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From molecular structure to metabolic regulation: How natural polysaccharides combat obesity via multiple pathways

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ABSTRACT: Obesity poses a pressing global health challenge, driving the search for safe and effective therapeutic strategies. Natural polysaccharides have emerged as promising anti-obesity agents due to their multifaceted bioactivities and favorable safety profiles. This review comprehensively summarizes the multi-target mechanisms underlying the anti-obesity effects of polysaccharides, including thermogenesis activation, adipogenesis suppression, lipid catabolism promotion, and gut microbiota modulation via prebiotic activity. Furthermore, we critically analyze the structure-activity relationships (SARs), highlighting how key structural features (molecular weight, monosaccharide composition, and chain conformation) dictate their biological efficacy. From an applied perspective, we also discuss the innovative utilization of polysaccharides as functional fat substitutes in healthier food formulations (e.g., dairy, meat, and bakery products). By integrating mechanistic insights with translational applications, this review provides a theoretical framework and practical guidance for designing polysaccharide-based functional foods to combat obesity.

Keywords: Natural polysaccharides; Anti-obesity; Structure-Activity Relationship; Food applications

1. Introduction

Obesity has emerged as one of the most critical public health challenges of the 21st century. Global epidemiological data from 2016 revealed that the number of overweight or obese children and adolescents (aged 5–19) had exceeded 340 million [1]. Furthermore, predictive models by Finkelstein et al. (2012) suggest that global obesity prevalence will increase by an additional 33% by 2030 [2]. More alarmingly, the latest 2022 statistics (WHO, 2022) indicate that over 50% of adults worldwide are now classified as overweight or obese. This global health crisis extends beyond abnormal fat accumulation, manifesting as complex metabolic disorders. In individuals with obesity, adipose tissue continuously secretes pro-inflammatory cytokines such as TNF-α and IL-6, triggering chronic low-grade inflammation and insulin

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resistance [3]. Concurrently, obesity significantly elevates the risk of type 2 diabetes, non-alcoholic fatty liver disease (NAFLD), cardiovascular diseases, and multiple cancers [4, 5]. Epidemiological studies confirm that severe obesity reduces life expectancy by 10–20 years compared to the general population [6], imposing a profound burden on both individual health and socioeconomic systems.

The Global Health Observatory (GHO) has conducted long-term monitoring, revealing the evolution of the obesity epidemic. The global adult obesity rate has tripled since 1975, and the childhood obesity rate is rapidly increasing [7]. This phenomenon is closely related to lifestyle changes brought about by economic development: the prevalence of high-calorie diets and reduced physical activity have combined to create an imbalance in energy metabolism [8]. The World Health Organization has classified obesity as a 'global epidemic', underscoring its significance as a pressing public health concern [9]. A comprehensive analysis of the pathophysiological mechanisms underlying obesity reveals its fundamental nature as a systemic metabolic disease, primarily characterised by adipose tissue dysfunction, marked by abnormal hypertrophy and hyperplasia of adipocytes, elevated serum triglyceride and cholesterol levels, and diminished insulin sensitivity across multiple organs [10].

Current clinical anti-obesity therapy is heavily reliant on pharmacological interventions and lifestyle management. Approved pharmaceuticals include orlistat (a lipase inhibitor), GLP-1 receptor agonists (e.g. liraglutide) and central appetite suppressants (e.g. the phentermine-topiramate combination) [11]. While these medications can yield 5-15% weight reduction in the short term, their clinical application is constrained by several limitations. Orlistat, for instance, has been associated with steatorrhea and fat-soluble vitamin deficiency, centrally acting drugs frequently lead to adverse effects such as palpitations and insomnia, and GLP-1 analogues necessitate long-term injections and are costly [12]. Moreover, weight regain is a common occurrence following drug withdrawal, and certain medications have been observed to induce liver injury or cardiovascular events [13]. Conversely, lifestyle interventions, encompassing dietary modification and physical activity, are considered safe as fundamental treatments. However, in practical settings, adherence remains a challenge, and the long-term implications are often constrained [14]. Timmers et al. (2011) demonstrated that only approximately 20% of obese individuals can achieve substantial weight loss through lifestyle modifications alone [15]. This 'treatment dilemma' has prompted researchers to seek safer and sustainable intervention strategies.

Against this backdrop, the regulation of dietary components has emerged as a new direction in anti-obesity research. Substantial evidence indicates that specific natural food compounds (tea polyphenols, caffeine, and resveratrol) can ameliorate obesity-related metabolic abnormalities through multi-target mechanisms. Among these, natural polysaccharides have attracted considerable attention due to their unique physicochemical properties and biological activities [16-18]. As major constituents of plant cell walls and microbial extracellular matrices, polysaccharides are high-molecular-weight polymers formed by monosaccharides linked via glycosidic bonds. Based on their origin, they can be categorized into plant polysaccharides (e.g., cellulose, pectin), animal polysaccharides (e.g., chitosan), and fungal polysaccharides

(e.g., β-glucans). A growing body of evidence has demonstrated that natural polysaccharides from various sources interfere with key processes in the development and progression of obesity through diverse mechanisms. They not only directly regulate metabolic pathways but also confer long-term benefits by improving gut health. However, available research remains fragmented, and the connections among their mechanisms of action, structural features, and practical applications have not yet been systematically summarized and integrated. This significantly limits the targeted development and efficient utilization of polysaccharide-based resources.

Therefore, this review aims to establish a comprehensive logical framework spanning from molecular mechanisms to practical applications, systematically elaborating the role and value of natural polysaccharides in the prevention and management of obesity. Firstly, the article will provide an in-depth analysis of the detailed anti-obesity mechanisms of natural polysaccharides, focusing on four major aspects: promoting energy expenditure, inhibiting fat accumulation, enhancing lipid metabolism, and their prebiotic properties. This section will offer a solid theoretical foundation for understanding their multi-target effects. Subsequently, the review will concentrate on the structure-activity relationship between the chemical structures of polysaccharides and their anti-obesity efficacy. By examining key parameters such as molecular weight (low, medium, and high), monosaccharide composition, and fundamental structural features (including chain conformation and branching degree), it seeks to elucidate the material basis of their bioactivity, thereby providing scientific guidance for the targeted screening and modification of highly active polysaccharides. Finally, moving beyond fundamental mechanistic studies, this review will explore the practical applications of natural polysaccharides as fat replacers in the food industry. It will evaluate their latest advances and potential in replacing fats, improving product texture, and enhancing health benefits in dairy products, meat products, as well as snacks and pastries, thereby building a bridge for translating theoretical research findings into functional food development.

In summary, given the global obesity epidemic and the limitations of current therapies, natural polysaccharides—with their multi-target mechanisms and low toxicity—offer a promising new approach for obesity prevention and management. This review systematically examines the anti-obesity mechanisms, current applications, and challenges of various natural polysaccharides, aiming to provide a theoretical foundation for developing novel anti-obesity strategies and advancing precision nutrition and personalized interventions. Through interdisciplinary collaboration to further elucidate the structure-activity relationships and functional networks of polysaccharides, we can pioneer innovative pathways for the prevention and control of metabolic diseases.

2. The detailed mechanism of natural polysaccharides in anti-obesity

Natural polysaccharides demonstrate distinctive advantages in obesity management through their multi-target and multi-level synergistic mechanisms of action. These bioactive compounds exert comprehensive anti-obesity effects through four primary mechanisms: (1) Energy Metabolism Modulation:

By activating the AMPK/SIRT1/PGC-1α signaling pathway, natural polysaccharides significantly enhance mitochondrial biogenesis and fatty acid oxidation capacity, thereby promoting energy expenditure; (2) Adipogenesis Suppression: They effectively inhibit adipocyte differentiation by downregulating key adipogenic transcription factors including PPARγ and C/EBPα; (3) Lipolysis Activation: Through upregulation of hormone-sensitive lipase (HSL) and adipose triglyceride lipase (ATGL) expression, they facilitate triglyceride hydrolysis and fat mobilization; (4) Gut Microbiota Regulation: Functioning as potent prebiotics, they selectively stimulate the growth of beneficial SCFA-producing bacteria, which improves intestinal barrier integrity and attenuates systemic inflammation. This integrated "quadruple-action" mechanism - simultaneously enhancing energy expenditure, inhibiting fat accumulation, promoting lipid breakdown, and modulating gut microbiota - establishes natural polysaccharides as promising anti-obesity therapeutic candidates (**Table 1**).

Table 1. The sources, structural characteristics, and mechanisms of anti-obesity polysaccharides.

Natural polysaccharides		Critical structural features			Anti-obesity mechanism		Potential applications	References
Source	Name	MW /kD	Monosaccharide composition （mol% or mole ratio）	Chemical structure	Classification	Main target		
Momordica charantia L.	MCPS-3	93.796	Rha:GlcA:GalA:Glc:Gal:Ara= 10.66:3.66:258.0:1.0:51.0:9.338	MCPS-3 was a complex polysaccharide, predominantly homogalacturonan domains with rhamnogalacturonan I side chains.	Promoting heat consumption	MCPS-3 enhanced the activities of hexokinase and pyruvate kinase.	Hypoglycemic supplements	[19]
Liriope spicata	LSP	4.742	β-Fru, α-Glc	The backbones of polysaccharides were formed by Fruf-(2→, →2)-Fruf-(6→, →6)-Glcp-(1→ and →1, 2)-Fruf-(6→ with a molar ratio of 5.0:18.2:1.0:5.3 (LSP), 6.8:15.8:1.0:5.8 (OJP), 8.3:12.3:1.0:3.9 (LMP), respectively.	Promoting heat consumption	LSP, LMP and OJP increased the expression of PI3K, AKT, InsR, PPARγ and decreased the expression of PTP1B in mRNA level and protein level in IR HepG2 cells.	Hypoglycemic supplements	[20]
Ophiopogon japonicus	OJP	4.925						
Liriope muscari	LMP	4.138						
Pseudostellaria heterophylla	H-1-2	14	D-Glc	H-1-2 contained pyranride, and had the characteristics of the α-iso-head configuration, a non-reducing end (T-), 4-, 1,6-, and 1,4,6-connection, in all four ways to connect glucose.	Promoting heat consumption	Oral absorption studies suggested potential intestinal mucosal uptake, supporting its anti-obesity and anti-diabetic potential.	Anti-diabetes material	[21]
Schisandra Chinensis (Trucz.) Baill	SCPP11	17.94	Gal, Glc, Man	SCPP11 was found that the repeating unit was a backbone composed of, (7.85%→1)-D-galp-(4→linkages, 62.34%→1)-D-glup-(4→linkages, 5.92%→1)-D-manp(6→linkages and 11.95%→1)-D-galp-(4,6→linkages), and with a single branch atthe C-4 positionof gal.	Promoting heat consumption	SCPP11 up-regulated the expression of GLUT-4 which might occur via insulin and AMPK signal pathway.	Anti-diabetes material	[22]
Ophiopogon japonicus	MDG-1	3.400	**D-Fructan, D-Glc**	Including a backbone composed of Fruf (2→1) and a branch of Fruf(2→6) Fruf(2→) per average 2.8 ofmainchainresidues;it also contains trace of -D-GLc.	Inhibiting fat accumulation	MDG-1 attenuated hepatic lipid accumulation, and increased the expression of genes related to lipid and energy metabolism in the liver.	Preventing high fat diet-induced obesity	[23]
Flaxseed	FP-1	2626	Rha:Ara:Fuc:Xyl:Man:Glc:Gal= 23.81%:10.62%:3.99%:35.24%:0.2%:2.66%:23.39%	The main glycosidic bonds of FP-1 are T-linked-β-D-xylan, (1→4)-linked-β-D-xylan, (1→2,3,4)-linked-β-D-xylan, (1→3)-linked-α-arabinose and T-linked-α-arabinose.	Promoting fat metabolism	Flaxseed polysaccharides promoted lipid metabolism by inducing the elimination of leptin resistance and through the AMP-activated protein kinase (AMPK) signalling pathway.	Anti-obesity supplements	[24]

