UNIVERSIDADE FEDERAL DE LAVRAS

GIZELE FONSECA DA SILVA

EVALUATION OF DIETARY FIBRE SOURCES ON THE PERFORMANCE AND INTESTINAL PERMEABILITY OF PIGLETS DURING NURSERY PHASE

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Master’s dissertation presented to the Federal University of Lavras, as part of the requirements of the Graduate Program in Animal Science, area of concentration in Production and Nutrition of Non-Ruminants, to obtain the title of Master of Science.

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GIZELE FONSECA DA SILVA

AVALIAÇÃO DE FONTES DE FIBRA DIETÉTICAS SOBRE O DESEMPENHO E A PERMEABILIDADE INTESTINAL DE LEITÕES DURANTE A FASE DE CRECHE

EVALUATION OF DIETARY FIBRE SOURCES ON THE PERFORMANCE AND INTESTINAL PERMEABILITY OF PIGLETS DURING NURSERY PHASE

Dissertação apresentada à Universidade Federal de Lavras, como parte das exigências do Programa de Pós-graduação em Zootecnia, área de concentração em Produção e Nutrição de Não Ruminantes, para obtenção do título de "Mestre".

Aprovada em 27 de julho de 2021.

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Este trabalho é dedicado aos meus pais, responsáveis diretos por tudo que eu fui, sou e serei. Vocês são o alicerce do meu caráter e personalidade. A eles, minha gratidão, amor, orgulho e respeito.

Dedico

A todos que acreditam que os sonhos movem o mundo!

Ofereço

“Correr atrás de um sonho tem um alto preço. Pode exigir que abandonemos nossos hábitos, nossas famílias e amigos, pode nos fazer passar por dificuldades, pode nos levar a decepções e desilusões. Porém, por mais caro que seja, nunca é tão alto quanto o preço pago por quem não viveu. Um dia essa pessoa vai olhar para trás e escutará o seu próprio coração dizer: Desperdicei minha própria vida, que tolo fui!”.

Paulo Coelho.

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BIOGRAFIA

GIZELE FONSECA DA SILVA, filha de Gérson Ribeiro da Silva e Rosenilde Ferreira da Fonseca (dona Rosa), nasceu em 12 de julho de 1993, na cidade de João Câmara, no estado do Rio Grande do Norte.

Em fevereiro de 2011, ingressou na Universidade Federal do Rio Grande do Norte, graduando-se em Zootecnia em julho de 2018.

Em agosto de 2018, foi admitida na Bretanha Suínos, atuando como Trainee em Reprodução de Suínos. Quatro meses após, foi promovida a Coordenadora de Produção de uma Unidade de Produção de Leitões.

Em agosto de 2019 iniciou o curso de pós-graduação em Zootecnia na Universidade Federal de Lavras, concentrando seus estudos na área de Nutrição e Produção de Não Ruminantes.

Em 27 de julho de 2021 submeteu-se à a banca de defesa de dissertação para obtenção do título de “Mestre”.

RESUMO GERAL

Objetivou-se avaliar o efeito de diferentes fontes de fibras em dietas pós-desmame, associadas ao uso reduzido de ZnO e/ou GEA sobre o desempenho, permeabilidade intestinal, incidência de diarreia, concentração de *E. Coli* nas fezes, excreção de Zn, cobre e proteína bruta nas fezes e a porcentagem de animais medicados a primeira semana pós-desmame. Um total de 90 leitões desmamados aos 25 dias (7.84±1.71 kg), foram distribuídos em um delineamento em blocos (peso) casualizado e divididos em 5 tratamentos: T1 - Tiamulina como GEA em associação com alta dosagem de ZnO (de 2500 a 1500 ppm); T2 - GEA negativo e fibra de lignocelulose (2%) em associação com alta dosagem de ZnO; T3 - GEA negativo e fibra de lignocelulose eubiótica (2%) em associação com alta dosagem de ZnO; T4 - GEA negativo e fibra de lignocelulose em associação com dosagem reduzida de ZnO (100 ppm); T5 - GEA negativo e fibra de lignocelulose eubiótica em associação com dosagem reduzida de ZnO (100 ppm), com seis repetições e três leitões por baia. O programa nutricional foi dividido em 4 fases (pré-inicial 1: 25 a 32 dias; pré-inicial II: 33 a 39 dias; inicial I: 40 a 53 dias; e inicial II: 54 a 67 dias). Todos os dados passaram pelo teste F. Adotou-se o teste de Tukey ($P < 0.05$), para comparar as médias. Embora tenha havido diferença entre o consumo de ração diário (CRD) em todos os períodos ($P < 0,05$), os tratamentos não influenciaram no peso final dos leitões. Na primeira semana, o maior CRD foi nos animais alimentados com fibra de lignocelulose eubiótica e dosagem reduzida de ZnO (T5). O CRD dos outros tratamentos não diferiu entre si. Porém, na segunda fase de creche, os maiores resultados do CRD foram obtidos com os animais do T1, T3 e T5. Analisando a somatória nos dois últimos períodos (0-28 e 0-42 dias), o ZnO influenciou negativamente o CRD dos leitões. O menor valor de ingestão de ração foi observado nos leitões alimentados com dieta contendo fibra de lignocelulose eubiótica e alta dosagem de ZnO (T3). Houve diferenças significativas entre as fases do teste de absorção de galactose (TAG). Quando houve diferença estatística pelo teste F ($P < 0.05$), Os valores do TAG na segunda fase foram menores em comparação com a primeira. Assim, pode-se inferir que a função de barreira intestinal foi garantida com o uso das fibras alimentares na fase de creche, tanto em altas quanto em baixas dosagens de ZnO. No geral, os animais alimentados com doses reduzidas de ZnO nas dietas tiveram menor excreção de Zn e Cobre nas fezes. Pode-se concluir que a inclusão de fibra eubiótica de lignocelulose nas dietas de leitões na fase de creche permite a retirada total da Tiamulina 80% como melhorador de desempenho e redução de 96% do óxido de zinco como antimicrobiano, sem prejudicar o desempenho dos animais, garantindo a manutenção da função de barreira no intestino e proporcionando menor excreção fecal de Zn no meio ambiente.

Palavras-chave: Diarreia, fibra dietética, saúde intestinal, sustentável, tight junctions

GENERAL ABSTRACT

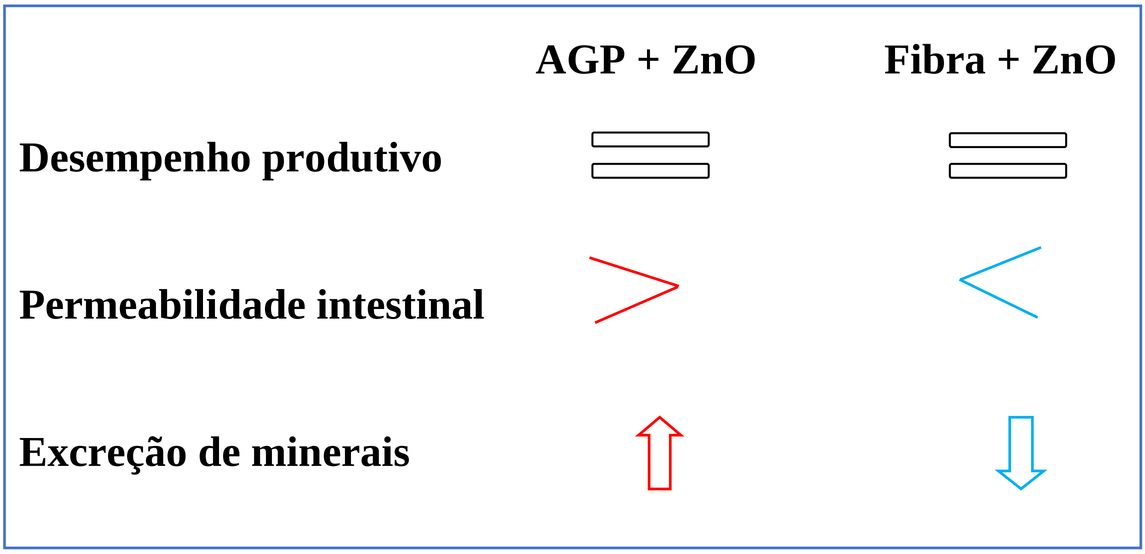
This study aimed to evaluate the effect of different fiber sources in post-weaning diets, associated with reduced use of ZnO and/or GEA on performance, intestinal permeability, incidence of diarrhea, *E. Coli* concentration in feces, Zn excretion, copper and crude protein in feces and the percentage of animals medicated the first week after weaning. A total of 90 piglets weaned at 25 days (7.84±1.71 kg) were distributed in a randomized block design (weight) and divided into 5 treatments: T1 - Tiamulin as GEA in association with high dosage of ZnO (from 2500 to 1500 ppm); T2 - negative GEA and lignocellulose fiber (2%) in association with high dosage of ZnO; T3 - negative GEA and eubiotic lignocellulose fiber (2%) in association with high dosage of ZnO; T4 - negative GEA and lignocellulose fiber in association with reduced dosage of ZnO (100 ppm); T5 - negative GEA and eubiotic lignocellulose fiber in association with reduced dosage of ZnO (100 ppm), with six replicates and three piglets per pen. The nutritional program was divided into 4 phases (pre-initial 1: 25 to 32 days; pre-initial II: 33 to 39 days; initial I: 40 to 53 days; and initial II: 54 to 67 days). All data passed the F test. The Tukey test (P < 0.05) was used to compare the means. Although there was a difference between the average daily feed intake (ADFI) in all periods (P < 0.05), the treatments did not influence the final weight of the piglets. In the first week, the highest ADFI was in animals fed with eubiotic lignocellulose fiber and reduced ZnO dosage (T5). The ADFI of the other treatments did not differ from each other. However, in the second stage of day care, the highest ADFI results were obtained with animals from T1, T3 and T5. Analyzing the sum in the last two periods (0-28 and 0-42 days), ZnO negatively influenced the ADFI of piglets. The lowest feed intake value was observed in piglets fed a diet containing eubiotic lignocellulose fiber and high ZnO (T3). There were significant differences between the phases of the sugar absorption test (SAT). When there was statistical difference by the F test (P < 0.05), SAT values in the second phase were lower compared to the first. Thus, it can be inferred that the intestinal barrier function was guaranteed with the use of dietary fiber in the nursery phase, both in high and low doses of ZnO. In general, animals fed reduced doses of ZnO in the diets had lower excretion of Zn and copper in feces. It can be concluded that the inclusion of eubiotic lignocellulose fiber in the diets of piglets in the nursery phase allows the total withdrawal of Tiamulin 80% as a performance enhancer and a 96% reduction of zinc oxide as an antimicrobial, without harming the performance of the animals, ensuring the maintenance of the barrier function in the intestine and providing less fecal excretion of Zn in the environment.

Keywords: Diarrhea, dietary fiber, intestinal health, sustainable, tight junctions

Performance and gut permeability of post-weaned piglets are influenced by different sources of lignocellulose fiber

Elaborado por **Gizele Fonseca da Silva** e orientado por **Márvio Lobão Teixeira de Abreu**

O uso dos antibióticos melhoradores de desempenho (AGP) e do óxido de zinco (ZnO) nas dietas pós-desmame é uma prática comum, com o objetivo de melhorar o desempenho e reduzir a diarreia. Porém, essa prática pode levar a resistência aos antibióticos e o uso do ZnO pode contribuir para poluição do zinco (Zn) ao ambiente. Desta forma, durante 42 dias foram avaliados os efeitos de diferentes fontes de fibras (lignocelulose e lignocelulose eubiótica) em dietas pós-desmame, associadas ao uso reduzido de ZnO e/ou AGP sobre o desempenho, permeabilidade intestinal e excreção de Zn, cobre e proteína bruta nas fezes. Um grupo de 90 leitões foram desmamados aos 25 dias de idade e divididos em cinco tratamentos: T1 - Tiamulina como AGP em associação com alta dosagem de ZnO; T2 - AGP negativo e fibra de lignocelulose (2%) em associação com alta dosagem de ZnO; T3 - AGP negativo e fibra de lignocelulose eubiótica (2%) em associação com alta dosagem de ZnO; T4 - AGP negativo e fibra de lignocelulose em associação com dosagem reduzida de ZnO (100 ppm); T5 - AGP negativo e fibra de lignocelulose eubiótica em associação com dosagem reduzida de ZnO (100 ppm). Em geral, o consumo de ração diário (CRD) melhorou em animais que consumiram dietas com menor quantidade de ZnO e lignocelulose eubiótica. Além disso, os mesmos animais tiveram menor excreção de Zn e Cobre nas fezes. A função de barreira intestinal foi garantida com o uso das fibras dietéticas na fase de creche. Portanto, a inclusão de lignocelulose eubiótica permite a retirada da Tiamulina 80% como melhorador de desempenho e redução de 96% do ZnO como antimicrobiano, sem prejudicar o desempenho dos animais, garantindo a manutenção da função de barreira no intestino e proporcionando menor excreção fecal de Zn no meio ambiente.



Principais efeitos do uso de diferentes fontes de fibras em substituição aos antibióticos e a redução do óxido de zinco como melhoradores de desempenho para suínos na fase de creche.

Dissertação de Mestrado em Zootecnia na UFLA, defendida em 27 de julho de 2021.

