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REVIEW ARTICLE

Probiotics as Feed Additives in Weaned Pigs: A Review

A. K. Patil[1*], Sachin Kumar[2], A. K. Verma[3] and R.P.S. Baghel[4]

Indian Veterinary Research Institute, Izatnagar, Bareilly (U.P.)- 243 122, India.

Present Address:
[1] Assistant Professor, Department of Animal Nutrition, [4] Dean, Veterinary College, Jabalpur (MP), India.
[2] Scientist, National Dairy Research Institute, Karnal (HR), India.
[3] Principal Scientist and Head, Centre of Advanced Faculty Training, Division of Animal Nutrition, IVRI, Izatnagar, Bareilly-243122.

*Corresponding Author:

A.K. Patil

Email:ashokdrpatil@gmail.com

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Abstract

Weaning is a complex phenomena which causes a great change in the magnitude and diversity of exposure to environmental antigens derived from food and potentially pathogenic microorganisms. Early weaning is a valuable way to get enhanced breeding efficiency and economical profits in modern intensive swine production. But this practice is accompanied by many challenges such as reduced feed intake, diarrhoea, body weight loss, damage to intestinal function and health. Antibiotics have traditionally been widely applied to nursery pigs to solve post weaning problems. However, development of antimicrobial resistance to these antibiotics urged scientists to find viable alternatives to the use of antibiotics that could enhance the natural defence mechanisms of animals. Probiotics have been established as a good alternative which can enhance intestinal health by stimulating the development of a healthy microbiota (predominated by beneficial bacteria), competing with pathogenic bacteria for nutrients in the gut, preventing enteric pathogens from colonizing the intestine, increasing digestive capacity and lowering the pH, or improving mucosal immunity. It is suggested that probiotic should be used as a feed additive in livestock.

Key words: Early weaning, Feed additive, Piglets, Probiotics.

1. Introduction

The weaning transition is a complex period during which the piglets have to cope up with abrupt separation from their dam, mixing with other litters in a usually new environment and switch from highly digestible feed (milk) to a less digestible more complex solid feed, hence weaning is a stressful experience for the piglets involving nutritional, psychological, environmental, microbiological and immunological stresses (Lalles, 2008). Breeding efficiency and economical profits in modern intensive swine production is enhanced by early weaning and it serves as effective way to enhance it (Yao *et al.*, 2008; Wang *et al.*, 2012). However, it is accompanied by many adverse effects viz. reduced feed intake, impaired intestinal health, diarrhoea and body weight loss (Lalles *et al.*, 2004; Pluske *et al.*, 1997). It leads to villous atrophy in the small intestine (Montagne *et al.*, 2007) thus impairing digestion and absorption of the nutrients in the gut. Antibiotics have traditionally been widely administered to nursery pigs to solve post weaning problems (Kong *et al.*, 2009). But worldwide concern about development of antimicrobial resistance to these antibiotics urged scientists to find viable alternatives to the use of antibiotics (Bach, 2001; Smith *et al.*, 2002) that could enhance the natural defence mechanisms of animals and reduce the massive use of antibiotics. Specific feed additives favorably affect animal performance and welfare, particularly through the modulation of the gut microbiota, which plays a critical role in maintaining host health (Tuohy *et al.*, 2005). The intestinal health can be enhanced by use of probiotic by stimulating the development of a healthy microbiota predominantly by beneficial bacteria by preventing the enteric pathogens from colonizing the intestine, increasing digestive capacity and lowering the pH, or improving mucosal immunity (Choct, 2009; De Lange *et al.*, 2010).

2. Probiotics

Parker (1974) coined the term “Probiotics” and described this as “microorganism or substance, which contributes to the intestinal microbial balance”. The term probiotic means “for life” and has a contrast with

the term antibiotic which means "against life". At present, probiotics are classified by the US Food and Drug Administration as generally recognized as safe (GRAS) ingredients. Probiotics are live microorganisms which have been found to confer a health benefit on the host when administered in adequate amounts (Weichselbaum, 2009). Many definitions have been proposed for the term "probiotic". The most widely accepted one is "live microorganisms, when they were administered in adequate amounts, confer a health benefits on the host" (FAO/WHO, 2002). This definition implies that a health effect must be demonstrated for the probiotic.

