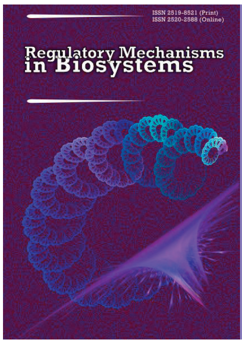

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Influence of modern treatment regimens on serum biochemical parameters in piglets with gastroenteritis

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The article presents analyses of biochemical parameters of blood serum in weaned piglets with non-contagious gastroenteritis and after their treatment with a probiotic (live spores of *Bacillus cereus* var. *toyoi*; silicic acid; calcium carbonate) and a phytobiotic (natural extracts of *Oreganum vulgare*, *Cinnamomun cassia* and *Capsicum annuum*; hydrogenated rapeseed oil) as part of the basic ration in combination with antibiotic (10% solution of enrofloxacin hydrochloride) on a modern pig farm. In animals of the experimental groups with gastroenteritis we established hypoproteinemia, hypoalbuminemia, hypoglycemia, hypoureaemia, hypercreatininemia, hyperbilirubinemia and increase of enzyme activity compared to parameters of clinically healthy piglets. The study established that the use of probiotics and phytobiotics for weaned piglets had a positive influence on protein synthesis function of the liver, as indicated by the normalization of serum total protein and albumins. Also, we found a positive influence of probiotics and phytobiotics on intensity of protein metabolism, as indicated by an increase of serum urea to the level of clinically healthy piglets. Use of phytobiotics for piglets had a positive influence on the process of gluconeogenesis in their body, which is indicated by the normalization of serum glucose to the level of clinically healthy piglets. Also, the use of probiotics and phytobiotics had a positive influence on the pigment-forming function of the liver, as indicated by the reduction of serum total bilirubin to the level of clinically healthy piglets. The use of probiotics and phytobiotics reduced activity of serum alanine and aspartate aminotransferases in the piglets of the experimental groups, indicating the stabilization of hepatocytes' cell structures (mitochondrial and cytosolic). The study established positive influence of probiotics and phytobiotics on the functioning of the liver and biliary tract, as indicated by decreased activity of serum alkaline phosphatase and gamaglutamiltranspeptidase to the level of clinically healthy piglets. So, addition of probiotics and phytobiotics to mixed fodder up to 45 days of age, normalizes functioning of the kidneys and liver in weaned piglets with gastroenteritis.

Keywords: antibiotic; probiotics; phytobiotics; protein synthesis function; pigment-forming function; enzymes activity.

Introduction

The digestive system of piglets is significantly different from that of adult pigs. It has a number of features necessary to adapt them to the new type of feeding, conditions of autonomous existence. Formation of gastrointestinal digestion in piglets is completed by 2.0–2.5 months of age (Pluske et al., 2003; Zabielski et al., 2008; Gutyj et al., 2017).

In the gastric juice of newborn piglets up to three weeks of age there is no free hydrochloric acid and a small amount of pepsin. This is a normal age phenomenon called achlorhydria. Thanks to it, the proteins of colostrum in the stomach are not broken down and getting into the small intestine, are absorbed by whole molecules, and with the undisturbed structure of immune bodies enter the blood, providing the body with immunity (Hedemann & Jensen, 2004; Lalles et al., 2004; Wheeler et al., 2008). At 2–3 weeks of life piglets have good digestion and use nutrients of animal feed (especially milk) and much worse – plant feed. Feed of vegetable origin with a high content of starch in the initial period is insufficiently digested by the piglets, but contributes to the restructuring of the digestive canal and earlier manifestation of physiological fullness of the stomach. They are also stimulants of intestinal motility for piglets and are involved in the formation of the microflora in the large intestine. Early (5–6 days of age) training in pigs for special compound feeds ensures the adaptation of the gastrointestinal canal to those feeds that they will receive after losing the sow's milk. In addition, feeding with prestarters stimulates digestion of digestive enzymes and secretory activity of the gastrointestinal canal, which increases the digestibility of protein and stabilizes the intestinal microflora, under the influence of which in the early neonatal period the formation of immune response occurs (Williams et al., 2002; De Lange et al., 2010; Kiczorowska et al., 2017; Trevisi & Pérez, 2017).

