Chapter

Swine Production: Probiotics as an Alternative to the Use of Antibiotics

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Abstract

Animal food production is one of the most powerful European economic sectors; however, this sector is facing new challenge due to the development of bacteria with resistant genes, and consequently, restriction on the administration of antibiotics. Limitation, at the moment, is focused on those antibiotics employed in human medicines. Therefore, it is necessary to improve as much as possible animals' health and reduce diseases. Among others, alternatives include adequate animal handling, hygienic facilities, quality food, or vaccines. Probiotics also arise as a good alternative due to their already known properties as intestinal microbiota modulators, improving the immune functions and reducing the risk and the development of illness. Significant data can found scientific literature that demonstrates probiotics benefits when they are administrated to the animals through diet. However, to be able to apply all these findings in a specific animal species, at a particular production animal life stage and at a industrialize scale, it is necessary to compile and organize reported information. This chapter presents the most recent and relevant finding on the use of probiotics in swine production.

Keywords: probiotics, swine, animal production, antibiotics, antimicrobial-resistant bacteria, pork

1. Introduction

The abuse on the use of antibiotics in veterinary and human medicine has triggered the exponential development of resistant genes. These genes gave to the microorganism the ability to resist antimicrobial treatments, especially antibiotics; therefore, infections become more a more difficult, since usual therapies are not effective anymore. Special attention is required for the development of superbugs, resistant bacteria to most antibiotics, such is the case of *Salmonella*, *Campylobacter*, and *Escherichia coli*, resistant to a wide range of commonly used antibiotic [1]. It is estimated that in 2050, there will be more deaths from multidrug-resistant bacteria than from cancer worldwide [2]. According to the Spanish Ministry of Health, Social Services and Equality (2014) [3] antibiotics with critical importance for human

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health are macrolides (7.5%), polymyxins (6.6%), fluoroquinolones (1.9%), and cephalosporins of third and fouth generation (0.2%).

Implications of resistant bacteria in food safety are no longer in doubt, and different studies and investigations have shown that food contain genes of resistant bacteria, and these genes can be transmitted from animal to human through the food chain [4–7]. Therefore, food safety authority must control transmission of pathogen, residue of veterinary medicines, resistant bacteria, and resistant genes. Maciel *et al*. [8] isolated resistant *Salmonella* spp. from swine and poultry products, and theirs results indicated that 55% of the isolated were resistant to three or more classes of antibiotics (amoxicillin, ampicillin, ceftiofur, enrofloxacin, florfenicol, gentamycin, tetracycline, and sulfa-trimethoprim). This is not only a human health problem, which causes more than 33000 deaths in Europe each year [9] compared to those caused by the combination of influenza, tuberculosis, and HIV/AIDS, but also a veterinary problem and, consequently, a food safety problem. Forslund and collaborators [10] observed in human stool samples higher resistance genes to antibiotics employed in human and veterinary medicine than to those antibiotics only employed in human medicine.

Aiming to control and reduce the development of resistant genes, international organizations and public bodies, organisms including WHO, have establish different strategies and protocols to reduce the use of antimicrobials in human and veterinary medicine with high restriction for the food animal production. As a result, the European Regulation 2019/6 was published in 2019 [11], this regulation established limitation on the use of antibiotics in veterinary medicine, avoiding their application for routine prophylactic and metaphylactic, with special restriction to those antimicrobials that are of critical importance for preventing or treating life-threatening infections in humans. The objective of this regulation is to warrant food safety and human health by protecting consumers from the consumption of resistant genes or residues of antibiotic through food of animal origin.

Therefore, the European animal food-producing sector must face the great challenge of reducing, and avoiding as much as possible, the use of antibiotics, without spreading pathogens. Possible alternatives include biosecurity plans, hygiene measures, infectious disease prevention protocols, correct housing design, production integration systems, correct animal management to reduce stress, the use of quality food and water, vaccination programs and the use of bioactive substances such as probiotics, prebiotics, antioxidants, and vitamins, among others [3, 12].

This chapter aims to collect the most employed probiotic species in swine production as well as to report the results to evaluate if, effectively, the use of specific probiotics, administered alone or as a mixture of species or strains may an interesting alternative to antibiotics to prevent diseases. Other aspects as the average daily feed intake or the daily weight gain have been evaluated.

2. Pig production

The livestock sector is the main produce of animal-based protein for human consumption and is the pork sector which accounts for more than one-fourth of the total protein consumed worldwide [13]. In the last decade, this sector has increase in number of pigs, number of pig farms, and meat production. According to the FAO statistical yearbook published in 2021 [14], in 2019 a total of 337 million tonnes of meat were produced, 44% more than in 2000. After China, the UE is the second leader pig meat producer, being Spain the fourth producer, after China, EEUU, and

Germany. Only in Europe, 150 million of pigs are reared representing the largest livestock category before bovines. Pork meat demand will certainly increase due to continuous human population growth, and this will increase farms size and numbers, leading to more animals' densities in the farms. The major problem of swine production is infection disease as they are transmitted easily between animals, and they decrease productivity by reducing animal growth and in many cases causing animal death. Pig diseases need to be controlled during meat production, not only to obtain major production benefits but also to warranty food safety.

2.1 Production cycle and diseases

The prevention of infection is of great importance in food-producing animals to guarantee and maintain animals' health to achieve good production rates and quality food. To control and reduce disease in swine production, it is important to understand the production cycle and the most prevalent pathogens in each phase.

