



# Bioactives and Bioactivities from Food Byproducts

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## Abstract

**Purpose of review** This paper examines the utilization of food byproducts as sources of bioactive compounds, aiming to reduce waste generation and enhance human health. It investigates the types of bioactive compounds present in food byproducts, their associated bioactivities, and their significance in functional food and nutraceutical development.

**Recent findings** Food processing generates significant quantities of byproducts rich in bioactive compounds, including vitamins, polyphenols, flavonoids, carotenoids, dietary fibers, and essential fatty acids. These compounds exhibit diverse bioactivities, such as antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. Incorporating them into food formulations enhances nutritional value and develops functional foods with enhanced health-promoting properties.

**Summary** Exploring bioactive compounds from food byproducts offers promising avenues for addressing environmental and public health concerns. By leveraging these resources, researchers can develop sustainable solutions to improve human health while reducing the environmental impact of food production

**Keywords** Food · Bioactives · Phenols · Bioactivities · Health benefit

## Introduction

Recently, there has been a significant surge in popularity of functional foods, plant-based nutraceuticals, and dietary supplements, all esteemed for their incorporation of health-promoting ingredients that fortify human well-being. These

products, encompassing functional foods, dietary supplements, and nutraceuticals, nutritional components, embracing bioactive compounds renowned for their positive effects on health [1–3]. The rapid expansion of the food processing industry globally has spurred the emergence of various health-benefitting functional foods. These foods, similar to

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conventional dietary items, seamlessly integrate into everyday diets while offering proven physiological benefits that surpass basic nutrition. This realization has fuelled extensive exploration into numerous functional ingredients, including carotenoids, lutein, lycopene, zeaxanthin, dietary fibre, phenolics, saponins, phytoestrogens, and lignans, among others [4, 5]. Among these bioactive ingredients, dietary fibre stands out as a crucial component due to its widespread availability in many food products and its efficacy in preventing and treating an array of ailments. From common afflictions such as constipation and gastrointestinal problems to more severe conditions like colon cancer, dietary fibre has garnered immense importance for its preventive and therapeutic properties [4]. In past, food was not merely recognized for its nutritional value but also as a repository of dietary substances and biologically active compounds that contributed to human health and overall well-being. The increasing consumer awareness regarding the profound impact of diet on health is evident in their preference for natural products abundant in minerals, bioactives including carotenoids, anthocyanins, polyphenols, and peptides and vitamins [6, 7]. Moreover, food industrial by-products (BPs) have emerged as abundant sources of functional components, including fiber, phytochemicals, minerals, and more. These by-products come from various origins and encompass a diverse array of components such as peel, stem, leaf, seed, shell, bran, kernel, pomace, and oil cake [8]. Utilizing these industrial by-products offers an opportunity to extract valuable functional ingredients, which promotes sustainability and enhances the nutritional profile of various food products. By-products, such as peels, bagasse, seeds and pomace, are recognized as valuable sources of bioactive compounds like polyphenols, vitamins, flavonoids and carotenoids. Beyond fresh fruits and vegetables, other by-products generated by the food industry are being repurposed to extract natural compounds with diverse pharmacological activities [9]. This underscores the potential for leveraging food by-products to not only reduce waste but also extract valuable bioactive compounds for various applications, thereby contributing to both environmental sustainability and human health. In this review, an up-to-date compilation of various bioactive compounds and health-promoting activities derived from food by-products has been presented.

## Sources of Bioactives and Extraction of Bioactives in Food Byproducts

From production to consumption, agriculture annually generates approximately 1.3 billion tonnes of waste [10]. In addition to agricultural waste, other sources of food waste

