

# Dietary strategies and feed additives to mitigate the infections caused by *Streptococcus suis* in weaned piglets.

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## 1. Introduction

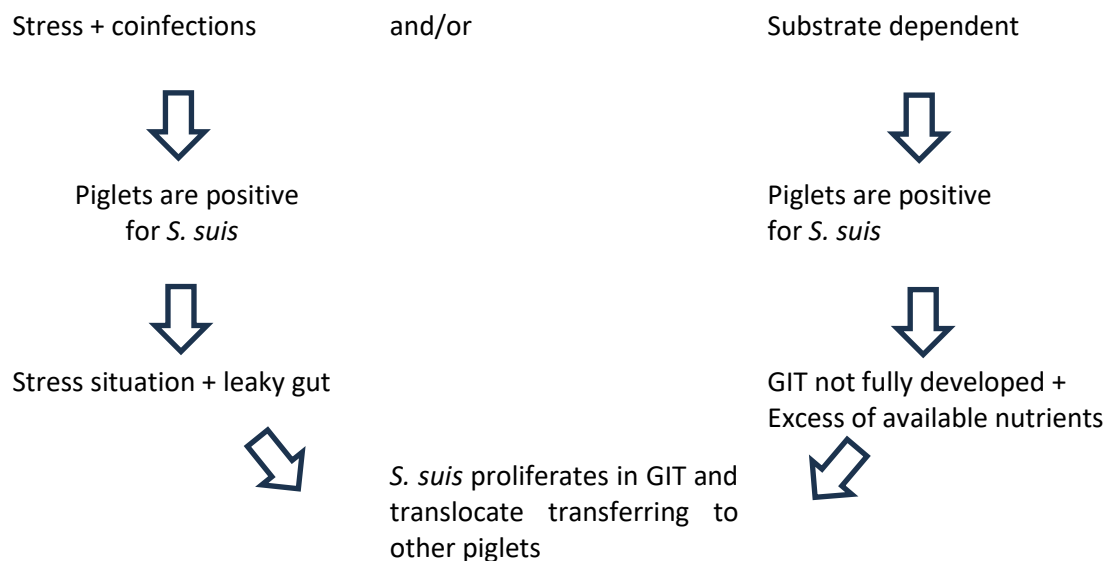
*Streptococcus suis* (*S. suis*) is a Gram-positive bacterium that ranks among the leading post-weaning killers of pigs, causing meningitis, arthritis and septicemia and provoking major economic losses. Because the organism is a frequent commensal of the upper airways and tonsils, eradication is difficult, and rising antimicrobial-resistance urges for non-antibiotic solutions.

*S. suis* is not a problem during lactation, although they are contaminated by the sow after farrowing, because the piglets have an immature microbiota, there are antibacterial compounds in the milk of the sow, maternal antibodies and probably a too low dose of bacteria to infect them. To cause clinical infections *S. suis* must:

- Adhere and colonize the host cells. *S. suis* can be transported by immune cells to the blood stream, reaching the lymph nodes and the brain or the joints,
- Invade and pass through the host epithelial barrier,
- Spread in connective tissues and lymphatic system and survive in the blood stream and
- Infect different organs.

All the piglets are positive against *S. suis* but not all of them are positive to the pathogenic strains of *S. suis*. Nose-to-nose contact in piglets after weaning is the main transmission route. Vectors as flies can carry *S. suis*.

There is currently one hypothesis to describe the infections of *S. suis*:



Nutrition can modulate the two main “windows of opportunity” that *S. suis* exploits after weaning:

- **Gastric barrier failure** – fine-ground, highly buffered feeds raise stomach pH, allowing *S. suis* to survive gastric passage, whereas coarser meals keep pH  $\leq 3$  and clear the pathogen.
- **Intestinal dysbiosis and inflammation** – excess undigested nutrients, oxidative stress and loss of maternal immunity favour bacterial translocation and systemic spread.

The following evidence-based feed interventions target these weaknesses and can be combined into an integrated formula.

