Dietary interventions for resilient poultry gut health in the AMR era

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Gut health is critical for profitable poultry production, as the gastrointestinal tract (GIT) plays a dual role in nutrient digestion and absorption while serving as a crucial defense against pathogens. A healthy gut enables efficient feed conversion, robust immune function, and resilience against diseases, reducing reliance on preventive and therapeutic antibiotics. Optimum gut health has become increasingly important in poultry production to combat antimicrobial resistance (AMR), a pressing global challenge threatening animal agriculture and public health.

AMR arises when bacteria develop antibiotic resistance, often due to overuse or misuse in human and animal settings. Predictive models suggest that by 2050, AMR could result in 10 million annual deaths and a 2.0%–3.5% reduction in global gross domestic production, amounting to economic losses between 60 and 100 trillion USD. In poultry, AMR compromises flock health, leading to higher mortality, reduced growth performance, and elevated treatment costs, directly impacting profitability. Additionally, resistant pathogens increase the risk of zoonotic disease transfer, posing serious food safety concerns.

Stricter regulations and rising consumer demand for antibiotic-free poultry products drive a shift toward sustainable, antibiotic-free production systems. However, A lack of understanding about strategies to replace AMU and their effectiveness under field conditions hampers change in farming practices (Afonso et al., 2024). Addressing AMR requires a holistic approach, encompassing enhanced biosecurity, innovative health-promoting strategies, and sustainable management practices. This paper explores practical dietary interventions to support poultry gut health while reducing dependency on antimicrobials, offering solutions for the long-term sustainability of poultry production.

Gut Mediated Immunity in Chickens

The gut is a critical component of the immune system, as it is the first line of defense against pathogens that enter the body through the digestive system. Chickens have a specialized immune system in the gut, known as gut-associated lymphoid tissue (GALT), which helps to identify and respond to potential pathogens. The GALT includes Peyer's patches, clusters of immune cells in the gut wall, and the gut-associated lymphocytes (GALs) found throughout the gut. These immune cells recognize and respond to pathogens that enter the gut.

The gut-mediated immune response in chickens involves several mechanisms, including activating immune cells, producing antibodies, and releasing inflammatory mediators. GALT and GALs play a crucial role in this response by identifying and responding to pathogens and activating other immune cells to help fight off the infection.

The gut microbiome is a diverse community of microorganisms that live in the gut. These microorganisms can significantly impact the immune response. Certain beneficial bacteria, for example, can help stimulate the immune response and protect the gut from pathogens.

Overall, the gut microbiome, GALT, and GALs work together to create an environment hostile to pathogens while supporting the growth and health of beneficial microorganisms.

Key Factors Affecting Poultry Gut Health

The key factors affecting broiler gut health can be summarized as follows:

1. Early gut development: Gut-associated immunity responds to early feeding and dietary nutrients and is critical for protecting against exogenous organisms during the first week of life post-hatch.
2. Feed and Water Quality: The form, type, and quality of feed provided to broilers can significantly impact their gut health. Consistently available cool and hygienic drinking water is crucial for optimum production performance.
3. Stressors: Stressful conditions, such as high environmental temperatures or poor ventilation, can lead to an imbalance in the gut microbiome and an increased risk of disease.
4. Infections and medications: Exposure to pathogens or other harmful bacteria can disrupt the gut microbiome and lead to gut health issues. A robust immune system is important for maintaining gut health, as it helps to prevent the overgrowth of harmful bacteria and promote the growth of beneficial bacteria.
5. Biosecurity: Keeping the poultry environment clean and free of pathogens is crucial for maintaining gut health, as bacteria and other pathogens can quickly spread and disrupt the gut microbiome.
6. Management practices: Best practices, including proper litter management, can help maintain gut health and prevent gut-related issues.

Dietary Interventions for Optimum Gut Health

Gut health means the absence of gastrointestinal disease, the effective digestion and absorption of feed, and a normal and well-established microbiota (Bischoff, 2011). Various dietary measures can be taken to support the healthy functioning of the GIT and host defense. Water and feed safety and quality, feeding

management, the form the feed is provided in (e.g., pellets), the composition of the diet, and the use of various feed additives are all tools that can be used to support health (Smits et al., 2021).

Various gut health-supporting feed additives, including organic acids, probiotics, prebiotics, phytochemicals/essential oils, etc., in combination or alone, have been explored as an alternative to antimicrobials in animal production. There were differences in the impacts of the strategies between and within species; this highlights the absence of a 'one-size-fits-all' solution. Nevertheless, some options seem more promising than others, as their impacts were consistently equivalent or positive when compared with animal performance using antimicrobials (Afonso et al., 2024). Including insoluble fibers, toxin binders, exogenous enzymes, and antioxidants in the feed formulations also play a crucial role in gut health optimization, which goes beyond their primary functions to combat AMR challenges.

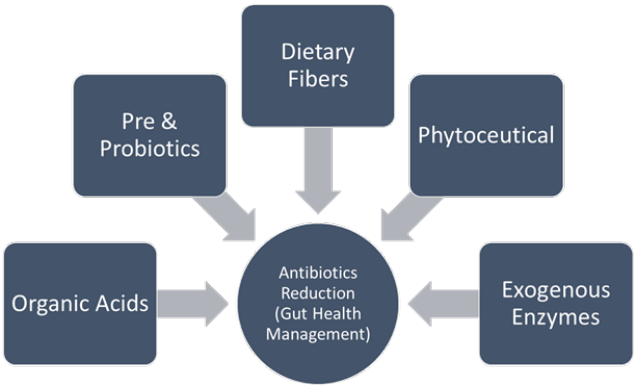


Fig. 1: Multifactorial approach to gut health management in reduced antimicrobial use

Organic Acids

The digestive process extensively includes microbial fermentation, and as a result, organic acids are commonly produced by beneficial bacteria in the crop, intestines, and ceca (Huyghebaert et al., 2010). Organic acids' inclusion in the poultry diet can improve growth performance due to improved gut health, increased endogenous digestive enzyme secretion and activity, and nutrient digestibility. Butyrate is highly bioactive in GIT. It increases the proliferation of enterocytes, promotes mucus secretion, and may have anti-inflammatory properties (Bedford and Gong, 2018; Canani et al., 2011; Hamer et al., 2008). These effects suggest that it supports mucosal barrier function. Butyrate is becoming a commonly used ingredient in diets to promote GIT health.

Including organic acids in the feed can decontaminate feed and potentially reduce enteric pathogens in poultry. Alternately, the formaldehyde treatment of feed is highly effective at a relatively low cost (Jones, 2011; Wales, Allen, and Davies, 2010).

Organic acids like formic and citric acid are also used in poultry drinking water to lower the microbial count by lowering the water's pH and preventing/removing biofilms in the water lines. By ensuring feed and water hygiene, producers can minimize pathogen exposure, enhance bird health, and significantly reduce their reliance on antibiotics.

Probiotics, Postbiotics, Prebiotics and Synbiotics

Probiotics and prebiotics have drawn considerable attention to optimizing gut health in animal feeds. Probiotic supplementation could have the following effects: (1) modification of the intestinal microbiota, (2) stimulation of the immune system, (3) reduction in inflammatory reactions, (4) prevention of pathogen colonization, (5) enhancement of growth performance, (6) alteration of the ileal digestibility and total tract apparent digestibility coefficient, and (7) decrease in ammonia and urea excretion (Jha et al., 2020). Certain Lactobacilli or Enterococci species may be used with newly hatched or newborn animals; single or

multi-strain starter cultures can be used to steer the initial microbiota in a desired direction (Liao and Nyachoti, 2017). Apart from using probiotics in feed and drinking water, probiotic preparations can be sprayed on day-old chicks in the hatchery or immediately after placement in the brooding house. This way, the probiotic strains/beneficial bacteria gain access to the gut at the earliest possible time (early seeding). Postbiotics are bioactive compounds produced by probiotics during fermentation, such as short-chain fatty acids, peptides, and bacterial cell wall components. Unlike live probiotics, postbiotics are stable, safer, and provide consistent health benefits.

Prebiotics like mannan-oligosaccharides (MOS), inulin, and its hydrolysate (fructo-oligosaccharides: FOS) play an important role in modulating intestinal microflora and potential immune response. Prebiotics reduce pathogen colonization in poultry and promote selective stimulation of beneficial bacterial species. Synbiotics are a combination of probiotics and prebiotics. This synergistic approach offers dual benefits by promoting the growth of beneficial bacteria and directly combating pathogens.

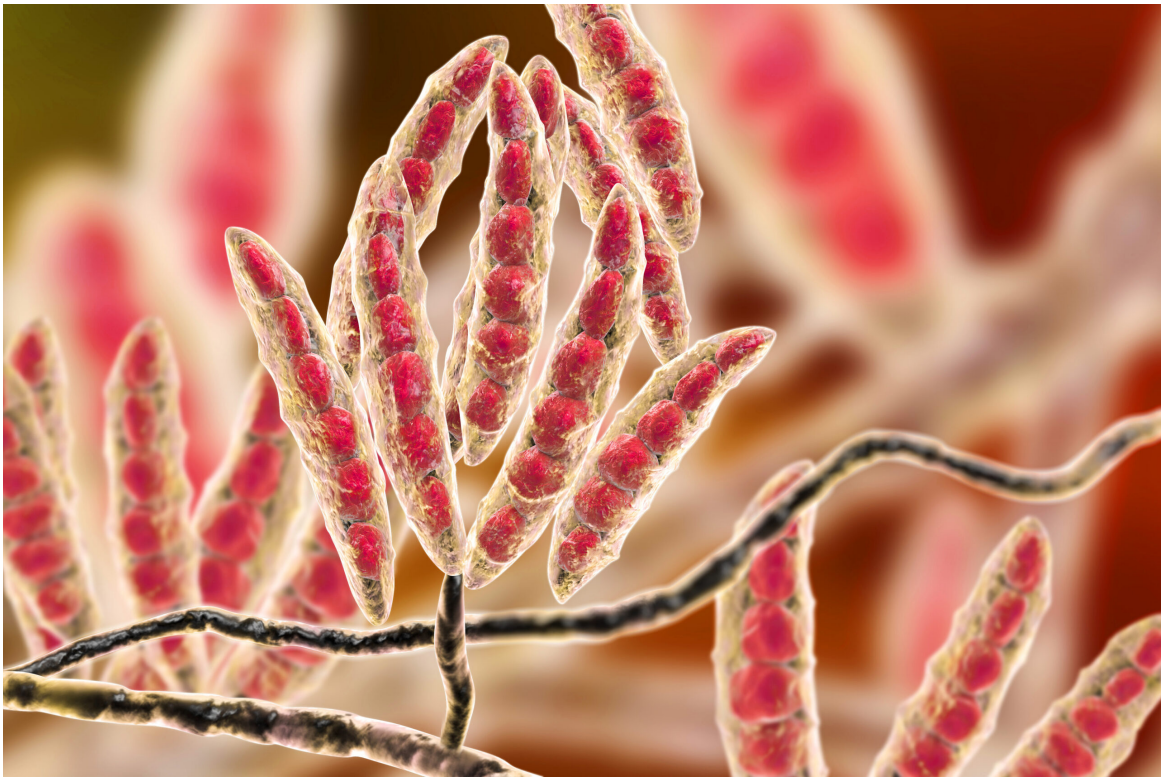
Dietary Fibers (DF)

The water-insoluble fibers are regarded as functional nutrients because of their ability to escape digestion and modulate nutrient digestion. A moderate level of insoluble fiber in poultry diets may increase chyme retention time in the upper part of the GIT, stimulating gizzard development and endogenous enzyme production, improving the digestibility of starch, lipids, and other dietary components (Mateos et al., 2012). The insoluble DF, when used in amounts between 3–5% in the diet, could have beneficial effects on intestinal development and nutrient digestibility.

Dietary fibers influence the development of the gizzard in poultry birds. A well-developed gizzard is a must for good gut health. Jiménez-Moreno & Mateos (2012) noted that coarse fiber particles are selectively retained in the gizzard, ensuring a complete grinding and a well-regulated feed flow. Secretion of digestive juices regulates GIT motility and feed intake. Including insoluble fibers in adequate amounts improves the gizzard function and stimulates HCl production in the proventriculus, thus helping control gut pathogens.

Toxin Risk Management

Mycotoxins may have a detrimental impact on the mucosal barrier function in animals (Akbari et al., 2017; Antonissen et al., 2015; Basso, Gomes and Bracarense, 2013; Pierron, Alassane-Kpembi and Oswald, 2016)**.** Mycotoxins like Aflatoxin B1, Ochratoxin A, and deoxynivalenol (DON) not only suppress immune responses but also induce inflammation and even increase susceptibility to pathogens (Yuhang et al., 2023). To avoid intestinal health problems, poultry producers need to emphasize avoiding levels of mycotoxins in feedstuffs and rancid fats that exceed recommended limits (Murugesan et al., 2015; Grenier and Applegate, 2013).



Fusarium mycotoxin

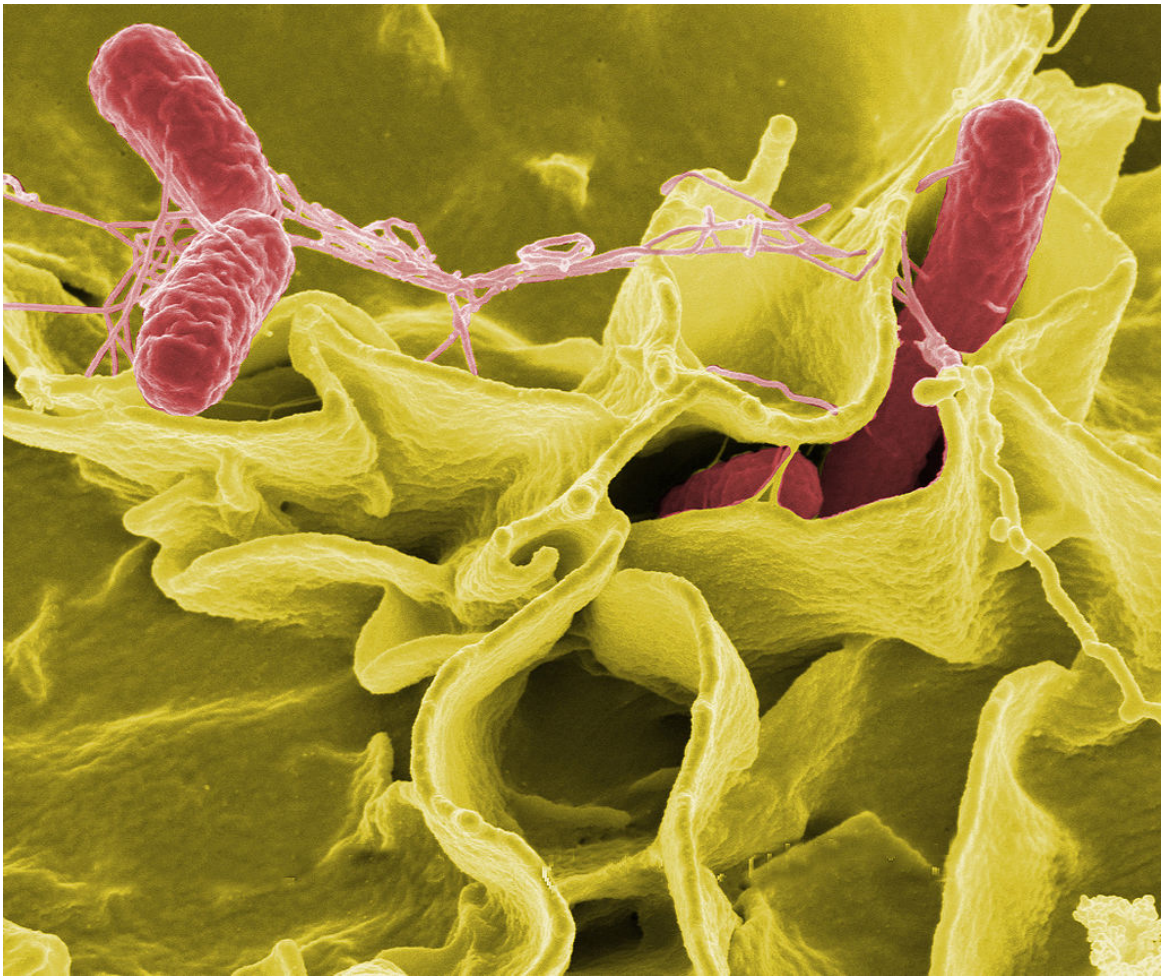
Bacterial lipopolysaccharides (LPS), also known as endotoxins, are the main components of the outer membrane of all Gram-negative bacteria and are essential for their survival. In stress situations, the intestinal barrier function is impaired, allowing the passage of endotoxins into the bloodstream. When the immune system detects LPS, inflammation sets in and results in adverse changes in gut epithelial structure and functionality. Dietary Intervention to bind these endotoxins in the GIT can help mitigate the negative impact of LPS on animals. Given this, toxin risk management with an appropriate binding agent able to control both mycotoxins and endotoxins appears to be a promising strategy for reducing their adverse effects. Further, adding antioxidants and mycotoxin binders to feed can reduce the effects of mycotoxins and peroxides and is more necessary in ABF programs (Yegani and Korver, 2008).

