

# Nutritional Strategies to Mitigate Post-Weaning Challenges in Pigs

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The pig-farming industry faces significant challenges in ensuring the health and growth of piglets, particularly during the weaning phase. This critical period involves multiple stressors, such as environmental changes, dietary shifts, and social separation, which can adversely affect the piglet's digestive health, immune system, and overall well-being.

pig

weaning

$\beta$ -glucans

mushrooms

## 1. Introduction

Weaning is a critical phase in the development of piglets, with profound effects on their gastrointestinal health, immune responses, and overall physiology <sup>[1]</sup>. This stage introduces a complex interplay of stressors, including environmental shifts, dietary changes, and social separations, all of which collectively impact production efficiency <sup>[2][3]</sup>. The nutritional transition during weaning, which involves a shift from a milk-based to a cereal-based diet, poses a significant challenge to the piglet's digestive capacities <sup>[4]</sup>. Additionally, the move from farrowing rooms to weaner houses exposes them to novel environments and increased pathogen exposure. Social stress is further intensified as piglets are abruptly separated from their mothers and integrated with new piglets. These multifaceted stressors result in decreased feed intake and a range of gastrointestinal issues <sup>[5]</sup>. In contrast, wild piglets undergo a gradual weaning process over 10–14 weeks, allowing for more robust gastrointestinal development <sup>[6]</sup>. Commercial weaning, typically occurring between 3 and 4 weeks, coincides with the peak development of the gastrointestinal barrier but leaves the piglet's immune systems underdeveloped. Delaying weaning can enhance disease resistance but comes at the cost of increased production costs.

Following weaning, piglets undergo significant alterations in intestinal morphology, which affect nutrient absorption <sup>[7][8]</sup>. These changes are linked to an increased incidence of post-weaning diarrhea (PWD) and reduced enzymatic activity, which is essential for nutrient digestion <sup>[9]</sup>. Consequently, disruptions in the intestinal barrier lead to heightened immune system responses <sup>[10]</sup>. The weaning process triggers inflammation in piglets due to their immature immune systems and exposure to various antigens <sup>[11]</sup>.

To address these intricate issues, various nutritional strategies have been explored in piglet rearing to enhance health and growth. Glucans, specifically  $\beta$ -glucans derived from sources like seaweed, mushrooms, cereals, and yeast, have gained attention for their potential to alleviate some of the weaning-related challenges. Additionally, the roles of Vitamin D and selenium, two essential nutrients, are emerging as important factors in piglet nutrition.

Casein hydrolysates, which are derived from milk protein casein, are also gaining attention as potential alternatives to antibiotic growth promoters in pig nutrition. Understanding the underlying physiological changes during this critical phase is vital for developing effective nutritional strategies. Until recently, the main focus on finding alternatives to in-feed antibiotic growth promoters and zinc oxide has been on dietary manipulations in pigs post-weaning using feed additives in the post-weaning diet.

## 2. The Physiological and Immunological Implications of Weaning on Piglets

Weaning is a critical period characterized by considerable stress, influencing the piglet's gut microbiology, immunology, and physiology, which in turn impacts growth, intake, and health [3]. Environmental changes, dietary shifts, and social reorganization contribute to this stress. Unlike the gradual weaning process observed in the wild, commercial weaning procedures are abrupt, potentially increasing health risks due to the piglet's reliance on maternal antibodies [12]. During the suckling period, the piglet's gut microbiota is significantly influenced by the constituents of milk, which promotes the growth of bacterial families such as *Bacteroidaceae*, *Clostridiaceae*, *Lachnospiraceae*, and *Lactobacillaceae* [13]. However, with the introduction of solid feed and cessation of milk at weaning, substantial changes occur in the intestinal microbiota composition, demonstrated by the emergence of substantial shifts in the population dynamics of gut bacteria [14]. The weaning transition, coupled with a decline in lactose availability, results in higher gastric pH levels, reducing the natural barrier to enteric infections [1][15]. Concomitantly, there is a decrease in beneficial microbes such as *Lactobacillus*, alongside an increase in opportunistic pathogens, including *Clostridium* and *E. coli*, the latter of which plays a pivotal role in the etiology of PWD [16][17]. As the piglet matures, the GIT microbiota diversifies and stabilizes, approximating an adult-like composition by three weeks post-weaning, characterized by a higher abundance of *Prevotellaceae*, *Ruminococcaceae*, *Lactobacillaceae* and *Veillonellaceae*, with a concurrent reduction in *Enterobacteriaceae* and *Bacteroidaceae* [18].

