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Gut dysbiosis: Nutritional causes and risk prevention in poultry, with reference to other animals

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Abstract

The poultry gastrointestinal microbiome consists of more than 900 bacterial species and their metabolites; it serves as an indicator of bird health and is influenced by nutrition, medication, and other factors. Dysbiosis is a form of reduced microbial diversity, characterised by the loss of beneficial microbes, the expansion of opportunistic microbes, and the disruption of tight junctions, as well as raised pro-inflammatory cytokines (interleukin-6 and interleukin-17), tumour necrosis factor-α, and *Enterobacteriaceae*, and decreased short-chain fatty acids. Dysbiosis leads to various disorders, including liver disorders, metabolic disease, cardiovascular disease, and neurological problems. It also impacts several bodily systems, such as the gastrointestinal tract, kidneys, the gut-liver axis (liver disease, hepatocellular carcinoma, autoimmune liver disease, and metabolic-associated fatty liver disease), the gut-lung axis (pneumonia and chronic obstructive pulmonary disease), the gut-microbiota axis (irritable bowel syndrome, inflammatory bowel disease, and constipation or stool hardness), and the gut-islet axis (hypertension, hyperglycaemia, diabetes, and hypercreatinaemia syndrome). Many factors, including medications (antibiotics, anti-tumour, and immunosuppressants), environmental pollutants (heavy metals, pesticides, microplastics, and atmospheric particulates), high levels of nutrients (protein, fat, salt, and sugar), and others (age, disease, habits, and genes), cause and enable gastrointestinal dysbiosis to develop. Nutritional strategies such as the administration of probiotics, prebiotics, antibiotics, or phytogenic feed additives, and the consumption of a high-quality, balanced diet, as well as early detection of gut health malfunction and an emphasis on increasing bird resilience, can reduce the risk of dysbiosis, modify the gut microbial balance, and make microbial eubiosis possible.

Keywords broiler, dysbiosis, gut microbiota, nutrition

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Introduction

The human microbiome is estimated to contain roughly 10^{13}–10^{14} microbial cells, with a ratio of one microbial cell for every human cell (Sender *et al*., 2016). The diverse gastrointestinal microbiome (GM) primarily consists of bacteria from three major phyla: *Firmicutes*, *Bacteroidetes*, and *Actinobacteria* (Marchesi *et al*., 2016). This intricate microbiome operates as an extension of the host's genetic material and is estimated to possess 50–100 times more genes than the host genome. The human GM weighs approximately 2 kg and consists of 5000 species, whereas in chickens, the GM consists of more than 900 bacterial species and 117 bacterial genera (Sender *et al.*, 2016). By the third day after hatching, every gram of ileal and caecal content contains 10^{11} and 10^{9} microbial cells, respectively, and in older chickens, the GM contains more than 10^{14} bacteria, fungi, viruses, and protozoa (Zmora *et al*., 2019). The dominant phyla in avian intestines are *Firmicutes* (particularly the *Clostridium*, *Enterococcus*, *Lactobacillus*, and *Ruminococcus* genera), *Bacteroidetes* (particularly the *Bacteroides* and *Prevotella* genera), and *Proteobacteria* (Choi *et al*., 2015).

Hippocrates, a Greek physician from 460–370 BC, believed that all diseases begin in the gut, and a Turkish proverb states, “A treacherous friend and a crazy enemy are both waiting; you will be in trouble” (Salahi & Raad, 2018), warning that many harmful bacteria are waiting for an opportunity to overcome the beneficial microbes and disrupt the GM balance. A healthy gut is the main foundation for poultry health, optimum performance, economic profit, immunity, and physio-endocrine functions. The maintenance of gut health depends on the intestinal mucous layer, the GM, the effectiveness of the immune system, and appropriate nutrition and feeding, in terms of feed quality, dietary antigens, anti-nutrients, and mycotoxins (Shehata *et al*., 2022a, b).

The small intestine produces enzymes that are responsible for the digestion and absorption of nutrients. Any alteration in the breeder flock's nutrition, in-ovo feeding, or hatched chick diet can influence the intestinal morphology and, thus, the performance of the chicks (Salahi *et al*., 2011; 2015). Despite the fact that six-week-old Hubbard F15, Ross 308 breeder, and yellow-feathered broiler chickens have small intestines that measure only 199, 198, and 164 cm in length, respectively, and caeca that are only 40.1, 41.1, and 38 cm long, respectively (Kokoszyński *et al*., 2017; Guo *et al*., 2023a), these birds face numerous pressures and challenges within this two-meter lumen world.

Eubiosis is the exact opposite of dysbiosis, with dysbiosis describing a disturbance in the GM balance and intestinal bacterial homeostasis, as well as an increase in the ratio of harmful to beneficial bacteria (Figure 1).

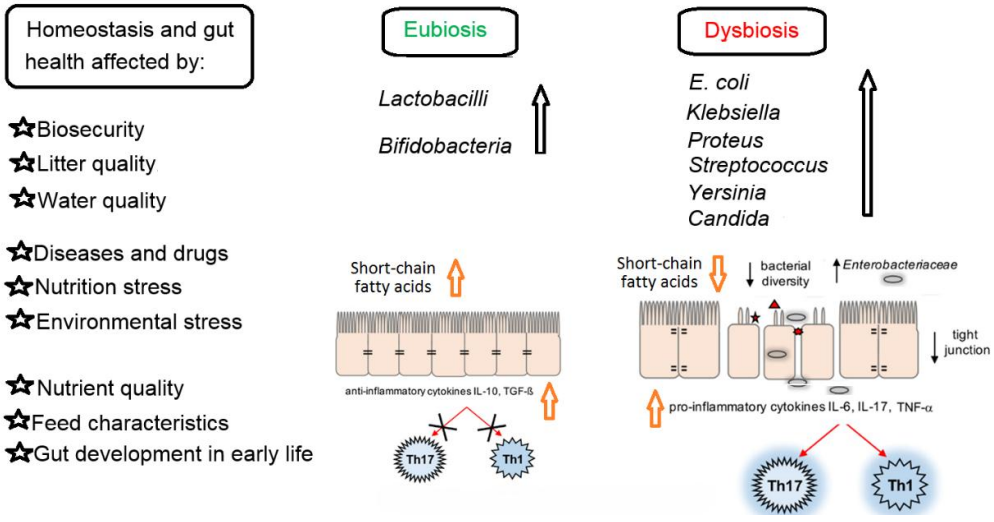

Figure 1 Factors affecting gut homeostasis and the comparison of eubiosis and dysbiosis (Baldelli *et al*., 2021). Th (1, 17): T helper cell (types 1, 17); IL (-6, -10, -17): interleukin (-6, -10, -17); TNF-α: tumour necrosis factor alpha; TGF-β: transforming growth factor beta.

DeGruttola *et al*. (2016) divided dysbiosis into three types: the loss of beneficial bacteria, the loss of overall bacterial diversity, and the overgrowth of pathogenic bacteria. Dysbiosis in poultry negatively influences growth, performance, health, flock uniformity, and welfare (Blachier *et al*., 2017;

2019; El-Saadony *et al*., 2021). Gut dysbiosis is also implicated in inflammatory diseases (Dahal *et al*., 2023), psychological manifestations of the gut-brain axis (Mohan *et al*., 2023), and endotoxemia due to the disruption of the gut barrier after heat stress (Ringseis & Eder, 2022). Healthy flocks with high productive performance and health indicate eubiosis, but not dysbiosis.

There are several causes of dysbiosis, including reduced microbial diversity following disease or antibiotic treatment, excessive heat stress or cold stress, high stocking densities, poor-quality water, the absence of probiotic administration, the presence of environmental toxins, and poor-quality sleep (typically caused by a short dark period or insufficient resting time). Dietary factors, such as a sudden change in diet, a poor-quality diet, malnutrition, the ingestion of mouldy maize or soybean meal, feed containing rancid fats or putrefied animal proteins, and a low fibre intake, will also increase the risk of dysbiosis. Dysbiosis following avian influenza virus infection reduces the number of gut microbes and increases the number of secondary pathogenic bacteria, such as *Escherichia coli*, as well as increasing the gene expression of pro-inflammatory cytokines such as interferon (IFN)-ɤ and IFN-α, and interleukin (IL)-1b, IL-6, IL-22, and IL-17A, and reducing the expression of genes responsible for the health of the intestinal mucin layer and mucosa (Abd El-Hack *et al*., 2022).

The quantity of feed and water intake and the environment surrounding poultry are important factors that are reflected in the risk of dysbiosis. The adverse effects of dysbiosis on bird health include decreasing performance, an increased risk of zoonotic pathogens and food contamination, as well as poorer health, welfare, and economic outcomes (El-Saadony *et al*., 2021). The duration of exposure to dysbiosis and pathogenic bacteria is also an important factor. Prolonged dysbiosis increases the sensitivity of the gut microorganisms to the overgrowth of harmful bacteria (Abd El-Hack *et al*., 2021).

Omics' sciences include genomics (DNA), transcriptomics (RNA), proteomics (proteins), and metabolomics (metabolite assays), and are strongly associated with bioinformatics and biostatistics to manage the large amounts of data that are generated. Omics technology is commonly used in human medicine to survey the microbial ecology of the digestive tract and gut health (Nibali & Henderson, 2016), but it has not received enough attention in poultry science. Extensive studies have been conducted on the human and mouse microbiomes, but few have focused on the microbiome's relevance in poultry production systems. Strict biosecurity measures and good nutrition, including high-quality diets, balanced diets, keeping anti-nutrients to a minimum, and the administration of next-generation probiotics, have been found to increase the proportion of beneficial microbes and reduce the numbers of pathogenic bacteria, thereby helping to optimise performance (Salahi & Abd El-Ghany, 2024) (Figure 2). This literature review therefore aims to discuss the relationship between gut dysbiosis and nutritional causes, as well as the assessment and amelioration of risk.

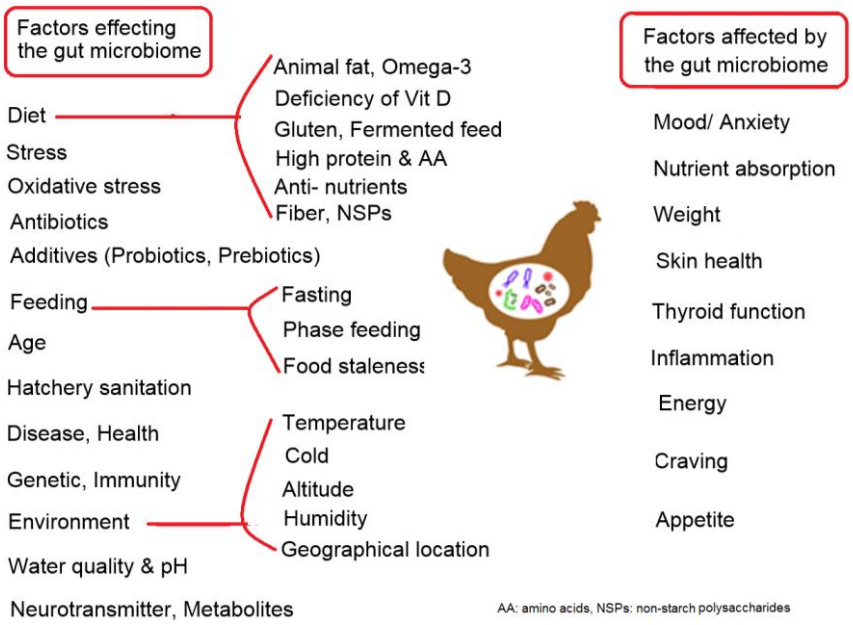

Figure 2 Factors affecting the gut microbiome and the effects of the microbiome on physiology and bird performance. AA: amino acids, NSPs: non-starch polysaccharides.

The relationship between nutrition and dysbiosis

The effects of dysbiosis on feed intake (FI) in poultry

A healthy GM is crucial for enhancing the absorption of dietary nutrients (Tassoni *et al*., 2023). Poultry, including chickens and turkeys, lack certain enzymes (such as cellulase) that are necessary to break down plant fibres (such as cellulose) in the diet. However, the GM can aid in the digestion of plant materials through fermentation. The GM is capable of producing enzymes that break down indigestible dietary polysaccharides and convert them into their compositional fermentable sugars and short-chain fatty acids (SCFAs), which can be utilised by poultry (Dunkley *et al*., 2007). The GM also stimulates nitrogen metabolism, which is essential for the formation of bacterial cellular proteins, allowing bacteria to act as a source of amino acids (AAs) and vitamins for the host (LeBlanc *et al*., 2013). Nevertheless, the ability of the GM to break down plant fibres is limited and cannot fully replace the function of digestive enzymes.

The SCFAs produced by bacterial fermentation include acetate, propionate, and butyrate (Morrison & Preston, 2016), which are important sources of energy for chickens. These SCFAs also contribute to maintaining the integrity of the intestinal mucosa, improving glucose and lipid metabolism, controlling energy consumption, and regulating the body's immune system and inflammatory responses (Agus *et al*., 2020; Shehata *et al*., 2022c). Short-chain fatty acids stimulate the proliferation of epithelial cells present in the gut, increasing the surface area available for nutrient absorption (Dibner & Richards, 2005). Furthermore, the bacteriostatic properties of SCFAs help inhibit foodborne pathogens, including *Salmonella* spp. (Ricke, 2003), and SCFAs improve feed efficiency by promoting sodium and water absorption (Clavijo & Flórez, 2018). Short-chain fatty acids also stimulate the production of IFN-α and IFN-β and enhance the function of T-regulatory cells. This process promotes the secretion of anti-inflammatory cytokines such as IL-22, as well as the humoral immune response through the production of immunoglobulin A and immunoglobulin G (Schuijt *et al*., 2016).

Over the past decade, few studies have focused on the role of the GM in the regulation of appetite, as most studies have focused on the interactions between the nervous and endocrine systems in this context. The GM generates metabolites (such as the SCFAs) that regulate appetite and stimulate gut hormone secretion by reducing energy intake and glucose output, consequently inducing energy homeostasis (Byrne *et al*., 2015; Chambers *et al*., 2015). The most dominant phyla in the gastrointestinal tracts of poultry are *Firmicutes*, which produce butyrate; *Bacteroidetes*, which produce acetate and propionate; and *Tenericutes*; *Proteobacteria*; and *Actinobacteria* (Wei *et al*., 2013). However, some *Clostridium* spp. (which belong to the *Firmicutes* phylum) can produce harmful metabolites that degrade cellulose and reduce SCFA production (Louis & Flint, 2009). In contrast, *Actinomycetes* produce nutrients and metabolise SCFAs, enhancing digestive efficiency and improving feed conversion rates (Polansky *et al*., 2016).

Acetate, propionate, and butyrate are produced by the GM in a ratio of 3:1:1 (Canfora *et al*., 2015), or a molar ratio of 60:25:15 (Mortensen & Clausen, 1996), and 70–140 mmol/L of SCFAs are produced in the human colon (Mortensen & Clausen, 1996). The fermentation of complex carbohydrates into SCFAs directly affects satiety; reduces appetite by changing the levels of glutamate, glutamine, gamma-aminobutyric acid (GABA), and neuropeptides (Babakhani & Hosseini, 2019); and stimulates gut hormone secretion, hypothalamus activity, and appetite regulation. The receptors involved in these pathways include the free fatty acid receptors, FFAR2 and FFAR3 (Kim *et al*., 2022).

Propionate, which makes up 15%–20% of the SCFAs produced in the gastrointestinal tract (Kim *et al*., 2022), is mainly used by the gut epithelium (Hosseini *et al*., 2011). Propionate is produced by a limited number of bacterial species, and propionate and butyrate are generated through three main pathways: the succinate pathway, which is the main pathway and is primarily used by *Bacteroidetes* and *Firmicutes* spp.; the acrylate pathway, which is used by *Firmicutes* spp.; and the propanediol pathway (also used by *Firmicutes* spp.). With the increase in pH from the caecum to the distal colon, the bacterial population shifts from butyrate-producing bacteria (*Faecalibacterium prausnitzii* and *Roseburia* spp.) to propionate and acetate-producing bacteria (*Bacteroides*) (Walker *et al*., 2005). Maintaining the balance of the gut SCFAs is important, as propionate reduces myeloperoxidase, while increasing catalase and superoxide dismutase in the serum and colons of mice (Tong *et al*., 2016). A ketogenic diet decreases the availability of glucose, and SCFAs are thus utilised as an energy source, whereas a high-fat diet increases the polyunsaturated fatty acid (PUFA), butyrate, and acetate uptake from the intestines (Eor *et al*., 2021). Propionate treatment for 40 days caused an increase in adenosine triphosphate, mitochondrial catalase, superoxide dismutase, glutathione peroxidase, and nicotinamide adenine

dinucleotide, while decreasing 8-hydroxy-2'-deoxyguanosine and hippocampal neuronal loss (Cheng *et al*., 2019). The intraperitoneal injection of propionate in mice was found to reduce FI (Goswami *et al*., 2018), but this result was not observed in humans (Darzi *et al*., 2016). In pigs, propionate infusion did not reduce FI in the long term, possibly because of the fast metabolism of propionate (Zhang *et al*., 2022) or the absorption of sodium propionate in the portal veins for gluconeogenesis in the liver (Yu *et al*., 2019). The intra-caecal inoculation of propionate in pigs stimulated the release of the gut hormones glucagon-like peptide 1 (GLP-1) and peptide YY (PYY), and upregulated the expression of both PYY and GLP-1R mRNA; it also upregulated FFAR2 and FFAR3 expression in the colon mucosa, consequently suppressing appetite (Zhang *et al*., 2022).

Acetate produced by the GM suppressed the appetites of rats either through its direct effect on the hypothalamus (Frost *et al*., 2014; Byrne *et al*., 2015) or by crossing the blood-brain barrier. Acetate was found to downregulate the expression of the agouti-related peptide (AgRP) in NPY/AgRP neurons and upregulate the expression of pro-opiomelanocortin (POMC) in POMC/CART neurons in the hypothalamus (Koda *et al*., 2005; Frost *et al*., 2014). Peptide YY and GLP-1 are intestinal hormones involved in satiety homeostasis that affect the main neural centre for feeding, behaviour, energy status sensing, and appetite signals in the hypothalamus (Zhang *et al*., 2022b), causing satiety (Greiner & Backhed, 2016). In addition, cholecystokinin and ghrelin secreted by enteroendocrine cells modulate FI (Han *et al*., 2021).

Feeding behaviour in mice is affected by the depletion of the GM, which leads to the over-consumption of palatable high-sucrose pellets and the reduction of *Lactobacillus johansson* colonisation (Ousey *et al*., 2023). More research is needed to understand how the serotonergic and acidergic systems affect appetite and FI, and to determine the relationship between these systems and changes in the GM. The intra-cerebro-ventricular injection of serotonin (5-HT) in broiler chickens results in a reduction in FI, and the central serotonergic system plays a major role in the modulation of ingestion behaviour (Zendehdel *et al*., 2012; 2013). The regulation of appetite is controlled by neurotransmitters in the central nervous system (Parker *et al*., 2014). In poultry, the brain opioid receptors, including the μ, δ, and κ receptors (Le Merrer *et al*., 2009), play a direct role in FI regulation (Kozlov *et al*., 2013); injection of a μ-opioid receptor agonist reduced FI, but injection of δ- and κ-opioid receptor agonists increased it (Bungo *et al*., 2005).

It may be concluded that dysbiosis of the GM in poultry alters the population of propionate-producing microbes that are able to produce larger amounts of propionate (such as *Bacteroidetes* and *Firmicutes*). Propionate, after absorption from the digestive system, stimulates the secretion of the hormones PYY and GLP-1, both of which act as appetite suppressants. These hormones send satiety messages to the central nervous system and decrease FI. Dysbiosis also influences appetite centres within the brain by increasing systemic inflammation through an increase in the production of inflammatory metabolites, such as bacterial lipopolysaccharide (LPS), and the activation of the immune system through the production of cytokines such as IL-6 and tumour necrosis factor-α.

The relationship between dysbiosis and feed quality and particle size

Feed quality should be optimised by ensuring the provision of a balanced, palatable diet with high nutrient digestibility, availability, and uniformity. This diet should be appropriately processed, and should provide an adequate supply of macronutrients and micronutrients; it should have an ideal AA profile, and be free of harmful substances such as mycotoxins, pesticides, heavy metals, and pathogens. The provision of an optimal diet could decrease oxidative stress and inflammation (Bärebring *et al*., 2018), enhance total serum antioxidant capacity and saliva and urine secretion (Hassimotto *et al*., 2008), promote a healthy GM, and reduce the risk of dysbiosis (Figure 3). A combination of fermentable fibres and polyphenols in the diet has been found to have a positive effect on bacterial growth and metabolite production in the gut, in terms of an increase in SCFA production and a decrease in indole and ammonia production (Whitman *et al*., 2024).