Essential oils/Phytomolecules

Essential oils (EOs) are important aromatic components of herbs and spices and are used as natural alternatives for replacing antibiotic growth promoters (AGPs) in poultry feed. The beneficial effects of EOs include appetite stimulation, improvement of enzyme secretion related to food digestion, and immune response activation (Krishan and Narang, 2014)

Essential oils (EOs), raw extracts from plants (flowers, leaves, roots, fruit, etc.), are an unpurified mix of different phytomolecules. The raw extract from Oregano is a mix of various phytomolecules (Terpenoids) like carvacrol, thymol and p-cymene. Whereas the phytomolecules are active ingredients of essential oils or other plant materials. Phytomolecule is clearly defined as one active compound.

These botanicals have received increased attention as possible growth performance enhancers for animals in the last decade via their beneficial influence on lipid metabolism, and antimicrobial and antioxidant properties (Botsoglou et al., 2002), ability to stimulate digestion (Hernandez et al., 2004), immune enhancing activity, and anti-inflammatory potential (Acamovic and Brooker, 2005). Many studies have been reported on supplementing poultry diets with some essential oils that enhanced weight gain, improved carcass quality, and reduced mortality rates (Williams and Losa, 2001). The use of some specific EO blends has been shown to have efficacy towards reducing the colonization and proliferation of Clostridium perfringens and controlling coccidia infection and, consequently, may help to reduce necrotic enteritis (Guo et al., 2004; Mitsch et al., 2004; Oviedo-Rondón et al., 2005, 2006a, 2010).



Salmonella

Antimicrobial properties of phytomolecules hinder the growth of potential pathogens. Thymol, eugenol, and carvacrol are structurally similar and have been proven to exert synergistic or additive antimicrobial effects when combined at lower concentrations (Bassolé and Juliani, 2012). In in-vivo studies, essential oils used either individually or in combination have shown clear growth inhibition of Clostridium perfringens and E. coli in the hindgut and ameliorated intestinal lesions and weight loss than the challenged control birds (Jamroz et al., 2006; Jerzsele et al., 2012; Mitsch et al., 2004). One well-known mechanism of antibacterial activity is linked to their hydrophobicity, which disrupts the permeability of cell membranes and cell homeostasis with the consequence of loss of cellular components, influx of other substances, or even cell death (Brenes and Roura, 2010; Solórzano-Santos and Miranda-Novales, 2012; Windisch et al., 2008; O'Bryan et al., 2015).

Apart from use in feed, the liquid phytomolecules preparations for drinking water use can prove to be beneficial in preventing and controlling losses during challenging periods of bird's life (feed change, handling, environmental stress, etc.). Liquid preparations can potentially reduce morbidity and mortality in poultry houses and thus the use of therapeutic antibiotics. Barrios et al. (2021) suggested that commercial blends of phytomolecule preparations may ameliorate the impact of Necrotic Enteritis on broilers. Further, they hypothesized that the effects of liquid preparation via drinking water were particularly important in improving overall mortality.

In modern, intensive poultry production, the imminent threat of resistant Eimeria looms large, posing a significant challenge to the sustainability of broiler operations. Eimeria spp., capable of developing resistance to traditional anticoccidial drugs, has become a pressing global issue for poultry operators. The resistance of Eimeria to traditional drugs, coupled with concerns over drug residue, has necessitated a shift towards natural, safe, and effective alternatives. It was found that if a drug to which the parasite has developed resistance is withdrawn from use for some time or combined with another effective drug, the sensitivity to that drug may return (Chapman, 1997).

Several phytogenic compounds, including saponins, tannins, essential oils, flavonoids, alkaloids, and lectins, have been the subject of rigorous study for their anticoccidial properties. Among these, saponins

and tannins in specific plants have emerged as powerful tools in the fight against these resilient protozoa. Botanicals and natural identical compounds are well renowned for their antimicrobial and antiparasitic activity so that they can represent a valuable tool against Eimeria (Cobaxin-Cardenas, 2016). The mechanisms of action of these molecules include degradation of the cell wall, cytoplasm damage, ion loss with reduction of proton motive force, and induction of oxidative stress, which leads to inhibition of invasion and impairment of Eimeria spp. development (Abbas et al., 2012; Nazzaro et al., 2013). Natural anticoccidial products may provide a novel approach to controlling coccidiosis while meeting the urgent need for control due to the increasing emergence of drug-resistant parasite strains in commercial poultry production (Allen and Fetterer, 2002).

Role of Feed Enzymes Beyond Feed Cost Reduction

Feed enzymes have traditionally been associated with improving feed efficiency and reducing feed costs by enhancing nutrient digestibility. However, their role can extend well beyond economic benefits, profoundly impacting gut health and supporting reduced antimicrobial use in poultry production. Exogenous enzymes reduce microbial proliferation by reducing the undigestible components of feed, the viscosity of digesta, and the irritation to the gut mucosa that causes inflammation. Enzymes also generate metabolites that promote microbial diversity which help to maintain gut ecosystems that are more stable and more likely to inhibit pathogen proliferation (Bedford, 1995; Kiarie et al., 2013).

High dietary levels of non-starch polysaccharides (NSPs) can increase the viscosity of digesta. This leads to an increase in the retention time of the digesta, slows down the nutrient digestion and absorption rate, and may lead to an undesired increase in bacterial activity in the small intestine (Langhout et al., 2000; Smits et al., 1997). Further the mucosal barrier function may also be adversely affected. To solve this problem, exogenous enzymes, such as arabinoxylanase and/ or ß-glucanase, are included in feed to degrade viscous fibre structures (Bedford, 2000). The use of xylanase and ß-glucanase may also cause oligosaccharides and sugars to be released, of which certain, for example, arabinoxylan oligosaccharides, may have prebiotic properties (De Maesschalck et al., 2015; Niewold et al., 2012).

New generation xylanases coming from family GH-10 are known to effectively breakdown both soluble and insoluble arabinoxylans into a good mixture of smaller fractions of arabino-xylo-oligosaccharides (AXOS) and xylo-oligosaccharides (XOS), which exert a prebiotic effect in the GIT. Awati et.al. (2023) observed that a novel GH10 xylanase contributed to positive microbial shift and mitigated the anti-nutritional gut-damaging effects of higher fiber content in the feed. With a substantial understanding of the mode of action and technological development in enzyme technology, nutritionists can reliably consider new-generation xylanases for gut health optimization in their antibiotic reduction strategy.

Conclusions

The challenge of mitigating antimicrobial resistance (AMR) in poultry production necessitates a multidimensional approach, with gut health at its core. Dietary interventions, such as organic acids, probiotics, prebiotics, phytomolecules, toxin binders, and feed enzymes, promote gut resilience, enhance immune responses, and reduce reliance on antimicrobials. These strategies not only support the health and productivity of poultry but also address critical global issues of AMR and food safety.

While no single solution fits all circumstances, integrating these dietary tools with robust biosecurity measures, sound management practices, and continued research on species-specific and field-applicable strategies can pave the way for sustainable, antibiotic-free poultry production. The transition to such systems aligns with regulatory requirements and consumer expectations while contributing to global efforts against AMR.

Ultimately, embracing holistic and innovative dietary strategies ensures a resilient gastrointestinal environment, safeguarding poultry health and productivity while protecting public health and environmental sustainability for future generations.

References: The references can be made available upon request to the author.

Rearing pigs without antibiotics

Conference Report

Holistic management is essential for successfully rearing pigs, particularly in systems that aim to minimize antibiotics. The method emphasizes the interconnectedness of various factors contributing to sustainable pig health and productivity. Some of the key components of this holistic management were discussed by Dr. Seksom.

Sow lifetime productivity

Suggested targets for sow lifetime productivity are

- >70 marketed fattening pigs
- At least 6 parities with at least 10.5 pigs marketed per parity
- 25 fattening pigs/sow/year (2.4 parities/year x 10.5 fattening pigs)

To achieve these targets, we need 29.2 born alive piglets/sow/year (or 12.2 born alive piglets/parity), and it is essential to control losses during each production period: <10% pre-weaning, <3% during nursery,

and <2% in fattening.

Since the occurrence of African swine fever (ASF), with improved genetics, we can now produce pigs with 120 kg+ bodyweight at slaughter without carcass problems and reach about 3 tons of bodyweight/sow/year, compared to around 2 tons before.

Modern pig genetics and subsequent problems

Despite the advancements in modern pig genetics leading to improved production and bigger litters, several ensuing problems have emerged:

- Less average body weight of piglets at birth
- Large number of piglets born with less than 1.0 kg (target <5%)
- High pre-weaning mortality
- High post-weaning mortality and morbidity

Dr. Seksom highlighted that birthweights decrease with increasing sow prolificacy. He stated that “piglets should be divided into groups with similar body weights at weaning” and that “a key objective for successful weaning is a piglet that weighs a minimum of 6-6.5 kg at three weeks of age, and that less than 25% of the piglets have a weight of ≤5.9 kg.”

Sow body condition

Sows should be fed to feed to body condition score (BCS), not a fixed amount of feed. Ideally, the sows have a BCS of 2.75 (the sow’s backbone is visible, and the tips of the short ribs can be felt but are smooth) or 3.0 (well-rounded appearance, hips, and spine can only be felt with firm pressure) at 12 weeks of pregnancy, so we can feed more in the last month to achieve a BCS of 3-3.25 at farrowing. This is essential to ensure that sows have sufficient energy reserves for lactation and overall health.

Target body condition score – 2.75 at three months of gestation

Feed intake must be increased gradually during the last month of gestation as most fetal growth and mammary gland development occur during this period. This may involve raising energy-dense feeds or adjusting protein levels as needed.

Dr. Seksom stressed that “nutrition is not just the feed; it’s about feeding as well. To feed sows to BCS,

assessments of BCS should be done regularly throughout gestation, ideally every 2-4 weeks. This allows for timely adjustments in feeding based on individual sow's needs. Ensure that staff are trained one-on-one to accurately assess the body condition of sows. This includes recognizing the visual and tactile indicators of different scores and understanding how BCS impacts reproductive performance, longevity, and overall farm profitability."

After farrowing, the sows must be monitored closely for any signs of excessive weight loss and feeding strategies adjusted accordingly to support recovery and lactation needs.

Piglet diarrhea

Many factors cause diarrhea and must be thoroughly investigated. For bacteria-caused diarrhea, Dr. Seksom advised a good hygiene program, whereas for viral causes, a vaccination program is essential. However, he emphasized that "for a vaccination program, you can't just copy from another farm; it needs to be created specifically using the titers for diseases on your farm."

Swine influenza is an often-overlooked cause of diarrhea in piglets. While it is primarily recognized for causing respiratory issues, the virus can also lead to scours in the first two weeks of piglets' life. So, sows should be checked for symptoms of swine influenza (such as nasal discharge, sneezing and coughing, and inappetence) before farrowing. If necessary, they must be treated with paracetamol to reduce fever and symptoms.

Main disease causes of pre-weaning diarrhea

	Nursery period				Mortality level
	Days 1-3	Days 3-7	Days 7-14	Days 14-21	
Agalactia	√	√	√	√	Moderate
Clostridia	√	√	√		High
Coccidiosis		√	√	√	Low
E. coli	√	√	√		Moderate
PED	√	√	√		Variable
PRRS	√	√	√	√	Variable
Rotavirus			√	√	Low
TGE	√	√	√	√	High
Influenza		√	√		Low

Ensuring colostrum intake

The intake of an adequate quantity of colostrum is crucial for piglets to be protected during the first days of life. Best practices to ensure that piglets get □250 mL of colostrum include:

- **Teat access –** if a sow has a large litter or is unable to nurse all her piglets effectively, consider split suckling by separating larger, more vigorous piglets from the litter for a couple of hours after birth. This allows smaller or weaker piglets better access to the udder without competition. Syringe-feeding colostrum to smaller piglets is also effective.
- **Early access –** six hours after farrowing, the quality of colostrum begins to decline significantly. Additionally, the piglet can only absorb intact large IgG molecules, the major source of passive immunity, during the first 24 h after birth, prior to gut closure. In any case, by this time, the sow will start producing milk and not colostrum.
- **Sow behavior –** if a sow experiences pain or discomfort from injuries caused by her piglets' teeth, she may become less willing to allow them to nurse, leading to delays in colostrum intake. Genetic background influences maternal behavior significantly. For example, some breeds

exhibit stronger maternal instincts and better nursing behaviors than others. Selecting sows with proven good maternal traits can lead to improved outcomes in piglet survival and growth.

- **Drafts –** newborn piglets are born with low fat reserves and are highly susceptible to hypothermia. Drafts significantly impact the effective temperature experienced by piglets.
- **Staff training –** Staff must be trained to recognize signs of distress in both sows and piglets; training in techniques enables them to assist with nursing and feeding, which is crucial for timely interventions.

Weaning is a process, not just a one-time event

Research has shown that heavier piglets at weaning have better lifetime performance than lighter ones. Weaning weight is a more accurate indication of post-weaning growth than either birth weight or age. It is, therefore, important to establish the weaner immediately post-weaning to maintain growth rates, reduce pen variation, and lessen the amount of 'tail-enders' at the point of sale.

