Effects of Probiotics on growth performance

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Abstract: Probiotics are products containing a single viable strain of beneficial bacteria or multiple bacterial strains that colonize the crop, small intestine, ceca, and cloaca**.** Beneficial microorganisms in probiotics (in feed or water) may inhibit enteric pathogens by competing for attachment sites on surface of enterocytes, competing for nutrients, and producing antibacterial compounds (volatile fatty acids, low pH, and bacterocins) Moreover, probiotic may negatively affect pathogen metabolism by increasing or decreasing enzyme activity and stimulating immunity by increasing antibody levels and macrophage activity Probiotics, prebiotics, and synbiotics can be used to modify the gut environment to prevent introbacterial pathogens colonization, invasion, multiplication, and shedding. The review discusses the modes of action like antibacterial, competitive exclusion (CE), and immunomodulatory properties of probiotics, particularly in poultry. it is necessary to conduct more researches with prebiotics and probiotics as well as other feed additives to understand the detailed mechanisms of action and identify better alternatives for poultry production and health.

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Introduction:

Probiotics are either mono or mixed culture of live microorganisms which beneficially affect the host animal by improving its intestinal microbial balance **(Fuller,1989)**. According to FAO/WHO, probiotics are live microorganisms which when administered in adequate amounts confer a health benefit on the host. The characteristics of good probiotics are: 1) they should be a strain capable of exerting beneficial effects on the host animal, 2) they should be non-pathogenic and non-toxic, 3) they should be present as viable cells, 4) they should be capable of surviving and metabolizing in the gut environment and 5) they should be stable and capable of remaining viable for periods under storage and field conditions **(Fuller, 1989)**. Probiotics are also called 'direct fed microbials'. Commonly used probiotics in animals are: LAB (*L. bulgaricus, L. plantarum, L. acidophilus, L. helveticus, L. lactis, L. salivarius, L. casei, Bacillus subtilis*), *Enterococcus* (*E. faecalis, E. faecium*), *Bifidobacterium* spp., *Streptococcus*, *Enterococcus, Lactococcus, E. coli* and fungi and yeast (*Aspergillus oryzae*, *Saccharomyces cerevisiae*) **(Huang et al., 2004)**. LAB and *Bifidobacterium* species have been used most extensively in humans as well. *Bacillus, Enterococcus*, and *Saccharomyces* yeast have been the most commonly used organisms in livestock **(Ferreira et al., 2011)**. Multiple strains may be more beneficial than single strain as they act on different sites and provide different modes of action that create synergistic effects **(Klose et al., 2006; Timmerman et al., 2004; Sanders and Huis in't Veld, 1999). Probiotics** are products containing a single viable strain of beneficial bacteria or multiple bacterial strains that colonize the crop, small intestine, ceca, and cloaca **(Fuller, 1989).** Beneficial microorganisms in probiotics (in feed or water) may inhibit enteric pathogens by competing for attachment sites on surface of enterocytes, competing for nutrients, and producing antibacterial compounds (volatile fatty acids, low pH, and bacterocins) Moreover, probiotic may negatively affect pathogen metabolism by increasing or decreasing enzyme activity and stimulating immunity by increasing antibody levels and macrophage activity **(Fuller 1989, Patterson and Burkholder 2003)**