Following inflammation, a decrease in the number of butyrate-producing bacteria facilitates the establishment of enteric pathogens such as *Salmonella* spp., as butyrate helps control pathogen proliferation and decreases the expression of pro-inflammatory cytokines (Chen & Vitetta, 2020). Feeding mice diets containing germinated barley malt resulted in increased butyric acid production in the caecum and increased the butyric acid concentration in the portal serum, with anti-inflammatory effects (Zhong *et al*., 2015). However, replacing maize-based diets with low-quality diets formulated using barley and wheat, which contain non-starch polysaccharides (NSPs), resulted in the activation of

pattern recognition receptors (PRRs) for the initiation of the immune response and maintenance of homeostasis. This increased the expression of the LPS-recognising toll-like receptor gene (TLR4), stimulated the innate immune response, activated the pro-inflammatory pathway, and enhanced the production of cytokines to reduce inflammation (Shi *et al*., 2006). Toll-like receptor signalling pathways activate nuclear factor-κB (NF-κB, a component of the innate host defence), and NSPs have negative regulatory effects on NF-κB. The effects of pathogen-associated molecular patterns on PRRs lead to cell death programmes, and the binding of microbial pathogen-associated molecular patterns activates the NF-κB and IFN regulatory factor pathways (Singh & Pollard, 2015). Four families of PRRs, including TLRs, C-type lectin receptors, nucleotide oligomerisation domain-like receptors, and retinoic acid-inducible gene I-like receptors, have extensive functions (Neerukonda & Katneni, 2020), and ten and 13 types of TLRs have been identified in chickens and mammals, respectively (Turin & Riva, 2008).

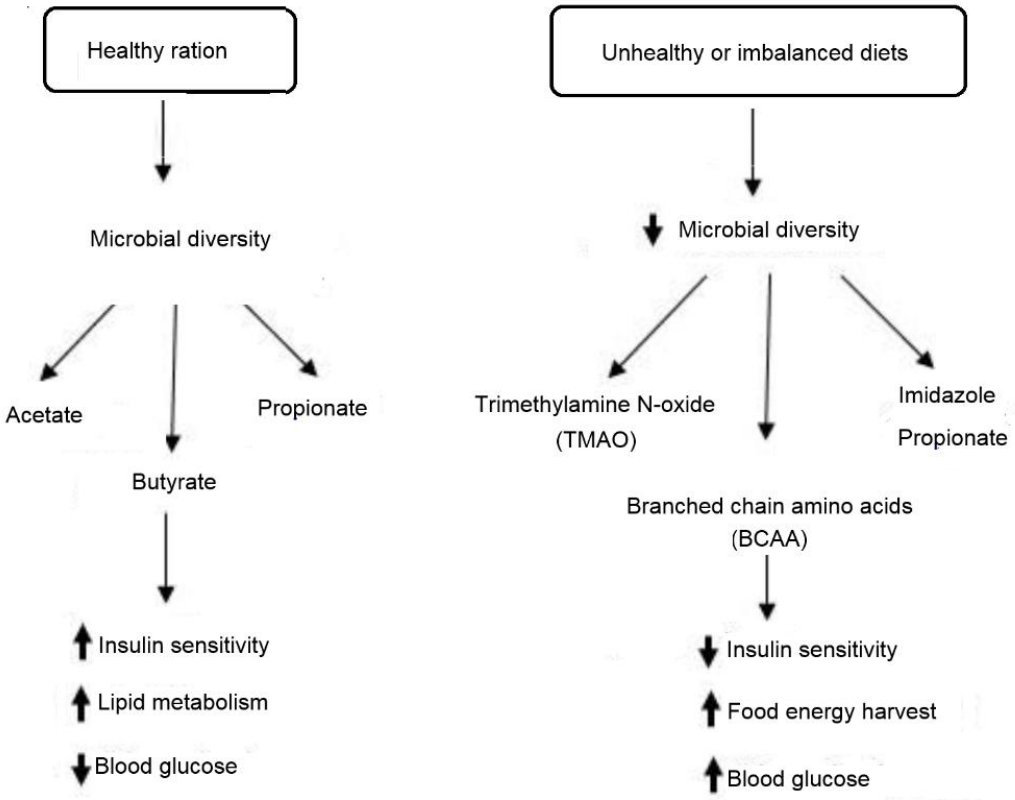

Figure 3 Effects of healthy (balanced) and unhealthy (imbalanced) diets on the gut microbiome (Tassoni *et al*., 2023).

Imbalanced rations may lead to an increase in gut permeability, intestinal dysbiosis, the abundance of harmful bacteria, disharmony of the GM, impairment of digestive system function, and acceleration of the onset of chronic liver disorders (Figure 4). There are more than 26 symptoms of dysbiosis, including those related to the digestive system (gas production, stomach rumbling and flatulence, constipation or diarrhoea, acid reflux or heartburn, thickened tongue, strong fluctuations in appetite, abdominal pain, nausea, irregular bowl movements, and belching and bloating) and other physiological systems (anxiety, nervousness, chronic fatigue, hair loss, heart failure, and chest pain).

Feed quality changes the diversity of the GM and the ratios of bacterial species. An increase in the ratio of *Firmicutes* to *Bacteroidetes* results in metabolic diseases such as obesity in humans, and causes changes in energy acquisition, digestive tract permeability, bile acid (BA) metabolism, central nervous system function, and immune system regulation (Thursby & Juge, 2017). In addition, increasing microbiome diversity in hens led to enhanced feed efficiency by optimising nutrient absorption and increasing the proportions of fibrolytic bacteria, such as *Alistipes* and *Anaerosporobacter* (Bernard *et al.*, 2024).

The recommended ratio for omega-6/omega-3 PUFAs is 4–6:1 (Tan *et al*., 2016), and the recommended ratio for saturated fatty acids/monounsaturated fatty acids/omega-3 and omega-6 PUFAs is 1:1.5:1 in humans (WHO, 2008), or 1:1:1 in mice (Tan *et al*., 2016). The optimal saturated fatty acid/monounsaturated fatty acid ratio is 1:1–2, and the recommended omega-3 to omega-6 ratio for broilers is 1:5. The consumption of diets rich in omega-6 fatty acids enhanced the growth of LPS-producing bacteria (Kaliannan *et al*., 2015). Dietary omega-3 PUFAs have been found to modulate the abundance and type of gut microbiota; alter the levels of the pro-inflammatory IL-17, LPS, SCFAs, and acid salts (Fu *et al*., 2021); and inhibit IL-17A secretion (Chehimi *et al.*, 2019). Polyunsaturated fatty acids have anti-inflammatory properties and cause the release of IL-10, thereby reducing intestinal inflammation (Zeyda *et al*., 2002; Wenderoth *et al*., 2024).

Microbial metabolites play a central role in metabolic homeostasis and the maintenance of physiological functions (Neis *et al*., 2015). These metabolites have been detected in human and bird faeces, urine, liver, cerebrospinal fluid, and blood serum samples. Short-chain fatty acids, AA, choline, lipid metabolites, vitamins, and BAs are the most important metabolites, as they are necessary for intestinal homeostasis and the pathogenesis of some diseases (Agus *et al*., 2020; Lavelle & Sokol, 2020). Other metabolites, including SCFAs and quorum-sensing agents, are produced only by the intestinal microbiota and not by the host (Li *et al*., 2018). The caecal microbiota produce vitamins, indole, SCFAs, and bacteriocins, which play a vital role in improving avian gut health and performance parameters (Aruwa *et al*., 2021).

Poultry ration feed particle size influences FI, growth rate, and gastrointestinal development (Gabriel *et al*., 2008; Safaa *et al*., 2009). For example, coarse feed particles increased gizzard weight by decreasing gut pH (Amerah *et al*., 2007); promoted intestinal motility (Ferket, 2000); triggered the secretion of cholecystokinin and pancreatic enzymes (Svihus, 2004); modulated gastrointestinal reflux (Duke, 1992); improved intestinal villi height, crypt depth, and surface area (Novotný *et al*., 2023); increased the acidification of the hindgut and stomach; controlled *E. coli* and *Salmonella* counts (Kiarie & Mills, 2019); and resulted in improved gut health. A coarse particle size (0.9 mm) has also been found to cause an increase in the death rate of *Salmonella enterica* serovar Typhimurium DT12 (Huang *et al*. 2006). Different-sized coarse maize particles increased the relative gizzard weight and quantity of *Peptostreptococcaceae*, but reduced *Lactobacillaceae* abundance. In contrast, fine-ground maize particles increased the relative abundance of *Acinetobacter* (Yan *et al*., 2022). Particle size is more important in mash diets than in crumble and pelleted diets. Therefore, the ideal particle size recommended for maize-soybean meal-based diets is 0.6–1.0 mm for starters and 1.0–1.5 mm for growers. It has also been suggested that particle size can be coarser in diets for male chickens than female chickens, and that the optimal feed pellet size is 3–4 mm.

The relationship between dysbiosis and AA

Although some intestinal AA are of host bacterial origin, most are of feed origin. All 20 types of AA play a role in the homeostasis of the GM (Li *et al*., 2017). The gut microbiota produce lysine and threonine, which influence diseases such as obesity and diabetes in humans (Neis *et al*., 2015). Amino acids such as arginine, glutamine, and threonine play a key role in maintaining the intestinal health of broilers, and it is recommended that their dietary levels are increased by 0.5%–1.0% in times of intestinal challenge (Chalvon-Demersay *et al*., 2021a). Amino acids have a protective effect on all four pillars of health of the digestive system, namely the microbiome, immunity, epithelial function, and oxidative stress (Chalvon-Demersay *et al*., 2021b). Threonine is necessary for the function of mucin-producing epithelial cell barriers (Bortoluzzi *et al*., 2018), and glycine, glutamate, and cysteine are constituents of glutathione, which is necessary for reducing free radicals and oxidative stress (Song *et al*., 2016). *Eimeria* spp.-induced coccidiosis was found to reduce FI, bird performance, AA transportation and availability (Tan *et al*., 2016), digestibility (Rochell *et al*., 2016), and plasma concentrations of arginine, glutamine, asparagine, and aspartate, but increased ornithine and lysine concentrations (Rochell *et al*., 2016).

Tryptophan is an α-AA used in protein biosynthesis, and is a precursor for the biosynthesis of 5-HT and melatonin, which are endocrine neurotransmitters (Agus *et al*., 2018; 2020). Serotonin 5-hydroxytryptamine is a biogenic amine that serves as a neurotransmitter in the gut and brain, which is produced by serotonergic neurons in the brain (1%–2%) and by enterochromaffin cells and intestinal mucosa (95%) (Gershon & Tack, 2007). Serotonin plays a key role in various physiological body functions, including feeding, temperature regulation, mood, aggression, stress, depression, sexual

behaviour, pain perception, motor control, circadian rhythm, and sleep (Walther *et al*., 2003; Nonogaki *et al*., 2008; 2009). Alberghina *et al*. (2020) reported that the normal plasma level of 5-HT in healthy layer hens was 4.24 µmol/L, and that this was significantly lower than in hens with foot pad dermatitis (6.88 µmol/L) (Figure 4). Approximately 95% of blood 5-HT is carried by platelets in mammals (Anderson *et al*., 1987). However, the measurement of 5-HT in plasma is more reliable than the measurement in whole blood for the assessment of the inflammatory response and the evaluation of chicken welfare (Alberghina *et al*., 2020).

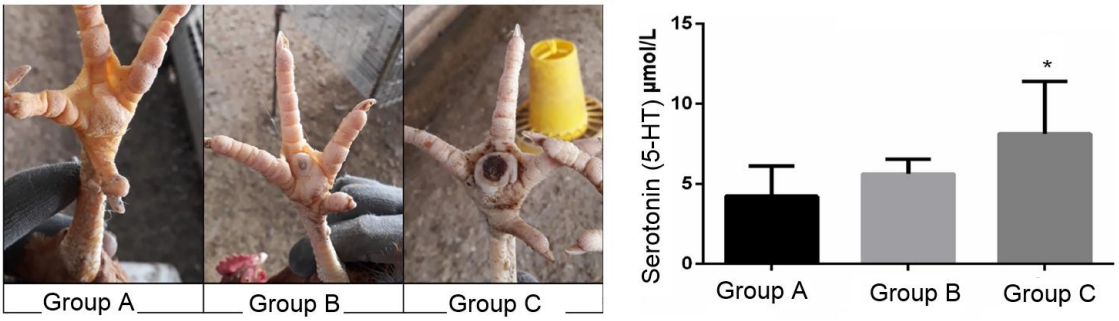

Figure 4 The plasma serotonin (5-HT) level in healthy laying hens (group A, 4.24 µmol/L) was significantly lower than in laying hens with foot pad dermatitis (group C, 6.88 µmol/L) (Alberghina *et al*., 2020).

Tryptamine is an indolamine metabolite of tryptophan that transmits local signals to the intestinal mucosa and the brain (Agus *et al*., 2018). Synbiotic bacteria, such as *Clostridium*, *Lactobacillus*, *Blautia*, and *Ruminococcus*, degrade tryptophan into tryptamine, which has a structure similar to that of 5-HT (Williams *et al*., 2014; Agus *et al*., 2018). The manipulation of the GM changes the balance of the microbial metabolism of tryptophan and thus the production of 5-HT. Bacteria belonging to the genera *Streptococcus*, *Lactobacillus*, *Lactococcus*, *Escherichia*, and *Klebsiella* produce 5-HT by expressing tryptophan synthase (Hoseini-Tavassol *et al*., 2022). Approximately 10% of humans have intestinal bacteria that encode decarboxylases and degrade tryptophan (Williams *et al*. 2014). The effects of tryptophan metabolites produced by intestinal microbes on metabolic diseases, such as fatty liver disease, osteoporosis, obesity, diabetes, inflammatory bowel disease (IBD), cardiovascular diseases, kidney diseases, nerve disorders, mental depression, anxiety, and autism, have been studied (Agus *et al*., 2018). In patients with diabetes, the oral administration of a probiotic containing *Lactobacillus rhamnosus* GG induced changes in the level of tryptophan and the qualitative pattern of metabolite formation, and also decreased the production of inflammatory cytokines (Mondanelli *et al*., 2020).

Tryptophan positively influences hormone secretion, immune organ development, and the quality and quantity of meat and eggs (Fouad *et al*., 2021). Tryptophan and its metabolites have the ability to pass through the blood-brain barrier and affect the metabolism of neurotransmitters; therefore, any decrease in dietary tryptophan can cause the induction of neurological diseases (Agus *et al*., 2018). Indole is the main tryptophan metabolite produced by the intestinal bacteria (Gao *et al*., 2018). Other microbial metabolites of tryptophan, including indole-3-acetic acid and indole-3-propionic acid, inhibit central nervous system inflammation (Rothhammer *et al*., 2016), intestinal permeability, and the innate and acquired immunity of the host. Gut microbiome dysbiosis affects intestinal tryptophan metabolism through the neurohormonal pathway in patients with chronic kidney disease (Jazani *et al*., 2019). Indole affects brain function and behaviour (Whitfield-Cargile *et al*., 2016) through communication with the intestinal epithelium (Jennis *et al*., 2018), the creation of resistance in tight junctions, and the expression of anti-inflammatory cytokines. In addition, indole-3-propionic acid is produced by *Peptostreptococcus russellii* and some *Lactobacillus* spp. (Jennis *et al*., 2018; Lavelle & Sokol, 2020), contributing to the anti-inflammatory effects of the intestinal microbiome (Jennis *et al*., 2018). The administration of grape extract containing polyphenols, in conjunction with L-arginine, L-threonine, and L-glutamine, was found to improve gut permeability (Barekatain *et al*., 2021) and the ileal digestibility of AAs in broiler chickens under stress (Chalvon-Demersay *et al*., 2021b).

Future research should focus on the precise mechanisms by which AA (particularly arginine, glutamine, threonine, and tryptophan) and microbial metabolites (particularly indole and tryptamine)

influence the balance of the GM, intestinal homeostasis, immune health, and neurological function in poultry under normal and challenging conditions. More investigation into the effects of combining AAs with probiotics, prebiotics, and polyphenols on bird health and performance is required, especially under stress or disease conditions. However, there are many research gaps, and a deeper understanding of these interactions could help reduce antibiotic use, improve meat and egg quality, and enhance disease resistance. Further investigations will be fundamental for creating more effective strategies in sustainable poultry farming, improving bird welfare, and ensuring overall health.

The relationship between dysbiosis and branched chain AAs (BCAAs)

Branched chain AAs, such as leucine, isoleucine, and valine, are essential AAs that positively impact performance, growth, immunity, intestinal health, energy homeostasis, and transamination. They also act as signalling molecules for glucose and lipid regulation, as well as protein synthesis in poultry (Kim *et al*., 2022). Moreover, BCAAs are important for liver cell proliferation, insulin resistance, and thermogenesis control in brown adipose tissue (Hoseini-Tavassol *et al*., 2022). Branched chain AAs are important nutrients for protein biosynthesis and the maintenance of intestinal barrier function (Zhou *et al*., 2018). However, the addition of cereals containing high levels of leucine to low-protein diets has a negative effect on growth (Kim *et al*., 2022). In contrast, the addition of arginine and BCAAs to diets with low crude protein contents improved the immune response and intestinal integrity of broiler chickens challenged with *Eimeria* spp. (Liu *et al*., 2023).

There is a complex relationship between the diet, the GM, and disease. The supplementation of mouse diets with BCAAs promoted the health of some microbiota, such as *Akkermansia* and *Bifidobacterium*, but reduced the counts of *Enterobacteriaceae* (Agus *et al*., 2020). In addition, supplementing the diets of colon cancer patients with high amounts of BCAAs and aromatic AAs aided in adjusting the intestinal microbiota and their metabolites, as well as preventing disease progression (Yachida *et al*., 2019).

A high level of BCAAs in the blood is considered a potential indicator of metabolically associated fatty liver disease in humans. Supplementing mice's diets with BCAAs was found to improve the diversity, composition, and abundance of the GM when the mice had high-fat diet-induced metabolically associated fatty liver disease (Zhang *et al*., 2022).

The relationship between dysbiosis and dietary protein balance

The GM stimulates nitrogen metabolism and produces bacterial cellular proteins, allowing bacteria to act as sources of AAs or proteins for the host (LeBlanc *et al*., 2013). Improving the balance of the GM can be achieved by ensuring a proper protein/carbohydrate ratio in the diet. High-protein diets have many effects on the intestinal microbiota (Alou *et al*., 2016), and increasing the dietary protein content decreases the share of carbohydrates but increases the abundance of butyrate-producing bacteria such as *Bacteroides*, *Clostridium* cluster XIV, *Roseburia*, *Eubacterium rectale*, *F. prausnitzii*, *Bifidobacteria*, and *Lactobacilli*, which exhibit proteolytic activity (Graf *et al*., 2015; Maukonen & Saarela, 2015; Alou *et al*., 2016)***.***

Imbalanced diets can induce intestinal dysbiosis directly or indirectly. For instance, a ration containing a high crude protein/metabolisable energy ratio may lead to the occurrence of excessive undigested protein in the caeca, and consequently the overgrowth of proteolytic microbes, producing hydrogen sulphide and ammonia. Rations with an imbalanced protein content also have harmful effects on the GM (Blachier *et al*., 2017; 2019), as a high protein content results in the production of toxic metabolites, N-nitroso compounds, amines, indolic and phenolic compounds, and gaseous products that suppress the expression of pro-inflammatory genes (Yao *et al*., 2016; Blachier *et al*., 2017; 2019; Tassoni *et al*., 2023) (Figure 5).

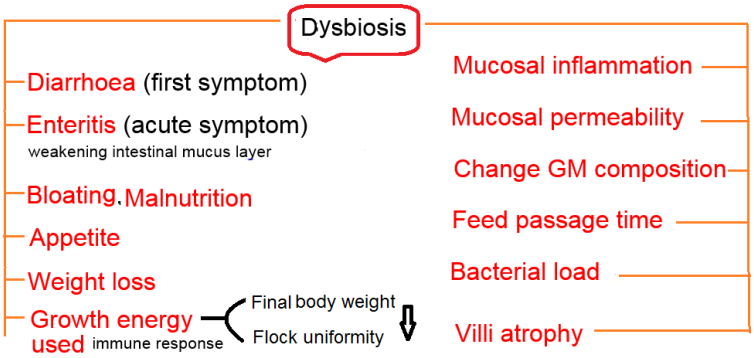

Figure 5 Symptoms of dysbiosis in poultry.