2.1.1 Gestation and lactation phase

This phase lasts for 114 days (gestation) and 21–28 days more for lactation. At the fourth week of gestation, sows are separated in groups of approximately 15–20 individuals. During gestion and lactation, sows are subject to various stress factors such as farrowing, lactation, housing conditions, management, as well as feeding [15]. Parvovirus is the most frequent disease at this stage, and sow vaccination is required. Additionally, numbers of newborn piglets can decrease by increasing mummified fetuses and neonatal deaths [16] by virus attacks such as porcine teschovirus (TVP), circovirus type-28 (PCV2), rotavirus, reproductive syndrome virus, and porcine respiratory virus (PRRS). In fact, mortality rate of piglet, at this stage, is one of the main problems for profitability in swine production [17].

Intestinal microbiota of both mother and piglet plays a relevant role in animals' health. At this stage, piglets are sensitive to diseases since they have an undeveloped digestive and immune systems, and they can easily die if infections are not treated quickly. Key aspects for piglet microbiota development include, among other, the type of parturition, use of antibiotics, and lactation period. Sow milk provides to the piglets all the necessary nutrients and antibodies to grow and face infections [18]. Piglet mortally, at this stage, is related to diarrhea caused by *E. coli*, *Salmonella* spp., *Campylobacter* spp., rotavirus, coronavirus, and protozoa of the genus *Cryptosporidium*. Other microorganisms and diseases that can also affect piglets' health are *Actinobacillus suis*, which causes respiratory processes, porcine circovirus type 1 and 2, responsible of swine dermatitis and nephropathy, *Streptococcus suis*, causing respiratory disease, African swine fever and Classical swine fever, causing respiratory and dermatological symptoms and sudden deaths, foot-and-mouth disease virus responsible for dermatological, respiratory, and lameness symptoms, and respiratory syndrome virus (PRRS) that can cause neonatal deaths [16].

2.1.2 Piglet weaning phase

Piglets are separated for theirs mothers at 3–4 weeks of age (21–28 days), although it will naturally occur at 17 weeks (119 days), and this transitional phase or weaning lasts until 60–70 days of life. Groups of animals, of 20 to 25 individuals from different litters, are now formed. Separation of piglet from their mothers is a sudden, quick, and stressful for the animals, because a lot of changes takes place; animal diet and social and environmental living conditions are modified. These modifications have an impact on the health status of the piglets and can cause decreases in its performance and even on his death. The critical moment are the first 5 days of the transition, which are very important, and the environmental, handling, and feeding conditions must be checked and verified very well in order to reduce the incidence of post-weaning and post-weaning diarrhea and improve the pig growth [16, 18, 19].

At this stage, the piglet intestinal microbiota undergoes changes, losing diversity, since in the previous stage it was largely modulated by lactation. Decrease has been observed in the bacteria of the *Lactobacillus* and *Clostridium* genera and *Escherichia coli* species, and their increase has been associated with the appearance of enteric infections that can lead to diarrhea [18, 19]. Among other, most common pathogens in this period are *A. suis*, *Pasteurella multocida*, *S. suis*, and *Bordetella Bronchiseptica* causing respiratory processes, porcine circovirus type 1 and 2, porcine herpesvirus type I responsible for Aujeszky's disease, *Staphylococcus hyicus* responsible for epidermitis exudative, porcine epidemic diarrhea virus, foot-and-mouth disease virus, and PRRS virus [16].

2.1.3 Fattering phase

This phase begins 60–70 days after birth, when the animal weighs around 30 kg. It lasts for 80–100 days, until the animals reach the optimum weight for slaughter, which is approximately 100 kg [16, 20]. Diseases most frequently reported in this phase are those caused by PRRS virus that causes respiratory symptoms and weight loss in pigs, swine circovirosis caused by PCV2, swine flu or influenza, caused by

