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Dietary glycans and their role in human health: implications for gut health, metabolism, and functional foods

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ABSTRACT

Dietary glycans, a diverse class of carbohydrate-based biomolecules, play a crucial role in human health by modulating gut microbiota, enhancing immune responses, and influencing metabolic processes. This review explores the physiological significance of dietary glycans, their classification, and their natural food sources. The prebiotic effects of glycans on gut microbiota composition and short-chain fatty acid (SCFAs) production are highlighted, emphasizing their role in digestive health and gut barrier integrity. Additionally, glycans contribute to immune modulation by interacting with immune receptors, showcasing anti-inflammatory properties beneficial in autoimmune conditions. Beyond gut health, dietary glycans are implicated in aging and metabolic health. Their antioxidative and anti-aging effects, alongside their influence on glucose metabolism, insulin sensitivity, and lipid homeostasis, underscore their potential in managing obesity, diabetes, and cardiovascular diseases. In food science, glycans are emerging as functional food ingredients, with innovations in glycan-enriched foods, fermented products, and dietary supplements. However, the stability and bioavailability of glycans during food processing remain critical challenges. Furthermore, glycans are gaining attention in sports nutrition, with potential applications in muscle recovery and exercise performance. The advent of glycomics and precision nutrition paves the way for personalized dietary interventions targeting metabolic and immune health. This review provides a comprehensive understanding of dietary glycans, their physiological roles, and their potential in functional food development. It underscores future directions in dietary glycan research and its implications for human health.

1. Introduction to dietary glycans and their importance in human health

Carbohydrates stand among the three main macronutrients in the nutrition of an individual with the primary importance of energy metabolism.[1] More than just simple sugars and starches, there exists a specialized subclass of carbohydrates called glycans, which are of paramount importance in the fields of food science and human physiology.[2] Glycans are complex carbohydrate molecules made of glycosidically linked monosaccharide units that are structurally formed as oligosaccharides, polysaccharides, glycoproteins, and glycolipids. In contrast to simple carbohydrates that are readily available as an energy source, glycans are biomolecules acting as biological structurally functional components, signaling molecules, and biological spare parts, modulating a myriad of biological activities.[3] Within dietary science, glycans are naturally found in many food sources such as fruits, vegetables, whole grains, dairy products, and marine foods.[4] As food ingredients, dietary glycans play important functional roles in enhancing food texture, stability, and nutritional values, thereby making them important constituents of both traditional diets and modern innovations of functional foods.[5]

The importance of glycans is not limited to food. One of the notable biological roles of glycan is that it affects the gut microbiota, which is the enormous variety of microorganisms living in the human digestive system.[6] Some dietary glycans, and especially prebiotic oligosaccharides, boost the growth of certain beneficial bacterial strains like *Bifidobacteria* and *Lactobacilli*.[7] These bacteria use glycans and ferment them to short-chain fatty acids (SCFA), which have several health benefits, such as enhancing the gut barrier, reducing inflammation, and improving energy metabolism. Such interplay of dietary glycans and gut microbiota is critical for digestion, nutrient absorption, and general gastrointestinal health.[8] Human milk oligosaccharides (HMOs) found in mother's milk are some of the most well-known examples of glycans that help in the development of the gut microbiome in infants and help

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them fight infections.[9] Likewise, beta-glucans in mushrooms and oats act as immune-modulating polysaccharides that foster gut health and boost immune defenses.[10]

Glycans are also implicated in the regulation of metabolism, especially of blood glucose, cholesterol, and lipids.[11] Some dietary slowly digestible carbohydrates, like certain beta-glucans, dietary fibers, or resistant starches, prevent the rapid increase of blood glucose levels while simultaneously boosting insulin's effectiveness, thereby fostering greater sensitivity towards it. Such properties make them useful for individuals vulnerable to type 2 diabetes and metabolic syndrome.[12] Moreover, beta-glucans from oats and barley have also been found to cut down on the levels of LDL cholesterol, which, in turn, reduces the likelihood of heart disease.[13] In addition, marine sulfated polysaccharides possess anti-inflammatory and antioxidant activity, which further enhances metabolic and cardiovascular health.[14] These results emphasize the importance of dietary glycans as prophylactic agents for various diseases as well as for the maintenance of health.

Even though there is a growing appreciation of the importance of glycans to human health, their functions are still not as well-studied in depth as are those of proteins and nucleic acids. The main reason for this is that glycan structures are complex and their various physiological interactions are multifaceted, requiring tools like mass spectrometry, glycan sequencing, and other advanced analytical approaches for systematic examination.[15] Nonetheless, progress in glycoscience is enabling a better understanding of the interactions that dietary glycans have with biological systems, which is opening new frontiers in nutrition, medicine, and biotechnology.[16] Their role in food and formulation, gastrointestinal health, immune system modulation, and prevention of chronic disease makes glycans a very important topic of study in contemporary food science.[17]

This study seeks to give an in-depth review of dietary glycans, with an emphasis on their taxonomy, natural sources, and physiological roles in human health. It will examine how glycans affect gut microbiota composition, immunological function, and metabolic health, emphasizing their role in functional foods and medicinal applications. Furthermore, the review will glance at current research advances and future goals in glycoscience, with a particular emphasis on how glycans might be used to enhance health outcomes and develop novel nutritional approaches.

2. Dietary glycans and natural food sources

Foods contain a varied class of carbohydrates called glycans, each of which has unique structural traits and biological roles.[18] They influence the texture, digestibility, and health effects of food and can be found in a variety of dietary sources. Investigating the role of glycans in human nutrition and health requires an understanding of the many forms of glycans and their natural sources.[19]

2.1. Classification of dietary glycans

The structure and function of dietary glycans allow for their general classification into several groups.[20] N-glycans, O-glycans, glycosaminoglycans, and glycolipids are the main types, as shown in Fig. 1, and each has a distinct function in physiological processes:

- **O-Glycans:** These glycans attach to the oxygen atoms of serine or threonine residues in proteins. They are high in mucins, which are critical for gut health and immunological function. O-glycans are found in plant-based foods such as fruits, vegetables, and cereals.[21]
- **Glycosaminoglycans (GAGs):** These are lengthy, unbranched polysaccharides made up of repeating disaccharide units that play an important role in tissue structure. Common kinds include chondroitin sulfate, heparan sulfate, and hyaluronic acid, which are found in animal-derived foods, including bone broth, cartilage, and shellfish.[22]
- **Glycolipids:** These glycans are connected to lipids and play an important role in cell membrane integrity and signaling. They are most commonly found in dairy products, certain fermented foods, and marine sources.[23]

Each form of glycan has distinct structural features that influence its digestibility, absorption, and bioactivity, ultimately impacting its role in human health.[24]

2.2. Major dietary sources of glycans

Dietary glycans are naturally present in a wide variety of foods, with their composition varying based on food type and processing methods, as shown in Table 1. These food sources contain a wide range of glycans, which contribute to several health benefits, including improved gut microbiota composition, immunological modulation, and metabolic balance.[25]

The bioavailability of dietary glycans is determined by food source, processing, digestion, and gut microbiota interactions.[26] Soluble fibers are fermentable by gut bacteria, which promotes gut health, whereas insoluble fibers resist digestion and aid with bowel movements.[27] Processing changes glycan structures, which affects digestibility and biological activity. Fermentation increases glycan bioavailability, as shown in kimchi, kefir, and sourdough bread, where microbial activity alters glycans to improve absorption.[28] Cooking can degrade glycans, increasing digestibility, as seen in cooked carrots, which release more bioactive pectin.[29] Furthermore, resistant starches in green bananas and raw potatoes are less digested but become more accessible when cooked and cooled.[30] Understanding these variations aids in optimizing glycan consumption for greater health advantages.