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SUMMARY

FIRST PART

1 INTRODUCTION

It is well known that the weaning is a stressful event in piglet's life, and can compromise the piglet gut health, leading to growth performance decrease. Nowadays, to achieve high production indexes in the swine industry, the weaning happens earlier than when the organism has established as a stable development, meaning, enzyme, immune system activity and microbial population. The stress caused at weaning will further disrupts the gut microbial ecosystem, increasing susceptibility to post-weaning diarrhea, leading to productive loss (LIU et al., 2018b).

The strong social, environmental and nutritional changes related to weaning are factors that cause great stress and may frequently cause the manifestation of factors, which can reduce or paralyze growth rates during the post-weaning period, mainly due to diarrhea. All of that can lead to a reduction in the secretion of some enzymes, which, consequently, affects the digestive and absorptive capacity of the nutrients in the small intestine, besides important changes in their morphology. The poorly digested food can be used as substrate for the growth of microorganisms, causing post-weaning diarrhea. For this reason, feed additives have been widely used in swine farming as growth-enhancing in order to minimize the incidence of post weaning diarrhea and compromised performance of the animals (JAYARAMAN; NYACHOTI, 2017).

The use of growth-enhancing antimicrobials (GEA's) tends to smooth these disturbances by decreasing the incidence of post weaning diseases. The exaggerated and indiscriminate use of GEA's has increased selective pressure for anti-microbial resistant bacteria. Zinc oxide (ZnO) has been widely used for diarrhea control and as an GEA's for post weaning diets. Among the benefits, it can prevent pathogenic bacteria adhesion (specially *Escherichia coli*) and also provide improvements in the immune system action and in the growth performance (PLUSKE, 2013; LIU et al., 2018).

The development of antibiotic resistance in several important pathogenic bacterial species becomes the most pressing issue in public health, requiring safe antibiotic alternatives for piglets. Although ZnO is widely used to decrease the incidence of diarrhea and to improve the growth performance of piglets, more attention ought to be paid on the excretion caused by the high doses of the conventional source of

ZnO. Due to its low absorption, nearly 76% of ZnO is excreted as zinc in the feces (BUFF et al., 2005). Likewise, antimicrobial resistant can be generated with high dietary ZnO inclusion, promoting persistent multi-bacteria *E. Coli* in pigs as reported by (MARON; SMITH; NACHMAN, 2013; CIESINSKI et al., 2018).

The use of zinc oxide in high dosages has the consequence of increasing its concentration of this mineral in animal waste, which can generate environmental contamination when they do not receive a suitable destination, since zinc is a heavy metal with a high accumulation capacity on the ground. Another point to be considered is that the use of zinc oxide in formulations with high doses and for prolonged periods, can contribute to bacterial resistance (MARON; SMITH; NACHMAN, 2013).

Based on the conclusion that the benefits of using zinc oxide to prevent diarrhea do not outweigh the risks to the environment, in 2017, the European Medicines Agency (EMEA) recommended restricting the use of all veterinary products that have the metal as a base in their formulations. And in the same year, the European Commission adopted this recommendation, determining that all member countries of the European Union should cease use, with a maximum term of five years (EMA, 2017).

In Brazil, restrictions of this type are not yet being applied, but they are already in discussions and it is to be expected that in the near future they will be implemented, mainly to guarantee an export agenda in the international market. For this reason, some studies have already been carried out in order to circumvent the negative effects of using zinc oxide in therapeutic doses, or even, replace both antibiotics and ZnO from the diets. Considering the severe restriction or total ban on the use of GEA’s and ZnO in swine production, different types feed additives have been suggested as an alternative (FERNANDES et al., 2020).

Current pig production faces two main challenges at nursery phase: maintaining intestinal health and consistently ensuring the high performance of animals in the face of the demand to reduce the use of GEAs. Diets for modern pigs are typically nutrient-dense and concentrated to meet nutritional requirements. However, these diets do not meet the fiber´s physiological requirements, as animals need fibers to obtain optimal health and intestinal digestion, with fibers in the nutrition of monogastric animals often associated with poor nutrient use and reduced energy values. However, fiber must be included in the diet to maintain normal physiological functions in the digestive tract. Fiber supplementation in piglet nutrition is of special interest, as it is a prerequisite for improving intestinal health and animal performance, playing an essential role in feeding strategies that aim to replace the use of GEAs (JARRETT; ASHWORTH, 2018).

In recent years, in-depth studies have been carried out on the physical, chemical, and nutritional physiology of dietary fibers for pigs. The source and type of fiber can cause beneficial or detrimental effects on the animals. In the past, fibers were almost always related to interference in the digestive capacity of the diet´s ingredients, due to its features on passage rate, viscosity, water holding capacity, solubility and fermentability. These characteristics can be more present in the common commercial vegetable products, like wheat bran and soybean hulls for example. Nowadays, this concept has evolved a lot, with many companies working on deliver to the market purified sources of fiber (lignocellulose and eubiotic lignocellulose), free of mycotoxins and with more favorable than deleterious effects (JHA; BERROCOSO, 2015). It was also found that depending on the source its use can improve the microbiological balance in the intestine, and that the fermentation carried out by the intestinal microorganisms can positively affect the health of the animals. Fermentation of dietary fiber in the large intestine produces short-chain fatty acids, which are used to maintain intestinal health. It was also observed that the fibers promote new benefits for the swine production systems, mainly due to the reduction in the use of antimicrobials worldwide, with the concern for the welfare of animals fed a restricted diet and the need to ensure that these systems are more sustainable. For example, the inclusion of dietary fiber can alter the intestinal microbiota in order to reduce the need for GEAs, while the controlled addition of certain types of fiber can reduce nitrogen losses in the environment and thus reduce the environmental cost of pig production (JARRETT; ASHWORTH, 2018).

It is also worth mentioning that the use of vegetable ingredients as sources of fiber in pig diets can have variable quality, and the inclusion of a low-quality raw material is not desirable, as it causes a worsening in the performance of the animals, and consequently, reduced profitability. In this sense, the use of new dietary fibers can be an interesting alternative, since their inclusion occurs at levels lower than those usually practiced on farms, and with less risk of adverse implications, in relation to the digestibility and suitability of the product, being mycotoxin-free dietary fibers (JHA; BERROCOSO, 2015; LIU et al., 2018a).

Based on this previous information, we hypothesized that the inclusion of different sources of dietary fiber in post-weaning piglet diets might be a potential substitute for the conventional dosages of Tiamulin and ZnO, improving growth performance, decreasing diarrhea incidence and fecal zinc excretion, as well as, for maintaining intestinal permeability and the hole healthy status of the animals. Therefore, this study was conducted to evaluate effects of the inclusion of different sources of dietary fiber on growth performance, intestinal permeability, copper, zinc and crude protein fecal excretion, incidence of diarrhea and concentration of *E. Coli* in the feaces and percentage of medicated animals in the post weaning period. The results of the present study might provide insights on the application of dietary fiber as an additive to replace or decrease the practiced high doses of ZnO and of the subtherapeutic levels of antibiotics as performance enhancers.

2 LITERATURE REVIEW

2.1 Post weaning challenges

In intensive pig production systems, in order to increase the number of farrowing/sow/year and piglets-weaned/sow/year, piglets are involuntarily separated from their mother with about three to four weeks to live. Unlike what happens in the nature, where animals are weaned at the age of twelve to sixteen weeks.

The weaning process can be defined as the separation of the piglets from the sow after the lactation period and represents one of the most critical and determinant moments of the piglet’s life. Throughout their lives, piglets are exposed to a lot of stressful factors, such as removal from the sow, dietary changes, adapting to a new environment among others. These factors may negatively affect the adequate development of them, which may lead to commitment on the growth performance and animal’s health in general (CAMPBELL; CRENSHAW; POLO, 2013; PLUSKE; TURPIN; KIM, 2018).

One of the main factors involved on the decrease of the piglet’s performance on the first two weeks after weaning is the low daily feed intake related to many stressful factors, such as the alterations in the diets (JAYARAMAN; NYACHOTI, 2017). The transition from the sow milk to a cereal-based solid diet with low digestibility and palatability results on a decrease on the daily feed intake. According to the same authors, when the low feed intake is associated with the other weaning stressful factors, it can compromise the health and the nutrient absorption of the post weaning piglets. Furthermore, many stress factors associated with the weaning period, such as removal from the sow, dietary changes, adapting to a new environment and histological and morphological changes in the small intestine, may negatively affect the maturation of the intestine (immune system, permeability, enzymes and microbiota) leading to decreased piglet`s performance in general (HEO et al., 2013).

The diet transition on the nursery period represents a big challenge for post weaned piglets due to anti-nutritional compounds in some feedstuffs. Some allergic proteins like β-conglycinin, glycinin, lectin are good examples of substances that can cause irritations and inflammations in the mucosa of the small intestine. Often, feed formulation does not apply the ideal protein concept, as a consequence, proteins antinutritional factors can cause nitrogenous fermentation in the large intestine (WANG et al., 2017). These can cause proliferation of pathogenic proteolytic bacteria, which acts against benefic lactogenic bacteria impacting in the good microbiota balance. Unbalanced microbiota and immune response in the small intestine cause intestinal diseases, affecting negatively growth performance and the average daily feed intake of the animals. According to Liu et al., (2018b), high incidence of inflammation can cause increases in the oxidative stress, which leads to disturbs in the integrity of enterocytes and compromise intestinal permeability. Intestinal leaking or “leak gut” contributes to pathogenic infection and, consequently, intestinal disorders. Therefore, post-weaning piglets with affected intestinal health will present reduced ability for nutrient digestion and absorption, having worse performance in the nursery and the phases that follows (PLUSKE; TURPIN; KIM, 2018).

In this specific phase, when piglets are weaned, hydrochloric acid secretion is still low (HEO et al., 2013; MODINA et al., 2019). If it were under natural conditions, the intrinsic behavior would be to maintain the intake of breast milk, resulting from its metabolism to the production of lactic acid, which in turn lowers the pH of the medium and favors the maintenance of a beneficial bacterial population, such as *Lactobacillus*. and *Bifidobacterium* (SANCHES et al., 2006; PIEPER et al., 2012; GRECCO et al., 2018). Due to the more alkaline pH, there is no stimulus for the activation of pepsinogen at the appropriate speed, producing undigested protein residues, which are used as a substrate for undesirable microbial growth, such as *Escherichia* and

Staphylococcus, which secrete enterotoxins, causing diarrhea (SANTOS, L. S.; MASCARENHAS, A. G.; OLIVEIRA, 2016).

In addition to physiological stress, weaning is also associated with psychological and social stress, which is evidenced by altered patterns of behavior, such as belling nosing behavior, higher rates of vocalization and aggression (IACOBUCCI et al., 2015), and increased activation of the hypothalamic-pituitary-adrenal (HPA) axis (MORMÈDE et al., 2007). This stimulus promotes the release of corticotrophin-releasing hormone (CRH) and subsequent activation of stress pathways, which can lead to the degranulation of intestinal mast cells and an increase in pro-inflammatory cytokines and proteases, which in turn alter the tight junctions between the intestinal enterocytes, increasing paracellular permeability and the risk of enteric disease, being diarrhea one of the majors issues (WANG et al., 2016; MOESER; POHL; RAJPUT, 2017).

Post-weaning diarrhea is an economically important disease and one of the most common causes that can lead to morbidity and mortality in swine production by affecting piglets during their first weeks on nursery facilities. Post-weaning diarrhea is usually associated with proliferation of enterotoxigenic *E. coli* (LUPPI et al., 2016). This pathotype is characterized by the production of enterotoxins inside of the enterocytes, which are essential for the disease development in the intestinal tract (RHOUMA et al., 2017). Roselli et al., (2003) suggested that the reduction of *E. coli* adhesion by ZnO action could be due to the binding of this metal to bacterial fimbriae, which interferes with *E. coli* recognition by the specific receptors on intestinal cells, since it has been shown that the fimbriae of *E. coli* are able to exclusively bind the oxide form of zinc (WANG et al., 2017).

During post-weaning diarrhea, there is a greater amount of mast cells present in the mucosa and submucosa of the intestine. Mast cells can suppress this inflammation produces and releases histamine, prostaglandins and tumor necrosis factors. These biomarkers have the capacity to increase the permeability of the intestinal epithelium, which can aggravate the diarrhea by increasing the endotoxin translocation enterocytes damaging thought the intestine (XIONG et al., 2019).

It is well documented that the occurrence of diarrhea is closed related to the increase in intestinal permeability (LI, 2017). Wang et al., (2017) stated that when supplemental pharmacological level of ZnO is used, it can reduce intestinal permeability by enhancing the expression and production of tight junction proteins (occludin and zonula occludens protein-1). Thus, the alleviated post-weaning diarrhea by conventional ZnO can be attributed to the decrease in intestinal permeability (ROSELLI et al., 2003).

These events also mark the approximately 50% decrease in the secretion of disaccharidase enzymes as lactase, sucrase and isomaltase over the first five days after weaning, causing the animal to poor digestion and absorption of certain nutrients, such as carbohydrates in the small intestine (XIONG et al., 2019). The association of all these changes leads to an appearance of osmotic diarrhea, resulting in a malnourished and dehydrated animal. Thus, with the incidence of diarrhea, the animal’s growth performance and health are remarkably affected and subsequently increasing the morbidity and mortality rates of the herd, causing high economic losses (RHOUMA et al., 2017; MODINA et al., 2019).

