



Improvement of Inflammation, Diabetes, and Obesity by Forest Product-Derived Polysaccharides through the Human Intestinal Microbiota

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ABSTRACT

The intestinal microbiota plays a crucial role in determining human health, rendering it a major focus of scientific investigation. Rather than eliminating all microbes, promoting the proliferation of beneficial microorganisms within the gut has been recognized as a more effective approach to improving health. Unfavorable conditions potentially alter gut microbial populations, including a reduction in microbial diversity. However, intentionally enhancing the abundance of beneficial gut microbes can restore a state of optimal health. Polysaccharides are widely acknowledged for their potential to improve the gut microbiota. This review emphasizes the findings of recent studies examining the effects of forest product-derived polysaccharides on enhancing the gut microbiota and alleviating inflammation, diabetes symptoms, and obesity. The findings of several studies reviewed in this paper strongly suggest that forest products serve as an excellent dietary source for improving the gut microbiota and potentially offer valuable dietary interventions for chronic health problems, such as inflammation, diabetes, and obesity.

Keywords: diabetes, forest products, inflammation, intestinal microbiota, obesity, polysaccharides

1. INTRODUCTION

The human microbiota is a complex and dynamic community of microorganisms that inhabit various human body parts, including the skin, mouth, gut, and vagina (Faust *et al.*, 2012; Gilbert *et al.*, 2018; Martínez *et al.*, 2021). It plays an important role in maintaining human health and is involved in a broad range of physiological processes, including inflammation and immune responses; diabetes; and obesity (Wang *et al.*, 2017). It has emerged as an increasingly important area of research in

recent years, as modifications of the microbiota have been found to be associated with a wide range of diseases (Bik, 2016). This review aims to provide an overview of findings on immunity, diabetes, and obesity in relation to alterations in the human microbiota by forest product-derived polysaccharides.

The human microbiota is composed of various microorganisms, including bacteria, viruses, fungi, and archaea (Hoffmann *et al.*, 2013; Kong, 2011; Wade, 2013). The bacterial population of the human microbiota is the most extensively studied and comprises more than 1,511 di-

Date Received June 12, 2023, Date Revised July 12, 2023, Date Accepted August 14, 2023

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fferent species (Arumugam *et al.*, 2011). The microbiota's viral component is less well understood than the bacterial component; however, recent studies have suggested that enteroviruses potentially serve an important role in the gut microbiota and influence host health (Dreyfus, 2013; Rowan-Nash *et al.*, 2019). The microbiota's fungal component, also known as the mycobiome, has also received increasing attention in recent years. Fungi exist in smaller numbers than bacteria; nevertheless, they play an essential role in maintaining gut health and are associated with various diseases (Baker *et al.*, 2017; Ghannoum *et al.*, 2010). In this study, we reviewed recent research on the most studied bacterial microbiota in the human gut.

The microbiota serves a key beneficial role in maintaining host health via diverse biological functions, such as producing essential nutrients (Uebanso *et al.*, 2020), including vitamins and short-chain fatty acids (SCFAs); regulating immune function (Round and Mazmanian, 2009); and preventing colonization by potentially harmful microorganisms. It is also involved in the breakdown of complex carbohydrates, including dietary fibers, that resist degradation by human digestive enzymes (Flint *et al.*, 2012). Carbohydrate metabolism in the microbiota yields SCFAs that play significant roles in the immune response (Ratajczak *et al.*, 2019), the regulation of inflammation (Aho *et al.*, 2021; Cait *et al.*, 2018), and obesity (De la Cuesta-Zuluaga *et al.*, 2018; Murugesan *et al.*, 2018). In addition to these functions, the microbiota is also involved in the metabolism of drugs and other xenobiotics, and alterations in the microbiota potentially lead to changes in drug efficacy and toxicity (Wilson and Nicholson, 2017; Zimmermann *et al.*, 2019).

The human gastrointestinal tract contains hundreds of trillions of microbial cells that play a vital role in maintaining host health (Hooper and Macpherson, 2010). Collectively known as the gut microbiota, these microbial communities are involved in the various health-promoting, essential physiological processes listed above.

The gut microbiota's components and diversity are influenced by various factors, including diet, lifestyle, environmental factors, health condition, and genetic factors (Askarova *et al.*, 2020; Gacesa *et al.*, 2022; Walker *et al.*, 2021). Although several studies have reported the effects of the overall gut microbiota on health, studies identifying specific microbes or biological mechanisms that are beneficial to host health are limited. In general, when disease develops, microbial diversity in the host's microbiota has commonly been observed to decrease, at which time the proportion of pathogenic microorganisms is expected to increase (Lloyd-Price *et al.*, 2016).

Dietary compounds are factors that directly affect the gut microbiota (Lindell *et al.*, 2022; Shondelmyer *et al.*, 2018). In recent years, interest in the role of dietary compounds in modifying the components and function of the gut microbiota has increased (Laparra and Sanz, 2010; Rinninella *et al.*, 2019). Numerous studies have demonstrated that dietary patterns rich in plant-based foods and fiber are associated with a more diverse and beneficial gut-microbiota composition, whereas those high in fat and sugar are associated with a less diverse and potentially harmful microbiota (De Filippis *et al.*, 2016; Rinninella *et al.*, 2019; Sakkas *et al.*, 2020; Wong, 2014). This review provides a comprehensive analysis of the results of studies focusing on gut microbiota improvement by forest-derived polysaccharides.

Various polysaccharides have been shown to improve the gut microbiota by promoting the growth of beneficial bacteria and providing additional beneficial effects. Dietary fiber is a complex carbohydrate that is not digested by human enzymes but is instead fermented by gut bacteria in the colon (Murga-Garrido *et al.*, 2021; Tanes *et al.*, 2021). This fermentation process produces SCFAs (Deehan *et al.*, 2020; Markowiak-Kopeć and Śliżewska, 2020). Probiotics are live microorganisms that are ingested for their health-promoting properties (Kaur *et al.*, 2022; Linares *et al.*, 2017). They potentially improve gut microbiota health by increasing the

abundance of beneficial bacteria in the gut. Prebiotics are compounds that are not digested by the human body but instead serve as food for beneficial gut bacteria (Enam and Mansell, 2019; Miqdady *et al.*, 2020). They also enhance gut microbiota health by selectively promoting the growth of beneficial bacteria and reducing the abundance of harmful bacteria (Bindels *et al.*, 2015; Rastall and Gibson, 2015). Polyphenols (Trošt *et al.*, 2018; Tuohy *et al.*, 2012) in several plant-based foods, including fruits, vegetables, and tea; omega-3 fatty acids (Costantini *et al.*, 2017; Kaliannan *et al.*, 2015) in fatty fish, nuts, and seeds; and butyrate (Di Costanzo *et al.*, 2021; Donohoe *et al.*, 2011) produced by gut bacteria during dietary-fiber fermentation have been shown to possess numerous health benefits, including improving gut microbiota health by promoting the growth of beneficial bacteria and reducing gut inflammation.

