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Physiological functions of fructooligosaccharides and its application progress in food

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ABSTRACT: Fructooligosaccharides (FOS) are naturally sourced, low-calorie carbohydrates that resist human digestive enzymes in the gastrointestinal tract. They are selectively fermented by certain *Lactobacillus* and *Bifidobacterium* species in the colon, thereby producing short-chain fatty acids (SCFAs). This process promotes the growth of beneficial microbiota while inhibiting pathogenic microorganisms. Consequently, they are classified as prebiotics. By interacting with the gut microbiota, FOS elicit various physiological effects and have attracted considerable research attention in functional food studies due to their favorable physicochemical and biological properties. This review systematically summarizes and critically evaluates recent advances on the physiological functions of FOS, covering their roles in maintaining intestinal microbial balance, reducing plasma levels of cholesterol, phospholipids, and triglycerides, regulating blood glucose levels, and enhancing immunity. Their potential involvement in tumour inhibition and mineral absorption is also discussed. Furthermore, this review examines recent progress in the application of FOS in food systems, including baked goods, meat products, dairy and non-dairy beverages, and animal feed. Special emphasis is placed on emerging in-situ enzymatic conversion technologies, which could enable more flexible and cost-effective utilization of FOS. Additionally, current common biosynthetic strategies are also outlined. Overall, this review highlights the key challenges and future prospects of FOS in functional foods, and provides critical insights for its application in personalized nutrition and disease management.

Key words: Fructo-oligosaccharides; physiological function; intestinal microbiota; short-chain fatty acids

1. Introduction

Prebiotics are dietary components that are generally resistant to digestion and absorption by the human body but can be selectively utilized by gut microorganisms. They can improve the composition and/or activity of intestinal microbiota, thereby benefiting human health [1]. Many fermentable carbohydrates, such as the non-digestible oligosaccharides fructans and galactans, human milk oligosaccharides, and certain soluble fermentable fibres, have demonstrated prebiotic effects. Moreover, certain non-carbohydrates, including plant polyphenols, polyunsaturated fatty acids, and organic acids, have also shown prebiotic activity [2]. Prebiotics contribute to a variety of physiological and pathophysiological processes across the human lifespan. These

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include enhancing mineral absorption, improving gastrointestinal and barrier functions, regulating energy metabolism and satiety, and reducing the risk of intestinal infections [3,4]. Meanwhile, growing consumer awareness of the link between prebiotics and gut health has driven increased interest in this field. Among various prebiotic compounds, fructooligosaccharides (FOS) have attracted particular attention due to their functional properties and economic potential in the sugar industry [5,6]. Accordingly, global demand for FOS has increased steadily [7].

FOS are composed of several β-D-fructofuranosyl units linked to an internal or terminal glucosyl unit via β-(2→1) and/or β-(2→6) glycosidic bonds, with a degree of polymerisation (DP) ranging from 3 to 30 [8]. According to the type of glycosidic linkage, FOS can be classified into three main types: inulin type, levan type, and branched type ("neo-series") [9]. The inulin type consists predominantly or exclusively of β-(2→1) fructose-fructose linkages, while the levan type is mainly or only composed of β-(2→6) fructose-fructose linkages. Branched FOS contain a mixture of both linkage types [10]. These compounds are naturally present in various plant sources, such as onions, chicory, asparagus, leeks, garlic, wheat, and tomatoes [11,12]. FOS are low-calorie, non-carcinogenic sweeteners with approximately 30%–60% of the sweetness of sucrose, making them suitable sugar substitutes in various food products. Owing to their glycosidic configuration, FOS are resistant to human enzymes and cannot be digested [13]. Therefore, they do not contribute to caloric intake and can be safely consumed by individuals with diabetes [14,15]. Additionally, FOS have been associated with multiple physiological effects. They enhance the gastrointestinal absorption of essential minerals such as Ca and Mg, strengthen resistance to infections, activate the immune system, and exhibit anti-tumor properties. They also contribute to reducing plasma cholesterol, phospholipids, and triglyceride levels [14]. These functional attributes have supported their widespread application in baked goods, meat products, beverages, dairy products, and animal feed.

Although some studies have investigated the health benefits of FOS as a prebiotic, existing reviews predominantly focus on general functions or specific application scenarios. A systematic analysis of the mechanisms underlying their effects remains limited. Concurrently, inconsistent conclusions regarding the health effects of FOS in the existing literature have not been sufficiently scrutinised or resolved. Therefore, this review aims to comprehensively summarise recent advances in the physiological functions of FOS, critically evaluate their applications in the food industry, and outline prevalent biosynthetic approaches. Furthermore, it aims to identify key challenges and provide targeted guidance for the future development of functional foods and advanced applications in pharmaceutical and healthcare sectors.

2. Physiological functions of FOS

FOS has various health benefits, and the consumption of FOS-rich foods has an ameliorative effect on a variety of diseases in the body (Table 1), which has been discussed in this section.

Table 1. Therapeutic potential of FOS

Disease Condition	Research Object	Health Benefits	Reference
Fatty Liver Disease	Mice with fatty liver disease induced by a high-fat diet	Reduces liver adipogenesis pathway and intestinal permeability via the microbiota-gut-brain axis	[16]
Liver Cirrhosis	Sprague-Dawley rats with cirrhosis induced by bile duct ligation	Alleviates hepatic vascular dysfunction in cirrhotic rats by at least partially ameliorating dysbacteriosis and oxidative stress	[17]
Kidney Injury	Wistar rats fed a high-fat diet	Reduces insulin resistance and hypercholesterolemia while inhibiting renal inflammation, oxidative stress, fibrosis, and apoptosis	[18]
Type 2 Diabetes	Male C57BL/6J mice fed a high-fat diet	Causes obvious intestinal ecosystem structure reorganization, improving type 2 diabetes-related metabolic disorders, including obesity, insulin resistance, systemic inflammation, oxidative stress, dyslipidemia, and hepatic steatosis	[19]
Autism Spectrum Disorders	Children with autism spectrum disorders	Probiotics + FOS intervention regulates gut microbiota, SCFAs production, and serotonin to improve the autism spectrum, while reducing high serotonin status and dopamine metabolic disorders.	[20]
Alzheimer's disease	Male Apse/PSEN 1dE9 transgenic mice	Reverses the altered microbial composition, increases the levels of GLP-1, and decreases the levels of GLP-1R in the transgenic mice	[21]
Mood Disorders (Anxiety Disorders, Depression)	Male C57BL/6 mice fed a high-fat diet	Regulates the microbiota-gut-brain axis reversed the symptoms of depression and anxiety in Huntington's disease mice	[22]
Osteoporosis	Young female adult mice	Acts on the gut-bone axis and has beneficial effects on bone and mineral metabolism	[23]
Allergy Prevention and Infection Protection	Male BALB/c mice under specific-pathogen-free conditions	FOS is metabolized to Immunoglobulin A by producing SCFAs in the intestine.	[24]
Prognosis in Acute Pancreatitis	110 patients with severe acute pancreatitis	Reduces the incidence of intra-abdominal infection and the level of inflammation	[25]
Colitis	C57BL/6J mice with colitis	Exerts intestinal anti-inflammatory activity in T lymphocyte-mediated colitis	[26]
Constipation	Elderly patients undergoing continuous ambulatory peritoneal dialysis	Significantly increases bowel frequency, softens stools, and speeds up colonic transit time	[27]

2.1. Regulating intestinal microecological balance

The human gastrointestinal tract harbors a diverse microbial community comprising over 100 trillion microorganisms, with bacterial cell densities in the colon of approximately 1011 to 1012 cells per milliliter. This multicellular "organ" is essential for maintaining a dynamic balance in various physiological processes [28,29]. In recent years, increasing attention has been directed toward the microbiota-gut-brain axis, a bidirectional communication network mediated by neural, endocrine, immune, and microbial pathways [30]. Microbial metabolites, especially short-chain fatty acids (SCFAs), mediate bi-directional communication of the gut-brain axis [31]. On the one hand, the central nervous system can indirectly influence the intestinal microbiota by altering the intestinal environment and a series of signaling pathways. On the other hand, gut microorganisms communicate with the host via Toll-like receptors, microbial metabolites, and metabolites of neuroactive substances such as 5-hydroxytryptamine, thereby influencing the enteric nervous system, the main neural network connecting the microbiota and the host [32–34]. As a typical prebiotic, FOS can be selectively fermented by specific beneficial bacteria, promoting SCFA production and thereby contributing to the regulation of gut-brain axis-related signals.

