



## Oligosaccharides: Sources, Biological Activities and Health Benefits in Animals and Humans

Collins Fiifi Anyimadu <sup>1#</sup>, Rinku Sudarshan Agrawal <sup>2#</sup>, Phanthipha Laosam <sup>3</sup>, Papungkorn Sangsawad <sup>4</sup>, Gitanjali S. Deokar <sup>5</sup>, Fahad Al-Asmari <sup>6</sup>, Li Li <sup>7</sup>, Kasim Sakran Abass <sup>8</sup>, Narashans Alok Sagar <sup>9</sup>, Nattira On-Nom <sup>1\*</sup> and Nilesh Nirmal <sup>1\*</sup>

<sup>1</sup>Institute of Nutrition, Mahidol University, 999 Phutthamonthon 4 Road, Salaya, Nakhon Pathom, 73170, Thailand

<sup>2</sup>School of Food Technology, MIT Art, Design and Technology University, Pune, Maharashtra, India

<sup>3</sup>Research and Development Institute Suranaree University of Technology, Nakhon Ratchasima, Thailand 30000

<sup>4</sup>School of Animal Technology and Innovation, Institute of Agricultural Technology, Suranaree University of Technology, Nakhon Ratchasima 30000, Thailand

<sup>5</sup>MET's Institute of Pharmacy, Bhujbal Knowledge City, Adgaon, Nashik, Maharashtra, India

<sup>6</sup>Department of Food Science and Nutrition, College of Agriculture and Food Sciences, King Faisal University, P.O. Box 400, Al-Ahsa 31982, Al-Hofuf, Saudi Arabia

<sup>7</sup>Gulbali Research Institute, Charles Sturt University, NSW 2800, Australia

<sup>8</sup>Department of Physiology and Pharmacology, College of Veterinary Medicine, University of Kirkuk, Kirkuk 36001, Iraq

<sup>9</sup>Department of Biotechnology, University Centre for Research and Development, Chandigarh University, Mohali, 140413, Punjab, India

#These authors contributed equally

\*Corresponding author: [nattira.onn@mahidol.ac.th](mailto:nattira.onn@mahidol.ac.th) (NON); [nilesh.nir@mahidol.ac.th](mailto:nilesh.nir@mahidol.ac.th) (NN)

### ABSTRACT

Oligosaccharides (OS), carbohydrates composed of a small number of monosaccharide units, have attracted growing interest due to their diverse biological activities and promising health benefits. OS, naturally present in plants, milk, and diverse dietary sources, functions as a prebiotic by selectively promoting the growth of beneficial gut microbiota, thereby supporting gastrointestinal health. In addition to their prebiotic effects, emerging evidence underscores their immunomodulatory, antioxidant, antimicrobial, and anti-inflammatory activities. This review comprehensively examined the types of OS and their health benefits, with particular emphasis on antioxidant, immunomodulatory, metabolic-regulating, and prebiotic functions. OS, defined by a degree of polymerization of 3–10 (e.g., fructo- and galacto-oligosaccharides), act primarily as selective substrates for *Bifidobacteria* spp. and *Lactobacilli* spp., promoting gut-brain axis signaling, immunomodulation, and glycemic control. Additionally, this review emphasizes current developments in personalized nutrition and biotechnology that open avenues for their incorporation into nutraceuticals and functional foods. Integrating OS with PS, either alone or in synergistic formulations with probiotics and antioxidants, represents a powerful approach for managing and preventing diseases. With continued scientific exploration, these natural carbohydrates will assume an increasingly important role in human nutrition, offering novel strategies for disease prevention and prospects in human health management.

**Keywords:** Oligosaccharides, Prebiotics, Bioactivities, Health benefits.

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### INTRODUCTION

Carbohydrates represent a fundamental class of biomolecules that occur naturally in plants

(Stylianopoulou, 2023), microorganisms, fungi, and animals, performing diverse structural and functional roles (Fernandes & Coimbra, 2023). Carbohydrates are sugars, starches, or dietary fibers. As short-chain carbohydrates,

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oligosaccharides (OS) consist of 3 to 10 monosaccharide units and have received growing scientific attention due to their unique structural characteristics and wide-ranging physiological functions. OS are increasingly recognized not only as nutritional components but also as bioactive compounds with significant health-promoting properties. Beyond their nutritional role, the biological activity of OS is mainly influenced by their structural properties (Wang et al., 2024a). The growing recognition of the bioactive properties of oligosaccharides has made them an important area of research in recent years. According to Fernandes and Coimbra (2023), negatively charged OS with low molecular weight (MW), such as pectin, carrageenan, and alginate fragments, exhibit the greatest antioxidant activity. This function of low-MW OS is related to the ease with which their terminal hydroxyl groups can be reduced (Wang et al., 2024b).

One of the well-documented roles of oligosaccharides is their prebiotic effect, wherein they selectively stimulate the growth and activity of beneficial gut microbiota, particularly *Bifidobacterium* (Magnoli et al., 2024; Nurhayati et al., 2025) and *Lactobacillus* species. The gut microbiota is essential for maintaining proper functioning of the gut-brain axis, producing short-chain fatty acids (SCFAs) and neuroactive substances such as gamma-aminobutyric acid (GABA), enhancing neuroplasticity, and reducing neurodegeneration (Oleskin & Shenderov, 2019; Palepu et al., 2024). Modulation of the intestinal microbiome improves gastrointestinal function, enhances nutrient assimilation, and strengthens immunity. Fructans, mostly found in plants, and glucans are among the most important prebiotics (Araújo-Rodrigues et al., 2024).  $\beta$ - and  $\alpha$ -glucans are sourced from plants and fungi, such as mushrooms. Beyond their prebiotic activity, OS also exhibit important biological activities, including anticancer, antitumor, antidiabetic, and immunoregulatory activities.

These bioactive properties make OS promising candidates for preventing and controlling chronic conditions as nutraceuticals for human health management. However, their biological activities depend on the molecular weight, monosaccharide composition, presence of functional groups, chain length, and branching structures (Wang et al., 2024a). Advancements in biotechnology and food science have facilitated the development and application of functional OS in nutraceuticals, pharmaceuticals, and functional foods (Bashir et al., 2025). As consumer interest in natural and health-promoting dietary components continues to rise, oligosaccharides are emerging as key candidates for improving overall health and well-being.

This paper aims to provide a comprehensive review of the different types of oligosaccharides, their bioactivities, health benefits, and bioavailability. It also highlights future perspectives of OS in human health management.