Forest products, such as wood and plants, have been used for medicinal purposes for centuries due to their bioactive compounds. Various bioactive compounds have been identified in forest products, including phenolic compounds, which constitute one of the largest groups of bioactive compounds found in forest products (Huh *et al.*, 2022; Yang *et al.*, 2022a). Phenolic compounds are characterized by their aromatic ring structure, and they have been shown to exhibit potent antioxidant (Huh *et al.*, 2022; Lee *et al.*, 2021; Yang *et al.*, 2022a) and anti-inflammatory (Yang *et al.*, 2019, 2022b) activities. Flavonoids are another group of bioactive compounds found in forest products that possess a broad range of pharmacological activities, including antioxidant, anti-inflammatory, and anticancer effects (Ella Nkogo *et al.*, 2022; Huh *et al.*, 2022). Terpenoids constitute a diverse group of compounds found in forest products that have been shown to have antimicrobial, anti-inflammatory, and antioxidant activities (Kim *et al.*, 2017). Forest products also contain lignans, which are polyphenolic compounds found in plant cell walls. Lignans have been shown to exhibit estrogenic and anticancer activities

(Basu and Maier, 2018; Mottaghi and Abbaszadeh, 2022), and they may also play a role in the prevention of cardiovascular disease (Peterson *et al.*, 2010). Alkaloids are another group of bioactive compounds found in forest products that possess a wide range of pharmacological activities, including antimicrobial, anti-inflammatory, and anticancer effects (Ella Nkogo *et al.*, 2022; Manurung *et al.*, 2019). All the above compounds have proven to have beneficial effects on human health, including antioxidant (Huh *et al.*, 2022; Lee *et al.*, 2021; Yang *et al.*, 2022a), anti-inflammatory (Yang *et al.*, 2019, 2022b), and antimicrobial (Ham *et al.*, 2020; Lee *et al.*, 2021) activities, and they have been proposed as potential therapeutic agents for various diseases (Ham and Kim, 2018; Yoon and Kim, 2023). However, knowledge regarding the impact of forest-product compounds on the gut microbiota remains limited.

Therefore, this study reviewed the effects of polysaccharides found in forest products on the components and function of the intestinal microbiota.

2. EFFECTS of FOREST PRODUCT-DERIVED POLYSACCHARIDES on INFLAMMATION and IMMUNE RESPONSES via the INTESTINAL MICROBIOTA

The human body has an innate immune system and an adaptive immune system. The adaptive immune system is trained by exposing pathogens and provides strong, selective immunity against exposed pathogens. The close correlation between the gut microbiota and the host's immunity has been shown in many experiments using germ-free animals, such as intestinal defects of lymphoid tissue and immune functions (Bauer *et al.*, 1963), a decrease in $\alpha\beta$ and $\gamma\delta$ intra-epithelial lymphocytes (Umesaki *et al.*, 1993), a normalization of IgA antibodies following colonization of the gut microbiota (Hapfelmeier *et al.*, 2010), and an absence of Th17 cells

(Ivanov *et al.*, 2008) and restoring by colonization of the gut microbiota (Ivanov *et al.*, 2009). The interaction between the gut microbiota and immunity to maintain a healthy condition has been summarized and presented in a previous study (Zheng *et al.*, 2020). In this section, we review the studies on the change in the gut microbiota by forest product-derived polysaccharides that improve inflammation and immune response (Table 1).

2.1. Polysaccharides from plants

Lycium barbarum polysaccharides potentially increase the abundance of *Lactobacillus acidophilus*, *Bifidobacterium longum*, Firmicutes, and Proteobacteria strains as well as stimulate the growth of *Akkermansia*, *Lactobacillus*, and Prevotellaceae, which in turn increase serum transforming growth factor (TGF)- β , interleukin (IL)-6, and secretory immunoglobulin A (sIgA) concentrations in the colon, rendering it an excellent source of immune-response improvement (Zhu *et al.*, 2020).

Nelumbo nucifera Gaertn. polysaccharides improved the gut microbiota by decreasing the Firmicutes/Bacteroidetes ratio and increasing *Bifidobacterium* relative abundance, suggesting their potential as a prebiotic for SCFA production (Guan *et al.*, 2022).

Polysaccharides in Mulberry (*Morus alba* Linné) leaves have also been demonstrated to act as prebiotics by modulating the Bacteroidetes, Firmicutes, *Butyrivibrio*, and *Eubacterium* microbiota to improve the immune response via SCFA production (Chen *et al.*, 2021).

Moringa oleifera polysaccharides were found to induce changes in the gut microbiota, including increasing the proportion of Muribaculaceae and decreasing that of Proteobacteria, *Helicobacter*, *Stenotrophomonas*, and others, resulting in a significant increment in thymus and spleen indices and decrement in IL-6 and tumor necrosis factor (TNF)- α concentrations (Wen *et al.*,

2022).

Dendrobium huoshanense polysaccharides altered the gut microbiota and improved the immune response (Xie *et al.*, 2019). They increased the population of several beneficial bacteria, such as *Lactobacillus*, and decreased that of bacteria such as *Clostridium*, *Psychrobacter*, and *Propionibacterium*. These polysaccharides have been suggested as potentially useful prebiotics that modulate mucosal structures; increase the expression of tight-junction proteins, mucin-2, β -defensins, and sIgA; and stimulate cytokine production and the functional development of immune cells.

Dendrobium aphyllum polysaccharides improved gut microbiota by increasing beneficial bacteria, such as Porphyromonadaceae, Ruminococcaceae, and Erysipelotrichaceae, thereby increasing SCFA production and balancing Th₁/Th₂ and Th₁₇/Treg (Liu *et al.*, 2019).

Scutellaria baicalensis Georgi polysaccharides potentially suppress inflammatory cytokine levels and increase SCFA levels (Cui *et al.*, 2021). In the gut microbiota, the populations of microorganisms such as Firmicutes, *Bifidobacterium*, *Lactobacillus*, and *Roseburia* increased, whereas the proportion of *Bacteroides*, Proteobacteria, and *Staphylococcus* decreased, suggesting that *S. baicalensis* polysaccharides may have therapeutic applications for colitis and in improving the immune response.

The root polysaccharides of *Pueraria thomsonii* promoted intestinal barrier integrity, reduced inflammation via the nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) signaling pathway, and ameliorated lipid peroxidation via the adenine monophosphate activated protein kinase (AMPK)/nicotinamide adenine dinucleotide phosphate oxidase signaling pathway (Li *et al.*, 2022a). These improvements have been associated with the enrichment of the gut bacteria *Parabacteroides* (promoting intestinal barrier integrity) and Prevotellaceae (activating the AMPK signaling pathway).

