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Role of prebiotics, probiotics and synbiotics on animal health and productivity

Vijay Kumar Matham, A Gopala Reddy and N Prakash

Abstract
Intensive production systems in livestock are playing an important role worldwide. The health benefits imparted by probiotics and prebiotics as well as synbiotics have been the subject of extensive research in the past few decades. These food supplements termed as functional foods have been demonstrated to alter, modify and reinstate the pre-existing intestinal flora. Prebiotics like FOS, GOS, XOS, Inulin; fructans are the most commonly used fibers. *Bifidobacterium, Lactobacillus, Bacillus, Enterococcus* and *Saccharomyces* are commonly utilized as probiotics in the animal feed. Prebiotics used together with probiotics are termed synbiotics and are able to improve the viability of the probiotics. The present review focuses on composition and roles of Prebiotics, Probiotics and Synbiotics on animal health and Productivity.

Keywords: Prebiotics, probiotics, synbiotics, livestock, productivity

Introduction
Livestock farming is one of the rapidly growing agricultural sectors. Around, 75% of the rural population and 25% of urban population depend on livestock for their sustenance (Grace, 2012) [15]. Livestock provides a major source of income for marginal people of developing countries and is a major entry point to fight against rural poverty (Randolph *et al.*, 2007;Smith *et al.*, 2013) [36, 46]. Livestock provides a draught power and manure as fuel and fertilizer. Livestock farming can give inflation-proof animal assets for both financing and insurance (Ehui *et al.*, 1998) [10]. Intensive production systems in livestock are playing an important role worldwide, however this increases the need to make sure that animal welfare issues are considered appropriately.

Despite the increased livestock production, there are two major public health issues. Firstly, sub-therapeutic uses of antibiotics as growth promoters for animals in feed has evoked widespread concern, with their use being banned in many of the countries because of the potential to develop antibiotic resistance among the microbial populations being associated with human and animal diseases. Secondly, some of the foodborne zoonotic infections like Campylobacteriosis, Salmonellosis and *Escherichia coli* infection are serious public health concerns of the world leading to serious economic losses. Antibiotics are broadly used mainly to modify the alimentary microbiota and to the boost productivity and growth of the animal along with treatment of infectious diseases. Long-term use of antibiotics has led to the development of drug-resistant microorganisms imposing threat to health of humans and exerting negative effect on the environment. Therefore, looking at the present scenario, there is an urgent requirement for discovery of non-toxic, novel and biosafe substances for. Use of probiotics, prebiotics and synbiotics is considered as suitable alternative for the treatment of infectious and non-infectious diseases (Silva *et al.*, 2020) [42].

Prebiotics
Prebiotics are used as natural feed additives. The prebiotic concept was first initiated in 1995 by Gibson and Roberfroid in 1995. Also, Prebiotic is “indigestible fermented diet substrates that selectively stimulate the composition, growth, and activity of microflora in gastrointestinal tract and thus improve hosts’ health” (Gibson RG and Roberfroid, 1995;Hamasalim, 2015) [15, 19]. Prebiotic carbohydrates are observed naturally in fruits and vegetables. It is considered necessary to determine the health bonuses that are associated with prebiotic intake (Hamasalim *et al.*, 2012) [18].

Prebiotic namely fructooligosaccharides can be utilized as dietary supplement for the animals to maintain gastrointestinal well-being (Lynn, 2010) [28]. Prebiotics are not broken down by the gastric enzymes, but they pass unaltered into large intestine, where they get selectively fermented leading to beneficial effects (Hamasalim, 2015) [19]. A study has shown that administration of prebiotic results in increased numbers of beneficial intestinal flora (especially *Bifidobacteria*) (Schiffrin, 2007) [40]. Probiotic, prebiotic and synbiotic administration have been documented to increase intestinal levels of beneficial *Bifidobacteria*, *Enterocooci* and *Lactobacilli*, with reduced levels of Enterobacter (Ahmed *et al.*, 2007) [1]. Prebiotic have shown to increase the mineral absorption (magnesium and calcium). Prebiotics play an important role in nutrition of both livestock and pet animals (Paulina and Katarzyna, 2018) [33].

