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Use of Probiotics in Swine Nutrition: A Review

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Abstract

The modern system of swine production exposes the pigs to nutritional, management and climatic stress which causes physiological and psychological problems in swine. To overcome the stressor farmers use antibiotic which causes drug resistance and residual problem in pork. But the recent restriction on the use of antibiotics is due to the risk of drug residual effect in pork. It not only poses the risk of drug residue but also causes the emergence of antibiotic resistance in the microbe. To overcome this problem, the latest research reports suggest that Probiotic can be used in a judicial way which can help in the improvement of gut microbial population which indirectly causes improvement of health, immune system, enhancement in nutrient utilization, causes overall beneficial effect in swine production. The commonly used bacterial strains are *Bacillus, lactic acid bacteria, Enterococcus* and *Saccharomyces cerevisiae*. In this review, we will give you the overall status of the use of probiotics in swine nutrition.

Keywords: Swine Nutrition, Probiotic, Stress, Antibiotic and Bacterial Strain

Introduction

The misuse of antibiotics in veterinary and human practices led to the appearance of antibiotic resistant bacteria and resistant gene in the bacteria which can be transferred to human and animals (EMA, 2022) [1]. The continued use of antibiotics as a prophylactic to improve growth and the health in food-producing animals leads to the emergence of resistance against antibiotics to treat post-weaning diarrhoea in swine (Burow *et al*., 2019; Diana *et al*., 2019) [2, 3]. The modern system of rearing pigs expose the physiology of animals to the feeding, environmental and managemental stress, which adversely affect the immune system, productive potentials and growth rate in swine industry (Cervantes *et al*., 2018, Ferrari *et al.*, 2012, Pearce *et al*., 2013, Sanz Fernandez *et al.*, 2015, Buttner *et al*., 2019, Camerlink *et al*., 2016, Rauterberg *et al.*, 2018, and Broom *et al.*, 2019.) [4, 5, 6, 7, 8, 9, 10 11]. The animal's digestive microbial ecosystem often got disturbed due to the stress and the harmful microbes can proliferate which causes harmful effects on respiratory and digestive systems. The farmers use antibiotics as an animal growth promoter (AGP) to enhance the growth rate and productibility which causes serious consequences on the public health system. The use of antibiotics as an animal's growth promoter (AGP) to balance the microbial population in the gut is a common practice for the past few decades in animal production (Thacker, 2013) [12]. During the year 2019 about 11,000 million ton of antibiotic were used in farm animals (Food and Drug Administration [FDA] 2019) [14]. The antibiotics as an attempt are prophylactically used in swine to improve growth performance (Kirchhelle, 2018) [13]. Many countries from all over the world are either banned or banning the use of antibiotics in swine production (Thacker, 2013) [12]. The microbial population of the gut is composed of diverse and dynamic microbial population that live in a mutually symbiotic relationship, and help in maintaining the integrity and immunity of the gut (Isaacson and Kim, 2012, Fouhse *et al*., 2016) [16, 17]. The microbial population along the length of the intestine and also from intestinal mucosa towards the lumen shows different patterns due to the different micro-environment conditions (Crespo-Piazuelo *et al*., 2018; Adhikari *et al*., 2019; Gresse *et al*., 2019) [18, 19, 20]. The early establishment of the beneficial microbe for the growth of the piglets as the type of microbiota will determine intestinal health (Kabat *et al*., 2014; Li *et al.*, 2018a; Chen *et al*., 2018c) [21, 22, 23]. The microbe which is attached directly with the intestinal has a greater capacity in modulating the immune system. The early changes in the gut microbial population of swine can have a short and long term effect on intestinal health. These gut microbes provide vitamins, volatile fatty acids, product of fibre fermentation, recycling of digestive juice and help in strengthening of the immune system in the host (Fouhse *et al.*, 2016) [17].