	FP-2	1182	Rha:Ara:Fuc:Xyl:Man:Glc:Gal:GalA=11.27%:4.03%:2.82%:7.12%:2.99%:4.41%:11.61%:55.75%	The main glycosidic bonds of FP-2 are (1→4)-linked-α-D-Gal, (1→2,4)-linked-α-D-Gal, (1→2)-linked-L-Rhap, with T-linked-D-Glu residues.				
Lycium barbarum L.	LICP009-2-1	13.5	Ara:Gal:Glc:GalA:GlcA= 40.2:31.5:4.2:5.8:5.7	LICP009-2-1 was consisted of a repeated unit of →3,6)-β-D-Galp-(1→ residues, with three branches composed of α-L-Araf-(1→, α-L-Araf-(1 → 5)-α-L-Araf-(1 → 5)-α-L-Araf-(1 → 3)-β-D-Galp-(1→, and α-L-Araf-(1 → 2)-α-L-Araf-(1→[4)-β-D-Galp-(1]3 → .	Promoting fat metabolism	LICP009-2-1 downregulated the expression of key transcription factors and proteins in the adipogenesis pathway.	Anti-obesity supplements	[25]
Bangia fusco-purpurea	BFP	133	D-Gal	The BFP was mainly composed of 1,3-linked-β-D-galactose that is partially sulfated at position O-6, followed by 1,4-linked-α-D-galactose and low level of 1,4-linked-α-L-3,6-anhydro-galactose.	Promoting fat metabolism	BFP activated the AMP-activated protein kinase and acetyl coenzyme A carboxylase signalling pathways and inhibited peroxisome proliferator-activated receptor gamma expression.	Nutritional supplements against obesity	[26]
Pearsonothuria graeffei	fuc-Pg	310	Fuc	Fuc-Pg had a highly repeating tetrasaccharide unit as [3Fuc (2S, 4S) α1 → 3Fucα1 →3Fuc (4S) α1 → 3Fucα1]$_n$.	Promoting fat metabolism	Fuc-Pg down-regulated the TLR4/NF-κB pathway.	Anti-obesity supplements	[27]
Inonotus hispidus (Bull.: Fr.) P. Karst	IHP3	22.0	**Gal:Man:Fuc:Me-Gal=51.8%:18.8%:11.2%:10.2%**	Its backbone was predominantly composed of →6)-α-D-Galp-(1→, →2,6)-α-D-Galp-(1→,→6)-α-D-O-Me-Galp-(1→ , →3)-α-D-Manp-(1→, and →3,4,6)-β-D-Galp-(1→ residues, branched at C2 of partial α-D-Galp, or C3 and C4 of β-D-Galp, and terminated by α-D-Manp, and α-L-Fucp.	Promoting fat metabolism	These suppressed the interleukin (IL)-17-mediated inflammatory response in obese mice.	Anti-obesity supplements	[28]
Grifola frondosa	GFPA	5570.17	Glc:Gal:Fuc=99.73:0.17:0.10	GFPA mainly consisted of →4)-aD-Glcp-(1→, β-D-Glcp-(1→ and →4,6)-β-D-Glcp-(1→.	Probiotic properties	GFPA exhibited strong anti-obesity effects via the modulation of chronic inflammation through Toll-like receptor 4/nuclear factor kappa-B signaling.	Slimming prebiotics	[29]
Ganoderma lucidum	BSGLP	26.0	Glc:Man:Gal=87.4:4.81:8.14	BSGLP was a β-D-glucan containing (1→3)-β-D-Glcp, (1→3,6)-β-D-Glcp, (1→6)-β-D-Glcp, and terminal-β-D-Glcp moieties.	Probiotic properties	BSGLP notably alleviated HFD-induced upregulation of TLR4/Myd88/NF-κB signaling pathway in adipose tissue.	Anti-obesity supplements	[30]
Lyophyllum decastes	LDP1-1	502	Man:Glc:Gal:Fuc=1:2.38:2.58:0.73	LDP1-1 appeared mainly as slices. LDP1-2 showed irregular fragments, with some of them intertwined with filamentous structures. The arrangement of LDP1-1 and LDP1-2 was loose,	Probiotic properties	LDP1 altered gut microbiota that showed enrichments of *B. intestinalis* and *L. johnsonii* and an increase in secondary bile acids.	Anti-obesity supplements	[31]
	LDP1-2	1130	Man:Glc:Gal:Fuc=1:2.33:2.51:0.78					

				indicating weak interactions among LDP1-1 and LDP1-2.				
Chachiensis	PCRCP	122.0	D-GalA, Ara, Gal	PCRCP may link 1,4-linked Gal(p)-UA, 1,4-linked Ara(f) and 1,4-linked Gal(p).	Probiotic properties	PCRCP significantly reduced the relative abundances of obesity-promoting bacteria, and selectively stimulated the growth of specific bacteria, especially *Lactobacillus johnsonii*.	Slimming prebiotics	[32]
Eurotium cristatum	PEC	32.305	Man, Gal, Glc	The main chain of PEC was →5)-β-D-Galf-(1 → 6)-α-D-Manp-(1 → glycosidic bond, and the branched chain →2)-α-D-Manp-(1 → through →2,6)-α-D-Manp-(1 → was connected to the main chain by an O-2 bond.	Probiotic properties	PEC decreased F/B ratio, *Clostridium leptum* and *Mucispirillum shaedleri* abundances, and increased *Parabacteroides goldsteinii*, *Parabacteroides distasonis*, *Faecalibaculum rodentium*, *Blautia producta*, *Bacteroides thetaiotaomicron*, and *Bacteroides uniformis* abundances.	Anti-obesity supplements	[33]
Strawberry juice	PFY06-EPS	8.08×10^3	Glc	Composed of α-(1,6)-D glucosyl residues.	Probiotic properties	PFY06-EPS reduced the *F*/*B* ratio and increased butyrate-producing bacteria (*Roseburia* and *Oscillibacter*).	Slimming prebiotics	[34]
Stichopus japonicus	SCSP	670	GlcA:Fuc:Gal=0.77 :9.11:1.00	SCSP had been reported as →4)-GlcA(1→3)-GalNAc(1→ with 2,4-di-O-sulfated and 3,4-di-O-sulfated fucose and →1)-Fuc(2S)(1→3)-Fuc(1→4)-Fuc(1→4)-Fuc(1 →3)-Fuc(2S)(3→.	Probiotic properties	SCSP could prevent diet-induced obesity and its associated diseases by modulating the gut microbiota, improving microbial metabolites, and enhancing gut tissue integrity.	Slimming prebiotics	[35]
Patinopecten yessoensis	SPYP	13.58	Man, GlcN, GlcA, GalN, Glc, and Fuc	SPYP was determined as heparin-like → 4)β-GlcA(1 → 4)α-GlcNAc → and chondroitin sulfate-like → 4)β-GlcA(1 → 3)β-GalNAc →.	Probiotic properties	SPYP exhibited anti-obesity effects by modulating gut microbiota, restoring short-chain fatty acids, and altering lipid/amino acid metabolism.	Slimming prebiotics	[36]
Saccharina japonica	J2H	5.1	Fuc	It was concluded that the primary structure of J2H is composed of 1,3-linked α-L-Fucp residues sulfated at C2, C4 or C2/C4.	Probiotic properties	J2H enriched *Bacteroides sartorii* and *Bacteroides acidifaciens*.	Slimming prebiotics	[37]

2.1 Promoting heat consumption

In recent years, natural polysaccharides have garnered significant attention in anti-obesity research due to their unique bioactivities and metabolic regulatory functions [38-40]. Numerous studies have demonstrated that polysaccharides derived from various plants and traditional Chinese medicines can effectively alleviate obesity and related metabolic disorders through multiple pathways, including promoting energy expenditure, improving glucose/lipid metabolism, and enhancing insulin sensitivity. The purified fraction MCPS-3, obtained from optimized extraction of *Momordica charantia* L. polysaccharides (MCP), exhibited remarkable α-amylase and α-glucosidase inhibitory activities. In insulin-resistant HepG2 cells, MCPS-3 significantly increased glucose consumption, enhanced glycogen synthesis, and activated key glycolytic enzymes (hexokinase and pyruvate kinase), thereby promoting energy metabolism and reducing lipid accumulation. These findings suggested that MCPS-3 may mitigate obesity risk by regulating critical enzymes in glucose metabolism to improve cellular energy utilization [19]. Similarly, polysaccharides LSP, OJP, and LMP isolated from *Ophiopogon japonicus* have been shown to significantly improve glucose uptake in insulin-resistant HepG2 cells. These polysaccharides enhanced insulin sensitivity by upregulating the PI3K/AKT/PPARγ signaling pathway while suppressing protein tyrosine phosphatase 1B (PTP1B) expression, thereby promoting glucose utilization and energy expenditure [20]. *Adenophora tetraphylla* (Thunb.) Fisch. polysaccharide (ARP) demonstrated potent glucose-consumption promoting activity under optimized extraction conditions, increasing glucose utilization by 75.86% in HepG2 cells without cytotoxicity, suggesting its potential to reduce hepatic lipid deposition through enhanced energy metabolism [41]. Studies on *Pseudostellaria heterophylla* polysaccharide (H-1-2) further elucidated how polysaccharides enhance energy expenditure by promoting glucose uptake in muscle and adipose cells. Structural analysis revealed H-1-2 was a glucose homopolymer with an α-1,4-glucan backbone and minor 1,6-branching. In vitro experiments demonstrated its ability to significantly increase glucose uptake in both 3T3-L1 adipocytes and L6 myocytes, indicating its potential to reduce fat accumulation by improving peripheral tissue energy utilization. Radioisotope tracing suggested H-1-2 might exert systemic effects after intestinal absorption, though its precise metabolic fate required further investigation [21]. Research on *Schisandra* polysaccharide (SCPP11) highlighted its regulation of the AMPK signaling pathway. In insulin-resistant hepatocytes, SCPP11 significantly upregulated GLUT-4 expression while activating both AMPK and PI3K/Akt pathways, thereby enhancing glucose uptake and oxidation. This dual mechanism not only improved cellular energy utilization but might also have reduced lipid accumulation through promoted fatty acid oxidation [22]. Furthermore, studies on *Camellia oleifera* Abel. seed cake polysaccharide (CCP) suggested that acidic structural features (e.g., glucuronic acid and galactosamine content) might critically have contributed to its glucose-lowering activity. Remarkably, CCP demonstrated superior hypoglycemic effects to metformin in HepG2 cells, underscoring the therapeutic potential of natural polysaccharides in metabolic regulation [42].

In summary, natural polysaccharides have been demonstrated to promote calorie consumption through a variety of mechanisms, including (1) the inhibition of carbohydrate digestive enzymes (e.g., α-amylase,

α-glucosidase) to reduce glucose uptake; (2) activation of insulin signalling pathways (PI3K/AKT/PPARγ) to enhance glucose uptake; (3) up-regulation of GLUT-4 and AMPK pathways to promote muscle and adipose tissue energy utilisation; (4) optimisation of hepatic glycogen synthesis and oxidative metabolism to reduce lipid accumulation.

2.2 Inhibiting fat accumulation

Obesity and its associated metabolic disorders have emerged as a global health challenge, creating an urgent need for safe and effective intervention strategies. In recent years, natural polysaccharides have attracted significant attention due to their remarkable anti-obesity potential, with primary mechanisms involving inhibition of adipogenesis, modulation of gut microbiota, and improvement of energy metabolism. Multiple studies have demonstrated that polysaccharides from various sources can reduce lipid accumulation and ameliorate metabolic disorders through multi-target interventions in the adipogenesis process.

The anti-obesity effects of flaxseed polysaccharide (FP) were closely associated with its gut microbiota metabolites. Studies found that bioactive metabolites produced through gut microbial fermentation of FP significantly inhibited the expression of glucose transporters SGLT1 and GLUT2 in intestinal epithelial cells (Caco-2), thereby reducing glucose uptake and decreasing energy intake. Furthermore, these metabolites suppressed 3T3-L1 preadipocyte differentiation by downregulating key adipogenic transcription factors—peroxisome proliferator-activated receptor γ (PPARγ) and CCAAT/enhancer-binding proteins (C/EBPα, C/EBPβ)—leading to reduced lipid droplet accumulation [43]. This dual inhibitory effect exhibited concentration dependence, with optimal efficacy observed at physiological concentrations, suggesting FP might exert anti-obesity effects through modulation of the gut microbiota-host metabolic axis.

Non-starch polysaccharides (NSPs), such as oat β-glucan and soybean pectin, were shown to inhibit fat accumulation by modulating SCFA production. Research demonstrated that soybean pectin had higher fermentation efficiency than cereal arabinoxylan in rat cecum and significantly increased cecal SCFA concentrations (particularly butyrate). Butyrate levels were negatively correlated with retroperitoneal adipose tissue weight, indicating its potential to reduce obesity risk through either adipogenesis inhibition or lipolysis promotion [44]. Additionally, oat β-glucan was confirmed to regulate energy metabolism through similar mechanisms, suggesting NSP-rich diets might serve as an effective strategy for obesity control.

The structural characteristics of *Lycium barbarum* L. polysaccharide (LICP009-2-1) were strongly correlated with its anti-adipogenic activity. Composed primarily of arabinose, galactose, and glucuronic acid, this polysaccharide possessed unique branched-chain structures. In 3T3-L1 adipocytes, LICP009-2-1 dose-dependently reduced lipid accumulation and downregulated adipogenesis-related gene expression. In high-fat diet-induced obese mice, oral administration of LICP009-2-1 significantly decreased body weight, adipose tissue mass, and serum lipid levels, demonstrating its potent anti-obesity effects both in vitro and in vivo. These findings suggested its potential application as a functional food ingredient or pharmaceutical adjuvant [25].