Dr. Seksom emphasized that "viewing weaning merely as a single event, rather than a process, overlooks the complexities involved in ensuring a smooth transition for the animals. He advocated for a comprehensive approach to weaning that includes the shown well-planned steps to support piglets during this critical phase. If the weaning process is managed effectively, you can significantly reduce the need for antibiotics."

Conclusion

"By integrating these holistic management strategies, pig producers can effectively raise pigs without antibiotics while promoting animal health, improving productivity, and addressing consumer concerns about antibiotic use in livestock production," summarized Dr. Seksom.

EW Nutrition's Swine Academy took place in Ho Chi Minh City and Bangkok in October 2024. Dr. Seksom Attamangkune, a leading expert in the nutrition and management of pigs in tropical conditions and former Head of the Animal Science Department and Dean of the Faculty of Agriculture at

Kamphaeng Saen, Kasetsart University, was a reputable guest speaker at this event.

Antimicrobial resistance in animal production workers, a serious challenge

With 73% of human-use antibiotics also used in food-animal production, antimicrobial resistance (AMR) is a pressing global health concern, particularly in contexts where humans and animals are in close proximity, such as in animal production facilities. This issue is exacerbated by the widespread use of antibiotics in livestock farming, which not only promotes resistance in bacteria but also poses direct risks to farm workers.

Antimicrobial resistance in farm workers

in Denmark

In Denmark, a country renowned for its robust agricultural monitoring systems, significant strides have been made in tracking AMR. A comprehensive report from 2015 emphasized the occurrence of antimicrobial-resistant bacteria, particularly in livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA). The Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP) highlighted that farm workers frequently came into contact with these resistant pathogens, which posed occupational hazards and public health challenges (Bager et al., 2015). The program found that 88% of pigs carried LA-MRSA, and farm workers had significantly elevated exposure risks, particularly in intensive swine operations (DANMAP 2015 Report).

Antimicrobial resistance in farm workers in the US

Studies in the United States have revealed even more alarming statistics. Farm workers in intensive animal farming environments were found to be 32 times more likely to develop antibiotic-resistant infections than the general population. This increased risk was attributed to prolonged exposure to resistant bacteria and antibiotic residues in animal feed and the environment (Silbergeld et al., 2008). The close interaction between humans and animals in confined spaces fosters the transfer of resistant genes, making these workers a vulnerable group.

Mechanisms of resistance spread

The spread of AMR from livestock to humans can occur through several pathways:

- Direct contact: Handling animals and exposure to manure or bodily fluids.
- Airborne transmission: Dust particles containing resistant bacteria.
- Contaminated food: Consumption of undercooked or improperly handled meat products.
- Environmental contamination: Water and soil contaminated with antibiotics or resistant bacteria.

What can be done?

Even in countries where antimicrobials reduction legislation has been in place for almost two decades, such as Germany or Sweden, new resistance cases are constantly discovered. In supermarkets around the world, meat contaminated with antibiotic-resistant superbugs is still a common occurrence. And in antibiotic resistance hot spots, “from 2000 to 2018, P50 increased from 0.15 to 0.41 in chickens—meaning that 4 of 10 antibiotics used in chickens had resistance levels higher than 50%. P50 rose from 0.13 to 0.43 in pigs and plateaued between 0.12 and 0.23 in cattle” (Dall, 2019). These hot spots are spread across the globe, from south and northeast India, northeast China, north Pakistan, Iran, and Turkey, to the south coast of Brazil, Egypt, the Red River Delta in Vietnam, and areas surrounding Mexico City, Johannesburg, and more recently Kenya and Morocco.

Globally, antimicrobial use in animals is projected to increase by 67% by 2030, especially in low- and middle-income countries where regulatory frameworks are weaker. Denmark provides a successful model for mitigating these risks. Policies such as the “Yellow Card” scheme have reduced antibiotic use in pigs by promoting alternative husbandry practices and strict monitoring. This approach has also reduced the prevalence of resistant bacteria in animal populations, offering a replicable strategy for other nations (Alban et al., 2017).

Recommendations for mitigation

- Strengthening surveillance: Programs like DANMAP should be implemented globally to monitor antibiotic usage and resistance trends in animals and humans.
- Reducing antibiotic use: Phasing out non-therapeutic uses of antibiotics, particularly as growth promoters, and avoiding Critically Important Antimicrobials for Human Medicine.
- Protecting workers: Providing personal protective equipment (PPE) and regular health screenings for farm workers.
- Public awareness: Educating communities about the risks of AMR and promoting safe food handling practices.

The evidence from Denmark and the U.S. underscores the urgent need to address AMR in animal production settings. Protecting farm workers from AMR not only safeguards their health but also prevents the spread of resistant pathogens across the wider public.

References

Bager, F., et al. (2015). *DANMAP 2014: Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food, and humans in Denmark*. Retrieved from DANMAP Report.

Silbergeld, E. K., Graham, J., & Price, L. B. (2008). *Industrial food animal production, antimicrobial resistance, and human health*. Annual Review of Public Health, 29(1), 151-169.

Alban, L., et al. (2017). *Assessment of the risk to public health due to use of antimicrobials in pigs—An example of pleuromutilins in Denmark*. Frontiers in Veterinary Science, 4, 74. DOI.

Magnusson, Ulf et al. (2024). *Chapter 3: Antimicrobial Resistance in Farm Workers and Its Public Health Implications. Advances in Animal Health and Welfare*, SpringerLink, https://link.springer.com/chapter/10.1007/978-3-031-51788-4_3.

Dall, Chris. (2019) *Antibiotic Resistance in Farm Animals Tied to Global Hot Spots*. Center for Infectious Disease Research and Policy (CIDRAP), https://www.cidrap.umn.edu/antimicrobial-stewardship/antibiotic-resistance-farm-animals-tied-global-hot-spots.

Vaughan, Adam. (17 June 2024). *Superbugs and E. coli present in Lidl chicken, campaigners find*. Retrieved from The Times. https://www.thetimes.com/uk/healthcare/article/superbugs-and-e-coli-present-in-lidl-chicken-campaigners-find-0cncb6s0n

World Animal Protection. (2021). *Antimicrobial resistance: The global threat of livestock antibiotic misuse*. Retrieved from https://www.worldanimalprotection.us/siteassets/reports-programmatic/amr-2021-report.pdf

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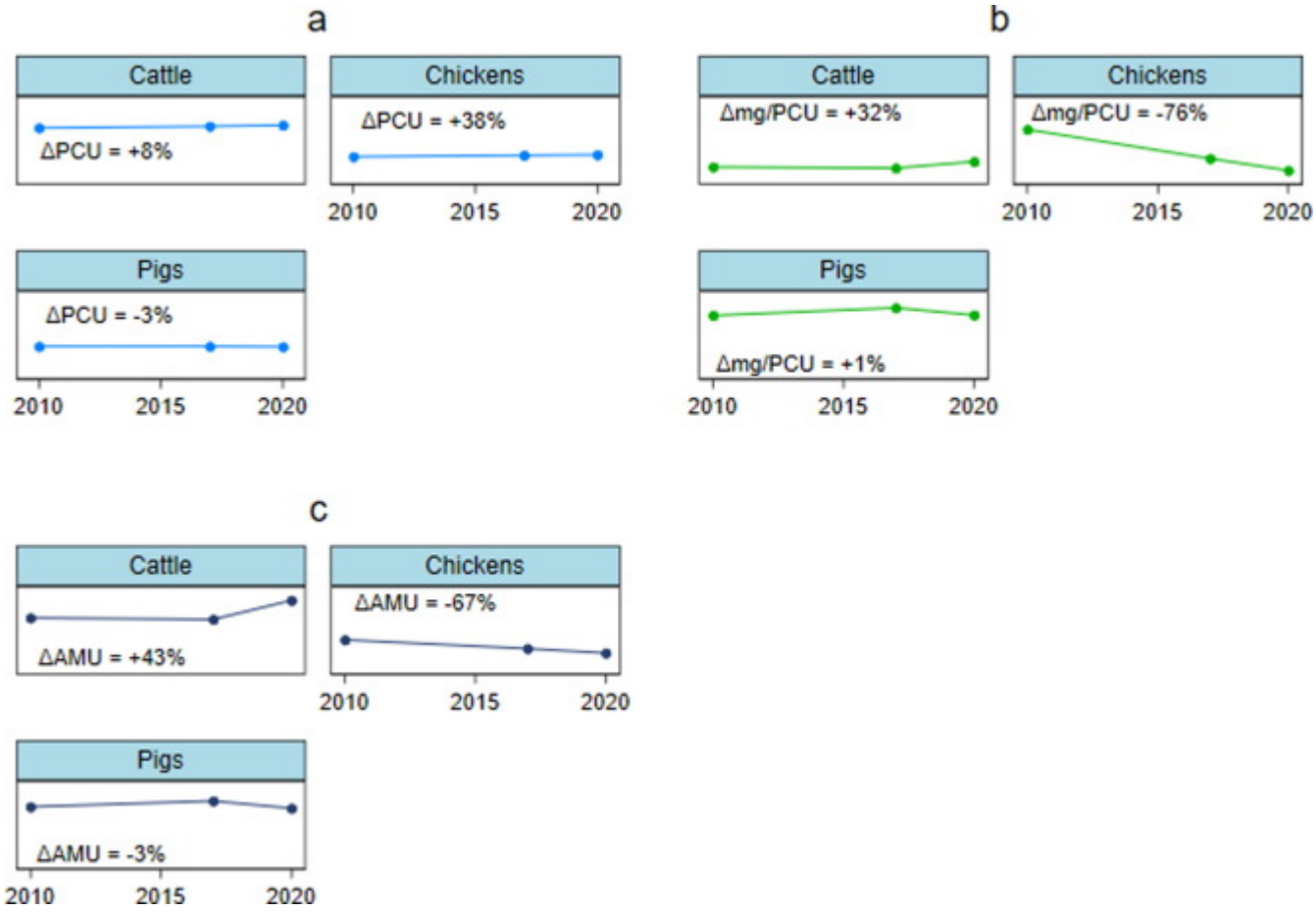
Global antimicrobial use in

livestock farming: A revised estimate



Antimicrobial resistance (AMR) poses a significant threat to global health, driven by the overuse and misuse of antibiotics in both human medicine and livestock farming. In livestock farming, antimicrobials are still used extensively for therapeutic and non-therapeutic purposes. However, estimates of the quantities used per species are notoriously hard to derive from fragmented, incomplete, or unstandardized data around the world.

A recent article ("Global antimicrobial use in livestock farming: an estimate for cattle, chickens, and pigs", *Animal*, 18(2), 2024) attempts to update the figures by estimating global biomass at treatment of cattle, pigs, and chickens, considering distinct weight categories for each species in biomass calculation, and using the European Medicines Agency's weight standards for the animal categories. With these more refined calculations, authors Zahra Ardakani, Maurizio Aragrande, and Massino Canali aim to provide a more accurate estimate of global antimicrobial use (AMU) in cattle, chickens, and pigs. Understanding these patterns is crucial for addressing AMR and developing strategies for sustainable livestock management.

Key Findings

The study estimates that the global annual AMU for cattle, chickens, and pigs amounts to 76,060 tons of antimicrobial active ingredients. This is a significant revision from previous estimates due to a more detailed evaluation of animal weights and categories:

1. Cattle: 40,697 tons (53.5% of total AMU)
2. Pigs: 31,120 tons (40.9% of total AMU)
3. Chickens: 4,243 tons (5.6% of total AMU)

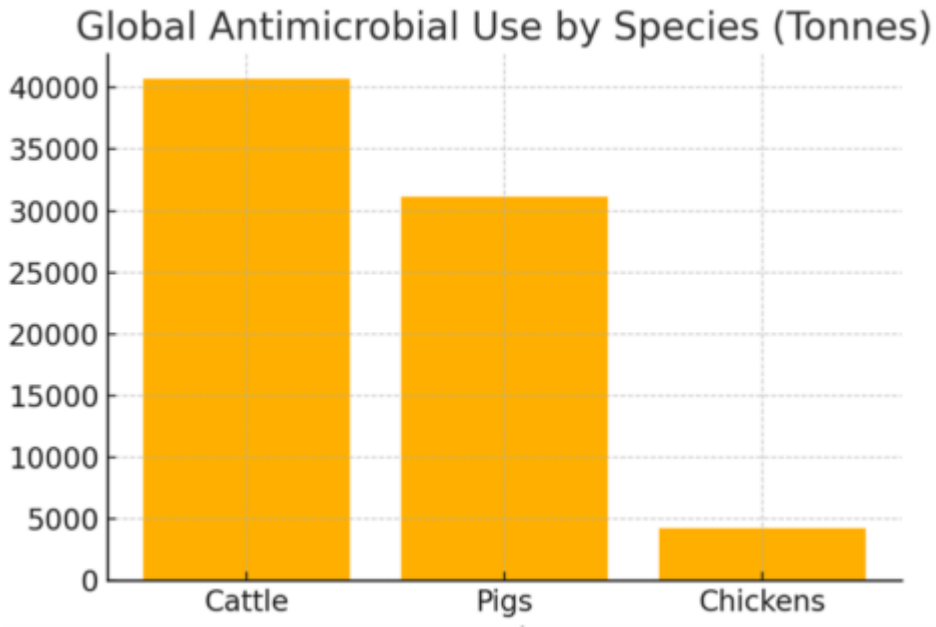


Figure 1: Distribution of global antimicrobial use among cattle, pigs, and chickens.

Methodology

The study utilizes the concept of Population Correction Units (PCU) to estimate antimicrobial usage, taking into account the weight and category of livestock at the time of treatment. This method differs from previous approaches that relied on live weight at slaughter, providing a more accurate representation of AMU.

The PCU is calculated by multiplying the number of animals by their average weight during treatment. This approach allows for differentiation by age and sex, which is particularly important for species like cattle and pigs.

Figure 2: (a) Changes in global PCU (million tonnes), (b) changes in global antibiotic use in mg per PCU, and (c) changes in global AMU (thousand tonnes) for cattle, chickens, and pigs; between 2010 and 2020. Abbreviations: PCU = Population Correction Unit; AMU = Antibiotic Use.