Following weaning, intestinal morphological changes, such as fluctuations in villous height and crypt depth, affect the organ's absorptive function and overall health [19]. Optimal nutrient uptake is compromised by the reduced activity of digestive enzymes such as lactase, sucrase, and maltase, which are critical for carbohydrate digestion [7][20]. These physiological alterations are further aggravated by disruptions to the intestinal barrier, mediated by the inflammatory response, and characterized by weakened tight junctions between epithelial cells [10][21]. Additionally, stress mediators, including cortisol and corticotropin-releasing factors, have been implicated in neuro-immune interactions that adversely affect gastrointestinal functionality [6]. Post-weaning also sees a marked reduction in feed intake, with subsequent negative repercussions for gastrointestinal health and growth [7]. Furthermore, PWD, primarily caused by *E. coli*, poses a significant challenge in pig production. The enterotoxigenic strains of this bacterium bind to the intestinal epithelium, facilitated by fimbriae such as F4 and F18, leading to infection and diarrheal outbreaks [22][23]. Various management strategies that focus on nutrition and the weaning process itself are critical for minimizing these episodes [17]. In summary, weaning represents a developmental stage with profound implications for the gastrointestinal health of piglets. Effective management of this phase, including the

understanding of associated stressors and implementation of nutritional interventions, is essential to promote health and growth in piglets, with the added benefit of reducing the need for medicinal supplements such as zinc oxide and in-feed medication in pig production.

### 3. Exploring Natural Dietary Interventions to Address Dysbiosis in Pig Nutrition

This research delves into the evolving dynamics and challenges within the pig industry, placing a strong emphasis on advancing the health and growth of weaned piglets. A central theme revolves around exploring natural compounds and nutrients as potential dietary supplements for pigs, with a particular focus on the advantages associated with incorporating  $\beta$ -glucans, casein hydrolysates, mushrooms, Vitamin D, and selenium and their synergisms into piglet and sow diets. These natural compounds are acknowledged for their multifaceted properties, encompassing anti-inflammatory, antimicrobial, antioxidant, immunomodulatory, and prebiotic effects. The research emphasizes the major role of maternal nutrition in shaping the health and well-being of piglets, examining how maternal dietary interventions significantly impact piglet development and resilience, both before and after weaning. Another aspect of the research lies in its examination of the unique capabilities of mushrooms, specifically their ability to synthesize Vitamin D and convert inorganic selenium into highly bioavailable organic forms. This positions mushrooms as invaluable additions to pig diets, presenting opportunities to enhance piglet health and performance post-weaning. The research stresses the importance of understanding the underlying mechanisms governing the functional properties of these feed ingredients. Key aspects of gut functionality, including digestive and absorptive capacity, villi architecture, nutrient transporter expression, chemical and physical barriers, microbiota diversity, and immune function, are considered to achieve an optimal response to these dietary interventions <sup>[11][24]</sup>.

### 4. Structural Specificity and Health Impact of Beta-Glucans in Pig Nutrition

The role of  $\beta$ -glucans in pig nutrition is increasingly recognized for its profound impact on enhancing the immune response and overall health of pigs. These naturally occurring polysaccharides, comprised of glucose molecules linked by  $\beta$ -glycosidic bonds, display a structural diversity that is crucial to their functionality. Depending on their botanical or microbial origin, ranging from cereals like barley and oats to yeasts and mushrooms—the arrangement of these linkages can be primarily 1,3, 1,4, or 1,6, each conferring different physical properties and biological activities. For example, the  $\beta$ -glucans from mushrooms have a 1,3 backbone with 1,6-linked side chains, a structure that has been shown to potentiate immune response through various mechanisms, including the activation of macrophages and other immune cells <sup>[25]</sup>. Yeast-derived  $\beta$ -glucans, with a higher proportion of 1,3 linkages, have been found to enhance pathogen recognition by the immune system <sup>[26]</sup>. Conversely, the  $\beta$ -glucans found in cereals, primarily with 1,3 and 1,4 linkages, exhibit a solubility that can influence gut health, which in turn can have a systemic effect on the immune status of pigs <sup>[27]</sup>. This specificity necessitates a nuanced approach to dietary inclusion, where factors like source, purity, solubility, synergisms, and molecular mass must be carefully

considered to ensure the  $\beta$ -glucans incorporated into pig feeds are optimized for the best possible health outcomes [28]. In essence, the structural complexity of  $\beta$ -glucans dictates their potential as a functional feed additive in pig nutrition.

