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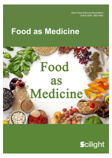

Expert Review

Agri-Food By-Products as Sources of Bioactive Compounds: Nutritional Value, Health Effects, and Functional Food Applications

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Abstract: The agri-food industry generates substantial quantities of by-products and processing residues that remain underutilized despite their significant nutritional and functional potential. Growing evidence indicates that these materials are rich sources of bioactive compounds, including polyphenols, flavonoids, dietary fibers, bioactive peptides, carotenoids, phytosterols, and omega-3 fatty acids. These constituents exhibit antioxidant, anti-inflammatory, antimicrobial, cardiometabolic, and gut-modulating properties supported by preclinical studies and emerging human evidence. This review provides an updated synthesis of the composition of major agri-food by-products, the mechanisms underlying their biological activities, and their applications in functional foods and nutraceutical formulations. Particular emphasis is placed on distinguishing evidence derived from *in vitro*, animal, and human studies, together with discussion of bioavailability, dose considerations, and translational relevance. Advances in sustainable recovery technologies, including ultrasound-assisted extraction, enzyme-assisted extraction, supercritical fluid extraction, and fermentation, have improved the yield, stability, and functionality of bioactive compounds, facilitating their incorporation into food systems. Valorized by-product ingredients have been successfully applied in fiber-enriched bakery products, antioxidant beverages, lipid-lowering supplements, marine collagen formulations, and prebiotic food products. However, important challenges remain, including compositional variability, extract standardization, regulatory approval, labeling, and robust clinical validation of health claims. Future research should prioritize well-designed human trials, optimized formulations, and comprehensive bioavailability assessment to ensure efficacy and safety. Overall, agri-food by-products represent valuable and sustainable sources of nutritionally relevant bioactive compounds with considerable potential for functional food innovation, chronic disease risk reduction, and the advancement of circular bioeconomy strategies.

Keywords: agri-food by-products; bioactive compounds; functional foods; nutraceuticals; green extraction; human health

1. Introduction

The increasing global prevalence of diet-related non-communicable diseases (NCDs), including obesity, type 2 diabetes, cardiovascular diseases, and certain cancers, has intensified scientific interest in food-derived bioactive compounds capable of modulating metabolic, inflammatory, and oxidative pathways [1,2]. Simultaneously, substantial quantities of agricultural and food-processing materials remain underutilized or are discarded across the food supply chain, generating economic losses and environmental burdens. It has been estimated that approximately one-third of food produced for human consumption is lost or wasted annually, representing not only a sustainability challenge but also the loss of valuable nutritional resources [3,4].

Agri-food by-products, including fruit peels, seeds, pomace, cereal bran, whey permeate, brewer's spent grain, oilseed press cakes, and marine processing residues, are generated during harvesting, handling, industrial processing, and manufacturing operations. Traditionally, many of these materials have been directed to low-value uses such as animal feed, composting, or energy recovery. However, growing evidence demonstrates that these side streams are rich sources of polyphenols, dietary fibers, carotenoids, bioactive peptides, essential fatty acids, phytosterols, vitamins, and minerals with recognized physiological benefits [5–8]. Importantly, phytochemical profiling studies indicate that several non-edible fractions, particularly peels, seeds, and pomace, often contain higher concentrations of bioactive compounds than corresponding edible tissues, making their disposal both a nutritional and economic loss [9–11].

Recovered compounds from agri-food by-products have attracted increasing attention because of their reported antioxidant, anti-inflammatory, antimicrobial, cardiometabolic, and cytoprotective properties [9,12–14]. These biological effects are mediated through multiple mechanisms, including modulation of oxidative stress pathways such as Nrf2 activation, regulation of inflammatory signaling cascades including NF-κB and MAPK, improvement of lipid and glucose metabolism, enhancement of endothelial function, and beneficial interactions with gut microbiota composition and activity [15,16]. Consequently, valorized by-product ingredients are increasingly investigated as components of preventive nutrition strategies and functional foods aimed at reducing chronic disease risk [17,18]. Soluble fibers such as β-glucans and pectins have demonstrated benefits in glycemic control and lipid regulation, whereas polyphenols and bioactive peptides may exert vascular, metabolic, and immunomodulatory effects supported by preclinical and emerging clinical evidence.

Technological progress has further accelerated this field. Advances in green extraction technologies and controlled bioprocessing methods have improved the recovery, purity, stability, and functional performance of bioactive compounds intended for incorporation into food systems and nutraceutical products. These developments are particularly relevant in view of increasing consumer demand for natural, clean-label, and health-promoting ingredients. In addition to enhancing nutritional value, the recovery of bioactives from by-products contributes to improved resource efficiency and reduced waste generation within modern food systems [19,20].

Despite substantial progress, important limitations remain. A large proportion of the available literature focuses on individual by-products or isolated classes of compounds without adequately integrating compositional variability, mechanistic pathways, bioavailability, and translational relevance [20,21]. Furthermore, industrial implementation is frequently constrained by variability in raw materials, processing costs, regulatory requirements, and consumer acceptance of upcycled ingredients [22,23]. Greater clarity is also needed regarding effective dosages, standardized extract characterization, long-term safety, and evidence-based health claims.

Accordingly, this review provides a comprehensive and evidence-based overview of agri-food by-products as sources of nutritionally relevant bioactive compounds. Specifically, it examines: (i) major sources and classification systems of agri-food by-products; (ii) their principal bioactive constituents and mechanisms of action; (iii) emerging valorization technologies for compound recovery; (iv) applications in functional foods, nutraceuticals, and health-oriented products; and (v) safety, regulatory, and translational considerations. By integrating nutritional science, food technology, and clinical relevance, this review aims to highlight the role of agri-food by-products in sustainable innovation, functional food development, and chronic disease prevention. Unlike previous largely descriptive reviews, this article integrates a multidimensional classification framework with evidence grading, translational applicability, and regulatory considerations.

2. Literature Search and Review Approach

Given the broad and multidisciplinary scope of this topic, a structured narrative review approach was adopted to synthesize current evidence relating to agri-food by-products, bioactive compounds, human health, food applications, and valorization technologies. The objective was to provide an integrative overview of nutritional relevance, mechanistic evidence, translational potential, and practical applications rather than a formal systematic review or meta-analysis.

Peer-reviewed literature was identified through electronic searches of major scientific databases, including PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar, with searches conducted through December 2025. Publications from January 2000 to December 2025 were prioritized to capture contemporary developments in food science, nutrition, and bioactive recovery, while earlier seminal studies were included where necessary to support foundational concepts and widely accepted mechanisms.

Search strategies combined keywords and Boolean operators related to the main themes of the review, including: “agri-food by-products,” “food processing residues,” “bioactive compounds,” “polyphenols,” “dietary fiber,” “bioactive peptides,” “phytosterols,” “carotenoids,” “functional foods,” “nutraceuticals,” “green extraction,” “fermentation,” “biorefinery,” “health effects,” “clinical trials,” and “circular bioeconomy.” Additional relevant studies were identified through manual screening of reference lists from eligible articles and key review papers.

Studies were considered for inclusion when they addressed one or more of the following areas: compositional characterization of agri-food by-products; extraction, stabilization, or processing technologies relevant to food applications; *in vitro*, animal, or human evidence of nutritional or health-related effects; mechanisms of action, bioavailability, or dose-response relationships; and safety, regulatory, or translational considerations relevant to functional foods and nutraceutical use.

Original research articles, narrative reviews, systematic reviews, meta-analyses, and relevant reports from regulatory or international organizations were considered when published in English. Studies focused exclusively on non-food waste management, fuel generation, or industrial applications without clear nutritional or health relevance were excluded from the main synthesis.

Priority was given to higher-quality evidence where available, particularly randomized controlled trials, human intervention studies, systematic reviews, and well-designed mechanistic investigations. Throughout the manuscript, efforts were made to distinguish findings derived from *in vitro*, animal, and human studies to avoid overstating the level of clinical support.

As a narrative review, this article does not claim exhaustive coverage of all published studies, and some degree of selection bias inherent to qualitative evidence synthesis cannot be completely excluded. Nevertheless, the structured search strategy and critical appraisal approach were designed to ensure balanced, relevant, and up-to-date coverage of the field.

3. Sources and Classification of By-Products

Agri-food by-products are generated throughout the food supply chain, from primary agricultural production and postharvest handling to industrial processing and product manufacturing. These materials represent an important yet frequently underutilized reservoir of nutritionally relevant compounds. Although a proportion is redirected to animal feed, composting, or other secondary uses, substantial quantities remain insufficiently valorized, resulting in the loss of valuable dietary fibers, polyphenols, proteins, lipids, and micronutrients [19,24]. Growing recognition of these materials as concentrated sources of functional ingredients has stimulated increasing research into their recovery and incorporation into foods, nutraceuticals, and health-oriented formulations [20,22].

