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Review paper

Alternatives to zinc oxide in pig production

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Abstract

Zinc oxide (ZnO) has been applied for many years in the production of pigs to reduce the number of diarrhoea in weaned piglets. In June 2022, the European Union banned the use of zinc oxide (ZnO) in pig feed. According to scientific reports, the may reason was the accumulation of this microelement in the environment of pig production. It has been shown that frequent application of ZnO can lead to increased antibiotic resistance in pathogenic swine microflora. The main alternatives to ZnO are probiotics, prebiotics, organic acids, essential oils, and liquid feeding systems.

Alternatives to ZnO can be successfully used in pig production to reduce the number of diarrhoea among piglets during the postweaning period. Additional reports indicated that bacteriophage supplementation has a positive effect on the health of pigs. The article provides an overview of current ZnO substitutes that can be used in pig farming.

Keywords: zinc oxide, alternatives, probiotics, organic acids, liquid feeding, bacteriophages

Introduction

Zinc represents a key element for the functioning of all living beings, as well as for the proper course of biological processes at the cellular level (Broadley et al. 2007, Prakash et al. 2015). This element is involved in actions of several enzymes and transcription factors (TFs) (Broadley et al. 2007). Zinc and especially zinc oxide (ZnO) have played an important role in pig production until the European Union (UE) has introduced a limitation on the use of antibiotics as feed additives, including natural growth promoters (AGP) and metaphylaxis (2006) (Casewell et al. 2002). According to the scientific reports and opinions of leading food safety authorities, ZnO has an adverse effect on the environment due to its accumulation and potential increase in resistance of certain bacterial species (European Commission 2003, Bednorz et al. 2013, Vahjen et al. 2015, European Commission 2017).

The exact way in which ZnO limits porcine diarrhea

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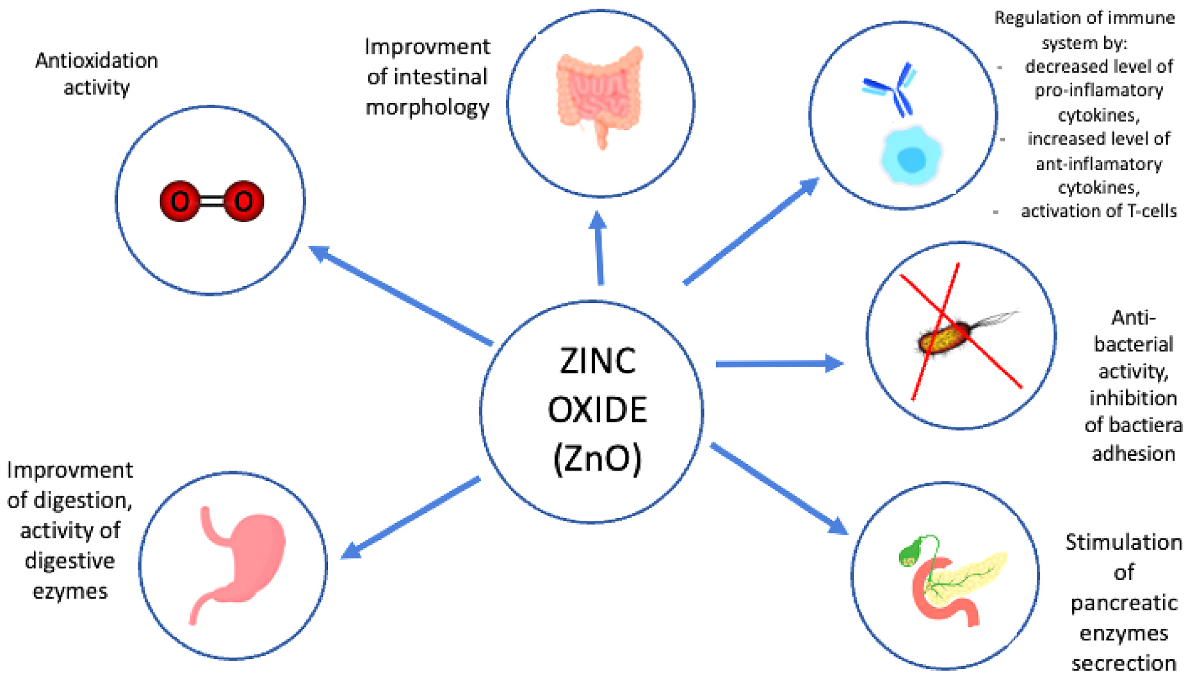