Table 1. Effects of forest product derived polysaccharides on inflammation and immune responses via the intestinal microbiota

Origin	Compound (constitutional monosaccharides)	Gut bacteria changed	Biological effects	References
Plants				
<i>Lycium barbarum</i>	Polysaccharides (arabinose, rhamnose, xylose, mannose, galactose, glucose)	<i>Lactobacillus acidophilus</i> ↑, <i>Bifidobacterium longum</i> ↑, <i>Akkermansia</i> ↑, <i>Lactobacillus</i> ↑, Prevotellaceae ↑, Proteobacteria ↓, Firmicutes ↑, Bacteroidetes ↓	Transforming growth factor (TGF)-β ↑, IL-6 ↑ in serum, sIgA ↑ in the colon	(Zhu <i>et al.</i> , 2020)
<i>Nelumbo nucifera</i> Gaertn.	Polysaccharides [(1→4)-α-D-glucan with α-D-glycopyranosyl moieties]	Veillonellaceae ↑, Negativicutes ↑, <i>Escherichia</i> ↑, <i>Shigella</i> ↑, Bacteroidetes ↑, <i>Megamonas</i> ↑, <i>Bifidobacterium</i> ↑, Firmicutes ↓, Actinomycetes ↓	Gut pH ↓, SCFAs ↑	(Guan <i>et al.</i> , 2022)
<i>Morus alba</i> Linné leaves	Polysaccharides (mannose, rhamnose, glucose, galactose, arabinose)	Bacteroidetes ↑, Firmicutes ↓, <i>Butyricimonas</i> ↓ <i>Eubacterium</i> ↓	SCFAs ↑	(Chen <i>et al.</i> , 2021)
<i>Moringa oleifera</i>	Polysaccharides (β-gluco-pyranose, mannose)	Muribaculaceae ↑, Proteobacteria ↓, <i>Helicobacter</i> ↓, <i>Stenotrophomonas</i> ↓	Thymus index ↑, spleen index ↑, IL-6 ↓, TNF-α ↓	(Wen <i>et al.</i> , 2022)
<i>Dendrobium huoshanense</i>	Polysaccharides (glucose, xylose, galactose)	Firmicutes/Bacteroidetes ↓, <i>Lactobacillus</i> ↑, <i>Clostridium</i> ↓, <i>Psychrobacter</i> ↓, <i>Propionibacterium</i> ↓	Cytokines ↑, immune cells ↑	(Xie <i>et al.</i> , 2019)
<i>Dendrobium aphyllum</i>	Polysaccharides (mannose, glucose)	Porphyromonadaceae ↑, Ruminococcaceae ↑, Erysipelotrichaceae ↑	Gastrointestinal transit time ↓, pH ↓, fecal water-binding capability ↑, SCFAs ↑	(Liu <i>et al.</i> , 2019)
<i>Scutellaria baicalensis</i> Georgi	Polysaccharides (mannose, ribose, rhamnose, glucuronic acid, glucose, xylose, arabinose, fucose)	Firmicutes ↑, <i>Bifidobacterium</i> ↑, <i>Lactobacillus</i> ↑, <i>Roseburia</i> ↑, <i>Bacteroides</i> ↓, Proteobacteria ↓ <i>Staphylococcus</i> ↓	Proinflammatory cytokines ↓, SCFAs ↑	(Cui <i>et al.</i> , 2021)
<i>Pueraria thomsonii</i>	Polysaccharides	<i>Parabacteroides</i> ↑, Prevotellaceae ↑	Hepatic injury ↓, steatosis ↓, intestinal barrier integrity ↑, inflammation ↓	(Li <i>et al.</i> , 2022a)
Mushrooms				
<i>Dictyophora indusiate</i>	Polysaccharides (glucose, mannose, galactose)	Proteobacteria ↓, <i>Bacteroides</i> ↓, Gammaproteobacteria ↓, Bacteroidaceae ↓, Enterobacteriaceae ↓, <i>Lactobacillus</i> ↑	Cytokine ↓, anti-inflammatory cytokine ↑, tight-junction proteins ↑	(Kanwal <i>et al.</i> , 2020)
<i>Pleurotus eryngii</i>	Polysaccharides (glucose)	Porphyromonadaceae ↑, Rikenellaceae ↑, Bacteroidaceae ↑, Lactobacillaceae ↑ Firmicutes ↓, Bacteroidetes ↑	pH ↓, moisture content ↑, SCFAs ↑	(Ma <i>et al.</i> , 2017)
<i>Inonotus obliquus</i>	Polysaccharides (mannose, rhamnose, glucose, galactose, xylose, arabinose)	Bacteroidetes ↑, Firmicutes ↓	Glutathione peroxidase ↑, total antioxidant capacity ↑, TNF-α ↓, TGF β ↓, lipase ↓, trypsin ↓	(Hu <i>et al.</i> , 2017)

Table 1. Continued

Origin	Compound (constitutional monosaccharides)	Gut bacteria changed	Biological effects	References
Mushrooms				
<i>Auricularia auricular-judae</i> (Bull.)	Polysaccharides (rhamnose, mannose, glucose, fucose, xylose, galactose)	Deferribacteres ↓, Actinobacteria ↓, <i>Ruminococcus</i> sp. ↓	Symptoms of colitis ↓	(Zhao <i>et al.</i> , 2020)
<i>Flammuliana velutipes</i>	Polysaccharides (glucose, mannose, galactose)	Lachnospiraceae ↑, <i>Ruminal butyrivibrio</i> ↑, <i>Roseburia</i> ↑	SCFAs ↑	(Zhang <i>et al.</i> , 2020)
<i>Hericium erinaceus</i>	Polysaccharides	Clostridiales ↑, <i>Akkermansia</i> ↑, <i>Desulfovibrio</i> ↑	Nitric oxide ↓, malondialdehyde ↓, total superoxide dismutase ↓, myeloperoxidase ↓	(Ren <i>et al.</i> , 2018)
<i>Lentinula edodes</i>	Polysaccharides	Firmicutes/Bacteroidetes ↓, Bacteroidia ↑, <i>Bacillus</i> ↓, Betaproteobacteria ↓, Bacteroidaceae ↑, Lactobacillaceae ↓, Alcaligenaceae ↓.	Immune responses ↑, cytokine ↑ in peripheral blood.	(Xu <i>et al.</i> , 2015)
<i>Ganoderma lucidum</i>	Polysaccharides	Bacteroidetes ↓, Firmicutes ↑, <i>Lactobacillales</i> ↑, <i>Roseburia</i> ↑, Lachnospiraceae ↑	Superoxide dismutase ↑, total antioxidant activity ↑, lipase ↓, amylase ↓, interferon γ ↓, TNF- α ↓	(Li <i>et al.</i> , 2016)
<i>Phellinus linteus</i>	Polysaccharide extracts (glucose, arabinose, fucose, galactose, xylose)	<i>Roseburia</i> ↑, <i>Prevotella</i> ↑, <i>Ruminiclostridium-9</i> ↑, Lachnospiraceae ↑, <i>Blautia</i> ↑, <i>Oscibacter</i> ↑, <i>Clostridium</i> ↓, <i>Escherichia</i> ↓, Bacteroidales ↓	SCFAs ↑, lipopolysaccharides ↓	(Liu <i>et al.</i> , 2020)

Please note that most of the results in the presented references are from studies performed on animal models, and additional experiments are required to determine if the results can apply to healthy individuals or humans.

↑: Increased, enhanced, promoted, or positively changed in terms of activity, expression, or concentration.

↓: Decreased, inhibited, repressed, reduced, or negatively changed in terms of activity, expression, or concentration.

IL: interleukin, sIgA: secretory immunoglobulin A, SCFAs: short-chain fatty acids, TNF: tumor necrosis factor.

2.2. Polysaccharides from mushrooms

Dictyophora indusiata polysaccharides reduced the number of harmful microorganisms in the gut, such as Proteobacteria, Gammaproteobacteria, *Bacteroides*, Bacteroidaceae, and Enterobacteriaceae, and increased that of *Lactobacillus*, thereby relieving colitis (Kanwal *et al.*, 2020). They were also found to reduce pro-inflammatory cytokine levels and increase the expression of anti-inflammatory cytokines and tight-junction proteins, especially in severe cases of colitis.