Agri-food by-products encompass a broad range of materials, including crop residues, fruit and vegetable pomace, cereal bran, brewer’s spent grain, whey permeate, oilseed press cakes, and fishery processing residues. Their composition varies considerably according to botanical or animal origin, cultivar, season, processing method, and storage conditions [25,26]. Importantly, many of these materials contain higher concentrations of bioactive constituents than their corresponding edible fractions, including polyphenols, β-glucans, arabinoxylans, carotenoids, bioactive peptides, unsaturated fatty acids, and essential minerals [21,27,28]. This compositional richness underlies their growing relevance in functional food development and sustainable nutrition strategies.

To facilitate systematic evaluation and practical utilization, this review adopts a three-axis classification framework widely used in valorization research. The three-axis of this framework are origin-based classification, composition-based classification, and application-based classification.

3.1. Origin-Based Classification

3.1.1. Agricultural By-Products (Field-Level Residues)

Primary agricultural activities generate large volumes of residues, including cereal straw, rice husks, wheat bran, corn stalks, sugarcane bagasse, and fruit culls. From a nutritional perspective, cereal brans and husks are particularly important because they are rich in insoluble and soluble dietary fibers such as arabinoxylans and β-glucans, as well as phenolic acids including ferulic and *p*-coumaric acids and essential minerals [29,30]. Wheat bran, for example, has been extensively investigated as a functional ingredient for improving fiber intake, glycemic response, and intestinal health.

Although residues such as straw and bagasse have traditionally been associated with non-food uses [19], their lignocellulosic fractions and bound phenolics are increasingly being explored for recovery of functional fibers, antioxidant compounds, and prebiotic ingredients suitable for food applications [31]. Accordingly, even field-level residues may serve as valuable raw materials for nutritionally oriented ingredient production when appropriately processed.

3.1.2. Food-Processing By-Products

Food-processing operations often concentrate nutrients and phytochemicals in side streams of direct relevance to human nutrition. Fruit and vegetable pomace, peels, and seeds are rich in polyphenols, carotenoids, and pectins with documented antioxidant, metabolic, and prebiotic properties [25,32]. Apple and citrus pomace, for instance, provide soluble fibers and flavonoids associated with improved lipid metabolism and modulation of gut microbiota composition.

Cereal-processing by-products such as bran, germ, and brewer’s spent grain contain considerable levels of proteins, β-glucans, arabinoxylans, and phenolic compounds [33,34]. These components support their application in fiber-enriched bakery products, protein supplements, and functional cereal-based foods.

Oilseed press cakes derived from soybean, sunflower, flaxseed, and grape seed are protein-rich materials that also contain polyphenols, phytosterols, and polyunsaturated fatty acids [35,36]. With protein levels frequently ranging between 30–40%, depending on seed type and processing conditions, these by-products are promising substrates for plant-based protein ingredients and bioactive peptide production [37]. Emerging plant-derived residues such as aquafaba, leaves, and vegetable trimming streams also provide emulsifying proteins and functional compounds suitable for innovative food formulations.

3.1.3. Animal-Derived By-Products (ADPs)

Animal-derived by-products generated during meat, dairy, and fish processing include skin, bones, offal, viscera, shells, and whey fractions. When appropriately handled, these materials are valuable sources of nutritionally relevant compounds. Low-risk Category 3 materials can yield collagen and gelatin from skin and tendons, widely used in functional foods and nutraceutical preparations [38].

Fish-processing residues are important sources of bioactive peptides and omega-3-rich oils with documented cardioprotective and anti-inflammatory properties [39–42]. Shrimp shells and crustacean residues provide chitin and chitosan, which have recognized applications in functional foods, encapsulation systems, and gut-health formulations [43]. These streams contribute substantially to the development of marine-derived supplements and protein hydrolysate-based products targeting metabolic and musculoskeletal health.

3.1.4. Industrial Fermentation and Herbal Extraction Residues

Residues generated by breweries, wineries, distilleries, and herbal extraction industries also retain considerable nutritional value. Spent yeast is rich in mannoproteins, peptides, amino acids, and B-vitamins with reported immune-supporting and prebiotic properties [44]. Wine lees and grape pomace contain anthocyanins and polyphenols associated with antioxidant and cardiometabolic benefits [45,46].

Herbal extraction residues may still contain flavonoids, terpenoids, saponins, and related phytochemicals with recognized biological activity [47]. Such materials can undergo enzyme-assisted extraction (EAE), ultrasound-assisted extraction (UAE), or fermentation to enhance recovery and improve functionality for incorporation into food and nutraceutical systems.

3.2. Composition-Based Classification

Classification according to biochemical composition is particularly relevant for nutritional applications because it guides the selection of suitable recovery methods and intended physiological outcomes. Major categories include carbohydrate-rich residues, protein-rich residues, lipid-rich residues, phytochemical-rich residues, and mineral-rich residues. Carbohydrate-rich residues (pomace, husks, bran, bagasse), which are important sources of pectin, β-glucans, cellulose, and arabinoxylans. These fibers contribute to glycemic control, cholesterol reduction, satiety, and prebiotic activity [48]. Protein-rich residues (whey, fish trimmings, oilseed cakes), which provide high-quality proteins that may be hydrolyzed into bioactive peptides with antihypertensive, antioxidant, and immunomodulatory effects [36]. Lipid-rich residues, particularly fish viscera and seed cakes, which contain nutritionally valuable lipids including omega-3 fatty acids, tocopherols, and phytosterols associated with cardiovascular protection [41,42]. Phytochemical-rich residues, such as grape pomace, citrus peels, and olive mill by-products, which are concentrated sources of polyphenols, flavanones, and carotenoids with documented antioxidant and anti-inflammatory properties [49,50]. Mineral-rich residues, including fish bones and cereal fractions, which supply calcium, phosphorus, iron, magnesium, and other essential minerals important for skeletal and metabolic health [41]. This compositional framework supports targeted extraction strategies and evidence-based formulation of functional foods and nutraceutical products.

3.3. Application-Based Classification

From a translational and food science perspective, agri-food by-products may also be classified according to their intended applications. Food and nutraceutical ingredients include polyphenol extracts, dietary fiber concentrates, bioactive peptides, specialty oils, and phytosterol-enriched fractions for health-oriented products [51,52]. Animal feed and aquafeed are secondary applications that may have an indirect impact on nutrient quality throughout the food chain [53]. Biomaterials and packaging systems, such as chitosan-based coatings and biodegradable materials, have the potential to improve food preservation and safety [43]. Fermentation substrates and enzyme production enable the development of additional functional ingredients and value-added metabolites [54]. Although applications extend beyond the food sector, the most direct impact on human health is the production of functional foods, nutraceuticals, and bioactive-enriched formulations. This application-based framework highlights the nutritional, industrial, and sustainability importance of agri-food by-products within modern food systems (Table 1).

Table 1. Classification of Agri-Food By-Products According to Origin, Biochemical Composition, and Nutritional/Functional Applications.

By-Product Category	Representative Sources	Major Bioactive Components	Main Functional/Nutritional Applications	Commercial Readiness
Agricultural field residues	Wheat bran, rice husk, corn husk, fruit culls	Dietary fibers (cellulose, arabinoxylans), phenolic acids (ferulic, *p*-coumaric), minerals [21,30]	Fiber concentrates, prebiotic ingredients, phenolic-rich extracts, glycemic-support formulations [28,30]	Emerging
Fruit and vegetable processing by-products	Citrus peels, grape pomace, apple pomace, tomato skins/seeds, mango peel	Flavonoids (hesperidin, naringin), anthocyanins, catechins, carotenoids, pectin, polyphenols [2,8,21,55])	Functional food enrichment, antioxidant beverages, cardiometabolic-support products, prebiotic fibers [21,55,56]	Established
Cereal and brewery by-products	Wheat bran, rice bran, oat hulls, brewer's spent grain	β-glucans, arabinoxylans, phenolic acids, proteins, tocols [21,33,34]	Fiber-enriched bakery products, β-glucan supplements, gut-health formulations, protein-fortified foods [21,33,34]	Established
Dairy industry by-products	Acid whey, sweet whey, cheese whey permeate, buttermilk	Whey proteins, bioactive peptides, lactoferrin, lactose [36,37]	Protein beverages, ACE-inhibitory nutraceuticals, peptide supplements, microbiome-support ingredients [36,37]	Established
Marine and fish-processing by-products	Fish skin, bones, heads, viscera, shrimp shells	Collagen, gelatin, bioactive peptides, omega-3 fatty acids (EPA/DHA), chitin/chitosan, minerals [40–42]	Marine collagen supplements, omega-3 products, anti-inflammatory peptide formulations, joint and cardiovascular support products [40–42]	Established
Fermentation and winery by-products	Spent yeast, wine lees, brewery residues, grape pomace	Mannoproteins, polysaccharides, peptides, B-vitamins, polyphenols [45,57]	Prebiotic ingredients, immune-support supplements, antioxidant formulations, functional fermented foods [45,57]	Emerging
Herbal extraction residues	Tea residues, coffee husks, medicinal plant residues	Catechins, chlorogenic acids, caffeine, terpenoids, saponins [47,58]	Polyphenol-rich powders, metabolic-support extracts, natural antioxidant ingredients for functional foods [47,58]	Emerging
Oilseed, nut, and seed by-products	Sunflower cake, soybean cake, flaxseed meal, peanut skins, olive pomace, grape seeds, tomato seeds, pumpkin seed cakes	Polyphenols, phytosterols, tocopherols, proteins, polyunsaturated fatty acids [45,46,50,52,59]	Plant protein isolates, phytosterol-enriched foods, specialty oils, antioxidant extracts, lipid-lowering nutraceuticals [45,46,50,52,59]	Established

4. Bioactive Components in By-Products

Growing global food demand has intensified interest not only in food production but also in the nutritional value of underutilized food fractions. Nearly one-third of food produced for human consumption is lost or wasted annually, representing a substantial loss of potentially valuable nutrients and health-promoting compounds [3,4]. Advances in phytochemical and compositional profiling have shown that non-edible fractions—particularly peels, seeds, pomace, husks, and bran—often contain higher concentrations of bioactive constituents than edible tissues, making their disposal both a nutritional and economic loss [10,11].