Therefore, it is of paramount importance in the nursery phase, especially in the first two weeks, to formulate diets based on highly palatable dairy ingredients. These will stimulate consumption, provide energy through lactose, as well as a reduction in stomach pH, through the production of lactic acid, favoring the reduction of undesirable microbial growth and enabling better development of the animal´s digestive tract (BROWNLEE, 2011; MOLINO et al., 2011; YOO et al., 2018).

Given this scenario, it is evident that the conservation of intestinal health through the maintenance of its gut barrier function (responsible for the physical protection against pathogens), is a key point for the proper development of the piglet, and, therefore, of the profitable sustainability of the entire pig production system.

2.2 Intestinal health of piglets in the nursery phase

In the swine specie, as in all mammals, there are hundreds of species of microorganisms in the intestine, the entire population of which is known as the microbiota (FOUHSE; ZIJLSTRA; WILLING, 2016), which plays an important role in intestinal health. Right after the birth of the animal, these species begin to colonize its intestine (KIM; ISAACSON, 2015) and when this process occurs in a balanced, healthy and normal way, it is called symbiosis (WILLING; MALIK; VAN KESSEL, 2012; PLUSKE; TURPIN; KIM, 2018). On the other hand, dysbiosis or microbiota imbalance causes physiological changes and disorders in the piglet's GIT (HEO et al., 2013), Dietary adjustments such as the use of zinc oxide and fiber, for example, can modify the metabolism of the microbiota of the gastrointestinal tract, producing antimicrobial peptides that can interfere with the development and adhesion of pathogens in the intestinal mucosa. In addition, the diet can stimulate the production of cytokines directly in the epithelium and consequently the activation of defense cells (DE LANGE et al., 2010; HEO et al., 2013; PLUSKE, 2013; LIU et al., 2018a).

It is worth mentioning that there is a gradual adaptation of the diets provided at this stage. One of the main characteristics of these diets is the presence of dairy ingredients in their composition, as it provides lactose, which is also found in the milk of the matrix, being the lactic acid resulting from the action of bacteria. Lactic acid is a precursor to the formation of lactate, which is part of the metabolism of propionate and butyrate, which are used as an energy source by the intestine itself and for the development of beneficial bacteria for the piglets' digestive system (STARKE et al., 2014; JAYARAMAN; NYACHOTI, 2017).

The development of pathogenic bacteria such as *E. coli*, *Streptococcus*, and *Clostridium*, occurs in an intestinal environment with little activity in the production of acid compounds, like lactic acid for example, causing an increase in the intestine's pH. This increase in pH favors the growth of pathogens, such as *E. coli*, a bacterium that attaches to the intestinal mucosa, causing post-weaning diarrhea and edema disease (TSILOYIANNIS et al., 2001; EVERAERT et al., 2017).

Adding this condition to immature immunity and compromised intestinal integrity, there is a tendency for increased levels of morbidity and mortality, which can reach 25% if effective preventive measures are not taken (KIRKDEN; BROOM; ANDERSEN, 2013). However, the incidence of diarrhea is not always due only to the presence of *E. coli*, it is also influenced be age at weaning, changes in the diet, variations in litter origins, other pathological agents and abrupt fluctuation in the thermal comfort zone of the animals (GOSWAMI et al., 2011; SUN; KIM, 2017).

Piglets in this phase need diets with good palatability and digestibility, thus enabling a better development of them (SOLÀ-ORIOL; GASA, 2017), since about 70% of the production costs of pigs come from feed (POMAR; REMUS, 2019). Nutritional strategies such as the use of acidifiers, probiotics, prebiotics, essential oils, short-chain fatty acids and functional fibers, for example, can be used, aiming to promote a better use of diet ingredients (LIU et al., 2018a), contributing to maintaining a healthy intestine and avoiding losses in performance, mainly due to post-weaning diarrhea (HEO et al., 2013; PLUSKE, 2013). It means that every nutritional strategy must be evaluated and discussed based on the objectives of the producer and the estimated budget. Nowadays, there are a lot of consolidated strategies applied to smooth the post weaning challenges and the post-weaning diarrhea.

2.3 Use of additives in swine production

When it comes to what is the most important thing in life, there is no doubt that the answer is, food. Moreover, the qualified professionals have in their hands a huge responsibility, which it is to improve the production and quality of animal protein products (meat, milk, egg and etc.) for human consumption. In this sense, applied research plays an important role in all the aspects of animal husbandry techniques (JAYARAMAN; NYACHOTI, 2017).

Pork is the second most consumed meat in the world. Nevertheless, in some cases it can be a source of pathogens, such as *Salmonella* and *E. Coli* (EVANGELOPOULOU et al., 2014; CAVALIN et al., 2018). Therefore, it becomes crucial to the animal producers to identify the best solutions to reduce the incidence of *Salmonella* and *E. coli* infection from pig meat (THACKER, 2013). That being said, in order to obtain high quality meat, producers must be concerned with controlling their systems, making an effort to do not end up with poor quality meat to the market. More than that, it is public health concern in all agribusiness sector (CAVALIN et al., 2018).

According to the European Parliament and the Council of the European Union (2003), feed additives are defined as substances, micro-organisms or preparations, other than feed material and premix, which are included on the water or/on the diets in order to perform important functions such as, positive effects on the ingredient's characteristics, attend the nutritional requirements, improve the performance and animal welfare and also increase digestibility of feeding stuffs.

Therefore, a feed additive must not perform any adverse effect on animal health or the environment, without any performance decrease. Among the feed additives currently used on swine production, plant extracts, acidifiers and ZnO are already consolidated and has registered positive effects, letting space in research for new approaches, like dietary fibers.

Acidifiers, for example, are often used as alternatives to GEA's, due to their ability to stimulate a favorable intestinal environment for healthy microorganisms, which might result in greater nutrient digestibility, increased growth performance, and significant reduction on the incidence of diarrhea (GRECCO et al., 2018).

Plant extracts have potential biological functions, such as antiviral, antimicrobial, antioxidant and anti-inflammatory effects. Based on previous studies, plant extracts may improve animal health through several mechanisms, such as direct suppression of the proliferation of pathogens, alteration of gut microbial populations and enhancement of immune functions (LIU et al., 2018b).

According to Raquipo et al., (2017), the inclusion of ZnO on post weaning diets improves growth performance and reduces the incidence of diarrhea. It possesses an antimicrobial function, mainly acting on *E. coli*, which is one of the main issues on nursery phase. Likewise, Starke et al. in 2014, suggested that the supplementation with high levels of zinc has a marked effect on the physiology of the gastrointestinal tract taking into account the enzymatic activity, since this supplementation leads to greater production of enzymes in the pancreatic tissue such as amylase, carboxypeptidase A, chymotrypsin, trypsin and lipase, which may lead to better digestion of the food.

It is known that the benefits of this additive are noticeable only with the inclusion of high doses (also known as therapeutic doses) in the diet, around 2400 to 4000 ppm (DAVIN et al., 2013; PLUSKE, 2013). However, the dosage currently used can contribute to environmental contamination and, in addition, to bacterial resistance. Due to these negative effects, the use of zinc oxide has been restricted all over the world (FERNANDES et al., 2020).

In the past, antibiotics were included at subtherapeutic levels, acting as growth-enhancers and reducing the pathogen load (MARON; SMITH; NACHMAN, 2013). Even so, there is a concern of the global population towards the use of antibiotics as growth-enhancers (GEA's) removal from animal production systems, due to health and environmental issues that are increasing the bacterial strain resistance against many antibiotics. Increases in the incidence of human infections from antibiotic-resistant bacteria have been inferred to be directly related to the indiscriminate and overuse of antibiotics required to therapeutics in animal production (MARTIN; THOTTATHIL; NEWMAN, 2015). Langlois et al., 1988 stated that complete removal of antibiotics from animal production has decreased the resistance of lactose-fermenting fecal coliform bacteria. Thus, a tremendous pressure on the livestock industry to develop alternatives against pathogens has been installed (MARQUARDT; LI, 2018; LEKAGUL; TANGCHAROENSATHIEN; YEUNG, 2019).

However, one of the main consequences of eliminating GEA's from diets, is the higher chance of pathogens causing diseases in the animals, affecting negatively their performance. Nevertheless, to avoid the negative effects of removing GEA's from the production systems, modifications and adaptations in management protocol and nutritional strategies are required (JAYARAMAN; NYACHOTI, 2017). Focusing in to improve the prevention of pathogenic bacteria colonize the intestinal system. This can be accomplished via feed additives, which can prevent the pathogens bacteria from compromising the animal`s health (LIU et al., 2018b).

Taking into consideration the severe restriction or total ban on the use of GEA's in swine production, different alternatives, such as ZnO, have been suggested as a viable solution (SUN; KIM, 2017). Even so, there are two important concerns on it, to star of, the zinc on its oxide form has a very low absorption, just about 25% is used by the animal, the other 75% is excreted in the feces, contributing to a none sustainable environment (JONDREVILLE; REVY; DOURMAD, 2003). The second issue would be the promotion of antimicrobial resistant with high dietary ZnO inclusion (CIESINSKI et al., 2018). Thus, new alternatives must be included in the production cycle, being dietary fibers good examples of tools to include as in feed additives in piglets diets (FERNANDES et al., 2020).

2.4 Fibers for piglets in the nursery phase

In pigs, most of the ingredients are digested in the small intestine, and their respective nutrients absorbed by it. In the large intestine, on the other hand, fermentation of previously undigested foods occurs, like fibers and insoluble proteins. The products of this fermentation, short-chain fatty acids, contribute mainly to the supply of energy, as well as to support of the eubiosis of the animal (JHA et al., 2019).

Dietary fibers are oligosaccharides and polymers of carbohydrates that are not hydrolyzed by endogenous enzymes in the small intestine (TURNER, A. N. D.; LUPTON, 2011), and can be classified as to solubility in soluble or insoluble (ASP, 1996). The insoluble ones reduce the time of passage of the digesta, in this way, they can reduce the proliferation of pathogens in the intestinal lumen (HEO et al., 2013). The inclusion of soluble fibers can have negative effects after weaning, as there is an increase in the viscosity of the digesta, which leads to exfoliation of the intestinal mucosa and atrophy of the villi, in addition to reducing the fermentability of the diet and the satiety of the animal (JHA; BERROCOSO, 2015; CHEN et al., 2020).

The contact between the piglets and the dietary fibers happens from the moment that the animals start to feed on diets based on products of vegetable origin. Although the amount of crude fiber in the diet may not impact the performance of weaned piglets (PIEPER et al., 2012; CHEN et al., 2015), fibers can still perform important functions related to intestinal health. An important role played by fibers is the modulation of the intestinal microbiota. For example, the use of Chicory and Plantago in the diet of weaned piglets favors the development of *Lactobacillus, Treponema* and *Prevotella*, and consequently, indirectly aiding the digestibility of diet components (DICKSVED; JANSSON; LINDBERG, 2015).

Soluble fibers can reduce the count of *E. coli* in the small intestine due to its property of blocking the adhesion of this bacteria to receptors in the intestinal mucosa of piglets (MOLIST et al., 2014). By altering the microbiota, due to reduction of the population of *E. coli* in the intestine, fibers can also provide improvements in intestinal morphology, such as an increase in villus density, which in turn promotes better absorption of nutrients, and consequently, the animals perform better in the post-weaning phase (PASCOAL et al., 2012, 2015; PLUSKE, 2013; CHEN et al., 2020).

Wheat bran has a large percentage of insoluble fibers in its composition, its inclusion in the feed as a fiber source increases the villus/crypt ratio and the amount of goblet cells in the small intestine (CHEN et al., 2020). Regarding fermentation, the fibers composed of insoluble non-starch polysaccharides and oligosaccharides, start in the ileum, whereas the fermentation of insoluble non-starch polysaccharides, by retaining more water, is fermented in the most distal portion of the intestine (JHA et al., 2019). Indirectly, insoluble fibers increase ileal and post-ileal fermentation, thus regulating the microbiota and can increase the concentration of volatile fatty acids, such as acetate, butyrate and propionate, which can have an important effect on metabolism, primarily, as source of energy (WENK, 2001; PIEPER et al., 2012).

Fibers do have very variable characteristics; hence, the fiber source and its composition are important for the expected result to be obtained. The physiological effect that the fiber will cause depends more on physical-chemical characteristics than on its monomeric composition itself (HEO et al., 2013; JARRETT; ASHWORTH, 2018). Therefore, the fiber source, the balance between insoluble and soluble, as well as the level of inclusion and particle size are key features to guarantee the microbiological and physicochemical integrity of the animal´s intestine (CHEN et al., 2020).

Lignocellulose and eubiotic lignocellulose fiber in this study were obtained from a commercial company (Agromed GmbH, Bad Haller Street 23, A-4550 Kremsmünster, Áustria). Agromed is specialized in natural feed concepts, it has been focusing for more than ten years on the research and development of dietary fibers in order to improve performance of animals in the agribusiness sector. Both products are patented manufacturing technology is at the origin of the sources of fiber. The main differences between them lie in the fermentability. Lignocelulose fiber is derived from trunk wood, and eubiotic lignocelulose fiber is a combination of trunk and bark. Trunk delivers insoluble, non-fermentable fibre, whereas the bark is insoluble but partly fermentable. Chemical analyzes and specified warranty levels of lignocelulose fiber: insoluble and non-fermentable fiber, with a low percentage of lignin (10%); Dry Matter: 96%; Crude Fiber: 70%; Acid Detergent Fiber: 75%. Chemical analyzes and specified warranty levels of eubiotic lignocelulose fiber: insoluble and partially fermentable fiber, with a high percentage of lignin (30%), DM: 96%; CF: 65%; A.D.F: 70%; ME: 1.400 Kcal/kg.

