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Probiotic Modes of Action and Its Effect on Biochemical Parameters and Growth Performance in Poultry

Review Article

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ABSTRACT

Provide a healthy diet is one of the major health challenges in the world to maintain health and nutritional status of populations. In this reason, new control strategies such as probiotics have been applied as prophylactic and therapeutic instead of antibiotics. In the same line, probiotics have antagonistic effects to various microorganisms proposed in several mechanisms including improvement of gut epithelial barrier function, competition on adhesive receptors, competition on available nutrients, antibacterial effects, degradation and neutralization of toxins and immunomodulatory effect. Furthermore, probiotics have significant impacts on biochemical parameters and could be used as substitutional supplements do health benefits including hypocholesterolemia and reduction of blood glucose. Probiotics have been explained to hypocholesterolemia and hypoglycemia through several mechanisms. Moreover, the use of probiotics in feeds enhances the protein utility in feedstuff. Thus, this review was attempted to spot generally insight on the modes of action of probiotics and its importance biochemically.

KEY WORDS biochemical parameters, growth performance, mechanisms of action of probiotics, poultry, probiotics.

INTRODUCTION

From many decades, antibiotics have been used in poultry feeds but now prohibited in many countries. The enteric pathogens are most common and associated diseases in poultry industry due to lack of knowledge about application of biosecurity measures that result to spread of infection. Antibiotics have been used for controlling the infection and as growth promoters. Due to several negative effects for antibiotics such as increasing the antibiotic resistances to pathogenic microorganisms and presence of their residues in poultry products that pose the health hazard to consumer therefore, it has brought a call for worldwide antibiotic prohibit. Concerning with food safety has given rise to challenge for productive efficiency. The poultry industry represents among the highest sources of protein production as well as increasing in the size of poultry industry is faster than other food producing animal industries (Lyayi, 2008; Ohimain and Ofongo, 2012). Unfortunately, overuse of antibiotics for veterinary purposes led to presence of resistant bacteria. Therefore, the issue of controlling pathogenic bacteria without antibiotics became the great challenge (Ohimain and Ofongo, 2012; Wallace *et al.* 2010). Such infections are responsible for loss productivity and increase of mortality in poultry industry (Patterson and Burkholder, 2003). In the light of growing concerns over excessive mortality rate because of gastrointestinal problems and restrictions in usage of antibiotics thus, it is a very necessary to find alternative method to improve gut health and reduce the productivity losses. Probiotics are used as prospective substitute for antibiotic in poultry because of its side effects on consumers and manufactures. Probiotics are defined as a group of beneficial live microorganisms to host by reducing the gut pathogens. This improves the health status, production performances and feed conversion rate as well as immune response of poultry and farm animals (Getachew, 2016; Sethiya, 2016; Smith, 2014). The lactic acid bacteria of genus *Lactobacillus* and *Bifidobacterium* are the main bacteria reported in probiotics. Besides, different bacteria species and yeast have been used in probiotics as *Bacillus*, *Lactococcus*, *Streptococcus*, *Enterococcus*, *Pediococcus*, *Saccharomyces cerevisiae* and *Toulopsis sphaerica* (Jadhav *et al*. 2015; Jeong and Kim, 2014; Lee *et al*. 2010a). Furthermore, killed bacteria cultures, bacterial metabolites and fungi such as mushroom have been also included (Jadhav *et al*. 2015; Mahfuz *et al*. 2017; Willis *et al*. 2011). *Bacillus subtilis* spores one of bacterial species used as probiotics that has several advantages in poultry industry like heat resistance during feed manufacture, bearing gastric acidicity, storage for long period at room temperature and have immune stimulant and antimicrobial activities (Cutting, 2011; Lee *et al*. 2010b; Lee *et al*. 2010c). This review is aimed to explain mechanism of probiotics action and investigate its effect on biochemical parameters and immune response in poultry.

Mechanisms of probiotics action

Under normal circumstances, the sources of microbial are either autochthonous bacterial colonies by environmental exposure and normal feeding activities or allochthonous by introducing them as dietary supplementation through feeding or drinking water as probiotics (Chichlowski *et al*. 2007a; Chichlowski *et al*. 2007b; Patterson and Burkholder, 2003).

Several studies have reported that commensal bacteria improve the gut health and inhibit pathogens but sometimes suffering from disturbances result in sensitivity to infection (reviewed byDhama *et al*. 2011). Besides, the size and complexity of microbial population are important factors in controlling pathogens (Mead, 2005). The probiotic may contain one or a cocktail of variant bacterial species/ strains and the mode of action of each one may differ. So, there are possibilities for probiotics action include competition between native organisms and pathogens for adhesive receptors in intestinal epithelium, competition for available nutrients, establishment environmental condition by decrease pH, direct antimicrobial effect by releasing antibacterial substances and neutralization of toxins, aggregation with pathogenic bacteria and stimulation of immune system (Dhama and Singh, 2010; Ng *et al*. 2009; Otutumi *et al*. 2012).

