Postprint on the Interplay Between Gut Microbiota and Bile Acid Metabolism

Authors: Fan Zheyu, Wang Jinbo, Qi Lili, Li Zhenbiao

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Abstract

The gut microbiota is intimately associated with bile acid metabolism. Gut bacteria influence bile acid synthesis by modulating the expression of the farnesoid X receptor and G protein-coupled receptors; bile salt hydrolases and steroid dehydrogenases produced by gut bacteria affect bile acid deconjugation, covalent modification, and isomerization; and gut bacteria impact bile acid reabsorption by influencing the expression of bile acid transporters in the intestinal mucosa. Bile acids can directly inhibit gut bacteria by disrupting cell membrane integrity, damaging DNA, or inducing protein denaturation and inactivation; they can also indirectly suppress the growth and proliferation of gut bacteria by stimulating intestinal epithelial cells to produce nitric oxide synthase, interleukins, and other factors; additionally, bile acids can serve as inducers to regulate the expression of virulence factors in pathogenic bacteria. Both gut microbiota and bile acids are closely related to livestock and poultry health, and they affect the physiological functions of the organism through intricate and sophisticated interaction mechanisms. This article summarizes the interactive relationship between gut microbiota and bile acid metabolism and its role in regulating the health and production performance of livestock and poultry.

Full Text

Interacting Relationship between Intestinal Microflora and Bile Acid Metabolism

FAN Zheyu[1], WANG Jinbo[1], QI Lili[1]*, LI Zhenbiao[1],[2]

[1] Ningbo Institute of Technology, Zhejiang University, Ningbo 315100, China
[2] College of Chemical and Biological Engineering, Zhejiang University, Hangzhou 310027, China

Corresponding author, lecturer, E-mail: qll@nit.net.cn

Abstract

Intestinal microflora is closely related to bile acid metabolism. The gut microbiota influences bile acid synthesis by regulating the expression of farnesoid X receptor (FXR) and G protein-coupled receptor (TGR5). Bacteria affect the deconjugation, covalent modification, and epimerization of bile acids through the production of bile salt hydrolases (BSHs) and hydroxysteroid dehydrogenases (HSDHs). The expression of intestinal mucosal bile acid transporters and the reabsorption of bile acids are also regulated by intestinal microflora. Bile acids can directly inhibit intestinal bacteria by destroying bacterial membrane integrity, damaging DNA, and denaturing proteins. Additionally, bile acids can indirectly suppress the growth and proliferation of intestinal bacteria by stimulating intestinal epithelial cells to produce inducible nitric oxide synthase (iNOS) and interleukins. Bile acids act as inducers that modulate the expression of virulence factors in pathogenic bacteria. The intestinal microflora and bile acids are intimately associated with animal health, influencing physiological functions through sophisticated mechanisms. This paper reviews the interacting relationship between intestinal microflora and bile acid metabolism and the roles of this interaction in regulating animal health and performance.

Keywords: intestinal microflora; bile acid; interaction; animal health

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2. Mechanisms of Interaction between Intestinal Microflora and Bile Acid Metabolism

2.1 Regulation of Bile Acid Synthesis by Intestinal Microflora The gut microbiota profoundly influences bile acid synthesis through modulation of nuclear receptor signaling pathways. The farnesoid X receptor (FXR) and TGR5 (G protein-coupled receptor 5) serve as critical sensors for bile acids, regulating hepatic synthesis via enterohepatic circulation. Activation of FXR in the ileum induces expression of fibroblast growth factor 15/19 (FGF15/19), which suppresses hepatic CYP7A1 (cholesterol 7 -hydroxylase) expression, thereby inhibiting bile acid synthesis [6-7]. Sayin et al. [7] demonstrated that modulation of gut microbiota with probiotics downregulates the FXR-FGF15 axis, leading to enhanced hepatic bile acid synthesis. Li et al. [14] showed that specific bacterial metabolites can inhibit intestinal FXR signaling, altering the bile acid pool composition. The microbiota also influences the expression of CYP8B1 (oxysterol 8 -hydroxylase), which controls the cholic acid/chenodeoxycholic acid ratio, through FXR-dependent mechanisms [11-13]. These regulatory networks illustrate the intricate crosstalk whereby intestinal bacteria shape the hepatic bile acid profile.

2.2 Regulation of Bile Acid Transport and Reabsorption Intestinal microflora modulate the expression and function of bile acid transporters, thereby controlling enterohepatic circulation. The apical sodium-dependent bile acid

transporter (ASBT) mediates bile acid reabsorption in the ileum, and its expression is regulated by microbial signals through GATA4 transcription factor [19-20]. Studies have shown that germ-free mice exhibit altered expression of ASBT and other transporters, leading to impaired bile acid reabsorption [8]. The microbiota also affects the expression of organic solute transporters and multidrug resistance proteins that facilitate bile acid export from enterocytes. This regulatory mechanism ensures proper bile acid homeostasis and prevents excessive accumulation in the intestinal lumen.

2.3 Microbial Modification of Bile Acid Structure Bacterial enzymes extensively modify bile acid structures, altering their physicochemical properties and signaling functions. Bile salt hydrolases (BSHs) deconjugate taurine- and glycine-conjugated bile acids, increasing their hydrophobicity and antimicrobial activity [17]. Hydroxysteroid dehydrogenases (HSDHs) catalyze oxidation and epimerization of hydroxyl groups at positions 3, 7, and 12, generating secondary bile acids such as deoxycholic acid and lithocholic acid [15,18]. These modifications affect bile acid solubility, receptor binding affinity, and toxicity. Approximately 95% of bile acids undergo microbial transformation in the colon, fundamentally reshaping the bile acid pool available for host signaling and antimicrobial defense [10,17].

3. Regulation of Intestinal Flora by Bile Acids

Bile acids exert potent antimicrobial effects through multiple mechanisms. Direct antimicrobial action involves disruption of bacterial cell membranes due to their detergent properties, induction of DNA damage through oxidative stress, and denaturation of bacterial proteins [28-32]. Indirect effects include stimulation of intestinal epithelial cells to produce antimicrobial peptides and inflammatory mediators such as iNOS and interleukins, creating a hostile environment for bacterial proliferation [33-34]. Furthermore, bile acids serve as environmental cues that regulate bacterial virulence gene expression. In pathogens such as *Vibrio parahaemolyticus* and *Campylobacter jejuni*, bile salts activate type III secretion systems and invasion antigens through transcriptional regulators like VtrA and Cia [37-40]. Conversely, bile acids can promote spore germination in *Clostridium difficile* via CspC receptor sensing [41]. The bidirectional relationship is further exemplified by bacterial adaptation mechanisms, including efflux pumps and bile acid modification enzymes that confer resistance [31,34].

4. Implications for Animal Health and Performance

The intricate interplay between intestinal microflora and bile acid metabolism significantly impacts animal physiological functions and health status. Bile acid-microbiota crosstalk influences nutrient absorption, lipid metabolism, and energy homeostasis through FXR and TGR5 signaling pathways [43-44]. Modulation of this interaction via dietary interventions, probiotics, or bile acid sequestrants can improve feed efficiency and growth performance in livestock [45-46].

Disruption of the normal bile acid-microbiota axis is associated with inflammatory bowel disease, metabolic disorders, and increased susceptibility to enteric pathogens [47-49]. Understanding these mechanisms provides novel strategies for enhancing animal health through targeted manipulation of the gut microbiome and bile acid pool composition.

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