BURLEIGH DODDS SERIES IN AGRICULTURAL SCIENCE

Improving gut health in poultry

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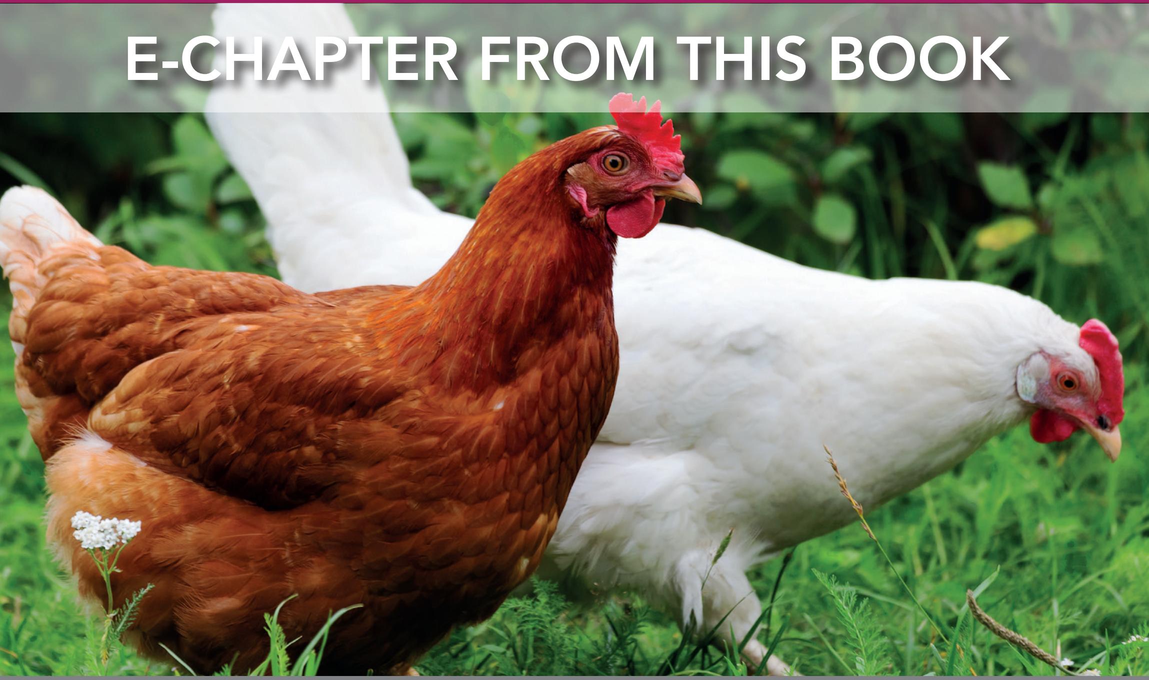
E-CHAPTER FROM THIS BOOK



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The role of synbiotics in optimizing gut function in poultry

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1 Introduction

There is a tendency to regard all microorganisms as harmful; to equate bacteria with germs. Nothing could be further from the truth. The number of non-pathogenic species far exceeds the number of pathogenic species, and many of the known bacteria are useful, even essential for the continued existence of life on earth (Fraune and Bosch, 2010). One example is microorganisms which inhabit the gastrointestinal tract (GIT) of animals. The GIT harbours an incredibly complex and abundant ensemble of microbes. The intestine is in contact with components of this microflora from birth, yet little is known about their influence on healthy development and physiology. The GIT is more densely populated with microorganisms than any other organ and is an interface where the microflora may have a pronounced impact on animal biology (López-Garcia et al., 2017). Throughout millions of years of evolution, animals have developed the means for supporting complex and dynamic consortia of microorganisms during their life cycle (Wren, 2000). An excellent view of vertebrate biology, therefore, requires an understanding of the contributions of these indigenous microbial communities to host development and adult physiology (McFall-Ngai, 2001). The fragile composition of the gut microflora can be affected by various factors such as age, diet, environment, stress and medication (Xu et al., 2007). As with most complex ecosystems, it appears that most species cannot be cultured

