



The effects of dietary fibers from rice bran and wheat bran on gut microbiota: An overview

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ARTICLE INFO

Keywords:

Dietary fibers
Rice bran
Wheat bran
Digestive behaviors
Gut microbiota
Metabolites
SCFAs

ABSTRACT

Whole grain is the primary food providing abundant dietary fibers (DFs) in the human diet. DFs from rice bran and wheat bran have been well documented in modulating gut microbiota. This review aims to summarize the physicochemical properties and digestive behaviors of DFs from rice bran and wheat bran and their effects on host gut microbiota. The physicochemical properties of DFs are closely related to their fermentability and digestive behaviors. DFs from rice bran and wheat bran modulate specific bacteria and promote SAFCs-producing bacteria to maintain host health. Moreover, their metabolites stimulate the production of mucus-associated bacteria to enhance the intestinal barrier and regulate the immune system. They also reduce the level of related inflammatory cytokines and regulate Tregs activation. Therefore, DFs from rice bran and wheat bran will serve as prebiotics, and diets rich in whole grain will be a biotherapeutic strategy for human health.

1. Introduction

Gut microbiota is a diverse and multiplex microbial community composed of trillions of microorganisms (Zheng, Chen, & Cheong, 2020). It has been considered as a crucial factor in the maintenance of human health and disease, such as the improvement of intestinal barrier function and regulation of host metabolism, intestinal homeostasis, and immune system (Rooks & Garrett, 2016; Singh et al., 2019). Various chronic diseases are associated with intestinal flora dysbiosis (Hand, Vujkovic-Cvijin, Ridaura, & Belkaid, 2016), including metabolic syndrome (Kjølbaek et al., 2020), colorectal cancer (Coker et al., 2019), cardiovascular disease (Bartolomeaus et al., 2019), type 2 diabetes (Zhou et al., 2019), obesity (Canfora, Meex, Venema, & Blaak, 2019; Huang et al., 2019), and inflammatory bowel disease (Franzosa et al., 2019; Han et al., 2020). In contrast, the composition of gut microbiota is changed by long-term diet adjustment or drug intervention (Fragiadakis, Wastyk, Robinson, Sonnenburg, Sonnenburg, & Gardner, 2020; Walsh, Griffin, Clarke, & Hyland, 2018). Gut health is maintained by probiotic substances and their metabolites. Short-chain fatty acids (SCFAs) have been considered essential metabolites, regulating gut microflora and defense diseases (Qiu et al., 2022; Xie & Cheong, 2021). Therefore, gut microbiota regulation has become a hot research topic in the treatment

of various diseases.

Whole grain is a whole, crushed or compressed caryopsis, including rice, wheat, corn, barley, oats, rye, black rice, and sorghum. Rice and wheat are principal food crops in Asia and Latin America, and Asia accounts for approximately 90% of global rice production (Muthayya, Sugimoto, Montgomery, & Maberly, 2014). Whole grain can reduce the risk of cancer (Xie, Liu, Tsao, Wang, Sun, & Wang, 2019), obesity (Zhang, Han, Wang, Wang, Sun, & Zhai, 2019), cardiovascular disease (Sawicki, Livingston, & McKeown, 2019), and type 2 diabetes (Kyro, Tjonneland, Overvad, Olsen, & Landberg, 2018). The potential reason is that whole grain is abundant in bioactive compounds, such as dietary fibers (DFs), polyphenols, vitamins, and minerals (Ozkaya, Turksoy, Ozkaya, & Duman, 2017; Zheng, Zhong, Tang, & Chen, 2020). As readily available as processing by-products, rice bran and wheat bran contain high content of DFs. Wheat bran accounts for 36.5–52.4% of DFs (Apprigh et al., 2014). Rice bran contains 50% of carbohydrates, majorly starch and DFs (Lavanya, Saikiran, & Venkatachalapathy, 2019). Wheat bran and rice bran are always utilized for animal feed and biogas production. However, they are beneficial for human consumption with remarkable values after appropriate processing (Aktaş & Akın, 2020).

DFs from rice bran and wheat bran are beneficial to human health by regulating host gut microbiota. DFs can induce the release of some

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beneficial metabolites during fermentation, particularly SCFAs, which are closely associated with defending various diseases (Dallie, Van Oudenhove, Vervliet, & Verbeke, 2019). They have the potential to be applied to food supplement or therapeutic purposes in the future. In this review, the physicochemical properties, digestive behaviors, and impacts on the gut microbiota of DFs (mainly from rice bran and wheat bran) are summarized. The review helps to further understand the interaction between DFs and gut microbiota and provides insight into a complete mechanism in the future.

