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Valorizing seafood processing by-products for prebiotic development: a circular economy approach to gut health

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ABSTRACT

Background: Approximately 50% of global seafood catch is discarded as processing by-products, creating both environmental burdens and untapped bioactive resources. Seafood-derived oligosaccharides and polysaccharides exhibit structure-dependent prebiotic activities through distinct mechanisms, yet a comprehensive framework linking extraction methods, structural features, and gut microbiota outcomes remains lacking.

Scope and approach: This review critically integrates mechanistic evidence on valorizing seafood by-products such as crustacean shells, fish waste, algal residues, and emerging sources as sustainable prebiotic feedstocks. It examines how structural characteristics such as molecular weight (Mw), degree of polymerization (DP), degree of acetylation (DA), and sulfation patterns determine fermentability, carbohydrate-active enzymes (CAZymes) accessibility, and microbial utilization, while systematically evaluating extraction and purification methods and their influence on bioactivity.

Key findings and conclusions: In vitro and animal studies demonstrate that prebiotic activity is strongly structure-dependent. Low-Mw chito-oligosaccharides (COS) specifically stimulate beneficial *Lactobacillus* and *Bifidobacterium* populations, while high-degree-of-deacetylation (DD) chitosan has antibacterial action through charge-mediated membrane disruption. Fish-derived glycosaminoglycans (GAGs) contribute to the modulation of short-chain fatty acids (SCFAs) profiles in fermentation models, with proposed GPR41/43-mediated pathways that require further validation. Preclinical evidence shows promising anti-obesity, antidiabetic, cardioprotective, and anti-inflammatory effects, though human data remain limited. However, critical translational gaps persist: limited human trials, inter-individual variability, lack of standardized production protocols, and the purity/bioactivity paradox, whereby extensive processing may enhance yield but compromise functional properties. Addressing these gaps requires integrated biorefinery approaches that preserve structural integrity while maximizing bioactivity, alongside harmonized regulations and rigorous human intervention studies to establish clinical relevance.

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1. Introduction

Large amounts of leftover biomaterials are produced worldwide during seafood production, frequently exceeding half of the collected mass. This generates severe environmental issues and represents a considerable loss of valuable biochemical resources (Xie, 2026). Nearly 35% of the global seafood catch is lost or wasted throughout the value chain annually. The main reasons for this include poor food quality due to spoilage, inadequate cold storage, and poor handling methods (Wu et al., 2026). Traditionally, leftovers have been used for low-value purposes such as animal feed, landfill disposal, or ocean dumping, which can pose risks to coastal communities, eutrophication of coastal waters, and uncontrolled decomposition leading to greenhouse gas emissions (Xie, 2026). These practices deplete valuable biochemical resources and increase environmental pressures on marine ecosystems. Consequently, there is an urgent need for circular economy-aligned sustainable valorization techniques that reframe seafood processing leftovers as key feedstocks for high-value bioproducts, mitigating pressure on natural resources while generating economic advantages (Xie, 2026; Advaitha et al., 2026; Cakmak et al., 2026).

The gut microbiota plays a pivotal role in regulating host metabolism, immune function, and energy homeostasis through the fermentation of dietary fibers into short-chain fatty acids (SCFAs), which enhance intestinal barrier integrity and modulate systemic inflammation (Fan & Pedersen, 2021). Disruption of mucosal integrity and translocation of bacterial endotoxins provide a mechanistic link between gut dysbiosis and obesity, type 2 diabetes, cardiovascular disease, and chronic inflammation, driving metabolic endotoxemia and insulin resistance. Through a variety of channels, the gut microbiota interacts with the host in both directions, and microbial metabolites have a direct impact on cardiovascular risk, obesity, and lipid metabolism (Van Hul et al., 2024). These interconnected pathways highlight the potential of prebiotics and other microbiome-targeted interventions as promising strategies for the prevention and management of metabolic diseases (Wang et al., 2025).

Prebiotics are defined as “substrates that are selectively utilized by host microorganisms conferring a health benefit” (Hutkins et al., 2025). Inulin, fructo-oligosaccharides (FOS), and galacto-oligosaccharides (GOS) are well-known prebiotics that support the growth of *Lactobacillus* and *Bifidobacterium* species. While terrestrial plants remain the primary source of conventional prebiotics, marine biomass and seafood processing by-products are gaining attention as sustainable alternative sources of structurally distinct oligosaccharides (Yun et al., 2026). Seafood processing by-products have shown promise as sustainable sources of prebiotic compounds. Chitin, chitosan, and chito-oligosaccharides (COS) from crustacean waste support beneficial microbes such as *Clostridium cluster* IV and *Bifidobacteriaceae*; waste-derived chitosan offers greater benefits than regular chitosan (Addazii et al., 2026). GAGs and protein hydrolysates derived from fish processing waste yield balanced SCFA profiles including 33-37% acetate, 29-36% propionate, and 34-36% butyrate during fermentation (Geetha et al., 2023). *Bacteroides, Bifidobacterium*, and *Lactobacillus* are stimulated by cellulose microparticles, ulvan, and agaro-oligosaccharides found in algal processing waste (Gotteland et al., 2020). Emerging sources like sea cucumber boiling liquid and swiftlet nest by-products have recently shown prebiotic promise through gut microbiota regulation (HuiYan et al., 2026; Sang et al., 2024).

The prebiotic activity of seafood-derived oligosaccharides is controlled by structural characteristics including degree of polymerization (DP), acetylation, molecular weight (Mw), and sulfation patterns. DP plays a key role in modulating the biological activity of chitosan derivatives, with low Mw-COS exhibiting prebiotic effects by stimulating the growth of lactic acid bacteria, whereas high Mw-COS and chitosan generally display antimicrobial activity through the inhibition of microbial growth (Ahn et al., 2014). Acetylation also regulates functionality: acetylated COS maintain prebiotic activity and promote beneficial bacteria; on the other hand, deacetylated COS exhibit antimicrobial properties through positive charge-mediated electrostatic interactions with bacterial cell surfaces (Mateos-Aparicio et al., 2016). For algal polysaccharides, higher sulfate content and lower Mw enhance fermentation and SCFA production (Karagöz et al., 2025). These structural features influence the fermentability, microbial accessibility, and metabolic effects of seafood-derived prebiotics. However, the extraction and purification processes that determine Mw, sulfation patterns, acetylation degree, and overall bioactivity are crucial to the recovery of bioactive compounds from seafood by-products (Rubak et al., 2026). Conventional chemical extraction methods often involve severe conditions that can induce depolymerization and desulfation. EAE (enzyme-assisted extraction) offers milder alternatives but presents mechanistic challenges such as enzyme competition and over-hydrolysis. Emerging technologies including UAE (ultrasound-assisted extraction), MAE (microwave-assisted extraction), and SWE (subcritical water extraction) provide rapid and solvent-minimized alternatives, although their processing conditions can differently affect molecular structure (Rout et al., 2025). Bioactivity is further influenced by purification methods, particularly membrane filtration and chromatography, with improved function not always correlating with higher purity (Li, Tang, et al., 2023).

Although the *in vivo* evidence is promising, several challenges remain in translating seafood-based prebiotics into clinical applications, including the lack of well-controlled human studies, inter-source and inter-population variability in efficacy, the lack of standardized extraction and characterization procedures, and limited industrial scalability. Previous reviews have addressed some of these aspects individually; however, the present review provides a critical and integrated synthesis linking seafood waste valorization, extraction and purification strategies, gut microbiota modulation mechanisms, metabolic health outcomes, and circular economy principles within a single framework. The aim is to address key challenges in the field by identifying major knowledge gaps, reconciling contradictory findings, and outlining the requirements for translation of seafood processing by-products into prebiotics supported by evidence for their potential use in sustainable gut health interventions.

2. Literature search methodology

An extensive and structured literature review was conducted to collect and analyze peer-reviewed literature on the valorization of seafood processing by-products, their prebiotic compounds, and the extraction and purification techniques used, as well as on the mechanisms by which these compounds modulate the gut microbiota and contribute to metabolic health. The literature search was conducted between January 2020 and January 2026 to identify recent mechanistic and translational studies, with additional seminal references from earlier years included to provide essential historical and foundational context, including the definition of prebiotics, key carbohydrate-active enzyme (CAZyme) families, and established structure-activity relationships for chitin and chitosan. Four main scientific databases, namely Scopus, Web of Science, PubMed, and Google Scholar, were used to retrieve the literature, and all were used to get a broad spectrum of multidisciplinary work in the fields of food science, nutrition, microbiology, biotechnology, and marine bioeconomy.

Eligible studies included original research articles, reviews, and meta-analyses published in peer-reviewed English-language journals that provided mechanistic, quantitative, or translational insights into the extraction, purification, structural characterization, gut microbiota modulation, or metabolic health outcomes of seafood-derived prebiotic compounds. Studies were excluded if they did not focus on seafood processing by-products or marine-derived sources, were published in languages other than English, consisted of conference abstracts, opinion pieces, or non-peer-reviewed reports, or lacked sufficient methodological detail or quantitative data.

Particular emphasis was dedicated to publications providing historical background and fundamental insights into the underlying mechanisms. The search strategy used included Boolean combinations of keywords related to the four themes: (i) seafood by-products (e.g., crustacean shell, fish waste, algal residues, sea cucumber cooking liquid, swiftlet nest by-products); (ii) prebiotic compounds (e.g., chitin, chitosan, COS, GAGs, ulvan, fucoidan, agaro-oligosaccharides, sialylated glycopeptides); (iii) extraction and purification technologies (e.g., conventional extraction, EAE, ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), subcritical water extraction (SWE), ultrafiltration (UF), chromatography); and (iv) gut microbiota modulation and metabolic health outcomes (e.g., SCFAs, gut barrier integrity, bacterial selectivity, tryptophan metabolism, anti-obesity, antidiabetic, cardioprotective, anti-inflammatory). These terms were combined to maximize literature retrieval. The initial search yielded 946 records. After removal of duplicates (n = 311), 635 records were screened by title and abstract. Of these, 441 full-text articles were assessed for eligibility, and 194 studies meeting the inclusion criteria were included in the final synthesis. Recent studies providing quantitative data, mechanistic insights, or translational relevance were prioritized to address the review's goals of identifying translational gaps, establishing mechanistic connections, and reconciling conflicting findings. The retrieved publications were screened by title, abstract, and full text for relevance. Given the interdisciplinary nature and the size and diversity of the literature in this area, the present study employs a structured narrative review approach rather than a systematic review or meta-analysis. The literature was critically synthesized to compare mechanistic evidence, areas of agreement and contradiction, current limitations, and opportunities for further research.

3. Seafood processing by-products: sources and prebiotic compounds

3.1. Crustacean processing waste

Crustacean processing waste, such as shrimp, crab, and lobster shells, is a significant but under-exploited chitin source, which is the second most abundant natural polysaccharide. Chitin can be deacetylated to chitosan, a more soluble derivative, which can be further depolymerized to COS through chemical or enzymatic hydrolysis (Ferri et al., 2025). Mw and degree of deacetylation (DD), which influence fermentability by bacterial CAZymes, play a key role in determining the prebiotic potential of these derivatives (Tao et al., 2026). While high-Mw chitosan shows decreased fermentability, low-Mw COS preferentially promotes *Lactobacillus acidophilus, Lacticaseibacillus casei*, and *Bifidobacterium bifidum* through improved enzymatic breakdown (Ahn et al., 2014; Kim et al., 2024).

The antimicrobial-prebiotic duality of chitosan derivatives has been associated with a DD threshold of approximately 85%. At high DD, the abundance of free amino groups imparts a strong positive surface charge, with zeta potential values ranging from +40 to +60 mV (Anusha & Fleming, 2016), enabling electrostatic interactions with negatively charged bacterial surfaces (Chen et al., 2010). This charge-mediated attraction disrupts membrane integrity, leading to cytoplasmic leakage and bactericidal effects (Kong et al., 2010; Kou et al., 2022). Conversely, at low DD, the reduced charge density diminishes membrane-disruptive activity, allowing bacterial CAZymes to access and hydrolyze chitosan chains more readily (Paudel et al., 2023; Zhang & Neau, 2001). Furthermore, DD determines the product profile of enzymatic hydrolysis: high-DD chitosan favors the formation of short fragments with limited prebiotic activity, whereas low-DD chitosan produces oligosaccharides with DP 2-6 that can serve as fermentable substrates for beneficial bacteria (Kim et al., 2024; Lee et al., 2002). Thus, the same structural feature regulates both the physico-chemical interaction and enzymatic availability of chitosan derivatives. Crustacean-derived chitin derivatives demonstrate prebiotic efficiency comparable to commercial prebiotics, supporting *Lactobacillus*, *Bifidobacterium*, and butyrate-producing *Roseburia* (Ferri et al., 2025).

3.2. Fish processing waste

Waste from fish processing represents a major overlooked source of bioactive compounds with prebiotic potential. These by-products contain valuable proteins and GAGs, which can be recovered as protein hydrolysates through chemical or enzymatic hydrolysis, as well as compounds such as hyaluronic acid and chondroitin sulfate (Olaniran et al., 2024). In addition to addressing environmental issues related to seafood industry waste, the valorization of fish processing waste offers a sustainable source of beneficial compounds for gut health applications (Rout et al., 2025). GAGs' prebiotic activity is derived from their uronic acid-rich backbone, which provides fermentable sites for gut bacteria equipped with polysaccharide lyases and glycosaminoglycan-degrading hydrolases (Ndeh et al., 2020; Overbeeke et al., 2022). Fish protein hydrolysates exert prebiotic effects through peptide sequences serving as nitrogen sources, with particular peptides possibly affecting bacterial quorum sensing and metabolic pathways. During *in vitro* fermentation with *L. plantarum* and *B. bifidum*, extracted GAGs from mackerel waste showed prebiotic action with SCFA production of about 33-37% for acetic acid, 29-36% for propionic acid, and 34-36% for butyric acid (Geetha et al., 2023). The butyrate-rich profile is functionally significant: butyrate fuels colonocytes and inhibits histone deacetylases (HDACs), thereby modulating host gene expression (Stilling et al., 2016). Fish protein hydrolysates similarly alter the gut microbiota composition through amino acid-derived metabolites, including branched-chain fatty acids and tryptophan catabolites that stimulate aryl hydrocarbon receptor (AhR) signaling (Lamminpää et al., 2024). Batch-to-batch variation in hydrolysate composition occurs by fish species, enzyme type, and hydrolysis conditions. This directly affects peptide bioactivity and requires standardized protocols for clinical translation. Nevertheless, fish processing by-products offer fermentable substrates that support healthy gut microbial ecosystems.

3.3. Algal processing residues

Algal processing residues represent an important source of insoluble fibers and bioactive oligosaccharides with prebiotic potential, as they are generated during the extraction of phycocolloids such as alginate, agar, and carrageenan. These wastes are particularly rich in cellulose, which can account for up to 42% of dealginated *Laminaria japonica* waste after agar extraction, and 40% of residual pulp from *Gracilaria verrucosa* biomass (Tang et al., 2024). Prebiotic activity is determined by residue composition: cellulose can serve as a fermentable substrate, whereas agaro-oligosaccharides and ulvan are degraded by bacterial enzymes, including agarases, ulvan lyases, and sulfatases (Gotteland et al., 2020; Zonfrillo et al., 2026).

Cellulose microparticles, made from dealginated seaweed waste, can alter the composition of the gut microbiota by stimulating populations of beneficial bacteria. This modulation involves a marked decrease in the Firmicutes/Bacteroidetes ratio and an increase in the production of SCFAs, indicative of a shift towards a healthier microbial profile. While a reduced F/B ratio was observed in association with these metabolic improvements, this single metric should be interpreted with caution. The F/B ratio is a controversial and context-dependent indicator that often fails to capture the functional complexity of the gut microbiome, and it cannot serve as a universal marker of health or prebiotic efficacy (Tang et al., 2024). Likewise, the agaro-oligosaccharides produced by red algae have a prebiotic effect by stimulating the growth of *Lactobacillus* and *Bifidobacterium*, as well as increasing the production of SCFAs (Kurasawa et al., 2026). The prebiotic properties of ulvan, a sulfated polysaccharide extracted from green macroalgae, have been demonstrated, with a positive impact on the growth of beneficial bacteria, such as *Lactobacillus* and *Bifidobacterium*. Nonetheless, its prebiotic activity

depends on sulfation patterns, as bacterial sulfatases can modulate ulvan desulfation and thereby subsequent degradation of the polysaccharide backbone (Yun et al., 2026; Zonfrillo et al., 2026).

Certain sulfation sites are crucial for bacterial sulfatases to recognize sulfated polysaccharides. Sulfatases have position-specific selectivity, with some enzymes exhibiting preferred activity toward C2-sulfated residues over C6-sulfated residues, as demonstrated by structural studies on fucoidan-degrading enzymes. PsFucS1, a fucoidan sulfatase from *Pseudoalteromonas sp.,* showed preferential docking to C2-sulfated fucobiose in its crystal structure, indicating that enzyme-substrate recognition is determined by the spatial arrangement of sulfate groups (Mikkelsen et al., 2021). Additionally, unlike glycoside hydrolases that act on neutral polysaccharides, the GH168 family of enzymes provides a unique identification mechanism for sulfated fucans with conserved active-site residues (Chen et al., 2025). This position-specific recognition highlights how the fine structure of marine polysaccharides controls their enzymatic degradation, with implications for their prebiotic activity.

3.4. Emerging by-product sources

Some new seafood by-products, such as cooking liquid from sea cucumber and waste from swiftlet nests, have been identified as potential sources of prebiotic compounds recently. The by-products of swiftlet nests contain abundant sialylated-mucin glycopeptides, which are resistant to gastric digestion (HuiYan et al., 2026); the cooking liquid of sea cucumber contains abundant sulfated polysaccharides with different monosaccharide compositions and sulfation patterns (Sang et al., 2024). The value of these streams to the gut microbiota is related to their structural composition, which may support the growth of beneficial bacteria with specific glycosidases; sulfated polysaccharides in sea cucumbers have a different monosaccharide profile and pattern of sulfation, which may influence fermentability by gut microbiota (HuiYan et al., 2026).

Sulfated polysaccharides, mainly fucosylated chondroitin sulfate (FCS) and sulfated fucan (SF), are present in sea cucumber cooking liquid. The repeated →4)-β-D-GlcA-(1 → 3)-β-D-GalNAc-(1→) units that make up FCS's chondroitin sulfate-like backbone include sulfated α-L-fucose branches connected to position three of the β-Residues of D-glucuronic acid (Ustyuzhanina et al., 2018, 2022). The fucose branches show a variety of sulfation sites and glycosidic links, with a majority of disaccharide units made up of 3,4-di-O-sulfo-α-L-fucopyranosyl units glycosidically linked by position 1 → 2 to 4-O-sulfo-α-L-fucopyranose (Felix et al., 2025). Sea cucumber sulfated fucans vary in the degree and location of sulfate substitution and have a typical tetrasaccharide repeat unit with 1→3-linked α-L-fucopyranose residues. Depending on the species and extraction techniques, the Mw of FCS normally ranges from 30 to 100 kDa.

The cooking liquid polysaccharides of sea cucumber reversed intestinal dysbiosis in mice induced by a high-fat diet (HFD) by enriching beneficial taxa and metabolites that were positively correlated with these bacteria. B cell receptor signaling, cytochrome P450 pathways, and amino acid metabolism were found to be associated with obesity prevention through transcriptome and metabolome integration (Sang et al., 2024). Sulfation patterns and monosaccharide composition may influence fermentability by particular bacterial sulfatases and glycosidases, and *Parabacteroides distasonis* is involved in the utilization of sulfated polysaccharides in sea cucumbers (Liu et al., 2023).

Sialylated-mucin (SiaMuc) glycoproteins, which are O-linked and N-linked glycoproteins high in sialic acid, are common in swiftlet nest by-products. Galβ (1-3) [GlcNAcβ (1-6)] is one of the basic monosialyl O-linked glycan structures. GalNAcα(1-3)GalNAc-ol, whereas the sequence Galβ1-4GlcNAcβ1-4 is present in N-linked glycans (Unal et al., 2024). Usually, galactose or N-acetylgalactosamine residues are connected to sialic acid through α2→3 or α2→6 glycosidic connections. EBN glycoproteins have Mw ranging from 42.0 to 148.8 kDa for glycoproteins and 21.1-254.3 kDa for proteins (Yan et al., 2021; You et al., 2015). Sialylated mucin glycopeptides from swiftlet nest by-products inhibited pathogenic *Clostridium* while promoting beneficial probiotics during *in vitro* human colonic fermentation. Both hydrolysates increased the production of SCFAs while reducing potentially hazardous branched-chain fatty acids (HuiYan et al., 2026). The effectiveness of prebiotics depends on sulfation patterns or glycan structure. In addition, edible bird's nest (EBN) by-product glycopeptides showed improved *L. plantarum* growth with >89% recovery (Noor et al., 2022).

3.5. CAZymes involved in seafood polysaccharide fermentation

A wide variety of CAZymes, arranged into specialized gene clusters called polysaccharide utilization loci (PULs), facilitate the gut microbiota's breakdown of polysaccharides obtained from seafood (Rüttiger et al., 2025). Several PULs are used by *Bacteroides thetaiotaomicron*, one of the human gut's most effective degraders of complex polysaccharides, to break down marine seaweed polysaccharides such as laminarin, fucoidan, sodium alginate, and *Pyropia haitanensis* polysaccharides (Yu et al., 2024). Effective oligosaccharide uptake and utilization are facilitated by the SusC/SusD transport systems, which enable the import of oligosaccharides generated during extracellular polysaccharide degradation (Pollet et al., 2021; Tauzin et al., 2016). The main degraders of macroalgal polysaccharides in marine herbivorous fish are *Bacteroidia* and *Clostridia*. *Alistipes* species are especially enriched in CAZyme gene clusters, suggesting an increased capacity to use macroalgal polysaccharides, such as alginate, laminarin, and sulfated polysaccharides (Facimoto et al., 2024). Few genomes have the necessary enzymes to completely break down any complex sulfated algal polysaccharide on its own, which is compatible with cooperative extracellular degradation in which several taxa contribute complementary CAZyme activity (Gotteland et al., 2020). GH20 β-N-acetylhexosaminidases produce N-acetylglucosamine monomers after bacterial GH18 and GH19 chitinases break β-1,4-glycosidic linkages to start depolymerization (Luo et al., 2024; Vera-Ponce de León et al., 2024). Sulfatases must work in conjunction to remove sulfate esters from sulfated polysaccharides like ulvan and fucoidan, and then GH and PL enzymes must break the glycosidic backbone (Adalsteinsson et al., 2025; Hettle et al., 2022). GH105 and PL families are engaged in ulvan degradation, whereas GH29 and GH95 are involved in fucoidan backbone degradation (Collén et al., 2014; Silchenko et al., 2022). GH16 (β-glucanases for laminarin), GH86 (β-agarases), and PL6, PL7, PL17, and PL18 (alginate lyases) are important CAZyme families for algal polysaccharides (Kabisch et al., 2014; Koch et al., 2019). PL8, PL12, PL29, and GH84 are involved in the breakdown of GAGs derived from fish waste (Ndeh et al., 2018). The distribution of CAZymes in the gut microbiota varies among bacterial phyla: *Clostridia* mainly contribute to the utilization of brown algae, whereas Bacteroidia dominate the degradation of macroalgal polysaccharides. This functional diversity enables the gut microbiota to adapt and utilize a wide range of dietary polysaccharides.

Seafood-derived polysaccharides are fermented by cooperative cross-feeding interactions between primary degraders and secondary fermenters rather than by a single bacterial species. Complex non-digestible carbohydrates are primarily broken down by Bacteroides species, producing oligosaccharides that are then broken down by secondary fermenters like *Bifidobacterium* (Fernandez-Julia et al., 2022). Although some gut bacteria have the complete enzymatic machinery for the degradation of complex polysaccharides, complete utilization of these substrates can involve cross-feeding between primary degraders and secondary fermenters. This cooperative metabolism facilitates the conversion of complex glycans into beneficial metabolites, such as SCFAs and tryptophan-derived compounds. As seen during ulvan fermentation, this cooperative network also produces IPA and IAA by cross-feeding between saccharolytic and indole-producing taxa (Zonfrillo et al., 2026).