## 2. Nutritional strategies

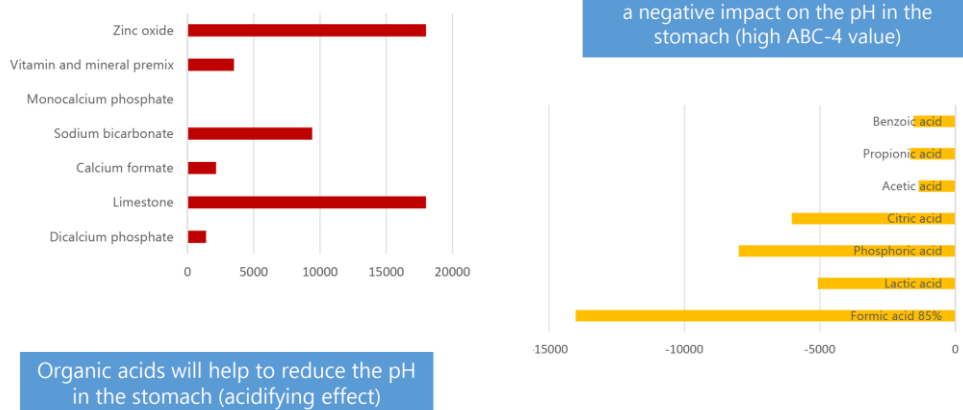
### 2.1 Feed particle size and structure

Grinding feed too finely ( $< 500 \mu\text{m}$ ) elevates gastric pH to  $\sim 5$ , enabling *S. suis* survival, while a coarsely ground meal maintains pH  $\approx 2.5$  and kills the pathogen within minutes. Coarser particles also prolong gastric retention and stimulate stomach function, reinforcing the acid barrier. Recommendation: mean particle size 600–700  $\mu\text{m}$ ; restrict pelleting pressure or include 20 % mash meal in the feed of piglets at risk or in herds with historical clinical symptoms or feeding coarse feed not pelleted in herds with high risk or historical records of *S. suis* infections

### 2.2 Dietary organic acids and buffer control

Stomach pH is governed by the diet's acid-binding capacity (ABC). Limestone, dicalcium phosphate and sodium bicarbonate are potent buffers, whereas formic, lactic and phosphoric acids lower ABC and acidify the chyme. Diets supplemented with protected formic acid (0.4–0.6 %) eliminated *S. suis* in the stomach and prevented oro-gastro-intestinal infection in vivo. Recommendation: formulate low-ABC diets, replace part of limestone with calcium formate and add 0.5 % micro-encapsulated formic / lactic acid.

Figure 1: Acid binding capacity (ABC, meq/kg)



*Ex-vivo* trials showed that *S. suis* serotypes 2 and 9 were cleared from porcine stomach contents within 60 minutes at pH 5.0 and within 30 minutes at pH 4.7, regardless of the bacterial growth phase. In a separate study, serotypes 2 and 9 were completely eliminated after 1 hour at pH 4.0 in Todd-Hewitt broth acidified with formic acid.

Blending OAs with different pKa values can create synergistic effects and maximise digestive health benefits.

Supplementing sows with a combination of OA and MCFA lowered *S. suis* counts and increased *Lactobacillus* spp. in the faeces of their piglets at weaning, indicating reduced vertical transmission.

### 2.3 Medium-Chain Fatty Acids (MCFA) and lauric acid delivery and monolaurin

- Efficacy and mode of action: MCFA—especially lauric acid (LA) and its monoglyceride derivative, glycerol monolaurate (GML)—display the strongest antimicrobial activity. Their primary mode of action is disruption of the bacterial cell membrane, making the development of resistance unlikely. MCFA can also modulate gut health by regulating IL-6 and TNF- $\alpha$  levels, improving intestinal morphology and function, and exerting immunomodulatory effects. Monolaurin has been shown to block staphylococcal exotoxin production and interfere with signal transduction, thereby inhibiting  $\beta$ -lactamase synthesis and the expression of virulence factors. Lauric acid itself has proven equally effective as monolaurin in these inhibitory effects.
- Sources: Coconut and palm oils are the principal natural sources of LA. However, certain edible insects—most notably *Hermetia illucens* (black soldier fly)—are attracting interest as feed ingredients because of their high LA content and other bioactive components. Meals derived from *H. illucens* have been effective in reducing *D*-streptococci and *Streptococcus* spp. while increasing *Lactobacillus* and *Bifidobacterium* in weaned piglets.
- Application: A combination of MCFA and a natural anti-inflammatory agent has been as effective as amoxicillin in lowering the prevalence of clinical signs consistent with *S. suis* infection in weaned piglets.
- Challenges and solutions: Direct inclusion of MCFA can be hampered by low stability, poor palatability, and limited availability in the lower intestine. Microencapsulation is a promising strategy that stabilizes MCFA, enables slow and targeted release in the desired intestinal regions, and improves ingredient protection during storage.