It is necessary for maintenance the healthy gut microflora to improve the microbial environment by replacing the pathogenic bacteria. Since the pathogenic bacteria multiply faster than the native bacteria occurrence the infection. The equilibrium between favorable and unfavorable is a crucial. This equilibrium may affect by environmental factors or internal factors like stress. Probiotics are capable of adherence and colonize to the epithelial surface of gut and competing with pathogen to adhesion site forming the enterocytes complexity and facilitate the interaction amongst cell types, thus raise the amplitude of phagocytosis (Bene *et al*. 2017; Trejo *et al*. 2006). For instance, *Lactobacillus plantarum* compete with *E. coli* for adhesion site by induction MUC3 mucins (Mack *et al*. 1999).

Probiotics help in utilization of nutrients such as digestible protein, vitamins, minerals and enzymes. In addition, they help in vitamin synthesis (Biotin, B_1, B_2, B_{12} and K) and mineral metabolism that are important for proper growth and metabolism (Dhama and Singh, 2010). Furthermore, probiotics compete with pathogens for available nutrients preventing them from growth and multiplication in intestine (Bajaj *et al*. 2015). For instance, *Bifidobacterium adolescentis* S2-1 competes with *Porphyromonas gingivalis* on vitamin K (Hojo *et al*. 2007).

A variety of primary and secondary metabolites such as volatile fatty acids, oraganic acids and lactic acid lowering the intestinal pH to inhibit the pathogens growth such as *Salmonella* and *E. coli* (Marteau *et al*. 2004). For example, *Lactobacilli* produce lactic acid and indirectly increase butyric acid concentration in gut that induce the growth and proliferation of butyric acid producing bacteria through cross-feeding phenomena (Van Immerseel *et al*. 2009). However, it inhibits the pathogens and enhances decomposing of organic matter such as cellulose and lignin without occurring any harmful effects arising from its fermentation (Higa and Parr, 1994).

Probiotics produce the antibacterial substances to kill / inhibit the pathogenic microorganisms including bacteriocins, organic acids such as acetate and lactate, lysosomes, lactoferrin, lactoperoxidase and hydrogen peroxide (Jin *et al*. 1997). For example, *Lactobacillus crispatus* F117 produce the highest level of hydrogen peroxide inhibiting *Staphylococcus aureus* growth (Ocana *et al*. 1999). In addition, they release anti-enterotoxin substances including acidophilin, acidolin and lactin like *Lactobacillus bulgaricus* capable of neutralizing and / or absorption of enterotoxins produced by pathogens. Furthermore, they produce useful substances such as enzymes, hormones and vitamins that vital for favorable microorganisms' multiplication. They decrease urease activity in gut subsequently, reducing the concentration of non protein nitrogen, uric acid, ammonia and urea that result in lowering the ammonia formation in litter. Excess of ammonia concentration in litter causes kerato-conjunctivitis and associated problems in poultry farms. Therefore, it was reported that *Bacillus subtilis* and

Streptococcus faecium have ability to reduce ammonia concentration in excreta (Fuller, 2001; Hajati and Rezaei, 2010; Vegad, 2004).

Probiotics have a significant impact on the immunity system of poultry against invading pathogens. Probiotics induce both innate immunity and adaptive immunity via regulation of Toll-like receptors expression, activation both dendritic cells and natural killer cells, in addition increasing the responses of T-helper cells, induction cytokines production and immunoglobines secretion like IgM, IgG and IgA (Alkhalf *et al.* 2010; Janardhana *et al.* 2009; Tsai *et al.* 2012). Probiotics increase the number of lymphocytes in gut associated lymphoid tissues like payer's patches and intestinal mucosal cells thereby providing the local immunity by IgA secretion producing plasma cells (Haghighi *et al.* 2006). The intestinal plasma cells participated in production of T-cells independent antibodies against pathogens as an evasive mechanism (Jiang *et al.* 2004). In addition, the intestinal enterocytes acts as a barrier to loss of nutrients to pathogens thereby help the immune system to recognize the pathogens.