Fig.1. Influence of zinc oxide on the functions of the digestive system and the activity of the immune system.

is not yet fully understood. Although previous studies have assumed that ZnO activity is related to the factors presented in Fig. 1. It seems that ZnO's primary mechanism of action is related to improve nutrient absorption and intestinal morphology, rather than simply fulfilling daily nutritional requirements (Pearce et al. 2015). Additional research has confirmed that pharmacological supplementation with ZnO improves performance by increasing the villi: crypt ratio, including protein levels, and promoting enterocyte proliferation (Grilli et al. 2015, Zhu et al. 2017). ZnO also enhances the expression of tight junctions, which reduces intestinal permeability, a crucial factor during a delicate phase for piglets that can lead to diarrhea (Zhang and Guo 2009). The antioxidant properties of ZnO may also play a role in its positive effect on the intestinal mucosa (Zhu et al. 2017).

Although ZnO has been shown to cause oxidative stress in microbial cells (Pasquet et al. 2014, Lee et al. 2018) its direct antimicrobial activity against *Escherichia coli* F4, the primary cause of porcine diarrhoea, is limited (Söderberg et al. 1990). Moreover, ZnO supplementation is mainly directed against Gram-positive bacteria rather than Gram-negative bacteria, with ZnO-supplemented animals showing higher coliforms and enterococci, but lower lactic acid bacteria (Söderberg et al. 1990, Højberg et al. 2005). Therefore, mechanisms other than direct antimicrobial activity may exist for ZnO.

ZnO has been shown to protect cultured enterocytes from ETEC-induced damage and inhibit bacterial adhesion to cells (Roselli et al. 2003). It also modulates cytokine expression, improving the transcription of the anti-inflammatory cytokine TGF-β while reducing the expression of several pro-inflammatory cytokines (Sargeant et al. 2011, Grilli et al. 2015, Zhu et al. 2017, Gammoh and Rink 2019). ZnO has a key action on the immune system (Gammoh and Rink 2019), promoting the development and function of macrophages (Ercan and Bor 1991), natural-killer lymphocytes (Rolles et al. 2018), and T helper cells (Honscheid et al. 2009). In weaned piglets, pharmacological doses of ZnO increase the number of regulatory T cells, modulating the immune response and maintaining homeostasis (Kloubert et al. 2018). ZnO can also stimulate ghrelin secretion and increase the activity of pancreatic digestive enzymes, leading to higher nutrient digestibility and improved systematic performance in weaning piglets (Yin et al. 2009, Mac Donald 2000, Hedemann et al. 2006).

ZnO partially solved problems in pig production associated with diarrhea in weaned piglets. Weaning is currently carried out in most farms between 21 and 28 days after farrowing (Jensen and Recén 1989, Bøe 1991). The current knowledge indicates the positive effects of early weaning of piglets from the age of 3 weeks. During the weaning process, there are several morphological, enzymatic, and physical changes in piglet organism, which increase the risk of gastrointestinal tract disorders, especially diarrhea. Piglet diarrhea leads to decrease in economically important production rates in farms (Rhouma et al. 2017). The use of ZnO after weaning has been shown to improve intestinal flora (Hu et al. 2013, Hu et al. 2015) and significantly reduces mortality, relieves symptoms, and improves breeding parameters such as weight gain and feed intake (Poulsen 1998, Case and Carlson 2002).