Pleurotus eryngii polysaccharides lowered intestinal pH, increased SCFA production in the cecum and colon, and increased water content (Ma *et al.*, 2017). They decreased the distribution of Firmicutes and increased that of Bacteroidetes in the gut, creating a healthy gut environment.

The administration of *Inonotus obliquus* polysaccharides to rats with chronic pancreatitis increased glutathione peroxidase levels and total antioxidant capacity and decreased TNF- α , TGF- β , lipase, and trypsin levels (Hu *et al.*, 2017). It also promoted gut health by in-

creasing gut microbiota diversity, with an increase in the population of Bacteroidetes bacteria, which exhibit beneficial interaction with glutathione peroxidase and total antioxidant capacity, and a relative decrease in Firmicutes.

Polysaccharides extracted from *Auricularia auricular-judae* (Bull.) display a considerably protective effect against dextran sulfate sodium-induced inflammatory disease. Rats fed a high content of polysaccharides have a decreased disease activity index, and this relieves diarrhea and bloody stool and also prevents an increase in diamine oxidase, which in turn increases the resistance of mucous membranes (Zhao *et al.*, 2020).

Flammuliana velutipes polysaccharides promoted SCFA production by microorganisms in rat gut, and they are known to be protective against inflammatory bowel disease (Zhang *et al.*, 2020). Moreover, they increased the population of SCFA-producing microbes in Lachnospiraceae, including *Butyrivibrio* and *Roseburia*.

Polysaccharides from *Hericium erinaceus* protect against oxidative damage to the mucosa by reducing nitric oxide, malondialdehyde, total superoxide dismutase, and myeloperoxidase levels (Ren *et al.*, 2018). They have been found to restore the gut microbiota, including *Clostridiales*, *Akkermansia*, and *Desulfovibrio*, and recover from the imbalanced microbiota in colitis caused by dextran sulfate sodium.

Polysaccharide L2, extracted from the fruiting body of *Lentinula edodes*, increased cytokine levels in the peripheral blood and potentially recovered age-related decreasing factors, including TNF- α , IL-1, IL-2, and especially IL-6 (Xu *et al.*, 2015). This allows polysaccharide L2 to mitigate the age-related diminishment of the immune response. It may also reduce age-related changes in the gut microbiota. Polysaccharide L2 reduced the Firmicutes/Bacteroidetes ratio in the gut; increased Bacteroidia and Bacteroidaceae; and decreased *Bacillus*, Betaproteobacteria, Lactobacillaceae, and Alcaligenaceae. Thus, polysaccharide L2 from *L. edodes*

mitigates the age-related diminishment of immunity and improves the gut microbiota.

Ganoderma lucidum polysaccharides improve pancreatitis via diverse physiological changes, including increased superoxide dismutase and total antioxidant activities as well as restored activities of lipase, amylase, interferon γ , and TNF- α (Li *et al.*, 2016). They were found to improve the gut microbiota by decreasing Bacteroidetes and increasing Firmicutes, *Lactobacillales*, *Roseburia*, and Lachnospiraceae.

Mice treated with *Phellinus linteus* polysaccharide extract (PLPE) have been found to increase the number of SCFA-producing bacteria, such as *Roseburia*, *Prevotella*, *Ruminiclostridium-9*, Lachnospiraceae, *Blautia*, and *Oscibacter*, in the gut, and SCFAs have an intestinal barrier function and reduce blood lipopolysaccharide levels, thereby alleviating systemic inflammation and insulin resistance (Liu *et al.*, 2020). In addition, PLPE was found to decrease the *Clostridium*, *Escherichia*, and Bacteroidales populations, thus increasing the level of lipopolysaccharide, an inflammatory factor in serum.

3. EFFECTS of FOREST PRODUCT-DERIVED POLYSACCHARIDES on DIABETES via the INTESTINAL MICROBIOTA

There are two types of diabetes mellitus. Type 1 diabetes is an inability to control blood sugar due to decreased production of insulin, often caused by a genetic defect. Type 2 diabetes is a condition in which blood sugar cannot be controlled by normal insulin secretion due to increased resistance to insulin. In many cases, resistance to insulin is acquired through the living condition. In this section, we review the studies on forest product-derived polysaccharides that have been shown to improve diabetes symptoms by improving gut microbiota, with a focus on Type 2 diabetes (Table 2). Compounds produced by the gut microbiota have been pro

Table 2. Effects of forest product derived polysaccharides on diabetes via the intestinal microbiota

Name	Compounds	Gut bacteria changed	Mechanisms	References
Plants				
<i>Ophiopogon japonicus</i>	Polysaccharides (fructose, glucose)	Actinobacteria ↑, <i>Bifidobacterium</i> ↑, Desulfovibrionaceae ↓, <i>Dorea</i> ↓, Ruminococcaceae ↓	Insulin resistance ↑, glucose tolerance ↑, SCFAs ↑	(Wang <i>et al.</i> , 2019)
<i>Salvia miltiorrhiza</i>	Polysaccharides	Cyanobacteria ↓, Firmicutes/Bacteroidetes ↓, <i>Bacteroides</i> ↑, <i>Lactobacillus</i> ↑, <i>Parabacteroides</i> ↑, <i>Oscillospira</i> ↓, <i>Alistipes</i> ↓	Liver total cholesterol ↓, triglyceride ↓, free fatty acid ↓, alanine transaminase ↓, aspartate transaminase ↓, LDL-C ↓	(Wang <i>et al.</i> , 2020b)
<i>Rosa roxburghii</i>	Polysaccharides (arabinose, galactose, glucose, mannose, xylose, fructose)	Bacteroidaceae ↑, Peptostreptococcaceae ↑, Prevotellaceae ↑, Rikenellaceae ↑, <i>Bacteroidales</i> ↑, <i>Lactobacillus</i> ↑, Enterococcaceae ↓, Desulfovibrionaceae ↓, Clostridiaceae ↓, Ruminococcaceae ↓, Erysipelotrichaceae ↓, Helicobacteraceae ↓, Ruminococcaceae ↓, Lachnospiraceae ↓, Clostridiales ↓, Desulfovibrionales ↓	PPAR-γ ↓, SREBP-1 ↓, ACC-1 ↓, fatty acid synthase ↓, glucose-6-phosphatase ↓	(Wang <i>et al.</i> , 2020a)
<i>Apocynum venetum</i> leaves	Polysaccharide-rich extracts	<i>Odoribacter</i> ↑, <i>Anaeroplasm</i> ↑, <i>Parasutterella</i> ↑, <i>Muribaculum</i> ↑, <i>Enterococcus</i> ↓, <i>Klebsiella</i> ↓, <i>Aerococcus</i> ↓	Fasting blood glucose ↓, serum insulin ↓, glycated serum protein ↓, serum lipid profiles ↓	(Yuan <i>et al.</i> , 2020)
<i>Momordica charantia</i> L.	Fermented polysaccharides (rhamnose, arabinose, galactose, glucose, xylose, mannose, galacturonic acid)	<i>Lactococcus laudensis</i> ↑, <i>Prevotella loescheii</i> ↑, <i>Prevotella oralis</i> ↑	Hyperglycemia ↓, hyperinsulinemia ↓, hyperlipidemia ↓, oxidative stress ↓, SCFAs ↑, pH ↓	(Gao <i>et al.</i> , 2018)
<i>Cyclocarya paliurus</i> (Batal.)	Polysaccharides (xylose, arabinose, glucose, galactose, rhamnose, mannose)	Ruminococcaceae ↑	SCFAs ↑, Bax ↓, Bcl-2 ↑, normalized hormone secretion, inflammation ↓	(Li <i>et al.</i> , 2021)
<i>Plantago asiatica</i> L.	Polysaccharides	<i>Bacteroides vulgatus</i> ↑, <i>Lactobacillus fermentum</i> ↑, <i>P. loescheii</i> ↑, <i>Bacteroides vulgatus</i> ↑	Blood glucose ↓, insulin, total cholesterol ↓, triglyceride ↓, non-esterified fatty acid ↓, maleic dialdehyde ↓, HDL cholesterol ↑, antioxidant enzyme activity ↑	(Nie <i>et al.</i> , 2019)
Mushrooms				
<i>Grifola frondosa</i>	Polysaccharides (mannose, rhamnose, glucuronic acid, galacturonic acid, glucose, galactose, fucose)	<i>Streptococcus</i> ↓, <i>Enterococcus</i> ↓, <i>Staphylococcus</i> ↓, <i>Aerococcus</i> ↓, <i>Alistipes</i> ↑	Fasting blood glucose ↓, oral glucose tolerance ↓, cholesterol ↓, triglyceride ↓, LDL-C ↓	(Guo <i>et al.</i> , 2020)
	Polysaccharides (arabinose, mannose, glucose)	<i>Porphyromonas gingivalis</i> ↑, <i>Akkermansia muciniphila</i> ↑, <i>Lactobacillus acidophilus</i> ↑, <i>Tannerella forsythia</i> ↑, <i>Bacteroides acidifaciens</i> ↑, <i>Roseburia intestinalis</i> ↑	IRS 1 ↑, phosphatidylinositol-3-kinase ↑, glucose transporter 4 ↑, JNK 1 ↓	(Chen <i>et al.</i> , 2019)