Bioactive compounds are naturally occurring constituents that exert physiological effects beyond basic nutrient provision. Although not classified as essential nutrients, they can modulate oxidative stress, inflammatory signaling, lipid and glucose metabolism, endothelial function, and gut microbiota composition, thereby contributing to chronic disease prevention and health promotion [9,60,61]. However, the strength of evidence differs markedly among compound classes and outcomes. While some effects are supported by human intervention studies, others remain based primarily on *in vitro* and animal research. An overview of major bioactive classes, representative sources, mechanisms of action, reported health outcomes, and level of evidence is summarized in Table 2.

Table 2. Major Bioactive Compounds from Agri-Food By-Products: Mechanisms, Reported Health Effects, and Level of Supporting Evidence.

Bioactive Class	Representative Sources	Principal Mechanisms of Action	Reported Health-Related Effects	Level of Evidence	Key References
Polyphenols (flavonoids, phenolic acids, anthocyanins)	Grape pomace, citrus peels, pomegranate peels, apple peels, olive leaves	Antioxidant activity; Nrf2 activation; NF-κB inhibition; modulation of gut microbiota; inhibition of lipid oxidation	Reduced oxidative stress; improved endothelial function; LDL reduction; anti-inflammatory effects; microbiota modulation	*In vitro* + animal studies; limited human trials (selected flavonoids such as hesperidin, oleuropein)	[9,27,62–64]
Dietary fibers (pectin, β-glucans, arabinoxylans)	Citrus pomace, cereal bran, apple pomace, beet pulp	Increased intestinal viscosity; bile acid binding; SCFA production via fermentation; modulation of gut microbiota	LDL cholesterol reduction; improved glycemic response; enhanced gut barrier integrity; microbiota shifts	Strong human evidence (β-glucans, pectin); supported by animal studies	[65–70]
Bioactive peptides (ACE-inhibitory, antioxidant peptides)	Whey, fish skin/bones, oilseed cakes	ACE inhibition; nitric oxide modulation; antioxidant activity; anti-inflammatory signaling	Blood pressure reduction; improved vascular function; skin elasticity; joint support	Animal + emerging human trials (marine collagen peptides)	[38,40,71–73]
Carotenoids (lycopene, β-carotene)	Tomato pomace, carrot peels, mango peels	Free radical scavenging; modulation of gene expression; provitamin A activity	Reduced oxidative stress; potential cardioprotective and immune-supportive effects	*In vitro* + animal studies; limited human evidence (lycopene-rich preparations)	[62,74–77]
Phytosterols	Oilseed press cakes, seed residues	Competitive inhibition of intestinal cholesterol absorption; modulation of lipid metabolism genes	LDL cholesterol reduction; improved lipid profile	Strong human evidence (dose-dependent effects)	[78–80]
Ellagitannins/ Punicalagins	Pomegranate peels	Antioxidant activity; apoptosis induction; modulation of inflammatory pathways	Anti-inflammatory effects; antiproliferative activity (cancer cell models)	Primarily *in vitro* + animal studies; limited clinical validation	[81–83]
Glucosinolates/ Isothiocyanates	Broccoli stems/leaves, Brassica residues	Induction of phase II detoxification enzymes; modulation of carcinogenesis pathways	Potential chemopreventive effects	*In vitro* + animal studies; limited human biomarker studies	[84–88]
Fermentable substrates producing SCFAs	Cereal bran, fruit pomace	Fermentation to acetate, propionate, butyrate; gut–immune signaling modulation	Improved metabolic markers; enhanced gut barrier function	Animal + limited human trials	[66–69]

4.1. Phenolic Compounds

Phenolic compounds are among the most abundant bioactive in plant-derived by-products and include flavonoids, phenolic acids, tannins, lignans, and anthocyanins. Their antioxidant and anti-inflammatory activities are attributed to direct free radical scavenging, metal-chelating properties, and modulation of signaling pathways such as NF-κB and Nrf2 [9,89–92].

Major sources include grape pomace (resveratrol, catechins, anthocyanins), citrus peels (hesperidin, naringin), pomegranate peels (punicalagin), eggplant skins (nasunin), and tropical fruit residues such as mango, avocado, and papaya peels and seeds [9,89–92]. Preclinical studies consistently report cardioprotective, antimicrobial, and metabolic regulatory effects. Human evidence is emerging but remains heterogeneous, with some trials demonstrating improvements in lipid profile, endothelial function, and inflammatory biomarkers depending on extract standardization, dose, and intervention duration. Accordingly, phenolic-rich by-products are promising ingredients for functional foods and nutraceuticals, although stronger clinical validation is still required.

4.2. Terpenoids and Carotenoids

Terpenoids, including carotenoids and essential oil constituents, are lipid-soluble compounds responsible for pigmentation and aroma in many plant materials. Tomato pomace is a major source of lycopene, while citrus and mango peels provide β-carotene, limonene, and citral with reported antioxidant and antimicrobial activities [62,93].

Root vegetable peels such as carrot, sweet potato, and pumpkin are rich in α- and β-carotene, contributing to provitamin A activity, immune support, and potential cardioprotective effects [74,94,95]. Carotenoids also act as singlet oxygen quenchers and modulators of cellular pathways involved in oxidative stress and inflammation. Although lycopene and selected carotenoid-rich preparations have been investigated in human studies, evidence specific to by-product-derived preparations remains limited compared with broader dietary evidence. Citrus essential oils are additionally relevant as natural preservatives and functional food ingredients [96,97].

4.3. Dietary Fibers and Polysaccharides

Dietary fibers derived from agri-food by-products—including pectin, cellulose, hemicellulose, lignin, resistant starch, and oligosaccharides—are among the most translationally relevant bioactive components. Apple and citrus pomace are important sources of pectin, whereas banana peels, date seeds, onion skins, and potato peels provide resistant starch and fructooligosaccharides associated with improved glycemic control, lipid regulation, and modulation of gut microbiota composition [65,98,99].

Fermentable fibers enhance production of short-chain fatty acids (SCFAs), strengthen intestinal barrier integrity, and influence appetite and glucose-regulating pathways relevant to obesity and type 2 diabetes. Compared with several other bioactive classes, fibers such as β-glucans and pectins have stronger human evidence supporting benefits in cholesterol lowering and glycemic management. Brassica leaves and stems also contain glucosinolates with potential chemoprotective properties, although evidence remains more mechanistic and epidemiological than intervention-based [84]. Fiber-rich by-products therefore represent leading candidates for large-scale functional food applications.

4.4. Bioactive Peptides and Proteins

Protein-rich by-products such as cheese whey, fish skin, bones, and oilseed residues are valuable substrates for the production of bioactive peptides. Whey-derived peptides, including glycomacropeptide, exhibit antimicrobial, antioxidant, and immunomodulatory properties [38,39]. Enzymatic hydrolysis of marine residues can generate collagen peptides and low-molecular-weight fractions with reported antihypertensive, antioxidant, neuroprotective, and antihyperglycemic activities.

Angiotensin-converting enzyme (ACE)-inhibitory effects have been demonstrated extensively in *in vitro* and animal models; while emerging human studies report modest blood-pressure-lowering effects depending on peptide composition, dose, and duration [40]. Marine collagen peptides also show comparatively stronger clinical evidence for skin elasticity, hydration, and joint health than for many other peptide applications. These findings support the inclusion of peptide-rich by-products in nutraceutical and protein-based formulations.

4.5. Fatty Acids and Lipid Fractions

Oil- and seed-derived by-products contain nutritionally relevant lipid fractions, including polyunsaturated fatty acids (PUFAs), phytosterols, and tocopherols. Grape and bell pepper seeds, for example, are rich in linoleic acid and vitamin E, contributing to antioxidant protection and lipid regulation [14,35,100].

Marine residues provide eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), for which cardiovascular and anti-inflammatory benefits are well established in the broader literature [41,42]. Phytosterols recovered from oilseed residues competitively inhibit intestinal cholesterol absorption and have strong human evidence for LDL-cholesterol reduction when consumed at appropriate doses. Orange seed oil and related by-product-derived oils have also been incorporated into functional food formulations with potential benefits in dyslipidemia management [101]. These lipid fractions are therefore highly relevant for cardiometabolic-targeted food innovation.