The lipid-lowering effects of bitter melon polysaccharide (BPS) were associated with its regulation of glucose metabolism and fatty acid desaturase pathways. Both water-soluble (WBPS) and alkali-soluble (ABPS) bitter melon polysaccharides inhibited fat accumulation, though ABPS exhibited more pronounced effects. The mechanism involved enhanced glucose uptake (via GLUT4) and gluconeogenesis (via PEPCK), coupled with modulation of fat-5-, fat-6-, and fat-7-mediated fatty acid desaturation processes, ultimately reducing triglyceride deposition. Furthermore, in Caenorhabditis elegans models, ABPS demonstrated stronger anti-lipid accumulation activity without significant toxicity, further supporting its potential as a safe anti-obesity agent [45].

Seaweed-derived fucoidan (ECC and ECF3) exerted anti-obesity effects through dual mechanisms. In vitro experiments revealed that ECC and its purified sulfate-rich fraction ECF3 significantly reduced lipid accumulation in 3T3-L1 cells. In obese mice, oral ECC administration decreased body weight, serum lipid levels, white adipose tissue mass, and hepatic fat deposition. Mechanistic studies demonstrated that ECC not only inhibited lipid storage in white adipose tissue but also promoted energy expenditure by upregulating thermogenic proteins UCP1 and UCP3 in brown adipose tissue (BAT), thereby ameliorating obesity-related metabolic abnormalities [26].

Additionally, IHP3 attenuated obesity in HFD-fed mice by reducing adiposity, glucose dysregulation, and hepatic steatosis. Mechanistically, it modulated gut-liver-adipose crosstalk through fecal metabolome remodeling, PPARγ signaling inhibition, and enhanced thermogenesis (UCP1-mediated browning), ultimately suppressing IL-17-driven inflammatory cascades [28] (Fig. 1). *Bangia fusco-purpurea* polysaccharide (BFP) showed superior anti-obesity efficacy compared to common prebiotic inulin (INU). Its mechanisms involved gut microbiota modulation (e.g., increased *Clostridium* and *Aerococcus* abundance) and metabolite regulation (e.g., biotin and G6P). BFP also activated the AMPK/ACC signaling pathway to promote fatty acid oxidation while suppressing PPARγ-mediated adipogenesis, demonstrating significant anti-obesity effects in both cellular and animal models [46].

In summary, it is evident that natural polysaccharides can inhibit adipogenesis through various mechanisms, including (1) modulation of intestinal flora and their metabolites (e.g., SCFA); (2) inhibition of key transcription factors for adipocyte differentiation (PPARγ, C/EBPα/β); (3) promotion of fatty acid oxidation (AMPK/ACC pathway); (4) enhancement of thermogenesis (UCP1/UCP3); and (5) improvement of glucose metabolism (GLUT4/PEPCK).

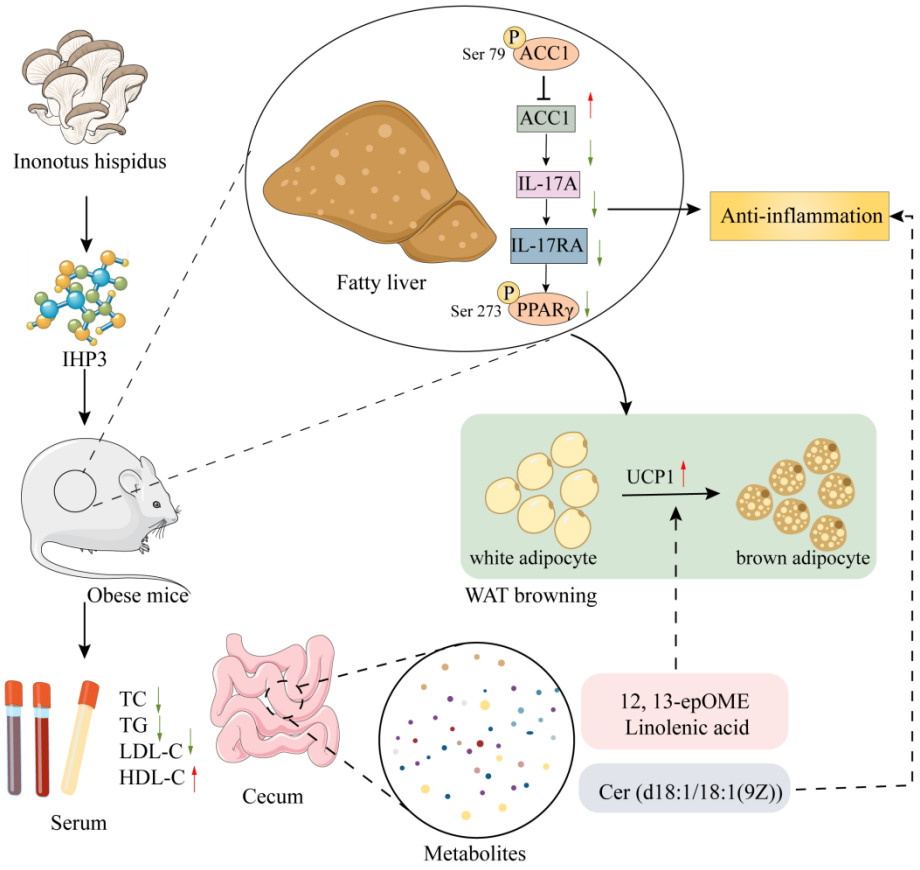

Fig. 1. IHP3, a heteropolysaccharide from *Inonotus hispidus*, counteracted high-fat diet-induced obesity in mice by suppressing PPARγ phosphorylation, promoting adipose tissue browning, modulating gut microbiota, and inhibiting IL-17-mediated inflammation, demonstrating its significant potential as an anti-obesity therapeutic.

2.3 Promoting fat metabolism

Natural polysaccharides have been demonstrated to possess distinctive advantages and potential in the treatment of lipid metabolism disorders and the management of obesity through the establishment of multi-target and multi-level regulatory networks. Recent studies have demonstrated that natural polysaccharides from diverse sources, despite exhibiting distinct structural characteristics, can play a significant role in the treatment of obesity through the systematic regulatory network of the 'intestinal flora-metabolite-signalling pathway'. The *Bangia fusco-purpurea* polysaccharide (UBFP) prepared by ultra-high pressure-assisted extraction technology demonstrated significantly enhanced bioactivity through structural optimization, exhibiting superior lipid-lowering effects compared to native BFP. The mechanisms of UBFP included: specifically promoting the proliferation of SCFA-producing bacteria such as *Allprevotella* and *Akkermansia* to improve gut microecological balance; regulating key metabolites in the tryptophan metabolic pathway; and simultaneously activating the AMPK/ACC signaling pathway to promote fatty acid β-oxidation while inhibiting the PPARγ-mediated adipogenesis process. This multi-target synergistic effect established UBFP as a highly promising anti-obesity agent [47]. Sea cucumber sulfated polysaccharide (SCSP) significantly altered the lipid metabolic profile by reducing saturated fatty acid levels (e.g., palmitic acid) in blood and urine while increasing the excretion of unsaturated fatty acids (e.g., linoleic acid) in feces. This

selective regulatory effect was closely associated with promoting the proliferation of specific gut microbiota including *Muribaculaceae* and *Clostridia_UCG-014* [48]. *Ophiopogon japonicus* polysaccharide (MDG-1) enhanced mitochondrial function, increasing oxygen consumption by 50% and significantly elevating energy expenditure. Concurrently, it regulated the expression of hepatic lipid metabolism-related genes, achieving weight loss effects without affecting appetite [23].

The acetylated *Stropharia rugoso-annulata* polysaccharide (ASRP) demonstrated excellent efficacy in ameliorating NAFLD through dual activation of both the AMPK/SREBP-1c signaling pathway and Nrf2 antioxidant pathway (**Fig. 2**). At a dose of 400 mg/kg, ASRP significantly improved hepatocyte steatosis and inflammatory responses [49]. Particularly noteworthy was the remarkable synergistic effect observed when soluble soybean polysaccharide (SSPS) was combined with genistein. This combination therapy dually activated PPAR-α/PPAR-γ nuclear receptors and the AMPK energy metabolism pathway while optimizing gut microbiota composition (reducing the *Firmicutes*/*Bacteroidetes* ratio). The formulation showed significantly superior effects compared to individual components in inhibiting adipogenesis, alleviating inflammation, and reducing oxidative stress, providing novel insights for developing composite anti-obesity formulations [50]. Black tea polysaccharides comprehensively improved obesity-related metabolic disorders by regulating a network of metabolic pathways, including upregulation of 8 pathways (e.g., glycerolipid metabolism) and downregulation of 5 pathways (e.g., fatty acid degradation) [51]. Microalgal polysaccharides (CPS and SPS) not only ameliorated obesity symptoms as effectively as β-glucan but also specifically increased beneficial bacteria like *Clostridium* and regulated the expression of key lipid metabolism proteins including CPT-1 and PPARγ [52]. The study on flaxseed polysaccharide (FP) first elucidated the complete mechanism of polysaccharide-mediated anti-obesity effects through the gut-brain axis: by suppressing NPY and upregulating GLP-1 expression to improve leptin resistance, subsequently activating the AMPK signaling pathway to promote lipolysis and fatty acid oxidation, ultimately achieving significant reductions in body weight and fat content (decreasing high-fat diet-induced obese rat weights from (530 ± 16) g to (478 ± 10) g, and abdominal fat content from 2.15% to 1.38%) [24]. Collectively, these studies established a systematic theoretical framework for understanding the anti-obesity effects of natural polysaccharides. Although different polysaccharides exhibited distinct primary mechanisms, they all achieved precise intervention in lipid metabolism networks through three interrelated aspects: modulating gut microbiota structure, optimizing metabolite profiles, and regulating key signaling pathways.

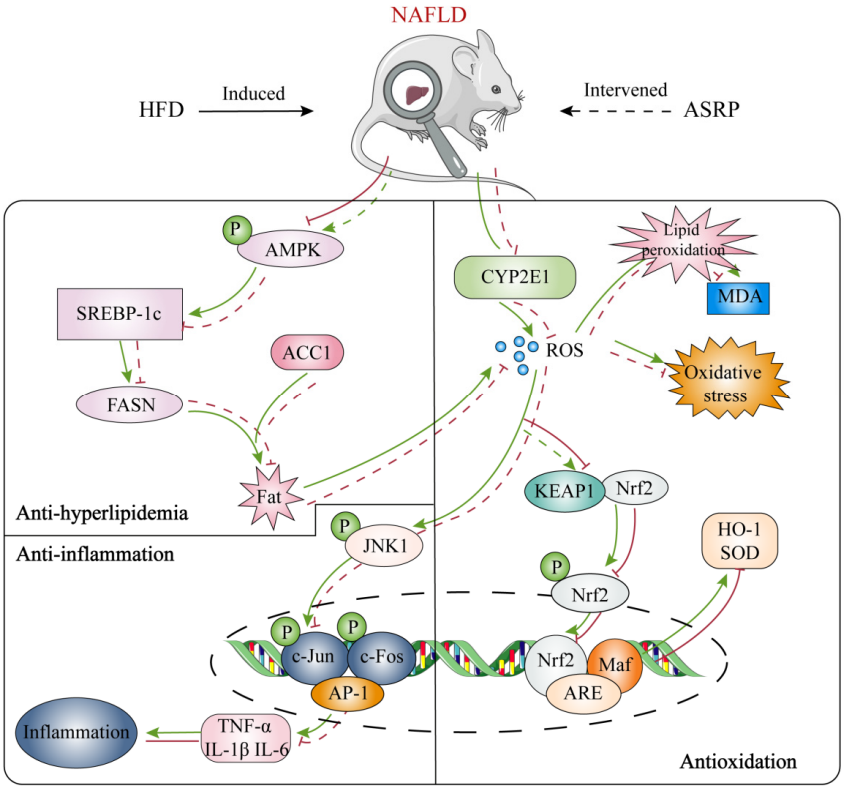

Fig. 2. ASRP attenuated NAFLD by simultaneously modulating AMPK/SREBP-1c and Nrf2 pathways. (Green arrows represented promotion, and red arrows represented inhibition. The solid lines represented the pathogenesis of HFD-induced NAFLD, and the dotted lines represented the intervention mechanism of ASRP.)

2.4 Probiotic properties

In recent years, natural polysaccharides, as bioactive substances with prebiotic properties, have demonstrated considerable potential in the field of obesity prevention and treatment. A substantial body of research has demonstrated that natural polysaccharides from diverse sources can efficaciously enhance obesity and associated metabolic disorders through multiple mechanisms, including specific regulation of gut microbiota structure, optimisation of metabolite profiles, and activation of host metabolic pathways. These findings contribute to a more profound understanding of the intricate relationship between gut microbiota and host metabolism, thereby providing a robust theoretical foundation for the development of novel anti-obesity strategies.