2. The physicochemical properties of DFs from rice bran and wheat bran on the digestive and fermentation behaviors

The physicochemical properties of DFs from rice bran and wheat bran, including particle size, branch degree, monosaccharide and linkage composition, molecular weight, solubility, viscosity, and hydration properties, are closely related to their behaviors in the digestive tract (Holscher, 2017; McRorie & McKeown, 2017). Fermentation of DFs could improve their digestibility and utilization (Gänzle, 2020). DFs can also be associated with side effects such as gastrointestinal symptoms, partly due to gas production or bloating caused by rapid fermentation (Rodriguez et al., 2020). The fermentability of DFs, which could be improved by decreasing the particle size of materials, was shown by the increasing amount of produced butyric acid in the colon (Iwai, Yoshikawa, Nyosmi, Fukutome, Asada, & Ohashi, 2017; Tuncil, Thakkar, Marcia, Hamaker, & Lindemann, 2018). The hydration and antioxidant properties of DFs were enhanced by decreasing the particle size of rice bran (Zhao et al., 2018). The digestive behaviors of DFs were also related to branch degree. The fermentation rate of DFs was increased due to a relatively high degree of arabinose substitution on the xylan backbone (Chen, Long, Zhang, Liu, Zhao, & Hamaker, 2017). The digestibility of DFs could be improved by decreasing their molecular weight, such as hydrolyzing DFs with xylanases and arabinofuranosidases (Vangsoe, Bonnin, Joseph-Aime, Saulnier, Neugnot-Roux, & Knudsen, 2020). DFs could be classified as soluble DFs and insoluble DFs according to their solubility in water. Prebiotic soluble oligosaccharides, such as galactose-oligosaccharides, fructose-oligosaccharides, and xyloligosaccharides, are fermented rapidly. Soluble polysaccharides, such as inulin, β -glucan, type 2 and type 3 resistant starches, were partially fermented. Cellulose is the most abundant biomacromolecule in nature, and although ruminants can degrade it, its fermentation by the human gut microbiota is minimal (Wang, Wichienchot, He, Fu, Huang, & Zhang, 2019). Classification of DFs as “soluble” or “insoluble” may not be sufficient to explain fermentation performance. For example, soluble sodium alginate cannot be fermented by human gut microbiota (Rose, Keshavarzian, Patterson, Venkatachalam, Gillevet, & Hamaker, 2009). The viscosity of DFs was associated with its concentration, defined as the resistance to flow. Wheat bran DFs possessed Newtonian fluid property by detecting apparent viscosity (Li, Liu, Wu, & Zhang, 2017; Yan, Wu, Cai, Xiao, Duan, & Zhang, 2019). DFs with high viscosity had more hydrophilic groups, which increased intestinal mucosal water film thickness and thus increased the viscosity of supernatant intestinal contents (He et al., 2022). However, if the viscosity of DFs was too high, fermentation would be inhibited due to the limited oxygen supply (van Leeuwe et al., 2020). The hydration properties of DFs mainly depended on the porous matrix structure formed by glycosidic linkages, which could hold plenty of water through hydrogen bonds (-H), considered as thermodynamics and dynamics of water absorption or desorption (Capuano, 2017; Zhao et al., 2018). The hydration capacities of DFs were related to their fermentation in the digestive tract (Cui et al., 2019). Low water-binding capacity would limit the fermentation rate, as the highly condensed fiber substrate provided an obstacle to efficient utilization of the carbohydrates within the granules (Gidley & Yakubov, 2019). Besides, after absorbing water, DFs had a lubricating effect, promoting intestinal peristalsis and intestinal motility. The specific hydration behavior is determined by the number of hydrophilic groups,

side chain reactivity, and binding force (Föste, Verheyen, Jekle, & Becker, 2020). In a word, the digestive behaviors and fermentation characteristics of DFs from rice bran and wheat bran are related to their physicochemical properties.

3. The digestive behaviors of DFs from rice bran and wheat bran

The mammalian digestive system is complex and highly derived, consisting of the digestive tract and digestive glands (Hartenstein & Martinez, 2019). Digestive behavior is a principal physiological approach to absorbing nutrients from food. It happens in the digestive tract, which contains the oral cavity, esophagus, stomach, and large intestine. Oral processing is the first step of food digestion by grinding DFs into small particles. Then in the stomach, pepsin and gastric lipase help to further mechanically stir DFs. The intestine is the major location of absorbing nutrients from foods. DFs cannot be digested by the enzymes in the upper gastrointestinal tract, such as lingual lipase, gastric lipase, and pepsin, and almost safely reach the large intestine (Tuncil, Thakkar, Arioglu-Tuncil, Hamaker, & Lindemann, 2018). They can be hydrolyzed by some specific enzymes released by microbial metabolism in the large bowel, like a cross-feeding enzyme system in the prominent gut symbiont *Bacteroides ovatus*, which can digest macromolecular substances (Rakoff-Nahoum, Foster, & Comstock, 2016).

Due to mechanical processes, the size and shape of DFs from rice bran and wheat bran have changed in the oral, stomach, and small intestine. The general digestive behaviors of DFs in the human body are summarized in Fig. 1, according to Capuano's report (2017). There is no significant change in the molecular weight of macromolecular substances (eg. polysaccharides and DFs) in the stomach (Chen et al., 2018; Han, Pang, Wen, You, Huang, & Kulikouskaya, 2020; Huang et al., 2019; Zhang et al., 2019). Molecular weight and monosaccharide composition have been changed in the large intestine due to the fermentation of gut microbiota (Huang et al., 2019). The fermentable DFs were degraded during the fermentation process. Then the remaining part (water-soluble not-fermentable DFs and other residues) were expelled out of the host in feces (Capuano, 2017). During *in vitro* fermentation, rice bran arabinoxylans are fermented by a debranching mechanism based on the change of monosaccharide composition by detecting carbohydrate loss and changes in arabinose/xylose ratio. In contrast, these unsubstituted xylose regions in wheat bran arabinoxylans are fermented preferentially. Then the remaining (highly branched oligosaccharides) are fermented (Rose, Patterson, & Hamaker, 2010). The physical and chemical properties of DFs from rice bran and wheat bran changed during their fermentation and digestive behaviors.