Under healthy conditions, the gut microbiota exhibits high diversity and stability, and maintains a dynamic symbiotic relationship with the host. On the contrary, the imbalance of microbiome composition and function (dysbacteriosis) is closely associated with a variety of metabolic disorders and neurological diseases [35]. For example, microbial metabolites can stimulate the secretion of satiety-related hormones, and these satiety signals regulate appetite through the gut-brain axis, thereby reducing the prevalence of obesity and metabolic syndrome [36]. An increasing number of studies have also linked gut microbiota dysregulation to neurological and psychiatric disorders, including Alzheimer's disease (AD), Parkinson's disease, and anxiety, and depression. Microbially derived neuroactive molecules can directly or indirectly affect the physiological functions of brain cells, thereby shaping cognitive and emotional processes [31,37]. For example, dysbiosis may result in the excessive production of amyloid, lipopolysaccharides, and other toxins. These substances can induce systemic inflammation, disrupt physiological barriers, and trigger neuroinflammation, thereby elevating the risk of AD [38]. However, administration of FOS to AD model rats improved learning and memory and inhibited the reduction of intestinal microbial diversity [39], suggesting a potential neuroprotective role mediated through modulation of the microbiota-gut-brain axis. Regulation of gut microbiota may be a promising way to treat neurodegenerative diseases such as AD [38,40,41]. SCFAs are considered to play an important regulatory role in the development of depression and anxiety. They are attached to the free fatty acid receptors of intestinal epithelial cells, interact with neurons, and exhibit neuroactive properties [37]. Accordingly, microbial flora intervention has emerged as a potential treatment for emotional disorders such as depression [42].

Beyond the gut–brain axis, gut microbiota dysbiosis can also affect distal organ function via pathways such as the gut-liver axis and gut-kidney axis. Intestinal barrier damage and microbial imbalance can induce abnormal

immune response or strong inflammation in the liver, weaken the ability of pathogen clearance and disturb metabolic function. In turn, abnormal liver function may further exacerbate intestinal barrier damage and microbial dysbiosis, forming a vicious circle [43]. Similarly, dysbiosis can contribute to renal injury and fibrosis by promoting endotoxemia and chronic low-grade inflammatory response. In turn, impaired renal function can further aggravate microbial imbalance and uremic toxin accumulation, forming a two-way pathological regulation relationship [44]. These findings suggest that FOS may exert systemic regulatory effects across multiple organ axes by modulating SCFA production (Fig. 1).

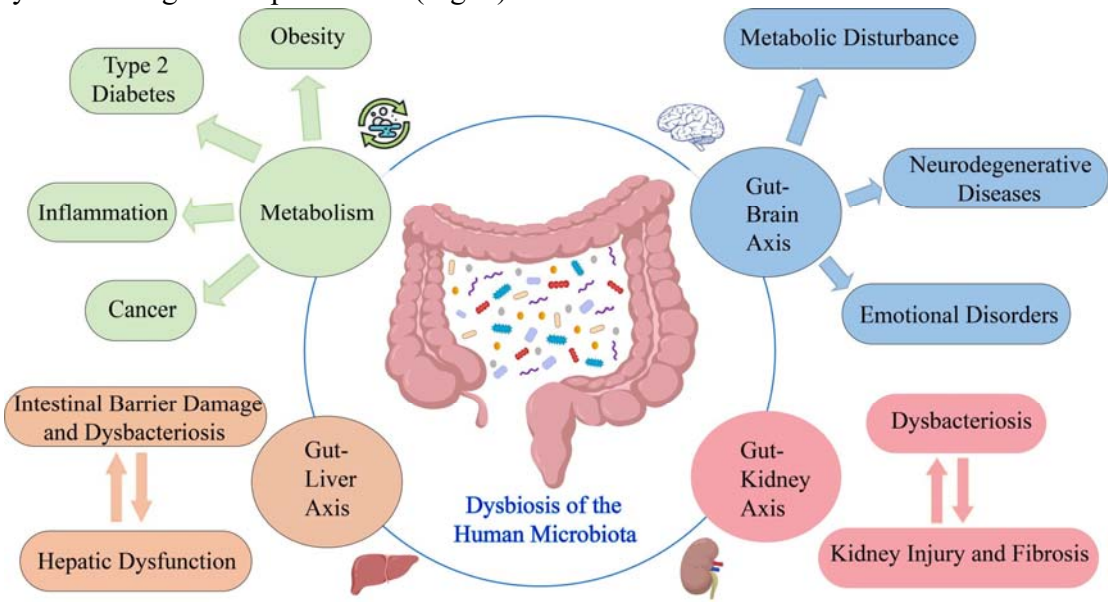


Fig.1 The human microbial dysbiosis in human diseases. Gut microbiota is implicated in the right functioning of many organs, such as brain, kidneys, and liver. However, any disruption to the microbiota homeostasis results in the malfunctioning of these affected organs, and the progression of many related diseases.

FOS is a natural, low-calorie carbohydrate, which can promote the growth of beneficial microorganisms while inhibiting harmful bacteria in the gastrointestinal tract. It is one of the recognized prebiotics with a high level of evidence at present [1]. FOS is not affected by intestinal enzymes and can only be fermented by Lactobacillus and Bifidobacterium species in the colon. Lactobacillus species primarily metabolize FOS through two mechanisms: hydrolysis before transport and transport before hydrolysis, whereas Bifidobacterium species predominantly utilize the transport-before-hydrolysis pathway [45]. The abundance of most bacteria, especially probiotics such as Bifidobacteria, is significantly positively correlated with SCFAs production and negatively correlated with intestinal pH [46]. FOS fermentation will reduce luminal pH, thereby promoting the growth and activity of beneficial bacteria, especially Bifidobacteria. They also inhibit the growth and reproduction of potentially spoilage bacteria, thus reducing the production of toxic products. Additionally, SCFAs produced during this process are absorbed in the colon and metabolized by peripheral tissues to generate butyrate, propionate, and acetate. These metabolites contribute to host energy metabolism and reduce intestinal pH, thus effectively inhibiting the growth and reproduction of pathogenic bacteria and enhancing nutrient absorption [8,14].

In addition, SCFAs play key roles in physiological related mechanisms such as mineral absorption, lipid metabolism, glucose homeostasis, and immune regulation [47,48].

In particular, FOS serve as potent bifidogenic factors, significantly stimulating the proliferation of Bifidobacteria. As one of the earliest bacterial communities to colonise the mammalian gut, Bifidobacteria possesses greater adaptive advantages, ecological adaptability and competitiveness within the human gut. They play essential roles in metabolite production (e.g., SCFAs and vitamins), immune system development, and protection against intestinal diseases [49]. Studies have demonstrated that maternal mice supplementation with synbiotics containing long-chain FOS during pregnancy and lactation increase Bifidobacteria abundance in the intestinal and cecum of their offspring [50]. Gao et al. [51] supplemented lactating dairy calves with FOS, which stimulated the survival of Bifidobacterium and promoted the maturation and stability of the hindgut microbiome. This effective proliferative effect has also been observed in humans. Van Harsselaar et al. [52] conducted a randomized, double-blind, crossover study with 64 volunteers, who were randomly assigned to consume either 2.5 g/day of chicory oligofructose or a placebo for two weeks. Following this initial phase, participants underwent a four-week washout period before crossing over to the alternate intervention. The results showed that compared with the placebo, FOS supplementation exhibited a significant increase in intestinal Bifidobacterium spp. and stool frequency. This study is the first to demonstrate that even a low dose of chicory oligofructose (2.5 g/day) can significantly promote Bifidobacteria proliferation in the human gut.