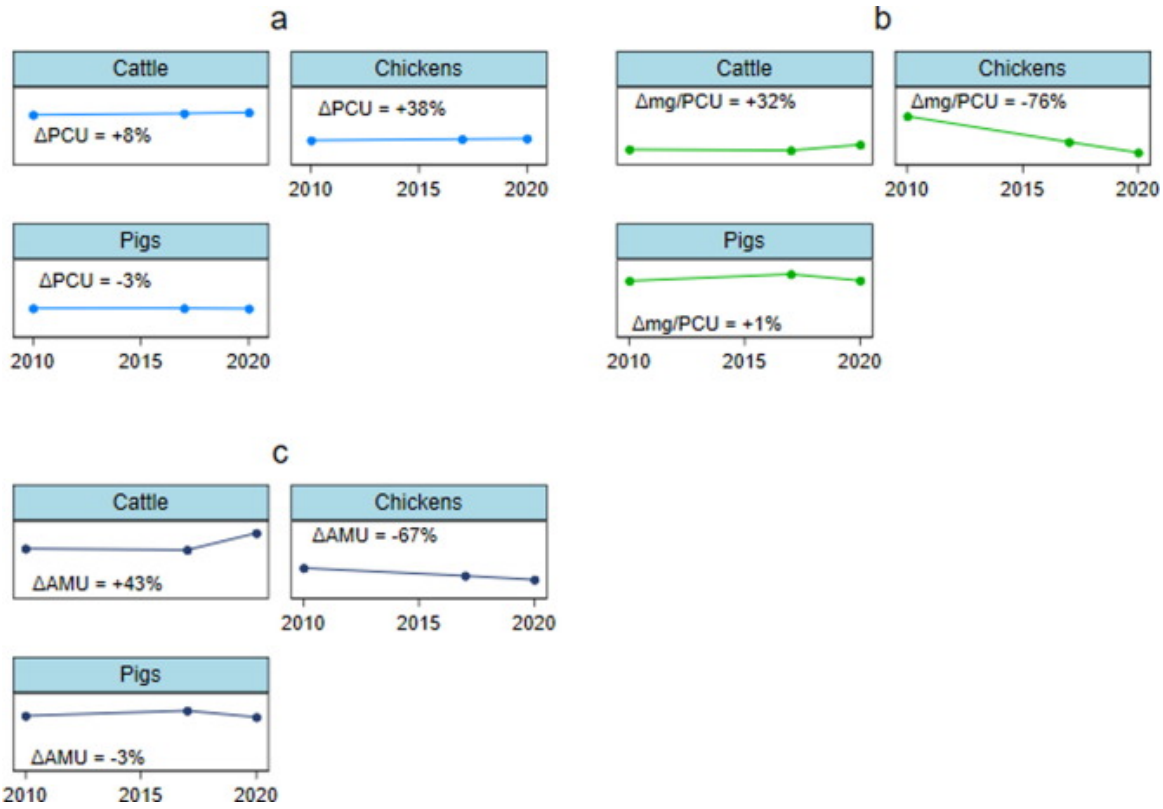


Figure 2: (a) Changes in global PCU (million tonnes), (b) changes in global antibiotic use in mg per PCU, and (c) changes in global AMU (thousand tonnes) for cattle, chickens, and pigs; between 2010 and 2020. Abbreviations: PCU = Population Correction Unit; AMU = Antibiotic Use.

Study shows lower AMU than previous estimates

The study highlights a significant shift in AMU patterns, with chickens showing a remarkable decrease in antimicrobial use despite increased production. This is indicative of improved management and more responsible use of antibiotics in the poultry industry.

The lower AMU in cattle and pigs, compared to previous estimates, underscores the importance of considering animal age and weight at treatment. These findings align closely with World Organization for Animal Health (WOAH) estimates, validating the methodology.

However, the study also acknowledges limitations, including reliance on European standards for average weight at treatment, which may not reflect global variations. Additionally, the lack of comprehensive global data on veterinary antibiotics presents challenges in creating fully accurate estimates.

Corrected estimate highlights improved production advances

This study provides a revised and potentially more accurate estimate of global antimicrobial use in livestock. By accounting for the weight and treatment categories of animals, it offers insights that could guide policy and management practices to mitigate the spread of antimicrobial resistance.

The article also indicates that the industry may have over-estimated antimicrobial usage in livestock and, just as importantly, that antimicrobial use has been kept in check or even reduced, despite increases in

farmed animal headcounts. The lower usage is likely due to regulatory oversight and improvements in alternative methods to control and mitigate health challenges.

Can phytogenics have a meaningful effect in coccidiosis control?

*by **Madalina Diaconu**, Global Manager Gut Health, EW Nutrition*

Coccidiosis, caused by Eimeria spp., is a major challenge in poultry production, leading to significant economic losses. Historically, control strategies have relied on chemical anticoccidials and ionophores. However, the emergence of drug-resistant Eimeria strains and consumer concerns about chemical residues necessitate alternative solutions. Phytogenics, especially tannins and saponins, offer promising natural solutions to be included in programs for coccidiosis control. More and more independent research highlights the potential of these natural compounds to enhance poultry health and productivity.

Efficacy of Tannins and Saponins in Coccidiosis Control

Phytogenics are plant-derived bioactive compounds known for their antimicrobial, antioxidant, and immunomodulatory properties. Among these, tannins and saponins have shown particular promise in supporting coccidiosis control.

The challenge: Preventing the spread of infections and mitigating subclinicial coccidiosis before it reaches this stage.

Tannins

Tannins are polyphenolic compounds found in various plants. They exhibit strong antimicrobial activity by binding to proteins and metal ions, disrupting microbial cell membranes, and inhibiting enzymatic activity.

Anticoccidial Activity: Tannins have been shown to interfere with the life cycle of Eimeria. Studies demonstrate that tannins can reduce oocyst shedding and intestinal lesion scores in infected birds (Abbas et al., 2017).

Immune Modulation: Tannins enhance immune responses by promoting the proliferation of lymphocytes

and the production of antibodies, which help in the clearance of Eimeria infections (Redondo et al., 2021).

Saponins

Saponins are glycosides with surfactant properties, capable of lysing cell membranes of pathogens. They also stimulate immune responses, enhancing the host's ability to fight infections.

Membrane Disruption: Saponins disrupt the cell membranes of Eimeria, leading to reduced parasite viability and replication (Githiori et al., 2004).

Immune Enhancement: Saponins stimulate the production of cytokines and enhance the activity of macrophages, improving the overall immune response against coccidiosis (Zhai et al., 2014).

Independent Research Evidences Phytogenics's Role in Supporting Programs for Coccidiosis Control

Numerous studies have evaluated the efficacy of phytogenics in coccidiosis control. Here, we highlight key findings from peer-reviewed research:

Abbas et al. (2012): This study reviewed various botanicals and their effects on Eimeria species in poultry. The authors concluded that tannins and saponins significantly reduce oocyst shedding and lesion scores, comparable to conventional anticoccidials.

Allen et al. (1997): The authors investigated the use of dietary saponins in controlling Eimeria acervulina infections. The study found that saponin-treated birds exhibited lower oocyst counts and improved weight gain compared to untreated controls.

Masood et al. (2013): This study explored the role of natural antioxidants, including tannins, in controlling coccidiosis. The results indicated that tannins reduced oxidative stress and improved intestinal health, leading to better performance in broiler chickens.

Idris et al. (2017): The researchers assessed the potential of saponin-rich plant extracts against avian coccidiosis. The findings demonstrated significant reductions in oocyst output and lesion severity, highlighting the potential of saponins as effective anticoccidials.

Hailat et al. (2023): The researchers studied three phytogenic formulations against a control group with chemical drugs. The study concluded that phytogenic blends can be safely used as alternatives to the chemically synthesized drugs, either alone or in a shuttle program, for the control of poultry coccidiosis.

El-Shall et al. (2021): This review article highlights research findings on phytogenic compounds which showed preventive, therapeutic, or immuno-modulating effects against coccidiosis.

Despite initial skepticism, the growing body of evidence supports the efficacy of phytogenics in supporting coccidiosis control. Tannins and saponins, in particular, have shown significant potential in reducing parasite load, improving intestinal health, and enhancing immune responses. These natural compounds offer several advantages over traditional chemical treatments, including lower risk of resistance development and absence of harmful residues in meat products.

Challenges and Promises

While the efficacy of phytogenics is well-supported, challenges remain, especially with lower-quality products that may display variability in plant extract composition, in their standardization of doses, and in ensuring consistent quality. At the same time, these compounds are not silver bullets, and no producer should make unreasonable claims.

As far as the mode of action is concerned, the evidence is becoming clear: phytogenics, particularly tannins and saponins, are effective in mitigating gut health challenges and supporting bird performance when challenged. Their natural origin, coupled with potent antimicrobial and immunomodulatory properties, makes them suitable for sustainable poultry production. As the poultry industry seeks to reduce reliance on chemical drugs, phytogenics represent a viable and promising solution.

References

Abbas, R. Z., Iqbal, Z., Blake, D., Khan, M. N., & Saleemi, M. K. (2011). “Anticoccidial drug resistance in fowl coccidia: the state of play revisited”. *World’s Poultry Science Journal*, 67(2), 337-350. https://doi.org/10.1017/S004393391100033X

Allen, P. C., Danforth, H. D., & Levander, O. A. (1997). “Interaction of dietary flaxseed with coccidia infections in chickens”. *Poultry Science*, 76(6), 822-828. https://doi.org/10.1093/ps/76.6.822

El-Shall, N.A., El-Hack, M.E.A., et al. (2022). “Phytochemical control of poultry coccidiosis: a review”. Poultry Science, 101(1) 101542. https://doi.org/10.1016/j.psj.2021.101542

Idris, M., Abbas, R. Z., Masood, S., Rehman, T., Farooq, U., Babar, W., Hussain, R., Raza, A., & Riaz, U. (2017). “The potential of antioxidant rich essential oils against avian coccidiosis”. *World’s Poultry Science Journal*, 73(1), 89-104. https://doi.org/10.1017/S0043933916000787

Hailat, A.M., Abdelqader, A.M., & Gharaibeh, M.H. (2023). “Efficacy of Phyto-Genic Products to Control Field Coccidiosis in Broiler Chickens”. International Journal of Veterinary Science, 13(3), 266-272. https://doi.org/10.47278/journal.ijvs/2023.099

Masood, S., Abbas, R. Z., Iqbal, Z., Mansoor, M. K., Sindhu, Z. U. D., & Zia, M. A. (2013). “Role of natural antioxidants for the control of coccidiosis in poultry”. *Pakistan Veterinary Journal*, 33(4), 401-407.

Redondo, L. M., Chacana, P. A., Dominguez, J. E., & Miyakawa, M. E. (2021). “Perspectives in the use of tannins as alternative to antimicrobial growth promoter factors in poultry”. *Frontiers in Microbiology*, 12, 641949. https://doi.org/10.3389/fmicb.2021.641949

Zhai, H., Liu, H., Wang, S., Wu, J., & Kluenter, A. M. (2014). “Potential of essential oils for poultry and pigs”. *Animal Nutrition*, 2(4), 196-202. https://doi.org/10.1016/j.aninu.2016.12.004

Sustainable use of veterinary antimicrobials in Europe: EEA report

The European Environment Agency (EEA) has recently published a briefing detailing the impact of veterinary antimicrobials on Europe's environment. Positive developments are to be applauded, however they do not tell the whole story.

The use of antimicrobials for farmed animals and in aquaculture decreased by around 28% between 2018 and 2022. Nonetheless, the rate of antimicrobial resistance continues to rise around the world, including as an important cause of death in the European Economic Area (the EEA includes all EU countries, as well as Norway, Lichtenstein, and Iceland). At present, antimicrobial-resistant infections are estimated to caused 35,000 deaths per year in the European Union. For reference, in the EU, traffic accidents cause around 20,000 deaths per year.

A large number of EU guidelines, policies, and regulations attempt to control and monitor the use of antimicrobials in food-producing animals. This makes the regulatory landscape somewhat confusing, especially that many implementation details are still left to the states.

Figure 1. Overview of the EU regulatory framework applicable to antimicrobials used in food-producing animals

One of the results of unequal implementation is that there is no standardized way of tracking the actual use of antimicrobials in food-producing animals. To collect the numbers, the EEA has used proxy numbers, especially antimicrobial sales data and self-reported data. With such broad strokes, it is to be expected that the actual figures might be higher.

Lower numbers…

According to the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) database, in the European Economic Area countries, plus Switzerland and the UK, total antimicrobial consumption for farmed animals and aquaculture was estimated at **73.9 mg/PCU*** in 2022. This signifies a 30% reduction over 5 years.

In numbers: 4,458 tons of active substances were sold in one years for farmed animals & aquaculture.

*PCU represents a population correction unit (PCU). The PCU takes into account the population and relative weight of animals and "is used the normalize antimicrobial sales data for the size of the animal population that could potentially be treated with these substances. Using this methodology, 1 PCU corresponds to 1 kilogram of animal biomass".

…But higher risks

In 2021, total antimicrobial consumption in humans – measured in 28 European countries – was estimated at **125.0 mg/kg**. This number has unfortunately not gone down. What is worse: a much larger volume of antimicrobials is sold for food-producing animals than for human medicine. Which means that, relative to the total population, the impact of veterinary-use antimicrobials remains disproportionately large.

Moreover, two outliers (Poland and Lithuania) exhibited a worrying increasing trend, showing that no good development is irreversible. The EEA also highlights this danger, in the context of growing global consumption of animal protein. Increased demand "may put pressure on farmers to adopt intensive production practices that require increased use of antimicrobials". The use of antimicrobials elsewhere in the world may lead to impacts in Europe, "not just by theoretically exposing consumers to antimicrobial residues but also by contributing to rising global rates of drug-resistant pathogens and infections".

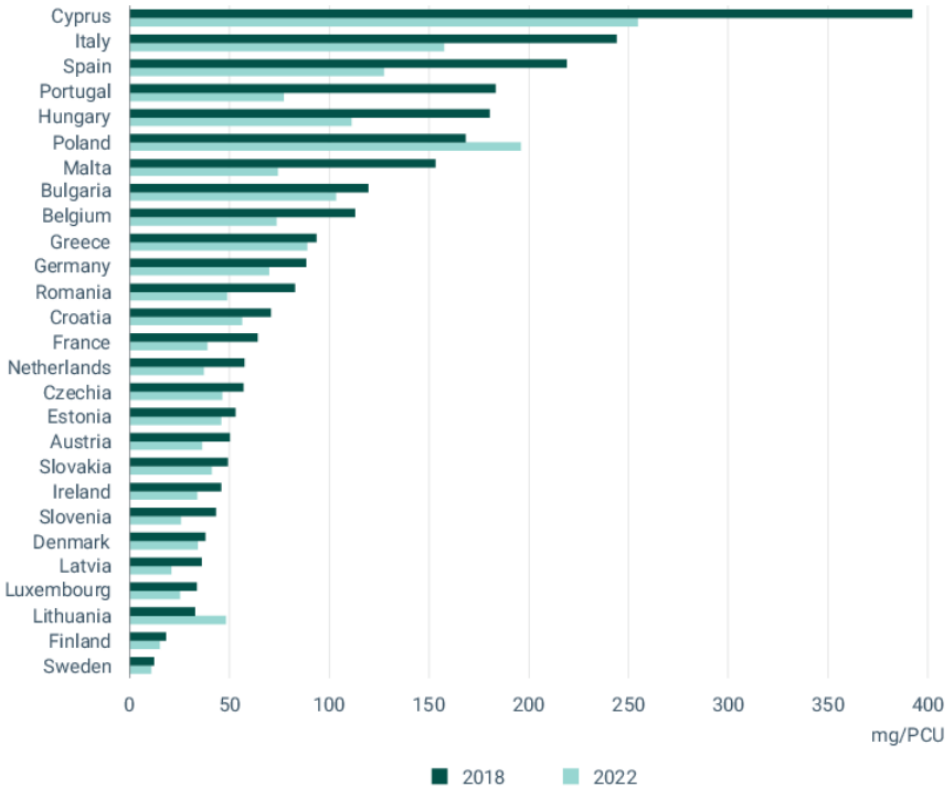


Figure 2. Sales by EU Member States in 2018 vs. 2022

Because of declining livestock populations in the last few years, while demand remained constant, EU-27 imports of animal products more than doubled between 2002 and 2022. There are no reliable global data on the veterinary use of antimicrobials, however it is generally believed that **over 70% of antimicrobials sold globally may be used in for animal protein production**.