4. Effect of DFs from rice bran and wheat bran on host gut microbiota

Soluble DFs can be utilized by gut microbiota. DFs exerted beneficial effects on the host primarily by fermentation and production of metabolites. Bacteroidetes, Firmicutes, and Actinobacteria are the three main phyla in the human large intestine, which can degrade complex substrates due to their degradative enzymes produced during the metabolic process (Scott, Gratz, Sheridan, Flint, & Duncan, 2013). The effect of DFs on gut microbiota is summarized in Fig. 2.

4.1. Effect of DFs from rice bran and wheat bran on gut microbiota composition

DFs can improve the composition and abundance of gut microbiota to maintain host health during fermentation. It is generally detected by 16S rRNA gene sequencing. The impact of DFs on gut microbiota is summarized in Table 1. DFs can maintain host health by promoting the growth of beneficial bacteria and preventing that of harmful bacteria. Traditionally, *Bifidobacterium* and *Lactobacillus* are considered as beneficial bacteria, which can defend against diseases by utilizing complex

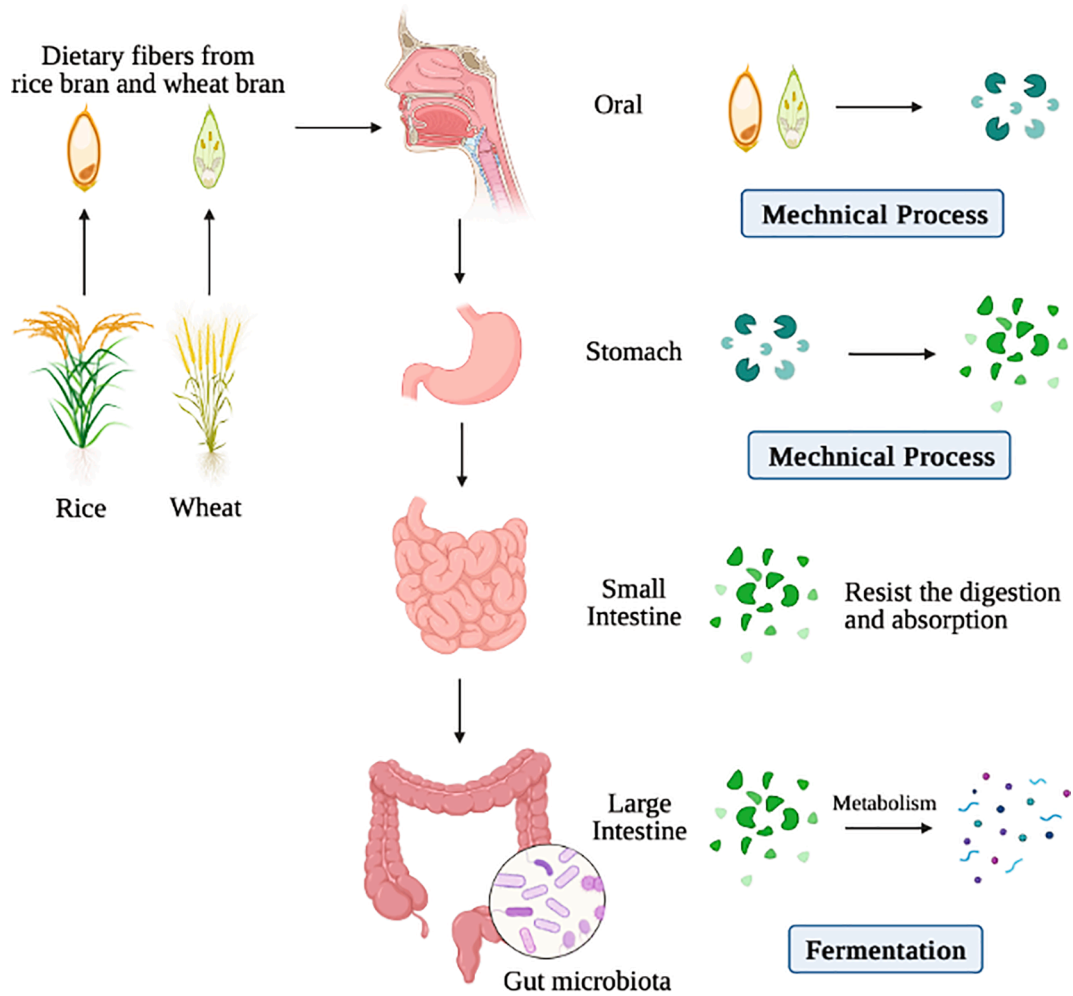


Fig. 1. The general digestive behaviors of DFs from rice bran and wheat bran in human body.

