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Synbiotic as Feed Additives Relating to Animal Health and Performance

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Abstract

According to the increasing of human population in the world, it reached about seven billion people and it continuously increased. In this background, the food source in both animal and plant origin must be increased accordingly. For these we must use and add some feed additives such as antibiotic, probiotic, prebiotic, postbiotic and synbiotic for the animal feed to increase production (meat, egg, milk and fish) and improve health. In early cases, probiotic as mono or mixed beneficial live microorganism was used as feed additive that plays a significant role in several health conditions and performances. In another way, the scientists use some ingredients indigestible with carbohydrates origin, especially oligosaccharides as a source of energy for beneficial microorganisms in the body which were called prebiotic, and it is indigestible fermented food substrates that stimulate the growth, composition and activity of microorganisms in gastrointestinal and improve host. Most of the scientists urged to use all the above in such way that have more benefits in animal health and performance which were therefore called synbiotic, that was a combination between probiotic and prebiotic which beneficially had significant effects on the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract, and thus improving animal health and performance. So, it was proposed that the synbiotic in this research increased beneficial microorganisms in the gastrointestinal tract and improved intestinal architect, and then promoted intestine environment. Consequently, it can improve blood indices, and especially decrease bad cholesterol (Low-density lipoprotein), decrease harmful microorganisms and toxins. However, it can also improve ingredient product, increase mineral absorption and nutrient. In conclusion, it can improve animal health and performance.

Keywords

Synbiotic, Animal, Intestinal Tract, Health and Performance

1. Introduction

People of the world have increased from 3 billion in 1959 to more than 7 billion in March 2012. As the world's

people grow, hunger persists in many locations and almost 1 billion people are reported to be malnourished [1]. By 2050, farmers will need to double crop production to meet the demand. In this background, the world needs food products with annual growth of 2.5% for the next 10 years [2]. Many scientists and nutrition specialists believe that animal production can play a role in increasing food production. A huge amount of antibiotics have been used to control diseases, improve performances and increase production in livestock. Additionally, the most commonly used alternatives to antibiotics have been probiotic, prebiotic, postbiotic and symbiotic.

Probiotic is defined as live microbial feed additive that beneficially affects the host animal by improving the intestinal microbial balance [3]-[6]. Also, prebiotic is "indigestible fermented diet substrates that selectively stimulate the composition, growth and activity of microflora in gastrointestinal tract" [7] [8]. Synbiotics refer to nutritional supplements combining probiotic and prebiotic in a form of synergism, hence, synbiotic can enhance their isolated beneficial effects. When two nutritional ingredients or supplements are given together, the resulting positive effect generally follows one of the three patterns: potentiation, synergism and additivity [9] [10]. Many studies have evaluated the effects of different symbiotic preparations [11] [12]. Further, Symbiotic affects the host by improving the survival and establishment of live microbial dietary supplements in the gastrointestinal tract by selectively stimulating the growth by activating the metabolism of one or a limited number of health promoting microorganisms and thus improving the host [7] [10] [13]. Furthermore, synbiotic can exert beneficial effects in the gastrointestinal tract as a result of alteration in whole body, feed consumption, and absorption of nutrient and beneficial changes in intestinal architecture [14]. In fact, intestinal microorganisms play an important role in the immunological, physiological, nutritional and protective functions of the host [15] and can be influenced by the food [16]. The most alternative additives for livestock and poultry feed include probiotic, prebiotic and synbiotic [17]. Though, the use of synbiotics may possibly produce greater benefits rather than the application of individual portions [18].

Synbiotics provide more additive benefits in growth performance, feed conversion ratio, hematological and biochemical parameters than probiotic and prebiotic individual use of these additives [19]. Moreover, synbiotic could increase the digestibility and availability of many nutrient elements such as, vitamins, mineral elements and proteins [20]. After all, limited data are available regarding the application of synbiotic [21]-[24].

The research questions that were asked in this review were as follows: Is the feeding of synbiotic supplement important while used in applied research and commerce? Does the use of synbiotic supplement in animal lead to improved intestinal microbiota and prevent pathogen? Does the use of synbiotic in animal benefit the performance and enhance blood picture and immunity? Hence, the aim of this review study is to update our information regarding the influences of synbiotic. This review focuses on the collection of the most scientific evidences concerning the aspects of synbiotic and its effect on animal growth, production and health, including the immune system, digestive tract, metabolic, intestinal organ and blood.