Effect of probiotics on enteric pathogens

The idea of competitive exclusion of pathogenic microorganisms by beneficial one such as *Lactobacilli*, prevent the pathogens from adherence to gut surface and removed from intestine via ingest. It was one of the spreading keys of probiotics in poultry and livestock production systems which inhibit the harmful effect of pathogens such as *E. coli*, *Salmonella*, *Clostridia*, *Campylobacter* (Jin *et al.* 1997). Mulder (1991) illustrated that administration of probiotics orally reduces occurrence of *Salmonella* infection in chicks. A mixture of three different probiotics has a therapeutic effect on post infectious irritable bowel syndrome caused by *Trichinella spiralis* (Wang *et al.* 2014). *Lactobacilli* and *Bifidobacteria* have been exhibited a strong killing activity against a wide range of pathogenic microorganisms like *E. coli*, *Salmonella*, *Listeria monocytogenes*, *Campylobacter pylori* and *Rotavirus* (Bermudez-Brito *et al.* 2012; Bujalance *et al.* 2014). Probiotics degrade toxin receptors on intestinal mucosa via enzymatic mechanism such as *Saccharomyces boulardii* protect the host against *Clostridium difficile* infection through suppression toxin production in ileum of rabbits and also can produce polyamines that inhibit secreted toxins of cholera infection in jejunum of rats (Bermudez-Brito *et al.* 2012; Valdes-Varela *et al.* 2018). Moreover, probiotics have a significant role in development of immune response against Newcastle disease, tetanus toxoid and *Clostridium perfringens* alpha-toxin (Anjum, 1998; Haghighi *et al.* 2006). Probiotics can enhance stimulation of nonspecific immunity like induction phagocytic activity of macrophages, promote the immunoglobulins secretion and immune cells proliferation (Kaur *et al.* 2009). Previous study was observed level of serum antibodies production usually IgG, IgM and interferon γ increased after addition of probiotic to diet (Ahmed, 2006).

Effect of probiotics on biochemical parameters

Many previous literatures reported impact of probiotics on biochemical parameters in poultry. Probiotics have a significant improvement levels of total unsaturated fatty acids, omega 6 and essential poly unsaturated fatty acids like linoleic acid and linolenic acid in egg yolk (Tang *et al.* 2016; Yi *et al.* 2014). Pervious study demonstrated that probiotics reduced total cholesterol and triglyceride in blood (Taranto *et al.* 2000). However, other studies reported that probiotics hadn't a significant difference on levels of total cholesterol (Greany *et al.* 2004; Pelicano *et al.* 2004). Previous studies have been demonstrated cholesterol lowering effect of probiotics through several mechanisms. It has been hypothesized that enzymatic deconjugation of bile acid by hydrolase enzyme. Cholesterol is the end product of bile which is stored and concentrated in gallbladder then released on ingested food in duodenum. Once deconjugation, part of bile salt reabsorption by enterohepatic circulation into liver. Cholesterol reused in new bile acid synthesis leading to lowering serum cholesterol. Probiotics can uptake cholesterol and exploit it in cell walls (Begley *et al.* 2006; Jones *et al.* 2004; Lye *et al.* 2009) and cellular membrane synthesis during growth in small intestine lead to increase the cell membrane strength thereby preserve the cellular resistance from fragmentation (Lye *et al.* 2010a).

Another mechanism occurs by cholesterol conversion into copresterol then directly excreted in feces. *Sterolibacterium denitrificans* secrete cholesterol dehydrogenase that catalyze transformation of cholesterol into copresterol via intermediate factor (Chiang *et al.* 2008). Furthermore, another study reported that *Lactobacillus acidophilus*, *L. bulgaricus* and *L. casei* ATCC 393 were also shared into conversion of cholesterol into copresterol (Lye *et al.* 2010b).

Probiotics can ferment probiotic in intestine producing short chain fatty acids such as propionate. Propionate acts as an effective inhibitor for fatty acids synthesis and control of cholesterol synthesis in the liver subsequently, it leads to decrease the plasma cholesterol levels (Trautwein *et al.* 1998).

Regarding to effect of probiotics on blood glucose levels, previous study showed increasing of blood glucose level by probiotic supplements in feeding (Das *et al.* 2005). However, other studies on human observed that *Lactobacillus* and *Bifidobacteria* reduce blood glucose level (Asemi *et al.* 2013; Ejtahed *et al.* 2012; Eslamparast *et al.* 2014). For example, some studies investigated a significant improvement in blood glucose level after ingestion of probiotics for

6 weeks (Ejtahed *et al*. 2012). It has been speculated that probiotics induce glucose absorption through insulinotropic polypeptides and glucagon like peptides production (Al-Salami *et al*. 2008). This mechanism has been explained that certain probiotics such as *Lactobacillus casei*, *L. plantarum*, *L. acidophilus*, *L. delbrueckii subsp. bulgaricus*, *Bifidobacterium longum*, *B. breve*, *B. infantis* and *Streptococcus salivarius subsp*. *Thermophilus* produce short chain fatty acids that promote the butyrate secretion of glucagon-like peptide-1. Glucagon-like peptide-1 hormone was secreted by L-cells in intestine resulting to stimulate insulin secretion and inhibits glucagon (Belenguer *et al*. 2006; Yadav *et al*. 2013). This secretion leads to delay gastric empty and reduce the appetite, food intake and body weight gain (Drucker and Nauck, 2006). Lactic acid bacteria produce lactate and then fermented into acetate and propionate via methylmalonyl-CoA or acrylyl-CoA reductase and then to butyrate via acetyl-CoA (Belenguer *et al*. 2006; Seeliger *et al*. 2002).