3. Glycans and immune modulation: enhancing immunity and reducing inflammation

Glycans play a crucial role in immune modulation by influencing host-microbe interactions, regulating inflammation, and enhancing immune surveillance. Glycans are important prebiotics that help maintain a healthy gut microbiota, which is necessary for immune system homeostasis. Glycans' immunomodulatory properties are especially important for controlling autoimmune disorders and reducing inflammatory reactions.[39]

3.1. Interaction of glycans with immune receptors

Glycans are bioactive substances that interact with host immunological receptors to alter immune signals. These interactions affect immunological pathways that are both innate and adaptive:

- Glycans interact with Toll-like receptors (TLRs), NOD-like receptors (NLRs), and C-type lectin receptors (CLRs) to modulate immune responses through downstream signaling cascades like NF-κB activation and MAPK pathways, which control cytokine expression and immune cell differentiation. These receptors are known as Pattern Recognition Receptors (PRRs).[40]
- Activation of Dendritic Cells and Macrophages: Glycans control the balance between pro-inflammatory (M1) and anti-inflammatory (M2) phenotypes in antigen-presenting cells (APCs), especially dendritic cells and macrophages. This strategy suppresses excessive inflammatory responses while promoting the development of regulatory T cells (Tregs).[41]
- GALT stands for Glycan-Gut-Associated Lymphoid Tissue Interactions: By interacting with Peyer's patches and mesenteric lymph nodes, the glycans generated from the gut microbiota promote mucosal immunity and immunological tolerance by triggering a regulated immune response against both commensal and pathogenic microorganisms.[42]

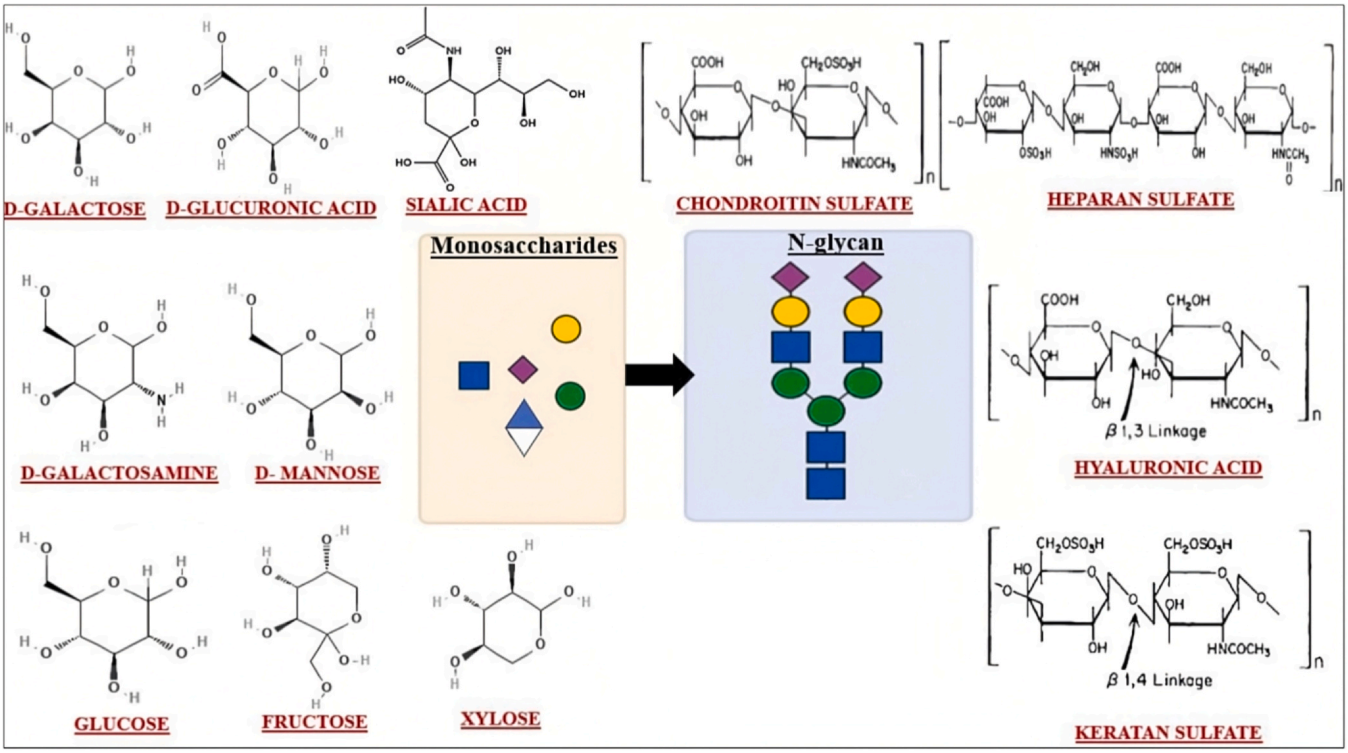

Fig. 1. Classification of typical dietary glycans.

Table 1
List of major dietary sources of glycans.

Food source	Major glycan type (S)	Health benefits	Reference
Fruits	Pectin, Hemicelluloses, Arabinogalactans	Supports gut health, acts as a prebiotic, regulates digestion	31
Vegetables	O-Glycans, Pectin, Fructooligosaccharides (FOS)	Enhances immune function, supports gut microbiota, anti-inflammatory	32
Whole Grains	Beta-glucans, Arabinoxylans, Cellulose	Lowers cholesterol, supports gut health, improves metabolic balance	33
Legumes	Galactooligosaccharides (GOS), N-Glycans, Hemicelluloses	Prebiotic activity, improves digestion, supports cardiovascular health	34
Dairy & Fermented Foods	Glycoproteins, HMOs, Modified Glycans	Enhances gut microbiota, strengthens immunity, supports digestion	35
Seafood & Marine Sources	Sulfated Polysaccharides (Fucoidans, Carrageenan, Chondroitin Sulfate)	Antioxidant, anti-inflammatory, supports joint and heart health	36
Mushrooms	Beta-glucans, Chitin	Boosts immune response, regulates cholesterol, supports gut microbiota	37
Nuts & Seeds	Galactomannans, Arabinogalactans	Provides dietary fiber, supports metabolic health, anti-inflammatory	38

3.2. Anti-inflammatory properties and their role in autoimmune diseases

By both direct and indirect means, glycans have strong anti-inflammatory qualities that make them essential for reducing autoimmune dysregulation and chronic inflammation.

- Immunomodulation Mediated by Short-Chain Fatty Acids (SCFAs): SCFAs, including butyrate, acetate, and propionate, are produced when glycans are fermented by microbes. These SCFAs act as inhibitors of histone deacetylase (HDAC) and activate G-protein-coupled receptors (GPCRs), including GPR41, GPR43, and GPR109A.[43] These interactions promote anti-inflammatory mediators like TGF-β and IL-10 while suppressing inflammatory cytokines including TNF-α, IL-6, and IL-1β.
- Autoimmune Regulation and Regulatory T Cell Expansion: SCFAs encourage Foxp3 + Treg differentiation and proliferation, which is critical for immune tolerance and the avoidance of autoimmune diseases like multiple sclerosis (MS), rheumatoid arthritis (RA), and inflammatory bowel disease (IBD).[44]
- Gut Barrier Integrity and Control of Systemic Inflammation: Glycans help to stabilize tight junction proteins (occludin, claudin) and secrete mucin, which lowers intestinal permeability and stops systemic inflammation associated with autoimmune diseases.[45]

3.3. Potential of glycan-rich foods in enhancing immune response

By altering the composition of the gut microbiota and boosting mucosal immunity, including foods high in glycans in the diet has promising immunological effects.

