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Formulation of Poultry Diet to Improve Immune Response: A Review

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ABSTRACT

Early in the past, poultry diet was mainly formulated to meet maintenance and production requirements, so the focus was on productive performance, and health of birds expected to be involved within these requirements. Thereafter the use of antibiotics as feed additives at sub-therapeutic dose was introduced to increase productivity by reducing bacterial colony count in the gut and improving gut equilibrium. That means more concern about health of birds. Recently, arises of poultry welfare concern in addition to the ban of the use of antibiotics as feed additives by European Union from 2006, rushed producers and nutritionists into more concentration on health of birds and immunity when they formulate poultry diets. Hence two ways were adopted to improve bird health and immunity by feed formulation without supplementation of antibiotics as growth promoters. The first one is by using antibiotic alternatives as growth promoters. The other one, which emerges recently, is formulation of feed to meet the needs of cells of the immune system. This means studying its needs for nutrients such as protein, energy, amino acids, vitamins and minerals. There is also, feeding of infected birds when the diet should be formulated in a way to avoid exacerbating the condition by feeding microorganisms and help them to proliferate. This review aims to discuss the role of nutrients and feed formulation in improving poultry health and immunity either through meeting requirements of cells of the immune system or through antibiotic alternatives supplementation or even as modified diet during infections.

INTRODUCTION

Recently, emerge of poultry welfare, sustainable agriculture and environment protection concerns in addition to produce high level of safety products leads to more investigation to find methods to improve bird immunity (Lara and Rostagno). However, use of antibiotics as growth promoters played a valuable part in improving health of birds in the past through their anti-inflammatory effects on the gut and consequently reducing loss of energy (Niewold, 2007). The author stated that this theory of mode of action doesn't show discrepancy with the previous theory of antibiotics action on the microflora. However, use of antibiotics as growth promoters in feed additives has been prohibited from January 2006 according to regulation 1831/2003 performed by European Union (Castanon, 2007). Antibiotic restriction besides, emerge of poultry welfare concern challenged researchers particularly nutritionists to look for antibiotic alternatives to fill the gap that expected to occur as a result of this restriction. At first nutritionists focused on antibiotic alternatives as growth promoters and finally they succeeded in finding growth promoters other than antibiotics such as prebiotics and probiotics (Hajati and Rezaei, 2010 and Takahashi *et al*., 2005), phytogenic (Helander *et al*., 1998, Giannenas *et al*., 2003 and Fascina *et al*., 2012), volatile short-chain fatty acids (Fernández-Rubio *et al*., 2009) and organic acids (Fascina *et al*., 2012). After that, studying nutrition-immunity relationship has given part of attention of nutritionist. Impact of feeding broiler chicks immediately post-hatch on immune system has been evaluated (Dibner *et al*., 1998, Noy and Uni 2010, El Rammouz *et al*., 2011 and Ao *et al*., 2012). Furthermore, nutrients in poultry diets have been considered as immune-modulators such as energy, unsaturated fatty acids, vitamin A, selenium and zinc (Rama *et al*., 2014). Nevertheless, more investigations in this area have been recommended (Klasing, 2007). The author claimed that, for the immune-modulators there is genetics-nutrition-environment interactions. In addition variation in nutrients needs for immune responses has been reported even in closely related strains (Kwak *et al*., 2001). Therefore studying optimum nutrients as immune-modulators for certain strain in a certain environment will be required.

ANTIBIOTIC ALTERNATIVES GROWTH PROMOTERS AND IMMUNE RESPONSE

The effect of considerable amount of antibiotic alternatives growth promoters on broilers and layers performance and immune response has been studied. Some of these growth promoters showed positive effect on performance and immune response.

a) PREBIOTICS

Prebiotic is "A selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefit upon host wellbeing and health" (Gibson *et al*., 2004). Commonly used prebiotics in human and animal diets are carbohydrate (fibre) and nondigestible oligosaccharides such as fructooligosaccharides, galactooligosaccharides, transgalacto-oligosaccharides and lactulose (Gaggìa *et al*., 2010). Mannan-oligosaccharide showed antimicrobial properties with lactic acid bacteria product (All-Lac