The relationship between dysbiosis and BAs

The Aviagen guides for Ross 308 broiler chickens show that energy requirements for starter, grower, finisher one, and finisher two diets were 3010, 3175, 3175, 3225, and 3225 kcal/kg, respectively, in 1999, decreasing to 2975, 3050, 3075, 3100, and 3125 kcal/kg, respectively, in 2022 (Aviagen, 2022). This indicates a decreasing trend in terms of the energy requirements of broiler chickens during the five periods of rearing. The dietary supplementation of BAs was found to increase growth and improve carcass quality and lipid metabolism in broiler chickens (Ge *et al*., 2019), decrease mortality rates and enhance lipid metabolism in layers (Sun *et al*., 2023), and treat non-alcoholic fatty liver disease in humans (Jiao *et al*., 2018). Bile acids are small molecules that are synthesised from cholesterol in liver cells and act as detergents for emulsifying fats, as well as being involved in the digestion and absorption of lipids and fat-soluble vitamins. Approximately 95% of BAs are absorbed in the ileum by active transport and reach the liver through the hepatic portal system (Ahn *et al*., 2003), whereas BAs are absorbed through passive diffusion in the jejunum (Tancharoenrat *et al*., 2014).

Bile acids enhance glycogen synthesis and insulin sensitivity in the liver; increase insulin secretion by the pancreas (Hoseini-Tavassol *et al*., 2022); facilitate energy consumption in the liver, brown adipose tissue, and muscle; and play a role in thermogenesis (Agus *et al*., 2020). There are two types of BAs: primary BAs (PBAs) and secondary BAs (SBAs). Primary BAs consist of chenodeoxycholic acid and cholic acid conjugated to glycine or taurine before secretion, and are necessary for the digestion and absorption of lipids and vitamins. Primary BAs are the products of cholesterol breakdown in the liver, where they are recycled and then passed into the intestine to be converted into SBAs by the intestinal microbiota (Ridlon *et al*., 2016). Secondary BAs include deoxycholic acid, lithocholic acid, and ursodeoxycholic acid (National Institute of Diabetes and Digestive and Kidney Diseases, 2012), and activate macrophages to produce inflammatory cytokines (Joyce & Gahan, 2017). Low concentrations of SBAs in humans have anti-inflammatory effects, whereas high concentrations cause heart damage (Rasouli & Zeighami, 2023). The dietary supplementation of BAs in broilers increased their body and breast muscle weights and improved the serum lipid profile and microbial diversity (Hu *et al*., 2024).

The GM plays an important role in BA metabolism. Bile acids are broken down by bile salt hydrolase produced by *Lactobacillus*, *Clostridium*, *Bifidobacterium*, and *Enterococcus* spp. in the gastrointestinal tracts of humans. In addition, *Clostridium scindens,* which has α/β-7 dehydroxylation activity, is capable of converting PBAs to SBAs, thereby decreasing the amount of BA entering the intestine and reducing the number of some gram-positive bacteria, such as *Blautia* and *Rumminococcaceae* (Hoseini-Tavassol *et al*., 2022). An increase in the concentration of PBAs is associated with an increase in *Firmicutes* and deoxycholic acid-producing *Clostridium* spp., and a decrease in *Bacteroidetes* and *Actinobacteria* (Ridlon *et al*., 2014; 2015). The *Ruminococcaceae* family promotes the production of SCFAs (specifically butyrate) and plays a key role in gut health, as their deficiency results in human IBD (Sokol *et al*., 2008; Morgan *et al*., 2012) and hepatic encephalopathy (Bajaj *et al*., 2012). Some probiotic-producing bacteria, such as *Lactobacillus*, *Bifidobacterium*, and *C. scindens*, show resistance to BAs due to the activation of glycolysis (Hoseini-Tavassol *et al*., 2022). Bile acids rapidly affect bacterial metabolism, causing membrane damage and altering AA, nucleotide, and carbohydrate metabolism (Tian *et al*., 2020). The BAs also play a key role in the function and permeability of the intestinal epithelium, and in maintaining intestinal homeostasis (Agus *et al*., 2020). They prevent the overgrowth of bacteria and the production of mucosal damage factors such as pro-

inflammatory cytokines, IL-8, inducible nitric oxide synthase, and carbonic anhydrase-12 (Hoseini-Tavassol *et al*., 2022). In obese individuals, dysbiosis, including changes in microbial metabolism, is associated with the occurrence of liver cancer (Yoshimoto *et al*., 2013). Dysbiosis induces SBA deficiency and reduces the abundance of *Ruminococcaceae*, whereas supplementation with SBA ameliorates inflammation-induced colitis (Sinha *et al.,* 2020). The protective effects of SBAs depend mainly on the Takeda G protein-coupled receptor 5, a BA receptor (Sinha *et al*., 2020).

The supplementation of BAs increased the microbial diversity in broiler chicken caecal digesta (increasing the abundance of *Firmicutes*, *Lactobacillus*, *Anaerostipes*, and *Sellimonas*), but reduced liver and abdominal fat weights, triglycerides, total cholesterol, the abundance of *Barnesiella* and *Akkermansia*, and the occurrence of fatty liver disease, via modulation of the GM (Hu *et al*., 2024). Most bile salts are not tolerated by *Akkermansia* (Hagi *et al*., 2020). Bile acids increase the permeability of bacterial cell membranes and produce antimicrobial activity, particularly against gram-negative bacteria (Tian *et al*. 2020). Moreover, BAs modulate the GM and its metabolites to resist heat stress in broiler chickens (Yin *et al*., 2021). *Proteobacteria* are an indicator of hepatic steatosis in mice; therefore, BAs could be used to inhibit the abundance of *Proteobacteria* that is induced by a high fructose diet (Vasques-Monteiro *et al*., 2021). In addition, the presence of *Ruminococcus torques* in the gastrointestinal tract is vital for lipid deposition in poultry (Lyu *et al*., 2021).

The relationship between dysbiosis and dietary carbohydrates and fats

Fermentable β-glucans, β-fructans, inulins, pectins, and oligosaccharides are fermented to produce SCFAs (Canfora *et al*., 2015), and carbohydrates are thus associated with GM changes in humans (Table 1).

Table 1 The main effects of different types of dietary carbohydrates on the gut microbiome in humans (adapted from Seo *et al*., 2020)

Effect on gut microbiome	References
High starch and fibre	De Filippo *et al*., 1979 Yatsunenko *et al*., 2012
Increased SCFAs, microbial diversity and richness, *Prevotella, Xylanibacter*	
Decreased *Bacteroides*, pathogenic bacteria	
Lactose (disaccharide)	Francavilla *et al*., 2012 Jeffery & O'Toole, 2013
Increased SCFAs, *Lactobacilli*	
Decreased *Clostridia*	
Fruits	Ruiz-Ojeda *et al*., 2019
Increased *Bifidobacteria*	
Decreased *Bacteroides*	
Resistant starch (type 2)	Martinez *et al*., 2010 Gori *et al*., 2011
Increased *Ruminococcus*, *Eubacteria*	
Resistant starch (type 4)	Martinez *et al*., 2010
Increased *Parabacteroides*, *Actinobacteria*, *Bacteroidetes*, *Bifidobacteria*	
Decreased *Firmicutes*	
Oligosaccharides, polysaccharides, fructo-oligosaccharides	Kapiki *et al*., 2007 Costabile *et al*., 2008 Gori *et al*., 2011 Yu *et al*., 2013
Increased *Bifidobacteria*	
Decreased *Clostridia*, *Enterococcus*	
Saccharin	Suez *et al*., 2014
Increased *Bacteroides*, *Clostridia*, dysbiosis	
Decreased *Bifidobacteria*, *Lactobacilli*	

SCFAs: short-chain fatty acids

Long- and short-term feeding of carbohydrates influences the GM, as there is a relationship between a high carbohydrate intake, the GM, and the health of the host (Seo *et al*., 2020).

Dietary fibres and fats also affect the GM (Alou *et al*., 2016), by enhancing the abundance of butyrate-producing bacteria (*Blautia*, *E. rectale*, *Roseburia*, *F. prausnitzii*, and other *Faecalibacterium* spp.), *Lactobacilli*, and *Bifidobacteria*. Different fibre fermentation processes occur in the distal colon of the human intestine to enhance the proportions of different *Bacteroidetes* spp. (Dominianni *et al*., 2015; Graf *et al*., 2015; Maukonen & Saarela, 2015). High-carbohydrate diets lead to an increase in the number of bacteria that are involved in fermentation, such as *Clostridium* cluster XVIII, *Lachnosporaceae* (*Clostridium colostridioforme*), *Ruminococcaceae* (*F. prausnitzii*), and *Prevotella* (Alou *et al*., 2016).

The effects of fats on the diversity of the intestinal microbiota are indirect. Increasing the quantity of dietary fat stimulates the production of BAs and consequently accelerates the growth of bacterial species that metabolise BAs (Graf *et al*., 2015; Maukonen & Saarela, 2015). Diets rich in fats therefore increase the abundance of BA-tolerant bacterial species, such as *Alisitpes*, *Bacteroides*, and *Bilophila* (Alou *et al*., 2016).

The relationship between dysbiosis and mycotoxins

Mycotoxins are metabolites produced by the fungi *Aspergillus*, *Fusarium*, and *Penicillium*. The most common mycotoxins in poultry feed are the fumonisins (FUM) and deoxynivalenol (DON), both of which negatively affect the GM composition. The main damaging effects of mycotoxins on the gut health of broiler chickens are changes in GM homeostasis, changes in the caecal microbiome composition, increases in diversity and microbial richness, intestinal damage, and the activation of gut inflammation (Elmassry *et al*., 2022; Shanmugasundaram *et al*., 2023). Changes in the intestinal microbiota due to various mycotoxins are summarised in Table 2.

Table 2 The main effects of various mycotoxins on the composition of the poultry gut microbiome (adapted from Guerre, 2020)

Poultry type	Effect	References
Aflatoxin B1 (40 µg/kg)		
Broiler (ID)	Increased *Staphylococcus xylosus, Escherichia coli, Shigella* Decreased *Lactobacillus aviarius*	Guo *et al*., 2023
Aflatoxins (0.5 and 2 mg/kg)		
Broiler (ID)	Increased *E. coli*, *Salmonella* spp., *Klebsiella* spp.	Jahanian *et al*., 2019
Aflatoxin B1 (40 µg/kg)		
Broiler (ID)	No observed effect on *Lactobacilli*, *Bifidobacteria*, *Clostridium perfringens*, *E. coli*	Liu *et al*., 2018
Aflatoxin B1 (20 µg/kg)		
Broiler (CD)	Increased gram bacteria and total aerobic bacteria	Galarza-Seeber *et al*., 2016
Deoxynivalenol/vomitoxin (2.5 and 10 mg/kg)		
Broiler (CD)	Relative increase in *Firmicutes, Clostridiales* Relative decrease in *Proteobacteria*, *Oscillospira*, *Clostridiaceae*, *Clostridium*, *Ruminococcaceae*	Lucke *et al*., 2018
Fumonisin B1 (10.4 mg/kg) + fumonisin B2 (8.2 mg/kg)		
Broiler (ID)	Increased total *C. perfringens* Decreased *Lactobaccilus* spp., *Candidatus savagella*,	Antonissen *et al*., 2015
Ochratoxin A (235 µg/kg body weight)		
Duck (EX)	Increased *Bacteroidetes*, *Bacteroides*, *Bacteroides plebeius*	Wang *et al*., 2019
Ochratoxin A (200–462 µg/kg feed)		
Turkey (CD, JD, CE)	Decreased *Lactobacillus* spp., *Bifidobacterium* spp.	Śliżewska *et al*., 2020

ID: ileal digesta, CD: caecal digesta, EX: excreta, JD: jejunum digesta, CE: caecal excreta

Mycotoxins mainly target intestinal epithelial cells; however, the GM plays a prominent role in mycotoxin detoxification (Grenier & Applegate, 2013). Gut microbial diversity can be increased by subclinical doses of DON (Lucke *et al*., 2018) and FUM (Antonissen *et al*., 2015). In piglets, feeding FUM (fumonisin B1) at a dose of 12 mg/kg increased intestinal *Lactobacillus* but decreased the abundances of *Lachnospiraceae* and *Veillonellaceae* families (Mateos *et al*., 2018). In addition, mycotoxins, including DON, fumonisin B1, aflatoxin B1, ochratoxin A, zearalenone, and patulin, have adverse effects on the number of goblet cells that produce mucus, epithelial cell function and integrity, and GM composition (Attia *et al*., 2016; Robert *et al*., 2017). Diets containing subclinical levels of FUM and DON (3 and 4 mg/kg, respectively), resulted in increases in *Defluviitaleaceae* and *Lachnospiraceae* counts, decreases in *Moraxellaceae* and *Streptococcaceae* counts, and changes in caecal microbial composition and intestinal function (Shanmugasundaram *et al*., 2023). The United States Food and Drug Administration recommends maximum levels of 5 and 50 mg/kg for DON and FUM, respectively, in poultry finisher diets.

Studies on the effects of mycotoxins on the GM, and vice versa, have typically been conducted using high doses of mycotoxins, and research on the interactions between the GM and mycotoxins is still in its initial stages. It is therefore not possible to reach a conclusion about the impact of mycotoxins on health (Guerre, 2020). Administering a detoxifying compound at a dose of 1 g/kg to broiler chickens fed an aflatoxin-contaminated ration resulted in a stable GM, reduced the histopathological lesions of organs, and decreased some serum enzyme activities (Guo *et al*., 2023b). It can therefore be concluded that to prevent intestinal dysbiosis, the use of mycotoxin binders in poultry rations should be mandatory in high-risk areas (areas with high temperatures and humidity), in cases where feed has been improperly stored, in unsafe and low-quality feed, or for preventative purposes. Furthermore, better results have been obtained with multi-component binders that combine clay (bentonite or montmorillonite), yeasts (including glucomannans), and enzymatic detoxifiers (fumonisin esterase and zearalenone hydrolase).

The relationship between dysbiosis and anti-nutrients

Anti-nutritional factors and low-quality diets adversely affect the GM, gut health (intestinal mucosal integrity), and immunity. Therefore, it is important to prevent factors that cause dysbiosis through nutritional manipulation.

Phytate and NSPs are soluble and non-digestible nutrients in monogastric animals, and they are the main anti-nutritional factors in poultry nutrition. High levels of anti-nutrients increase the viscosity of the intestinal contents and consequently create the opportunity for infection, as they produce a suitable environment for the growth of harmful bacteria such as *E. coli* and *Clostridium perfringens*, and decrease the nutrient passage rate and adsorption (Raza *et al*., 2019). Some physico-chemical intestinal conditions, such as mucus secretion and composition, acidity, inflammation, and the secretion of bacteriostatic peptides by the pancreas, decrease nutrient absorption and change the GM and metabolite composition (Bushra *et al*., 2020). Generally, the total NSP contents and soluble NSP contents of poultry diets are 10%–12% and 1%–2.5%, respectively (Bach Knudsen, 1997). The most important NSPs are the arabinoxylans, β-mannans, and galactomannans (sugar gum). Some enzymes, such as xylanases, are used in carbohydrate degradation, while NSPs change the composition of the avian GM (Saeed *et al*., 2019). Feeding poultry with barley containing high levels of NSPs increases the incidence of *C. perfringens* infections and leads to necrotic enteritis in the intestines of broilers (Choct, 2002). Dysbiosis caused by necrotic enteritis, associated with a decrease in ileal fungal populations, leads to dysregulation of the GM (Xu *et al*., 2023).

The relationship between dysbiosis and nucleic acids

DNA damage plays an important role in cancer progression. Reactive oxygen species, ionising radiation, and polycyclic aromatic hydrocarbons are DNA-damaging agents that lead to cell apoptosis and mutations (tumour formation). Gut dysbiosis has an undesirable effect on the GM and cancer progression, but the underlying mechanism is not well understood. The interactions between the host‘s microbiota and methylome DNA can influence the gene functions associated with metabolic disease, inflammation, and oxidative stress of the intestinal wall and blood cells in Crohn’s disease (Xu *et al*., 2023). Also, this issue leads to inflammation and immune system activation, as well as gut barrier integrity damage, leading to an increase in permeability and the entrance of toxins into the blood and liver. Gut microbiome metabolites, vitamins, bioactive compounds, and mRNAs affect DNA and histone methylation, acetylation, or lactylation, which then influences the levels of gene expression. Furthermore,

mRNAs produced by the GM cause RNA degradation and inhibit viral RNA and transposons. However, the methylation of DNA and interference of RNA prevents gene expression and the methylation of histones. In contrast, the acetylation and lactylation of histones stimulates gene expression (Mostafavi Abdolmaleky & Zhou, 2024). An increase in pathogenic bacteria leads to the production of genotoxins that damage DNA in poultry host cells. Responses to DNA damage can cause the arrest of the cell cycle, apoptosis, or the induction of natural killer group 2-member D ligands (Espinoza & Minami, 2018). It has been reported that *Helicobacter pylori*, genotoxins, and colibactin from *Enterobacteriaceae* spp. affect DNA alkylates (Hsiao *et al*., 2023). Gram-negative bacteria such as *E. coli*, *H. pylori*, *Campylobacter* spp., *Shigella dysenteriae*, *Haemophilus ducreyi*, *Proteus mirabilis*, and *Klebsiella pneumonia* release genotoxins, cytolethal distending toxins, colibactin, and uropathogen-specific proteins that cause DNA pathway damage (Espinoza & Minami, 2018). The normalisation of sialic acid metabolism reduces dysbiosis, whereas the zebrafish tp53-mutant gene disrupts sialic acid metabolism and induces inflammation, pathogen overgrowth, and dysbiosis (Lee *et al.*, 2022).

Dietary competitive exclusion compounds play a key role in ameliorating the effects of the composition of the GM and its metabolites (Aleksandrova *et al*., 2017; Al Theyab *et al*., 2020). For instance, a diet containing high concentrations of carbohydrates or fats enhanced the production of *Firmicutes* (*Clostridium* spp.), *Prevotella*, and *Methanobrevibacter*, but reduced *Lactobacillus*, *Bacteroides*, *Bifidobacterium*, and *Akkermansia*, changing the production of SCFAs. These changes are usually linked to compromised intestinal barrier integrity, increased production of reactive oxygen species, and dyslipidaemia (Amabebe *et al*., 2020). Moreover, a high-fibre diet and acetate supplementation could alleviate gut dysbiosis by increasing the abundance of *Bacteroides acidifaciens* and modulating the ratio of *Firmicutes* to *Bacteroidetes* (Marques *et al*., 2017).

The relationship between dysbiosis and vitamins

The choline requirements for Ross 308 starter, grower one, grower two, and finisher rations were 1600, 1500, 1500, and 1400 mg/kg, respectively, in 2007, and increased to 1700, 1600, 1500, and 1450 mg/kg, respectively, in 2022. Choline, phosphatidylcholine, and L-carnitine are precursors that are used to produce trimethylamine N-oxide (TMAO) and betaine by the GM (Ebrahimzadeh Leylabadlo *et al*., 2020). Trimethylamine N-oxide negatively influences human health (Yu *et al*., 2020), reducing renal function (Zixin *et al*., 2022), increasing inflammatory and cardio-metabolic risks (Fu *et al*., 2020), and inducing chronic diseases such as metabolic syndrome (Yu *et al*., 2020), obesity, insulin resistance, cancer, and arteriosclerosis. Trimethylamine N-oxide metabolites also play a role in cholesterol changes, BA metabolism, and inflammatory pathway activation (Velasquez *et al*., 2016; Janeiro *et al*., 2018). Trimethylamine N-oxide also increases the incidence of cardiovascular complications, such as vessel blockage or coronary failure, by a factor of 1.5 (Heianza *et al*., 2017), and type 2 diabetes by 54% (Zhuang *et al*., 2019). Trimethylamine N-oxide is a sign of a change in the intestinal microbiome balance or dysbiosis (Landfald *et al*., 2017), while some species of *Eubacterium*, *Bacteroides*, *Clostridium*, and *Collinsella* have the potential to reduce this dysbiosis (Romano *et al*., 2015; Rath *et al*., 2017).

Bifidobacteria and lactic acid-producing bacteria in the intestines produce vitamin B complex groups and vitamin K_2 (a pathogen survival factor). Vitamin B_2 increases non-specific resistance against pathogens. Vitamin B_6 strengthens cellular and humoral immunity in the body and prevents pathogen growth (Li *et al*., 2018). Vitamin B_9 is produced by *Bifidobacteria* and *Lactobacilli* spp. in the human body, and its deficiency reduces lymphocyte proliferation and natural killer cell activity, as it plays a central role in the survival of regulatory T (Treg) cells. *Propionibacterium freudenreichii* and *Lactobacillus reuteri* synthesise vitamin B_{12} (LeBlanc *et al*., 2013). In addition, different *Bifidobacterium* and *Lactobacillus* spp. produce folate in the intestines (LeBlanc *et al*. 2013).