- **Effects of Microbiota and Prebiotics:** Foods high in glycans, such as inulin, Arabinoxylans, fructooligosaccharides (FOS), and β-glucans, specifically promote the growth of *Lactobacillus* and *Bifidobacterium*, which help to maintain immunological homeostasis.[46]

- **Improved Systemic and Mucosal Immunity:** The production of secretory IgA (sIgA), which is essential for pathogen neutralization and gut barrier defense, is influenced by dietary glycans.[47]
- **Immunonutrition's Potential for Therapy:** Glycan-enriched functional foods and nutraceuticals are being investigated as potential therapeutic agents to reduce inflammation, stop gut dysbiosis[48] and improve the effectiveness of vaccines.

4. The impact of dietary glycans on aging and longevity

4.1. Role of glycans in cellular aging and oxidative stress reduction

Oxidative stress, caused by an imbalance between pro-oxidants and antioxidants, affects glycan expression by altering glycosyltransferase gene activity. This leads to structural and functional changes in glycoproteins, contributing to chronic diseases like diabetes, Alzheimer's, multiple sclerosis, and COPD. The integration of glycoscience and redox biology, termed "glyco-redox research," offers new insights into disease mechanisms and aging.

Aging and age-related diseases share key mechanisms such as inflammation, metabolic dysfunction, proteostasis loss, and stem cell depletion. These processes are influenced by oxidative stress and glycomic alterations. Though glycan changes have been well-studied in cancer and diabetes, fewer studies focus on aging-related glycomic shifts. Emerging evidence links chronic stress, including PTSD and Alzheimer's,[49] to immune dysregulation and accelerated cellular aging, with changes observed in N-glycan profiles and metabolomic signatures in humans and animals.[50] Glycan-based biomarkers hold promise for differentiating biological age from chronological age and diagnosing age-related conditions. Clinically used glycoprotein markers and serum/plasma-derived N- and O-linked glycans are being explored for their diagnostic potential, with levels varying in diseases compared to healthy states. Understanding glycan dynamics could aid in the early detection and management of aging-related disorders.[51]

4.2. Glycan-rich diets and their impact on longevity biomarkers

Identifying potential biomarkers is crucial for early diagnosis, allowing timely treatment and a better understanding of disease mechanisms. Clinical glycomics focused on glycosylation analysis, offers significant potential across medical fields. Analytical methods such as gel electrophoresis, mass spectrometry, and lectin-based techniques enable the study of free glycans and intact glycoproteins. More refined methods, including lectin capture, improve specificity, especially when combined with protein levels. This integrative approach enhances early diagnosis and therapy monitoring in diseases like cancer, diabetes, Alzheimer's, and inflammatory disorders. Clinical validation remains vital, as glycosylation is influenced by both genetic and environmental factors.[52]

One notable biomarker, Leucine-rich alpha-2 glycoprotein (LRG), shows a strong association with inflammatory conditions, including bacterial and aseptic meningitis. Another study optimized biomarker isolation from blood using prolonged ultracentrifugation and electrostatic repulsion-hydrophilic interaction chromatography (PUC-ERLIC), followed by mass spectrometry-based quantification. Meanwhile, noninvasive approaches examine skin biomarkers like collagen, hyaluronan, proteoglycans, and glycoproteins, useful in monitoring chronic inflammatory diseases and impaired wound healing.[53]

The GlycoAgeTest is a promising aging biomarker, based on the logarithmic ratio of two glycans (NGA2F/NA2F). This ratio remains stable until age 40, then increases progressively, peaking in individuals over 90. Elevated GlycoAgeTest values have been noted in dementia and Cockayne syndrome patients, suggesting its utility in assessing biological versus chronological aging. It offers potential for predicting disease progression and identifying early age-related dysfunctions.

Age-related glycosylation changes in proteins are increasingly recognized.[54] For instance, Immunoglobulin G (IgG) exhibits altered glycosylation with age, shifting toward a pro-inflammatory profile that contributes to chronic inflammation and tissue damage. Similarly, α1-antitrypsin (αAT) glycosylation is linked to cardiovascular and metabolic disorders. Other glycoproteins like protein C, plasminogen, and α2-macroglobulin (α2M) also undergo age-related changes. Although one study found no major differences in α2M glycosylation between newborn and adult plasma, microheterogeneity varied, with higher sialic acid content in newborn samples. Age-related shifts included increased α2,6-linked sialic acid, mannose, N-acetylglucosamine, and multiantennary N-glycans.[55]

In cancer, typical glycosylation changes involve increased sialylation, enhanced branching, and core fucosylation. Clinically used glycoprotein biomarkers include PSA (prostate), AFP (liver), CA125 (ovary), CA15–3 (breast), and β-HCG (reproductive cancers). CA19–9, derived entirely from a glycan (sialyl Lewis A), is a notable biomarker for digestive cancers. However, many of these markers lack optimal sensitivity and specificity, prompting continued research into refining glycan-based diagnostics for improved early detection and disease monitoring.

5. Glycan diversity and function across human organ systems

5.1. Role of glycans in cardiovascular system

Glycosylation, the most prevalent post-translational protein modification, plays a crucial role in regulating protein function. Many acute-phase proteins, which are released by the liver in response to inflammation, undergo enzymatic glycosylation and circulate at measurable levels detectable by proton nuclear magnetic resonance (NMR) spectroscopy.[56] The glycosylated serum protein components N-acetylglucosamine/galactosamine and sialic acid serve as nonspecific indicators of inflammation and exhibit a strong correlation with C-reactive protein (CRP).[57] Elevated GlycA (Glycan-associated biomarker) levels have been linked to common cardiovascular disease (CVD) risk factors, including smoking, diabetes, hypertension, dyslipidemia, and obesity. Longitudinal studies, such as the Women's Health Study and the Multi-Ethnic Study of Atherosclerosis (MESA), have shown that GlycA independently predicts the onset of coronary heart disease and CVD events, with its association with CVD being comparable to that of CRP. However, after adjusting for CRP levels, the association between GlycA and CVD was no longer statistically significant.[58]

Protein glycosylation, the process of attaching carbohydrates to proteins, is one of the most prevalent co-translational and post-translational modifications. Technological advancements have significantly expanded our understanding of the biosynthetic pathways involved in glycosylation and how alterations in this process can impact cellular function.[59] In the heart, alterations in protein glycosylation are involved in the development of heart failure, cardiac hypertrophy, and the detrimental effects of diabetes mellitus. In the vascular system, glycosylation dysregulation affects cell–cell interactions, promotes inflammation, and contributes to vascular remodelling processes, including atherosclerosis.[60]

5.2. Functional roles of glycans in the human respiratory system

Pathogens such as influenza A virus (IAV) recognize glycans in the human lungs, yet the structural details of these glycans remain largely unexplored. In this study, we provide the first comprehensive characterization of N-glycans, O-glycans, and glycosphingolipid (GSL) glycans from whole human lung tissue, alongside histological assessments of IAV binding. The lung N-glycome features unusually large complex-type N-glycans with linear poly-N-acetyllactosamine (PL) [−3Galβ1–4GlcNAcβ1-] n chains, predominantly capped with α2,3-linked sialic acid. In contrast, smaller N-glycans lack these PL extensions and are enriched with α2,6-linked sialic acids. Large GSL-glycans comprising linear PL structures, similarly terminating mainly in α2,3-linked sialic acid. Histological staining showed that IAV binds to both sialylated and non-sialylated glycans, and this binding pattern does not align directly with that observed using sialic acid-specific lectins.[61]