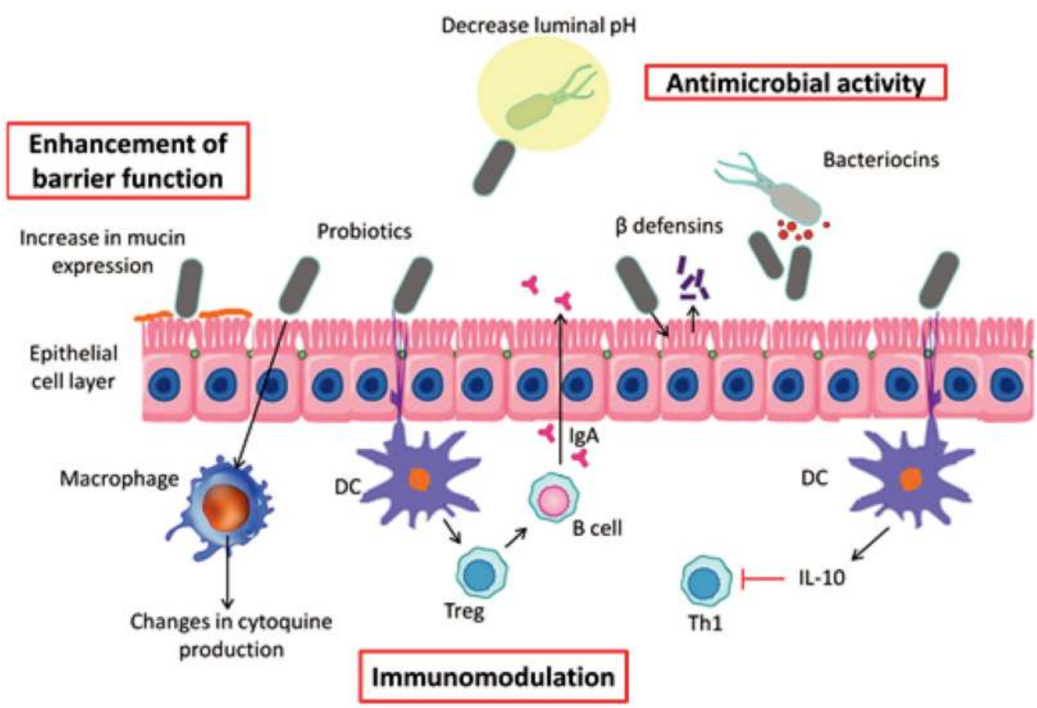

Figure 1.
A schematic diagram about probiotic mechanisms within the intestine. Reproduced from Cerdó et al. [26] (CC BY license).

influenza virus type A, and swine enzootic pneumonia caused by the bacterium *Mycoplasma Hyopneumoniae*. Other agents that also cause relevant diseases during this phase are coronavirus, that gives rise to transmissible gastroenteritis (TGE), *Salmonella* spp., mainly associated with diarrhea, *Lawsonia intracelluralis*, that causes ileitis [21, 22], *Brachyspira hyodysenteriae*, a spirochete that causes swine dysentery in fattening pigs [23] and, *Actinobacillus pleuroneumoniae*, that causes porcine pleuro-pneumonia and pastry/streptococcal pneumonia [16].

3. Probiotics: an alternative to reduce antibiotics

The use of bioactive substances is a possible and good alternative to reduce the use of antibiotics. Probiotics, in particular, have attracted attention from the scientific community and producers due to their already recognized efficacy in humans.

According to the Food and Agriculture Organization of the United Nations (FAO)/WHO, a probiotic is defined as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" [24]. Numerous studies have been shown the beneficial effects of probiotics for human and animal, including the swine sector. Positive effects include modulation of the intestinal microbiota, regulation of the immune system, as well as improvement of growth, efficiency of feed conversion, and reproductive improvement of pregnant sows [25].

Probiotics can act against pathogenic microorganisms through various mechanisms including anti-adhesive effect, production of antimicrobial substances, strengthening of the epithelial barrier of the intestine, and modulation of the immune system (**Figure 1**) [19]. The anti-adhesive effect is characterized by the ability of probiotic bacteria to adhere to intestinal epithelial cells, taking place a competition between probiotic and the pathogen for the same receptor. In addition to competitive exclusion, other modes of probiotic anti-adhesion described are degradation of carbohydrate receptors through the secretion of proteins, establishment of a biofilm, production of analogs receptor, and induction of biosurfactants [27]. Probiotics can also produce antimicrobial substances such as antimicrobial peptides, also called bacteriocins, which are produced, among others, by lactic acid bacteria, and they can also generate deconjugated bile acids with superior antimicrobial activity to bile salts synthesized by the body itself [28]. Another mode of action of probiotics is through the strengthening of the intestine epithelial barrier [28]. Probiotics are also capable to modulate the immune system as it can be observed in **Figure 1**.

4. Probiotics applied in swine production

Probiotics tested in swine include a variety of bacteria, and they were tested in the three main stages of production: gestation and lactation, piglet weaning, and growing and finishing phase. The most employed species include *Bacillus subtilis*, *Clostridium butyricum*, *Lactobacillus acidophilus, Bacillus licheniformis*, *Enterococcus faecalis*, and *Saccharomyces cerevisiae*.

4.1 *Bacillus* spp.

From the genus *Bacillus*, different species were tested such as *Bacillus coagulans* [29], *Bacillus cereus* var. Toyoi [30, 31], *Bacillus licheniformis* [32], *Bacillus mesentericus* [33], *Bacillus pumilus* [34], and *Bacillus subtilis* [35]. Even though the strain is a very important factor, not all the strains from the same species have the same effects and, therefore, for the reproduction of the study, not all the studies available in the literature reported the strain tested. In fact, out of eight studies that administrated *B. subtilis* to pig, only four indicate the strain, and in each case, a different strain was reported: *B. subtilis* PB6, C-3102, DSM 5750, and DSM 32540.

B. subtilis is the species for which more studies were found. Data indicate an increase in reproductive performance when probiotic was administrated to sows. Additionally, Zhang *et al*. in 2020 [36] reported an increase of 34% weight of the litter and an increment of 10% of survival in suckling piglets when *B. subtilis* PB6 was administrated to 32 pregnant and lactating sows. On the other hand, Menegat *et al*. in 2019 [35] did not observe an increase in litter size and weight when sows received a dietary supplement with *B. subtilis* C-3102, but they did find a 2.1% higher piglet survival rate in the supplemented sows group and 2% increase in piglet intake compared to the control group. According to Zhang *et al*. [36], *B. subtilis* PB6 can inhibit the growth of pathogenic bacteria in the intestine of the pig as it has survival and germination characteristics in the tract, capable of forming a biofilm and secreting antimicrobial compounds. Likewise, Menegat *et al*. [35] observed that the administration *B. subtilis* C-3102 increased *Lactobacillus* population approximately 2% (1.08 $\log_{10}$ CFU/g) during pregnancy and (0.8 $\log_{10}$ CFU/g) lactation in supplemented sows. Improvement of sow milk quality was also reported, and improvement in fat and protein contents on the milks' sows supplemented *B. subtilis* DSM 5750 and *B. licheniformis* DSM 5749 were 3.28% and 5.81% higher than in the control group. Sow's milk of supplemented animals also increased lactose content, 2% compared to the control group, having a better nutritional value for the piglets [32].