In poultry, vitamin K synthesis in the intestine is insufficient to meet the body's requirements. The Ross 308 requirements for menadione (vitamin K) in starter, grower, and finisher rations were 3.2, 3.0, and 2.2 IU/kg, respectively, in 2019, and 4.0, 3.6, and 3.2 IU/kg, respectively in 2022, whereas the 1994 NRC recommendations were 0.5, 0.5, and 0.5 mg/kg, respectively. The administration of sulfaquinoxaline increased vitamin K requirements by four to seven times in chickens and eight times in pheasants (Korver, 2023).

Although vitamin D_3 has a positive influence on the abundance of *Bacteroides* in the human gut, it has a negative effect on the abundance of *Prevotella* (Wu *et al*. 2011). Administration of vitamin D_3 for eight weeks decreased *Proteobacteria* but increased the abundance of *Bacteroidetes* in the human gut (Bashir *et al*., 2016). Mice supplemented with vitamin E (DL-α-tocopherol) showed a decrease in some

caecal microbiome diversity measures, such as the *Firmicutes*/*Bacteroides* ratio (Choi *et al*., 2019), while vitamin B_{12} supplementation increased *Enterobacteriaceae* abundance (Zhu *et al*., 2019). It can therefore be concluded that it is necessary to slightly increase the vitamin intake of broilers to meet their requirements according to breed-specific recommendations. Furthermore, the standard recommendations for vitamin supplementation should be revised.

Relationship between dysbiosis and other bacterial metabolites

Bacteriocins are antimicrobial compounds that are produced more by gram-positive bacteria than by gram-negative bacteria. They produce cell pores, leading to bacterial cell destruction and the inhibition of pathogenic agent release (Li *et al*., 2018). Bacteriocins synergise with beneficial bacteria to increase the speed of pathogen clearance from infected cells (Hoseini-Tavassol *et al*., 2022). For instance, bacteriocin-producing bacteria such as *Enterococcus faecium* and *Pediococcus pentosaceus* have been used as probiotics to prevent the growth of pathogenic bacteria in chickens (Shin *et al*., 2008).

Succinate is produced by both host cells during energy metabolism and the Krebs cycle and by the intestinal microbiota. It acts as an important pro-inflammatory signal (Mills *et al*., 2016), as its level increases in diseases related to metabolism and inflammation, such as high blood pressure, ischemic heart disease, type-2 diabetes, obesity, and IBD (Fernández-Veledo & Vendrell, 2019; Lavelle & Sokol, 2020). Oral gavage of Hyline brown hens with 3 mL of probiotic solution containing *Prevotella melaninogenica* and *Prevotella copri* (10^7 colony forming units/mL), along with the dietary supplementation of 0.25% sodium succinate, changed the caecal GM and reduced the fatty livers of the treated layers (Liu *et al*., 2024). Imidazole propionate (ImP) is a metabolite produced by the GM, with the level of production being affected by the populations of some microbes, such as *Clostridium bolteae*, *Ruminococcus gnavus*, and *Cenarchaeum symbiosum* (Fujisaka *et al*., 2023). Imidazole propionate levels have been found to be higher in patients with prediabetes, type-2 diabetes, and chronic inflammation, and elevated levels of ImP are thus considered an early warning sign for these diseases. An increase in the level of ImP is associated with a reduction in the *Bacteroides* count (Agus *et al*., 2020).

Increasing the host's resilience and reducing the risk of dysbiosis

The gut is a dynamic, adaptable organ, and various methods can be used to adjust and modulate its function and reduce the risk of dysbiosis. Improving the balance of the GM can be achieved by avoiding high-fat diets, high NSP diets, and a high protein/carbohydrate ratio in the diet, as well as by administering certain microbiome-promoting factors, such as whole grains, fermented foods, prebiotics, probiotics, phytogenic plants, herbal extracts, or organic acids. In addition, genetics, age, and improving environmental conditions can also help alter the GM composition towards a more favourable balance (Gill *et al*., 2006; Shehata *et al*., 2022a). Food additives can either have a positive effect on the microbial composition of the intestine, such as the addition of curcumin, omega-3, or polyphenols, or a negative effect that increases the incidence of diseases caused by microbial changes (such as the use of emulsifiers and the sweeteners intended to reduce obesity and diabetes) (Dudek-Wicher *et al*., 2018).

Antibiotics

Although the use of antibiotics in animal production systems decreased by 13% between 2017 and 2019 (WOAH, 2022), the global use of antimicrobials increased to 99500 t in 2020, with a predicted increase to 107470 t (an 8% increase) by 2030 (Mulchandani *et al*., 2023). Abuse of antibiotics influences the gut microbiota (Borre *et al*., 2014), and can increase the risks of cardiovascular diseases (Rasouli & Zeighami, 2023) and degenerative skeletal diseases (Lyu *et al*., 2023). Antibiotic administration suppresses TMAO levels, but these levels increase following the discontinuation of antibiotic treatment (Tang *et al*., 2013). Plasma TMAO levels are potential markers for predicting the risk of cardiovascular disorders in patients with chest pain (Tang *et al*., 2013; Rasouli & Zeighami, 2023).

Most research on antibiotics focuses on their effectiveness and mechanisms, while the pathophysiology of dysbiosis in poultry remains poorly understood. Another important issue regarding antibiotics is the duration of their use, with long-term use causing a decrease in microbial diversity and a change in the ratio of *Bacteroidetes* to *Firmicutes*, leading to the overgrowth of *Clostridium* and opportunistic bacteria such as *Salmonella typhimurium*, *E. coli*, and *Klebsiella* (Dudek-Wicher *et al*.,

2018). A comprehensive study on the effects of antibiotics on dysbiosis risk and the resilience of poultry, and the emergence of diseases due to the indiscriminate and unprincipled use of antibiotics, has not been conducted. One antibiotic-related disease known in humans is called drug-induced liver injury. Drug-induced liver injury has an occurrence of 2–19 cases per 100000 people, and is attributed to the use of amoxicillin-clavulanate, which can affect the diversity of the GM and its metabolites, potentially causing liver damage (Fu *et al*., 2022).

Dietary supplementation with antibiotic growth promoters (AGPs) has been used in poultry production to improve digestion, growth, and health (Rafiq *et al*., 2022), and reduce enteric bacterial infections with *C. perfringens* (Gadbois *et al*., 2008), *S. enterica* (The European Food Safety Authority, 2019), *E. coli*, and *Staphylococcus aureus* (de Mesquita Souza Saraiva *et al*., 2022). However, the misuse and long-term administration of AGPs induces adverse effects on the host's health and modifies the GM, leading to resistance in commensal and pathogenic microbiota (Rodrigues *et al*., 2021). The addition of AGPs to poultry diets could decrease the proportions of *C. perfringens* and other gram-positive bacteria, including *Lactobacilli*, *Streptococcus*, and *Bifidobacteria*, which are considered beneficial gut bacteria in the gastrointestinal tract (Broom, 2017), and increase the abundance and propagation of gram-negative bacteria such as *Salmonella* and *Campylobacter* spp., because of the absence of competition for nutrients (Kairmi *et al*., 2022).

Abbas *et al*. (2024) demonstrated that the administration of a broad-spectrum antibiotic cocktail (neomycin, ampicillin, metronidazole, vancomycin, and kanamycin, 0.5 g/L each) in the drinking water of broilers for seven or 14 days increased the abundance of antibiotic-resistant species, produced dysbiosis of the GM, delayed intestinal development, disturbed intestinal barrier function, and lowered immunity. Administration of this cocktail for two weeks also significantly decreased the abundances of *Firmicutes*, *Lactobacillus*, and *Bacillus*, and increased the abundances of *Bacteroidetes*, *Proteobacteria*, *Cyanobacteria*, and *Enterococcus* in the ileums of the broiler chickens. Furthermore, the administration of this cocktail for more than a two-week period significantly reduced the abundances of *Firmicutes*, *Lachnospiraceae*, *Oscillospiraceae*, *R. torques*, and *Ruminococcaceae*, but elevated the abundance of *Enterococcus*. Moreover, the addition of the antibiotic cocktail to the drinking water for one and two weeks significantly downregulated the ileal germinal centre cell numbers and the expression of occludin, zonula occludens-1, and mucin 2 genes (Abbas *et al*., 2024). The levels of claudin 1 mRNA were significantly diminished after 14 days of antibiotic cocktail treatment, which suggested the dysfunction of the intestinal tight junction barrier (Abbas *et al*., 2024). Similarly, the antibiotic cocktail disturbed the tight junction proteins, including claudin, occludin, and zonula occludens, which maintain the gut barrier, possibly leading to increased permeability of the intestines (Feng *et al*., 2019). A significant decrease in the abundance of *Lactobacillus* spp. in chickens' caecal contents was noticed after treatment with bacitracin methylene disalicylate, ampicillin, neomycin, tylosin, virginiamycin, and the ionophores, monensin and salinomycin (Engberg *et al*., 2000; Murai *et al*., 2016; Robinson *et al*., 2019). Treatment of broiler chickens with monensin, monensin–virginiamycin, and monensin–tylosin induced a marked reduction in the caecal abundance of *Bacilli* (Danzeisen *et al*., 2011). Moreover, the addition of a coccidiostat and antibiotic complex to the diets of broiler chickens decreased the abundances of caecal *Ruminococcaceae* and *Lactobacillaceae* (Kairmi *et al*., 2022). Also, antibiotic treatment with a cocktail containing neomycin and ampicillin increased the abundances of *Firmicutes*, *Ruminococcaceae*, and *Lachnospiraceae*, and introduced *Rikenellaceae* and *Enterobacteriaceae* (Zhang *et al*., 2021).

Probiotics, prebiotics, and synbiotics

Antibiotic alternatives, including probiotics, prebiotics, antimicrobial peptides, organic acids, hyperimmune serum, phytobiotics, enzymes, bacteriophages, clays, and others, have shown a positive influence on dysbiosis modification (Shehata *et al*., 2022c). Modification of the GM composition and health restoration are possible through the administration of a mixed combination of probiotics and prebiotic compounds (synbiotics) (Attia *et al*., 2023). The prevention and treatment of cardiovascular diseases is being advanced by the ability of synbiotics to alter the intestinal microbiome (Jin *et al*., 2019). Probiotics containing *Lactobacillus plantarum* and *L. rhamnosus* can reduce blood lipid levels in patients with coronary artery disease (Akbarzadeh *et al*., 2012) and myocardial infarction, improve left ventricular hypertrophy and endothelial vessel function (Lam *et al*., 2012), and reduce systemic inflammatory biomarkers (Malik *et al*., 2018).

Table 3 shows the effects of dietary nutrients on dysbiosis (Brown *et al*., 2012). Rations enriched with probiotics increased the gut counts of *Lactobacilli*, *Lachnospiraceae*, *F. prausnitzii*, and *Bacteroides*

(Flint *et al*., 2015; Maukonen & Saarela, 2015; Chung *et al*., 2016). Moreover, the short-term administration of synbiotics reduced the symptoms of inflammatory diseases; however, the long-term effects are not known, as dysbiosis in most inflammatory diseases changes the GM composition and the immune response (Brown *et al*., 2011).

Piglets' resistance to cold stress was increased by the dietary addition of probiotics or by the adjustment of the composition of the diet to modify the GM structure (Zhang *et al*., 2024). Cold stress has significantly adverse effects on energy balance and increases purine degradation by *Acholeplasma*, *Proteiniphilum*, and *Olsenella* spp. in the colon and ileum; *Ruminococcaceae* spp., *Butyricicoccus*, and *Lachnospiraceae* FCS020 in the mucosa of the colon; and *Sphingomonas*, *Helicobacter*, *Cutibacterium*, and *Bradyrhizobium* in the mucosa of the ileum (Zhang *et al*., 2024).

Table 3 The effects of dietary nutritional characteristics on the gut microbiome (adapted from Brown *et al*., 2012)

Effect on the gut microbiome	References
Low carbohydrate	
Increased *Bacteroidetes* in humans	Walker *et al*., 2011
Complex carbohydrates	
Increased *Bacteroides thetaiotaomicron*, *Bacteroides longum* (*longum*), *Bacteroides breve* in humans	Walker *et al*., 2011 Pokusaeva *et al*., 2011
Decreased *Enterobacteriaceae, Mycobacterium avium* (*paratuberculosis*) in humans	
Low calorie	
Decreased *Lactobacillus*, *Bifidobacteria*, *Clostridium coccoides* in humans	Santacruz *et al*., 2009
High fat	
Decreased *Bifidobacteria* spp. in mice	Zhang *et al*., 2010
High fat (+ high sugar)	
Increased *Enterococcus* spp., *Clostridium innocuum*, *Catenibacterium mitsuokai* in humans	Turnbaugh *et al*., 2009
Decreased *Bacteroides* in humans	
High n-6 polyunsaturated fats (safflower oil)	
Increased δ-*Proteobacteria*, *Firmicutes*, *Actinobacteria*, *Proteobacteria* in mice and rats	De la Serre *et al*., 2010 Hildebrandt *et al*., 2009 Turnbaugh *et al*., 2008
Decreased *Bacteroidetes* in mice and rats	

Probiotics can modify behaviour and brain function by suppressing the production of IL-6 and IL-4, stimulating the production of IL-10, and consequently preventing and treating neurological diseases and high blood pressure (Babakhani & Hosseini, 2019). In broiler chickens, treatment with probiotics containing *Bacillus subtilis* increased 5-HT levels in the hypothalamus (raphe nuclei), decreased norepinephrine and dopamine levels in the hypothalamus, and improved bone mineral density (Yan *et al*., 2018). *L. rhamnosus* administration to broiler chickens prevented tibial dyschondroplasia (TD) by improving tibia weight, length, and diameter (Liu *et al*., 2021), and improved trabecular bone volume and bone formation in mice (Tyagi *et al*., 2018). In rats, *Bifidobacterium longum* increased bone mineral density and stimulated calcium and phosphorous absorption (Rodrigues *et al*., 2012).

Faecal microbiota transplantation (FMT)

During the past decades, the total microbial communities from healthy adult chickens have been transplanted to newly hatched chicks via FMT. Faecal microbiota transplantation from healthy donors assists in the modulation and alteration of the GM in patients with IBD, reaching a remission rate of 35%–40% (Cammarota *et al*., 2017; Imdad *et al.*, 2023). Inoculating young broilers with the microbiomes from highly feed-efficient donors positively affected the composition of the caecal microbiota and the

host's intestinal development (Metzler-Zebeli *et al*., 2019). Nonetheless, the use of FMT to control enteric foodborne infections in poultry (e.g., *Salmonella* and *Campylobacter* spp.) has had varying results (Gilroy *et al*., 2018; Chintoan-Uta *et al*., 2020; Aruwa *et al*., 2021; Taha-Abdelaziz *et al*., 2023; Pottenger *et al*., 2023).

Reshaping the GM using FMT could enhance chicken growth by balancing T helper 17 (Th17) and Treg cells. Transferring the faecal microbiota from healthy chicks that have good growth performance parameters and a high abundance of *Lactobacillus* in droppings to one-day-old chicks enhanced their growth performance, reduced Th17 cell-associated transcriptional factors and cytokines, and elevated jejunal cytokines and Treg cell-associated transcriptional factors (Ma *et al*., 2023). Faecal microbiota transplantation and inulin supplementation synergistically affected both the intestinal barrier and immune function in chicks (Song *et al*., 2024). It promoted the development of gut-associated lymphoid tissue, which promoted early intestinal immunity by regulating the cluster of differentiation 28 protein and the cytotoxic T-lymphocyte-associated protein 4 in broilers (Song *et al*., 2024). Moreover, FMT used synergistically with inulin supplementation elevated the secretion of transforming growth factor-β, and increased the intestinal goblet cell number and mucin 2 expression in week two of treatment. The β-cell activating factor, the transcription factor Pax5, the C-X-C motif chemokine ligand 12, and IL-2 expression were elevated in week one, and C-X-C motif chemokine receptor 4 and IL-2 expression in the caecal tonsils were elevated in week two of treatment (Song *et al*., 2024). Moreover, oral treatment of young broilers with FMT using adult caecal microbiota could enhance the development of the GM, and has been found to prevent the colonisation of *Campylobacter* (Pang *et al*., 2023). Further research on the use and effectiveness of FMT using a synthetic microbiome designed for the control of foodborne pathogens in poultry would be of interest.

Reducing stress and inflammation

Lactobacillus johnsonii and *L. reuteri* increased oxytocin production by cells in the brain (Bray, 2016), while *Bacteroidetes*, *Actinobacteria*, and *Firmicutes* decreased oxytocin production in mice (Dinan & Cryan, 2017). Mice reared under conditions inducing stress and anxiety showed changes in the intestinal microbiota, with a concomitant reduction in brain-derived neurotrophic factor, which is involved in the prevention of β cell exhaustion, and the regulation of glucose and energy metabolism (Autry & Monteggia, 2012; Prinsloo & Lyle, 2015). Decreases in the brain-derived neurotrophic factor level are associated with three neurodegenerative diseases (Bathina & Das, 2015).

Gamma-aminobutyric acid produced by *Lactobacillus brevis* can affect brain health and assist in the treatment of diabetes (Dinan & Cryan, 2016); can help regulate blood pressure, heart rate, anxiety, and depression; and can regulate neuronal pain (Hyland & Cryan, 2016). In addition, GABA is regarded as a neurotransmitter inhibitory substance and is used for stress reduction (Park *et al*., 2023). A dietary concentration of GABA of 100 mg/kg downregulated AgRP (NPY/AgRP) neuropeptides and stimulated the FI of broilers (El-Naggar *et al*., 2019).

Gut microbial modification leads to a reduction in inflammation in patients with chronic kidney disease (Li & Tang, 2018). Short-chain fatty acids regulate immunity and modulate inflammation by inhibiting deacetylases or G protein-coupled receptors (Chang *et al*., 2014). The loss of butyrate-producing bacteria causes the passive leakage of microbial receptors, such as LPSs, and these bind to TLRs and other intrinsic innate immune receptors, causing colonic inflammation (Furusawa *et al*., 2013). The levels of SCFAs produced by the intestinal microbiota are reduced in type-1 diabetic patients (Siljander *et al*., 2019), as these fatty acids reduce serum glucose levels, insulin resistance, and inflammation, and increase the secretion of GLP-1 in type-2 diabetic patients (Puddu *et al*., 2014). T-regulatory cells and SCFAs produced by intestinal microbiota such as *Lactobacilli*, *Bifidobacteria*, and *Saccharomyces boulardii* reduce bone loss by regulating inflammatory factors (Celiberto *et al*., 2018). Administration of glycerol monolaurate also induces anti-inflammatory and anti-apoptotic properties by suppressing ROS and the tumour necrotising factor-κB signalling pathway in avian macrophages (Kong *et al*., 2024).

Regarding the environment, climatic and litter conditions could affect the complex poultry GM (Shang *et al*., 2018). It has been reported that the diversity and richness of the caecal microbiome was higher in summer than in winter (Oakley *et al*., 2018; Diaz Carrasco, 2019). Other management factors in poultry flocks, such as feed type, feeding time, free-range access, stocking density, litter type, heating, ventilation, biosecurity, hygiene, medical treatment, and vaccination, could also influence the birds' GM (Wang *et al*., 2018; Diaz Carrasco *et al*., 2019; Göransson *et al*., 2023). Reusing moist litter increases

the pathogenic bacterial load on poultry farms and increases the possibility of pathogen transfer to humans or consumers through the poultry supply chain (Cressman *et al*., 2010).

Modification of the microbiome to reduce stress levels is possible through the administration of probiotics, prebiotics, synbiotics and postbiotics, as well as through the development of the early-life microbiome, nutritional interventions (herbal extracts, essential oils, and yeast extracts), the reduction of antibiotic use, the improvement of water quality, the monitoring and adjustment of the diet, and the management of stressors. The best strategies to minimise stress in poultry farming are to optimise environmental conditions (temperature, humidity, ventilation, and lighting), improve housing conditions, avoid overcrowding, provide a balanced diet, reduce handling and disturbances, implement disease prevention and health management, and offer enrichment and behavioural support (perches and pecking objects).

Increasing FI and appetite

The administration of GABA, or its producer *L. brevis*, increased the FI of commercial broiler chickens (El-Naggar *et al*., 2019). *Clostridium sporogenes* and *R. gnavus* affect appetite and mood by producing tryptamine, a product of tryptophan decarboxylation (Williams *et al*., 2014). Tryptophan is involved in the production of 5-HT, which is necessary for the regulation of colon movement and the improvement of appetite, behaviour, and mood (Neuman *et al*., 2015; Jenkins *et al*., 2016; Agus *et al*., 2018; Malinova *et al*., 2018).