5.3. Role of glycans in the urinary system

Bladder cancer ranks among the most prevalent malignant tumors of the urogenital tract and is associated with high rates of illness and death globally. Achieving early detection and implementing personalized therapies are essential for effective treatment. However, due to frequent postoperative recurrence and poor outcomes, there is a pressing need to identify effective therapeutic targets and biomarkers. Glycans, one of the four major classes of biological macromolecules alongside proteins, nucleic acids, and lipids are involved in critical cellular functions such as protein folding, processing, and translation; cell adhesion; receptor-ligand interactions; and signal transduction. Glycans are categorized into N-glycans, O-glycans, proteoglycans, and glycosphingolipids. This review focuses on glycans associated with bladder cancer and explores their potential clinical applications in its diagnosis and treatment. Aberrant glycan structures may serve as promising biomarkers for bladder cancer.[62]

5.4. Glycans in neural development and function

Cells of the central nervous system contain at least ten distinct monosaccharides, which contribute to a diverse array of oligosaccharides essential for proper brain function. The synthesis of monosaccharides and sugar nucleotides demonstrates considerable metabolic flexibility, utilizing multiple precursor pathways. N-linked glycans play a vital role in a wide range of neuronal activities, including regulation of the resting membrane potential, axonal signaling, and synaptic vesicle release. Additionally, N-linked glycosylation is a key regulator of the unfolded protein response (UPR), which influences the survival or death of neurons. Many components of the innate immune system, such as cytokines, nitric oxide synthase, and other related proteins and enzymes, undergo N-linked glycosylation, highlighting the important role of these glycans in neuroinflammatory processes.[63]

6. Functional foods and glycan fortification: innovations in food science

Functional foods are gaining attention for their potential to improve health beyond basic nutrition.[64] Glycans, complex carbohydrates found in dietary sources, have emerged as promising functional food components due to their prebiotic, immunomodulatory, and metabolic health benefits.[65]

6.1. Functional roles of glycans in food science

Glycans contribute to various functional roles in food formulations.[66] Table 2 highlights the diverse functional roles of glycans in food products, showcasing their impact on texture, preservation, and health benefits. These bioactive carbohydrates contribute to gut health, immune modulation, and antimicrobial properties, enhancing both food quality and consumer well-being.[67]

6.2. Sources and extraction of glycans for functional foods

Glycans, a diverse group of bioactive carbohydrates, play a crucial role in food functionality and health benefits. They can be derived from plant-based sources, microbial sources, and marine sources.[76] The extraction and purification of glycans are essential to enhance their bioavailability, functional properties, and potential applications in the food and nutraceutical industries.[77]

Fig. 2 illustrates glycans extraction and purification methods, highlighting their natural sources, extraction techniques, refinement processes, and applications in glycan-enriched functional foods.

Different methods are employed to extract glycans from raw materials, each influencing their structure and functionality:

- **Hot Water Extraction (HWE)**: Common for beta-glucans and pectin, as it facilitates the release of polysaccharides from plant and fungal sources.[78]
- **Enzymatic Hydrolysis**: Used primarily for producing oligosaccharides by breaking down complex polysaccharides into bioactive components.[79]
- **Ultrasound-Assisted Extraction (UAE)**: Enhances extraction efficiency and bioactivity, reducing processing time and energy consumption.[80]
- **Supercritical Fluid Extraction (SFE)**: Ensures high purity with minimal solvent residues, making it a sustainable and efficient method for glycan recovery.[81]

Once extracted, glycans undergo purification to remove impurities and enhance their functionality. Purified glycans are incorporated into various glycan-enriched functional foods.[82]

6.3. Glycan fortification in functional foods

Fortification with glycans aims to improve the nutritional and health-promoting properties of food products.[83] Table 3 presents various glycan-fortified functional foods, highlighting the incorporation of bioactive carbohydrates into different food categories to enhance their health benefits. Glycans such as inulin, beta-glucans, chitosan, and oligosaccharides are widely used to improve gut health, cardiovascular function, immune support, and antimicrobial properties.[84] These functional ingredients are commonly found in dairy, cereals, beverages, meat products, and plant-based foods, with several commercially available examples demonstrating their efficacy in promoting human health.[85]

This table underscores the growing application of glycans in functional food formulations**,** providing nutritional and therapeutic benefits while improving food texture, stability, and preservation.

Table 2
Functional roles of glycans in food products.

Glycan Type	Functional Role	Example Foods	Health Benefits	References
Inulin	Prebiotic	Yogurt, cereal bars	Gut microbiota modulation	68
Beta-glucans	Immune-modulating	Oatmeal, mushroom-based products	Anti-inflammatory effects	69
Pectin	Textural enhancer	Jams, juices	Gut health, cholesterol reduction	70
Chitosan	Antimicrobial	Edible coatings, meat products	Pathogen inhibition, obesity management	71
Arabinoxylans	Prebiotic, Texturizer	Whole grains, baked goods	Improves digestion, regulates blood sugar	72
Fucoidans	Antioxidant, Anti-inflammatory	Seaweed, marine algae	Supports immune function, reduces inflammation	73
Hyaluronic Acid	Moisture retention, Anti-aging	Functional beverages, supplements	Skin hydration, joint health	74
Dextran	Emulsifier, Prebiotic	Bakery products, fermented foods	Enhances texture, promotes gut health	75

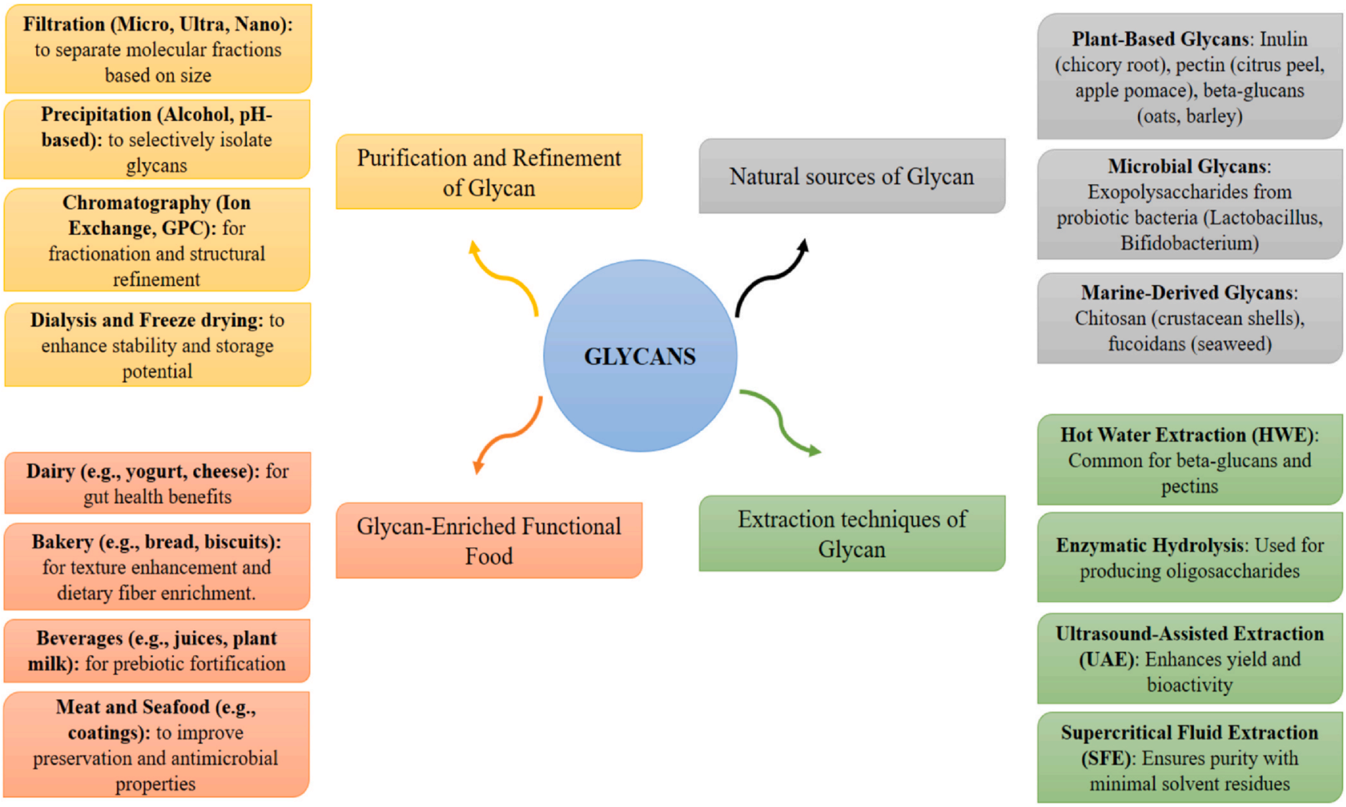

Fig. 2. Extraction and purification methods for glycans.