In conclusion, by-products of seafood processing provide a variety of prebiotic compounds with functions that depend on their structure. Crustacean-derived chitin/chitosan activity is influenced by Mw and DD; fish-derived GAGs and protein hydrolysates produce distinct SCFA profiles; algal residues provide cellulose, agaro-oligosaccharides, and ulvan, whose degradation involves agarases, ulvan lyases, and sulfatases; and emerging sources provide additional sulfated polysaccharides and sialylated glycopeptides. The major CAZyme families involved in the depolymerization of seafood-derived polysaccharides, along with their associated bacterial genera and mechanistic steps, are summarized in Table 1. Table 2 summarizes structural features, bacterial targets, enzymatic mechanisms, SCFA profiles, host signaling pathways, functional outcomes, and model systems for seafood-derived prebiotic compounds. Seafood processing by-products from crustacean, fish, algal, and emerging sources yield diverse prebiotic compounds with gut-modulating potential, as illustrated in Fig. 1.

4. Extraction and purification process

4.1. Conventional extraction methods

Conventional extraction approaches for recovering polysaccharides and bioactive compounds from seafood by-products often rely on sequential chemical treatments. In crustacean shells, chitin is typically isolated through alkaline deproteinization followed by acid demineralization, while alkaline deacetylation converts the chitin into chitosan (Ahmed et al., 2026). For algal biomass, hot water extraction remains a widely used method for recovering polysaccharides. For example, *Ulva papenfussii* yielded 29% ulvan with a sulfate content of 50% when extracted in water at 80°C for 6 h. In contrast, alkaline extraction resulted in lower yields and reduced sulfate content (Gonzales et al., 2025). Sulfate content is mechanistically critical, as it determines recognition by bacterial sulfatases and subsequent fermentability. The pH-shift approach enables the sequential recovery of proteins and sulfated polysaccharides from fish by-products, with alkaline processing achieving almost twice the polysaccharide recovery obtained through acid processing (Naghdi et al., 2025a).

Nevertheless, these chemical processes have limitations that directly affect the bioactivity of prebiotics. Sulfate ester linkages are broken by acid-catalyzed hydrolysis, reducing the sulfate concentration from 50% to 15-20%. This severely prevents recognition by bacterial sulfatases and ulvan lyases, resulting in a 40% reduction in fermentation efficiency (Gotteland et al., 2020). Similarly, high-alkaline conditions cause β-elimination of glycosidic bonds, reducing Mw from >50 kDa to <10 kDa. Although lower Mw generally improves fermentability, excessive depolymerization results in oligosaccharides with DP < 3 that are too short for bacterial GH18/GH19 chitinase recognition and transporter uptake, which paradoxically reduces prebiotic activity despite improved solubility (Lamarque et al., 2004; Monge & Gardner, 2021). The pH-shift method has additional trade-offs: acid processing better preserves native structure but produces lower recovery, whereas alkaline processing increases polysaccharide recovery but deacetylates GAGs, changing their uronic acid-rich backbone and decreasing recognition by polysaccharide lyases (Naghdi et al., 2025a, 2025b).

Gut microbiota interactions are significantly impacted by these extraction-induced structural changes. Gastrointestinal resistance is affected by decreased crystallinity and Mw, which restricts the intestinal transport of intact polysaccharides. Contradictory results of chitosan activity can be explained by the simultaneous generation of prebiotic and antibacterial fractions from broad DP distributions from conventional extraction (Ahn et al., 2014; Mateos-Aparicio et al., 2016). Because bacterial sulfatases are unable to identify desulfated substrates, desulfation lowers the production of SCFAs (Zonfrillo et al., 2026). Prebiotic efficacy varies from batch to batch due to variations in Mw and sulfation patterns, and the disposal of chemical waste poses environmental issues that go against the concepts of the circular economy. Therefore, even if traditional approaches provide well-established procedures, their extreme conditions result in structural alterations that essentially influence gut microbiota modulation, pressing for a change to more moderate approaches.

4.2. Enzyme-assisted extraction (EAE)

EAE represents a selective and environmentally benign alternative that preserves the structural integrity and bioactivity of prebiotic compounds. By breaking down the cell wall matrix enzymatically, EAE improves recovery and increases access to intracellular bioactive compounds. This has been demonstrated to have a major impact on prebiotic potential since the content and fermentability of seaweed extracts are affected by various extraction techniques (Charoensiddhi et al., 2016). For instance, EAE of ulvan from *Ulva lactuca* produced a yield of 29.85% as opposed to 12.22% using non-enzymatic techniques; enzymatic extracts showed better prebiotic action. EAE generated larger quantities of polysaccharide, reducing sugar, and uronic acid, while non-enzymatic extraction maintained higher sulfate content. This suggests that better bioactivity is driven by improved substrate accessibility rather than native structure preservation.

However, EAE efficacy is not uniform. Although multienzyme systems are expected to enhance polysaccharide release through complementary catalytic activities, a combination of cellulase, pectinase, and protease did not improve ulvan extraction compared with cellulase alone. This unexpected finding may result from enzyme competition, substrate preference, or excessive hydrolysis. The observation that a multienzyme system failed to outperform cellulase alone represents a significant mechanistic finding with important implications for process optimization (Rubak et al., 2026). Several interrelated mechanisms may explain this counterintuitive outcome. Enzyme competition for overlapping substrate binding sites within the Ulva cell wall matrix can reduce the effective concentration of each enzyme, as multiple enzymes may target similar polysaccharide structures within the complex cell

Table 1
Key CAZyme families in seafood polysaccharide fermentation.

Polysaccharide	CAZyme families	Bacterial genera	Mechanism	References
Chitin/Chitosan	GH18, GH19, GH20, AA10	*Bacteroides*, Enterobacterales, Lactobacillales	Hydrolytic and oxidative depolymerization	Paudel et al. (2023)
Fucoidan	GH29, GH95; Sulfatases (S1 families)	*Bacteroides*, *Alistipes*, *Pseudoalteromonas*	Desulfation → glycosidic cleavage	(Gotteland et al., 2020; Silchenko et al., 2022)
Ulvan	GH105, PL families; Sulfatases	*Bacteroides*, *Alistipes*	Desulfation → lyase cleavage	(Collén et al., 2014; Gotteland et al., 2020)
Alginate	PL6, PL7, PL17, PL18	*Alistipes*, Bacteroidia	β-elimination cleavage	Koch et al. (2019)
Laminarin	GH16 (β-glucanases)	Bacteroidia, Clostridia	Endo-β-glucanase cleavage	Kabisch et al. (2014)
Agarose	GH86 (β-agarases)	*Alistipes*, Bacteroidia	Endo-β-agarase cleavage	Kabisch et al. (2014)
Carrageenan	GH16_13 (κ), GH150 (λ)	*Alistipes* clades C2 and C4	Endo-carrageenase cleavage	Facimoto et al. (2024)
Glycosaminoglycans	PL8, PL12, PL29, GH84	*Bacteroides*	Lyase and hydrolase cleavage	Ndeh et al. (2018)

Abbreviations: AA: Auxiliary Activity, CAZymes: Carbohydrate-Active Enzymes, GH: Glycoside Hydrolase, PL: Polysaccharide Lyase, S1: Sulfatase Family 1, κ: kappa-carrageenan, λ: lambda-carrageenan.

Table 2
Structural features, bacterial targets, enzymatic mechanisms, SCFA profiles, host signaling pathways, functional outcomes, and model systems for seafood-derived prebiotic compounds.

Prebiotic compound	Source	Key structural features	Bacterial targets	Mechanism	SCFA production (mmol/L)	bioactivity	References
Chitosan	Crustacean shells	Mw: >50 kDa; DD: >85%	Inhibits: *Bifidobacterium*, *Roseburia*, *Bacteroides*	Electrostatic; no CAZymes	↓ SCFA (0.5–1.2)	Antimicrobial	Mateos-Aparicio et al. (2016)
COS	Crustacean shells	Mw: 1-3 kDa; DP: 2-6; DD: 30-50%	Promotes: *Lactobacillus* (↑2.5 log), *Bifidobacterium* (↑2.0 log)	GH18/GH19 chitinases; transporters	15.2 ± 2.1	Anti-obesity; antidiabetic	Kim et al. (2024)
COS	Crustacean shells	Mw: 10-50 kDa; DP: >10; DD: >85%	Inhibits: LAB (↓1.5 log)	Electrostatic; membrane disruption	4.5 ± 0.8	Antibacterial	Ahn et al. (2014)
COS (Acetylated)	Crustacean shells	Acetylation: >50%; Mw: 3-5 kDa	Maintains: *Lactobacillus*/*Enterococcus*	Reduced positive charge; CAZymes	10.3 ± 1.5	Prebiotic; maintains microbiota	Mateos-Aparicio et al. (2016)
Ulvan	*Ulva lactuca*	Sulfate: 15-25%; Mw: 10-50 kDa	↑ *Bifidobacterium* (↑1.8 log), *Lactobacillus* (↑1.5 log)	Sulfatases; ulvan lyases	18.7 ± 2.3	Immunomodulatory; IPA/IAA	Zonfrillo et al. (2026)
Agaro-oligosaccharides	Red algae	DP: 2-8; sulfate: 5-10%	↑ *L. acidophilus* (↑2.0 log), *Bifidobacterium*	Agarases	20.5 ± 1.8	Prebiotic > inulin	Gomes-Dias et al. (2026)
Cellulose microparticles	Algal residues	Crystallinity: 85.51%; size: 10-50 μm	↑ *Akkermansia* (↑2.0 log), *Lactobacillus*	Cellulases	22.3 ± 2.5	Hypolipidemic; ↓F/B ratio	Tang et al. (2024)
Sea cucumber polysaccharides	Cooking liquid	Sulfate: 20-30%; Mw: 15-30 kDa	↑ *Akkermansia*; ↓ F/B ratio	Sulfatases; glycosidases	16.5 ± 1.9	Anti-obesity; hepatoprotective	Sang et al. (2024)

Abbreviations: CAZymes: Carbohydrate-Active Enzymes, COS: Chito-oligosaccharides, DD: Degree of Deacetylation, DP: Degree of Polymerization, F/B ratio: Firmicutes/Bacteroidetes ratio, GH: Glycoside Hydrolase, IAA: Indole-3-acetic acid, IPA: Indole-3-propionic acid, LAB: Lactic Acid Bacteria, Mw: Molecular Weight, SCFA: Short-Chain Fatty Acid.

wall network (Charoensiddhi et al., 2016). pH incompatibility between enzymes can compromise overall activity, as each enzyme has distinct optimal pH ranges; cellulase functions optimally at acidic pH (4.5-5.5), pectinase at pH 4.0-5.0, protease at pH 6.0-8.0, and the working pH of the extraction system may not simultaneously satisfy all enzyme requirements (Pinheiro et al., 2021). Product inhibition may also occur when the oligosaccharides released by one enzyme inhibit the activity of another enzyme in the cocktail (Egharevba et al., 2025). Several strategies should be taken into consideration in order to maximize the performance of the enzyme cocktail for the extraction of seafood polysaccharides. By enabling each enzyme to function on its particular substrate at its ideal pH and temperature before the next enzyme is added, sequential enzyme addition can reduce competition (Cheng et al., 2009; Zhao et al., 2007). The ideal ratios of each enzyme in the cocktail can be found using RSM or design of experiments (DoE), which maximizes synergistic interactions while reducing competitive inhibition. Pre-treatment of the substrate, such as gentle mechanical or thermal disturbance, can improve substrate accessibility and lower the amount of enzyme needed for efficient extraction (Nawawi et al., 2022). High enzymatic activity may generate oligosaccharides below the optimal DP range required for bacterial CAZyme recognition and transporter uptake, thereby reducing both recovery yields and potentially prebiotic activity (Rubak et al., 2026). This mechanistic trade-off directly impacts interactions between gut microbiota. Excessive enzymatic activity that results in DP < 3 fragments restricts CAZyme recognition, reducing the supply of fermentable substrate and perhaps preventing prebiotic activity (Mateos-Aparicio et al., 2016). While decreased bioactivity indicates that substrate accessibility to bacterial enzyme binding is more important for prebiotic activity than structural preservation alone, the higher sulfate content in non-enzymatic extracts suggests preservation of native structure (Rubak et al., 2026). Gut microbiota outcomes are determined by structural traits that are shaped by EAE. While reducing antibacterial fractions, optimal DP specifically promotes *Lactobacillus* and *Bifidobacterium*. Preservation of sulfate groups maintains recognition sites for bacterial sulfatases, potentially enhancing fermentation and SCFA production. On the other hand, excessive hydrolysis may reduce DP below the optimal range required for bacterial recognition and utilization. Additionally, EAE efficiency depends on the biomass source, as different seaweed species and by-product types exhibit distinct cell wall compositions, requiring tailored enzyme formulations (Charoensiddhi et al., 2016).

4.3. Emerging technologies

Among emerging extraction technologies, SWE, MAE, and UAE provide rapid, solvent-minimized alternatives with improved recovery yields while preserving bioactivity. UAE employs sound waves to create cavitation, breaking down cell walls and enhancing solvent penetration, while MAE exploits dielectric heating to disrupt cell structures, enhancing the release of intracellular compounds (Shehzadi et al., 2025). SWE employs pressurized hot water to modify the dielectric constant of water, enabling efficient extraction without organic solvents. According to comparative studies, SWE demonstrates superior performance compared with other extraction techniques. For example, from *Sargassum ilicifolium*, SWE achieved a yield of 7.86% compared to 6.60% for MAE and 5.97% for conventional extraction. Fucoidans extracted using SWE had the highest sulfate content, the smallest Mw, and superior antimicrobial, antiviral, and anticancer activities, all of which are attributed to the enhanced sulfate and total phenol content preserved under subcritical conditions (Bahrami et al., 2025). Similarly, SWE yielded 13.15% fucoidan from *Nizamuddinia zanardinii*, whereas UAE achieved 3.6% (Alboofetileh et al., 2019).

However, a combination of SWE and mild electric fields improved ulvan extraction efficiency while preserving inherent polysaccharide characteristics and lowering Mw to 92 kDa (Pereira et al., 2025). Emerging technologies, however, have opposing effects on molecular

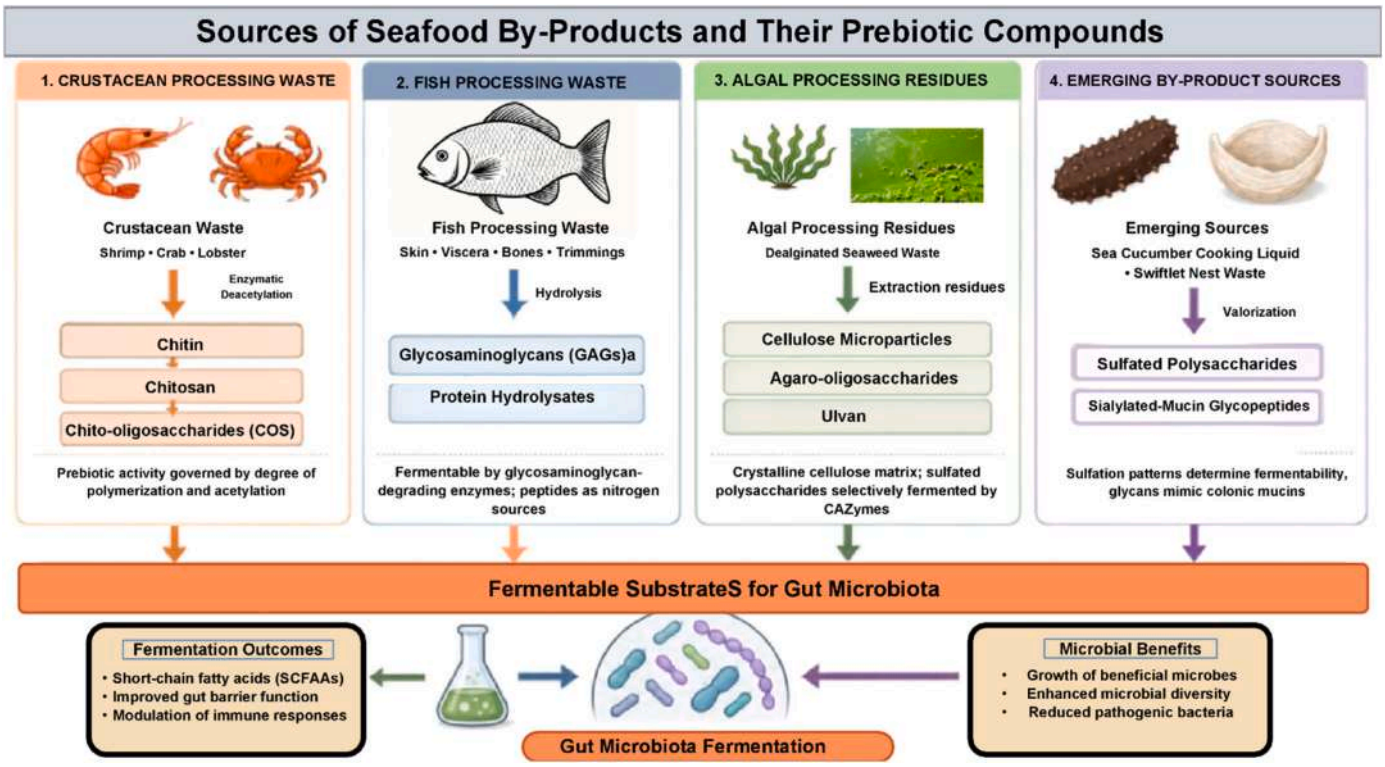


Fig. 1. Sources of seafood processing by-products and their prebiotic compounds, illustrating crustacean shells, fish waste, algal residues, and emerging sources and their derived prebiotic compounds.

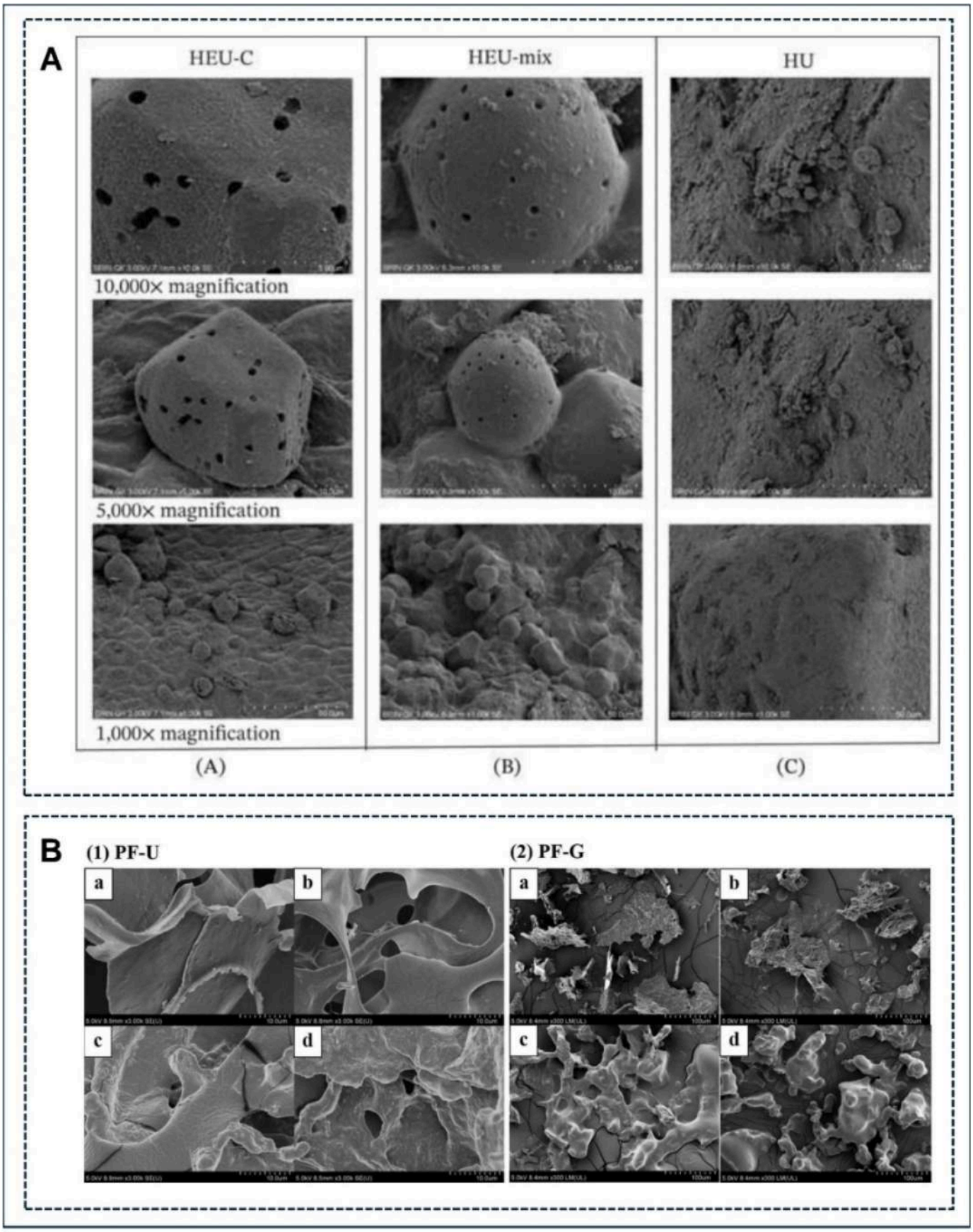
structure that have a significant impact on prebiotic function. Due to partial hydrolysis, MAE and SWE frequently create smaller Mw polysaccharides, which can improve fermentability by increasing bacterial CAZymes accessibility (Bahrami et al., 2025). It is important to underline that increased solubilization can release non-prebiotic components or produce fragments too short for bacterial identification; therefore, higher yield does not always equate to better prebiotic efficacy (Teixeira-Guedes et al., 2023). Similarly, decreased Mw can improve fermentability by making CAZymes more accessible. However, excessive degradation results in oligosaccharides with DP below the bacterial transporters' recognition threshold, which paradoxically reduces prebiotic activity. Additionally, prebiotic functionality is mechanistically different from antibacterial, antiviral, or anticancer capabilities, which are indicative of bioactivity but require selective use by beneficial gut microorganisms to provide health benefits. Therefore, rather than being inferred from other biological activities or yield alone, prebiotic activity should be precisely assessed using validated assays that measure the selective stimulation of beneficial bacteria and the synthesis of health-relevant compounds (Zhang et al., 2018).

On the other hand, UAE frequently produces greater Mw fractions that might be less fermentable (Yin et al., 2021). This leads to a mechanistic paradox: excessive depolymerization during SWE at higher temperatures may negatively impact structural integrity and bioactivity, whereas reduced Mw normally enhances prebiotic activity through enhanced substrate accessibility. The results of gut microbiota are directly impacted by these structural changes. By making bacterial GH families and oligosaccharide transporters more accessible, lower Mw polysaccharides from MAE and SWE improve fermentability (Li et al., 2022). Nevertheless, CAZyme identification is restricted by excessive depolymerization that produces fragments below the DP threshold for bacterial recognition, which lowers SCFAs synthesis and prebiotic efficiency (Ji et al., 2022). On the other hand, because of decreased substrate accessibility, UAE-generated greater Mw fractions may restrict fermentability while maintaining native structure. Additionally, while maintaining intrinsic polysaccharide properties and reducing Mw to 92 kDa, the combination of SWE and mild electric fields increased ulvan extraction efficiency by 9-17% (Pereira et al., 2025).