http://dx.doi.org/10.19103/AS.2019.0059.19

Chapter taken from: Ricke, A. (ed.), *Improving gut health in poultry*, Burleigh Dodds Science Publishing, Cambridge, UK, 2019, (ISBN: 978 1 78676 304 4; www.bdspublishing.com)

when removed from their niches. Biodiversity awaits systematic application of molecular enumeration techniques, such as genotyping DNA or encoding 16S rRNA genes. Colonization begins at birth and is followed by mounting assembly of a complex and dynamic microbial society (Kikuchi et al., 2009). Assembly is presumably regulated by elaborate and combinatorial microbial–microbial and host–microbial interactions predicated on principles refined throughout animal evolution (Tellez, 2014). Comparisons of rodents raised without exposure to any microorganisms to animals that have assembled a microbiota since birth, or those that have been colonized with components of the microbiota during or after completion of postnatal development, have revealed a range of host functions affected by indigenous microbial communities (Blaser, 2006). For example, the microbiota directs the assembly of the gut-associated lymphoid tissue, helps educate the immune system, affects the integrity of the intestinal mucosal barrier, modulates proliferation and differentiation of its epithelial lineages, regulates angiogenesis, modifies the activity of the enteric nervous system and plays a crucial role in extracting and processing nutrients consumed in the diet (Kau et al., 2011; Hadrich, 2018). The microflora can metabolize proteins and protein degradation products, sulphur-containing compounds, and endogenous and exogenous glycoproteins (O'Hara and Shanahan, 2006). Some organisms grow on intermediate products of fermentation such as H_2, lactate, succinate, formate and ethanol and convert these to end products including short-chain fatty acids (SCFA), a process which has a direct impact on digestive physiology (Van Der Wielen et al., 2000). These and other mechanisms of bacteria biology remain virtually unknown. Researchers in this area are focusing on elucidating these mechanisms as well as manipulating the bacteria and the gastrointestinal environment towards achieving optimal health a number of foods or food components, that provide beneficial roles (for growth and health) beyond ordinary nutrition, leading to the development of the concept of nutraceuticals (Subbiah, 2007). In general, nutraceuticals can be defined as food or food components that have a role in modifying and maintaining normal physiological functions that support the healthy host (Sugiharto, 2016). These nutraceuticals also help in protecting the host against infectious diseases (Hailu et al., 2009). Nutraceuticals may range from isolated nutrients (vitamin, mineral, amino acids, fatty acids), herbal products (polyphenols, herbs, spices), dietary supplements (probiotics, prebiotics, synbiotics, organic acids, antioxidants, enzymes) to genetically modified foods. In this chapter, we will only focus on probiotics, prebiotics and synbiotics.

The use of lactic acid bacteria (LAB) as feed supplements goes back to pre-Christian times when humans consumed fermented milk. It was not until the last century that Eli Metchnikoff, working at the Pasteur Institute in Paris, evaluated the subject from a scientific basis. Metchnikoff documented a direct link between human longevity and the necessity of maintaining a healthy balance of the beneficial and pathological microorganisms residing in the human gut. Metchnikoff was awarded the Nobel Prize in Physiology in 1908 for his discovery of phagocytes and other immune system components, but his accurate description of vital elements in the body's intestinal flora is equally notable (Metchnikoff, 1907). He developed and prescribed to his patients bacteriotherapy, that is the use of LAB in dietary regimens. In support of this, he cited the observation that Bulgarian peasants consumed large quantities of soured milk and lived long lives (Metchnikoff, 1907). He did not doubt the causal relationship, and subsequent events have, in part, confirmed his thesis. He isolated what he called the 'Bulgarian bacillus' from soured milk and used this in subsequent trials. This organism was probably what became known as *Lactobacillus bulgaricus* and is now called *L. delbrueckii* subsp. *bulgaricus* which is one of the organisms used to ferment milk and produce yogurt. After Metchnikoff's death in 1916 the centre of activity moved to the United States. In the late 1940s interest in the gut microflora was stimulated by two research developments. First, the finding that antibiotics included in the feed of farm animals promoted their growth (Dhama et al., 2014). A desire to discover the mechanism of this effect led to increased study on the composition of the gut microflora and the way in which it might be affecting the host animal. Secondly, the increased ready availability of germ-free animals provided a technique for testing the effect that the newly discovered intestinal inhabitants were having on the host (Tlaskalová-Hogenová et al., 2011). This increased knowledge also showed that *L. acidophilus* was not the only *Lactobacillus* in the intestine and a wide range of different organisms came to be studied and later used in probiotic preparations.