### Types of Oligosaccharides

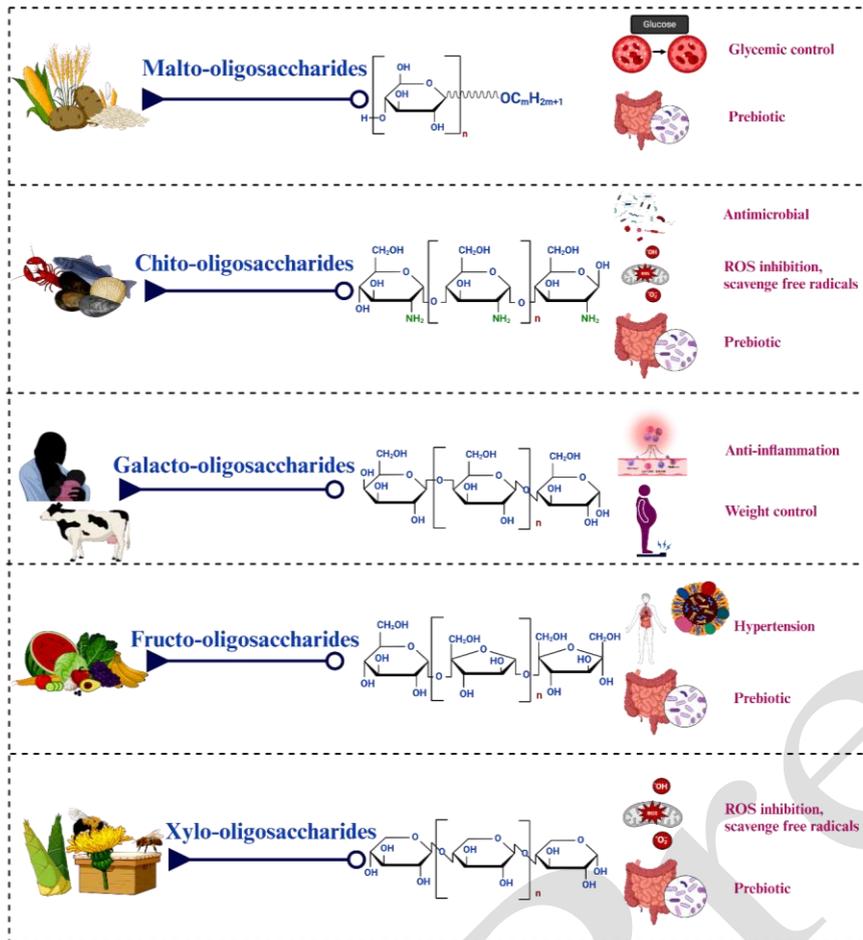
OS are typically extracted from natural sources or produced through the physical, chemical, or biochemical breakdown of polysaccharides. They can also be

synthesized by enzymatic and/or chemical methods. It is crucial to select the most appropriate preparation method based on the specific application areas being targeted. OS are derived from a wide range of natural sources, which determine their chemical structure and bioactivity. Key sources include fungi, algae, plants, and animals. The OS structural diversity arises from the composition and linkage pattern of monosaccharides. The chemical structure, sources, and bioactivities of a few commercially important OS have been illustrated in Fig. 1.

Maltooligosaccharides (MIOS) are among the simplest OS, consisting of 3-10 glucose units derived from starch components (Lang et al., 2025). As a result, MIOS has all its glucose units in  $\alpha$ -(1-4) linkages, or an additional  $\alpha$ -(1-6) linkage in the case of isomaltooligosaccharides (iMIOS) (Shinde & Vamkudoth, 2022). As starch fragments, MIOS are hydrolysed into glucose units by intestinal brush-border enzymes; however, they have been shown to persist into the colon and to be utilised by gut microbiota, giving them "prebiotic" status (Bláhová et al., 2023). In addition, several of its physicochemical properties, such as its low sweetness, low osmolarity, moderate viscosity, non-hygroscopicity, and ability to inhibit retrogradation, make it well-suited for application in diverse food products. MIOS are not abundant in nature, and extraction from starch-laden sources proves non-productive. Instead, they are obtained from hydrolysis, transglycosylation or isomerisation by the glycoside hydrolase family of enzymes isolated from bacteria or fungi (Shinde & Vamkudoth, 2022).

Chitooligosaccharides (COS) are low-MW products from the hydrolysis of chitin, a biopolymer of N-acetyl D-glucosamine units, found in the cell walls of fungi and the exoskeleton of arthropods, making it the second most abundant polymer on earth (Km et al., 2025). Chitin is highly insoluble in water and most organic solvents, necessitating hydrolysis for broader application (Liu et al., 2023b). Accordingly, chitinases of the glycosyl hydrolase family are able to break down the  $\beta$ -(1-4) bonds within the polymer, releasing acetylated glucosamine subunits of various lengths (Minguet-Lobato et al., 2025). Of note are COS of 2-6 units, which have shown anti-inflammatory, antimicrobial, immune stimulation and prebiotic properties among other bioactivities. Another COS of similar biological relevance but less abundance is lacto-N-triose II, which, along with other OS, is found in human milk (Liu et al., 2023a). COS, unlike chitin, is soluble in water and pH- and heat-stable, offering many food and pharmaceutical applications.

Galactooligosaccharides (GOS) are also structurally similar to human milk OS, having up to 9 galactose subunits in various glycosidic bonds, including  $\beta$ -(1-2),  $\beta$ -(1-3),  $\beta$ -(1-4) and  $\beta$ -(1-6), and having a terminal glucose or galactose (Costa et al., 2025; Zhao et al., 2025). GOS is naturally uncharged, which hinders its extraction and yields low impure yields, thereby favoring enzymatic synthesis by  $\beta$ -galactosidases via transgalactosylation reactions with lactose as the primary substrate (Costa et al., 2025).  $\beta$ -galactosidases can be classified into six families, most



**Fig. 1:** The chemical structure of oligosaccharides, their natural sources, and bioactivities.

belonging to GH2, which are produced by bacteria and yeasts such as *Aspergillus oryzae* and *Kluyveromyces lactis* (Koirala et al., 2026; Zhao et al., 2025). GOS are also water-soluble, moderately sweet, thermally stable at pH 7, and possess moderate thickness, hence commonly used as fillers for baked products (Koirala et al., 2026). GOS are non-digestible and mostly serve as prebiotic soluble fiber but may also enhance the absorption of certain minerals such as iron (Giorgetti et al., 2022).

Fructooligosaccharides (FOS) can be obtained naturally from many vegetables, including, Jerusalem artichokes, garlic, onions, apple pomace, rice bran and beetroot peels (Rahim et al., 2021). However, they may also be synthesized by transfructosylation enzymes such as  $\beta$ -fructofuranosidases and  $\beta$ -D-fructosyltransferases obtained from fungi, acting on sucrose as substrate (Amoedo et al., 2025). FOS may contain up to 20 fructosyl units held in  $\beta$ -(1-2) glycosidic linkages (Huang et al., 2025). FOS can reduce water activity of products, prolonging storage quality, prevent ice recrystallisation through hydrogen bond interaction with water and has high water holding capacity due to its hygroscopicity (Liu et al., 2025). The glucosidic linkages in FOS make them undigestible by mammals, making them potent prebiotics and glycosylation agents that improve the bioavailability of other bioactive agents (Li et al., 2023).