Data collected by the World Organization for Animal Health (WOAH) from its member countries suggest that, between 2017-2019, “the use of antimicrobials in animals decreased by 25% in the Asia, Far East and Oceania regions, while it increased in Africa (+45%) and the Americas (+5%). Despite these partial improvements, a recent study forecasted that global use of antimicrobials in food-producing animals could rise by 8% in 2030, compared to 2020 levels (Mulchandani et al., 2023)”.

Quick summary

Reduction in Antimicrobial Use: There has been a significant reduction in the use of antimicrobials in farming and aquaculture across the EU. From 2018 to 2022, there was a decrease of approximately 28%, which aligns with the EU’s Farm to Fork strategy targeting a 50% reduction by 2030.

Antimicrobial Resistance (AMR): Despite the decrease in use, antimicrobial resistance remains a severe public health threat, causing an estimated 35,000 deaths annually in the European Economic Area. The resistance is attributed to the use of antimicrobials, which – as has been widely documented and discussed – can promote the evolution of resistant microorganisms.

Environmental Impact: The briefing underscores significant knowledge gaps in monitoring antimicrobial residues, resistant bacteria, and resistance genes in the environment. Improved surveillance could help identify pollution hotspots and assess the impact of reduction measures.

Regulatory and Policy Framework: The EU has implemented several policies to regulate the use of antimicrobials, including banning their use as growth promoters and setting stricter conditions for prescriptions. These measures are crucial for managing the risk of AMR.

Further efforts are needed to decrease the reliance on antimicrobials in food production. These include enhanced monitoring, promoting alternative practices in animal farming, and better animal welfare and biosecurity measures.

While improvements are clear and commendable in the EU-27 states, increased antimicrobial usage in some EU countries and in various areas around the world represent a significant concern.

For further details on the use of veterinary antimicrobials in Europe’s environment, you can refer to the EEA’s full report.

Organic acids can play a crucial role in zinc oxide replacement

Dr. Inge Heinzl, Editor EW Nutrition &
Juan Antonio Mesonero Escuredo, GTM Swine/GPM Organic Acids EW Nutrition

The use of high levels of Zinc Oxide (ZnO) in the EU before 2022 was one of the most common methods to prevent postweaning diarrhea (PWD) in pig production. Pharmacologically high levels of ZnO (2000-3000 ppm) increase growth and reduce the incidence of enteric bacterial diseases such as post-weaning diarrhea (PWD)(Carlson et al., 1999; Hill et al., 2000; Hill et al., 2001; Poulsen & Larsen, 1995; De Mille et al., 2019).

However, ZnO showed adverse effects, such as the accumulation of heavy metal in the environment, the risk for antimicrobial resistance (AMR), and problems of mineral toxicity and adverse growth effects when feeding it longer than 28 days (Jensen et al., 2018; Cavaco et al., 2011; Vahjen, 2015; Romeo et al., 2014; Burrough et al., 2019). To replace ZnO in pig production, let us first look at its positive effects to know what we must compensate for.

ZnO has a multifactorial mode of action

ZnO shows several beneficial characteristics that positively influence gut health, the immune system, digestion, and, therefore, also overall health and growth performance.

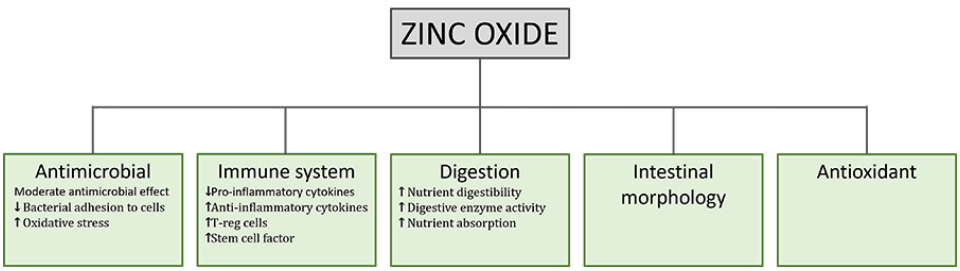


Figure 1. Beneficial effects and ZnO mode of action in postweaning piglets

1. ZnO acts as an antimicrobial

Concerning the antimicrobial effects of ZnO, different possible modes of action are discussed:

- ZnO in high dosages generates reactive oxygen species (ROS) that can damage the bacterial cell walls (Pasquet et al., 2014)
- The death of the bacterial cell due to direct contact of the metallic Zn to the cell (Shearier et al., 2016)
- Intrinsic antimicrobial properties of the ZnO^{2+} ions after dissociation. The uptake of zinc into cells is regulated by homeostasis. A concentration of the ZnO^{2+} ions higher than the optimal level of 10^{-7} to 10^{-5} M (depending on the microbial strain) allows the invasion of Zn^{2+} ions into the cell, and the zinc starts to be cytotoxic (Sugarman, 1983; Borovanský et al., 1989).

ZnO shows activity against, e.g., *Staphylococcus aureus, Pseudomonas aeruginosa, E. coli, Streptococcus pyogenes*, and other enterobacteria *(*Ann et al., 2014; Vahjen et al., 2016). However, Roselli et al. (2003) did not see a viability-decreasing effect of ZnO on ETEC.

2. ZnO modulates the immune system

Besides fighting pathogenic organisms as described in the previous chapter and supporting the immune system, ZnO is an essential trace element and has a vital role in the immune system. ZnO improves the innate immune response, increasing phagocytosis and oxidative bursts from macrophages and neutrophils. It also ameliorates the adaptative immune response by increasing the number of T lymphocytes (T cells) in general and regulatory T lymphocytes (T-regs) in particular. These cells control the immune response and inflammation (Kloubert et al., 2018). Macrophage capacity for phagocytosis (Ercan and Bor, 1991) and to kill parasites (Wirth et al., 1989), and also the killing activity of natural killer cells depends on Zn (Rolles et al., 2018). By reducing bacterial adhesion and blocking bacterial invasion, ZnO disburdens the immune system (Roselli et al., 2003).

ZnO reduces the expression of several proinflammatory cytokines induced by ETEC (Roselli et al., 2003). Several studies have also shown a modulation effect on intestinal inflammation, decreasing levels of IFN-γ, TNF-α, IL-1ß and IL-6, all pro-inflammatory, in piglets supplemented with ZnO (Zhu et al., 2017; Grilli et al., 2015).

3. ZnO improves digestion and promotes growth

Besides protecting young piglets against diarrhea, the goal is to make them grow optimally. For this target, an efficient digestion and a high absorption of nutrients is essential. Stimulating diverse pancreatic enzymes such as amylase, carboxypeptidase A, trypsin, chymotrypsin, and lipase increases digestibility (Hedemann et al., 2006; Pieper et al., 2015). However, Pieper et al. (2015) also showed that a long-term supply of very high dietary zinc triggers oxidative stress in the pancreas of piglets.

By stimulating the secretion of ghrelin at the stomach level and thereby promoting the release of insulin-like growth factor (IGF-1) and cholecystokinin (CCK), ZnO enhances muscle protein synthesis, cell proliferation, and feed intake (Yin et al., 2009; MacDonald et al., 2000)).

The result of improved digestion is increased body weight and average daily gain, which can be seen, e.g., in a study by Zhu et al. (2017).

4. ZnO protects the intestinal morphology

ZnO prevents the decrease of the trans-endothelial electrical resistance (TEER), usually occurring in the case of inflammation, by downregulating TNF-α and IFN-γ. TNF-α, as well as IFN-γ, increase the permeability of the epithelial tight junctions and, therefore, the intestinal barrier (Al-Sadi et al., 2009).

The enterotrophic and anti-apoptotic effect of ZnO is reflected by a higher number of proliferating and PCNA-positive cells and an increased mucosa surface in the ileum (higher villi, higher villi/crypt ratio)(Grilli et al., 2015). Zhu et al. (2017) also saw an increase in villus height in the duodenum and ileum and a decrease in crypt depth in the duodenum due to the application of 3000 mg of ZnO/kg. Additionally, they could notice a significant ($P<0.05$) upregulation of the mRNA expression of the zonula occludens-1 and occluding in the mucosa of the jejunum of weaned piglets.

In a trial conducted by Roselli et al. (2003), the supplementation of 0.2 mmol/L ZnO prevented the disruption of the membrane integrity when human Caco-2 enterocytes were challenged with ETEC.

5. ZnO acts antioxidant

The antioxidant effect of ZnO was shown in a study conducted by Zhu et al., 2017. They could demonstrate that the concentration of malondialdehyde (MDA), a marker for lipid peroxidation, decreased on day 14 or 28, and the total concentration of superoxide dismutase (SOD), comprising enzymes that transform harmful superoxide anions into hydrogen peroxide, increased on day 14 ($P<0.05$). Additionally, Zn is an essential ion for the catalytic action of these enzymes.

Which positive effects of ZnO can be covered by organic acids (OAs)?

1. OAs act antimicrobial

OAs, on the one hand, lower the pH in the gastrointestinal tract. Some pathogenic bacteria are susceptible to low pH. At a $pH<5$, the proliferation of, e.g., Salmonella, E. coli, and Clostridium is minimized. The good thing is that some beneficial bacteria, such as lactobacilli or bifidobacteria, survive as they are acid-tolerant. The lactobacilli, on their side, can produce hydrogen peroxide, which inhibits, e.g., Staphylococcus aureus or Pseudomonas spp. (Juven and Pierson, 1996).

Besides this more indirect mode of action, a more direct one is also possible: Owing to their lipophilic character, the undissociated form of OAs can pass the bacterial membrane (Partanen and Mroz, 1999). The lower the external pH, the more undissociated acid is available for invading the microbial cells. Inside the cell, the pH is higher than outside, and the OA dissociates. The release of hydrogen ions leads to a decrease in the internal pH of the cell and to a depressed cell metabolism. To get back to “normal conditions”, the cell expels protons. However, this is an energy-consuming process; longer exposure to OAs leads to cell death. The anion remaining in the cell, when removing the protons, disturbs the cell’s metabolic processes and participates in killing the bacterium.

These theoretical effects could be shown in a practical trial by Ahmed et al. (2014). He fed citric acid (0.5 %) and a blend of acidifiers composed of formic, propionic, lactic, and phosphoric acid + SiO_2 (0.4 %) and saw a reduction in fecal counts of Salmonella and E. coli for both groups.

2. OAs modulate the immune system

The immune system is essential in the pig’s life, especially around weaning. Organic acids have been shown to support or stimulate the immune system. Citric acid (0.5%), as well as the blend of acidifiers mentioned before (Ahmed et al., 2014), significantly increased the level of serum IgG. IgG is part of the humoral immune system. They mark foreign substances to be eliminated by other defense systems.

Ren et al. (2019) could demonstrate a decrease in plasma tumor necrosis factor-α that regulates the activity of diverse immune cells. He also found lower interferon-γ and interleukin (Il)-1ß values in the OA group than in the control group after the challenge with ETEC. This trial shows that inflammatory response can be mitigated through the addition of organic acids.

3. OAs improve digestion and promote growth

In piglets, the acidity in the stomach is responsible for the activation and stimulation of certain enzymes. Additionally, it keeps the feed in the stomach for a longer time. Both effects lead to better digestion of the feed.

In the stomach, the conversion of pepsinogen to pepsin, which is responsible for protein digestion, is catalyzed under acid conditions (Sanny et al., 1975)group. Pepsin works optimally at two pH levels: pH 2 and pH 3.5 (Taylor, 1959). With increasing pH, the activity decreases; at pH 6, it stops. Therefore, a high pH can lead to poor digestion and undigested protein arriving in the intestine.

These final products of pepsin protein digestion are needed in the lower parts of the GIT to stimulate the secretion of pancreatic proteolytic enzymes. If they do not arrive, the enzymes are not activated, and the inadequate protein digestion continues. Additionally, gastric acid is the primary stimulant for bicarbonate secretion in the pancreas, neutralizing gastric acid and providing an optimal pH environment for the digestive enzymes working in the duodenum.

As already mentioned, the pH in the stomach influences the transport of digesta. The amount of digesta being transferred from the stomach to the small intestine is related to the acidity of the chyme leaving the stomach and arriving in the small intestine. Emptying of the stomach can only take place when the duodenal chyme can be neutralized by pancreatic or other secretions (Pohl et al., 2008); so, acid-sensitive receptors provide feedback regulation and a higher pH in the stomach leads to a faster transport of the digesta and a worse feed digestion.

4. OAs protect the intestinal morphology

Maintaining an intact gut mucosa with a high surface area is crucial for optimal nutrient absorption. Research suggests organic acids play a significant role in improving mucosal health:

Butyric acid promotes epithelial cell proliferation, as demonstrated in an *in vitro* pig hindgut mucosa study (Sakata et al., 1995). Fumaric acid, serving as an energy source, may locally enhance small intestinal mucosal growth, aiding in post-weaning epithelial cells' recovery and increasing absorptive surface and digestive capacity (Blank et al., 1999). Sodium butyrate supplementation at low doses influences gastric morphology and function, thickening the stomach mucosa and enhancing mucosal maturation and differentiation (Mazzoni et al., 2008).

Studies show that organic acids affect gut morphology, with a mixture of short-chain and mid-chain fatty acids leading to longer villi (Ferrara et al., 2016) and Na-butyrate supplementation increasing crypt depth and villi length in the distal jejunum and ileum (Kotunia et al., 2004). However, the villi length and mucosa thickness in the duodenum were reduced. Dietary sodium butyrate has been linked to increased microvilli length and cecal crypt depth in pigs (Gálfi and Bokori, 1990).

5. OAs show antioxidant activity

The last characteristic, the antioxidant effect, cannot be provided at the same level as with ZnO; however, Zhang et al. (2019) attest to OAs a certain antioxidant activity. Oxalic, citric, acetic, malic, and succinic acids, which were extracted from Camellia oleifera, also showed good antioxidant activity in a trial conducted by Zhang et al. (2020).

Organic acids are an excellent tool to compensate for the ban on ZnO

The article shows that organic acids have similar positive effects as zinc oxide. They act antimicrobial, modulate the immune system, maintain the gut morphology, fight pathogenic microbes, and also act – slightly – antioxidant. Additionally, they have a significant advantage: they are not harmful to the

environment. Organic acids used in the proper pH range and combination are good tools for replacing zinc oxide.

References on request

INFOGRAPHIC – Target measurements for water quality

Water is a main nutrient and carrier for vaccines, medicine – including antibiotics, but also for pathogens

Chemistry

pH and pKa

Acidity and dissociation index
Target: pH 3,5-3,8 Important for acids application (E.g. organic acids, etc), and ORP

Hardness

Content of Ca, sometimes plus Mg
Target: better TDS Important for acid binding capacity (ABC, buffer capacity)

Oxidation Reduction Potential (ORP)

Target: 650 mV>700 mV » reduces water intake Important for biocides application (E.g. chlorination)

Total Dissolved Solids (TDS)

Sum of dissolved salts, minerals, metals, carbonates, organics Target: 2000 ppm>3000 ppm » laxation
Important for buffer capacity and ORP

Microbiology

Yeast

Target: < 5000 cfu/gr

Enterobacterias

Target: < 100 cfu/gr

Moulds

Target: < 100 cfu/gr

Nutritional considerations for immunity and gut health

Conference report

At the recent EW Nutrition Poultry Academy in Jakarta, Indonesia, Dr Steve Leeson, Professor Emeritus, University of Guelph, Canada, opened his presentation by stating that “it is obvious that any nutrient deficiency will impact bird health, but not so obvious is that nutrition *per se* can positively impact immunity and health in an otherwise healthy and high-producing bird.”