Importantly, all three types of  $\beta$ -glucans have been linked to improved growth performance and feed efficiency in pigs, operating through distinct mechanisms. Yeast and seaweed-derived  $\beta$ -glucans likely enhance growth by boosting health and disease resistance, while cereal-derived  $\beta$ -glucans improve growth through better gut health and nutrient absorption. The selection of  $\beta$ -glucan source should be guided by specific production goals, like enhancing immune function, improving gut health, or optimizing growth performance in pigs.

## 5. Yeast-Derived $\beta$ -Glucans: Enhancing Swine Nutrition and Health during Weaning

### 5.1. Immunomodulatory Potential of Yeast-Derived $\beta$ -Glucans

$\beta$ -Glucans, a class of vital polysaccharides, have gained increasing recognition for their health-promoting roles in functional foods and animal nutrition. These molecules are diverse and can be found in various sources, including bacteria, fungi, algae, and cereals, each displaying unique structural attributes. Yeast-derived  $\beta$ -glucans are characterized by having  $\beta$  (1,6)-linked branches on a  $\beta$  (1,3) backbone, in contrast to the primarily linear  $\beta$  (1,4) linkages interspersed with  $\beta$  (1,3) chains typically found in cereal  $\beta$ -glucans [25]. One of the prominent features of yeast-derived  $\beta$ -glucans is their capacity to stimulate the immune system, as they activate a wide range of immune cells, including macrophages, T helper cells, and natural killer cells [29]. This immune activation occurs through their interaction with pattern recognition receptors, which identify these polysaccharides as pathogen-associated molecular patterns, therefore triggering innate immune responses [30][31]. Among these receptors, Dectin-1 plays a crucial role in recognizing  $\beta$ -glucans and initiating immune responses, encompassing processes such as phagocytosis, oxidative burst, and cytokine production [32][33][34].

The immunomodulatory activity of  $\beta$ -glucans is significantly influenced by their structure and solubility. Insoluble  $\beta$ -glucans activate the dectin-1 pathway, while soluble forms often interact with the complement system, with their action being dependent on specific antibodies [33]. The effectiveness of dectin-1 receptor activation by  $\beta$ -glucans requires a  $\beta$  (1,3) backbone of sufficient length, typically consisting of at least seven glucose units, and often necessitates at least one  $\beta$  (1,6)-side-chain branch [33].

### 5.2. Enhancing Growth Performance with Yeast-Derived $\beta$ -Glucans

In the field of pig nutrition,  $\beta$ -glucans, particularly those derived from yeast, have been associated with improved growth performance in weaned pigs. Multiple studies have demonstrated that  $\beta$ -glucans sourced from organisms like *Agrobacterium* spp. and yeast can positively influence the gut microbiota, increasing the abundance of beneficial bacterial taxa such as *Lactobacillus* while reducing harmful species like *E. coli* [28][35][36][37][38][39]. Moreover, yeast  $\beta$ -glucans are known for their anti-inflammatory and antioxidant properties, which may provide

added resilience against chronic inflammation and oxidative stress. A recent meta-analysis [40] quantified these benefits, revealing a 7.6% increase in weight gain and a 5.3% increase in feed intake among nursery pigs fed with yeast  $\beta$ -glucans sourced from *Saccharomyces cerevisiae*. Even more substantial growth improvements were observed with *Agrobacterium*-derived  $\beta$ -glucans. The meta-analysis recommended an optimal use of 50 mg/kg of *Saccharomyces cerevisiae*-derived  $\beta$ -glucans in nursery pig diets based on these findings [40].

