 7.55, and 60.22–71.86, respectively [15, 16]. Grapefruit peels, which contain moisture and sugars and are perishable, can pose environmental problems and, therefore seek apt utilization. They are the source of polyphenols, which are confirmed to possess diverse bioactivities, beneficial to human health. TPC was reported to be 77.3 mg of gallic acid equivalent/g peels [17]. In particular, naringin is the most abundant flavonoid present in peels followed by isonaringin, and hesperidin, which can be used as functional ingredients in food and therapeutically [18]. Apart from this, peels account for 59.77% of the insoluble dietary fiber (IDF) fraction [19, 20], and can also be harnessed to yield pectin, EO, and peel extract, making them a valuable resource for valorization.

Seeds

Grapefruit seeds are the premier repositories for limonoids (triterpenoid dilactones chemically related to limonin), from which 77% are neutral while 2% are acidic limonoids [21]. The number of seeds present in grapefruits varies with varieties, with Duncan having around 50–70, while Marsh seedless, has very few to no seeds, as the name illustrates [22]. The chemical composition might vary among the seeds from different cultivars and geographical niches, though oil content lies from 40.2 to 45.5%, similar to that of seeds

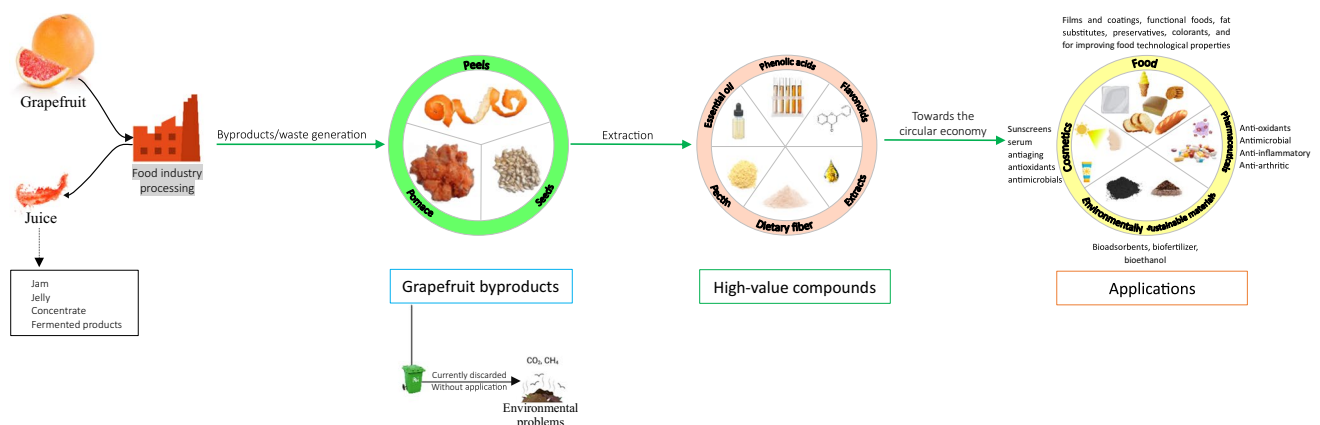


Fig. 1 Overview of grapefruit byproducts utilization towards the circular economy

from the same genus. Grapefruit seed oil consists of both saturated and unsaturated or omega fatty acids, with palmitic acid, oleic acid, and linoleic acid as key constituents accounting for more than 20% of most grapefruit seed oils [23], apart, fat-soluble bioactive compounds such as tocopherols, carotenoids, and phytosterols are present in seeds. Different fatty acids were quantified in the oil such as linoleic acid (40.78–40.95%), palmitic acid (28.19–28.66%), and oleic acid (20.74–20.78%), linolenic (5.45–5.71%), stearic (3.77–3.81%), and palmitoleic (0.40–0.75%) acids [24]. Seeds are often transformed into extracts for various food and pharma applications [21]. The typical proximate for grapefruit seed divulges 36.54% oil content, 3.90% protein, 8.50% fiber, and 5.03% ash content [25].

Pomace

Following the juice extraction, the solid residue left is called pomace. Proximate analysis of grapefruit pomace unveiled 7.69 ± 0.02 crude protein, 50.33 ± 2.1 carbohydrate, 6.13 ± 0.01 crude fat, 2.16 ± 0.01 ash, 24.79 ± 2.4 as nonfibrous carbohydrates such as starch and sugars [16]. Like other citrus fruits, grapefruit pomace is a sound source of dietary fiber, along with health-promoting compounds, and hence therefore can be used to improve the nutritional content of foods. Since pomace is indexed by its high moisture and soluble sugar content, it makes it highly susceptible biomass to fermentation and microbial degradation. The conventional management route follows dried pellet production at a commercial scale. However, ascribable to the reported dietary fiber and polyphenols present, grapefruit pomace can be explored for edible packaging [26], nutritional content improvement [27], and as a functional agent [16, 28]. Pectin from grapefruit pomace with significant emulsifying and gelling properties can be used as a food additive [29].

High-value Components from Grapefruit byproducts

Dietary Fiber

Often referred to as the “seventh nutrient”, dietary fiber (DF) is an important component of the human diet [30]. The total dietary fiber of grapefruit waste (peel and pomace) is reported as 90.34%, with 7.03% as soluble and 83.31% as insoluble fraction [31]. DF mainly comprises soluble dietary fibers (SDF) and insoluble dietary fibers (IDF) and are linked with various health benefits including improving digestive health, serum-lipid concentrations, and reduced risk of cancers [32, 33]. SDF content in grapefruit peel is reported as $3.62 \pm 0.13\%$, however, extraction with modifications in microwave-assisted extraction increased yield

significantly ($7.94 \pm 0.20\%$) [19]. In recent times investigations have been conducted to improve the IDF/SDF ratio from grapefruit byproducts. SDF from grapefruit peel IDF (GP-IDF-SDF) obtained with microwave and enzymatic methods given $9.2 \pm 0.36\%$ yield, with excellent glucose adsorption, water and oil retention capacity 14.49 ± 0.068 mg/g, 13.43 ± 1.19 g/g, and 22.10 ± 0.85 g/g, respectively [34]. Arabinose (100.72 mg/g db) equates to the main monosaccharide in grapefruit peel SDF, followed by glucose (84.00), fructose (31.40), galactose (17.60), and rhamnose (10.85). Compared to orange and lemon peels, grapefruit peels contain a higher amount of uronic acid (UA) (130.72 GUAE/g db), alluding to higher pectic polysaccharide contents [33], ascribable to which, it could find applications in the pharmaceutical industry for its beneficial effects on gastrointestinal health.

Pectin

Pectin, a soluble fiber, finds extensive use as a thickener, stabilizer, and gelling agent and replacement for fat or sugar in low-calorie foods. Pectin is a key ingredient in various pharmaceutical formulations, particularly in producing dietary supplements and oral dosage forms like tablets and capsules. Global pectin consumption as an additive has reached more than 60,000 tonnes, with industry experts projecting a steady 5.8% compound annual growth rate by 2024 in the global pectin market [35, 36]. Grapefruit peel pectin comprises shorter side chains and is richer in rhamnogalacturonan I backbones, which also imparts its valuable bioactivities [33, 35]. Different innovative extraction approaches can be useful tools to increase pectin yield and quality. DES (betaine-citric acid) based extraction from grapefruit peels provided a significant yield of 36.47% pectin with higher RG-I value, more arabinan side chains, and bigger Mw and Mn values, better emulsifying activity and stability than conventional HCl-extracted pectin [36], while microwave-assisted High-Pressure $\text{CO}_2/\text{H}_2\text{O}$ system (147°C , 3 min, and 10 mL g^{-1}) of 27.53% [37], and monosonication-assisted with 17.10% pectin yield [38].