Modern high-performing broilers are characterized by extremely high feed intake. This puts a lot of stress on the physiology of the entire gastrointestinal tract, but particularly so on the absorptive epithelial cells of the small intestine. Any organism requires a nutrient source for survival and reproduction. Dr Leeson asked “can we significantly reduce nutrient supply to pathogens, while sustaining bird productivity?”

He reminded the audience that no cellular function comes for free: so there is always a “cost”. A general conclusion is that 10% of nutrients can be used for immune function during disease challenge, and always get priority. Therefore, you don’t want to overstimulate the immune system, which in extreme situations leads to an inflammatory response. In his presentation, Dr Leeson considered factors determining gut health and nutritional tools which are available to support gut health.

Gut microflora

Gut pathogens impact the bird and/or the consumer. *Clostridia* and *E. coli* are the major concerns regarding bird health and productivity, whereas *Salmonella* and *Campylobacter* are major pathogens important for human health.

The chick hatches with a gut virtually devoid of microbes, so early colonizers tend to predominate quite quickly. Microbial species present on the hatching tray, during delivery and during the first few days at the farm will likely dictate early gut colonization. In some instances, the chick's microflora may be established by the time it gets to the farm, so the probiotic faces more of a challenge to establish itself as the predominant species.

Antibiotic alternatives

Gut villi development matures at around 10-15 days of age. The broiler pre-starter diet therefore is a target for feed additives that positively impact gut structure and development.

- Among the **short chain fatty acids**, butyric acid is considered the prime energy source for enterocytes and it is also necessary for the correct development of the gut-associated lymphoid tissue (GALT). Butyric acid can also be added indirectly via fermentation of judicious levels of soluble fiber to encourage optimal gut villi development. Dr Leeson added that he is a big believer in butyric acid, encouraging a good gut structure at 10 days, which can be worth about 50 kcal.
- **Exogenous enzymes** should also be considered in an attempt to maximize digestion and limit the flow of nutrients to the large intestine and ceca. Protease enzymes have great potential in this regard, since they allow nutritionists to reduce dietary crude protein and hopefully reduce the supply of nitrogen that fuels proteolytic Clostridia bacteria in the large intestine and ceca.
- **Amino acids**, particularly threonine, play a critical role in the maintenance of intestinal mucosal integrity and barrier function, especially for mucin synthesis, which protects enterocytes from adherence by pathogenic bacteria, and from attack by endogenous enzymes and acids.
- **Polyunsaturated fatty acids** (PUFAs) – Omega-3s and especially DHA from fish oil help to reduce inflammatory response (overstimulation). Omega-3s are poorly converted to DHA by the chicken, so conventional sources such as flax are of limited application for immunity.
- **Blood plasma** from pigs or cattle is a complex spray-dried mixture of proteins and amino acids, many of which are immunoglobulins that "temper" the immune system, much like PUFAs.
- **Vitamins A, D, E and C** have vital roles in the normal function of the immune system and have antioxidant capacity.
- Certain **complex carbohydrates**, such as ß-glucans, influence gut health due to their fermentation, leading to the production of short-chain fatty acids, such as butyrate.
- **Antioxidants** – to firstly control oxidation of fats and fat-soluble vitamins in feed, and secondly to optimize birds' cellular oxidative capacity, to prevent cell damage, therefore maintaining healthy cellular and immune function.
- **Betaine** increases intracellular water retention, reducing "dehydration" of microvilli and increasing their volume/surface area.
- **Fiber** – moderate levels (1-2%) of soluble (fermentable) and insoluble fiber can be beneficial to early gut development by stimulating gizzard development and endogenous enzyme production.
- **Phytogenics** are becoming very common in combination with acidifiers (upper tract) and probiotics. Essential oils are becoming more mainstream the more we know about them.

Recommendations for optimizing gut health and immunity

Fast growth rate and high egg output are negatively correlated with immune response. Consequently, nutrient-dense diets are not optimal for immunity. With bacteria, it's a numbers game – but these numbers quickly multiply. The first 7 days are important, therefore probiotics must be established early. Consider

the role of targeted feed additives, such as butyrate, phytogenics, antioxidants, PUFAs etc.

Also, maximize feed particle size – the limit is usually pellet quality. Mitigate nutrient transition at any diet change. Review the supply of trace minerals, as there is a trend to lower levels of organic minerals. With all the factors that weigh into production performance, any support that can be rallied through nutrition needs to be considered.

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EW Nutrition's Poultry Academy took place in Jakarta and Manila in early September 2023. Dr. Steve Leeson, an expert in Poultry Nutrition & Production with nearly 50 years' experience in the industry, was the distinguished keynote speaker.

Dr. Leeson had his Ph.D. in Poultry Nutrition in 1974 from the University of Nottingham. Over a span of 38 years, he was a Professor in the Department of Animal &Poultry Science at the University of Guelph, Canada. Since 2014, he has been Professor Emeritus at the same University. As an eminent author, he has more than 400 papers in refereed journals and 6 books on various aspects of Poultry Nutrition & Management. He also won the American Feed Manufacturer's Association Nutrition Research Award (1981), the Canadian Society of Animal Science Fellowship Award (2001), and Novus Lifetime Achievement Award in Poultry Nutrition (2011).

Salmonella in pigs: a threat for humans and a challenge for pig producers

*By **Dr. Inge Heinzl**, Editor, EW Nutrition*

Salmonellosis is third among foodborne diseases leading to death (Ferrari, 2019). More than 91,000 human cases of Salmonellosis are reported by the EU each year, generating overall costs of up to €3 billion a year (EFSA, 2023), 10-20% of which are attributed to pork consumption (Soumet, 2022). The annual costs arising from the resulting human health losses in 2010 were about €90 million (FCC Consortium, 2010). Take the example of Ireland, where a high prevalence of Salmonella in lymph nodes still shows a severe issue pre-slaughter and a big challenge for slaughterhouses to stick to the process hygiene requirements (Deane, 2022).

Several governments already have monitoring programs in place, and the farms are categorized according to the salmonella contamination of their pigs. In some countries, e.g., Denmark, an economic penalty of 2% of the carcass value must be paid if the farm has level 2 (intermediate seroprevalence) and 4-8% if the level is 3. Other countries, e.g., Germany, the UK, Ireland, or the Netherlands, use quality assurance schemes. The farmers can only sell their carcasses under this label if their farm has a certain level.

Let’s take a quick look at the genus of Salmonella

Salmonellas are rod-shaped gram-negative bacteria of the family of enterobacteria that use flagella for their movement. They were named after the American vet Daniel Elmer Salmon. The genus of Salmonella consists of two species (S. bongori and S. enterica with seven subspecies) with in total more than 2500 serovars (see Figure 1). The effects of the different serovars can range from asymptomatic carriage to severe invasive systemic disease (Gal-Mor, 2014). All Salmonella serovars generally can cause disease in humans; the rosa-marked ones already showed infections.

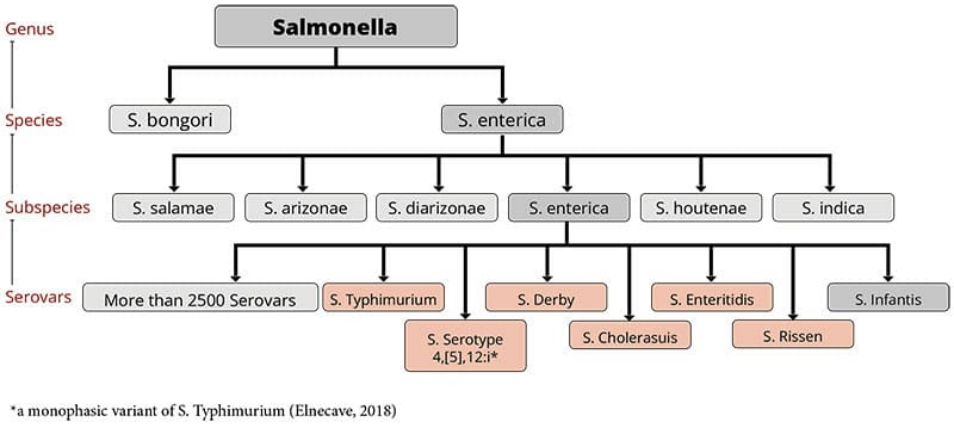


Figure 1: the genus of Salmonella with Salmonella serovars relevant for pigs (according to Bonardi, 2017: Salmonella in the pork production chain and its impact on human health in the European Union)

Within the group of Salmonella, some serovars can only reside in one or few species, e.g., S. enterica spp. enterica Serovar Dublin (S. Dublin) in bovines (Waldron, 2018) or S. Cholerasuis in pigs (Chiu, 2004). An infection in humans with these pathogens is often invasive and life-threatening (WHO, 2018). On the contrary, serovars like S. Typhimurium and S. Enteritidis are not host-specific and can cause disease in various species.

The serotypes S. Typhi and S. Paratyphi A, B, or C are highly adapted to humans and only for them pathogenic; they are responsible for the occurrence of typhus.

Serovars occurring in pigs and relevant for humans are, for example, S. Typhimurium (Hendriksen, 2004), S. Serotype 4,[5],12:I (Hauser et al., 2010), S. Cholerasuis (Chiu, 2004), S. Derby (Gonzalez-Santamarina, 2021), S. Agona (Brenner Michael, 2006) and S. Rissen (Elbediwi, 2021).

Transmission of Salmonella mostly happens via contaminated food

The way of transmission to humans depends on the serovar:
Human-specific and, therefore, only in humans and higher primates residing serovars S. Typhi and Paratyphi A, B, or C (typhoidal) are excreted via feces or urine. Therefore, any food or water contaminated with the feces or urine of infected people can transmit this disease (Government of South Australia, 2023). Typhoid and paratyphoid Salmonellosis occur endemic in developing countries with the lack of clean water and, therefore, inadequate hygiene (Gal-Mor, 2014).

Serovars which can cause disease in humans **and** animals (non-typhoidal), can be transmitted by
– animal products such as milk, eggs, meat
– contact with infected persons/animals (pigs, cows, pets, reptiles…) or
– other feces- or urine-contaminated products such as sprouts, vegetables, fruits….

Farm animals take salmonellas from their fellows, contaminated feed or water, rodents, or pests.

Symptoms of Salmonellosis can be severe

In the case of typhoid or paratyphoid Salmonellosis, the onset of illness is gradual. People can suffer from sustained high fever, unwellness, severe headache, and decreased appetite, but also from an enlarged spleen irritating the abdomen and dry cough.

A study conducted in Thailand with children suffering from enteric fever caused by the typhoid serovars S. Typhi and Paratyphi showed a sudden onset of fever and gastrointestinal issues (diarrhea), rose spots, bronchitis, and pneumonia (Thisyakorn et al., 1987)

The non-typhoid Salmonellosis is typically characterized by an acute onset of fever, nausea, abdominal pain with diarrhea, and sometimes vomiting (WHO, 2018). However, 5% of the persons – children with underlying conditions, e.g., babies, or people who have AIDS, malignancies, inflammatory bowel disease, gastrointestinal illness caused by non-typhoid serovars, and hemolytic anemia, or receiving an immunosuppressive therapy can be susceptible to bacteremia. Additionally, serovars like S. Cholerasuis or S. Dublin are apt to develop bacteremia by entering the bloodstream with little or no involvement of the gut (Chiu, 1999). In these cases, consequences can be septic arthritis, pneumonia, peritonitis, cutaneous abscess, mycotic aneurysm, and sometimes death (Chen et al., 2007; Chiu, 2004, Wang et al., 1996).

In pigs, S. Cholerasuis causes high fever, purple discolorations of the skin, and thereinafter diarrhea. The mortality rate in pigs suffering from this type of Salmonellosis is high. Barrows orally challenged with S. Typhimurium showed elevated rectal temperature by 12h, remaining elevated until the end of the study. Feed intake decreased with a peak at 48h after the challenge and remained up to 120h after the challenge. Daily gain reduced during the following two weeks after infection. A higher plasma cortisol level and a lower IGF-I level could also be noticed. All these effects indicate significant changes in the endocrine stress and the somatotropic axis, also without significant alterations in the systemic pro-inflammatory mediators (Balaji et al., 2000)

To protect humans, Salmonella in pork must be restraint

There are three main steps to keep the contamination of pork as low as possible:

1. Keeping Salmonella out of the pig farm
2. Minimizing spreading if Salmonella is already on the farm
3. Minimizing contamination in the slaughterhouse

1. How to keep Salmonella out of the pig farm?

To answer this question, we must look at how the pathogen can be transported to the farm. According to the Code of Practice for the Prevention and Control of Salmonella on Pig Farms (Ministry of Agriculture, Fisheries and Food and the Scottish Executive Rural Affairs Department), there are several possibilities to infiltrate the pathogen into the farm:

- Diseased pigs or pigs which are ill but don’t show any symptoms
- Feeding stuff or bedding contaminated with dung
- Pets, rodents, wild birds, or animals
- Farm personnel or visitors
- Equipment or vehicles

Caution with purchased animals!

To minimize/prevent the entry of Salmonella into the livestock, bought-in animals must come from reputable breeding farms with a salmonella monitoring system in place. As possible carrier animals are more likely to excrete Salmonella when stressed; they should be kept in isolation after purchasing. Additionally, the animals must go through a disinfectant foot bath before entering the farm.

Keep rodents, wild animals, and vermin in check!

Generally, the production site must be kept clean and as unattractive as possible for all these animals. Rests of feed must be removed, and dead animals and afterbirths must be promptly and carefully disposed of. A well-planned baiting and trapping policy should be in place to effectively control rodents.

Only selected people should enter the hog houses

In any case, the number of persons entering the hog house must be kept as low as possible. Farmworkers should be trained in the principles of hygiene. They should wear adequate clothing (waterproof boots and protective overalls) that can be easily cleaned/laundered and disinfected. The clothes/shoes should always be used only at this site. Thorough hand washing and the disinfection of the boots when entering and leaving the pig unit are a must.

If visits are necessary, the visitors should take the same measures as the farm workers. And, of course, they should not have had contact with another pig farm during the last 48 hours.

Keep pens, farm equipment, and vehicles clean!

Farm equipment should not be shared with other farms. If this cannot be avoided, it must be cleaned and disinfected before re-entering the farm. Also, the vehicles for the transport of the animals must be cleaned and disinfected as soon as possible after usage, as contaminated transporters always pose the risk of infection.

Feed should be Salmonella-free!