Polysaccharides derived from various medicinal fungi demonstrated significant gut microbiota-modulating effects. *Cordyceps militaris* polysaccharide (CMP) significantly increased the abundance of beneficial bacteria such as Alloprevotella and Parabacteroides while reducing populations of negative bacilli, thereby improving intestinal barrier function and glucose metabolism [53]. More remarkably, the high-molecular-weight polysaccharide from *Cordyceps sinensis* (H1>300 kDa) achieved a 50% reduction in body weight of high-fat diet (HFD)-induced obese mice by selectively promoting the growth of *Parabacteroides goldsteinii*. Fecal microbiota transplantation (FMT) experiments confirmed that H1's anti-obesity effects were entirely dependent on its modulated gut microbiota, and direct supplementation with live P. goldsteinii could replicate H1's metabolic improvements. These findings provided crucial evidence for

developing "prebiotic-probiotic" combination therapies [54]. In addition, BSGLP from *Ganoderma lucidum* alleviated HFD-induced obesity by restoring gut microbiota balance, enhancing SCFA production and GPR43 signaling, strengthening intestinal barrier function, and suppressing the TLR4/Myd88/NF-κB pathway in adipose tissue, with FMT confirming microbiota-mediated effects [30] (**Fig. 3**).

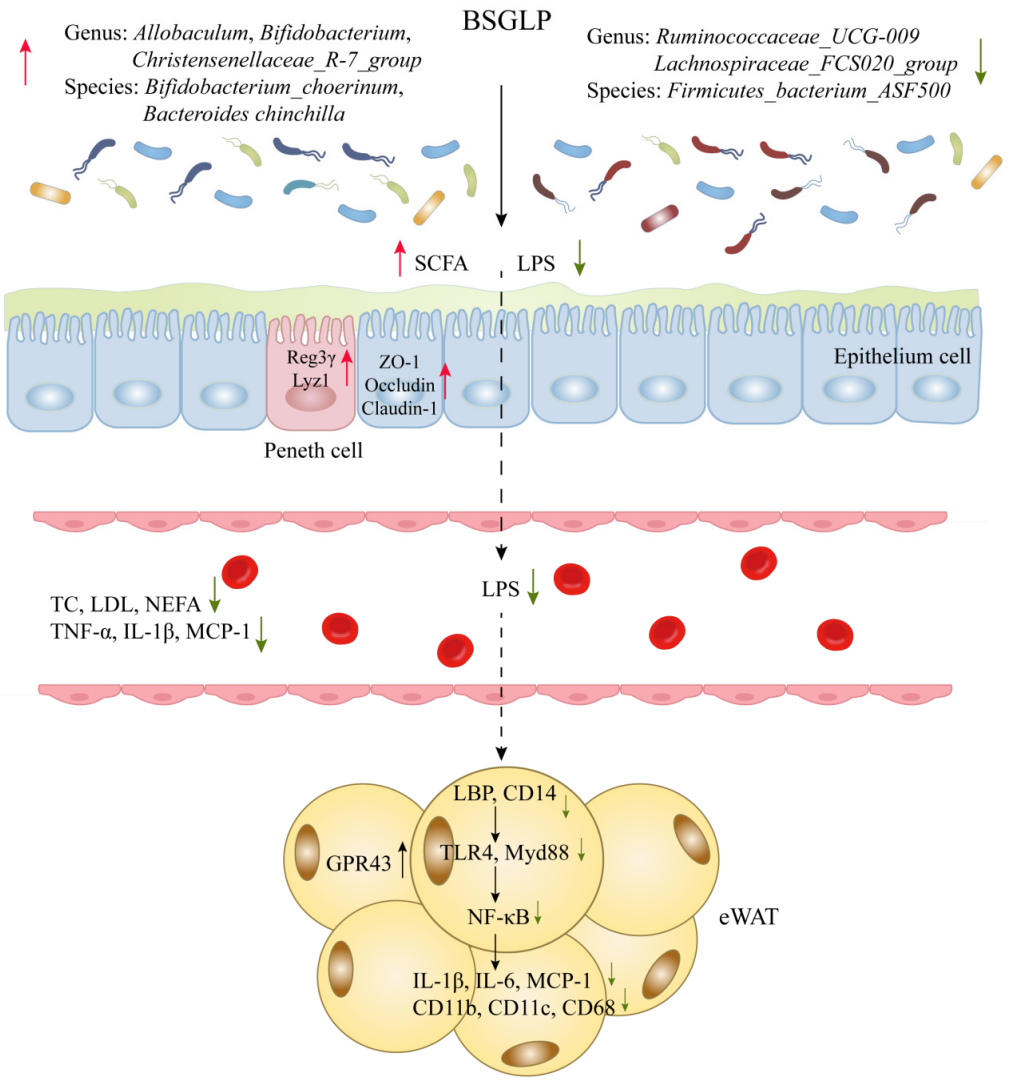

Fig. 3. BSGLP attenuated HFD-induced obesity by rebalancing gut microbiota, elevating SCFA production, activating GPR43-dependent pathways and enhancing intestinal barrier integrity, and suppressing adipose tissue inflammation through TLR4/Myd88/NF-κB inhibition, with FMT validation of microbiota-dependent effects.

Systematic comparative studies revealed differential regulation of gut microbiota by various polysaccharides. Dietary fibers including β-glucan, arabinoxylan, and apple pectin significantly increased the abundance of beneficial bacteria like *Akkermansia* and *Oscillospira* while improving 15-18 obesity-related biomarkers. Notably, the abundance of *Butyricimonas* and *Prevotella* showed significant negative correlations with lipid parameters (TC, TG, LDL-C) but positive correlations with beneficial metabolites like phosphatidylcholine, suggesting these specific microbiota might play key roles in lipid metabolism regulation [55].

SCFAs, as primary end-products of microbial polysaccharide fermentation, played central roles in polysaccharides' anti-obesity mechanisms. Fermented garlic polysaccharide (BGP) significantly elevated

acetate and butyrate levels by increasing SCFA-producing bacteria like Lachnospiraceae_UCG_006, consequently reducing serum triglycerides and free fatty acids in obese mice [56]. Flaxseed polysaccharide (FSP) specifically restored propionate and butyrate levels. These SCFAs not only provided energy for intestinal epithelial cells but also regulated systemic energy metabolism through GPR41/43 activation [57]. The polysaccharide derived from *Agrocybe cylindracea* (ACP) exerted its anti-obesity effects by modulating the gut microbiota (reducing pro-inflammatory *Desulfovibrio* while increasing anti-inflammatory *Parabacteroides* abundance) and associated metabolites (e.g., decreasing solavetivone levels) in high-fat diet-induced obese mice. ACP significantly enriched SCFA-producing bacteria (such as *Butyricimonas* and *Dubosiella*), thereby suppressing the expression of pro-inflammatory factors (TNF-α and IL-6), improving gut barrier function, and ultimately alleviating obesity-associated weight gain, fat accumulation, insulin resistance, and hepatic damage. These findings demonstrated that ACP operates through the "gut microbiota-SCFA-inflammatory regulation" axis [58], confirming that polysaccharides exert multi-target regulatory effects via the "microbiota-metabolite" axis.

Natural polysaccharides also directly or indirectly activated various host metabolic pathways. The exopolysaccharide from *Weissella cibaria* PFY06 (PFY06-EPS) reduced the *Firmicutes*/*Bacteroidetes* ratio while increasing butyrate-producers like *Roseburia* and *Oscillospira*, thereby improving gut barrier function, promoting gastrointestinal hormone secretion, and suppressing inflammatory factors [34] (**Fig. 4**). The polysaccharide from *Flammulina velutipes* (FVP) ameliorated metabolic syndrome symptoms including obesity, hyperlipidemia and insulin resistance by modulating gut microbiota composition (enriching SCFA-producing bacteria) and activating the AMPKα1/PPARα signaling pathway, thereby significantly elevating SCFA levels. Fecal microbiota transplantation (FMT) experiments further confirmed that these beneficial effects of FVP were mediated through the "gut microbiota-SCFA-metabolic regulation" axis, wherein SCFAs promoted lipid metabolism by activating the AMPKα1/PPARα pathway, ultimately exerting anti-metabolic syndrome effects [59]. Oyster polysaccharide (OPS) modulated the gut microbiota structure in high-fat diet-induced obese mice by enriching beneficial bacteria (such as *Bifidobacterium*, *Lactobacillus*, *Dobosiella*, and *Faecalibaculum*) and reducing harmful bacteria (such as *Erysipelatoclostridium*, *Helicobacter*, and *Mucispirillum*). This significantly promoted the production of SCFAs, which subsequently activated the p-AMPKα signaling pathway and downregulated the expression of SREBP-1c, PPARγ, and p-ACC-1. As a result, OPS improved lipid metabolism in adipose tissue and the liver, ultimately alleviating obesity-related symptoms, including weight gain, dyslipidemia, and metabolic endotoxemia [60]. *Morchella esculenta* polysaccharide (MPF) modulated the gut microbiota structure in high-fat diet-induced obese mice by restoring the *Firmicutes*/*Bacteroidetes* ratio and altering the abundances of *Lactobacillus*, *Dubosiella*, and *Faecalibaculum*. This significantly increased the production of SCFAs and downregulated the expression of hepatic glucose metabolism-related genes (Glucose-6-phosphatase, glucose transporter 1) and lipogenesis-related genes (PPARγ, CCAAT/enhancer-binding protein α). Concurrently, MPF upregulated the expression of fatty acid oxidation-related genes (PPARα, PPAR coactivator-1α), thereby reducing fat

accumulation, obesity, and liver injury. These findings revealed the molecular mechanism by which MPF exerted its anti-obesity effects via the 'gut microbiota–SCFA–liver metabolism' axis [61].

The extant research has collectively erected a multi-level theoretical framework for the anti-obesity effect of natural polysaccharides. At the microbial level, it has been demonstrated that there is a promotion of functional bacteria such as *Akkermansia* and *Bifidobacterium*, alongside an inhibition of harmful bacteria such as *Desulfovibrio*. At the metabolite level, an increase in beneficial metabolites such as SCFA and glycerophospholipids has been observed. At the host level, metabolic disorders have been shown to be improved through multiple signalling pathways. These findings provide important insights for the development of targeted anti-obesity agents. As our understanding of the "microbiota metabolism host" interaction network continues to deepen, natural polysaccharides are poised to emerge as a novel intervention modality for the prevention and treatment of obesity and associated metabolic diseases. The integration of multi-omics technologies, artificial intelligence-assisted design, and precise nutrition strategies is set to elevate polysaccharide-based prebiotic therapy to a pivotal role in the future of personalised health management.

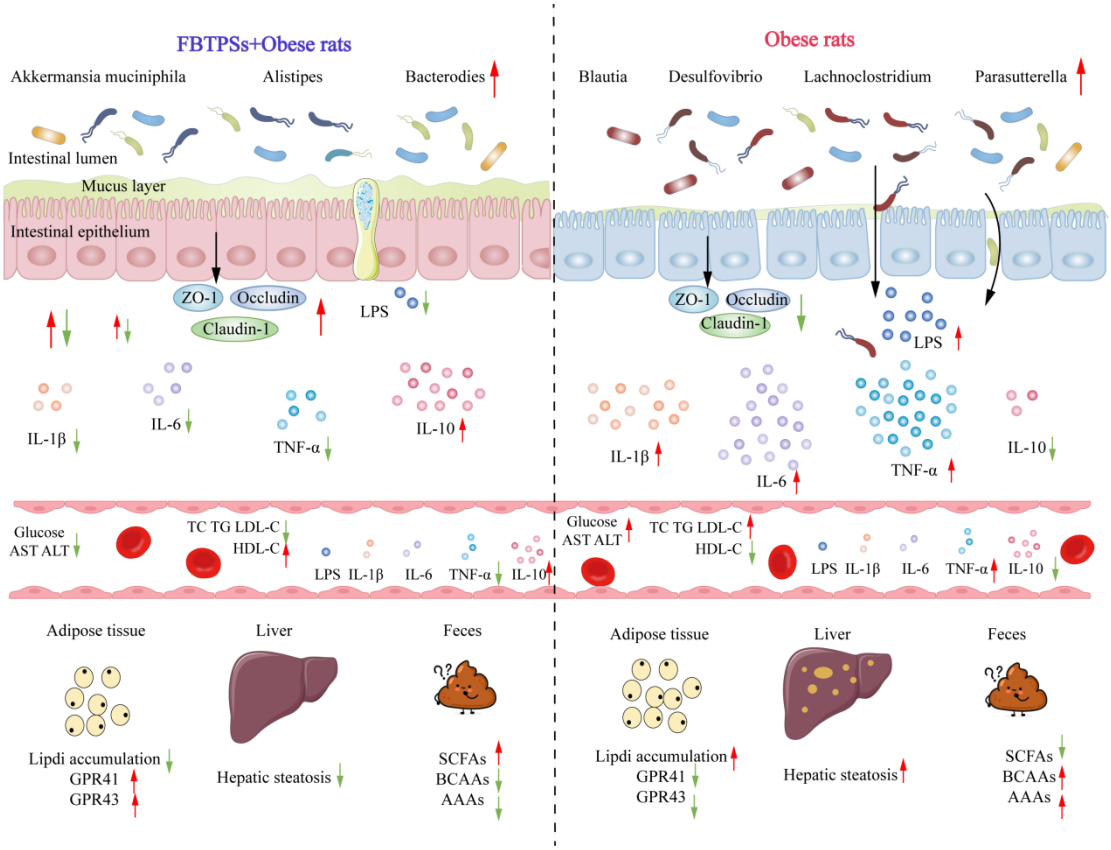

Fig. 4. PFY06-EPS exerted anti-obesity effects by modulating gut microbiota (↓F/B ratio, ↑butyrate-producers), enhancing gut barrier integrity, and improving metabolic inflammation in HFD-fed mice.