encompass cereals, pulses, fruits, vegetables, dairy, seed oil, poultry, meat, eggs, and aquatic life. Often overlooked, these sources serve as rich reservoirs of nutritionally and biologically active compounds, including minerals, phenols, sugars and dietary fiber. With a wide range of health effects such as cardioprotective, antimicrobial, and antibacterial activities [11, 12], these compounds are valuable. Focusing on fruit and vegetable waste, by-products include peels, seeds, hull, skins, bran, husk, germ, fiber, and other discarded parts, each varying in phenolic compound levels. For instance, banana peels contain a significant amount of flavan-3-ols [13], while apple peels are notable for chlorogenic acid, epicatechin, and phloridzin [14]. Similarly, pineapple peels are rich in polyphenolics like gallic acid, catechin, epicatechin, and ferulic acid [15], and pomegranate peels are abundant in flavonoids and hydrolyzable tannins [16]. Papaya seed and peel contain abundant phenolic compounds, including p-hydroxybenzoic acid, gallic acid-deoxyhexoside, kaempferol-3-O glucoside, protocatechuic acid hexoside, protocatechuic acid, caffeoyl hexose-deoxyhexoside, chlorogenic acid, caffeic acid, ferulic acid, rutin, p-coumaric acid and myricetin [17] (Table 1). Other sources, such as guava seed [18], dried onion skin [19], and garlic skin [20], are also rich in phenolic compounds. Similarly, cereal by-product contains phenolic compounds with numerous health benefits. The primary cultivated cereal crops, like wheat, barley, maize, rye, rice, sorghum, millets and oats contribute to about 3200 million tons of grains produced annually [21]. Residues from milling industries, such as wheat and rice bran, are valuable for animal feeding due to their high fiber content, minerals, vitamins, and polyphenols [22, 23]. In seafood or aquatic by-products, chitosan derived from crustacean waste exhibits antibacterial properties [24]. Waste from slaughterhouses is a rich source of nutrients that can be used to produce a variety of value-added products such as biogas, biomass, and methane [25–27]. Therefore, food waste serves as a cost-effective reservoir of bioactive and functional compounds, enhancing the nutritional value of by-products. Utilizing novel technologies to extract these compounds (Table 1) from food waste is necessary for developing healthy and functional food ingredients, dietary supplements, contributing to environmental and economic sustainability.

## Health-Promoting Bioactivities of Food Byproducts

### Antioxidant Properties

Choe and coworkers reported notably significant antioxidant potential of varieties tomato seed flours [60]. In another

**Table 1** Bioactive compounds isolated from fruit and vegetable waste

Source	Extraction method	Classification	Compound name	Reference
Cranberry pomace, blueberry waste, carrot waste	Chemical extraction, superficial CO <sub>2</sub> extraction, ultrasound assisted extraction	Anthocyanidin	Cyanidin	[28, 29]
Orange peel, beetroot waste	Chemical extraction	Catechin	Ferulic acid	[30, 31]
Citrus peel, tea leaves	Ultrasound assisted extraction, Chemical extraction, microwave assisted extraction, subcritical water extraction	Catechin/flavan-3-ol	Catechin/Epicatechin	[32, 33]
Grape pomace	Solvent assisted extraction	Polyphenols, triterpenoid	-	[34]
Peanut waste, grape pomace	Chemical waste, microwave assisted extraction,	Stilbene	Resveratrol	[35, 36]
Tomato waste, apple pomace, grape skin	Chemical extraction, liquid extraction	Flavonol	Quercetin	[37, 38]
Citrus peel, citrus waste	Chemical extraction	Flavonoid	Hesperidin	[39]
Poultry and meat	Fermentation, transesterification, anaerobic digestion	-	Lactic acid, probiotics	[40, 41]
Cheese, yogurt, casein	Fractionation, enzymolysis producing single cell protein, fermentation, transglycosidation,	-	Whey protein, lactose, single cell protein, galactooligosaccharides	[42, 43]
Onion	Macroporous resin adsorption, chemical extraction		Fructans, phenolic compounds	[44–46]
Tomato pomace	Solvent extraction	Carotenoids	-	[47]
Vaccinium berry press residue	Ultrasound assisted extraction	Anthocyanin, Phenolic acids	Glycoconjugates of delphinidin cyaniding petunidin malvidin, chlorogenic acid	[48]
Mango kernel seed	Pressurized-liquid extraction	Phenolic acid, flavonoids, catechins, hydrolysable tannins, xanthanoids	Gallic acid, quercetin, isoquercetin, fisetin, epicatechin, epigallocatechin, epicatechin gallate, mangiferin	[49–51]
Mango peel	Supercritical fluid extraction	Carotenoids	β-cryptoxanthin, lutein β-carotene	[52, 53]
Beetroot pomace	Ultrasonic and solvent assisted extraction	Phenolic acids, flavonoids	p-Hydroxy-benzoic acid, ferulic acid, caffeic acid, vanillic acid, catechin, rutin, protocatechuic acid, epicatechin	[54]
Beetroot stems and leaves	Supercritical CO <sub>2</sub> extraction	Betalains, phenols	Betacyanins (betanin and isobetanin) Betaxanthins (vulgaxanthin I)	[55]
Pomegranate epicarp	-	Phenolic acids, hydrolysable tannins, flavonoids, anthocyanins	-	[56]
Blackthorn fruit epicarp and fig peel	Lyophilization, ultrasonic assisted extraction	Anthocyanins	-	[57]
Pumpkin peel	Supercritical fluid and subcritical water extraction	Phenolics, carotenoid	-	[58]
Jabuticaba epicarp	Ultrasound-assisted extraction	Anthocyanins	-	[59]