3. Commonly Used Probiotics

A number of microorganism strains are being used as probiotics with different efficacies; some of them may provide certain benefits for the host whereas others do not (Weichselbaum, 2009). The most commonly used species of probiotics are strains of lactic acid bacteria such as *Lactobacillus*, *Bifidobacterium* and *Streptococcus*. These species can resist gastric and bile acid and ability to colonize in the intestine or antagonism of potentially pathogenic microorganism (Verdenelli *et al.,* 2009). The most frequently used microorganisms as probiotics for livestock are *Lactobacillus- acidophilus, casei, brevis, fermentum, gallinarum, plantarum, gasseri, johnnsonii, reuteri, salivaris, Bifidobacterium- bifidum, lactis, Saccharomyces- cerevisiae, boulardii, Aspergillus- oryzae, Bacillus- cereus, coagulans, licheniformis, subtilis, Enterococcus- faecium and Pediococcus- pentosaceus* (Ohashi and Ushida, 2009).

4. Mode of Action of Probiotics

The normal gut microflora has a supportive role in disease protection and digestion of food. However, stressful conditions such as introduction of weaning results in change of diet and increase gut pH, which favours growth of pathogenic organisms. The probiotics bring about its beneficial effects through one of the following mechanisms.

4.1 Neutralization of Toxin

The various enterotoxins produced by various pathogenic microorganisms in gastrointestinal tract. A variety of substances such as organic acids, antioxidants and bacteriocins which are inhibitory to both Gram-positive and Gram-negative bacteria are produced by different probiotic bacteria (Cho *et al.,* 2011). Murali *et al.* (2010) reported that these compounds may reduce not only the number of viable pathogenic organisms but may also affect bacterial metabolism and toxin production. *Lactobacillus acidophilus* produces anti-metabolites such as *acidophilin, lactocidin* and *acidolin* and *L. plantarum* produces lactolin as reported by Vila *et al.* (2010). The protective effect of *Saccharomyces cerevisiae* is due to the reduction in the available amounts of the toxins secreted by pathogens and by competition for its adhesion sites in the presence of the yeast. Generally, toxins bind to specific receptors on intestinal epithelial cells and induce changes resulting in loss of water and electrolytes. Certain strains of *Saccharomyces cerevisiae* can excrete a serine protease that can hydrolyze toxin A produced by *Clostridium difficile,* which is resistant to trypsin and inhibits binding of this toxin to its brush border glycoprotein receptor (Castagliulo *et al.,* 1996).

4.2 Enhancement of Epithelial Barrier Integrity

Probiotics can inhibit the pathogens by enhancement of intestinal barrier function through modulation of cytoskeletal and tight junction protein phosphorylation (Sherman *et al.,* 2005)

4.3 Competition for Adhesion Sites

The competitive exclusion is the ability of normal microflora to protect against the harmful establishment of pathogens (Cho *et al.,* 2011). The competition for the space to adhere between indigenous bacteria and exogenous pathogens result in the competitive exclusion of exogenous pathogens from the intestinal lumen (Brown, 2011). The concept of competitive exclusion indicates that cultures of selected, beneficial microorganisms, supplemented to the feed, compete with potentially harmful bacteria in terms of adhesion sites and organic substrates (mainly carbon and energy sources). Probiotics may exclude the harmful bacteria in two ways. First, these may compete for nutrients and absorption sites with pathogenic bacteria which prevent proliferation of pathogenic bacteria in the gut environment (Brown, 2011; Malago and Koninkx, 2011). Secondly, after establishment in the gut may produce substances such as lysozyme, hydrogen peroxide as well as several other organic acids and volatile fatty acids with bactericidal or bacteriostatic properties (bacteriocins by lowering the gut pH below the optimum level for survival of harmful species such as enteropathogenic *E. coli* or *Salmonella*. These substances have detrimental effect on these bacteria (Brown, 2011). The adhesion of bacteria to epithelial cells is an early stage in bacterial infection of mucous membranes. Bacteria possess binding molecules on their surfaces that are capable of interacting stereo-specifically with host-cell membranes in a manner analogous to antigens-