Mechanism of action of probiotics

The most common mechanism of probiotics to work is competitive exclusion (CE), which was originated on the finding that the newly hatched chicken could be protected against *Salmonella* colonization of the gut by providing it with a suspension of gut content prepared from healthy adult chickens **(Nurmi and Rantala, 1973)**. By competing for the common niche in the gut, probiotics exclude the sites for pathogen replication **(Wu et al., 2008)**. CE refers to the physical blocking of opportunistic pathogen colonization and altering the environmental niches within the intestinal tract like intestinal villus and crypts leading to better immune system **(Duggan et al., 2002)**. It involves the addition of a non pathogenic culture either single or multiple strains in order to reduce the pathogenic bacteria in the GI tract **(Fuller,1989)**. CE due to probiotics includes competition for physical attachment sites, enhancement of host immune system, and production of antimicrobial compounds like SCFAs and bacteriocins or colicins from metabolic reactions **(Callaway et al., 2008; Stahl et al., 2004)**. Enhancement of the epithelial barrier, increased adhesion to intestinal mucosa, production of antimicrobial substances and modulation of immune system are other mechanisms of action by probiotics **(Bermudez-Brito et al., 2012)**. A front line of defense against the adverse effect of pathogens is provided by probiotics showing their antimicrobial effect. For example, lactic acid producing probiotics show antimicrobial effects by reducing the pH of the gut **(Fayol-Messaoudi et al., 2005; Corr et al., 2007)**. On the other hand, some strains of LAB that are used as probiotics inhibit the virulence factor expression of pathogens like in *Shigella* and *Yersinia* and directly reduce their invasiveness **(Carey et al., 2008; Lavermicocca et al., 2008)**. It has been shown that lactic acid producing bacteria produce lactic acid, which is used by anaerobic butyrate producing bacteria for producing large amount of butyric acids, and this is called cross feeding **(Duncan et al., 2004)**. A study showed that cross feeding mechanism, particularly due to butyric acid was able to promote growth performance **(Qaisrani et al., 2015)**. Mechanisms of action of probiotics to modulate immune system mostly depend on the strains of bacteria or microorganisms used (Huang et preparation method, routes of administration and environment where birds are raised **(Ajuwon, 2015)**. Through the interaction of host and the probiotic cultures, enhancement of both natural and specific antibodies, interferon or cytokines as well as activation or suppression of T-cells that eventually leads to the cytokine expression have been observed in many studies **(Haghighi et al., 2008; Castellazzi et al., 2007; Haghighi et al., 2005).**

Probiotics in chickens

The major effects observed in poultry due to probiotics including yeast cultures supplementation are in growth performance, meat quality, immune response, intestinal morphology, and intestinal microbiota **(Gao et al., 2008; Samanya and Yamauchi, 2002; Bai et al., 2013)**. In poultry, probiotics feeding has been shown to maintain normal flora mainly by CE **(Kizerwetter-Swida and Binek, 2009),** improve feed consumption/digestion and gut health (Awad et al., 2009), and stimulate the immune system **(Brisbin et al., 2008)**. Probiotics may potentially stimulate growth through increased SCFA production in poultry and through selective regulation of insulin signaling in different tissues **(Ichikawa et al., 2002).** Short chain fatty acids like acetate, propionate and butyrate are used as energy source in tissues. Particularly in chickens, butyrate has shown beneficial effects by selectively partitioning the nutrients away from liver and adipose tissues towards muscles through up regulation of insulin receptors **(Matis et al., 2015).** Another mechanism by which probiotics may stimulate growth is by regulating the immune system. When immune system is regulated, it suppresses the negative effects of chronic immune activation. When immune system is activated, there is diversion of nutrients from production process towards immune response **(Gabler et al., 2008).** On the other hand, there is direct effect on epithelial barrier, thus producing better growth **(Awad et al., 2010).** Some studies that used probiotics of *Bacillus* and LAB complex were able to improve egg production and other traits like reduction of serum and egg cholesterol level in laying hens **(Li et al., 2006).** Combination of humane and probiotics (*Lactobacillus, Bifidobacterium, Streptococcus*, and *Enterococcus* spp.) in late laying age of hens improved egg quality and feed conversion whereas decreased mortality **(Yörük et al., 2004)**. Growth performance as well as immune modulation by production of mucosal IgA were the best with yeast culture supplemented diets at level of 2.5 g/kg among the various levels provided (0, 2.5, 5.0 and 7.5 g/kg) **(Gao et al., 2008).** Similarly, probiotics containing LAB and *Saccharomyces cerevisiae* supplemented at 0.2% enhanced growth performance as well as T-cell function in broilers **(Bai et al., 2013)**. Chickens fed dietary *B. subtilis* for 28 days had a tendency to display greater growth performance as well as pronounced intestinal morphology, including prominent villus height, extended cell area and consistent cell mitosis compared to those fed a control diet **(Samanya and Yamauchi, 2002)**. Probiotic strains differentially modulate, and especially balance pro- and anti-inflammatory cytokines **(Foligné et al., 2010).** Pro-inflammatory cytokines like TNFα, IL-1β and IL-6 released from monocytes and macrophages are augmented by LAB and *Bifidobacteria* (**Helwig et al., 2006; Miettinen et al., 1998)**. Anti-inflammatory cytokine like IL-10 is also released from cells like dendritic cells and monocytes due to LAB or *Bifidobacteria* feeding **(Braat et al., 2004; Smits et al., 2005)**. It has been shown that LAB increased production of anti- and pro-inflammatory cytokines such as IL-12, IFN-γ, IL-10, and TNF-α from the intestinal epithelium of broiler chicken **(Arvola et al., 1999)**. Production of cytokines leads to the overall immune modulation in the chicken. LAB has shown the modulating effects on the immune system of both layer- and meat-type chickens. The ability of LAB to modulate chicken cytokines, toll-like receptors and chemokine gene expression has been demonstrated **(Haghighi et al.,2008; Brisbin et al., 2011).** Increase in the antibody secretion due to increase in Blymphocytes (humoral immunity) is a potential mechanism by LAB in boosting the immunity in broiler chicks **(Apata, 2008)**. The increase in the population of white blood cells may be attributed to the presence of LAB in the diet stimulating the production of lymphocytes, particularly the B-cells that are responsible for forming antibodies that provide humoral immunity. Enhancement of gut barrier function through modulation of the cytoskeleton and epithelial tight junctions in the intestinal mucosa is one of the mechanisms of probiotics in preventing pathogens (Ng et al., 2009). Pathogens like *Salmonella*, *Campylobacter*, *Clostridium* and *E. coli* are displaced or reduced by probiotic bacteria supplemented in chickens Supplementation of probiotics in feed helps in reducing *Salmonella* colonization in ceca and other internal organs either by the mechanism of CE **(Nurmi and Rantala, 1973**) or reduction of the colonization of opportunistic bacteria in the GI tract **(Patterson and Burkholder,2003 and Callaway et al., 2008)**.