Zinc is a one of the heavy metals with low bioavailability (European Commission 2003) and must be administered in high doses (2000-4000 ppm) to allow optimal absorption in the small intestine of piglets. As a result of poor absorption, most zinc is excreted through urine and feces, *leading* to accumulation in the environment, similarly to other heavy metals such as mercury or lead (Ociepa-Kubicka and Ociepa 2012).

There are numerous reports regarding antimicrobial resistance caused partially by ZnO administration. For instance, the study conducted by Bendorz et al. (2013) showed a probable role of ZnO in *Escherichia coli* antibiotic resistance. Similar observations were made in case of *Staphylococcus aureus*, where the possibility of the increased resistance to methicillin caused by ZnO administration was demonstrated. Vahjen et al. (2015) concluded that high supplementation with ZnO in piglet diet may increase the appearance of resistance genes among Gram-negative bacteria to tetracyclines and sulfonamides.

The aim of this paper is to provide the current review on pig supplements and alternatives that may replace the effect of ZnO administration in feed for piglets.

Low protein concentration in feed

The post-weaning time represents one of the most stressful times for piglets. One of the most important stressing factors is represented by a change from colostrum to solid feed. The potential problems are associated with low feed intake, non-effective digestion, lack of micro- and microelements, anorexia as well as immune deficiency. Additionally in weaned piglets, the HCl production is too low to ensure the proper digestion of regular feed (Halas et al 2007). In general, the protein concentration in feed for this age group exceeds 200 g/kg of feed, which may overpass the capacity of piglet stomach and proper digestion. The undigested protein that concentrates in the large intestine leads to diarrhea and replication of pathogenic microflora including enterotoxigenic *E.coli* (ETEC) (Nyachoti et al. 2006, Wellock et al. 2008, Pieper et al. 2016). On the other hand, the accumulation of toxic fermentation metabolites, excessive growth of pathogenic microflora as well as not fully developed immune system of piglets may lead to diarrhea and increased mortality. Therefore, it is very important to carefully choose the feed considering the protein content, including individual amino acids, and to plan the moment of introduction of solid feed for unweaned piglets (Yue and Qiao 2008, Byrgesen et al. 2021).

It has been shown that piglets fed containing from 15 to 18% of protein showed better resistance to *E. coli* F4 infection during the animal trial (Yue and Qiao 2008, Heo et al. 2010). A low-protein diet can reduce diarrhea symptoms up to 30% in piglets up to 15 kg of body weight. Furthermore, some researchers pointed out that the levels of IL-1, TNF-α, IL-2, IL-6, and IL-10 and IL-13 in the colonic mucosa of weaned piglets decreased, which is most likely due to lower concentration of protein in the feed (Wan et al. 2020).

However, low weight gain and amino acid deficiency can be a serious problem in a low protein diet in piglets (Yue and Qiao 2008). Several studies have shown that threonine, arginine, glutamine, methionine, and cysteine are responsible for the proper functioning of the intestinal immune barrier, anti-inflammatory and antioxidant functions, and stress reduction after weaning. Methionine, lysine, threonine, and glutamate also influenced the normal growth and composition of the intestinal bacterial flora (Wang et al. 2009, Liao 2021, López-Gálvez et al. 2021). Threonine is an essential component of mucins contained in intestinal mucin, since it represents between 28% and 35% of amino acids in mucinous proteins. Stimulation of the immune system, e.g., in case of *E. coli* infection, *increases* mucus production as well as requirement for threonine in piglets (Lien et al. 1997, Le Floc'h and Seve 2007, Trevisi et al. 2015, McGilvray 2019). The results of other studies indicate that a 2 g/kg of threonine feed supply as recommended by the National Research Council (NRC 2012) improves the intestinal barrier function and intestinal morphology, increasing the probability that piglets avoid diarrhea (Ren et al. 2014, Zhang et al. 2019, Koo et al. 2020, Table 1).