2. Gut Microflora

The intestinal microbiota (a term that has now replaced the old denomination of "microflora" [25]-[27] is an ecosystem shaped by a diversity of ecological niches, made of several bacterial species and a very large amount of strains [27] [28]. Also, intestine is populated by 100 trillions of microorganisms (called "microbiota") that are important for health [29] [30]. While, the transition from soil and plants to the animal gut, has three areas of genomic adaptation [31]. The intestine's normal microflora is a metabolically active but as yet unexplored area of host defense [32] [33]. Major functions of the gut microbiota include metabolic activities that result in salvage of energy and absorbable nutrients, trophic effects on the intestinal epithelium and protection of the host against invasion by harmful microorganism [34] [35]. The gastrointestinal tract which places a huge microbial ecosystem; the colon alone is estimated to contain over seventy percentage of all the microbes in the body [36] [37]. The gut microbiota or microflora has an important role in disease and well-being [38]. Commensal intestinal flora plays an essential role in the maintenance of the host health. However, reports of shifts in the composition of intestinal microbiota with age, with increased numbers of bacteria (mainly Enterobacter) and a decrease in the number of beneficial organisms such as Lactobacilli and Bifidobacteria [39]. These changes, along with a general decrease in species diversity in most bacterial groups, and changes to diet and digestive physiology such as intestinal transit time, may result in increased putrefaction in the colon and a greater susceptibility to infection and disease [40]. The three major units of the gastrointestinal tract are the stomach, the small intestine, and the large intestine. Every unit has its own distinct microbiota [41] [42]. The amount and composition of microbial

species differs along the digestive tract. Families, phyla and genera of the microbiota enriched in each particular niche are listed. Main bacterial phyla are represented in the mammalian gut microbiota; *Streptococcus*, *Lactobscilus*, *Bacteroides*, *Clostridium*, *Streptococci*, *Lactobacilli*, *Eubacterium*, *Peptococcus*, *Streptococcus Fusobacterium* and *Bifidobacterium* [43].

3. Probiotic

Probiotic was first defined by Metchnikoff in 1908 based on his observations on the longevity of individuals who lived in a certain part of Bulgaria and which he attributed to their ingestion, on a regular basis, of a fermented milk product [44] [45]. Which contain of rod-shaped bacteria (Lactobacillus spp). Therefore, these bacteria affect the gut microflora positively and reduction the microbial toxic activity in intestine [46]-[49]. The expression "probiotic" comes from the Greek word "pro bios" which means "for life" as different to "antibiotics" which means "against life". The history of probiotic began with the consumption of fermented diets by Greek and Romans [46]. Probiotic is defined as mono or mixed cultures of "live microorganisms which, when administered in adequate amounts confer a health benefit on the host" [43] [50] [51]. A new description by the American Academy of Pediatric Committee on Nutrition states that probiotic is "microorganisms that generate small molecular metabolic by-products that exert beneficial regulatory effect on host biological functions and may function as immunomodulators" [52]. Probiotic is mainly lactic acid creating bacilli, mostly Lactobacilli (L. acidophilus DDS-1, Lactobacillus casei (L. casei), L. lactis, L. rhamnosus, L. salviarius) and Bifi dobacteria (B. longum, B. infantis, B. bifi dum), and the yeasts Sacharomyces boulardii (Brewer's yeast) and Sacharomyces cervisiae (Baker's yeast) [53]. Probiotic may play a beneficial role in several health conditions and performance, including Intestinal microbial composition, therapeutic effects, metabolic effects and immunomodulation [43] [54] [55]. The overall performance and well-being benefits of probiotic microorganisms are repre-sented in Figure 1.

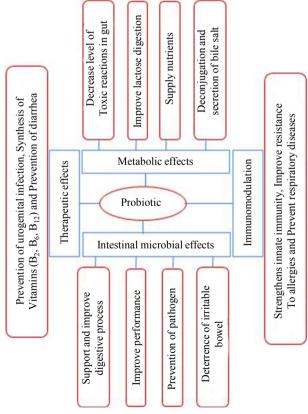


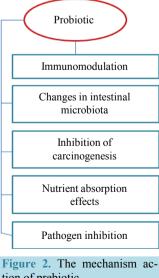
Figure 1. General benefits of probiotic on health and performance.