XCL) in preventing necrotic enteritis (Hofacre *et al*., 2003) and assists in control of *Eimeria* species with anticoccidial vaccine (Nollet *et al*., 2007). Inulin is another example of prebiotics that examined for their effect on immune response. It has been reported that application of inulin in broiler diet resulted in significant increase in total anti-SRBCs (Sheep Red Blood Cells) and IgM titer in addition to WBCs, heterophils and heterophils to lymphocytes ratio (Nabizadeh *et al*., 2012) . Furthermore, nutrigenomic and a report of a microarray based gene expression study of the impact of inulin on gene activity revealed improvement of broilers immunity as a result of dietary inulin supplementation (Sevane *et al*., 2014). Considering mechanisms of action of prebiotics, it has been noticed that each compound has its own properties. Fructooligosaccharides support endogenous defensive lactic acid bacilli to become dominant, and inulin enhances release of cytoprotective butyrate (Sartor, 2004).

b) *PROBIOTICS*

Probiotic is "A preparation of or a product containing viable, defined microorganisms in sufficient numbers, which alter the microflora (by implantation or colonization) in a compartment of the host and by that exert beneficial health effects in this host" (Schrezenmeir and De Vrese, 2001). Microorganisms that frequently used as probiotic in animal feed are *Lactobacillus* and *Bifidobacterium* species in addition to yeast (*Saccharomyces spp*.) (Binns, 2013). It has been stated that lactobacillus spp. has the ability to improve humeral and proliferative immune response of layers and broilers in a specific conditions (Koenen *et al*., 2004). However, authors concluded that improvement effects of lactobacillus depend on strain, age of bird, dose and duration of supplementation. These findings were confirmed by Brisbin *et al*. (2011). Authors found variation in effects of 3 species of *Lactobacillus* administered orally on immune response of chickens. The authors observed considerable immunomodulation effect due to application of *Lactobacillus acidophilus*, and week effects of *Lactobacillus reuteri* and *Lactobacillus salivarius*. Contrary to these results, Huang *et al*. (2004) failed to obtain immunomodulation effects of *Lactobacillus* species in spite of detection of their ability to promote broiler growth. Modes of actions of probiotics that have been concluded are: First, reduction in gut pH leading to growth of acidophilic commensal organisms those affect pathogens adherence, growth, translocation through epithelium and gut colonization. Second, some probiotic bacteria release bacteriocin which regarded as bacteriostatic. Third, decrease pathogens virulence by modifying their gene expression. Fourth, some probiotics may support defensive mechanism of mucous layer of gut against pathogens translocation. Fifth, probiotics may stimulate paneth cells in the small intestine to release antibacterial substance called defensins. Sixth, probiotics also act through competitive property with pathogens for receptors, so inhibiting their translocation. Finally, probiotic may adhere to pathogens preventing their gut colonization (Binns, 2013).

c) PHYTOGENICS

Include various kinds of herbs spices and plant extract, mainly essential oil

(Hashemi and Davoodi, 2010), such as black cumin seeds, Artemisia leaves and Camellia L. plant extract which introduced into poultry diets to evaluate their effects on performance and immunity (Khalaji *et al*., 2011). Authors reported that Artemisia leaves improve the condition of gastrointestinal tract, whereas black cumin seeds promote boiler growth but Camellia L. plant extract is not recommended to use in broiler diet. In addition, positive effect of mushroom and herb polysaccharide extracts on gut microbial environment in diseased birds has been recorded (Guo *et al*., 2004a). Their improvement of cellular and humoral immune response in chickens infested with *Eimeria tenella* has been also detected (Guo *et al*., 2004b). Phytochemicals in phytogenic show various modes of action on microorganisms (Hashemi and Davoodi, 2010), tannic acids produce their antimicrobial effect through suppression of extracellular enzymes of pathogens, affecting oxidative phosphorylation and iron degradation (Scalbert, 1991), alkaloids acts through suppression of DNA synthesis (Bonjean *et al*., 1998 and Van Miert *et al*., 2004), saponins may act through interference with catabolic enzymes and affecting electron transport chain and bacterial and fungal energy metabolism (Mandal *et al*., 2005), Finally, antimicrobial effect of essential oils have been thought to occur through degradation of microbial membrane altering pH homeostasis and imbalance of inorganic ions (Lambert *et al*., 2001 and Lv *et al*., 2011)