Currently, various concepts are being used to create a scheme for the "ideal protein." One of the more well known is InraPorc which acts as a tool for determining the ratio of amino acids relative to the standarised ileal digestible (SID) lysine (Lys=100%) (Van Milgen et al. 2008, Van Milgen and Dourmad 2015, Dourmad et al. 2008).

Therefore, when choosing a low-protein diet, supplementation with amino acids is recommended to avoid deficiencies that affect animal performance (Halas et al. 2007).

Probiotics

Probiotics are living microorganisms that reach the intestine in sufficient quantity and active to induce

Table1. Expressed as a percentage of the standarised ilal digestible (SID) Lys requirement (Lys=100%) (Dourmad et al. 2008, Van Milgen et al. 2008, Van Milgen and Dourmad 2015).

Items	Growing pigs 20-140 kg	Gestating sows	Lactating sows
Lys (base)	100	100	100
Met	30	28	30
Met+Cys	60	65	60
Thr	65	72	66
Trp	18	20	19
Val	70	75	85
Ile	55	65	60
Leu	100	100	115
Phe	50	60	60
Phe+Tyr	95	100	115
His	32	30	42
Arg	42	-	-

a positive effect on health of the host, and improving the functioning of the digestive system. The microorganisms contained in probiotics should not contain pathogenic, toxic, or antibiotic resistant strains. The colonization of the intestine by microorganisms contained in probiotics has a few advantages including maintaining the integrity of the intestinal barrier, competitiveness of the pathogenic microflora, production of antimicrobial compounds and inactivation of toxins. Other indirect advantages include stimulation of host's immune response and improvement of performance, better weight gain, reduction of animal stress, and reduction of methane emissions (Dianawati 2016, Dubreuil 2017, Lan 2017, Wang 2017, Barba-Vidal et al. 2019). Currently there are number probiotics for pigs available on the market, containing *Bacillus* spp., *Bifidobacterium* spp., *Clostridium* spp., *Enterococcus* spp., *Lactobacillus* spp. and *Pediococcus* spp. Parallelly yeast probiotics belonging to the species *Saccharomyces cerevisiae* are widely used. Commercial products generally contain different strains of one or more types of bacteria and/or yeast. They are applied as feed additives in quantities between 10^8 and 10^{11} colony formation units per kg of feed (CFU/kg) (López-Gálvez et al. 2021).

Studies have shown that *Bacillus* spp. preparations have a positive effect on intestinal flora by the reduction of diarrhea incidence and improved body growth of weaned piglets. Supplementation with *B. subtilis* (10^9 CFU/kg of feed) reduced diarrhea caused by the enterotoxic *E. coli* (ETEC) F18 fimbriae. From a clinical point of view, *B. subtilis* and *B. licheniformis* are the most frequently used probiotics. It has been shown that the supplementation with *B. subtilis* KN-42 at a dose of 2.0×10^9 and 4.0×10^9 CFU/kg feed had a comparable effect that caused by application of neomycin, especially in piglets during the first 14 days post-weaning (Hu et al. 2014). Similarly, *B. licheniformis* ATCC 21424 at dose of 1.6×10^9 CFU spores/g of feed or 4.8×10^9 CFU spores/g of feed reduced the prevalence of piglet diarrhea also (Dumitru et al. 2020). Both species stimulated the growth of *Lactobacillus* spp. and reduced the amount of *E. coli* in the intestines. The combination of several strains of *Bacillus* spp. during the studies did not provide the same results as their separated administration (Zhang et al. 2017).

Bifidobacterium spp. bacteria are rods that physiologically colonize the intestinal flora in pigs. They are responsible for fermentation of glucose into lactic acid, which lowers the pH value. The study conducted by Rhouma et al. (2017) showed that *B. lactis* HN019 supplementation (10^9 CFU/Ferkel) may inhibit rotavirus A (RVA) and *E. coli* caused diarrhea. Supplementation with a multi-strain probiotic *B. longum* subsp. *infantis* CECT 7210 or *B. animalis* subsp. *lactis* BPL6 (1.0×10^9 CFU) had a positive effect on the reduction of infection with *Salmonella typhimurium* in piglets, what was observed as a decreasing incidence of diarrhea and increasing feed intake (Barba-Vidal 2017).