Phenolic Compounds

Phenolic compounds are natural bioactive molecules that are ubiquitous in fruits and are of significant merit due to their health-promoting bioactivities. Grapefruit byproducts have been investigated and affirmed as a good source of phenolic antioxidants. Grapefruit byproducts are rich in flavonoids. Among these, high levels of bioactive flavanones glycosides, namely, naringin and narirutin, and their aglycones, naringenin has been reported in peel and seed residues [39]. Apart, eritrocin, poncirin, neoponcirin, and neohesperidin are also effective antioxidants attributable

to their ability to stabilize and inhibit free radicals [40, 41]. The HPLC analysis also pointed out the presence of phenolic acids (resveratrol, gallic acid, ellagic acid, and caffeic acid), and tannin (catechin) in grapefruit byproducts [42]. Levels of polymethoxylated flavones, sinensetin, nobilletin, and tangeretin range from 1.03 to 3.45 mg/g DW in fresh grapefruit peels, while dried (oven or freeze-dried) peels exhibit lower concentrations [39]. Peels also contain ferulic, sinapic, p-coumaric, and caffeic acids (32.3, 31.9, 13.1, and 5.6 mg/100 g, respectively) [43]. The presence of hydroxyl groups on phenolic rings and their ability to attract free radicals with available hydrogen atoms is deemed to be the reason for the antioxidant activity of these compounds [44]. Extraction of different bioactive compounds can be done with different approaches such as microwave-assisted (MAE) [45], ultrasound-assisted (UAE) [46], and enzyme-assisted extractions (EAE) [47]. Nishad et al. [47] divulged higher TPC yields of 2116.71 and 3170.35 mg GAE/100 g with UAE and EAE, respectively, compared with conventional solvent extraction (CSE) of 1528 mg GAE/100 g [20]. Garcia-Castello et al. [46] also reported better yields for UAE (on average TPC 50% and TAA 66% higher) with lower temperatures and extraction times, compared to CSE. Among individual phenolic compounds, naringin was the most abundant flavonoid in the UAE (24–36 mg/g dw) followed by hesperidin (0.72–1.14 mg/g dw) and narirutin (0.42–0.98 mg/g dw). Grapefruit peel waste may potentially turn out to be a good source of flavonoids, especially naringin, that could be used for food fortification [48] or as therapeutic agents for pharmacological propositions [39].

Essential oil

Grapefruit essential oil obtained from peels is one of the primary grapefruit byproducts, known for its characteristic aroma with wide applications. The major components of essential oil (EO) are terpene oxides, including alcohols, ethers, aldehydes, ketones, and esters, which are attributed to the aroma [49]. Grapefruit EO, primarily extracted through cold pressing, is now being explored through steam distillation and hydrodistillation. GC–MS analysis identified 25 compounds, with D-limonene being the main component. [50–52]. Other compounds include β -Phellandrene (4.17%), β -Myrcene (2.51%), and *o*-Cymene (1.18%) [51, 53]. Grapefruit EO is promoted to exhibit apoptotic, antioxidant, olfactory stimulation, antibacterial, antifungal, insecticidal, acaricidal, and repellency properties [49]. Denkova-Kostova et al. [52] reported 87.5% DPPH free radical inhibition at a concentration of 1 mg/cm³ for grapefruit EO and also highlighted antimicrobial activity against saprophytic microorganisms, spore-forming bacteria, yeast, and fungi. Apart, EO sensibility to external agents like ultraviolet light, high temperatures, and water, may affect their composition, which

facilitates the loss of some specific properties, especially D-limonene is prone to oxidation, which is why encapsulation is feasible for stability, controlled release and enhancement the various characteristics of EO [54–56].

Seed Extract

Grapefruit seed extract (GSE) is a natural product containing tocopherols, citric and ascorbic acids, and flavonoids, with significant antioxidant and antimicrobial properties [57]. Phenolic acids, i.e., trans-ferulic acid, rosmarinic acid, trans-2-hydroxycinnamic acid, and flavonoids, are deemed to be the chief antioxidant active ingredients responsible for antioxidant activity [23, 58]. GSE is a natural food preservative to maintain food quality of various types of foods, including meat, fish, poultry, fruits, cheese, and vegetables [59]. It can be applied directly and can be used to fabricate various composite functional films [60, 61]. The antimicrobial activity of GSE equates to the bacterial membrane disruption and liberation of the bacterial cytoplasmic contents within a relatively short time [23, 59]. GSE also finds applications in the pharma and health sector for wound healing applications [62], oral health-care [63], treating urinary tract infections [64], gastritis and gastric ulcers [65], improving kidney activity, purifying the blood, and help keep cholesterol levels under control. Owing to the reported biological properties, GSE can be explored for the line-up of cosmetic products, including facial cleansers, creams, and serums. [66].

Minerals and Vitamins

Micronutrients include minerals and vitamins because small amounts of these components are needed for the body. Peels of the grapefruit grown in Turkey are reported for minerals, including potassium (K) (111–117), calcium (Ca) (34.8–38.9), phosphorus (P) (19–22.5), magnesium (Mg) (9.50–11.1) (mg 100 g⁻¹), respectively [67]. In another study, Saleem et al. [68] quantified the micro- and macro-elements and reported for Fe (3.53), Mn (0.36), Cu (0.14), Zn (0.14), Mg (79.33), K (984.33), and Ca (801) (mg/100 g). Reported different values are attributable to the differences in soil conditions, climate, and cultivars. The vitamin C content of grapefruit peels was found to be 113.3 mg/100 g [17], while Vitamin E, which is a fat-soluble vitamin, has been confirmed. Further authors have quantified α -, γ -, δ - tocopherol as 380.00, 43.41, and 9.08 mg/kg, respectively [25].

Various studies indicate that all these high-value components are interesting for the food, pharma, and cosmetic industries, and their reutilization would promote a circular and sustainable economy around the grapefruit industry. This strategy is relevant to harmonize with the SDGs, specifically to minimize grapefruit waste, in line

with the circular economy model which pivots on bringing the waste back into the streamline of production so that it goes back into the production loop and can either become the resource for the next cycle of production or is channeled for an independent new product. However, to maximize the environmental benefits of reusing these wastes, it is required the application of green extraction techniques to obtain optimal production yields ecologically and economically.

Extraction Technologies for Extraction of Various Components

The extraction of bioactive compounds from food processing waste is a critical step. Conventional methods have drawbacks like higher energy expenditure and toxic solvents, prompting the search for efficient technologies like ultrasound, microwave, enzyme-assisted, and supercritical fluid [69–74]. Extraction of functional and bioactive compounds from grapefruit byproducts using various techniques has been framed in Table 1 and discussed hereunder.

Ultrasound-assisted Extraction

Ultrasound follows the acoustic cavitation principle. When ultrasound propagates through any medium it generates a series of compressions and rarefactions in the molecules of the medium, such alternate pressure changes induce the formation, growth, and consequently implosion of air bubbles in a liquid medium. Such violent collapse produces extremely high pressures and temperatures at the surface of cell membranes of bio matrices, due to which cell destruction occurs, causing localized damage to the plant tissues termed ‘erosion’. This event creates microchannels, making the intercellular content more available to the solvent, and increasing the yield of extraction [86, 87]. Ultrasound applications are versatile and can be used to treat grapefruit byproducts for extraction of polyphenols, pectin, polysaccharides, dietary fibers, and oils. For instance, Garcia-Castello et al. [46] reported a higher TPC range for UAE (29.4 to 80.0 mg GAE/g dw) than for the conventional approach (25.3 to 55.8 mg GAE/g dw) from grapefruit solid wastes. In the latest investigation, Islam et al. [75] reported TPC (78.5 mg GAE/g dw), TFC (53.5 mg naringin/g dw), naringin (40.8 mg/g dw), and TAA by DPPH (25.5 mM Trolox/g dw), and FRAP assay (17.45 Fe [II]/g dw), for treated 2 g grapefruit peel powder with ultrasonication. Ultrasound is a rapid process, provides higher extraction yields, easy to operate, and requires less investment costs,

and versatility, strengthens its ability to be implemented at the industrial level, among others.

Microwave-assisted Extraction

Microwave-assisted extraction functions the application of non-ionizing electromagnetic waves with frequencies ranging from 300 MHz to 300 GHz to a sample matrix that induces changes in the cell structures. Responsible mechanisms for energy transfer in MAE involve ionic conduction and dipole rotation [69, 70]. Ionic conduction in particular pertains to the movement of ions through a solution, eliciting a homogeneous heat in the media ascribable to the resistance of the solvent to the ionic migration upon application of electromagnetic waves. Dipole rotation is enacted by the interaction of dipoles with polar components and elicits the dipoles to realign with the applied field, instigating coerced molecular movements that produce heat [88]. The moisture content in the sample significantly influences MAE, as water evaporation increases intracellular pressure, breaking cell walls, and leaching high-value compounds [89]. Taşan & Akpınar [79] reported a 20.93% pectin yield from grapefruit peels using MAE (pH 1, 30 ml/g solvent/solid ratio, 90 s) with significantly lower extraction times than conventional extraction without compromising on yield and quality of pectin. In a different study, a 17.19 ± 0.35% increased yield of soluble DF was obtained with MAE treatment of grapefruit peels [19]. Merits for the technology include operational ease and low running costs. Apart, higher outputs can be generated with a punctilious selection of operating conditions such as temperature, solid-to-liquid ratio, extraction duration, microwave power, and stirring [90].