In addition, pathogens can adhere to the surface of the intestinal mucosa, compromising its integrity, invading the intestinal tract, and proliferating, thereby posing a threat to human health. While Bifidobacterium and other probiotics can attach to epithelial cells via phosphatidic acid, forming a protective biofilm barrier. This barrier effectively prevents the invasion, colonization, and proliferation of harmful bacteria [53]. Therefore, the bifidogenic effect of FOS plays a crucial role in maintaining intestinal homeostasis and overall gut health.

2.2. Improved blood parameters

2.2.1. Lipid metabolism regulation

FOS modulates the composition of the gut microbiota and its metabolites, particularly SCFAs and bile acids (BA), thereby improving lipid metabolism and exerting systemic effects. Hyperlipidaemia is commonly characterised by elevated triglyceride and low-density lipoprotein cholesterol levels. This pathological process is associated with multiple health issues, including liver and pancreatic damage, hypertension, stroke, fatty liver disease, atherosclerosis, obesity, and type 2 diabetes [14,54]. By regulating the processes of digestion, absorption, storage, and secretion of dietary lipids, gut microbes can regulate lipid metabolism. Therefore, their diversity and richness affect energy absorption and are negatively correlated with obesity risk. Firmicutes and Bacteroidetes are the two dominant phyla, accounting for over 90% of the human gut microbiota. Certain Firmicutes (e.g., Faecalibacterium, Ruminococcaceae, Lachnospiraceae, and Anaerofilum) are more efficient at extracting energy

from food, thereby promoting calorie absorption and weight gain. In contrast, members of the phylum Bacteroides are generally associated with promoting leanness in animals [55,56]. FOS intake enhances gut microbiota diversity and richness, accompanied by a significant reduction in the Firmicutes/Bacteroidetes ratio, thereby improving energy utilisation patterns and exerting beneficial effects on lipid metabolism. This therapeutic potential has been validated across multiple animal and human models, including high-fat diet-induced type 2 diabetic mice and exogenously obese children [19,57].

Beyond altering microbial composition, FOS modulates lipid metabolism via two key metabolites: SCFAs and secondary BAs. FOS enhances SCFAs production by gut microbiota, particularly propionic acid, which plays a pivotal mediating role in lipid metabolism regulation through multiple potential mechanisms: (1) Compromised intestinal barrier integrity may promote lipopolysaccharide translocation, triggering systemic inflammation and resulting in abnormal lipid metabolism [58]. SCFAs increased by FOS fermentation can strengthen the intestinal barrier, enhance immunity, reduce inflammatory responses, and thereby improve lipid metabolism [59]. (2) SCFAs stimulate the expression of G-protein-coupled receptors, such as Ffar2 and Ffar3 (GPR43 and GPR41), thereby promoting the secretion of hormones including glucagon-like peptide-1 and peptide YY, which regulate hepatic lipid accumulation [60]. (3) SCFAs effectively suppress the release of inflammatory mediators [61]. Therapeutic FOS supplementation may reduce pro-inflammatory cytokine secretion (including tumour necrosis factor-alpha) and lower blood lipid levels by modulating SCFAs [62]. Furthermore, FOS intake synergises with the gut microbiota to accelerate BA cycling, thereby regulating lipid metabolism. As mediators facilitating lipid digestion and absorption [63], primary BAs synthesised from cholesterol can be converted into secondary BAs within the liver. Due to their limited reabsorption, Secondary BAs are typically excreted with food residues, thereby prompting the liver to consume more cholesterol for de novo BA synthesis. This process simultaneously accelerates the "enterohepatic circulation of BA", further reducing cholesterol levels [14,58]. Hu et al. [64] demonstrated via a piglet model that FOS intake alters BA composition and concentration, thereby reducing lipid synthesis. Furthermore, studies indicate FOS directly downregulates key lipid synthesis regulators such as SREBPs and ChREBP, alongside inflammation-related gene expression, thus inhibiting hepatic lipid synthesis [64–66].

Evidence from multiple animal models, including chronic low-grade inflammation [67], non-alcoholic fatty liver disease [68], and high-fat diet-induced metabolic disorder [69], consistently demonstrates that FOS supplementation—either alone or in combination with dietary/pharmacological interventions—improves lipid metabolism, reduces abnormal fat accumulation, and alleviates hepatic steatosis and inflammation. Notably, recent studies have shown for the first time that maternal FOS intake during pregnancy improves offspring lipid metabolism and immune responses by mitigating intrauterine inflammatory conditions [70]. Collectively, the existing evidence collectively supports FOS as a potential dietary strategy for preventing and managing

dyslipidaemia-related metabolic disorders. However, rigorously controlled clinical trials remain necessary to validate its long-term efficacy and mechanism-specific effects in human populations.

2.2.2. Controlling blood sugar level

FOS, as a promising dietary component, demonstrates potential for regulating blood glucose levels by modulating the composition of the gut microbiota and its derived metabolites (particularly SCFAs), while reshaping intestinal immune homeostasis. Diabetes is a serious health problem with an alarming growth rate worldwide, and it is reported to be the 16th leading cause of death worldwide. Type 2 diabetes mellitus represents the predominant form of diabetes and is associated with insulin resistance, obesity, hyperlipidemia, chronic inflammation, and a variety of other symptoms. Among these factors, insulin resistance stands out as the primary etiological contributor to the development of type 2 diabetes [71]. When gut microbiota dysbiosis occurs, increased production of lipopolysaccharides and heightened release of pro-inflammatory cytokines trigger a series of non-specific inflammatory responses. These disrupt insulin signalling pathways, thereby inducing insulin resistance [72]. Conversely, FOS selectively stimulate the growth of beneficial bacteria, particularly Bifidobacteria, whose abundance has been observed in multiple studies to exhibit a negative correlation with the risk of type 2 diabetes [73]. At the same time, FOS can be fermented in the colon to produce SCFAs. SCFAs play an important role in glucose homeostasis through a variety of potential mechanisms: (1) activating G protein-coupled receptors on L-cells and promoting the release of glucagon-like peptide-1 and peptide YY, thereby enhancing insulin secretion, reducing glucagon levels, and suppressing appetite [74,75]; (2) upregulating tight junction proteins, improving intestinal barrier integrity, and reducing circulating endotoxins, inflammation, and oxidative stress; and (3) inhibiting lipolysis in adipocytes, mainly acetate [76], and upregulating 5'-AMP-activated protein kinase signaling in muscle and liver tissues, thereby reducing insulin resistance through energy consumption processes such as fat synthesis and reduction of gluconeogenesis [73,77]. Beyond metabolic signalling, emerging evidence suggests that FOS's beneficial effects on glucose metabolism may also stem from its capacity to remodel intestinal immune subsets. Studies indicate that under high-fat dietary conditions, FOS supplementation restores the homeostasis of RORγt+ CD4 T cells subsets via 2 conventional dendritic cells-dependent pathway, thereby improving glucose tolerance and metabolic regulation [78]. Furthermore, the inability to suppress lipolysis constitutes a significant contributor to insulin resistance in type 2 diabetes patients. Consequently, FOS's improvement of the lipid profile may indirectly enhance glycaemic control by reducing ectopic fat deposition [73,79].