Regarding conditionally pathogenic microorganisms, the system of local immunity of the intestine exhibits adequate protective properties, with regard to norm flora – tolerance, promotes the adhesion, survival and reproduction of indigenous flora representatives. Immunoglobulins form complexes with antigens, interfere with the contact of microorganisms with target cells of the macroorganism due to agglutination and bacteriostasis, promote the rapid removal of microorganisms from the gastrointestinal canal. Normal intestinal microflora causes antigenic irritation of its mucous membrane, potentiating the inclusion of systemic and local immunity mechanisms: increases the synthesis of immunoglobulin E (IgE), propherdine, complement, lysozyme. The mucus containing secretory immunoglobulin A (IgA) protects the gastrointestinal mucosa from the degradation of macromolecules, physical and chemical aggression, as well as from attacks by microorganisms, bacterial toxins and parasites (Konstantinov et al., 2006; Metzler et al., 2006; Chen et al., 2018; Han et al., 2019). Therefore, the development peculiarities of organs and functional systems in newborn animals largely determine the state of health and resistance of the organism in subsequent periods of animal life.

Gastrointestinal diseases, in particular gastroenteritis, are registered at large industrial complexes throughout the entire technological cycle. The gastroenteritis development leads to impaired function of the liver and pancreas, which affects the alteration of gastrointestinal canal motility and reduce the digestibility of feed mass and nutrients absorption. As a result, putrefactive and fermentative processes develop, which create favourable conditions for the reproduction of microflora with subsequent intoxication of the animal's body. Decomposition products and microbial toxins are absorbed into the body through the damaged digestive canal mucous membranes. They pass through the broken liver barrier and cause damage to the central nervous system, heart and kidneys. The secretion of bile and pancreatic juice decreases. Toxic substances that are absorbed into the blood, excite the vagus nerve and increase intestinal peristalsis. As a result, nutrient absorption is slowed down and profuse diarrhea develops, which has a debilitating effect on the general condition of sick piglets, causing severe dehydration of the body, which results in blood clotting and circulatory disorders (Pittman, 2010; Gonzalez et al., 2015; Sun & Kim, 2017). As a result, farms have significant economic losses in the form of lack of production and death of animals (Heo et al., 2012; Adewole et al., 2016).

Besides, diseases of piglets in the suckling period lead to decrease in their body weight during weaning, which negatively affects their further development and preservation (Ariza-Nieto et al., 2011; Lukashchuk et al., 2018). The stable health of the digestive system in pigs is based on three main factors: the physiological state of the gastrointestinal canal, proper functioning of the immune system, optimal ration and natural balance of the digestive canal ecosystem. Due to neurohumoral regulation of processes, the body provides close functional communication of all digestive organs. Therefore, the mismatch between the functional load on digestive system and their morpho-physiological capabilities is the basis of pathogenesis of non-contagious gastrointestinal diseases (Solà-Oriol & Gasa, 2017; Trevisi & Pérez, 2017).

The occurrence of gastrointestinal diseases is associated with critical periods in the life of piglets, among which can be distinguished three main ones. The first critical period is the first two days of life. There are almost no immunoglobulins in the blood of piglets after birth, which together with a small amount of leukocytes, low lysozyme and bactericidal activity of blood serum contributes to the development of the first phase of age-related immune deficiency. If full-fledged colostrum arrives in a timely manner, age-related immune deficiency is compensated, general and local immunity develops, and the number of immunoglobulins of all classes increases in the blood. However, the late intake of colostrum in piglets impairs the formation of immune protection and develops diseases of the gastrointestinal canal. The second critical period lasts from the 14th to the 21st day of life. This is due to the fact that the immunoglobulins that came with the colostrum are decayed and the pig's immune system is still underdeveloped, contributing to the second phase of age-related immune deficiency. In addition, the synthesis of a piglet's own immunoglobulins occurs from 7–14 days of age at a low level (Sinkora et al., 2002; Bulter et al., 2006; Wheeler et al., 2008; Pluske et al., 2018).