3. The structure-activity relationship between the chemical structure of natural polysaccharides and their anti-obesity activity

Natural polysaccharides, as an important class of bioactive macromolecules, have shown broad application prospects in anti obesity research due to their structural diversity and good biocompatibility.

Research has shown that the anti obesity activity of polysaccharides is closely related to their chemical structure, including key factors such as molecular weight (Mw), monosaccharide composition, glycosidic bond type, and branching degree. In depth analysis of the structure-activity relationship between these structural features and anti obesity effects not only helps to elucidate the mechanism of action of polysaccharides, but also provides theoretical basis for the development of efficient and safe anti obesity functional components.

3.1 Molecular weight

The anti-obesity effects of natural polysaccharides are closely associated with their Mw, with polysaccharides from different Mw ranges exhibiting distinct metabolic regulatory functions through unique structural characteristics and bioactive mechanisms. Low-molecular-weight polysaccharides (<10 kDa), owing to their excellent solubility and bioavailability, primarily serve as high-efficiency prebiotics that are rapidly fermented by gut microbiota to promote SCFA production and optimize microbial composition. Medium-molecular-weight polysaccharides (10-500 kDa) combine fermentability with physical barrier functions, enabling simultaneous regulation of lipid metabolism gene expression and moderate delay of nutrient absorption. In contrast, high-molecular-weight polysaccharides (> 500 kDa) rely on their high viscosity and gel-forming capacity to exert anti-obesity effects through physical mechanisms including lipase inhibition, gastric emptying delay, and lipid adsorption/excretion. This molecular-weight-dependent structure-activity relationship not only provides a theoretical foundation for the precise design of polysaccharide-based functional foods but also suggests that rational combinations of polysaccharides with different Mw ranges may yield synergistic effects, opening new avenues for intervention strategies against obesity and related metabolic disorders.

3.1.1 Low molecular weight

Low-molecular-weight polysaccharides (< 10 kDa) demonstrate significant advantages in anti-obesity intervention strategies due to their unique structural characteristics. These oligosaccharide substances possess smaller molecular dimensions and more free hydroxyl groups, endowing them with excellent solubility and high bioavailability. Such structural properties enable their rapid passage through the intestinal epithelial barrier and efficient fermentation by gut microbiota [62]. Studies have shown that Mw is one of the key determinants of polysaccharide physiological functions, with low-molecular-weight polysaccharides exhibiting distinct advantages in modulating gut microbiota balance and improving metabolic disorders.

From a structure-function relationship perspective, the prebiotic properties of low-molecular-weight polysaccharides are particularly prominent. Taking lactulose and its derivatives as examples, research has found that lactulose oligosaccharides such as 3-O-β-D-galactopyranosyl-D-fructose demonstrate stronger activity in promoting Lactobacillus acidophilus proliferation compared to ordinary lactulose. This difference primarily stems from the easier recognition and utilization of low-molecular-weight oligosaccharides by specific bacterial strains [63]. Similarly, studies on blackberry polysaccharides (BBPs) revealed that while

BBPs of different Mw could all modulate gut microbiota, the low-molecular-weight components were more readily utilized by bacteria, exhibiting higher fermentation efficiency [64]. This efficient fermentation capacity is closely related to their molecular structure: the smaller molecular size increases contact area with microbial enzymes, while the abundant free hydroxyl groups provide more enzymatic action sites.

In terms of metabolic regulation, low-molecular-weight polysaccharides demonstrate multiple beneficial effects. First, they significantly promote the production of SCFAs, particularly butyrate. Studies have found that guar gum with a Mw of 10-15 kDa yields the highest proportion of butyrate during fermentation [65]. As the primary energy source for colonic epithelial cells, butyrate not only maintains intestinal barrier function but also exerts anti-obesity effects by regulating the secretion of appetite-related hormones.

Second, low-molecular-weight polysaccharides such as 5.1 kDa fucoidan (J2H) can specifically enrich probiotic bacteria with polysaccharide-degrading potential (e.g., *Bacteroides sartorii* and *Bacteroides acidifaciens*). The proliferation of these strains helps improve gut microecological balance. Notably, J2H also effectively suppresses high-fat diet-induced obesity, glucose metabolism dysfunction, and dyslipidemia, suggesting that low-molecular-weight polysaccharides may exert systemic effects through the "microbiota-metabolism" axis [37].

3.1.2 Medium molecular weight

Medium Mw polysaccharides (10-500 kDa) exhibit unique structural advantages in anti obesity, with a mechanism of action that combines fermentation dependent and non fermentation dependent pathways. These polysaccharides have moderate molecular size and structural complexity, allowing them to be partially degraded by gut microbiota to produce SCFAs, while maintaining partial structural integrity to exert physical effects, forming a multi-level anti obesity effect. Multiple studies have confirmed that medium Mw polysaccharides often exhibit better effects than low Mw and high Mw polysaccharides in regulating metabolism and improving obesity related indicators.

From a structure-function relationship perspective, medium-molecular-weight polysaccharides exhibit unique advantages. Studies on *Dendrobium officinale* polysaccharide (DOP) revealed that the medium-molecular-weight fraction DOP5 demonstrated not only remarkable antioxidant properties that significantly extended the lifespan of Caenorhabditis elegans, but also improved lipid metabolism by regulating key lipid metabolism genes including fat-4 and fat-5 [66]. The study revealed that medium-molecular-weight konjac glucomannan (KGM-M, 757.1 kDa) more significantly reduced fasting blood glucose, improved insulin resistance, and alleviated inflammation in type 2 diabetic rats compared to the low-molecular-weight component (KGM-L, 87.3 kDa). These effects primarily depended on its superior capacity to: 1) modulate gut microbiota composition (e.g., increasing abundances of *Ruminococcus* and *Clostridium*); 2) enhance SCFA production; 3) upregulate G protein-coupled receptor (GPCR) expression; and 4) inhibit bile acid synthesis. Antibiotic treatment confirmed the gut microbiota-dependent nature of these effects, while fecal microbiota transplantation (FMT) experiments further demonstrated that KGM-M's

superior hypoglycemic activity was closely associated with its stronger regulatory effects on the gut microbiota-SCFA-GPCR-bile acid metabolic axis [67].

The anti-obesity mechanisms of medium-molecular-weight polysaccharides primarily operate through three distinct pathways: Firstly, they undergo moderate fermentation to produce SCFAs, which modulate the intestinal microenvironment and influence host metabolism. Secondly, their physical properties (e.g. viscosity enhancement) delay gastric emptying, promote satiety, and interfere with fat absorption. Thirdly, they have been demonstrated to directly regulate adipocyte differentiation, as evidenced by kefir grain-derived exopolysaccharides (EPS) that have been shown to inhibit adipogenesis in 3T3-L1 preadipocytes in a dose-dependent manner [68]. It is notable that these polysaccharides exhibit exceptional efficacy in maintaining intestinal barrier integrity, a property likely attributable to their partial resistance to digestive processes and ability to form protective gel layers in the colon. This dual functionality, combining partial fermentability with persistent macromolecular structure, enables simultaneous modulation of both microbial and physiological pathways, representing a unique advantage over other Mw fractions in obesity intervention strategies.

Current research suggests that the optimal bioactivity of medium-molecular-weight polysaccharides may exist within specific Mw ranges. For instance, both 1129.5-kDa KGM-H and 87.3-kDa KGM-L exhibited inferior metabolic improvement in comparison to 757.1-kDa KGM-MM1, suggesting that moderate Mw is imperative for achieving optimal efficacy [69]. The molecular-weight-dependent effect is hypothesised to originate from three key factors: (1) medium Mw maintains sufficient structural integrity for physical functions while retaining appropriate fermentability; (2) enhanced capacity for targeted interactions with specific gut microbiota; and (3) formation of ideal rheological properties in intestinal contents. Future studies should further elucidate the optimal Mw ranges for medium-molecular-weight polysaccharides from different sources and establish universal structure-activity relationships. Such investigations will provide a scientific foundation for developing precision nutrition intervention strategies. The identification of these optimal parameters will be particularly valuable for designing functional foods with maximised anti-obesity effects while minimising required dosages.

3.1.3 High molecular weight

High Mw polysaccharides with a Mw greater than 500 kD have been shown to possess unique structural characteristics that make them particularly well suited to anti-obesity interventions. These polysaccharides form a distinctive three-dimensional reticulated gel structure within the gastrointestinal tract, a property that arises from their substantial molecular size and notable spatial barrier effect. This physical property enables them to increase the viscosity of coeliacs by 5-10 times, thus generating multiple anti-obesity effects. The mechanism of action of these polysaccharides can be summarised as follows: firstly, they reduce postprandial glycaemic response by slowing down the gastric emptying rate by 30%-50%; secondly, they form a physical barrier in the intestinal tract, hindering the contact between lipase and the substrate, so as to significantly reduce the digestive and absorption rate of dietary fats; and thirdly, they promote the lipid discharge through the adsorption and excretion mechanism.

The study demonstrated that high-molecular-weight oat β-glucan (compared to its low-molecular-weight counterpart) significantly enhanced anti-obesity effects through its superior viscosity and fermentability. The underlying mechanisms involved: 1) modulating gut microbiota (reducing *Faecalibacterium* while increasing *Lactobacillus* and *Bifidobacterium*), thereby promoting 7-ketodeoxycholic acid (an FXR antagonist) production; 2) inhibiting the ileal FXR-FGF15 signaling pathway to stimulate alternative bile acid synthesis; and 3) upregulating CYP27A1 to increase chenodeoxycholic acid, which subsequently activated hepatic FXR and accelerated fat breakdown via the PPARα-CPT1A pathway. These findings revealed that oat β-glucan exerted its molecular-weight-dependent anti-obesity effects through the "gut microbiota-bile acid metabolism-hepatic lipolysis" axis [70]. These macromolecules induced gastric distension and prolonged intestinal lipid absorption time, while their hydrated network structures effectively blocked contact between lipases and chylomicrons, thereby inhibiting lipid digestion. More importantly, high-molecular-weight polysaccharides displayed exceptional adsorption capacity, binding to lipid components including bile acids, cholesterol, and triglycerides to promote their excretion. Similarly, *Ganoderma lucidum* polysaccharides (>300 kDa) [71] and *Auricularia auricula* polysaccharides [72] exhibited extraordinary bile salt-binding capacity that effectively inhibited bile salt reabsorption.

In metabolic regulation, high-molecular-weight polysaccharides demonstrated multi-target characteristics. The study revealed that the higher-molecular-weight component (KGM-1, 90 kDa) of konjac-derived β-glucan (KGM) significantly inhibited high-fat high-fructose diet-induced hepatic lipid accumulation in mice by downregulating hepatic Pparg gene expression and upregulating Hsl and Cpt1 gene expressions. Concurrently, it improved β-diversity through modulation of gut microbiota (increasing *Faecalibacterium*, *Streptococcus*, *Clostridium IV*, and *Parasutterella*). These mechanisms collectively enabled KGM-1 to demonstrate superior anti-obesity effects compared to lower-molecular-weight components (KGM-2, 5 kDa; KGM-3, 1 kDa), including more pronounced reductions in body weight and improvements in insulin resistance [73]. *Artemisia sphaerocephala* polysaccharide (551 kDa fraction 60P) further confirmed this pattern by effectively upregulating colonic barrier integrity genes while suppressing hepatic lipid metabolism genes and colonic inflammatory response genes [74]. These findings suggested high-molecular-weight polysaccharides functioned through dual "physical barrier-gene regulation" pathways.

It was noteworthy that high-molecular-weight polysaccharides exhibited unique patterns in modulating gut microbiota. Although these polysaccharides were difficult to absorb directly, their gel matrices created specialized microenvironments that selectively enriched beneficial bacteria (e.g., *Bifidobacterium* and *Olsenella*) while inhibiting harmful species (e.g., *Mucispirillum* and *Helicobacter*). Studies on CMP40 (Mw >100 kDa) demonstrated that these high-molecular-weight fractions restored intestinal health by increasing SCFA levels, modulating microbial community structure, and repairing tight junctions [75]. This "local action-systemic impact" characteristic enabled high-molecular-weight polysaccharides to produce significant metabolic improvements even without complete fermentation.