study by Ghasemi and Ebrahimzadeh (2009) suggests a positive correlation between the antioxidative property of fruits and vegetables and total phenolics and total flavonoids concentration [61]. For instance, as study reported the antioxidative potential of polyphenols extracted from dried and frozen apple peels for stabilizing fish oil enriched in omega-3 polyunsaturated fatty acid. The findings revealed that frozen apple peels (ethanolic extract of polyphenols) exhibited significantly elevated FRAP, DPPH and FC

scavenging values compared to those derived from dried apple peels ( $p < 0.05$ ). Moreover, fractions rich in flavonols demonstrated the ability to inhibit 40–62% fish oil oxidation at 200 µg/mL of phenolic concentration. Further, frozen and dried apple peels derived fractionated polyphenols showed high inhibition of lipid oxidation in comparison to butylated hydroxytoluene, apple peel extract and α-tocopherol [62]. Habeebullah et al. (2010) reported significant DPPH scavenging activity in both crude extracts and phenolic-rich

fraction derived from potato peels [63]. Low  $IC_{50}$  value indicates greater radical scavenging ability of plant extract [64], suggesting an inverse relationship between radical scavenging activity and total phenol. This phenolic activity is attributed to its rapid electron transfer process [65]; further, it is important to note that only phenolics with specific structural configurations and hydroxyl groups at defined positions exhibit radical scavenging activity [66]. Chen et al. (2017) examined *Camellia oleifera* defatted seeds (hexane, isopropanol and diethyl ether extracts) for antioxidant capacity. The study revealed isopropanolic extract shown high yield of phenolic compounds. Subsequently, the antioxidant activity of these extracts was evaluated in terms of their ability to mitigate lipid oxidation in corn oil. Results indicated that the isopropanolic extract demonstrated superior effectiveness in reducing peroxide value, thiobarbituric acid reactive substances (TBARS), anisidine value and conjugated dienes. These findings underscore the potential of *Camellia* seed byproducts as valuable sources of antioxidants for enhancing stability corn oil stability [67] (Table 2). In summary, from the findings of above-mentioned studies it is demonstrated that high phenolic and flavonoid content in these byproducts is related (such as apple peels, potato peels, and *C. oleifera* seeds) with strong antioxidative properties, which are effective in stabilizing oils and preventing lipid oxidation. This indicates the potential for these byproducts to be used as natural antioxidants in food preservation and health promotion. It is clear that incorporating these byproducts into the diet or food systems could enhance the nutritional and functional quality of foods, contributing to better health outcomes.

### Anti-inflammatory Effects

A study investigated the anti-inflammatory properties of bioactive compounds extracted from *Crataegus pinnatifida* seeds. This was done by subjecting them to lipopolysaccharide (LPS)-induced TNF- $\alpha$  and NO production in RAW264.7 cell line. The MTT assay at a concentration of 100  $\mu$ M indicated that the bioactive compound did not impact cell viability. Hence, the impact of these compounds on the lipopolysaccharide (LPS)-induced production of TNF- $\alpha$  and NO in RAW 264.7 cells was investigated using concentrations below 100  $\mu$ M. The compounds exhibited potent inhibition of NO and TNF- $\alpha$  production, surpassing the activity of the control. The observed inhibitory activities of NO and TNF- $\alpha$  seem to be linked to the structures of the compounds [68]. Similarly, in another study, tomato seed flour's anti-inflammatory properties were investigated using two different batches (TSF1 and TSF2). Both batches exhibited anti-inflammatory effects in a dose-dependent manner against interleukin (IL)-1 $\beta$ , IL-6, and TNF- $\alpha$ . Treatment