POST-HATCH EARLY FEEDING AND IMMUNE RESPONSE

Nutritionists tried other strategies to improve bird health and immunity in addition to the use of antibiotic-alternatives as feed additives. Studying of feeding chicks post-hatch and its impact on immune response has been performed. El Rammouz *et al*. (2011) noticed that deprivation post-hatch chick of feed significantly affects immune response. Juul-Madsen *et al*. (2004) confirmed negative effect of deprivation chicks of feed for 48 hours post-hatch on the immunity through their detection of development interception of circulating $CD4^+$, $CD8^+$, $BU\text{-}1^+$ cells and antibody responses. This because development of the immune system starts pre-hatch and goes on for several weeks post-hatch and this development required earlier feed supplementation (Juul-Madsen *et al*., 2004). In addition, the development of gut associated lymphoid tissue (GALT) is correlative with the development of the digestive system and both are influenced by early and late feeding immediately post-hatch. GALT has been suggested to play a role in the prevention of gut from microorganisms (Friedman *et al*., 2003 and Bar Shira et *al*., 2005). Bar Shira *et al*. (2005) examined the impact of post-hatch fasting (72 hours) on GALT development in chicken. Findings obtained were delayed response of systemic and intestinal antibody to rectal immunization, reduced GALT efficiency in the caecum and colon in addition to gut-related cloacal bursa, delayed proliferation of T and B lymphocytes in the hind gut and cloacal bursa and chIL-2mRNA expressed more slowly in the hindgut T lymphocytes. Dibner *et al*. (1998) observed improvement in immune response of broiler chicks fed balanced ration immediately post-hatch. This immunity improvement exhibited in the form of increase in bursa weight, faster occurrence of biliary IgA and germinal centers in the caecal tonsils and better response against disease challenge. It has been observed that feeding chick during the first 3 days post-hatch showed better resistance to Newcastle disease, Infectious Bronchitis disease and Gumboro (El Rammouz et *al*., 2011). Furthermore, Ao *et al*. (2012) concluded that supplementation of feed additives to broiler chicks diet offered immediately post-hatch improve the immune response to *Clostridium perfringens*.

NUTRITION-DISEASE-IMMUNITY INTERACTIONS

An important role of nutrition in modulating immune response of birds has been reported (Kidd, 2004). Kogut and Klasing (2009) concluded that all dietary nutrients participate in achievement of optimum immune response therefore lack or excess of each of these nutrients might produce negative impact on the immune response.

a) PROTEIN

It has been reported that supplementation of lower level of protein to broilers diet reduced total antibodies against Sheep Red Blood Cells (SRBCs) (Malik et *al*., 2013). This finding is in line with that of (Bunchasak *et al*., 2005). Authors found that introduction of crude protein into layers diet at level of 18% showed higher antibody titer against Newcastle Disease than those introduced at levels of 14% and 16%.

b) AMINO ACIDS

Interaction of dietary essential amino acids and immunity has been detected, particularly branch-chain amino acids (isoleucine, leucine and valine) (Konashi et *al*., 2000). Effect of other essential amino acids on the immune response also has been examined. Dietary arginine supplementation showed significant increase in thymus, spleen and bursa weights in addition to increase in nitric oxide release by peritoneal macrophages and delayed-type hypersensitivity response (Kwak *et al*., 2001). Abdulkalykova and Ruiz-Feria (2006) noticed that addition of higher level of arginine to broiler diet enhances antibody production. Bouyeh (2012) observed increase in blood lymphocytes and Newcastle antibody beside decrease in heterophyls and heterophyls: lymphocytes ratio, which considered as a stress index, as a result of applying broiler diet with lysine and methionine at levels above (NRC, 1994) recommendations. It has been reported that at 42 day of broiler age threonine improved antibody titer against Newcastle disease (Rezaeipour *et al*., 2012) and against SRBCs (Abbasi *et al*., 2014). Furthermore, improvement of systemic immune response (interferon-α, interferon-γ and immunoglobulin G) against infectious bursal disease has been detected due to supplementation of broiler diet with arginine and tryptophan combination (Emadi *et al*., 2011).