Rubak et al. (2026) used SEM analysis to compare different extraction technologies and demonstrated that each method produced distinct surface morphologies, with enzymatic treatments generating more porous structures. The resistance of seafood-derived polysaccharides to upper gastrointestinal digestion is essential for their prebiotic function, as shown in Fig. 2. Surface morphology is greatly influenced by extraction techniques, as shown in Fig. 2 (Panel A). Enzyme-assisted treatments result in more porous structures that improve fermentability. Through simulated oral, gastric, and intestinal phases, Fig. 2 (Panel B) shows that polysaccharide-enriched extracts from Ulva rigida and *Gracilaria fisheri* preserve structural integrity, confirming their resistance to digestion and ensuring colonic delivery for fermentation by gut microbiota (Charoensiddhi et al., 2022). When compared to non-enzymatic extraction, the HEU-C (cellulase-assisted ultrasonication) method produced the highest ulvan yield. Enzymatic extracts showed better prebiotic activity, whereas non-enzymatic extracts maintained the highest sulfate level. This suggests that substrate accessibility for bacterial enzyme binding is more important for prebiotic activity than native structure retention alone. These results highlight the need for extraction method selection to maintain a balance between Mw preservation and yield maximization, since effective prebiotic activity requires retaining significant chain length for microbial fermentation while ensuring appropriate solubility and accessibility. The key process parameters, structural outcomes, and functional properties of each extraction technology are compared in Table 3.

4.4. *Purification techniques*

Purification is a critical step in the recovery of seafood-derived prebiotic compounds, as co-extracted impurities, including proteins, salts, polyphenols, and low-Mw chemicals, can affect their bioactivity



(caption on next page)

Fig. 2. Structural characterization and gastrointestinal digestibility of seaweed-derived polysaccharides from processing residues. **(A)** Scanning electron micrographs of *Ulva lactuca* polysaccharides showing surface morphology differences among extraction treatments: HEU-C (mild hydrothermal-enzymatic with cellulase-ultrasonication), HEU-Mix (mild hydrothermal-enzymatic with cellulase–pectinase-protease–ultrasonication), and HU (mild hydrothermal-ultrasonication without enzymes). Surface morphology varied with extraction methods, with enzymatic treatments producing more porous structures. Reproduced from Rubak et al. (2026) under the terms of Creative Commons Attribution (CC BY 4.0) License. **(B)** Gastrointestinal digestibility of polysaccharide-enriched extracts from *Ulva rigida* (PF-U, 3000×) and *Gracilaria fisheri* (PF-G, 300×) showing morphological changes after passage through simulated oral (b), gastric (c), and intestinal (d) phases compared to undigested samples (a), Reproduced from Charoensiddhi et al. (2022) under the terms of Creative Commons Attribution (CC BY 4.0) License.

Table 3
Comparison of extraction technologies for seafood-derived prebiotic compounds: process parameters, structural outcomes, and functional properties.

Parameters	Conventional	EAE	UAE	MAE	SWE
Temperature (°C)	60-100	40-60	25-50	60-150	100-180
Time (h)	4-24	2-12	0.5-2	0.1-1	0.1-0.5
Solvent	Acid/alkali; hot water	Aqueous buffer	Water; ethanol	Water; ethanol	Water only
Polysaccharide yield (%)	5-30	20-45	15-40	20-50	25-60
Ulvan yield (%)	12.22	29.85	-	-	-
Fucoidan yield (%)	5.97	-	3.6	6.60	7.86
Mw	↓↓ (>50→<10 kDa)	Moderate	Variable (higher)	↓ (partial)	↓↓
Sulfation	↓↓ (50 → 15-20%)	Preserved	Preserved	↓ (high T)	↓ (high T)
DP range	Broad (DP < 3−>10)	Optimal (DP 2-6)	Higher DP	Lower DP	Lower DP
Prebiotic activity	Moderate	High	Moderate	Moderate	High
CAZymes accessibility	↓ (DP < 3)	↑↑ (DP 2-6)	Limited	↑	↑
Scalability	High	Moderate	High	High	Moderate
Green score	Poor	Good	Very good	Very good	Excellent
References	(Gotteland et al., 2020; Naghdi et al., 2025a; Rubak et al., 2026)	(Charoensiddhi et al., 2016; Rubak et al., 2026)	(Shehzadi et al., 2025; Yin et al., 2021)	Bahrami et al. (2025)	(Bahrami et al., 2025; Pereira et al., 2025)

Abbreviations: CAZymes: Carbohydrate-Active Enzymes, DD: Degree of Deacetylation, DP: Degree of Polymerization, EAE: Enzyme-Assisted Extraction, MAE: Microwave-Assisted Extraction, Mw: Molecular Weight, SWE: Subcritical Water Extraction, UAE: Ultrasound-Assisted Extraction, UF: Ultrafiltration.

and functional consistency. Polysaccharides and GAGs are frequently fractionated by Mw using membrane filtration, especially UF. Sequential UF using 10, 3, and 1 kDa membranes allowed for selective fractionation, with the 3 kDa retentate recovering 93.51% of ulvan precipitate. Dialysis of ulvan extracts produced carbohydrate content up to 55.34% and sulfate level up to 21% (Baltrusch et al., 2024). Although membrane fouling and concentration polarization ultimately decreased permeate flux, UF successfully separated glucosamine from low-molecular-weight chitosan for chitosan hydrolysis products (Rokhati et al., 2020). Ion-exchange and size-exclusion chromatographic techniques yield greater purity for agaro-oligosaccharides and sulfated polysaccharides, with neoagaro-oligosaccharide purities exceeding 97% (Li, Tang, et al., 2023; Lin et al., 2018). However, chromatographic procedures are time-consuming, expensive, and less scalable, whereas membrane technologies suffer from fouling and loss of low-molecular-weight bioactive fractions (Rokhati et al., 2020).

These purification methods involve key mechanistic trade-offs that directly influence their effect on gut microbiota. By separating polysaccharides according to Mw, membrane filtration generates fractions with distinct DP values, which can differentially influence bacterial selectivity. While intermediate fractions with DP 4-10 offer the best fermentable substrates for CAZymes identification and SCFAs synthesis, high-Mw fractions may show antibacterial activity against beneficial bacteria (Ahn et al., 2014; Wu et al., 2023). On the other hand, low-Mw fractions can limit the effectiveness of prebiotics by decreasing below the DP threshold for bacterial transporter uptake (Hou et al., 2022; Monge & Gardner, 2021).

The purity-bioactivity paradox represents a fundamental challenge in the development of seafood-derived prebiotic compounds. Since purification may partially remove associated proteins, polyphenols, or sulfate groups that contribute to synergistic effects, increased purity does not necessarily translate into enhanced prebiotic bioactivity. For example, when sulfate groups are removed during purification, bacterial sulfatases may have reduced ability to recognize and degrade these structures, which limits the fermentation of fucoidan and ulvan and the subsequent SCFAs production (Gotteland et al., 2020; Liu et al., 2024, 2025). Similarly, the loss of protein-polysaccharide complexes might affect colonic delivery by reducing the structural integrity needed for GI resistance. This is in line with research showing that crude extracts frequently have more prebiotic activity than highly purified fractions, indicating that overall bioactivity is influenced by the complex matrix of related compounds (Tao et al., 2026).

In another example, Karuppusamy et al. (2024) reported that crude laminarin and fucoidan extracts from brown macroalgae exhibited significantly higher antioxidant activity than purified samples and commercial standards, while also showing stronger anti-inflammatory and antidiabetic effects. Similarly, Rubak et al. (2026) demonstrated that while non-enzymatic ulvan extracts retained higher sulfate content than enzymatic extracts, the enzymatic extracts exhibited superior prebiotic activity, suggesting that substrate accessibility, rather than structural preservation alone, is more critical for bioactivity. The synergistic interactions of co-extracted chemicals provide the molecular foundation for higher efficacy of crude extracts. Through a variety of complementary processes, proteins, polyphenols, and other co-extracted biomolecules may enhance prebiotic action. By directly altering the composition of the gut microbiota, polyphenols can increase the number of taxa that produce SCFAs (Cheng et al., 2023). Protein-polysaccharide complexes may enhance GI resistance and colonic delivery by protecting polysaccharides from enzymatic degradation (Tao et al., 2026). Co-extracted phenolic chemicals have the potential to function as electron donors, increasing the antioxidant activity of the extracts and lowering oxidative stress in the gut environment (Zeng et al., 2019). Additionally, the combined effects of polysaccharides and polyphenols can enhance SCFA production more than either component alone. (Maiuolo et al., 2024).

The idea of “optimal purity windows”, a purity range that maximizes bioactivity rather than maximal purity, is supported by these findings. According to this concept, bioactivity exhibits a biphasic response, whereby the initial removal of contaminants enhances activity, while excessive purification may reduce efficacy through the loss of synergistic co-factors. The ideal purity window creates a balance between eliminating contaminants and protecting bioactive co-factors. Manufacturers

should aim for a degree of functional purity that preserves the complex matrix underlying enhanced bioactivity, given its significant industrial implications. From a translational standpoint, clinical efficacy and batch-to-batch uniformity are determined by the purification process selected. Scalability is provided by membrane filtration, but fouling may cause Mw distribution fluctuations. Although chromatography offers greater purity, it is less practical for large-scale manufacturing (Luiz-Santos et al., 2020). The structural characteristics necessary for the best regulation of the gut microbiota must be evaluated against these trade-offs. Therefore, rather than just maximizing purity, purifying procedures should be developed to maintain the structural features that control prebiotic activity.

In conclusion, the structural integrity and prebiotic bioactivity of compounds obtained from seafood are significantly determined by extraction and purification. The need for balanced, structure-guided process optimization in prebiotic production is highlighted by contradictions such as multienzyme underperformance, the Mw-dependent fermentability paradox, and the purity-bioactivity disconnect. Conventional, enzymatic, and emerging technologies all present trade-offs between yield and structural preservation.

5. Gut microbiota modulation by by-product-derived prebiotics

5.1. Resistance to upper gastrointestinal digestion

The ability of seafood-derived polysaccharides to remain stable under the harsh conditions of the upper gastrointestinal tract is essential for their prebiotic function. Their chemical structure determines their susceptibility to acidic environments and digestive enzymes. Charoensiddhi et al. (2022) used *Ulva rigida* and *Gracilaria fisheri* to obtain polysaccharide-enriched extracts. They showed that these extracts were resistant to digestion because small intestinal enzymes could not break them down. Compared to the control, the extracts significantly improved total SCFA synthesis after 24 h of *in vitro* fermentation. PF-G promoted beneficial bacteria like *Roseburia* and *Faecalibacterium* and produced butyric acid at a rate similar to that of inulin. Similarly, ulvan oligosaccharides (UOS), which are produced by the enzymatic hydrolysis of *Ulva rigida* polysaccharides, also protect probiotic bacteria. As a result, the bacteria are now more resilient in acidic environments and when α-amylase is present (Krangkratok et al., 2023).

From the dealginated remains of giant kelp, Tang et al. (2024) separated highly crystalline cellulose microparticles. Colonic transport is ensured by the high crystallinity, which restricts enzymatic breakdown. The Firmicutes to Bacteroidetes ratio was significantly reduced, and the relative abundance of *Lactobacillus*, *Bifidobacterium*, and *Akkermansia* was significantly enhanced when SC was given to HFSD-fed mice at a dose of 500 mg/kg BW/day for six weeks. The quantities of total SCFAs, acetate, propionate, and butyrate in the rectal contents increased significantly as a result. This demonstrates that highly crystalline cellulose microparticles can reduce HFSD-induced metabolic syndrome in mice and regulate gut microbiota dysbiosis. Additionally, the prebiotic benefits of cellulose as an insoluble dietary fiber may be significantly influenced by particle size. However, structural characteristics and processing techniques affect the degree of GI resistance, which varies across molecules produced from by-products. Particle size can affect these compounds' fermentability and, thus, their prebiotic potential, even though crystalline cellulose from seaweed waste exhibits high resistance due to its crystallinity. This has significant effects on how seaweed processing leftovers are valued. While direct study on dealginated waste is limited, research on ulvan extracted from whole *U. rigida* provides mechanistic insight, confirming its high resistance to gastric and intestinal juice hydrolysis (Kansandee et al., 2024). Cellulose's 85.51% crystallinity is mechanistically crucial because it limits the surface area available for cellulase binding, which slows down degradation and ensures colonic delivery (Lehocký, 2026). Particularly, chitosan derived from seafood waste has demonstrated varying biological and functional effects based on its Mw, particle size, and DD (Addazii et al., 2026). The balance between crystalline domains and amorphous regions, which vary depending on the source and extraction technique, is the cause of this heterogeneity.

5.2. Selective stimulation of beneficial bacteria

Studies using direct fermentation have shown that by-products of seafood processing specifically support gut bacteria that are favorable to health, such as *Bifidobacterium, Lactobacillus*, and *Akkermansia*. However, structural characteristics that are directly influenced by extraction techniques have a significant impact on selectivity. While EAE produces the best DP for the selective growth of beneficial bacteria, conventional extraction produces both prebiotic and antimicrobial portions. While UAE yields greater Mw fractions that can restrict fermentability, SWE and MAE improve CAZymes accessibility through reduced Mw. The varying bacterial selectivity observed in various studies can be explained by these extraction-dependent variations. The molecular basis of this selectivity lies in specialized transport systems that are predominantly found in beneficial Bacteroidetes and are less common in most enteropathogens.

PULs, co-regulated gene clusters expressing proteins necessary for the detection, binding, breakdown, and import of particular complex carbohydrates, are responsible for glycan utilization in Gram-negative beneficial Bacteroidetes (Grondin et al., 2017). The sus (starch utilization system) locus of *Bacteroides thetaiotaomicron*, which encodes genes for proteins that regulate the full breakdown of starch, is the prototypical PUL (Foley et al., 2016). Over 100 SusCD pairs are encoded by numerous sequenced intestinal Bacteroides species, each of which is likely unique to a particular glycan substrate (Foley et al., 2016; Glenwright et al., 2017). The SusC/D transporter complex is the functional center of PUL-mediated glycan consumption. SusD is a surface-exposed lipoprotein that binds oligosaccharide substrates with great selectivity, while SusC is a TonB-dependent transporter that forms a β-barrel porin in the outer membrane (Bolam & Koropatkin, 2012; Foley et al., 2016). In Gram-positive beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*, PUL variants have been identified, which incorporate ATP-binding cassette (ABC) transporters rather than the TonB-dependent systems of Gram-negative organisms (Glowacki & Martens, 2020; Sheridan et al., 2016). These PULs typically consist of ABC transport proteins, transcriptional regulators, and glycoside hydrolases, with solute-binding proteins that exhibit broad specificity for oligosaccharides (Glowacki & Martens, 2020).

According to Geetha et al. (2023), viable counts increased from 8 to 12 log CFU mL^{-1} over 48 h when *L. plantarum* and *B. bifidum* used GAGs isolated from mackerel fish waste as a fermentable substrate. Chitosan made from seafood waste demonstrated more prebiotic effects than normal chitosan, suggesting that the structural features of waste-derived chitosan promoted *Bifidobacteriaceae* and *Clostridium* cluster IV (Addazii et al., 2026). In the same way, Kim et al. (2024) found that mealworm-derived chitosan oligosaccharides (MCOS) containing DP 2-6 considerably increased the development of *B. bifidum, L. acidophilus*, and *L. casei* in a concentration-dependent way. Mechanistically, bacterial CAZymes may more easily access lower Mw oligosaccharides, which speeds up the breakage of glycosidic bonds and the release of monosaccharides (Lee, 2008).

Shrimp waste chitin oligosaccharides selectively increased beneficial enteric bacteria but did not stimulate enteropathogens such as *S. enterica* and *E. coli*. This selection effect most likely derives from differences in carbohydrate transport systems: enteropathogens generally lack the specialized SusC/D-like transport systems and associated glycan-degrading enzymes encoded by PULs. The sensing and regulation of PUL expression is mediated by hybrid two-component systems (HTCS) in Bacteroidetes, where membrane-spanning proteins contain extracellular sensor domains that directly bind oligosaccharide fragments, triggering expression of the associated PUL (Bolam & Koropatkin, 2012;

Grondin et al., 2017; Lynch & Sonnenburg, 2012). When marine oligosaccharides are present, pathogens lacking these complex regulatory mechanisms may have a reduced capacity to initiate specific catabolic pathways. Additionally, a mechanistic basis for selectivity is provided by the structural requirements for oligosaccharide recognition by SusD-like proteins. The binding pocket of SusD proteins is structurally complementary to particular oligosaccharide configurations, and the limited occurrence of these proteins in pathogens may restrict the binding, transport, and metabolism of marine oligosaccharides (Bolam & Koropatkin, 2012). By favoring *L. casei* while protecting *E. coli*, shrimp shell COS further demonstrated pathogen selectivity (Halder et al., 2013).

5.3. Metabolic outputs and pathogen inhibition

SCFAs, which are important mediators of host-microbiome interactions, are produced when the gut microbiota ferments prebiotics obtained from seafood byproducts. The increased production of acetate, propionate, and butyrate after supplementing with seafood-derived oligosaccharides is a recurring pattern in several studies. GAGs from mackerel fish waste, recovered via enzymatic extraction, demonstrated notable SCFA production during *in vitro* fermentation with *L. plantarum* and *B. bifidum*, with a pH decrease from 6.23 to 3.32 (Geetha et al., 2023). Over the course of 48 h, the viable cell count increased from 8 to 12 log CFU mL^{-1}, demonstrating that the enzymatically extracted GAGs were an efficient fermentable substrate. Additionally, e-GAG supplementation significantly reduced the Firmicutes to Bacteroidetes ratio from 6.23 to 5.26 in HFD-fed C57BL/6 mice, indicating that enzymatic extraction maintained the structural integrity required for gut microbiota regulation.

Another important mechanism of seafood-derived prebiotics is their ability to inhibit pathogenic microorganisms, with most supporting evidence derived from seafood processing by-products. Enteropathogens such as *Salmonella enterica*, *E. coli*, and *Pseudomonas* were not stimulated by the COS produced from shrimp waste through solid-state fermentation (López-García et al., 2024). COS have shown structure-dependent antibacterial action against both Gram-positive and Gram-negative bacteria. Prebiotic properties decrease while antimicrobial qualities increase with increasing polymerization; on the other hand, prebiotic potential rises while antimicrobial potential falls with increasing acetylation (Guan & Feng, 2022). The amino groups of deacetylated COS confer a net positive charge, enabling electrostatic interactions with negatively charged microbial cell surfaces and leading to cell wall disruption. The reason for this inverse association is that deacetylated chitin oligosaccharides have free amino groups that give them a net positive charge. This allows them to engage electrostatically with negatively charged microbial surfaces and rupture cell walls (Darweesh et al., 2020). Shrimp shell COS further confirmed pathogen selectivity by promoting *L. casei* while sparing *E. coli* (Halder et al., 2013).

Through two main G-protein-coupled receptors, GPR41 (FFA3) and GPR43 (FFA2), the biological activity of SCFAs goes beyond local gut effects to systemic signaling. The chemical structure of the SCFAs ligand controls the unique ligand selectivity profiles that these receptors exhibit. GPR41 is preferentially activated by ligands with sp^3-hybridized α-carbons (propionate, butyrate), while GPR43 is preferred by ligands with sp^2-or sp-hybridized α-carbons (acetate, acrylate) (Schmidt et al., 2011). Receptor binding affinity and signaling specificity are influenced by the spatial orientation of the carboxyl group and the geometry of the α-carbon. This structure-activity relationship (SAR) has been demonstrated through comprehensive examination of synthetic orthosteric agonists. Certain basic residues in the receptor binding pockets mediate this selectivity at the molecular level. GPR41's Arg185 (transmembrane domain V), His245 (transmembrane domain VI), and Arg258 (transmembrane domain VII) are essential for identifying the negatively charged carboxyl group of SCFAs via electrostatic interactions (Priyadarshini et al., 2018). It has been shown that mutations in these conserved arginine and histidine residues prevent SCFA-mediated receptor activation, highlighting their crucial role in ligand recognition (Stoddart et al., 2008).

The comparable residues in GPR43 are Arg180, His242, and Arg255. These residues serve similar functions but differ slightly in their spatial location, which helps explain each receptor's unique ligand preferences. Both GPR41 and GPR43 couple to Gαi/o proteins upon ligand binding, thereby inhibiting adenylyl cyclase, lowering intracellular cAMP, and activating downstream signaling pathways such as ERK1/2, PI3K, and AMPK (Lee et al., 2024; Qian et al., 2022). Additionally, GPR41 and GPR43 differ in β-arrestin recruitment and G-protein coupling effectiveness, which may lead to biased signaling and different physiological effects. While GPR41 mostly signals through Gαi/o, GPR43 can connect to both Gαi/o and Gαq pathways, adding another level of signaling complexity (Le Poul et al., 2003). The different biological effects of various SCFAs reflect the physiological significance of these SARs. Propionate (C3) and butyrate (C4) activate both receptors with different affinities, affecting metabolic and neuroendocrine pathways, while acetate (C2) mainly activates GPR43, exerting anti-inflammatory actions in immune cells (Koh et al., 2016). Thus, differences in the SCFA fermentation profile may contribute to different GPR41/43 activation and downstream host signaling. This receptor-level selectivity may contribute to the pleiotropic effects associated with seafood-derived prebiotics, such as anti-inflammatory, anti-diabetic, and anti-obesity activities.

5.4. Production of other bioactive metabolites

Seafood-derived prebiotics regulate the synthesis of bioactive metabolites that have important health effects in addition to SCFAs, especially through tryptophan metabolism. Using an *in vitro* human colonic fermentation model, Zonfrillo et al. (2026) examined the fermentability and prebiotic potential of ulvan, a sulfated polysaccharide from *Ulva lactuca L.* Supplementing with ulvan greatly increased the production of SCFAs, especially acetic acid, to levels similar to those of the well-known prebiotic inulin. Simultaneously, ulvan enhanced the production of health-associated metabolites including indole-3-propionic acid (IPA) and indole-3-acetic acid (IAA) by selectively modulating tryptophan metabolism. This observation is of particular significance because IPA and IAA function as key ligands for the aryl hydrocarbon receptor (AhR), a ligand-activated transcription factor widely distributed in intestinal epithelial and immune cells. In its inactive state, AhR, a member of the basic helix-loop-helix/Per-ARNT-Sim (bHLH/PAS) transcription factor family, is found in the cytoplasm as a component of a multiprotein complex. AhR undergoes conformational changes that result in nuclear translocation, heterodimerization with the AhR nuclear translocator (ARNT), and binding to xenobiotic response elements (XREs) in target gene promoters upon ligand interaction with indole metabolites (Mahdiabadi et al., 2026).

In the intestinal epithelium, AhR activation upregulates tight junction proteins and maintains the structural integrity of the apical junctional complex. In immune cells, particularly type 3 innate lymphoid cells (ILC3s) and T helper 17 (Th17) cells, AhR signaling plays a key role in interleukin-22 (IL-22) production (Kang et al., 2025). IL-22, in turn, promotes epithelial repair, enhances mucus and antimicrobial defenses, and strengthens tight junctions. Additionally, AhR signaling induces IL-10 receptor expression in intestinal epithelia, enhancing responsiveness to this key anti-inflammatory cytokine. The physiological importance of this pathway is underscored by findings that AhR-deficient mice exhibit increased susceptibility to experimental colitis and impaired epithelial barrier function (Mahdiabadi et al., 2026). IPA functions as a dual agonist for AhR and PXR, exerting anti-inflammatory effects by inhibiting NF-κB signaling (Min et al., 2024; Pan et al., 2024). IAA enhances M2 macrophage polarization, downregulates TLR4 and NF-κB p65 phosphorylation, activates AhR, and suppresses macrophage pro-inflammatory cytokines (TNF-α, IL-1β) (Min et al., 2024). IAA also

promotes Treg differentiation via the AhR-TAZ-Tip60 pathway, reducing Foxp3 ubiquitination. Elevated IPA is associated with lower arterial stiffness, while IAA correlates with decreased LDL-cholesterol (Pan et al., 2024). In MASLD, IPA and IAA ameliorate hepatic steatosis and inflammation by suppressing NF-κB activation (Min et al., 2024).