Multiple experimental and clinical studies further substantiate the role of FOS intake in lowering blood glucose levels, improving insulin response, and reducing the risk of metabolic syndrome. An in vitro batch fermentation model has demonstrated the potential of FOS as a dietary intervention to enhance gut health and metabolic outcomes in women with gestational diabetes mellitus [80]. Clinical intervention studies indicate that FOS supplementation, either alone or in combination with metformin, improves glycaemic control, reduces

inflammatory markers, and decreases adverse pregnancy outcomes in women with gestational diabetes mellitus [81,82]. Supplements utilising yacon syrup as a FOS source have been shown to enhance postprandial glucose and insulin responses in women with polycystic ovary syndrome or in healthy adult females [83,84]. Synbiotic supplements combining FOS with multiple probiotics significantly improved fasting plasma glucose, serum insulin levels, and insulin resistance indices in elderly patients with type 2 diabetes mellitus [85], demonstrating beneficial effects in controlling blood glucose and inflammation in diabetic individuals [86]. Beyond its role in blood glucose regulation, FOS supplementation may exert a potential protective effect against diabetic nephropathy by reducing inflammatory responses triggered by dysbiosis. However, knowledge of the underlying mechanisms remains limited, necessitating further detailed evidence to substantiate these findings [87–89]. Recent studies further indicate that the structural characteristics of FOS may influence its metabolic efficacy. High-molecular-weight FOS fractions demonstrated enhanced intestinal α-amylase inhibitory activity in diabetic animal models, alongside improvements in glycaemic and lipid metabolic parameters. This research first revealed that the molecular weight of pure FOS may be a crucial structural factor regulating its effects on glucose and lipid metabolism [90]. In summary, existing evidence supports the potential of FOS as an adjunct dietary strategy for blood glucose regulation. However, current research remains predominantly based on short-term interventions. Rigorous long-term clinical trials are required to further elucidate its therapeutic efficacy in human populations and the structure-function relationship.

2.3. Immunity Enhancement

FOS enhances immune regulation through multiple mechanisms. It is hypothesized that prebiotics and Biostime exert multiple immunomodulatory effects by altering the colonic microbiota, and through both direct and indirect interactions with epithelial cells and intestinal permeability, and innate immune cells, such as dendritic cells, mononuclear/macrophages, neutrophils, and natural killer cells [91,92]. Indirect effects are mediated by the elimination of pathogenic bacteria and the production of metabiotic compounds such as SCFAs [93]. These SCFAs facilitate communication between the gut microbiota and the immune system, contributing to both intestinal and systemic health by regulating the balance between pro-inflammatory and anti-inflammatory factors. As immunomodulatory metabolites, SCFAs also serve as a primary energy source for colonic cells, playing a crucial role in immune protection [28,94]. Previous studies have found that FOS exhibits immunostimulatory properties, including the activation of phagocytes and neutrophils, enhancement of serum immunoglobulin levels and lysozyme activity, and stimulation of the alternative complement pathway. Nevertheless, among the observed FOS-induced changes in the gut microbiota, increasing Bifidobacterium abundance appears to be the first step toward their beneficial effects on gut immune modulation and systemic immune responses [95]. In addition, oxidative stress is associated with immune system dysfunction. FOS can inhibit the production of pro-inflammatory cytokines such as interleukin (IL)-1β, IL-6, and interferon-gamma (IFN-γ) through multiple mechanisms. For example, FOS reduces ovalbumin-induced IFN-γ and IL-4 levels in food allergy animal models

[96]. And alleviates oxidative stress, for example by reducing D-galactose-induced oxidative molecular damage in BALB/cJ mice [97]. These effects collectively contribute to the enhancement of the body's immunity [98,99]. However, the possible mechanisms behind the beneficial effects on the immune system remain unclear, involving a combination of factors rather than just one [95].

Evidence from multiple animal models and population studies supports the potential application of FOS in immunomodulation. For instance, several aquatic animal model studies indicate that FOS supplementation—particularly when combined with probiotics as synbiotics—significantly improves growth performance, immune indices, and anti-inflammatory and antioxidant functions. It also enhances survival following pathogen challenges, such as infection with Streptococcus agalactiae [98,100,101]. Although aquatic models differ physiologically from mammals, their innate immune regulation and oxidative stress pathways exhibit high conservation. Consequently, these findings provide valuable insights into the fundamental biological functions of FOS in regulating host immune homeostasis. The immunoregulatory potential of FOS is particularly prominent in infants and children. Synbiotic supplements containing FOS have improved growth performance, gut microbiota balance, and immune status in early animal models [102,103], while clinical studies demonstrate beneficial effects on gastrointestinal and immune function in human children [104]. Multiple studies indicate that adding FOS to infant formula significantly increases Bifidobacteria abundance, reduces pathogen adhesion, and strengthens intestinal barrier function. This promotes alignment of infant gut microbiota composition and intestinal immune responses with those observed in breastfed infants [105,106]. Furthermore, supplementation with synbiotics containing FOS during pregnancy and lactation improves maternal immune status and promotes neonatal immune system development, reducing the incidence and severity of rotavirus-associated diarrhoea [50,107]. In healthy adults, synbiotic supplementation with FOS has also been observed to improve immune parameters by inducing changes in gut microbiota [108]. However, most current clinical research focuses on synbiotic interventions, with relatively limited evidence regarding pure FOS supplementation alone. Furthermore, studies targeting the elderly and populations with compromised immune function or elevated inflammatory states remain scarce [109]. Consequently, future research should conduct more rigorously designed and well-stratified clinical trials to systematically evaluate the personalised immunomodulatory effects of pure FOS across different age groups, genders, and health statuses.

2.4. Inhibition of tumour

Cancer is a global health problem that affects more than 18.1 million individuals worldwide, according to the latest (2022) data from GLOBOCAN [110]. A variety of tumours (e.g., gastrointestinal and breast cancers) have a complex relationship with gut microbiota. A balanced and functional intestinal microbial community helps maintain immune integrity to eliminate invading pathogens and initiate an anti-cancer immune response [111]. As prebiotics, FOS can enhance host immunity by altering the gut microbiota involved in immune response to emerging tumour. The gut microbiota can continuously mediate immune responses based on its composition,

thereby altering innate and adaptive immunity at different levels. These immune responses are critical for suppressing tumour cell metabolism and enhancing antitumour T-cell activity, ultimately limiting cancer progression [112]. Furthermore, Bifidobacteria ferment FOS to produce metabolites such as lactate and acetate. These are subsequently utilised by other microorganisms such as butyrate producers (e.g., Faecalibacterium prausnitzii) to generate butyrate. Butyrate is a unique SCFA that can reduce the etiologic risk of colon cancer and adenoma development. It also protects against genotoxic carcinogens by enhancing the expression of detoxification enzymes [12,112,113]. Furthermore, butyrate can also strengthen tight junctions and improve the energy balance of epithelial cells, thereby inhibiting tumourigenesis by maintaining barrier integrity and reducing inflammatory signalling [114].

Substantial evidence supports the potential of FOS in tumours inhibition. In vitro experiments have demonstrated that FOS exhibits anticancer activity against the human colon cancer cell lines (HCT-116) and the human adenocarcinoma cell lines (HT-29) [115]. FOS inhibits the proliferation of HCT-116 cells by arresting the cell cycle and eliminates these cells by inducing apoptosis [116]. Similarly, its cytotoxic effects on HT-29 cells involve apoptotic signalling pathways, as evidenced by the upregulation of caspase-3, caspase-9, and Bax genes [117]. These findings highlight the potential of FOS in colon cancer prevention. In a mouse model of colitis-associated colorectal cancer, administration of FOS (2 mg/kg b.w.) significantly reduced tumour numbers, lowered serum levels of pro-inflammatory cytokines, and regulated T-helper (Th) cell differentiation in the colon by reducing Th17 cell proportions whilst increasing the Th1/Th2 ratio [118]. These findings suggest that FOS may influence the development of colorectal cancer through immune modulation and inflammation control. However, clinical evidence regarding colorectal cancer remains inconsistent. One perioperative trial showed that prebiotic supplements containing FOS improved serum immune markers and the gut microbiota composition in colorectal cancer patients [119], whereas, a case–control study found no clear association between dietary FOS intake and colorectal cancer risk [120].