Considering the severe restriction or total ban on the use of GEA’s and ZnO in swine production, different alternatives, such as dietary fibers have been suggested as an alternative tool to be implemented in the nutritional protocol of the production system, as they can influence positively to the both removals and reduce in its dosage, by modulating the microbiota, contributing to energy supply (fermentation) and improving the digestibility of the ingredients, giving the animal more chances to perform better.

3. GENERAL CONSIDERATIONS

The weaning is a critical transition phase for the piglets, being characterized by several physical and physiological changes that can compromise the health and growth performance in the post weaning period. Nutritional and farm managements become the major challenges on this phase, in order to minimize stressors and ensuring adequate productive conditions throughout the nursery phase and until the slaughter.

In the last decades, different additives have been developed focusing on reducing or smoothing the post weaning challenges. Moreover, sustainability is increasingly present in production systems, giving more space in academic field to look for alternatives to replace and/or reduce GEA's and ZnO from the diets. In this sense, private companies are developing new products in a very high speed, in order to attend the demands from the market. As it was explained earlier in this paper, the alternative sources of dietary fiber have a great potential for improving growth performance, decreasing incidence of diarrhea and mineral fecal excretion. Furthermore, these alternatives can be included at low inclusion, might leading to economics benefits.

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SECOND PART

Performance and gut permeability of post-weaned piglets are influenced by different sources of lignocellulose fiber

ABSTRACT

The use of growth-enhancing antibiotics (GEA) and zinc oxide (ZnO) in post-weaning diets is a common practice, with the aim of improving performance and reducing post-weaning diarrhea. However, this practice can lead to antibiotic resistance and the use of ZnO can contribute to zinc (Zn) pollution to the environment, since most of the ingested amount is excreted in the feces. Therefore, the present study aimed to evaluate the effect of different fiber sources (lignocellulose and eubiotic lignocellulose) in post-weaning diets, associated with reduced use of ZnO and/or GEA on performance, intestinal permeability, incidence of diarrhea, *E. Coli* concentration in feces, excretion of Zn, copper and crude protein in feces and the percentage of animals medicated in the first week after weaning. A total of 90 piglets weaned at 25 days (7.84±1.71 kg) were distributed in a randomized block design (weight) and divided into 5 treatments: T1 - Tiamulin as GEA in association with high dosage of ZnO (from 2500 to 1500 ppm); T2 - negative GEA and lignocellulose fiber (2%) in association with high dosage of ZnO; T3 - negative GEA and eubiotic lignocellulose fiber (2%) in association with high dosage of ZnO; T4 - negative GEA and lignocellulose fiber in association with reduced dosage of ZnO (100 ppm); T5 - negative GEA and eubiotic lignocellulose fiber in association with reduced dosage of ZnO (100 ppm), with six replicates and three piglets per pen. The nutritional program was divided into 4 phases (pre-initial 1: 25 to 32 days; pre-initial II: 33 to 39 days; initial I: 40 to 53 days; and initial II: 54 to 67 days). All data passed the F test. The Tukey test (P < 0.05) was used to compare the means. Plasma galactose was analyzed in one animal from each pen. Although there was a difference between the average daily feed intake (ADFI) in all periods (P < 0.05), the treatments did not influence the final weight of the piglets. In the first week, the highest ADFI was in animals fed with eubiotic lignocellulose fiber and reduced ZnO (T5) dosage. The ADFI of the other treatments did not differ from each other. However, in the second stage of day care, the highest ADFI results were obtained with animals from T1, T3 and T5. The lowest consumption was with T4, with T2 no different from the others. Analyzing the sum in the last two periods (0-28 and 0-42 days), ZnO negatively influenced the ADFI of piglets. The lowest feed intake value was observed in piglets fed a diet containing eubiotic lignocellulose fiber and high dosage of ZnO (T3). There were significant differences between the phases of the sugar absorption test (SAT). When there was statistical difference by the F test (P < 0.05), SAT values in the second phase were lower compared to the first. Thus, it can be inferred that the barrier function was guaranteed with the use of dietary fiber, both in high and low doses of ZnO. In general, animals fed reduced doses of ZnO in the diets had lower excretion of Zn and copper in feces. It can be concluded that the inclusion of eubiotic lignocellulose fiber in the diets of piglets in the nursery phase allows the total withdrawal of Tiamulin 80% as a performance enhancer and a 96% reduction of ZnO as an antimicrobial, without harming the performance of the animals, ensuring the maintenance of the barrier function in the intestine and providing less fecal excretion of Zn in the environment.

Keywords: diarrhea, dietary fiber, intestinal health, sustainable, tight junctions.

1. INTRODUCTION

The weaning is responsible for many physiological changes that have a negative impact in the animals, mainly due to factors that occur in this period, such as separation from the mother and litter mates, substitution of liquid milk for solid foods, fights in nursery pens, sanitary and management challenges, and changes in temperature.

This scenario leads to important changes in their morphology, besides a reduction in the secretion of some enzymes, which consequently affects the digestive and absorptive capacity of the nutrients in the small intestine. With all these reasons, growth-enhancer antibiotics (GEA) have been widely used in pig production as growth promoters in order to minimize the incidence of diarrhea after weaning and to improve the performance of the piglets in the nursery and in the phases that follows (LI, 2017).

However, increases in the incidence of human infections from antibiotic-resistant bacteria have been hypothesized to be directly related to the overuse of antibiotics required for human medical prophylactics and therapeutics in the feeding programs for animal production (LEKAGUL; TANGCHAROENSATHIEN; YEUNG, 2019). Considering the severe restriction or total ban on the use of GEA in swine production, ZnO have been suggested as an alternative to GEA. Nevertheless, the issue regarding the high doses of ZnO in piglet’s diets is the environmental pollution, since approximately 80% of the amount ingested is excreted in the feces (FERNANDES et al., 2020). Thus, new approaches are being already developed as an effort to replace both GEA and ZnO, in order to maintain and/or improve the animal´s performance, being the dietary fiber a good example of an alternative for that matter.

In recent years, in-depth studies have been carried out on the physical, chemical, and nutritional physiology of dietary fibers for pigs. It was found that its use can improve intestinal morphology, the microbiological balance in the intestine, decrease of gut permeability, and that the fermentation carried out by the intestinal microorganisms can positively affect the health of the animals in times of high challenges, such as weaning (PASCOAL et al., 2012; JARRETT; ASHWORTH, 2018).

2. OBJECTIVE

The present study aimed to evaluate the effect of different fiber sources (lignocellulose and eubiotic lignocellulose fiber) in post-weaning diets, associated with reduced use of ZnO and/or growth-enhancing antibiotics on the productive performance, intestinal permeability, incidence of diarrhea, concentration of *E. Coli* in the feces, zinc, copper and crude protein excretion in the feces and the percentage of animals medicated in the first week post-weaning.

3. MATERIALS AND METHODS

All methods involving animal handling were performed in accordance with the regulations approved by the Institutional Animal Welfare and Ethics/Protection committee from the Universidade Federal de Minas Gerais (UFMG) - Campus Montes Claros (UFMG - CETEA), Brazil, under the protocol number 101/2020.

3.1 Local, animals, facilities, experimental design and diets

The study was performed between March and June 2020 and it was conducted in the nursery facilities of the swine production farm of UFMG - Campus Montes Claros. A total of 90 piglets were obtained from a commercial pig herd (45 castrated males and 45 females - TN70 * Talent) and weaned at 25 days of age, presenting an initial body weight of 7.84 ± 1.71 kg. The piglets were housed in groups (three animals) in pens of 1.20m length, 1.00m width and 0.80m height (0.40cm per animal), with a semi-automatic collective feeder, nipple drinker and plastic slatted floor, with access to feed and water *ad libitum*. The pens were suspended from the floor at a height of 0.90cm, for fecal score analysis on the ground. Variations in ambient temperature, relative humidity and photoperiod closely followed outside conditions during the day and during the night buildings were insulated with curtains to protect against wind and the lower temperatures of the night. Each pen was equipped with individual heating infrared lamps and all rooms were lighted at night. The pigs were allocated in a randomized block design using the initial body weight as the main criteria for the formation of the blocks, and divided among five treatments and sex repetitions per treatment, with 3 piglets per pen. The treatments consisted of the inclusion of Tiamulina 80%, ZnO, lignocellulose fiber and eubiotic lignocellulose fiber in different amounts in four phases in the nursery, as shown in Table 1. The fibers were added volumetrically in substitution of the corn. The nutrient compositions of the experimental diets are shown from Table 2 to Table 5. Due to the pandemic, we were not able to perform laboratory analysis in the samples of the diets.

Table 1 - Description of the tretaments in all phases at nursery*.

Additives	Treatments				
	1	2	3	4	5
Phase 1 (Pre-starter I: 25 to 32 days of age)					
Tiamulin 80%, ppm	150	--	--	--	--
Zn, ppm	2000	2000	2000	80	80
Lignocellulose fiber, %	--	2,0	--	2,0	--
Eubiotic lignocellulose fiber, %	--	--	2,0	--	2,0
Phase 2 (Pre-Starter II:33 to 39 days of age)					
Tiamulin 80%, ppm	150	--	--	--	--
Zn, ppm	1600	1600	1600	80	80
Lignocellulose fiber, %	--	2,0	--	2,0	--
Eubiotic lignocellulose fiber, %	--	--	2,0	--	2,0
Phase 3 (Starter I: 40 to 53 days of age)					
Tiamulin 80%, ppm	150	--	--	--	--
Zn, ppm	1200	1200	1200	80	80
Lignocellulose fiber, %	--	1,0	--	1,0	--
Eubiotic lignocellulose fiber, %	--	--	1,0	--	1,0
Phase 4 (Starter II: 54 to 67 days of age)					
Tiamulin 80%, ppm	150	--	--	--	--
Zn, ppm	80	80	80	80	80
Lignocellulose fiber, %	--	1,0	--	1,0	--
Eubiotic lignocellulose fiber, %	--	--	1,0	--	1,0

*The diets were formulated to meet the requirements of this animal category according to Rostagno et al., (2017). T1 – Tiamulin as GEA in association with high dosage of ZnO (from 2500 to 1500 ppm); T2 – GEA negative and lignocellulose fibre (2%) in association with high dosage of ZnO; T3 – GEA negative and eubiotic lignocellulose fibre (2%) in association with high dosage of ZnO; T4 – GEA negative and lignocellulose fibre in association with reduced dosage of ZnO (100 ppm); T5 – GEA negative and eubiotic lignocellulose fibre in association with reduced dosage of ZnO (100 ppm).

Table 2 - Experimental diets used on phase 1 (25 to 32 days of age).

Ingredients (%)	**Phase 1 - Pre-starter I**				
	T1	**T2**	**T3**	**T4**	**T5**
Corn (7.86%)	31.315	28.650	28.650	28.550	28.550
Milk whey	21.000	21.000	21.000	21.000	21.000
Soybean meal (46%)	16.000	16.000	16.000	16.000	16.000
Pre-Cooked corn	10.000	10.000	10.000	10.000	10.000
Soybean protein concentrate	8.000	8.000	8.000	8.000	8.000
Swine plasma	5.000	5.000	5.000	5.000	5.000
Soybean oil	3.550	4.200	4.200	4.300	4.300
Sugar	3.500	3.500	3.500	3.500	3.500

Lignocellulose fiber	0.000	2.000	0.000	2.000	0.000
Eubiotic Lignocellulose fiber	0.000	0.000	2.000	0.000	2.000
Dicalcium fosfate	1.635	1.650	1.650	1.650	1.650
L-Lysina HCL (98.5%)	0.402	0.400	0.400	0.400	0.399
Sodium cloride	0.400	0.400	0.400	0.400	0.400
DL-Methionine (99%)	0.283	0.290	0.290	0.280	0.281
Zinc oxide 80%	0.250	0.250	0.250	0.010	0.010
Premix micromineral SALUS®[1]	0.200	0.200	0.200	0.200	0.200
Ultracid® (Organic acid blend)[2]	0.200	0.200	0.200	0.200	0.200
L-Threonine (98.5%)	0.167	0.197	0.167	0.171	0.171
L-Triptophane (98%)	0.100	0.095	0.095	0.095	0.095
L-Valine (98%)	0.100	0.110	0.110	0.110	0.110
Toxi-Nil® (Mycotoxin binder)[3]	0.100	0.100	0.100	0.100	0.100
Premix vitamin growing OVN®[4]	0.050	0.050	0.050	0.050	0.050
Powersweet® (Flavoring)[5]	0.030	0.030	0.030	0.030	0.030
Tiamulin 80%	0.015	0.000	0.000	0.000	0.000
TOTAL	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**
Nutritional Specifications					
Metabolizable energy, (kcal/kg)	3.442	3.404	3.404	3.417	3.417
Crude protein, (%)	22.4	22.2	22.2	22.2	22.2
Lactose, (%)	17.9	17.8	17.8	17.8	17.8
Total calcium, (%)	0.68	0.69	0.69	0.69	0.69
Digestible phosphorus, (%)	0.44	0.44	0.44	0.44	0.44
Crude fiber, (%)	2.19	2.13	3.51	2.14	3.51
Neutral detergent fiber, (%)	6.67	6.39	6.39	6.41	6.41
Acid fetergent fiber, (%)	2.69	2.62	4.05	2.62	4.05
SID[6] AAS. %					
Lysine	1.67	1.66	1.66	1.66	1.66
Methionine + Cysteine	1.00	1.00	1.00	0.99	0.99
Threonine	1.13	1.15	1.12	1.12	1.12
Valine	1.21	1.21	1.21	1.21	1.21
Tryptophan	0.38	0.37	0.37	0.37	0.37

[1]Carbo-amino-phospho chelate of Cobalt (Cobalt 102 mg/kg). Carbo-amino-phospho chelate of Copper (Copper 7.500.00 mg/kg). Carbo-amino-phospho chelate of Chromium (Chromium 100.00 mg/kg). Carbo-amino-phospho chelate of Iron (Iron 52.00 g/kg). Carbo-amino-phospho chelate of Manganese (Manganese 23.00 g/kg). Carbo-amino-phospho chelate of Selenium (Selenium 184.00 mg/kg). Carbo-amino-phospho chelate of Zinc (Zinc 57.50 g/kg). Butylated Toluene Hydroxide (BTH). Calcium Iodine (Iodine 665 mg/kg). [2]Acids: Formic Acid, Propionic Acid, Lactic Acid, Citric acid. [3]Mycotoxin Binder. [4]Vitamin A (225.00000 UI/kg). Vitamin D3 (380.0000 UI/kg). Vitamin E (200.000 UI/kg). Vitamin K (10.000 mg/kg). Biotin (1.000 mg/kg). Folic acid (9.000 mg/kg). Nyacin (120.000 mg/kg). Pantotenic acid (60.000 mg/kg). Vitamin B2 (20.000 mg/kg). Vitamin B1 (8.000 mg/kg). Vitamin B6 (12.000 mg/kg) and Vitamin B12 (100.000 mcg/kg). [5]Feed sweetener. [6]Standardized ileal digestibility.