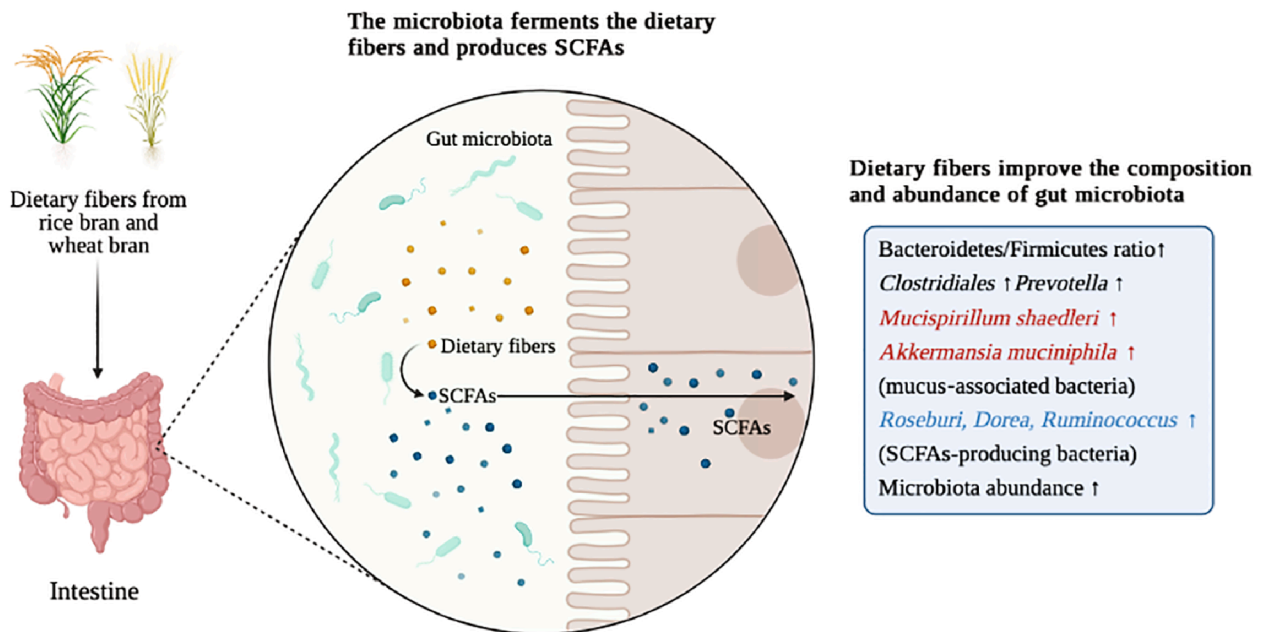


Fig. 2. The effects of DFs from rice bran and wheat bran on gut microbiota.

Table 1
The impacts of DFs from rice bran and wheat bran on gut microbiota.

Fiber sources	Physicochemical properties	Research methods/objects	Intervention intake/ time	Changes of bacteria	Other results	Conclusions	References
Rice bran	–	<i>In vivo</i> / male C57BL/KsJ db/db mice	10% of AIN-93G standard diet/8 weeks	↓Enterobacteriaceae, Streptococcaceae, Enterococcaceae (phylum Proteobacteria) ↑Lachnospiraceae and Ruminococcaceae (phylum Firmicute)	↓fasting blood glucose levels ↓fasting serum insulin levels ↑butyric acid, activating the insulin IRS1/AKT/GLUT4 signaling pathway	Bound phenolics ensured the anti-hyperglycemic effect of rice bran dietary fibers.	(Zhang et al., 2020)
Wheat bran	A gel-like network with cavities, fissures, and holes on the surface	<i>In vivo</i> and <i>in vitro</i> / 15 healthy subjects (male: 7, female: 8, at age 22–32 years old) with mean body mass index of 21.4 kg/m ²	50 g/3 days	↑fermentability	↓digestibility ↑breath H ₂ ↓postprandial blood glucose	Wheat bran with microstructure modification improved glycemic response and sustain colonic fermentation	(Liu, Zhao, Wang, & Liu, 2020)
Wheat bran	High viscosity	<i>In vitro</i> /human feces (20 to 41 years old)	5, 10 and 20 g diluted in 300 mL of colonic contents (without rutin and with rutin)/0, 6, 24 h	–	↑3,4 diHPAA (rutin metabolite) at 24 h with an 2.3-fold increase	Eating fiber and polyphenols together was beneficial to human health with the phenolic acids and SCFAs production	(Havlik et al., 2020)
Wheat bran	Particle sizes: D50 = 53 μm (powdered) D50 = 350 μm (granulated)	<i>In vivo</i> /eight-week-old male Balb/c mice	4 weeks	↑α-diversity and β-diversity ↑ <i>Clostridiales</i>	↑acetic acid, propionic acid, and butyric acid ↑IgA	Wheat bran enhanced Tfh-mediated IgA production in the intestine by SCFA increment through the modulation of gut microbiota	(Matsuzaki et al., 2020)
Rice bran (heat-stabilized)	Glycan and arabinoxylan	<i>In vivo</i> /29 colorectal cancer survivors, more than four months post cancer treatment (e.g. chemotherapy or radiation)	0, 14, 28 days/30 g/day rice bran	↑ <i>Bacteroidetes</i> (<i>Bacteroides ovatus</i>) ↑ <i>Coprococcus</i> , <i>Lachnobacterium</i> ↓ <i>Firmicutes</i> , <i>Ruminococcus</i> , <i>Ethanoligenens</i> (after 14 days)	↑acetic and propionic (after 14 days)	Heat-stabilized rice bran modulated gut microbiota	(Sheflin et al., 2017)
Wheat bran	–	<i>In vivo</i> /male C57BL/6J mice (obesity model)	10% w:w/12 weeks	↑Microbial α-diversity	↑hepatic TGs and the higher hepatic ↑butyrate	Regulated hepatic lipid metabolism	(Graf et al., 2019)
Fermented rice bran	–	<i>In vivo</i> / male ICR mice (IBD model)	–	↑ <i>Bacteroides acidifaciens</i> , and Enterobacteriaceae (operational taxonomic units)	–	Ameliorated the symptoms of IBD	(Shibayama et al., 2018)
Whole-grain wheat products	–	<i>In vivo</i> /50 overweight 45 to 70 years old men and postmenopausal women	98 g·day ⁻¹ / 12 weeks	↑gut microbiota diversity	Prevented a substantial increase in intrahepatic TGs, ↓the lipid in the liver	Maintained live health	(Schutte et al., 2018)
Whole grain	–	<i>In vivo</i> /62 participants with increased waist circumference	26 weeks	↑ <i>Prevotella</i>	↓body fat (0.88–3.15 Kg)	Subjects with high P/B ratio appeared more susceptible to lose body fat on diets high in fiber and whole grain than subjects with a low P/B ratio	(Hjorth et al., 2018)
Whole grain	β-Glucan, arabinoxylan, and cellulose More soluble DFs	<i>In vivo</i> /49 subjects with overweight or obesity and low intakes of whole grains, fruit, and vegetable	6 weeks	No significant changes	↓ TNF-α↓LBP (- 3.7 pg/mL; p < 0.001)	Kept metabolic health in individuals affected by overweight or obesity with normally low intake of whole grains	(Kopf et al., 2018)
Rice bran (with <i>Lactobacillus paracasei</i>)	–	<i>In vitro</i> / <i>Salmonella</i> Typhimurium culture medium	16 h	↓ <i>Salmonella</i> Typhimurium	–	The metabolism by <i>Lactobacillus paracasei</i> increases antimicrobial activity against <i>Salmonella</i> Typhimurium	(Nealon et al., 2017)
Cereal products from wheat and rice	–	<i>In vitro</i> /infant feces	1% (w/v)/ 0, 24 and 48 h	↑ <i>Bacteroidaceae</i> , <i>Veillonellaceae</i> , <i>Bifidobacteriaceae</i> , <i>Lachnospiraceae</i> and <i>Lactobacillaceae</i> ↓ <i>Enterobacteriaceae</i>	↑butyrate	Altered the infant gut microbiota and increased the production of SCFAs	(Gamage, Tetu, Chong, Ashton, Packer, & Paulsen, 2017)