### 2.4 Spray-Dried Porcine Plasma (SDPP)

SDPP provides high levels of immunoglobulins (IgG, IgM) and bioactive peptides that neutralise pathogens, down-regulate cytokine storms and improve gut barrier integrity. Meta-analyses show 5 % SDPP lowers post-weaning mortality and reduces systemic inflammation markers; inclusion up to 6 % is practical in the first 14 days post-weaning. For herds with historical data of *S. suis* infection is highly recommended the inclusion of SDPP at least at 3 % with the rest of the measures mentioned in this report.

### 2.5 Functional fibre – Alfalfa Inclusion

A moderate (1.3 %) inclusion of alfalfa in creep feed increased *Clostridium* cluster XIVb and *Sporobacter termitidis* and—critically—produced the lowest abundance of *S. suis* in both caecum and distal colon of suckling piglets. Likely mechanisms include butyrate production and competitive exclusion. Recommendation: 1.0% to 1.5% % milled dehydrated alfalfa in creep and

prestarter feeds; maintain an insoluble: soluble fibre ratio < 1 during the first week after weaning to avoid overload.

This effects of fibre inclusion in weaned piglets have been shown in different studies. Using dietary fibre in post-weaning diets is controversial, but moderate levels of inert, non-fermentable fibre (ICHO) are recommended to dilute the diet, prevent diarrhoea, enlarge stomach capacity and help restore brush-border enzyme activity—thereby limiting pathogenic bacterial overgrowth in the small intestine. In contrast, high levels of fermentable fibre (FCHO) can pose an additional health and growth risk immediately after weaning, especially under poor sanitary conditions.

Feed particle size strongly influences gastric function. Coarser feed promotes a lower stomach pH and better nutrient digestion, reducing the risk of gastrointestinal infections. In contrast, finely ground particles raise gastric pH and facilitate *S. suis* colonisation in the stomach.

## 2.6 Antioxidants (Vitamin E, selenium, and bioflavonoids)

- **Managing oxidative stress:** Weaning induces oxidative stress, which can exacerbate the pathogenicity of *S. suis*. Field experience shows that adding primary antioxidants to pre- and post-weaning diets helps curb pathogen spread and lessen tissue damage.
- **Immune support:** Combined supplementation with vitamin E and selenium exerts synergistic effects on immune function. During the post-weaning window (days 7–14), serum levels of both nutrients drop sharply, a change associated with higher mortality.
- **Citrus bioflavonoids:** Powerful antioxidants with anti-inflammatory and immunomodulatory properties; they support epithelial health and enhance productive performance. Citrus bioflavonoids such as hesperidin, naringin and their aglycones act as potent scavengers of reactive oxygen species and activate the Nrf2-antioxidant response while simultaneously dampening NF- $\kappa$ B-driven cytokines (IL-1 $\beta$ , TNF- $\alpha$ ). This dual antioxidant/anti-inflammatory action protects gut epithelium and limits the tissue damage that amplifies *S. suis* septicaemia. Beyond host support, several flavonoids (e.g., fisetin, myricetin) have been shown to directly weaken *S. suis* serotype 2 virulence by inhibiting the pore-forming toxin sullysin, thereby reducing haemolysis and lethality in experimental models. Recent piglet studies further report that dietary citrus flavonoids improve villus height, strengthen tight-junction protein expression and skew TLR2/NF- $\kappa$ B signalling toward a less inflammatory phenotype, translating into better growth and a lower pathogen load after weaning. Together, these properties make citrus bioflavonoids a valuable adjunct for mitigating oxidative stress, inflammation and toxin-mediated damage during *S. suis* outbreaks in piglets.