Other mechanisms for probiotics could be correlated with improvement immune system through increased anti-inflammatory cytokine production, decreased intestinal permeability and inhibit oxidative stress (Ma *et al*. 2004; Paszti-Gere *et al*. 2012; Yadav *et al*. 2008). Probiotic additions accompanied with an elevation of glutathione peroxidase, superoxide dismutase activities and total antioxidant status. Under nuclear factor-κB regulation, probiotics can inhibit the inhibitor of NF-κB kinase subunit β breakdown subsequently, prevent NF-κB move into the nucleus and inhibit pro-inflammatory cytokines expression as well as up-regulated nerve growth factor (Lambiase *et al*. 1997; Ma *et al*. 2003; Pierucci *et al*. 2001). Therefore, these findings showed increasing probiotics efficacy to inhibit streptozotocin-induced changes in blood glucose by increasing antioxidants on pancreatic β-cells (Yadav *et al*. 2008).

Several studies drew an attention towards importance of probiotics in improving the feed utilization efficacy. Probiotic supplementation enhanced digestibility, improved animal growth performance and reduced the quantity of feed consumed (Bedford and Schulze, 1998). Addition of probiotics to low protein diets of broiler chickens showed a significant positive effect on body weight gain, and reduced the protein degradation and ammonia formation (Mehr *et al*. 2007). However, probiotics feeding had no any influence serum protein level (Gohain and Sapcota, 1998).

While serum uric acid levels were significantly increased with the increasing of probiotics levels in broiler (Hamid and Qureshi, 2009; Sultan and Abdul- Rahman, 2011). However, there were no any changes in kidneys of mice that treated with probiotics may be as a result to serum uric acid level was at tolerance level (Salahuddin *et al*. 2013).

Influence of probiotics on growth performance

Several studies have been illustrated that probiotics promote growth performance in the poultry production system compared with non-supplement diets (Kalavathy *et al*. 2003; Mountzouris *et al*. 2010; Shim *et al*. 2010). Midilli and Tuncer (2001) showed significantly improved growth performance in broiler that administered with probiotic orally. Administration of probiotics in diets enhances organic acid production like lactic acid can prevent the gastrointestinal disorders and improve feed efficiency. Therefore, it was observed a significant improve in weight gain between 21day and 42 day in broiler (Jin *et al*. 1998). However, some studies reported that probiotics had no influence on food consumption, but it improve growth rate and carcass weight of broiler (Djouvinov *et al*. 2005a; Djouvinov *et al*. 2005b).

From the best of my knowledge there is limited information about the effective doses of probiotics that used in poultry and animal production systems. Meanwhile, the application of probiotics on poultry production differs than animal production because of difference of their life span and physiological status. Furthermore, the impact of probiotics poultry health and their productivity depends on many factors such as the type of probiotic (lactobacilli, bifidobacteria, yeasts, …), the daily dose, the timing and the frequency of daily administration, the method of delivery, the duration of administration, and the viability of the probiotic. It is very important to keep the viability of probiotic from destroying the external factors via microencapsulation.

CONCLUSION

This article attempted to spot an overview on the modes of action of probiotics and their impacts on biochemical parameters and growth performance. Recently, many research centers focused the importance of probiotics usage as antibiotic substitution. Moreover, probiotics have a significant potential effect for different diseases. Several important mechanisms demonstrate the antagonistic effect of probiotics on pathogens including competition on adhesion receptors, competition for available nutrients and production inhibitory substances, improvement the gut epithelial barrier function, degradation and neutralization of toxins and immune-stimulatory effect. Biochemically, probiotics have beneficial effect in treatment of chloesterolemia and alleviation of blood glucose. It is necessary for enhancement the poultry resistance to bacterial and viral diseases through promoting the immune response to the pathogens. It was recommended that dietary inclusion of probiotics from 21 day to 42 day of age in broiler chicken, while it had a significant effect on growth performance. The efficacy of probiotic depends on the type of bacteria present in probiotic, dose (10^7-10^{10} CFU/bird/day) and types of the gastrointestinal microbial population.

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