Xylooligosaccharides (XOS) are produced from the targeted degradation of xylan, a component polymer of hemicellulose, which is the second most abundant

polysaccharide (PS) after cellulose (Katić et al., 2025). Alternatively, they may be synthesized from arabinoxylans using endo-xylanases in a cocktail of enzymes targeting arabinose substitutions (Kim et al., 2026). XOS produced in this manner will have 2-10 xylose units in  $\beta$ -(1-4) linkages, with high water solubility and thermal stability. XOS also serves as a prebiotic, with different beneficial microorganism species preferring XOS of different lengths. For example, *Levilactobacillus brevis* efficiently utilizes xylobiose, while bifidobacteria prefer medium-chain XOS (Zhang et al., 2025b). XOS is also water-soluble and heat-stable. Chen et al. (2021) reported that XOS possesses various biological activities, including antioxidant, antimicrobial, anti-inflammatory, antitumor, etc. Further, the authors stated that XOS reported a reduction in disease condition in humans and improved growth and disease resistance in animals (Chen et al., 2021). In their study, Xiong et al. (2024) investigated the effect of XOS supplementation on the growth and production performance, gut health, and intestinal morphology in laying hens. The study indicated that XOS supplementation improved intestinal morphology, gut health, and production performance in laying hens. In conclusion authors recommended supplementation of 200 mg/Kg in the diet of hens (Xiong et al., 2024). Recently, Kim et al (2026) confirmed that mid-length XOS support the gut health in broilers. The prebiotic effect of XOS could alleviate aging-associated phenotype in a D-galactose-induced aging mouse by reducing oxidative

stress, inflammatory markers, and supporting cognitive function (Feng et al., 2025).

Fungi-derived OS, such as mannoooligosaccharides (MOS), which come from fungal cell wall mannans. These are known for their immune-boosting and prebiotic effects (Yoo et al., 2024). Another type is chitooligosaccharides (COS), which are developed from the partial breakdown of chitin and crustacean shells. COS shows antimicrobial, antioxidant, and anti-inflammatory properties (Kong et al., 2020). Moreover, mannan oligosaccharides (MOS) from yeast cell walls act as immune boosters and pathogen blockers in both human and animal nutrition (Zhang et al., 2025a). Algae-derived OS, like porphyrin OS from red algae (*Porphyra* spp.), have shown antioxidant and anti-tumor effects. Fucooidan OS from brown algae (*Fucus vesiculosus*) is known for its blood-thinning and antiviral effects (Jutur et al., 2016). Plant-derived OS are some of the most common. They include raffinose, found in beans, cabbage, and brussels sprouts, maltose, produced during seed germination; and sucrose, which is abundant in sugarcane and sugar beets. Fructooligosaccharides (FOS), extracted from chicory root, wheat, and onions, act as prebiotics that promote gut health. Galactooligosaccharides (GOS) found in legumes and dairy support beneficial gut bacteria (Rastall & Gibson, 2015).

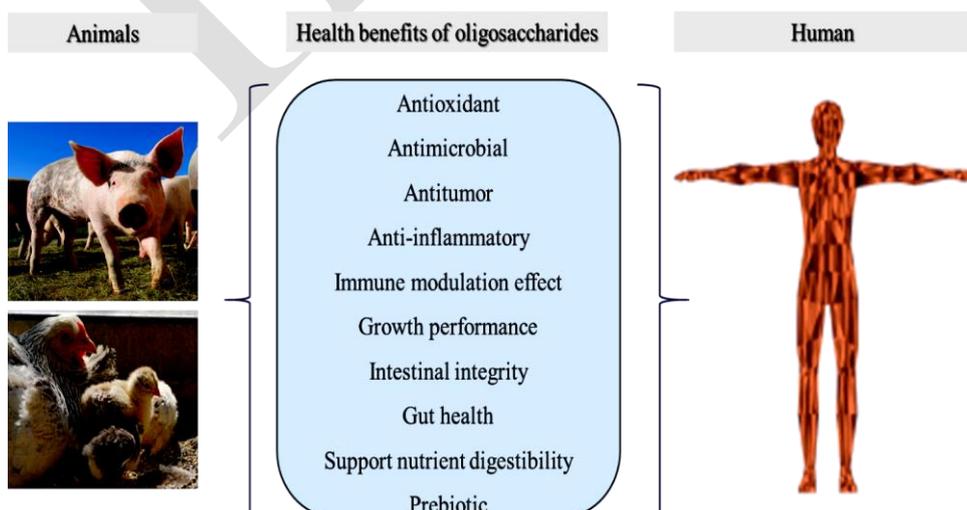
Similarly, animal-derived oligosaccharides primarily include lactose and GOS, both of which are naturally present in milk and are important for infant nutrition (van der Toorn et al., 2023). Bacterial oligosaccharides, such as fucosyllactose, are part of human milk oligosaccharides (HMOs). They help with infant immunity and gut bacteria balance (Tang et al., 2025). Overall, these various OS provide multiple benefits that are important for the food, pharmaceutical, and nutraceutical industries. Various therapeutic effects of oligosaccharides on animals and human health are depicted in Fig. 2.

### Bioactivities of OS

The structural diversity and biological activities of OS have attracted considerable attention in recent biomedical research due to their therapeutic potential and natural abundance, as shown in Table 1. Recent studies have identified their functions in various physiological processes, including antioxidant defense, antimicrobial activity, metabolic regulation, and the promotion of gastrointestinal health across different natural sources. Their capacity to modulate various biological pathways is noteworthy, as distinct structural characteristics, including molecular weights and degrees of polymerization, affect bioavailability and functional properties.

**Table 1:** Bioactive properties of oligosaccharides

Source	Activity	Indicator	Dose	References
Red Seaweed	Antioxidant	-SOD, 44% -GSH-Px 21% -MDA, AST, ALT 22.6%	400 mg/kg,	(Chen et al., 2006)
Chitosan	Antioxidant	-DPPH** -ABTS** -·OH	0.31mg/mL 0.39 mg/mL 0.73 mg/mL	(Xia et al., 2022)
Shrimp shell	Antibacterial	- <i>E. coli</i> - <i>S. aureus</i> ATCC 25923 - <i>S. aureus</i> ATCC 43300	0.1% (w/v)	(Benhabiles et al., 2012)
Chitosan	Antibacterial	- <i>Staphylococcus aureus</i> - <i>Bacillus subtilis</i> - <i>Listeria monocytogenes</i> - <i>Escherichia coli</i> - <i>Pseudomonas aeruginosa</i>	-	(Xia et al., 2022)
Chitosan	Antibacterial	- <i>Escherichia coli</i> - <i>Staphylococcus aureus</i>	0.14 mg/mL	(Yue et al., 2021)
Pullulan oligosaccharides (POS) and curdlan oligosaccharides (COS)	Prebiotic properties	enhanced bacterial growth and lactic and acetic acid production	2 g/L	(Xu et al., 2021)
Ganoderma lucidum spore	Prebiotic properties	<i>Lactobacillus</i>	1%, w/v	(Yang et al., 2020)



**Fig. 2:** Various health benefits of oligosaccharides. Source: The figure adopted and modified from Chen et al. (2021).