Kim et al. [39] observed that dietary  $\beta$ -glucans led to a substantial improvement in the daily gain of weaned pigs, with this improvement attributed to enhanced nutrient absorption and improved intestinal health. These findings align with previous research [37], which noted an enhancement in feed conversion ratios with  $\beta$ -glucan supplementation. The pivotal role of  $\beta$ -glucans in promoting gut health has been well emphasized [41].  $\beta$ -glucans contribute to maintaining the integrity of the gut barrier and support the establishment of a healthy gut microbiome [41], which is critical for preventing post-weaning diarrhea. Additionally,  $\beta$ -glucans also have the potential to alleviate weaning stress in pigs [40]. This study revealed that  $\beta$ -glucans reduced stress-related behaviors and improved feed intake in post-weaned pigs, a factor crucial for ensuring steady growth during the post-weaning period. Research on  $\beta$ -glucans from *Agrobacterium* sp. ZX09, known for its high purity compared to yeast, has shown positive effects on weaned piglet growth and intestinal health [42]. Both low and high molecular weight  $\beta$ -glucans from *Agrobacterium* sp. ZX09 enhanced piglet growth, emphasizing the importance of source and purity. Low molecular weight  $\beta$ -glucans had strong antioxidant effects, improved mucosal barrier function, and positively affected gut microbiota. High molecular weight  $\beta$ -glucans specifically benefited hindgut bacteria [42].

In summary, current research provides compelling evidence for the significant advantages of incorporating microbial  $\beta$ -glucans, particularly those derived from yeast and bacteria, into the diets of nursery pigs. These  $\beta$ -glucans contribute to enhanced growth, intestinal health, and immune function, ultimately resulting in improved growth performance and overall well-being.

## 6. The Role of Cereal-Derived $\beta$ -Glucans in Piglet Diets

### 6.1. Impact on Gastrointestinal Microbiota

Cereal  $\beta$ -glucans have a significant impact on the gastrointestinal microbiota of pigs, enhancing beneficial bacteria populations such as *Lactobacillus* and *Bifidobacteria*, which are vital to pig health [43]. These polysaccharides also modulate the cycling of nutrients within the pig's system, as indicated by their effect on the excretion patterns of urinary and fecal nitrogen, suggesting improved nutrient utilization [44]. Moreover,  $\beta$ -glucans have been shown to contribute to the reduction of emissions from pig manure, aligning pig-farming practices with environmental sustainability goals [45][46]. However, the inclusion of high levels of intact  $\beta$ -glucans may impede nutrient digestibility, potentially affecting the economic efficiency of pig nutrition [44]. Studies by Metzler and Zebeli [46] have correlated high  $\beta$ -glucan content with a decrease in the apparent ileal digestibility and the total tract digestibility of crude protein and energy, highlighting the necessity for careful dietary inclusion to prevent negative effects on nutrient utilization. At optimal concentrations, cereal  $\beta$ -glucans can increase caecal volatile fatty acids and butyrate levels, conferring a gut health advantage [46]. However, their water-soluble nature can also lead to increased

digesta viscosity, which may interfere with feed digestion and nutrient absorption, a concern particularly relevant to the growth and health of nursery pigs [46].

## 6.2. Structural Configurations and Physiological Impact

The structural configurations of  $\beta$ -glucans, especially the ratios of  $\beta$  (1,3) to  $\beta$  (1,4) linkages, are key determinants in their physicochemical properties, influencing their solubility and the extent of microbial degradation in the pig's gastrointestinal tract [47]. A higher ratio of  $\beta$  (1,3) linkages is known to increase solubility and viscosity, impacting the digestive process. The concentration and solubility of  $\beta$ -glucans differ among cereal grains; for instance, barley has a higher  $\beta$ -glucan content in its endosperm and is characterized by a greater proportion of water-insoluble  $\beta$ -glucans compared to oats [48].

Meta-analytic insights indicate inconsistent growth and feed intake responses to dietary cereal  $\beta$ -glucans [40], suggesting that while certain levels can promote intestinal health, demonstrated by prebiotic effects that bolster beneficial gut microbiota and reduce pathogenic bacteria adhesion, the responses are not uniform. The source of  $\beta$ -glucans plays a significant role; oat-derived  $\beta$ -glucans affect gut microbiota differently from barley-derived  $\beta$ -glucans [48][49]. Therefore, formulating pig diets with  $\beta$ -glucans requires a strategic approach that considers both the type and amount, particularly in cases of soluble  $\beta$ -glucans from barley that could heighten digesta viscosity and associate with digestive issues such as PWD [40]. By contrast, the research of Bach Knudsen and Jørgensen [50] underlines the importance of soluble fiber  $\beta$ -glucans in improving the gut environment of weaned pigs. These fibers increase the viscosity of gut contents, which slows the passage rate and facilitates better nutrient absorption, which is beneficial during the weaning phase when pigs are prone to nutritional upsets and often exhibit inefficient digestion. Therefore, the formulation of pig diets with cereal  $\beta$ -glucans calls for a strategic approach that weighs the type and amount, particularly in the case of soluble  $\beta$ -glucans from barley that could increase digesta viscosity and be associated with digestive issues such as PWD [40].