2 Probiotics

Probiotics are a single or mixed culture of living microorganisms which when administrated in adequate numbers exerts health benefits for the host by improving the host intestinal microbial balance, enhancing of colonization resistance against pathogens and improving the immune responses (Schrezenmeir and de Vrese, 2001). The species of microorganisms currently being used in probiotic preparations are varied, and LAB, that is *Lactobacillus* spp., *Streptococcus thermophilus, Enterococcus faecium, Enterococcus faecalis* and *Bifidobacterium* spp., are the most common type of bacteria used as probiotics. The definite mechanism through which probiotics may improve the defence and performance of chickens remains unclear, but some possible modes of action have been proposed: (1) maintaining a healthy balance of bacteria in the gut by competitive exclusion (the process by which beneficial bacteria exclude potential pathogenic bacteria through competition for attachment site in the intestine and nutrients) and antagonism (inhibit the growth of pathogenic bacteria by producing, for example lactic acids); (2) promoting gut maturation and integrity; (3) modulating the immune system and preventing inflammation; (4) improving the metabolism by increasing digestive enzyme activity and decreasing bacterial enzyme activity and ammonia production; (5) improving feed intake and digestion (as a result from the improved microbial balance in the gut); and (6) neutralizing enterotoxins and stimulating the immune system (Yurong et al., 2005; Howarth and Wang, 2013). Many probiotic effects are mediated through immune regulation, mainly through balance control of pro-inflammatory and anti-inflammatory cytokines (Vanderpool et al., 2008). However, other studies have shown that some probiotics also exert antioxidant properties and enhance barrier integrity (Prado-Rebolledo et al., 2017). Also, several investigators have demonstrated the benefits of probiotics on innate immunity (Molinaro et al., 2012) as well as on humoral immunity (Howarth and Wang, 2013).

Our laboratory has worked to identify probiotic candidates for use in poultry. FloraMax-B11® is a defined LAB-based probiotic that was confirmed to increase the resistance of poultry to *Salmonella* spp. infections (Farnell et al., 2006; Higgins et al., 2007). Extensive laboratory and field research conducted with this defined LAB culture has demonstrated accelerated development of healthy microflora in chickens and turkeys, providing increased resistance to *Salmonella* sp. infections (Vicente et al., 2007; Higgins et al., 2007; Menconi et al., 2011). Published experimental and commercial studies have shown that these selected probiotic organisms can reduce idiopathic diarrhoea in commercial turkey brooding houses (Higgins et al., 2005). Large-scale commercial trials have indicated that proper administration of this probiotic mixture to turkeys and chickens increased performance and reduced costs of production (Torres-Rodriguez et al., 2007; Vicente et al., 2007). More recently, microarray analysis of gut mRNA expression showed differences in birds treated with this probiotic in genes associated with the NFκB complex (Higgins et al., 2011). These data have demonstrated that the selection of therapeutically efficacious probiotic cultures with marked performance benefits in poultry is possible, and that defined cultures can sometimes provide an attractive alternative to conventional antimicrobial therapy.