4.6. Structure–Activity Relationships of Bioactive Compounds

The biological effects of valorized by-product-derived compounds are closely linked to their molecular structure. For polyphenols, antioxidant and anti-inflammatory properties are strongly influenced by hydroxylation pattern, degree of polymerization, and conjugation, which determine redox potential, metal-chelating capacity, and interactions with signaling pathways such as Nrf2 and NF-κB [9,63]. Glycosylation state and molecular size further affect intestinal absorption, microbial biotransformation, and systemic bioavailability [102,103].

For dietary fibers, solubility, viscosity, molecular weight, and branching structure govern bile acid binding, fermentability, SCFA production, and glycemic modulation [65,66,98,99]. Bioactive peptides exhibit sequence-dependent functionality, where specific amino acid residues and lower molecular weight fractions may enhance ACE inhibition and antioxidant activity [38–40,71]. Similarly, the conjugated double-bond system in carotenoids underlies their free radical scavenging and membrane-stabilizing properties [62,93–95], while the sterol nucleus and side-chain configuration of phytosterols determine their competitive inhibition of intestinal cholesterol absorption [78,79].

Importantly, processing techniques such as enzymatic hydrolysis, fermentation, encapsulation, and controlled extraction may modify these structural features, thereby enhancing bioactivity, stability, or bioavailability [103–107]. Understanding these structure–activity relationships is essential for optimizing extraction strategies, formulation design, and clinically relevant dosing.

4.7. Critical Perspective and Translational Relevance

Collectively, agri-food by-products constitute concentrated sources of polyphenols, carotenoids, dietary fibers, bioactive peptides, and functional lipid fractions with significant nutritional potential. However, not all compound classes are supported by the same level of evidence. Stronger human data currently exist for β-glucans, pectin, phytosterols, selected flavonoids, and marine collagen peptides, whereas many anticancer, neuroprotective, and immunomodulatory claims remain largely preclinical.

Future progress in this field requires standardized compositional characterization, dose harmonization, improved bioavailability assessment, and well-designed randomized clinical trials using clearly defined endpoints. Such advances are essential to translate compositional richness into evidence-based functional foods and nutraceutical products capable of supporting chronic disease prevention and public health.

5. Valorization Technologies and Processing Strategies for Nutritional Applications

The recovery of bioactive compounds from agri-food by-products requires processing strategies that preserve chemical integrity, biological activity, and nutritional functionality while remaining feasible for industrial implementation. Conventional extraction methods often rely on large volumes of organic solvents, prolonged heating, and extended processing times, which may reduce the stability of thermolabile compounds such as polyphenols, carotenoids, and bioactive peptides [103]. In contrast, emerging valorization technologies aim to improve extraction efficiency, reduce environmental burden, and generate food-grade ingredients with reproducible composition. An overview of major technologies, their nutritional relevance, and key limitations is presented in Table 3, while the integrated valorization pathway is summarized in Figure 1.

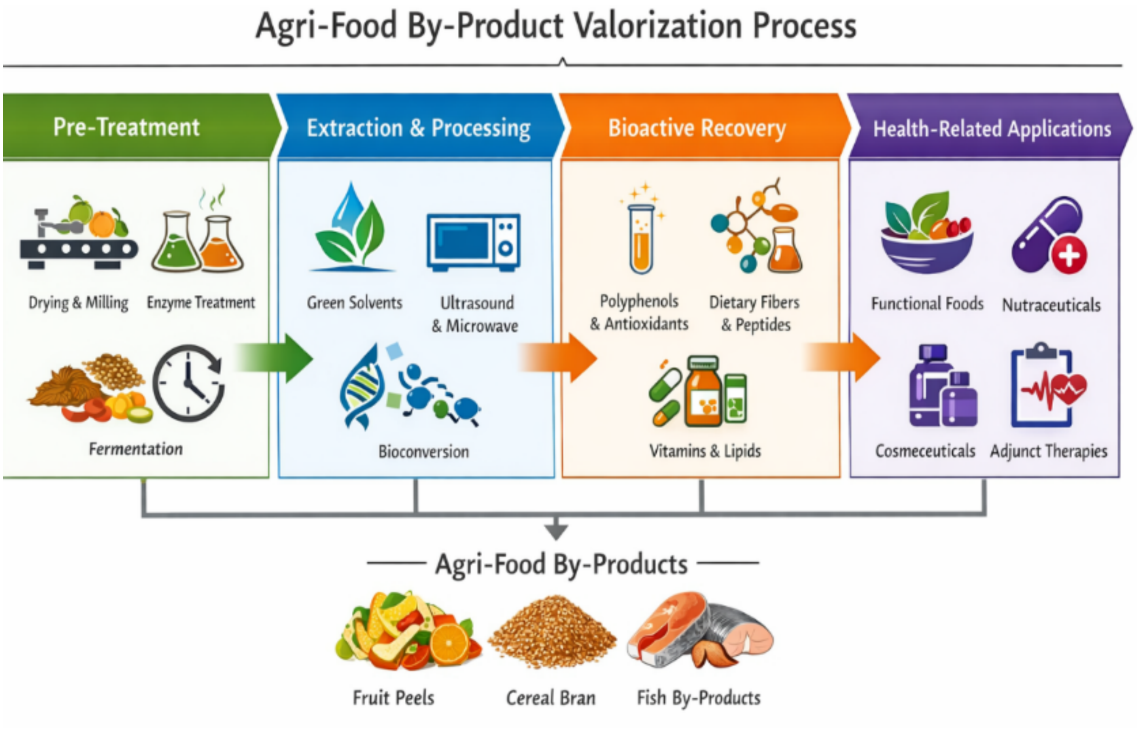

Figure 1. Overview of the valorization process of agri-food by-products into bioactive-rich applications.

Table 3. Green Processing and Biotransformation Technologies for Recovery of Nutritionally Relevant Bioactive Compounds from Agri-Food By-Products.

Technology	Principle	Nutritional/Functional Advantages	Key Limitations for Food Applications	Key References
Ultrasound-Assisted Extraction (UAE)	Acoustic cavitation disrupts plant/matrix structures, enhancing solvent penetration and mass transfer	Short extraction time; relatively low temperatures help preserve thermolabile antioxidants; improved recovery of polyphenols and polysaccharides; compatible with food-grade solvents	Limited penetration in dense matrices; possible degradation at excessive intensity; scale-up and process consistency challenges	[108–110]
Microwave-Assisted Extraction (MAE)	Rapid heating of solvent–matrix systems increases diffusivity and solubilization of target compounds	Fast extraction; high recovery of phenolics and carotenoids; reduced solvent use; concentrated extracts for food enrichment	Risk of thermal degradation if not optimized; requires strict parameter control; uneven heating at industrial scale	[111,112]
Supercritical Fluid Extraction (SFE, CO_2-based)	Supercritical CO_2 selectively solubilizes non-polar and moderately polar compounds under controlled pressure and temperature	Solvent-free extracts suitable for food use; high purity carotenoids and omega-3 oils; preserves lipid integrity; minimal solvent residues	High equipment cost; technical complexity; limited extraction of highly polar compounds without co-solvents	[21,75,76,113]
Enzyme-Assisted Extraction (EAE)	Enzymatic degradation of cell wall polymers releases bound bioactives under mild conditions	Moderate temperatures and pH preserve sensitive compounds; improved release of pectins, phenolics, and peptides; may enhance digestibility and bioavailability	Enzyme cost; longer processing time; need for process optimization; risk of over-hydrolysis affecting sensory quality	[104–107]
Fermentation (Submerged or Solid-State)	Microbial metabolism transforms substrates and increases availability of phenolics, peptides, and functional metabolites	Enhances bioavailability; increases free phenolic content; generates ACE-inhibitory peptides and exopolysaccharides; reduces antinutritional factors	Longer processing times; microbial control required; variability between batches; possible sensory changes	[44,57,114,115]
Pressurized Liquid/Subcritical Water Extraction	Uses water or solvents under high pressure and moderate–high temperature to improve solubility and mass transfer	Water-based green solvent system; effective recovery of phenolics and polysaccharides; suitable for food-grade extracts	Elevated temperatures may degrade sensitive compounds; specialized equipment required	[70,113]
Deep Eutectic Solvent (DES) Extraction	Hydrogen-bond-based designer solvents enhance solubilization of targeted bioactives	High extraction efficiency for polyphenols; potentially biodegradable; tunable solvent properties	Limited regulatory approval for food use; solvent recovery challenges; high viscosity may hinder processing	[70,72]
Hybrid Technologies (e.g., UAE + EAE)	Combination of physical and enzymatic mechanisms to intensify extraction efficiency and selectivity	Improved yield and selectivity; better preservation of antioxidant activity; potential reduction in solvent use and processing time	Increased process complexity; higher capital cost; optimization required for reproducibility	[110,111]

A critical consideration highlighted by recent literature is that extraction yield alone should not be regarded as the sole indicator of success. For nutritional applications, technologies must also be evaluated according to compound stability, bioaccessibility, batch-to-batch consistency, regulatory compatibility, sensory impact, scalability, and cost-effectiveness. These factors are essential for translating laboratory findings into commercial functional foods and nutraceutical products.