4. Prebiotic

The word prebiotic was first used by Gibson and Roberfroid in 1995 [7]. Dietary fiber is the most generally utilized prebiotic [7] [8]. 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" [56]-[58]. Prebiotic carbohydrates are found naturally in such fruit and vegetables tomatoes, Jerusalem artichoke, as oatmeal, bananas, flaxseed, asparagus, barley, berries, garlic, wheat, onions and chicory, greens and legumes [59]. It is considered important to determine the definite health bonuses associated with prebiotic intake in people and their mechanisms of action [60] [61]. Prebiotic, such as fructooligosaccharides can be used as a dietary supplement for animals like, dogs and cats to maintain gastrointestinal well-being [62]. Prebiotic is not broken down by gastric enzymes, but pass unaltered into the large intestine, where they are then selectively fermented, creating beneficial effects [63] [64]. A study has shown that administration of prebiotic also results in increased numbers of beneficial intestinal flora (especially Bifidobacteria) [65] [66]. Probiotic, prebiotic and synbiotic administration have been documented to increase intestinal levels of beneficial Bifidobacteria, Enterocooci and Lactobacilli, with reduced levels of Enterobacter [67] [68]. Prebiotic have been demonstrated to increase mineral absorption, chiefly that of magnesium and calcium [69] [70]. The main prebiotic functions are shown in Figure 2.

5. Synbiotic

Synbiotic refers to nutritional supplements combining prebiotic and probiotic and in a form of synergism. The main aim for using a synbiotic is that a true probiotic, without its prebiotic food, does not survive well in the digestive system. Synbiotic refers to nutritional supplements combining Probiotic and Prebiotic that are thought to act together; i.e. synergism. It has been suggested that a combination of a probiotic and a prebiotic, i.e. Synbiotics, might be more effect than either a probiotic or prebiotic alone [71]-[75]. Furthermore, synbiotic is a mixture of probiotic and prebiotic which beneficially affect the host by improving the survival and the implantation of live microorganisms dietary supplements in the gastrointestinal tract, and thus improving host health [76]. The United Nations Food and Agriculture Organization (FAO) recommend that the word "synbiotic" be used only if the net health benefit is synergistic [77]. The first attempts should be to combine Probiotic and Prebiotic which have demonstrated individual benefits to determine if there are additive effects, alternatively, a more structured approach would be to determine the specific properties that a prebiotic requires to be beneficial to the probiotic and select the prebiotic accordingly [78]. Synbiotic is designed not only to present beneficial microorganisms populations, but also to promote proliferation of autochthonous-specific strains in the intestinal tract [79]. Studies on the effects of synbiotic on metabolic health still are limited. It is worth mentioning that the health effect will likely depend on the synbiotic combination. Therefore, synbiotics seem promising for the modulation of the gut microbiota composition [80].



tion of prebiotic.

6. Probiotic, Prebiotic and Synbiotic as Compared with Each Other

Unlike probiotic, prebiotic do not add to an existing colony of bacteria, rather they provide nourishment for existing flora, allowing the colony to grow naturally and flourish. As probiotic is principally active in the small intestine and prebiotic is only effective in the large intestine, the combination of the two may give a synergistic influence. Probiotic is a live microbial food ingredient which is beneficial to host [3] [76] [81]-[83] while prebiotic is a non-digestible food ingredient which beneficially affects the host by selectively stimulating the growth and activity of one or a limited number of microorganisms in the colon having the potential to improve host well-being [76] [84] [85] nevertheless, synbiotic is a mixture of probiotic and prebiotic which beneficially affect the host and thus improving host health and well-being [74] [76] [86]. Examples of list of probiotic, prebiotic and synbiotic applied or studied for application in animal feed are included in **Table 1**.

7. Action Mechanism of Synbiotic

The gastrointestinal tract has a compound community of microbiota that provides benefits to its host in numerous different ways, including drug metabolism, nutrient production, and protection against pathogens, detoxification and regulation of the immune system. Animal studies have demonstrated that changes in these gut microbial communities can cause immune dysregulation; improve growth and influence on performance and there are information that support the use of probiotic and prebiotic and especially synbiotic. The synbiotic concepts about mechanism of action: altering the composition of intestinal microbiota by viable benefit organism and non-absorbable organism substrates are shown in **Figure 3**.