The existing research also suggested that high-molecular-weight polysaccharides from different sources might share common functional features: 1) Mw threshold effects, typically requiring >100 kDa to exhibit significant activity; 2) viscosity-dependent properties that positively correlated with lipase inhibitory activity; and 3) microbiota modulation specificity favoring intestinal barrier function improvement. Future studies should focus on: 1) identifying optimal Mw ranges for different polysaccharides; 2) elucidating quantitative relationships between gel properties and metabolic effects; and 3) developing processing techniques that preserve high-molecular-weight characteristics. These findings provided important theoretical foundations for developing functional foods based on high-molecular-weight polysaccharides.

3.2 Monosaccharide Composition

The monosaccharide composition of natural polysaccharides was a determinant structural feature for their anti-obesity activity, with different monosaccharide types and their specific linkage patterns influencing polysaccharides' physiological functions and metabolic regulatory effects through multiple mechanisms. Extensive research demonstrated that the monosaccharide composition of polysaccharides not only directly affected their physicochemical properties, intestinal fermentation characteristics, and interaction patterns with biomolecules, but also determined the molecular mechanisms and efficacy intensity of their anti-obesity effects. This structure-activity relationship provided important theoretical foundations and practical guidance for developing targeted anti-obesity polysaccharide products.

The study demonstrated that glucosyl polysaccharides, as the most extensively studied anti-obesity polysaccharides, primarily exerted their effects through physical regulation and anti-inflammatory mechanisms. The water-soluble glucan (GFPA) derived from *Grifola frondosa* served as a typical representative of this category, characterized by its β-1,4-glucan backbone with 1,4,6-branching structures. Its molecular mechanisms were manifested through: 1) inhibition of lipid accumulation via regulation of the ceramide metabolic pathway, resulting in reduced adipocyte size and improved hepatic steatosis; 2) activation of the TLR4/NF-κB signaling pathway through its specific monosaccharide composition, which significantly decreased pro-inflammatory cytokine levels in white adipose tissue and liver, thereby ameliorating chronic inflammation; and 3) systemic metabolic regulation, effectively reducing body weight, blood glucose, and lipid levels in obese mice while decreasing serum AST/ALT activities. These findings confirmed a clear structure-activity relationship between its monosaccharide composition and anti-obesity efficacy [29]. Similarly, *Anoectochilus roxburghii* polysaccharide (ARPs-p) demonstrated significant anti-hyperglycemic effects, further confirming the crucial role of β-configuration glucans in metabolic regulation [76]. Mannose-containing polysaccharides (e.g., konjac glucomannan) exhibited distinctive physicochemical properties. The mannose residues in these molecules formed stable three-dimensional networks through intermolecular hydrogen bonding, endowing them with exceptional hydration capacity (water absorption up to 100 times their own weight). This characteristic generated multiple anti-obesity effects: significantly increasing gastric content volume and prolonging satiety duration; effectively encapsulating dietary fats to reduce enzyme contact area; delaying gastric emptying and intestinal absorption rates. These physical

mechanisms established them as ideal dietary fibers for obesity prevention and management. Galactose-based polysaccharides (e.g., arabinogalactan, carrageenan) primarily functioned through microbiome modulation and immunoregulation. The water-soluble galactomannan (PEC) from *Eurotium cristatum*, composed mainly of mannose, galactose and minor glucose, represented a characteristic example. Studies revealed PEC prevented obesity development and metabolic disorders by reversing high-fat diet-induced gut dysbiosis [33]. Its functional features included: specifically promoting beneficial bacteria (e.g., *Bifidobacterium*); suppressing obesity-associated microbiota (e.g., *Desulfovibrio*); improving intestinal barrier function; and modulating host immune responses. These combined effects constituted the unique anti-obesity mechanism of galactose-based polysaccharides.

Polysaccharides composed of acidic monosaccharides (e.g., glucuronic acid, galacturonic acid) typically demonstrated enhanced bioactivity, primarily attributed to the negative charges conferred by their carboxyl groups. Studies revealed that these negatively charged uronic acid residues could significantly inhibit fat digestion processes through electrostatic interactions with positively charged digestive enzymes (e.g., pancreatic lipase). Research on fucoidan provided compelling evidence: low-molecular-weight fucoidan rich in uronic acids downregulated SREBP-1 and FAS expression to suppress lipid synthesis; high-uronic-acid fucoidan fractions markedly reduced serum triglyceride levels; while hydrothermal degradation-induced decarboxylation of uronic acids substantially diminished the polysaccharides' anti-obesity activity [77]. These findings confirmed the pivotal role of uronic acids in mediating fucoidan's anti-obesity effects.

Sulfated polysaccharides (e.g., fucoidan) demonstrated remarkable metabolic regulatory capacities due to their unique sulfate groups. Fucoidan extracted from *Undaria pinnatifida*, characterized by its high sulfate content, exhibited enhanced bioactivity by preventing oral glucose-induced hyperglycemia and reducing blood glucose and serum insulin levels in diabetic mice [78]. Studies on fucoidan further elucidated the mechanisms of sulfated polysaccharides. The research revealed that high-molecular-weight fucoidan (FUC) exerted significant anti-obesity effects through dual mechanisms: 1) molecular regulation via downregulation of hepatic SREBP-1c and FAS expression to inhibit fatty acid synthesis, while upregulating CYP7A1 and CYP27A1 to promote cholesterol metabolism; and 2) specific modulation of gut microbiota composition to optimize lipid metabolism. In contrast, hydrothermally degraded low-molecular-weight fucoidan (LF), despite having higher bioavailability, showed reduced regulatory capacity for key lipogenic genes (SREBP-1c/FAS) due to decreased glucuronic acid content, along with diminished effects on obesity-promoting gut microbiota. Consequently, LF demonstrated significantly weaker anti-obesity activity than native FUC, revealing a ternary structure-activity relationship among fucoidan's molecular weight, glucuronic acid content, and microbiota-modulating capacity [79]. These combined effects established the distinctive "non-adipogenic" anti-diabetic mode of action characteristic of sulfated polysaccharides.

Minor monosaccharides (e.g., fucose, rhamnose), despite their low abundance in polysaccharide compositions, made non-negligible contributions to anti-obesity activities. These special monosaccharides typically functioned through: 1) serving as specific structural domains for host receptor interactions; 2)

influencing polysaccharide spatial conformation and solubility; and 3) participating in forming unique active sites. Even subtle modifications in these components could lead to significant alterations in polysaccharide bioactivities.

In summary, natural polysaccharides exhibited clear structure-activity relationships between their monosaccharide composition and anti-obesity effects: glucose-based polysaccharides primarily functioned through physical effects and inflammation regulation; mannose-containing polysaccharides relied on their gelling properties to create mechanical barriers; galactose-based polysaccharides focused on microbiome modulation; acidic monosaccharides inhibited digestive enzymes via charge interactions; while sulfated polysaccharides demonstrated superior insulin-sensitizing effects. This diverse mechanistic profile suggested that polysaccharide products with specific monosaccharide compositions could be selected or designed for targeted intervention against different obesity subtypes and pathogenic mechanisms.

3.3 Basic Chemical Structure

The fundamental structural characteristics of natural polysaccharides, encompassing chain conformation, branching degree, and glycosidic bonding, serve as the pivotal structural elements that govern their anti-obesity efficacy. The mechanism of action and the strength of efficacy of polysaccharides in body weight regulation are ultimately determined by these structural parameters. This is achieved by affecting their physicochemical properties, bioaccessibility and interactions with biomolecules.

3.3.1 Chain conformation

There exists a close structure-activity relationship between polysaccharide chain conformation and anti-obesity effects, primarily mediated through two key mechanisms: digestive enzyme inhibition and gut microbiota modulation. Research demonstrated that β-glucans with rigid helical conformations (e.g., oat β-glucan) formed stable three-dimensional networks that dramatically increased chyme viscosity (up to 100-1000 times that of aqueous phase). This unique physical property effectively hindered lipase-substrate contact through steric hindrance effects, reducing triglyceride hydrolysis rates by 40%-60%. Undigested oat β-glucan exhibited primary aggregates with fringed micelle structures and supramolecular secondary aggregates of high molar mass - this hierarchical ordered structure formed the basis of its exceptional bile acid-binding capacity [80]. In contrast, flexible linear arabinoxylans, despite lower viscosity, demonstrated 30%-50% greater bile acid-binding affinity due to their larger specific surface area and more open molecular conformation, resulting in more pronounced cholesterol excretion effects. Regarding molecular conformation and digestive enzyme inhibition, green tea-derived acidic tea polysaccharide (TPSA) displayed unique structure-activity relationships. TPSA possessed spherical homogeneous conformations (20-40 nm), with molecular docking analyses revealing its hyperbranched structure could function as a competitive α-amylase inhibitor. This inhibitory effect originated from its branch segments mimicking starch substrate structures to occupy enzyme active sites [81]. Notably, polysaccharide conformational characteristics profoundly influenced their intestinal fermentation properties. Comparative studies between fucoidan and alginate oligosaccharides

showed that while both increased Bacteroidetes relative abundance and decreased Proteobacteria proportions, their microbial utilization efficiency differed significantly due to conformational differences. Alginate oligosaccharides, with their lower Mw, better solubility, and more flexible chain conformations, were more readily degraded by gut microbiota than rigid-chain fucoidan [82, 83]. This conformation-dependent utilization difference provides crucial guidance for designing gut microbiota-targeted polysaccharide preparations. Collectively, polysaccharide chain conformations play pivotal roles in anti-obesity effects by regulating their physicochemical properties and bioaccessibility. The conformation-dependent mechanisms operate through: 1) modulating viscosity-dependent physical barriers; 2) determining enzyme inhibitory potency; 3) influencing bile acid binding capacity; and 4) regulating microbiota fermentation efficiency-together constituting a multidimensional structure-activity framework for anti-obesity polysaccharide development.

3.3.2 Branching degree

There is a close conformational relationship between the branching degree of polysaccharide chains and their anti-obesity activity, which mainly works through multiple mechanisms, such as regulating the digestive and absorption properties, the fermentation efficiency of intestinal flora, and the lipase inhibition ability. Low-branched polysaccharides are susceptible to enzymatic degradation in the upper gastrointestinal tract due to their linear structure, which enhances satiety by delaying gastric emptying for 30-50 minutes, while highly branched polysaccharides resist enzymatic degradation by virtue of their complex spatial structure, and are able to be delivered to the colon for fermentation by specific probiotic bacteria. It was found that moderately branched dextran (1 branch point per 10-15 sugar residues) had the best SCFAs production efficiency, with butyric acid production up to 2-3 times higher than that of linear polysaccharides, a structure that balances the fermentation rate with colony selectivity. Notably, hyperbranched polysaccharides can bind multiple lipase molecules simultaneously due to the dense surface functional groups, and the inhibition efficiency of lipase is 1.5-2 times higher than that of linear polysaccharides, which provides a new perspective on the physical fat reduction mechanism of polysaccharides.

The anti-obesity effect of pectin-like polysaccharides further validates the critical role of branching degree. Pectin (WRP) with a high content of branched rhamnogalacturonans (RG-I) has been shown to significantly inhibit body weight gain and promote white fat browning in mice on a high-fat diet. In contrast, its low-branched oligosaccharides (DWRP) have been found to be ineffective, a phenomenon that has been attributed to the ability of intact RG-I structural domains to selectively modulate intestinal flora, such as Rousseaus, butyric acid-producing bacteria. Retention of the neutral sugar side chains is essential to maintain the prebiotic activity of RG-I oligosaccharides, as the branching structure preferentially stimulates the proliferation of specific flora during fermentation [84]. The study demonstrated that the anti-obesity activity of hawthorn pectin oligosaccharides (POS) was closely associated with their degree of polymerization (DP), with DP5-POS showing optimal efficacy. The mechanisms were manifested through: 1) significant improvement of glucose and lipid metabolism by elevating serum GLP-1 levels and upregulating ileal Gcg/Pcsk1 gene expression; 2) specific upregulation of 9,10-DHOME to enhance linoleic acid metabolism;

and 3) dual modulation of gut microbiota (reducing opportunistic pathogens while increasing microbial diversity) and intestinal barrier function (upregulating claudin-1/occludin/ZO-1/MUC2 genes). Although high-molecular-weight pectin (HP) showed similar directional effects, it exhibited weaker metabolic regulation. These results confirmed that reduced branching degree (DP5) significantly enhanced anti-obesity effects through a synergistic "gut-brain axis (GLP-1)-microbiota-metabolite" multi-target mechanism, providing clear evidence of structure-activity relationships for polysaccharide optimization [85]. These findings imply that the 'golden branching point' for the anti-obesity activity of polysaccharides needs to satisfy the balance between spatial resistance and microbial accessibility.