Table 2. Continued

Name	Compounds	Gut bacteria changed	Mechanisms	References
Mushrooms				
<i>Morchella esculenta</i>	Polysaccharides (mannose, ribose, rhamnose, glucuronic acid, galacturonic acid, glucose, galactose, arabinose, fucose)	<i>Lactobacillus</i> ↑, <i>Firmicutes</i> ↑, <i>Actinobacteria</i> ↓, <i>Corynebacterium</i> ↓, <i>Facklamia</i> ↓	Endotoxemia ↓, insulin resistance-related proinflammatory cytokines IL-1β ↓, TNF-α ↓, IL-6 ↓	(Rehman <i>et al.</i> , 2022)
<i>Phellinus linteus</i>	Polysaccharides (glucose, mannose, galactose, xylose, arabinose, rhamnose)	<i>Porphyromona</i> ↑	Fasting blood glucose ↓, glucose tolerance ↑	(Feng <i>et al.</i> , 2018)
	Polysaccharide extracts (glucose, arabinose, fucose, galactose, xylose)	<i>Roseburia</i> ↑, <i>Prevotella</i> ↑, <i>Ruminiclostridium-9</i> ↑, <i>Lachnospiraceae</i> ↑, <i>Blautia</i> ↑, <i>Oscibacter</i> ↑, <i>Clostridium</i> ↓, <i>Escherichia</i> ↓, <i>Bacteroidales</i> ↓	SCFAs ↑, lipopolysaccharides ↓	(Liu <i>et al.</i> , 2020)
<i>Ganoderma lucidum</i>	Polysaccharides (mannose, glucose, galactose, rhamnose, arabinose)	<i>Aerococcus</i> ↓, <i>Ruminococcus</i> ↓, <i>Corynebacterium</i> ↓, <i>Proteus</i> ↓, <i>Blautia</i> ↑, <i>Dehalobacterium</i> ↑, <i>Parabacteroides</i> ↑, <i>Bacteroides</i> ↑	Fasting blood glucose ↓, insulin ↓, butyric acid ↑, valeric acid ↑, amino acid metabolism ↑, carbohydrate metabolism ↑, bacterial toxin ↓	(Chen <i>et al.</i> , 2020)

Please note that most of the results in the presented references are from studies performed on animal models, and additional experiments are required to determine if the results can apply to healthy individuals or humans.

↑: Increased, enhanced, promoted, or positively changed in terms of activity, expression, or concentration.

↓: Decreased, inhibited, repressed, reduced, or negatively changed in terms of activity, expression, or concentration.

SCFAs: short-chain fatty acids, LDL-C: low-density lipoprotein cholesterol, PPAR: peroxisome proliferator-activated receptor, SREBP: sterol regulatory element-binding protein, ACC: acetyl-CoA carboxylase, HDL: high-density lipoprotein, IRS: insulin receptor substrate, JNK: c-Jun N-terminal kinase, IL: interleukin, TNF: tumor necrosis factor.

posed to be involved in type 2 diabetes through various mechanisms, and it has been suggested that the distribution of the gut microbiota is abnormally changed by host molecules, which may contribute to the development of type 2 diabetes (Zhou *et al.*, 2022). Thus, in the studies reviewed in this section, restoring the abnormal gut microbiome to normal through the consumption of forest product-derived polysaccharides has been shown to improve diabetes symptoms.

3.1. Polysaccharides from plants

A homogeneous polysaccharide fraction from *Ophio-*

pogon japonicus improved insulin resistance, glucose tolerance, diabetes-associated gut microbiota, and SCFA metabolism in mice with high-fat diet-induced type-2 diabetes (Wang *et al.*, 2019). It increased the population of Actinobacteria and *Bifidobacterium* and decreased that of Proteobacteria and type 2 diabetes-associated bacteria.

Salvia miltiorrhiza polysaccharides fortified probiotic activity by reducing total cholesterol and total triglyceride levels in the liver; free fatty acid levels in the serum; and alanine aminotransferase, aspartate aminotransferase, and low-density lipoprotein cholesterol (LDL-C) levels (Wang *et al.*, 2020b). Gut microbiota

alterations, such as an increase in the abundance of Cyanobacteria, *Bacteroides*, *Lactobacillus*, and *Parabacteroides* and a decrease in that of *Oscillospira* and *Alistipes*, were induced by these polysaccharides.

Rosa roxburghii-originated polysaccharides have been reported to significantly reduce fat, liver hypertrophy, fasting blood glucose levels, and serum insulin and lipids as well as attenuate the expression levels of peroxisome proliferator-activated receptor (PPAR)- γ , sterol regulatory element-binding protein-1, acetyl-CoA carboxylase (ACC)-1, fatty acid synthase (FAS), and glucose-6-phosphatase (Wang *et al.*, 2020a). Gut microbiota balance was altered by lowering the Firmicutes/Bacteroidetes ratio; increasing the relative abundances of beneficial bacteria, Bacteroidaceae, Peptostreptococaceae, Prevotellaceae, Rikenellaceae, Bacteroidales, and *Lactobacillus*; and decreasing the relative abundances of Enterococcaceae, Desulfovibrionaceae, Clostridiaceae, Ruminococcaceae, Erysipelotrichaceae, Helicobacteraceae, Ruminococcaceae, Lachnospiraceae, Clostridiales, and Desulfovibrionales.