B. subtilis also improved growth performance when it was administrated during piglet weaning phase. Thus, He *et al.* [34] indicated that supplementation with *B. subtilis* DSM 32540 to piglet, at the weaning phase, challenged with F18 enterotoxigenic *E. coli* (ETEC F18) improving their growth performance; the increase was 11% for the daily weight gain and 10% for the average daily feed intake. Results indicate that that supplemented piglets improved metabolization of nutrients and optimized the energy, improving their growth and fighting against infection; however, these finding were not observed when the strain *B. pumilus* DSM 32539 were employed as probiotic for the piglets [34].

At the growing and finishing phase, administration during 104 days of *B. coagulans* (strain no reported) improved a 4% the daily weight gain and the average daily feed intake and modulated the intestinal microbiota, increasing 3% the abundance of Lactobacillus and decreasing a 6% the *E. coli* [29]. Other authors administrated *B. subtillis* combined with *L. acidophilus* and *S. cerevisiae* to 150 pigs, and at the growing and finishing stage, for 10 weeks, the mixture of bacteria showed to increase 1% the *Lactobacillus* population (0.07 $\log_{10}$ CFU/g) and decrease 1% the *E coli* (0.05 $\log_{10}$ CFU/g).

Three different studies reported supplementation with *B. licheniformis*, but only one indicated the strain. Alexopoulos *et al.* [32] supplemented pregnant and lactating sows with *B. licheniformis* DSM 5749 and *B. subtilis* DSM 5750, for 14 days before farrowing and until wean. Supplemented animals lost less body weight during lactation, approximately 3.5 kg. Similar findings were evidenced in litters of supplemented sows, showing 0.1 kg more per piglet in the 14 days postpartum. Possible due to the fact that incidence of diarrhea during the lactation period was significantly lower. Pan *et al*. [37] also reported lower (55%) severity of diarrhea caused by enterotoxigenic

E. coli K88 in piglet to which a mixture of *B. licheniformis* and the yeast *S.* cerevisiae was administrated, 12 days after weaning. In fact, in supplemented animals, *E. coli* concentration decreased 5% and *Lactobacillus* increased 9%. He *et al.* [34] also observed 10% reduction of diarrhea in piglet supplemented with *B. pumilus* DSM 32539, probably due to a reduction of 50% of coliforms. Additionally, in piglets supplemented with a probiotic, mixture of *B. licheniformis* and *S. cerevisiae*, IgA secreted by the intestinal mucosa increased 31%, improving the immune system through the modulation of intestinal microbiota in treated piglets [37].

Regarding sows' serum biochemical parameters, level of cholesterol and total lipid increase 4% in animals treated with *B. subtilis* DSM 5750 and *B. licheniformis* DSM 5749, with beneficial effect in piglets' growth [32]. Piglets growth improvement was reported by Lan *et al*. [38] after the administration of a mixture of *B. coagulance*, *B. licheniformis*, *B. subtilis*, and *C. butyricum*, for 42 days. Average daily gain increased 8 % but not significantly the average daily feed intake possibly due to the improvement of nutrient digestibility that improved 3% due to the use of the probiotic [38].

B. cereus var. Toyoi was investigated by Alexopoulos *et al*. [31], Baum et *al*. [39], Taras *et al*. [40], and Schierack *et al*. [30]. Schierack *et al*. [30] observed that the administration of these bacteria with feed showed to improve blood immune cells of piglets by modulating composition and activities, and the authors indicated that the probiotic also improved the effect of vaccination against influenza and *Mycoplasma*.

4.2 *Clostridium* spp.

C. butyricum was administrated to lactating sows and piglets, and what should be highlighted regarding the application of the bacteria is the fact that most researchers report its administration combined with another bacteria. Hayakawa *et al.* [15] employed *B. mesentericus*, *C.butyricum,* and Enterococcus faecalis; Lan et al. [38] employed *B. coagulance*, *B. lincheniformis*, *B.* subtilis, and *C. butyricum*: *Tsukahara et al.* [33] tested B. mesentericus, *C.butyricum,* and *E. faecalis;* and Wang *et al*. [41] investigated the combination of *C. butyricum* and *E. faecalis.*

Even if the bacteria were suministrated on a different formulation, *Tsukahara et al.* [33] and Wang *et al.* [41] observed similar results, an improvement of serum immunoglobulin (IgA and IgM), and the study of Wang *et al*. [41] was conducted with piglet and the one of Tsukahana *et al*. [33] with pregnant sows. Specifically, Tsukahana *et al.* [33] investigated the probiotic supplementation in unvaccinated and infected sow with porcine epidemic diarrhea virus. The probiotic BIO-THREE PZ (composed of *C. butyricum* TO-A, *Enterococcus* T-110, and *B. mesentericus* TO-A) improved the immune system of unvaccinated, PED-infected sows and their reproductive performance. On the other hand, Wang *et al*. [41] administrated the probiotic to weaned piglets and observed that the probiotic increased the jejunal villus length and jejunal villus height-to-crypt-depth ratio and decreased the jejunal crypt depth. They also reported a relative higher level of *C. butyricum* in supplemented animals and concluded that the mixture can promote growth performance, protect the intestinal pilli morphology, improve immunity, and optimize the intestinal flora in weaned piglets.