To get high feed quality, the feed should be purchased from feed mills/sources with a well-functioning bacterial control to guarantee the absence of Salmonella. It is essential that birds, domestic and wild animals cannot enter the feed stores.
It is also advised to keep dry feed dry as possibly contaminating Salmonella can multiply in such humid conditions. Additionally, all feed bins and delivery pipes for dry and wet feed must be consciously cleaned, and the damp feed pipes also disinfected.
The change from pellets to mash could be helpful as the pellets facilitate Salmonella colonization by stimulating the secretion of mucins (Hedemann et al., 2005).

For sanitation of the feed, we offer organic acids (Acidomix product range) or mixtures of organic acids and formaldehyde in countries where formaldehyde products are allowed (Formycine) to decrease the pathogenic load of the feed materials. In vitro trials show the effectiveness of the products:

For the in vitro trial with Formycine, autoclaved feed samples were inoculated with Salmonella enteritidis serovar Typhimurium DSM 19587 strain to reach a Salmonella contamination of 10^6 CFU/g of feed. After incubating at room temperature for three hours, Formycine Liquido was added to the contaminated feed samples at 0, 500, 1000, and 2000 ppm. The control and inoculated feed samples were further incubated at room temperature, and Salmonella counts (CFU/g) were carried out at 24, 48, 72 hours and on day 15.

The limit of Salmonella detection was set at 100 CFU/g (10^2). Results are shown in figure 2.

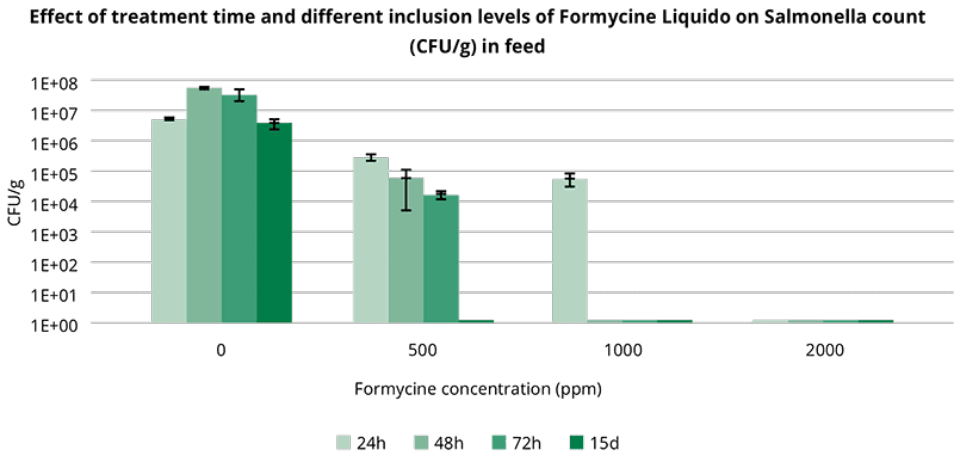


Fig. 2: Effect of treatment time and different inclusion levels of Formycine Liquido on the Salmonella count in feed

As important as uncontaminated feed is clean water for drinking. It can be achieved by taking the water from a main or a bacteriologically controlled water borehole. Regular cleaning/disinfection of the tanks, pipes, and drinkers is essential.

Bedding should be Salmonella-free

Straw material containing feces of other animals (rodents, pets) always carries the risk of Salmonella contamination. Also, wet or moldy bedding is not recommended because it is an additional challenge for the animal. To optimize the quality of bedding, the straw should be bought from reliable and as few as possible sources. The material must be stored dry and as far as practicable from the pig buildings (Ministry of Agriculture, Fisheries and Food & Scottish Executive Rural Affairs Department, 2000).

Vaccination is a beneficial measure

For the control of Salmonella in swine herds, vaccination is an effective tool. De Ridder et al. (2013) showed that an attenuated vaccine reduced the transmission of Salmonella Typhimurium in pigs. The vaccination with an attenuated S. Typhimurium strain, followed by a booster vaccination with inactivated S. Cholerasuis, showed better effects than an inactivated S. Cholerasuis vaccine alone (Alborali et al., 2017). Bearson et al. (2017) could delimitate transmission through less shedding and protect the animals against systemic disease.
To achieve the best effects, the producer must understand the diversity of Salmonella serovars to choose the most promising vaccination strategy (FSIS, 2023).

2. How to minimize the spreading of Salmonella on the farm?

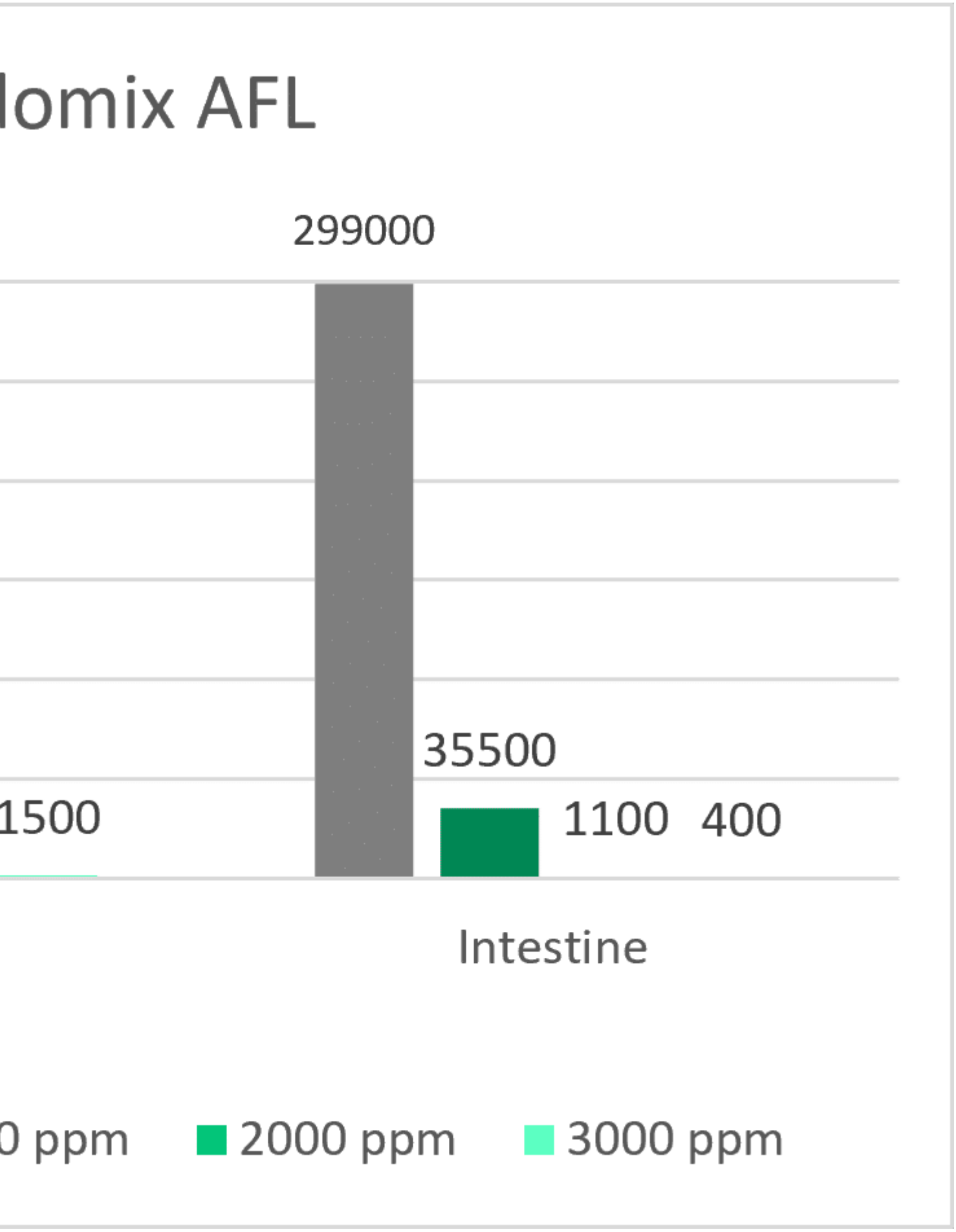
If there are already cases of Salmonella on the farm, infected animals must be separated from the rest of the herd. Small batch sizes are beneficial, as well as not mixing different litters after weaning. If feasible, separate units for different production phases with an all-in/all-out system could break the reinfection cycle and help reduce Salmonella contamination on the farm. And also in this case, vaccination is helpful.

Salmonella doesn’t like acid conditions

An effective tool is acidifying the feed with organic acids, as Salmonella doesn’t like acid conditions. A trial was conducted with Acidomix AFG and Acidomix AFL to show their effects against Salmonella. For the test, 10^5 CFU/g of Salmonella enterica ser. Typhimurium was added to feed containing 1000 ppm, 2000 ppm, and 3000 ppm of Acidomix AFG or AFL. The stomach and intestine were simulated in vitro by adjusting the pH with HCl and NaHCO3 as follows:

Stomach	2.8
Intestine	6.8-7.0

After the respective incubation, the microorganisms were recovered from feed and plated on an appropriate medium for CFU counting. The results are shown in figures 3 and 4.


lomix AFL
299000
35500
1500
1100
400
Intestine
0 ppm
2000 ppm
3000 ppm

Figures 3 + 4: Effects of different concentrations of Acidomix AFG and Acidomix AFL against Salmonella enterica ser. Typhimurium in feed

Phytomolecules can support pigs against Salmonella

Plant compounds or phytomolecules can also be used against Salmonella in pigs. Some examples of phytomolecules to be used are Piperine, Allicin, Eugenol, and Carvacrol. Eugenol, e.g., increases the permeability of the Salmonella membrane, disrupts the cytoplasmic membrane, and inhibits the production of bacterial virulence factors (Keita et al., 2022; Mak et al., 2019). Thymol and Carvacrol interact with the cell membrane by H bonding, also resulting in a higher permeability.

An already published in vitro trial conducted with our product Ventar D also showed excellent effects against Salmonella while sparing the beneficial gut flora. A further trial once more demonstrated the susceptibility of Salmonella to Ventar D. It showed that Ventar D controls Salmonella by suppressing their motility and, at higher concentrations, inactivating the cells (see figures 5 + 6):

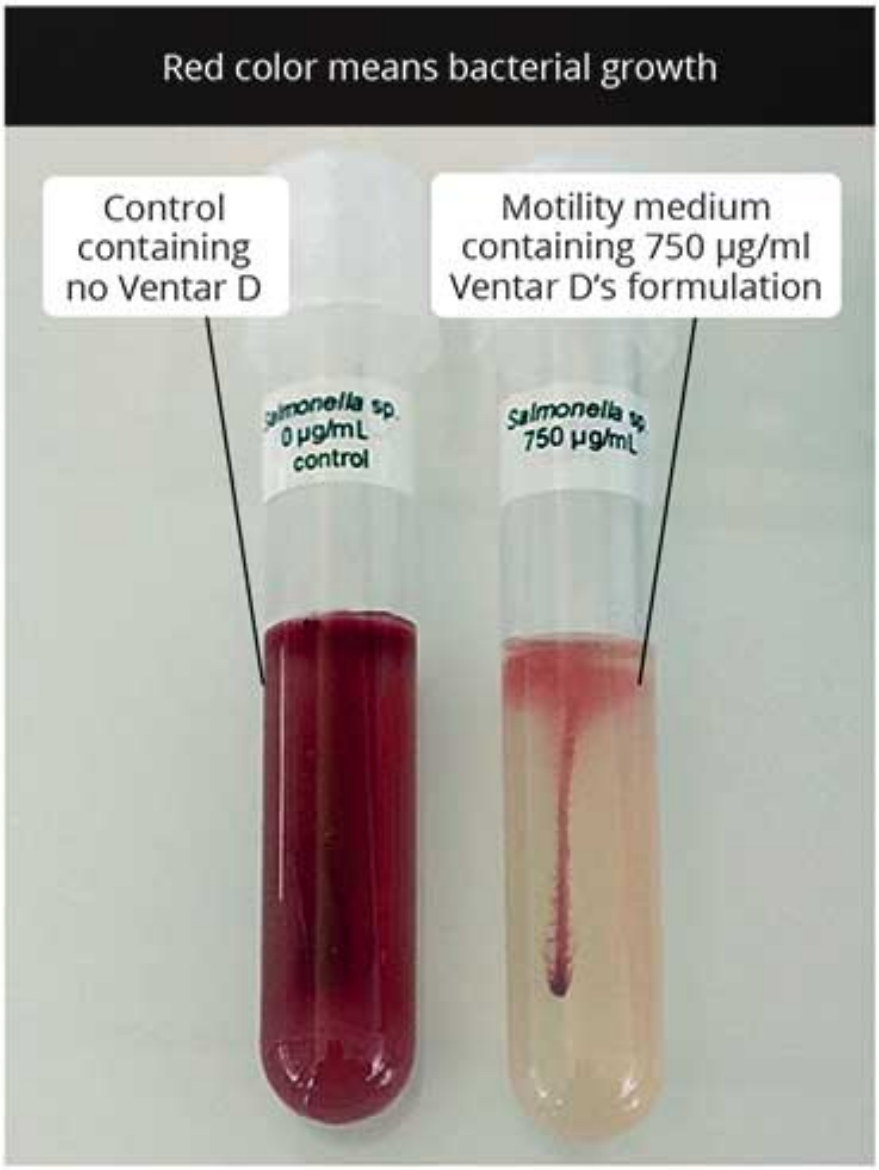


Figure 5: S. enterica motility test: on the left side – control; on the right side – motility medium containing.750 µg/mL of Ventar

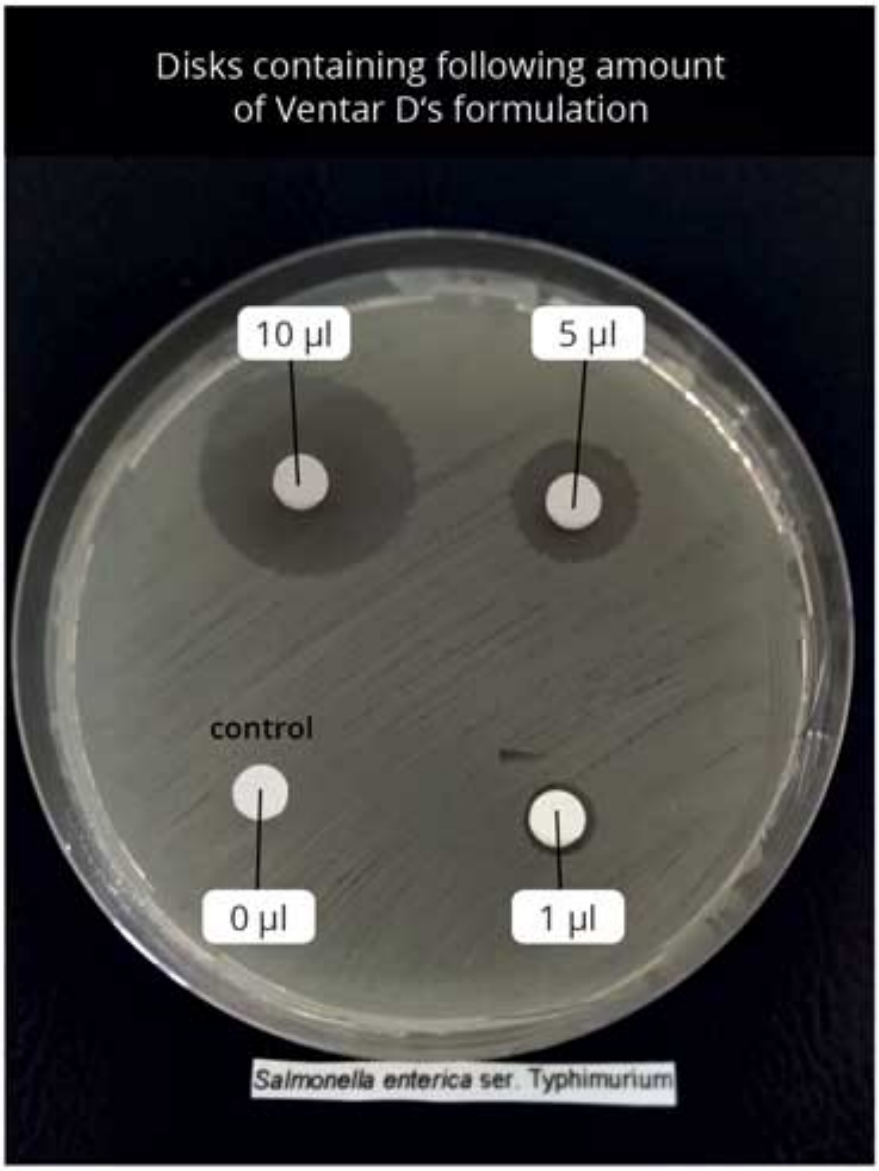


Fig 6 . Disk diffusion assay employing S. enterica. upper left side – disk containing 10 µL of Ventar; upper right – 5 µL; lower left – control; lower right – 1µL.