Effects of Prebiotics on Animal health and Productivity

Smiricky-Tjardes *et al.* (2003) [44] administered prebiotic to pigs for 6 weeks @ of 35 g/kg feed. A significant increase in stool *Lactobacillus* and *Bifidobacterium* count was noticed compared to the control group. Tzortzis *et al.* (2005) [52] studied a novel blend of prebiotic produced as a result of the activity of galactosyl transferase in bacteria *Bifidobacterium bifidum*. The administration of prebiotic to pigs @ 40 g/kg feed lead to a significant elevation of *Bifidobacterium* and of acetic acid levels, with a simultaneous decrease in intestinal pH compared to control group and diet with an addition of inulin. Moreover, the studied mixture of oligosaccharides lead to a strong inhibition of the adhesion of *Salmonella enterica* serotype Typhimurium and *Escherichia coli* (ETEC) to HT29 cells in in-vitro studies. An interesting study on the effect of oat and barley varieties was carried with different composition of carbohydrate on intestinal microbiota of weaned piglets for 15 days. It was observed that increased β-glucan levels along with the changes in the ratio of amylose and amylopectin led to selective modulation in growth of butyric acid bacteria that could hydrolyse complex carbohydrates like xylan or β-glucan. Therefore, differences between cereal varieties in amount and form of carbohydrates influenced the piglets intestinal microbiota and appropriate selection of cereals caused positive effect on *Lactobacillus* and *Bifidobacterium* count.

Xu *et al.* (2003) [55] studied the effects of FOS at different doses of 0, 2, 4 and 8 g/kg feed upon the activity of digestive system enzymes and intestinal morphology along with the microbiota. It was observed that administration of FOS at dose of 4 g/kg feed showed a positive effect on mean daily growth of animals and also on the growth of *Lactobacillus* and *Bifidobacterium* bacteria, with a concurrent inhibition on growth of *Escherichia coli* in gastrointestinal tract of birds. Whereas, Juskiewicz *et al.* (2006) [22] reported that FOS in turkeys used for 6 weeks had no effect at concentrations of 0.5, 1 and 2% on animal growth and productivity. However, the reduction in intestinal pH was observed in case of FOS at the 2% concentration. Ziggers, (2000) [60] reported that supplementation of prebiotics in broiler chickens diet showed reduction of gastrointestinal pH and elevated levels of *Bifidobacterium* and *Lactobacillus* counts caused by increased levels of volatile fatty acids. Yusrizal and Chen (2003) [59] conducted an experiment on 96 broiler chickens for 6 weeks with fructane (of chicory origin) containing feed upon growth of birds and structure and length of the intestine of animals and observed an improved feed turnover, body weight gain and reduced serum cholesterol. Feed supplementation with fructanes lead to an increase of bacterial count of *Lactobacillus* genus and reduction in counts of potential pathogens like *Campylobacter* and *Salmonella* in the gastrointestinal tract of broiler chicken. Kleessen *et al.* (2003) [25] used 380 chickens for 35 days for breeding by giving them drinking water with artichoke-based fructane having (0.5%) syrup to know the effect of fructane supplementation upon the intestinal microbiota of animals. It was noted that addition of fructanes to drinking water caused decline in *Clostridium perfringens* count and decrease in levels of bacterial endotoxin. Stanczuk *et al.* (2005) [48] studied the effect of MOS and inulin administered in two different concentrations (0.1 and 0.4%) to turkeys ad libitum as feed supplement for 8 weeks of rearing. There was no increase in feed consumption or body weight of turkeys. However, in prebiotic-fed groups higher concentration of SCFA was noted compared to control group. Sims *et al.* (2004) [43] analysed 180 turkeys bred for 18 weeks by MOS supplemented feed leading to better growth in studied animals. Spring *et al.* (2000) [47] studied the effect of *Saccharomyces cerevisiae* yeast containing MOS supplementation in their cellular wall on reduction of various intestinal pathogen counts in chickens. It was noted that administration of MOS-containing yeast showed reduced count of *Salmonella* in the intestines of chicken by 26% compared to control animals receiving a non-modified diet. Effect of isomalto-oligosaccharides (IMO) administration in the following concentrations of 1, 2 and 4% (by weight) on intestinal microbiota was verified in broiler chickens infected with *Salmonella typhimurium*. Animal feed supplementation with IMO caused a significant decrease of *Salmonella typhimurium* count. However, digestion, chewing and effectiveness of administered feed were non-significant compared to the control group. It was also noted that addition of IMO to feed showed an increase in the bacterial count of *Bifidobacterium* genus. Moreover, a significant decrease in weight was seen in birds fed 1% IMO compared to control animals that were fed with non-modified feed.