Oral administration of *Klebsiella pneumoniae*, *Citrobacter diversus*, and *E. coli* significantly reduced *Campylobacter jejuni* colonization of chickens **(Stern et al., 2001)**. Down regulation of some flagellar genes like fla A by LAB supplementation was able to reduce pathogenesis due to the *Campylobacter* in chicken **(Ding et al., 2005).** Similarly, a study reported that dietary probiotics were able to provide the better cell-mediated immunity and the reduction in shedding of fecal oocysts of *Eimeria acervulina* **(Dalloul et al., 2005)**. The authors further demonstrated that the probiotic continued to afford some measure of protection through immune modulation despite a fairly overwhelming dose of *E. acervulina*. Mortality due to necrotic enteritis was reduced from 60 to 30% due to lactic acid bacteria added in feed **(Hofacre et al., 2003).** Dietary supplementation of *Bacillus subtilis* reduced FCR as well as reduced intestinal lesions in broilers challenged with *Clostridium* and *Eimeria* **(Jayaraman et al., 2013)**. The effect of *Bacillus* on *Eimeria maxima* infection in broiler chickens was studied and it was found that *Bacillus subtilis* reduced the clinical signs of experimental avian coccidiosis and increased various parameters of immunity in broiler chickens **(Lee et al., 2010 b)**. Such inconsistencies exist among the studies with probiotics. Beneficial effect of *Lactobacillus* spp. bacteria on chicken livability was observed without any effect on BWG and FCR **(Brzóska et al., 2012)**. Feeding DFM containing *Bacillus* did not affect the growth performance **(Lee et al., 2010 a)**. The use of probiotics did not influence the performance of the birds challenged with *Salmonella* enteritidis, neither the production of anti-*Salmonella* antibodies and intestinal morphology were observed **(Ribeiro et al., 2007)**. The effects of probiotics on chickens also depend on rearing system (cage vs. floor pen) especially *Salmonella* challenge condition and this can be due to differences in hygienic conditions **(Pirgozliev et al., 2014; Santos et al.,2008)**. A study has shown that the beneficial effects of additives like organic acids are pronounced in less hygienic housing conditions **(Pirgozliev et al., 2014)**. Broilers raised in litter had lower cecal *Salmonella* count than in cages as litter birds may have more chance to get the modulated gut microbes due to CE and thus reduced *Salmonella* **(Santos et al., 2008)**. Such results may question the effectiveness of similar feed additives as potential growth promoters. The factors behind the variability due to probiotics may include physiological state of bird, actual microbiota already present in the gut, dose and nature of strains used for probiotics culture, probiotics species, method of preparation of probiotic strains, route of administration and timing of application relative to any pathogen challenge **(Brisbin et al., 2011; Ajuwon, 2015; Huyghebaert et al., 2011)**.

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