Modifications in physiological conditions

Tibial dyschondroplasia accounts for 30% of all skeletal afflictions in chickens worldwide (Mehmood *et al*., 2018). According to Xu *et al*. (2023b), TD in broilers resulted in distinguishable GM structures, with perturbations in the GM effecting bone homeostasis through unknown mechanisms. Specifically, there was a 45.5% decrease in the *Bacteroidetes* count and a 53.6% increase in the *Firmicutes* count, when compared to the abundance of each phylum in the control group (*Bacteroidetes* 73% and *Firmicutes* 26.3%). The abundance of *Blautia* and *Coprococcus* in TD-affected broilers was also higher than that in the control group, leading to higher blood glucose levels (Xu *et al*., 2023b). In the same study, the treatment of TD-affected broilers with total flavonoids from *Rhizoma drynariae* for two weeks led to the modulation of blood glucose levels, the recovery of gut barrier damage, the modification of the diamine oxidase enzyme level in plasma, and the upregulation of intestinal tight junction proteins (claudin 1 and occludin), by reducing gut barrier permeability (Xu *et al*., 2023).

In humans, the reduction of disease incidence by nutrition modification is particularly important. For instance, SCFA levels in faecal samples decrease in active IBD (ulcerative colitis and Crohn's disease) (Parada Venegas *et al*., 2019), and rectal inoculation with butyrate has been shown to help treat patients with colitis (Scheppach *et al*., 1992). Any imbalance in the GM composition leads to an increase in uremic toxicity compounds, including TMAO, indoxyl sulphate and p-cresyl sulphate, as well as dysbiosis and intestinal permeability.

Conclusions

There are many strategies for optimising poultry gut health, including supplementing feed additives such as prebiotics, probiotics, synbiotics, and postbiotics; providing a balanced AA profile; reducing the use of antibiotics; synergising the effects of fibres and probiotics; reducing stress and inflammatory agents; optimising drinking water quality; avoiding sudden changes in diet; and striving to provide maximum welfare and comfort for the birds. Despite this article and others focusing on understanding the poultry microbiome and its impact on general health and disease, further investigations are required to explore the factors affecting the gut ecosystem and its interactions with the host, especially in poultry. Furthermore, it is important to develop various effective methodologies to identify the beneficial strains of bacteria that play key roles in maintaining poultry health.

In this review, we have attempted to provide an insight into the world of the poultry microbiome and the many research gaps in understanding the precise mechanisms of GM dysbiosis and its impacts on the immune system, reproduction, oxidative stress, egg and meat quality, growth and performance, gut health, and vaccines. In addition, the use of advanced genomics and metagenomics technologies, such as next-generation sequencing, the development of specific probiotics and prebiotics to reduce

GM dysbiosis, and the creation of animal models to study GM dysbiosis in greater detail will also be valuable contributions to the field.

Author contributions

AS: concept and study design and writing of the first draft. WAAE: Critical review, and editing of the article, YAA, NMZ, FB, VT, revision, editing and overall review of the manuscript. All authors read and approved the final version.

Conflicts of interest declaration

The authors declare no conflict of interest.

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References

Abbas, W., Bi, R., Hussain, M.D., Tajdar, A., Guo, F., Guo, Y., & Wang, Z. 2024. Antibiotic cocktail effects on intestinal microbial community, barrier function, and immune function in early broiler chickens. Antibiotics, 13(5), 413. doi 10.3390/antibiotics13050413

Abd El-Hack, M.E., El-Saadony, M.T., Shehata, A.M., Arif, M., Paswan, V.K., Batiha, G.E., Khafaga, A.F., & Elbestawy, A.R. 2021. Approaches to prevent and control *Campylobacter* spp. colonization in broiler chickens: a review. Environ. Sci. Pollut. Res. Int., 28, 4989–5004.

Abd El-Hack, M.E., El-Saadony, M.T., Alqhtani, A.H., Swelum, A.A., Salem, H.M., Elbestawy, A..R., Noreldin, AE., Babalghith, A.O., Khafaga, A.F., Hassan, M.I., & El-Tarabily, K.A. 2022. The relationship among avian influenza, gut microbiota and chicken immunity: an updated overview. Poult. Sci., 101(9), 102021.

Agus, A., Clément, K., & Sokol, H. 2020. Gut microbiota-derived metabolites as central regulators in metabolic disorders. Gut, 70(6), 1174–1182.

Agus, A., Planchais, J., & Sokol, H. 2018. Gut microbiota regulation of tryptophan metabolism in health and disease. Cell Host Microbe 23, 716–724.

Ahn, Y.T., Kim, G.B., Lim, K.S., Baek, Y.J., & Kim, H.U. 2023. Deconjugation of bile salts by *Lactobacillus acidophilusisolates*. Int. Dairy J., 13, 303–311.

Akbarzadeh, F. & Homayouni, A. 2012. Dairy probiotic foods and coronary heart disease: A review on mechanism of action. In: Probiotics. Ed: Rigobelo, E. InTech: London, UK. 121–128.

Alberghina, D., Biondi, V., Passantino, A., Giunta, F., & Panzera, M. 2020. Plasma serotonin in laying hens (*Gallus gallus domesticus*) with and without foot pad dermatitis. Int. J. Tryptophan Res., 13, 1178646920927380.

Aleksandrova, K., Romero-Mosquera, B., & Hernandez, V. 2017. Diet, gut microbiome and epigenetics: Emerging links with inflammatory bowel diseases and prospects for management and prevention. Nutrients, 9, 962.

Al Theyab, A., Almutairi, T., Al-Suwaidi, A.M., Bendriss, G., McVeigh, C., & Chaari. 2020. Epigenetic effects of gut metabolites: Exploring the path of dietary prevention of type 1 diabetes. Front. Nutr., 7, 563605.

Alou, M.T., Lagier, J.C., & Raoult, D. 2016. Diet influence on the gut microbiota and dysbiosis related to nutritional disorders. Hum. Microbiome J., 1, 3–11. doi 10.1016/j.humic.2016.09.001

Amabebe, E., Robert, F.O., Agbalalah, T., & Orubu, E.S. 2020. Microbial dysbiosis-induced obesity: Role of gut microbiota in homoeostasis of energy metabolism. Br. J. Nutr., 123, 1127–1137.

Amerah, A.M., Ravindran, V., Lentle, R.G., & Thomas, D.G. 2007. Influence of feed particle size and feed form on the performance, energy utilization, digestive tract development, and digesta parameters of broiler starters. Poult. Sci., 86, 2615–2623. doi 10.3382/ps.2007-00212

Anderson, G.M., Feibel, F.C., & Cohen, D.J. 1987. Determination of serotonin in whole blood, platelet-rich plasma, platelet-poor plasma and plasma ultrafiltrate. Life Sci., 40, 1063–1070.

Antonissen, G., Croubels, S., Pasmans, F., Ducatelle, R., Eeckhaut, V., Devreese, M., & Van Immerseel, F. 2015. Fumonisins affect the intestinal microbial homeostasis in broiler chickens, predisposing to necrotic enteritis. Vet. Res., 46, 98. doi 10.1186/s13567-015-0234-8

Aruwa, C.E., Pillay, C., Nyaga, M.M., & Sabiu, S. 2021. Poultry gut health – microbiome functions, environmental impacts, microbiome engineering and advancements in characterization technologies. J. Animal Sci. Biotechnol., 12, 119. doi 10.1186/s40104-021-00640-9

Attia, Y.A., Abd Al-Hamid, A.E., Allakany, H.F., Al-Harthi, M.A., & Mohamed, N.A. 2016. Necessity of continuing of supplementation of non-nutritive feed additive during day 21-42 of age following three weeks of feeding aflatoxin to broiler chickens. J. Appl. Anim. Res., 44(1), 87–98.

Attia, Y.A., Basiouni, S., Abdulsalam, N.M., Bovera, F., Aboshok, A.A., Shehata, A.A., & Hafez, H.M. 2023. Alternative to antibiotic growth promoters: Beneficial effects of *Saccharomyces cerevisiae* and/or

Lactobacillus Acidophilus supplementation on the growth performance and sustainability of broilers' production. Front. Vet. Sci., 10, 1259426. doi 10.3389/fvets.2023.1259426.
The European Food Safety Authority, 2019. The European Union one health 2018 zoonoses report. EFSA Journal, 17(12) , 17, e05926.
Autry, A.E. & Monteggia, L.M. 2012. Brain-derived neurotrophic factor and neuropsychiatric disorders. Pharmacol. Rev. 64(2), 238–258.
Aviagen. 2022. ROSS broiler nutrition specifications (All plant protein based feeds). pp 1–6.
Babakhani, S. & Hosseini, F. 2018. Gut microbiota: An effective factor in the human brain and behavior. Neurosci. J. Shefaye Khatam, 7, 106–118. doi 10.29252/shefa.7.1.106.
Bach Knudsen, K.E. 1997. Carbohydrate and lignin contents of plant materials used in animal feeding. Anim. Feed Sci. Tech., 67, 319–338.
Bajaj, J.S., Ridlon, J.M., Hylemon, P.B., Thacker, L.R., Heuman, D.M., Smith, S., Sikaroodi, M., & Gillevet, P.M. 2012. Linkage of gut microbiome with cognition in hepatic encephalopathy. Am. J. Physiol. Gastrointest. Liver Physiol., 302(1).
Bärebring, L., Winkvist, A., Gjertsson, I., & Lindqvist, H.M. 2018. Poor dietary quality is associated with increased inflammation in Swedish patients with rheumatoid arthritis. Nutrients, 10, 1535.
Barekatain, R., Chalvon-Demersay, T., McLaughlan, C., & Lambert, W. 2021. Intestinal barrier function and performance of broiler chickens fed additional arginine, combination of arginine and glutamine or an amino acid-based solution. Animals, 11, 2416.
Bashir, M., Prietl, B., Tauschmann, M., Mautner, S.I., Kump, P.K., Treiber, G., Wurm, P., Gorkiewicz, G., Högenauer, C., & Pieber, T.R. 2016. Effects of high doses of vitamin D3 on mucosa-associated gut microbiome vary between regions of the human gastrointestinal tract. Eur. J. Nutr., 55, 1479–1489.
Bathina, S. & Das, U.N. 2015. Brain-derived neurotrophic factor and its clinical implications. Arch. Med. Sci., 11(6), 1164-1178. doi 10.5114/aoms.2015.56342.
Bernard, M., Lecoeur, A., Coville, J.L., Bruneau, N., Jardet, D., Lagarrigue, S., Annabelle, M., Fanny, C., Géraldine, P & Zerjal, T. 2024. Relationship between feed efficiency and gut microbiota in laying chickens under contrasting feeding conditions. Sci. Rep., 14(1), 8210. doi 10.1038/s41598-024-58374-3.
National Institute of Diabetes and Digestive and Kidney Diseases, 2012. LiverTox: Clinical and research information on drug-induced liver injury. National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD.
Blachier, F., Beaumont, M., Andriamihaja, M., Davila, A.M., Lan, A., Grauso, M., Armand, l., Benamouzig, R., & Tomé, D. 2017. Changes in the luminal environment of the colonic epithelial cells and physiopathological consequences. Am. J. Pathol., 187, 476–486.
Blachier, F., Beaumont, M., Portune, K.J., Steuer, N., Lan, A., Audebert, M., Khodorova, N., Andriamihaja, M., Airinei, G., Benamouzig, R., & Sanz, Y. 2019. High-protein diets for weight management: Interactions with the intestinal microbiota and consequences for gut health. A position paper by my new gut study group. Clin. Nutr., 38, 1012–1022.
Borre, Y.E., Moloney, R.D., Clarke, G., Dinan, T.G., & Cryan, J.F. 2014. The impact of microbiota on brain and behavior: mechanisms & therapeutic potential. In: Microbial endocrinology: The microbiota-gut-brain axis in health and disease. Eds: Lyte, M., Cryan, J., Springer, New York, NY. pp. 373-403. doi 10.1007/978-1-4939-0897-4_17
Bortoluzzi, C., Rochell, S.J., & Applegate, T.J. 2018. Threonine, arginine, and glutamine: Influences on intestinal physiology, immunology, and microbiology in broilers. Poult. Sci., 97, 937–945.
Bray, N. 2016. Gut-brain communication: Making friends with microbes. Nat. Rev. Neurosci., 17(9), 533. doi 10.1038/nrn.2016.93
Broom, L.J. 2017. The sub-inhibitory theory for antibiotic growth promoters. Poult. Sci., 96, 3104–3108.
Brown, K., DeCoffe, D., Molcan, E., & Gibson D.L. 2012. Diet-induced dysbiosis of the intestinal microbiota and the effects on immunity and disease. Nutrients, 4(8), 1095–1119.
Brown, C.T., Davis-Richardson, A.G., Giongo, A., Gano, K.A., Crabb, D.B., Mukherjee, N., Casella, G., Drew, J.C., Ilonen, J., Knip, M., & Hyöty, H. 2011. Gut microbiome metagenomics analysis suggests a functional model for the development of autoimmunity for type 1 diabetes. PloS One, 6, e25792.
Bungo, T., Dodo, K.I., Kawamura, K., Izumi, T., & Ueda, H. 2005. Effects of various μ-, δ- and κ-opioid ligands on food intake in the meattype chick. Physiol. Behav., 8, 519–523.
Bushra, M., Al-Obaidi, B., Fayyadh, M.H., & Dakheel K. 2020. The potential influence of fractional substitute of soybean meal with guar meal supplement of salinomycine and mycofixe on performance and GUT ecosystem of broiler. Int. J. Pharm. Res., 12, 848–854.
Byrne, C., Chambers, E., Morrison, D.J., & Frost, G. 2015. The role of short chain fatty acids in appetite regulation and energy homeostasis. Int. J. Obes., 39(9), 1331–1338.
Cammarota, G., Ianiro, G., Tilg, H., Rajilić-Stojanović, M., Kump, P., Satokari, R, Sokol, H., Arkkila, P., Pintus, C., Hart, A., & Segal, J. 2017. European consensus conference on faecal microbiota transplantation in clinical practice. Gut, 66(4), 569–580.

Canfora, E.E., Jocken, J.W., & Blaak, E.E. 2015. Short-chain fatty acids in control of body weight and insulin sensitivity. Nat. Rev. Endocrinol., 11, 577–591. doi 10.1038/nrendo.2015.128

Celiberto, L.S., Graef, F.A., Healey, G.R., Bosman, E.S., Jacobson, K., Sly, L.M., & Vallance, B.A. 2018. Inflammatory bowel disease and immunonutrition: novel therapeutic approaches through modulation of diet and the gut microbiome. Immunology, 155, 36–52.

Chalvon-Demersay, T., Luise, D., Le Floc'h, N., Tesseraud, S., Lambert, W., Bosi, P., Trevisi, P., Beaumont, M., & Corrent, E. 2021a. Functional amino acids in pigs and chickens: implication for gut health. Front. Vet. Sci., 25(8), 663727.

Chalvon-Demersay, T., Yamphet, T., Srinongkote, S., Ohara, H., & Lambert, W. 2021b. Supplementing functional amino acids and polyphenols at low dose can restore performance and amino acid digestibility in broilers challenged with coccidiosis. Livest. Sci., 254, 104769.

Chambers, E.S., Viardot, A., Psichas, A., Morrison, D.J., Murphy, K.G., Zac-Varghese, S.E., MacDougall, K., Preston, T., Tedford, C., Finlayson, G.S., & Blundell, J.E. 2015. Effects of targeted delivery of propionate to the human colon on appetite regulation, body weight maintenance and adiposity in overweight adults. Gut, 64(11), 1744–1175.

Chang, P.V., Hao, L., Offermanns, S., & Medzhitov, R. 2014. The microbial metabolite butyrate regulates intestinal macrophage function via histone deacetylase inhibition. PNAS, 111(6), 2247–2252.

Chehimi, M., Ward, R., Pestel, J., Robert, M., Pesenti, S., Bendridi, N., Michalski, M.C., Laville, M., Vidal, H., & Eljaafari, A. 2019. Omega-3 polyunsaturated fatty acids inhibit il-17a secretion through decreased icam-1 expression in t cells co-cultured with adipose-derived stem cells harvested from adipose tissues of obese subjects. Mol. Nutr. Food Res., 63(11), e1801148. doi 10.1002/mnfr.201801148

Chen, J. & Vitetta, L. 2020. The role of butyrate in attenuating pathobiont-induced hyperinflammation. Immune Netw., 20(2), e15. doi 10.4110/in.2020.20. e15.

Cheng, Y., Mai, Q., Zeng, X., Wang, H., Xiao, Y., Tang, L., Li, J., Zhang, Y., & Ding, H. 2019. Propionate relieves pentylenetetrazol-induced seizures, consequent mitochondrial disruption, neuron necrosis and neurological deficits in mice. Biochem. Pharmacol., 169, 113607.

Chintoan-Uta, C., Wisedchanwet, T., Glendinning, L., Bremner, A., Psifidi, A., Vervelde, L., Watson, K., Watson, M., & Stevens, M.P. 2020. Role of cecal microbiota in the differential resistance of inbred chicken lines to colonization by *Campylobacter jejuni*. Appl. Environ. Microbiol., 86, e02607-19.

Choct, M. 2022. Chapter 13. Non-starch polysaccharides: effect on nutritive value. In: Poultry feedstuffs: Supply, Composition and Nutritive Value. Eds: McNab, J.M., Boorman, K.N. CAB International. pp 221–235.

Choi, K.Y., Lee, T.K & Sul, W.J. 2015. Metagenomic analysis of chicken gut microbiota for improving metabolism and health of chickens—a review. Asian-Australas. J. Anim. Sci., 28, 1217–1225.

Choi, Y., Lee, S., Kim, S., Lee, J., Ha, J., Oh, H., Lee, Y., Kim, Y., & Yoon, Y 2019. Vitamin E (α-tocopherol) consumption influences gut microbiota composition. Int. J. Food Sci. Nutr., 71, 1–5.

Chung, W.S.F., Walker, A.W., Louis, P., Parkhill, J., Vermeiren, J., Bosscher, D., Duncan, S.H., & Flint, H.J. 2016. Modulation of the human gut microbiota by dietary fibres occurs at the species level. BMC Biol., 14, 3.

Clavijo, V. & Flórez, M.J.V. 2018. The gastrointestinal microbiome and its association with the control of pathogens in broiler chicken production: a review. Poult. Sci., 97, 1006–1021. doi 10.3382/ps/pex359

Costabile, A., Klinder, A., Fava, F., Napolitano, A., Fogliano, V., Leonard, C., Gibson, G.R., & Tuohy, K.M. 2008. Whole-grain wheat breakfast cereal has a prebiotic effect on the human gut microbiota: A double-blind, placebo-controlled, crossover study. Br. J. Nutr., 99, 110–120.

Cressman, M.D., Yu, Z., Nelson, M.C., Moeller, S.J., Lilburn, M.S., & Zerby, H.N. 2010. Interrelations between the microbiotas in the litter and in the intestines of commercial broiler chickens. Appl. Environ. Microbiol., 76(19), 6572–6582. doi 10.1128/AEM.00180-10

Dahal, R.H., Kim, S., Kim, Y.K., Kim, E.S., & Kim, J. 2023. Insight into gut dysbiosis of patients with inflammatory bowel disease and ischemic colitis. Front. Microbiol., 14, 1174832.

Danzeisen, J.L., Kim, H.B., Isaacson, R.E., Tu, Z.J., & Johnson, T.J. 2011. Modulations of the chicken cecal microbiome and metagenome in response to anticoccidial and growth promoter treatment. PLoS ONE, 6, e27949.

Darzi, J., Frost, G.S., Swann, J.R., Costabile, A., & Robertson, M.D. 2016. L-rhamnose as a source of colonic propionate inhibits insulin secretion but does not influence measures of appetite or food intake. Appetite, 98, 142–149.

De Filippo, C., Di Paola, M., Ramazzotti, M., Albanese, D., Pieraccini, G., Banci, E., Miglietta, F., Cavalieri, D., & Lionetti, P. 2017. Diet, environments, and gut microbiota. A preliminary investigation in children living in rural and urban Burkina Faso and Italy. Front. Microbiol., 8, 1979.

de Mesquita Souza Saraiva, M., Lim, K., do Monte, D.F.M., Givisiez, P.E.N., Alves, L.B.R., de Freitas Neto, O.C., Kariuki, S., Júnior, A.B., de Oliveira, C.J.B., & Gebreyes, W.A. 2022. Antimicrobial resistance in the globalized food chain: A One Health perspective applied to the poultry industry. Vet. Microbiol., 53, 465–486.

