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Abstract

Enterococcus faecium is one of the commonly used probiotics in piglet production. This probiotic not only survives in the gastrointestinal tract of piglets and maintains intestinal microbiota balance, but also regulates small intestinal villus development, nutrient absorption, immune function, and the ability to resist Chlamydia, rotavirus, and Salmonella typhimurium infections, thereby exerting an important influence on piglet intestinal health. This article reviews the aforementioned research progress.

Full Text

The Influence of *Enterococcus faecium* on Gut Health of Piglets

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Abstract: *Enterococcus faecium* is one of the most commonly used probiotics in piglet production. This probiotic not only survives in the gastrointestinal tract of piglets and maintains intestinal microbial balance but also regulates small intestinal villus development, nutrient absorption, immune function, and resistance to *Chlamydia*, rotavirus, and *Salmonella* Typhimurium infection, thereby exerting important effects on piglet gut health. This review summarizes recent research progress in these areas.

Keywords: *Enterococcus faecium*; piglets; intestinal microbiota; small intestinal villus; nutrient absorption; immune regulation; disease resistance

Enterococcus faecium, a Gram-positive, facultatively anaerobic bacterium belonging to the family Streptococcaceae and genus *Enterococcus*, is classified as a lactic acid bacterium due to its ability to ferment carbohydrates into lactic acid. It can grow at temperatures ranging from 10–45 °C, pH 9.6, 6.5% NaCl, and 40% bile salt concentrations, and is commonly cultured in MRS medium at 37 °C under constant temperature conditions [1]. Among the *Enterococcus* genus, only *E. faecium* and *E. faecalis* possess probiotic properties, and most *E. faecium* strains have been confirmed as safe [2–4]. Consequently, *E. faecium* was listed by the U.S. Food and Drug Administration (FDA) in 1989 as a probiotic strain approved for direct-fed use, has been permitted by China' s Ministry of Agriculture as a microbial additive for animal production since 1999, and is also approved by the European Union as a safe feed additive for all animal species, making it the predominant strain in European animal probiotic products. Most probiotic *E. faecium* strains originate from the intestines of healthy humans or animals, with a smaller proportion derived from fermented foods. These probiotics promote piglet growth, increase daily weight gain, and prevent diarrhea [5–16]. The beneficial effects of *E. faecium* on piglets are closely linked to its survival capacity in the gastrointestinal tract and its regulatory effects on gut health, including intestinal microbial balance, small intestinal villus development, immunity, and disease resistance. This review focuses on these aspects.

1. Survival of *Enterococcus faecium* in the Piglet Gastrointestinal Tract

Tolerance to gastric acid and bile salts is a prerequisite for oral probiotics to survive and proliferate in the host gastrointestinal tract. The gastric pH in piglets under 8 weeks of age is approximately 4.0, gradually decreasing to near 2.0 after 8–10 weeks. Strompfová et al. [17] isolated *E. faecium* from the rectum and feces of healthy piglets that could adhere to porcine colonic mucosa and survive for over 3 hours at pH 3.0, maintaining viable counts exceeding 10 CFU/mL after coexisting with 1% ox bile and lysozyme for one day. Marcináková et al. [18] isolated *E. faecium* strains from animal feces and digestive tracts that, despite adhesion rates of only 2–4%, could tolerate 0.3% ox bile and hydrochloric acid at pH 3.0. Guerra et al. [6] reported that the commercial *E. faecium* CECT 410 strain could withstand conditions simulating the stomach (pH 2.0, 3 g/L pepsin, and 5 g/L NaCl) and small intestine (pH 8.0, 1 g/L pancreatin, and 5 g/L NaCl), retained strong viability after 3 months of storage at -20 °C, and showed minimal viability loss when added to pig feed and stored at room temperature for 8 days. These findings demonstrate that *E. faecium* strains from various sources can survive in the piglet gastrointestinal tract.