Supercritical fluid Extraction

The supercritical fluid extraction (SFE) approach follows the solvation of compounds of interest in a solvent maintained typically above its critical pressure and temperature. CO₂ is commonly used for SFE applications and behaves as supercritical fluid above the critical temperature and pressure and shows improved productivity for solubilizing non-polar compounds. Elevating the temperature and pressure of supercritical fluid beyond 4000 psi significantly improves solubility for highly efficient extractions in shorter periods [91]. Supercritical fluid carries target compounds past the pressure release valve into the separator, where lower pressure separates CO₂ from the extracted compounds and routed back into the CO₂ tank to be used again. Priyadarsani et al. [92] reported for 93% extraction efficiency of lycopene from grapefruit endocarp at 305 bar pressure, 35 g/min CO₂ flow rate, 135 min of extraction time, and 70 °C temperature. Latesty, Yaldiz et al. [93] reported TPC values of 79.60 mg

Table 1 Recent studies for extraction of bioactive compounds from grapefruit byproducts

Grapefruit byproduct	Extracted compound	Technique employed	Treatment conditions	Yield/potential outcomes	References
Peels	Polyphenols	Ultrasound-assisted extraction	48% (v/v) ethanol concentration; amplitude: 40%; time: 13 min	TPC=78.5 mg GAE/g dw; TFC=53.5 mg naringin/g dw; naringin content=40.8 mg/g dw; DPPH=25.5 mM Trolox/g dw; ABTS=4050 mM Trolox/100 g dw; FRAP=17.45 Fe [III]/g dw	[75]
	Polyphenols	Ultrasound-assisted extraction bath	50% (v/v) ethanol concentration; time: 30 min; temperature: 50 ± 2 °C	Naringin yield = 17.45 ± 0.872 mg/g (from albedo)	[76]
	Polyphenols	Microwave-assisted extraction	Time: 45 s; power: 275 W	TPC = 17.22 mg GAE/g; TFC = 1.71 mg CE/g	[47]
	Polyphenols	Enzyme-assisted extraction	Time: 4.81 h; pH: 4.8; temp: 60 °C; enzyme concentration: 0.9%; solvent-solid ratio: 40 mL/g	TPC = 3170.35 ± 8.72 mg/GAE/100 g; TFC = 329.89 ± 1.37 mg QE/100 g	[77]
	Polyphenols	Deep eutectic solvents coupled with High voltage electrical discharges (HVED)	Distance between electrodes: 5 mm; Voltage: 40 kV; current: 10 kA; Pulse frequency: 0.5 Hz; HVED energy input: 7.27 – 218 kJ/kg; Number of pulses (n): 10–300	Naringin extraction improved by 3 times than conventional extraction	[18]
	Pectin	Microwave-assisted high-pressure CO ₂ /H ₂ O	Temperature: 147 °C; time: 3 min; and liquid–solid ratio: 10 mL g ⁻¹	27.53%	[37]
	Pectin	Deep eutectic solvent (DES) (betaine-citric acid)	Temperature: 85 °C; time: 120 min; L/S ratio of 25 mL/g; pH of 2.0	36.47%	[36]
	Pectin	Steam explosion technology	Time: 90 s; pressure: 0.8 MPa	17.50%	[78]
	Pectin	Microwave-assisted extraction	Time: 90 s; pH: 1; solvent solid ratio: 30 mL/g	20.93%	[79]
	Pectin	Acoustic cavitation-assisted extraction	Time: 28 min; temp.: 67 °C; amplitude: 58%; pulse duty cycle: 50% (2 s on and 2 s off)	23.49%	[80]
	Pectin	Ultrasound-assisted heating extraction	Time: 27.95 min; power: 12.56 W/cm ² ; temp: 66.71 °C; frequency: 20 kHz; pulse duty cycle: 50% (2 s on and 2 s off)	27.34%	[81]
	Pectin	Array-induced voltages assisted extraction	Excitation voltage: 1000 V; frequency: 20 kHz; phase difference: 0 °C	10.34%	[82]
	Soluble dietary fiber	Microwave-assisted extraction	Time: 40 min; temp: 80 °C; power: 500 W	17.19 ± 0.35% increased yield	[19]
	Essential oil (EO)	Pilot scale twin-screw extruder	The extruder barrel comprised 10 modules of length 20 cm each with a filtration unit stationed in module 4 and an outlet in module 10; temp: 150 °C; rotation speed: 80 rpm	2.21 g EO/ (kg of dry base peel.min)	[83]
	Essential oil	Solvent-free microwave extraction	Oven frequency: 2450 MHz; Microwave irradiation: 85 W; time: 20 min; temp: 100 °C	0.44%	[84]

Table 1 (continued)

Grapefruit byproduct	Extracted compound	Technique employed	Treatment conditions	Yield/potential outcomes	References
Seeds	Seed oil	Enzyme treatment followed by cold pressing	Enzymes: Naringinase (0.06 U/g seed activity) and hesperidinase (0.033 U/g seed activity); incubation temp: 65 °C; shaking: 55 rpm for 4 h	65.35 ± 1.51% oil yield	[24]
	Dietary fiber	Ultrasound-assisted aqueous extraction	Ultrasound power: 280W; frequency: 20 kHz; time: 20 min (pulse duration of 5 s on and 25 s off); filtration: 100 mesh screens; vacuum drying: 50 °C for 3 days	SDF: 4.59—7.95%; IDF: 75.95—82.24%	[85]
Pulp, pomace, solid waste	Flavonoids	Ultrasound-assisted extraction	Frequency: 40 ± 2 kHz; power: 100W; ethanol concentration: 0.2–0.8 g/g (20–80 g/100 g); temp: 34–61 °C; time: 15–48 min	29.4–80.0 mg GAE/g dw TPC; naringin was the most abundant flavonoid in the extract ranging from 24 to 36 mg/g dry-weight	[46]
	Dietary fiber	Ethanol extraction	Pulp homogenates were mixed with anhydrous ethanol (1:4, w/v); centrifugation: 3.22 × 104 × g (4000 rpm)	TDF content: 22.0 g/100 g, with an IDF/SDF ratio of 3.5 ± 0.3	[32]

GAE/g from grapefruit peel waste when treated at 150 bar, 70 °C, and a cosolvent ratio of 20% (v/v) ethanol. Short extraction time, a low amount of solvent requirement, and rapid solvent recovery, account for the advantages of the technology [94], while the major setbacks are the high cost of the equipment and operation and optimization complexity.

Enzyme-assisted Extraction

This approach involves exclusive enzymes (such as cellulases, amylases, pectinases) to break down bound chemicals, and resultantly enhance the extraction through cell wall breakdown and polysaccharide hydrolysis. Phenolic compounds are entangled within the cell wall polysaccharides like cellulose, hemicellulose, and pectin and are linked by hydrophobic interactions and hydrogen bonds. In particular grapefruit peel flavonoids, are covalently linked by a glycosidic bond with sugar moieties through an OH group (O-glycosides) or carbon–carbon bonds (C-glycosides) [20, 95]. Enzymes pounce upon the internal spots of the amorphous region of the polysaccharide chains which prompts small oligosaccharides generation of uneven length that facilitates easy release of entrapped molecules [96]. Pectinase and cellulase (5, 6, 7 U g⁻¹ enzyme concentration) used to extract phenolic compounds at different temperatures (40–60 °C) and time (6–24 h) combinations from grapefruit peels enhanced the extraction yields (p < 0.05) [97].

Natural Deep eutectic Solvents

Natural deep eutectic solvents (NADES) are sustainable solvents fabricated by blending a hydrogen bond acceptor (e.g. choline-chloride) with a hydrogen bond donor (such as sugars, alcohols, and amines), and up to 50% (v/v) water; at a precise ration to develop a liquid solvent mixture. DESs are liquid at low temperatures, miscible with water, non-flammable, and highly viscous [18]. NADES are widespread in nature and are more based on biological than chemical concepts since ionic liquids or deep eutectic solvents might exist in nature with specific physiological functions [98]. In the latest investigation, Lin et al. [36] extracted pectin from grapefruit peels with betaine-citric acid (BC-P) at an L/S ratio of 25 mL/g, 2.0 pH, and 85 °C for 120 min with a higher yield (36.47%), compared to HCl-extracted pectin (HCl-P, 8.76%) under a pH of 2.0. BC-P exhibited a higher RG-I (Rhamnogalacturonan I) value, Mw, and more arabinan side chains, than HCl-P. The authors also stated higher viscosity, emulsifying activity, and stability compared to HCl-P and commercial pectin. NADES is a versatile method for extracting bioactive compounds from grapefruit byproducts, offering high

solubilization strength and easy extraction. Drawbacks such as high viscosity and very low vapor pressure are there, but anti-solvents can be used to confront the issue, moreover, liquid–liquid or solid–liquid extraction can be performed [99].

Pooling Technologies

Numerous studies have reported the integration of novel extraction technologies with beneficial and efficient results [100]. The food industry is heavily focused on lowering manufacturing costs, either by increasing process speed or increasing yield. This refers to either using one thriving technique or combining two or more techniques to achieve its goal. For grapefruit peel, Peng et al. [20] combined microwave (600 W, 85 °C, and 37 min) and enzymatic treatment (8% cellulose, 60 °C, 2 h) (ME-BP) to free insoluble bound phenolic compounds. The obtained results showed higher values for the combined treatment (12.46 ± 0.028 GAE mg/100 g) compared to enzymatic (7.17 ± 0.044 GAE mg/100 g) and microwave (9.95 ± 0.049 GAE mg/100 g) alone.