This suggests cross-feeding interactions between saccharolytic and indole-producing taxa. Different compounds linked to ulvan treatment were identified by untargeted metabolomics, including cyclic proline dipeptides, which suggests a selective promotion of advantageous microbial species. Similarly, Zhang et al. (2021) showed that in loperamide-induced constipated mice, COS treatment significantly increased intestinal motility, inhibited inflammatory responses, and prevented damage to the gut barrier. The production of intestinal metabolites, such as bile acids, SCFAs, and tryptophan catabolites, was partially recovered by COS treatment, which statistically reversed the abundance changes of several intestinal bacteria at the phylum, family, and genus levels by 16S rDNA gene sequencing. Additionally, COS failed to reduce constipation in mice with intestinal flora reduction, demonstrating the importance of gut microbiota in COS-induced constipation prevention.

Qin et al. (2025) showed that fucoidan from *Apostichopus japonicus* enhanced beneficial microbes and maintained gut structural integrity while upregulating metabolites linked to tryptophan metabolism. After a three-week intervention, the gut microbiota in mice developed a new homeostasis, and the effect of Aj-FUC on intestinal immunity was related to the regulation of tryptophan metabolism by gut microbiota. These metabolites are generated through bacterial tryptophanase and decarboxylase activities, with indole-3-lactic acid serving as a precursor for IPA via reductive pathways. However, contradictory findings reveal that metabolite production is not universal across all prebiotic compounds and is influenced by structural characteristics. Although recent *in vitro* research has demonstrated acetate and lactate generation with enrichment of *Bifidobacterium* and *Lactobacillus*, earlier studies found that SCFA production during ulvan fermentation was modest and equivalent to growth controls (Zonfrillo, 2025). This variability likely reflects differences in the initial structure and functionality of microbial communities, as dietary fiber responses are not uniform across individuals. Beyond substrate structure, inter-individual variations in gut microbiota composition and metabolic ability significantly influence the effectiveness of prebiotics derived from seafood. Research employing *in vitro* fermentation models with several human donors regularly shows that oligosaccharides cause donor-dependent changes in the microbiota and metabolite production patterns (Hoevenaars et al., 2025; Silva et al., 2026; Wang et al., 2026). Individual hosts can account for up to 50-70% of the entire variation in microbiota composition and activity, whereas diet contributes only around 10%. This means that the gut microbiota response to dietary treatments can differ significantly between individuals. The baseline gut microbiota composition before intervention, including the presence or lack of particular CAZyme-encoding genes and oligosaccharide transporters such as SusC/D-like systems, is a major factor in this variability. Baseline gut microbiota composition can reasonably predict responders versus non-responders to prebiotic therapies, using machine learning techniques (Fehlner-Peach et al., 2019; Kok et al., 2024; Salonen et al., 2014). Additionally, metabolic modeling has demonstrated that there is substantial inter-individual variation in the anticipated butyrate production in response to fiber intervention, and non-responders might profit from a customized choice of substitute prebiotics (Quinn-Bohmann et al., 2023, 2026). Studies on chitosan with varying Mw showed that it has a significant impact on the effectiveness of gut microbiota modulation and metabolite production, with COS30K showing better effects on tryptophan metabolism than COS1K and COS3K (Liang et al., 2025).

In summary, prebiotics derived from seafood affect the gut microbiota through pathogen suppression, selective bacterial activation, GI tolerance, and the production of SCFAs and tryptophan metabolites. The Trp-AhR pathway represents a critical mechanistic axis linking dietary substrates, gut microbial metabolism (IPA and IAA), and host physiological regulation, maintaining intestinal immune homeostasis while contributing to systemic metabolic health through modulation of lipid metabolism, inflammation, and vascular function. However, efficacy varies with structural features, indicating a structure-activity paradox in which low-DD chitosan retains prebiotic activity, but high-DD chitosan exhibits antimicrobial qualities. The synthesis of bioactive metabolites is largely dependent on the extraction process; EAE preserves sulfation patterns that may support tryptophan metabolism, whereas conventional extraction may undermine these effects by depolymerization and desulfation. There is still little human evidence supporting these metabolite-mediated benefits, and conflicting results emphasize the need for standardized extraction procedures and human intervention studies. Table 4 summarizes seafood by-products, prebiotic compounds, extraction methods, yields, bioactivities, mechanisms, and translational status. The prebiotic activity of seafood-derived compounds is mediated through four key mechanisms: resistance to gastrointestinal digestion, selective stimulation of beneficial bacteria, short-chain fatty acid production, and biosynthesis of bioactive metabolites, as presented in Fig. 3.

6. Metabolic health benefits

6.1. Obesity and metabolic syndrome

Seafood-derived prebiotics have demonstrated anti-obesity effects by modulating adipogenesis, lipid homeostasis, and energy metabolism. The extraction method critically determines the structural features that govern these biological activities. As discussed in Section 4.2, EAE preserves sulfation patterns and optimal Mw that enhance fermentability and SCFAs production, while conventional extraction may reduce bioactivity through depolymerization and desulfation. When administered to C57BL/6 mice fed an HFD, a polysaccharide from the red seaweed Bangia fusco-purpurea (BFP) reduced body weight gain and fat accumulation more effectively than inulin. BFP suppressed PPARγ expression, promoted lipolysis and fatty acid oxidation, and inhibited adipogenesis while activating the AMPK and ACC signaling pathways (Zheng et al., 2024). Similarly, through dose-dependent downregulation of PPARγ and C/EBPα, COS derived from crustacean shells inhibited adipogenesis and lipid accumulation in 3T3-L1 preadipocytes. Transcriptomic analysis revealed coordinated modulation of PPAR signaling, PI3K-Akt, AMPK, and insulin signaling pathways (Songkoomkrong et al., 2026). By increasing energy expenditure and UCP1 expression in brown adipose tissue, the glycosaminoglycan dermatan sulfate protected HFD-fed mice against increased adiposity, visceral fat mass, and adipocyte size (Stojnić et al., 2024). When HFD-fed animals were treated with chitin oligosaccharide, the mRNA expression of lipogenesis regulators, adipocyte differentiation markers, and gluconeogenesis enzymes in adipose tissues was inhibited (Zheng et al., 2018).

However, the anti-obesity efficacy of seafood-derived prebiotics is not uniform and is influenced by structural characteristics. Sulfation patterns, Mw, and DP influence fermentability and resulting metabolic effects, with increased sulfation and lower Mw typically associated with enhanced activity. Seaweed-derived sulfated polysaccharides significantly reduce body weight gain, adiposity, liver weight, blood insulin, TNF-α, and lipid profiles, according to meta-analytic data from 11 animal studies. The influence of seaweed species and experimental design was highlighted by the variability in efficacy observed across studies and the lack of statistical significance for some parameters (Magwaza et al., 2024). While these findings suggest an association between microbiota modulation and metabolic improvements, the F/B ratio alone is an unreliable predictor of health outcomes. A lower F/B ratio should be interpreted as one of many ecological shifts rather than as a definitive marker of prebiotic efficacy, as functional outcomes depend on metabolic activity, strain-level variation, and overall gut ecosystem context.

Table 4
Seafood processing by-products, extraction methods, yields, bioactivity, mechanisms, and translational status of derived prebiotic compounds.

Source	Compound	Yield & Method	Bioactivity	Mechanism	Translational Stage	Key Limitations	References
Crustacean shells	COS	16.4 mg/g (Enzymatic)	Prebiotic	GH18/GH19; transporter	Lab scale	Enzyme cost; scale-up	(A Ismail & A Emran, 2020)
Fish (Mackerel)	GAGs	Enzymatic	SCFAs	Polysaccharide lyases; GPR41/43	*In vitro*; animal	Source variation	Geetha et al. (2023)
Fish (Skipjack)	Protein hydrolysates	15-25% (Enzymatic)	Antidiabetic	Peptide; AhR	Rat	Batch variation	Riyadi et al. (2025)
Algae (*U. lactuca*)	Ulvan	29.85% (EAE) vs. 12.22% (Hot water)	Prebiotic	Sulfatases; ulvan lyases	*In vitro*	Source variation	Rubak et al. (2026)
Algae (*U. rigida*)	Ulvan oligosaccharides	Enzymatic	Prebiotic; pathogen inhibition	Ulvan lyases; transporters	*In vitro*	Enzyme costs	Krangkratok et al. (2023)
Algae (Red)	Gluco/Galacto-oligosaccharides	5-10% (Autohydrolysis)	Prebiotic > inulin	Agarases; GH16/GH86	*In vitro*	Residue variability	Gomes-Dias et al. (2026)
Algae (Brown)	Fucoidan	7.86% (SWE) vs. 6.60% (MAE)	Antimicrobial; anticancer	Sulfatases; Nrf2	*In vitro*	Temp-dependent depolymerization	Bahrami et al. (2025)
Algae (Green)	Cellulose microparticles	Chemical	Hypolipidemic; antidiabetic	F/B ratio ↓; SCFAs	Mice	Scale-up; purity	Tang et al. (2024)
Sea cucumber	Sulfated polysaccharides	Hot water	Anti-obesity; hepatoprotective	Gut-liver axis	Mice	Seasonality; supply	Sang et al. (2024)
Swiftlet nests	Sialylated glycopeptides	Enzymatic	Prebiotic	Sialidases	*In vitro*	Cost; supply	HuiYan et al. (2026)

Abbreviations: AhR: Aryl hydrocarbon receptor, COS: Chito-oligosaccharides, EAE: Enzyme-assisted extraction, F/B ratio: Firmicutes/Bacteroidetes ratio, GAGs: Glycosaminoglycans, GH: Glycoside hydrolase, GPR41/43: G protein-coupled receptors 41 and 43, MAE: Microwave-assisted extraction, Nrf2: Nuclear factor erythroid 2-related factor 2, SCFAs: Short-chain fatty acids, SWE: Subcritical water extraction.

The degree of reaction varies greatly, even though most of the research shows consistent anti-obesity effects. Notably, whereas N-acetylchitooligosaccharide (NACOS) supplementation improved inflammation and glucose metabolism in HFD-fed mice, it did not lower liver or abdominal fat tissue weight. Furthermore, as discussed in the above sections, emerging technologies such as SWE and MAE produce lower Mw fractions that enhance accessibility to bacterial CAZymes, while UAE generates higher Mw fractions that may limit fermentability. These extraction-dependent structural differences may contribute to the variability in anti-obesity efficacy observed across studies.

6.2. *Type 2 diabetes*

Seafood processing byproducts have emerged as promising antidiabetic agents due to their ability to modulate the gut microbiota, enhance insulin sensitivity, and regulate glucose metabolism. In rats fed a high-fat, high-sugar diet, cellulose microparticles from dealginated seaweed waste reduced insulin resistance. This effect was linked to a decrease in the Firmicutes/Bacteroidetes ratio and an increase in the number of *Lactobacillus, Bifidobacterium*, and *Akkermansia*, which improved the production of SCFAs (Tang et al., 2024). In diabetic rats, fish protein hydrolysates made from skipjack tuna by-products substantially reduced blood glucose levels. They also improved TNFα levels and decreased leukocyte and lymphocyte numbers, indicating immunomodulatory pathways (Riyadi et al., 2025). Crustacean shell-derived COS inhibited α-glucosidase activity in a DP-dependent manner. Shorter-chain COS (DP2-4) showed greater inhibitory activity than longer-chain COS, indicating that structural characteristics significantly affect antidiabetic efficacy (Khaisaat et al., 2022). Likewise, the antidiabetic potential of fish protein hydrolysates depends on both the raw material and the hydrolysis process. Pepsine-derived hydrolysates exhibited greater antidiabetic activity than those produced using other proteases, highlighting the importance of processing conditions in determining bioactivity. Furthermore, it has been demonstrated that *Pinctada martensii* hydrolysate (PMH) modulates central nervous system proteins and neuropeptides involved in insulin regulation, thereby contributing to blood glucose homeostasis through the gut-brain axis (Li et al., 2024).

While the available evidence indicates clear antidiabetic potential, inconsistencies and variability among studies require careful consideration. A meta-analysis of 33 randomized controlled trials (RCTs) found that inulin-type fructans significantly reduced fasting blood glucose, Hemoglobin A1c (HbA1c), and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) in T2D patients (Wang et al., 2019). However, another RCT showed that inulin supplementation led to increases in HbA1c, HOMA-IR, and fasting blood glucose, highlighting the need for careful consideration of study design and population. These conflicting data could be the result of variations in the baseline microbiota composition, the length of the intervention, or the dosage (Mitchell et al., 2021). Additionally, the types of enzymes and raw material affect the antidiabetic properties of fish protein hydrolysates; skipjack tuna by-products and particular hydrolysis conditions produced hydrolysates with greater antidiabetic potential (Riyadi et al., 2025). Several translational challenges still exist despite the effectiveness shown in animal models, such as the requirement for uniform prebiotic components and the significant variation in gut microbial responses between seaweed species and individual subjects.

6.3. *Cardiovascular disease*

Seafood by-products exert cardioprotective effects by modulating lipid metabolism and regulating blood pressure. In mice fed a high-fat, high-sugar diet, cellulose microparticles extracted from dealginated seaweed waste significantly reduced serum total cholesterol, triglycerides, and LDL cholesterol while increasing HDL cholesterol. These beneficial effects were associated with a reduced Firmicutes/Bacteroidetes ratio and enhanced SCFA production, as reflected by higher fecal

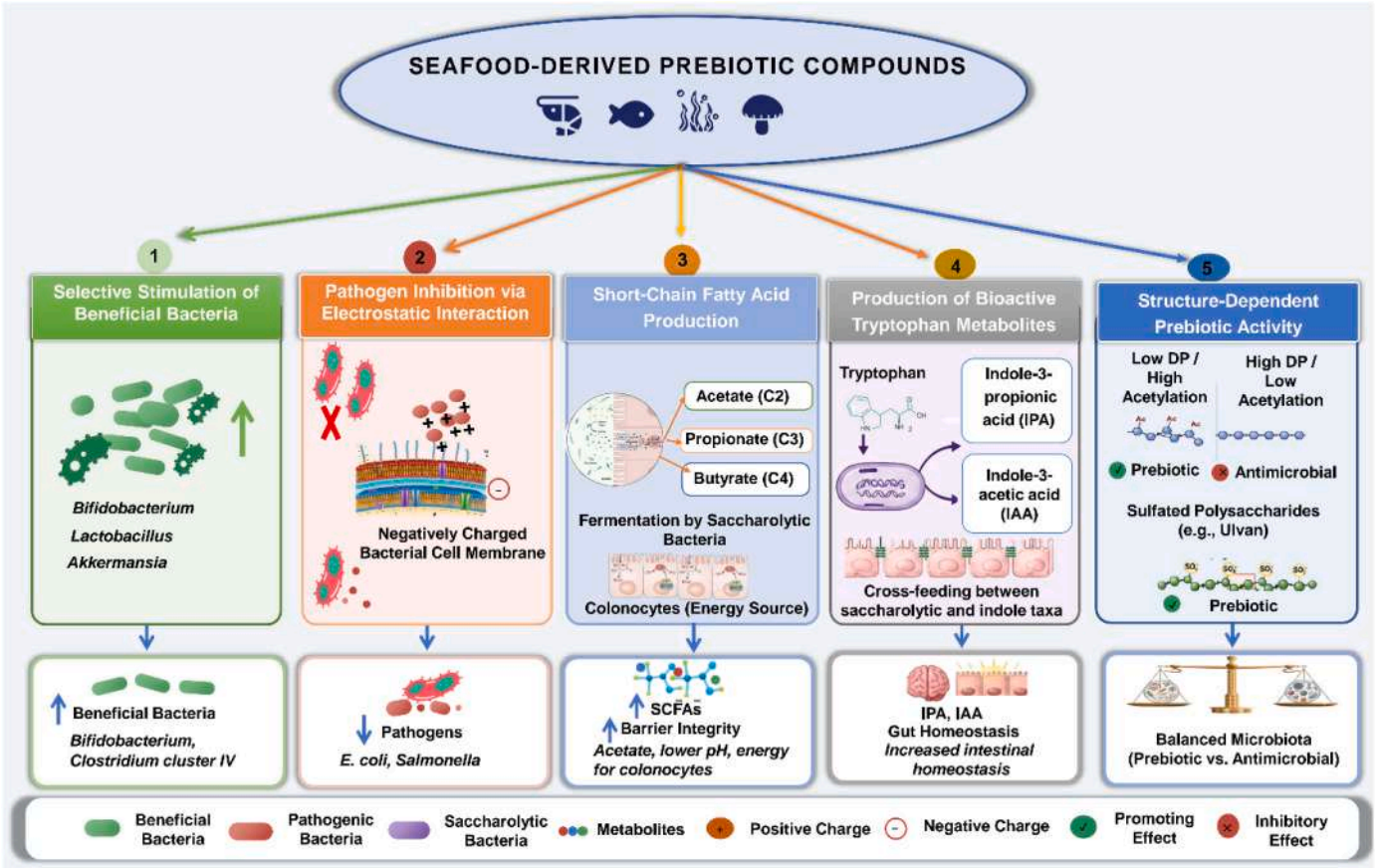


Fig. 3. Seafood-derived prebiotics modulate gut microbiota through GI resistance, selective bacterial stimulation, SCFAs and tryptophan metabolite production, and pathogen inhibition via structure-dependent mechanisms.

concentrations of total SCFAs, acetate, propionate, and butyrate (Tang et al., 2024). Similarly, over the course of a six-week experiment, fish protein hydrolysate and oil derived from fish waste reduced plasma triglycerides and angiotensin-converting enzyme activity in adult dogs without having any negative effects on cardiac anatomy or function. Angiotensin-converting enzyme (ACE) inhibition reduces angiotensin II production, lowering blood pressure and improving vascular function. The experimental diet, with higher DHA and EPA contents, also tended to decrease total cholesterol. However, no effects were observed on serum levels of pro-inflammatory cytokines or cardiac structure and function during the 6-week trial (Cabrita et al., 2024). In Bama pigs fed a high-fat diet, COS derived from shrimp and crab shells reduced weight gain and improved dyslipidemia, insulin resistance, and inflammation. COS upregulated intestinal ATP-binding cassette transporters G5 and G8 (ABCG5/ABCG8) in an RCT to promote cholesterol excretion, increased ATP-binding cassette transporter A1 (ABCA1) expression in the intestine and liver to enhance reverse cholesterol transport, and upregulated hepatic LDL-R to facilitate LDL-C clearance from circulation while modulating hepatic cholesterol synthesis via SREBP2 downregulation and RNF145 upregulation. Additionally, COST decreased fecal secondary bile acid levels, reshaped gut microbiota composition, and increased SCFAs production, with significant correlations among these factors (Zhou et al., 2026).

However, these trends are not uniform in terms of effectiveness in cardioprotection, particularly when it comes to seafood by-products. Triglycerides and ACE activity were reduced in dogs fed fish waste hydrolysate and oil, but there were no significant effects on pro-inflammatory cytokines, cardiac structure, and function during the 6-week trial (Cabrita et al., 2024). These findings indicate that either short-term systemic anti-inflammatory effects are not evident or that systemic anti-inflammatory pathways are not the predominant mechanisms responsible for the observed cardiovascular effects. Longer interventions may be required to observe systemic anti-inflammatory benefits, as cardioprotection includes gradual modification of gene expression and metabolic pathways. In animal models, various fish proteins, peptides, and algal components have been found to possess cardioprotective effects, but their translation to humans is limited (Lamminpää et al., 2024). Additionally, in zebrafish models, marine-derived phospholipids from shrimp heads, codfish roe, and squid gonads have shown strong antithrombotic, anti-inflammatory, and cardioprotective effects, indicating that the interaction of various lipid nutrients rather than just n-3 PUFA content alone contributes to cardiovascular benefits (Xie et al., 2022).

6.4. *Anti-inflammatory effects*

The anti-inflammatory effects of seafood processing by-products have been consistently observed by reducing pro-inflammatory cytokines and increasing gut barrier integrity. Ahmad et al. (2019) used chloroform/methanol extraction to extract lipid fractions from the viscera and heads of octopus, squid, sardines, and salmon. In lipopolysaccharide-stimulated macrophages, these lipid extracts significantly decreased the production of nitric oxide (NO) and tumor necrosis factor-alpha (TNF-α), with cephalopod by-products exhibiting the strongest efficacy because of their higher omega-3 polyunsaturated fatty acid (PUFA) content. However, the combined effects of saturated, monounsaturated, and polyunsaturated fatty acids all contributed to efficacy, suggesting that the entire fatty acid profile is more significant than omega-3 concentration alone. Carotenoids isolated from the shells of Atlantic blue crab and European lobster were described by Di et al.

(2026). By preventing Nrf2 from binding to Keap1, these compounds triggered the Nrf2 pathway, which caused cells to produce antioxidant and anti-inflammatory reactions. Chaklader et al. (2023) showed that enzymatic hydrolysis of fish protein hydrolysates from kingfish, carp, and tuna waste reduced inflammation in barramundi's guts. As demonstrated by reduced villus damage and enhanced neutral mucin production, the hydrolysates protected the intestinal mucosal barrier through downregulation of TNF-α and upregulation of IL-10.

Although current evidence of anti-inflammatory activity is mostly consistent, some discrepancies and limitations must be considered. Yamabhai et al. (2024) reported that COS exhibited a limited therapeutic window, where doses above optimal levels triggered inflammatory responses. According to the research, COS has a biphasic dose-response (hormetic) profile, based on the research. The most beneficial dose range of COS in a murine model of inflammatory bowel disease was 10-20 mg/kg/day, whereas a higher dose of 100 mg/kg/day did not significantly decrease colitis symptoms (Yousef et al., 2012). Studies using human cells support this conclusion, showing that although COS doses of 10-200 μg/mL enhanced antioxidant activity without causing cytotoxicity, a higher concentration of 400 μg/mL caused oxidative stress and reduced cell viability (Çeriğ, 2021). Overstimulation of immune pathways is probably the mechanism underlying this pro-inflammatory shift at high doses; in the context of pre-existing inflammation, excessive COS may paradoxically amplify NF-κB signaling or upset the delicate balance of gut microbiota, resulting in dysbiosis and endotoxin release (Ghattas et al., 2025). The DA significantly affects bioactivity; oligochitosan demonstrated maximum immunostimulatory activity at an acetylation degree of 6 mol%, while cytotoxicity was absent at a concentration of ≤2.5 mg/mL for Mw below ~50 kDa. Therefore, structural parameters must be taken into account when establishing safe dosage guidelines (Markushin et al., 2018). Although a human clinical trial using 100 mg/day COS in elderly type 2 diabetes patients showed no adverse effects and improved therapeutic outcomes (Zhao et al., 2017), and a protocol for non-alcoholic fatty liver disease using chitosan at 2.5-3 g/day is under investigation (Markushin et al., 2018). These findings are based on single-dose evaluations conducted in specific populations. Taken together, the animal data and mechanistic evidence regarding endotoxin release suggest that the safe dosage range of COS is not universal, but rather depends on Mw, DA, and the host's baseline inflammatory state. The effectiveness of COS was dependent on the production process; products derived from lactic acid were hygroscopic and unstable, while those from HCl were stable. Christensen (2025) demonstrated that fucoidan fractions from brown seaweed showed varying immunomodulatory effects based on their Mw: low Mw fractions inhibited Th1 responses and suppressed IL-12p40 secretion by dendritic cells, while alginate oligosaccharides increased the production of IL-6, IL-10, and IL-12p40 and stimulated Th1 responses. Collectively, seafood-derived prebiotics exert multi-targeted metabolic benefits through activation of AMPK, suppression of PPARγ and C/EBPα, α-glucosidase inhibition, ACE inhibition, cholesterol transporter upregulation, Nrf2-mediated antioxidant responses, and SCFAs-dependent GPR41/43 signaling. However, the anti-obesity, anti-diabetic, cardioprotective, and anti-inflammatory activities are strongly influenced by their structural characteristics, source, processing conditions, and dosage. Furthermore, as demonstrated by Ahmad et al. (2019) and Di et al. (2026), extraction methods play a critical role in shaping the bioactive profiles responsible for their anti-inflammatory efficacy.