# 7. Seaweed: A Sustainable $\beta$ -Glucan Source for Swine Nutrition

## 7.1. Immunomodulatory Benefits of Algae $\beta$ -Glucan

Algae-derived  $\beta$ -glucans are attracting increasing attention as a promising dietary supplement for weaned pigs, offering unique advantages for both growth and health during this crucial developmental stage. One of the primary advantages of incorporating algae  $\beta$ -glucans into the diets of piglets lies in their substantial immunomodulatory capabilities. Algae-derived  $\beta$ -glucans play a vital role in boosting the immune response of weaned pigs [24][51]. This enhancement of the immune system is of paramount importance as it contributes to reducing the occurrence of common post-weaning issues such as diarrhea and respiratory infections. By fortifying the immune defenses, algae  $\beta$ -glucans provide piglets with increased resilience against the microbial threats they encounter in the post-weaning phase [24].



## 7.2. Laminarin: Antibacterial and Prebiotic Effects

Laminarin, a low molecular weight  $\beta$ -glucan found in various seaweeds, is particularly noteworthy for its antibacterial activity. It is characterized by a linear backbone of (1,3)- $\beta$ -linked glucopyranose residues with varying  $\beta$ -(1,6)-branching [52][53]. The water solubility of laminarin is influenced by its branching levels, and it accumulates in algal cells during specific seasons to support survival and growth during adverse conditions, such as winter. Laminarin has demonstrated antibacterial properties against a wide range of bacteria in vitro, including pathogenic strains like *E. coli*, *S. Typhimurium*, *L. monocytogenes*, and *St. Aureus* [52][54]. This antibacterial activity extends to purified laminarin extracted from various seaweed species, with a more pronounced effect observed against Gram-negative bacteria [55][56].

When applied in pig nutrition, the inclusion of laminarin-rich extracts in the diet has been associated with reduced populations of *Enterobacteriaceae* and attaching-effacing *Escherichia coli* (AEEC) in the caecum and colon of weaned pigs [57][58]. Moreover, laminarin exhibits prebiotic activity, as demonstrated by an increase in the populations of beneficial *Lactobacillus* species in pig colonic and fecal microbiota following supplementation with both crude and highly purified laminarin-rich extracts [59]. Additionally, investigations in weaned pigs have revealed an increased relative abundance of *Prevotella* spp. following laminarin supplementation, which has been correlated with improved pig performance and maturity [60].

The impact of laminarin supplementation goes beyond microbiota modulation and extends to the production and profiles of short-chain fatty acids (SCFAs) in the gastrointestinal microbiota, particularly affecting butyrate production [35][61]. The SCFAs, including butyrate, are crucial for gut health and have been linked to various physiological benefits. In terms of immunomodulatory activity, dietary supplementation with crude or highly purified laminarin-rich extracts has demonstrated an anti-inflammatory effect on the small intestine and colon of weaned and growing pigs [35]. This anti-inflammatory effect is characterized by the reduced expression of pro-inflammatory cytokine genes, pattern recognition receptors, and the transcription factor NF $\kappa$ B1 [62]. In the colon, laminarin has an immunosuppressive effect, primarily down-regulating genes associated with the Th17 pathway [63]. Furthermore, laminarin-rich extracts have been associated with several performance improvements in weaned pigs, including enhanced final body weight, daily gain, feed intake, and gain-to-feed ratio [63][64]. Additionally, laminarin supplementation has proven effective in reducing diarrhea, particularly in the post-weaning period, as indicated by lower fecal scores in supplemented weaned pigs [57][64]. Importantly, under both hygienic and unsanitary conditions, laminarin-rich extracts have shown promise in reducing the incidence of post-weaning diarrhea and improving daily gains, making them a potential dietary alternative to antibiotic growth promoters and zinc oxide for managing post-weaning diarrhea in pigs [61].

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