2.1 A Bacillus *spore-based probiotic for* Salmonella *control and performance enhancement in poultry*

Despite the success shown by the development of the LAB probiotic for use in commercial poultry (above), there is still an urgent need for commercial probiotics that are shelf-stable, cost-effective and feed-stable (tolerance to heat pelletization process) to increase compliance and widespread utilization. Among a large number of probiotic products in use today some are bacterial spore formers, mostly of the genus *Bacillus*. Used primarily in their spore form, some (though not all) have been shown to prevent selected gastrointestinal disorders and the diversity of species used, and their applications are astonishing. While not all *Bacillus* spores are highly heat tolerant, some specific isolates are the most robust life form known on earth and can be used under extreme heat conditions (Vreeland et al., 2000). At present, our laboratory's aim is to develop a novel, cost-effective, feed-stable probiotic with widespread utilization and improve probiotic production, delivery and clinical efficacy for human and animal use. We have demonstrated that one *Bacillus subtilis* spore isolate was as effective as FloraMax-B11® for *Salmonella* reduction (Shivaramaiah et al., 2011; Wolfenden et al., 2011). Other isolates or combinations of isolates with increased potency and efficacy may be identified with continued research. Some of these environmental *Bacillus* isolates have been evaluated *in vitro* for antimicrobial activity against selected bacterial pathogens, heat stability and the ability to grow to high numbers. Unpublished experimental evaluations have confirmed improved body weight gain as well as *Salmonella* sp. or *Clostridium perfringens* reduction in commercial turkey and broiler operations when compared with medicated (nitarsone) or control non-medicated diets, respectively. Our preliminary data suggest that these isolates could be an effective alternative to antibiotic growth promoters for commercial poultry. Importantly, improved efficiency of amplification and sporulation is essential to gain widespread industry acceptance of a feed-based probiotic for ante-mortem food-borne pathogen intervention, as well as cost-effectiveness. Recently, both vegetative growth and sporulation rate have been optimized in our laboratory, which may lead to new efficiencies for commercial amplification and manufacture of a cost-effective product at very high spore counts (Wolfenden et al., 2010).

3 Prebiotics

The concept of prebiotics is relatively new; it developed in response to the notion that non-digestible food ingredients (e.g. non-digestible oligosaccharides) are selectively fermented by one or more bacteria known to have positive effects on gut physiology (Schrezenmeir and de Vrese, 2001). Bacteria fed by a preferential food substrate have a proliferative advantage over other bacteria. Some prebiotics have shown to selectively stimulate the growth of endogenous LAB and bifidobacteria in the gut to improve the health of the host (Pourabedin and Zhao, 2015).

Prebiotics may provide energy for the growth of endogenous favourable bacteria in the gut, such as bifidobacteria and lactobacilli, thus improving the host microbial balance. In this notion, prebiotics may have more benefits compared with probiotics, in that prebiotics stimulate the bacteria (commensal bacteria) which have adapted to the environment of the GIT (Liu et al., 2015). Prebiotics have been reported to enhance the host defence and reduce mortality of bird caused by the invasion of gut pathogens (Ducatelle et al., 2015). The mechanism by which prebiotics exert this feature remains less elucidated, but it is likely that the capacity of prebiotics to increase the number of LAB in the gut may aid the competitive exclusion of pathogens from the GIT of birds (Pourabedin and Zhao, 2015). The increased production of SCFAs with the administration of prebiotics resulting in increased intestinal acidity may also contribute to the suppression of pathogens in the gut of chicken. Prebiotics have also been reported to enhance the immune response of chicken, resulting in rapid clearance of pathogens from the gut (Ajuwon, 2016).

With regard to the immune-enhancing effect of prebiotics, this may in part be due to direct interaction between prebiotics and gut immune cells as well as due to an indirect action of prebiotics via preferential colonization of beneficial microbes and microbial products that interact with immune cells (Collins and Gibson, 1999). Overall, prebiotics may have a similar mechanism as probiotics in supporting the gut health of chicken. The most common prebiotics used in poultry are oligosaccharides, including inulin, fructooligosaccharides (FOS), mannan-oligosaccharides (MOS), galactooligosaccharides (GOS), soya oligosaccharides (SOS), xylo-oligosaccharides (XOS), pyrodextrins, isomaltooligosaccharides (IMO) and lactulose (Molinaro et al., 2012; Pandey et al., 2015).

Prebiotic research on poultry has been performed since 1990 and, as a result, an extensive database of research is accessible in this area. Prebiotics in broiler diets have been shown to increase lactobacilli counts in the GIT. Also, increased bifidobacteria and decreased clostridia have been reported in some studies that investigated the microbial effects of prebiotic supplementation (Van den Broek et al., 2008). Some authors reported decreased *Salmonella* and coliforms (Dhama et al., 2008; Janssens et al., 2004). Some other pathogenic bacteria like streptococci, staphylococci, bacilli and yeast have also been reported to decrease with prebiotic supplementation (Parracho et al., 2007). Regarding intestinal morphology, increased intestinal villus height was reported when prebiotics were included in the broiler diet. Other changes of intestinal characteristics have been observed, including increased gut length (Hamilton-Miller, 2004).