6.4. *Technological innovations in glycan-enriched functional foods*

Microencapsulation for Glycan Stability: Encapsulation techniques such as spray drying and freeze-drying are employed to improve glycan stability and bioavailability.[86]

Glycan-Based Edible Coatings and Films:

- Chitosan-based edible coatings for meat and fruit preservation.
- Pectin-infused biofilms for biodegradable packaging.[87]

Symbiotic Formulations: Combining glycans with probiotics (e.g., *Lactobacillus* with inulin) enhances gut microbiome synergy.[88]

6.5. *Challenges and future perspectives*

While glycan fortification offers numerous health benefits, several challenges must be addressed to enhance its commercial viability and consumer acceptance.[89] Regulatory approvals play a crucial role, as novel glycans require rigorous safety evaluations before being incorporated into food products.[90] Another key concern is the stability of glycans during processing, as some are heat-sensitive and may degrade under high-temperature conditions, affecting their functional properties.[91] Additionally, consumer acceptance remains a challenge, as glycan fortification can sometimes alter the taste, texture, or mouthfeel of food products, necessitating formulation adjustments.[92] The cost of production is another barrier, as advanced extraction and purification techniques often require sophisticated technology, making large-scale implementation expensive.[93]

Looking ahead, future directions in glycan research and application hold great promise. One emerging area is the development of smart glycan-based packaging, where bioactive glycans can be incorporated into food packaging materials to enhance preservation and antimicrobial properties.[94] Another exciting prospect is glycan-enriched personalized nutrition, where dietary interventions can be tailored based on an individual's gut microbiota and metabolic needs.[95] Furthermore, biotechnological advances in glycan synthesis are expected to drive innovation, enabling cost-effective and sustainable production of functional glycans with enhanced bioavailability and targeted health benefits.[96]

Table 3
Examples of glycan-fortified functional foods.

Food Category	Glycan Added	Health Benefit	Commercial Examples
Dairy	Inulin, GOS	Gut microbiome modulation	Prebiotic yogurt
Cereal	Beta-glucans	Heart health, immune support	Oat-based breakfast cereals
Beverages	Pectin, FOS	Digestive support	Fiber-enriched juices
Meat Products	Chitosan	Antimicrobial, fat reduction	Low-fat meat patties
Plant-Based Foods	Xylo oligosaccharides (XOS)	Prebiotic function	Fortified soy milk
Confectionery	Fructo-oligosaccharides (FOS)	Supports gut microbiota, reduces sugar load	Prebiotic chocolate, candy
Infant Nutrition	Galactooligosaccharides (GOS)	Enhances gut flora, immune development	Probiotic infant formula
Bakery Products	Arabinoxylans	Improves digestion, regulates blood sugar	Whole grain bread, fortified biscuits
Seafood Products	Fucoidans	Anti-inflammatory, antioxidant effects	Seaweed-based functional foods

7. Prebiotic effects of glycans: gut microbiota and digestive health

As complex carbohydrate structures, glycans are essential for regulating the composition of the gut microbiota, promoting microbial fermentation, and impacting host digestion and gut barrier function.[97] Their capacity to act as specific substrates for advantageous gut bacteria, which results in the synthesis of short-chain fatty acids and other bioactive compounds that influence host metabolism, immunological responses, and general gut health, accounts for their prebiotic potential.[98]Gaining knowledge about how glycans affect digestion and gut flora is essential for using them in functional foods and treatments.[99]

7.1. Role of glycans on the composition of the gut microbiota

The immune system, gut integrity, and host metabolism are all significantly impacted by the complex and dynamic collection of bacteria known as the gut microbiota.[100]By providing substrates for specific bacterial development, glycans influence the microbial environment by promoting the growth of helpful bacteria and inhibiting the growth of harmful ones.[101]Glycans affect the composition of the microbiome through the following mechanisms:

7.1.1. Beneficial microbiota-mediated selective fermentation

Glycans function as a substrate for specific microbial communities, including *Bifidobacterium, Lactobacillus*, and *Akkermansia muciniphila*,[102] each of which plays a crucial role in intestinal health. The fermentation of glycans provides these bacteria with necessary nutrients, allowing them to outcompete potentially dangerous microorganisms.[103] The selective nature of glycan consumption contributes to a healthy microbial environment, which is essential for host metabolism and immunological function.

7.1.2. Competitive exclusion of pathogens

Beneficial bacteria that feed on glycans serve to control harmful bacteria through a variety of processes. They compete with pathogenic species for glycan-derived substrates, limiting disease development.[104] Furthermore, antimicrobial metabolite synthesis during glycan fermentation causes the release of organic acids like lactic acid and short-chain fatty acids (SCFAs),[105] which reduce gut pH and produce an unfavorable environment for pathogens like *Clostridium difficile* and *Escherichia coli*.[106]Furthermore, glycans help to reinforce the mucosal barrier by increasing mucin synthesis, which improves gut barrier integrity and reduces pathogen adhesion, resulting in a healthy gut microbiome.[107]

7.1.3. Impact on Immunomodulation

Through its interactions with gut-associated lymphoid tissue (GALT), glycans also affect immune system activity.[108] Glycan fermentation produces SCFAs, which have immunomodulatory effects through:

- Enhancing regulatory T cell (Treg) production, which aids in immune response regulation[109]
- Lowering pro-inflammatory cytokine release to lessen inflammation in the stomach[110]
- Strengthening the tight junctions of the gut epithelium prevents increased intestinal permeability and helps reduce systemic inflammation.[111]

7.2. Role of glycans in fermentation and production of short-chain fatty acids

Glycan Function in Fermentation and Short-Chain Fatty Acid (SCFAs) Production Fermentation, a microbially driven process that converts complex carbohydrates into bioactive metabolites, including SCFAs, is a crucial byproduct of glycan metabolism. These metabolites are important modulators of immunological response, metabolism, and gut homeostasis.[112] Dietary glycans, like inulin and pectin, are fermented by gut bacteria into SCFAs (acetate, propionate, and butyrate), acting as prebiotics. Butyrate fuels colonocytes, strengthens the gut barrier, and enhances tight junctions. SCFAs inhibit HDACs, reduce inflammation, and modulate immunity through GPR receptors.[113] They lower gut pH, suppress harmful bacteria, and improve mineral absorption. SCFAs also regulate metabolism, influence the gut-brain axis, and support antioxidant and mucin production.[114]

7.2.1. Functions of glycans in gut health and metabolism

- Promote the growth of beneficial gut microbes as prebiotics: Glycans act as prebiotic fibers that selectively feed helpful bacteria like *Bifidobacteria* and *Lactobacilli*, improving gut microbiota balance and overall digestive health.[115]
- Act as substrates for fermentation to produce SCFAs: In the colon, undigested glycans are fermented by gut microbes to generate short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate, which are vital for gut and metabolic health.[116]
- Strengthen gut barrier by enhancing tight junctions: SCFAs, particularly butyrate, help reinforce the tight junctions between intestinal epithelial cells, reducing permeability and protecting against harmful substances entering the bloodstream.[117]
- Regulate immune function and reduce inflammation: SCFAs derived from glycan fermentation modulate immune cell activity, promote the development of regulatory T cells, and suppress inflammatory responses in the gut.[118]
- Maintain acidic gut pH to inhibit harmful pathogens: The SCFAs produced during glycan fermentation lower the colon's pH, creating an environment that inhibits the growth of pathogenic bacteria and favors beneficial microbes.[119]
- Influence host metabolism through SCFA-related pathways: SCFAs impact metabolic processes by regulating glucose and lipid metabolism, enhancing insulin sensitivity, and influencing appetite through gut-brain signaling.[120]

7.3. Possible advantages for digestion and gut barrier function

By enhancing digestion processes and fortifying the gut barrier, glycans support gut health in addition to modifying the microbiota.