## 2.7 Nucleotides

- **Intestinal repair and immune function:** Purified nucleotides promote intestinal regeneration and strengthen immune responses.
- **Documented benefits:** Maternal nucleotide supplementation improves intestinal morphology and immunity in newborn piglets challenged with lipopolysaccharide. Nucleotides also increase villus height, boost antibody production, and speed recovery from intestinal lesions.

## 2.8 Prebiotics and Probiotics

- **Microbiota and immunity modulation:** Mannan-oligosaccharides (MOS) and  $\beta$ -glucans interact with phagocytic cells, prevent bacterial adhesion, and act as immunostimulants by engaging macrophages, granulocytes, and natural killer cells.
- **Gut-health effects:** Oral supplementation with prebiotics (e.g., inulin,  $\beta$ -glucans, other oligosaccharides) and functional amino acids (e.g., glutamine) can produce lasting improvements in intestinal morphology and function. Fructo-oligosaccharides and galacto-oligosaccharides exhibit bifidogenic effects, strengthen the intestinal barrier, and modulate barrier- and immunity-related gene expression.

## 2.9 Copper hydroxychloride

Copper hydroxychloride has been investigated as a nutritional strategy to mitigate the effects of *S.suis* infections in weanling piglets. Its benefits are attributed chiefly to a direct antimicrobial effect and to modulation of the intestinal microbiota.

- **Reduction of *Streptococcus spp.* counts:** A study by Villagómez-Estrada et al. (2020) reported that copper hydroxychloride, compared with copper sulphate at 160 mg kg<sup>-1</sup>, lowered the abundance of *Streptococcus spp.* in the large intestine of piglets. Similar findings indicate that non-ionic copper sources (hydroxychloride) reduce *Streptococcus* levels in the gut.
- **Antimicrobial mode of action:** The observed decline in *Streptococcus spp.* suggests a direct antimicrobial activity of copper hydroxychloride, which may help curb intestinal colonisation by the pathogen.
- **Modulation of the intestinal microbiota:** In addition to direct antimicrobial effects, copper hydroxychloride can help reshape the gut microbiota. By shifting microbial populations, it may create an environment less favourable for the growth and proliferation of *S. suis*.

When formulating nutritional products, inclusion of copper hydroxychloride at authorised levels (around 160 mg kg<sup>-1</sup>) is recommended to reduce intestinal colonisation. Nonetheless, local regulations governing mineral use in animal feed must be respected because of potential environmental and food-safety implications.

## 4. Conclusion

*Streptococcus suis* exploits two main vulnerabilities after weaning: loss of the gastric acid barrier and post-weaning intestinal dysbiosis/inflammation. An integrated nutritional programme should therefore (1) keep stomach pH  $\leq 3$ , (2) limit readily fermentable substrates, and (3) reinforce mucosal immunity while exerting direct antimicrobial pressure.

The following list is a sort of recommendation to produce diets for piglets at high infection *S. suis* in a decreasing power:

- **Physical feed structure** (600–700  $\mu\text{m}$ , coarse mash) is the first line of defence, ensuring rapid bactericidal action in the stomach.

- **Low-buffer organic-acid blends** acidify the chyme and synergise with other bactericidal agents; protected formic/lactic acids at 0.5 % are practical.
- **MCFAs, especially lauric acid or monolaurin—optionally supplied via black-soldier-fly meal—** disrupt bacterial membranes and down-regulate virulence; micro-encapsulation secures distal delivery.
- **Spray-dried porcine plasma** supplies functional IgG and IgM and anti-inflammatory peptides, cutting mortality during the critical first 14 days.
- **Alfalfa-based functional fibre** fosters butyrate producers and competitively excludes *S. suis* in the large intestine; inclusion of 1–1.5 % is sufficient.
- **Copper hydroxychloride** at 160 mg Cu kg<sup>-1</sup> offers an additional non-antibiotic antimicrobial lever, provided local environmental limits are respected.
- **Antioxidant support** (200 IU Vit E kg<sup>-1</sup> + 0.3 ppm Se + 150–300 ppm citrus bioflavonoids) mitigates weaning-induced oxidative stress, blunts inflammatory cascades and directly neutralises the suilyisin toxin.
- **Nucleotide enrichment** accelerates villus repair and enhances secretory immunity; benefits are amplified when provided to both sows and piglets.
- **Pre- and probiotics** (MOS,  $\beta$ -glucans, FOS/GOS, selected *Lactobacillus* strains) maintain a resilient microbiome and reinforce barrier function.