antibodies interaction. Evidence has been established that certain strains of *E. coli* or *Salmonella* possess a fimbrial adhesin, which binds to mannose residues on epithelial cell membranes (Ofek *et al.*, 1977). Such bacteria or their isolated fimbriae will also agglutinate yeast containing mannan in the outer layer of their cell wall (Korhonen, 1979). This agglutination is inhibited by solutions of D-mannose. Gedek (1989) reported that binding of pathogens to yeast cell wall induces a protective effect. Competition between yeast and pathogens for binding to intestinal cells could help to explain the beneficial action of yeast, since adhesion is crucial to the expression of the cytopathogenic effect.

4.4 Stimulation of Immunity

Probiotics can stimulate the immune system by increased production of antibodies and activation of lymphocytes (Ng *et al.*, 2009). The action of yeast cell wall material on the complement system has been known for a long time (Pillemer *et al.*, 1954). These properties are due to the presence of glucans in the inner part of their cell wall that are constituted of main chains of beta-(1-3)-linked D-Glucose molecules to which linear side chains of beta-(1-6) linked residues are attached. These macromolecules stimulate immune system in mammals mainly inflammatory response and reticuloendothelial system (RES). Intestinal immune response is modulated by *Lactobacillus* through the stimulation of certain cytokine secretion by epithelial cells.

4.5 Prevention of Amine Synthesis

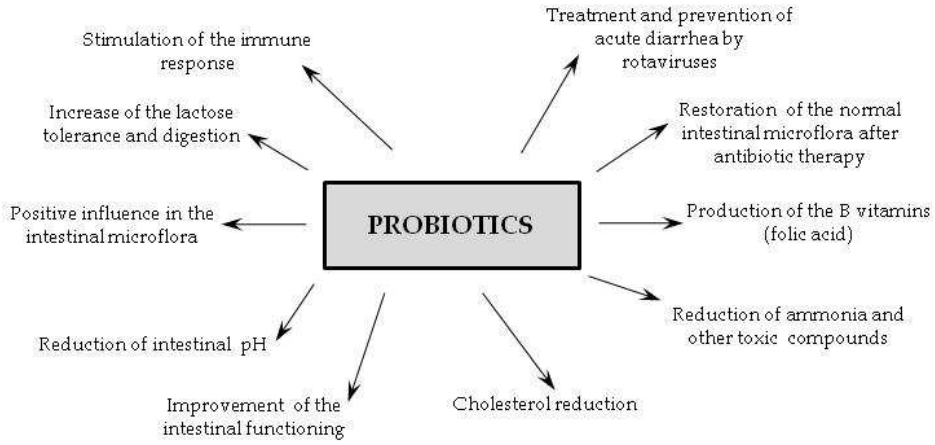
Amines are produced from amino acids by decarboxylation by Coliform bacteria, are toxic which may irrigate the gut and leads to diarrhoea. Probiotic reduce the count of coliform bacteria thus resulting in prevention of amine production.