with tomato seed flour extracts in varying concentration (0.2, 0.5, 1.0, and 2.0 mg tomato seed flour (TSF)/mL) resulted in the inhibition of lipopolysaccharide (LPS)-induced IL-1 $\beta$  mRNA expression by 69, 97, 99, and 99%, respectively. Additionally, TSF1 and TSF2 dose-dependently suppressed IL-6 and TNF- $\alpha$  mRNA expressions (refer to Table 2). Importantly, all tomato seed flour extracts used in this investigation did not exhibit adverse effects on THP-1 macrophage viability, as assessed by MTT assay [60]. Park and coworkers evaluated the anti-inflammatory activity of the tannin fraction from black raspberry seed extract (BSTE) [69]. The analysis revealed that the tannin fraction is primarily composed of pedunculagin, sanguin H6 and H10 isomers, and galloyl-bis-HHDP glucose isomer. The results of the anti-inflammatory activity assessed through LPS-induced NO production in RAW 264.7 cells treated with BSTE, showed that BSTE exhibits significantly higher NO inhibition in comparison to grape seed extract (GSTE) at concentrations of 5–40  $\mu$ g/mL. Furthermore, the black raspberry fraction at 2.5  $\mu$ g/mL reduces NO production by 19%, while the grape seed fraction at 5  $\mu$ g/mL reduces it by just 10%. These findings indicate that the anti-inflammatory properties of black raspberry seeds are significantly higher compared to grape seeds, suggesting that black raspberry seed extracts and their tannin fractions could serve as potent natural antioxidant agents, similar to grape seed extracts. From the findings, it was evaluated that food by products contain novel bioactive compounds which offer certain health benefits; thus, there is need to further explore other by products for their application in pharmaceutical, food and cosmetic industry.

### Antimicrobial Activity

Numerous studies have investigated the antimicrobial potential of various by-products, evaluated the efficacy of different extracts and characterizing the bioactive compounds [70–72]. Avocado peels, for example, have been found to contain phenolic compounds such as hydroxy-benzoic and -cinnamic acids, as well as various flavonoids. Research has shown that avocado extracts exhibit inhibitory effects against a range of microbes, including *Pseudomonas* spp., *S. aureus*, *E. coli*, *B. cereus*, *L. monocytogenes* and *Y. lipolytica*, with zones of inhibition ranging from 5.07 to 6.33 mm. This study imply that extracts derived from avocados hold promise as viable reservoirs of antimicrobial properties, potentially serving as efficacious natural supplements to prolong the preservation duration of perishable food items [70]. Similarly, the peel of *Citrus aurantium*, or bergamot, a by-product of essential oil extraction, has been identified as a rich flavonoid source, including hesperetin, naringenin and eriodictyol which have been found to be active