Probiotics

Metchnikoff in 1908 defined probiotic based on his observations based on the longevity of individuals who lived in certain parts of Bulgaria. He attributed to their ingestion based on fermented milk product containing rod-shaped *Lactobacillus* spp bacteria (Chauhan and Chorawala, 2012) [6]. Food and Agriculture Organization of United Nations (FAO) along with World Health Organization (WHO) defined probiotics as "live micro-organisms which when administered in adequate amounts confer a health benefit on the host." This is widely accepted and adopted by International Scientific Association for Probiotics and Prebiotics. Probiotics are recognized as non-pathogenic microbes worldwide with health benefits. The beneficial effects of probiotics are related to the immunomodulatory activity in gut by stimulating the secretions of immune modulators i.e., IgA and cytokines in the intestinal mucosa. Probiotics in ruminants are administered to target the rumen (feed digestion) where they effect the rumen fermentation especially on the feed digestibility along with degradability and rumen microbiota. Probiotics positively affect the celluloysis and synthesis of microbial protein during digestion process and stabilizes the lactate levels and rumen pH. In addition, probiotics can increase the nutrient absorption. Feed probiotics have shown to reduce the ruminal acidosis (Wahrmund *et al.*, 2012) [53].

Lactic-acid bacterial strains i.e., *Bifidobacterium*, *Lactobacillus*, *Bacillus, Enterococcus* and *Saccharomyces* are commonly utilized as probiotics in the functional foods and animal feed. *Bifidobacterium* and *Lactobacillus* species have shown to provide protection against enteric infections. These beneficial microbes consist of various species of microorganisms like bacteria and yeast and they could be used as single or multi-strain. The probiotics of multi-strain have a broad-spectrum effect compared to different strains against infections and could elevate the beneficial effects of probiotics due to synergistic adhesion effects (Timmerman *et al.*, 2004; Collado *et al.*, 2007) [51, 7].

Effects of Probiotics on Animal Health and Productivity

Utilization of probiotics (live or dry) as natural feed additives have shown to favorably improve the animal welfare and performance, via modulation of the gut microbial community essential in ensuring the host homeostasis. Probiotics have positive effects on the growth rate and production performance of animals when given as single or multi-strain feed supplements. Oral administration of probiotic have shown to improve the daily weight gain, feed intake and overall weight gain in goats, sheep and cattle (Hasunuma *et al.*, 2011) [20]. Population of beneficial microbes i.e., *Bifidobacteria* and *Lactobacillus* are lower in neonatal calves but studies have depicted that supplementation of probiotics containing these microbes increases the growth. In dairy cows, probiotics composed of live yeast increased the feed intake, improved average daily gain, improved feed efficiency and overall total body weight. Additionally, probiotic increased the quality and milk yield (Stein *et al.*, 2006*;Poppy et al., 2012)* [49;34]. Spanish Boer kid-goats were drenched with probiotic mixture consisting of *Bifidobacterium breve*, *Bifidobacterium longum*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus and Lactobacillus reuteri* (Gyenai *et al.* 2016) [16]. Ekwemalor *et al.*, (2017) [11] opined that in goats probiotic supplementation affected the two indicators of anemia i.e., FAMACHA and packed cell volume.

Probiotics are typically utilized to improve the gastrointestinal health, bloating, reduce diarrhea and protect against infectious diseases. Researchers have reported various benefits of oral administration of probiotics in ruminants. Probiotics balance and regulate the gut microbes, development of animals and improvise the host resistance for diseases. Studies suggest that use of probiotics as feed supplements in ruminants improve the production, growth performance and enhance the health and overall well-being of animals. Application of probiotics have shown to decrease the negative environmental impact like methane emission associated with the ruminant production (Liong, 2007;Xu *et al.*, 2017) [27;56].