### Antioxidant

OS, despite their shorter chain length, also show considerable antioxidant potential, with studies revealing their capacity to protect against oxidative stress-induced cellular damage (An et al., 2025). The antioxidant efficiency of OS is similarly influenced by their structural characteristics, with lower-molecular-weight fractions often demonstrating superior cellular permeability and free-radical-scavenging capabilities. Recent studies have demonstrated the significant antioxidant potential of marine-derived oligosaccharides, particularly highlighting the efficacy of agar-oligosaccharides extracted from red seaweed (Table 2). Chen et al. (2006) indicated that these compounds showed remarkable antioxidant activities across multiple organ systems in rat models, demonstrating their ability to enhance key antioxidant enzyme activities while reducing harmful oxidative markers. The study revealed that at an optimal dosage of 400 mg/kg, these compounds achieved impressive results, including a 44% reduction in liver malondialdehyde (MDA) levels and a 21% reduction in heart MDA levels, while simultaneously boosting superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activities to peak levels in both liver tissue and serum, accompanied by a notable 22.16% decrease in serum ALT levels. Furthermore, Perumal et al. (2024) demonstrated that oligosaccharides from *Sargassum* sp. (SAR-OSC) possess exceptional antioxidant capacity across multiple assays, achieving near-complete inhibition in FRAP tests. Additionally, OS exhibit synergistic effects when combined with other antioxidant compounds, enhancing their potential for therapeutic applications in oxidative stress-related conditions.

### Antibacterial

OS, as shorter chain carbohydrates, demonstrate their distinct antibacterial properties through mechanisms that often complement those of polysaccharides. Extensive research has demonstrated the significant antimicrobial potential of these compounds against a broad spectrum of pathogenic bacteria. Benhabiles et al. (2012) investigated the antimicrobial efficacy of chito-oligosaccharides extracted from shrimp shells, revealing substantial inhibitory effects against both Gram-positive and Gram-negative bacteria, including clinically significant pathogens such as *Escherichia coli* ATCC 25922, *Vibrio cholerae*,

*Shigella dysenteriae*, and *Bacteroides fragilis*. Further advancing our understanding of these compounds, Yue et al. (2021) conducted comprehensive *in-vitro* analyses of novel chitosan oligosaccharide derivatives, specifically examining their antibacterial activity against *Escherichia coli* and *Staphylococcus aureus*. OS often demonstrate their antibacterial effects by competitively inhibiting bacterial adhesion to host cells, thereby preventing colonization and subsequent infection (Reigada et al., 2020). The antibacterial efficacy of OS is influenced by its structural characteristics, including its degree of polymerization, substitution pattern, and specific functional groups.

### Anti-hypertensive

OS contribute to cardiovascular health through distinct mechanisms that complement the actions of polysaccharides. These short-chain carbohydrates demonstrate significant ability to modulate vascular function and lipid metabolism, thereby contributing to blood pressure regulation and overall cardiovascular health (Rony et al., 2015). OS has shown particular promise in reducing systolic and diastolic blood pressure while simultaneously improving vascular elasticity and reducing arterial stiffness (Hill & Newburg, 2015). Their cardiovascular benefits extend to cholesterol metabolism, with studies showing significant reductions in total cholesterol, triglycerides, and low-density lipoprotein levels. Marine-derived OS have demonstrated remarkable efficacy in improving endothelial function, a critical factor in maintaining healthy blood pressure. These compounds can enhance nitric oxide production and bioavailability, promoting vasodilation and reducing peripheral resistance.

### Anti-diabetic and Weight Loss

OS, with its shorter chain structure, offers unique advantages in diabetes management and weight control through distinct mechanisms. These simple carbohydrate molecules play pivotal roles in activating insulin-dependent cellular pathways, increasing the expression of glucose transport proteins (especially GLUT4), and enhancing the production of glucose-regulating hormones, thereby improving glycemic regulation (Chaiyasut & Sivamaruthi, 2017; Zhang et al., 2017). Chaiyasut & Sivamaruthi (2017) investigated the therapeutic potential of an extract of *Hericium erinaceus*,

**Table 2:** Prebiotic effect of oligosaccharides

Type of oligosaccharides	Source	Molecular structure	Beneficial microbe	Health benefits	Reference
Fructo-oligosaccharide	Fruits, Vegetables, Honey	Fructose	<i>Bifidobacteria</i> <i>Lactobacilli</i>	Better digestive health, boosts immunity, and controls bowel movement	(Zielińska et al., 2021)
Galacto-oligosaccharide	Human milk, Cow milk	Galactose	<i>Bifidobacteria</i>	Balanced gut microbiota	(Wang et al., 2021)
Arabino-oligosaccharide	Cell walls of cereals	Arabinose	<i>Bifidobacteria</i> , <i>Lactobacilli</i> and <i>Enterococci</i>	Promotes innate immunity	(Bhattacharya et al., 2020)
Xylo-oligosaccharides	fruits, Vegetables, milk, honey, and bamboo shoots	Xylose	<i>Bifidobacteria</i> , <i>Lactobacilli</i>	Antimicrobial, Antioxidant, growth-regulating	(Valladares-Diestra et al., 2023)
Mannan- oligosaccharide	Yeast cell-wall	Mannose	<i>Akkermansia</i> <i>Bacteroides</i>	Increases digestion, immunomodulatory, and hypolipidemic	(Chen et al., 2024b)
Maltooligosaccharide	Corn, potato, rice, wheat, tapioca starch	Glucose	<i>Bifidobacteria</i>	Improves colon health, prevents constipation	(Bláhová et al., 2023)
Raffinose	Legume, peas, lentils, soy, seeds, roots	Glucose, Galactose, Fructose	<i>Lactobacillus</i> <i>Bifidobacteria</i>	Reduces constipation, modulate gut microbiota	CVDs risk, (Anggraeni, 2022)

which contains bioactive oligosaccharides, demonstrating its dual efficacy in glyceimic control and weight management. The study revealed that supplementation with 20-100 mg/kg body weight of *H. erinaceus* extract resulted in significant reductions in blood glucose levels while promoting weight loss. OS contributes significantly to weight management through beneficial modifications to the intestinal microbial ecosystem, enhancing the growth of beneficial bacteria that influence energy harvest and metabolism. Their prebiotic effects promote the production of short-chain fatty acids that can modulate appetite, energy expenditure, and fat storage, offering a unique pathway for weight management. This dual action highlights the potential of OS as a comprehensive therapeutic agent for managing both diabetes and obesity, suggesting its value in developing integrated treatments for metabolic disorders with minimal side effects.