**Table 2** Health promoting activities of food byproduct extracts

Name of food byproduct	Type of extract	Bioactive compounds	Type of cell lines/type of study	Results/outcome of study	Reference
<b>Antioxidant properties</b>					
Apple peel (dried and frozen)	Aqueous ethanolic extract	Polyphenol: Quercetin-3-O-glycosides, Epicatechin, Cyanidin-3-O-galactoside, Chlorogenic acid	DPPH, FRAP	DPPH: IC <sub>50</sub> = 1.7–18.9 µg/mL; FRAP: 4.6–3976.4 µg/mL Inhibition of fish oil oxidation by 40–62%	[62]
Potato peel	Hydroethanolic extract	Chlorogenic acid, ferulic acid, polyphenol and flavonoid	Lipid oxidation	Peel extract proved to be effective in retarding lipid oxidation, even at low concentration (14.01–31.94 ppm)	[94]
Potato peel	Aqueous and ethanolic extract	Protocatechuic acid, gentisic acid, p-hydroxybenzoic acid, chlorogenic acid	In-vitro lipid peroxidation	Prevention of lipid oxidation in emulsions and oil, while water extracts had no antioxidant activity in oil and were pro-oxidant in emulsions	[63]
<i>Crataegus pinnatifida</i> seeds	Hydroethanolic extract sequentially extract with ethyl acetate and n-BuOH	Lignans	DPPH, ABTS	Seed extract showed good antioxidant capacity with IC <sub>50</sub> 71.1–309.9 µM for DPPH assay and IC <sub>50</sub> 10.6–49.8 µM in case of ABTS assay	[68]
<i>Camellia oleifera</i> defatted seeds	Isopropanol, hexane, diethyl ether extract	Epicatechin, naringenin, and catechin	FRAP	Exhibited best inhibition with FRAP value of 3.29 mM; useful antioxidant for stabilization of corn oil	[67]
Pineapple peel	n-hexane, methanol	Gallic acid, catechin, epicatechin, ferulic acid	DPPH	Total antioxidant capacity was 0.037 g ascorbic acid equivalents/g with IC <sub>50</sub> of 1.13 mg/mL for DPPH	[15]
<b>Anti-inflammatory effects</b>					
<i>Crataegus pinnatifida</i> seeds	Hydroethanolic extract sequentially extract with ethyl acetate and n-BuOH	Lignans	LPS-induced murine macrophage cell line RAW264.7	Extract showed potent inhibitory action against the production of TNF-α with IC <sub>50</sub> of 15.2 to > 100 µM; and for NO IC <sub>50</sub> 8.8 to > 100 µM	[68]
Tomato seed flour	Acetone extract	Malic acid, 2-hydroxyadipic acid, salicylic acid, quercetin-di-O-hexoside, kaempferol-di-O-hexoside	THP-1 macrophages	Inhibition of pro-inflammatory markers (IL-1β, IL-6, TNF-α). Inhibition of the lipopolysaccharide stimulated IL-1β mRNA expression (69–99%)	[60]
Tomato pomace	Alcoholic extract	Flavonoids, phenolic acids	Human colon epithelial cell line Caco-2	Extract shows excellent reduction (0.06–7.1%) in release of IL-8 expression from Caco-2	[95]
Black raspberry and grape seed	-	Tannin	LPS-induced NO production in RAW 264.7 cell	Inhibition of NO production in dose dependent manner (1–10 µg/mL). Black raspberry showed significantly higher NO inhibition (19%) than GSTF at 2.5–10 µg/mL (10%)	[69]
<b>Antimicrobial activity</b>					
Apricot peel	Ethyl acetate, 70% acetone, and 70% methanol	Phenolic compounds: catechins, procyanidins, and hydroxycinnamic acids	In-vitro: <i>B. cereus</i> , <i>S. aureus</i> , <i>E. coli</i> , <i>Y. lipolytica</i> , <i>L. monocytogenes</i>	Significant zone of inhibition of tested microbial strains viz., zone <i>B. cereus</i> (6.33 mm), <i>S. aureus</i> (5.73–5.80 mm), <i>L. monocytogenes</i> (5.07–5.80 mm), <i>E. coli</i> (5.73 mm), <i>Pseudomonas</i> spp. (5.73 mm) and <i>Y. lipolytica</i> (5.53–6.00 mm)	[70]
Bermagot peel	Ethanolic fraction	Flavanones: Neohesperidin, Hesperetin, Neoeriocitrin, Eriodictyol, Naringin, Naringenin	<i>E. coli</i> , <i>L. innocua</i> , <i>S. aureus</i> , <i>P. putida</i> , <i>S. enterica</i> , <i>B. subtilis</i> , <i>S. cerevisiae</i> , <i>L. lactis</i>	Inhibition against the growth of tested strains with MIC of 200–800 µg/mL; fraction showed both synergistic and indifferent interactions	[71]