At the molecular level, the branching degree of polysaccharides modulates their interactions with digestive enzymes through three-dimensional structural control. Highly branched pectins (e.g., SAP), lacking triple-helical structures, adopt more open conformations that increase binding sites for lipase (PL) and cholesterol esterase (ACE), significantly inhibiting enzyme activity via steric hindrance effects. This inhibitory effect intensifies with increasing degree of esterification (DE), as high DE promotes gel network formation that further restricts enzyme-substrate contact [86]. Moreover, branched structures critically influence polysaccharides' water-holding capacity (WHC) and oil-holding capacity (OHC): The C-OH functional groups of galacturonic acid at branching points construct hydrophilic networks, while hydrophobic side chains bind lipid molecules. This dual functionality enables polysaccharides to physically entrap fat micelles while directly adsorbing lipases to form inhibitory barriers [87-90]. These findings provide clear structural optimization principles for designing targeted anti-obesity polysaccharides—by precisely regulating branching frequency, side-chain length, and functional group distribution, researchers can develop precision nutritional interventions that simultaneously enhance satiety, modulate gut microbiota, and inhibit digestive enzymes.

3.3.3. Glycosidic bond

The anti-obesity activity of natural polysaccharides is closely related to their fundamental structures, particularly the type, position, and configuration of glycosidic bonds. As the key chemical bonds linking monosaccharide units, the structural features of glycosidic bonds directly affect the spatial conformation, solubility, stability, and interactions with biological macromolecules of polysaccharides, thereby regulating their biological effects on energy metabolism, fat digestion, and gut microbiota modulation. For example, β-glycosidic bonds (such as β-(1→4) and β-(1→3)), which are commonly found in polysaccharides like cellulose and β-glucans, resist hydrolysis by mammalian digestive enzymes. This allows them to reach the colon intact as dietary fiber, where they are fermented by gut microbiota to produce short-chain fatty acids (SCFAs). These SCFAs activate the GPR41/GPR43 receptor signaling pathway, promoting the secretion of glucagon-like peptide-1 (GLP-1) and peptide YY (PYY), enhancing satiety, and increasing energy expenditure [91-93]. In contrast, polysaccharides containing α-(1→4) glycosidic bonds (e.g., starch) are readily hydrolyzed by human enzymes into glucose, leading to postprandial hyperglycemia and fat accumulation. However, modified polysaccharides or those with specific structural features such as α-(1→6) branching (e.g.,

certain resistant starches and inulin) exhibit similar prebiotic activity due to their resistance to digestion [94, 95]. Furthermore, the anomeric configuration (α/β) and linkage positions (e.g., 1→6, 1→2) of glycosidic bonds influence the chain rigidity, degree of polymerization, and solution behavior of polysaccharides: linear β-(1→4)-linked glucans often form rigid chain structures that enhance bile acid binding capacity, thereby inhibiting fat absorption [96, 97]; while branched polysaccharides (e.g., yeast β-glucans with 1→6 linkages) can delay gastric emptying and modulate gut microbiota composition more effectively by increasing specific surface area and viscosity [98, 99]. It is noteworthy that the type of glycosidic bond also indirectly affects the molecular weight distribution and functional group accessibility of polysaccharides. These factors collectively determine the ability of polysaccharides to effectively regulate signaling pathways such as AMPK and PPARα, which are involved in lipid metabolism. Therefore, in-depth analysis of the relationship between glycosidic bond characteristics and anti-obesity functions will not only facilitate the targeted design and modification of highly efficient polysaccharide-based prebiotics or fat substitutes, but also provide a theoretical foundation for developing precise nutritional intervention strategies against obesity-related metabolic disorders.

4. The application of natural polysaccharides as fat substitutes in food production

Natural polysaccharides demonstrate significant potential as fat substitutes in the food industry due to their unique gelling properties, water-holding capacity, and prebiotic characteristics (**Fig. 5)**. In dairy products, polysaccharides such as carrageenan and konjac glucomannan effectively mimic the rheological properties of fats, substantially improving the texture and mouthfeel of low-fat yogurt and cheese while enhancing product stability. For meat products, polysaccharides including β-glucan and pectin not only reduce fat content but also optimize water retention and texture, enabling low-fat sausages and patties to maintain desirable tenderness and juiciness. In the snack and bakery sector, composite polysaccharide systems like sodium alginate and guar gum can partially or completely replace conventional fats, reducing calorie content while preserving the softness and sensory qualities of baked goods. Furthermore, the dietary fiber attributes of polysaccharides provide additional health benefits to these products, such as regulating gut microbiota and lowering cholesterol levels (**Table 2**). This multifunctionality - combining technological performance with nutritional enhancement-positions polysaccharides as ideal ingredients for developing next-generation reduced-fat food products that meet both processing requirements and consumer health expectations.

Table 2 From lab-scale findings to commercial food products.

Food category	Fat substitutes	Critical functional benefit	Potential product application	Example formulation	Mechanism	References
Dairy products	Peach gum polysaccharide (PGP)	Sensory properties of skimmed milk	Skimmed milk	0.5% PGP + skimmed milk	Skimmed milk containing 0.5% PGP showed a similar creamy mouthfeel to full-fat milk.	[100]
	λ-carrageenan	Stabilizing emulsions	Milk powders	λ-carrageenan (0.3% w/w) + milk powders	Reduction of surface fat formation on spray-dried milk powders through emulsion stabilization with λ-carrageenan	[101]
	Konjac glucomannanand konjac flours	Fat loss	Low fat processed cheese	0.5% of commercial konjac glucomannan (CKG) or konjac flour (KF) + low fat processed cheese	Processed cheese with 50% fat reduction with added CKG (CKG50) showed the highest hardness value (327 g) and a strong elastic behavior.	[102]
	Gum ghatti or gum arabic (GA)	Improving probiotic bacterial survival	Yogurt	Gum ghatti or gum arabic + NaCas	NaCas-LMF combined with GA may provide effective protection to probiotic bacterial cells not only during spray drying, but also during storage and in vitro digestion.	[103]
Meat product	β-glucans	Mimicking the “fattiness” of chicken patties	Chicken patties	β-glucans (49.6 ± 1.9 mg/100 g) + chicken patties	Chicken patties with added mushroom extract were notable in retaining moisture, cooking yield and its structure.	[104]
	Dietary polysaccharides pectin (PEC)	Superior stability and textural properties	Low fat lamb patties	PEC + sheep hoof gelatin	PEC-IPN significantly improved the quality stability during storage, without affecting the sensory quality.	[105]
	Flammulina velutipes polysaccharide (FVPN)	Improving animal fat in meat products	Sausage	20% FVPN + sausage	Emulsion improved the springiness and cohesiveness of sausage and significantly reduced the hardness and chewiness.	[106]
	Konjac glucomannan	Superior water retention and gel strength	Muscle food	Konjac glucomannan (1%，w/w) + myofibrillar protein	Adding konjac glucomannan gel exhibited excellent water retention, gel strength and higher digestibility.	[107]
	Konjac glucomannan	Simulating the swallowing feeling and lubricity of natural fat	Pork fat	1% Soybean Protein Isolate + 4% konjac glucomannan	Protein/polysaccharide composite emulsion gel significantly improved the brightness, elasticity, and hardness of fat substitutes.	[108]
Snacks and pastries	Sodium alginate	Producing a low-calorie cake by replacing sugar and fat	Reduced fat and sugar cakes	Whey protein isolate + sodium alginate + licorice extract	The cake samples with 0 % and 50 % substitution levels had the lowest and highest values for hardness (0.76 . 2.38 N), cohesiveness, and chewiness, respectively.	[109]
	Aloe vera and guar gum	Producing a low-calorie cake	Cake	1 % mucilage + 1 % guar gum + cake	The cake containing a 50 % substitution of vegetable fat with AGB (C50) supplied desirable physicochemical, textural, and sensory properties.	[110]
	Mangosteen peels polysaccharides (MPPS)	Reduce heat, improve oxidative stability, retain viscoelasticity, and enhance taste	Reduced-fat mayonnaise	MPPS + mayonnaise	MPPS directly replaced the oil phase, reducing calories.	[111]
	Carrageen polysaccharide	Polysaccharide coating inhibited fat absorption on the surface of fried potato chips.	Deep-Fat Fried Potato Chip	1% Okra + carrageen polysaccharide	Better moisture retention capacity	[112]

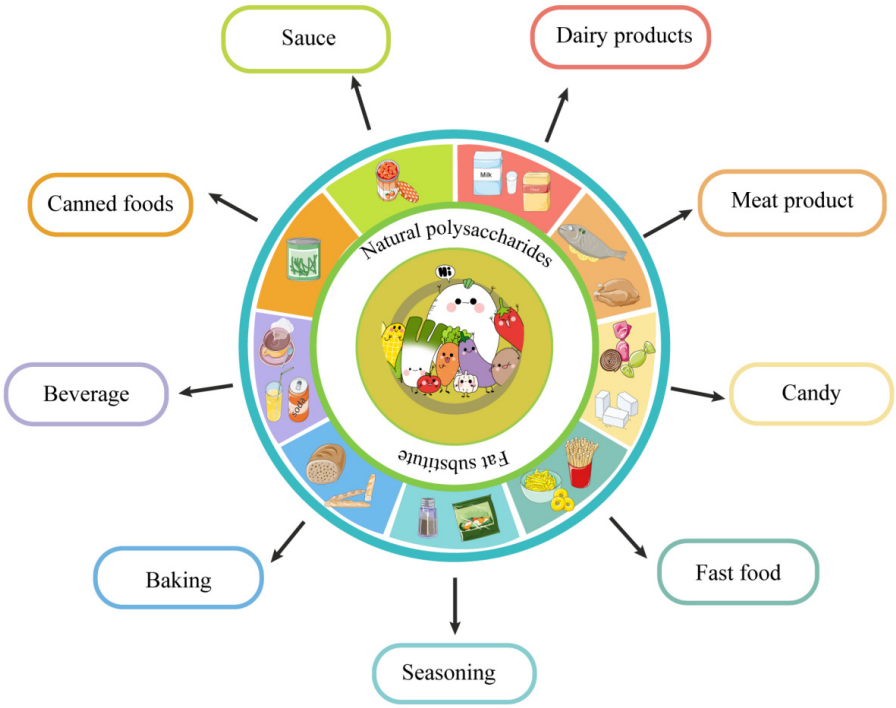

Fig. 5. The application of natural polysaccharides as fat substitutes in the food industry.

4.1 Dairy products

Significant progress has been made in the application of natural polysaccharides as fat substitutes in dairy products. Leveraging their unique rheological properties and structural simulation capabilities, these polysaccharides effectively reduce fat content while maintaining product sensory quality. Research on peach gum polysaccharide (PGP) demonstrated that adding 0.5% PGP eliminated significant differences ($P>0.05$) in rheological behavior (n, k values) and viscoelasticity (G′, G″ and η∗) between skim milk and whole milk. Tribological tests revealed comparable average surface roughness (2.390 vs 2.287) and root mean square values (2.908 vs 2.855) to whole milk. Electron microscopy confirmed PGP's ability to stabilize milk protein structures, enabling skim milk to achieve a creaminess similar to whole milk [100]. In spray drying processes, λ-carrageenan significantly improved milk powder quality by regulating emulsion stability. At 0.3% concentration, it formed optimal milk fat globule membrane adsorption structures that simultaneously avoided bridging flocculation and depletion flocculation, minimizing fat globule size. Its characteristic elongational viscosity enhancement increased fat encapsulation efficiency by over 40% in spray-dried particles while reducing surface fat content to one-third of conventional processes. This approach also enhanced product solubility and oxidative stability [101]. The incorporation of konjac glucomannan in low-fat processed cheeses demonstrated that the addition of 0.5% commercial konjac gum (CKG) resulted in a maximum hardness value of 327 g for a cheese with a 50% fat reduction. Dynamic rheological measurements revealed a significant increase in the modulus of elasticity (G'), and the structure remained stable and did not melt at 28 °C, whereas the standard full-fat cheeses were already completely melted at this temperature [102]. In the domain of

probiotic microencapsulation, the composite system of gum arabic (GA) and sodium caseinate (NaCas) exhibited remarkable protective properties, with an enhancement in the glass transition temperature (Tg) that sustained over 50% of the probiotic storage viability for a period of 16 weeks within the water activity range of 0.11-0.76. This finding was substantiated by porcine intestinal digestion experiments, which demonstrated that this system can facilitate the complete release of probiotic bacteria within a span of less than 1 hour [103]. Together, these studies reveal a triple advantageous mechanism of polysaccharides as fat substitutes: (1) modulation of protein aggregation state through hydrogen bonding and hydrophobic interactions to mimic the rheological properties of fat; (2) formation of a three-dimensional network structure to replace the textural function of fat; and (3) some polysaccharides (e.g., β-glucan) can also confer additional dietary fibre value to the product. The current technical challenge lies in the selection of optimal polysaccharides and optimisation of compounding ratios in different dairy systems. Future research should focus on: (1) molecular modification of polysaccharides to enhance their compatibility with milk proteins; (2) development of polysaccharide combination prediction models based on artificial intelligence; (3) synergistic mechanism of polysaccharides and probiotics in fermented dairy products, in order to promote the wider application of natural polysaccharides in low-fat dairy products.