Bacteria fed by a preferential food substrate have a proliferative advantage over other bacteria. Prebiotics selectively modify the colonic microflora and can potentially influence gut metabolism (Hedin et al., 2007). The presence of healthy gut microflora may improve the metabolism of host birds in various ways, including absorptive capacity, protein metabolism, energy metabolism and fibre digestion and gut maturation (Everard et al., 2011). A healthy population of these beneficial bacteria in the digestive tract enhances the digestion and absorption of nutrients, detoxification and elimination processes, and helps boost the immune system (Teitelbaum and Walker, 2002). Some studies have shown that prebiotics enhance the performance of egg-laying birds and positively affect mineral utilization and improve eggshell and bone quality.

3.1 *Prebiotic properties of* Aspergillus niger *to control food-borne pathogens improve performance and bone mineralization in poultry*

The commercially available mycelium product of *Aspergillus niger*, Fermacto®, referred to as *Aspergillus* meal (AM), has no live cells or spores and is proven to enhance the digestive efficiency of the GI tract. AM contains 16% protein and 45% fibre, and may be used with low levels of protein and amino acid diets to improve performance in commercial poultry (Harms and Miles, 1988; Torres-Rodriguez et al., 2005). Even though the exact mechanisms of action for prebiotics have not been defined, it may be speculated that the effect is due to changing intestinal flora that promote the growth of beneficial bacteria. This product has also been shown to benefit poultry through stimulation of growth, most probably by increasing absorption of feed ingredients and improving digestibility. Additionally, *Aspergillus* fibre contains beta-glucans, FOS, chitosan and mannan-oligosaccharides (MOS) (Uchima et al., 2011; Hernandez-Patlan et al., 2018). Beta-glucan is a powerful immune-enhancing nutritional supplement (Jonker et al., 2010). This unique compound affects the intestinal villi and primes the innate immune system to help the body defend itself against viral and bacterial invaders (Teitelbaum and Walker, 2002; Hooge et al., 2003). MOS protects the GIT from invading toxins by binding the active toxin sites. FOS and chitosan refer to a class of host non-digestible carbohydrates that are readily fermented by the beneficial bacteria in the intestine (Kim et al., 2006). A healthy population of these beneficial bacteria in the digestive tract enhances the digestion and absorption of nutrients, detoxification and elimination processes, and helps boost the immune system.

In previous work, we have shown that dietary AM induces significant changes on intestinal morphometry in turkey poults. Increased number of acid mucin cells in the duodenum, neutral mucin cells in the ileum and sulphomucin cells in the duodenum and ileum, as well as increased villi height and villi surface area of both duodenum and ileum when compared to control, suggest that AM prebiotic has an impact on the mucosal architecture and goblet cell proliferation in the duodenum and ileum of neonate poults (Tellez et al., 2010). In another study, dietary AM prebiotic supplemented for 30 days, significantly increased the body weight of neonate poults and improved feed conversion when compared with poults that received the basal control diet. Interestingly, energy and protein content in the ileum was significantly lower in poults that received dietary AM prebiotic compared with control poults, suggesting better digestibility and absorption of those nutrients, which are in agreement with the morphometric changes observed previously (Reginatto et al., 2011). Furthermore, we also observed significant increases in tibia weight, diameter, breaking strength, ash, calcium and phosphorus in poults that received dietary AM when compared with neonatal poults that received the basal control diet (Reginatto et al., 2011). FOS have been shown to stimulate calcium (Ca) and magnesium (Mg) absorption in the intestine and increase bone mineral concentrations (Scholz-Ahrens et al., 2007).