**Table 2** (continued)

Name of food byproduct	Type of extract	Bioactive compounds	Type of cell lines/type of study	Results/outcome of study	Reference
Coconut husk fiber	Crude extract, ethyl acetate phase, aqueous phase	Gallic acid, Ellagic acid, Catechin, Procyanidin, Epicatechin, Tannin	<i>S. aureus</i>	Minimum inhibitory concentration for <i>S. aureus</i> is 0.25–1000 µg/mL	[72]
Tomato seeds	Methanol, chloroform, sulfuric acid (0.005 M), ethyl acetate and hexane and	Rutin	<i>S. aureus</i> , <i>Proteus mirabilis</i> , <i>S. epidermidis</i> , <i>Candida albicans</i> , <i>Salmonella typhimurium</i> , <i>Micrococcus luteus</i> , <i>Trichophyton rubrum</i> , <i>Enterococcus faecalis</i> , <i>Aspergillus fumigatus</i> , <i>B. cereus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> ,	Significant inhibition against all tested strains with <i>C. albicans</i> as most susceptible one (MIC: 5–10 mg/mL)	[73]
Cacao bean husk	Chloroform fraction	Caffeine, theobromine, polyphenols, theophylline	<i>S. agalactiae</i> , <i>B. cereus</i>	Inhibition percentage of 34.90% for <i>B. cereus</i> and 52.40% for <i>S. agalactiae</i>	[96]
Sugarcane bagasse	Ethanol extract	Phenolics, flavonoid	<i>S. aureus</i> , <i>S. typhimurium</i> , <i>L. monocytogenes</i> , <i>E. coli</i>	Inhibitory activity due to toxicity of polyphenolics	[97]
Anticancer activity					
Grape Seed Proanthocyanidin (GSP)	Lipophilic Grape Seed Proanthocyanidin (LGSP)	Proanthocyanidins	HeLa cell lines, HeLa-derived xenograft zebrafish model	Increased levels of ROS induced cell apoptosis LGSP effectively suppressed growth of HeLa xenograft tumor in zebrafish model	[78]
Robusta Coffee Beans	Freeze-Dried Extract	Polyphenols, Caffeine	In-vitro: ER- (MDA-MB-231) and ER+ (MCF-7)	Induced increase in S phase. Suppressed clonogenic capacity of MDA-MB-231 breast cancer cells	[79]
Pomegranate peel	-	Punicalagin (PCN)	In-vitro: ME-180 cell line	PCN cause reduced viability of ME-180 cells by up to 80% (dose: 10–100 µM) Stimulation of apoptosis due to downregulation of NF-kB protein expression and upregulation of caspase-3, -9, Bax, and p53 mRNA expression	[81]
Pomegranate Peels	-	Granatin B, Punicalagin	Human Colorectal Cancer Cell Line (HT-29) (In vitro), Xenograft Tumor Models (In vivo), Lipopolysaccharide-induced RAW264.7 Cells (In vitro), 5-FU-treated Rats (In vivo)	Induced ROS-mediated S-phase cell cycle arrest and apoptosis in HT-29 cells Cell cycle arrest in S-phase and sensitization of HT-29 cells to 5-FU-induced cell death	[82]
Cardioprotective activity					
Oat Bran	-	Dietary Fiber	Randomized Controlled Trial (Patients with Hypertension)	Oat bran supplementation significantly lowered 24-hour maximum heart rate (24 h maxHR) compared to control group	[88]
Grape Pomace	Seasoning	Polyphenols, Dietary Fiber	Randomized intervention study (Healthy and high risk-cardiovascular subjects)	Significant decreases in blood pressure (SBP, MBP, DBP) and fasting blood glucose (dose: 2 g/day) Decreased in MBP of 16 out of 17 subjects with a mean reduction of 14.32% Reductions in blood pressure and fasting blood glucose were observed in both healthy subjects and high-risk cardiovascular subjects	[93]

DBP-Diastolic blood pressure, ROS-Reactive oxygen species, MBP-Mean blood pressure, MIC- Minimum inhibitory concentration, SBP- Systolic blood pressure

against all bacterial strains. Flavanones from *C. aurantium* peel have been shown to exhibit synergistic effects against pathogenic bacteria, possibly because of collective interactions with the bacterial cell membrane, as well as slight antagonistic interactions, which could be attributed due to the particular target sites competition or the bacterial cells inhibition uptake [71]. Additionally, extracts from coconut palm husk fibers, which yield phenolic-rich extracts containing flavonoids (like catechins), gallic and ellagic acids and procyanidins, have demonstrated antimicrobial activity against *S. aureus* [72]. Additionally, an investigation was conducted on extracts derived from seeds of two tomato varieties to assess their phenolic and compound composition. The constituents of these extracts comprised phenolic glycosides (including derivatives of kaempferol, quercetin and isorhamnetin), alongside organic acids and fatty acids. Notably, these extracts exhibited efficacy against Gram-positive bacteria, with *E. faecalis* demonstrating high susceptibility. Regarding antifungal properties, the most prominent activity was observed against “Bull’s heart,” with *C. albicans* displaying the high susceptibility among species tested [73]. In conclusion, the antimicrobial activity of by-product extracts, particularly those from avocado peels, *Citrus aurantium* peel, and coconut palm husk fibers, highlights their potential as natural antimicrobial agents for numerous applications, comprising food preservation and healthcare.

### Anticancer Potential

Anticancer bioactives found in food byproducts offer a promising approach for cancer prevention and treatment. Derived from various plant sources, these bioactive compounds possess inherent properties that can hinder the growth and proliferation of cancer cells [74]. Polyphenols, flavonoids, carotenoids, and other phytochemicals found abundantly in fruits, vegetables, nuts, seeds, and their processing by-products have garnered significant attention for their anticancer potential. Specific compounds like resveratrol from grape skins, quercetin from onions, lycopene from tomatoes and, epigallocatechin gallate (EGCG) from green tea exhibit remarkable anticancer properties [75]. Additionally, phytochemicals such as sulforaphane from broccoli and curcumin from turmeric have shown promising anticancer activity through various mechanisms. These bioactive compounds exert their effects by scavenging reactive oxygen species (ROS), modulating signalling pathways related to cell proliferation and apoptosis, inhibiting angiogenesis, and suppressing metastasis [76, 77]. By targeting these critical processes involved in cancer development and progression, bioactive compounds from food byproducts present promising opportunities for both preventing and treating cancer. For example, a study was undertaken to explore the