Taras et al. [13] and Simon [14] confirmed that microencapsulated *E. faecium* NCIMB 10415 could rapidly colonize the stomach, jejunum, and colon of sows and piglets, be detected in feces, and transmit from sow feces to newborn piglets, colonizing their ileum and colon. This indicates that *E. faecium* NCIMB 10415 adapts well to the gastrointestinal environment of both sows and piglets.

While survival in the gastrointestinal tract is necessary for probiotic function, *E. faecium* must achieve viable counts exceeding 10 CFU/g of intestinal content to exert beneficial effects on piglets. This requires dietary supplementation of *E. faecium* at levels above 10 CFU/kg [14]. High doses of viable bacteria (over 10 CFU/d) should ideally be administered from birth, although supplementing sow diets during gestation and lactation does not significantly affect post-weaning viable counts in piglet intestines [14].

2. Effects of *Enterococcus faecium* on Piglet Intestinal Microbiota

In healthy piglet gastrointestinal microbiota, lactic acid bacteria are among the most dominant and beneficial groups, whereas many *Enterobacteriaceae* species are pathogenic or opportunistic pathogens. Therefore, promoting beneficial lactobacilli while reducing pathogenic bacteria is key to maintaining intestinal microecological balance and ensuring gut health. Klar [19] fed sows and their piglets with *E. faecium* NCIMB 10415 and observed changes in gastric, jejunal, and colonic microbiota before and after weaning. The results showed that *E. faecium* increased microbiota diversity and created high consistency within piglet groups. Specifically, *Enterococcus* species (primarily *E. faecium*) and beneficial lactobacilli such as *L. johnsonii* significantly increased across all gastrointestinal segments, while *L. reuteri* counts in the colon of 56-day-old piglets also increased significantly. *L. acidophilus* remained unchanged, bifidobacteria were unaffected, and pathogenic *E. coli* counts decreased slightly, with significant reductions observed in the colon of 7-day-old piglets.

Twardziok et al. [16] also reported that *E. faecium* NCIMB 10415 significantly increased commensal *E. faecium* counts in the ileal content of weaned piglets. However, Vahjen et al. [20] found that *E. faecium* NCIMB 10415 did not affect total *E. faecium* counts in pre- or post-weaning piglet intestinal content but significantly reduced *E. faecalis* and total enterococci counts in pre-weaning colonic content and post-weaning jejunal and colonic content. These inconsistent results may be related to piglet breed, weaning age, and varying viable counts of *E. faecium* in piglet diets. Mallo et al. [8] found that feeding *E. faecium* CECT 4515 to weaned piglets significantly increased lactobacilli counts in the ileum and feces while reducing coliform bacteria in the ileum. Wen et al. [9] similarly reported that *E. faecium* supplementation significantly increased fecal lactobacilli and decreased *E. coli* and *Salmonella* counts in weaned piglets. Huang et al. [15] observed that oral administration of *E. faecium* to newborn piglets significantly reduced pathogenic enterobacteria counts in cecal content without affecting total bacterial or lactobacilli counts in suckling piglets.

Scharek et al. [21] and Simon [14] reported that feeding *E. faecium* NCIMB 10415 to sows and their piglets significantly reduced the proportion of diarrhea-causing pathogenic *E. coli* serovars (such as O141 and -hemolytic types) in weaned piglet colonic content without affecting total coliform counts. Collectively, these findings demonstrate that *E. faecium* strains can modulate intesti-

nal microbiota balance in piglets both pre- and post-weaning, with some strains remaining effective even after inactivation [11]. The mechanism likely involves increasing lactic acid-producing bacteria and inhibiting pathogen adhesion and growth [19, 22].