When *C. butyricum*, and other bacteria, was administrated to the pregnant and lactating sows and weaned piglets, a modulation occurs not only in the sows but also in the piglets' intestinal microbiota. In sows, *Lactobacillus* increased approximately 2% but *E. coli* decreased 12%, while in piglets *Lactobacillus* increased the same percent than in sows (2%) but E coli decreased much lower (1%) [15]. Li *et al*. [42] also indicated that *C. butyricum* plays an important role in feed addition, and they concluded that *C. butyricum* enhanced intestinal barrier function and inhibited apoptosis-associated speck-like protein-independent NLRP3 inflammasome signaling pathway in weaned piglets after ETEC K88 challenge. Even if beneficial results were observed when *C. butyricum* was supplemented to infected animals, Peeters *et al*. [43] in an assay developed in 2019 did not observe a significant difference in the daily weight gain, serological analysis, or bacteriological analysis when *C. butyricum* alone was supplemented to piglet challenged to *S. typhimurium*. However, this resolves that supplementation should be conducted with the combination of *C. butyricum* and other bacteria to achieve an improvement in swine production.

4.3 *Enterococcus* spp.

E. faecalis and *E. faecium* were supplemented to pigs, and most studies were conducted with their application in combination with other bacteria. Wang *et al*. [41] combined *E. faecalis* with C. *butyricum* and administered the mixture to piglets. Tsukahara *et al*. [33] and Hayakawa et al. [15] administrated a probiotic mixture formulated with three species *E. faecalis*, *C. butyricum*, and *B. mesentericus* to pregnant and lactating sows. Hayakawa *et al*. [15] aimed to reduce diarrhea, while Tsukahara *et al.* [33] aimed to improve the immune systems of sows and piglets, achieving both research groups their objectives.

Regarding *E. faecium*, the study conducted by Scharek *et al*. [44] who administered the strain *E. faecium SF68* to pregnant and lactating sows showed satisfactory results. They observed lower levels of cytotoxic T cells in the jejunal epithelium of piglets of the probiotic group. According to the authors, the difference in T population was not due to the modification of the epithelial cell numbers but due to the reduction of the frequency of β-hemolytic and O141 *E. coli* serovars in the intestinal contents of probiotic piglets. Zhang *et al*. [45] also administrated the bacterial species *E. faecium,* but in combination with *B. subtilis* to piglets. They observed a reduction of diarrhea (16%) that resulted in an increase of 23% of the daily weight gain, certainly due to an improvement of the microbiota composition caused by the administration of the probiotic.

4.4 *Lactobacillus* spp.

Lactobacillus spp. together with *Bifidobacterium* spp. are the genera most used as probiotics in human and veterinary medicine. However, in swine production, there are not many scientific works reporting supplementation with *Lactobacillus*, and generally the species of Lactobacillus are administrated combined with other bacteria to obtain more benefits from the supplementation. Dowarah *et al*. [46], Joysowal *et al.* [47], and Liu *et al*. [6] reported *L. acidophilus* supplementation at growing and finishing stage. Dowarah *et al*. [46] and Joysowal *et al.* [47] combined the strain *L. acidophilus* NCDC-15 and the strain *Pediococcus acidilactici* FT28. The first one administered the mixture to 36 pigs for 180 days. Diarrhea was reduced up to 41%, due to the modulation of the microbiota and an increase in the beneficial genera *Bifidobacterium* (4%) and *Lactobacillus* (7%) and a decrease (10%) in *E. coli* and *Clostridium*, bacterias whose increases are associated with disease. Joysowal et al. [47] supplemented 27 pigs for 90 days and observed, as Dowarah *et al*. [46], an improvement in the microbiota composition and increase of 12% of the final animal weight.

Liu *et al*. [6] tested the probiotic mixture of *L. acidophilus*, *B. subtilis,* and *S. cerevisiae* and reported an improvement of microbiota composition; however, the increase of *Lactobacillus* was only of 1% and the reduction of *E. coli* was only of 1%. The difference in this results between Liu *et al*. [6] and Dowarah *et al*. [46] could be due to various factors, and one of the most important is that in the first case a mixture of three probiotics was used, whereas in the other case only two were employed being *Lactobacillus* the only coincident species, so results can strongly differ. In addition, it is important to highlight that the supplementation was shorter in 2020 and in 2017, 110 days less of treatment with the probiotic mixtures.