Table 3 - Experimental diets used on phase 2 (33 to 39 days of age)

Ingredients (%)	**Phase 2 - Pre-starter II**				
	T1	**T2**	**T3**	**T4**	**T5**
Corn (7.86%)	39.273	36.103	36.316	36.316	36.316
Milk whey	15.000	15.000	15.000	15.000	15.000

Soybean meal (46%)	19.000	19.000	19.000	19.000	19.000
Pre-Cooked corn	10.000	10.000	10.000	10.000	10.000
Soybean protein concentrate	5.000	5.000	5.000	5.000	5.000
Swine plasma	3.000	3.000	3.000	3.000	3.000
Soybean oil	3.350	4.500	4.300	4.300	4.300
Sugar	3.500	3.500	3.500	3.500	3.500
Lignocellulose fiber	0.000	2.000	0.000	2.000	0.000
Eubiotic Lignocellulose fiber	0.000	0.000	2.000	0.000	2.000
Dicalcium fosfate	1.877	1.897	1.884	1.884	1.884
L-Lysina HCL (78.5%)	0.553	0.568	0.565	0.563	0.563
Sodium cloride	0.400	0.400	0.400	0.400	0.400
DL-Methionine (99%)	0.307	0.318	0.318	0.317	0.317
Zinc oxide 80%	0.200	0.200	0.200	0.010	0.010
Premix micromineral SALUS®[1]	0.200	0.200	0.200	0.200	0.200
Ultracid® (Organic acid blend)[2]	0.150	0.150	0.150	0.150	0.150
L-Threonine (98.5%)	0.243	0.250	0.245	0.245	0.245
L-Triptophane (98%)	0.119	0.119	0.119	0.119	0.119
L-Valine (98%	0.175	0.180	0.175	0.175	0.180
Toxi-nil® (Mycotoxin binder)[3]	0.100	0.100	0.100	0.100	0.100
Premix vitamin growing OVN®[4]	0.050	0.050	0.050	0.050	0.050
Powersweet® (Flavoring)[5]	0.030	0.030	0.030	0.030	0.030
Tiamulin 80%	0.015	0.000	0.000	0.000	0.000
TOTAL	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**
Nutritional Specifications					
Metabolizable energy, (kcal/kg)	3.418	3.403	3.394	3.400	3.401
Crude protein, (%)	20.4	20.2	20.2	20.2	20.2
Lactose, (%)	13.6	13.6	13.6	13.6	13.6
Total calcium, (%)	0.72	0.72	0.72	0.72	0.72
Digestible phosphorus, (%)	0.43	0.43	0.43	0.43	0.43
Crude fiber, (%)	2.26	2.29	3.67	2.30	3.67
Neutral detergent fiber, (%)	7.47	7.14	7.17	7.19	7.19
Acid detergent fiber, (%)	2.90	2.82	4.25	2.83	4.26
SID[6] AAS. %					
Lysine	1.59	1.59	1.59	1.59	1.59
Methionine + Cysteine	0.95	0.95	0.95	0.95	0.95
Threonine	1.07	1.07	1.06	1.06	1.06
Valine	1.15	1.14	1.14	1.14	1.14
Tryptophan	0.36	0.36	0.36	0.36	0.36

[1]Carbo-amino-phospho chelate of Cobalt (Cobalt 102 mg/kg). Carbo-amino-phospho chelate of Copper (Copper 7.500.00 mg/kg). Carbo-amino-phospho chelate of Chromium (Chromium 100.00 mg/kg). Carbo-amino-phospho chelate of Iron (Iron 52.00 g/kg). Carbo-amino-phospho chelate of Manganese (Manganese 23.00 g/kg). Carbo-amino-phospho chelate of Selenium (Selenium 184.00 mg/kg). Carbo-amino-phospho chelate of Zinc (Zinc 57.50 g/kg). Butylated Toluene Hydroxide (BTH). Calcium Iodine (Iodine 665 mg/kg). [2]Acids: Formic Acid, Propionic Acid, Lactic Acid, Citric acid. [3]Mycotoxin Binder. [4]Vitamin A (225.00000 UI/kg). Vitamin D3 (380.0000 UI/kg). Vitamin E (200.000 UI/kg). Vitamin K (10.000 mg/kg). Biotin (1.000 mg/kg). Folic acid (9.000 mg/kg). Nyacin (120.000 mg/kg). Pantotenic acid (60.000 mg/kg). Vitamin B2 (20.000 mg/kg). Vitamin B1 (8.000 mg/kg). Vitamin B6 (12.000 mg/kg) and Vitamin B12 (100.000 mcg/kg). [5]Feed sweetener. [6]Standardized ileal digestibility.

Table 4 - Experimental diets used on phase 3 (40 to 53 days of age).

Ingredients (%)	**Phase 3 - Starter I**				
	T1	**T2**	**T3**	**T4**	**T5**
Corn (7.86%)	51.086	40.056	49.878	50.078	50.078
Milk whey	6.000	6.000	6.000	6.000	6.000
Soybean meal (46%)	25.000	25.000	25.000	25.000	25.000
Pre-Cooked corn	7.000	7.000	7.000	7.000	7.000
Soybean protein concentrate	3.000	3.000	3.000	3.000	3.000
Soybean oil	3.700	3.700	3.900	3.700	3.700
Sugar	2.000	2.000	2.000	2.000	2.000
Lignocellulose fiber	0.000	1.000	0.000	1.000	0.000
Eubiotic Lignocellulose fiber	0.000	0.000	1.000	0.000	1.000
Dicalcium fosfate	2.214	2.244	2.222	2.222	2.222
L-Lysina HCL (78.5%)	0.625	0.638	0.625	0.625	0.625
Sodium cloride	0.400	0.400	0.400	0.400	0.400
DL-Methionine (99%)	0.285	0.295	0.285	0.285	0.285
Zinc oxide 80%	0.150	0.150	0.150	0.010	0.010
Premix micromineral SALUS®[1]	0.200	0.200	0.200	0.200	0.200
Ultracid® (Organic acid blend)[2]	0.100	0.100	0.100	0.100	0.100
L-Threonine (98.5%)	0.281	0.287	0.281	0.282	0.281
L-Triptophane (98%)	0.117	0.117	0.117	0.117	0.117
L-Valine (98%	0.191	0.195	0.191	0.191	0.191
Toxi-nil® (Mycotoxin binder)[3]	0.100	0.100	0.100	0.100	0.100
Premix vitamin growing OVN®[4]	0.050	0.050	0.050	0.050	0.050
Powersweet® (Flavoring)[5]	0.030	0.030	0.030	0.030	0.030
Tiamulin 80%	0.015	0.000	0.000	0.000	0.000
TOTAL	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**
Nutritional Specifications					
Metabolizable energy, (kcal/kg)	3.391	3.370	3.366	3.361	3.361
Crude protein, (%)	19.3	19.1	19.2	19.2	19.0
Lactose, (%)	7.60	7.30	7.50	7.60	7.60
Total calcium, (%)	0.71	0.72	0.71	0.71	0.71
Digestible phosphorus, (%)	0.42	0.42	0.42	0.42	0.42
Crude fiber, (%)	2.82	2.81	3.28	2.80	3.29
Neutral detergent fiber, (%)	8.91	8.79	8.79	8.82	8.83
Acid detergent fiber, (%)	3.44	3.40	4.13	3.42	4.14
SID[6] AAS. %					
Lysine	1.47	1.48	1.47	1.47	1.47
Methionine + Cysteine	0.88	0.88	0.87	0.87	0.87
Threonine	0.99	0.99	0.98	0.98	0.98
Valine	1.06	1.06	1.05	1.05	1.05
Tryptophan	0.32	0.32	0.32	0.32	0.32

[1]Carbo-amino-phospho chelate of Cobalt (Cobalt 102 mg/kg). Carbo-amino-phospho chelate of Copper (Copper 7.500.00 mg/kg). Carbo-amino-phospho chelate of Chromium (Chromium 100.00 mg/kg). Carbo-amino-phospho chelate of Iron (Iron 52.00 g/kg). Carbo-amino-phospho chelate of Manganese (Manganese 23.00 g/kg). Carbo-amino-phospho chelate of Selenium (Selenium 184.00 mg/kg). Carbo-amino-phospho chelate of Zinc (Zinc 57.50 g/kg). Butylated Toluene Hydroxide (BTH). Calcium Iodine (Iodine 665 mg/kg). [2]Acids: Formic Acid, Propionic Acid, Lactic Acid, Citric acid. [3]Mycotoxin Binder. [4]Vitamin A (225.00000 UI/kg). Vitamin D3 (380.0000 UI/kg). Vitamin E (200.000 UI/kg). Vitamin K (10.000 mg/kg). Biotin (1.000 mg/kg). Folic acid (9.000 mg/kg). Nyacin (120.000 mg/kg). Pantotenic acid (60.000 mg/kg). Vitamin B2 (20.000 mg/kg). Vitamin B1 (8.000 mg/kg). Vitamin B6 (12.000 mg/kg) and Vitamin B12 (100.000 mcg/kg). [5]Feed sweetener. [6]Standardized ileal digestibility.

Table 5 - Experimental diets used on phase 4 (54 to 67 days of age).

Ingredients (%)	**Phase 2 - Pre-starter II**				
	T1	**T2**	**T3**	**T4**	**T5**
Corn (7.86%)	65.681	64.174	64.174	64.174	64.170
Soybean meal (46%)	28.000	28.000	28.000	28.000	28.000
Soybean oil	4.000	4.500	4.500	4.500	4.500
Lignocellulose fiber	0.000	1.000	0.000	1.000	0.000
Eubiotic Lignocellulose fiber	0.000	0.000	1.000	0.000	1.000
Dicalcium fosfate	2.319	2.326	2.326	2.326	2.330
L-Lysina HCL (78.5%)	0.574	0.574	0.574	0.574	0.574
Sodium cloride	0.400	0.400	0.400	0.400	0.400
DL-Methionine (99%)	0.226	0.236	0.236	0.236	0.236
Zinc oxide 80%	0.010	0.010	0.010	0.010	0.010
Premix micromineral SALUS®[1]	0.200	0.200	0.200	0.200	0.200
Ultracid® (Organic acid blend)[2]	0.100	0.100	0.100	0.100	0.100
L-Threonine (98.5%)	0.247	0.257	0.257	0.257	0.257
L-Triptophane (98%)	0.112	0.112	0.112	0.112	0.112
L-Valine (98%	0.145	0.145	0.145	0.145	0.145
Toxi-nil® (Mycotoxin binder)[3]	0.100	0.100	0.100	0.100	0.100
Premix vitamin growing OVN®[4]	0.050	0.050	0.050	0.050	0.050
Powersweet® (Flavoring)[5]	0.030	0.030	0.030	0.030	0.030
Calcitic limestone	0.021	0.018	0.018	0.018	0.018
Tiamulin 80%	0.015	0.000	0.000	0.000	0.000
TOTAL	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**
Nutritional Specifications					
Metabolizable energy, (kcal/kg)	3.374	3.363	3.363	3.363	3.363
Crude protein, (%)	18.4	18.3	18.3	18.3	18.3
Lactose, (%)	3.30	3.30	3.30	3.30	3.30
Total calcium, (%)	0.70	0.70	0.70	0.70	0.70
Digestible phosphorus, (%)	0.40	0.40	0.40	0.40	0.40
Crude fiber, (%)	3.05	3.02	3.70	3.02	3.70
Neutral detergent fiber, (%)	9.76	9.60	9.60	9.60	9.60
Acid detergent fiber, (%)	3.68	3.64	4.36	3.64	4.36
SID[6] AAS %					
Lysine	1.35	1.35	1.35	1.35	1.35
Methionine + Cysteine	0.81	0.81	0.81	0.81	0.81