In ruminants, use of probiotics as feed supplements have shown beneficial effects on milk quality milk production and functional components i.e., fat and protein content. Studies have depicted that probiotic dairy products are safer for large-scale consumption. Study conducted by Yu *et al.* (1997) [58] in dairy cows showed that treatment with probiotic species of *Saccharomyces cerevisiae* and *Aspergillus oryzae* increased the milk proteins and production. Stein *et al.* (2006) [49] reported that probiotic supplementation improved the milk yield, feed utilization rate and component profiles along with elevation in dry matter intake in dairy cows. Xu *et al.* (2017) [56] reported that probiotic use could reduce the udder inflammation and increase the milk yield while decreasing the somatic cell count (SCC). These positive effects of probiotics on milk quality and milk production characteristics are mainly attributed to the subsequent effects of probiotic on number of fiber-degrading and cellulolytic bacteria as well as changes in volatile fatty acid concentration of the rumen (Paulina and Katarzyna, 2018) [33].

The beneficial effects of probiotics on health have been partly due to the ability of probiotic bacterias to modulate the immune system of animal, increase both adaptive and innate immune response. Research from various *in vitro* and *in vivo* studies have shown that probiotics promote the gut health via stimulation of innate immune response. Probiotic with different bacteria i.e., *Lactobacillus casei* strain Shirota, *Lactobacillus casei*, *Lactobacillus fermentum*, *Streptococcus thermophilus* and yeast have been analysed to elicit immune response (Matsuzaki, 2000) [29]. The oral administration of *Lactobacillus casei* activated the immune cells of innate immune response and elevated the expression of innate immune receptor (TLR2) (Galdeano & Perdigon, 2006) [12]. Ghadimi *et al.* (2008) [13] opined that probiotic enhanced the secretion of IFN-γ (a TH1 cytokine) and inhibited the TH2 cytokines stimulation such as IL4 and IL5. Research by Yan and Polk (2002) [57] depicted that immunomodulatory effect of probiotic (*Lactobacillus rhamnosus* GG) in prevention of cytokine-induced apoptosis on the intestinal epithelial cells. Results from their study showed that probiotic inhibited the activation of p38/mitogen activated protein kinase which is pro apoptotic kinase induced by the cytokines IL-1α, IFN-γ or TNF. Furthermore, *Lactobacillus rhamnosus* GG probiotic activated the Akt/protein kinase B (anti-apoptotic) in colon cells of mice and humans. *In vivo* and ex vivo studies have demonstrated the effect of probiotics on inflammasome (Schmitz *et al.*, 2015) [41]. Inflammasome are found in various immune cells (dendritic cells and macrophages) and intestinal epithelial cells having cytosolic proteins i.e., NOD-like receptors, caspase-1 (the serine protease) and apoptosis-associated speck-like protein having a CARD domain. Activation of the inflammasome receptors further produced the activation of Interleukin (IL)-1β and IL-18 and caspase-1. Activation and secretion of inflammatory cytokines Interleukin (IL)-1β and IL-18 enhance and stimulates the antimicrobial effect of immune cells against the intracellular pathogen infection and activates the death of inflammasome-activated cells (Miao *et al.*, 2011) [31]. In ruminants, *Lactobacillus rhamnosus* GR-1 probiotic have shown to amend the *E. coli* induced inflammation in primary mammary epithelial cells pf bovines. Study showed that probiotic pretreatment impaired activation ASC-independent NLRP3 inflammasome, and reduced the protein expression of caspase 1 and NLRP3 (NOD -like receptor family member pyrin domain-containing protein 3) induced by *E. coli* (Wu *et al.*, 2016) [54].

Synbiotics

Synbiotic refers to the nutritional supplements combining the prebiotic and probiotic in the form of a synergism. The main aim of using synbiotic is as a true probiotic, without its prebiotic food, does not survive well in digestive system.

Synbiotic are to nutritional products combining the probiotic and prebiotic to act together. It has been suggested that combination of probiotic and prebiotic, i.e., Synbiotics, might be more effective than either probiotic or prebiotic alone. Synbiotic is a mixture of prebiotic and probiotic which beneficially affect the host by improving the survival and implantation of live microorganisms dietary supplements into the gastrointestinal tract thus improving the host health. The United Nations Food and Agriculture Organization (FAO) recommends that word "synbiotic" can be used only if the net health benefit is synergistic (Cecic and Chingwaru, 2010) [5]. Synbiotic not only have beneficial microorganisms populations, but also promote proliferation of autochthonous-specific strains in intestinal tract. Studies on effects of synbiotic on metabolic health still are limited and lacking. It is worth mentioning that health effect will likely depend on synbiotic combination. Therefore, synbiotics seem promising in modulation of the composition of gut microbiota (Scavuzzi *et al.*, 2014; Hozan at al., 2016) [39, 21].