The polysaccharides obtained via alkaline extraction from *Apocynum venetum* leaves were effective in improving fasting blood glucose, serum insulin, glycosylated serum protein, and serum lipids profiles (Yuan *et al.*, 2020). In terms of intestinal microbial changes, the extracts increased the abundance of bacteria, *Odoribacter*, *Anaeroplasma*, *Parasutterella*, and *Muribaculum* and decreased that of *Enterococcus*, *Klebsiella*, and *Aerococcus*. Therefore, this polysaccharide extract is expected to be a potentially useful anti-diabetic food.

Polysaccharides from *Momordica charantia* L. exhibited antidiabetic activity, such as improving hyperglycemia, hyperinsulinism, and hyperlipidemia in diabetic rats, and increased the abundance of beneficial gut bacteria, such as *Lactococcus laudensis*, *Prevotella loescheii*, and *Prevotella oralis*, resulting in increased SCFA production (Gao *et al.*, 2018).

Cyclocarya paliurus (Batal.) is a deciduous tree pre-

dominantly found in eastern and central China. Polysaccharides extracted from *C. paliurus* potentially inhibit Bax protein expression in the pancreas, enhance β -cell lymphoma (Bcl)-2 expression to improve pancreatic β -cell regeneration and insulin resistance, normalize hormone secretion, and control inflammation (Li *et al.*, 2021). They have also been found to increase Ruminococcaceae UCG-005 bacteria and elevate SCFA production.

Plantago asiatica L., a perennial herb, has been shown to reduce blood glucose, insulin, total cholesterol, triglyceride, free fatty acid, and malaldehyde concentrations; increase high-density lipoprotein levels and antioxidant enzyme activity; and promote the diversity of bacteria such as *Bacteroides vulgatus*, *Lactobacillus fermentum*, and *P. loescheii*, which potentially exert antidiabetic effects through increased SCFA production (Nie *et al.*, 2019).

3.2. Polysaccharides from mushrooms

Polysaccharides extracted from the fruiting body of *Grifola frondosa* have the effect of reducing blood glucose and blood lipid levels (Guo *et al.*, 2020). The administration of these polysaccharides to rats fed a high-fat diet decreased fasting blood glucose, oral glucose tolerance, cholesterol, triglyceride, serum LDL-C, and free fatty acid levels in the liver. Oral administration decreased the relative abundance of *Streptococcus*, *Enterococcus*, *Staphylococcus*, and *Aerococcus* and increased that of *Alistipes*, thereby alleviating gut microbiota imbalance. A polysaccharide from *G. frondosa* also improved the symptoms of type 2 diabetes (Chen *et al.*, 2019). When administered to rats, it activated insulin receptor substrate 1, phosphatidylinositol-3-kinase, and glucose transporter 4 and decreased c-Jun terminal kinase 1, thus improving type 2 diabetes. It was also observed to increase the distribution of gut microbes beneficial to diabetes, including *Porphyromonas gingivalis*, *Akkermansia muciniphila*, *L. acidophilus*, *Tanne-*

rella forsythia, *Bacteroides acidifaciens*, and *Roseburia intestinalis*.

Polysaccharides extracted from the fruiting body of *Morchella esculenta* reduced insulin resistance-related proinflammatory cytokines IL-1 β , TNF- α , and IL-6 in rats with type 2 diabetes induced by a high-fat diet with streptozotocin (Rehman *et al.*, 2022). Among the gut microbes, there was an increase in the relative abundance of *Lactobacillus* and *Firmicutes*, which are beneficial against type 2 diabetes, and a decrease in the relative abundance of *Actinobacteria*, *Corynebacterium*, and *Facklamia*, which are opportunistic pathogens. The polysaccharides also regulated the expression of colon tight-junction proteins, such as zonula occludens-1, occludin, claudin-1, and mucin-2.

Oral administration of PLPE to rats fed a high-fat, high-fructose diet decreased fasting blood glucose levels and improved glucose intolerance (Feng *et al.*, 2018). It also increased the proportion of *Porphyromonas* bacteria, which are capable of producing vitamin B12 in the gut, and activated insulin-signaling transduction by increasing the phosphatidylcholine/phosphatidylethanolamine ratio. PLPE also exerts hypoglycemic effects, modulates the gut microbiota, and induces insulin resistance (Liu *et al.*, 2020).

G. lucidum polysaccharides decreased the populations of diabetes-causing *Aerococcus*, *Ruminococcus*, *Corynebacterium*, and *Proteus* in the gut and increased those of diabetes-modifying *Blautia*, *Dehalobacterium*, *Parabacteroides*, and *Bacteroides* (Chen *et al.*, 2020). These polysaccharides potentially alleviate type 2 diabetes by reducing fasting blood glucose and insulin levels.

4. EFFECTS of FOREST PRODUCT-DERIVED POLYSACCHARIDES on OBESITY via the INTESTINAL MICROBIOTA

In mice with the same diet and the same body weight,

germ-free mice with an obese microbiota had increased total body fat content compared to individuals with a lean microbiota (Turnbaugh *et al.*, 2006). The involvement of the gut microbiota in obesity is suggested by promoting nutrient absorption of the host with obese microbiota (Petersen *et al.*, 2019), regulating gastrointestinal function through the production of neuromodulators such as serotonin (Shajib and Khan, 2015), and modulating fat storage in the host by gut microbiota (Bäckhed *et al.*, 2004). In addition, reduced gut microbiota diversity has been commonly observed in obese hosts (Turnbaugh *et al.*, 2009). In this section, we review the studies showing an association between gut microbiota improved by forest product-derived polysaccharides and obesity (Table 3).

4.1. Polysaccharides from plants

L. barbarum polysaccharides are potentially useful as prebiotics in improving obesity by modulating gut microbiota composition and SCFA metabolism. They have been found to promote beneficial gut bacteria, such as *Lactobacillus* (Yang *et al.*, 2021).

A water-soluble β -D-fructan from *O. japonicus* was found to have potent anti-obesity and blood sugar-lowering effects (Shi *et al.*, 2015). It reduced the Firmicutes/Bacteroidetes ratio and potentially restored the abnormal gut microbial composition to its normal state and modified its metabolic profiles. It can be degraded and utilized by the gut microbiota, which can be absorbed and used by the host, contributing to weight loss and increased energy metabolism.