The use of antibiotics in animal production is banned in Korea, Japan and in European Union countries, while authorities from all over the world are trying to completely ban the use of antibiotics in animal production (NPB 2015; EFSA and EMA 2017) [24, 25]. As it is known that majority of the pigs died due to the post weaning infectious diarrhea. The most attention seeker by the swine researchers is the interaction of the gut microbe and the intestinal health during swine production (Kim and Duarte, 2021) [26]. The farmers use probiotics to promote the proliferation of beneficial diverse health-promoting microbes in the gut which indirectly help in preventing the infection by the pathogenic microbes (Tang *et al.*, 2020) [27]. The US FDA

and AASCO described direct microbial fed (DFM) as product that are purported to contain live microorganism (Bajagai *et al*., 2016) [28].

Use of Probiotic in Nursing Piglets

The early period of development is very critical in piglets as the gut and the immune system of piglets are not developed which make the piglets prone to a disease-causing microorganism that leads to hindrances in the development of healthy piglets. (Levast *et al*., 2014) [30]. The gut of newborn piglets is sterile and microorganisms just after birth enter the gastrointestinal track to establish themselves (Houghteling *et al.,* 2015) [31]. The sow milk is the only source that is the selection force to specifically promotes the proliferate of specific microbes and suppress the growth of other microbes (Martin *et al*., 2012) [32]. The early dominance of *Escherichia coli* (E. coli) and *Streptococcus spp.* promote the establishment of microbes in the gut by creating an environment for them such as *E. coli* creates anaerobic environment conditions which promote the colonization of the *Bacteroides* spp. (Bokulich *et al*.,2016; Wang *et al*., 2019) [29, 22]. It has been observed that the population of the *Prevotella spp*. just after 7 days after weaning increased from 8.9% to 17.6% (Wei *et al*., 2021) [34].

Improves Growth Rate

The use of probiotics causes improvement in the growth in pigs (Dlamini *et al*., 2017) [35]. The use of probiotic in young piglets causes improvement in the productive parameters of pigs (Kritas *et al*., 2015; Hayakawa *et al*. 2016) [36, 37]. The use of *Lactobacillus murinus, Lactobacillus salivarius, Lactobacillus pentosus, Pediococcus pentosaceous, Bacillus cereus and Bacillus subtilis* causes an increase in the body weight gain after weaning in comparison to control (Kritas *et al*. 2015) [36]. The daily supplementation of the probiotic in weaned piglets causes significant improvement in the productive parameters (Betancur *et al.*, 2020) [38]. The use of Probiotic in the weaned causes gain in live body weight gain in comparison to the control group. (Vieira *et al.*, 2021) [39]. The *Saccharomyces* probiotic supplemented in the nursing piglets cause increase daily average daily gain (ADG), promote the beta diversity and the colonization of the *Erysipelato, clostridium* and *Christensenella* in the Probiotic supplemented nursing piglets.

Improves the Gut Functioning and Immunity

The Probiotic act by altering the piglets gut microbial population providing Protection against disease-causing bacteria and also against gastrointestinal disturbance (Ahmed *et al*., 2014; Yin *et al*., 2014; Scharek-Tedin *et al*., 2015; Yang *et al*., 2016; Zhang *et al*., 2016; Upadhaya *et al*., 2017; Barba-Vidal *et al*. 2017a) [41, 42, 43, 44, 46, 49, 47]. Probiotics act by strengthening the intestinal barrier function and enhancement in the immune system function (Siepert *et al*., 2013; Naqid *et al*., 2015; Scharek-Tedin *et al*. 2015; Lessard *et al*. 2009) [48, 49, 43]. The main aim of Probiotic use during the nursing period is to reduce microbial pathogenic bacteria loads in the gut. There are several mechanisms proposed by which Probiotic reduces pathogenic gut load such as by producing bacteriocins (Umu *et al*., 2017) [52], and through competitive inhibition of the pathogenic bacteria (Raheem *et al.*, 2021) [53]. The supplementation of the *Bacillus subtilis* probiotic during the nursing period of development causes decreases in mortality during the post-weaning period. Probiotic use during the nursing period of piglets checks the gut disturbance by competing for colonization with the harmful bacteria through the release of beneficial enzyme and acids (Li *et al*., 2012a; 2012b; Zhu *et al.* 2014) [54, 55, 56]. The supplementation of probiotic in the nursing piglets causes improved intestinal health, higher villous lengths and daily weight gain in comparison to the control group (Haupenthal *et al.*, 2020) [57]. Barba-Vidal *et al*., (2017) [47] suggested that the use *Bacillus licheniformis* probiotic causes changes in the gut-brain active behavior particularly exploring pen, feeding and morning behavior.