Field application of this multi-modal formula has consistently reduced clinical signs and pathogen shedding, offering producers a robust alternative to preventive antibiotics while supporting growth and feed efficiency in modern, high-performance pig herds.

## 5. Summary Table

Nutritional strategy	Mode of action	Practical inclusion / Dose	Key Evidence / Outcomes
Feed Particle Size & Structure	Keeps gastric pH $\leq 3$ , increases retention time, mechanical stomach stimulation	600–700 $\mu\text{m}$ mean particle size; $\geq 20\%$ mash meal or coarse meal	Fine < 500 $\mu\text{m}$ raises pH $\sim 5$ and allows <i>S. suis</i> survival; coarse particles kill within minutes
Dietary Organic Acids & Buffer Control	Lower diet ABC, acidify stomach, bactericidal and synergistic blend effects	0.4–0.6 % protected formic acid; 0.5 % encapsulated OA; low-ABC formulation	Serotypes 2 & 9 cleared within 60 min at pH 5; OA+MCFA in sows reduced piglet <i>S. suis</i> shedding
MCFA (Lauric Acid / Monolaurin incl. Insect-Derived)	Membrane disruption, immunomodulation, anti-virulence toxin inhibition	0.3–0.4 % protected LA or 1–3 $\text{kg t}^{-1}$ MCFA blend; 5–8 % <i>H. illucens</i> meal	MCFA + phyto blend matched amoxicillin; insect meal lowered Streptococci, raised Lactobacillus
Spray-Dried Porcine Plasma (SDPP)	Passive IgG/IgM, anti-inflammatory peptides, barrier protection	3–6 % first 14 d post-weaning (typical 5 %)	Meta-analysis: $\downarrow$ mortality, $\downarrow$ cytokines; recommended in herds with <i>S. suis</i> history
Functional Fibre – Alfalfa	Prebiotic butyrate producers, competitive exclusion of pathogens	1.0–1.5 % dehydrated alfalfa; keep insoluble:soluble < 1	1.3 % alfalfa yielded lowest <i>S. suis</i> in caecum & colon; supports Clostridium XIVb
Antioxidants (Vit E, Se, Bioflavonoids)	Scavenge ROS, activate Nrf2, suppress NF- $\kappa$ B cytokines, inhibit suilysin	150–200 IU Vit E $\text{kg}^{-1}$ + 0.3 ppm Se; 150–300 ppm citrus bioflavonoids	Improved villus height, $\downarrow$ IL-1 $\beta$ /TNF- $\alpha$ , $\downarrow$ toxin activity, better growth under challenge
Nucleotides	Accelerate mucosal repair, enhance antibody synthesis	0.1 % in piglet feed; 1 $\text{g kg}^{-1}$ in late gestation-lactation sow diets	$\uparrow$ villus height, $\uparrow$ IgA, faster recovery from lesions; maternal transfer benefits
Prebiotics & Probiotics	Modulate microbiota, block adhesion, stimulate innate immunity	0.2–0.5 % MOS / $\beta$ -glucans / FOS / GOS; functional aa (glutamine)	$\uparrow$ Lactobacillus, strengthened barrier, reduced pathogen load in Safe-concept diet
Copper Hydroxychloride	Direct antimicrobial, shifts gut microbiota	$\approx 160 \text{ mg Cu kg}^{-1}$ (regulatory max) as hydroxychloride	Lower Streptococcus spp. in large intestine vs $\text{CuSO}_4$ ; aids colonisation control

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