A homogalacturonan-type pectic polysaccharide extracted from *Ficus pumila* Linn. fruits effectively alleviated obesity by reducing body weight, blood total cholesterol, and LDL-C levels (Wu *et al.*, 2020). A decrease in the Firmicutes/Bacteroidetes ratio, an increase in *Akkermansia*, and a decrease in *Blautia* were induced by this polysaccharide in mice with high-fat diet-induced

Table 3. Effects of forest product-derived polysaccharides on obesity via the intestinal microbiota

Name	Compounds (constitutional monosaccharides)	Gut bacteria changed	Mechanisms	References
Plants				
<i>Lycium barbarum</i>	Polysaccharides (xylose, glucose, rhamnose, mannose, galactose, arabinose, fructose, fucose, ribose)	Firmicutes/Bacteroidetes ↓, <i>Lactobacillus</i> ↑	Gut microbiota diversity ↑, SCFAs ↑	(Yang <i>et al.</i> , 2021)
<i>Ophiopogon japonicus</i>	A water-soluble β-D-fructan	<i>Bacteroidetes</i> ↑, <i>Firmicutes</i> ↓	SCFAs ↑, related metabolites ↑	(Shi <i>et al.</i> , 2015)
<i>Ficus pumila</i> Linn.	Homogalacturonan-type pectic polysaccharide	<i>Firmicutes/Bacteroidetes</i> ↓, <i>Akkermansia</i> ↑, <i>Blautia</i> ↓	Body weight ↓, serum total cholesterol ↓, LDL-C ↓	(Wu <i>et al.</i> , 2020)
Bamboo	Polysaccharide (arabinoxylan)	<i>Firmicutes/Bacteroidetes</i> ↓, <i>Enterobacter</i> ↓, <i>Desulfovibrio</i> ↓, <i>Akkermansia muciniphila</i> ↑, <i>Lactobacillus</i> ↑	Richness and diversity of gut microbiota ↑, lipid metabolism ↑	(Chen <i>et al.</i> , 2018)
Soybean	Soybean insoluble dietary fiber	<i>Lactobacillus</i> ↑, Lachnospirace ↑, Lachnospiraceae ↓	Total cholesterol ↓, triglyceride ↓, LDL-C ↓, HDL cholesterol ↑, SCFAs ↑	(Wang <i>et al.</i> , 2021)
<i>Hippophae rhamnoides</i> Linn.	Polysaccharides (fructose, rhamnose, arabinose, galactose, glucose, xylose, galacturonic acid)	Muribaculaceae ↑, <i>Bifidobacterium</i> ↑, Rikenellaceae ↑, <i>Alistipes</i> ↑, <i>Bacteroides</i> ↑, <i>Lactobacillus</i> ↓, Firmicutes ↓, <i>Dubosiella</i> ↓, <i>Bilophila</i> ↓, <i>Streptococcus</i> ↓	Body weight gain ↓, serum lipids ↓, liver triglycerides ↓, p-adenine monophosphate activated protein kinase (AMPK)α ↑, PPARα ↑, ACC1 phosphorylation ↑, FAS ↓, PPARγ ↓, CD36 ↓, SCFAs ↑	(Lan <i>et al.</i> , 2022)
Guava	Polysaccharides (galacturonic acid, galactose, arabinose)	Firmicutes/Bacteroidetes ↓, <i>Clostridium</i> XIVa ↑, <i>Parvibacter</i> ↑, <i>Enterorhabdus</i> ↑, <i>Mucispirillum</i> ↓	Induced body weight gain ↓, visceral obesity ↓, serum cholesterol ↓, triglyceride ↓, LDL-C ↓, hepatic lipid accumulation ↓	(Li <i>et al.</i> , 2022b)
<i>Hylocereus undatus</i>	Polysaccharides	Muribaculaceae ↓, Lactobacillaceae ↑, Lachnospiraceae ↑, Ruminococcaceae ↑	Obesity ↓ via amino acid, carbohydrate, and glycan metabolism.	(Lee <i>et al.</i> , 2022)
Mushrooms				
<i>Ophicordyceps sinensis</i> and <i>Cordyceps militaris</i>	Carbohydrates, amino acids	Firmicutes/Bacteroidetes ↓, <i>Phascolarctobacterium</i> ↑, <i>Bifidobacterium</i> ↑	Gut pH ↓, SCFAs ↑	(Ji <i>et al.</i> , 2020)
<i>Ganoderma lucidum</i>	Polysaccharides (mannose, glucose, galactose)	Firmicutes/Bacteroidetes ↓, <i>Parabacteroides goldsteinii</i> ↑, <i>Bacteroides</i> spp. ↑, <i>Anaerotruncus colihominis</i> ↑, <i>Roseburia hominis</i> ↑, <i>Clostridium methylpentosum</i> ↑, <i>Clostridium</i> XIVa and XVIII ↑, <i>Eubacterium coprostanoligenes</i> ↑	Gut barrier integrity ↑, endotoxemia ↓, TLR4 signaling ↓, inflammation ↓	(Chang <i>et al.</i> , 2015)

Table 3. Effects of forest product-derived polysaccharides on obesity via the intestinal microbiota

Name	Compounds (constitutional monosaccharides)	Gut bacteria changed	Mechanisms	References
Mushrooms				
<i>Oudemansiella radicata</i>	Polysaccharides	<i>Firmicutes/Bacteroidetes</i> ↓, <i>Bacteroidete</i> ↑, <i>Parabacteroides</i> ↑	SCFAs ↑	(Liu <i>et al.</i> , 2021)
<i>Grifola frondosa</i>	Polysaccharides (mannose, rhamnose, glucose, galactose, fucose)	<i>Oscillibacter</i> ↑, <i>Barnesiella</i> ↑, <i>Defluvitalea</i> ↑	AMPK- α ↑, PPAR- α ↑, glucokinase ↑, sterol regulatory element-binding transcription factor-1c ↓, ACC ↓	(Pan <i>et al.</i> , 2020)

Please note that most of the results in the presented references are from studies performed on animal models, and additional experiments are required to determine if the results can apply to healthy individuals or humans.

↑: Increased, enhanced, promoted, or positively changed in terms of activity, expression, or concentration.

↓: Decreased, inhibited, repressed, reduced, or negatively changed in terms of activity, expression, or concentration.

SCFAs: short-chain fatty acids, LDL-C: low-density lipoprotein cholesterol, HDL: high-density lipoprotein, PPAR: peroxisome proliferator-activated receptor, ACC: acetyl-CoA carboxylase, FAS: fatty acid synthase, CD36: cluster of differentiation 36, TLR4: toll-like receptor 4.

obesity.

Bamboo-derived polysaccharides reduced the Firmicutes/Bacteroidetes ratio, decreased the number of harmful bacteria (*Enterobacter* and *Desulfovibrio*), increased the number of beneficial bacteria (*A. muciniphila* and *Lactobacillus*), and improved lipid metabolism (Chen *et al.*, 2018).

Insoluble dietary fiber from soybeans significantly modulated gut microbiota composition by increasing the number of beneficial bacteria, such as Lactobacillales, *Lactobacillus*, and Lachnospiraceae, and decreasing the number of potentially harmful bacteria, such as Lachnospiraceae and *B. acidifaciens* (Wang *et al.*, 2021). It also reduced body weight, the adiposity index, total cholesterol, triglycerides, and LDL-C in high-fat diet-fed mice.

Sea buckthorn (*Hippophae rhamnoides* Linn.) polysaccharide consumption increased AMPK α and PPAR α protein expression, stimulated ACC1 phosphorylation, and inhibited the protein expression of FAS, PPAR γ , and cluster of differentiation 36 (Lan *et al.*, 2022). Regarding gut microbiota changes, these polysaccharides increased the proportions of Muribaculaceae, *Bifidobacterium*, Rikenellaceae, *Alistipes*, and *Bacteroides* and

decreased those of *Lactobacillus*, Firmicutes, *Dubosiella*, *Bilophila*, and *Streptococcus*. They were also found to be involved in increasing SCFA production.

Guava-derived polysaccharides restored the Firmicutes/Bacteroidetes ratio; induced the growth of beneficial bacteria, namely, *Clostridium* XIVa, *Parvibacter*, and *Enterorhabdus*; reduced the inflammation-associated bacterium *Mucispirillum*; and promoted the production of SCFAs, which potentially mitigate weight gain and visceral obesity and reduce serum cholesterol, triglyceride, and LDL-C levels (Li *et al.*, 2022b).