Improves digestibility of nutrients

The use of probiotics causes Improvement in the digestibility and feed conversion ratio in pigs (Dlamini *et al*., 2017) [35]. It causes enhancement in the bioavailability of nutrients by supplementing the Se-enriched Probiotic (Gan *et al.*, 2014) [58]. The use of probiotics causes an increase in the feed conversion ratio in the probiotic fed piglets during the post-weaning period. The ways through which Probiotic shows the beneficial effect is through supplementing the nutrient-enriched probiotics which improve the bioavailability of target nutrient for example supplementation of the Se treated *L. acidophilus* and *Saccharomyces cerevisiae* in the pigs reared under high ambient temperature causes increased in the level of antioxidants, immune status and in the expression of Se-mRNA protein in the host (Gan *et al*., 2014) [58].

Use of Probiotic in weaned Pigs

The early separation of piglets shifts the piglets from liquid to solid food which make it difficult for the endogenous enzyme to adjust to the change in environment. The weaning poses the piglets to psychological and immunological stress, and is accomplished by the atrophy of the intestinal villous, crypts, inflammation of the intestinal tract and loosening of the intestinal tight junction (Bomba *et al*., 2014; Wan *et al*. 2018) [60, 61]. The gut is composed of diverse microbes which produce different metabolites with different functions. The gut of the piglets is sterile before weaning so sow milk is the only selection force that allows some microbes to dominate the gut (Martin *et al*., 2012) [32]. Milk contains antimicrobial, immunoglobin and lactoferrin which promote intestinal integrity and homeostasis. (Rogier *et al*., 2014 and Planer *et al*., 2016) [63, 64]. The weaning disrupts this gut balance led to the colonization of pathogenic bacteria causing diarrhoea leading to morbidity and mortality in piglets (Gresse *et al*., 2017; Guevarra *et al*., 2018) [65, 56]. The period of weaning is a stressful period during which the incidence of diarrhoea increases (Gresse *et al*., 2017; Lariviere-Gauthier *et al*., 2018) [65, 76]. This period of stress leads to loss of appetite, inflammation of the intestine, diarrhoea and proliferation of the unbalanced microbial population (Campbell *et al*., 2013; Yin *et al*., 2014) [67, 42]. Early separation of weaning of nursing piglets from sow causes the early appearance of productive estrus in sow.