### Prebiotic

Prebiotics in human and animal diets have risen to prominence since identifying microorganisms in/on hosts as being beneficial to their health. The current definition of prebiotics states that they are substrates that are selectively utilized by microorganisms to confer health benefits to their host (Singh et al., 2025; Kumalasari et al., 2025). These will include microorganisms not only in the intestinal tract, but also in the mouth and skin. As substrates, prebiotics promote the growth of beneficial microorganisms (probiotics) and/or increase the production of useful metabolites, such as SCFAs, bile acids, and peptidoglycan fragments (Li et al., 2022). OS and other functional carbohydrates remain the leading prebiotic compounds; however, some polyphenols have been shown to exhibit prebiotic activity (Rodríguez-Daza et al., 2021). It is also observed that different microbial species utilize different substrates as prebiotics, sometimes even preferring specific lengths of a particular OS and utilizing them via different metabolic pathways (Zeng et al., 2023; Zhang et al., 2025b). Utilization of prebiotics by beneficial microorganisms is essential, as hosts house a diverse community of microbes, some beneficial and some not, which must be held in a tight balance for optimal health. This includes phyla like actinobacteria, proteobacteria, and verrucomicrobia as minor communities with firmicutes and Bacteroidetes as the two major ones, whose ratio (F/B) can indicate a balance or imbalance (dysbiosis) (Shariff et al., 2024). An increased F/B ratio, in addition to low microbial diversity, signifies dysbiosis, and this has been implicated in several diseases, including colitis, irritable bowel syndrome/disease, leaky gut syndrome, liver disease, and colon and rectum cancers (Dahiya & Nigam, 2023).

FOS are among the most extensively studied prebiotics. FOS releases gases such as carbon dioxide, methane and hydrogen, along with SCFAs, which lower the colon's pH and suppress harmful bacteria (Costa et al., 2021b). A combination of low pH and increased colon water content due to FOS fermentation also allows for absorption of minerals such as calcium and magnesium by colonic epithelial cells (Costa et al., 2021a; Tolmacheva et al., 2024). In in-vitro fermentation of FOS, using fecal

bacteria of healthy students, a suppression of *Escherichia-Shigella* and *Bacteroides*, and an increase in *Bifidobacteria* and *Lactobacillus* were observed (Fu et al., 2024). Ripple effects of improved CO<sub>2</sub> production, and enhanced pathways of carbon and pyruvic acid metabolism were also observed due to increased growth of *Lactobacillus*. The prebiotic activity of FOS has also been shown in mouse models. A study induced non-alcoholic fatty liver disease in mice, using either a high-fat, high-cholesterol diet or a methionine and choline-deficient diet. Whereon supplementation with FOS attenuated hepatic steatosis, which correlated with an increase in the beneficial microbial phylum, Bacteroidetes, and species, *Klebsiella variicola*, *Lactobacillus gasseri*, and *Clostridium perfringens* (Huang et al., 2023). Another showed that FOS can increase *Lactobacillus* in mice with neurodegenerative diseases, an effect that correlated with reduced oxidative stress, inflammation, and apoptosis (Liu et al., 2026). In human infants, a combination of FOS and GOS suppressed *Klebsiella pneumoniae*, increased the abundance of *Bifidobacterium* and *Actinobacteria*, and accompanied an increase in SCFA production (Yao et al., 2022). Despite its enormous benefits to gut microbiota, FOS, may cause bloating and abdominal stress on heavy consumption, and may necessitate the use of other agents to slow down its fermentation (Cheng et al., 2025).

MIOS at 2 % v/v in a culture medium for human fecal bacteria also increased *Bifidobacteria* and SCFA production, while suppressing pathogenic bacteria (Jang et al., 2020). Isomaltooligosaccharides were similarly fermented by infant faecal bacteria as GOS, which are more familiar substrates due to their presence in human milk (Logtenberg et al., 2021). iMIOS and GOS increased the abundance of *Bifidobacterium* and enhanced the production of lactate and acetate. A mixture of OS or other dietary fiber components can also provide potent prebiotic effects as was tested in tumor-induced mice (Butorac et al., 2025). A prebiotic mixture including FOS, GOS, inulin, and corn dextrin improved the abundance of *Bifidobacterium pseudolongum*, the best indicator for ameliorated dysbiosis in oncomicrobiomes. Although *Lactobacillus* and *Bifidobacterium* have traditionally been observed for symbiosis of the gut microbiota, new genera such as *Akkermansia*, *Christensenella*, *Propionibacterium*, and *Faecalibacterium*, are recently being monitored due to their ability produce SCFAs and other relevant metabolites, contributing to health, especially in certain diseased conditions (Losada-Garcia et al., 2025). This also opens up the possibility for studying less popular OS like manooligosaccharides (MOS), pullulan (POS), and curdlan (COS) OS, respectively. For instance, after purging mice with a cocktail of antibiotics, MOS was most potent in improving the abundance of *Akkermansia* and *Bacteroides*, while suppressing the pathogenic *Proteus*, among counterparts like iMIOS, GOS, and resistant starch. Xu et al. (2021) also showed that pullulan oligosaccharides (POS) and curdlan oligosaccharides (COS) specifically enhanced the growth of *Lactobacillus* and *Bifidobacterium* strains, resulting in increased production of beneficial organic acids, particularly lactic and acetic acids (Table 2).

These findings highlight the selective nature of OS in promoting the growth of health-beneficial bacteria while potentially inhibiting pathogenic organisms. The fermentation of OS by probiotic bacteria produces beneficial metabolites, including short-chain fatty acids such as butyrate, acetate, and propionate, which serve as energy sources for colonic epithelial cells and help regulate various physiological processes. The degree of polymerization of OS significantly influences their prebiotic efficacy, with shorter chains often being more readily fermentable by beneficial bacteria. These studies collectively underscore the versatility and effectiveness of OS as natural prebiotics, suggesting their potential applications in functional foods and therapeutic interventions to improve gut health and overall well-being.