The third critical period occurs after the early weaning of piglets from a sow and their transfer to another age group. This period is accompanied by the development of immune deficiency, associated with complete transition of animals to plant food against the background of reducing natural resistance of the organism and the action of stress factors, which leads to dysbiosis (Gresse et al., 2017; Jayaraman & Nyachoti, 2017; Hu et al., 2018; Pluske et al., 2018). The combination of these factors leads to the development of inflammatory processes in the digestive tract.

Therefore, the period of weaning piglets from sows is one of the most critical for their growth, which together with low functional activity of the immune system, which forms the immune response to the action of antigenic stimulus, is one of the main causes of gastrointestinal canal diseases of animals at an early age.

Along with other factors in the etiology of gastroenteritis, it is important to note that the intestinal microflora due to the close (symbiotic) relationship with the macroorganism always responds to changes in conditions of retention, feeding, the presence of pathological process, therefore, the disturbance of its balance (dysbacteriosis) is another reason for the development of digestive disorders and disruption of the gastrointestinal canal. Dysbacteriosis disrupts wall digestion, absorption of nutrients and biologically active substances and increases the pathogenic impact on the body of putrefactive, gram-negative microflora, which inhabits not only the large but also the small intestine and stomach. Therefore, in the early postnatal period, animals have "natural dysbacteriosis" or "age-related dysbacteriosis", which together with insufficiently expressed immune reactivity and immunodeficiency state create favourable conditions for the development of gastroenteric pathology (Konstantinov et al., 2006; Gresse et al., 2017; Han et al., 2019).

In addition, the inappropriate use of antibiotics for treatment of pigs with gastroenteritis leads to the emergence of pathogenic and conditionally pathogenic microorganisms resistant to them, which reduces the therapeutic effect and increases the cost of treatment (Cromwell, 2002; Chowdhury et al., 2009; Holman & Chénierab, 2015).

Therefore, veterinary specialists are increasingly looking for natural and safe means, which include medicines or feed additives containing natural biologically active components.

Today the most popular among such means for prevention and treatment of gastrointestinal diseases are probiotics – biological medicines consisting of symbiotic microorganisms (lactobacillus, bifidobacteria, gram-positive cocci, yeast) or products of their metabolism, which are harmless to the organism of animals and environmentally friendly. They are a good alternative to antibiotics, and the mechanism of their action is aimed at colonization of the intestine by representatives of normal or exogenous microflora, which are antagonists of pathogenic microorganisms and delay their development (Jacela et al., 2010; Silva et al., 2010; Živković et al., 2011). They occupy a leading place, performing a number of other functions: producing bacteriocins that have antimicrobial action against pathogenic strains of intestinal microflora; produce lactic acid, determining the acidity of the gastrointestinal canal; take part in the synthesis of vitamins, enzymes, antibiotics, hormone-like substances, essential amino acids, low-molecular fatty acids, peptides; responsible for the body's heat supply and epithelial energy supply; regulate intestinal peristalsis, support ion homeostasis; remove exogenous and endogenous substrates from the body; stimulate the immune system and local immunity (Brown, 2010; Ross et al., 2010; Simon, 2010).

The attention of scientists has been drawn to phytobiotics – drugs containing plant extracts, essential oils, natural alcohols and alkaloids derived from herbs or spices that have aromatic and functional properties. These include medicines containing an extract of oregano (carvacrol), cinnamon (cinnamaldehyde) and Mexican pepper (capsaicin). They can stimulate appetite, provide antioxidant protection, modify the pH of the intestines, improve digestion of feed and the efficiency of feed conversion. Also, phytobiotics act as flavours and fungistatics. However, their most important effect is that they modify functioning of the digestive glands by providing optimal conditions for competitive growth of intestinal lactobacilli and inhibiting the growth of pathogenic intestinal microorganisms (Verstegen & Williams, 2002; Vidanarachchi et al., 2005; Hanczakowska & Swiatkiewicz, 2012).