Purification and Detection of Bioactive Compounds

Impurities are introduced during the extraction process and must be isolated immediately to validate the safety and purity of the compound of interest. Different methodologies for purification and characterization are employed as post-extraction treatments. In particular, citrus waste comprises different polysaccharides and other phytochemicals in tandem with bioactive compounds. These compounds are also extracted during the solid–liquid extraction process. To separate a particular bioactive compound, it should be available in concentrated form in the solution, which can be done by the polarity and pH of the solvent engaged. Non-polar solvents are commonly utilized for lipid fractions, whereas, polar ones are preferable to isolate the ionic compounds [101, 102]. Solid-phase extraction is carried out for the removal of carbohydrates. Sugars, polar nonphenolic compounds, and organic acids could interfere with the total polyphenol content analysis, therefore crude polyphenolic extracts from grapefruit solid wastes are quite commonly purified by using C18 chromatography cartridges [46]. Fractionalization of polyphenols is brought about with methanol and/or acetone from the polyphenol concentrate [101]. In particular, for flavonoid, i.e., naringenin, Chen et al. [103] reported improved performance of CMIPs when employed to enrich naringenin in grapefruit peel extract

compared with the common adsorbent materials including AB-8, D101, cationic exchange resin, and active carbon. Flavonoids can also be adsorbed with Indion PA 800 and later desorbed using ethanol. The purification phase culminates in different scaled filtrations, while the identification and characterization of bioactive phytochemicals from grapefruit byproducts is done using different chromatographic and spectrophotometric techniques, such as HPLC–DAD [39], HPLC–MS [103, 104], thin layer chromatography (TLC) [105, 106], ultrahigh performance liquid chromatography (UPLC) [107], gas chromatography–mass spectrometry (GC–MS) [53], nuclear magnetic resonance (NMR) and UV-spectrophotometry [75]. The schematic representation of extraction to the identification of bioactive compounds utilizing innovative approaches is illustrated in Fig. 2.

Grapefruit byproduct Utilization

Food sector

Bioactive ingredients work well as an ingredient to produce nutritious goods and nutraceuticals with improved technological and biofunctional qualities. The following section catalogs and discusses the uses of various grapefruit byproducts for different food applications (Table 2).

Food Packaging

The rejection of synthetic materials and the shift toward renewable and eco-friendly materials for packaging has fueled research for green alternatives [123, 124]. Moreover, the global market for edible coatings and films has been projected to grow at a rate of 7.70% (CAGR) during the next five years to reach a value of 4.54 billion US\$ in 2028 [125]. Grapefruit waste yields pectin, essential oils, and seed extracts that can be used in bio-based coatings and films. Moreover, active ingredients may enhance the flavors, colors, antimicrobial, and antioxidant properties of films, ultimately improving food quality [126]. In a study, Zanganeh et al. [127] fabricated a *Lallemantia iberica* seed mucilage (LISM) coating incorporated with grapefruit EO (0–2% v/v), which reduced microbial growth and lipid oxidation. The authors also reported that lamb with 2% v/v EO concentration had better quality maintenance and extended shelf life (>9 days). Chiabrando & Giacalone [128] tested the potential of alginate-based grapefruit EO coating for fresh-cut kiwifruit quality preservation. The results showed a lowered respiration rate, increased firmness, and vitamin C content, and curbed yeast and mold flourishing. Roy & Rahim [60] tested the antioxidant potential of grapefruit seed extract (GSE) after addition to a poly(vinyl

alcohol)-based film. The obtained results showed escalated DPPH scavenging activity of 50.3% with GSE in comparison to the control film (0.7%), while ABTS activity reached 90.2% with GSE incorporation.

Baek et al. [129] investigated the potential of sodium alginate nanoparticle-based grapefruit seed extract (GSE) coating for safety and quality maintenance of shrimp stored at 4 °C for 8 days. Upon coating on shrimp, nanoparticles (1% alginate + 1% GSE) prevented the microbiological limit from exceeding during 8 days of storage, while uncoated shrimp exceeded the limit on the 4th day. Additionally, nanoparticles markedly attenuated the TVB-N values and showed the lowest weight loss when compared to other samples. Chitosan coating with GSE (1.0% w/w) inactivated *Salmonella* by 2.0 ± 0.3 log CFU without affecting the lycopene content, color, or sensorial properties of fruits, as reported by Won et al. [130]. Bionanocomposites based on halloysite-encapsulating grapefruit seed oil (GO) (2.5 wt%) showed marked mold prevention and better preservation of the fruit texture and appearance for strawberries [131]. Citrus peels are among the major industrial sources for pectin extraction, and grapefruit peel pectin is another component that needs to be studied further for use as a packaging film/coating biomaterial.

Antimicrobial Agent

The use of natural antimicrobials as food preservatives prevents the extremities of physical and chemical processing [132]. In a study, grapefruit EO was tested against food-borne pathogens. The results revealed bacteriostatic properties against most of the tested bacterial strains. Essential oil at concentrations up to 25 mg/mL effectively suppressed *Salmonella paratyphi* A, *Vibrio vulnificus*, and *Serratia liquefaciens* growth. Grapefruit EO, when used in a nanoemulsion system, ameliorated bacteriostatic potency [51].

Grapefruit seed extract (GSE) in particular has a broad antimicrobial spectrum against a variety of microbial strains. Choi et al. [133] reported MIC values of GSE against the food-borne pathogens *B. subtilis*, *C. albicans*, *E. coli* O157:H7, *P. aeruginosa*, *S. enteritidis*, and *S. aureus* in the range 0.0061 to 0.7813 $\mu\text{L/mL}$, and promoted GSE as an efficacious natural additive that prolonged the shelf-life of fresh Makgeolli with no significant loss in quality. Antibacterial mechanism of GSE accounts for the bacterial membrane disruption and liberation of cytoplasmic contents [59], while antifungal action is attributed to causing loss of spore contents and damage to the thick cell wall and cell membrane of the spore [58]. Although the conventional use of GSE in foods is its sole application, it is

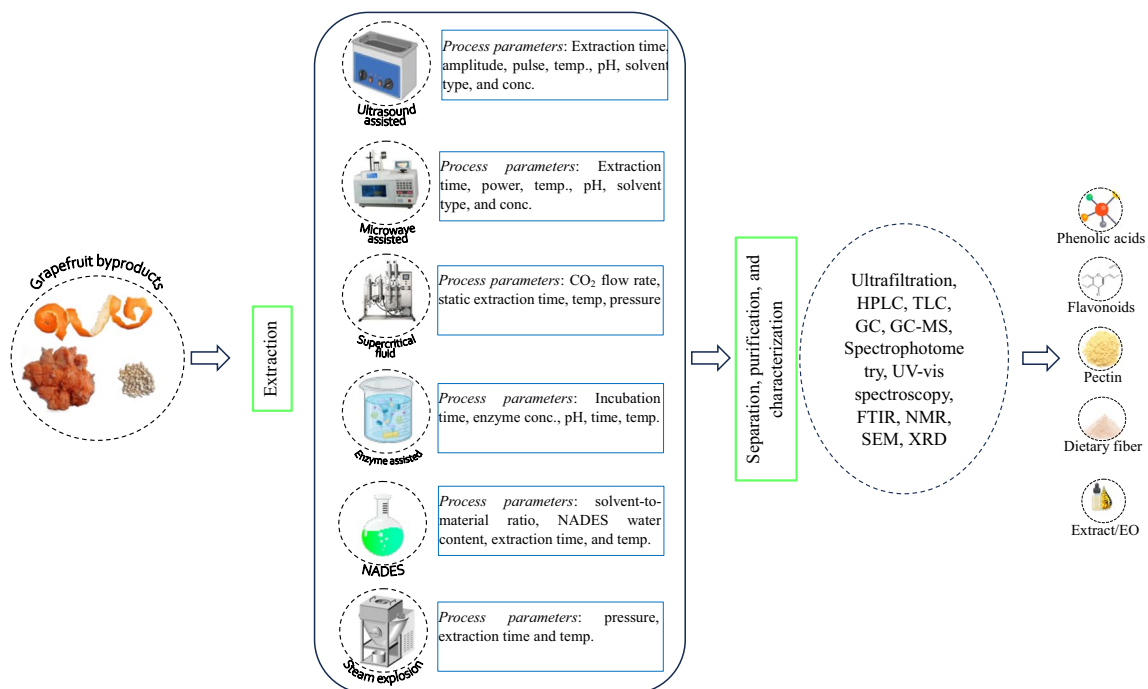


Fig. 2 Schematic representation of recovery of high-value compounds from grapefruit byproducts

Table 2 General spectrum regarding utilization of bioactive compounds from grapefruit wastes in the food sector