3. Effects of *Enterococcus faecium* on Small Intestinal Villus Development and Nutrient Absorption

The small intestinal epithelium serves as both a physical barrier against foreign antigens and a critical site for nutrient absorption, making villus development essential for gut health. Studies show that *E. faecium* enhances the integrity and metabolic activity of piglet small intestinal epithelial cells [23], significantly promotes jejunal villus growth in weaned piglets, with some heat-inactivated strains producing similar effects [11], while other strains can promote jejunal villus development in *Salmonella*-infected piglets and strengthen intestinal barrier function [24]. *E. faecium* NCIMB 10415 has also been reported to enhance glucose absorption capacity in piglet jejunal epithelium [25], significantly increase sodium/glucose co-transport capacity in jejunal mucosa of 26- and 54-day-old piglets, and improve ion transport capacity in 54-day-old piglet jejunal epithelium without affecting mRNA expression of the sodium/glucose co-transporter SGLT1 or chloride channel CFTR [26]. However, other studies indicate that *E. faecium* NCIMB 10415 does not affect jejunal villus length or crypt depth in pre- or post-weaning piglets [21] nor impact intestinal transport, barrier function, or nutrient digestibility [14, 27]. These discrepancies may be related to piglet age or rearing conditions, and the mechanism by which *E. faecium* NCIMB 10415 promotes glucose absorption may be SGLT1-independent, warranting further investigation.

4. Effects of *Enterococcus faecium* on Piglet Immune Function

Probiotics possess immunostimulatory properties that influence immune system function and host health. The intestinal mucosa is the first site to encounter orally administered probiotics and mount immune responses. Huang et al. [28] demonstrated that *E. faecium* EF1 modulates cytokine expression in newborn piglet small intestinal mucosa by significantly inhibiting pro-inflammatory cytokines (TNF- , IFN- , IL-1, IL-6, IL-12, and IL-8) while increasing anti-inflammatory cytokines (IL-10 and TGF- 1), suggesting anti-inflammatory and gut homeostasis-promoting effects. Twardziok et al. [16] fed *E. faecium* NCIMB 10415 to gestating sows and their piglets, observing significant downregulation of multiple immune-related genes in 34-day-old piglet Peyer' s patches, including peptidoglycan recognition proteins (PGLYRP-1, PGLYRP-2A, PGLYRP-2B), IL-8, IL-10, NOD1, NOD2, CD86, acetylase 1, and CTLA4, suggesting that reduced diarrhea incidence correlates with immunomodulatory effects.

Furthermore, *E. faecium* NCIMB 10415 significantly reduced activated T cells

and IgM B cells in ileal mesenteric lymph nodes of suckling piglets [29], increased CD1 expression on Peyer' s patch B cells, and decreased CD4 CD8 cells [30], while also reducing fecal IgA content [31] and jejunal epithelial CD8 cytotoxic T cell counts in weaned piglets [14, 21, 32] without affecting CD4 and CD8 T cell numbers in jejunal Peyer' s patches [21]. These findings indicate that *E. faecium* NCIMB 10415 attenuates intestinal mucosal immune responses. Similar patterns were observed systemically, with reduced serum total IgG levels in weaned piglets [14, 21, 31] and altered blood lymphocyte composition, including decreased CD16 cell proportions but increased T cell and CD4 T cell counts in piglets fed *E. faecium* NCIMB 10430 from early life [30]. Long-term supplementation also reduced circulating CD8 T lymphocyte counts [14, 32]. However, some *E. faecium* strains significantly increase serum IgA, IgG, or IgM levels in weaned piglets [9, 33], with inactivated strains producing similar effects [11]. These results demonstrate strain-specific immunomodulatory effects, though piglets generally mount weak immune responses to oral *E. faecium*, particularly strain NCIMB 10415, possibly indicating immune tolerance.

Enterococcus faecium NCIMB 10415 may directly modulate immune function by regulating intraepithelial lymphocyte populations or indirectly influence host immune responses by altering intestinal microbiota [14, 29]. Although the mechanisms remain unclear, studies indicate that Toll-like receptors 2 and 9 (TLR2 and TLR9) are involved in *E. faecium* EF1-mediated modulation of innate immune responses in newborn piglet small intestinal mucosa [34], suggesting that TLR-related signaling pathways play important roles.