A structured assessment of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework is presented in Fig. 4, which reveals that while *in vitro* studies consistently demonstrate mechanisms such as AMPK activation, PPARγ inhibition, α-glucosidase inhibition, and Nrf2-mediated antioxidant responses, and animal studies show reproducible benefits across multiple models, human evidence remains severely limited. For anti-obesity, antidiabetic, and anti-inflammatory effects, the certainty of evidence is low due to indirectness (animal models do not fully replicate human metabolic disease), risk of bias (lack of blinding and randomization in many animal studies), and imprecision (small sample sizes). For cardioprotective effects, the evidence is very low due to minimal human data and inconsistent results across models. No randomized controlled trials have evaluated seafood-derived prebiotics for these metabolic outcomes in humans, highlighting a critical translational gap that must be addressed through well-designed human intervention studies. In summary, seafood-derived prebiotics demonstrate multi-targeted metabolic benefits through AMPK, PPARγ, α-glucosidase, ACE, ABC transporters, and Nrf2-mediated pathways. However, the strength of evidence is predominantly derived from *in vitro* and animal studies, with

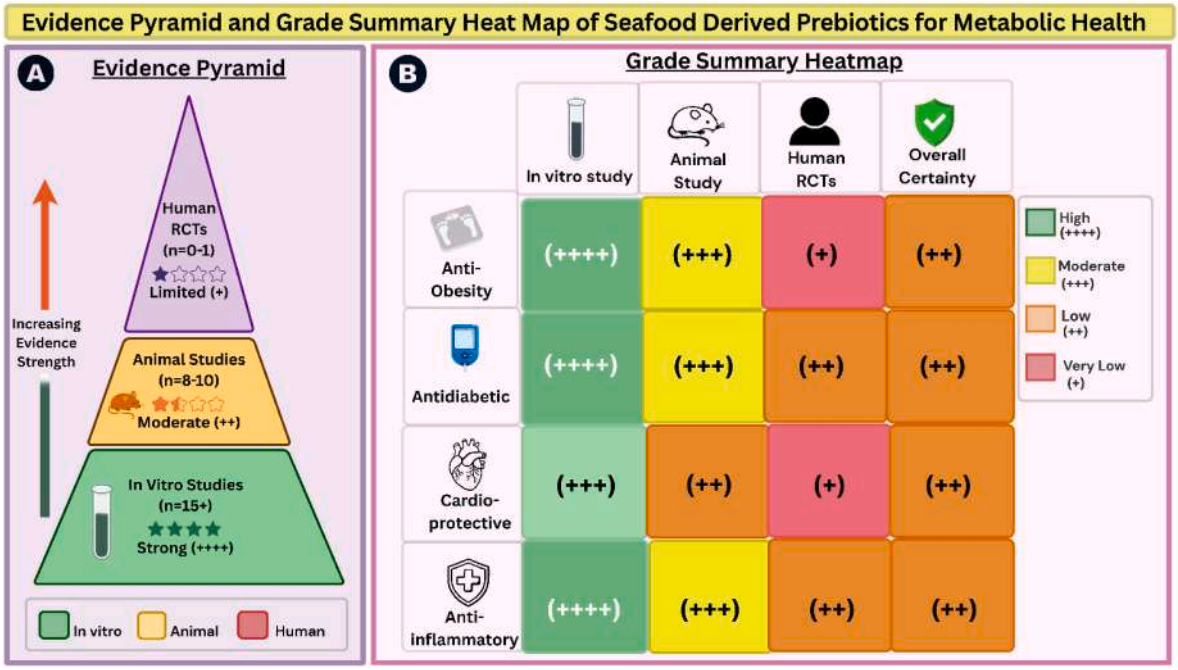


Fig. 4. GRADE evidence certainty assessment for metabolic health benefits of seafood-derived prebiotics.

human clinical validation remaining a critical priority for translating these preclinical findings into therapeutic applications. These findings highlight the need for standardized production processes, reliable human trials, and optimized techniques accounting for baseline microbiota composition to verify and optimize clinical translation. Fig. 5 depicts the metabolic health benefits of seafood-derived prebiotics: anti-obesity through AMPK and PPARγ, antidiabetic via α-glucosidase and GLP-1, cardioprotective through ACE and ABC transporters, and anti-inflammatory via Nrf2 and cytokine modulation.

7. Valorization and sustainability

7.1. Circular economy and environmental impact

The processing of fish in the world produces a significant amount of fish waste, which is equivalent to more than 50% of the catch, and has environmental problems and losses as a resource (Xie, 2026). Methane, which has an impact 25 times greater than carbon dioxide, accounts for an estimated 8% of all man-made greenhouse gas emissions, with an estimated 35% of the world's seafood harvest lost or wasted every year (Grever, 2026). Traditionally, these residues have been utilized in low-value applications such as animal feed, landfill disposal, or ocean disposal, thereby increasing risks of pathogenicity, eutrophication, and GHG emissions. The circular economy reframes these leftovers as strategic feedstocks for valuable bioproducts (Xie, 2026). An example of this change is the HORIZON-JU-CBE-2024 Marmade Project, which focuses on minimizing the waste generated by crustaceans by 95%. It generates integrated biorefinery processes to extract vitamins, peptides, oligosaccharides, prebiotics, and postbiotics from locally available crustacean wastes and macroalgae biomass (Marmade, 2025). The Fish4fish project, funded by the European Maritime and Fisheries Fund (EMFF), is an example of cascaded valorization, using shellfish bio-waste to create active packaging with prebiotic, antioxidant, and antimicrobial properties. This extends seafood shelf life, reduces plastic waste, and provides additional income for the fishing industry (FISH4FISH - European Commission, 2022). According to these models, seafood by-products are renewable feedstocks for the manufacture of sustainable, useful ingredients rather than environmental liabilities when viewed through the perspective of the circular bioeconomy.

7.2. Economic viability and scalability

Quantitative evaluations are progressively supporting the economic viability of seafood waste valorization. Although profitability is mostly dependent on the selling price and quality of recovered protein hydrolysates, a techno-economic analysis of fish waste biorefineries revealed revenues of about €955 per ton of waste treated, with expected payback periods of 2.9 to 6.9 years (Andreola et al., 2023). Scalable methods are provided by enzymatic and microbial bioprocessing. For example, the sequential fermentation of crab shell waste by lactic acid bacteria and proteolytic fungi has allowed for full demineralization and deproteinization, producing high-purity chitin suitable for prebiotic uses (Jung et al., 2007). Similarly, molluscan manufacturing effluents have shown promise as inexpensive sources of nitrogen for the production of probiotics, saving three to 371 times as much as commercial medium (Pedreira et al., 2025). Despite these developments, capital-intensive extraction and transportation expenses make it difficult to compete on price with well-established terrestrial prebiotics (Advaitha et al., 2026; Xie, 2026). To increase overall profitability and facilitate industrial-scale adoption, multi-product biorefinery techniques that progressively recover pigments, peptides, and polysaccharides from a single waste stream are required (Xie, 2026).

7.3. Challenges, regulatory frameworks, and quality standards

Despite substantial progress, several challenges continue to hinder large-scale implementation, including sanitary requirements, the need for standardization, pollutant management, and high capital investment costs, particularly for small-scale operators in developing countries. Although results depend on feedstock logistics, stability, and process

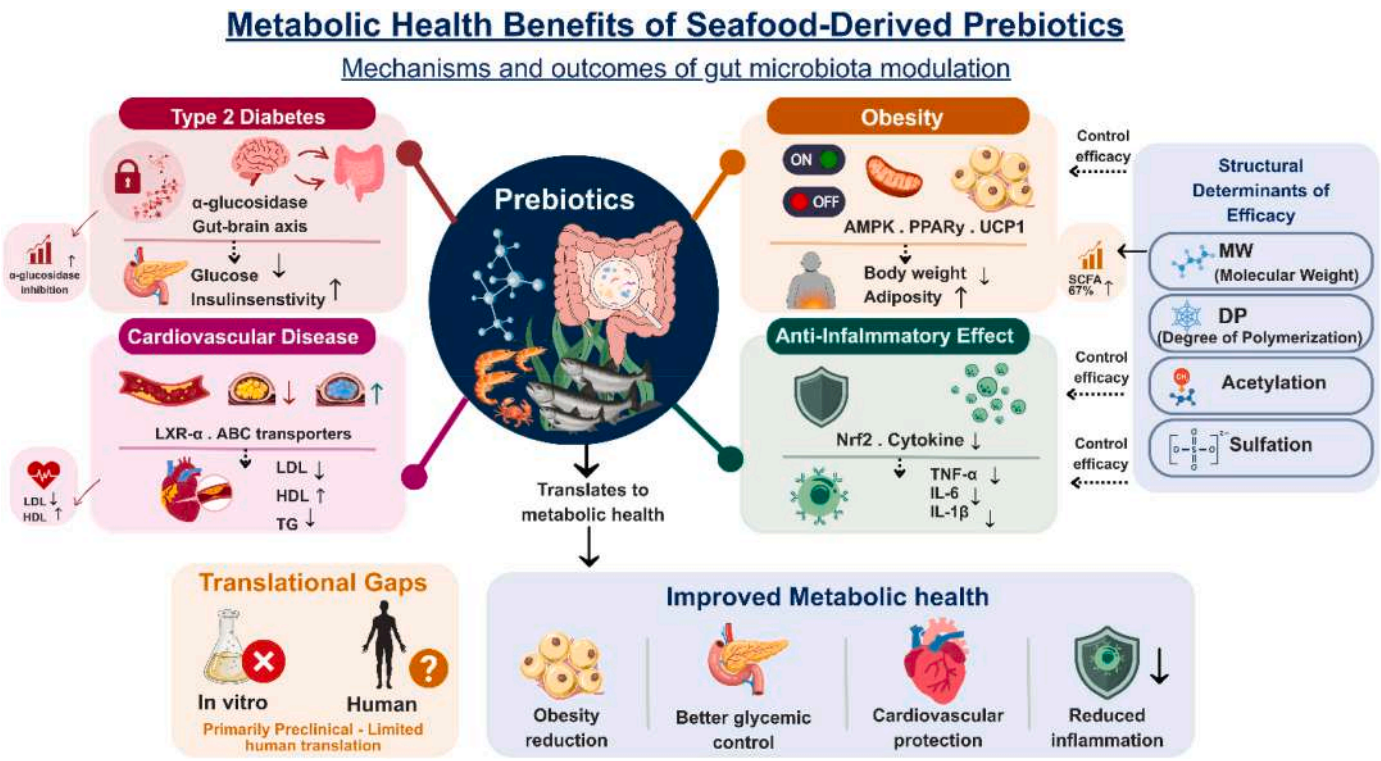


Fig. 5. Seafood-derived prebiotics exert anti-obesity, antidiabetic, cardioprotective, and anti-inflammatory effects through AMPK, PPARγ, α-glucosidase, ACE, ABC transporters, and Nrf2-mediated pathways.

integration, integrated biorefineries can achieve >70% resource recovery and 50-75% GHG reduction compared to disposal (Haque et al., 2026). Regulatory barriers, consumer acceptance, financial viability, and technical challenges continue to be major barriers to wider implementation (Advaitha et al., 2026). The legal framework for valorization is complicated by regulatory fragmentation, with international bodies such as MARPOL, the Basel Convention, and EU circular economy directives all setting out the rules and requirements for compliance (Ijaz et al., 2026). The main challenges associated with extraction and purification remain depolymerization and desulfation induced by conventional procedures, enzyme competition during EAE, and changes in Mw and sulfation patterns caused by emerging extraction technologies. In addition, purification presents a purity-bioactivity paradox, as increasing purity may compromise structural features essential for biological activity.

Regulatory approval pathways for prebiotics derived from seafood processing by-products remain highly fragmented across jurisdictions, with no globally harmonized definition or standardized approval framework (Teferi et al., 2026; EFSA Panel on Dietetic Products et al., 2016). Under EFSA, human clinical trials must thoroughly demonstrate a cause-and-effect relationship to substantiate health claims; *in vitro* and animal studies are considered supportive but insufficient on their own. Only specific claims, such as the impact of inulin on bowel function, have received favorable evaluations under the Article 13.5 procedure after thorough reports were submitted; thus far, EFSA has not authorized any general claims for prebiotic effects (Chatonidi & Vaughan, 2025). The 2017 ISAPP consensus statement defined prebiotics as "a substrate that is selectively utilized by host microorganisms conferring a health benefit" (Gibson et al., 2017), while the Global Prebiotic Association has recently proposed an expanded definition that removes selectivity requirements to include non-carbohydrate ingredients and extra-intestinal microbiomes (Deehan et al., 2024).

Standardized quality control and analytical requirements for prebiotics remain insufficient. In particular, there is a lack of validated and standardized analytical methods for shellfish-derived prebiotic compounds, such as fucoidan, ulvan, and COS, representing a critical gap in quality assurance. Driven by a 2008 FAO Technical Meeting that proposed criteria for assessing prebiotics and a 2018 submission from Sudan to the Codex Committee on Nutrition, the Codex Alimentarius Commission has begun work on unified prebiotic standards. International trade and product innovation remain restricted by the lack of globally unified definitions, with some nations using the FAO definition and others using ISAPP or the original 1995 definition (Deehan et al., 2024). Addressing the complex regulatory landscape surrounding seafood-derived prebiotic compounds requires coordinated efforts among food scientists, microbiologists, clinicians, and regulatory agencies to establish harmonized standards and overcome existing regulatory challenges.

7.4. Techno-economic analysis of emerging extraction technologies

The economic feasibility and scalability of emerging extraction technologies are critical factors influencing their industrial adoption for seafood-derived prebiotic development. Recent techno-economic assessments have provided quantitative insights into the capital costs, operational costs, and energy requirements of UAE, MAE, and SWE compared to conventional methods. The combined SWE-MEF technology demonstrated the lowest energy consumption for agar extraction from red seaweeds, with 67 MJ/kg agar for *Gracilaria vermiculophylla* and 100 MJ/kg agar for *Gelidium sesquipedale*, while achieving a carbon footprint reduction of up to 94% compared to conventional extraction, with carbon emissions of 15.9 kg CO_2 eq./kg agar for G. *vermiculophylla* and 20.4 kg CO_2 eq./kg agar for *G. sesquipedale.* Critically, cost analysis confirmed that the combined SWE-MEF technology was the most cost-effective extraction method, demonstrating that environmental sustainability and economic viability can be simultaneously achieved (Pereira et al., 2024).

For seaweed multiproduct biorefineries, EAE has become a viable sustainable technique. Techno-economic modeling shows that, when laminarin and fucoidan are prioritized as the primary products, EAE can yield a value of up to €1.07 per kilogram of fresh weight biomass. However, the most significant impacts on biorefinery profitability are found in extraction yields and raw biomass alginate composition, highlighting the significance of optimizing both upstream cultivation and downstream processing (Herrera Barragán et al., 2022). Green chemistry-driven optimization produced chitosan from shrimp exoskeleton waste at a total equivalent cost of 29.81 USD/kg as opposed to 54.65 USD/kg for conventional methods, significantly reducing the impact on human health by more than 75% (Leon-Pulido et al., 2025). MAE extraction demonstrated yield improvements of 70.37%, 64.31%, and 20.71% for *Sargassum sp.*, *Gracilaria sp.*, and *Enteromorpha sp.*, respectively, compared with conventional solvent extraction. However, because of higher capital costs, the return on investment for MAE was lower than that of conventional methods (Golshan et al., 2025). Together, these results suggest that high-value product applications, efficient drying methods, and renewable energy sources could be combined to attain economic viability. Enzyme recycling and process integration could also be used to reduce high operating costs.

7.5. Safety assessment of seafood-derived prebiotics

Based on current scientific literature, the safety profile of chitosan and COS is well-established through comprehensive toxicological evaluations. Acute toxicity studies have demonstrated that COS exhibits an LD_{50} exceeding 30,000 mg/kg body weight, classifying it as practically non-toxic according to acute toxicity grading standards. The lack of mutagenic potential has been confirmed by the negative findings of genotoxicity studies, such as Ames tests, mouse spermatocyte chromosome aberration tests, and mammalian erythrocyte micronucleus assays. All tested doses showed no negative effects on body weight, organ coefficients, hematological parameters, or histological examinations during a 28-day feeding toxicity study (Qiao et al., 2025). According to long-term safety data from the National Toxicology Program, high-Mw chitosan is primarily linked to negative effects, such as altered calcium and phosphorus metabolism and decreased serum vitamin E and vitamin A levels, which occur at very high doses well beyond therapeutic ranges. In addition, it has been shown that there are gender differences in chitosan toxicity; when given higher dosages for longer periods of time, female mice are more vulnerable to hepato-renal toxicity than male mice (Omara et al., 2012).

The main allergenicity concern associated with seafood-derived prebiotics is the potential presence of residual proteins from the source material, particularly tropomyosin, a major allergen in crustaceans. Effective deproteinization techniques are required since ionic liquid extraction of chitin has been demonstrated to leave 1.3-1.9% protein contamination, including allergenic proteins like tropomyosin (Lyon Jr et al., 2022). However, the Maillard reaction with COS showed a considerable reduction in this risk, lowering tropomyosin allergenicity by up to 60% by changing immunodominant epitopes and converting from α-helix to β-sheet (Fu et al., 2019). In addition to being environmentally friendly and preserving the Mw of chitosan, enzymatic hydrolysis and immobilized enzyme-based purification techniques can effectively reduce the Mw of residual proteins and, consequently, their allergenicity (Li et al., 2012). A safe dose range of 10-200 μg/mL has been found for COS specifically in human cell-based experiments; concentrations up to 200 μg/mL increased antioxidant activity without cytotoxicity, whereas 400 μg/mL caused oxidative stress and decreased cell viability. Mw and dosage must be considered when determining acceptable daily intake; in subacute studies, chitosan has an established "No-Observed-Adverse-Effect Level" (NOAEL) of 1 g/kg orally (Lagarto et al., 2015). Both animal toxicology studies and human cell-based assays support the favorable safety profile of properly characterized and

purified seafood-derived prebiotics, especially low-Mw COS, with established NOAEL values. However, gender-specific considerations and stringent quality control for residual allergens remain crucial during manufacturing and clinical translation (Mukhopadhyay et al., 2015; Omara et al., 2012).

7.6. Roadmap for clinical translation

A systematic translational roadmap is necessary to convert the encouraging preclinical findings for seafood-derived prebiotics into therapeutic uses. Since these factors directly affect bioactivity and prebiotic efficacy, the first goal is to design standardized production processes that ensure batch-to-batch consistency in structural properties, particularly Mw, DP, DA, and sulfation patterns (Monteiro et al., 2026; Swackhamer et al., 2025). Clinical reproducibility and regulatory approval depend on this uniformity. To more precisely recreate human gut physiology and forecast clinical reactions, sophisticated preclinical platforms like gut-on-a-chip systems and humanized microbiota models should be used in addition to conventional *in vitro* fermentation and animal models (Gibbons et al., 2022; Ojima et al., 2022; Peñaherrera-Pazmiño et al., 2025). These advanced systems represent a significant paradigm shift from demonstrating correlations to finding causative linkages by enabling the analysis of complex tripartite interactions between prebiotics, the microbiota, and host cells (Peñaherrera-Pazmiño et al., 2025). To establish causal relationships between specific structural features, microbial shifts, metabolite production, and clinical outcomes, rigorous and well-controlled human intervention trials incorporating mechanistic endpoints, such as multi-omics analyses, should take precedence over observational or feasibility studies. Clinical trial designs should incorporate baseline microbiome stratification and "responder analysis" to determine which populations benefit most from certain prebiotics, given the substantial inter-individual heterogeneity in prebiotic responsiveness (Bedu-Ferrari et al., 2022; Ojima et al., 2022). This stratification approach enables a shift from generic, "one-size-fits-all" supplementation toward personalized prebiotic interventions (Ali et al., 2025; Bedu-Ferrari et al., 2022). Strategies should move toward "synbiotics 2.0," which entails the methodical pairing of particular prebiotics with known degrading bacteria, to ensure fermentation independent of the host's natural microbiota composition (Razzak et al., 2026).

In conclusion, the valorization of seafood processing by-products within a circular bioeconomy framework integrates waste reduction, biorefinery processes, and the sustainable production of prebiotic ingredients, as depicted in Fig. 6. Although this approach is technically feasible and economically promising, its translation into clinical applications requires harmonized regulations, standardized safety protocols, and robust human trials. Addressing these interconnected challenges through integrated biorefinery approaches and interdisciplinary collaboration will be essential to fully realize the potential of seafood-derived prebiotics for gut health. Valorization of seafood processing by-products within a circular bioeconomy framework integrates waste reduction, biorefinery processes, and sustainable production of prebiotic ingredients, as depicted in Fig. 6.

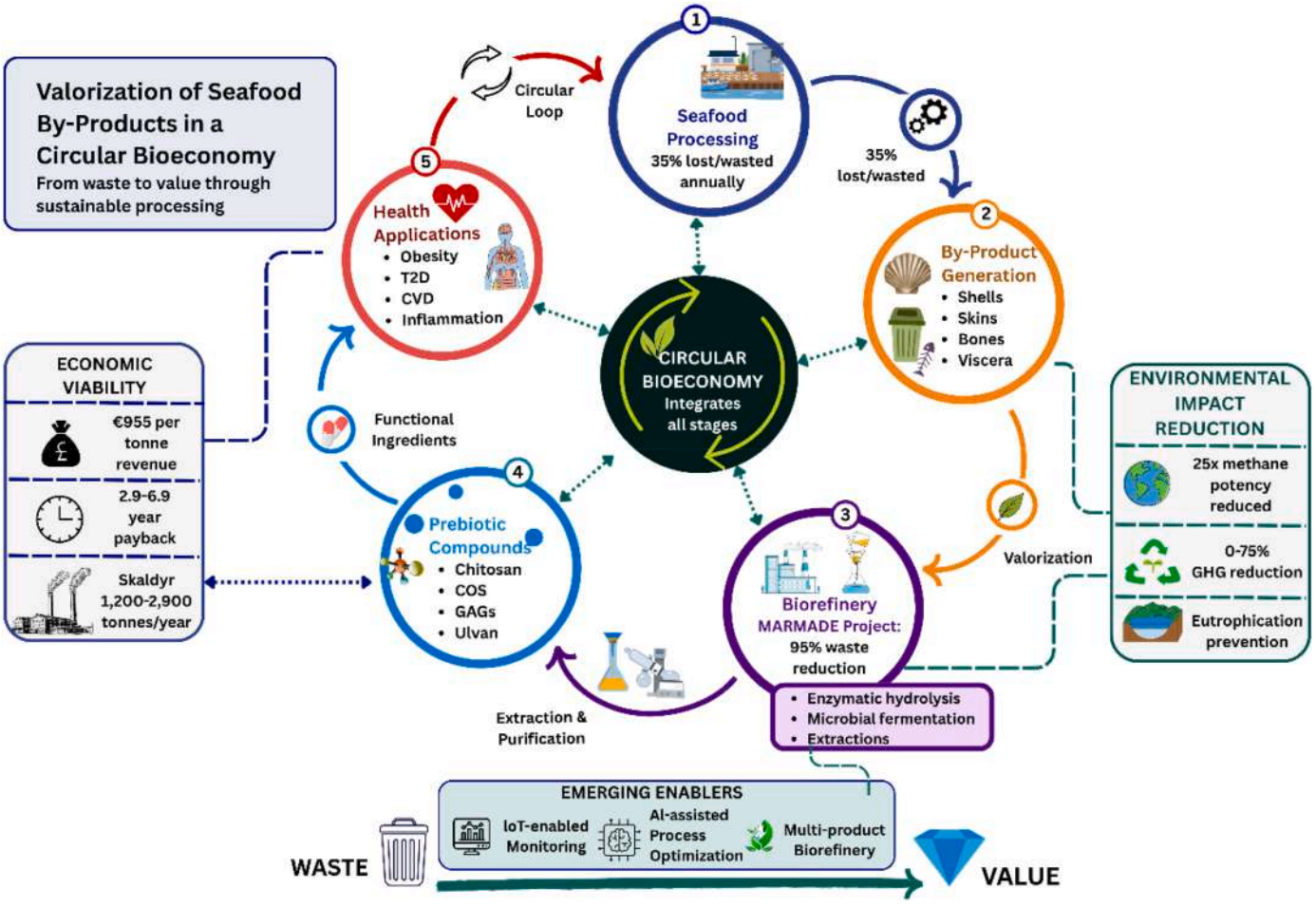


Fig. 6. Circular bioeconomy framework showing the valorization of seafood processing by-products into gut-modulating prebiotics via integrated biorefinery processes, contributing to environmental sustainability and the production of health-promoting ingredients.