Therefore, these means are competitive and cost-effective in pig breeding, as their widespread use improves the physiological state of animals, balances rational nutrition and enriches the body with the necessary biologically active substances, and also increases the resistance of animals to diseases and improves the quality of products. The research objective was to determine the influence of the probiotic Toyocerin 10^9 and the phytobiotic Extract™ 6930 in combination with the antibiotic (10% solution of enrofloxacin hydrochloride) on the blood serum biochemical parameters of weaned piglets with gastroenteritis.

Material and methods

The research was conducted in the agro-enterprise "Agroprodservice" ,which is safe regarding infectious diseases. For the research we selected four groups (clinically healthy animals, control and two experimental groups, n = 10) of weaned piglets (Landrace breed) aged 30 days on the principle analogues. In order to prevent the activation of conditionally pathogenic microflora and its distribution in the body, the piglets of the control and experimental groups were treated with 10% solution of enrofloxacin hydrochloride injected intramuscularly at a dose of 0.5 mL/10 kg of body weight once a day for 5 days. The choice of this medicinal drug is based on the analysis conducted on the sensitivity to antibiotics. Piglets of the first experimental group were additionally given probiotic Toyocerin 10^9 (Lohmann Animal Nutrition, Germany) at a dose of 0.5 g/kg of mixed fodder, the second group – phytobiotic Extract™ 6930 (Pancosma S.A., Switzerland) at a dose of 0.15 g/kg of mixed fodder up to 45 days of age. 1 g of probiotic contains: live spores of *Bacillus cereus* var. *toyoi* not less than 1 x 10^9 CFU; silicic acid 1%; calcium carbonate 98%. 100 g of phytobiotic contains: carvacrol (natural extract of *Oreganum vulgare*) – 5.5 ± 0.55 g; cinnamaldehyde (*Cinnamomun cassia* natural extract) – 3.3 ± 0.33 g; capsicum oleoresin (natural *Capsicum annuum* extract) – 2.2 ± 0.22 g; hydrogenated rapeseed oil – up to 100 g.

The material for the study was blood, obtained from the vena cava cranialis before and after treatment. Serum samples were tested for total protein (TP), albumin (Alb), urea (Urea), creatinine (Crea), glucose (Glu), total bilirubin (TB); activity of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamaglutamiltranspeptidase (GGT). Biochemical blood tests were performed at the laboratory of animal internal diseases and clinical diagnostic at Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv using an automatic biochemical analyzer BS-120 (Shenzhen Mindray Bio-Medical Electronics Co., Ltd., China) with PZ Cormay S.A. (Poland) reagents.

Clinical status was checked 24 hours per day, throughout the research period by standard methods of veterinary medicine.

All manipulations with animals were carried out in accordance with the European Convention for the Protection of Vertebrate Animals, used for Experimental and Scientific Purposes (Strasbourg, 1986). The mathematical processing of the research results was worked out statistically using a program package Statistica 6.0 software (Stat Soft, Tulsa, USA). Differences between the mean values were considered statistically significant at $P < 0.05$ (ANOVA, taking into account the Bonferroni Correction).

Results

Before treatment, statistically significant differences between biochemical parameters of the blood serum in piglets of control and experimental groups with gastroenteritis were not established. However, in animals of these groups hypoproteinemia (100.0%), hypoalbuminemia (73.3%), hypoglycemia (63.3%), hypercreatininemia (40.0%), hyperbilirubinemia (60.0%), hyperenzymemia (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase – in 100.0% of piglets, and gamaglutamiltranspeptidase – in 93.3%) was established, and in 33.3% of animals decrease of serum urea content was established compared to parameters of clinically healthy piglets.

In animals with gastroenteritis the established hypoproteinemia is due to absorption violation of protein in the intestine and protein synthesis dysfunction of the liver. After treatment, the total protein content in serum of weaned piglets in the control group was increased by 11.4% ($P < 0.01$, Fig. 1). In the first and second experimental groups, this parameter was ($P < 0.001$) increased by 12.6% and 16.4%, compared to animals before treatment, and was also significantly higher by 5.6% ($P < 0.05$) and 8.6% ($P < 0.01$) compared to control group after treatment.

