Effects of Dietary Fiber on Porcine Intestinal Barrier Function: Postprint

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Abstract

The intestinal barrier primarily comprises the normal gut microbiota, mucus layer, intestinal epithelial cells, and immune barrier, whose function is intimately associated with diet. Dietary fiber refers to carbohydrates that cannot be digested and absorbed by endogenous digestive enzymes in the mammalian intestine, commonly known as non-starch polysaccharides (NSP), which mainly include cellulose, hemicellulose, lignin, and -glucan. Dietary fiber exerts multiple beneficial effects, including enhancing the intestinal mucosal barrier, improving microbial community structure, and modulating the ratio of probiotics to pathogenic bacteria. This review summarizes the effects of dietary fiber on intestinal barrier function in pigs and the underlying mechanisms, aiming to promote the rational and effective utilization of fiber in swine production.

Full Text

Effects of Dietary Fiber on Intestinal Barrier Function in Pigs

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Abstract

The intestinal barrier comprises four main components: the normal gut microbiota, mucus layer, intestinal epithelial cells, and immune barrier. Its function is intimately linked to dietary composition. Dietary fiber refers to carbohydrates that cannot be digested and absorbed by mammalian endogenous digestive enzymes, commonly known as non-starch polysaccharides (NSP), which primarily

include cellulose, hemicellulose, lignin, and -glucan. Dietary fiber enhances intestinal mucosal barrier function, improves microbial community structure, and optimizes the ratio of beneficial to pathogenic bacteria. This review summarizes the effects and underlying mechanisms of dietary fiber on intestinal barrier function in pigs, aiming to promote the rational and effective utilization of fiber in swine production.

Keywords: fiber; pigs; intestinal barrier; gut microbiota

The intestine is a vital organ for digestion and immunity, determining not only nutrient digestion and absorption but also playing a crucial role in defending against pathogenic microorganisms, maintaining immune status, and ensuring overall health. Characterized by low digestibility and low energy value, fiber has traditionally been viewed in pig production as reducing feed digestibility, diluting nutrient concentrations, and impairing growth performance. Consequently, numerous studies have investigated the use of exogenous enzymes to digest cellulose or hemicellulose that pigs cannot break down endogenously, aiming to mitigate fiber' s negative effects on growth. However, emerging research reveals that fiber and its metabolites exert significant positive effects on porcine intestinal health, particularly in modulating gut microbiota and enhancing intestinal immunity. This review examines fiber' s regulatory effects on the intestinal barrier and related mechanisms to advance understanding and scientific application of dietary fiber.

1.1 Definition of Fiber

Fiber is widely present in various plant feedstuffs and possesses complex composition, which has precluded a precise, universally accepted definition to date. Hipsley first defined fiber in 1953 as "the indigestible portion of plant cell walls" [1]. In 2001, the American Association of Cereal Chemists (AACC) defined fiber as edible carbohydrates and analogous substances that resist digestion by intestinal enzymes in the small intestine but can be fermented by certain microorganisms in the large intestine. Despite historical variations in definition, scholars universally recognize its core characteristic: plant substances that escape digestion and absorption in the small intestine but can be fermented by microorganisms in the large intestine.

1.2.1 Viscosity

Viscosity critically influences fiber functionality. The viscous properties of fiber arise from the intertwining of polysaccharide molecules through covalent or noncovalent bonds, forming network structures that impart viscosity to aqueous solutions. Viscosity depends primarily on molecular weight and side chains of polysaccharides. Generally, insoluble fibers such as cellulose and lignin exhibit low viscosity, whereas soluble fibers like arabinoxylan and pectin display high viscosity [2].

1.2.2 Hydration Properties

Fiber hydration encompasses water solubility and water-holding capacity. Water solubility, a key criterion for fiber classification, refers to the ability of fiber to form colloidal suspensions when combined with water [3]. Based on solubility, fiber is categorized as soluble or insoluble; lignin and cellulose are insoluble, while guar gum and pectin are soluble. Water-holding capacity, defined as the mass of water absorbed per unit mass of fiber, reflects the binding affinity between fiber and water [4]. Both soluble and insoluble fibers demonstrate strong water-holding capacity, though insoluble fiber typically exhibits lower capacity than soluble fiber.

1.2.3 Fermentability

Fiber fermentability varies with its source and degree of lignification. Different fiber sources exhibit distinct fermentability profiles, with highly lignified fibers showing low fermentability. For instance, pectin is highly fermentable, whereas lignin is virtually non-fermentable. Generally, higher lignification corresponds to lower fermentability. Dietary fiber cannot be digested by monogastric animal endogenous enzymes and is only fermented by microorganisms in the large intestine to produce short-chain fatty acids (SCFAs) for utilization. The total amount and types of SCFAs produced through fiber fermentation vary depending on the fiber source.