8. Conclusions

Seafood processing by-products represent a sustainable and largely untapped source of structurally diverse compounds with prebiotic potential, as demonstrated by consistent *in vitro* and animal studies. However, human evidence remains limited, with most data derived from fermentation models and preclinical studies. Structural characteristics such as Mw, DP, DA, and sulfation patterns determine fermentability, CAZyme accessibility, and microbial utilization, driving selective stimulation of beneficial bacteria, SCFAs and tryptophan metabolite production, and pathogen inhibition. The metabolic effects of seafood prebiotics are mediated through pathways with varying experimental validation. Direct evidence exists for AMPK activation and PPARγ/CEBPα suppression by COS. In contrast, mechanisms involving GPR41/43, HDAC inhibition, and AhR signaling remain largely inferred from general metabolite knowledge rather than demonstrated for specific seafood-derived compounds. This distinction underscores a key knowledge gap requiring hypothesis-driven validation. Precise structural control is critical due to the structure-activity paradox: high-DDA chitosan is antimicrobial, while low-DDA chitosan is prebiotic. Over-depolymerization yields fragments below the DP threshold for bacterial recognition, and excessive purification may reduce bioactivity by removing synergistic co-factors. Microbiota changes, including shifts in the Firmicutes/Bacteroidetes ratio and increased abundance of genera such as *Bifidobacterium* or *Lactobacillus*, should be interpreted with caution; these taxonomic shifts alone do not establish prebiotic efficacy, as functional outcomes depend on metabolic activity, strain-level variation, and broader ecological context. Key translational challenges include limited human trials, inter-individual variability, lack of standardized protocols, scalability issues, and regulatory fragmentation. Addressing these requires integrated biorefineries, harmonized regulations, and well-designed human studies. Moving forward, personalized prebiotic strategies based on baseline microbiota composition, alongside interdisciplinary collaboration among food scientists, microbiologists, clinicians, and policymakers, will be essential to realize the full potential of seafood processing by-products for gut health within a circular bioeconomy framework.

Informed consent

Informed consent was not required as no human subjects were involved in this study.

CRediT authorship contribution statement

Ali Hassan: Writing – original draft, Methodology, Data curation, Conceptualization, Writing – review & editing. Nadia Yasin: Writing – review & editing, Visualization. Sana Shahid: Writing - Review & Editing, Software. Giovanna Gomez d'Ayala*: Supervision, Writing – review & editing, Visualization, Conceptualization. Donatella Duraccio: Software, Writing – review & editing, Visualization. Domenico Zannini: Writing – review & editing, Visualization. Mudassar Hussain**: Writing - review & editing, Formal analysis, Resources, Supervision. Muneeba Naseer Chaudhary: Writing – review & editing, Visualization.

Research involving human participants and/or animals

This research did not involve any studies with human participants or animals performed by any of the authors.

Declaration of generative AI in scientific writing

The authors conceived, designed, and finalized all figures themselves. External tools were used only to support visual drafting and language refinement. No external tool was used to generate original data, perform analyses, or make scientific conclusions. All scientific content, interpretations, and final presentations were developed, verified, and approved by the authors, who take full responsibility for the manuscript and figures.

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Data availability

Data will be made available on request.

References

A Ismail, S., & A Emran, M. (2020). Direct microbial production of prebiotic and antioxidant chitin-oligosaccharides from shrimp byproducts. *Egyptian Journal of Aquatic Biology and Fisheries, 24*(4), 181–195. https://doi.org/10.21608/ejabf.2020.104067

Adalsteinsson, B. T., Guðmundsson, H., Jasilionis, A., Schiøtt, M., Mikkelsen, M. D., Guðmundsdóttir, E. E., Sivakumar, P., Malmgren, A., Kaushik, T., & Apelqvist, E. (2025). Targeted metagenomics–enrichment for enzymes active on sulfated polysaccharides from seaweeds. *Enzyme and Microbial Technology, 182*, Article 110528. https://doi.org/10.1016/j.enzmictec.2024.110528

Addazii, D., Pinheiro, A. C. D. A. S., Nissen, L., Tappi, S., Bordoni, A., Rocculi, P., & Gianotti, A. (2026). Bridging the gap of gut microbiome effects of new food additives in food risk assessment: MICODE gut model to test new chitosan from seafood waste. *Food Chemistry, 512*, Article 148927. https://doi.org/10.1016/j.foodchem.2026.148927

Advaitha, S., Sunooj, K. V., Vellaisamy, S. K., Negi, S., Navaf, M., Sabu, S., Sasidharan, A., & Venugopal, V. (2026). Valorization of side streams to enhance seafood sustainability. *Sustainable Food Technology, 4*(1), 89–109. https://doi.org/10.1039/d5fb00236b

Ahmad, T. B., Rudd, D., Kotiw, M., Liu, L., & Benkendorff, K. (2019). Correlation between fatty acid profile and anti-inflammatory activity in common Australian seafood by-products. *Marine Drugs, 17*(3), 155. https://doi.org/10.3390/md17030155

Ahmed, M. S., Rafi, M. O. S., & Muslim, T. (2026). Valorization of crab shell waste into chitin, chitosan, and carboxymethyl chitosan: Extraction, chemical modification, and characterization. *Next Materials, 11*, Article 101710. https://doi.org/10.1016/j.nxmate.2026.101710

Ahn, G., Lee, W., & Jeon, Y.-J. (2014). Effect of different molecular weights of chitosans on the growth of lactic acid bacteria from traditional fermented foods. *Journal of Chitin and Chitosan, 19*(3), 194–200.

Alboofetileh, M., Rezaei, M., Tabarsa, M., Rittà, M., Donalisio, M., Mariatti, F., You, S., Lembo, D., & Cravotto, G. (2019). Effect of different non-conventional extraction methods on the antibacterial and antiviral activity of fucoidans extracted from *Nizamuddinia zanardinii*. *International Journal of Biological Macromolecules, 124*, 131–137. https://doi.org/10.1016/j.ijbiomac.2018.11.153

Ali, S., Hamayun, M., Siraj, M., Khan, S. A., Kim, H.-Y., & Lee, B. (2025). Recent advances in prebiotics: Classification, mechanisms, and health applications. *Future Foods, 12*, Article 100680. https://doi.org/10.1016/j.fufo.2025.100680

Andreola, C., González-Camejo, J., Tambone, F., Eusebi, A. L., Adani, F., & Fatone, F. (2023). Techno-economic assessment of biorefinery scenarios based on mollusc and fish residuals. *Waste Management, 166*, 294–304. https://doi.org/10.1016/j.wasman.2023.05.014

Anusha, J. R., & Fleming, A. T. (2016). Synthesis and characterization of chitosan nanoaggregates from gladius of *Uroteuthis duvauceli*. *International Journal of Biomaterials, 2016*(1), Article 5379424. https://doi.org/10.1155/2016/5379424

Bahrami, S., Nateghi, L., Rashidi, L., Nobandegani, B. K., & Ghorbanpour, M. (2025). Evaluation of the properties of polysaccharides extracted from brown macroalgae (*Sargassum ilicifolium*) by methods of conventional, microwave, and subcritical water extraction. *Innovative Food Science & Emerging Technologies, 102*, Article 103975. https://doi.org/10.1016/j.ifset.2025.103975

Baltrusch, K. L., Torres, M. D., & Domínguez, H. (2024). Characterization, ultrafiltration, depolymerization and gel formulation of ulvans extracted via a novel ultrasound-enzyme assisted method. *Ultrasonics Sonochemistry, 111*, Article 107072. https://doi.org/10.1016/j.ultsonch.2024.107072

Bedu-Ferrari, C., Biscarrat, P., Langella, P., & Cherbuy, C. (2022). Prebiotics and the human gut microbiota: From breakdown mechanisms to the impact on metabolic health. *Nutrients, 14*(10), 2096. https://doi.org/10.3390/nu14102096

Bolam, D. N., & Koropatkin, N. M. (2012). Glycan recognition by the Bacteroidetes Sus-like systems. *Current Opinion in Structural Biology, 22*(5), 563–569. https://doi.org/10.1016/j.sbi.2012.06.006

Cabrita, A. R. J., Barroso, C., Fontes-Sousa, A. P., Correia, A., Teixeira, L., Maia, M. R. G., Vilanova, M., Yergaliyev, T., Camarinha-Silva, A., & Fonseca, A. J. M. (2024).

Assessing functional properties of diet protein hydrolysate and oil from fish waste on canine immune parameters, cardiac biomarkers, and fecal microbiota. *Frontiers in Veterinary Science, 11*, Article 1449141. https://doi.org/10.3389/fvets.2024.1449141

Cakmak, E. K., Owusu-Agyeman, I., Caglar Balkis, N., Aksu, A., Taskin, O. S., Cetintasoglu, M. E., Yenipazar, H., Saygun, A., Sahin Yesilcubuk, N., Kocatürk-Schumacher, N. P., Moges, M. E., Morken, J., Salazar, S. A., Gomez d'Ayala, G., Cerruti, P., Muñana, S., Ruiz Rubio, L., Yuksel Imer, D., Cagrican Gok, E. Cetecioglu, Z., … (2026). Unlocking the potential of blue food- and feed-centered marine biorefineries. *Resources, Conservation and Recycling, 233*, Article 109001. https://doi.org/10.1016/j.resconrec.2026.109001. https://linkinghub.elsevier.com/retrieve/pii/S0921344926002259

Çeriğ, S. (2021). In vitro cytotoxic assessment of chitosan oligosaccharide lactate on human blood and lymphocyte cells. *Eskişehir Teknik Üniversitesi Bilim ve Teknoloji Dergisi - C Yaşam Bilimleri Ve Biyoteknoloji, 10*(1), 79–89. https://doi.org/10.18036/estubtdc.798520

Chaklader, M. R., Howieson, J., Foysal, M. J., Hanif, M. A., Abdel-Latif, H. M. R., & Fotedar, R. (2023). Fish waste to sustainable additives: Fish protein hydrolysates alleviate intestinal dysbiosis and muscle atrophy induced by poultry by-product meal in *Lates calcarifer* juvenile. *Frontiers in Nutrition, 10*, Article 1145068. https://doi.org/10.3389/fnut.2023.1145068

Charoensiddhi, S., Conlon, M., Methacanon, P., Thayanukul, P., Hongsprabhas, P., & Zhang, W. (2022). Gut microbiome modulation and gastrointestinal digestibility in vitro of polysaccharide-enriched extracts and seaweeds from *Ulva rigida* and *Gracilaria fisheri*. *Journal of Functional Foods, 96*, Article 105204. https://doi.org/10.1016/j.jff.2022.105204

Charoensiddhi, S., Conlon, M. A., Vuaran, M. S., Franco, C. M. M., & Zhang, W. (2016). Impact of extraction processes on prebiotic potential of the brown seaweed *Ecklonia radiata* by in vitro human gut bacteria fermentation. *Journal of Functional Foods, 24*, 221–230. https://doi.org/10.1016/j.jff.2016.04.016

Chatonidi, G., & Vaughan, E. E. (2025). Prebiotics and health claims: Bridging the gap in EU regulation. *Agro Food Industry Hi-Tech, 36*(1). https://digital.h5mag.com/agrofood_industry_hi_tech_36_1_2025/biotics_-_prebiotics_and_health_claims_bridging_the_gap_in_eu_regulation.

Chen, G., Shen, J., Li, X., Sun, M., Dong, S., Sun, Y., Khamleng, A., Mei, X., Zhang, Y., & Liu, G. (2025). Structure-function relationship of the GH168 fucanase reveals an unusual enzyme recognition mechanism for sulfated polysaccharide. *Nature Communications, 16*(1), 9216. https://doi.org/10.1038/s41467-025-54365-w

Chen, L.-C., Kung, S.-K., Chen, H.-H., & Lin, S.-B. (2010). Evaluation of zeta potential difference as an indicator for antibacterial strength of low molecular weight chitosan. *Carbohydrate Polymers, 82*(3), 913–919. https://doi.org/10.1016/j.carbpol.2010.06.017

Cheng, H., Zhang, D., Wu, J., Liu, J., Zhou, Y., Tan, Y., Feng, W., & Peng, C. (2023). Interactions between gut microbiota and polyphenols: A mechanistic and metabolomic review. *Phytomedicine, 119*, Article 154979. https://doi.org/10.1016/j.phymed.2023.154979

Cheng, J. W., Wu, X. Q., He, L. A., Wu, Q. Q., Fu, L. Z., Wei, H. L., & Li, H. B. (2009). Extraction of polysaccharide from *Lentinula edodes* fruit bodies using stepwise enzymic hydrolysis. In *Proceedings of the 2009 international conference on environmental science and information application technology* (pp. 382–385). https://doi.org/10.1109/ESIAT.2009.427

Christensen, M. D. (2025). *Refining marine polysaccharides and their immunomodulatory effects [Master's thesis, University of Iceland]. Skemman*. https://opinvisindi.is/items/6aa96801-11ce-4806-b97c-219f14e97ccc.

Collén, P. N., Jeudy, A., Sassi, J.-F., Groisillier, A., Czjzek, M., Coutinho, P. M., & Helbert, W. (2014). A novel unsaturated β-glucuronyl hydrolase involved in ulvan degradation unveils the versatility of stereochemistry requirements in family GH105. *Journal of Biological Chemistry, 289*(9), 6199–6211. https://doi.org/10.1074/jbc.M113.520775

Darweesh, W. A., Mohamed, S. A. E.-R., Emam, W. M., Abd El Moniem, O., & El-Khateeb, M. A. (2020). Evaluation of antibacterial activity of chitosan against different bacterial strains. *Egyptian Journal of Chemistry, 63*(7), 2265–2275. https://doi.org/10.21608/ejchem.2020.32119.2674

Deehan, E. C., Al Antwan, S., Witwer, R. S., Guerra, P., John, T., & Monheit, L. (2024). Revisiting the concepts of prebiotic and prebiotic effect in light of scientific and regulatory progress—A consensus paper from the Global prebiotic association. *Advances in Nutrition, 15*(12), Article 100329. https://doi.org/10.1016/j.advnut.2024.100329

Di, L., Gabriella, P., Francesca, C., Chiara, M., Maria, B., Albini, A., Noonan, D., & Serangeli, C. (2026). Chemophysical characterization of carotenoproteins from crustacean shell waste for pharmaceutical applications. *International Journal of Food Science, 2026*(1), Article 1042650. https://doi.org/10.1155/ijfo/1042650

Egharevba, I., Salau, H., Omonedo, M., & Ogbeide, S. (2025). Optimizing enzyme synergy in the hydrolysis of cassava bagasse for biofuel production using multi-enzyme cocktails: A response surface methodology approach. *NIPES-Journal of Energy Technology and Environment, 7*(4), 111–123. https://doi.org/10.70711/njetev7i4.123

Facimoto, C. T., Clements, K. D., White, W. L., & Handley, K. M. (2024). Bacteroidia and Clostridia are equipped to degrade a cascade of polysaccharides along the hindgut of the herbivorous fish *Kyphosus sydneyanus*. *ISME Communications, 4*(1), Article ycae102. https://doi.org/10.1093/ismeco/ycae102

Fan, Y., & Pedersen, O. (2021). Gut microbiota in human metabolic health and disease. *Nature Reviews Microbiology, 19*(1), 55–71. https://doi.org/10.1038/s41579-020-0433-9

Fehlner-Peach, H., Magnabosco, C., Raghavan, V., Scher, J. U., Tett, A., Cox, L. M., Gottsegen, C., Watters, A., Wiltshire-Gordon, J. D., & Segata, N. (2019). Distinct polysaccharide utilization profiles of human intestinal *Prevotella copri* isolates. *Cell Host & Microbe, 26*(5), 680–690. https://doi.org/10.1016/j.chom.2019.10.013

Felix, A. L., Penno, S. M., Bezerra, F. F., & Mourão, P. A. S. (2025). Fucosylated chondroitin sulfate, an intriguing polysaccharide from sea cucumber: Past, present, and future. *Glycobiology, 35*(2), Article cwae098. https://doi.org/10.1093/glycob/cwae098

Fernandez-Julia, P., Commane, D. M., Van Sinderen, D., & Munoz-Munoz, J. (2022). Cross-feeding interactions between human gut commensals belonging to the *Bacteroides* and *Bifidobacterium* genera when grown on dietary glycans. *Microbiome Research Reports, 1*(2), 12. https://doi.org/10.20517/mrr.2022.02

Ferri, I., Canala, B., & Rossi, L. (2025). Unravelling the role of chitin and chitosan in prebiotic activity and correlation with cancer: A narrative review. *Nutrition Reviews, 83*(7), e2015–e2024. https://doi.org/10.1093/nutrit/nuae168

FISH4FISH - European Commission. (2022). FISH4FISH [Project]. *CINEA - European Climate, Infrastructure and Environment Executive Agency*. https://cinea.ec.europa.eu/featured-projects/fish4fish_en.

Foley, M. H., Cockburn, D. W., & Koropatkin, N. M. (2016). The Sus operon: A model system for starch uptake by the human gut Bacteroidetes. *Cellular and Molecular Life Sciences, 73*(14), 2603–2617. https://doi.org/10.1007/s00018-016-2242-x

Fu, L., Wang, C., Wang, J., Ni, S., & Wang, Y. (2019). Maillard reaction with ribose, galacto-oligosaccharide or chitosan-oligosaccharide reduced the allergenicity of shrimp tropomyosin by inducing conformational changes. *Food Chemistry, 274*, 789–795. https://doi.org/10.1016/j.foodchem.2018.09.068. https://linkinghub.elsevier.com/retrieve/pii/S0308814618316388

Geetha, V., Chathur, K. N., Prakash, M. H., & Suresh Kumar, G. (2023). In vitro fermentation of glycosaminoglycans from mackerel fish waste and its role in modulating the antioxidant status and gut microbiota of high fat diet-fed C57BL/6 mice. *Food & Function, 14*(15), 7130–7145. https://doi.org/10.1039/d3fo00660a

Ghattas, M., Dwivedi, G., Chevrier, A., Horn-Bourque, D., Alameh, M.-G., & Lavertu, M. (2025). Chitosan immunomodulation: Insights into mechanisms of action on immune cells and signaling pathways. *RSC Advances, 15*(2), 896–909. https://doi.org/10.1039/d4ra06783g

Gibbons, S. M., Gurry, T., Lampe, J. W., Chakrabarti, A., Dam, V., Everard, A., Goas, A., Gross, G., Kleerebezem, M., Lane, J., Maukonen, J., Penna, A. L. B., Pot, B., Valdes, A. M., Walton, G., Weiss, A., Zanzer, Y. C., Venlet, N. V., & Miani, M. (2022). Perspective: Leveraging the gut microbiota to predict personalized responses to dietary, prebiotic, and probiotic interventions. *Advances in Nutrition, 13*(5), 1450–1461. https://doi.org/10.1093/advances/nmac075

Gibson, G. R., Hutkins, R., Sanders, M. E., Prescott, S. L., Reimer, R. A., Salminen, S. J., Scott, K., Stanton, C., Swanson, K. S., & Cani, P. D. (2017). Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nature Reviews Gastroenterology & Hepatology, 14*(8), 491–502. https://doi.org/10.1038/nrgastro.2017.75

Glenwright, A. J., Pothula, K. R., Bhamidimarri, S. P., Chorev, D. S., Baslé, A., Firbank, S. J., Zheng, H., Robinson, C. V., Winterhalter, M., Kleinekathöfer, U., Bolam, D. N., & van den Berg, B. (2017). Structural basis for nutrient acquisition by dominant members of the human gut microbiota. *Nature, 541*(7637), 407–411. https://doi.org/10.1038/nature20828

Glowacki, R. W. P., & Martens, E. C. (2020). If you eat it, or secrete it, they will grow: The expanding list of nutrients utilized by human gut bacteria. *Journal of Bacteriology, 203*(9), Article e0048120. https://doi.org/10.1128/JB.00481-20

Golshan, M., Osfouri, S., Azin, R., Jalali, T., & Moheimani, N. R. (2025). A techno-economic analysis of marine algae for dye-sensitized solar cells: Process optimization and scale-up. *Biomass Conversion and Biorefinery, 15*(10), 15777–15793. https://doi.org/10.1007/s13399-024-05355-9

Gomes-Dias, J. S., Gonzalez, A., Teixeira-Guedes, C. I., Oliveira, K., Ferreira, A. S., Nunes, C., Nobre, C., Teixeira, J. A., & Rocha, C. M. R. (2026). The bioactive potential of red seaweed oligosaccharides obtained using autohydrolysis: Correlation between extract composition and prebiotic activity. *International Journal of Biological Macromolecules, 370*, Article 152905. https://doi.org/10.1016/j.ijbiomac.2026.152905

Gonzales, K. N., Troncoso, O. P., & Torres, F. G. (2025). Controlled extraction and characterization of ulvan from *Ulva papenfussii* with potential applications in sustainable energy. *Journal of Applied Phycology, 37*(3), 2051–2059. https://doi.org/10.1007/s10811-025-03429-7

Gotteland, M., Riveros, K., Gasaly, N., Carcamo, C., Magne, F., Liabeuf, G., Beattie, A., & Rosenfeld, S. (2020). The pros and cons of using algal polysaccharides as prebiotics. *Frontiers in Nutrition, 7*, 163. https://doi.org/10.3389/fnut.2020.00163

Grever, M. (2026). *Food loss and waste in fish value chains*. FAO. https://www.fao.org/flw-in-fish-value-chains/resources/articles/climate-change-and-fish-loss-and-waste/en/.

Grondin, J. M., Tamura, K., Déjean, G., Abbott, D. W., & Brumer, H. (2017). Polysaccharide utilization loci: Fueling microbial communities. *Journal of Bacteriology, 199*(15), Article e0086016. https://doi.org/10.1128/JB.00860-16

Guan, Z., & Feng, Q. (2022). Chitosan and chitooligosaccharide: The promising non-plant-derived prebiotics with multiple biological activities. *International Journal of Molecular Sciences, 23*(12), 6761. https://doi.org/10.3390/ijms23126761

Halder, S. K., Adak, A., Maity, C., Jana, A., Das, A., Paul, T., Ghosh, K., Mohapatra, P. K. D., Pati, B. R., & Mondal, K. C. (2013). Exploitation of fermented shrimp-shells hydrolysate as functional food: Assessment of antioxidant, hypocholesterolemic and prebiotic activities. *Indian Journal of Experimental Biology, 51*(11), 924–934.