4.5 *Pediococcus* spp

Pediococcus is a genus of lactic acid bacteria usually isolated from fermented food, but it can be also isolated from aquatic products, raw animal, plant products, and even human feces. Many species of *Pediococcus* are proven to have links of the human gastrointestinal tract. The species *Pediococcus acidilactici* is one of these species. *P acidilactici* produces bacteriocins, specifically, pediocins with antimicrobial properties. This particular bacterium was employed in pig at the growing and finishing stage and always combined with other bacteria. Supplementation of pigs during 180 days with the strain *P. acidilactici* FT28 combined with *L. acidophilus* NCDC-15 showed a modulation in the animals' intestinal microbiota with a consequently reduction of diarrhea [46]. In another study developed by Joysowal *et al.* [47], pigs were supplemented with the same strain, *P. acidilactici* FT28, alone and compared the results with pigs supplemented with *L. acidophilus* a NCDC-15 and without supplementation. The obtained results showed an improvement in growth performance, feed intake, digestibility of crude protein, and nitrogen retention in *P. acidilactici* FT28-fed group. Authors also reported a better serum albumin/globulin (A/G) ratio and cholesterol and triglyceride levels in the *P. acidilactici* group, compared to the control and *L. acidophilus* supplemented group.

4.6 *Saccharomyces* spp.

Saccharomyces spp. is a live yeast extensively used as probiotic, more specifically *S. boulardii* and *S. cerevisiae*. In human medicine, they have been used for years to prevent the diarrhea associated with antibiotic consumption and as a coadjuvant treatment for *Helicobacter pylori* eradication, so it is expected to have the same effects in pigs. Studies have been carried out with piglets at the post-weaning stage to investigate this objective. Thus, Trevisi *et al*. [48] and Trckova *et al*. [49] evaluated the effect of feeding supplementation with *S. cerevisiae* on diarrhea, and both authors found that supplementation reduced the duration and severity of post-weaning diarrhea caused by ETEC in piglet. In addition, trevisi et al. observed that administration of S. cerevisiae in concomitance with ETEC infections reduced pig illness and mortality.

On the other way, in the growing and finishing stage, production and rentability depend basically on the increment of pig weight. *Saccharomyces* was tested with pigs at this final stage; in 2017, Liu and collaborators [50] administrated, to 100 pigs, *S. cerevisia*e with *B. subtilis*, strain not indicated, for 42 days. The probiotics increased the daily feed intake up to 40 g/day, and consequently the animals daily weight gain was also increased by 57.5 g per day. Later, Liu *et al*. [6] included in the probiotic mixture *L. acidophilus*, and this work was conducted with 150 pigs, and the administration of supplementation was for 70 days. In this case, the incremented in the animal daily weight gain was lower than in 2017, i.e. 28 g/day. This may be due to a lower duration of the treatment or to the strain combination. So, other studies should be developed to confirm these results; however, as none of the studies indicate the strain, data cannot be compared so easily and conclusion cannot be made.

5. Conclusions

In general, all the studies included in this chapter show good results in terms of weight gain, daily intake, reduction of infection, reduction of illness severity, etc. However, in most cases, the studies cannot be compared since they use different strains or combination of probiotics. Since beneficial effects of probiotics are strain-dependent, it is important to highlight that in most of the studies conducted with probiotics, the strain or strains used are not indicated. Therefore, although the use of probiotics seems to be an interesting alternative to the use of antibiotics as prophylactic, more studies and research with solid results which indicate the dose, strain/s, age and health status of animals, type of feed, feed composition, administration mode, duration of treatment period are required. Well-defined studies must be carried out to really determine which strain/strains are effective for a specific objective (diarrhea prevention, increase in weight gain, respiratory pathologies, etc).

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References

[1] European Medicine Agency (EMA). CVMP strategy on antimicrobials 2021-2025. [Internet]. 2020. Available from: https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/cvmp-strategy-antimicrobials-2021-2025. [Accessed: September 16, 2022]

[2] Rubio J. Las bacterias resistentes se generan por un proceso de selección natural. [Internet] Available from: https://www.elsevier.com/es-es/connect/medicina/las-bacterias-resistentes-se-generan-por-un-proceso-de-seleccion-natural. [Accessed: September 16, 2022]

[3] Alonso Herreras M, Aracil García B, Saiz BI, Campos Marqués J, Durán Ferrer M, de Frutos Escobar C. Primer análisis integrado del consumo de antibióticos y su relación con la aparición de resistencia. AEMPS Plan Nac Resist Antibióticos. 2018:1-165

[4] Bennani H, Mateus A, Mays N, Eastmure E, Stärk KD, Häsler B. Overview of evidence of antimicrobial use and antimicrobial resistance in the food chain. Antibiotics. 2020;**9**(2):49

[5] El-Seedy FR, Samy AA, Khairy EA, Koraney AA, Salam HSH. Molecular determinants of multiple antibiotic resistant *E. coli* isolated from food of animal origin. Advances in Animal and Veterinary Sciences. 2020;**8**(4):347-353

[6] Liu X, Kim SH, Kim IH. Effects of the combination of multistrain probiotics and Castanea crenata shell extract on growth performance, nutrient digestibility, fecal microbial shedding, meat quality, noxious gas emissions, and blood parameters in finishing pigs. Livestock Science. 2020;**240**:104185

[7] Elghaieb H, Tedim AP, Abbassi MS, Novais C, Duarte B, Hassen A, et al. From farm to fork: Identical clones and Tn6674-like elements in linezolid-resistant Enterococcus faecalis from food-producing animals and retail meat. Journal of Antimicrobial Chemotherapy. 2020;**75**(1):30-35

[8] Maciel MJ, Machado G, Avancini CAM. Investigation of resistance of Salmonella spp. isolated from products and raw material of animal origin (swine and poultry) to antibiotics and disinfectants. Revista Brasileira de Saúde e Produção Animal. 2019;**20**:1-13