8. Synbiotic and Intestinal Flora

The gastrointestinal tract is an important immune organ and the largest defense barrier protecting the host from toxins, pathogens and subsequent inflammation while allowing commensal microorganisms to grow [87]. Also, the intestinal tract is a host to a vast ecology of microbes [88]. The notion of modulating bacterial activities directed towards improving gut microbial function has a long history [89]. The importance of the natural gut microflora for decreasing diseases in animals has long been recognized and it is now apparent that the composition of the microflora plays a crucial role both in digestion and in resistance to diseases [90] [91]. When, probiotic and prebiotic are administered at the same time, the combination is called Synbiotic. The prebiotic in the synbiotic mixture improves the survival of the probiotic microorganisms in the intestinal tract, and stimulates the activity of the host's endogenous bacteria [79] [92] [93]. Then, supplemental probiotic from anaerobic microflora with prebiotic improved crude protein and dry matter digestibility as well as reducing noxious gas emission and enter pathogenic bacteria in early-weaning pigs [94].

Smith and Jones [95] reported that supplemental symbiotic increased the production of lactate and antibody, altered intestinal bacteria colonies and reduced harmful bacteria growth in animals. In addition, symbiotic is also

Table1. Examples of list of probiotic, prebiotic and synbiotic applied or studied for application in animal feed.

Probiotic	Prebiotic	synbiotic
Lactobacillus sps.	Inulin	Lactobacilli + inulin
Bifidobacterium sps.	Galactooligosaccharides (GOS)	Bifidobacteria + FOS
Saccharomyces sps.	Fructo-oligosaccharides (FOS)	Lactobacilli + FOS
Streptococcus sps.	Lactulose	Bifidobacteria and Lactobacilli + inulin
Bacillus coagulans	Lactitol	${\it Bifidobacteria} \ {\rm and} \ {\it Lactobacilli+FOS}$
Propionibacterium	Cereals fibres	Lactobacilli + lactitol
Bacillus coagulans	Xylooligosaccharides	Bifidobacteria + GOS
Enterococcus faecium	Isomaltooligosaccharides	
Freudenreichii		
Homeostatic Soil		

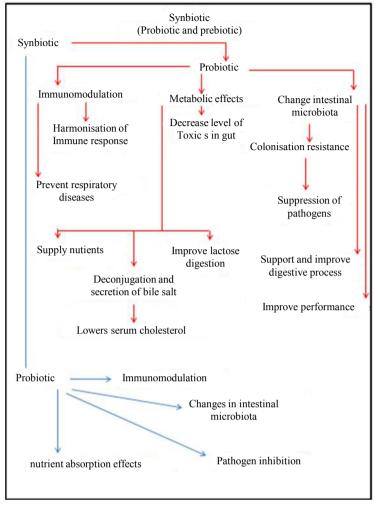


Figure 3. The mechanism action of synbiotic.

considered to reduction harmful bacteria counts and aid the adhesion of beneficial bacteria through the decrease of intestinal pH [96]. Also, Synbiotic supplementation maintaining populations of unprofitable or potential pathogens (*E. coli*) at relatively low levels (numerically) in the cecal digesta and small intestinal [97]. Further, synbiotic reduced *Escherichia coli* and total coliform populations in the intestines of broiler chickens. On the contrary, concentrations of the synbiotic higher than the suggested levels in the diet increased the lactic acid bacteria population in the gut of broiler chickens [98]. Furthermore, the addition of synbiotic increased the villus height/crypt depth ratio and villus height in ileum. However, the ileal crypt depth was reduced by dietary supplementation of synbiotic compared with control of broiler Chickens [14].

9. Synbiotic and Performance

Supplemental antibiotic in animal feed improve feed efficiency and growth performance [99]. However, supplemental antibiotic increases the hazard of antibiotic residues and increases bacterial resistance [100], making their use in animal production harmful to human health. Recently, the most commonly used replacements to antibiotic have been synbiotic. Supplemental synbiotic can be expected to improve swine production by improving the feeding environment of early weaning pigs [94]. Further, Supplemental synbiotic with *ficus-indica var. saboten* could decrease sulfide gas emissions and ammonia of finishing pigs [101]. Synbiotic had significant effect on growth performance in *Danio rerio* [102]. Conversely, supplemental probiotic from anaerobic microflora with prebiotic did not affect performance in Weaning Pigs [94]. Likewise, the results clarify that using synbiotic in sheep diet did not influence on performance traits such as feed conversion rate, daily gain and dry matter in-

take. However, Digestibility of dry matter, crude protein and organic matter were not affected with synbiotic [103]. Combination of mannan oligosaccharides and *Bacillus* spp. as synbiotic in European lobster larvae (*Hommarus gammarus* L.) [104], combination of mannan oligosaccharides and *Enterococus faecalis* as synbiotic in rainbow trout (*Oncorhyncchus mykiss*) [21] and combination of *Bacillus subtilis* and fructooligosaccharides as synbiotic in yellow croaker, Larimichtys crocea [22], synbiotic added to feed was not able to increase the growth and survival rate in grass carp but the best survival rate was obtained in feed added synbiotic [10].

