Research Progress on the Effects of Probiotics on Nutrient Digestion, Absorption, and Hepatic Metabolism in Animals: Postprint

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Abstract

Probiotics are live microorganisms that confer health benefits to the host by improving gut microecological balance, and they are widely applied as feed additives in animal husbandry. Probiotics can not only promote the digestion and absorption of nutrients in the gastrointestinal tract, thereby improving animal production performance, but also regulate organismal metabolism and effectively prevent metabolic diseases. This paper summarizes recent research progress at home and abroad regarding the effects of probiotics on nutrient digestion and absorption in animals and hepatic metabolism, with the aim of providing a theoretical foundation for the application of probiotics in livestock and poultry production.

Full Text

Research Progress on the Effects of Probiotics on Animal Nutrient Digestion, Absorption, and Liver Metabolism

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Abstract: Probiotics are live microorganisms that confer health benefits to the host by improving intestinal microecological balance, and they have been widely used as feed additives in livestock production. Probiotics not only enhance the digestion and absorption of nutrients in the gastrointestinal tract to improve animal performance, but also regulate host metabolism and effectively prevent metabolic diseases. This review summarizes recent research progress on the effects of probiotics on nutrient digestion, absorption, and liver metabolism in animals, aiming to provide theoretical evidence for the application of probiotics in livestock and poultry production.

Keywords: probiotics; intestine; liver; digestion and absorption; metabolism

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The intestine serves as the primary site for food digestion and absorption, and its digestive and absorptive functions directly determine nutrient utilization efficiency, thereby affecting animal growth. The intestinal mucosa also acts as a crucial barrier against invasion by microorganisms and harmful substances. The liver is the central metabolic organ in animals, and disruption of its metabolic homeostasis can lead to metabolic syndrome. Probiotics are defined as live microbial feed additives that benefit the host by enhancing intestinal microecological balance [1], with common strains including *Lactobacillus plantarum*, *Streptococcus thermophilus*, *Enterococcus faecium*, *Bifidobacterium*, and *Bacillus subtilis* [2]. As microecological preparations, probiotics have been widely applied in livestock and aquaculture, and their growth-promoting effects and underlying mechanisms have become research hotspots in recent years. Numerous studies have demonstrated that probiotics can improve livestock performance, and their growth-promoting mechanisms are closely associated with improved intestinal microbial balance and mucosal structure [3], enhanced nutrient digestion, absorption, and metabolism [4], strengthened intestinal mucosal immune function [5], inhibition of pathogenic infections, and maintenance of intestinal health [6]. This article reviews recent research on the effects of probiotics on animal nutrient digestion, absorption, and liver metabolic function.

1.1 Effects of Probiotics on Intestinal Digestive and Absorptive Enzymes

The small intestine is the main site for nutrient digestion and absorption, where dietary nutrients including carbohydrates, proteins, and fats undergo extracellular digestion through the action of microorganisms and various digestive enzymes. The digested end products are then absorbed into the bloodstream through various transporters on intestinal epithelial cells [7]. Impaired nutrient digestion and absorption can cause various diseases such as diarrhea, constipation, and abdominal distension or pain [8]. Microbial communities enriched in the proximal small intestine exhibit tolerance to bile acids and low pH, thereby utilizing dietary nutrients to promote their digestion and absorption. Studies have shown that certain intestinal microorganisms can decompose carbohydrates and proteins due to their enrichment in genes encoding amylases and proteases [9]. Numerous studies have demonstrated that feeding probiotics to different animals can significantly increase the populations of *Bifidobacterium*, *Lactobacillus*, and *Streptococcus* in the colon and cecum [10-11]. Therefore, probiotics can promote nutrient digestion by improving intestinal microbial structure. Additionally, dietary probiotic supplementation can enhance digestive enzyme activities in intestinal contents of aquatic animals [12], poultry [13], and pigs [14]. Huang [14] found that pancreatic digestive enzyme activities in suckling piglets increased with age, and confirmed that *Lactobacillus delbrueckii* (viable count 5×10 CFU/mL) could regulate the mRNA expression of pancreatic lipase and protease, thereby promoting enzyme synthesis and secretion and increasing feed intake. These findings indicate that probiotics can promote animal nutrient digestion by regulating enzyme gene transcription levels or digestive enzyme activities.