DeGruttola, A.K., Low, D., Mizoguchi, A., & Mizoguchi, E. 2016. Current understanding of dysbiosis in disease in human and animal models. Inflamm. Bowel Dis., 22(5), 1137–1150. doi 10.1097/MIB.0000000000000750.

Diaz Carrasco, J.M. 2019. Seasonality as a driver of cecal and litter microbiota variation in commercial broiler chickens. In: Proceedings of the Symposium on Gut Health in Production of Food Animals. St. Louis, USA.

Diaz Carrasco, J.M., Casanova, N.A., & Miyakawa, M.E. 2019. Microbiota, gut health and chicken productivity: what is the connection? Microorganisms, 7, 374. doi 10.3390/microorganisms7100374

Dinan, T.G. & Cryan, J.F. 2016. Microbes, immunity, and behavior: psychoneuroimmunology meets the microbiome. Neuropsychopharmacology, 42(1), 178–192.

Dinan, T.G. & Cryan, J.F. 2017. Gut-brain axis in 2016: Braingut- microbiota axis - mood, metabolism and behaviour. Nat. Rev. Gastroenterol. Hepatol., 14(2), 69–70.

Dominianni, C., Sinha, R., Goedert, J.J., Pei, Z., Yang, L., Hayes, R.B., & Ahn, J. 2015. Sex, body mass index, and dietary fiber intake influence the human gut microbiome. PLoS One, 10, e0124599. doi 10.1371/journal.pone.0124599

Dudek-Wicher, R., Junka, A., & Bartoszewicz, M. 2018. The influence of antibiotics and dietary components on gut microbiota. Prz. Gastroenterol. 13(2), 85–92. doi 10.5114/pg.2018.76005

Duke, G.E. 1992. Recent studies on regulation of gastric motility in turkeys. Poult. Sci. 71, 1–8. doi 10.3382/ps.0710001

Dunkley, K.D., Dunkley, C.S., Njongmeta, N.L., Callaway, T.R., Hume, M.E., Kubena, L.F., Nisbet, D.J. & Ricke, S.C. 2007. Comparison of in vitro fermentation and molecular microbial profiles of high-fiber feed substrates incubated with chicken cecal inocula. Poult. Sci., 86(5), 801–810.

Ebrahimzadeh Leylabadlo, H., Sanaie, S., Heravi, F.S., Ahmadian, Z., & Ghotaslou, R. 2020. From role of gut microbiota to microbial-based therapies in type 2-diabetes. Infect. Genet. Evol., 81, 104268. doi 10.1016/j.meegid.2020.104268

Elmassry, M.M., Zayed, A., & Farag, M.A. 2022. Gut homeostasis and microbiota under attack: Impact of the different types of food contaminants on gut health. Crit. Rev. Food Sci. Nutr., 62, 738–763. doi 10.1080/10408398.2020.1828263.

El-Naggar, K., El-Kassas, S., Abdo, S.E., & Kirrella, A.A. 2019. Role of gamma-aminobutyric acid in regulating feed intake in commercial broilers reared under normal and heat stress conditions. J. Therm. Biol., 84, 164–175. doi 10.1016/j.jtherbio.2019.07.004.

El-Saadony, M.T., Zabermawi, N.M., Zabermawi, N.M., Burollus, M.A., Shafi, M.E., Alagawany, M., Yehia, N., Askar, A.M., Alsafy, S.A., Noreldin, A.E., & Khafaga, A.F. 2021. Nutritional aspects and health benefits of bioactive plant compounds against infectious diseases: a review. Food Rev. Int., 37, 1–23.

Engberg, R.M., Hedemann, M.S., Leser, T.D., & Jensen, B.B. 2000. Effect of zinc bacitracin and salinomycin on intestinal microflora and performance of broilers. Poult. Sci., 79(9), 1311–1319.

Eor, J.Y., Son, Y.J., Kim, J.Y., Kang, H.C., Youn, S.E., Kim, J.H., & Kim, S.H. 2021. Neuroprotective effect of both synbiotics and ketogenic diet in a pentylenetetrazol-induced acute seizure murine model. Epilepsy Res., 174, 106668.

Espinoza, J.L. & Minami, M. 2018. Sensing bacterial-induced DNA damaging effects via natural killer group 2-member D immune receptor: From dysbiosis to autoimmunity and carcinogenesis. Front. Immunol. 9, 52. doi 10.3389/fimmu.2018.00052

Feng, Y., Huang, Y., Wang, Y., Wang, P., Song, H., & Wang, F. 2019. Antibiotics induced intestinal tight junction barrier dysfunction is associated with microbiota dysbiosis, activated NLRP3 inflammasome and autophagy. PloS one, 14(6), e0218384.

Ferket, P. 2000. Feeding whole grains to poultry improves gut health. Feedstuffs. 72, 12–13.

Fernández-Veledo, S., & Vendrell, J. 2019. Gut microbiotaderived succinate: Friend or foe in human metabolic diseases? Rev. Endoc. Metab. Discord, 20, 439–447. doi 10.1007/s11154-019-09513-z

Flint, H.J., Duncan, S.H., Scott, K.P., & Louis, P. 2015. Links between diet, gut microbiota composition and gut metabolism. Proc. Nutr. Soc., 74(1), 13–22. doi https://doi.org/10.1017/S0029665114001463

Fouad, A.M., El-Senousey, H.K., Ruan, D., Wang, S., Xia, W., & Zheng, C. 2021. Tryptophan in poultry nutrition: Impacts and mechanisms of action. J. Anim. Physiol. Anim. Nutr. (Berl)., 105(6), 1146–1153. doi 10.1111/jpn.13515.

Francavilla, R., Calasso, M., Calace, L., Siragusa, S., Ndagijimana, M., Vernocchi, P., Brunetti, L., Mancino, G., Tedeschi, G., Guerzoni, E., & Indrio, F. 2012. Effect of lactose on gut microbiota and metabolome of infants with cow's milk allergy. Pediatr. Allergy Immunol., 23, 420–427.

Frost, G., Sleeth, M.L., Sahuri-Arisoylu, M., Lizarbe, B., Cerdan, S., Brody, L., Anastasovska, J., Ghourab, S., Hankir, M., Zhang, S., & Carling, D. 2014. The short-chain fatty acid acetate reduces appetite via a central homeostatic mechanism. Nat. Commun., 5, 3611. doi 10.1038/ ncomms4611

Fu, B.C., Hullar, M.A., Randolph, T.W., Franke, A.A., Monroe, K.R., Cheng, I., Wilkens, L.R., Shepherd, J.A., Madeleine, M.M., Le Marchand, L., & Lim, U. 2020. Associations of plasma trimethylamine N-oxide, choline, carnitine, and betaine with inflammatory and cardiometabolic risk biomarkers and the fecal microbiome in the Multiethnic Cohort Adiposity Phenotype Study. Am. J. Clin. Nutr., 111(6), 1226–1234. doi 10.1093/ajcn/nqaa015.

Fu, L., Qian, Y., Shang, Z., Sun, X., Kong, X., & Gao, Y. 2022. Antibiotics enhancing drug-induced liver injury assessed for causality using Roussel Uclaf Causality Assessment Method: Emerging role of gut microbiota dysbiosis. Front. Med., 9, 972518.

Fu, Y., Wang, Y., Gao, H., Li, D., Jiang, R., Ge, L., Tong, C., & Xu, K. 2021. Associations among dietary omega-3 polyunsaturated fatty acids, the gut microbiota, and intestinal immunity. Mediat. Inflamm., 1–11.

Fujisaka, S., Watanabe, Y., & Tobe, K. 2023. The gut microbiome: a core regulator of metabolism. J. Endocrinol., 256(3), e220111. doi 10.1530/JOE-22-0111

Furusawa, Y., Obata, Y., Fukuda, S., Endo, T.A., Nakato, G., Takahashi, D., Nakanishi, Y., Uetake, C., Kato, K., Kato, T., & Takahashi, M. 2013. Commensal microbe-derived butyrate induces the differentiation of colonic regulatory T cells. Nature, 504(7480), 446–450.

Gabriel, I., Mallet, S., Leconte, M., Travel, A., & Lalles, J.P. 2008. Effects of whole wheat feeding on the development of the digestive tract of broiler chickens. Anim. Feed. Sci. Technol., 142, 144–162. doi 10.1016/j.anifeedsci.2007.06.036

Gadbois, P., Brennan, J.J., Bruce, H.L., Wilson, J.B., & Aramini, J.J. 2008. The role of penicillin G potassium in managing *Clostridium perfringens* in broiler chickens. Avian dis., 52(3), 407–411.

Gao, J., Xu, K., Liu, H., Liu, G., Bai, M., Peng, C., Li, T., & Yin, Y. 2018. Impact of the gut microbiota on intestinal immunity mediated by tryptophan metabolism. Front. Cell. Infect. Microbiol., 8, 13. doi 10.3389/fcimb.2018.00013.

Ge, X.K., Wang, A.A., Ying, Z.X., Zhang, L.G., Su, W.P., & Cheng, K. 2019. Effects of diets with different energy and bile acids levels on growth performance and lipid metabolism in broilers. Poult. Sci. 98, 887–895.

Gershon, M.D. & Tack, J. 2007. The serotonin signaling system: from basic understanding to drug development for functional GI disorders. Gastroenterology. 132, 397–414.

Gill, S.R., Pop, M., DeBoy, R.T., Eckburg, P.B., Turnbaugh, P.J., Samuel, B.S., Gordon, J.I., Relman, D.A., Fraser-Liggett, C.M., & Nelson, K.E. 2006. Metagenomic analysis of the human distal gut microbiome. Science, 312, 1355–1359.

Gilroy, R., Chaloner, G., Wedley, A., Lacharme-Lora, L., Jopson, S., & Wigley, P. 2018. *Campylobacter jejuni* transmission and colonisation in broiler chickens is inhibited by faecal microbiota transplantation. BioRxiv., 23, 476119.

Gori, A., Rizzardini, G., Van't Land, B., Amor, K.B., Van Schaik, J., Torti, C., Quirino, T., Tincati, C., Bandera, A., Knol, J., & Benlhassan-Chahour, K. 2011. Specific prebiotics modulate gut microbiota and immune activation in HAART-naive HIV-infected adults: results of the “COPA” pilot randomized trial. Mucosal Immunol., 4(5), 554–563.

Göransson, L., Abeyesinghe, S., Yngvesson, J., & Gunnarsson, S. 2023. How are they really doing? Animal welfare on organic laying hen farms in terms of health and behaviour. Brit. Poult. Sci., 64(5), 552–564.

Goswami, C., Iwasaki, Y., & Yada, T. 2018. Short-chain fatty acids suppress food intake by activating vagal afferent neurons. J. Nutr. Biochem., 57, 130–135.

Graf, D., Di Cagno, R., Fåk, F., Flint, H.J., Nyman, M., Saarela, M., & Watzl, B. 2015. Contribution of diet to the composition of the human gut microbiota. Microb. Ecol. Health Dis., 26, 26164.

Greiner, T.U. & Backhed F. 2016. Microbial regulation of GLP- 1 and L-cell biology. Mol. Metal. 5(9), 753–758.

Grenier, B. & Applegate, T.J. 2013. Modulation of intestinal functions following mycotoxin ingestion: Meta-analysis of published experiments in animals. Toxins, 5, 396–430. doi 10.3390/toxins5020396

Guerre, P. 2020. Mycotoxin and gut microbiota interactions. Toxins (Basel), 12(12), 769. doi 10.3390/toxins12120769.

Guo, H., Wang, P., Liu, C., Chang, J., Yin, Q., Wang, L., Jin, S., Zhu, Q., & Lu, F. 2023. Compound mycotoxin detoxifier alleviating aflatoxin B1 toxic effects on broiler growth performance, organ damage and gut microbiota. Poult. Sci., 102(3), 102434. doi 10.1016/j.psj.2022.102434

Guo, P., Lin, S., Lin, Q., Wei, S., Ye, D., & Liu, J. 2023. The digestive tract histology and geographical distribution of gastrointestinal microbiota in yellow-feather broilers. Poult. Sci., 102(10), 102844. doi 10.1016/j.psj.2023.102844.

Hagi, T., Geerlings, S.Y., Nijsse, B., & Belzer, C. 2020. The effect of bile acids on the growth and global gene expression profiles in *Akkermansia muciniphila*. Appl. Microbiol. Biotechnol., 104, 10641–10653.

Han, H., Yi, B., Zhong, R., Wang, M., Zhang, S., Ma, J., Yin, Y., Yin, J., Chen, L., & Zhang, H. 2021. From gut microbiota to host appetite: gut microbiota-derived metabolites as key regulators. Microbiome, 9 (1), 162.

Hassimotto, N.M.A., Pinto, M.D.S., & Lajolo, F.M. 2008. Antioxidant status in humans after consumption of blackberry (*Rubus fruticosus* L.) juices with and without defatted milk. J. Agric. Food Chem., 56, 11727–11733.

Heianza, Y., Ma, W., Manson, J.E., Rexrode, K.M., & Qi, L. 2017. Gut microbiota metabolites and risk of major adverse cardiovascular disease events and death: a systematic review and meta-analysis of prospective studies. J. Am. Heart Assoc., 6, e004947. doi 10.1161/JAHA.116.004947

Tavassol, Z.H., Ejtahed, H.S., Soroush, A., Shahriari, A., Siadat, S.D., Ranjbar, S.H., Nikfar, S., & Larijani, B. 2022. Clinical application of gut microbiota metabolites: A novel opportunity in personalized medicine. Koomesh, 24(2), 197–209.

Hosseini, E., Grootaert, C., Verstraete, W., & Van de Wiele, T. 2011. Propionate as a health-promoting microbial metabolite in the human gut. Nutr. Rev., 69(5), 245–258.

Hsiao, Y.C., Liu, C.W., Yang, Y., Feng, J., Zhao, H., & Lu, K. 2023. DNA damage and the gut microbiome: from mechanisms to disease outcomes. DNA, 3(1), 13–32.

Hu, D., Hou, M., Song, P., Chen, Q., Feng, Y., Wu, X., & Ni, Y. 2024. Dietary bile acids supplementation improves the growth performance and alleviates fatty liver in broilers fed a high-fat diet via improving the gut microbiota. Poult. Sci., 103(2), 103270.

Huang, D.S., Li, D.F., Xing, J.J., Ma, Y.X., Li, Z.J., & Lv, S.Q. 2006. Effects of feed particle size and feed form on survival of *Salmonella typhimurium* in the alimentary tract and cecal *S. typhimurium* reduction in growing broilers. Poult. Sci., 85, 831–836. doi 10.1093/ps/85.5.831

Hyland, N.P. & Cryan, J.F. 2016. Microbe-host interactions: influence of the gut microbiota on the enteric nervous system. Dev. Biol., 417(2), 182–187.

Imdad, A., Pandit, N.G., Zaman, M., Minkoff, N.Z., Tanner-Smith, E.E., Gomez-Duarte, O.G., Acra, S., & Nicholson, M.R. 2023. Fecal transplantation for treatment of inflammatory bowel disease. Cochrane Database Syst. Rev., 4(4), CD012774. doi 10.1002/14651858.CD012774

Janeiro, M.H., Ramírez, M.J., Milagro, F.I., Martínez, J.A., & Solas, M. 2018. Implication of trimethylamine N-oxide (TMAO) in disease: potential biomarker or new therapeutic target. Nutrients, 10, 1398. doi 10.3390/nu10101398

Jazani, N.H., Savoj, J., Lustgarten, M., Lau, W.L., & Vaziri, N.D. 2019. Impact of gut dysbiosis on neurohormonal pathways in chronic Kidney Disease. Diseases, 7, 21. doi 10.3390/diseases7010021

Jeffery, I.B. & O'Toole, P.W. 2013. Diet-microbiota interactions and their implications for healthy living. Nutrients, 5, 234–252.

Jenkins, T.A., Nguyen, J.C., Polglaze, K.E., & Bertrand, P.P. 2016. Influence of tryptophan and serotonin on mood and cognition with a possible role of the gut-brain axis. Nutrients, 8(1). doi 10.3390/nu8010056

Jennis, M., Cavanaugh, C.R., Leo, G.C., Mabus, J.R., Lenhard, J., & Hornby, P.J. 2018. Microbiota-derived tryptophan indoles increase after gastric bypass surgery and reduce intestinal permeability in vitro and in vivo. Neurogastroenterol. Motil., 30, e13178. doi 10.1111/nmo.13178

Jiao, N.A., Baker, S.S., Chapa-Rodriguez, A., Liu, W., Nugent, C.A., Tsompana, M., Mastrandrea, L., Buck, M.J., Baker, R.D., Genco, R.J., & Zhu, R. 2018. Suppressed hepatic bile acid signalling despite elevated production of primary and secondary bile acids in NAFLD. Gut, 67, 1881–1891.

Jin, M., Qian, Z., Yin, J., Xu, W., & Zhou, X. 2019. The role of intestinal microbiota in cardiovascular disease. J. Cell. Mol. Med., 23(4), 2343–350.

Joyce, S. & Gahan, C. 2017. Disease-associated changes in bile acid profiles and links to altered gut microbiota. Dig. Dis., 35, 169–177.

Kaliannan, K., Wang, B., Li, X.Y., Kim, K.J., & Kang, J.X. 2015. A host-microbiome interaction mediates the opposing effects of omega-6 and omega-3 fatty acids on metabolic endotoxemia. Sci. Rep., 5(1), 11276.

Kapiki, A., Costalos, C., Oikonomidou, C., Triantafyllidou, A., Loukatou, E., & Pertrohilou, V. 2007. The effect of a fructo-oligosaccharide supplemented formula on gut flora of preterm infants. Early Hum. Dev. 83(5), 335–339.

Kairmi, S.H., Taha-Abdelaziz, K., Yitbarek, A., Sargolzaei, M., Spahany, H., Astill, J., Shojadoost, B., Alizadeh, M., Kulkarni, R.R., Parkinson, J., & Sharif, S. 2022. Effects of therapeutic levels of dietary antibiotics on the cecal microbiome composition of broiler chickens. Poult. Sci., 101(6), 101864.

Kiarie, E.G. & Mills, A. 2019. Role of feed processing on gut health and function in pigs and poultry: Conundrum of optimal particle size and hydrothermal regimens. Front. Vet. Sci., 6, 19. doi 10.3389/fvets.2019.00019

Kim, W.K., Singh, A.K., Wang, J., & Applegate, T. 2022. Functional role of branched chain amino acids in poultry: a review. Poult. Sci. 101(5), 101715. doi 10.1016/j.psj.2022.101715

Kim, S., Park, S., Choi, T.G., & Kim, S.S. 2022. Role of short chain fatty acids in epilepsy and potential benefits of probiotics and prebiotics: targeting "health" of epileptic patients. Nutrients, 14, 2982. doi 10.3390/nu14142982

Koda, S., Date, Y., Murakami, N., Shimbara, T., Hanada, T., Toshinai, K., Niijima, A., Furuya, M., Inomata, N., Osuye, K., & Nakazato, M. 2005. The role of the vagal nerve in peripheral PYY3-36-induced feeding reduction in rats. Endocrinology, 146(5) 2369–2375.

Kokoszyński, D., Bernacki, Z., Saleh, M., Stęczny, K., & Binkowska, M. 2017. Body conformation and internal organs characteristics of different commercial broiler lines. Braz. J. Poult. Sci., 19(1), 47–51. doi 10.1590/1806-9061-2016-0262

Kong, L., Sun, P., Pan, X., Xiao, C., Song, B., & Song, Z. 2024. Glycerol monolaurate regulates apoptosis and inflammation by suppressing lipopolysaccharide-induced ROS production and NF-κB activation in avian macrophages. Poult. Sci., 103870. doi 10.1016/j.psj.2024.103870

Korver, D. 2023. Vitamin deficiencies in poultry. Available from: https://www.msdvetmanual.com/poultry/nutrition-and-management-poultry/vitamin-deficiencies-in-poultry.

Kozlov, A.P., Nizhnikov, M.E., Kramskaya, T.A., Varlinskaya, E.I., & Spear, N.E. 2013. Mu-opioid blockade reduces ethanol effects on intake and behavior of the infant rat during short-term but not long-term social isolation. Pharmacol. Biochem. Behav., 103, 773–782.

Landfald, B., Valeur, J., Berstad, A. & Raa, J. 2017. Microbial trimethylamine-n-oxide as a disease marker: something fishy? Microb. Ecol. Health Dis., 28, 1327309. doi 10.1080/16512235.2017.1327309

Lavelle, A. & Sokol, H. 2020. Gut microbiota-derived metabolites as key actors in inflammatory bowel disease. Nat. Rev. Gastroenterol. Hepatol., 17(4), 223–237. doi 10.1038/s41575-019-0258-z

Le Merrer, J., Becker, J.A.J., Befort, K., & Kieffer, B.L. 2009. Reward processing by the opioid system in the brain. Physiol. Rev., 89, 1379–1412.