Application of synbiotic treatment combination of probiotic and prebiotic, showed improvement of digestive enzyme activity (lipase, protease and amylase) of Humpback Grouper (*Cromileptes altivelis*) [105]. Common carp fed dietary synbiotic showed better digestive enzyme activities and significantly higher trypsin and chymotrypsin activities compared with the control treatment [106]. Synbiotic could significantly improve growth parameters (length gain, specific growth rate, percentage weight gain and weight gain) but did not display any effect on survival rate of common carp [106]. Administration of synbiotic (E. faecalis and MOS/PHB) in rainbow trout for periods not affects the survival rate of fish [21]. Japanese flounder feeding B. clausii and MOS/FOS, in which fish maintained active ingestion, exhibited proper growth and survived for all time [107]. In yellow croaker and cobia, administration of B. subtillis/FOS or B. subtillis/chitosan respectively, not affects the survival rate, with no alterations among different dietary treatments [22] [108]. The study of Mehrabi et al. showed that after 60 days groups fed diets containing different levels of synbiotics (0.5, 1.0 and 1.5) improved body weight gain about 50, 59 and 53%, respectively, in comparison with the control group [109]. Body composition has been investigated by Rodriguez-Estrada [21], Ye [107] and Mehrabi [109]. First of these studies, reported no significant differences in crude ash, moisture, crude proteins and crude lipids contents among all the experimental groups. Contrary to our finding, Jung [110] and Erdogan [111] reported that the diet supplemented with synbiotic had no effect on feed intake, body weight, feed conversion efficiency and weight gain, of broilers. The final body weight, feed conversion efciency, weight gain were significantly higher in synbiotic supplemented broilers compared with the control group [97]. Body weight gain was increased significantly in birds' supplemented synbiotic compared with control and probiotic treated group [112]. The results showed that 1 g/kg synbiotic inclusion in the diet significantly improved body weight and feed conversion ratio of the ostrich chicks compared to control group [113]. Also, synbiotic substantially increased blood glucose but reduced cholesterol while Serum total protein and uric acid also decreased in the all dietary levels of synbiotic compared to control group of the ostrich chicks. Synbiotic has the ability to reduction the concentration of cholesteryl esters CE in LDL-cholesterol [114]. Prebiotic that present in the synbiotic mixture has hypocholesterolemic effects thereby decreasing the absorption of lipids in the intestine through binding bile acids, increasing cholesterol elimination and hepatic synthesis of new bile acid [115]. Finally, supplemental Aspergillus oryzae, one kind of prebiotic, increased growth performance and nitrogen retention in pigs, while supplemental Fermacto 500® from Aspergillus oryzae culture increased the digestibility of protein and fat in pigs [116].

10. Synbiotic Hematological and Biochemical Parameters

Among the hematological and biochemical parameters evaluated in animal after treatments with synbiotic find triglyceride, cholesterol, high-density protein cholesterol, low-density protein cholesterol, albumin, globulin, total serum protein, glucose and hematocrit. Accordingly, a positive contact of prebiotic and probiotic was found concerning the number of leukogram and white blood cells while supplements to feed rations for ewes [117]. Also, Lambs fed on diet contain probiotic and prebiotic plasma was significant decrease of the level of total cholesterol and HDL-cholesterol fraction increase were observed [117]. But, supplementation of synbiotic had no influence on blood urea nitrogen, glucose and albumin concentrations in sheep [103]. Application of synbiotic treatment showed improvement of biochemical plasma (glucose and triglyceride) and haematology parameter (hematocrit, haemoglobin and phagocytic activity) of Humpback Grouper (Cromileptes altivelis) [105]. Rodriguez-Estrada and colleagues [21] found synbiotic influence on hematocrit value and significant higher hematocrit value was recorder in the feed added feed additives while compare control group. Serum biochemical parameters evaluated by Ye et al. [107], reported the following results: The triglyceride level was lower or tended to be lower in fish fed the MOS, FOS and/or B. clausii-containing diets as opposed to the control diet. Dietary administration of commercial synbiotic in rainbow trout resulted in an increase of total serum protein content but other recorded parameters such as albumin/globulin ratio and triglycerides in fish fed with different levels of synbiotic did not show any significant difference in comparison with that from the control group at the end of the experiment [109]. In addition, diets containing synbiotic had no significant effect on total serum protein [118] [119]. Ashayerizadeh [120] and Mokhtari [121] found enhanced serum cholesterol level in broiler chickens in response to synbiotics supplementation and Shams [122] and Sharifi [123] also reported better hematological and cholesterol picture in broiler chickens when synbiotic was given in the diet. Liong and Shah [124] presented that the use of synbiotic consumption in broilers regulates the concentration of the organic acids and decrease cholesterol levels. Also, Sahin *et al.* [125] reported that adding a synbiotic supplements in the diet had a significant effect on blood parameters, including total serum protein and cholesterol. Uric acid, creatinine, Packed cell volume and urea concentration were increased significantly in birds' supplemented synbiotic compared with control group [112].