A similar tendency was established with the serum albumin content of the control and experimental groups of piglets, which was significantly increased by 20.9% ($P < 0.01$), 24.7% ($P < 0.01$) and 32.0% ($P < 0.001$) compared to parameters before treatment. This parameter was significantly higher in piglets of the experimental groups by 12.6% ($P < 0.05$) and 17.3% ($P < 0.01$) compared to the control group (Fig. 2).

It is important to note that after treatment the serum albumins content in piglets of the first and total protein content and albumins in piglets of the second experimental group reached the parameters of clinically healthy animals. An increase of total protein content and albumins in the blood serum indicates the normalization of protein intestinal absorption. In addition, albumins are synthesized in hepatocytes, so the use of probiotics and phytobiotics had positive effect on formation of liver protein synthesis function. The reduction of serum urea content is due to alimentary depletion of animals and involvement of liver and kidneys in the pathological process. After treatment, the serum urea content increased in piglets of the control group by 12.9% ($P < 0.05$), by 19.4% ($P < 0.01$) and 24.1% ($P < 0.001$) in the first and second experimental groups compared to before treatment and reached the parameters of clinically healthy animals (Fig. 2). An increase of serum urea content in piglets is characterized by increase in intensity of protein metabolism.

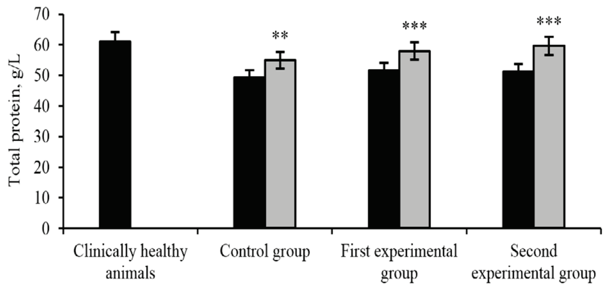

Fig. 1. Influence of different treatment regimens on total protein content in the blood serum of weaned piglets with gastroenteritis: black – before treatment, grey – after treatment (g/L, x ± SE, n = 10)

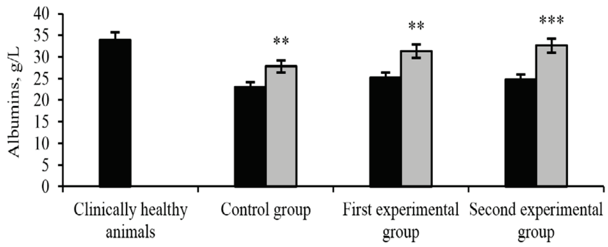

Fig. 2. Influence of different treatment regimens on albumin content in the blood serum of weaned piglets with gastroenteritis: black – before treatment, grey – after treatment (g/L, x ± SE, n = 10)

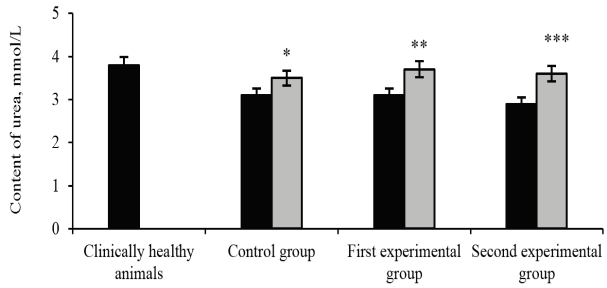

Fig. 3. Influence of different treatment regimens on urea content in the blood serum of weaned piglets with gastroenteritis: black – before treatment, grey – after treatment (mmol/L, x ± SE, n = 10)

A slight hypercreatininemia in piglets of the control and first experimental groups was due to the development of inflammatory and dystrophic processes in the kidneys. After treatment, the serum creatinine content in piglets of control and the first experimental groups reached the level of the clinically healthy animals' parameter (Fig. 4). However, this parameter significantly ($P < 0.05$) decreased by 7.3% in piglets of the first experimental group.