LeBlanc, J.G., Milani, C., De Giori, G.S., Sesma, F., Van Sinderen, D., & Ventura, M. 2013. Bacteria as vitamin suppliers to their host: a gut microbiota perspective. Curr. Opin. Biotechnol. 24, 160–168. doi 10.1016/j.copbio.2012.08.005

Lee, J.G., Lee, S., Jeon, J., Kong, H.G., Cho, H.J., Kim, J.H., Kim, S.Y., Oh, M.J., Lee, D., Seo, N., Park, K.H. Yu, K., An, H.J., Ryu, C.M., & Lee, J.S. 2022. Host tp53 mutation induces gut dysbiosis eliciting inflammation through disturbed sialic acid metabolism. Microbiome, 10, 3. doi 10.1186/s40168-021-01191-x

Li, Q., Lauber, C.L., Czarnecki-Maulden, G., Pan, Y., & Hannah, S.S. 2017. Effects of the dietary protein and carbohydrate ratio on gut microbiomes in dogs of different body conditions. MBio, 8(1). doi 10.1128/mbio.01703-16

Li, Z., Quan, G., Jiang, X., Yang, Y., Ding, X., Zhang, D., Wang, X., Hardwidge, P.R., Ren, W., & Zhu, G. 2018. Effects of metabolites derived from gut microbiota and hosts on pathogens. Front. Cell. Infect. Microbiol., 8, 314. doi 10.3389/fcimb.2018.00314

Li, D.Y. & Tang, W.W. 2018. Contributory role of gut microbiota and their metabolites toward cardiovascular complications in chronic kidney disease. Semin. Nephrol., 38, 193–205.

Liu, G., Ajao, A.M., Shanmugasundaram, R., Taylor, J., Ball, E., Applegate, T.J., Selvaraj, R., Kyriazakis, I., Olukosi, O.A., & Kim, W.K. 2023. The effects of arginine and branched-chain amino acid supplementation to reduced-protein diet on intestinal health, cecal short-chain fatty acid profiles, and immune response in broiler chickens challenged with *Eimeria* spp. Poult. Sci., 102(7), 102773. doi 10.1016/j.psj.2023.102773

Liu, F., Kong, A., Fu, P., Cao, Q.Q., Tao, K.S., Liu, D.Y., Wang, X.B., Tong, Z.X., Rehman, M.U., & Huang, S.C. 2021. *Lactobacillus rhamnosus* JYLR-005 prevents thiram-induced tibial dyschondroplasia by enhancing bone-related growth performance in chickens. Probiotics Antimicrob. Proteins, 13(1), 19–31. doi 10.1007/s12602-020-09670-7

Liu, H.Q., Qiu, Y., Mu, Y., Zhang, X.J., Liu, L., Hou, X.H., Zhang, L., Xu, X.N., Ji, A.L., Cao, R., & Yang, R.H. 2013. A high ratio of dietary n-3/n-6 polyunsaturated fatty acids improves obesity-linked inflammation and insulin resistance through suppressing activation of TLR4 in SD rats. Nutr. Res., 33, 849–858.

Liu, M., Kang, Z., Cao, X., Jiao, H., Wang, X., Zhao, J., & Lin, H. 2024. *Prevotella* and succinate treatments altered gut microbiota, increased laying performance, and suppressed hepatic lipid accumulation in laying hens. J. Anim. Sci. Biotechnol., 15(1), 26. doi 10.1186/s40104-023-00975-5

Louis, P. & Flint, H.J. 2009. Diversity, metabolism and microbial ecology of butyrate-producing bacteria from the human large intestine. FEMS Microbiol. Lett., 294(1), 1–8.

Lucke, A., Böhm, J., Zebeli, Q., & Metzler-Zebeli, B.U. 2018. Dietary deoxynivalenol contamination and oral lipopolysaccharide challenge alters the cecal microbiota of broiler chickens. Front. Microbiol., 9. doi 10.3389/fmicb.2018.00804

Lyu, Z., Hu, Y., Guo, Y., & Liu D. 2023. Modulation of bone remodeling by the gut microbiota: a new therapy for osteoporosis. Bone Res., 11(1), 31. doi 10.1038/s41413-023-00264-x

Lyu, W., Liu, X., Lu, L., Dai, B., Wang, W., Yang, H., & Xiao, Y. 2021. Cecal microbiota modulates fat deposition in Muscovy ducks. Front. Vet. Sci., 8, 609348.

Ma, Z., Akhtar, M., Pan, H., Liu, Q., Chen, Y., Zhou, X., You, Y., Shi, D., & Liu, H. 2023. Fecal microbiota transplantation improves chicken growth performance by balancing jejunal Th17/Treg cells. Microbiome, 11(1), 137.

Malik, M., Suboc, T.M., Tyagi, S., Salzman, N., Wang, J., Ying, R., Tanner, M.J., Kakarla, M., Baker, J.E., & Widlansky, M.E. 2018. *Lactobacillus plantarum* 299v supplementation improves vascular endothelial function and reduces inflammatory biomarkers in men with stable coronary artery disease. Circ. Res., 123 (9), 1091–1102.

Malinova, T.S., Dijks tra, C.D., & de Vries, H.E. 2018. Serotonin: a mediator of the gut-brain axis in multiple sclerosis. Mult. Scler., 24(9), 1144–1150.

Marques, F.Z., Nelson, E., Chu, P.Y., Horlock, D., Fiedler, A., Ziemann, M., Tan, J.K., Kuruppu, S., Rajapakse, N.W., El-Osta, A., & Mackay, C.R. 2017. High-fiber diet and acetate supplementation change the gut microbiota and prevent the development of hypertension and heart failure in hypertensive mice. Circulation, 135(10), 964–977.

Martínez, I., Kim, J., Duffy, P.R., Schlegel, V.L., & Walter, J. 2010. Resistant starches types 2 and 4 have differential effects on the composition of the fecal microbiota in human subjects. PloS one, 5(11), e15046.

Marchesi, J.R., Adams, D.H., Fava, F., Hermes, G.D., Hirschfield, G.M., Hold, G., Quraishi, M.N., Kinross, J., Smidt, H., Tuohy, K.M., & Thomas, L.V. 2016. The gut microbiota and host health: a new clinical frontier. Gut, 65(2), 330–339. doi 10.1136/gutjnl-2015-309990

Mateos I., Combes S., Pascal G., Cauquil L., Barilly C., Cossalter A-M., Mateos, I., Combes, S., Pascal, G., Cauquil, L., Barilly, C., Cossalter, A.M., Laffitte, J., Botti, S., Pinton, P., & Oswald, I.P. 2018. Fumonisin-exposure impairs age-related ecological succession of bacterial species in weaned pig gut microbiota. Toxins, 10, 230. doi 10.3390/toxins10060230

Maukonen, J. & Saarela, M. 2015. Human gut microbiota: does diet matter? Proc. Nutr. Soc., 74, 23–36. doi 10.1017/S0029665114000688

Mehmood, K., Zhang, H., Li, K., Wang, L., Rehman, M.U., Nabi, F., Iqbal, M.K., Luo, H., Shahzad, M., & Li, J. 2018. Effect of tetramethylpyrazine on tibial dyschondroplasia incidence, tibial angiogenesis, performance and characteristics via HIF-1α/VEGF signaling pathway in chickens. Sci. Rep., 8, 2495. doi 10.1038/s41598-018-20562-3

Metzler-Zebeli, B.U., Siegerstetter, S.C., Magowan, E., Lawlor, P.G., O′ Connell, N.E., & Zebeli, Q. 2019. Fecal microbiota transplant from highly feed efficient donors affects cecal physiology and microbiota in low-and high-feed efficient chickens. Front. Microbiol., 10, 1576.

Mills, E.L., Kelly, B., Logan, A., Costa, A.S., Varma, M., Bryant, C.E., Tourlomousis, P., Däbritz, J.H.M., Gottlieb, E., Latorre, I., & Corr, S.C. 2016. Succinate dehydrogenase supports metabolic repurposing of mitochondria to drive inflammatory macrophages. Cell, 167, 457–470.

Mohan, A., Godugu, S., Joshi, S.S., Shah, K.B., Vanka, S.C., Shakil, H., Dhanush, P., Veliginti, S., Sure, P.S., & Goranti, J. 2023. Gut-brain axis: Altered microbiome and depression—Review. Ann. Med. Surg., 85, 1784–1789.

Mondanelli, G., Orecchini, E., Volpi, C., Panfili, E., Belladonna, M.L., Pallotta, M.T., Moretti, S., Galarini, R., Esposito, S., & Orabona, C. 2020. Effect of probiotic administration on serum tryptophan metabolites in pediatric type 1 diabetes patients. Int. J. Tryptophan Res., 13, 1178646920956646.

Morgan, X.C., Tickle, T.L., Sokol, H., Gevers, D., Devaney, K.L., Ward, D.V., Reyes, J.A., Shah, S.A., LeLeiko, N., Snapper, S.B., & Bousvaros, A. 2012. Dysfunction of the intestinal microbiome in inflammatory bowel disease and treatment. Genome Biol., 13, 1–8. doi 10.1186/gb-2012-13-9-r79

Morrison D.J. & Preston T. 2016. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. Gut Microbes, 7(3), 189–200.

Mortensen, P.B. & Clausen, M.R. 1996. Short-chain fatty acids in the human colon: relation to gastrointestinal health and disease. Scand. J. Gastroenterol., 31(sup216), 132–148.

Mostafavi Abdolmaleky, H. & Zhou, J.R. 2024. Gut microbiota dysbiosis, oxidative stress, inflammation, and epigenetic alterations in metabolic diseases. Antioxidants, 13(8), 985. doi 10.3390/antiox13080985

Mulchandani, R., Wang, Y., Gilbert, M., & Van Boeckel, T.P. 2023. Global trends in antimicrobial use in food-producing animals: 2020 to 2030. PLOS Glob. Public Health, 3(2), e0001305.

Murai, A., Kitahara, K., Okumura, S., Kobayashi, M., & Horio, F. 2016. Oral antibiotics enhance antibody responses to keyhole limpet hemocyanin in orally but not muscularly immunized chickens. Anim. Sci. J., 87(2), 257–265.

Neerukonda, S.N., & Katneni, U. 2020. Avian pattern recognition receptor sensing and signaling. Vet. Sci. 7, 14. doi 10.3390/vetsci7010014

Neis, E.P., Dejong, C.H., & Rensen, S.S. 2015. The role of microbial amino acid metabolism in host metabolism. Nutrients, 7, 2930–2946. doi 10.3390/nu7042930

Neuman, H., Debelius, J.W., Knight, R., & Koren, O. 2015. Microbial endocrinology: the interplay between the microbiota and the endocrine system. FEMS Microbiol. Rev., 39(4), 509–521.

Nibali, L. & Henderson, B. (eds). 2016. The human microbiota and chronic disease: Dysbiosis as a cause of human pathology. John Wiley & Sons, Inc. New Jersey, USA.

Nonogaki, K., Kaji, T., Ohba, Y., Sumii, M., Wakameda, M., & Tamari, T. 2008. Serotonin 5-HT2C receptor-independent expression of hypothalamic NOR1, a novel modulator of food intake and energy balance, in mice. Biochem. Biophys. Res. Commun., 386, 311–315.

Nonogaki, K., Ohba, Y., Sumii, M., & Oka, Y. 2008. Serotonin systems upregulate the expression of hypothalamic NUCB2 via 5-HT2C receptors and induce anorexia via leptin-independent pathway in mice. Biochem. Biophys. Res. Commun., 372, 186–190.

Novotný, J., Horáková, L., Řiháček, M., Zálešáková, D., Šťastník, O., Mrkvicová, E., Kumbár, V., & Pavlata, L. 2023. Effect of different feed particle size on gastrointestinal tract morphology, ileal digesta viscosity, and blood biochemical parameters as markers of health status in broiler chickens. Animals (Basel), 13(15), 2532. doi 10.3390/ani13152532

Oakley, B.B., Vasconcelos, E.J., Diniz, P.P., Calloway, K.N., Richardson, E., Meinersmann, R.J., Cox, N.A., & Berrang, M.E. 2018. The cecal microbiome of commercial broiler chickens varies significantly by season. Poult. Sci., 97(10), 3635–3644.

O'Mahony, S.M., Clarke, G., Borre, Y.E., Dinan, T.G., & Cryan, J.F. 2015. Serotonin, tryptophan metabolism and the brain-gut microbiome axis. Behav. Brain Res., 277, 32–48.

Ousey, J., Boktor, J.C., & Mazmanian, S.K. 2023. Gut microbiota suppress feeding induced by palatable foods. Curr. Biol., 33(1), 147–157.

Pang, J., Beyi, A.F., Looft, T., Zhang, Q., & Sahin, O. 2023. Fecal microbiota transplantation reduces *Campylobacter jejuni* colonization in young broiler chickens challenged by oral gavage but not by seeder birds. Antibiotics, 12(10), 1503. doi 10.3390/antibiotics12101503

Parada Venegas, D., De la Fuente, M.K., Landskron, G., González, M.J., Quera, R., Dijkstra, G., Harmsen, H.J., Faber, K.N., & Hermoso, M.A. 2019. Short chain fatty acids (SCFAs)-mediated gut epithelial and immune regulation and its relevance for inflammatory bowel diseases. Front. Immunol. 10, 277.

Park, K.T., Oh, M., Joo, Y., & Han, J.K. 2022. Effects of gamma aminobutyric acid on performance, blood cell of broiler subjected to multi-stress environments. Anim. Biosci., 36(2), 248.

Parker, K.E., Johns, H.W., Floros, T.G., & Will, M.J. 2014. Central amygdala opioid transmission is necessary for increased high-fat intake following 24-h food deprivation, but not following intra-accumbens opioid administration. Behav. Brain Res., 260, 131–138.

Polansky, O., Sekelova, Z., Faldynova, M., Sebkova, A., Sisak, F., & Rychlik, I. 2016. Important metabolic pathways and biological processes expressed by chicken cecal microbiota. Appl. Environ. Microbiol., 82, 1569–1576. doi 10.1128/AEM.03473-15

Pottenger, S., Watts, A., Wedley, A., Jopson, S., Darby, A.C., & Wigley, P. 2023. Timing and delivery route effects of cecal microbiome transplants on *Salmonella typhimurium* infections in chickens: potential for in-hatchery delivery of microbial interventions. Anim. Microbiome, 5(1), 11.

Prinsloo, S. & Lyle, R.R. 2015. The microbiome, gut-brain axis, and implications for brain health. NeuroRegulation, 2(4), 158–161.

Puddu, A., Sanguineti, R., Montecucco, F., & Viviani, G.L. 2014. Evidence for the gut microbiota short-chain fatty acids as key pathophysiological molecules improving diabetes. Mediators Inflamm., 162021. doi 10.1155/2014/162021

Rafiq, K., Tofazzal Hossain, M., Ahmed, R., Hasan, M.M., Islam, R., Hossen, M.I., Shaha, S.N., & Islam, M.R. 2022. Role of different growth enhancers as alternative to in-feed antibiotics in poultry industry. Front. Vet. Sci., 8, 794588.

Rasouli, E. & Zeighami, H. 2023. The relationship between gut microbiota dysbiosis and cardiovascular diseases. Lab. Diagn., 15(60), 36–46.

Rath, S., Heidrich, B., Pieper, D.H., & Vital, M. 2017. Uncovering the trimethylamine-producing bacteria of the human gut microbiota. Microbiome, 5, 1–14. doi 10.1186/s40168-017-0271-9

Raza, A., Bashir, S., & Tabassum, R. 2019. An update on carbohydrases: growth performance and intestinal health of poultry. Heliyon, 5(4), e01437.

Ricke S.C. 2003. Perspectives on the use of organic acids and short chain fatty acids as antimicrobials. Poult. Sci., 82(4), 632–639.

Ridlon, J.M. & Bajaj, J.S. 2015. The human gut sterolbiome: bile acid-microbiome endocrine aspects and therapeutics. Acta Pharm. Sin. B., 5(2), 99–105. doi 10.1016/j.apsb.2015.01.006

Ridlon, J.M., Harris, S.C., Bhowmik, S., Kang, D.J., & Hylemon, P.B. 2016. Consequences of bile salt biotransformations by intestinal bacteria. Gut Microbes, 7(1), 22–39.

Ridlon, J.M., Kang, D.J., Hylemon, P.B., & Bajaj, J.S. 2014. Bile acids and the gut microbiome. Curr. Opin. Gastroenterology, 30, 332.

Ringseis, R. & Eder, K. 2022. Heat stress in pigs and broilers: role of gut dysbiosis in the impairment of the gut-liver axis and restoration of these effects by probiotics, prebiotics and synbiotics. J. Anim. Sci. Biotechnol. 13(1), 126.

Robert, H., Payros, D., Pinton, P., Theodorou, V., Mercier-Bonin, M., & Oswald, I. 2017. Impact of mycotoxins on the intestine: Are mucus and microbiota new targets? J. Toxicol. Environ. Health B, 20, 249–275. doi 10.1080/10937404.2017.1326071

Robinson, K., Becker, S., Xiao, Y., Lyu, W., Yang, Q., Zhu, H., Yang, H., Zhao, J., & Zhang, G. 2019. Differential impact of subtherapeutic antibiotics and ionophores on intestinal microbiota of broilers. Microorganisms, 7(9), 282.

Rochell, S.J., Parsons, C.M., & Dilger, R.N. 2016. Effects of *Eimeria acervulina* infection severity on growth performance, apparent ileal amino acid digestibility, and plasma concentrations of amino acids, carotenoids, and α1-acid glycoprotein in broilers. Poult. Sci., 95, 1573–1581.

Rodrigues, F.C., Castro, A.S.B., Rodrigues, V.C., Fernandes, S.A., Fontes, E.A.F., de Oliveira, T.T., Martino, H.S.D., & de Luces Fortes Ferreira, C.L. 2012. Yacon flour and *Bifidobacterium longum* modulate bone health in rats. J. Med. Food, 15, 664–670.

Rodrigues, G., Maximiano, M.R., & Franco, O.L. 2021. Antimicrobial peptides used as growth promoters in livestock production. Appl. Microbiol. Biotechnol., 1, 1–7.

Romano, K.A., Vivas, E.I., Amador-Noguez, D., & Rey, F.E. 2015. Intestinal microbiota composition modulates choline bioavailability from diet and accumulation of the proatherogenic metabolite trimethylamine-N-oxide. MBio, 6. doi 10.1128/mBio.02481-14

Rothhammer, V., Mascanfroni, I.D., Bunse, L., Takenaka, M.C., Kenison, J.E., Mayo, L., Chao, C.C., Patel, B., Yan, R., Blain, M., & Alvarez, J.I. 2016. Type I interferons and microbial metabolites of tryptophan modulate astrocyte activity and central nervous system inflammation via the aryl hydrocarbon receptor. Nat. Med., 22, 586–597. doi 10.1038/nm.4106

Ruiz-Ojeda, F.J., Plaza-Díaz, J., Sáez-Lara, M.J., & Gil, A. 2019. Effects of sweeteners on the gut microbiota: a review of experimental studies and clinical trials. Adv. Nutr., 10, S31–48.

Saeed, M., Ayaşan, T., Alagawany, M., El-Hack, M.E.A., Abdel-Latif, M.A., & Patra, A.K. 2019. The role of ß-mannanase (Hemicell®) in improving poultry productivity, health and environment. Braz. J. Poult. Sci., 21, 1–8.

Safaa, H.M., Jiménez-Moreno, E., Valencia, D.G., Frikha, M., Serrano, M.P., & Mateos, G.G. 2009. Effect of main cereal of the diet and particle size of the cereal on productive performance and egg quality of brown egg-laying hens in early phase of production. Poult. Sci. 88, 608–614.

Salahi, A. & Abd El-Ghany, W.A. 2024. Beyond probiotics, uses of their next-generation for poultry and humans: A review. J. Anim. Physiol. Anim. Nutr., 1–12.

Salahi, A., Moosanezhad Khabisi, M., & Mousavi, S.N. 2011. Optimum time of in ovo injection in eggs of young broiler breeder flock. In: Proceedings of the 18th European Symposium on Poultry Nutrition, Izmir, Turkey.

Salahi, A. & Raad, M.R. 2018. Turkish Idiom and expression. Yas e Bakhshayesh publication, Qom, Iran, pp. 1–1316,

Salahi, A., Adabi, S.G., Khabisi, M.M., Anissian, A., & Cooper, R.G. 2015. Effect of in ovo administration of butyric acid into broiler breeder eggs on chicken small intestine pH and morphology. Slovak J. Anim. Sci., 48(1), 8–15.