Haque, S. A., Al Jufaili, S. M., Islam, M. F., Hasan, M., Mamdouh-Lotfy, M., Rahman, M. S., & Al-Habsi, N. (2026). Sustainable valorisation of fish processing

byproducts through integrated biorefinery approaches. *Discover Food, 6*(1), 45. https://doi.org/10.1007/s44187-026-00222-0

Herrera Barragán, J. A., Olivieri, G., Boboescu, I., Eppink, M., Wijffels, R., & Kazbar, A. (2022). Enzyme assisted extraction for seaweed multiproduct biorefinery: A techno-economic analysis. *Frontiers in Marine Science, 9*, Article 948086. https://doi.org/10.3389/fmars.2022.948086

Hettle, A. G., Vickers, C. J., & Boraston, A. B. (2022). Sulfatases: Critical enzymes for algal polysaccharide processing. *Frontiers in Plant Science, 13*, Article 837636. https://doi.org/10.3389/fpls.2022.837636

Hoevenaars, F. P. M., Scheithauer, T. P. M., Eveleens Maarse, B. C., De Oliveira, I. M., Warnke, I., Sybesma, W., Moerland, M., Van Den Broek, T. J., & Schuren, F. H. J. (2025). Translating in vitro gut microbiota models to human context: Compositional correlations under dietary fiber intervention. *Frontiers in Microbiology, 16*, Article 1708906. https://doi.org/10.3389/fmicb.2025.1708906

Hou, Y., Liu, L., He, Q., Zhang, D., Jin, J., Jiang, B., & Zhao, L. (2022). Adsorption behaviors and kinetics studies of chitooligosaccharides with specific degree of polymerization on a novel ion-exchange resin. *Chemical Engineering Journal, 430*, Article 132630. https://doi.org/10.1016/j.cej.2021.132630

HuiYan, S. T., Sarbini, S. R., Chang, L. S., Joe, L. S., & Babji, A. S. (2026). Eco-recovery of edible swiftlet's nest (ESN) by-product in the form of bioactive sialylated-mucin (SiaMuc) glycopeptide: A prebiotic assessment using in vitro human colonic fermentation. *Journal of Food Science and Technology*, 1–13. https://doi.org/10.1007/s13197-026-06283-y

Hutkins, R., Walter, J., Gibson, G. R., Bedu-Ferrari, C., Scott, K., Tancredi, D. J., Wijeyesekera, A., & Sanders, M. E. (2025). Classifying compounds as prebiotics—Scientific perspectives and recommendations. *Nature Reviews Gastroenterology & Hepatology, 22*(1), 54–70. https://doi.org/10.1038/s41575-024-00981-y

Ijaz, H., Farooqi, M. H., Abbas, A., Qaiser, M., Ullah, A., Emenike, C., Goksen, G., Jambrak, A. R., & Zubair, M. (2026). Global policies and regulations in aquatic waste valorization: Standards, challenges, and opportunities. In *Aquatic waste valorization* (pp. 443–463). https://doi.org/10.1016/B978-0-443-23729-8.00018-5

Ji, X., Zhu, L., Chang, K., Zhang, R., Chen, Y., Yin, H., Jin, J., & Zhao, L. (2022). Chitooligosaccharides: Digestion characterization and effect of the degree of polymerization on gut microorganisms to manage the metabolome functional diversity in vitro. *Carbohydrate Polymers, 275*, Article 118716. https://doi.org/10.1016/j.carbpol.2021.118716

Jung, W. J., Jo, G. H., Kuk, J. H., Kim, Y. J., Oh, K. T., & Park, R. D. (2007). Production of chitin from red crab shell waste by successive fermentation with *Lactobacillus paracasei* KCTC-3074 and *Serratia marcescens* FS-3. *Carbohydrate Polymers, 68*(4), 746–750. https://doi.org/10.1016/j.carbpol.2006.08.011

Kabisch, A., Otto, A., König, S., Becher, D., Albrecht, D., Schüler, M., Teeling, H., Amann, R. I., & Schweder, T. (2014). Functional characterization of polysaccharide utilization loci in the marine Bacteroidetes 'Gramella forsetii' KT0803. *The ISME Journal, 8*(7), 1492–1502. https://doi.org/10.1038/ismej.2014.4

Kang, H., Chen, Z., Wang, B., & Chen, Z. (2025). The AhR/IL-22 axis in chronic gut inflammation: Unraveling mechanisms and therapeutic prospects. *Frontiers in Immunology, 16*, Article 1668173. https://doi.org/10.3389/fimmu.2025.1668173

Kansandee, W., Moonmangmee, S., Vangpikul, S., Kosawatpat, P., & Tamtin, M. (2024). Physicochemical properties and in vitro prebiotic activity of *Ulva rigida* polysaccharides. *Biocatalysis and Agricultural Biotechnology, 59*, Article 103252. https://doi.org/10.1016/j.bcab.2024.103252

Karagöz, M. F., Ünaldı, B.Ö., Buhurcu, C. A., Şen, N., Aydoğdu, G. S., Demirci, K.Ş., Gündüz, Z. G., Güler, M. S., Ağagündüz, D., & Coreta-Gomes, F. (2025). Seaweed polysaccharides and their potential health effects via gut microbiota modulation. *Carbohydrate Polymers.* , Article 124621. https://doi.org/10.1016/j.carbpol.2025.124621

Karuppusamy, S., Wanigasekara, J., Fitzpatrick, S., Lyons, H., Curtin, J., Rajauria, G., Tiwari, B. K., & O'Donnell, C. (2024). Investigation of biological activity of fucoidan and laminarin as bioactive polysaccharides from Irish brown macroalgae. *Cells, 13*(23), 1938. https://doi.org/10.3390/cells13231938

Khaisaat, S., Chancharoensin, S., Wipatanawin, A., Suphantharika, M., & Payongsri, P. (2022). Influence of degree of polymerization of low-molecular-weight chitosan oligosaccharides on the α-glucosidase inhibition. *Molecules, 27*(23), 8129. https://doi.org/10.3390/molecules27238129

Kim, H., Cheon, G. Y., Kim, J. H., Choi, R.-Y., Kim, I.-W., Suh, H. J., Hong, K.-B., & Han, S. H. (2024). Preparation of chitosan oligosaccharides from chitosan of *Tenebrio molitor* and its prebiotic activity. *Applied Biological Chemistry, 67*(1), 84. https://doi.org/10.1186/s13765-024-00944-0

Koch, H., Freese, H. M., Hahnke, R. L., Simon, M., & Wietz, M. (2019). Adaptations of *Alteromonas* sp. 76-1 to polysaccharide degradation: A CAZyme plasmid for ulvan degradation and two alginolytic systems. *Frontiers in Microbiology, 10*, 504. https://doi.org/10.3389/fmicb.2019.00504

Koh, A., De Vadder, F., Kovatcheva-Datchary, P., & Bäckhed, F. (2016). From dietary fiber to host physiology: Short-chain fatty acids as key bacterial metabolites. *Cell, 165*(6), 1332–1345. https://doi.org/10.1016/j.cell.2016.05.041

Kok, C. R., Rose, D. J., Cui, J., Whisenhunt, L., & Hutkins, R. (2024). Identification of carbohydrate gene clusters obtained from in vitro fermentations as predictive biomarkers of prebiotic responses. *BMC Microbiology, 24*(1), 183. https://doi.org/10.1186/s12866-024-03340-0

Kong, M., Chen, X. G., Xing, K., & Park, H. J. (2010). Antimicrobial properties of chitosan and mode of action: A state of the art review. *International Journal of Food Microbiology, 144*(1), 51–63. https://doi.org/10.1016/j.ijfoodmicro.2010.09.012

Kou, S. G., Peters, L., & Mucalo, M. (2022). Chitosan: A review of molecular structure, bioactivities and interactions with the human body and micro-organisms. *Carbohydrate Polymers, 282*, Article 119132. https://doi.org/10.1016/j.carbpol.2022.119132

Krangkratok, W., Chantorn, S., Choosuwan, P., Phomkaivon, N., La-ongkham, O., Kosawatpat, P., Tamtin, M., & Praiboon, J. (2023). Production of prebiotic ulvan-oligosaccharide from the green seaweed *Ulva rigida* by enzymatic hydrolysis. *Biocatalysis and Agricultural Biotechnology, 54*, Article 102922. https://doi.org/10.1016/j.bcab.2023.102922

Kurasawa, R., Hirota, R., & Muto, G. (2026). Agaro-oligosaccharides: Recent advances in production, bioactivities, and functional applications for human health. *Preventive Medicine Research, 3*(4), 133–138. https://doi.org/10.60219/pmr.3.4_133

Lagarto, A., Merino, N., Valdes, O., Dominguez, J., Spencer, E., de la Paz, N., & Aparicio, G. (2015). Safety evaluation of chitosan and chitosan acid salts from *Panurilus argus* lobster. *International Journal of Biological Macromolecules, 72*, 1343–1350. https://doi.org/10.1016/j.ijbiomac.2014.10.030

Lamarque, G., Viton, C., & Domard, A. (2004). Comparative study of the first heterogeneous deacetylation of α- and β-chitins in a multistep process. *Biomacromolecules, 5*(3), 992–1001. https://doi.org/10.1021/bm034454v

Lamminpää, I., Amedei, A., & Parolini, C. (2024). Effects of marine-derived components on cardiovascular disease risk factors and gut microbiota diversity. *Marine Drugs, 22*(11), 523. https://doi.org/10.3390/md22110523

Le Poul, E., Loison, C., Struyf, S., Springael, J.-Y., Lannoy, V., Decobecq, M.-E., Brezillon, S., Dupriez, V., Vassart, G., & Van Damme, J. (2003). Functional characterization of human receptors for short chain fatty acids and their role in polymorphonuclear cell activation. *Journal of Biological Chemistry, 278*(28), 25481–25489. https://doi.org/10.1074/jbc.M301403200

Lee, D.-H., Kim, M.-T., & Han, J.-H. (2024). GPR41 and GPR43: From development to metabolic regulation. *Biomedicine & Pharmacotherapy, 175*, Article 116735. https://doi.org/10.1016/j.biopha.2024.116735

Lee, H.-S. (2008). Classification and characteristics of chitin/chitosan hydrolases. *Journal of Life Science, 18*(11), 1617–1624. https://doi.org/10.5352/JLS.2008.18.11.1617

Lee, H.-W., Park, Y.-S., Jung, J.-S., & Shin, W.-S. (2002). Chitosan oligosaccharides, dp 2–8, have prebiotic effect on the *Bifidobacterium bifidium* and *Lactobacillus* sp. *Anaerobe, 8*(6), 319–324. https://doi.org/10.1016/S1075-9964(03)00030-1

Lehocký, M. (2026). Recent advances in cellulose depolymerization: Mechanistic insights, catalytic innovations, and scalable pathways for biomass valorization. *Polymers, 18*(13), 1565. https://doi.org/10.3390/polym18131565

Leon-Pulido, J., Meramo, S., & González-Delgado, Á. D. (2025). Green chemistry-driven chitosan production from seafood waste: Insights from life cycle and techno-economic assessments. *SSRN*. https://doi.org/10.2139/ssrn.5095657

Li, B., Zhang, J., Dai, F., & Xia, W. (2012). Purification of chitosan by using sol–gel immobilized pepsin deproteinization. *Carbohydrate Polymers, 88*(1), 206–212. https://doi.org/10.1016/j.carbpol.2011.11.092

Li, C., Tang, T., Du, Y., Jiang, L., Yao, Z., Ning, L., & Zhu, B. (2023). Ulvan and *Ulva* oligosaccharides: A systematic review of structure, preparation, biological activities and applications. *Bioresources and Bioprocessing, 10*(1), 66. https://doi.org/10.1186/s40643-023-00685-w

Li, J., Lv, Y., Wei, Y., Wang, X., Yan, S., Zhao, B., Sun, J., Liu, R., & Lai, Y. (2024). *Pinctada martensii* hydrolysate modulates the brain neuropeptidome and proteome in diabetic (db/db) mice via the gut–brain axis. *Marine Drugs, 22*(6), 249. https://doi.org/10.3390/md22060249

Li, N., Xiong, Y.-X., Ye, F., Jin, B., Wu, J.-J., Han, M.-M., Liu, T., Fan, Y.-K., Li, C.-Y., & Liu, J.-S. (2023). Isolation, purification, and structural characterization of polysaccharides from *Codonopsis pilosula* and their anti-tumor bioactivity by immunomodulation. *Pharmaceuticals, 16*(6), 895. https://doi.org/10.3390/ph16060895

Li, Q.-Y., Dou, Z.-M., Chen, C., Jiang, Y.-M., Yang, B., & Fu, X. (2022). Study on the effect of molecular weight on the gut microbiota fermentation properties of blackberry polysaccharides in vitro. *Journal of Agricultural and Food Chemistry, 70*(36), 11245–11257. https://doi.org/10.1021/acs.jafc.2c03686

Liang, Y., Jiang, K., Liu, Z., Tu, J., Gong, W., Hu, Y., Li, J., Hardiman, G., Guo, X., & Zhu, B. (2025). The role of molecular weight on chitosan and chitosan oligosaccharides in sleep regulation: Integrating network pharmacology and multi-omics analysis in Drosophila. *International Journal of Biological Macromolecules, 308*(3), Article 142147. https://doi.org/10.1016/j.ijbiomac.2025.142147

Lin, F., Huang, Y., Zhang, N., Ye, J., & Xiao, M. (2018). Simple and rapid separation of diverse neoagaro-oligosaccharides. *bioRxiv*. , Article 363739. https://doi.org/10.1101/363739

Liu, G.-L., Wu, S.-L., Sun, Z., Xing, M.-D., Chi, Z.-M., & Liu, Y.-J. (2024). ι-Carrageenan catabolism is initiated by key sulfatases in the marine bacterium *Pseudoalteromonas haloplanktis* LL1. *Applied and Environmental Microbiology, 90*(7), Article e0025524. https://doi.org/10.1128/aem.00255-24

Liu, Z., Hu, Y., Tao, X., Li, J., Guo, X., Liu, G., Song, S., & Zhu, B. (2023). Metabolites of sea cucumber sulfated polysaccharides fermented by *Parabacteroides distasonis* and their effects on cross-feeding. *Food Research International, 167*, Article 112633. https://doi.org/10.1016/j.foodres.2023.112633

Liu, Z., Wang, M., Li, J., Zhao, Z., Wang, Z., Hu, Y., Guo, X., Guo, Q., & Zhu, B. (2025). Sulfated polysaccharide from *Hizikia fusiforme* selectively utilized by *Bacteroides caccae* and regulates its metabolite profile during in vitro fermentation. *Food Bioscience, 69*, Article 106816. https://doi.org/10.1016/j.fbio.2025.106816

López-García, C. L., Guerra-Sánchez, G., Santoyo-Tepole, F., & Olicón-Hernández, D. R. (2024). Chitinase induction in *Trichoderma harzianum*: A solid-state fermentation approach using shrimp waste and wheat bran/commercial chitin for chitooligosaccharides synthesis. *Preparative Biochemistry & Biotechnology, 54*(8), 1040–1050. https://doi.org/10.1080/10826068.2024.2308731

Luiz-Santos, N., Prado-Ramírez, R., Arriola-Guevara, E., Camacho-Ruiz, R.-M., & Moreno-Vilet, L. (2020). Performance evaluation of tight ultrafiltration membrane

systems at pilot scale for agave fructans fractionation and purification. *Membranes, 10*(10), 261. https://doi.org/10.3390/membranes10100261
Luo, X., Zhang, Z., Zheng, Z., Zhang, W., Ming, T., Jiao, L., Su, X., Xu, J., & Kong, F. (2024). Characterization of a bacterium isolated from hydrolyzed instant sea cucumber *Apostichopus japonicus* using whole-genome sequencing and metabolomics. *Foods, 13*(22), 3662. https://doi.org/10.3390/foods13223662
Lynch, J. B., & Sonnenburg, J. L. (2012). Prioritization of a plant polysaccharide over a mucus carbohydrate is enforced by a *Bacteroides* hybrid two-component system. *Molecular Microbiology, 85*(3), 478–491. https://doi.org/10.1111/j.1365-2958.2012.08120.x
Lyon, J. D. R., Smith, B. R., Abidi, N., & Shamshina, J. L. (2022). Deproteinization of chitin extracted with the help of ionic liquids. *Molecules, 27*(13), 3983. https://doi.org/10.3390/molecules27133983
Magwaza, S. N., Chabalala, V. N., Hlongwane, N. P., Ismail, H., & Islam, M. S. (2024). Anti-obesity effects of sulphated polysaccharides derived from marine macro algae or seaweeds: A systematic review and meta-analysis. *Marine Drugs, 22*(12), 528. https://doi.org/10.3390/md22120528
Mahdiabadi, M. A., Moghaddam, A., & Erfanian, N. (2026). Microbiome-derived tryptophan metabolites regulate AhR signaling to restore epithelial barrier integrity in inflammatory bowel disease. *MicrobiologyOpen, 15*(5), Article e70386. https://doi.org/10.1002/mbo3.70386
Maiuolo, J., Bulotta, R. M., Ruga, S., Nucera, S., Macrì, R., Scarano, F., Oppedisano, F., Carresi, C., Gliozzi, M., Musolino, V., Mollace, R., Muscoli, C., & Mollace, V. (2024). The postbiotic properties of butyrate in the modulation of the gut microbiota: The potential of its combination with polyphenols and dietary fibers. *International Journal of Molecular Sciences, 25*(13), 6971. https://doi.org/10.3390/ijms25136971
Markushin, S. G., Akopova, I. I., Blagodatskikh, I. V., Kulikov, S. N., Bezrodnykh, E. A., Muranov, A. V., Yamskov, I. A., & Tikhonov, V. E. (2018). Effect of molecular weight and degree of acetylation on adjuvantive properties of chitosan derivatives. *Applied Biochemistry and Microbiology, 54*(5), 512–517. https://doi.org/10.1134/S0003683818050084
MARMADE. (2025). *Circular bio-based Europe joint undertaking (CBE JU)*. MARMADE. https://www.cbe.europa.eu/projects/marmade.
Mateos-Aparicio, I., Mengibar, M., & Heras, A. (2016). Effect of chito-oligosaccharides over human faecal microbiota during fermentation in batch cultures. *Carbohydrate Polymers, 137*, 617–624. https://doi.org/10.1016/j.carbpol.2015.11.011
Mikkelsen, M. D., Cao, H. T. T., Roret, T., Rhein-Knudsen, N., Holck, J., Tran, V. T. T., Nguyen, T. T., Tran, V. H. N., Lezyk, M. J., & Muschiol, J. (2021). A novel thermostable prokaryotic fucoidan active sulfatase PsFucS1 with an unusual quaternary hexameric structure. *Scientific Reports, 11*(1), Article 19523. https://doi.org/10.1038/s41598-021-98911-2
Min, B. H., Devi, S., Kwon, G. H., Gupta, H., Jeong, J.-J., Sharma, S. P., Won, S.-M., Oh, K.-K., Yoon, S. J., & Park, H. J. (2024). Gut microbiota-derived indole compounds attenuate metabolic dysfunction-associated steatotic liver disease by improving fat metabolism and inflammation. *Gut Microbes, 16*(1), Article 2307568. https://doi.org/10.1080/19490976.2024.2307568
Mitchell, C. M., Davy, B. M., Ponder, M. A., McMillan, R. P., Hughes, M. D., Hulver, M. W., Neilson, A. P., & Davy, K. P. (2021). Prebiotic inulin supplementation and peripheral insulin sensitivity in adults at elevated risk for type 2 diabetes: A pilot randomized controlled trial. *Nutrients, 13*(9), 3235. https://doi.org/10.3390/nu13093235
Monge, E. C., & Gardner, J. G. (2021). Efficient chito-oligosaccharide utilization requires two TonB-dependent transporters and one hexosaminidase in *Cellvibrio japonicus*. *Molecular Microbiology, 116*(2), 366–380. https://doi.org/10.1111/mmi.14721
Monteiro, C. R. A. V., Bogea, E. G., Campos, C. D. L., Pereira-Filho, J. L., Almeida, V. S. S., Vale, A. A. M., Azevedo-Santos, A. P. S., & Monteiro-Neto, V. (2026). Prebiotics and gut health: Mechanisms, clinical evidence, and future directions. *Nutrients, 18*(3), 372. https://doi.org/10.3390/nu18030372
Mukhopadhyay, P., Bhattacharya, S., Nandy, A., Bhattacharyya, A., Mishra, R., & Kundu, P. P. (2015). Assessment of in vivo chronic toxicity of chitosan and its derivates used as oral insulin carriers. *Toxicology Research, 4*(2), 281–290. https://doi.org/10.1039/C4TX00139A
Naghdi, S., Rezaei, M., Tabarsa, M., & Abdollahi, M. (2025a). Expanding the pH-shift technique for sequential extraction of intact proteins and sulfated polysaccharide from fish heads: A novel biorefinery approach. *Food Science and Nutrition, 13*(8), Article e70673. https://doi.org/10.1002/fsn3.70673
Naghdi, S., Rezaei, M., Tabarsa, M., & Abdollahi, M. (2025b). Structure, functionality and bioactivity of sulfated polysaccharide extracted from rainbow trout byproducts: pH-shift method vs enzymatic hydrolysis. *Food Chemistry, 479*, Article 143665. https://doi.org/10.1016/j.foodchem.2025.143665
Nawawi, M. H., Ismail, K. I., Sa'ad, N., Mohamad, R., Tahir, P. M., Asa'ari, A. Z., & Saad, W. Z. (2022). Optimisation of xylanase–pectinase cocktail production with *Bacillus amyloliquefaciens* ADI2 using a low-cost substrate via statistical strategy. *Fermentation, 8*(3), 119. https://doi.org/10.3390/fermentation8030119
Ndeh, D., Baslé, A., Strahl, H., Yates, E. A., McClurgg, U. L., Henrissat, B., Terrapon, N., & Cartmell, A. (2020). Metabolism of multiple glycosaminoglycans by *Bacteroides thetaiotaomicron* is orchestrated by a versatile core genetic locus. *Nature Communications, 11*(1), 646. https://doi.org/10.1038/s41467-020-14509-4
Ndeh, D., Munoz, J. M., Cartmell, A., Bulmer, D., Wills, C., Henrissat, B., & Gray, J. (2018). The human gut microbe *Bacteroides thetaiotaomicron* encodes the founding member of a novel glycosaminoglycan-degrading polysaccharide lyase family PL29. *Journal of Biological Chemistry, 293*(46), 17906–17916. https://doi.org/10.1074/jbc.RA118.004087
Noor, H. S. M., Ariff, R. M., Chang, L. S., Chai, X. Y., Tan, H. Y., Daud, N. A., Babji, A. S., & Lim, S. J. (2022). Enzymatic recovery of glycopeptides from different industrial grades edible bird's nest and its by-products: Nutrient, probiotic and antioxidant activities, and physicochemical characteristics. *Food Science and Human Wellness, 11*(6), 1555–1564. https://doi.org/10.1016/j.fshw.2022.06.013
Ojima, M. N., Yoshida, K., Sakanaka, M., Jiang, L., Odamaki, T., & Katayama, T. (2022). Ecological and molecular perspectives on responders and non-responders to probiotics and prebiotics. *Current Opinion in Biotechnology, 73*, 108–120. https://doi.org/10.1016/j.copbio.2021.06.023
Olaniran, A. F., Adeoye, O. E., Oyadeyi, O. M., Okonkwo, C. E., Erinle, O. C., Malomo, A. A., Iranloye, Y. M., Olaniran, O. D., & Faloye, O. R. (2024). Utilization and application of bioactive compounds generated from fish waste and by product as functional food ingredient: A review. *IOP Conference Series: Earth and Environmental Science, 1342*(1), Article 012014. https://doi.org/10.1088/1755-1315/1342/1/012014
Omara, E. A., Aly, H. F., & Nada, S. A. (2012). Chitosan induced hepato-nephrotoxicity in mice with special reference to gender effect in glycolytic enzymes activities. *Regulatory Toxicology and Pharmacology, 62*(1), 29–40. https://doi.org/10.1016/j.yrtph.2011.11.010
Overbeeke, A., Hausmann, B., Nikolov, G., Pereira, F. C., Herbold, C. W., & Berry, D. (2022). Nutrient niche specificity for glycosaminoglycans is reflected in polysaccharide utilization locus architecture of gut *Bacteroides* species. *Frontiers in Microbiology, 13*, Article 1033355. https://doi.org/10.3389/fmicb.2022.1033355
Pan, Y., Li, Y., Peng, Z., Zhang, X., Ye, S., Chen, N., Zhang, Z., & Yang, W. (2024). Indole derivatives and their associated microbial genera are associated with the 1-year changes in cardiometabolic risk markers in Chinese adults. *Nutrition Journal, 23*(1), 160. https://doi.org/10.1186/s12937-024-01070-1
Paudel, L., Pardhe, B. D., Han, S.-R., Lee, J. H., & Oh, T.-J. (2023). Identification and evaluation of CAZyme genes, along with functional characterization of a new GH46 chitosanase from *Streptomyces* sp. KCCM12257. *International Journal of Biological Macromolecules, 253*(8), Article 127457. https://doi.org/10.1016/j.ijbiomac.2023.127457
Pedreira, A., Valcarcel, J., & Vázquez, J. A. (2025). Sustainable valorisation of molluscan wastewaters for the cost-effective production of human and aquaculture probiotics. *Journal of Water Process Engineering, 79*, Article 108927. https://doi.org/10.1016/j.jwpe.2025.108927
Peñaherrera-Pazmiño, A. B., Rosero, G., Criollo, M., & Peñaherrera, J. P. (2025). In vitro gut-models to elucidate how human milk oligosaccharides shape the gut microbiota. *Journal of Functional Foods, 133*, Article 107011. https://doi.org/10.1016/j.jff.2025.107011
Pereira, S. G., Martins, A. A., Mata, T. M., Pereira, R. N., Teixeira, J. A., & Rocha, C. M. R. (2024). Life cycle assessment and cost analysis of innovative agar extraction technologies from red seaweeds. *Bioresource Technology, 414*, Article 131649. https://doi.org/10.1016/j.biortech.2024.131649
Pereira, S. G., Pereira, R. N., Ferreira, S., Nunes, C., Teixeira, J. A., & Rocha, C. M. R. (2025). Advancements in ulvan valorization from *Ulva rigida*: Unveiling a combined approach of electric fields and subcritical water extraction. *Innovative Food Science & Emerging Technologies*. , Article 104318. https://doi.org/10.1016/j.ifset.2025.104318
Pinheiro, V. E., Horvath, I. S., Lundin, M., Polizeli, M., & de, L. T. de M. (2021). Screening and cocktail optimization using experimental mixture design: Enzymatic saccharification as a biological pretreatment strategy. *Biofuels, Bioproducts and Biorefining, 15*(5), 1447–1460. https://doi.org/10.1002/bbb.2241
Pollet, R. M., Martin, L. M., & Koropatkin, N. M. (2021). TonB-dependent transporters in the Bacteroidetes: Unique domain structures and potential functions. *Molecular Microbiology, 115*(3), 490–501. https://doi.org/10.1111/mmi.14659
Priyadarshini, M., Kotlo, K. U., Dudeja, P. K., & Layden, B. T. (2018). Role of short chain fatty acid receptors in intestinal physiology and pathophysiology. *Comprehensive Physiology, 8*(3), 1091–1115. https://doi.org/10.1002/cphy.c170036
Qian, X., Xie, R., Liu, X., Chen, S., & Tang, H. (2022). Mechanisms of short-chain fatty acids derived from gut microbiota in Alzheimer's disease. *Aging and Disease, 13*(4), 1252–1269. https://doi.org/10.14336/AD.2022.0110
Qiao, C., Wang, R., Niu, S., & Huang, D. (2025). Study on the edible safety and immunomodulatory effects of chitosan oligosaccharide taurine aqueous solution in mice. *Chinese Journal of Food Hygiene, 37*(8), 707–714. https://doi.org/10.13590/j.cjfh.2025.08.001
Qin, W., Wei, B., Ren, P., Chang, Y., Xue, C., & Tang, Q. (2025). Fucoidan from *Apostichopus japonicus* enhances intestinal barrier function and promotes intestinal immunity via regulating the gut microbiota and tryptophan metabolism. *International Journal of Biological Macromolecules, 301*, Article 139929. https://doi.org/10.1016/j.ijbiomac.2025.139929
Quinn-Bohmann, N., Carr, A. V., & Gibbons, S. M. (2026). Metabolic modeling reveals determinants of prebiotic and probiotic treatment efficacy across multiple human intervention trials. *PLoS Biology, 24*(2), Article e3003638. https://doi.org/10.1371/journal.pbio.3003638
Quinn-Bohmann, N., Wilmanski, T., Sarmiento, K. R., Levy, L., Lampe, J. W., Gurry, T., Rappaport, N., Ostrem, E. M., Venturelli, O. S., Diener, C., & Gibbons, S. M. (2023). Microbial community-scale metabolic modeling predicts personalized short chain fatty acid production profiles in the human gut. *bioRxiv*. https://doi.org/10.1101/2023.02.28.530516
Razzak, M. A., Kim, H., Haque, M. A., Jang, M. J., Song, S., Talari, A., Chittepu, L. D., & Ku, S. (2026). The prebiotic and techno-functional potential of microbial exopolysaccharides for human health and food systems. *Comprehensive Reviews in Food Science and Food Safety, 25*(2), Article e70406. https://doi.org/10.1111/1541-4337.70406
Riyadi, P. H., Susanto, E., Agustini, T. W., Atho'illah, M. F., Arifah, S. N., & Rifa'i, M. (2025). Immunomodulatory potential of protein hydrolysate by-products derived from skipjack (*Katsuwonus pelamis* (Linnaeus, 1758)) against nicotinamide-