Enterococci also have a positive effect on intestinal functions in weaned piglets. The conducted experiments pointed out that administration of *E. faecium* R1 (6.5×10^6 CFU/g feed) had a positive influence onto the reduction on diarrhea symptoms in piglets. The bacteria stimulated renewal of the intestinal mucosa, appetite, and detoxication (Zeyner and Boldt 2006, Hu et al. 2015, Zhang et al. 2021).

Administration of *Lactobacillus plantarum* ZJ316 (1×10^9 CFU/day), *L. plantarum* PFM105 (2×10^7 CFU/g feed) or a combination of *L. plantarum* and *L. reuteri* (after 2×10^8 CFU/g feed) via drinking water resulted in a similar effect that caused by antibiotic administration (Suo et al. 2012, Wang et al. 2019).

Many researchers believe that supplementation with a nonpathogenic strain of *E. coli* carries a relatively high risk of diarrhea. However, it has been shown that *E. coli* administration is effective to reduce inflammation of intestines in pigs. This is because the presence of the pathogenic and non-pathogenic strains of *E. coli* within the common biological niche (Canibe et al. 2022). Furthermore, the study conducted by Hrala et al. (2021) showed 100% effectivity in diarrhea inhibition during administration of three human *E.coli* strains including 582, B771 and B1172 at the dose of 1.0×10^9 CFU. However, there still little is known about the positive effect of *E.coli* on the pig organism.

As it has been mentioned, yeasts, in particular *S. boulardii mafic*-1701 at the dose of 1.0×10^8 CFU/kg feed), *S. cerevisiae* (2.0×10^8 CFU/ml, 10 ml/day), *Candida utilis* (1.0×10^9 CFU/ml, 1 ml per day), improve growth parameters in weaned piglets and reduce diarrhea. The applied mixture of probiotics reduced mortality of piglets, increased the diversity of intestinal flora, and had an antioxidant effect. Supplementation of *C. utilis* may be enhanced with Yucca schidigera extract. This combination has been shown to have a better effect than administration *Candida utilis* alone (Zhang et al. 2020, Zhaxi et al. 2020, Yang et al. 2021).

In conclusion, application of probiotics has several benefits and should be considered as an alternative to zinc oxide and antibiotics. However, administration of probiotics in excessive doses may significantly alter intestinal flora and affect the immune system in pigs (Canibe et al. 2022).

Organic acids

Application of organic acids in pig farming has been found to lower the pH of the digestive tract and reduce the incidence of diarrhea in weaned piglets, especially during the change from liquid to solid feed (Suiryanrayna and Ramana 2015). Short-chain acids such as formic acid, acetate acid, propionic acid, lactic acid, malic acid, oxalic acid, citric acid, as well as fumaric and sorbic acid are the best alternatives to antibiotics or zinc oxide. The additive of organic acids to feed introduces a sour taste, which is attractive to pigs (Woźniakowska et al. 2017). Organic acids have antibacterial and antifungal properties and are applied by many farmers to acidify drinking water. The addition of 0.5% of citric acid to feed for piglets reduced the infection with *Salmonella typhimurium* causing inflammation of small intestines and colon caused by the *E. coli* serotype KCTC 2571 (Ahmed et al. 2014). Application of organic acids leads to an increase in proteolytic enzymes activity enabling better protein digestion. Acidification leads to the transformation of the pepsinogen proenzyme into endopeptidase, a pepsin that is necessary for proper functioning of the digestive system. Organic acids may influence the morphology of mucosa and stimulation of the pancreatic secretion and serve as substrates in metabolic pathways. The frequent disease in weaned piglets is oedema disease (*Morbus oedematosus*) caused by the *E. coli* serotypes K88 (F4) or F18, which produce Stx2e toxin. The poison damages walls of small blood vessels, including those in the brain, and causes fluid retention or swelling. Vascular damage is associated with characteristic neurological symptoms (Moxley 2000). The studies conducted by Tsilotiannis et al. (2001) showed that application of citric acid in piglets leads to significantly lower mortality. They also pointed out that application of organic acids may be useful in control or prevention of odema disease. In summary, the use of organic acids in pig feed allows the reduction of intestinal bacteria, especially *E. coli*, stimulates the immune system, improves digestibility parameters, and reduces the occurrence of diarrhea in piglets. Therefore, they present very strong alternative zinc oxide (Bonetti et al. 2021).