potential anti-cervical cancer properties of lipophilic grape seed proanthocyanidin (LGSP), a compound produced from grape seed proanthocyanidin and lauric acid. Findings revealed that LGSP elicited notable anti-proliferative effects on HeLa cells by increasing levels of ROS thereby arresting the cell cycle at G2/M phase and inducing cell apoptosis. Furthermore, treatment with LGSP led to diminished mitochondrial membrane potential, enhanced Bax/Bcl-2 ratio, release of cytochrome c into the cytoplasm, activation of caspase-9/3, alongside PARP cleavage, signifying LGSP-induced apoptosis through intrinsic mitochondrial/caspase-mediated pathway [78]. In a separate investigation, the influence of Robusta coffee (bean extract) on apoptosis, viability, proliferation of various human cancer types was explored, with a specific emphasis on breast cancer cell lines. Findings demonstrated that both green and dark coffee extracts exerted significant reductions in viability across diverse cancer cell lines, encompassing breast, colorectal, brain, and bone cancers. Notably, the anticancer efficacy of coffee extract was prominently observed in MDA-MB-231 (ER-) and MCF-7 (ER+) breast cancer cells, while displaying minimal effects on normal breast cell lines. Moreover, treatment with coffee extract resulted in an augmentation of the S phase and a reduction in the G2/M population within breast cancer cells, accompanied by alterations in mitochondrial morphology and induction of apoptosis [79]. Another study investigates the potential anti-tumor effects of compounds found in citrus peels on breast cancer, focusing on their ability to interfere with estrogen signaling and aromatase activity. Among these compounds, naringenin, naringin, and quercetin showed the most promising results, demonstrating the lowest IC<sub>50</sub> values. In vivo assays confirmed anti-estrogenic activity, while in vitro studies showed inhibition of aromatase by naringenin, naringin, and quercetin. Crucially, these compounds exhibited significant anticancer efficacy in vivo, as indicated by diminished tumor volumes observed in treated groups in comparison to controls. Collectively, the results of this investigation indicate that naringenin, and quercetin, isolated from citrus peels, harbor anti-tumor characteristics in breast cancer through the modulation of estrogen signaling and aromatase activity inhibition [80]. In another study the effect of punicalagin (PCN) treatment on the viability of the cervical cancer cell line ME-180. Results showed that PCN administered at concentrations ranging from 10 to 100  $\mu$ M, significantly reduced cell viability by up to 80% which was attributed to increase in the generation of ROS, induced alterations in mitochondrial membrane potential. Furthermore, the study showed changes in the expression levels of key regulatory proteins and genes associated with apoptosis, specifically downregulation of NF- $\kappa$ B protein expression, upregulation of expression of caspase-3 and -9, Bax, and p53 mRNA

was observed following PCN treatment. This study showed that PCN exerts its cytotoxic effects on cervical cancer cells by inducing oxidative stress, disrupting mitochondrial function, and promoting apoptotic pathways through modulation of key regulatory proteins and gene expression [81]. Another investigation was conducted to identify potential therapeutic agents in herbal medicine with anti-mucositis and anti-colorectal cancer, wherein pomegranate peels emerged as a promising candidate through comprehensive analyses. Subsequent examination revealed punicalagin and granatin B as the most potent antioxidant compounds present in pomegranate peels. Notably, both *in vitro* cell culture and xenograft tumor models demonstrated the robust anti-colorectal cancer efficacy of punicalagin and granatin B. Furthermore, these compounds exhibited considerable anti-inflammatory and anti-mucositis properties in RAW264.7 cells induced by lipopolysaccharide and 5-FU-treated rats, respectively. Mechanistic elucidation unveiled punicalagin and granatin B induced apoptosis in HT-29 cells via reactive oxygen species mediation and S-phase cell cycle arrest. Additionally, these compounds enhanced the susceptibility of HT-29 cells to 5-FU-induced cell death and facilitated S-phase cell cycle arrest [82].