Research on other cancer types also shows mixed results. A meta-analysis indicated that probiotic supplements containing Lactobacillus, Bifidobacteria, and Streptococcus, in combination with FOS, had potential benefits in combating obesity and dyslipidemia in breast cancer patients [121]. In contrast, a large hospital-based case-control study in Italy reported heterogeneous associations between specific FOS components and the risk of certain cancers (breast, ovarian, and endometrial). Among the selected FOS, nystose intake was slightly and directly associated with the risk of all three cancers. High intake of 1F-β-fructofuranosylnystose was inversely associated with ovarian cancer risk, whereas kestose intake showed no significant association with any of the three cancers [122]. However, another PrebiotiCa study by Turati et al. [123] did not support the main role of these FOS components in some upper gastrointestinal cancers (oral and pharyngeal, nasopharyngeal, and oesophageal cancers).

Other studies highlight the supportive role of FOS in cancer management. In a mouse model of in situ lung cancer, an intervention diet containing FOS, delayed the cachectic endpoint, slowed progression of cachexia, and thereby prolonged the maintenance of muscle function [124]. In a randomised controlled trial involving paediatric cancer patients undergoing chemotherapy, an enteral formula containing FOS significantly increased the abundance of Lactobacilli and Bifidobacterium in faecal samples, producing a mild prebiotic effect without gastrointestinal discomfort [125]. These studies suggest that FOS-based nutritional interventions can improve quality of life and reduce treatment-related burdens in cancer patients, and thus holds potential value in cancer management.

The discrepancies among these findings may arise from several factors. First, the effects of FOS may vary depending on cancer type. Although some inconsistencies exist in epidemiological studies, the overall consensus suggests a beneficial role of FOS in colorectal cancer, whereas its effects on other cancers remain more controversial. This may reflect differences in the role of the gut microbiota in the gastrointestinal tract compared with other tissues. Second, structural variations in FOS (e.g., nystose, kestose, and 1F-β-fructofuranosylnystose) and differences in dosage may lead to distinct biological effects. Third, variations in study design—including in vitro experiments, animal studies, observational studies, and clinical trials—may contribute to inconsistent outcomes. Fourth, limited research has examined the interactions between prebiotics and other dietary components or medications [126]. Differences may also arise between studies using FOS alone and those using synbiotic formulations. Finally, individual factors such as age, diet, health status, baseline microbiota composition, and genetic variation can all influence an individual's response to prebiotics [127,128].

In summary, although preclinical evidence is promising, clinical evidence for the anti-tumour effects of FOS in humans remains limited and inconsistent, particularly for non-colorectal cancer. Future research should prioritise well-designed clinical trials that comprehensively consider cancer type, FOS structure and dosage, as well as individual patient characteristics to clarify the role of FOS in cancer prevention and management.

2.5. Improvement of mineral absorption

The consumption of FOS-rich foods enhances intestinal absorption of minerals and trace elements, which are vital for numerous physiological processes in the humans. The underlying mechanisms involve multiple pathways: FOS is fermented in the colon to produce SCFAs and lactic acid, reducing intestinal luminal pH and thereby increasing the solubility of minerals such as Ca and Mg. This acidic environment facilitates the formation of SCFA-mineral complexes, promoting their absorption [15,112]. At the same time, SCFAs, mainly butyrate and lactate, mediate the proliferation of epithelial cells in the colon, expanding the absorptive surface and thus enhancing absorptive capacity [129]. Other studies have shown that the SCFAs produced by the anaerobic fermentation of FOS increase cecal content and wall thickness, thereby enhancing the concentration of the soluble mineral pool in the cecum and facilitating absorption [130]. In addition, phytic acid, an anti-nutritional factor found in many plant-based foods, can bind to minerals and prevent their absorption. Intestinal bacteria, especially

beneficial species, produce phytases, which are not endogenously produced by humans or monogastric animals, and hydrolyse phytic acid to release minerals such as Ca, Mg, and Zn, enabling their absorption in the small intestine [131,132].

Numerous animal studies (Table 2) have demonstrated that FOS supplementation improves the absorption of various minerals (e.g., Ca, Mg) and trace elements (mainly Cu, Fe, Zn). In contrast, evidence from human studies remains less consistent and somewhat unclear [133]. For instance, one study reported that the intake of 15 g/day of FOS has no significant effect on the absorption of Fe and Ca in healthy young men [134]. Conversely, other research has indicated that inulin rich in FOS can enhance the intestinal absorption of Ca and Mg in postmenopausal women and favourably influence bone turnover markers [135]. In summary, while animal data robustly support the mineral-enhancing effects of FOS, human findings are limited and contradictory. Therefore, the influence of FOS on mineral and trace element absorption in humans requires further rigorous investigation to clarify its potential as a dietary strategy for improving mineral bioavailability.

Table 2. The effect of FOS on mineral absorption in animals

Mineral	FOS interventional dose/duration	Animal	Number of subjects	Main findings	Reference
Ca, Mg, P	5 g/100 g FOS/60 days	Male Wistar rats (42 days old)	16	There was a significant increase in Ca and Mg absorption in FOS-fed rats. FOS feeding increased femoral volume in rats. FOS feeding enhanced mineral concentrations (Ca, Mg, and P) in each region of the rat bone surface.	[136]
Ca, Mg, Fe, Cu	100 g/kg inulin (FOS)/21 days	Male Wistar rats weighing about 160 g	32	FOS enhanced the apparent absorption of minerals (Ca, Mg, Fe, and Cu). FOS mitigated the harmful effects of phytic acid on mineral homeostasis in rats.	[137]
Mg, Ca, P, Fe, Cu	1%, 3%, 5% FOS/22 days	Adult male Sprague-Dawley rats	40	With increasing FOS concentration in the diet, the apparent absorption rate of Mg increased, whereas that of Ca, P, and Fe remained unchanged, and Cu absorption decreased. Dietary FOS supplementation was able to reduce urinary N excretion.	[138]
Ca	55 g/kg inulin and FOS mixture/21 days	Ovariectomized rats	26	Nondigestible oligosaccharides feeding had a positive effect on Ca absorption and retention in ovariectomized rats.	[139]
Ca	30 g/kg FOS/28 days	Male Sprague-Dawley rats (four weeks of age) undergoing total gastrectomy	54	FOS feeding partially restored the reduced Ca absorption and femoral variables induced by total gastrectomy.	[140]
Fe	30 g/kg FOS/28 days	Male Sprague-Dawley rats (four weeks of age) undergoing total gastrectomy	50	FOS increased the Fe absorption rate of rats in the sham operation group. Feeding FOS diet partially restored the reduced Fe absorption rate in rats after gastrectomy.	[141]

Fig. 2 summarises the hypothetical mechanisms underlying the health benefits of FOS. FOS promote specific fermentation processes in the gut microbiota, thereby selectively enhancing the growth and activity of beneficial bacteria. The fermentation of FOS produces organic acids, reduces pH, inhibits the growth of pathogenic microorganisms and enhances the absorption of minerals [142,143]. In addition, as previously mentioned, metabolites such as SCFAs play an important role in physiologically relevant mechanisms such as mineral absorption, lipid metabolism, glucose homeostasis, immune regulation, colorectal cancer prevention, and maintenance of the mucosal barrier [47,48,144].