Scheppach, W., Sommer, H., Kirchner, T., Paganelli, G.M., Bartram, P., Christl, S., Richter, F., Dusel, G., & Kasper, H. 1992. Effect of butyrate enemas on the colonic mucosa in distal ulcerative colitis. Gastroenterology,103, 51–56.

Schuijt, T.J., Lankelma, J.M., Scicluna, B.P., e Melo, F.D.S., Roelofs, J.J., de Boer, J.D., Hoogendijk, A.J., de Beer, R., de Vos, A., Belzer, C., & de Vos, W.M. 2016. The gut microbiota plays a protective role in the host defence against pneumococcal pneumonia. Gut, 65(4), 575–583.

Sender, R., Fuchs, S., & Milo, R. 2016. Revised estimates for the number of human and bacteria cells in the body. PLoS Biol., 14, e1002533. doi 10.1371/journal.pbio.1002533

Seo, Y.S., Lee, H.B., Kim, Y., & Park, H.Y. 2020. Dietary carbohydrate constituents related to gut dysbiosis and health. Microorganisms, 8(3), 427. doi 10.3390/microorganisms8030427

Shang, Y., Kumar, S., Oakley, B., & Kim, W.K. 2018. Chicken gut microbiota: importance and detection technology. Front. Vet. Sci., 5, 254.

Shanmugasundaram, R., Lourenco, J., Hakeem, W.A., Dycus, M.M., & Applegate, T.J 2023. Subclinical doses of dietary fumonisins and deoxynivalenol cause cecal microbiota dysbiosis in broiler chickens challenged with *Clostridium perfringens*. Front. Microbiol., 14, 1106604.

Shehata, A.M., Paswan, V.K., Attia, Y.A., Abougabal, M.S., Khamis, T., Alqosaibi, A.I., Alnamshan, M.M., Elmazoudy, R., Abaza, M.A., Salama, E.A., & El-Saadony, M.T. 2022c. In ovo inoculation of *Bacillus subtilis*, raffinose affects growth performance, cecal microbiota, volatile fatty acid, and ileal morphology and gene expression and sustainability of broiler chickens (*Gallus gallus*). Front. Nutr., 9, 903847.

Shehata, A.A., Attia, Y., Khafaga, A.F., Farooq, M.Z., El-Seedi, H.R., Eisenreich, W., & Tellez-Isaias, G. 2022a. Restoring healthy gut microbiome in poultry using alternative feed additives with particular attention to phytogenic substances: Challenges and prospects. Ger. J. Vet. Res., 2(3), 32–42. doi 10.51585/gjvr.2022.3.0047

Shehata, A.A., Yalçın, S., Latorre, J.D., Basiouni, S., Attia, Y.A., Abd El-Wahab, A., Visscher, C., El-Seedi, H.R., Huber, C., Hafez, H.M., & Eisenreich, W. 2022b. Probiotics, prebiotics, and phytogenic substances for optimizing gut health in poultry. Microorganisms, 10(2), 395.

Shi, H., Kokoeva, M.V., Inouye, K., Tzameli, I., Yin, H., & Flier, J.S. 2006. Tlr4 links innate immunity and fatty acid–induced insulin resistance. J. Clin. Invest., 116(11), 3015–3025.

Shin, M.S., Han, S.K., Ji, A.R., Kim, K.S., & Lee, W.K. 2008. Isolation and characterization of bacteriocin-producing bacteria from the gastrointestinal tract of broiler chickens for probiotic use. J. Appl. Microbiol. 105(6), 2203–2212.

Siljander, H., Honkanen, J., & Knip, M. 2019. Microbiome and type 1 diabetes. EBioMedicine, 46, 512–521.

Singh, V.K. & Pollard, H.B. 2015. Patents for Toll-like receptor ligands as radiation countermeasures for acute radiation syndrome. Expert Opin. Ther. Pat., 25(10), 1085–1092.

Sinha, S.R., Haileselassie, Y., Nguyen, L.P., Tropini, C., Wang, M., Becker, L.S., Sim, D., Jarr, K., Spear, E.T., Singh, G., & Namkoong, H. 2020. Dysbiosis-induced secondary bile acid deficiency promotes intestinal inflammation. Cell Host Microbe, 27(4), 659–670.

Sokol, H., Pigneur, B., Watterlot, L., Lakhdari, O., Bermúdez-Humarán, L.G., Gratadoux, J.J., Blugeon, S., Bridonneau, C., Furet, J.P., Corthier, G., & Grangette, C. 2008. *Faecalibacterium prausnitzii* is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proc. Natl. Acad. Sci. USA, 105(43), 16731–16736.

Song, Y., Cui, Y., Wang, Y., Wang, T., Zhong, Y., Liu, J., & Zheng, X. 2024. The effect and potential mechanism of inulin combined with fecal microbiota transplantation on early intestinal immune function in chicks. Sci. Rep., 14(1), 16973. doi 10.1038/s41598-024-67881-2

Song, Z.H., Tong, G., Xiao, K., Jiao, L.F., Ke, Y.L., & Hu, C.H. 2016. L-cysteine protects intestinal integrity, attenuates intestinal inflammation and oxidant stress, and modulates NF-κB and Nrf2 pathways in weaned piglets after LPS challenge. Innate Immun., 22, 152–161.

Suez, J., Korem, T., Zeevi, D., Zilberman-Schapira, G., Thaiss, C.A., Maza, O., Israeli, D., Zmora, N., Gilad, S., Weinberger, A., & Kuperman, Y. 2014. Artificial sweeteners induce glucose intolerance by altering the gut microbiota. Nature, 514, 181–186.

Sun, L., Xin, Q., Jiao, H., Wang, X., Zhao, J., Li, H., Zhou, Y., Cao, A., Wang, J., & Lin, H. 2023. Effect of exogenous bile salts supplementation on the performance and hepatic lipid metabolism of aged laying hens. J. Anim. Sci., doi 10.1093/jas/skad334

Svihus, B., Kløvstad, K.H., Perez, V., Zimonja, O., Sahlström, S., Schüller, R.B., Jeksrud, W.K., & Prestløkken, E. 2004. Physical and nutritional effects of pelleting of broiler chicken diets made from wheat ground to different coarsenesses by the use of roller mill and hammer mill. Anim. Feed. Sci. Technol., 117, 281–293. doi 10.1016/j.anifeedsci.2004.08.009

Taha-Abdelaziz, K., Singh, M., Sharif, S., Sharma, S., Kulkarni, R.R., Alizadeh, M., Yitbarek, A., & Helmy, Y.A. 2023. Intervention strategies to control *Campylobacter* at different stages of the food chain. Microorganisms, 11(1), 113.

Tan, L., Weng, M., Wu, X., Qiu, Z., & Shen, L. 2016. Design and application of batching software used to prepare nutritional blend oil with fatty acid balance. J. Chin. Cereals Oils Assoc., 31, 128–133. doi 10.3969/j.issn.1003-0174.2016.06.024

Tancharoenrat, P., Ravindran, V., Zaefarian, F., & Ravindran, G. 2014. Digestion of fat and fatty acids along the gastrointestinal tract of broiler chickens. Poult. Sci., 93, 371–379.

Tang, W.W., Wang, Z., Levison, B.S., Koeth, R.A., Britt, E.B., Fu, X., Wu, Y., & Hazen, S.L. 2013. Intestinal microbial metabolism of phosphatidylcholine and cardiovascular risk. N. Engl. J. Med., 368(17), 1575–1584.

Tassoni, D.S., Macedo, R.C., Delpino, F.M., & Santos, H.O., 2023. Gut microbiota and obesity: The chicken or the egg? Obesities, 3(4), 296–321. doi 10.3390/obesities3040024

Thursby, E. & Juge, N. 2017. Introduction to the human gut microbiota. Biochem. J., 474(11), 1823–1836.

Tian, Y., Gui, W., Koo, I., Smith, P.B., Allman, E.L., Nichols, R.G., Rimal, B., Cai, J., Liu, Q., & Patterson, A.D. 2020. The microbiome modulating activity of bile acids. Gut Microbes, 11(4), 979–996. doi 10.1080/19490976.2020.1732268

Tong, L.C., Wang, Y., Wang, Z.B., Liu, W.Y., Sun, S., Li, L., Su, D.F., & Zhang, L.C. 2016. Propionate ameliorates dextran sodium sulfate-induced colitis by improving intestinal barrier function and reducing inflammation and oxidative stress. Front. Pharmacol., 7, 253.

Turin L. & Riva F. 2008. Toll-like receptor family in domestic animal species. Crit. Rev. Immunol., 28, 513–538.

Tyagi, A.M., Yu, M., Darby, T.M., Vaccaro, C., Li, J.Y., Owens, J.A., Hsu, E., Adams, J., Weitzmann, M.N., Jones, R.M., & Pacifici, R. 2018. The microbial metabolite butyrate stimulates bone formation via T regulatory cell-mediated regulation of WNT10B expression. Immunity, 49, 1116.

V Vasques-Monteiro, I.M.L., Silva-Veiga, F.M., Miranda, C.S., de Andrade Gonçalves, É.C.B., Daleprane, J.B., & Souza-Mello, V. 2021. A rise in *Proteobacteria* is an indicator of gut-liver axis-mediated nonalcoholic fatty liver disease in high-fructose-fed adult mice. Nutr. Res., 91, 26–35.

Velasquez, M.T., Ramezani, A., Manal, A., & Raj, D.S. 2016. Trimethylamine N-oxide: the good, the bad and the unknown. Toxins, 8, 326.

Walker, A.W., Duncan, S.H., McWilliam Leitch, E.C., Child, M.W., & Flint, H.J. 2005. pH and peptide supply can radically alter bacterial populations and short-chain fatty acid ratios within microbial communities from the human colon. Appl. Environ. Microbiol., 71, 3692–3700. doi 10.1128/AEM.71.7.3692-3700.2005

Walther, D.J., Peter, J.U., Winter, S., Höltje, M., Paulmann, N., Grohmann, M., Vowinckel, J., Alamo-Bethencourt, V., Wilhelm, C.S., Ahnert-Hilger, G., & Bader, M. 2003. Serotonylation of small GTPases is a signal transduction pathway that triggers platelet alpha-granule release. Cell, 115(7), 851–862.

Wang ShuMei, W.S., Chen Li, C.L., He MaoZhang, H.M., Shen JunDa, S.J., Li GuoQin, L.G., Tao ZhengRong, T.Z., Wu RuRong, W.R., & Lu LiZhi, L.L. 2018. Different rearing conditions alter gut microbiota composition and host physiology in Shaoxing ducks. Sci. Rep., 8(1), 7387.

Wei, S., Morrison, M., & Yu, Z. 2013. Bacterial census of poultry intestinal microbiome. Poult. Sci. 92, 671–683.

Wenderoth, T., Feldotto, M., Hernandez, J., Schäffer, J., Leisengang, S., Pflieger, F.J., Bredehöft, J., Mayer, K., Kang, J.X., Bier, J., Grimminger, F., Paßlack, N., & Rummel, C. 2024. Effects of omega-3 polyunsaturated fatty acids on the formation of adipokines, cytokines, and oxylipins in retroperitoneal adipose tissue of mice. Int. J. Mol. Sci., 25(18), 9904. doi 10.3390/ijms25189904

Whitfield-Cargile, C.M., Cohen, N.D., Chapkin, R.S., Weeks, B.R., Davidson, L.A., Goldsby, J.S., Hunt, C.L., Steinmeyer, S.H., Menon, R., Suchodolski, J.S., & Jayaraman, A. 2016. The microbiota-derived metabolite indole decreases mucosal inflammation and injury in a murine model of NSAID enteropathy. Gut Microbes, 7, 246–261.

Whitman, J.A., Doherty, L.A., Pantoja-Feliciano de Goodfellow, I.G., Racicot, K., Anderson, D.J., Kensil, K., Karl, J.P., Gibson, G.R., & Soares, J.W. 2024. In vitro fermentation shows polyphenol and fiber blends have an additive beneficial effect on gut microbiota states. Nutrients, 16, 1159.

World Health Organization (WHO). 2008. Fats and fatty acids in human nutrition. Available from: https://www.who.int/news-room/events/detail/2008/11/10/default-calendar/fats-and-fatty-acids-in-human-nutrition

Williams, B.B., Van Benschoten, A.H., Cimermancic, P., Donia, M.S., Zimmermann, M., Taketani, M., Ishihara, A., Kashyap, P.C., Fraser, J.S., & Fischbach, M.A. 2014. Discovery and characterization of gut microbiota decarboxylases that can produce the neurotransmitter tryptamine. Cell Host Microbe, 16, 495–503.

World Organization for Animal Health (WOAH). 2022. Annual report on Antimicrobial Agents Intended for Use in Animals, 7th Edition.

Wu, G.D., Chen, J., Hoffmann, C., Bittinger, K., Chen, Y.Y., Keilbaugh, S.A., Bewtra, M., Knights, D., Walters, W.A., Knight, R., & Sinha, R. 2011. Linking long-term dietary patterns with gut microbial enterotypes. Science, 334, 105–108.

Xu, S., Li, X., Zhang, S., Qi, C., Zhang, Z., Ma, R., Xiang, L., Chen, L., Zhu, Y., Tang, C., & Bourgonje, A.R. 2023. Oxidative stress gene expression, DNA methylation, and gut microbiota interaction trigger Crohn's disease: a multi-omics Mendelian randomization study. BMC Med. 21(1), 179.

Xu, T.T., Chen, P., Zhang, C.D., Shaukat, A., Lin, L.X., Yue, K., Ding, W.L., Tong, X., Liu, K.L., He, Y.F., & Xie, J.F. 2023b. Gut microbiome dysregulation drives bone damage in broiler tibial dyschondroplasia by disrupting glucose homeostasis. NPJ Biofilms Microbiomes, 9, 1. doi 10.1038/s41522-022-00360-6

Yachida, S., Mizutani, S., Shiroma, H., Shiba, S., Nakajima, T., Sakamoto, T., Watanabe, H., Masuda, K., Nishimoto, Y., Kubo, M., & Hosoda, F. 2019. Metagenomic and metabolomics analyses reveal distinct stage-specific phenotypes of the gut microbiota in colorectal cancer. Nat. Med., 25, 968–976.

Yan, F.F., Wang, W.C., & Cheng, H.W. 2018. *Bacillus subtilis* based probiotic improved bone mass and altered brain serotoninergic and dopaminergic systems in broiler chickens. J. Funct. Foods, 49, 501–509.

Yan, L., An, S., Lv, Z.Z., Choct, M., Zhou, G.L., Li, Y., Zhuo, J.S., Wang, Z.G., Lai, J.L., Lv, M.B., & Guo, Y.M. 2022. Effects of corn particle size on growth performance, gastrointestinal development, carcass indices and intestinal microbiota of broilers. Poult. Sci., 101(12), 102205.

Yao, C.K., Muir, J.G., & Gibson, P.R. 2016. Review article: Insights into colonic protein fermentation, its modulation and potential health implications. Aliment. Pharmacol. Ther., 43, 181–196.

Yatsunenko, T., Rey, F.E., Manary, M.J., Trehan, I., Dominguez-Bello, M.G., Contreras, M., Magris, M., Hidalgo, G., Baldassano, R.N., Anokhin, A.P., & Heath, A.C. 2012. Human gut microbiome viewed across age and geography. Nature, 486, 222–227.

Yin, C., Xia, B., Tang, S., Cao, A., Liu, L., Zhong, R., Chen, L., & Zhang, H. 2021. The effect of exogenous bile acids on antioxidant status and gut microbiota in heat-stressed broiler chickens. Front. Nutr., 8, 747136.

Yoshimoto, S., Loo, T.M., Atarashi, K., Kanda, H., Sato, S., Oyadomari, S., Iwakura, Y., Oshima, K., Morita, H., Hattori, M., & Honda, K. 2013. Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome. Nature, 499(7456), 97–101.

Yu, K., Zhang, Y., Chen, H., & Zhu, W. 2019. Hepatic metabolomic and transcriptomic responses induced by cecal infusion of sodium propionate in a fistula pig model. J. Agric. Food Chem. 67(47), 13073–13081.

Yu, Z.T., Liu, B., Mukherjee, P., & Newburg, D.S. 2013. Trametes versicolor extract modifies human fecal microbiota composition in vitro. Plant Foods Hum. Nutr., 68, 107–112.

Yu, Z.L., Zhang, L.Y., Jiang, X.M., Xue, C.H., Chi, N., Zhang, T.T., & Wang, Y.M. 2020. Effects of dietary choline, betaine, and L-carnitine on the generation of trimethylamine-N-oxide in healthy mice. J. Food Sci., 85(7), 2207–2215.

Zendehdel, M., Mokhtarpouriani, K., Hamidi, F., & Montazeri, R. 2013. Intracerebroventricular injection of ghrelin produces hypophagia through central serotonergic mechanisms in chicken. Vet. Res. Commun., 37, 37–41.

Zendehdel, M., Taati, M., Jonaidi, H., & Amini, E. 2012. The role of central 5-HT (2C) and NMDA receptors on LPS induced feeding behavior in chickens. J. Physiol. Sci., 62, 413–419.

Zeyda, M., Staffler, G., Hořejší, V., Waldhäusl, W., & Stulnig, T.M. 2002. LAT Displacement from lipid rafts as a molecular mechanism for the inhibition of T cell signaling by polyunsaturated fatty acids. J. Biol. Chem., 277, 28418–28423.

Zhang, R., Mu, H., Li, Z., Zeng, J., Zhou, Q., Li, H., Wang, S., Li, X., Zhao, X., Sun, L., & Chen, W. 2022. Oral administration of branched-chain amino acids ameliorates high-fat diet-induced metabolic-associated fatty liver disease via gut microbiota-associated mechanisms. Front. Microbiol., 13, 920277.

Zhang, S. & Chen, DC. 2019. Facing a new challenge: the adverse effects of antibiotics on gut microbiota and host immunity. Chin. Med. J., 132(10), 1135–1138.

Zhang, S., Li, Y., Wang, J., Zhu, R., Sun, L., & Mi, J. 2024. Cold stress changes the composition and function of microbiota in the content and mucosa of the ileum and colon in piglets. Anim. Prod. Sci., 64, AN23374.

Zhang, Y., Li, X., Huang, G., Wang, H., Chen, H., Su, Y., Yu, K., & Zhu, W. 2022b. Propionate stimulates the secretion of satiety hormones and reduces acute appetite in a cecal fistula pig model. Anim. Nutr., 10, 390–398.

Zhang, T., Ding, H., Chen, L., Lin, Y., Gong, Y., Pan, Z., Zhang, G., Xie, K., Dai, G., & Wang, J. 2021. Antibiotic-induced dysbiosis of microbiota promotes chicken lipogenesis by altering metabolomics in the cecum. Metabolites, 11(8), 487.

Zhong, Y., Teixeira, C., Marungruang, N., Sae-Lim, W., Tareke, E., Andersson, R., Fåk, F., & Nyman, M. 2015. Barley malt increases hindgut and portal butyric acid, modulates gene expression of gut tight junction proteins and toll-like receptors in rats fed high-fat diets, but high advanced glycation end-products partially attenuate the effects. Food Funct., 6(9), 3165–3176.

Zhou, H., Yu, B., Gao, J., Htoo, J.K., & Chen, D. 2018. Regulation of intestinal health by branched-chain amino acids. Anim. Sci. J., 89(1), 3–11.

Zhu, X., Xiang, S., Feng, X., Wang, H., Tian, S., Xu, Y., Shi, L., Yang, L., Li, M., Shen, Y. & Chen, J. 2019. Impact of cyanocobalamin and methylcobalamin on inflammatory bowel disease and the intestinal microbiota composition. J. Agric. Food Chem. 67:916–926.

Zhuang, R., Ge, X., Han, L., Yu, P., Gong, X., Meng, Q., Zhang, Y., Fan, H., Zheng, L., Liu, Z., & Zhou, X. 2019. Gut microbe-generated metabolite trimethylamine N-oxide and the risk of diabetes: A systematic review and dose response meta-analysis. Obesit. Rev., 20, 883–894.

Zixin, Y., Lulu, C., Xiangchang, Z., Qing, F., Binjie, Z., Chunyang, L., Tai, R., & Dongsheng, O. 2022. TMAO as a potential biomarker and therapeutic target for chronic kidney disease: A review. Front. Pharmacol., 13, 929262.

Zmora, N., Suez, J., & Elinav, E. 2019. You are what you eat: Diet, health and the gut microbiota. Nat. Rev. Gastroenterol. Hepatol., 16, 35–56.