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Table 1 (continued)

Fiber sources	Physicochemical properties	Research methods/objects	Intervention intake/ time	Changes of bacteria	Other results	Conclusions	References
Whole grain	Mostly insoluble	<i>In vivo</i> /49 men and 32 postmenopausal women [age range: 40–65 years old, body mass index (in kg/m ²) < 35]	98 g·day ⁻¹ / 6 weeks	↓ <i>Enterobacteriaceae</i> ↑ <i>Lachnospira</i>	↑stool weight and frequency ↑acetate and total SCFAs	Had a modest effect on gut microbiota and immune	(Vanegas et al., 2017)
Wheat bran	Soluble arabinoxylan A linear backbone of xylose with arabinose as an attached monosaccharide	<i>In vivo</i> / seven-week-old male Balb/c mice, <i>in vitro</i> / splenocytes	100 mg/kg, 500 mg/kg, and 2500 mg/kg/4 weeks	–	↓IL-4 ↑IgA ↑splenic CD4 T cells	Affected systemic and intestinal immunity	(Choi et al., 2017)
Wheat bran	Insoluble non-starch polysaccharides, including arabinoxylan, cellulose, and β-glucan	<i>In vivo</i> / C57BL/6J mice (IBD model)	117 g·kg ⁻¹ / 28 days	↓ <i>Mucispirillum schaedleri</i> ↑ <i>Akkermansia muciniphila</i> ↑ <i>Dorea</i> , <i>Ruminococcus</i> and <i>Roseburia</i> spp.	↓food intake ↓IL-1β, IFN-γ, TNF-α (Th1 cytokines) ↓IL-17A (Th17 cytokines)↑butyrate↑total SCFAs	Improved intestinal health	(Jiminez et al., 2016)
Wheat bran	Insoluble	<i>In vitro</i> /fresh feces from four volunteers	0, 2, 4, 8, 24, 48, 72 h	↑ <i>Eubacterium xylanophilum</i> and <i>Butyrivibrio</i> spp., <i>Roseburia</i> spp.	↑ferulic acid	Breakdown of wheat bran involves specialist primary degraders	(Duncan et al., 2016)
Wheat bran	–	<i>In vivo</i> /female ICR mice (cadmium toxicity model)	100 g·kg ⁻¹ /8 weeks	↑Bacteroidetes (55.7%–70.7%)↓ Firmicutes (33.2%–23.1%) ↑Verrucomicrobia	↓Cd ↑propionate and butyrate	More effective against chronic Cd toxicity than traditional treatments	(Li et al., 2016)
Wheat bran	A mixture of arabinoxylan oligosaccharides (AXOSs), high-molecular-weight arabinoxylans, cellulose, and lignin	<i>In vivo</i> /male C57BL/6J mice (obese model)	20% w:w/10 weeks	↑Bacteroidetes↓Firmicutes	↓body weight and liver TGs ↑liver ROS ↓liver carbohydrate metabolites-glucose ↓hepatic arachidonic acid ↑liver and plasma β-hydroxybutyrate	Regulated hepatic metabolism concurrently with specific gut bacteria	(Kieffer et al., 2016)

“↑- increase; ↓ - decrease; IgA, immunoglobulin A; TNF-α, tumor necrosis factor-α; IL, interleukin; IFN-γ, interferon-γ; Th, regulate T helper; TGs, triglycerides; IBD, inflammatory bowel disease; ROS, reactive oxygen species; LBP, lipopolysaccharide binding protein; Cd, cadmium; w, weight; v, volume; P/B, *Prevotella/Bacteroides*.