Polyphenols from plant extracts

Polyphenols are among the biologically active substances that are present in large quantities in vegetables and fruits. Polyphenols include flavonoids, tannic acid, and ellagitannin (Quideau et al. 2011). Polyphenols used as food supplements are generally assumed to improve the function of the digestive system and are involved in metabolic pathways associated with the intestinal flora (Del Rio et al. 2013, Catalkaya et al. 2020). It is believed that an economically and health-optimal source of polyphenol compounds may be fruit pomace, which are by-products of the food industry, which could be frequently found in animal farms. The results of recent studies showed that the dried grape marc as a 5% of the feed had a positive effect on young piglets (Catalkaya et al. 2020). Both the polyphenols present in the pomace and their metabolites can be detected in the intestines of pigs fed with the enriched feed. The action mechanism of phenols affects the cattle digestive tract similarly to growth promoters increasing the secretion of digestive enzymes and reducing several unwanted bacteria in the gastrointestinal tract or modulating intestinal morphology due to their antioxidants and anti-inflammatory effects. Similar to organic acids, polyphenols in sufficient concentration promote pigs interest in feed due to their attractive taste (Mahfuz et al. 2021). Luna et al. (2010) investigated the effects of polyphenols on the quality of poultry meat. Thymol and carvacrol are polyphenols that occur naturally in thyme (Bouchra et al. 2003, Goodner et al. 2006). The authors pointed out that these additives can be used to improve meat quality (Luna et al. 2010). It has been also reported that phenol compounds may increase fat metabolism. Supplementation with phenol compounds has been believed to stimulate sterol excretion in feces and reduce lipid absorption resulting in lower plasma and liver cholesterol levels (Park et al. 2002). Chrisaki et al. (2012) have reported that dietary supplementation with phenol carriers can effectively inhibits *E.coli* and *Clostridium perfringens* colonization due to the antimicrobial properties of existing phenol compounds. Considering these features of polyphenols they may present an alternative to zinc oxide or antibiotics in the future. More studies on these substances in pig feed are needed to clearly determine whether a food supplement containing polyphenols could replace tried and tested remedies and which ones.

One of the current scientific project conducted by one of the authors of this paper (prof. Grzegorz Woźniakowski) is focused on examination of natural plant extracts influence on replication inhibition of an economically important coronaviruses infecting pigs. As it turns out, an effective solution is offered by a modern method of supercritical extraction with carbon dioxide in a supercritical state (scCO_2, supercritical fluid extraction – SFE), which guarantees the extraction of biologically active compounds without losing their properties and is completely neutral to the environment, plants and animals. Supercritical fluid extracts of plant raw materials are mixtures of several active substances including polyphenols. As the SFE is considered appropriate for the extraction of lipid compounds mainly, the addition of polar co-solvents (water, ethanol) to carbon dioxide widens the possibility of the extraction of polar substances (polyphenols).