2 Effects of Dietary Fiber on Intestinal Barrier Function

The intestine serves as both a critical site for nutrient digestion and absorption and the first line of defense against foreign substances. It separates the luminal environment from internal tissues, protecting the body from dietary antigens, pathogenic microorganisms, and their harmful metabolites, thereby maintaining homeostasis. The intestinal barrier comprises four main components: normal gut microbiota, mucus layer, intestinal epithelium, and intestinal immune system [Figure 1: see original paper] [5].

SIgA: secretory immunoglobulin A.

Fig.1 Intestinal barrier function[5]

2.1 Effects on Normal Gut Microbiota

The intestinal tract harbors a complex and relatively stable ecosystem containing vast bacterial populations. Bacterial counts are lower in the small intestine, with approximately 10^3–10 cells/mL in the duodenum and about 10 cells/mL in the terminal ileum [6]. In contrast, the large intestine contains substantially more bacteria, approximately 10^{11} cells/mL [6], representing over 500 species [7]. The gut microbiota constitutes a vital component of the intestinal defense barrier and plays a crucial role in host health. Under normal conditions, various

microbial genera constrain and depend on each other, maintaining a balanced microecosystem and healthy physiological state.

Dietary fiber influences not only the quantity and diversity of intestinal microorganisms but also their activity. Research demonstrates that adding 4% wheat bran to weaned piglet diets reduces *Escherichia coli* counts in ileal digesta while increasing *Lactobacillus* populations [8]. Owusu-Asiedu et al. [9] reported that compared with a control diet, a 7% soluble guar gum fiber diet significantly increased total aerobes, total anaerobes, lactobacilli, clostridia, and enterobacteria in the ileum of growing pigs, whereas a 7% insoluble cellulose fiber diet markedly elevated bifidobacteria and enterobacteria, with modest increases in total aerobes and anaerobes. In finishing pigs, Che et al. [10] found that pea fiber diets significantly increased colonic *Lactobacillus* populations without significantly affecting bifidobacteria or *E. coli*. Chen et al. [11] observed in weaned piglets that pea fiber significantly increased colonic *Lactobacillus* counts, while wheat bran fiber significantly increased bifidobacteria; both fiber types reduced colonic *E. coli* compared with soybean fiber. These results indicate that different fiber types exert distinct regulatory effects on gut microbiota, with soluble fiber generally promoting microbial proliferation more effectively than insoluble fiber.

Insoluble fiber can be partially utilized by intestinal microorganisms, thereby influencing microbial abundance and activity. Wang et al. [12] supplemented finishing pig diets with 10% insoluble alfalfa meal and reported that the relative abundance of the dominant phylum *Firmicutes* increased from 79.84% in the control group to 81.28% in the 10% alfalfa meal group, while the second dominant phylum *Bacteroidetes* decreased from 8.33% to 7.56%. Haenen et al. [13] demonstrated that resistant starch supplementation increased the relative abundance of *Faecalibacterium prausnitzii* and *Megasphaera elsdenii* in the colon while reducing pathogenic microorganisms such as *Leptospira*. Moreover, measuring ATP concentration revealed that microbial activity in the hindgut increased 5–6-fold in pigs fed high-fiber diets. Studies have identified highly active fibrolytic and hemicellulolytic bacteria in porcine gut microbiota, including *Ruminococcus albus*, *Butyrivibrio* spp., and *Fibrobacter succinogenes* [14]. These microorganisms obtain energy for growth through fiber fermentation, and the resulting SCFAs, particularly butyrate, can be absorbed and utilized by intestinal epithelial cells.

2.2 Effects on Intestinal Mucus Layer

The intestinal mucus layer consists of an outer and inner layer. The outer layer, adjacent to the intestinal lumen, is relatively thin and serves as a habitat for commensal bacteria. The inner layer, closely attached to the intestinal epithelium, is dense and forms a barrier that separates bacteria from epithelial cells, protecting the intestine from bacterial and mechanical damage. Thus, mucus layer impairment directly threatens intestinal health. Mucus comprises water, inorganic salts, and mucins secreted by goblet and intestinal epithelial cells,

along with trefoil factors, secretory immunoglobulin A (SIgA), and various cytokines [7]. The mucus layer is dynamic, regulated by goblet cell synthesis and secretion of mucins to maintain homeostasis [15]. Intestinal trefoil factor, a small peptide secreted by goblet cells, binds to mucus glycoproteins to form stable gel complexes that enhance the defensive barrier function and reduce damage from harmful substances or mechanical forces. Fiber can enhance intestinal barrier function by increasing goblet cell numbers, promoting mucin secretion, and elevating trefoil factor levels.