Polysaccharides from *Hylocereus undatus* fruits increased gut anti-obesity microbes, such as *Lactobacillus plantarum*, thereby alleviating obesity via amino acid, carbohydrate, and glycan metabolism (Lee *et al.*, 2022).

4.2. Polysaccharides from mushrooms

Both *Ophicordyceps sinensis* and *Cordyceps militaris* mitigate obesity by reducing the Firmicutes/Bacteroidetes ratio in the gut (Ji *et al.*, 2020). In particular, *O. sinensis* has a differential ratio of carbohydrates (glucose, mannitol, and trehalose) and amino acids (aspartate,

glutamate, lysine, and threonine) compared with *C. militaris*, and this has the effect of lowering gut pH, promoting SCFA production, and enriching probiotics, such as *Phascolarctobacterium* and *Bifidobacterium*.

A high-molecular-weight polysaccharide in a water extract from *G. lucidum* mycelium attenuated obesity in rats fed a high-fat diet (Chang *et al.*, 2015). This polysaccharide was found to reduce obesity-induced inflammation by increasing intestinal barrier integrity, reducing endotoxemia, and reducing toll-like receptor 4 signaling. It was also observed to inhibit intestinal bacteria, such as *Parabacteroides goldsteinii*, *Bacteroides* spp., *Anaerotruncus colihominis*, *Roseburia hominis*, *Clostridium methylpentosum*, *Clostridium* XIVa and XVIII, and *Eubacterium coprostanoligenes*.

Polysaccharides extracted from *Oudemansiella radicata* increased the number of *Bacteroides* and *Pareabacteroides* bacteria in the gut microbiota, thus promoting SCFA production in the gut (Liu *et al.*, 2021). In addition, the relative increase in *Bacteroides* was found to decrease the Firmicutes/Bacteroidetes ratio, thereby improving gut health.

G. frondosa water extract potentially prevents metabolic diseases, such as obesity, hyperlipidemia, and hyperglycemia (Pan *et al.*, 2020). This extract mainly contains polysaccharides as well as other substances, such as fatty acids, glycerophospholipids, steroids, and alkaloids. It has been found to increase the expression of AMPK- α , PPAR- α , and glucokinase and decrease the expression of sterol regulatory element-binding transcription factor-1c and ACC. It has also been observed to increase the number of *Oscillibacter*, *Barnesiella*, and *Defluvitalea* bacteria in the caecum, thereby reducing serum glucose and lipid parameters and increasing SCFA production.

5. CONCLUSIONS

The gut microbiota serves a critical role in main-

taining host health, and its significance has increasingly been acknowledged in scientific research. This review explored recent studies suggesting that forest-product derivatives possibly mitigate inflammation, ameliorate diabetes symptoms, and alleviate obesity, with the improvements potentially stemming from their impact on the gut microbiota. A common observation was that consumption of forest product-derived polysaccharides reduced the Firmicutes/Bacteroidetes ratio and increased beneficial microbes such as *Lactobacillus* in the gut microbiota. Some observations of increased Firmicutes (Cui *et al.*, 2021; Rehman *et al.*, 2022; Zhu *et al.*, 2020) were small enough to be interpreted as individual-specific phenomena.

Most forest products discussed in the reviewed studies were polysaccharides, and their consumption demonstrated symptom relief in animal models. Notably, various forest products containing diverse polysaccharides exhibited comparable health improvements, indicating that enhancing the gut microbiota may be one of the mechanisms by which different forest products confer health benefits. It is conceivable that optimizing the modes of forest-product consumption may maximize their impact on improving the gut microbiota and contribute to overall health enhancement. However, besides that on polysaccharides, research on compounds that promote forest product-derived gut microbiota diversity remains scarce. Therefore, further investigation is necessary to identify and develop compounds, beyond polysaccharides, that enhance forest product-derived gut microbiota.

The limited research on compounds other than polysaccharides can be attributed to the nascent stage of gut microbiota studies. As we delve into the exploration of microbial ecology, which encompasses diverse microorganisms, novel methodologies that elucidate the precise beneficial effects of the gut microbiota are warranted. To address these challenges and enhance our understanding, the following aspects require attention:

First, a crucial step is to distinguish between the

beneficial and detrimental bacteria within the gut microbiota. Determining the health implications of taxonomic changes in the gut at phylum or order level poses challenges, as bacteria within the same species can exhibit both beneficial and harmful characteristics. Thus, investigating the impact of alterations in microbial distribution on overall host health becomes imperative. In certain cases, emphasizing the assessment of broader physiological phenomena rather than focusing solely on taxonomic changes in microbial distribution may be more pertinent. This approach will provide a more comprehensive understanding of how gut microbiota modifications influence host health.

Second, to ascertain which metabolic processes are advantageous to host health, unravelling the diverse biological mechanisms by which the microbiota influences the host is essential. One approach toward measuring bioactivity is by examining enhanced SCFA production. The increased production of SCFAs, which are organic acids, has been widely recognized as beneficial to host health in numerous ways. Consequently, gut microbiota alterations that foster SCFA production are believed to confer health benefits. However, exploring additional methodologies for assessing the positive impacts of microbes on host health, beyond SCFA production, is important. This broader investigation will enhance our understanding of the multifaceted interactions between the microbiota and host well-being.

Third, elucidating the mechanisms by which the gut microbiota is positively modulated by various compounds, leading to health benefits, is imperative. Gaining insight into the specific mechanisms by which certain compounds enhance the gut microbiota and subsequently promote health can serve as a roadmap for the development of novel probiotics. By comprehending the intricate pathways and interactions involved, targeted interventions that optimize gut microbiota composition and function can be formulated, ultimately improving overall health.

Finally, establishing an effective means of administering compounds that promote the distribution of gut microbes is crucial. The distribution of the gut microbiota can be influenced by various factors, and even if a compound is ingested to improve the gut microbiota, its effects may diminish if the microbiota deteriorates due to other reasons. Therefore, developing delivery methods that potentially enhance the distribution of gut microorganisms is imperative, even when administered in minute quantities. Such delivery methods should consider factors such as targeted delivery, stability in the gastrointestinal environment, and optimal dosing strategies to ensure sustained and consistent effects on the gut microbiota. By addressing these challenges, the potential of substances to exert long-lasting positive effects on gut microbial distribution and ultimately contribute to improved health outcomes can be maximized.

Addressing these requirements will possibly lead to the discovery of various forest-product compounds, other than polysaccharides, that improve gut microbiota distribution.

The studies examined in this review demonstrated that diverse forest product-derived polysaccharides have the capacity to stimulate SCFA production in the gut, leading to decreased pH levels. These findings provide empirical evidence for SCFA production, which is a well-known mechanism for improving host health, thereby supporting the notion that forest products can enhance host health. Various forest products possess a broad range of compounds, and as the relationship between the microbiota and host health is further elucidated, further research on the health-promoting effects of forest products is anticipated.

CONFLICT of INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENT

This study was carried out with the support of 'R&D Program for Forest Science Technology (Project No.: 2023473B10-2325-EE02)' provided by Korea Forest Service (Korea Forestry Promotion Institute).

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