streptozotocin induced diabetic rat. *Veterinary Integrative Sciences, 24*(1), Article e2026006. https://doi.org/10.12982/VIS.2026.006

Rokhati, N., Istirokhatun, T., Hamada, N., & Apriyanti, D. T. (2020). Membrane technology application for fractionation process to obtain high quality glucosamine. *Reaktor, 20*(2), 103–108. https://doi.org/10.14710/reaktor.20.2.103-108

Rout, R. K., Sivaranjani, S., Puja, N., Singh, S. M., Kumar, T. D., T, J. J., & Rao, P. (2025). Valorization of fish wastes and by-products towards green circular bio-economy. *Next Research, 2*(4), Article 101037. https://doi.org/10.1016/j.nexres.2025.101037

Rubak, Y. T., Lalel, H. J. D., Ngurah, B. I. G. M., Turupadang, W. L., Mahara, F. A., & Yusuf, D. (2026). Ulvan polysaccharide of *Ulva lactuca* from coastal Indonesia: Functional prebiotic properties via enzymatic and nonenzymatic extraction. *International Journal of Food Science, 2026*(1), Article 4529168. https://doi.org/10.1155/ijfo/4529168

Rüttiger, A.-S., Ryan, D., Spiga, L., Lamm-Schmidt, V., Prezza, G., Reichardt, S., Langford, M., Barquist, L., Faber, F., & Zhu, W. (2025). The global RNA-binding protein RbpB is a regulator of polysaccharide utilization in *Bacteroides thetaiotaomicron*. *Nature Communications, 16*(1), 208. https://doi.org/10.1038/s41467-025-55734-1

Salonen, A., Lahti, L., Salojärvi, J., Holtrop, G., Korpela, K., Duncan, S. H., Date, P., Farquharson, F., Johnstone, A. M., & Lobley, G. E. (2014). Impact of diet and individual variation on intestinal microbiota composition and fermentation products in obese men. *The ISME Journal, 8*(11), 2218–2230. https://doi.org/10.1038/ismej.2014.63

Sang, X., Guan, X., Tong, Y., Wang, F., Zhou, B., Li, Y., & Zhao, Q. (2024). Sulfated polysaccharides from sea cucumber cooking liquid prevents obesity by modulating gut microbiome, transcriptome, and metabolite profiles in mice fed a high-fat diet. *Foods, 13*(13), 2017. https://doi.org/10.3390/foods13132017

Schmidt, J., Smith, N. J., Christiansen, E., Tikhonova, I. G., Grundmann, M., Hudson, B. D., Ward, R. J., Drewke, C., Milligan, G., & Kostenis, E. (2011). Selective orthosteric free fatty acid receptor 2 (FFA2) agonists: Identification of the structural and chemical requirements for selective activation of FFA2 versus FFA3. *Journal of Biological Chemistry, 286*(12), 10628–10640. https://doi.org/10.1074/jbc.M110.210872

Shehzadi, F., Shoaib, M., Munir, S., & Abdi, G. (2025). Ultrasound-assisted extraction of bioactive compounds from pomegranate peel and seed: A comprehensive review of key parameters and optimization strategies. *Ultrasonics Sonochemistry*. , Article 107722. https://doi.org/10.1016/j.ultsonch.2025.107722

Sheridan, P. O., Martin, J. C., Lawley, T. D., Browne, H. P., Harris, H. M. B., Bernalier-Donadille, A., Duncan, S. H., O'Toole, P. W., Scott, K. P., & Flint, H. J. (2016). Polysaccharide utilization loci and nutritional specialization in a dominant group of butyrate-producing human colonic Firmicutes. *Microbial Genomics, 2*(2), Article e000043. https://doi.org/10.1099/mgen.0.000043. https://www.microbiologyresearch.org/content/journal/mgen/10.1099/mgen.0.000043

Silchenko, A. S., Rubtsov, N. K., Zueva, A. O., Kusaykin, M. I., Rasin, A. B., & Ermakova, S. P. (2022). Fucoidan-active α-L-fucosidases of the GH29 and GH95 families from a fucoidan degrading cluster of the marine bacterium *Wenyingzhuangia fucanilytica*. *Archives of Biochemistry and Biophysics, 728*, Article 109373. https://doi.org/10.1016/j.abb.2022.109373

Silva, S. P., González, A., Roupar, D., Dias, M. S., Salvador, A. F., Teixeira, J. A., Almeida, R. D., Nobre, C., Coimbra, M. A., & Coelho, E. (2026). Glycosidic linkage-dependent fermentation of polysaccharide mixtures by human gut microbiota in vitro. *Carbohydrate Polymers, 388*, Article 125497. https://doi.org/10.1016/j.carbpol.2026.125497

Songkoomkrong, S., Nonkhwao, S., Saetan, J., Duangprom, S., Amonruttanapun, P., Janpan, P., Sobhon, P., & Kornthong, N. (2026). Chitosan oligosaccharides suppress adipogenesis and lipid accumulation in 3T3-L1 preadipocytes via multi-pathway transcriptomic reprogramming. *International Journal of Molecular Sciences, 27*(11), 4970. https://doi.org/10.3390/ijms27114970

Stilling, R. M., Van De Wouw, M., Clarke, G., Stanton, C., Dinan, T. G., & Cryan, J. F. (2016). The neuropharmacology of butyrate: The bread and butter of the microbiota-gut-brain axis? *Neurochemistry International, 99*, 110–132. https://doi.org/10.1016/j.neuint.2016.06.011

Stoddart, L. A., Smith, N. J., Jenkins, L., Brown, A. J., & Milligan, G. (2008). Conserved polar residues in transmembrane domains V, VI, and VII of free fatty acid receptor 2 and free fatty acid receptor 3 are required for the binding and function of short-chain fatty acids. *Journal of Biological Chemistry, 283*(47), 32913–32924. https://doi.org/10.1074/jbc.M805601200

Stojnić, B., Galmés, S., Serrano, A., Sulli, M., Sušak, L., Seye, N., Palou, A., Diretto, G., Bonet, M. L., & Ribot, J. (2024). Glycosaminoglycan dermatan sulfate supplementation decreases diet-induced obesity and metabolic dysfunction in mice. *BioFactors, 50*(3), 493–508. https://doi.org/10.1002/biof.2031

Swackhamer, C., Jang, S., Park, B.-R., Hamaker, B. R., & Jung, S. K. (2025). Structure-based standardization of prebiotic soluble dietary fibers based on monosaccharide composition, degree of polymerization, and linkage composition. *Carbohydrate Polymers, 367*, Article 123949. https://doi.org/10.1016/j.carbpol.2025.123949

Tang, S., Dong, X., Ma, Y., Zhou, H., He, Y., Ren, D., Li, X., Cai, Y., Wang, Q., & Wu, L. (2024). Highly crystalline cellulose microparticles from dealginated seaweed waste ameliorate high fat-sugar diet-induced hyperlipidemia in mice by modulating gut microbiota. *International Journal of Biological Macromolecules, 263*(2), Article 130485. https://doi.org/10.1016/j.ijbiomac.2024.130485

Tao, X., Wu, X., Wu, H., Tu, L., Dong, M., Xiao, Y., Yu, X., & Zhong, T. (2026). A structural roadmap to gut health: A comprehensive review of edible insect chitin–protein complexes as alternative protein-derived, structure-specific prebiotics. *International Journal of Biological Macromolecules, 354*, Article 151312. https://doi.org/10.1016/j.ijbiomac.2026.151312

Tauzin, A. S., Laville, E., Xiao, Y., Nouaille, S., Le Bourgeois, P., Heux, S., Portais, J., Monsan, P., Martens, E. C., & Potocki-Veronese, G. (2016). Functional characterization of a gene locus from an uncultured gut *Bacteroides* conferring xylo-oligosaccharides utilization to *Escherichia coli*. *Molecular Microbiology, 102*(4), 579–592. https://doi.org/10.1111/mmi.13482

Teferi, D. A., Kassa, M. G., Belachew, M. T., Asemu, A. M., Abera, B. D., Erku, E. G., & Ayalew, D. B. (2026). A review on valorizing sugarcane bagasse for prebiotic production with insights on health benefits, applications, regulations, and challenges. *Food Production, Processing and Nutrition, 8*(1), 51. https://doi.org/10.1186/s43014-026-00218-6

Teixeira-Guedes, C., Gomes-Dias, J. S., Cunha, S. A., Pintado, M. E., Pereira, R. N., Teixeira, J. A., & Rocha, C. M. R. (2023). Enzymatic approach for the extraction of bioactive fractions from red, green and brown seaweeds. *Food and Bioproducts Processing, 138*, 25–39. https://doi.org/10.1016/j.fbp.2022.12.005

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), Turck, D., Bresson, J., Burlingame, B., Dean, T., Fairweather-Tait, S., Heinonen, M., Hirsch-Ernst, K. I., Mangelsdorf, I., & McArdle, H. (2016). Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283. *EFSA Journal, 14*(11), Article e04594. https://doi.org/10.2903/j.efsa.2016.4594

Unal, K. I., Chang, L. S., Mustapha, W. A. W., Razali, N. S. M., Babji, A. S., & Lim, S. J. (2024). Extraction, structural analysis and biological activities of edible bird's nest sialylated mucin (SiaMuc) glycoproteins: A review. *Food Bioscience, 61*, Article 104791. https://doi.org/10.1016/j.fbio.2024.104791

Ustyuzhanina, N. E., Bilan, M. I., Anisimova, N. Y., Dmitrenok, A. S., Tsvetkova, E. A., Kiselevskiy, M. V., Nifantiev, N. E., & Usov, A. I. (2022). Depolymerization of a fucosylated chondroitin sulfate from *Cucumaria japonica*: Structure and activity of the product. *Carbohydrate Polymers, 281*, Article 119072. https://doi.org/10.1016/j.carbpol.2021.119072

Ustyuzhanina, N. E., Bilan, M. I., Dmitrenok, A. S., Nifantiev, N. E., & Usov, A. I. (2018). Fucosylated chondroitin sulfates from the sea cucumbers *Holothuria tubulosa* and *Holothuria stellati*. *Carbohydrate Polymers, 200*, 1–5. https://doi.org/10.1016/j.carbpol.2018.07.035

Van Hul, M., Neyrinck, A. M., Everard, A., Abot, A., Bindels, L. B., Delzenne, N. M., Knauf, C., & Cani, P. D. (2024). Role of the intestinal microbiota in contributing to weight disorders and associated comorbidities. *Clinical Microbiology Reviews, 37*(3), Article e0004523. https://doi.org/10.1128/cmr.00045-23

Vera-Ponce de León, A., Hensen, T., Hoetzinger, M., Gupta, S., Weston, B., Johnsen, S. M., Rasmussen, J. A., Clausen, C. G., Pless, L., Veríssimo, A. R. A., Rudi, K., Snipen, L., Karlsen, C. R., Limborg, M. T., Bertilsson, S., Thiele, I., Hvidsten, T. R., Sandve, S. R., Pope, P. B., & La Rosa, S. L. (2024). Genomic and functional characterization of the Atlantic salmon gut microbiome in relation to nutrition and health. *Nature Microbiology, 9*(11), 3059–3074. https://doi.org/10.1038/s41564-024-01830-7

Wang, J., Wei, Y., Chen, D., Li, X., Zhang, H., Feng, S., Lu, S., Yang, J., Zeng, Q., He, X., & Wu, L. (2025). Targeted therapy for gut microbiota: Candidates for a novel strategy to ameliorate type 2 diabetes mellitus. *Microbial Biotechnology, 18*(12), Article e70283. https://doi.org/10.1111/1751-7915.70283

Wang, L., Yang, H., Huang, H., Zhang, C., Zuo, H.-X., Xu, P., Niu, Y.-M., & Wu, S.-S. (2019). Inulin-type fructans supplementation improves glycemic control for the prediabetes and type 2 diabetes populations: Results from a GRADE-assessed systematic review and dose-response meta-analysis of 33 randomized controlled trials. *Journal of Translational Medicine, 17*(1), 410. https://doi.org/10.1186/s12967-019-02159-0

Wang, S., De Paepe, K., Onyango, S. O., Zhang, B., Huang, Q., Wang, S., & Van de Wiele, T. (2026). Starch-entrapped microspheres selectively promote propionate or butyrate production through individual-specific modulation of the human fecal microbiome. *Carbohydrate Polymers, 373*, Article 124614. https://doi.org/10.1016/j.carbpol.2025.124614

Wu, C., Yu, X., Zheng, P., Chen, P., & Wu, D. (2023). Rational redesign of chitosanase to enhance thermostability and catalytic activity to produce chitooligosaccharides with a relatively high degree of polymerization. *Journal of Agricultural and Food Chemistry, 71*(41), 15213–15223. https://doi.org/10.1021/acs.jafc.3c04632

Wu, H., Zhang, J., Zhu, H., Peñarubia, O., & Willer, D. F. (2026). Technology-driven reduction of fish post-harvest loss could enhance food security and economic resilience. *Communications Sustainability, 1*(1), 45. https://doi.org/10.1038/s44284-026-00045-0

Xie, D., Li, P., Zhu, Y., He, J., Zhang, M., Liu, K., Lin, H., Zhai, H., Li, X., & Ma, Y. (2022). Comparative bioactivity profile of phospholipids from three marine byproducts based on the zebrafish model. *Journal of Food Biochemistry, 46*(9), Article e14229. https://doi.org/10.1111/jfbc.14229

Xie, S. (2026). Transforming seafood processing residues into a circular blue bioeconomy: Modern advances, integrated pathways and industrial translation. *Food Chemistry, 517*, Article 149479. https://doi.org/10.1016/j.foodchem.2026.149479

Yamabhai, M., Khamphio, M., Min, T. T., Soem, C. N., Cuong, N. C., Aprilia, W. R., Luesukprasert, K., Teeranitayatarn, K., Maneedaeng, A., & Tuveng, T. R. (2024). Valorization of shrimp processing waste-derived chitosan into anti-inflammatory chitosan-oligosaccharides (CHOS). *Carbohydrate Polymers, 324*, Article 121546. https://doi.org/10.1016/j.carbpol.2023.121546

Yan, T. H., Babji, A. S., Lim, S. J., & Sarbini, S. R. (2021). A systematic review of edible swiftlet's nest (ESN): Nutritional bioactive compounds, health benefits as functional food, and recent development as bioactive ESN glycopeptide hydrolysate. *Trends in Food Science & Technology, 115*, 117–132. https://doi.org/10.1016/j.tifs.2021.06.042

Yin, D., Sun, X., Li, N., Guo, Y., Tian, Y., & Wang, L. (2021). Structural properties and antioxidant activity of polysaccharides extracted from *Laminaria japonica* using

various methods. *Process Biochemistry, 111*, 201–209. https://doi.org/10.1016/j.procbio.2021.10.017

You, Y., Cao, Y., Guo, S., Xu, J., Li, Z., Wang, J., & Xue, C. (2015). Purification and identification of α2–3 linked sialoglycoprotein and α2–6 linked sialoglycoprotein in edible bird's nest. *European Food Research and Technology, 240*(2), 389–397. https://doi.org/10.1007/s00217-014-2341-y

Yousef, M., Pichyangkura, R., Soodvilai, S., Chatsudthipong, V., & Muanprasat, C. (2012). Chitosan oligosaccharide as potential therapy of inflammatory bowel disease: Therapeutic efficacy and possible mechanisms of action. *Pharmacological Research, 66*(1), 66–79. https://doi.org/10.1016/j.phrs.2012.03.013

Yu, B., Lu, Z., Zhong, S., & Cheong, K.-L. (2024). Exploring potential polysaccharide utilization loci involved in the degradation of typical marine seaweed polysaccharides by *Bacteroides thetaiotaomicron*. *Frontiers in Microbiology, 15*, Article 1332105. https://doi.org/10.3389/fmicb.2024.1332105

Yun, Y. R., Kim, S., Lee, D. Y., Yu, S., Kim, K. H., & Yun, E. J. (2026). Valorizing renewable biomass into potential prebiotic oligosaccharides: Enzymatic, microbial, and synthetic biology strategies. *Bioresource Technology, 458*, Article 134974. https://doi.org/10.1016/j.biortech.2026.134974

Zeng, X., Li, P., Chen, X., Kang, Y., Xie, Y., Li, X., Xie, T., & Zhang, Y. (2019). Effects of deproteinization methods on primary structure and antioxidant activity of *Ganoderma lucidum* polysaccharides. *International Journal of Biological Macromolecules, 126*, 867–876. https://doi.org/10.1016/j.ijbiomac.2018.12.220

Zhang, C., Jiao, S., Wang, Z. A., & Du, Y. (2018). Exploring effects of chitosan oligosaccharides on mice gut microbiota in in vitro fermentation and animal model. *Frontiers in Microbiology, 9*, 2388. https://doi.org/10.3389/fmicb.2018.02388

Zhang, H., & Neau, S. H. (2001). In vitro degradation of chitosan by a commercial enzyme preparation: Effect of molecular weight and degree of deacetylation. *Biomaterials, 22*(12), 1653–1658. https://doi.org/10.1016/S0142-9612(00)00326-3

Zhang, X., Yang, H., Zheng, J., Jiang, N., Sun, G., Bao, X., Lin, A., & Liu, H. (2021). Chitosan oligosaccharides attenuate loperamide-induced constipation through regulation of gut microbiota in mice. *Carbohydrate Polymers, 253*, Article 117218. https://doi.org/10.1016/j.carbpol.2020.117218

Zhao, L., Sun, T., & Wang, L. (2017). Chitosan oligosaccharide improves the therapeutic efficacy of sitagliptin for the therapy of Chinese elderly patients with type 2 diabetes mellitus. *Therapeutics and Clinical Risk Management, 13*, 739–750. https://doi.org/10.2147/TCRM.S134039

Zhao, Q. C., Teng, Z., Wang, Q. K., Liu, J. R., Jin, Q., Wang, C., & Bai, H. (2007). Laminaria polysaccharide extraction by compound enzymes. *Food Science and Technology, 32*(8), 125–127.

Zheng, J., Cheng, G., Li, Q., Jiao, S., Feng, C., Zhao, X., Yin, H., Du, Y., & Liu, H. (2018). Chitin oligosaccharide modulates gut microbiota and attenuates high-fat-diet-induced metabolic syndrome in mice. *Marine Drugs, 16*(2), 66. https://doi.org/10.3390/md16020066

Zheng, M., Chao, X., Zheng, Y., Hong, T., Wu, W., Zhu, Y., Ni, H., & Jiang, Z. (2024). A polysaccharide from edible red seaweed *Bangia fusco-purpurea* prevents obesity in high-fat diet-induced C57BL/6 mice. *International Journal of Biological Macromolecules, 283*(Pt 2), Article 137545. https://doi.org/10.1016/j.ijbiomac.2024.137545

Zhou, M., Lei, K., Zhang, J., Yan, Q., Cao, H., Bai, Y., Wei, K., & Su, Z. (2026). Marine-derived chitooligosaccharide attenuates obesity and metabolic syndrome in Bama pigs through LXR-mediated cholesterol metabolism and gut microbiota modulation. *Nutrients, 18*(8), 1233. https://doi.org/10.3390/nu18081233

Zonfrillo, B. (2025). *Ulvan from Ulva lactuca L.: A multitarget approach for chemical characterization combined with in vitro tests on human gut microbiota* [Master's thesis, University of Florence].

Zonfrillo, B., C, M. S. A., Mulinacci, N., & Rubert, J. (2026). Ulvan acts as a prebiotic polysaccharide enhancing the production of indoles and short-chain fatty acids in vitro: A metabolomics study. *Food Chemistry, 514*, Article 149100. https://doi.org/10.1016/j.foodchem.2026.149100