Several studies have demonstrated that feeding probiotics can achieve prevention of *Salmonella* colonization in chickens (Janssens et al., 2004; Van Immerseel et al., 2002; Burkholder et al., 2008). Finally, chitosan is a modified, natural biopolymer derived by deacetylation of chitin, the main component of the cell walls of fungi and exoskeletons of arthropods. As mentioned before, chitosan exhibits numerous beneficial effects, including strong anti-microbial and antioxidative activities (Filipkowska et al., 2014). Its application in agriculture, horticulture, environmental science, industry, microbiology and medicine are well reported (Hernandez-Patlan et al., 2018). There have been numerous studies that report the use of chitosan as a mucosal adjuvant, by enhancing IgA levels (Ravi Kumar, 2000). The commercial prebiotic supplement derived from *Aspergillus niger* mycelium is unique because it contains all of the above mentioned prebiotic ingredients.

In another study conducted in our laboratory, we evaluated the effect of 0.2% dietary AM against horizontal transmission of *Salmonella* spp. in turkeys and chickens (Londero et al., 2011). The results of this study showed that dietary supplementation with 0.2% AM was able to reduce *Salmonella* Enteritidis horizontal transmission in turkeys, and *Salmonella* Typhimurium horizontal transmission in broiler chickens, by reducing the overall colonization levels in birds. Although the mechanism of action is not entirely understood, the reduction in *Salmonella* colonization may be related to a synergistic effect between beta-glucan, MOS, chitosan and FOS present in the *Aspergillus niger* mycelium. The GIT serves as the interface between diet and the metabolic events that sustain life. Intestinal villi, which play a crucial role in digestion and absorption of nutrients, are underdeveloped at hatch and maximum absorption capacity is attained by 10 days of age. Understanding and optimizing the maturation and development of the intestine in poultry will improve feed efficiency, growth and overall health of the bird (Pourabedin and Zhao, 2015).

4 Synbiotics

Both probiotics and prebiotics have been shown to provide beneficial effects on the gut of birds. When probiotics and prebiotics are combined, they form synbiotics (Schrezenmeir and de Vrese, 2001). This combination could improve the survival and persistence of the health-promoting organism in the gut of birds because its specific substrate is available for fermentation. Several studies have shown the potential benefits of synbiotics on the intestinal microbial ecosystem and immune functions of chicken (Pandey et al., 2015; Téllez et al., 2015).

Regarding performance, Synbiotics have have been found to be more effective than prebiotics in improving growth of broilers when administered *in ovo* (Madej et al., 2015). The improvement of intestinal morphology and nutrient absorption due to feeding synbiotics seems to contribute to the enhanced performance of broiler chicken (Dunislawska et al., 2017). It has been suggested that synbiotics are much more efficient when used in combination than singly (Scholz-Ahrens et al., 2007). The balance of healthy gut microflora may improve the metabolism of the host bird in various ways, including absorptive capacity, protein metabolism, energy metabolism and fibre digestion, energy conversion and gut maturation (Sugiharto, 2016). The consumption of synbiotics thus contributes to immunostimulation and a beneficial balance of microbiota in the gut (Awad et al., 2009).

Probiotic numbers have been enhanced by prebiotics that selectively stimulate the growth and activity of one or a limited number of bacterial species already resident in the large intestine, and, thus, improves host health. In this way, prebiotics selectively modify the colonic microflora and can potentially influence gut metabolism. However, the bacterial nutrient package will not be advantageous without the presence of the targeted, beneficial bacteria and likewise, the live microbial product will not succeed if the environment into which it is introduced is unfavourable (Liu et al., 2015; Dhama et al., 2008).

4.1 Role of synbiotics in digestive physiology: SCFA production

SCFA increases from undetectable levels in the caeca of day-of-hatch chicks to the highest concentration at day 15 of age as the enteric microflora become established (Yang et al., 2011). The primary fermentative reaction in the human colon or chicken caecum is similar to that in obligate herbivores: hydrolysis of polysaccharides, oligosaccharides and disaccharides to their constituent sugars, which are then fermented resulting in increased biomass. Carbohydrate hydrolysis is promoted by hydrolases secreted by bacterial cells that are able to digest a range of carbohydrates which monogastric animals would not otherwise be able to digest (Xu et al., 2003). Fermentation yields metabolizable energy for microbial growth and maintenance and also metabolic end products. Nitrogen for protein synthesis can come from either urea, undigested dietary protein or endogenous secretions (Van den Broek et al., 2008). The principal products are SCFA together with gases (CO_2, CH_4