11. Synbiotic and Health

The gut-associated lymphoid tissue and gut microbiota are fundamental components of the both digestive and immune system function and homeostasis. Microbes of the GIT can be generally separated into potentially pathogenic or beneficial groups. Harmful microorganisms may be involved in localized or systemic infections. toxin formation, and intestinal putrefaction. Some intestinal organisms may have useful effects such as vitamin production, stimulation of the immune system through nonpathogenic mechanisms, and inhibition of the growth and establishment of harmful microbial groups [126]. Antimicrobial action of Probiotic (Bifidobacterium sp), Prebiotics (chicory roots) and Inulin and synbiotic: (Bifidobacterium sp + chicory) and (Bifidobacterium sp + Inulin) against Pathogenic bacteria was tested by using agar diffusion assay [127]. The synergistic inhibitory influence of Synbiotic (Bifidobacterium sp + inulin) and (Bifidobacterium sp + chicory) on Pathogenic bacteria was higher than the effect of Bifidobacterium sp alone, chicory alone and inulin alone [128]. The microbiota of the GIT of mammals can be considered a metabolically active organ with its wide biodiversity in term of species and the high number of cells [129]-[131]. The positive effects of both probiotic and prebiotic on immune system in different animal strains have been confirmed [91] [132] [133]. Supplementation of synbiotic had influence blood metabolites, both non-esterifies fatty acids and total immunoglobulin of in sheep [103]. Lysozyme activity: Lysozyme is one of the significant bactericidal enzymes of innate immunity, and constitutes an essential defense mechanism against pathogens in fish [134]. As synbiotic therapy may offer a suitable alternative for controlling pathogens, the effectiveness of synbiotic in terms of protection against infectious agents could be evaluated by a challenge test. To date, challenge test carried out in fish following to symbiotic administration, have employed Vibrio sp species as pathogens, specifically V. anguillarum and V. harveyi [100] [107] [108]. Today, specific health effects are being investigated and documented, including alleviation of chronic intestinal inflammatory diseases [135], and prevention and treatment of pathogen induced diarrhea [136], urogenital infections [137], and atopic diseases [138]. The combination of a probiotic and prebiotic as single administration, is called synbiotic which is characterized by antimicrobial, anticarcinogenic, immune stimulating actions and antiallergic. It also improves the absorption of minerals, protects from diarrhea and optimizes nutrient digestion processes [139]. Supplemental synbiotic from Lactobacillus sp reduced diarrhea, as well as increased feed efficiency and performance in initial weaning pigs [140].

12. Conclusion and Future Perspective

From the research, we could conclude that the intestine was a variable niche of beneficial and harmful microorganisms. And in a different way they benefit or harm their host. The gastrointestinal tract has a compound community of microbiota that provides benefits to its host in many different methods, including nutrient production, protection against pathogens, detoxification, drug metabolism and regulation of the immune system. Animal studies have demonstrated changes in these gut microbial communities, and there are documents funding the use of probiotic, prebiotic and synbiotic. Though, the practice of synbiotic may possibly produce greater benefits rather than the application of individual portions. In recent years, synbiotic has become an integral part of the animal practices for improving the growth, enhancing blood picture, stimulating intestinal architecture, improving performance and competing against the pathogenic microbes. But limited information is available regarding the application of synbiotic in animal science. Experts recommend further research to substantiate preventive and therapeutic health benefits, mechanism of action, optimal intake, duration of treatment and selection of the best synbiotic (specific probiotic strains and type of prebiotic) for a targeted outcome in agriculture's animals.

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