5.1 Anti-*Chlamydia* and Anti-Rotavirus Effects

Swine chlamydiosis is a chronic contagious disease particularly affecting pregnant sows and young piglets, while rotavirus infection causes acute intestinal disease. Both pose serious threats to piglet health. Feeding *E. faecium* NCIMB 10415 to gestating sows and their piglets delayed *Chlamydia* infection time and significantly reduced natural infection rates [35], possibly by enhancing immune responses. *Enterococcus faecium* NCIMB 10415 also promoted rotavirus shedding in naturally infected piglets, with efficacy depending on viral type and potentially influenced by immune status [36]. These findings demonstrate that *E. faecium* NCIMB 10415 enhances resistance to *Chlamydia* and rotavirus infections, though the underlying mechanisms require further investigation.

5.2 Anti-*Salmonella* Effects

Salmonella Typhimurium is the primary pathogen causing salmonellosis in piglets, with both humoral and cellular immunity playing important defensive roles. Szabó et al. [37] continuously fed *E. faecium* NCIMB 10415 to sows during gestation and lactation and to their piglets from 14–56 days of age, then challenged the 28-day-old weaned piglets with *S.* Typhimurium DT104 via gavage. Infected piglets showed significantly reduced weight gain and increased *S.* Typhimurium colonization in tonsils, colon, and forelimb muscles,

while serum anti-*Salmonella* IgG, IgM, and IgA levels were upregulated to varying degrees. More recently, Rieger et al. [24] reported that piglets fed *E. faecium* NCIMB 10415 showed increased intraepithelial lymphocyte counts and enhanced intestinal barrier function on day 28 post-*S.* Typhimurium DT104 infection, but not on day 2 post-infection, indicating that infection duration is a critical factor influencing immune responses.

In contrast, Kreuzer et al. [38] found that *E. faecium* NCIMB 10415 did not affect humoral or cellular immune responses in *Salmonella*-infected piglets, including specific anti-*Salmonella* IgG, non-specific humoral immunity, and T helper cells, cytotoxic T cells, regulatory T cells, T cells, and B cell responses in lymph nodes, jejunal and ileocecal Peyer' s patches, ileal papillae, and blood. These results suggest that under experimental high-dose challenge conditions, *E. faecium* NCIMB 10415 cannot induce rapid, effective humoral and cellular immunity against *Salmonella* infection. However, this does not negate its probiotic function, as environmental *Salmonella* loads under natural conditions are far lower than experimental challenge doses. *Enterococcus faecium* can inhibit *Salmonella* adhesion and growth in the intestine by increasing lactobacilli counts, thereby maintaining intestinal microbial balance and ensuring piglet health.

Studying host innate immune responses to *E. faecium* is crucial for elucidating its mechanisms of action [39]. In vitro experiments show that *E. faecium* NCIMB 10415 expresses an extracellular factor that blocks *S.* Typhimurium invasion of porcine jejunal epithelial IPEC-J2 cells, though this factor remains unidentified and may be strain-specific [14]. Therefore, the role and mechanisms of *E. faecium* in anti-*Salmonella* infection require further investigation.

Enterococcus faecium improves piglet gut health by modulating intestinal microbiota, small intestinal villus development, and immune function. However, its efficacy is influenced by numerous factors, including strain specificity and individual piglet intestinal physiological conditions, with multiple mechanisms often acting simultaneously, leading to inconsistent research results. Therefore, probiotics should not be used for therapeutic purposes until their exact mechanisms are clarified. Future research should explore the mechanisms of *E. faecium* in modulating piglet gut health at the cellular and molecular levels, including identification of bioactive components (e.g., cell wall components, metabolites), effects on intestinal microbial homeostasis and nutrient metabolism, and signaling pathways regulating intestinal mucosal immunity. The signaling pathways modulating intestinal mucosal immunity represent a particularly promising research focus.

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