Nutrient absorption is the process by which digested food products, water, and electrolytes pass through digestive tract mucosal epithelial cells into blood and lymph. Among different digestive tract segments, the esophagus has no absorptive function, the gastric mucosa can only absorb alcohol and small amounts of water, and the large intestine generally absorbs only water and inorganic salts. Consequently, the small intestine is the primary site for nutrient absorption. Four mechanisms exist for nutrient transport across intestinal epithelial cells: passive transport, membrane transport, carrier-coupled transport, and paracellular pathway transport [15-16]. Polysaccharides and oligosaccharides must first be broken down into disaccharides by digestive enzymes, then further hydrolyzed into monosaccharides by disaccharidases (lactase, sucrase, and maltase) before absorption [17]. Probiotics can increase the activities of digestion- and absorption-related enzymes in intestinal mucosa. Dietary supplementation with *Bacillus* and *Lactobacillus* (6×10 CFU/g) effectively alleviated LPS-induced decreases in jejunal lactase activity and increases in ileal sucrase activity in piglets [18]. Dubey et al. [19] found that oral administration of probiotic GS4 (1.1×10 CFU/mL) significantly mitigated azoxymethane-induced reductions in intestinal mucosal sucrase and lactase activities and restored brush border structure in mice. Barrenetxe et al. [20] demonstrated that dietary *Lactobacillus casei* and *Bifidobacterium* (10 CFU/mL) significantly increased maltase, sucrase, and aminopeptidase N activities, enhancing intestinal epithelial absorption of monosaccharides and small peptides.

Fat absorption differs considerably from carbohydrate and protein absorption. Under the action of lipase, fats form fatty acids and monoglycerides, which combine with bile salts to form mixed micelles. These micelles then enter absorptive cells through diffusion via microvilli gaps, eventually forming chylomicrons that are transported through lymphatic vessels throughout the body [21]. Although few studies have reported on probiotics' effects on fat absorption, Ueda et al. [22] found that oral administration of *Pediococcus acidilactici* reduced serum triglyceride levels, consistent with the findings of Wang et al. [23], suggesting that probiotics can reduce fat accumulation. The potential mechanism may involve inhibition of intestinal fat absorption or enhancement of fat catabolism pathways by *P. acidilactici.*

Other enzymes such as alkaline phosphatase (AKP), Na /K -ATPase, and -glutamyl transpeptidase (-GT) also participate in nutrient absorption and transport. AKP plays a critical role in maintaining intestinal homeostasis, barrier function, and host health, with both diet and intestinal microorganisms influencing its expression and activity [24]. Na /K -ATPase is particularly important for maintaining glucose transport mediated by Na -dependent transporters such as sodium-glucose cotransporter 1 (SGLT1). -GT primarily participates in the uptake and transport of amino acids and small peptides in cells [25]. Dietary supplementation with *Bacillus* or *Lactobacillus* can ameliorate LPS-induced decreases in duodenal and jejunal mucosal AKP activity [18], effectively alleviating intestinal injury and improving intestinal health. Probiotic supplementation can also increase Na /K -ATPase mRNA expression in broiler ileal mucosa [26] and -GT activity in jejunal and ileal mucosa [27], further demonstrating that probiotics promote intestinal absorption of small peptides.

1.2 Effects of Probiotics on Intestinal Absorption Transporters

The small molecular nutrients produced by digestion must be transported into cells by corresponding transporters in the intestine and other tissues before being utilized by the body. Major intestinal transporters include peptide transporters [oligopeptide transporter 1 (PepT1)], amino acid transporters [L-type amino acid transporter 1 (LAT1), alanine/serine/cysteine/threonine transporter 1 (ASCT1), neutral amino acid transporter 1 (B AT1), and excitatory amino acid transporter 1 (EAAC1)], and glucose transporters [SGLT1 and glucose transporter 2 (GLUT2)] [28]. Studies have shown that probiotics can promote expression of these transporters. For instance, *Bacillus subtilis* significantly increased PepT1 mRNA expression in broiler ileal mucosa [26], and a compound *Lactobacillus* preparation (0.1% supplementation) significantly increased expression of sodium-glucose cotransporter 4 (SGLT4) under heat stress conditions, as well as GLUT2, GLUT5, and SGLT4 under normal conditions in broiler small intestine [29]. Additionally, while *Escherichia coli* K88 significantly downregulated mRNA expression of glucose transporter SGLT1, amino acid transporters y LAT1 and CAT1, and ASCT2 in porcine intestinal epithelial cells, dietary supplementation with 1×10 CFU of *L. plantarum* significantly inhibited these effects [30]. These findings collectively demonstrate that probiotics promote nutrient transport by enhancing transporter expression.