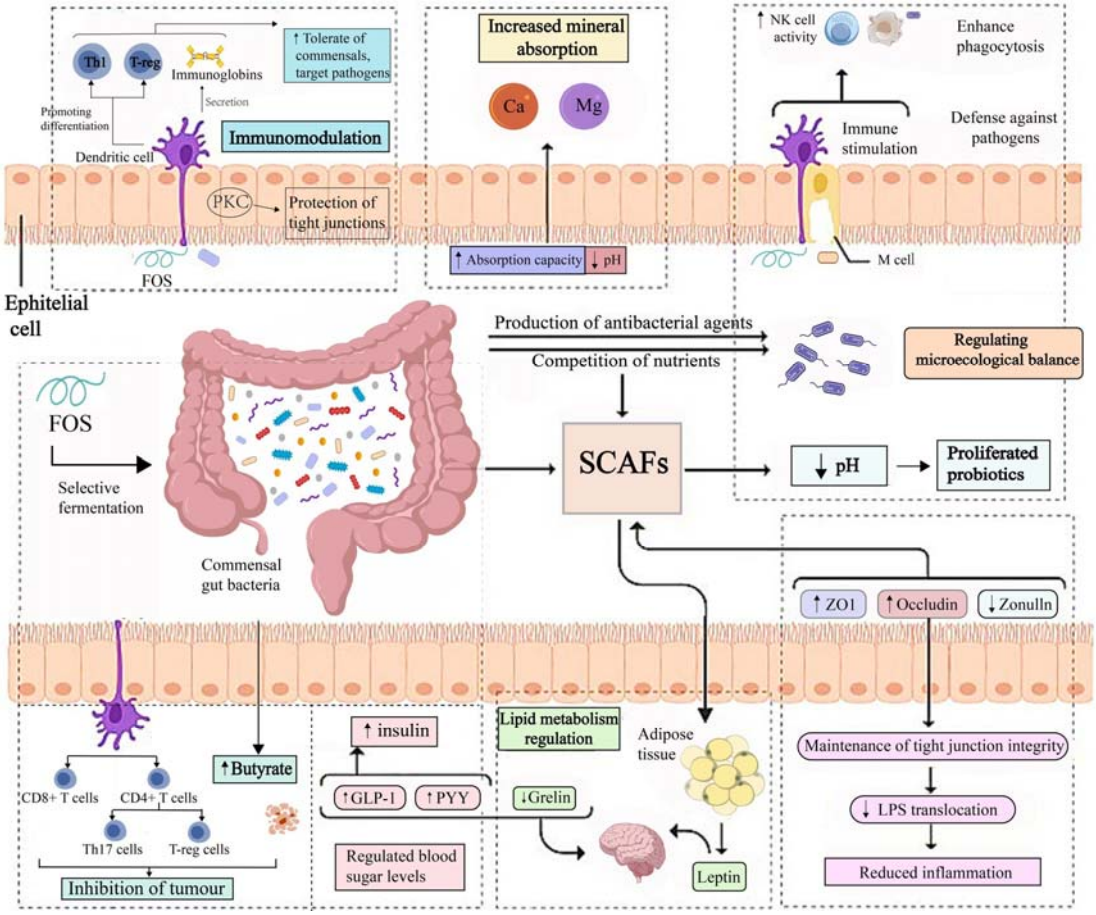


Fig.2 Hypothesized action mechanisms for human health benefits of FOS; TH1 cell, type 1 T helper cell; TH17 cell, T helper 17 cells; T-reg cell, regulatory T cell; NK cell, natural killer cell; M cell, microfold cell; PKC, protein kinase; GLP-1, glucagon-like peptide-1; PYY, peptide YY; ZO1, zonula occludens 1; LPS, lipopolysaccharide.

3. Applications of FOS

FOS has been widely used in the fields of baked goods, meat products, beverages, dairy products, and feeds (Table 3), which has been discussed in this section.

Table 3. FOS application cases in different foods

Product type	Application	Does	Main remarks	Reference
Low carb pound cake	Sugar substitutes	0%–100% of sucrose substitutes	FOS partially replaces sucrose. The low carb pound cake has a moderate glycemic index, low glycemic load, and good sensory evaluation.	[145]
Dry fermented sausages	Fat substitute	2%	FOS significantly reduces fat content. It does not affect microbial growth, lipid oxidation, and proteolysis.	[146]
Low-fat, low-sodium beef burger	Fat substitute	5%	FOS reduces fat content. It has little effect on physicochemical parameters and sensory acceptance.	[147]
Acidophilous milk	Prebiotics supplement	3%	The presence of FOS does not change most of the assessed texture parameters, but may increase dehydration shrinkage. FOS has no effect on the physical and optical aspects of a well-designed formulation	[148]
Carbonated dairy drinks	Prebiotics supplement	100 g FOS/4.5 L milk percolate	FOS exhibits excellent sensory acceptance and good rheological properties.	[149]
Laying hens feed	Intestinal enhancer	0.6%	FOS increases the concentration of antioxidant enzymes and immunoglobulins. It can improve the production performance, egg quality, amino acid digestibility, jejunum morphology, and physiological response of laying hens during the peak period.	[150]
Broiler feed	Antioxidants and Immunomodulators	0.3%, 0.5%, 0.7%	Various levels of FOS can be safely used to improve the antioxidant activity and cellular immune response of broilers. The use of 0.7% FOS can increase the weight of broilers.	[151]
Weaned piglet feed	Early nutrition intervention	5 g/day	Oral administration of FOS during early lactation has a significant bifid effect on colonic microbiota and jejunal mucosal gene expression in piglets.	[152]

3.1. Baked goods

Sugar is a key component in many baked goods, serving both structural and sensory function. However, excessive long-term intake of digestible carbohydrates, particularly mono- and disaccharides, is associated with metabolic disorders such as diabetes and contributes to a growing public health burden. Consequently, the food industry is actively developing low-sugar alternatives. FOS have been widely adopted as a sucrose substitute in baked goods [142]. When used in products like croissants, short-chain FOS (sc-FOS) not only replaces sucrose but also acts as a dough enhancer. It increases dough firmness by strengthening the gluten network adhesion, while simultaneously reducing sugar content and boosting dietary fiber levels [153]. Sc-FOS is added to bread as a humectant to control the flow of water in the bread matrix during storage and produce softer products. Moreover, it serves as an effective sucrose substitute, making such products more suitable for individuals with diabetes [154].

Traditionally, prebiotics like FOS are incorporated into foods via direct fortification before or during processing [155]. However, in-situ production of FOS during the baking process offers a novel alternative, which is less commonly reported. Specifically, by adding fructosyltransferases (FTases) to dough or batter, FOS can be synthesised from sucrose via enzymatic reactions, enabling direct formation of prebiotics within the product. This technique allows prebiotics to be generated within the product itself, overcoming limitations associated with direct FOS addition, such as potential impacts on taste or texture [156]. Na et al. [157] have successfully produced low-sugar sweet dough bread containing FOS without compromising quality by using the in situ method of invertase. Similarly, using a β-fructofuranosidase from Aspergillus niger to produce prebiotic bread with FOS content of 3.3 g/100 g by in situ enzymatic conversion of sucrose was also reported [158].

In-situ generation of FOS during baking presents several advantages over the addition of pre-formed FOS. First, it enables customisation of FOS production schemes for specific baking processes. Second, it enhances the functional properties of the product without causing significant sensory changes, whilst simultaneously reducing the sugar content and caloric value of the final product. Third, the enzymes can be reused, demonstrating the potential to reduce overall production costs and minimise environmental pollution [157,159,160]. Despite these benefits, this technology remains predominantly confined to laboratory or pilot-scale stages and is limited to a very restricted range of product types, such as baked goods and beverages. Several challenges hinder its broader adoption. Enzyme production currently depends on liquid or solid-state fermentation systems. Although mathematical modelling and statistics have aided in optimising fermentation conditions to enhance enzyme yield and productivity, further increases in enzyme output face certain constraints. Future endeavours aim to enhance enzyme production efficiency by designing genetically modified microorganisms with superior catalytic activity [14,158]. A second challenge is that enzymes involved in fructosylation exhibit both transferase and hydrolytic activities, leading to the formation of by-products such as glucose and fructose, which results in relatively low FOS yields (55%–60%) [11]. This process may intensify Maillard browning reactions during baking, affecting crust colour formation, aroma development,

and overall sensory acceptability [161]. In addition, enzyme dosage must be carefully controlled, as excessive amounts increase dough viscosity and negatively affect texture [162]. Building upon enzyme applications, the exploration of innovative functional food development presents vast opportunities for in situ enzymatic conversion methods [155].