### Cardioprotective Activities

Cardioprotective bioactives play a crucial role in safeguarding cardiovascular health, serving as essential components in the prevention and management of cardiovascular diseases (CVDs). These bioactive compounds, derived from various food sources, offer a multifaceted approach to maintaining heart health and reducing the risk of CVDs [83]. Among the diverse array of bioactive compounds, polyphenols, omega-3 fatty acids, dietary fibers, and peptides stand out as notable contributors to cardiovascular health [84, 85]. Bioactive compounds derived from food byproducts have been recognized for their cardioprotective attributes. Polyphenols, prominently present in fruits, vegetables, and plant-based foods, demonstrate formidable anti-inflammatory and antioxidant capabilities. These properties play a pivotal role in alleviating the oxidative stress and inflammation linked to CVDs [86]. Dietary fibers, present in whole grains, legumes, and fruits, aid in cholesterol management, glucose regulation, and weight control, thereby reducing the risk of cardiovascular events [87]. Oat bran, a byproduct of oat processing, is renowned for its high soluble fiber content, which helps lower cholesterol levels and regulate blood sugar. For example, a study was conducted to explore the impact of dietary fiber supplementation, specifically oat bran, on heart rate (HR) among patients diagnosed with hypertension (HTN). Seventy patients were randomly assigned to receive either regular DASH dietary

care or DASH care with oat bran supplementation. After 3 months, the intervention group showed significantly lower 24-hour maximum HR compared to the control group. Within the intervention group, reductions in various HR parameters were observed, suggesting that oat bran supplementation may lower HR in HTN patients [88]. In another study, the effects of a low-energy diet, either supplemented with oat bran and olive oil or without, were documented concerning changes in body mass index (BMI), blood pressure, and serum lipid levels among women diagnosed with diabetes over a three-month duration. Seventy-eight participants were divided into six groups, each receiving different dietary interventions. Results revealed reductions in BMI ranging from 0.9 to 6.0%, along with decreases in SBP and DBP by 1.0–9.0% and 4.8–12.6%, respectively. While reductions in serum triglycerides were observed in some groups, they were not statistically significant. Notably, a significant decrease in total cholesterol (8.3%) was observed only in obese subjects when the low-energy diet is supplemented with oat bran. Additionally, a notable reduction in LDL cholesterol (20.0%) was seen when supplements (oat bran and olive oil) were combined in subjects with elevated serum triglyceride levels [89]. Antioxidant and anti-inflammatory activities help neutralize ROS and suppress inflammatory cytokines, thus attenuating endothelial dysfunction and atherosclerosis progression [90]. Grape pomace extract, a byproduct of winemaking, contains polyphenols with potent antioxidant and anti-inflammatory effects, beneficial for cardiovascular health [91, 92]. A study investigated the potential health benefits of consuming grape pomace (GP)-derived seasonings on cardiovascular health and glycemia. A randomized intervention trial was conducted involving healthy individuals and high-risk of cardiovascular subjects, with participants either consuming 2 g per day of GP seasoning and control group with no seasoning for six weeks. Results reported significant reductions in fasting blood glucose levels and blood pressure among those consuming GP-derived seasoning compared to the control group. Notably, analysis of microbiota composition revealed modulation of gut bacteria and their metabolites by GP seasoning. Additionally, certain leukocyte populations, specifically eosinophils, increased significantly following GP seasoning consumption [93]. These examples underscore the potential of food byproducts as valuable sources of cardioprotective bioactives, contributing to a holistic approach to cardiovascular health promotion and disease prevention (Table 2).



## Conclusion and Future Perspectives

The exploration of bioactive and bioactivities from food byproducts offers a promising avenue for addressing both environmental sustainability and public health concerns. By repurposing these often-underutilized resources, valuable compounds such as antioxidants, antimicrobials, and anti-inflammatories can be extracted, contributing to the development of functional foods with enhanced nutritional profiles and health benefits. Moving forward, further research should prioritize development of innovative extraction techniques aimed at maximizing bioactive compound yield while minimizing resource consumption and environmental impact. Additionally, gaining a deeper understanding of synergistic interactions between bioactive compounds and exploring their potential as sources of bioactive peptides, prebiotics, and probiotics could significantly expand scope of functional food development. The ongoing innovation and exploration in this field have the potential to transform food industry towards a more sustainable and health-conscious direction. By using bioactive from food byproducts, we can ease waste generation, promote resource efficiency, and substitute economic viability within food industry. Moreover, this concerted effort aligns with the global agenda for sustainable development, contributing to a more resilient and environmentally friendly food system while improving public health and well-being. Whereas the continued research and application of bioactive from food byproducts hold promise for revolutionizing the food industry, offering sustainable solutions that benefit both human health and the planet.

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

## Declarations

**Human/Animal Rights** Not applicable.

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