Category	Grapefruit byproduct	Compound extracted	Additional material(s)	Final product/activity	Remarks	References
Food packaging	Seed	Seed oil	Hemp Hurd; rice flour (0.9 g in 30 ml DW); sodium alginate (0.1 g); glycerol (0.5 w/w); ethanol	Biodegradable composite edible films	<ol style="list-style-type: none"> The hydrophobic character of EO led to a reduction of either the sorption parameter (about 85%) or the diffusion one (up to 96%) Can be employed as potential packaging material for foods where antimicrobial activity is required as a tuned release profile 	[108]
	Peel	EO	Soy protein isolates-gum acacia conjugate (5 g in 100 ml DW); glycerol (2 g)	Edible film	<ol style="list-style-type: none"> Films comprising GF-EO showed the best moisture barricade properties, the highest tensile strength, and T_g compared to the films prepared from other EOs Film comprising GF-EO showed the lowest swelling ability 	[109]
	Seed	Seed extract	Chitosan (0.75 g); Acetic acid (1% v/v); corn starch (5 g); sorbitol (30% w/w)	Bio-nanocomposite film	<ol style="list-style-type: none"> Bread samples packed with nanocomposite coating containing 1.5 (v/v) grapefruit seed extract (GFSE) retarded fungal growth till 20 days Fabricated films displayed high crystallinity, low hydrophilicity, high water barrier, and mechanical properties 	[110]
	Seed	Seed extract	Corn starch (4% w/w); chitosan (2.5% w/w); glycerol (25% w/w)	Edible film	<ol style="list-style-type: none"> Films containing GSE presented less stiffness and resistance but were more stretchable than the control ones O_2 permeability remained unaffected by GSE incorporation 	[111]
	Seed	Seed extract	Melamin nanoparticles (0.02 g)	Functional film	<ol style="list-style-type: none"> The pectin/agar composite film showed intense antioxidant activity and excellent antibacterial activity against foodborne pathogens by adding MNP and GSE 	[61]
	Seed	Seed extract	Sodium alginate; CMC; potato starch in 1:1:1 ratio	Coating	<ol style="list-style-type: none"> GSE incorporation reduced the water vapor permeability properties and enhanced the flexibility and thermal stability of the film The prepared blend solution with 0.5 g of GSE effectively enhanced the shelf life of green chili by 25 days 	[112]

Table 2 (continued)

Category	Grapefruit byproduct	Compound extracted	Additional material(s)	Final product/activity	Remarks	References
Antimicrobial agent	Peel	Peel powder	Aerobic plate count (APC), psychrotrophs, <i>S. aureus</i>	Antibacterial activity	1. Samples treated with grapefruit peel powder (1%) showed lower bacterial counts (log ₁₀ CFU/g) for APC. Psychrotrophs and <i>S. aureus</i> as 3.57 ± 0.03, < 2.00 ± 0.00, < 2.00 ± 0.00, upon 3-month storage period at -18 °C, as compared to control samples	[113]
	Peel	EO	Bacterial strain – <i>S. aureus</i> , <i>E. faecalis</i> , <i>K. pneumoniae</i> , <i>S. Paratyphi A</i> , <i>V. vulnificus</i> , <i>P. mirabilis</i> , <i>S. liquefaciens</i> , <i>P. luteola</i>	Antibacterial activity	1. Grapefruit peel EO displayed bacteriostatic properties against the majority of tested bacterial strains; however, only the growth of <i>Salmonella paratyphi A</i> , <i>Vibrio vulnificus</i> and <i>Serratia liquefaciens</i> was inhibited by the EO with conc. up to 25 mg/mL 2. Incorporation of EO in nanoemulsion system resulted in increased bacteriostatic potency but no bactericidal effect was observed, probably due to too low EO conc	[51]
	Peel	EO	<i>E. coli</i> ATCC 25922, <i>S. aureus</i> ATCC 25923, <i>P. aeruginosa</i> NBIMCC 1390, <i>C. albicans</i> NBIMCC 74; Saprophytic test-microorganisms: <i>B. subtilis</i> ATCC 6633, <i>P. chrysogenum</i> ATCC 10106, <i>F. moniliforme</i> ATCC 38932, <i>A. niger</i> ATCC 9029, <i>A. flavus</i> ATCC 9643, <i>S. cerevisiae</i> ATCC 7754	Antimicrobial activity	1. Grapefruit EO demonstrated high antimicrobial activity against saprophytic microorganisms, spore-forming bacteria, yeast, and fungi, with significant inhibitory activity	[52]
	Seed	Seed extract	Bacterial strain – <i>Listeria monocytogenes</i>	Antibacterial activity	1. Supplementing döner kebab with 0.5 – 1% GSE rendered the pathogen more sensitive to the lethal effect of heat 2. Results suggest that 0.5 – 1% GSE supplementation in sous vide processed döner kebab, can benefit with adequate degree of protection against <i>L. monocytogenes</i>	[114]
	Seed	Seed extract	Bacterial strain – <i>E. coli</i> O157:H7, <i>S. Typhimurium</i> , and <i>L. monocytogenes</i>	Antibacterial activity	1. Potential of 1% Malic acid + 0.5% GSE was tested on artificially inoculated lettuce during storage at 5 °C for 14 days which showed maximum reductions of <i>E. coli</i> O157:H7, <i>S. Typhimurium</i> , and <i>L. monocytogenes</i> as 4.96, 4.80, and 3.95 log CFU/g, respectively	[115]

Table 2 (continued)

Category	Grapefruit byproduct	Compound extracted	Additional material(s)	Final product/activity	Remarks	References
Food additives	Peel	Nano-fibrillated cellulose (NFC)	–	Fat substitute	1. Gross energy showed a decreasing trend with an increase in NFC, highlighting lower calorie content	[116]
					2. NFC addition also showed an inhibitory effect on the digestion of protein and fat in ice cream during the digestion process with maximum inhibition rates of 21.70% and 59.53%, respectively	
	Peel	–	–	Functional agent	1. Functional drinks showed enhanced physicochemical profile, and improved storage stability with sensory score	[16]
					2. Can be successfully utilized as coloring agents in food products	
Prebiotics	Peel	Lycopene	–	Coloring agent	1. 93% lycopene extraction using supercritical CO ₂ extraction	[92]
					2. A reduction in the lipid oxidation of 73.45% was obtained in samples with added grapefruit peel extract	
	Peel	Peel extract	–	Antioxidant agent	1. A reduction in the lipid oxidation of 73.45% was obtained in samples with added grapefruit peel extract	[117]
					2. Lower peroxide value (PV) of 15.5 ± 0.7 meq kg ⁻¹ for samples with added extract after 13-day storage at 4 °C, compared to control (72 ± 1.9 meq kg ⁻¹)	
Prebiotics	Peel	Dietary fiber	–	Functional agent	1. Yogurt fortified with modified SDF showed lower syneresis, higher gel strength and hardness, and stronger odor characteristics compared to blank control yogurt	[118]
					2. Pectin utilization in preparing jam formulation resulted in a significant effect on the texture of the final product	
	Peel	Pectin	–	Gelling agent	1. The highest acceptability for the biscuits reported for the samples which were prepared with 5% grapefruit powder	[28]
					2. Grapefruit peel flour concentration the specific growth rate was higher, and with a lower duplication time	
Peel	Albedo and flavedo flour	–	Prebiotic activity	1. Short-chain fatty acids production confirmed the prebiotic potential of flours, validating their potential as functional ingredients in foods	[120]	
				2. SDFs extracted from grapefruit peel by ultrafine grinding treatment promoted bacteria proliferation and stimulated probiotic strains to produce more short-chain fatty acids		

Table 2 (continued)

Category	Grapefruit byproduct	Compound extracted	Additional material(s)	Final product/activity	Remarks	References
Encapsulation	Peel	Pectin	–	<i>Lactobacillus plantarum</i> encapsulated in pectin	1. Bacterial viability did not significantly decrease after freeze-drying and storage of the beads at 4 °C for 45 days	[121]
	Peel	Lycopene	Trehalose; β-cyclodextrin; Arabic gum	Lycopene encapsulated in alginate-based beads	1. Higher lycopene content (> 80%) after freezing and drying, regardless of the method involved	[122]

also used to fabricate edible coatings with antimicrobial properties. Carboxymethyl cellulose (CMC)-based films incorporated with chitin nanocrystals (ChNCs) and GSE displayed strong antimicrobial efficacy against both gram-negative bacteria (*E. coli*) and gram-positive bacteria (*L. monocytogenes*) Oun and Rahim [57], due to the release of polyphenol compounds (e.g., naringin, limonin), that breach the cell membrane and bind to cellular proteins, thereby impairing function [60].