5.1. Green Extraction Technologies

5.1.1. Ultrasound-Assisted Extraction (UAE)

Ultrasound-assisted extraction employs acoustic cavitation to disrupt plant or biological matrices, thereby enhancing solvent penetration and mass transfer. From a nutritional perspective, UAE is advantageous because it can operate at relatively low temperatures and short extraction times, reducing degradation of heat-sensitive antioxidants and other labile compounds [108–110].

UAE has been successfully applied to recover polyphenols, carotenoids, and polysaccharides from grape pomace, citrus peels, olive leaves, and nut-processing residues [108–110]. In many cases, improved retention of antioxidant activity has been reported compared with conventional extraction. However, extraction outcomes depend strongly on solvent type, ultrasound intensity, treatment duration, and matrix characteristics. Scale-up and process standardization remain important challenges for industrial adoption.

5.1.2. Microwave-Assisted Extraction (MAE)

Microwave-assisted extraction uses microwave energy to rapidly heat solvent–matrix systems, increasing diffusion rates and facilitating release of target compounds. Compared with conventional methods, MAE can markedly reduce extraction time and solvent consumption [111,112].

This approach has been applied to recover phenolics and carotenoids from olive pomace, grape residues, and citrus by-products [111,112]. When process conditions are carefully optimized, MAE can improve extract concentration and preserve antioxidant functionality. However, excessive heating may degrade sensitive compounds, alter flavor, or reduce biological activity. Therefore, parameter optimization and real-time temperature control are critical for food applications.

5.1.3. Supercritical Fluid Extraction (SFE)

Supercritical fluid extraction, particularly using carbon dioxide (CO_2), is widely recognized for its selectivity and suitability for recovering lipophilic compounds. Because it operates at moderate temperatures and leaves minimal solvent residues, SFE is especially attractive for food and nutraceutical applications [21,113].

SFE has been used to extract lycopene from tomato and carrot by-products as well as omega-3-rich oils from fish-processing residues [75–77]. The resulting extracts often show high purity and good oxidative stability, supporting their incorporation into cardiometabolic-targeted products and lipid-based formulations. Nevertheless, high equipment costs, technical complexity, and limited efficiency for highly polar compounds without co-solvents remain major barriers to widespread industrial use.

5.1.4. Enzyme-Assisted Extraction (EAE)

Enzyme-assisted extraction uses cellulases, hemicellulases, pectinases, proteases, and related enzymes to degrade structural barriers and release entrapped bioactive compounds under relatively mild conditions [104,105]. This strategy is particularly relevant for preserving compound integrity while enhancing recovery from complex plant matrices.

EAE has demonstrated effectiveness in improving extraction of pectins, phenolics, and protein hydrolysates from fruit peels, cereal brans, and oilseed meals. Enzymatic hydrolysis may also generate peptides with improved digestibility and enhanced bioactivity, increasing potential physiological efficacy [106,107]. However, enzyme cost, process time, substrate specificity, and the need for precise optimization may limit commercial scalability.

5.2. Fermentation and Biotransformation

Microbial fermentation represents a biologically driven approach for improving the nutritional functionality of agri-food by-products. Lactic acid bacteria, fungi, and yeasts can hydrolyze bound phytochemicals, release phenolic aglycones, synthesize exopolysaccharides, and generate bioactive peptides with ACE-inhibitory or antioxidant properties [44,114].

Fermentation of cereal bran may enhance β-glucan solubility, reduce antinutritional factors, and improve digestibility and metabolic functionality [57,115]. Similarly, fermentation of fruit pomace has been associated with increased free phenolic content and antioxidant capacity [57,115]. Solid-state fermentation (SSF) has also been applied to produce phenolic-enriched extracts and protein hydrolysates with enhanced functional properties (57). Despite these advantages, batch variability, microbial control, sensory changes, and regulatory compliance for microbial cultures must be carefully managed.

5.3. Integrated Biorefinery Approaches

Integrated biorefinery systems aim to fractionate biomass into multiple value-added streams through coordinated sequential processing [116–118]. In the context of nutritional applications, such systems may enable recovery of pectins, polyphenols, carotenoids, proteins, oils, and fermentable substrates from the same raw material.

For example, citrus peels and grape pomace can be processed to obtain fiber fractions, antioxidant extracts, and fermentation substrates within a single framework [119–121]. This approach can improve overall resource efficiency and economic feasibility while reducing waste generation. However, commercial implementation requires robust logistics, consistent feedstock quality, regulatory compliance across multiple outputs, and careful economic assessment.

5.4. Environmental and Economic Assessment

Life cycle assessment (LCA) and techno-economic analysis (TEA) are increasingly used to evaluate the sustainability and feasibility of valorization systems [122,123]. These tools are particularly important because a process with high extraction yield may still be unsuitable if associated with excessive energy use, water consumption, or prohibitive production costs.

Current evidence suggests that technologies such as UAE, EAE, and SFE may reduce solvent use and, in some cases, energy demand compared with conventional extraction systems [124,125]. However, outcomes are highly context-dependent and influenced by process scale, matrix type, and downstream purification requirements. Integrating environmental and economic metrics with nutritional performance is therefore essential for realistic commercialization pathways.

5.5. Standardization, Scale-Up, and Future Directions

Despite substantial technological progress, several barriers continue to limit large-scale implementation. Natural variability in raw material composition may lead to inconsistent extract profiles, making standardization and batch-to-batch reproducibility challenging. High capital investment, process complexity, and limited harmonization of analytical quality standards further constrain industrial uptake [31,126–128]. In addition, regulatory acceptance requires clear ingredient specifications, contaminant control, validated analytical methods, and safety documentation.

Future research should prioritize the optimization of extraction conditions to maximize compound stability and bioavailability; the development of food-grade green solvents, including deep eutectic solvents with regulatory compatibility [111]; and standardized reporting of yield, purity, active compound content, and dose equivalence. Also, scalable modular processing systems adaptable to diverse by-product streams [129]; integration of omics tools, digital monitoring, and predictive modeling for quality control; and well-designed human studies linking processing methods with biological efficacy.

Ultimately, the success of valorization technologies should be judged not only by extraction efficiency, but by their ability to deliver safe, standardized, bioavailable, and clinically relevant ingredients suitable for functional foods and nutraceutical applications.

6. Health-Promoting Potentials of Valorized By-Products

Valorized agri-food by-products are rich in bioactive constituents including polyphenols, flavonoids, dietary fibers, oligosaccharides, bioactive peptides, essential fatty acids, phytosterols, and micronutrients that may influence multiple physiological pathways relevant to chronic disease prevention and health maintenance [130]. Evidence supporting these effects derive from *in vitro* experiments, animal studies, and a growing but still heterogeneous body of human trials. Reported outcomes include modulation of gut microbiota composition, antioxidant and anti-inflammatory activity, improvements in lipid and glucose metabolism, vascular protection, and support of skin, joint, or cognitive function [27]. However, the strength of evidence differs considerably according to compound class, formulation, dose, and study design [102]. Accordingly, clear distinction between mechanistic promise and clinically validated outcomes remains essential.

6.1. Gut Microbiota and Metabolic Signaling

Fermentable fibers and non-digestible oligosaccharides derived from pomace, cereal brans, and vegetable residues can serve as substrates for beneficial gut microorganisms, increasing production of short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate [66]. SCFAs contribute to intestinal barrier integrity, modulation of inflammatory signaling, appetite regulation, and improved insulin sensitivity [67].

Polyphenols also interact bidirectionally with the gut microbiota. Many polyphenols are transformed by microbial enzymes into lower-molecular-weight metabolites with altered bioavailability and biological activity, while certain compounds may selectively stimulate beneficial taxa such as *Bifidobacterium* and selected *Lactobacillus* species in preclinical models [102].

Animal studies consistently show that supplementation with grape pomace, citrus extracts, or cereal bran can increase SCFA production, enrich butyrate-producing bacteria, and improve adiposity, glucose tolerance, and hepatic lipid accumulation [68]. Human trials remain more limited in size and duration but report modest improvements in microbiota composition and selected metabolic biomarkers following standardized fiber or polyphenol interventions [69]. Among the various reported health effects of valorized by-products, microbiota modulation is one of the most consistently observed and biologically plausible outcomes.

Importantly, processing conditions—including drying, thermal treatment, milling, and extraction methods—can alter fiber solubility and polyphenol composition, thereby influencing fermentability and biological response [71]. Standardized reporting of soluble fiber content, polyphenol profile, and dose is therefore necessary for cross-study comparison and product development.

6.2. Antioxidant, Anti-Inflammatory, and Immunomodulatory Effects

Polyphenols such as anthocyanins, catechins, oleuropein, and hesperidin exert antioxidant effects through direct free radical scavenging and activation of endogenous defense pathways, including Nrf2-mediated signaling. These compounds may also suppress pro-inflammatory pathways such as NF-κB and reduce expression of mediators including TNF-α, IL-6, COX-2, and iNOS [63].