The multiple study on natural extracts obtained from fruits, herbs, algae and lichens against human and animal viruses showed the inhibiting potential of the extracts on the replication of the viruses *in vitro* and *in vivo*. Taking into account the antiviral and biocidal potential of natural plant extracts as well as the technological progress in chemical sciences including supercritical extraction with carbon dioxide the efficient procedures have been developed to obtain antiviral compounds including phenols, terpenes, flavonoids and flavones from numerous plants. The antiviral extracts have been obtained from chokeberries (*Aronia melanocarpa*), cloves (*Syzygium aromaticum*), raspberries (*Rubus idaeus*) as hop (*Humulus lupulus*). The main goal of the currently ongoing studies is to determine to single and synergistic effect of 4 natural extracts against porcine epidemic coronavirus PEDV. Meanwhile, in countries with intensive pig production, including the United States of America or the Republic People of China, losses caused by the occurrence of PEDV reached hundreds millions of US dollars. Due to the very high contagiousness and morbidity of porcine coronaviruses, especially PEDV the most important is the prevention of swine infection by the effective biosecurity rules implementation. Therefore, the influence of natural extracts on PEDV replication inhibition *in vitro* and *in vivo* is going to be performed within the realized project.

Essential oils

Essential oils are extracts of plant origin that are produced as secondary metabolites stored by the plant in secretion cells, cavities, ducts, or epidermis cells. They usually have a typical smell or taste of the plant from which they originate (Nazzaro et al. 2013, Puvača et al. 2013). The biological activity of oils depends on the number of active substances and the relationship between them. For many years, essential oils have been attributed an antimicrobial effect due to a cascade of reactions that affect the entire bacterial cell. In addition, they not only inhibit the growth of bacteria or fungi, but also inhibit the production of their toxic metabolites (Burt and Reinders 2003, Chorianopoulos et al. 2008, De Martino et al. 2009).

In pig farming, essential oils can be used as antibacterial, antioxidant, anti-inflammatory, and anticoccidial agents. They improve the palatability, odor, and digestibility of food (Kroismayr et al. 2006, Brenes and Roura 2010, Sutaphanit and Chitprasert 2014). The conducted studies have shown that cinnamon, thyme, and clove oil are among the most effective extracts against Gram-negative and Gram-positive bacteria, fungi, and yeasts (Abbaszadeh et al. 2014). The MICs of the cinnamon oil and thyme oil components against *E. coli* and *S. typhimurium* DT104 ranged from 100 to 140 μg/ml or μl/ml. In comparison, MICs of clove oil between ranged between 230 and 300 μg/ml or μl/ml (Si et al. 2006). Since the MIC values of the oils are comparable to those of the antibiotics used in pig production, essential oils may be a very good substitute to them. In addition, *Lactobacillus plantarum* and *L. acidophilus* are significantly less sensitive to plant extracts (Zeghib et al. 2017). Other studies suggested that essential oil supplementation may increase the number of *Lactobacillus* spp. and its biodiversity (Zeng et al. 2015, Li et al. 2017, Wei et al. 2017).

Piglets and weaners are very susceptible to stressors such as weaning, heat stress, overcrowding or transport. This results in a cascade of reactions leading to oxidative stress, which in turn leads to a decrease in the performance of the animals, a decrease in immunity, appetite, the occurrence of diarrhea, and miscarriages in sows. Many studies pointed to the antioxidant effect of essential oils (Tan et al. 2015, Zou et al. 2016, Baschieri et al. 2017, Liu et al. 2017). Zou et al. (2016) have shown that oregano oil in the porcine intestine significantly reduces reactive oxygen and malondialdehyde, which are responsible for oxidative stress (Zou et al. 2016). The same essential oil that was administered to pregnant sows as well as during lactation period improved the performance of piglets by reduction of the oxidative stress in the sows (Tan et al. 2015).

It is possible to use different oils at the same time without antagonistic effect between them. The addition of cinnamon and thyme oil ingredients (100 mg/kg) for piglets from birth to the age of 28 days leads to tangible results. After 14 days of supplementation, the average daily body mass increase, food intake, and the incidence of diarrhea, were comparable to those caused by antibiotics or ZnO. In addition, intestinal morphology improves and oxidative stress decreases (Li et al. 2012, Tian and Piao 2019).

Liquid feeding

Two different feeding systems are distinguished in pig production. The first one is dry feeding, while the second is liquid feeding (Byrgesen et al. 2021). The possibilities of feeding with dry feed are running out and on the verge of economic profitability.