5. Responses of Probiotic Addition in Pigs

5.1 Growth Performance and Nutrient Utilization

A summary of influence of probiotic strains on performance of pigs (Table 1). Growth is one of the most important features during post-natal life of piglets. From economic point of view the growth performance of pig is very important and it is one of the key indicators affecting the profitability of pig meat production. It is generally measured as an increase in body weight. Campbell (1997) reported that improvement in growth rate and feed to gain ratio resulted in improved profitability due to greater output and reduction in overhead cost. An increased growth rate due to high dry matter intake and better feed conversion efficiency have been reported by feeding probiotics. However, the dietary composition and environmental conditions influence the growth response of animals to yeast supplementation. Datt *et al.* (2011) observed that probiotics supplementation did not affect feed intake, however, it improved digestibility of DM, OM, CP, CF and NDF significantly ($P<0.01$) without affecting the digestibility of EE and ADF. Animals in the probiotic supplemented group showed significantly higher ($P<0.01$) growth rate and better FCR as well as the lower cost of feeding per kg gain. Age and weight at weaning are closely related to post-weaning growth (Mahan *et al.*, 1998; Quiniou *et al.*, 2002). Many studies have demonstrated that weaning weight influences post-weaning growth performance and also influence performance during the subsequent grower and finisher phases (Le Dividich and Seve, 2000). An increase in pig weight at weaning with one kg will result in a pig which reaches slaughter weight at least 10 days faster (Cole and Cole, 2001) and accepted that average daily gain during the first week post-weaning has a major impact on subsequent growth performance (Tokach *et al.*, 1992). Jurgens *et al.* (1997) studied the effect of dietary active dry yeast supplementation on post-weaning pig performance in piglets. They reported that dry yeast supplementation has little difference in feed intake but significant improvement in average daily gain ($P<0.05$) and feed efficiency ($P<0.05$) by pigs whose dams, as well as themselves, received supplemental active dry yeast. Pigs fed with the yeast diets has shown better total intake as well as overall gains when compared with pig fed with the control diet (Mathew *et al.*, 1998). Bontempo *et al.* (2006) studied the effect of yeast supplementation (2g/kg of diet providing 2×10^6 cfu /g of feed) on piglet growth. They observed that control piglets were heavier ($P<0.05$) than treated piglets at weaning but the later ones were significantly heavier at 30 days post weaning ($P<0.01$). They also observed that piglets fed yeast had a significantly greater ADG (474±0.01g) from weaning throughout 30 days post weaning than non-supplemented group (432± 0.01g). Van Heugten *et al.* (2003) evaluated the effects of live yeast supplementation on nursery pig performance, nutrient digestibility and faecal microflora. They also carried out a study to determine whether live yeast could replace antibiotic and growth promoting concentration of Zn and Cu in nursery pigs. They observed that live yeast supplementation had a positive effect on nursery pig performance when diets contained growth promoting antimicrobials. However, results are variable, as some workers have reported no benefit -

General mechanism of action



of yeast supplementation (Kornegay *et al.,* 1995).

5.2 Immune Response

The pig placenta does not transport maternal immunoglobulin and therefore newborn piglets acquire maternal immunoglobulin from colostrums during the first 24 to 48 h of life. The mucosal immune system and more especially the T-cell component of the intestinal mucosa of the newborn piglet is poorly developed at the time of birth and during the first few weeks of life, it undergoes a rapid period of expansion and specialization (Lalles *et al.,* 2007). The immune-modulatory effects of probiotics are related to important parts of their beneficial effects. Initially, ingested probiotic bacteria interact with gut epithelial cells. In studies using cell lines, such as, Delcenserie *et al.* (2008) observed that probiotic *Lactobacillus* stimulated the production of pro and anti- inflammatory cytokines by Caco-2 or HT-29 cell lines in a strain dependent manner. These can influence the immune system by products like metabolites, cell wall components and DNA. Probiotic *Lactobacillus* may modulate the intestinal immune response through the stimulation of certain cytokine secretion by epithelial cells (Delcenserie *et al.,* 2008). Shen *et al.* (2009) observed that IFN-γ, which can activate phagocytosis by macrophages, was increased in gut mucosa by yeast culture (YC) supplementation. In addition they reported that number of CD4+ lymphocyte numbers increased after weaning in the case of control group, whereas the number of CD4+ lymphocytes in YC group did not increase by 14 days post-weaning. The supplementation of probiotics (*Bacillus cereus var toyoi*) was shown to affect the intestinal immune system of the piglets at the time of weaning and shortly thereafter such that the intestinal epithelium CD8/CD3 double positive cell populations were enhanced in the probiotics group. In addition, they observed that the frequency of pathogen-associated *E. coli* serogroups were less frequent in the probiotics treated piglets (Scharek *et al.,* 2007). Davis *et al.* (2004) reported that supplementation with phosphorylated mannans derived from cell wall of *S. cerevisiae* improves growth response and modulates immune function of weaning pigs.