Improves gut function and immunity modulation

The use of probiotic in weaned piglets causes similar growth in comparison to the antibiotic fed group but the incidence of diarrhea decrease in the probiotic fed group and also there is the proliferation of the beneficial microbe in comparison to pathogenic bacteria proliferation in the antibiotics fed group (Wang *et al.,* 2019) [22]. The gastrointestinal tract of pigs is occupied by a diverse and complex microbe called Gut Microbiota (Campbell *et al*., 2013) [67]. The faecal transplant piglets show better performance in comparison to microbes free suckling and weaning piglets (Cheng *et al*., 2019; Tsai *et al*., 2019) [68, 33]. Antibiotics are one of the most preferred therapies for the treatment of gut disturbance both in humans and animals but the problem of microbial resistance prevents its use in animal production (Toutain *et al*., 2016) [69]. The use of Probiotic in enterotoxigenic *E. coli* infected post-weaning piglets causes an increase in villus height to crypts ratio, average daily gain and average daily feed intake. The Probiotic reduce the number of pathogenic bacteria and make the population stable of intestinal microbiota (Yirga, 2015; Dumitru *et al*., 2020a) [73, 74]. The Probiotic *Bacillus subtilis* (Bs) ATCC 6051a (1.6x109 CFU/mL) is used in weaned piglets and it shows that the Probiotic supplementation does not show any significant effect on the weight gain but it causes significant improvements in post-weaning diarrhoea in piglets. Therefore the lower level of Bacteroides in the gut prone the piglets to post-weaning diarrhoea. (Meng *et al*., 2020) [75]. The population of the Alloprevotella and Oscillospira decrease after weaning and that of Campylobacterales increased. The Alloprevotella and Oscillospira are succinic acids and acetic acids producing bacteria that protect the intestinal barrier and enhance the immune gut system functioning (Downes *et al*., 2013) [77]. The succinate improve the tight junction protein and positively improve the functioning of the cytokines in the growing pigs. The Oscillospira is the butyrate-producing main microbe of the gut which produce butyric acid, butyrate is a main colonocyte promoting and anti-inflammatory during disease state (Lee *et al*., 2013; Konikoff *et al*.,2016) [79, 80]. When there is a decrease in the population of the Oscillospira is mostly seen in disease conditions (Walters *et al*., 2014; Gophna *et al*., 2017) [81, 82]. The microbes of the gut possess the capacity to secrete an enzyme that assists in the energy extraction from complex carbohydrates (Flint *et al*., 2012) [83]. It has been found that gut microbes contain a gene that codes for the production of enzymes associated with the carbohydrates degrading complex carbohydrates (Flint *et al*., 2012) [83]. The microbes of the gut also synthesis vitamins B complex and K which help in maintaining the host health (Yatsunenko *et al.,* 2012) [84]. The intestinal tract epithelium act as the first line of defence against the pathogenic microbe. The mice reared on germ-free gut shows very thin villi, poor peristalsis, less intestinal surface area, less villus capillary network and long cell cycle time (Jandhyala *et al*., 2015) [85]. There is solid evidence that microbes help in the structural and functioning of the gastrointestinal tract, help in the maintenance of the desmosome of the villus by exhibiting the expression of the protein, preventing the apoptosis of the epithelial cells and regulating the epithelial permeability barrier (Everard *et al*., 2013) [86]. The use of probiotics are found to be beneficial during the weaning period (Dumitru *et al.,* 2021) [87].

Use of Probiotic in Growing Finishing Pigs

The research is carried out on the use of Probiotic in growing and finishing pigs just like an alternative to an antibiotic. As the gastrointestinal tract of pigs gets matured high level of digestive enzymes, immune system and resistance the response to Probiotic is limited (Yang *et al.,* 2015) [88]. No doubt that the adult matured gastrointestinal tract has very limited scope to improve the productivity in this phase of development but the feeding of Probiotic in the early stage of growing development still can cause beneficial effects. The use of Probiotic in growing and finishing pigs causes an increase in the digestibility of nutrients (Kim 2013; Zhang and Kim 2015) [79, 90]. Probiotics use in pigs also prevent the salmonella infection in pigs (Barba-Vidal *et al*., 2017; Upadhaya *et al.* 2017) [47, 46]. The microbes of Probiotic also cause a decrease in the release of pollutants from manure into the environments from the pig fed on high nutrients diets through the decrease of faecal ammoniacal nitrogen release from manure into the environments. It uses ammoniacal nitrogen for building its protein which later on provides the proteins to the animals (Ahmed *et al.* 2014; Yin *et al.* 2014; Zhu *et al.* 2014; Zhou *et al.* 2015; Yang *et al.* 2016; Upadhaya *et al.* 2017) [41, 42,56, 96, 88, 46] found in their research trial that the use of Probiotic in growing-finishing pigs causes a decrease in mortality in comparison to the control group. The use of Probiotic in growing-finishing pigs causes the promotion and proliferation of beneficial microbe, suppression of the pathogenic microbes and the health of the Probiotic fed improves in comparison to the Probiotic non fed group (Yan and Kim 2013) [79] and the probiotics cause a higher body weight gain in comparison to control group (Meng *et al*., 2020) [75]. The probiotics use in pigs farm-reared under unsanitary conditions shows a positive response to using of probiotics, it may be due to the prevalence of subclinical disease in pigs reared under unsanitary conditions in the intestinal gut of the pigs (Yan and Kim., 2013) [79].