Finally, although FOS are generally recognised as safe, high intakes may cause gastrointestinal discomfort in sensitive individuals [163]. This tolerance threshold limits the maximum feasible inclusion level in commercial products, underscoring the need for formulation strategies that align with both technological functionality and physiological tolerability.

3.2. Meat products

Meat is an important part of a healthy, balanced diet. However, commercial meat products often contain high levels of saturated fat, cholesterol, and salt, and long-term intake may adversely affect consumer health [164]. Nevertheless, fat content is closely related to the sensory quality of meat products, and excessively low fat levels often negatively affect flavour and overall quality. Therefore, developing solutions to reduce or replace animal fat has become a major research focus in recent years [142]. In the existing literature, studies have explored the use of FOS as a structuring agent in meat products to form a gel network that retains moisture and mimics the lubricating properties of fat, thereby serving as a fat substitute. Currently, FOS has been applied as a fat substitute in beef burger formulations to reduce the lipid content while maintaining acceptable flavour perception and overall preference [165]. Additionally, incorporating FOS into fermented sausage formulations to reduce the fat content has shown positive effects, improving the stability of volatile compounds, increasing ester compounds, and reducing the undesirable taste of hexaldehydes [166]. Moreover, recently, in the field of emerging plant-based meat substitutes, FOS has been utilized as a prebiotic fiber binder to replace conventional refined binders such as methyl cellulose, improving the adhesion of the remaining ingredients. Soy burgers containing a gel of 2 g FOS have demonstrated favourable technical and sensory properties [167].

Despite these promising applications, several key challenges persist. A primary limitation is the inability to fully replicate the texture and sensory profile of fat. The removal of fat itself alters the microstructure of food, resulting in a firmer and drier texture with reduced juiciness. Furthermore, fat substitutes based on FOS cannot replace fat as a flavour carrier [168]. A fundamental technical limitation lies in the fact that most dietary fibre-based oil gels and emulsion gels exhibit poor thermal responsiveness, failing to mimic the reversible gel-sol-gel transition characteristic of conventional fats. This severely restricts their application as structured oil systems [169]. Advancing this field requires a deeper understanding of the underlying mechanisms, including the use of advanced in situ techniques to investigate molecular interactions governing their assembly and behaviour.

In addition, acidity, as one of the key factors influencing product quality and taste, is also closely related to the bacterial composition of fermented foods [170]. FOS can significantly promote the growth of Lactobacillus species, which in turn may increase the content of organic acids (including lactate, acetate,

citrate, succinate, malate, and tartrate) in fermented sausages [171]. Among these, succinate, malate, and tartrate are associated with astringency and bitterness [172]. Therefore, when adopting a strategy of adding FOS to reduce fat content in fermented sausage formulations, process parameters should be optimised to avoid the development of off-flavours.

3.3. Drinks

FOS is used in yogurt, whey drinks and other dairy drinks as a sucrose substitute while providing functional properties. Its addition accelerates yogurt acidification during fermentation, enhances the vitality of Lactobacillus, and may contribute to the development of lactose-free yogurt products suitable for lactose-intolerant consumers [173]. It also improves water retention and viscosity, reduces syneresis, and does not negatively affect the sensory acceptability of the product [174]. Enzymes used for in situ FOS production can be conveniently introduced during processing and are readily inactivated during pasteurisation, effectively terminating enzymatic reactions [159]. Gonçalves et al. [175] converted inherent sucrose content into FOS to successfully produced reduced-sugar, low-calorie strawberry preparations with prebiotic potential. Beyond dairy systems, FOS can also be applied to non-dairy beverages to support the viability of probiotic strains [142]. In corn- and rice-based fermented beverages, FOS was found to be important for maintaining viable amounts of probiotic starter cultures during fermentation and cold storage. Furthermore, the mixture of acetic acid, lactic acid, and some ester compounds provided the unique taste and aroma of the beverage, and formulations containing FOS achieved higher sensory scores [176]. In addition to direct addition, the production of endogenous FOS via enzymatic processing can eliminate the need for preliminary purification steps [177], an approach that has already been successfully validated in orange, pineapple juice, honeydew melon juice and carrot juice [178,179].

From an industrial perspective, the higher cost of FOS compared with sucrose may limit its widespread adoption. Furthermore, to successfully develop functional drinks, it is essential to optimise the dosage of FOS and the processing conditions. Otherwise, the quality of the final product may be significantly compromised, and consumer acceptance may decline, posing additional technical challenges.

3.4 Feed

FOS has been widely incorporated into animal feed due to its demonstrated benefits in improving feed conversion rate, promoting weight gain, enhancing animal immunity, and increasing resistance to pathogenic bacteria such as Salmonella and Escherichia coli in the digestive tract. Rybicka et al. [180] randomly divided 387 male broilers into three groups, and the experimental groups were given lignocellulosic and mixed diets containing lignocellulosic and FOS, respectively. The FOS-containing group exhibited the best growth performance during the trial and achieved the highest final body weight. The results indicated that the combination of insoluble fiber (lignocellulose) and highly fermentable fiber (FOS) can significantly improve nutrient digestibility and fattening performance in broilers. Similarly, Hanning et al. [181] reported that Cornish White Rock hybrid broilers fed FOS as a feed additive had the highest eight-week body weight compared to other prebiotic groups. In aquaculture, Sukul et al. [182] observed that FOS feeding alone significantly

improved the growth performance, feed utilization rate, and immunity of Labeo rohita, and that its combination with probiotics in a synbiotic formulation yielded even greater benefits.

Although current research has yielded promising technical results and satisfactory organ adaptability, there remain significant gaps in our understanding of the specific metabolic mechanisms in poultry following the consumption of FOS, as well as the safety of meat products and their impact on consumer health [183]. Furthermore, in the highly price-sensitive feed industry, economic viability is a key determinant of adoption. Future efforts to improve cost-effectiveness may focus on strain selection and bio-process optimization to lower the production costs of FOS [184].

4. Common pathways of FOS biosynthesis

4.1 By enzymatic synthesis from sucrose

FOS is primarily produced from sucrose by FTases (β-fructofuranosidases (EC.3.2.1.26) or fructosyltransferases (EC.2.4.1.9) [11]. FTases cleaves the glycosidic bond of the donor substrate (sucrose) and transfers the released D-fructose unit to the β-(2→1)/ β-(2→6) position of the fructose unit on the acceptor molecule (sucrose or fructan) [12,185]. Fig. 3 illustrates the process of synthesising Sc-FOS. Sc-FOS are composed of sucrose molecules bound to 1–3 fructose units, mainly including 1-kestose (GF2), 1-nystose (GF3), and 1-β-fructofuranosyl nystose (GF4). The glucose unit is linked to the terminal fructose unit of the fructan chain through a β-(2→1) glycosidic bond [11,185]. Further elongation of the side chains will result in the formation of inulin-type fructans [186]. Depending on the type of trisaccharide initially synthesised, FOS can be classified as inulin-type or levan-type. The commercially available inulin-type β-(2→1)-FOSs are limited by their low DP, which causes them to ferment in the proximal colon region. The levan-type β-(2→6)-FOSs exhibit higher Bifidobacteria formation and stronger prebiotic activity [187,188]. Their types depend on the enzymes in biosynthesis [7]. However, a key limitation of the enzymatic synthesis is the dual activity of FTases, which display both transfructosylation and hydrolysis functions, leading to by-products such as glucose and fructose and typically low FOS yields (55%–60%). In addition, glucose acts as an inhibitor of the enzyme, affecting the reaction efficiency [11]. Currently, most studies related to FOS production have focused on Aspergillus and Penicillium that produce inulin-type FOS [189]. However, FTases often possess low transfructosylation activity, limiting their industrial applicability [190]. Therefore, genetic engineering of microbial strains to enhance enzyme performance and FOS yield is regarded as a crucial direction toward sustainable and efficient FOS production.