macromolecular substances via various pathways (Aizawa et al., 2016; Schroeder et al., 2018). Arabinoxylans from Argentinian soft and hard wheat enhanced the growth of *Lactobacillus reuteri* ATCC23272 and *Bifidobacterium breve* 286 *in vitro* and exceed inulin serving as prebiotics (Paesani, Salvucci, Moiraghi, Fernandez Canigia, & Perez, 2019). *Staphylococcus aureus*, *Salmonella*, and several *Enterobacter* are considered as harmful bacteria, which cause diseases by producing spoilage metabolites in the degradation of proteins (Lehman et al., 2019; Velazquez et al., 2019). However, there is no exact boundary between harmful bacteria and beneficial bacteria. For instance, a double effect is existed in some neutral bacteria that are beneficial to health under normal circumstances, like *Escherichia coli* (Al-Zyoued, Nasereddin, Aljarajah, & Saket, 2019; Barroso-Batista et al., 2020).

There is a higher content of Firmicutes and lower content of Bacteroidetes in obese individuals than those in normal individuals. In other words, the ratio of Bacteroidetes and Firmicutes is closely related to some diseases, especially obesity. DFs could modulate gut microbiota by increasing the proportion of Bacteroidetes and Firmicutes (Han et al., 2018; Li, Liu, Shen, & Liu, 2016). DFs could increase the abundance of *Bacteroides acidifaciens* and Enterobacteriaceae (operational taxonomic units) associated with inflammatory bowel disease (Shibayama et al., 2018), inhibit the growth of *Salmonella* (Kumar et al., 2012), and stimulate the growth of butyrogenic bacteria and Verrucomicrobia (Li et al., 2016). Additionally, wheat bran diets can increase the abundance of *Clostridiales* in the mice, which contains the bacteria related to polysaccharide degradation and SCFAs production (Matsuzaki et al., 2020).

Akkermansia muciniphila is a dominant bacterium belonging to Verrucomicrobia, colonized on the outer layer of intestinal mucus (Ottman, Geerlings, Aalvink, de Vos, & Belzer, 2017). Recent studies have shown that *Akkermansia muciniphila* is a new important contributor involved in metabolic syndrome, immune function, and gut permeability (Cani & de Vos, 2017; Chelakkot et al., 2018; Depommier et al., 2019; Ottman et al., 2017). The abundance of *Akkermansia muciniphila* was higher in the colonic digesta of rats with wheat diets than that with rice diets (Han et al., 2018). *Prevotella* is related to the improvement of glucose tolerance, whose abundance can be modulated with high fiber intake from DFs (Kovatcheva-Datchary et al., 2015). Interestingly, the ratio of *Prevotella* and *Bacteroides* may influence the fermentation of DFs. Diets rich in DFs lead to a high ratio of *Prevotella* and *Bacteroides*, which helps individuals to lose body fat (Hjorth et al., 2018). In summary, DFs-rich diet intervention mainly caused changes in Firmicutes, Verrucomicrobia, Enterobacteriaceae, *Prevotella*, and *Bacteroides*. DFs possess prebiotic activity of selectively modulating the abundance of bacteria in the gut.

4.2. Effect of metabolites on gut microbiota in host health

The production of metabolites during DFs fermentation by microbes can maintain gut health and intestinal homeostasis. It can be detected and analyzed by gas chromatography and metabolomics. DFs can stimulate the growth of beneficial bacteria, and then the corresponding bacteria can produce beneficial metabolites, like SCFAs. As typical and critical metabolites, SCFAs mainly include acetate, propionate, and butyrate, which account for more than 95% of the total content (Cummins, Pomare, Branch, Naylor, & Macfarlane, 1987; Koh, De Vadder, Kovatcheva-Datchary, & Backhed, 2016). SCFAs individually elicit positive effects on the gut. SCFAs are considered as an important energy source for intestinal epithelial cells to regulate gut barrier function (Liu et al., 2018; Makki, Deehan, Walter, & Backhed, 2018). Pyruvate is a source for acetate production through two pathways: acetyl-CoA by Enterobacteria and Wood-Ljungdahl by acetogens. Acetate plays a key role in regulating appetite, promoting fat oxidation, and improving immune function (Frost et al., 2014; van der Beek et al., 2016). Some acetate can be transformed into butyrate by luminal bacteria. Propionate can be synthesized through three pathways, including succinate, acrylate, and propanediol pathways. The succinate pathway is the most common path for propionate formation, involving the participation of

Bacteroidetes and several harmful bacteria (Reichardt et al., 2014). Propionate improves pancreatic function and modulates hepatic lipid metabolism (Chambers et al., 2019; Pingitore et al., 2017). Butyrate is an important metabolite produced by Acetyl-CoA via Firmicutes (Louis, Hold, & Flint, 2014). Butyrate can ameliorate the gut mucosal barrier by enhancing tight junction protein expression and stimulating mucus secretion (Czajkowska & Szponar, 2018; Gaudier, Rival, Buisine, Robineau, & Hoebler, 2009; Ploeger et al., 2012; Wrzosek et al., 2013). It also could upregulate the expression of regulatory T-cells (Tregs) via inhibiting histone deacetylase enzyme (Furusawa et al., 2013).