Food Additives

Food additives are used for shelf-life extension, nutritional quality improvement, and appearance. Grapefruit byproducts and derivatives can be used as a natural substitute for chemical additives in various roles. Soluble dietary fiber from grapefruit peels added to blueberry jam formulation enhanced the stability of jam while maintaining the color, texture, and spreadability of jam [34]. Soluble dietary fibers (SDF) obtained by microwave-ultrasonic treatment from grapefruit peels were used for bread formation and improved the structural, functional, and in vitro digestion properties of the prepared bread. The authors also highlighted its low glucose release rate and potential as a functional food ingredient [19]. In another investigation, Ukom et al. [134] utilized grapefruit peel powder (3.7–5 g) in cake preparation that improved the DPPH, ABTS, and FRAP percentages up to 2–threefold over the control samples. Grapefruit peel nanofibrillated cellulose (GNFC) has been used as a fat substitute in the preparation of ice cream with lower gross energy and calorie content. Furthermore, GNFC incorporation demonstrated digestion impediments of 21.70% and 59.53% for protein and fat, respectively [116]. Kaanin-Boudraa et al. [107] used grapefruit EO as an alternative to vitamin E in margarine and found that it was more resistant to oxidation than control samples. Functional foods can be considered to be those fortified, enriched, or enhanced foods that are destined to provide additional health benefits. Ajtonty et al. [48] prepared functional chocolate fortified with grapefruit peel extract and confirmed it as a satisfactory carrier for naringin. Qin et al. [118] improved SDF quality from grapefruit peel by using superfine grinding combined with *L. paracasei* fermentation and used SDF to prepare functional yogurt, which exhibited lower syneresis, higher gel strength and hardness, and stronger odor characteristics compared to control yogurt. Moreover, functional drinks enriched with grapefruit peel and pomace showed improved phytochemical profile, which therefore could be promoted as a nutraceutical product with multiple benefits to the consumers [16].

Prebiotics

Prebiotics can help to nourish gut bacteria and eventually promote health-promoting bacteria that colonize the gastrointestinal tract, healthy digestive and therefore, immune systems [135]. Grapefruit albedo and flavedo peel flour evaluated with two lactic acid bacteria strains (*P. pentosaceus* UAM21 and *A. viridans* UAM22) showed the viability of the employed strains during the fermentation period employing the alternative carbon sources. Short-chain fatty acid production confirmed the prebiotic potential of grapefruit peel flours authenticating their potential as a functional ingredient in foods [120]. GSLSDF-1 obtained from the grapefruit peel sponge layer soluble dietary fiber (GSLSDF) possessed a low molecular weight and crystallinity, a loose and porous microstructure, and a high glucose content. GSLSDF-1 showed a better prebiotic activity, increasing the relative abundances of *Lactobacillus*, *Bacteroides*, *Bifidobacterium*, and *Faecalibacterium*. Furthermore, GSLSDF-1 promoted the production of short-chain fatty acids (SCFAs) by modulating the SCFAs synthesis pathway of intestinal microorganisms, while the NH₃-N synthesis of intestinal microorganisms was inhibited by GSLSDF-1 [5]. Qin et al. [30] reported that ultrafine ground SDF from grapefruit peel more effectively promoted bacteria proliferation and stimulated probiotic strains to produce more short-chain fatty acids, compared to untreated SDF when tested for in vitro prebiotic activity. These investigations confirm grapefruit peel is an apt and sustainable contender for developing products with prebiotic properties.

Encapsulating Agents

Encapsulation is an apt tailored option to improve the stability, bioavailability, quality, safety, and applicability of the bioactive compounds [136]. Encapsulation finds wide applications in the food and pharma sector, conferring micro (1–1000 µm) and nano (1–several hundred nm) levels of fabrications. Calvo and Santagapita [122] encapsulated grapefruit lycopene in alginate-based beads to improve its stability and shelf life. Alginate beads comprising trehalose with β-cyclodextrin retained a higher lycopene content (> 80%) after freezing and drying. In a separate study, Ko et al. [137] extracted flavanones (naringin, narirutin, naringenin, hesperidin, and hesperetin) from grapefruit peels, treated the extracts with 60% β-cyclodextrin and analyzed the extracts using field emission-scanning electron microscopy (FE-SEM). The results showed that encapsulation in β-cyclodextrin improved the solubilization. Nishad et al. [77] encapsulated grapefruit peel phenolics (GPP) into the nano-emulsion-based delivery system and reported extended oxidative stability of mustard oil.

Cosmetic Industry

The cosmetic industry is shifting towards safer, natural compounds due to health concerns over harmful chemical constituents. Consumers are demanding natural, organic, and certified organic ingredients, therefore high-value compounds from grapefruit waste can be explored in cosmetics and toiletries [138, 139] (Table 3).

Flavonoids present in grapefruit peels could preferably be used in cosmetics due to reported anti-inflammatory activity, as they prevent the release of arachidonic acid caused by oxidative processes of membrane lipids [146]. Naringin, hesperidin, and isonaringin are important flavonoids present in grapefruit peels and seed residues [39] that possess anti-carcinogenic, anti-oxidative, anti-aging, antimicrobial, anti-inflammatory, and free radical scavenging activity [147]. It has been reported that naringin scavenges free radicals in vitro [142] and, therefore could be used to develop skin creams and topical lotions. Phenolic acid i.e., such as resveratrol present in grapefruit byproducts is known to safeguard against photo-oxidative damage to the skin [42], while gallic acid, which is a major phenolic acid in grapefruit different parts, followed by chlorogenic acid, caffeic acid, and ferulic acid are often associated with preservation of hair color, strength, and growth. Limonene is a predominant component (93.33%) of monoterpenes present in light-phase grapefruit EO [49], therefore can be explored against acne due to its antibacterial properties. Cosmetic composition developed with natural extracts from rosemary and grapefruit seeds and pulp showed no bacterial colonies neither after one day nor after three months of storage period, divulging good antibacterial properties, being quite a satisfactory substitute for the parabens [148]. Grapefruit peel ethanolic extract with a concentration of 2% has the best anti-aging activity attributable to significant antioxidant activity [149]. Ha et al. [150] tested the antimicrobial effects of (GSE) against human skin pathogens: *Malassezia furfur*, *M. restricta*, *Propionibacterium acnes*, *Trichophyton mentagrophytes*, and *T. rubrum* and reported MIC values of 3.91, 3.91, 0.004, 0.024, and 0.012 µl/ml, respectively. The study indicated GSE as a promising source of antibacterial agents that could be utilized in skin and hair care products and alternative medicine for certain skin ailments. Grapefruit EO contains limonene, myrcene, and α-pinene that could be looked into as fragrance ingredients in cosmetics [49].

Pharma and Health Sector

Grapefruit byproducts, rich in phytochemicals and value-added compounds, are being explored for nutraceutical, pharmacological effects, and drug development. They offer a lucrative, sustainable, and cost-effective source of

biologically active compounds [6, 22, 42]. Pectin from grapefruit peels can be utilized as a natural prophylactic for the active elimination of toxic metals from the digestive and respiratory systems, in tablet formulations as a carrier material in colon-specific drug delivery systems. Pectin from grapefruit peels is also reported for inhibitory activity against pancreatic cholesterol esterase, pancreatic lipase, and α -glucosidase [73]. Grapefruit IntegroPectin, a potent antioxidant, has potential as a therapeutic and preventive agent for treating oxidative stress-related brain disorders and may also aid in cancer research. [151]. Dietary fibers are often associated with preventive action against constipation, elevating smooth bowel movements, helping with diabetes, and lowering cholesterol. Grapefruit pomace with an SDF/total DF ratio (w/w) of 0.76, followed by peels (0.15) [22] can be used as a reliable source of dietary fibers. Recently, Qin et al. [30] reported that ultrafine ground SDF from grapefruit peels effectively promoted bacteria proliferation and stimulated probiotic strains to produce more short-chain fatty acids. Apart from this, vitamin C is present in grapefruit peels, while vitamin E or tocopherol, a fat-soluble vitamin possibly found in seed oil can be harnessed for topical applications [44]. These byproducts can be exploited for the potential possibilities in the pharma and health sector (Table 4).

Hydroxycinnamic acids are present in grapefruit peels, which as dietary supplements are known to reduce inflammation, improve digestion, and promote cardiovascular health [43]. Naringin, abundantly present in grapefruit peels encompasses antioxidant, anticancer, and anti-osteoporosis, and serves as a facilitator for the absorption of other drugs [158]. It is also used for lipid-lowering functions and to treat obesity and diabetes [18]. Grapefruit peel flavonoids, naringin, and hesperidin have shown potential as neuroprotective agents in animal models of Parkinson's disease and neurodegenerative diseases, though clinical use is still a long way off [39].