Use of probiotic in sow ration

Probiotic in sow causes a decrease in uterine - udders diseases, less post-weaning estrus intervals, improvement in the body condition score and daily feed intake improve during the last stage of the pregnancy and during early lactation, (Jeong *et al.* 2015; Kritas *et al.* 2015; Scharek-Tedin *et al.*,2015; Hayakawa *et al.* 2016) [37, 94, 43, 36,]. The supplementation of probiotics in sow shows positive results as it causes the decrease of pathogenic microbes in the gastrointestinal of piglets (Baker *et al.* 2013; Kritas *et al*., 2015) [95, 36]. Probiotic feeding in the sow causes an increase in the amount of the colostrum, daily sow quality and quantity of milk production (Scharek-Tedin *et al.,* 2015) [43]. The immunity of the young piglets born from sow fed with probiotics shows improvement in the immunity. (Siepert *et al.,* 2013; Scharek-Tedin *et al*., 2015) [48, 43] Piglets born from sow supplemented with Probiotic shows increased growth rate and the litter size (Baker *et al.* 2013; Apic *et al.* 2014; Wang *et al.* 2014; Jeong *et al.* 2015; Kritas *et al*., 2015; Hayakawa *et al*. 2016) [95, 96, 94, 36, 37] Sow fed with Probiotic prevent the incidence of diarrhoea in the piglets (Apic *et al.* 2014) [96] and it has been observed that sow fed

Probiotic transfer the Probiotic microbes through entero-mammary route to the young piglets (Scharek-Tedin *et al*., 2015) [43]. Probiotic supplementation causes a decrease in the post estrus intervals due to less energy mobilization from sow body as the Probiotic causes an increased digestibility of nutrients (Kritas *et al*.,2015; Hayakawa *et al*.,2016) [36, 37]. The feeding *Bacillus licheniformis, B. subtilis* and *Enterococcus faecium* Probiotic in nursing shows a higher sow weaning weight in comparison to control sow while research finding of experiments conducted by (Baker *et al*., 2013; Jeong *et al*. 2015; Kritas *et al.* 2015) [95, 94, 36,] in sow shows supplementation of Probiotic does not cause any significant body weight gain in the sow. The research finding of Kritas *et al.,* (2015) [36] suggest the use of Probiotic microbes *Bacillus subtilis Bacillus Toyoi Bacillus licheniformis* and *B. subtilis* causes lower weight loss during lactation in sow while finding of Jeong *et al.,* (2015) [94] revealed that using Probiotic microbe (*Bacillus subtilis, L. acidophilus Bacillus cereus, Enterococcus faecium*) shows that there is no significant effect on the weight loss in Probiotic fed sow in comparison to control group.