Besides, there are many other metabolites produced by microbes after DFs intervention, including amino acid, peptide, carbohydrate, lipid, nucleotide, cofactor, and vitamin, phytochemical, and several gases (Canfora et al., 2019; Folkerts et al., 2018; Nealon, Worcester, & Ryan, 2017). Some can act as substrates of synthesizing nutrient components and supplying energy. The secreted proteins by probiotics have been found to protect the intestinal barrier by inhibiting the growth of pathogens (Liu et al., 2020). Some metabolites have been confirmed to benefit host metabolism. Other products of DFs fermentation like indole and enterolactone can also lower the risk of type 2 diabetes (Sun et al., 2014; Tuomainen et al., 2018). Indole promotes intestinal epithelium function by attenuating tumor necrosis factor α -mediated Nuclear factor-kappa B activation and Interleukin-8 secretion (Bansal, Alaniz, Wood, & Jayaraman, 2010). Especially, symbiotic *E. coli*-secreted indole can attenuate the adherence of pathogenic *E. coli* by increasing the impression of adhesion junctions and tight junctions, which enhance the intestinal barrier function (Bansal et al., 2010).

As shown in Table 1, DFs promote the concentration of butyrate. It is probably because DFs can promote the growth of butyrate-producing bacteria, including Firmicutes, *Dorea*, *Ruminococcus*, *Roseburia* spp., and *Lachnospiraceae* (Antharam et al., 2013; Vanegas et al., 2017). *Roseburia* spp. is the most abundant butyrate-producing bacteria accounting for 0.9–5.0% of the total microbiota (Hiippala et al., 2018). *Roseburia* has a positive effect on colonic health maintenance and metabolic diseases, including obesity and type 2 diabetes (Tamanai-Shacoori et al., 2017). Furthermore, butyrate can stimulate the production of mucus-associated bacteria to enhance the intestinal barrier function in the host. *Mucispirillum shaedleri* is a mucus-associated bacterium (Berry et al., 2012; Robertson et al., 2005). Besides, butyrate can improve inflammatory symptoms by lowering the concentration of related inflammatory cytokines and regulating Tregs activation (Jiminez, Uwiera, Abbott, Uwiera, & Inglis, 2016).

5. The possible mechanism of DFs from rice bran and wheat bran and their metabolites on maintaining host gut health

DFs can maintain host gut health via modulating gut microbiota through multiply mechanisms, including the production of metabolites, regulation of the immune system, and enhancement of gut barrier function (Flint, Scott, Louis, & Duncan, 2012). The fermentation of DFs and metabolic product-SCFAs create a harmonious intestinal microbial environment. DFs can promote the abundance of particular bacteria, which attenuated inflammation and strengthened the epithelial barrier to maintain gut health. Then SCFAs can be further recognized and received by relevant cells to regulate the immune system by inhibiting the activity of neutrophils, macrophages, dendritic cells, and effector T cells and promoting the activity of Tregs, particularly butyrate (Goncalves, Araujo, & Di Santo, 2018). In addition, there are generally three ways of SCFAs entering cells-passive diffusion, mediating vector transportation via SMCT1/Slc5a8, MCT1/Slc16a1 pathways, and activating G-protein-coupled receptors (GPCR) (Sun, Wu, Liu, & Cong, 2017). The G-protein-coupled receptors activating plays a critical role in regulating the immune system (Kim, Kang, Park, Yanagisawa, & Kim, 2013; Macia et al., 2015), decreasing some cytokines like Th1 (IL-1 β , IFN- γ , TNF- α), Th17 (IL-17A) (Jiminez et al., 2016), and Th2 (IL-4) (Choi, Lee, Lee, Lee, Jeong, & Kang, 2017), and increasing an anti-inflammation cytokine (IL-

18), which is related to mucins production and gut microbiota composition regulation (Levy et al., 2015; Macia et al., 2015; Singh et al., 2014). DFs intervention can also stimulate the secretion of IgA in the intestine (Choi et al., 2017; Matsuzaki et al., 2020), which is considered as a significant antibody to maintain a balance in gut microbiota (Kawamoto et al., 2014). IgA is secreted by producing IgM in the intestinal secondary lymphoid tissues such as Peyer's patches through activating B cells (Gutzeit, Magri, & Cerutti, 2014), which may be stimulated by T follicular helper (Tfh) cells from Tregs (Foxp3 +) differentiation with SCFAs production (Chung et al., 2011; Matsuzaki et al., 2020).

DFs and their metabolites can also enhance the intestinal barrier function and improve gut permeability together by improving the abundance and growth of mucus-associated bacteria. These bacteria play a fundamental role in human health and disease by resisting the invasion of pathogenic substances (Desai et al., 2016; Vancamelbeke & Vermeire, 2017). The gut permeability can be adjusted by tight junctions

(Chelakkot et al., 2018) and mucins (Bhatia et al., 2019), in which tight junctions are intercellular junctions that can connect the epithelial cells tightly together (Ulluwishewa, Anderson, McNabb, Moughan, Wells, & Roy, 2011), and mucins are the major components produced by goblet cells in mucus layer (Ma, Rubin, & Voynow, 2018). Tight junctions and mucins can be regulated by some bacteria like *Akkermansia muciniphila* colonized on the intestinal mucus (Chelakkot et al., 2018). Additionally, DFs and their metabolites can upregulate particular cytokines to promote mucins production, like IL-18 mentioned above.

The possible mechanisms involved in DFs associated-beneficial activities are summarized in Fig. 3, including inflammation improvement and intestinal barrier enhancement (Goncalves et al., 2018; Jiminez et al., 2016; Sun et al., 2017). In conclusion, DFs from rice bran and wheat bran and their metabolites appear to be mutual and simultaneous during the fermentation of DFs.