Arsène et al. [159] highlighted the antibacterial properties of grapefruit peel that can be effectively used against antibiotic resistance and for developing new drugs for treating bacterial diseases. Bokhary et al. [160] prepared Al_2O_3 nanoparticles using grapefruit extract, which showed antioxidant, anti-inflammatory, and immunomodulatory potentials. Fabricated Al_2O_3 nanoparticles displayed a potential to curtail the production of pro-inflammatory cytokines interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α), as well as the signaling pathway of the transcription factor NF-B, in addition to lowering NO and O_2 generation. Han et al. [161] reported for antibacterial activity of GSE against methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA), and vancomycin-resistant *S. aureus* (VRSA) in the disk and microdilution MIC tests highlighting its potential as a

natural substitute to traditional antibiotics to fight multidrug-resistant pathogens. Antimicrobial properties of GSE are ascribable to involve bacterial membrane disruption and release of cytoplasmic contents in a relatively short time. Quercetin and naringenin, significant GSE flavonoids, show potent anti-inflammatory and antiviral effects via NF κ B, TLR, and IL-6 signaling [59]. The presence of flavonoids in GSE is also equated with anticancer activity against various human breast cancers and is associated with the ability to inhibit platelet aggregation, thereby lowering the risk of coronary thrombosis and myocardial infarction [21]. GSE has significant gastroprotective properties against gastric lesions by preserving antioxidizing enzyme activity, reducing lipid peroxidation, enhancing gastric blood flow, and influencing plasma gastrin levels [21].

Development of Environmentally Sustainable Materials

Biosorbents

SDG's 6th goal is associated with clean water and sanitation. Researchers have been focusing on a new process for the remediation of heavy metals, dyes, pesticides, and organic and inorganic pollutants from water [162, 163]. Numerous water-soluble and insoluble monomers and polymers are found in grapefruit peels. Glucose, fructose, sucrose, and some xylose are present in the water-soluble fraction, whereas between 50 and 70 percent of the insoluble fraction is made up of lignin, pectin, cellulose, and hemicellulose. The carboxyl and hydroxyl functional groups are abundant in these polymers [164]. Grapefruit peels can be used as biosorbents in their natural state [165] or can be amended with physical (drying, grinding, heat treatment) and/or chemical modifications (graft co-polymerization, deamination, saponification, disulfide treatment, pyrolysis, protonation), to ameliorate the potential and adsorption capacity [166]. The maximum uptakes of Cd(II) and Ni(II) by grapefruit peel are found to be 42.09 and 46.13 mg/g, respectively. The kinetics of the biosorption process are found to follow the pseudo-second-order kinetic model [164]. Grapefruit peels pretreated with H_2O_2 (1 M) showed high levels of uptake, q_{max} of 37.4270 mg/g and 39.0628 mg/g for dye mixture and Cr (VI), respectively [167]. Apart, the adsorption of ciprofloxacin pollutants (CIP) using modified waste grapefruit peel was investigated by Fu et al. [168]. Obtained results showed a maximum uptake of $1.71 \text{ mmol}\cdot\text{g}^{-1}$ under optimal experimental conditions, with the adsorption process following pseudo-second-order kinetics, and fitting the Langmuir isotherm model. The latest investigations covering

the utilizing grapefruit byproducts for fabricating biosorbents have been tabulated in Table 5.

Biofertilizer

Although citrus biofertilizers have been reported to improve the quantities of native nutrients such as nitrogen (N), carbon (C), and potassium (K) in the soil which enhances the growth and development of plants [174, 175], in particular, reports on the utilization of the grapefruit peels for the same are scarce. Grapefruit peel utilization for the co-composting of poultry manure is conferred to increase the C/N ratio, and thus minimize N losses caused by increased pH [44]. Biochar materials made from

grapefruit peels have the potential to be used as a soil amendment. They can help immobilize lead and copper in the surrounding soil and enhance the establishment of vegetation in the treated soil. [176].

Bioethanol

SDG's 7th Goal contemplates affordable and clean energy. Bioethanol is a clean potential biofuel [177], and grapefruit peel represents a lucrative biomass for bioethanol production as it comprises cellulose, pectin, and hemicellulose that can be hydrolyzed by enzymes to monomer sugars, for bioethanol production [178]. In one study, glucose,

Table 3 Latest studies on the application of grapefruit processing byproducts in the cosmetic sector

Grapefruit byproduct	Compound/extract	Role in cosmetics	Potential outcomes	Reference
Peel	Essential oil	Anti-aging potential	1. Exhibited the highest enzyme inhibitory activity, with IC ₅₀ values of 12.82, 27.58, and 18.16 µg/mL for tyrosinase, elastase, and collagenase, respectively 2. In silico studies showed that the volatiles can inhibit the tested anti-aging enzymes	[140]
Peel	Ethanollic extract (GPE) and ethyl acetate extract (GPEA)	Anti-Wrinkle and Tyrosinase Inhibitory Activities	1. GPE and GPEA showed tyrosinase inhibitory activity, IC50 values were respectively 3312.5 ± 222.74; 2985.17 ± 122.80 µg/ml 2. In addition, GPE and GPEA inhibited elastase and collagenase enzymes	[141]
Peel	Naringin	Photostabilizer in sunscreen products	1. Naringin incorporated polystyrene films upon exposure to ultraviolet light, substantially reducing the photodegradation of the material	[142]
Peel	Essential oil	Repair and alleviate skin inflammation caused by <i>S. aureus</i>	1. Grapefruit EO promoted HaCaT cell proliferation, reduced reactive oxygen species (ROS) production induced by <i>S. aureus</i> metabolites, and inhibited the upregulated expression of IL-1 and COX-2	[143]
Peel	Extract	Prevention against UVB-induced skin photo-aging	1. Combination of grapefruit and rosemary extract prevented UVB-induced skin photo-aging due to collagen/elastin degradation via activation of MAPKs, MMPs, and the NF-κB signaling pathway in vitro and in vivo	[144]
Peel	Extract	Skin lightening cosmetic	1. Mixed extract from grapefruit and bitter orange showed upon testing for cellular human tyrosinase inhibition assay resulted in stronger tyrosinase inhibition, there the estimated IC50 was 0.24 mg/ml of flavonoid mixture 2. No cytotoxicity has been observed in concentrations that were applied	[145]

Table 4 Utilization of grapefruit byproducts in the pharmaceutical and health sector

Grapefruit byproduct	Compound/extract	Bioactivity	Experimental model	Potential outcomes	References
Peel	Essential oil and extract	Anti-cytotoxic	in Vitro model	1. Treatment with essential oil and extract (25:75%) formulation for 8 h exhibited slight cytotoxicity toward HeLa cells, no toxicity toward HaCaT and HUVECs, whereas inhibition of <i>C. albicans</i>	[93]
Peel	Extract	Erectogenic potential	Rat	1. Peel extract reversed PDE-5, ADA, and antioxidant activities to normal levels, and raised the concentration of nitric oxide 2. These results suggest the erectogenic effects and protective potentials of peel extract against paroxetine-induced erectile dysfunction	[152]
Peel	Essential oil	Anti-inflammatory	Wistar rats	1. An anti-inflammatory bioassay divulged that oil caused a significant ($p < 0.05$ – 0.01) reduction in oedema size when compared to the negative control group throughout the 5 h post-induction assessment period 2. The presence of Vitamin C, A, and lycopene in grapefruit peel has been reported to help fight inflammation caused by free-radical damage in the body	[153]
Peel	Hydroethanolic extracts	Anti-arthritic	Wistar rats	1. Oral administration of grapefruit fruit peel hydroethanolic extracts for 9 and 18 days, significantly reduced the complete Freund's Adjuvant (CFA)-induced paw swelling and edema in arthritic rats as manifested by a significant decrease in right hind paw circumference, volume, and thickness	[154]
Peel	Hydroethanolic extracts	Anti-arthritic	Wistar rats	1. Grapefruit peel hydroethanolic extracts have anti-arthritic effects which may be mediated via modulation of Th1/Th2/Th17 cytokine production and enhancement of the antioxidant defense system	[155]
Peel	Extract	Testicular toxicity inhibition	Male albino rats	1. Grapefruit peel extracts overcame the toxicity of sulfasalazine on the testis and protected testicular tissue from the detrimental effects of sulfasalazine, attributable to flavonoid phytoconstituents	[156]
Peel	Aqueous extract	Anti-histamine release and anti-inflammatory activities	Male Sprague–Dawley rats	1. Inhibited the release of histamine from rat peritoneal exudate cells, and also suppressed the effusion of Chicago sky blue through capillary vessels caused by the intraperitoneal injection of acetic acid in mice 2. Heating of the extracts increased both the inhibitory activity and the suppression 3. Extracts have beneficial activities such as antioxidative, anti-hydrogen peroxide, and anti-allergic effects and may serve as sources of new supplements	[157]