Effects of Synbiotics on Animal Health and Productivity

Smith and Jones (1963) [45] reported that symbiotic supplements elevated the production of antibody and lactate, altered the intestinal bacterial colonies and decreased the harmful bacterial growth in animals. In addition, synbiotic is also considered to reduce the harmful bacterial counts and aid the adhesion of beneficial bacteria by decreasing the intestinal pH. Also, synbiotic supplementation maintaining the populations of unprofitable or *E. coli* (potential pathogens) at relatively lower levels (numerically) in small intestinal and cecal digesta. Further, synbiotic reduced the *Escherichia coli* and total coliform populations in broiler chicken intestine. On the contrary, concentrations of synbiotic more than the suggested levels in diet elevated the lactic acid bacterial population in broiler chickens gut (Dibaji *et al.*, 2012) [9]. Furthermore, addition of synbiotic increased the villus height/crypt depth ratio and ileum villus height. However, the ileal crypt depth was decreased by dietary supplementation of synbiotic compared to the control group (Awad *et al.*, 2008) [4].

Synbiotics improve the swine production by improving the feeding environment of early weaning pigs. Further, synbiotic with ficus-indica var. saboten supplementation could decrease the sulfide gas emissions and ammonia in finishing pigs (Ra *et al.*, 2004) [35]. Synbiotics had a significant effect on the growth performance in Danio rerio. Conversely, in weaning pigs probiotic from anaerobic microflora with prebiotic did not affect performance (Lee *et al.*, 2009) [26]. Likewise, the results clarify that by using synbiotic in sheep diet, there was no influence on performance traits such as daily gain, feed conversion rate and dry matter in take. However, the digestibility of dry matter, organic matter and crude protein were not affected with symbiotic (Kazemi-Bonchenar *et al.*, 2013) [23]. Combination of Bacillus spp. And mannan oligosaccharides as synbiotic in European lobster larvae (*Hommarus gammarus* L.), combination of *Enterococus faecalis* and mannan oligosaccharides as synbiotic in rainbow trout (*Oncorhyncchus mykiss*) and combination of fructooligosaccharides and *Bacillus subtilis* as synbiotic in yellow croaker, *Larimichtys crocea* synbiotic added to the feed was not able to increase the growth and survival rate in grass carp but the best survival rate was obtained in feed supplemented with symbiotic (Rodriguez-Estrada *et al.*, 2009;Ai *et al.*, 2011;Nekoubin and Sudagar, 2012) [37, 2, 32]. Application of synbiotic treatment by combination of prebiotic and probiotic, depicted improvement in digestive enzyme activity (protease, lipase, and amylase) of Humpback Grouper (*Cromileptes altivelis*). Common carp fed dietary synbiotics showed a better digestive enzyme activity, significantly higher trypsin and chymotrypsin activities compared to control treatment. Synbiotics could significantly improve the growth parameters (specific growth rate, length gain, weight gain and percentage weight gain) but did not display any effect on the survival rate of common carp. Administration of synbiotic (*E. faecalis* and MOS/PHB) in rainbow trout didnot affect the survival rate of fish (Rodriguez-Estrada *et al*., 2009; Paulina and Katarzyna, 2018) [37, 33]. Japanese flounder feeding *B. clausii* and MOS/FOS, fish maintained active ingestion, exhibited proper growth, and survived for all time. In yellow croaker and cobia, administration of *B. subtillis*/FOS or *B. subtillis*/chitosan respectively, didnot affect the survival rate with no alterations among the different dietary treatment groups (Ai *et al.*, 2011) [2]. Mehrabi *et al.* (2012) [30] showed that experimental groups fed diet containing different levels of synbiotics (0.5, 1.0 and 1.5) improved the body weight gain by about 50, 59 and 53%, respectively in comparison with control group. Prebiotics present in the synbiotic mixture has a hypocholesterolemic effect thereby decreasing the absorption of lipids in intestine by binding bile acids, hepatic synthesis of new bile acid and increasing the cholesterol elimination (Klebaniuk and Czech, 2007) [24]. Al-Kassi *et al.* (2009) [3] reported that *Aspergillus oryzae* supplementation increased the growth performance and nitrogen retention in pigs, while supplemental product from *Aspergillus oryzae* culture elevated the digestibility of fat and protein in pigs.

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