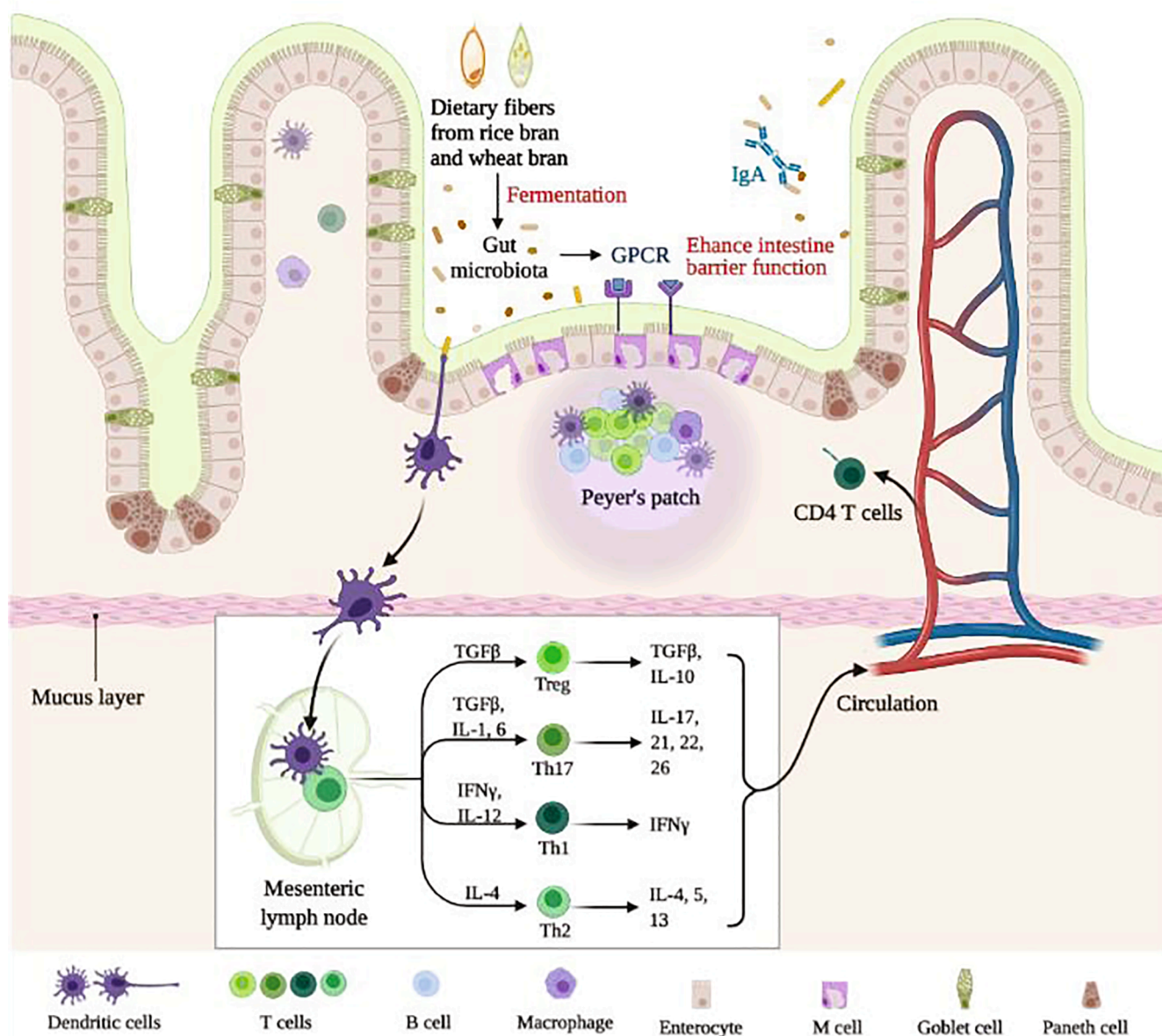


Fig. 3. The possible mechanisms involved in DFs from rice bran and wheat bran and their metabolites associated beneficial activities including attenuating inflammation and strengthening the intestinal barrier.

6. Conclusions

It has been demonstrated that whole grain consumption is an ideal diet with many gut health-promoting benefits. The physicochemical properties of DFs from rice bran and wheat bran, such as particle size, molecular weight, branch degree, monosaccharide and linkage composition, solubility, viscosity, and hydration properties, have a close relationship with their digestive behaviors. DFs from rice bran and wheat bran and their metabolites—SCFAs have beneficial effects on host gut health by selectively regulating gut microbiota, including improving some particular bacteria, like butyrate-producing and mucus-associated bacteria. DFs and their metabolites could enhance gut barrier function and immune function by regulating some bacteria associated with inflammatory and gut barriers. The mechanism of diverse biological activities of DFs by regulating intestinal flora remains to be further studied. To sum up, DFs from rice bran and wheat bran are natural, prebiotic, and promising ingredients with various benefits to host gut health. Whole grain consumption will be a global and popular diet in the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was supported by Fund of Key Laboratory of Aquatic Product Processing, Ministry of Agriculture and Rural Affairs, China (NYJG201902), National Natural Science Foundation of China (31972011 and 3211101620), Excellent Youth Foundation of Guangdong Scientific Committee (2021B1515020037), Natural Science Foundation of Guangdong Province (2019A1515011670), Guangzhou Science and Technology Program (201907010035), and Program of Department of Natural Resources of Guangdong Province (GDNRC [2021]53 and GDNRC [2021]49).

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