According to recent reports, liquid feed is currently being applied in many parts of the world, especially in western Europe. Approximate figures indicate that more than 60% of fatteners in Denmark and Sweden, as well as the majority of sows there, are fed liquid feed. Another example from the Netherlands and France indicated that about a third part of all pigs are fed with liquid feed, of which 50 to 60% of fatteners in the Netherlands and over 70% of fatteners in France. Around 40% of fattening pigs in Germany and far fewer sows, receive liquid feed. It is estimated that approximately 70% of pigs are fed according to this system in Ireland (Byrgesen et al. 2021).

Liquid feeding, due to the availability and low prices of maize, is less popular in North America than in Europe. The exception is Ontario, Canada, where in 2012 approximately 20% of fatteners were fed liquid feed.

It should be mentioned that in Poland there is no precise data on the number of pigs fed liquid feed. This may give the impression that the scale of the discussed issue is small. Currently, only about 100 liquid feed systems are installed in Poland. Considering the data available for several years on the effectiveness of feeding with liquid feed, not paying enough attention to the discussed issue should be a cause for reflexion.

Fermented feeds

Fermented pig feed is showing promise as an alternative to zinc oxide. According to reports, application of fermented feed can lead to improved growth of te small intestinal villi and hind gut mucosa, improve gut barrier function in the jejunum and colon (including the integrity of the mucosal and brush border, the presence of GALT structures and minimal inflammation indices), and shift the colon microbiota toward greater microbial diversity and robustness (Shi et al. 2016, Yuan et al. 2017, Zhu et al. 2017). Furthermore, fermented feeds show better digestibility because they are more easily digested by young animals. It is likely that the process of pre-fermentation of rapeseed meal through microbial control enhances its nutritional value. Studies have shown that microbial fermentation can improve the digestibility of feedstuffs such as rapeseed meal, as well as neutralises antinutritional components such as tannins, glucosinolates, and phytic acid (Satessa et al. 2020).

Bacteriophages

Since the beginning of the 20th century, "phage therapy" has been known to applied in human and veterinary medicine (Sulakvelidze et al. 2001). It is used successfully in the treatment of certain bacterial infections. A bacteriophage is a type of virus that attacks and destroys bacterial cells by an induction process (Howard-Varona et al. 2017). It turns out that it is possible to use phages to supplement piglets. According to Zeng et al. (2021), the phage cocktail added to the food maintained the performance at the level observed in other animal groups administered antibiotics. Furthermore, supplementing an antibiotic diet with phages had no effect on serum IgA, IgG, IgM proteins used by the immune system to identify and neutralize risks (Janeway 2001), IL-2, IL-12 – signaling molecules relevant for immune defense (Gołąb et al. 2007) and IFN-γ – interferon type II as macrophages activator (Schoenborn and Wilson 2007). However, piglets fed a 400 mg/kg bacteriophage-containing diet had lower IL-1β and TNF-α concentrations and higher serum IL-10 concentrations than antibiotic-fed piglets (Kim et al. 2014). In summary, this could mean that the bacteriophage diet had a stronger anti-inflammatory effect (Moore et al. 2001, Masters et al. 2009, Gołąb et al. 2011). Earlier, it was also shown that phages can be growth promoters in pigs. Administration of 400 mg/kg bacteriophages was found to increase final body weight and reduce the incidence of diarrhea in weaning piglets compared to the antibiotic group. This means that 400 mg / kg of phage supplementation significantly improved growth performance compared to an antibiotic diet (Kim et al. 2014). There are also reports showing that phage therapy is effective against bacterial infections such as *Salmonella* spp. (Wall et al. 2009, Won et al. 2021); *E. coli* (Smith and Huggins 1983, Lee et al. 2017) and *Clostridium* spp. (Kim et al. 2017). Lee et al. (2017) in their study also argue that the use of phages could be an alternative to antibiotics and zinc compounds.

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