1.3 Effects of Probiotics on Intestinal Epithelial Structure

The intestinal tract possesses a vast surface area that is constantly challenged by dietary antigens and microorganisms, serving as the first line of defense against such assaults. The morphological integrity of the intestinal mucosa is not only the morphological basis for maintaining intestinal barrier function but also a prerequisite for normal intestinal function. Normal intestinal mucosal cell turnover involves simultaneous cell proliferation and apoptosis [31]; however, abnormal apoptosis can lead to intestinal dysfunction and diseases such as intestinal wall necrosis and luminal hemorrhage [32]. Recent studies have revealed that probiotics not only alleviate apoptosis induced by external stimuli but also promote apoptosis of intestinal cancer cells. For example, *Clostridium butyricum* (1×10

CFU/mL) significantly inhibited *E. coli*-induced apoptosis in chicken embryo intestinal cells by downregulating expression of apoptotic factors and caspase-3 [33], while *Lactobacillus reuteri* alleviated LPS-induced intestinal apoptosis by downregulating caspase-3 protein expression [34]. Co-culture of *Lactobacillus* with human colon cancer HT-29 cells resulted in a Bax/Bcl-2 ratio greater than 1, indicating that *Lactobacillus* promoted HT-29 cell apoptosis [35]. Another study found that *Lactobacillus* could also promote Caco-2 cell apoptosis [36], suggesting that probiotics maintain intestinal structural integrity and restore normal physiological function by regulating apoptosis.

Another critical component of the intestinal barrier is the intercellular junction complex—tight junctions. These multi-protein complexes composed of transmembrane proteins seal the gaps between adjacent epithelial cells and are located near the apical membrane, including proteins such as claudin, occludin, and zonula occludens-1 (ZO-1) [37]. Broiler feeding trials have shown that yeast and *Bacillus* (1×10 CFU/kg) increased mRNA expression of occludin and claudin [38], consistent with findings from Eun et al. [39] and Endo et al. [40]. Additional studies have demonstrated that dietary probiotic supplementation in broilers, whether under heat stress, pathogen challenge, or normal conditions, not only alleviated stress-induced reductions in villus height, increases in crypt depth, decreases in villus-to-crypt ratio, and declines in epithelial electrical resistance, but also increased cecal villus height and crypt depth in normal groups [41-43]. Furthermore, diamine oxidase (DAO) is an intracellular enzyme primarily located in the upper villi of small intestinal mucosa. The activity of DAO in intestinal mucosa and plasma serves as an important marker reflecting intestinal mucosal epithelial cell structure repair, injury, and permeability [44]. Dou [18] found that LPS challenge increased plasma DAO activity while decreasing intestinal mucosal DAO activity in piglets, indicating small intestinal mucosal cell damage and increased permeability. Dietary supplementation with *Bacillus* or *Lactobacillus* preparations reduced both mucosal and plasma DAO activities, demonstrating that probiotics can alleviate LPS-induced intestinal mucosal injury and maintain intestinal functional integrity. However, some reports have indicated that probiotics have no significant effects on intestinal morphology [45-46].

2 Effects of Probiotics on Liver Metabolism

The liver is the central metabolic organ in the body. Nutrients absorbed by the intestine are metabolized by the liver and transported to various target organs and tissues for utilization, thereby promoting growth and development. The liver plays a primary role in maintaining homeostasis of glucose, lipid, and amino acid metabolism. Hepatic glycogen metabolic enzymes enable the liver to sense blood glucose levels and store or mobilize glycogen according to peripheral blood requirements. Major glucose metabolic pathways include glycolysis, gluconeogenesis, and the pentose phosphate pathway, with key metabolic enzymes such as phosphofructokinase, pyruvate kinase, and glucose-6-phosphatase [47]. Amino acid metabolic enzymes in the liver, including glutamic-oxaloacetic transaminase, glutamic-pyruvic transaminase, and lactate dehydrogenase, exhibit high activity and serve as important indicators of liver function [48]. Additionally, key enzymes in fatty acid synthesis and oxidation include fatty acid synthase, carnitine palmitoyltransferase 1, and acetyl-CoA carboxylase [49].