In addition to the direct Salmonella-reducing effect, essential oils / secondary plant compounds / phytomolecules improve digestive enzyme activity and digestion, leading to increased nutrient absorption and better feed conversion (Windisch et al., 2008).

3. How can the farmer keep Salmonella contamination low in the slaughterhouse?

In general, the slaughterhouse personnel is responsible for adequate hygiene management to prevent contamination of carcasses and meat. However, also the farmer can make his contribution to maintain the risk of contamination in the slaughterhouse as low as possible. A study by Vieira-Pinto (2006) revealed that one Salmonella-positive pig can contaminate several other carcasses.

According to a trial conducted by Hurd et al. (2002), infection and, therefore, "contamination" of other pigs can rapidly occur, meaning that cross-contamination is a topic during transport to the slaughterhouse and in the lairages when the pigs come together with animals from other farms. The stress to which the pigs are exposed influences physiological and biochemical processes. The microbiome and animal's immunity are affected, leading to higher excretion of Salmonella during transport and in the lairages. So, the animals should not be stressed during loading and unloading or transportation. The trailer poses a further risk of

infection if it was not cleaned and disinfected before. So, reliable people who treat the animals well and keep their trailers clean should be chosen for transportation.

Pig producers are obliged to keep Salmonella in check – phytomolecules can help

At least in the EU, pig producers have the big duty to keep Salmonella low in their herds; otherwise, they will have financial losses. They are not only responsible for their farm, but also the slaughterhouses count on them. Besides the standard strict hygiene management and vaccination, farmers can use products provided by the industry to sanitize feed but also to support their animals directly with phytomolecules acting against pathogens and supporting gut health.

All these measures together should be a solution to the immense challenge of Salmonella, to protect people and prevent economic losses.

References:

Alborali, Giovanni Loris, Jessica Ruggeri, Michele Pesciaroli, Nicola Martinelli, Barbara Chirullo, Serena Ammendola, Andrea Battistoni, Maria Cristina Ossiprandi, Attilio Corradi, and Paolo Pasquali. “Prime-Boost Vaccination with Attenuated Salmonella Typhimurium Δznuabc and Inactivated Salmonella Choleraesuis Is Protective against Salmonella Choleraesuis Challenge Infection in Piglets.” *BMC Veterinary Research* 13, no. 1 (2017): 284. https://doi.org/10.1186/s12917-017-1202-5.

Balaji, R, K J Wright, C M Hill, S S Dritz, E L Knoppel, and J E Minton. “Acute Phase Responses of Pigs Challenged Orally with Salmonella Typhimurium.” *Journal of Animal Science* 78, no. 7 (2000): 1885. https://doi.org/10.2527/2000.7871885x.

Bearson, Bradley L, Shawn M. Bearson, Brian W Brunelle, Darrell O Bayles, In Soo Lee, and Jalusa D Kich. “Salmonella Diva Vaccine Reduces Disease, Colonization, and Shedding Due to Virulent S. Typhimurium Infection in Swine.” *Journal of Medical Microbiology* 66, no. 5 (2017): 651–61. https://doi.org/10.1099/jmm.0.000482.

Brenner Michael, G, M Cardoso, and S Schwarz. “Molecular Analysis of Salmonella Enterica Subsp. Enterica Serovar Agona Isolated from Slaughter Pigs.” *Veterinary Microbiology* 112, no. 1 (2006): 43–52. https://doi.org/10.1016/j.vetmic.2005.10.011.

Chen, P.-L., C.-M. Chang, C.-J. Wu, N.-Y. Ko, N.-Y. Lee, H.-C. Lee, H.-I. Shih, C.-C. Lee, R.-R. Wang, and W.-C. Ko. “Extraintestinal Focal Infections in Adults with Non-typhoid Salmonella Bacteraemia: Predisposing Factors and Clinical Outcome.” *Journal of Internal Medicine* 261, no. 1 (2007): 91–100. https://doi.org/10.1111/j.1365-2796.2006.01748.x.

Chiu, Cheng-Hsun, Lin-Hui Su, and Chishih Chu. “*Salmonella Enterica*Serotype Choleraesuis: Epidemiology, Pathogenesis, Clinical Disease, and Treatment.” *Clinical Microbiology Reviews* 17, no. 2 (2004): 311–22. https://doi.org/10.1128/cmr.17.2.311-322.2004.

De Ridder, L., D. Maes, J. Dewulf, F. Pasmans, F. Boyen, F. Haesebrouck, E. Méroc, P. Butaye, and Y. Van der Stede. “Evaluation of Three Intervention Strategies to Reduce the Transmission of Salmonella Typhimurium in Pigs.” *The Veterinary Journal* 197, no. 3 (2013): 613–18. https://doi.org/10.1016/j.tvjl.2013.03.026.

Deane, Annette, Declan Murphy, Finola C. Leonard, William Byrne, Tracey Clegg, Gillian Madigan, Margaret Griffin, John Egan, and Deirdre M. Prendergast. “Prevalence of Salmonella spp. in Slaughter Pigs and Carcasses in Irish Abattoirs and Their Antimicrobial Resistance.” *Irish Veterinary Journal* 75, no. 1 (2022). https://doi.org/10.1186/s13620-022-00211-y.

Edel, W., M. Schothorst, P. A. Guinée, and E. H. Kampelmacher. “Effect of Feeding Pellets on the Prevention and Sanitation of Salmonella Infections in Fattening Pigs1.” *Zentralblatt für Veterinärmedizin Reihe B* 17, no. 7 (2010): 730–38. https://doi.org/10.1111/j.1439-0450.1970.tb01571.x.

EFSA. “Salmonella.” European Food Safety Authority. Accessed August 7, 2023. https://www.efsa.europa.eu/en/topics/topic/salmonella.

Elbediwi, Mohammed, Daiwei Shi, Silpak Biswas, Xuebin Xu, and Min Yue. “Changing Patterns of Salmonella Enterica Serovar Rissen from Humans, Food Animals, and Animal-Derived Foods in China, 1995–2019.” *Frontiers in Microbiology* 12 (2021). https://doi.org/10.3389/fmicb.2021.702909.

Elnekave, Ehud, Samuel Hong, Alison E Mather, Dave Boxrud, Angela J Taylor, Victoria Lappi, Timothy J Johnson, et al. “Salmonella Enterica Serotype 4,[5],12:I:- In Swine in the United States Midwest: An Emerging Multidrug-Resistant Clade.” *Clinical Infectious Diseases* 66, no. 6 (2018): 877–85. https://doi.org/10.1093/cid/cix909.

FCC Consortium. “Final Report – Food Safety.” European Commission, 2010. https://food.ec.europa.eu/system/files/2016-10/biosafety_food-borne-disease_salmonella_fattening-pigs_slaughthouse-analysis-costs.pdf.

Ferrari, Rafaela G., Denes K. Rosario, Adelino Cunha-Neto, Sérgio B. Mano, Eduardo E. Figueiredo, and Carlos A. Conte-Junior. “Worldwide Epidemiology of *Salmonella s*erovars in Animal-Based Foods: A Meta-Analysis.” *Applied and Environmental Microbiology* 85, no. 14 (2019). https://doi.org/10.1128/aem.00591-19.

“FSIS Guideline to Control Salmonella in Swine Slaughter and Pork Processing Establishments.” FSIS Guideline to Control Salmonella in Swine Slaughter and Pork Processing Establishments | Food Safety and Inspection Service. Accessed August 14, 2023. https://www.fsis.usda.gov/guidelines/2023-0003.

Gal-Mor, Ohad, Erin C. Boyle, and Guntram A. Grassl. “Same Species, Different Diseases: How and Why Typhoidal and Non-Typhoidal Salmonella Enterica Serovars Differ.” *Frontiers in Microbiology* 5 (2014). https://doi.org/10.3389/fmicb.2014.00391.

González-Santamarina, Belén, Silvia García-Soto, Helmut Hotzel, Diana Meemken, Reinhard Fries, and Herbert Tomaso. “Salmonella Derby: A Comparative Genomic Analysis of Strains from Germany.” *Frontiers in Microbiology* 12 (2021). https://doi.org/10.3389/fmicb.2021.591929.

Government of South Australia. Typhoid and paratyphoid – including symptoms, treatment, and prevention, April 3, 2022. https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/conditions/infectious+diseases/typhoid+and+paratyphoid/typhoid+and+paratyphoid+-+including+symptoms+treatment+and+prevention.

Hauser, Elisabeth, Erhard Tietze, Reiner Helmuth, Ernst Junker, Kathrin Blank, Rita Prager, Wolfgang Rabsch, Bernd Appel, Angelika Fruth, and Burkhard Malorny. “Pork Contaminated with *Salmonella Enterica* Serovar 4,[5],12:I:−, an Emerging Health Risk for Humans.” *Applied and Environmental Microbiology* 76, no. 14 (2010): 4601–10. https://doi.org/10.1128/aem.02991-09.

Health and Wellbeing; address=11 Hindmarsh Square, Adelaide scheme=AGLSTERMS.AglsAgent; corporateName=Department for. “Sa Health.” Typhoid and paratyphoid – including symptoms, treatment, and prevention, April 3, 2022. https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/conditions/infectious+diseases/typhoid+and+paratyphoid/typhoid+and+paratyphoid+-+including+symptoms+treatment+and+prevention.

Hedemann, M. S., L. L. Mikkelsen, P. J. Naughton, and B. B. Jensen. “Effect of Feed Particle Size and Feed Processing on Morphological Characteristics in the Small and Large Intestine of Pigs and on Adhesion of Salmonella Enterica Serovar Typhimurium DT12 in the Ileum in Vitro1.” *Journal of Animal Science* 83, no. 7 (2005): 1554–62. https://doi.org/10.2527/2005.8371554x.

Hendriksen, Susan W.M., Karin Orsel, Jaap A. Wagenaar, Angelika Miko, and Engeline van Duijkeren. “Animal-to-Human Transmission of*Salmonella*Typhimurium DT104A Variant.” *Emerging Infectious Diseases* 10, no. 12 (2004): 2225–27. https://doi.org/10.3201/eid1012.040286.

Keita, Kadiatou, Charles Darkoh, and Florence Okafor. “Secondary Plant Metabolites as Potent Drug Candidates against Antimicrobial-Resistant Pathogens.” *SN Applied Sciences* 4, no. 8 (2022). https://doi.org/10.1007/s42452-022-05084-y.

Ministry of Agriculture, Fisheries and Food, and Scottish Executive Rural Affairs Department. “Salmonella on Pig Farms – Code of Practice for the Prevention and Control Of.” ReadkonG.com, 2000.

https://www.readkong.com/page/code-of-practice-for-the-prevention-and-control-of-5160969.

Morrow, W.E. Morgan, and Julie Funk. Ms. *Salmonella as a Foodborne Pathogen in Pork*. North Carolina State University Animal Science, n.d.

Soumet, C., A. Kerouanton, A. Bridier, N. Rose, M. Denis, I. Attig, N. Haddache, and C. Fablet. Report, Salmonella excretion level in pig farms and impact of quaternary ammonium compounds based disinfectants on Escherichia coli antibiotic resistance § (2022).

Thisyakorn, Usa. “Typhoid and Paratyphoid Fever in 192 Hospitalized Children in Thailand.” *Archives of Pediatrics & Adolescent Medicine* 141, no. 8 (1987): 862. https://doi.org/10.1001/archpedi.1987.04460080048025.

Ung, Aymeric, Amrish Y. Baidjoe, Dieter Van Cauteren, Nizar Fawal, Laetitia Fabre, Caroline Guerrisi, Kostas Danis, et al. “Disentangling a Complex Nationwide Salmonella Dublin Outbreak Associated with Raw-Milk Cheese Consumption, France, 2015 to 2016.” *Eurosurveillance* 24, no. 3 (2019). https://doi.org/10.2807/1560-7917.es.2019.24.3.1700703.

Vieira-Pinto, M, R Tenreiro, and C Martins. “Unveiling Contamination Sources and Dissemination Routes of Salmonella Sp. in Pigs at a Portuguese Slaughterhouse through Macrorestriction Profiling by Pulsed-Field Gel Electrophoresis.” *International Journal of Food Microbiology* 110, no. 1 (2006): 77–84. https://doi.org/10.1016/j.ijfoodmicro.2006.01.046.

Waldron, P. “Keeping Cows and Humans Safe from Salmonella Dublin.” Cornell University College of Veterinary Medicine, December 25, 2018. https://www.vet.cornell.edu/news/20181218/keeping-cows-and-humans-safe-salmonella-dublin.

Wang, J.-H., Y.-C. Liu, M.-Y. Yen, J.-H. Wang, Y.-S. Chen, S.-R. Wann, and D.-L. Cheng. “Mycotic Aneurysm Due to Non-Typhi Salmonella: Report of 16 Cases.” *Clinical Infectious Diseases* 23, no. 4 (1996): 743–47. https://doi.org/10.1093/clinids/23.4.743.

WHO. “Salmonella (Non-Typhoidal).” World Health Organization, February 20, 2018. https://www.who.int/news-room/fact-sheets/detail/salmonella-(non-typhoidal).

Windisch, W., K. Schedle, C. Plitzner, and A. Kroismayr. “Use of Phytogenic Products as Feed Additives for Swine and Poultry1.” *Journal of Animal Science* 86, no. suppl_14 (2008). https://doi.org/10.2527/jas.2007-0459.

Windisch, W., K. Schedle, C. Plitzner, and A. Kroismayr. “Use of Phytogenic Products as Feed Additives for Swine and Poultry1.” *Journal of Animal Science* 86, no. suppl_14 (2008). https://doi.org/10.2527/jas.2007-0459.