Threonine	0.91	0.91	0.91	0.91	0.91
Valine	0.98	0.97	0.97	0.97	0.97
Tryptophan	0.30	0.30	0.30	0.30	0.30

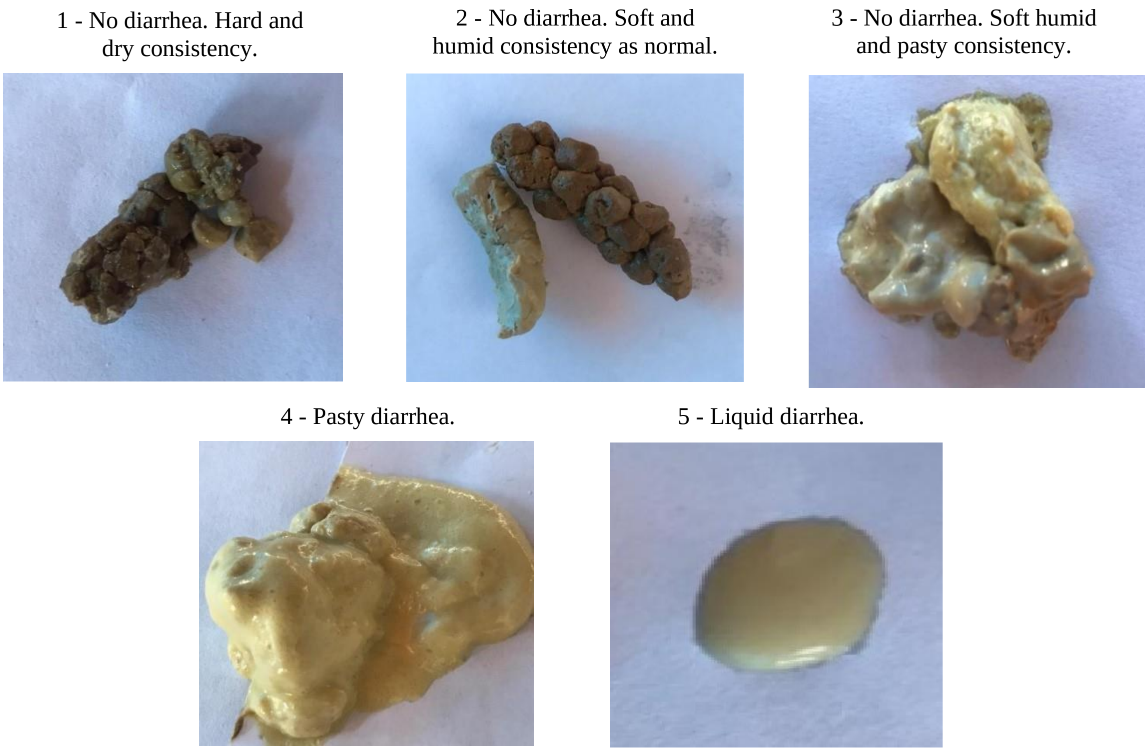
[1]Carbo-amino-phospho chelate of Cobalt (Cobalt 102 mg/kg). Carbo-amino-phospho chelate of Copper (Copper 7.500.00 mg/kg). Carbo-amino-phospho chelate of Chromium (Chromium 100.00 mg/kg). Carbo-amino-phospho chelate of Iron (Iron 52.00 g/kg). Carbo-amino-phospho chelate of Manganese (Manganese 23.00 g/kg). Carbo-amino-phospho chelate of Selenium (Selenium 184.00 mg/kg). Carbo-amino-phospho chelate of Zinc (Zinc 57.50 g/kg). Butylated Toluene Hydroxide (BTH). Calcium Iodine (Iodine 665 mg/kg). [2]Acids: Formic Acid, Propionic Acid, Lactic Acid, Citric acid. [3]Mycotoxin Binder. [4]Vitamin A (225.00000 UI/kg). Vitamin D3 (380.0000 UI/kg). Vitamin E (200.000 UI/kg). Vitamin K (10.000 mg/kg). Biotin (1.000 mg/kg). Folic acid (9.000 mg/kg). Nyacin (120.000 mg/kg). Pantotenic acid (60.000 mg/kg). Vitamin B2 (20.000 mg/kg). Vitamin B1 (8.000 mg/kg). Vitamin B6 (12.000 mg/kg) and Vitamin B12 (100.000 mcg/kg). [5]Feed sweetener. [6]Standardized ileal digestibility.

3.2 Experimental procedures

Every morning, feed refusals were collected when available, and fresh feed was immediately distributed once per day between 6:30 am and 7:30 am. Feed intake was determined as the difference between feed allowance and the refusals collected on the next morning. Feed samples (1 sample per treatment and per phase) were collected for further analyzes of the composition. The variations in ambient temperature (maximum and minimum), relative humidity (RH) and photoperiod were following closely the outdoor conditions, meaning, it was an open building with curtains. Ambient temperature and RH was continuously recorded (two measurements every day at 8:00 am and 4:00 pm) in the barns, using an infrared thermometer placed inside the facilities (Didai Tecnologia Ltda., Campinas, Brazil). Pigs were individually weighed at the beginning and at the end of each period of the experiment. For each growing stage, the average daily gain, average daily feed intake and gain: feed ratios were calculated.

During the experiment, piglets that presented intense diarrhea (score 4-5) were medicated with an intramuscular injection of Tylan® and Quinotril® during three consecutive days at a dosage of 3.0 mL/piglet. The diarrhea score of each pen was assessed daily, according to the method proposed by Guedes, 2019 (Figure 1). The incidence of diarrhea was observed by a visual inspection of the consistency of fecal material on the floor of each pen on a scale of 1-5: whereas, 1, no diarrhea hard and dry consistency; 2, no diarrhea soft and humid consistency considered as normal; 3, no diarrhea soft, humid and pasty consistency; 4, pasty diarrhea; and 5, liquid diarrhea. Diarrhea scores were taken from all repetitions in each treatment group daily, in two periods (8:00 am and 4:00 pm). The presence of diarrhea was recorded when at least a piglet of the pen developed pasty or watery fecal consistency (scores 4 to 5). The fecal score was analyzed based on the number of positive observations of diarrhea during each phase (phase 1: 7 d x 6 repetitions x 2 periods of observations = 84 possible observations; phase 2: 84; phase 3: 168; phase 4:168). The diarrhea incidence (%) was calculated as the sum of daily diarrheal piglet observations over the period and then divided by the number of days in the period, and the quotient multiplied by 100.

Figure 1 - Faecal scoring (Guedes, 2019).



Samples of fresh feces were collected for posterior laboratory of *E. Coli* concentration analyses. We did not analyze it only in the first phase because there was not enough amount of feces. The fecal sampling was followed a standard protocol: three non-consecutive days of collection throughout each phase of approximately 40g of feces from every pen. They were sampled, pooled, marked and frozen in a temperature of -72 ºC in a Consul® Freezer. Afterwards, the samples were thawed at room temperature, oven-dried at 55 °C for three days and grinded to be analyzed about the excretion of Cu, Zn and Crude Protein using the technique proposed by DETMANN et al., (2012).

Five piglets from each treatment choose randomly were subjected to sugar absorption tests (SAT) as markers of intestinal absorption based on methodologies described by COX; LEWIS; COOPER, 1999; THYMANN et al., 2006; BERKEVELD et al., 2008). Briefly, one piglet was selected per repetition per treatment and sugar absorption across the GIT using 20% galactose (≥98%; Sigma Aldrich. St Louis. MO. USA) (2.5 mL/kg body weight (BW)) was assessed. The galactose SAT was a longitudinal study performed during 2 periods after weaning (32 and 60 days of age). Piglets were fasted for three hours by blocking of the feeder access. but they had free access to water. An oral dose containing the sugar solution (galactose + distilled water) was then administered via a nasogastric tube. Twenty minutes after administration, a blood sample was taken by venepuncture of the jugular vein. The samples were collected in a lithium-heparin coated and an ethylenediaminetetraacetic acid (EDTA)-coated tube and immediately chilled on ice. The blood was centrifuged for 20 min at 2000 × g at 4 °C and aliquots of plasma were stored at -80 °C. Plasma galactose concentrations were then determined using commercial kits (D-Galactose Assay Colorimetric kit. Sigma-Aldrich) in accordance with the manufacturer's instructions.

3.3 Calculations and statistical analyses

The data were submitted to the statistical software SAS INSTITUTE INC, 2011. The Shapiro-Wilk test was used to analyze the normality of the data and when they did not present this distribution the transformation was performed using PROCRANK (SAS INSTITUTE INC, 2011). The initial weight of the piglets was considered as a covariate in the model. All variables were submitted to analysis of variance. When there was a statistical difference by the F test ($P < 0.05$), the Tukey test was adopted to compare the means. For the variable of incidence of diarrhea, the influence of each treatment on the occurrence of diarrhea was analyzed by applying the generalized linear model (GLM) in the GENMOD procedure (SAS INSTITUTE INC, 2011). Plasma galactose was analysed on a per pig basis using the GLM procedures of SAS, Tukey test was applied to compare the means.

4. RESULTS AND DISCUSSION

4.1 Environmental indexes

Average minimum, maximum, mean temperatures and relative humidity levels measured during experimental trial were disposed on Table 6. These parameters indicate that the pigs were kept in a comfortable thermoneutral environment. The local weather conditions in the city of Montes Claros, can be classified as a sub-humid tropical climate weather. Thus, the environment did was not an influencing factor in the results, especially the ones related to fecal scoring in the last two phases (Figure 3). Also, it did not have a major impact in the performance of the animals (Table 6).

Table 6 - Average minimum and maximum temperature and relative humidity during the experimental period*.

Indexes	**Values**			
	1-7 days	**8-14 days**	**15-28 days**	**29-42 days**
Minimum Temperature (ºC)	21.9	20.4	19.8	18.7
Maximum Temperature (ºC)	33.4	33.8	33.8	31.6
Mean Temperature (ºC)	27.7	27.1	26.8	25.2
Relative Humidity (%)	69.3	74.3	77.3	75.4

*The experiment was conducted in the city of Montes Claros, which can be classified as a sub-humid tropical climate weather.

4.2 Performance

Although there was difference (P < 0.05) between the ADFI on all periods, treatments did not influence on the final weight of the piglets (Table 6). In the first week, the highest consumption was in the animals fed with eubiotic lignocellulose fiber and reduced dosage of ZnO (T5). The ADFI of the other treatments did not differ from each other. However, in the second stage of nursery, the best results of ADFI were obtained with the animals from the T1, T3 and T5. The lowest consumption was with the T4, and the T2 that not differ from the others. Analyzing the last two periods (0-28 and 0-42 days), the ZnO negatively influenced the ADFI of the piglets. The lowest value of feed intake was observed on the piglets fed with diet eubiotic lignocellulose fiber and high dosage of ZnO (T3).

These ADFI differences can be explained by the amount inclusion of ZnO, and also by the physicochemical characteristic of the fibers. The ZnO has a bitter taste, which can limit the animal´s willingness to eat the diet (REYNOLDS; FORBES; MILLER, 2010). The fibers due to its influence on the motility, digestibility and fermentation can make the animal feel satisfied for more or less period of time (PLUSKE, 2013). The environment also plays an important role in the piglet´s feed intake. When the animal is not on its thermal comfort zone, it changes the eat habits, in order to keep the internal homeostasis. In other words, high temperature and RH will decrease feed intake, as the process of digestibility generates caloric increase. However, in this trial, we able to witness that the animals were not out of their comfort zone, and the changes occurred in eating behaviors were due to the different palatability features of the diets, with specific amount of each ingredient as the time went by, especially lack of ingredients of high digestibility features in the last two phases (Tables 2, 3, 4, and 5).

In 2020, Fernandes et al., evaluated dietary fiber (eubiotic lignocelulose) and zinc additives on performance and intestinal health of *E. coli* challenged piglets. In their analyses, they concluded that low levels of ZnO encapsulated with this source of dietary fiber guaranteed piglets the same final weight as did high levels of ZnO. It is good to point out the correlation between insoluble and soluble fibers on intestinal transit of the digesta and the amount of feed intake by the animal (satiety). These finding are in accordance with the results of this study.

Table 7 - Evaluation of dietary fiber on the performance of piglets during nursery phase.