and H_2) and some heat. Carbohydrates entering the large intestine can alter gut physiology in two ways: physical presence and fermentation. Effects of SCFA can be divided into those occurring in the lumen and those arising from their uptake and metabolism by the cells of the large bowel wall. SCFA are the principal luminal anions. They are relatively weak acids with pKa values of 4.8, and raising their concentrations through fermentation lowers digesta pH. SCFA also serves as an indispensable source of energy for the gut wall, providing up to 50% of the daily energy requirements of colonocytes (Dimitrov, 2011). Fermentable carbohydrates can alter the microbial ecology significantly by acting as substrates or supplying SCFA. Much attention has been directed towards the study of specific beneficial LAB, rather than the flora as a whole. However, the SCFA have diverse functions with regard to host and microbial physiology (Tellez et al., 2006).

4.1.1 Blood flow and muscular activity

In vitro studies have shown that incubation with SCFA at concentrations as low as 3 mM dilate precontracted colonic resistance arterioles in separate human colonic segments (Molinaro et al., 2012). Greater colonic blood flow has been observed with the infusion of acetate, propionate or butyrate (Plöger et al., 2012). The mechanism of action of SCFA on blood flow does not involve either prostaglandins or α- or β-adrenoreceptor-linked pathways. The mechanisms of action may involve local neural networks as well as chemoreceptors together with direct effects on smooth muscle cells (Van Der Wielen et al., 2000). SCFA produced in the colon and entering the portal circulation seem to influence the upper gut musculature. These actions are essential for the maintenance of the function of the whole gastrointestinal system, not just the colon. It is expected that greater blood flow enhances tissue oxygenation and transport of absorbed nutrients (Braniste et al., 2014).

4.1.2 Enterocyte proliferation

In rats, SCFA stimulates the growth of colorectal and ileal mucosal cells when they are delivered colorectal or intraperitoneally. In addition to promoting growth, the major SCFA (especially butyrate) appears to lower the risk of malignant transformation in the colon (Shen et al., 2013). Secondary bile acids are cytotoxic, and in rats fed deoxycholate plus cholesterol, cell proliferation as measured by incorporation of [3*H*]thymidine was increased (Begley et al., 2005). Some of the effects of SCFA may be due to low intra-colorectal pH rather than any specific SCFA. At pH 6, bile acids are mostly protonated and insoluble and so would not be taken up by colonocytes. Additionally, lower pH inhibits the bacterial conversion of primary to secondary bile acids and therefore lowers their carcinogenic potential (Hofmann, 1999).

4.1.3 Mucin production

Evidence has been presented that mucus production and release is stimulated locally by endogenous production of SCFA by gut microflora. Additionally, some studies have been completed evaluating the influence of specific beneficial or probiotic organisms on mucin production (Plöger et al., 2012). *In vitro* studies with *Lactobacillus plantarum* 299v suggest that the ability of organisms to inhibit adherence of attaching and effacing organisms to intestinal epithelial cells is mediated through their ability to increase expression of MUC2 and MUC3 intestinal mucins (Montagne et al., 2004). The benefits of probiotics mediated through intestinal mucin upregulation may have broader applicability than enteropathogen intervention in poultry. Several investigators have shown that the increase in mucin production following probiotic administration inhibited replication, disease symptoms and shedding of rotavirus. In the proximal colon, an increase in the butyrate concentration altered crypt depth and the number of mucus-containing cells; the increase in butyrate was highly correlated with the number of neutral mucin-containing cells (Van Immerseel et al., 2002; Schippa and Conte, 2014).