### Bioavailability of OS

Bioavailability of OS refers to the extent and rate at which they are absorbed and utilized by the body after ingestion (McClements & Xiao, 2017). Complex carbohydrates, such as OS, have bioavailability that depends on molecular structure, source, and digestive processing (Ullah et al., 2019). In the mouth and upper small intestine, human salivary and pancreatic  $\alpha$ -amylases initiate PS hydrolysis, but many linkages especially  $\beta$ -glycosidic bonds, remain resistant, allowing large PS ( $>10^5$  Da) to transit largely intact to the colon (Li et al., 2019; Ullah et al., 2019), whereas smaller OS may undergo partial hydrolysis yet still rely heavily on gut bacteria for conversion into absorbable metabolites (McClements & Xiao, 2017). To enhance bioavailability, processing methods such as heat treatment, extrusion, or enzymatic debranching reduce molecular size and improve water dispersibility, facilitating both host enzyme access and microbial fermentation (Liu et al., 2021). In addition, encapsulation strategies, such as microemulsions, liposomes, or nanocarriers, can further protect sensitive carbohydrates from gastric acid and release them at targeted intestinal sites (Jumazhanova et al., 2023).

OS, including raffinose, fructo-oligosaccharides (FOS), and galacto-oligosaccharides (GOS), are small enough to escape complete digestion yet too large for direct transporter-mediated uptake. They primarily function as prebiotics, selectively nourishing beneficial taxa (e.g., *Bifidobacterium* and *Lactobacillus*) and promoting SCFA production (Chen et al., 2024a; Jiang et al., 2025). Despite their smaller size, OS remain resistant to host enzymes and undergo colonic fermentation. Additionally, OS have been employed as wall materials for probiotic and bioactive encapsulation, improving viability and targeted delivery (Jumazhanova et al., 2023). MIOS, GOS, FOS, and XOS cannot be digested by gastrointestinal enzymes and gastric acid due to their physicochemical characteristics (Valladares-Diestra et al., 2023; Wang et al., 2024a; Atta et al., 2025; Ferrarotti & Costa, 2026).

Upon reaching the lower intestine, these OS are fermented by probiotic bacteria, mainly *Bifidobacterium* and *Lactobacillus* genera (Valladares-Diestra et al., 2023). However, recent studies on COS permeability, bioavailability and tissue distribution indicated that the

COS degree of polymerization (DP) affects its bioavailability, with lower DP associated with higher bioavailability (Chen et al., 2022; Zhang et al., 2022). Chen et al. (2022) examined the oral bioavailability and tissue distribution of chitobiose (COS2) and chitotriose (COS3) in Wistar rats. The results show that the bioavailability of COS2 was 0.32% and COS3 was 0.52%. Furthermore, COS2 and COS3 were widely distributed in rat tissues. In another study, Zhang et al. (2022) investigated the impact of different DP (COS 2-7) on permeability (Caco-2 cells) and pharmacokinetics in rats. The study shows that increasing DP reduced bioavailability. The low bioavailability of COS was related to the low permeability and structural variation in COS2-7. All these studies suggested that MIOS, GOS, FOS, and XOS are not digested by the upper or lower intestine but fermented by gut bacteria to produce SCFA. While COS can be distributed to the tissue based on its DP, lower-DP COS has greater bioavailability than higher-DP COS.

### Health Benefits of OS

#### Microbiome-nourishing Effect

Prebiotics are non-digestible OS that can help to address gastrointestinal issues and are well recognized for their numerous health benefits. OS cannot be broken down by the human digestive tract. Instead, they are fermented in the colon, where they encourage the growth and activity of a health-promoting bacterial population. Numerous preclinical and clinical studies have demonstrated the positive impact of OS on *Lactobacillus* growth via the metabolism of short-chain fatty acids (Bhola & Bhadekar, 2024). OS can facilitate *Lactobacilli* adhesion to the intestinal epithelium, thereby enhancing their colonization and persistence in the gut (Jana et al., 2021). Fructooligosaccharides (FOS) are a widely recognized class of prebiotics that stimulate the growth of *bifidobacteria* in the gut, promoting digestive health. Mao et al. (2018) evaluated how different doses of FOS influence the composition of gut microbiota in mice, with a particular focus on *Bifidobacterium* levels. During the study, 7-week-old male C57BL/6J mice were divided into a control group (standard diet), a low-dose group (5% FOS diet), and a high-dose group (25% FOS diet) for 4 weeks. The study concluded that FOS supplementation, especially at higher doses, selectively promotes the growth of *B. pseudolongum* in the mouse gut. This highlights the prebiotic potential of FOS in modulating gut microbiota composition.

#### Improved Gut Health

OS have been shown to play a crucial role in modulating gut microbiota. OS supplementation presents a promising strategy that supports a healthy gut microbiota while inhibiting the growth of harmful bacteria (Cheong et al., 2023). The fermentation of non-digestible carbohydrates like OS by gut microbiota promotes the production of functional metabolites such as SCFAs, including butyric acid, lactic acid, and propionic acid. SCFAs help lower the pH of the colon, which limits the growth of harmful bacteria (Lordan et al., 2020). Multiple studies have demonstrated the positive effect of short-

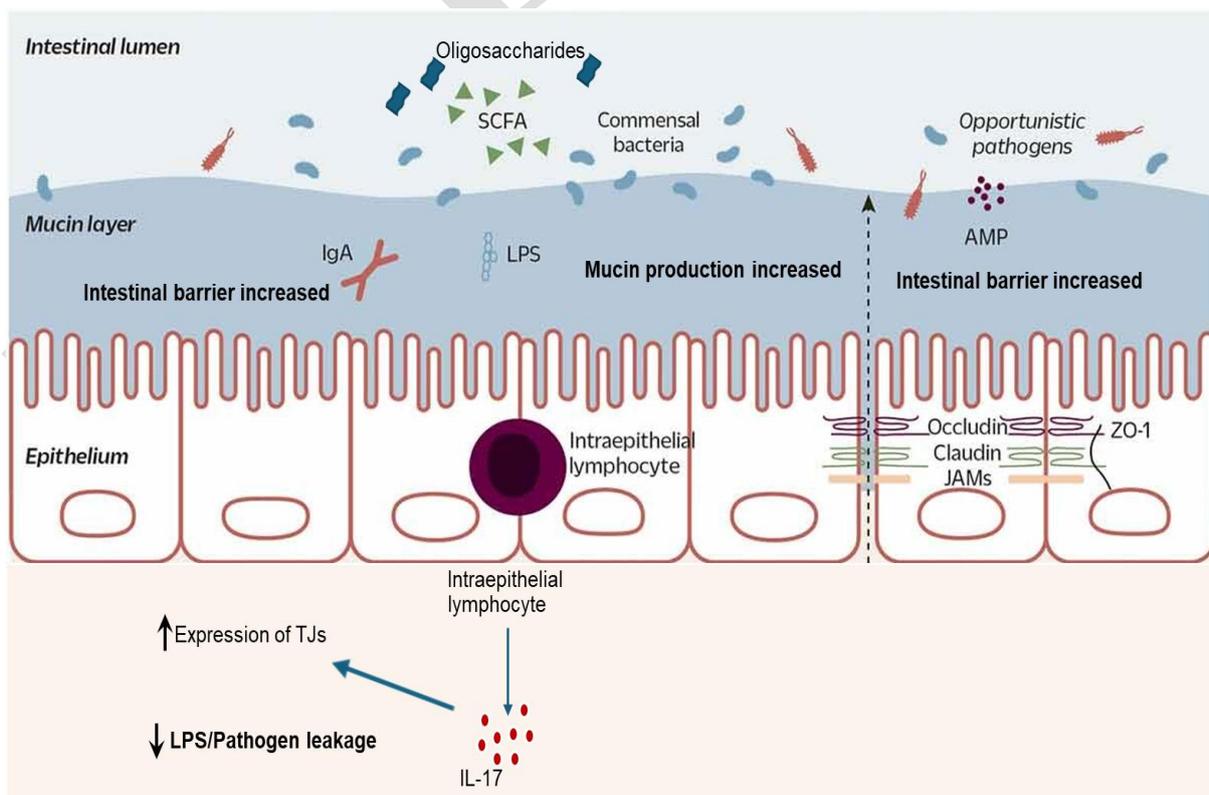
chain fructooligosaccharide supplementation in patients with type 2 diabetes, with a significant reduction in serum LDL cholesterol (García et al., 2023). Park et al. (2022) investigated the protective effects of *Porphyra tenera* (a type of red algae) against cognitive and immune function improvement in mice. The study included 6-week-old male BALB mice fed with 50 and 200 mg/kg of body weight for 12 weeks. The research highlighted that *P. tenera* helped maintain gut microbiota balance and intestinal barrier integrity by producing short-chain fatty acids, which are crucial for overall health and may influence cognitive function.