Liver proteomic analysis revealed that *Enterococcus faecium* (viable count >10 CFU/g) upregulated expression of amino acid metabolism-related proteins in broiler chickens, including betaine-homocysteine methyltransferase (BHMT), cystathionine- -lyase (CTH), and glutamic-oxaloacetic transaminase 1 (GOT1), indicating that *E. faecium* enhanced amino acid metabolic rates and provided abundant substrates for protein synthesis [50]. Probiotic mixtures (*L. plantarum* and *L. curvatus*) or individual strains reduced expression of hepatic lipogenic enzymes and their genes in mice fed high-fat, high-cholesterol diets [51]. When mice and SD rats were fed high-sucrose diets, supplementation with *Lactobacillus rhamnosus* or *Lactobacillus gasseri* significantly increased expression of fatty acid oxidation-related enzyme genes while decreasing expression of the lipogenic enzyme acetyl-CoA carboxylase [52-53], demonstrating that probiotics can reduce hepatic fat accumulation. Another study found that a probiotic isolated from the mucus layer reduced glucose-6-phosphatase gene expression while increasing fatty acid oxidation-related enzyme gene expression in the livers of high-fat diet-fed mice, thereby decreasing gluconeogenesis, controlling fat deposition, alleviating hyperglycemia induced by high-fat diets, and maintaining glucose metabolic homeostasis [54].

Glucose metabolism involves multiple processes including digestion and absorption, glucose uptake and catabolism, glycogen synthesis and breakdown, and gluconeogenesis [55]. Blood levels of triglycerides, total cholesterol, and free fatty acids are important indicators of lipid metabolism in animals. Additionally, cholinesterase is a hydrolytic enzyme reflecting liver synthetic function, and elevated cholinesterase activity may indicate fatty liver and steatohepatitis. Studies have found that *Lactobacillus* supplementation (viable count >1×10 CFU/g) significantly reduced cholinesterase activity while markedly increasing creatine kinase, lipase, and lactate dehydrogenase activities, with concurrent reductions in triglyceride and total cholesterol levels, indicating improved lipid metabolism [56]. Dietary supplementation with approximately 1×10 CFU/g of probiotics (*B. subtilis* and *Lactobacillus*) decreased serum triglyceride levels while increasing high-density lipoprotein and cholesterol levels in normal-protein diet groups of Qingjiaoma chickens, suggesting lipid-lowering effects [57]. Chen [58] reported that dietary *Lactobacillus* preparation increased serum total protein (TP) content while reducing non-protein nitrogen in broiler chickens, indicating significantly improved protein deposition. Cui et al. [59] demonstrated that feeding probiotic compound fermented feed significantly increased serum glucose and TP content while decreasing serum urea nitrogen levels in weaned piglets. Zhang [60] confirmed in rat studies that pre-administration of 4×10 CFU/mL of *Lactobacillus casei* Zhang could prevent high-fructose water-induced hyperinsulinemia, and continuous feeding for four weeks improved hyperinsulinemia levels. Serum glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase (GPT) are important enzymes in amino acid metabolism and key indicators of liver function [61]. *Clostridium butyricum* significantly alleviated GPT elevation induced by non-alcoholic fatty liver disease in rats [40], thereby reducing liver injury to some extent. These results collectively demonstrate that probiotics can promote lipid and glucose metabolism, enhance protein deposition, and alleviate liver injury. The underlying mechanisms may involve probiotic modulation of intestinal microbiota, altered bacterial enzyme activity and expression, and participation in signaling pathways of carbohydrate metabolism [62-63].

3 Summary

The ability of livestock and poultry to digest and absorb feed is a critical factor for improving growth and production performance, while liver metabolic status forms the essential basis for maintaining whole-body homeostasis. Research has demonstrated that probiotics can improve intestinal morphology, restore normal intestinal function, enhance intestinal digestive and absorptive enzyme activities, and alleviate stress-induced damage to intestinal mucosa and liver. Probiotic therapy can reduce the risk of certain diseases; however, the effects of probiotics on digestive and metabolic systems still lack many validated biomarkers. The interplay between probiotics and intestinal microbiota and its relationship with digestion and absorption, as well as the relevant signaling pathways in liver metabolism, require further in-depth investigation.

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