c) VITAMINS

Several researches investigated the effect of vitamins on immune response and showed that vitamins play important role in enhancing bird immunity. Abdulkalykova and Ruiz-Feria (2006) exhibited the role of vitamin E in improving antibody titer against SRBCs. This result is in agreement with that of Lin and Chang (2006). Authors observed increase in antibody titer against (SRBCs) and Infectious Bursal Disease virus in cockerels fed diet supplemented with moderate level of vitamin E (20 mg/ kg diet), author noticed that excess of vitamin E may suppress the immune response. The role of vitamin A in supporting immune response has been examined (Dalloul *et al*., 2002). Authors found reduction in intraepithelial lymphocytes, mainly $CD4^+$, and local cell-mediated immunity in broilers fed diet deficient in vitamin A. Furthermore, Safarizadeh and Zakeri (2013) reported enhancement of immune response against Newcastle Disease as a result of addition of vitamin A to broiler diet. Vitamin C (ascorbic acid) also, has been reported to play a role in immune response improvement (Lohakare *et al*., 2005). Authors observed increase in lymphocytes particularly $CD4^+$ and T-cell receptor-Π in addition to antibody titer against Infectious Bursal Disease as a result of application of ascorbic acid to broiler diet. Al-Masad (2012) agreed with this result, the author found increase in total IgM and IgG antibody titer when birds under heat stress fed combination of vitamin C and Zn.

d) TRACE MINERALS

A number of experiments was conducted to study the impact of trace minerals on the immunity. It has been declared that supplementation of broiler diets with higher levels of zinc (Zn) 80 ppm produced better humoral and cell mediated immune response than lower level (29 ppm) (Sunder *et al*., 2008). Sunder *et al*. (2013) found that Zn and manganese (Mn) work synergistically in improving humoral immune response when their combination is supplemented to broiler diet at 80 and 60 ppm levels, respectively. Positive effect of selenium (Se) on the immune response, also, has been obtained (Hegazy and Adachi, 2000). Authors detected increase in antibody titer against salmonellosis with or without aflatoxicosis due to addition of Se to chick diet. Furthermore, it has been noticed that the use of Se and vitamin E complex in broiler diet enhance humoral immune response (Safarizadeh and Zakeri, 2013 and Yamuna and Thangavel, 2011).

FEEDING INFECTED BIRDS

Some nutrients are very important for many pathogens such as iron and biotin. One of the defensive actions of the immune system during acute infection is the removal of iron from extracellular fluids into hepatocytes and binding of avidin with biotin to make them unavailable to pathogen (Klasing, 2007). Therefore supplementation of these substances to diets during some infections is unadvisable. It has been reported that requirements for vitamin A and K during coccidiosis are much more than their requirements under normal conditions (Das *et al*., 2011). This seems to be in line with the opinion of Kidd (2004) who mentioned that nutrient requirements for broilers immunity may not be met by requirements for growth and breast yield. Das *et al*. (2011) also, reported that higher levels of dietary protein and calcium may exacerbate coccidian infection by coccidia. Authors attributed this to their role in activation of trypsin enzyme which favour oocyst establishment. Hence application of lower levels of protein and calcium to poultry diets during coccidiosis is recommended.

CONCLUSION

It was concluded that nutrition can play important role in improvement of poultry immune response, and consequently health and welfare. To achieve optimum immunity more investigations should be performed to determine nutrient requirements for defensive mechanisms of the cells of the immune system. This because nutrient needs for higher productive performance are insufficient for defensive mechanisms against pathogens.

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