7.3.1. Improvement of the integrity of the gut barrier

- Mucosal Defense and Mucin Production: The intestinal mucus layer is strengthened and pathogen adhesion is inhibited by the stimulation of mucin secretion by certain glycans (galactans, arabinoxylans).[121]
- Reinforcement at Tight Junctions: Butyrate and propionate decrease intestinal permeability and stop leaky gut syndrome by upregulating tight junction proteins (occludin, claudin, and ZO-1).[122]

7.3.2. Increased effectiveness of digestion

- SCFAs-Mediated Stimulation of Enzymes: SCFAs improve the digestion of proteins and carbohydrates by increasing the production of pancreatic enzymes.[123]
- Improved Absorption of Nutrients: Butyrate maximizes the absorption of nutrients by increasing the height of intestinal villi and the depth of crypts.[124]
- Regulation of Gut Motility: By influencing the functioning of the enteric nervous system, SCFAs-GPCR signaling encourages normal peristalsis and lessens constipation.[125]

7.3.3. The impact of the gut-brain axis

- GPR41 and GPR43-mediated SCFAs signaling affect neurotransmitter synthesis, controlling mood, hunger, and cognitive performance[126]

- Gut microbiota activity is linked to mental health and stress resilience through the modulation of serotonin and dopamine levels by glycan fermentation products.[127]

8. Processing and bioavailability of glycans in food products

8.1. Impact of food processing on glycans

Food processing techniques, including thermal treatments, mechanical processing, and enzymatic modifications, can significantly alter the structure and functionality of glycans.[128]

8.1.1. Thermal processing

- Pasteurization, Sterilization, and Cooking: High temperatures can hydrolyze glycans, leading to a reduction in molecular weight and changes in their physiological function.[129]
- Baking and Roasting: Maillard reactions can occur between glycans and proteins, affecting their digestibility and potential prebiotic properties.[130]
- Extrusion Cooking: Used in cereal processing, this technique alters the solubility and fermentability of glycans.[131]

8.1.2. Mechanical processing[132]

- Grinding and Milling: These processes reduce particle size, enhancing the surface area for enzymatic digestion, but may also lead to oxidation.[133]
- High-Pressure Processing (HPP): This non-thermal technique can preserve glycan integrity while improving microbial safety.[134]

8.1.3. Enzymatic and fermentation processing

- Enzymatic Hydrolysis: Enzymes like amylase and cellulase can modify glycans to improve their digestibility and functional properties.[135]
- Fermentation: Utilization of probiotics can transform glycans into bioactive oligosaccharides, enhancing their prebiotic potential.[136]

Fig. 3 illustrates the different processing methods of glycans, including thermal, mechanical, enzymatic, and fermentation techniques, and their effects on glycan properties. It also highlights the final bioavailability of glycans in the gut, where they are either absorbed or fermented by gut microbiota.

8.2. Bioavailability of glycans

Bioavailability refers to the extent to which dietary glycans are absorbed and utilized in the body.[137] Factors affecting glycan bioavailability include:

8.2.1. Structural complexity

Highly branched and polymerized glycans have lower digestibility, necessitating microbial fermentation in the colon.[138]

8.2.2. Interaction with other food components

Glycans may form complexes with proteins, lipids, and polyphenols, affecting their solubility and absorption.[139]

8.2.3. Gastrointestinal digestion and microbial fermentation

- Enzymatic Breakdown: Human digestive enzymes primarily target simple carbohydrates, leaving complex glycans for microbial metabolism.[140]
- Gut Microbiota Utilization: Certain bacterial species (e.g., *Bifidobacterium*, *Lactobacillus*) ferment glycans, producing beneficial short-chain fatty acids (SCFAs).[141]

Table 4 categorizes various glycan types based on their digestibility and primary site of action in the digestive system. While some, like starch, are readily digested in the small intestine, others, such as inulin and pectin, undergo fermentation in the colon. The digestibility and site of action influence their prebiotic potential and physiological effects.[142]

Fig. 4 outlines the bioavailability pathway of glycans, starting from ingestion and digestion in the small intestine to microbial fermentation in the colon. Undigested glycans serve as substrates for gut microbiota, leading to the production of short-chain fatty acids (SCFAs). SCFAs contribute to gut health, immune modulation, and metabolism regulation.[143]

8.3. Strategies to enhance glycan bioavailability

To improve the bioavailability of glycans in food products, the following strategies can be employed:

8.3.1. Encapsulation technologies

- Microencapsulation and Nanoencapsulation: Protects glycans from thermal degradation and enzymatic breakdown, enhancing controlled release.[144]
- Lipid-Based Delivery Systems: Improves absorption and bioactivity.[145]

8.3.2. Combination with probiotics

- Symbiotic Formulations: Combining glycans with probiotic strains can enhance fermentation and bioactivity.[146]
- Targeted Fermentation: Utilizing specific microbial strains to preferment glycans before consumption.[147]

8.3.3. Modified processing techniques

- Cold Extrusion and Freeze Drying: Preserve glycan integrity while improving solubility.
- Low-Temperature Fermentation: Maintains bioactivity while promoting microbial metabolism.[148]

9. Glycans in sports nutrition and muscle recovery

9.1. Glycans as an energy source

The significance of glycans in sports nutrition is gaining attention due to their potential to enhance athletic performance and overall wellbeing. This review explores the role of glycans in sports nutrition, focusing on their contribution to energy production, muscle repair, immune support, and gut health.[149]

Glycans, primarily in the form of glycogen, serve as a crucial energy reservoir for athletes. Glycogen, a polysaccharide stored in muscles and the liver, acts as a readily available energy source during high-intensity exercise.[150] The breakdown of glycogen into glucose provides immediate fuel, delaying fatigue and sustaining endurance. Adequate glycogen replenishment through carbohydrate-rich diets ensures sustained athletic performance and prevents energy depletion.[151]

9.2. Glycans in muscle repair and recovery

Post-exercise muscle recovery is essential for maintaining peak performance. Glycans contribute to muscle repair by regulating protein synthesis and cellular signaling pathways.[152] Glycoproteins and