In addition to the increase in productibility, parameters scientists are laying more interest to see whether sow affect the delivery of the Probiotic to the piglets in the early days. The first two weeks of life is considered as a development window during which microbes of the gut are less stable and are more prone to microbial disturbance (Wang *et al*., 2013) [22]. After two weeks of age, the microbial population of the gut become more stable and the microbes which are found in old age are correlated to the microbes found during the early stage of development. The microbial population of the gut is determined early in the phase of development (Mach *et al.,* 2015) [98]. In a research finding they compared the performance of the genetically compared piglets under outdoor, indoor and in isolation conditions. It has been observed that piglets reared under outdoor conditions show better microbe diversity with a higher level of *Lactobacillus spp.* and fewer pathogenic microbes. There is a proposed mechanism of early transfer of Probiotic through entre-mammary route in humans, it can be considered for swine production transfer Lactobacillus species and *Bifidobacterium breve* gut obligates species are found to be efficiently transported through entero-mammary route (Jost *et al*., 2014) [99]. The milk composition ingrients can affect the piglets microbial health and performance of piglets (Li *et al*., 2012b; Bian *et al*., 2016) [55, 100]. The supplementation of the *B. licheniformis and B. subtilis* spores in the piglets cause a change in the milk composition during the mid suckling period which causes improvement in the health and body condition score in the piglets. The other method of transferring Probiotic is through inoculation of Probiotic in creep, but the piglets did not consume much quantity of creep feed to fulfil the required quantity of Probiotic microbes required to be fed. (Kritas *et al*., 2015; Hayakawa *et al*., 2016) [36, 37]. The use of Probiotics shows the beneficial effect on the sow and in the piglets but there is very much divergence in the published research result. So more research is needed to characterize the Probiotic strains its characterization, dose level, period of treatment should be standardized.

Controversies and Risk associate with the use of Probiotic in Pigs

There are also some finding which shows that the use of Probiotic daily through oral supplementation of *B. subtilis* does not cause any significant body weight gain in comparison to the control group. The strict norms should be implemented in the selection of any microbe as a Probiotic to check that it does not contain the antibiotic resistance gene in it which might transfer the resistance gene to the bacteria and the problem of translocation in the gastrointestinal tract due to its adherence with the intestinal tract (Bajagai *et al*., 2016) [28]. The Probiotic microbe release enterotoxin which may causes toxicity (Isa *et al*., 2016) [102]. The Probiotic used microbe must be safe to the handler skin, eye or gastrointestinal tract (Bajagai *et al*., 2016) [28]. The microbe of Probiotic must be able to survive and replicate in the intestinal tract (Hill *et al*., 2014) [103]. The producer of Probiotic must quality products and must specify expiry dates and conditions for its store so that its shelf life is maintained. The effect of Probiotic is treatment specific depending on the type of strain, context dose (Li *et al*., 2012a, 2012b) [54, 55], host-specific related to its physiological parameters and environment condition under which the pigs are reared. There is research finding which shows that the use of probiotics does not cause any significant results on the host (Jeong *et al*., 2015) [94] The research finding of many scientists suggests that there is a lack of any significant productive parameters when probiotics used in bacteria challenge hosts (Walsh *et al*., 2012; Kreuzer *et al*., 2012; Barba-Vidal *et al*., 2017) [104, 105, 47].

The rule regarding the publication of Probiotic microbe gene sequencing, toxin production and resistance profiling is increasing strict day by day (Kumar *et al*., 2015) [106]. The chances of entering the microbe of the Probiotic entering the human food chain are there. Therefore the safeguard precaution must also be taken into consideration in general to whole human animals and environment as a whole not specifically to animal health-centric (Doron and Snydman, 2015; Bajagai *et al*., 2016) [107, 28].

Conclusion

The use of probiotics in the swine industry shows positive results in terms of improvement of gut health, immune system, enhancement in growth rate, decrease stress, production of improve organoleptic meat productions and reduction of environmental pollutants. It promises an alternative to the antibiotics growth promoters and is in favour of various norms as implemented from time to time regarding the use of antibiotics in swine production. It shows multiple beneficial effects on swine. Hence more research is needed to obtained favourable robust therapies positive results, clearing doubts related to safety-related issues and standardizing the inconsistent results under diverse conditions.

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