[9] OECD, E. Antimicrobial Resistance—Tackling the Burden in the European Union—Briefing Note for EU/EEA Countries. [Internet] 2019. Available from: https://www.oecd.org/health/health-systems/AMR-Tackling-the-Burden-in-the-EU-OECD-ECDC-Briefing-Note-2019.pdf [Accessed: September 16, 2022]

[10] Forslund K, Sunagawa S, Kultima JR, Mende DR, Arumugam M, Typas A, et al. Country-specific antibiotic use practices impact the human gut resistome. Genome Research. 2013;**23**(7):1163-1169

[11] Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. Official Journal of the European L4. 2019;**43**:167

[12] Thacker PA. Alternatives to antibiotics as growth promoters for use in swine production: A review. Journal of Animal Science and Biotechnology. 2013;**4**(1):35

[13] FAO, F. Agriculture Organization of the United Nations. Rome, Italy: FAO; 2018, 2019

[14] FAO. World Food and Agriculture – Statistical Yearbook 2021. Rome, Italy: FAO; 2021

[15] Hayakawa T, Masuda T, Kurosawa D, Tsukahara T. Dietary administration of probiotics to sows and/or their neonates improves the reproductive performance, incidence of post-weaning diarrhea and histopathological parameters in the intestine of weaned piglets. Animal Science Journal. 2016;**87**(12):1501-1510

[16] Carr J. Swine Disorders Guide. Zaragoza: Grupo Asís Biomedia; 2014. p. 50

[17] Ortiz J. Soluciones posibles para la disminución de las principales causas de mortalidad en lechones. [Internet] 2013. Available from: https://www.produccion-animal.com.ar/produccion_porcina/00-produccion_porcina_general/10-causas_mortalidad_lechones.pdf [Accessed: September 16, 2022]

[18] Barba-Vidal E, Martín-Orúe SM, Castillejos L. Practical aspects of the use of probiotics in pig production: A review. Livestock Science. 2019;**223**:84-96

[19] Gresse R, Chaucheyras-Durand F, Fleury MA, Van de Wiele T, Forano E, Blanquet-Diot S. Gut microbiota dysbiosis in postweaning piglets: Understanding the keys to health. Trends in Microbiology. 2017;**25**(10):851-873

[20] Forcada F, Babot D, Vidal A, Buxadé C. Ganado porcino: diseño de alojamientos e instalaciones. 2009; Edit: Servet Diseño y Comunicación SL

[21] Lunney JK, Fang Y, Lading A, Chen N, Li Y, Rowland B, et al. Porcine Reproductive and Respiratory Syndrome Virus (PRRSV): Pathogenesis and Interaction with the Immune System. The Annual Review of Animal Biosciences. 2016;**4**(1):129-154

[22] Guedes RM, Machuca MA, Quiroga MA, Pereira CE, Resende TP, Gebhart CJ. Lawsonia intracellularis in Pigs: Progression of Lesions and Involvement of Apoptosis. Veterinary Pathology. 2017;**54**(4):620-628

[23] Burrough ER. Swine dysentery: Etiopathogenesis and diagnosis of a reemerging disease. Veterinary Pathology. 2016;**54**(1):22-31

[24] Food and Agricultural Organization of the United Nations and World Health Organization. Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. World Health Organization [Internet]. 2001. Available from: https://www.fao.org/3/a0512e/a0512e.pdf [Accessed: September 16, 2022]

[25] Shin D, Chang SY, Bogere O, Won K, Choi J-Y, Choi Y-J, et al. Beneficial roles of probiotics on the modulation of gut micobiota and immune response in pigs. PLoS ONE. 2019;**14**(8):e0220843

[26] Cerdó T, García-Santos JA, Bermúdez MG, Campoy C. The role of probiotics and prebiotics in the prevention and treatment of obesity. Nutrients. 2019;**11**(3):635

[27] Oelschlaeger TA. Mechanisms of probiotic actions–Areview. International Journal of Medical Microbiology. 2010;**300**(1):57-62

[28] FAO. Probiotics in Animal Nutrition – Production, Impact and Regulation. Rome, Italy: FAO; 2016

[29] Fu R, Chen D, Tian G, Zheng P, Mao X, Yu J, et al. Effect of dietary supplementation of Bacillus coagulans or yeast hydrolysates on

growth performance, antioxidant activity, cytokines and intestinal microflora of growing-finishing pigs. Animal Nutrition. 2019;**5**(4):366-372

[30] Schierack P, Filter M, Scharek L, Toelke C, Taras D, Tedin K, et al. Effects of Bacillus cereus var. toyoi on immune parameters of pregnant sows. Veterinary Immunology and Immunopathology. 2009;**127**(1-2):26-37

[31] Alexopoulos C, Karagiannidis A, Kritas SK, Boscos C, Georgoulakis IE, Kyriakis SC. Field evaluation of a bioregulator containing live Bacillus cereus spores on health status and performance of sows and their litters. Journal of Veterinary Medicine A: Physiology, Pathology, Clinical Medicine. 2001;**48**(3):137-145

[32] Alexopoulos C, Georgoulakis IE, Tzivara A, Kritas SK, Siochu A, Kyriakis SC. Field evaluation of the efficacy of a probiotic containing Bacillus licheniformis and Bacillus subtilis spores, on the health status and performance of sows and their litters. Journal of Animal Physiology and Animal Nutrition. 2004;**88**(11-12):381-392