Zhou et al. [16] reported that high resistant starch diets significantly increased colonic mucin levels compared with control diets. Vila [17] demonstrated that both corn fiber and wheat bran fiber significantly increased mucin 2 levels in the ileum and colon of pigs. Che et al. [10] found that pea fiber diets increased colonic mucin levels by 16% compared with controls. Chen et al. [18] observed in weaned piglets that wheat bran fiber significantly increased ileal goblet cell numbers and colonic trefoil factor levels, while pea and soybean fibers also increased goblet cell numbers, albeit non-significantly.

2.3 Effects on Intestinal Epithelium

Intestinal epithelial cells selectively absorb luminal substances through selective permeability, representing a critical component of the mucosal barrier. While permitting nutrient absorption, this barrier prevents pathogenic microorganisms and toxic substances from entering the body [19]. Intercellular connections include tight junctions, adherens junctions, gap junctions, and desmosomes, among which tight junctions—composed of multiple interacting proteins—play a pivotal role in nutrient absorption and pathogen defense by regulating epithelial permeability and cell proliferation [20].

Villus height and crypt depth in the small intestine are important indicators of intestinal permeability. An increased villus height-to-crypt depth ratio signifies improved mucosal function and enhanced absorptive capacity [20]. Zhang et al. [21] reported that dietary supplementation with 7.5% rice bran significantly increased the jejunal villus height-to-crypt depth ratio in finishing pigs. Wu et al. [22] demonstrated that inulin fiber and microcrystalline cellulose significantly increased ileal villus height, while microcrystalline cellulose reduced duodenal crypt depth and inulin fiber increased the ileal villus height-to-crypt depth ratio. Both fiber types also significantly increased colonic epithelial goblet cell numbers. Research indicates that wheat and pea fiber diets significantly increased mRNA expression of the tight junction protein zonula occludens 1 (ZO-1) and Toll-like receptor 2 in ileal and colonic epithelial cells [18].

2.4 Effects on Intestinal Immune Function

The intestinal immune system comprises diffusely distributed immune cells (e.g., macrophages, dendritic cells) and molecules (e.g., SIgA, cytokines) within the mucosal epithelium and lamina propria, as well as gut-associated lymphoid tis-

sues such as Peyer' s patches [23]. This system plays a vital role in defending against bacterial, viral, and toxin invasion. Upon stimulation, the intestinal immune system secretes immunoglobulins, interferons, and interleukins to maintain intestinal health through immunomodulation. SIgA, produced by B cells differentiating into plasma cells and secreted across intestinal epithelial cells into the lumen, is a crucial component of intestinal immunity [24]. SIgA not only neutralizes viruses and toxins but, more importantly, prevents bacterial adhesion to epithelial surfaces.

Studies show that long-term feeding of pea fiber diets significantly increased colonic mucosal SIgA content in pigs, thereby enhancing mucosal immune function [10]. In weaned piglets, pea fiber significantly increased colonic mucosal major histocompatibility complex class II and transforming growth factor- levels compared with controls [11]. A key mechanism by which fiber modulates intestinal immunity involves its fermentation products—SCFAs. SCFAs promote secretion of pro-inflammatory cytokines interleukin-6 (IL-6) and tumor necrosis factor- (TNF-), as well as anti-inflammatory cytokine interleukin-10 (IL-10) and chemokine monocyte chemoattractant protein-1 (MCP-1), thereby strengthening intestinal immune barrier function [25].

3 Mechanisms of Fiber Regulation on Intestinal Barrier

Microbial modulation represents a primary pathway through which fiber regulates intestinal barrier function. The four barrier components—gut microbiota, mucus layer, intestinal epithelium, and mucosal immunity—are interrelated and mutually influential. First, gut microbial metabolism produces SCFAs and can degrade the mucus layer under certain conditions. Second, mucus layer alterations directly affect intestinal epithelial integrity and permeability. Third, SCFAs directly influence immune barrier function and epithelial cell proliferation. Consequently, impairment of any single barrier component disrupts overall barrier function, as illustrated in [Figure 2: see original paper].

Dietary fiber influences gut microbiota through two mechanisms: first, through its water-holding capacity, which increases digesta moisture content and reduces gastrointestinal transit time; second, by serving as a direct or indirect energy source for specific microorganisms, thereby increasing microbial quantity, abundance, and activity to enhance the microbial barrier. Additionally, fiber fermentation by gut microbiota produces SCFAs that promote microbial growth and intestinal immune function. This process not only provides energy for microbial survival but also reduces hindgut pH and promotes intestinal epithelial cell proliferation [26]. The lowered pH creates a favorable environment for beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*, promoting their proliferation and enabling them to become dominant populations that occupy intestinal niches, thereby inhibiting pathogen expansion and preventing colonization. Generally, soluble fiber is extensively fermented, whereas insoluble fiber exhibits low fermentability and is primarily fermented in the distal gut, though it increases digesta water-holding capacity and reduces gastric emptying time [28], thereby

decreasing opportunities for harmful bacteria to exert toxic effects. Numerous studies demonstrate that dietary fiber increases the relative abundance of beneficial bacteria while reducing potential pathogens, favoring the establishment of a healthy microbiota that maintains intestinal health. Different fibers possess distinct structural features—including monosaccharide types, glycosidic linkages, conformations, and configurations—that determine their selective stimulation of specific microorganisms [29].