4.2 Meat products

The utilisation of natural polysaccharides as a functional fat substitute in meat products has achieved a significant breakthrough. The unique gel characteristics and nutritional control advantages of this material have been shown to be effective in reducing fat content while maintaining the sensory quality of products. A multitude of studies have demonstrated that polysaccharides from diverse origins exhibit varied fat replacement effects in meat products. For instance, mushroom-derived β-glucan (e.g., mushroom extract) has been shown to reduce the crude fat content of chicken patties to (79.9 ± 4.5) mg/100 g, while concomitantly increasing the proportion of polyunsaturated fatty acids to (49.6 ± 1.9) mg/100 g [104]. The completely interpenetrating polymer network (IPN) gel formed by pectin (PEC) and gelatin has been shown to not only maintain the texture characteristics of the product, but also improve its storage stability when replacing 80% of the fat in mutton cake [105]. In the emulsion sausage system, the Pickering lotion (FPOE) stabilised by Flammulina velutipes polysaccharide nanoparticles reduced the fat content of the product from 27.28% to 18.76% at a 20% substitution rate, while reducing the cooking loss by 46% (from 18.87% to 8.63%), and forming a denser pore structure. In contrast, yeast mannoprotein MP112 lotion, at a substitution rate of 50-75%, not only enhanced the texture characteristics of sausage (hardness increased by 35%, chewability increased by 28%), but also increased the PUFA/SFA ratio by 2.3 times, and the oxidation stability was linearly enhanced [106]. The research on the application of konjac glucomannan (KGM) in myofibrillar protein gel shows that a 1% addition can increase the water-holding capacity of the gel by 40%, forming a uniform and dense three-dimensional network structure. Furthermore, its ability to limit the migration of water molecules is significantly better than that of inulin and κ - carrageenan [107]. The fat simulant prepared by combining soy protein isolate (SPI) and konjac flour (4%) has rheological properties (G 'and G "increased by 3 times) and an

oral friction coefficient ($\mu < 0.15$) that are closest to natural lard. Sensory evaluation demonstrates that its overall acceptance is equivalent to 92% of commercial product levels [108]. These application cases reveal three major mechanisms by which polysaccharides can replace fat: (1) the regulation of protein gel network through hydrogen bonding and hydrophobic interaction to simulate the texture characteristics of fat; (2) the compensation of the loss of taste caused by fat reduction through the water-holding capacity of polysaccharide molecular chains; and (3) the increase of the dietary fibre content of the product by 2-3 times through the use of certain polysaccharides, such as β-glucan and konjac polysaccharides. The current technical challenge lies in the selection of the most suitable polysaccharides in different meat product systems and the optimization of their synergistic ratios. Future research should focus on the following: Firstly, molecular dynamics simulation of polysaccharide protein interaction mechanisms should be conducted. Secondly, biomimetic fat structures should be constructed based on 3D printing technology. Thirdly, strategies for enhancing the structural stability of polysaccharides during thermal processing should be formulated to promote the large-scale application of natural polysaccharides in healthy meat products.

4.3 Snacks and Pastries

In recent years, significant progress has been made in the application of natural polysaccharides as functional fat replacers in snacks and baked goods, driven by growing consumer demand for healthier food options. Extensive research has demonstrated that polysaccharides from various sources can effectively maintain the sensory qualities and textural properties of traditional products while reducing calorie and fat content, leveraging their unique rheological characteristics and structural simulation capabilities. In cake systems, a ternary foam composed of whey protein isolate/sodium alginate/licorice extract exhibited outstanding performance as a sugar and fat substitute: at 50% replacement level, the product's caloric content decreased significantly from 371.37 kcal/100g to 252.57 kcal/100g (a 32% reduction), with fat content reduced by 47% (8.91→4.73 g/100g) and carbohydrates by 31% (67.92→47.09 g/100g). While texture analysis revealed a 213% increase in hardness for the full replacement group (0.76→2.38 N), sensory evaluation showed that the 25% replacement group most closely resembled the control, confirming the feasibility of partial substitution strategies [109].

The study of guar gum-based nanopolysaccharide blends (AGB) provides a new technological solution for bakery products. The nanoparticles (761.03 ± 62) nm obtained by optimising the preparation process (4 h magnetic stirring) were able to form a stable gel network at 1% addition concentration. The presence of active monomers, such as mannose and arabinose, was confirmed by Fourier transform infrared spectroscopy (FTIR), and scanning electron microscopy (SEM) revealed a uniform spherical structure. It is noteworthy that AGB exhibited not only broad-spectrum antimicrobial activity (inhibition circle 19.33-22.32 mm), but also maintained desirable thermal stability (Tg 16-50 °C) and organoleptic properties when replacing 50% of vegetable fats in cakes. This provides a novel concept for the development of clean-labelled products [110].

Research on the application of mangosteen pericarp polysaccharides (MPPS) in sauces has been groundbreaking. When utilised to substitute for 25%-55% of the fat in mayonnaise, the calorie content of the

product was reduced by 25.6%-67.4%, thereby meeting the criteria of 'light food'. Rheological analyses demonstrated that the 25%-35% replacement group (MP25/MP35) could preserve comparable viscoelasticity to the full-fat product (G' and G' changed by < 15%), with an oil droplet size distribution ranging from 1.214-1.332 (control 0.992). Notably, the oil droplets increased to 12.27 μm (control 2.81 μm) in the high-replacement group (MP55). However, all MPPS formulations exhibited superior oxidative stability, and the overall acceptability of the MP25 group (7.53 points) was even slightly higher than that of the full-fat control group (7.28 points) in the organoleptic evaluation [111].

Research in the field of fried foods has also made important breakthroughs. The okra-carrageenan composite polysaccharide coating (1% concentration) could reduce the oil absorption of crisps by more than 35% ($P \leq 0.05$), and confocal laser scanning microscopy confirmed that the coating could effectively block fat penetration and form a protective barrier under the frying conditions of 170-180 ℃. This technology provides a cost-effective solution to the high-fat problem of traditional fried foods [112].

Recent research has revealed three major mechanisms of polysaccharide fat replacement: firstly, the construction of a three-dimensional network through hydrogen bonding and hydrophobic interactions to mimic the textural properties of fats; secondly, the water-holding capacity of polysaccharide hydrophilic groups to compensate for the loss of lubrication due to the reduction of fats; and thirdly, the gel properties of certain polysaccharides (e.g. sodium alginate, guar gum) to stabilise the emulsion system. The principal technical challenges pertain to achieving optimal taste balance and ensuring heat processing stability under conditions of high substitution rates. Future research should focus on the following: Firstly, there is a necessity to enhance the heat resistance of polysaccharide molecules through molecular modification. Secondly, there is a requirement to optimise the synergistic effects of composite polysaccharide systems. Thirdly, there is a need to develop substitution ratio prediction models based on artificial intelligence to promote the industrialisation of low-fat health foods. These innovations not only respond to the global consumption trend of reducing sugar and fat, but also provide a scientific basis for the development of functional food ingredients.

Conclusion and perspective

Natural polysaccharides, as an important class of bioactive substances, demonstrate unique comprehensive value in anti-obesity applications. From an efficacy perspective, although the short-term weight loss effects of natural polysaccharides may be slightly inferior to some chemically synthesized drugs, their mechanisms of action are more comprehensive and gentler. Current clinical data indicate that polysaccharides exert anti-obesity effects through multiple pathways, including regulating gut microbiota balance, improving insulin sensitivity, and inhibiting lipogenic enzyme activity. These synergistic effects give them distinct advantages in ameliorating metabolic syndrome. Compared to gastrointestinal lipase inhibitors like orlistat, polysaccharides not only reduce fat absorption but also promote fat catabolism; while in comparison to GLP-1 receptor agonists, their effects are milder without causing significant gastrointestinal discomfort. Regarding safety, numerous studies have confirmed the exceptionally high safety profile of natural polysaccharides, with their incidence of adverse reactions typically being much lower than that of

synthetic drugs. Particularly noteworthy is that long-term use of natural polysaccharides does not induce significant metabolic adaptation or drug resistance, nor does it interfere with normal energy metabolism balance, making them uniquely valuable for special populations such as children, the elderly, and pre-pregnancy women. From a health economics standpoint, natural polysaccharides offer significant cost advantages. Firstly, their raw materials are widely available and production processes relatively simple, resulting in substantially lower manufacturing costs compared to synthetic drugs. Secondly, polysaccharides can generally be used as functional food ingredients without stringent prescription regulations, greatly reducing the burden on healthcare systems. Furthermore, their excellent safety and tolerability mean long-term use does not incur additional medical monitoring costs.

The future applications of natural polysaccharides in anti-obesity and food production show tremendous promise. In anti-obesity research, we must not only delve deeper into elucidating the molecular mechanisms of natural polysaccharides - clarifying their interactions with key receptors such as TLR4 and FXR, and detailing their effects on signaling pathways including NF-κB and PPARγ to establish theoretical foundations for developing novel anti-obesity drugs and functional supplements - but also establish a systematic research framework. A critical breakthrough will be the construction of a comprehensive polysaccharide structure-function database that integrates structural parameters (molecular weight distribution, glycosidic bond types, branching degree, substitution patterns) with multidimensional data including in vitro activity, animal study results, and human clinical trial outcomes. Building upon this foundation, the introduction of deep learning-based artificial intelligence algorithms to develop structure-activity prediction models will enable machine learning analysis of hidden patterns between polysaccharide structural features and bioactivities. This will allow accurate prediction of key indicators like anti-obesity efficacy and bioavailability, significantly accelerating the screening and design process for high-performance anti-obesity polysaccharides. Concurrently, traditional structure-activity relationship studies should continue advancing through structural optimization via chemical modification and enzymatic engineering, combined with modern biotechnologies like genetic and protein engineering to develop polysaccharide derivatives with enhanced targeting specificity. Notably, computer-aided drug design techniques such as molecular docking and molecular dynamics simulations can be adapted for polysaccharide drug development, guiding rational molecular design by simulating polysaccharide-target protein interactions.

Natural polysaccharides exhibit tremendous potential as functional food ingredients in industrial applications, serving as ideal fat substitutes that not only replicate the textural properties of lipids but also deliver the health benefits of dietary fiber. Future development should focus on expanding their utilization across diverse food matrices through tailored polysaccharide formulations designed for specific food systems to enhance product quality, sensory attributes, and nutritional value. Critical challenges in clinical translation require particular attention, including optimizing human bioavailability through structural modifications (e.g., sulfation, acetylation) or advanced delivery systems (e.g., nanoemulsions, liposomal encapsulation) to improve gastrointestinal absorption rates; establishing standardized dosing protocols by developing

evidence-based dose-response relationships to determine optimal intake regimens for target populations (e.g., obese or diabetic individuals); and implementing comprehensive long-term safety assessments beyond conventional toxicological testing through 6-12 month clinical trials monitoring gut microbiota homeostasis, hepatic/renal function markers, and metabolic syndrome-related parameters. Such systematic evaluation processes are essential to ensure the safe incorporation of polysaccharides in food products while establishing the foundation for their transition into clinical nutritional interventions.

From a broader perspective, the future development of polysaccharide research and applications will be characterized by deep interdisciplinary convergence. On one hand, it requires integrating multidisciplinary approaches from systems biology, synthetic biology, and computational science to establish a comprehensive knowledge framework spanning molecular structures, biological functions, and practical applications. Particular emphasis should be placed on leveraging multi-omics technologies - including gut microbiomics, metabolomics, and transcriptomics - to holistically decipher the mechanistic actions of polysaccharides. On the other hand, big data analytics and artificial intelligence will assume increasingly pivotal roles in polysaccharide research. Beyond the aforementioned structure-activity prediction models, AI-powered systems for polysaccharide formulation optimization and personalized recommendation algorithms can be developed to advance polysaccharide products toward precision nutrition and tailored health interventions. Furthermore, establishing industry-wide standardized quality criteria, analytical methodologies, and science-based regulatory frameworks for polysaccharides will form the essential foundation for sustainable industrial development.

In conclusion, research on the application of natural polysaccharides in anti-obesity and food industries is currently at a critical stage of rapid development. By deepening fundamental research, strengthening technological innovation, promoting interdisciplinary collaboration, and improving standardization systems - particularly through full utilization of modern technological approaches such as polysaccharide structure-function databases and AI-based predictive models - we will undoubtedly propel polysaccharide research and industrial applications to new heights, making greater contributions to human health and food industry development. This process requires close collaboration among academia, industry and regulatory bodies to jointly address technical challenges, facilitate effective translation of research achievements, and ultimately realize the scientific utilization and value maximization of polysaccharide resources.

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Data availability

No data was used for the research described in the article.

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