Parameters	**Treatments**					**CV%**	***P*-value**
	T1	**T2**	**T3**	**T4**	**T5**		
			0-7 days				
Initial BW kg	7.780	7.850	7.777	7.924	7.878	2.33	0.9746
Final BW kg	9.375	9.364	9.464	9.594	9.883	2.49	0.5286
ADWG kg/d	0.228	0.216	0.245	0.239	0.287	8.14	0.1296
ADFI kg/d	0.304[b]	0.306[b]	0.314[b]	0.298[b]	0.344[a]	2.79	0.0032
F:G	1.98	1.70	1.67	1.36	1.39	17.43	0.5134
			8-14 days				
Final BW kg	12.543	12.645	12.822	12.503	12.878	2.77	0.9483
ADWG kg/d	0.452	0.469	0.457	0.416	0.428	6.38	0.6719
ADFI kg/d	0.571[a]	0.563[ab]	0.604[a]	0.529[b]	0.595[a]	2.19	0.0005
F:G	1.38	1.31	1.38	1.31	1.55	7.74	0.4715
			15-28 days				
Final BW kg	19.137	18.705	18.818	18.439	19.847	2.73	0.3730
ADWG kg/d	0.470	0.450	0.428	0.424	0.498	5.79	0.2439
ADFI kg/d	0.797[a]	0.835[a]	0.727[b]	0.730[b]	0.819[a]	2.05	<0.0001
F:G	1.76	1.87	1.97	1.94	1.70	8.10	0.6563
			29-42 days				
Final BW kg	29.944	28.456	27.897	27.774	29.800	2.55	0.0962
ADWG kg/d	0.769	0.697	0.648	0.672	0.711	4.80	0.1279
ADFI kg/d	1.324[a]	1.243[b]	1.171[c]	1.214[bc]	1.259[b]	1.67	<0.0001
F:G	1.72	1.78	1.82	1.75	1.80	4.52	0.9384
			0-42 days				
Total BW gain kg	22.168[a]	20.782[b]	19.980[c]	19.905[c]	21.922[a]	13.72	0.0489
ADWG kg/d	0.528[a]	0.495[b]	0.476[c]	0.474[c]	0.522[a]	13.72	0.0485
ADFI kg/d	0.825[a]	0.774[b]	0.745[c]	0.758[c]	0.849[a]	10.80	<0.0001
F:G	1.59	1.59	1.65	1.62	1.65	15.43	0.9477

BW – body weight; ADFI – average daily feed intake; ADWG – average daily weight gain; F:C – feed conversion ratio; T1 – Tiamulin as GEA in association with high dosage of ZnO (from 2500 to 1500 ppm); T2 – GEA negative and lignocellulose fibre (2%) in association with high dosage of ZnO; T3 – GEA negative and eubiotic lignocellulose fibre (2%) in association with high dosage of ZnO; T4 – GEA negative and lignocellulose fibre in association with reduced dosage of ZnO (100 ppm); T5 – GEA negative and eubiotic lignocellulose fibre in association with reduced dosage of ZnO (100 ppm). The lowercase letters mean statistical difference between treatments within each phase ($P < 0.05$).

4.3 Incidence of diarrhea

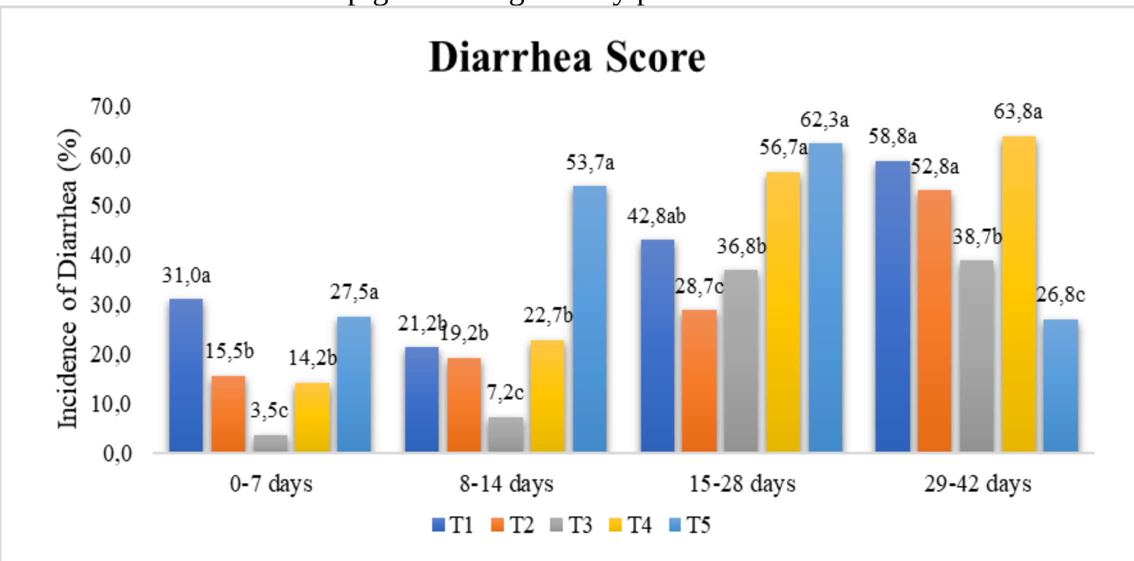
Due to nutritional, psychological and environmental stressors, weaning is often associated with diarrhea (JAYARAMAN; NYACHOTI, 2017). Analyzing data of incidence of diarrhea, in the first week post weaning, the treatment with eubiotic lignocellulose fiber in association with high dosage of ZnO (T3) decreased the incidence of diarrhea comparing with the others treatments (Figure 2). Treatments with lignocellulose, both with high and reduced dosage of zinc oxide had the same results (T2 and T4), they were better than the treatment with antibiotic as GEA, and eubiotic lignocellulose fiber in association with reduced dosage of ZnO, T1 and T5 respectively. The use of tiamulin as GEA with high dosage of zinc oxide as well as lignocellulose fiber both with high and reduced dosage of ZnO has promoted reduction in the incidence of diarrhea in the second phase of nursery, T1, T2 and T3 respectively. In the period from 15-28 days, the highest results of diarrhea score were originated from the T4 and T5. The T2 had the best outcome in decreasing diarrhea. The T1 and T3 were intermediate, not differing either from the highest and lowest values of diarrhea score. In the last stage of nursery phase (29-42 days), T1. T2 and T4, were the treatments with the worst performance in keeping the incidence of diarrhea low. The T3 was the intermediate, and the T5 was the one with the best outcome, meaning, it had less animals presenting diarrhea (Figure 2). Summarizing, there was a lot of interaction and variables influencing the treatments, mainly due to the local weather features. Nevertheless, it had no impact in the animal´s performance (Table 6). It is also worth mentioning that in the experimental trial, was necessary to wash the facilities twice a day, after every fecal score mensuration, in order to not gather many flies that could interfere in the normal behavior of the animals, especially the feed and water consumption. This washing was a contributing factor to increase the humidity inside the facilities, but this took just a few minutes and the water in the air dissipate really quick, not making the made animals feel out of their comfort zone.

The findings of this study are different to the ones reported by Fernandes et al., (2020) which showed that groups of piglets challenged with *E. Coli* fed with fiber (eubiotic lignocelulose) and ZnO (8000 ppm) showed better outcomes in the incidence of diarrhea during in the first week after weaning and subsequently during the entire trial. However, this trial was performed in another location of Brazil (Lavras, MG), which is directly correlated with the contrasting results in both experiments.

In order to infer about the digestibility of the diet, the majority of researchers perform the scoring of the feces, as an indicator of more or less suitability of the ingredients in periods when the animal is facing great amount stress (post weaning). In this study, the results (Figure 2) show higher score of diarrheas in the last phases of nursery, which can be explained by the different palatability features of the diets. As we know, the change of stages withing a phase should be done smooth, orderly not to cause sudden changes into the metabolism of the animal, that was guaranteed here in this experiment. Nevertheless, in the last two stages, there are more corn and soybean meal, which can contribute to the diet's buffering effect in the TGI, leaving substrate to be used by pathogenic organisms or to be left out in the feces. As well as, less highly digestible ingredients in the diet, like milk whey (Tables 2, 3, 4, and 5).

On the other hand, these higher feces scores in the last two stages of nursery did not have impact on the performance of the animals (Table 7). The only parameter influenced by the treatments was the ADFI within the stages. This data proves that, diarrhea score can be caused by many factors, and is not always related to performance.

Figure 2 - Evaluation of dietary fibre sources on the incidence of diarrhea based on the faecal score in the feces of piglets during nursery phase.



T1 – Tiamulin as GEA in association with high dosage of ZnO (from 2500 to 1500 ppm); T2 – GEA negative and lignocellulose fibre (2%) in association with high dosage of ZnO; T3 – GEA negative and eubiotic lignocellulose fibre (2%) in association with high dosage of ZnO; T4 – GEA negative and lignocellulose fibre in association with reduced dosage of ZnO (100 ppm); T5 – GEA negative and eubiotic lignocellulose fibre in association with reduced dosage of ZnO (100 ppm). The lowercase letters mean statistical difference between treatments within each phase *(P* < 0.05).

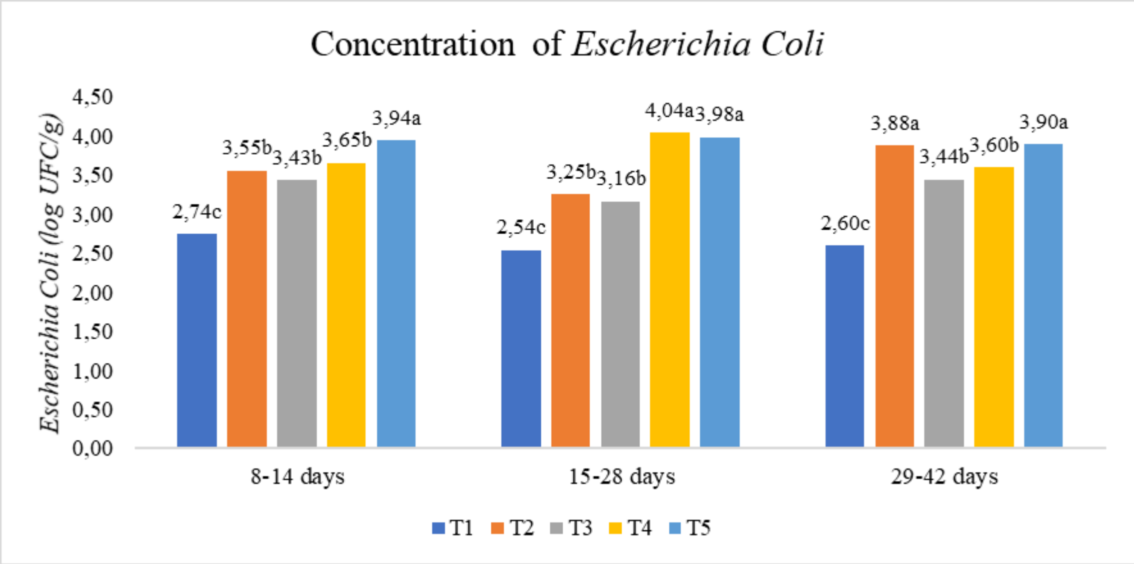
4.4 Concentration of *Escherichia coli*

The first week after weaning was not analyzed due to the small amount of sample. Overall, the animals belonging to the treatment with tiamulin as GEA in association with high dosage of ZnO (T1) had better results in the concentration of *E. Coli* in the feces of piglets during nursery phase (Figure 3). The T5 was the one with higher concentration, and the others treatments did not differ from the T1 and T5 in the second week of nursery. Analyzing the period from 15-28 days, the T2 and T3 were in between the best and the worst values, T1, T4 and T5, respectively. However, in the last two weeks of nursery, the T3 and T4 were the ones in between the best and the worst values, that came from the T1, T2 and T5, respectively. Moreover, in these three periods of nursery, the treatment with eubiotic lignocellulose fiber in association with high dosage of ZnO (T3) was the one with second best outcomes (numerically). Contrastingly, in the same three phases, the T5 had the highest results of *E. coli* concentration, but this effect had no impact on the performance, as the animals from this treatment were the ones equal statistically with the T1. The incidence of diarrhea was not directly correlated with *E. Coli* concentration between the treatments and among the phases of nursery. As is showed in Figure 3 and 4 the is no pattern in these results.

According to Fernandes et al., (2020), the association of dietary fiber and ZnO is able to reduce the amount *E. coli* in the cecum of piglets. Mainly due to the adhesion of ZnO to the pathogenic bacteria and the better dilatability of the diet, not leaving indigestible remains that could contribute to higher development of non-desirable species in the intestine, like *E. coli*. In this trial, we were able to observe similar effect.

Moreover, Pascoal et al., (2012) evaluated the effects of purified cellulose (1.5%), soybean hulls (3.0%) and citrus pulp (9.0%) in the diet of weaned piglets (21 days). They conclude that the inclusion of these fibers in diets of weaned piglets did not affect negatively the performance or transit time of diets in the TGI. However, the use of purified cellulose reduced incidence of diarrhea, being positive in control the diarrhea in weaned piglets. Also, in the same train of thought, they noted that, among the fiber sources, purified cellulose in piglet diets promotes better performance of animals, due to the modulation of the small intestine microbiota, with lower *E. coli* occurrence resulting in higher villus density (PASCOAL et al., 2015). These results are in contrast to the ones in Figure 3, but in accordance with the performance features (Table 7).

Figure 3 - Evaluation of dietary fibre sources on the concentration of *Escherichia coli* in the feces of piglets during nursery phase.