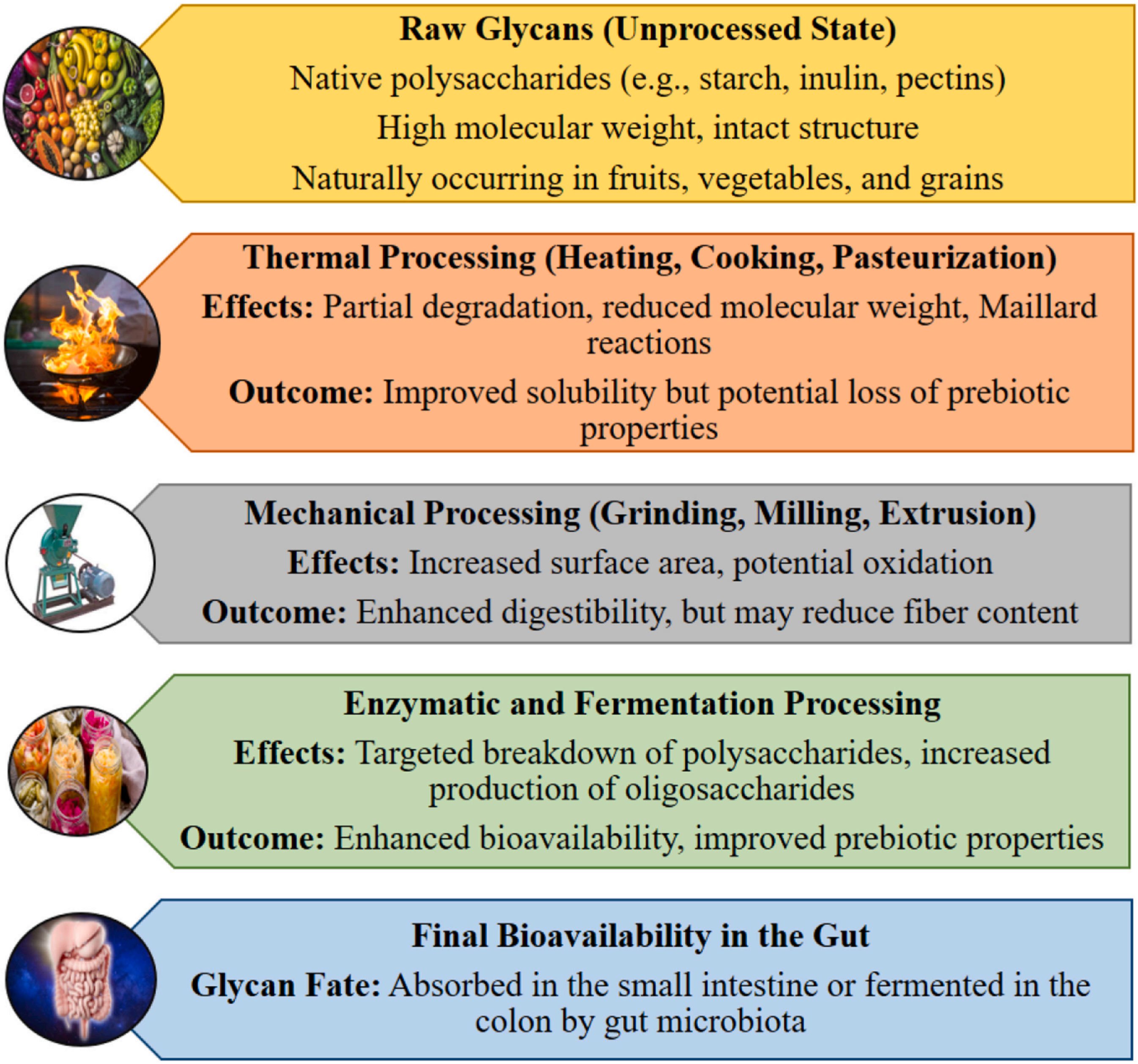

Fig. 3. Schematic representation of glycan transformations during different processing techniques.

Table 4
Digestibility and main site of action of different glycan types.

Glycan type	Digestibility	Main site of action
Starch	High	Small intestine
Inulin	Low	Colon (fermentation)
Beta-glucans	Moderate	Small intestine & colon
Pectin's	Low	Colon
Cellulose	Very Low	Colon (fermentation, minimal digestion)
Arabinoxylans	Moderate	Small intestine & colon
Galactooligosaccharides (GOS)	Low	Colon (fermentation)

proteoglycans, structural components of connective tissues, support muscle regeneration and reduce inflammation.[153] Consuming glycans post-workout, in combination with proteins, accelerates muscle recovery and minimizes the risk of injury.[154]

9.3. Dietary sources of glycans for athletes

Glycans are fundamental to sports nutrition, influencing energy metabolism, muscle recovery, immune function, and gut health. Athletes can optimize their performance and overall well-being by incorporating glycan-rich foods into their diets.[155] Continued research into glycans' role in sports nutrition may uncover new strategies to enhance endurance, recovery, and resilience in athletes. Understanding and utilizing glycans effectively can provide a competitive edge, ensuring sustained physical excellence and long-term health benefits.[156]

9.4. Potential of glycan-rich foods in sports nutrition

Athletes can obtain glycans from various natural sources, including:

- **Whole Grains**: Oats, brown rice, and quinoa provide essential glycans for sustained energy.[157]

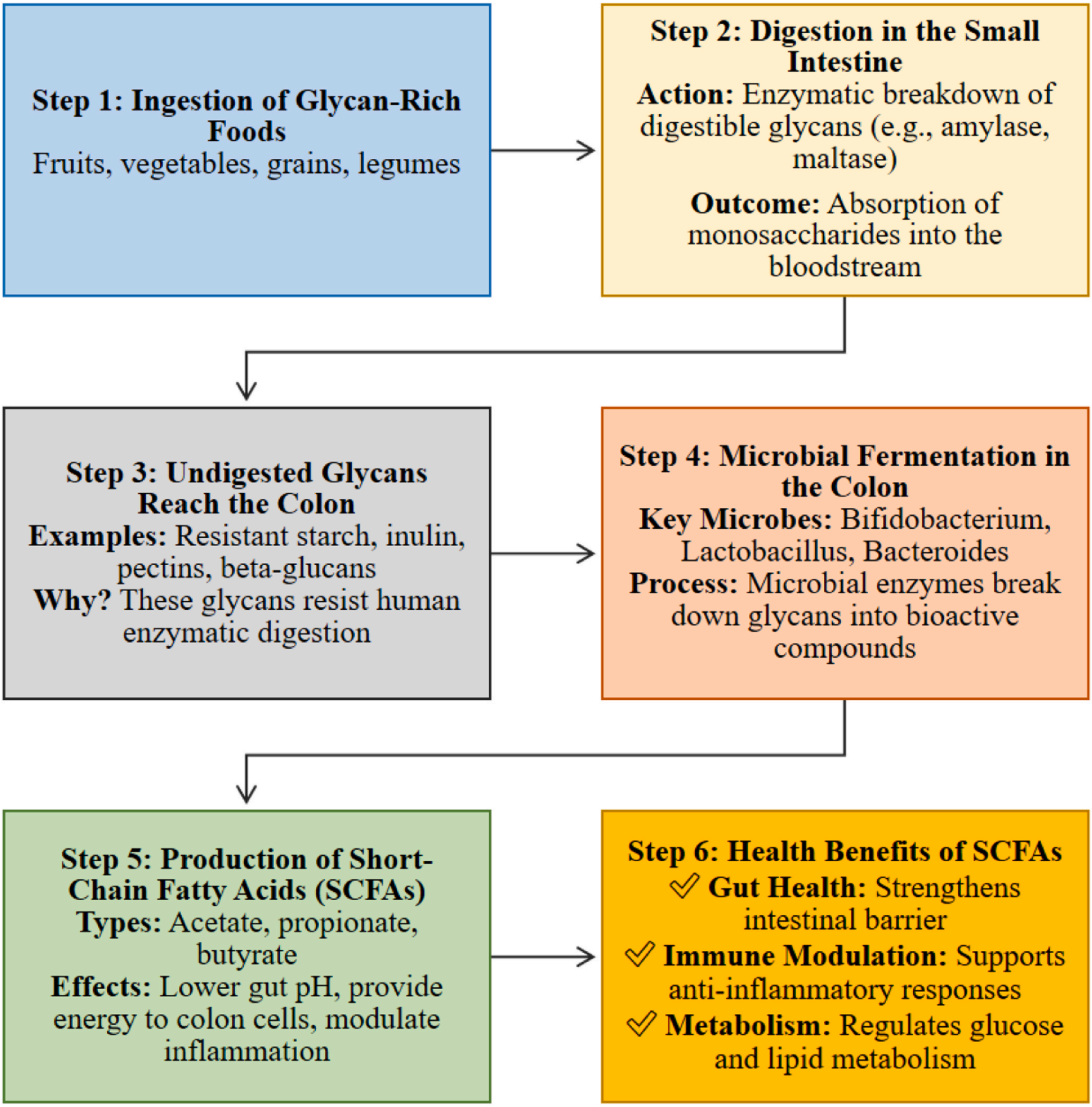

Fig. 4. Bioavailability pathway of glycans from ingestion to microbial fermentation and SCFAs production in the gut.