4.2 Role of synbiotics in poultry production

The GIT serves as the interface between diet and the metabolic events that sustain life. In poultry, intestinal villi, which play a crucial role in digestion and absorption of nutrients, are underdeveloped at hatch and maximum absorption capacity is attained by 10 days of age. Understanding and optimizing the maturation and development of the intestine in poultry will improve feed efficiency, growth and overall health of the bird. In the immediate post-hatch period birds must undergo the transition from energy supplied by the endogenous nutrients of the yolk to exogenous carbohydrate-rich feed (Awad et al., 2009). During that critical time, dramatic changes occur both in the intestinal size and morphology. Maturational changes also affect the epithelial cell membranes, a primary mechanical interface between the internal environment of the host and the luminal contents. Studies on nutrition and metabolism during the early phase of growth in chicks may help in optimizing nutritional management for maximum growth. By dietary means, it is possible to affect the development of the gut and the competitiveness of both beneficial and harmful bacteria, which can alter not only gut dynamics but also many physiological processes due to the end products metabolized by symbiotic gut microflora (Maiorano et al., 2012). Additives such as probiotics and prebiotics are now extensively used throughout the world. The chemical nature of these additives are well understood, but the manner by which they benefit the animal is not (Sugiharto, 2016).

4.3 Synbiotics as an alternative to antibiotics for control of bacterial pathogens and improved performance in poultry

Bacterial antimicrobial resistance in both the medical and agricultural fields has become a serious problem worldwide. Antibiotic-resistant strains of bacteria are an increasing threat to animal and human health, with resistance mechanisms having been identified and described for all known antimicrobials currently available for clinical use (Kiser, 1976). There is currently increased public and scientific interest regarding the administration of therapeutic and sub-therapeutic antimicrobials to animals, due primarily to the emergence and dissemination of multiple antibiotic-resistant zoonotic bacterial pathogens (Shea, 2003). Social pressures have led to the creation of regulations to restrict antibiotic use in poultry and livestock production (Niewold, 2007). There is a need to evaluate potential antibiotic alternatives to improve disease resistance in high-intensity food animal production. Nutritional approaches to counteract the debilitating effects of stress and infection may provide producers with useful alternatives to antibiotics (Joerger, 2003). Improving the disease resistance of animals grown without antibiotics will not only benefit the animals' health, welfare and production efficiency but is also a key strategy in the effort to improve the microbiological safety of poultry products. Most of the experiments conducted with pro-, pre- and synbiotics have focused on improving the microbial health, performance and decreasing carcass contamination of young meat birds (Teillant and Laxminarayan, 2015; Ajuwon, 2016).

5 Conclusion and future trends

Overall in this chapter pro-, pre- and synbiotics have been discussed concerning the systemic effects they exert on the host's health, metabolism and immune system. Probiotics and synbiotics have systemic effects on the host's healthy metabolism and immune system. Utilization of prebiotics by probiotics should be a prerequisite for symbiotic selection, in order to maintain a good synergy between the two and maximize the beneficial effects. By establishing the underlying mechanisms of probiotics, prebiotics and their combination (synbiotics), scientists would be able to design enhanced functional foods to improve host health. The ability to regulate the composition of the microbiota by symbiotic products is an exciting approach in the control and treatment of some major diseases and to increase performance. The recent advances in technology have enabled the deep sequencing and analysis of the beautiful diversity of the microorganisms in the GIT, and should be able to prevent diseases and lead to maintain better health.

6 Where to look for further information

During the last decade, the increasing interest in renewable energy sources changed the distribution of corn utilization from human and animal consumption to biofuel production, leading to a continuous rise in feed costs of livestock diets. Therefore, alternative feed ingredients such as distillers dried grains with solubles (DDGS) as well as cereals like wheat, barley and sorghum have become part of the feed matrix to maintain or reduce production costs. However, these raw materials often contain a higher concentration of anti-nutritional factors in comparison to corn, including non-starch polysaccharides which increase digesta viscosity and reduce nutrient absorption in monogastric animals. As a result, the addition of exogenous enzymes in poultry feed has steadily increased to maximize nutrient utilization and maintain performance parameters with diets containing less digestible ingredients. On the other hand, the poultry industry is also facing social concerns regarding the use of antibiotic growth promoters and the development of antibiotic-resistant microorganisms. One alternative among others is the utilization of direct-fed microbials as substitutes for antibiotics growth promoters and also as a prophylactic practice to reduce the incidence of bacterial gastrointestinal diseases. Currently, our laboratories are also working on evaluating and selecting different *Bacillus* spp. strains as DFM candidates based on enzyme production profiles to improve nutrient absorption and intestinal integrity, as well as to maintain a healthy microflora balance in poultry-consuming commercial and alternative diets.

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