Bioactive peptides may contribute additional antioxidant and vascular-modulating actions through metal chelation, nitric oxide regulation, and ACE inhibition [72]. Preclinical studies consistently report reductions in oxidative stress markers and inflammatory mediators following supplementation with grape pomace, olive leaf, and citrus-derived extracts [131].

Human studies involving olive leaf extracts and hesperidin supplementation have shown modest reductions in systolic blood pressure, LDL cholesterol, and circulating inflammatory markers [64]. However, most available trials are short-term, heterogeneous in formulation and dose, and not designed to evaluate hard clinical outcomes such as cardiovascular events or disease incidence. Larger randomized controlled trials with dose-response assessment and metabolite profiling are still required.

6.3. Cardiometabolic Benefits

Among the most clinically relevant effects of valorized by-products are improvements in lipid metabolism, blood pressure regulation, and glycemic control. Soluble fibers such as β-glucans and pectins can lower LDL cholesterol by increasing intestinal viscosity and reducing bile acid and cholesterol reabsorption [70]. Phytosterols derived from oilseed residues competitively inhibit cholesterol absorption, contributing to clinically meaningful LDL reductions [78,79].

Clinical studies indicate that phytosterol supplementation and standardized citrus extracts rich in hesperidin (≥500 mg/day in several trials) may modestly improve lipid profile and vascular function, although effect sizes vary across studies [80]. Marine-derived peptides exhibit ACE-inhibitory activity in mechanistic models and antihypertensive effects in animals, with emerging human studies reporting moderate blood-pressure reductions depending on peptide fraction, purity, and dose [71].

For successful translation into functional foods and nutraceutical products, consistency of dosage and clear labeling of active constituents (e.g., milligrams of hesperidin, percentage of oleuropein, grams of β-glucan) are essential to support efficacy and regulatory compliance [132].

6.4. Anticancer and Chemopreventive Potential

Polyphenols may influence carcinogenesis through multiple mechanisms including antioxidant effects, induction of apoptosis, cell-cycle arrest, inhibition of angiogenesis, and modulation of pathways such as PI3K/Akt and MAPK [85]. *In vitro* and animal studies indicate that olive leaf extracts, grape pomace extracts, and berry-derived polyphenols can inhibit tumor cell proliferation and modulate epigenetic regulators [86].

Epidemiological evidence links diets rich in polyphenol-containing foods with reduced cancer risk [87,88]. However, direct randomized clinical trials evaluating valorized by-product extracts for cancer prevention remain scarce. Therefore, current evidence should be considered promising but predominantly preclinical. Future studies should prioritize well-designed phase II trials using validated intermediate biomarkers of carcinogenesis.

6.5. Neuroprotection and Cognitive Function

Polyphenols may exert neuroprotective effects by reducing oxidative stress, attenuating neuroinflammation, improving synaptic plasticity, and enhancing cerebral blood flow. Some compounds or their metabolites may cross the blood–brain barrier, whereas others may act indirectly through modulation of the gut–brain axis and microbial metabolites such as SCFAs [133].

Preclinical studies demonstrate improved cognitive performance and reduced neuroinflammation following administration of grape and berry pomace extracts [134]. Small human studies involving polyphenol-rich interventions suggest possible improvements in memory and executive function among older adults; however, evidence specific to valorized by-product extracts remains limited and requires confirmation in larger trials [135].

6.6. Dermatological and Musculoskeletal Outcomes

Marine collagen peptides derived from fish-processing by-products have demonstrated improvements in skin elasticity, hydration, and joint discomfort in human studies, commonly at doses of 2.5–10 g/day administered for

8–12 weeks [73]. Compared with several other by-product-derived interventions, this area currently has relatively stronger clinical support.

Nevertheless, many available studies are industry-sponsored and differ in peptide characterization, comparator selection, and methodological rigor. Independent replication, transparent reporting, and standardized peptide profiling remain necessary to strengthen confidence in these findings.

6.7. Antimicrobial and Food-Safety Implications

Polyphenol-rich extracts from agri-food by-products exhibit antimicrobial and antifungal activity in *in vitro* systems, supporting their potential use as natural food preservatives with added functional value. Pomegranate peel extracts rich in ellagic acid and punicalagins have demonstrated antifungal and antibiofilm properties [136].

Although promising, efficacy within real food matrices may differ from laboratory models because of interactions with proteins, lipids, pH, and storage conditions. Sensory impact, optimal dose, and regulatory acceptance must also be considered before commercialization [137].

6.8. Bioavailability, Matrix Effects, and Formulation Strategies

Bioavailability is a critical determinant of efficacy. Many polyphenols show limited absorption, extensive metabolism, and substantial interindividual variability. Strategies such as microencapsulation, protein–polyphenol complexation, phospholipid delivery systems, and co-administration with bioavailability enhancers (e.g., piperine) may increase systemic exposure [103].

Fermentation and enzymatic treatment can improve release of bound phenolics and generate more absorbable metabolites. Future studies should routinely report pharmacokinetic parameters such as area under the curve (AUC), maximum concentration (Cmax), metabolite profiles, and dose-response relationships to improve translational validity.

6.9. Synthesis of Evidence and Future Priorities

Taken together, current evidence demonstrates a clear gradient in support across health domains. Antioxidant, anti-inflammatory, microbiota-modulating, and ACE-inhibitory effects are strongly supported by mechanistic and animal data, with emerging human trials reporting improvements in surrogate biomarkers such as LDL cholesterol, blood pressure, glycemic indices, and inflammatory mediators. In contrast, anticancer, neuroprotective, and several immunomodulatory claims remain largely preclinical.

Marine collagen peptides and selected phytosterol- or flavonoid-rich preparations currently possess the most consistent human evidence, whereas many polyphenol-rich extracts still require standardized dosing, pharmacokinetic characterization, and adequately powered long-term clinical trials. Future research should prioritize randomized controlled studies with clearly defined endpoints, dose-response assessment, safety monitoring, and harmonized reporting standards to bridge the gap between experimental promise and clinically meaningful health outcomes.

7. Applications in Functional Foods, Nutraceuticals, and Pharmaceuticals

The incorporation of agri-food by-products into value-added formulations has expanded considerably in response to increasing consumer demand for nutrient-dense, sustainable, and clean-label ingredients. These materials provide concentrated sources of dietary fibers, polyphenols, carotenoids, peptides, essential fatty acids, and micronutrients that may enhance nutritional quality, technological functionality, oxidative stability, and shelf life [138–140]. Their valorization has therefore gained relevance across functional foods, nutraceuticals, pharmaceutical systems, and related health-oriented products. Representative translational applications are summarized in Table 4.

A critical issue emphasized by current literature is that successful application depends not only on bioactive composition, but also on standardization, sensory acceptability, dose delivery, regulatory compliance, and evidence of efficacy in humans. Accordingly, the following sections distinguish established applications from emerging or primarily preclinical uses.

Table 4. Clinical and Translational Applications of Valorized Agri-Food By-Products in Functional Foods, Nutraceuticals, and Health-Oriented Formulations.

By-Product Source	Principal Bioactives	Application Format	Reported Health Outcomes	Level of Evidence	Key Considerations	Key References
Citrus peels	Pectin, hesperidin, naringenin, essential oils	Functional beverages, bakery enrichment, dietary supplements	LDL reduction, improved endothelial function, antioxidant activity	Preclinical + human trials (dose-dependent; ≥500 mg/day hesperidin in some studies)	Standardization of flavonoid content; bioavailability variability	[96,141–143]
Apple peels	Quercetin, chlorogenic acid, phloridzin, fiber	Bakery fortification, prebiotic dairy products, nutraceutical capsules	Improved antioxidant status, lipid modulation, enhanced probiotic viability	Mostly preclinical; limited controlled human trials	Fiber–polyphenol matrix interactions may affect absorption	[143–149]
Banana peels	Dopamine, carotenoids, polyphenols, tannins	Functional flour, fiber enrichment	Antioxidant and antihyperglycemic effects	Primarily preclinical	Sensory optimization and standardization required	[150,151]
Grape pomace	Resveratrol, anthocyanins, catechins, fiber	Polyphenol extracts, functional snacks, capsules	Improved lipid profile, reduced oxidative stress, microbiota modulation	Strong preclinical; emerging small human trials	Bioavailability influenced by matrix and metabolism	[68,86,131]
Pomegranate peels	Punicalagins, ellagic acid, ellagitannins	Nutraceutical extracts, meat preservatives	Anti-inflammatory, antioxidant, potential anticancer effects	Preclinical dominant; limited human validation	Dose-response data lacking	[81–83]
Onion peels	Quercetin	Weight-management supplements, capsules	Reduced LDL cholesterol, fasting glucose, body fat mass	Animal + small human studies	Standardized quercetin dosage essential	[152–155]
Potato peels	Phenolics, glycoalkaloids	Gluten-free pasta, yogurt enrichment, experimental pharmaceutical matrices	Increased antioxidant capacity; antiproliferative activity (*in vitro*)	Preclinical	Glycoalkaloid safety threshold must be monitored	[156–159]
Beetroot pulp/peel	Betalains, dietary fiber	Functional yogurt, flours, powders	Glycemic modulation, antioxidant effects; neuroprotection (animal models)	Preclinical + limited human food trials	Stability of betalains during processing	[160–164]
Olive leaves/pomace	Oleuropein, hydroxytyrosol	Cardiometabolic supplements	Reduced blood pressure, inflammatory markers	Human trials (mainly short-term)	Long-term clinical endpoints needed	[64,85]
Marine by-products (fish skin/bones)	Collagen peptides, ACE-inhibitory peptides, omega-3 fatty acids	Collagen powders (2.5–10 g/day), antihypertensive peptide supplements	Improved skin elasticity, joint comfort; modest blood pressure reduction	Moderate human evidence	Peptide characterization and independent replication required	[71,73]
Avocado peel (APN)	Polyphenols, anti-inflammatory phytochemicals	Experimental nutraceuticals	Anti-inflammatory effects; microbiota modulation (animal models)	Preclinical	Clinical translation pending	[9]