[33] Tsukahara T, Inatomi T, Otomaru K, Amatatsu M, Romeo-Pérez GA, Inoue R. Probiotic supplementation improves reproductive performance of unvaccinated farmed sows infected with porcine epidemic diarrhea virus. Animal Science Journal. 2018;**89**(8):1144-1151

[34] He Y, Jinno C, Kim K, Wu Z, Tan B, Li X, et al. Dietary Bacillus spp. enhanced growth and disease resistance of weaned pigs by modulating intestinal microbiota and systemic immunity. Journal of Animal Science and Biotechnology. 2020;**11**:101

[35] Menegat MB, DeRouchey J, Woodworth JC, Dritz SS, Tokach MD, Goodband RD. Effects of Bacillus subtilis C-3102 on sow and progeny performance, fecal consistency, and fecal microbes during gestation, lactation, and nursery periods1,2. Journal of Animal Science. 2019;**97**(9):3920-3937

[36] Zhang Q, Li J, Cao M, Li Y, Zhuo Y, Fang Z, et al. Dietary supplementation of Bacillus subtilis PB6 improves sow reproductive performance and reduces piglet birth intervals. Animal Nutrition. 2020;**6**(3):278-287

[37] Pan L, Zhao PF, Ma XK, Shang QH, Xu YT, Long SF, et al. Probiotic supplementation protects weaned pigs against enterotoxigenic Escherichia coli K88 challenge and improves performance similar to antibiotics. Journal of Animals Science. 2017;*95*(6):2627-2639

[38] Lan RX, Lee SI, Kim IH. Effects of multistrain probiotics on growth performance, nutrient digestibility, blood profiles, faecal microbial shedding, faecal score and noxious gas emission in weaning pigs. Journal of Animal Physiology and Animal Nutrition. 2016;**100**(6):1130-1138

[39] Baum B, Liebler-Tenorio EM, Enss ML, Pohlenz JF, Breves G. Saccharomyces boulardii and Bacillus cereus var. Toyoi influence the morphology and the mucins of the intestine of pigs. Zeitschrift fur. Gastroenterologie. 2002;**40**(5):277-284

[40] Taras D, Vahjen W, Macha M, Simon O. Response of performance characteristics and fecal consistency to long-lasting dietary supplementation with the probiotic strain Bacillus cereus var. toyoi to sows and piglets. Archives of Animal Nutrition. 2005;**59**(6):405-417

[41] Wang K, Cao G, Zhang H, Li Q, Yang C. Effects of Clostridium

butyricum and Enterococcus faecalis on growth performance, immune function, intestinal morphology, volatile fatty acids, and intestinal flora in a piglet model. Food & Function. 2019;**10**(12):7844-7854

[42] Li HH, Li YP, Zhu Q, Qiao JY, Wang WJ. Dietary supplementation with Clostridium butyricum helps to improve the intestinal barrier function of weaned piglets challenged with enterotoxigenic Escherichia coli K88. Journal of Applied Microbiology. 2018;**125**(4):964-975

[43] Peeters L, Mostin L, Wattiau P, Boyen F, Dewulf J, Maes D. Efficacy of Clostridium butyricum as probiotic feed additive against experimental Salmonella Typhimurium infection in pigs. Livestock Science. 2019;**221**:82-85

[44] Scharek L, Guth J, Reiter K, Weyrauch KD, Taras D, Schwerk P, et al. Influence of a probiotic Enterococcus faecium strain on development of the immune system of sows and piglets. Veterinary Immunology and Immunopathology. 2005;**105**(1-2):151-161

[45] Zhang S, Yoo DH, Ao X, Kim IH. Effects of dietary probiotic, liquid feed and nutritional concentration on the growth performance, nutrient digestibility and fecal score of weaning piglets. Asian-Australian Journal of Animal Sciences. 2020;**33**(10):1617-1623

[46] Dowarah R, Verma AK, Agarwal N, Patel BH, Singh P. Effect of swine based probiotic on performance, diarrhoea scores, intestinal microbiota and gut health of grower- finisher crossbred pigs. Livestock Science. 2017;**195**(1):74-79

[47] Joysowal M, Saikia BN, Dowarah R, Tamuly S, Kalita D, Dev Choudhury KB. Effect of probiotic Pediococcus acidilactici FT28 on growth performance, nutrient digestibility, health status, meat quality, and intestinal morphology in growing pigs. Veterinary World. 2018;**11**(12):1669-1676

[48] Trevisi P, Colombo M, Priori D, Fontanesi L, Galimberti D, Calò G, et al. Comparison of three patterns of feed supplementation with live Saccharomyces cerevisiae yeast on postweaning diarrhea, health status, and blood metabolic profile of susceptible weaning pigs orally challenged with Escherichia coli F4ac. Journal of Animal Science. 2015;**93**(5):2225-2233

[49] Trckova M, Faldyna M, Alexa P, Sramkova Zajacova Z, Gopfert E, Kumprechtova D, et al. The effects of live yeast Saccharomyces cerevisiae on postweaning diarrhea, immune response, and growth performance in weaned piglets. Journal of Animal Science. 2014;**92**(2):767-774

[50] Liu W, Devi S, Park J, Kim I. Effects of complex probiotic supplementation in growing pig diets with and without palm kernel expellers on growth performance, nutrient digestibility, blood parameters, fecal microbial shedding and noxious gas emission. Animal Science Journal. 2017;**89**(3):552-560