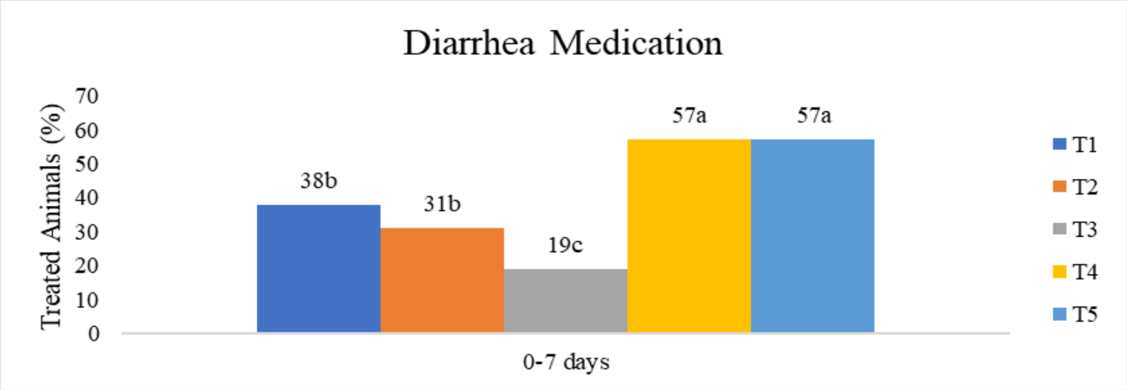
T1 – Tiamulin as GEA in association with high dosage of ZnO (from 2500 to 1500 ppm); T2 – GEA negative and lignocellulose fibre (2%) in association with high dosage of ZnO; T3 – GEA negative and eubiotic lignocellulose fibre (2%) in association with high dosage of ZnO; T4 – GEA negative and lignocellulose fibre in association with reduced dosage of ZnO (100 ppm); T5 – GEA negative and eubiotic lignocellulose fibre in association with reduced dosage of ZnO (100 ppm). The lowercase letters mean statistical difference between treatments within each phase ($P < 0.05$).

4.5 Diarrhea medication

The results from the first week diarrhea medication after weaning is presented on Figure 4. The treatments with reduced dosage of zinc oxide received had the highest number of animals with severe diarrhea (T4 and T5). Among the other treatments, the one with eubiotic lignocellulose in association with high dosage of ZnO (T3) had the best result. In other words, less animals needed medication. However, this result did not have influence on the animal´s performance. The animals with best performances were the ones from the T1 and T5. Also, the best outcome for diarrhea medication obtained in the T3 had no impact on the diarrhea score, with T1 and T5 being the best and worst respectively. Meaning that, performance, incidence of diarrhea, presence of *E. Coli* and diarrhea medication are not always related, there are a lot factors involved (diet adaptation, palatability, buffer effect and environment for example). Indicating that, the only treatment capable to be considered as equal with the T1 was T2 (2% of lignocellulose fiber high dosage of ZnO), meaning that in the conditions of this study, both strategies are a suitable alternative for removal of GEA from the piglet's diets.

Every time an animal needs to be treated, three major concerns are installed in the production system, labor time, medication costs and animal recovery time, which is always related to productive losses in some way. That being said, all the efforts made to go in the opposite direction are worth it, which means more efficiency in general.

Figure 4 - Evaluation of dietary fibre sources on the diarrhea medication of piglets during the first week of nursery phase.



T1 – Tiamulin as GEA in association with high dosage of ZnO (from 2500 to 1500 ppm); T2 – GEA negative and lignocellulose fibre (2%) in association with high dosage of ZnO; T3 – GEA negative and eubiotic lignocellulose fibre (2%) in association with high dosage of ZnO; T4 – GEA negative and lignocellulose fibre in association with reduced dosage of ZnO (100 ppm); T5 – GEA negative and eubiotic lignocellulose fibre in association with reduced dosage of ZnO (100 ppm). The lowercase letters mean statistical difference in the first week post weaning ($P < 0.05$).

4.6 Mineral excretion and crude protein concentration

The ZnO inclusion became a routine tool in nursery diets after the discovery of its property of bind the *E. coli* fimbriae, and as its principal positive result, decrease in the number of piglets with severe diarrhea, especially in the first two weeks post weaning (DAVIN et al., 2013; LIU et al., 2018b). On the other hand, sustainability in agriculture sector is not a long run reality anymore, it is a current drive is all sectors of animal protein production. In this sense, try to find ways to produce more with fewer and fewer resources is a massive demand from the market.

The copper excretion had a linear increasing in the first phase after weaning according to the treatment, where the T1 had the lower and T5 the higher excretion. Due to the no inclusion of Tiamulin as GEA and lower dosage of ZnO in treatments 1 to 4.

In the second, third and fourth phase post weaning, there was a lot of variation between treatments, in this case the nutritional adaptation within the nursery was a important aspect of it, being the T2, T4 the ones with least excretion, and in the phase four, the T4 and T5 were the lowest. Overall, the treatments with reduced dosage of zinc oxide (T4 and T5), had better zinc excretion outcomes during all nursery phase (Table 8). Analyzing the statistical difference between treatments and phases (the uppercase letters in the table), the highest amount of copper excretion from the T1 and T2 was in the last stage of nursery. For the T3, the more relevant value of copper excretion was in the first week and in the last phase (0-42 days). Nevertheless, T4 and T5 had higher values for copper excretion in the first period of nursery. The interaction between treatment and phase for zinc excretion had a different pattern, where the treatments with high dosage of zinc in the diets were the ones with higher zinc excretion values, with exception to the T5 in the third and second period. It is worth mentioning that these results were already expected, as the diets from T4 e T5 has less inclusion of ZnO, 100 ppm each, in all phases.

Not just the level of inclusion, but the physicochemical feature of ZnO can influence on its harnessing by the animal, resulting in less excretion to the environment. One fair statement is that the diets containing ZnO nanoparticles reduces zinc and phosphorus fecal excretion during the period from day 7 to day 42 (MOITA, 2019).

As observed in the present study, the fibers sources can be a suitable alternative to include less ZnO in the diets, decreasing Zn fecal excretion and keeping the animal´s performance, being beneficial to reduce the environmental Zn contamination.

These feeding and nutritional strategies are the primary tools inside a complex logistic system, meaning, animal protein production. Thus, finding ways to improve performance and keeping as profitable and sustainable as possible, is mandatory. This trial can give many valuable information about the on-farm implementation of it. As we know, nutrition is the foundation of any agriculture sector. There are a lot of options available, moreover, each farm has its particular way of doing things to achieve their specific goals. That being said, there is no right or wrong protocol, no best or worse additive, what should be it is a strategic protocol established directed to its needs.

Table 8 - Evaluation of dietary fibre sources on the copper, zinc excretion and crude protein concentration in the feces of piglets during nursery phase.

Parameters	Treatments					CV%	*P*-value
	T1	T2	T3	T4	T5		
0-7 days							
Cu (mg/kg)	137.00^{eB}	141.67^{dB}	158.83^{cA}	163.73^{bA}	181.07^{aA}	0.92	<0.0001
Zn (mg/kg)	8.665^{bA}	10.769^{aA}	10.689^{aA}	1.947^{cA}	1.682^{cA}	1.21	<0.0001
CP (%)	31.69	30.31	32.00	30.26	30.55	0.27	0.2133
8-14 days							
Cu (mg/kg)	129.05^{bC}	114.79^{cD}	133.50^{bB}	147.12^{aB}	132.37^{bC}	0.76	<0.0001
Zn (mg/kg)	8.774^{aA}	7.057^{bB}	7.561^{bB}	1.471^{cB}	1.218^{cC}	1.11	<0.0001
CP (%)	30.67	29.30	28.39	27.85	29.61	0.22	0.3516
15-28 days							
Cu (mg/kg)	134.47^{aBC}	135.90^{aC}	135.02^{aB}	126.63^{bC}	132.49^{aC}	0.76	<0.0001
Zn (mg/kg)	5.959^{bB}	6.311^{aC}	6.438^{aC}	1.425^{cB}	1.401^{cB}	1.34	<0.0001
CP (%)	30.04	27.85	27.73	29.28	28.38	0.22	0.1712
29-42 days							
Cu (mg/kg)	149.26^{aA}	150.88^{aA}	151.57^{aA}	141.89^{bB}	142.30^{bB}	0.47	<0.0001
Zn (mg/kg)	2.143^{aC}	2.442^{aD}	2.021^{bD}	1.317^{cC}	1.531^{cA}	2.49	<0.0001
CP (%)	26.56	27.13	25.89	27.32	26.41	0.19	0.5164

T1 – Tiamulin as GEA in association with high dosage of ZnO (from 2500 to 1500 ppm); T2 – GEA negative and lignocellulose fibre (2%) in association with high dosage of ZnO; T3 – GEA negative and eubiotic lignocellulose fibre (2%) in association with high dosage of ZnO; T4 – GEA negative and lignocellulose fibre in association with reduced dosage of ZnO (100 ppm); T5 – GEA negative and eubiotic lignocellulose fibre in association with reduced dosage of ZnO (100 ppm). The lowercase letters mean statistical difference between treatments within each phase ($P < 0.05$). The uppercase letters mean statistical difference within the treatment in all phases by Tukey test ($P < 0.05$).

4.7 Gut permeability

One the main issues related to worse performance in the nursery is the disfunction of the tight junctions. They are the key components in the intestinal barrier function. Once they are not able to keep its function anymore, the animal will have higher chances of get sick, as important pathogens, such as *Salmonella*, will now have the chance to enter the GIT (HEO et al., 2013).

The gut permeability results are presented in Figure 5. There was no significant difference between treatments on the galactose absorption test with the piglets within the phases. However, there were significant differences between phases. Despite the minor values of galactose absorption in the second phase compared with the first one, we presume that the intestinal permeability was guaranteed with the use of the dietary fibers thought the nursery, in association with both high and reduced dosage of ZnO.

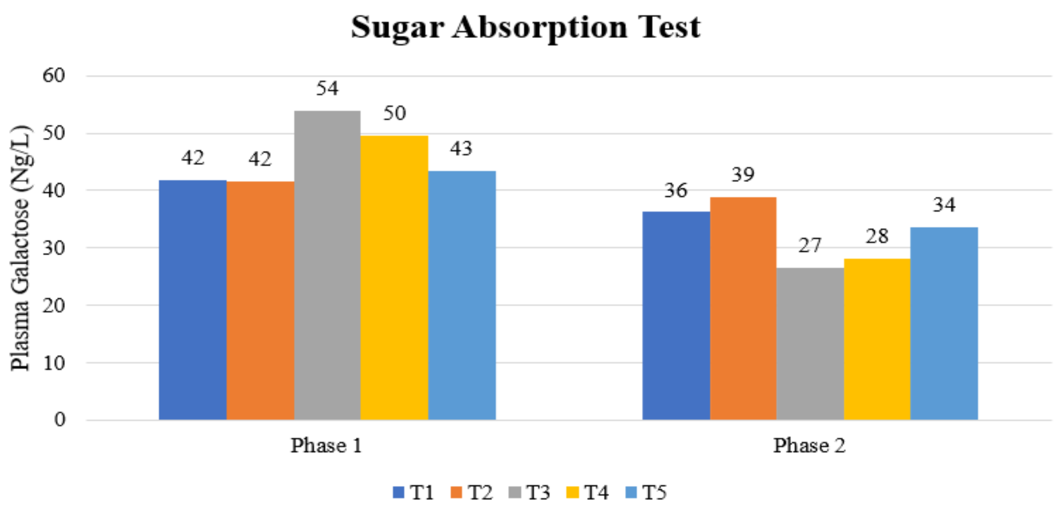
In 2017, Turpin; Langendijk and Pluske, conducted as innovative trial analyzing the potential use of mannitol and galactose as markers of intestinal morphology. They are both monosaccharides with no interaction in the GIT. Their hypothesis was that them could indicate superficial changes in the gut, which was confirmed be a strong correlation with the jejunum villus height. Their findings were the start point for this project, and as was showed in the Figure 5, eubiotic lignocellulose fiber with reduce dosage of ZnO (T5) can be a potential tool the maintain intestinal permeability.

When we talk about intestinal health, we have to look in the big picture, as many factors could interfere on it. Weaning age, use creep-feeding in the farrowing phase, environment, nutritional strategies and the healthy status of the piglets. Permeability is just one the ways to access it, morphology, enzyme activity, microbiota and immune response can be included as key aspects of it (XIONG et al., 2019).

The results of this trial are similar to those stated by Chen et al., (2015), who worked two sources of fiber, arabinoxylan in wheat bran and cellulose. They conclude that arabinoxylan in wheat is more responsible for improving various functional components of the intestinal barrier function. This paper reinforces our hypothesis, in other word, dietary fiber sources can contribute in a positive way the intestinal healthy.

Accordingly, also our findings are alike to those found by Chen et al., (2020), who have reported that diets supplemented with both soluble fiber and insoluble fiber were more effective than supplementation alone to improve blood biochemical indices, nutrients digestibility, hindgut microbe and gut barrier function.

Figure 5 - Evaluation of dietary sources of fibre on the gut permeability of piglets one week after weaning and one week before the end of the nursery phase.



T1 – Tiamulin as GEA in association with high dosage of ZnO (from 2500 to 1500 ppm); T2 – GEA negative and lignocellulose fibre (2%) in association with high dosage of ZnO; T3 – GEA negative and eubiotic lignocellulose fibre (2%) in association with high dosage of ZnO; T4 – GEA negative and lignocellulose fibre in association with reduced dosage of ZnO (100 ppm); T5 – GEA negative and eubiotic lignocellulose fibre in association with reduced dosage of ZnO (100 ppm). Phase 1 – One week after weaning (piglets were with 32 days of age). Phase 2 – One week before the end of the nursery phase (piglets were with 60 days of age).

5. CONCLUSION

It can be concluded that the inclusion of eubiotic lignocellulose fiber in the diets of piglets in the nursery phase allows the total withdrawal of Tiamulin 80% as a performance enhancer and a 96% reduction of zinc oxide as an antimicrobial, without harming the performance of the animals, ensuring maintenance of the barrier function in the intestine and providing less fecal excretion of zinc into the environment.

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