- **Fruits and Vegetables**: Bananas, apples, and leafy greens contain fiber-rich glycans beneficial for digestion and immune support.[158]
- **Dairy Products**: Milk and yogurt offer glycoproteins that aid in muscle repair and immune modulation.[159]
- **Legumes and Nuts**: Beans, lentils, and almonds supply complex carbohydrates essential for endurance.[160]
- **Seaweed and Mushrooms**: Rich in bioactive glycans, these foods enhance immune function and gut health.[161]

10. Emerging trends in glycan research for personalized nutrition

Glycan research is rapidly advancing, offering new insights into the role of complex carbohydrates in human health and nutrition.[162] As personalized nutrition gains traction, the study of glycans has become essential for understanding individual dietary needs, gut microbiome interactions, and metabolic responses. With the integration of cutting-edge technologies such as glycomics, artificial intelligence, and bioengineering, researchers are uncovering how glycans influence digestion, immune function, and chronic disease prevention. This review explores emerging trends in glycan research and their implications for personalized nutrition.

10.1. The potential role of glycans in individualized diet plans

Glycans, complex carbohydrate structures attached to proteins and lipids, play critical roles in digestion, metabolism, immune function, and cell signaling.[163] Unlike DNA and proteins, which have predictable structures, glycans exhibit high structural diversity, making their study challenging.[164] However, recent advances in glycomics have allowed for better characterization of glycan functions and their impact on human health. The potential of glycans in individualized diet plans, emphasizing their role in metabolic regulation, disease prevention, and gut health.[165]

10.2. Glycans and metabolic regulation

Metabolism is intricately linked to glycans, as they modulate glucose absorption, insulin sensitivity, and lipid metabolism.[166] Dietary glycans, such as those found in fiber and prebiotics, influence glycemic control by slowing carbohydrate digestion and absorption. Personalized diet plans can incorporate specific glycans to manage conditions like diabetes by optimizing blood sugar levels.[167] Additionally, variations in glycan structures between individuals can affect metabolic responses, necessitating tailored dietary recommendations.[168]

10.3. Glycans in disease prevention

The role of glycans in disease prevention is significant, particularly in conditions like cardiovascular diseases, obesity, and inflammatory disorders.[169] Certain glycans exhibit anti-inflammatory properties, reducing the risk of chronic diseases.[170] For example, glycan-rich foods such as seaweed and legumes contain bioactive compounds that regulate inflammatory markers. Moreover, glycans influence lipid metabolism and cholesterol levels, contributing to heart health. Understanding an individual's glycan profile can help formulate diets that minimize disease risk.[171]

10.4. Omics intervention in glycans

10.4.1. Omics approaches to glycans in personalized nutrition

The field of personalized nutrition is transforming, driven by advancements in omics sciences such as genomics, proteomics, metabolomics, and glycomics.[172] Among these, glycomics, the study of glycans and their biological functions, is emerging as a key player in understanding individualized dietary needs.[173] The interplay between glycans, genes, proteins, and metabolites is now recognized as essential for tailoring nutrition to improve health outcomes.[174] The current review explores the role of omics interventions in glycans and their implications for the future of personalized nutrition.

10.4.2. Genomics and glycans

Genomic studies have identified genes responsible for glycan biosynthesis and metabolism. Variations in these genes influence an individual's ability to digest and utilize dietary glycans.[175] For example, genetic differences in lactase persistence affect lactose digestion, while mutations in glycosylation pathways can impact immune responses and disease susceptibility.[176] Understanding these genetic variations enables personalized dietary recommendations.

10.4.3. Proteomics and glycans

Glycoproteins, which are proteins with glycan modifications, play vital roles in digestion and nutrient absorption. Proteomic analysis helps identify glycan-modified proteins involved in metabolic regulation, immune function, and gut health.[177] By studying these interactions, researchers can develop functional foods tailored to an individual's glycoprotein profile.

10.4.4. Metabolomics and glycans

Metabolomics investigates the metabolic products influenced by dietary intake and microbiome activity. Glycans interact with gut microbiota to produce metabolites that impact energy balance, inflammation, and overall health.[178] Personalized nutrition strategies can be developed by analyzing glycan-related metabolites and their effects on an individual's metabolic health.

10.4.5. Glycomics and the microbiome

The gut microbiome plays a crucial role in digesting dietary glycans, producing bioactive compounds that influence immune function and metabolism.[179] Advances in glycomics allow for the identification of specific glycans that promote beneficial bacterial growth. Personalized diets incorporating prebiotic glycans, such as human milk oligosaccharides (HMOs) and resistant starches,[180] can be tailored to optimize gut microbiota composition.

10.5. Advances in glycomics and precision nutrition

Precision nutrition is an approach that tailors dietary recommendations to an individual's unique genetic, metabolic, microbiome, and lifestyle factors to optimize health and prevent disease.[181]

10.5.1. Major components

- **Personalized Dietary Plans** – Based on genetic markers, metabolic responses, and gut microbiota composition.
- **Glycomics in Nutrition** – Glycans play a role in metabolism, immune function, and gut health, making them important in personalized diets.
- **Microbiome Influence** – Individual gut bacteria affect nutrient absorption and metabolism, guiding diet customization.
- **Metabolic Adaptation** – Monitoring an individual's metabolic responses to optimize macronutrient intake.
- **Disease Prevention** – Targeting conditions like diabetes, cardiovascular diseases, and inflammation through diet.
- **Nutrigenomics** – Studying gene-diet interactions to predict dietary effects on health.

11. Conclusion

Dietary glycans are vital to human health, influencing gut microbiota, metabolism, immune function, and overall well-being. Their structural diversity supports key physiological processes, making them important in nutrition and functional food development. Beyond digestive and immune health, glycans show promise in managing aging, metabolic disorders, and enhancing sports nutrition.

Rising interest in glycans has driven progress in glycan-enriched functional foods and supplements. However, challenges remain, including limited bioavailability, stability during processing, and individual metabolic responses. Advances in glycomics and personalized nutrition are enabling more precise, targeted dietary interventions.

Future research should aim to uncover the mechanisms of glycan-host interactions, discover new dietary sources, and improve glycan efficacy through innovative processing techniques. With ongoing study, dietary glycans have the potential to transform health management and support the development of next-generation functional and therapeutic foods.

CRediT authorship contribution statement

Suneetha Chinta: Writing – original draft, Investigation, Conceptualization. **L Sonali:** Writing – original draft, Investigation, Conceptualization. **R Pavithra:** Writing – original draft, Investigation, Conceptualization. **M P Drisya Raj:** Writing – original draft, Investigation, Conceptualization. **N V Kanimozhi:** Writing – original draft, Investigation, Conceptualization. **M Sukumar:** Writing – review & editing, Supervision, Conceptualization.

Consent to participate/publication

All the authors are aware of the submission of this manuscript to this journal.

All authors reviewed the manuscript.

Ethics approval

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Declaration of Competing Interest

This manuscript is not being submitted concurrently elsewhere and the other author is also aware of its submission. I hope you would agree with me on the significance of these interesting results and consider the paper for publication. We look forward to hearing from you at your earliest convenience. I declare that the authors have no conflict of interest.

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