SCFAs from OS fermentation can be absorbed and utilized by colon enterocytes for energy, promoting their growth and differentiation (Schönfeld & Wojtczak, 2016). In the context of improved gut health, this manifests as increased mucus production, tightening of barrier or junctional structures, and reduced inflammation (Fig. 3) (Wasiewska et al., 2025). Acetate, propionate, and butyrate, in a ratio of 3:1:1, make up the majority of SCFAs situated in the gut and absorbed by enterocytes (Yue et al., 2022; Chang et al., 2024). In addition to serving as energy sources, SCFA act as signalling agents for energy homeostasis by activating free fatty acid receptors (FFARs) such as GPR40, GPR41, GPR43, and GPR120 (Kimura et al., 2020). In such a manner, they influence the synthesis and storage of fat in adipose tissue, improve barrier tissue, and suppress pro-inflammatory responses (Sankarganesh et al., 2025). Conversely, a reduction in OS in the gut may deplete SCFA-producing bacterial taxa and promote Proteobacteria (Kotlyarov, 2022). Consequently, while SCFA

levels decrease, opportunistic taxa can begin to degrade the mucus layer, utilizing its glycan components, such as sialic acid, as a food source (Wongkuna et al., 2025). The result is thinning of the dense outer mucus layer and a possible penetration of the inner mucus layer by microorganisms to reach the epithelial cells (Luis & Hansson, 2023). In addition, metabolites from these microbes are also translocated across the epithelial barrier, causing inflammation and redox imbalance (Chen et al., 2026).

### Immunity Booster

OS are well known as low-energy sweeteners that offer a diverse array of functions, one of which is modulating the immune response. Human milk oligosaccharides (HMOs) are a diverse group of complex and indigestible sugars that play a key role in the development of an infant's gut microbiota and immune system. They have been shown to exert antiviral, anti-bacterial, and anti-inflammatory effects and reduce the risk of developing allergies, eczema, and asthma in early childhood (Wiciński et al., 2020). Galacto-oligosaccharides and fructo-oligosaccharides have also demonstrated numerous benefits in promoting immune system and microbiome development in infants. Numerous studies have reported the immunomodulatory and antioxidant properties of oligosaccharides, making them valuable for the treatment of various diseases. Wen et al. (2022) conducted a study to investigate the effect of Chitosan oligosaccharides by administering it into C57/BL6 mice and revealed enhancement in intestinal mucosal immunity in mice by promoting the secretion of secretory immunoglobulin A (SIgA).



**Fig. 3:** Oligosaccharides generate short-chain fatty acids in the gut, which can be utilized by colon enterocytes for energy production as well as enhance mucin production, thereby increasing intestinal barrier functions. This results in a reduction of pathogen and LPS leakage into tissue and blood. SCFA: short-chain fatty acid, IL-17: interleukin -17, TJ: tight junction, LPS: lipopolysaccharides, AMP: Antimicrobial peptide, JAMs: Junctional adhesion molecules, Zo-1: Zonulin-1. Source: The figure adopted and modified from Stoeva et al. (2021).

SCFAs produced from OS fermentation are key to sustaining immune function in the host (Fig. 4). While most of the SCFAs produced would be utilised by colonocytes, some still diffuse into the blood and are transported to the liver to be used by hepatocytes, while others go further to cross the blood-brain barrier (Wasiewska et al., 2025). As a result, in colonocytes and other cells of the body where SCFAs may reach, immunoregulatory activities are enhanced through inhibition of nuclear factor- $\kappa$ B, dephosphorylation of phosphorylated mitogen-activated protein kinase, and inhibition of histone deacetylase (Liu et al., 2023a). In the central nervous system, SCFA, can influence neuroplasticity, gene expression and immune response (Dalile et al., 2019). As such, the fermentation of OS by gut microbiota to produce SCFA initiates a two-way communication via complex signalling systems among the colonic environment and the vagus nerve, neuroendocrine system, hypothalamus-pituitary-adrenal axis and the immune system (Rodrigues de Paiva et al., 2025).