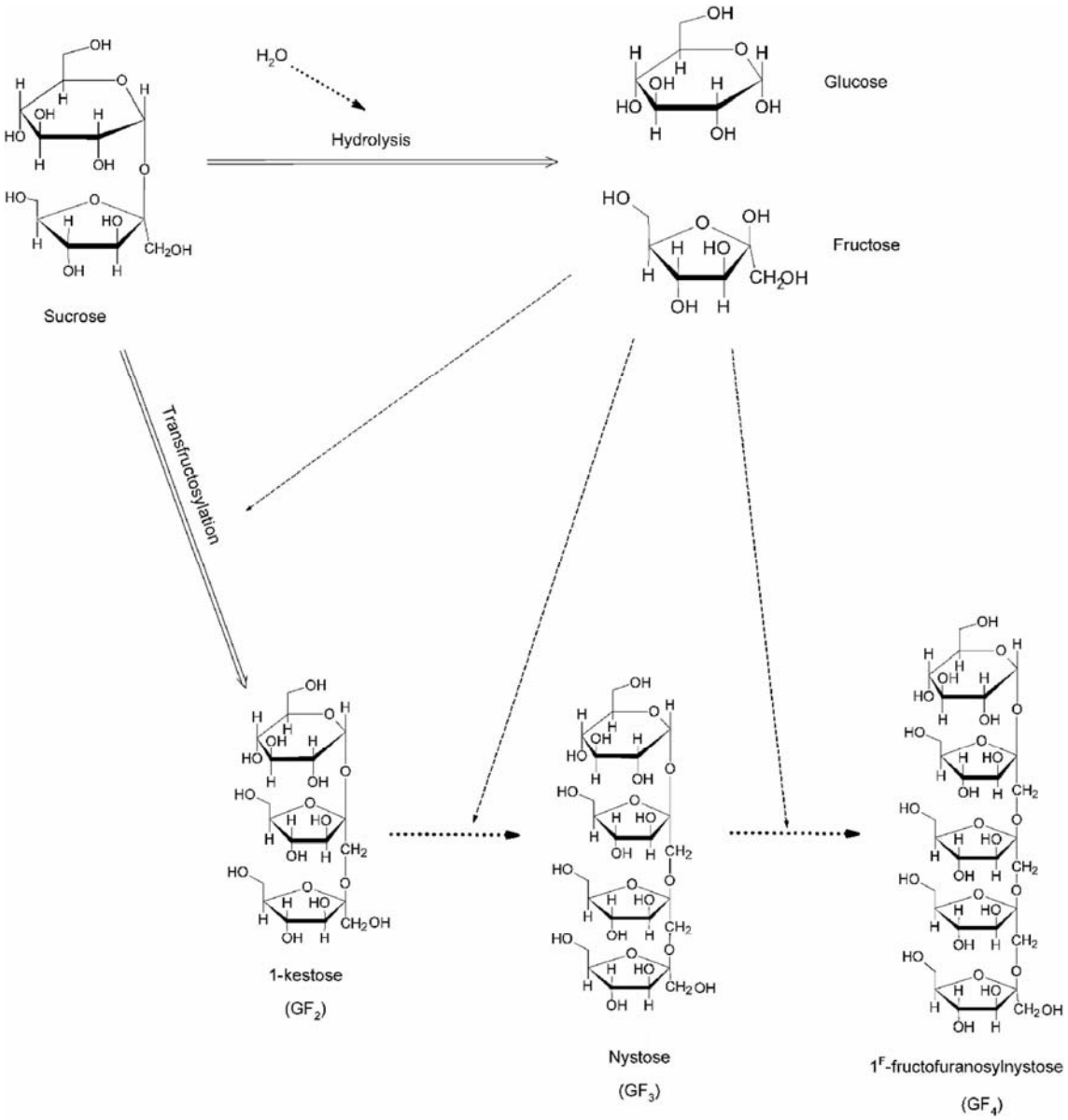


Fig.3 Enzymatic synthesis of sc-FOS from sucrose. Where: G-glucose, F-fructose (own elaboration) [185].

4.2 By enzymatic degradation of inulin

Inulin is a linear β-(2→1)-linked fructan that functions, with chicory root serving as the primary industrial source [191]. Microbial endoinulinases (2,1-β-d-fructan-fructan hydrolase, EC 3.2.1.7) act on inulin, randomly hydrolysing the internal β-(2→1) glycosidic bonds to produce FOS (DP 2–8) [189,192]. Compared with FOS prepared from sucrose (DP < 4), inulin-derived FOS possess a higher DP, which significantly influences their site of fermentation within the colon: sc-FOS are fermented predominantly in the proximal colon, whereas longer-chain fractions persist to the distal colon [193]. Furthermore, FOS produced by partial hydrolysis of inulin by inulinase usually lacks glucose terminal residues, because inulinase does not have invertase activity that hydrolyzes sucrose residues [7].

5. Conclusion and future perspectives

FOS exerts its considerable prebiotic potential primarily through selectively fermented by Lactobacillus and Bifidobacterium species, yielding SCFAs which stimulate the proliferation of beneficial intestinal

microbiota. By maintaining the gut microbiota balance and acting in synergy with it, FOS regulates key physiological functions. Specifically, it can lower plasma levels of cholesterol, phospholipids, and triglycerides and modulate blood glucose; with the magnitude of these glucolipid-metabolic effects being influenced by its molecular weight. Additional benefits also include immune enhancement, potential tumorigenesis inhibition, and improved absorption of minerals and trace elements.

Complementing these health benefits are FOS's favourable physicochemical properties: (1) a sweet, non-bitter taste profile suitable for sucrose substitution; (2) low caloric value (1.0–1.7 kcal/g) and resistance to digestive enzymes, effectively reducing the energy density of foods; (3) good water solubility; (4) superior thermal stability to sucrose and stability within the common food pH range (4.0–7.0); and (5) effective moisture retention [15,185,194,195]. Owing to this combination of bioactivity and physicochemical properties, FOS has gained significant attention in functional food research and has been widely incorporated into baked goods, meat products, beverages, and animal feed.

Despite this promise, several challenges remain in improving its application. First, dosage is critical; while the recommended average intake of FOS is 2–7 g/day [163]. Excessive intake can cause adverse effects, including abdominal distress, bloating, diarrhea, and intestinal inflammation, and has been linked to enhanced Salmonella in mice [48,196,197]. Second, the precise molecular mechanisms and structure-function relationships underlying FOS's actions require elucidation to inform targeted interventions. Third, current evidence relies heavily on short-term trials, necessitating longitudinal clinical studies to establish the long-term safety and efficacy profiles essential for sustained health promotion [198]. Fourth, despite substantial supportive evidence, inconsistencies exist in the literature, underscoring the need for more standardized clinical protocols and stricter control of confounding variables in future research [126]. Finally, accurate quantitative detection methods for FOS remain limited, highlighting the importance of advancing analytical standards and technologies to meet the demands of evolving food products [199].

In summary, FOS holds significant potential for health-promoting functional foods and the global market. Moving forward, leveraging interdisciplinary approaches spanning food science, nutrition, physiology and medicine, alongside tools from genomics, microbiomics, and metabolomics, will be key. A deeper understanding of FOS will enable the design of precise, personalized nutritional interventions, ultimately contributing to improved human health and quality of life.

Declaration of competing interest

The authors declared that they have no conflicts of interest to this work.

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