Table 5 Utilization of grapefruit byproducts for transformation into biosorbents

Grapefruit byproduct	Product developed	Fabrication	Application and potential outcomes	References
Peel	Adsorbent	Peels oven-dried at 70 °C for 48 h, crushed to reduce particle sizes, followed by drying at 85 °C for 4 h ↓ For the bio-adsorption study, grapefruit peels were in the natural state with no chemical treatment	1. Cadmium metal ions (Cd ²⁺) were removed efficiently from aqueous solutions by the grapefruit peel-based bio-adsorbents which were treated with tartaric acid 1% with a maximum capacity and removed all the 10.01 mg/Lit cadmium in wastewater 2. The adsorption process was well described by the pseudo-second-order kinetic model with correlation coefficients greater than 0.994. The adsorption isotherm could be well-fitted by the Langmuir model	[165]
Peel	Adsorbent	Peels soaked in 0.2 M NaOH for 180 min ↓ Washed with 0.05 M HCl and deionized water until the pH of the washing water reached 6.5 ↓ Dried at 343 K for 1440 min and stored in the dryer at 298 K	1. Maximum uptake of ciprofloxacin (CIP) was 1.71 mmol.g ⁻¹ under optimal experimental conditions 2. Adsorption data fit the Langmuir isotherm model and the adsorption process follows pseudo-second-order kinetics 3. Mechanistic studies showed that electrostatic, hydrophobic, hydrogen bonding, and π - π interactions are the main driving forces for CIP adsorption on modified peels	[168]
Peel	Biochar/pectin/alginate (BPA) hydrogel beads	Peels oven-dried at 50° for 2 days (step I) ↓ Pyrolysis = Biomass feedstock (~65 g) pyrolyzed at 450 °C (15 °C/min) for 1 h in the absence of air. After cooling to room temperature residues were repeatedly rinsed with water and oven-dried at 50 °C (step II) ↓ Low esterified pectin 20 g peel powder mixed with 600 mL of HCl solution (pH 1.5) followed by vigorously (at 85 °C for 1.5 h). Prepared slurry kept at 4 °C for 1 h. Centrifuged at 4000 rpm for 20 min, followed by pectin precipitation. Crude pectin filtration and mixed with 200 mL of 0.1 M NaOH for 5 min followed by repeatedly rinsing with 75% ethanol and oven-drying of pectin at 50 °C for 24 h. (step II) ↓ BPA = Biochar (0–1.5%) + pectin (1.5–5%) + Sodium alginate (0.5%) (step III)	1. Cu(II) removal from aqueous solution, with maximum adsorption capacity of optimized BPA-9 beads (mass ratio of pectin to alginate = 10:1) with 0.25% biochar, was ~80.6 mg/g at pH 6 2. The adsorption isotherms were fitted well by the Freundlich model and the experimental 3. The kinetic process was well described by the pseudo-second-order model and film diffusion primarily governed the overall adsorption rate, followed by intraparticle diffusion	[169]
Peel	Modified grapefruit peel aerogel (M-GPA)	Hydrothermal treatment of grapefruit peels (180 °C, 10 h) to prepare hydrogel ↓ Immersed in hot water (around 70 °C) for several times ↓ freeze-dried at –80 °C for 48 h to get GPA ↓ Immersed in coating solution (polydimethylsiloxane and 0.4 g melamine) for 3 min to improve the hydrophobicity of GPA, followed by curing at 120 °C for 2 h to form the final M-GPA	1. M-GPA showed a mesoporous structure with a high specific surface area of 36.42 m ² /g and a large pore volume of 0.0371 cm ³ /g 2. The excellent hydrophobicity of M-GPA with a water contact angle of 141.2° 3. The high adsorption capacity of M-GPA for a series of oils and organic solvents was 8 to 52 times as much as its weight 4. Moreover, the M-GPA was easily regenerated and a high adsorption capacity recovery above 97% was maintained after five adsorption–regeneration cycles	[170]
Peel	Biosorbent	1.5 g of peels and 150 mL of H ₂ O ₂ (1 M) were added to an Erlenmeyer flask 250 mL and stirred at 110 rpm for 24 h ↓ Oven drying at 60°C for 24 h, followed by grinding to reach size below 0.5 mm	1. Pretreated peels with H ₂ O ₂ (1 M) showed the highest removal capacity of 80% and 100%, for the mixture of leather dyes and Cr (VI), respectively 2. Adsorption isotherms data fitted well to the Langmuir model with a maximum uptake of 37,427 mg/g for dyes mixture and 39,0628 mg/g for Cr (VI)	[171]
Peel	Biosorbent	Peels modified by using Instant Controlled Pressure Drop (DIC) with sudden vacuum (30 mbar) and pressurizing the reactor up to 3 bars for 90 s. Cycle repeated thrice. Overnight dried at 105 °C ↓ Modified with 0.1 mol L ⁻¹ NaOH solution and then dried overnight at 105 °C. Modified with citric acid and stirred for 2 h at 80 °C ↓ Finally, the materials were rinsed with distilled water and dried at 105 °C	1. Chemical treatment with sodium hydroxide and citric acid enhanced the Cu(II) adsorption capacity due to the interaction of oxygen-containing groups with the metal cation in the solution. The results indicate that a high adsorption capacity (52.48 mg g ⁻¹ and 24 g L ⁻¹) can be achieved in fixed-bed columns, working in continuous mode	[171]

Table 5 (continued)

Grapefruit byproduct	Product developed	Fabrication	Application and potential outcomes	References
Peel	Hydrochar and activated carbon (AC)	Hydrothermal carbonization (HTC) of grapefruit peels (GP) in the liquid from HTC of swine manure was conducted at 220 to 260 °C	<ol style="list-style-type: none"> The HTC in SM liquid at 220 °C retained abundant aliphatic structures in hydrochar and produced AC with developed pore structures (1056.7 m²/g) The superior porosity of the ACs with micro-mesopores texture rendered good removal efficiencies (91.4%) of Cr (VI) in aqueous solution 	[172]
Peel	Grapefruit peel based biochar (GPBC)	<p>Grapefruit peels mixed with water were crushed. Filtrate was stored and residual solid was dried at 80°C for 24 h, and pyrolyzed at 600 °C for 1 h</p> <p>↓</p> <p>The powder was washed with 0.1 M HCl 3 times</p> <p>↓</p> <p>Obtained carbon was further impregnated into the GP extracts with various solid-solution ratios (1:10, 1:20, and 1:30, g/mL) for 4 h at room temperature</p>	<ol style="list-style-type: none"> GPBC-20 showed excellent performance for tetracycline (TC) adsorption (37.92 mg/g) The pseudo-second-order kinetic model and Langmuir isotherm model were well-fitted The mechanism of TC adsorption by GPBC was a combined result of the pore filling, electrostatic adsorption, hydrogen bond, and π–π interaction 	[173]

fructose, galactose, arabinose, xylose, and galacturonic acid (GA) were produced using the enzymes pectinase, cellulase, and beta-glucosidase, with a pH range of 3.8–4.8 found to be optimal for sugar yields from peel hydrolysis [179]. However, D-limonene in grapefruit peels could act as a native inhibitor, which before bioethanol production, must be removed due to its antibacterial action against yeast or bacteria used in fermentation to produce ethanol [180]. Teke et al. [181] employed an ultrasound-assisted pretreatment (14.6 °C, 25.81 W/cm²) to extract D-Limonene with a validation yield of 134 ± 4.24 mg/100 g dry CPW, and reported bioethanol yield with a 66% increase. Following grapefruit peel fermentation in an immobilized cell reactor (ICR), Choi et al. [182] observed reduced ethanol concentrations and created a D-limonene removal column (LRC) that effectively eliminated this inhibitor from the fruit waste. Yeast fermentation using an LRC in conjunction with an ICR produced yields of 90.7% and ethanol concentrations of 21.6 g/L, which were twelve times higher than those obtained from ICR fermentation alone.

Conclusion and Future Directions

Grapefruit processing generates important volumes of disposals such as peels, pomace, and seeds that could be attractive raw materials for the recovery of compounds such as dietary fiber, polyphenols, flavonoids, essential oil, and pectin. These could be natural alternatives to cope with the high demand for natural compounds for the development of healthy matrices for different industries, favoring a circular economy model. This manuscript also spotlights advanced and innovative extraction techniques for processing grapefruit byproducts, allowing an efficient, easier, quick, cost-effective, and appreciable recovery of bioactive compounds that could be used in food, cosmetic, or pharma sectors for various applications. The recovery of byproducts from grapefruit can not only benefit the environment, but could commence businesses, and will keep valuable resources and materials in the economy. Future works should focus on optimizing the extraction parameters and researchers should prioritize the gap between in-vitro trials and commercial-scale applications for the sustainable valorization of grapefruit byproducts. However, a multidisciplinary approach with the collaboration of academics, engineers, economists, and policymakers, is critical to understand and pave the valorization route to a level of innovation where it is possible to achieve a broader landscape of zero waste and a sustainable society. Moreover, consonance of capital investments, policy amendments, and commercial, social, and consumer acceptance is vital for unraveling the true potential of grapefruit waste.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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