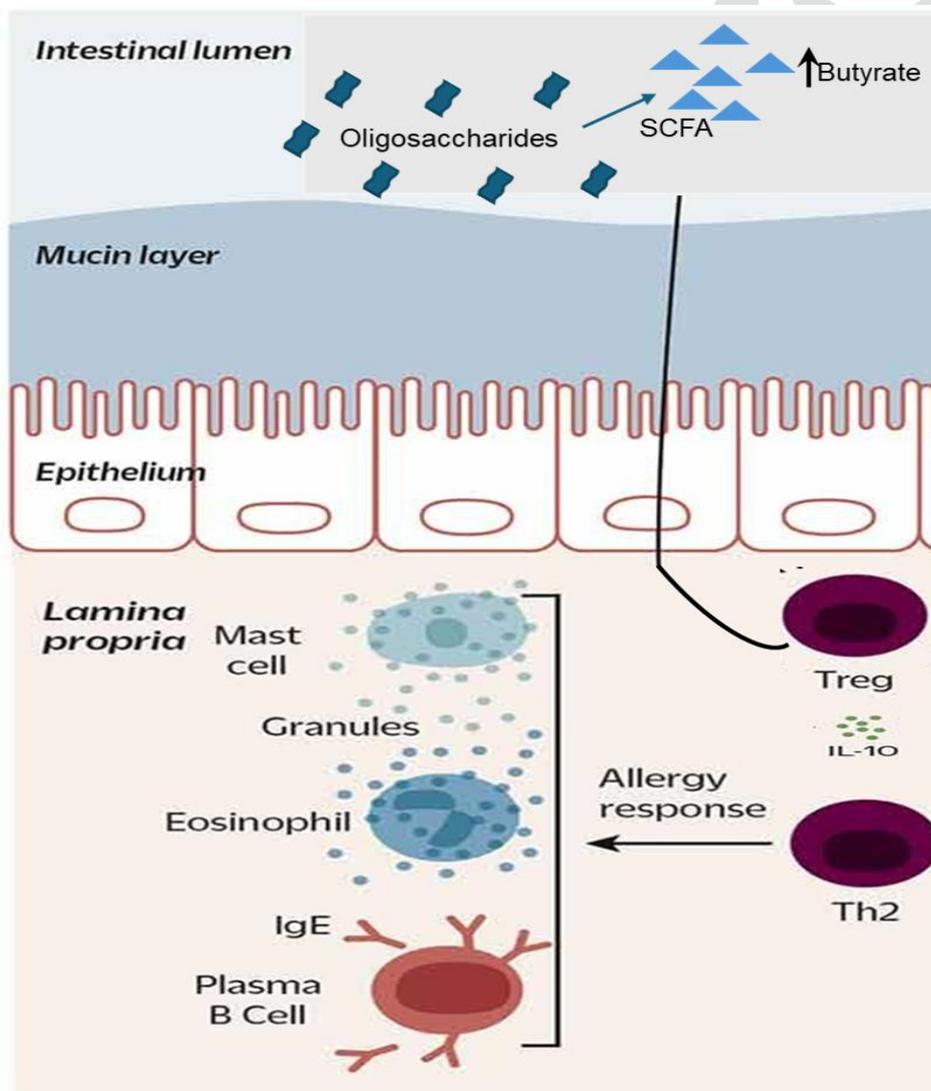
#### Future Prospects of OS in Human Nutrition

The importance of oligosaccharides (OS) in human nutrition is being strengthened by ongoing research and

developments, particularly in functional foods and nutraceuticals. Due to the increasing demand for diet-based therapies, their ability to address diseases and enhance health is increasingly recognized. Future research is focusing on several key areas:

#### i) Individualized Nutritional Interventions

The creation of customized nutrition plans is a key area for OS going forward. This method adjusts the intake of specific OS to each person's health profile, considering their underlying medical conditions, gut microbiota composition, and genetic predispositions (Vandeputte, 2020). For instance, those with gut dysbiosis, in which abnormalities in the gut microbiota lead to metabolic illnesses, chronic inflammation, or digestive issues, may be targeted with polysaccharides such as beta-glucans and oligosaccharides such as FOS (Gibson et al., 2017). OS may also be utilized to treat metabolic disorders and enhance immunological function, especially in those with weakened immune systems. Healthcare professionals may be able to suggest dietary therapies that boost immune function and lower the risk of infections and autoimmune diseases by choosing OS with particular immune-modulating qualities (Vulevic et al., 2013).



**Fig. 4:** Oligosaccharides generate short-chain fatty acids in the gut, which activate butyrate signalling and boost the immune system. SCFA: short-chain fatty acid, Treg: regulatory T-cell, IL-10: interleukin-10, Th2: T helper-2. Source: The figure adopted and modified from Stoeva et al. (2021).

### ii) Novel Technologies Applications

OS extraction, modification, and bioavailability could all be improved with rapid advances in new technologies. Enzymatic hydrolysis and nanotechnology are being developed to enhance the effectiveness and accessibility of OS across a range of products, including pharmaceuticals, functional foods, and dietary supplements. Enhancing the solubility can maximize their health advantages by improving their absorption in the gastrointestinal tract (McClements, 2020).

### iii) Biotechnological Advantages

Researchers can create specific kinds of OS with improved qualities, such as higher prebiotic activity or more potent immune-modulating effects, by genetically altering bacteria or fungi. This invention may lead to the development of more economical and environmentally friendly processes for producing OS, enabling their extensive application in food and medicine (Ma et al., 2022).

### iv) Synergistic Effects with Other Nutrients

Another fascinating topic for further study is the mixing of OS with other useful components, including probiotics, prebiotics, and antioxidants. The health benefits of each component alone may be enhanced by the synergistic effects of certain mixtures. To promote the growth of beneficial bacteria in the gut, probiotics (live bacteria) that support gut health work in concert with prebiotics, such as OS (synbiotics) (Markowiak & Śliżewska, 2017; Rahmi et al., 2025). Additionally, to combat oxidative stress and inflammation, research should focus on combining OS with antioxidants. By adding these substances to nutraceuticals or functional foods, the overall health benefits might be increased, and a more comprehensive strategy for illness prevention and health promotion could be offered.

### Conclusion

OS have emerged as multifunctional bioactive compounds with profound implications for human health. Their unique structural characteristics enable them to act not only as prebiotics, but also as modulators of antioxidant defense, immune responses and metabolic regulation. Evidence from both experimental and clinical studies highlights their ability to enhance gastrointestinal health, improve immune function, and mitigate risks associated with chronic diseases. Advances in biotechnology are paving the way for improved bioavailability, while research on synergistic formulations combining probiotics, polysaccharides, and antioxidants offers promising strategies for developing functional foods and nutraceuticals. Continued scientific exploration and technological innovation will further unlock their value, positioning oligosaccharides as vital components in future approaches for human health management.

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Rinku Sudarshan Agrawal: Data curation, formal analysis, methodology, Writing-original draft.

Phanthipha Laosam: Data curation, formal analysis, methodology, Writing-original draft.

Papungkorn Sangsawad: Validation, Writing-review & editing.

Gitanjali S. Deokar: Data curation, methodology, Writing-original draft.

Fahad Al-Asmari: Data curation, formal analysis, Writing-original draft.

Li Li: Validation, Writing-review & editing.

Kasim Sakran Abass: Validation, Writing-review & editing

Narashans Alok Sagar: Resources, Software

Nattira On-nom: Conceptualization, Investigation, Methodology, Supervision, visualization, Writing-review & editing.

Nilesh Nirmal: Conceptualization, Funding acquisition, Investigation, Project administration, Supervision, Validation, Visualization, Writing-review & editing.

All authors agree to be accountable for their contributions and approval of the manuscript.

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