Intestinal diseases are prevented by probiotic administration through both humoral and cell mediated immune modulation (Erickson and Hubbard, 2000). Probiotics may lead to an increased IgA production and stimulation of macrophage (Perdigon *et al.,* 1999). Moreover, several studies have reported that probiotics are able to regulate both anti- and pro-inflammatory cytokine productions. Some studies reported that treatment of piglets with *B. lactis* increases blood leukocyte phagocytic and T-lymphocyte proliferative responses (Shu, 2001). Administration of *P. acidilactici* or *S. cerevisiae boulardii* was effective in reducing ETEC F4 attachment to the illeal mucosa, whereas the presence of *P. acidilactici* was required to modulate the expression of intestinal inflammatory cytokines in pigs challenged with ETEC F4 (Huang *et al.,* 2004).

5.3 Effect on Microflora

A summary of influence of probiotic strains on microflora of pigs (Table 2). Weaning of pigs is associated with the change of diet from sow's milk to a solid weaner diet and other post-weaning stressors. Microflora in the digestive system of pigs plays a very vital role in the health and nutrition of the body. The -

Table 1: Summary of influence of probiotic strains on performance of pigs

Stage of Pig	Probiotic	Effect	Reference
Weaning	*Lactobacillus acidophilus* or *Pediococcus acidilactici*	Improved Performance	Wang *et al.* (2012)
Weaning	*Enteroccocus faecium DSM 7134*	Better feed conversion ratio Higher daily gain Lower percentage of mortality	Lojanica *et al.* (2010)
Growing finishing	*Bacillus subtilis endospore Clostridium butyricum endospore complex*	Growth performance (↑) Beneficial effects on apparent total tract digestibility	Meng *et al.* (2010)
Growing	*Saccharomyces cerevisiae + Lactobacillus*	Improved digestibility Higher growth rate and better FCR	Datt *et al.* (2011)
Weanling	*E. farcium*	Growth (↑) FCR (↑)	Malloa *et al.* (2010)
Nursery	*Saccharomyces cerevisiae*	Positive effect on growth performance	Shen *et al.* (2009)
Weaning	*Saccharomyces cerevisiae*	Body weight (↑) Greater ADG	Bontempo *et al.* (2006)
Weaning	*Saccharomyces cerevisiae*	Better total intake as well as overall gains	Mathew *et al.* (1997)
Nursery	*Saccharomyces cerevisiae*	Positive effect on nursery pig performance when diets contained growth promoting antimicrobials	Van Heugten *et al.* (2003)
Weanling	*Bacillus licheniformis*	Weight gain (↑)	Collinder *et al.* (2000)
Weaning	*Saccharomyces cerevisiae*	Little difference in feed intake but ADG (↑) and feed efficiency (↑)	Jurgens *et al.* (1997)
Weanling	*B. licheniformis* *Bacillus toyoi*	Growth (↑) Growth (↑)	Kyriakis *et al.* (1999)
Weanling	*Bacillus toyoi*	Growth and feed efficiency (↑) Diarrhoea Mortality (↓)	Kyriakis *et al.* (1999)
Weanling	*Saccharomyces cerevisiae*	No benefit of yeast supplementation	Kornegay *et al.* (1995)
Weanling	*L. acidophilus* and *Streptococcus faecium* or *Bacillus toyoi*	Growth and feed efficiency (↑) Feed intake (No effect) Nitrogen retention (↑) Biological Value (↑)	Fialho *et al.* (1998)

* (↓) and (↑) are either significantly increased or decreased

Table 2: Influence of probiotic strains on the microflora in pigs

Stage of Pig	Probiotics	Effects	Reference
Nursery	*Saccharomyces cerevisiae*	E. coli (↓)	Shen *et al.* (2009)
Weanling	*Saccharomyces cerevisiae*	Total faecal bacteria (↓)	Van Heugten *et al.* (2003)
Weanling	*Saccharomyces cerevisiae*	No influence on intestinal microflora	Mathew *et al.* (1998)
Weanling	*Bacillus cereus, Lactobacillus spp. Streptococccus*	No influence on mortality, clinical symptoms and fecal hemolytic E. coli	Cupere *et al.* (1992)
Weanling	*Bifidobacterium globosum A*	No consistent effect on scour scores, faecal or gastrointestinal pH and cell-mediated immune response	Apgar *et al.* (1993)