7.1. Functional Food Applications

Agri-food by-products are increasingly incorporated into conventional food matrices to improve fiber content, antioxidant capacity, and technological performance. Among the most extensively studied examples are citrus-derived ingredients because of their high pectin, flavonoid, and essential oil content. Citrus pectin functions as a natural gelling agent, stabilizer, and emulsifier, improving viscosity, texture, and shelf life in beverages, dairy systems, and bakery products [165,166]. Citrus peel powders and extracts may also increase dietary fiber content and antioxidant potential, while flavonoids such as hesperidin and naringenin have shown lipid-lowering and endothelial-supportive effects in clinical and preclinical studies depending on dose and formulation [97,141,142].

Apple peels are rich in dietary fiber and polyphenols including quercetin, chlorogenic acid, phloridzin, and tannins. Their incorporation into bakery products has been associated with improved total fiber content, antioxidant capacity, and rheological properties when used at optimized inclusion levels [143,144]. Apple peel fiber has also been explored in fermented dairy products, where it may enhance probiotic viability, viscosity, and texture while providing prebiotic functionality [145].

Banana peels, which contain carotenoids, dopamine, quercetin, and tannins, have been evaluated as ingredients in composite flours and fiber-enriched foods. Preclinical studies report antioxidant, antimicrobial, and antihyperglycemic properties, although robust human evidence remains limited [150,151]. Similarly, fiber-rich matrices such as psyllium husk incorporated into synbiotic systems have demonstrated cardioprotective effects in animal models, supporting the broader relevance of soluble fibers in metabolic modulation [167].

Vegetable-processing residues also show promising food applications. Potato peel extracts have been incorporated into gluten-free pasta and yogurt, improving antioxidant activity and nutritional profile without compromising sensory acceptability when appropriately formulated [156,157]. Beetroot pulp and peel, rich in betalains and dietary fiber, have been used as natural colorants and antioxidant enhancers in baked goods and dairy products [160,161]. Probiotic-fortified beetroot-enriched yogurt has demonstrated improvements in glycemic and oxidative stress markers in experimental models of type 2 diabetes [162].

Broccoli stems and leaves, frequently discarded during processing, contain phenolic compounds and glucosinolates and have been incorporated into fermented foods and bakery products, contributing phytochemical enrichment and antioxidant activity [168,169]. Overall, successful food incorporation requires balancing bioactive concentration with sensory quality, technological functionality, storage stability, and consumer acceptance.

7.2. Nutraceutical and Pharmaceutical Applications

Beyond conventional food matrices, by-product-derived compounds are increasingly formulated as nutraceuticals and adjunct therapeutic ingredients. These applications typically allow more precise dose delivery and standardization than whole-food formulations, although regulatory requirements may be more stringent.

Citrus peel-derived pectin has been investigated in controlled drug delivery systems because of its gelling, mucoadhesive, and biocompatible properties [170,171]. Citrus flavonoids, particularly hesperidin and naringenin, exhibit anti-inflammatory, lipid-lowering, antimicrobial, and endothelial-supportive effects, supporting their use in cardiometabolic health supplements [143].

Apple peel polyphenols demonstrate antioxidant and anti-inflammatory effects in mechanistic and animal studies, with reported improvements in lipid metabolism and glycemic markers [146–149]. However, robust human intervention trials using standardized peel-derived preparations remain limited.

Pomegranate peel extracts, rich in ellagitannins and punicalagin, show strong antioxidant and anti-inflammatory activity in preclinical models [81,82]. Their incorporation into nutraceutical capsules and use as natural preservatives in meat systems have demonstrated improved oxidative stability and microbial quality [83].

Avocado peel-derived nutraceutical preparations (APN) have shown anti-inflammatory and anti-arthritic effects in experimental studies, together with modulation of gut microbiota composition [9]. While promising, these findings require validation in controlled human studies.

Onion peel extracts standardized for quercetin content have demonstrated reductions in body fat mass, LDL cholesterol, and fasting glucose in limited human and animal studies, although dose standardization and bioavailability remain critical considerations [152,153].

Potato peel-derived phenolics and glycoalkaloids exhibit antioxidant and antiproliferative properties in laboratory models [158,159]. Beetroot pulp supplementation has shown neuroprotective effects in murine models of neurodegeneration [166]. At present, most of these applications should be considered emerging rather than clinically established.

7.3. Cosmeceutical Applications

By-product-derived bioactives are increasingly incorporated into dermatological and cosmetic formulations because of their antioxidant, anti-inflammatory, and barrier-supportive properties. Although not equivalent to therapeutic claims, these applications represent an important commercial pathway for valorized ingredients.

Citrus peel extracts are used in topical systems for antimicrobial and antioxidant functions, contributing to oxidative stability and skin protection [167]. Pomegranate peel extracts have shown protective effects against oxidative stress and ultraviolet-induced damage and are increasingly explored in anti-aging and dermatological formulations [172,173].

Apple and onion peel extracts, rich in quercetin, demonstrate anti-tyrosinase and skin-brightening activity in experimental systems [174,175]. Broccoli-derived extracts show potential protective effects against ultraviolet-induced oxidative stress [176]. Beetroot and ginger peel extracts contribute antioxidant activity and may support collagen synthesis and anti-aging mechanisms in topical formulations [177,178].

Despite growing commercial interest, many cosmeceutical claims are supported primarily by laboratory or small-scale studies. More rigorous clinical trials evaluating efficacy, tolerability, and long-term safety are needed.

7.4. Translational Challenges and Future Opportunities

The expanding use of agri-food by-products in food, nutraceutical, pharmaceutical, and cosmeceutical systems demonstrates considerable translational potential. However, successful progression from experimental concept to commercial product requires consistent standardization of bioactive composition, validated analytical methods, scientifically justified dosing, contaminant control, and regulatory compliance.

Equally important are formulation strategies that enhance stability and bioavailability without compromising sensory quality or consumer trust. Clear labeling, including transparent declaration of active ingredient content and alignment with "upcycled" or "clean-label" expectations, may further influence market acceptance and purchasing decisions.

Commercial translation of valorized by-products is already evident in several established product categories. Examples include citrus pectin widely used as a gelling and stabilizing ingredient in jams, beverages, and dairy products; phytosterol-enriched spreads and dairy alternatives marketed for cholesterol reduction; whey protein isolates and hydrolysates incorporated into sports and medical nutrition products; marine collagen powders and beverages positioned for skin and joint health; and oat or barley β-glucan products formulated to support heart health and glycemic management. These examples demonstrate that when safety, standardization, efficacy, and consumer acceptance are adequately addressed, by-product-derived ingredients can achieve successful large-scale commercialization.

Future research should prioritize well-designed human trials, head-to-head comparisons of formulation systems, shelf-life validation, and cost-effective scalable manufacturing approaches. With these advances, valorized by-products may become increasingly important components of sustainable health-oriented product innovation.

8. Safety and Regulatory Considerations

The successful translation of agri-food by-products into functional foods, nutraceuticals, and related health-oriented products depends not only on biological efficacy, but also on rigorous safety assessment, regulatory compliance, and consumer confidence. Although these materials frequently originate from edible raw materials, concentration of bioactive compounds, processing conditions, and potential contamination risks require careful evaluation before commercialization. In addition, regulatory classification and permitted claims differ substantially across jurisdictions, making harmonized quality standards and transparent labeling particularly important.

8.1. Safety Evaluation and Quality Control

The assumption that all by-products are inherently safe because they derive from foods is not always justified. During cultivation, storage, and processing, by-products may accumulate undesirable substances or undergo compositional changes that alter safety profiles. Potential concerns include natural toxins, pesticide residues, heavy metals, mycotoxins in cereal-derived materials, histamine and other biogenic amines in marine residues, and process-generated contaminants such as residual solvents or polycyclic aromatic hydrocarbons (PAHs) [179–181].

Accordingly, comprehensive safety assessment should include compositional characterization of the raw material and final extract; screening for chemical contaminants and microbiological hazards; evaluation of allergenicity where relevant; stability and shelf-life testing; toxicological assessment when concentration or novel processing substantially changes exposure; and verification that manufacturing practices ensure reproducible quality.