FIGURE:2 Dietary fiber' s regulatory effects on intestinal barrier

Furthermore, fiber influences the mucus layer through microbial interactions. Desai et al. [30] demonstrated that fiber and colonic mucus barrier interact bidirectionally: in fiber-deprived conditions, gut microbiota can utilize colonic mucus glycoproteins as a nutrient source, leading to corrosive degradation of the mucus barrier ([Figure 3: see original paper]). These mucus-degrading microbes increase intestinal epithelial permeability and susceptibility to lethal colitis induced by *Citrobacter*. This finding underscores the critical role of microbiota in fiber' s effects on the mucus layer and epithelium.

FIGURE:3 Model of how a fiber-deprived gut microbiota mediates degradation of the colonic mucus barrier and heightened pathogen susceptibility[30]

While fiber itself does not directly modulate intestinal immunity, its metabolite SCFAs directly affect immune function and epithelial cell proliferation. SCFAs provide 60–70% of the energy required by colonic epithelial cells, with butyrate being the most significant contributor [31]. Studies show that long-term pea fiber feeding significantly increased acetate, propionate, butyrate, and total SCFA concentrations in cecal digesta of weaned piglets, and significantly elevated acetate and total SCFA levels in finishing pigs [32]. Carneiro et al. [33] reported that wheat fiber significantly reduced cecal and colonic pH while increasing cecal acetate and butyrate and colonic butyrate concentrations.

SCFAs primarily participate in immune regulation by inhibiting histone deacetylase (HDAC) activity and activating G protein-coupled receptors (GPRs), with butyrate serving as the main effector [34]. Histone acetylation generally facilitates DNA-histone octamer dissociation, relaxes nucleosome structure, and enables transcription factors to bind DNA, thereby activating gene transcription. Histone deacetylation produces the opposite effect. In the nucleus, histone acetylation and deacetylation are dynamically balanced and co-regulated by histone acetyltransferases (HAT) and HDAC. HAT transfers acetyl groups from acetyl-CoA to specific lysine residues on histone N-termini, whereas HDAC removes acetyl groups, enabling tight binding with negatively charged DNA, chromatin condensation, and transcriptional repression. Studies demonstrate that sodium butyrate, an HDAC inhibitor (HDACi), plays a crucial role in gene transcription [35]. Sodium butyrate inhibits HDAC activity, thereby activating the activator protein 1 (AP-1) signaling pathway in intestinal epithelial cells to modulate release of inflammatory factors including IL-2, IL-6, IL-8, and TNF- , ultimately exerting positive immunomodulatory effects [36].

GPRs play important roles in inflammatory responses. Research indicates that sodium butyrate regulates monocyte function through GPR43 and GPR41 to exert anti-inflammatory effects [37]. GPR activation triggers multiple transcription factors, including cAMP response element binding protein (CREB), c-Jun, nuclear factor- B (NF- B), and signal transducer and activator of transcription 3 (STAT3). These receptors influence macrophage migration and aggregation at inflammatory sites, thereby modulating inflammation and facilitating macrophage recognition and phagocytosis of foreign substances. Studies show that sodium butyrate influences the MEK-ERK downstream pathway through GPRs to promote secretion of the antimicrobial peptide LL-37, thereby suppressing inflammatory responses [23]. Additionally, sodium butyrate effectively regulates T lymphocyte function through GPR43, significantly reducing pro-inflammatory IL-2 levels while increasing anti-inflammatory IL-4 levels [38], ultimately inhibiting inflammation and maintaining intestinal health.

4 Summary

Different fiber types exert distinct regulatory effects on porcine intestinal barrier function. Accumulating evidence demonstrates that dietary fiber plays a significant role in enhancing intestinal barrier function and promoting gut health. Moreover, the various barrier components are tightly interconnected and mutually influential. Although fiber research in pigs has gained increasing attention in recent years, several challenges remain: (1) The mechanisms underlying fiber's regulation of intestinal barrier function, particularly regarding immune modulation, require further elucidation; (2) A comprehensive and quantifiable standard for using different fiber types is still lacking.

In conclusion, continued in-depth, comprehensive, and systematic investigation into fiber' s improvement of porcine intestinal health and its regulatory mechanisms is essential for achieving antibiotic alternatives, promoting sustainable swine production, ensuring food safety, and protecting the environment.

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Note: Figure translations are in progress. See original paper for figures.