* (↓) and (↑) are either significantly increased or decreased

major intestinal flora of pig *is Lactobacilli, Saccharomyces, Bifidobacteria, Streptococci, Bacteriodes, Clostridium perfringes* and *E. coli*, this microflora changes with age. When piglets are weaned, the intestinal microflora of piglets is altered involving an increase in *E. coli* populations, especially haemolytic *E. coli* in the anterior small intestine. Enteropathogenic *E. coli* is the major infectious agent for post-weaning diarrhoea. Lactic acid bacteria (LAB) fed weaned piglets had higher *Lactobacilli* populations and lower *E. coli* counts along the intestine (Huang *et al.,* 2004). Inclusion of lactic acid bacteria complex together with the mixture of *Bacillus* and *Saccharomyces* increased faecal LAB counts and decreased faecal *E. coli* counts in the grower pigs, but not in finisher pig (Giang *et al.,* 2011). The lower count of *E. coli* may be due to inhibited growth through the production of organic acids by the LAB (Jin *et al.,* 2000) and through the release of proteinaceous component that will inhibit the adhesion of *E. coli* in the mucus in the ileum of piglets (Blomberg, 1993). Similarly, YC or yeast cell wall component can affect the composition of intestinal microflora (White *et al.,* 2002). Changes in the microflora, due either to mannans or to a direct effect of live yeast, could reduce pathogenic bacteria and toxic metabolites and subsequently improve animal health and growth performance (Anderson *et al.,* 1999). Enzymes, vitamins and other nutrients or growth factors contained in yeast have been proposed to produce beneficial production responses in pig. Dietary supplementation of YC and antibiotic growth promoter (AGP) did not affect microbial populations tested however, only the number of *E. coli* in the caecum of YC and AGP group was decreased compared with the control group.

5.4 Small Intestine Morphology

Villus height and crypt depth are indirect indicators of maturity and functional capacity of enterocytes. At weaning there are a number of well documented changes in the histology and morphology of the small intestine. There is a reduction in villous height (villous atrophy) and an increase in crypt depth (crypt hyperplasia) at weaning (Hampson, 1986). Villous atrophy was associated with either an increased rate of cell loss from the villous apex or a reduced rate of cell renewal. Similar changes are clear at 5 days post-weaning and continued in the first to second week after weaning. The villous height was reduced to 50-75% of pre-weaning values (Kelly *et al*., 1991). Jejunal villus height and villus height to crypt depth ratio of pigs fed YC were greater than controls. Bontepmo *et al.* (2006) observed that villus height and crypt depth were greater and villous to crypt ratio was smaller in treated piglets than controls. Baum *et al.* (2002) also reported that villus length was greater in the small intestine of piglets fed yeast than controls. Gebert *et al.* (2011) concluded that pigs administered with probiotics had lower *E. coli* counts in the jejunum and illeum and lower coliform counts in the jejunum compared to unsupplemented pigs. The villous height: crypt depth ratio was greater in the illeum at 9 days of age when pigs were provided *L. brevis* 1E1 compared to unsupplemented pigs as well as in the duodenum of pigs supplemented with *L. brevis* 1E1 at 22 days of age. Changes in histometry occurred predominantly in the small intestine, showing higher jejunal villi when probiotics were administered alone. Inulin decreased the number of acidic goblet cells in jejunal villi, whereas probiotics increased neutral goblet cells in illeal villi (Mair *et al.,* 2010). Rekiel *et al.* (2010) concluded that feed additives and probiotics had a varied effect on the morphological characteristics and the proliferation capacity of crypt epithelium.

6. Conclusion

It may be concluded that weaning in piglets is accompanied by stress and reduced performance. Probiotics feeding may be good strategy to combat these challenges. It would furnish the scientists with better options, which would help them to search for a median path regarding the use and to optimize more feeding strategy to these live microorganism culture.

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