Standardization of extraction and processing methods is essential to minimize batch-to-batch variability and ensure that active compounds remain within safe and efficacious ranges during storage and distribution. This issue is particularly important for phytochemical-rich extracts and peptide concentrates, where biological activity may vary considerably according to raw material source, season, and process conditions.

Dose justification is another critical requirement. Experimental studies often use doses that may not directly correspond to realistic intake from commercial products. Therefore, clinical translation requires alignment between efficacious doses reported in research settings and actual levels delivered in food matrices, supplements, or fortified products. Clear declaration of active constituent content is necessary to support both safety and expected functionality.

8.2. Regulatory Frameworks and Market Authorization

Regulatory classification of valorized by-product ingredients depends on composition, intended use, processing history, and jurisdiction. In the European Union, the European Food Safety Authority evaluates novel foods and health claims. Ingredients without a documented history of significant consumption may require authorization under Regulation (EU) 2015/2283 (Novel Foods), while food supplements are regulated under Directive 2002/46/EC [23,182]. These pathways require evidence of safety, nutritional suitability, and substantiation of proposed health claims before market entry.

In the United States, the Food and Drug Administration oversees food ingredients through frameworks such as Generally Recognized as Safe (GRAS) and regulates dietary supplements under the Dietary Supplement Health and Education Act (DSHEA) [154]. Manufacturers are responsible for safety substantiation, compliant labeling, and adherence to current good manufacturing practices. Structure/function claims may be permitted under defined conditions, whereas disease-treatment claims require a different regulatory pathway.

At the international level, Codex Alimentarius Commission principles and FAO/WHO guidance provide reference standards for contaminant limits, microbiological criteria, labeling, and general food safety management [155]. Although national regulations differ, these frameworks support global harmonization and facilitate international trade of food ingredients.

8.3. Labeling, Consumer Acceptance, and Market Trust

Regulatory approval alone may not guarantee market success. Consumer perception of ingredients derived from by-products can strongly influence adoption, particularly when sustainability messaging is not accompanied by clear evidence of safety, quality, and functionality. Terms such as “upcycled ingredients,” “recovered bioactives,” and “clean label” may enhance acceptance when supported by transparent communication and scientifically substantiated claims.

Accurate labeling should include ingredient identity, relevant allergen information, storage conditions, and, where appropriate, quantitative declaration of active constituents (e.g., milligrams of hesperidin, percentage of oleuropein, grams of β-glucan). Transparent labeling is especially important for products marketed for cardiometabolic, digestive, or cosmetic benefits, where consumer expectations may be strongly influenced by health-related messaging.

In addition to general labeling requirements, several valorized ingredients are already established in commercial markets and provide practical examples of successful regulatory and consumer acceptance. These include citrus pectin used as a stabilizer and gelling agent in foods and beverages, whey protein isolates widely marketed in sports and clinical nutrition products, phytosterol-enriched spreads and dairy alternatives authorized in many regions for cholesterol-lowering claims, marine collagen supplements promoted for skin and joint health, and oat β-glucan products recognized for heart-health and glycemic-support applications. The commercial success of these ingredients illustrates how robust safety assessment, standardized composition, compliant health claims, and clear consumer communication can facilitate market adoption of by-product-derived products.

8.4. Current Gaps and Future Priorities

Despite rapid growth in this field, several challenges remain. Regulatory pathways for some emerging ingredients are still unclear, especially when novel extraction technologies or unconventional raw materials are used. In addition, analytical methods for standardizing complex extracts are not always harmonized across laboratories or jurisdictions. Long-term safety data are also limited for many newly commercialized formulations.

Future progress should prioritize the harmonized specifications for identity, purity, and active compound content; validated analytical methods for complex mixtures; stronger post-market surveillance where appropriate; long-term human safety studies for concentrated extracts; clearer international guidance for ingredients derived from sustainable side streams; and consumer-centered labeling strategies that combine transparency with scientific accuracy.

Overall, robust safety assessment, regulatory clarity, and trustworthy communication are fundamental for converting agri-food by-products from promising raw materials into credible and widely accepted health-oriented products.

9. Conclusions

The valorization of agri-food by-products has evolved beyond a waste-management strategy into a scientifically relevant and nutritionally meaningful approach for generating bioactive-rich ingredients with potential health benefits. As highlighted throughout this review, residues from fruit, vegetable, cereal, oilseed, dairy, and marine processing streams contain concentrated levels of polyphenols, dietary fibers, bioactive peptides, functional lipids, and micronutrients that can be recovered and incorporated into value-added products. This transition aligns with current priorities in sustainable food systems, resource efficiency, and circular bioeconomy development.

Evidence from *in vitro* and animal studies consistently supports antioxidant, anti-inflammatory, microbiota-modulating, antihypertensive, lipid-lowering, and tissue-protective effects of many by-product-derived compounds. However, the level of support is not uniform across all applications. Human studies currently provide the strongest evidence for selected interventions such as β-glucans, pectin, phytosterols, certain flavonoid-rich preparations, and marine collagen peptides, where improvements in cardiometabolic markers, glycemic control, vascular function, skin health, or joint comfort have been reported. In contrast, several anticancer, neuroprotective, and broader immunomodulatory claims remain promising but are still supported predominantly by preclinical findings.

Technological advances—including ultrasound-assisted extraction, enzyme-assisted processing, fermentation, hybrid systems, and integrated biorefinery approaches—have significantly improved the recovery, stability, and functionality of bioactive compounds from complex side streams. Nevertheless, extraction efficiency alone should not be considered sufficient for successful translation. Standardization of raw materials, reproducibility of extract composition, dose characterization, bioavailability, sensory acceptability, scalability, and economic feasibility are equally important determinants of practical application.

Despite rapid progress, several challenges continue to limit broader commercialization. These include natural variability in source materials, inconsistent analytical characterization, incomplete long-term safety data, regulatory complexity across jurisdictions, and limited numbers of adequately powered randomized clinical trials. Addressing these barriers will require coordinated efforts among food scientists, nutrition researchers, clinicians, toxicologists, process engineers, industry stakeholders, and regulatory authorities.

Future research priorities should include the rigorous compositional standardization and batch-to-batch quality control; improved bioavailability assessment, metabolite profiling, and pharmacokinetic evaluation; validation of clinically relevant dosages and mechanisms in well-designed human trials; harmonized safety and regulatory frameworks for emerging valorized ingredients; formulation strategies that optimize stability, efficacy, and consumer acceptability; and integration of digital tools and predictive models to support process optimization and quality assurance.

Among near-term opportunities, functional foods and nutraceuticals represent the most immediately translatable applications because they can incorporate standardized by-product-derived ingredients into everyday dietary patterns. With robust evidence generation and responsible commercialization, these products may contribute meaningfully to prevention and management of cardiometabolic disorders, inflammatory conditions, and other diet-related chronic diseases.

In conclusion, agri-food by-product valorization represents a multidisciplinary nutrition framework that combines sustainability with evidence-based health innovation. Continued progress will depend on bridging the gap between promising mechanistic findings and clinically validated outcomes, thereby enabling underutilized biological resources to become credible components of future health-oriented food systems.

Author Contributions

D.A.M. conceived the study topic, reviewed the data, and prepared the final version of the manuscript. A.A.R. contributed to literature collection, drafting the manuscript, and English language editing. S.E.M., H.B.M., R.A.B., E.S.K.A.-S., H.F.E., and I.H. contributed to literature collection and preparation of the initial manuscript draft. All authors reviewed and approved the final submitted version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

List of Abbreviations

ACE	Angiotensin-Converting Enzyme
ADPs	Animal-Derived By-Products
AUC	Area Under the Curve
BP	Blood Pressure
CO_2	Carbon Dioxide
DES	Deep Eutectic Solvents
DSHEA	Dietary Supplement Health and Education Act
DHA	Docosahexaenoic Acid
EPA	Eicosapentaenoic Acid
EAE	Enzyme-Assisted Extraction
EFSA	European Food Safety Authority
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
GRAS	Generally Recognized as Safe
IL-6	Interleukin-6
iNOS	Inducible Nitric Oxide Synthase
LCA	Life Cycle Assessment
LDL	Low-Density Lipoprotein
MAE	Microwave-Assisted Extraction
MAPK	Mitogen-Activated Protein Kinase
NCDs	Non-Communicable Diseases
NF-κB	Nuclear Factor Kappa B
Nrf2	Nuclear Factor Erythroid 2–Related Factor 2
PAHs	Polycyclic Aromatic Hydrocarbons
PI3K/Akt	Phosphoinositide 3-Kinase/Protein Kinase B
PUFAs	Polyunsaturated Fatty Acids
ROS	Reactive Oxygen Species
SCFAs	Short-Chain Fatty Acids
SFE	Supercritical Fluid Extraction
SSF	Solid-State Fermentation
TEA	Techno-Economic Analysis
TNF-α	Tumor Necrosis Factor Alpha
UAE	Ultrasound-Assisted Extraction
WHO	World Health Organization

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