Hypoglycemia may indicate increased use of glucose for energy supply (increased use of fatty acids in energy metabolism) in the presence of typical symptoms of gastroenteritis (starvation, exhaustion, diarrhea). It was established that after treatment, the serum glucose content in weaned piglets of the control and experimental groups significantly increased by 40.6% ($P < 0.001$), 44.1% ($P < 0.001$) and 44.4% ($P < 0.001$) compared to parameters before treatment (Fig. 5). This parameter was significantly higher by 15.6% ($P < 0.05$) in piglets of the second experimental group compared to the control group and reached the level of clinically healthy animals. Consequently, the use of phytobiotics for animals positively influenced the process of gluconeogenesis in their body.

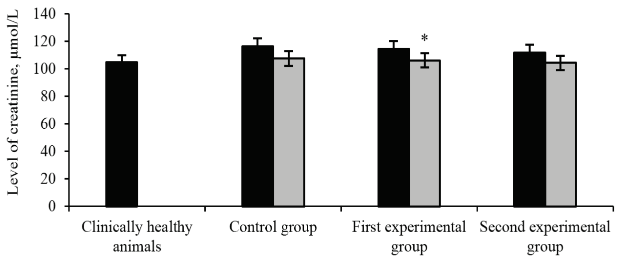

Fig. 4. Influence of different treatment regimens on creatinine content in the blood serum of weaned piglets with gastroenteritis: black – before treatment, grey – after treatment (µmol/L, x ± SE, n = 10)

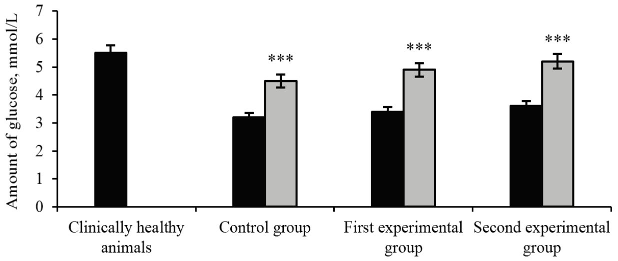

Fig. 5. Influence of different treatment regimens on glucose content in the blood serum of weaned piglets with gastroenteritis: black – before treatment, grey – after treatment (mmol/L, x ± SE, n = 10)

Hyperbilirubinemia may indicate a violation of the pigment-forming function of liver and development of hepatic cholestasis. In the piglets of the control group after the treatment, the serum total bilirubin content was significantly (P < 0.01) decreased by 19.4%. In the first and second experimental groups this parameter decreased by 21.1 (P < 0.001) and 22.1% (P < 0.01) compared to before treatment and reached the level of the clinically healthy animals. Also, the serum total bilirubin content was significantly lower in piglets of the second experimental group by 8.6% (P < 0.05) compared to the control group after treatment (Fig. 6). Normalizing of total bilirubin content may indicate a positive effect on the pigment-forming function of the liver.

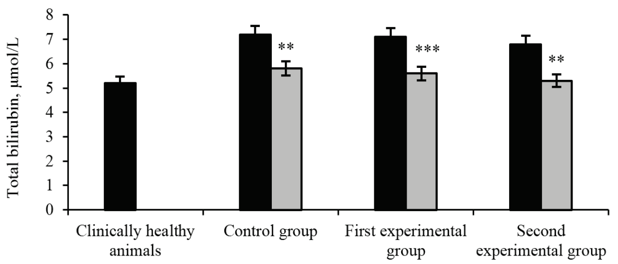

Fig. 6. Influence of different treatment regimens on total bilirubin content in the blood serum of weaned piglets with gastroenteritis: black – before treatment, grey – after treatment (µmol/L, x ± SE, n = 10)

Hyperenzymemia of aspartate aminotransferase and alanine aminotransferase in piglets with gastroenteritis before treatment is due to the development of hepatocyte cytolysis. It was established that after treatment, the activity of alanine aminotransferase in the blood serum of the control group weaned piglets was significantly (P < 0.001) decreased by 20.8%. In the first and second experimental groups, its activity was (P < 0.001) decreased by 28.9% and 35.8%, compared to the parameter before treatment, and reached the level of clinically healthy piglets. Also, this parameter was significantly lower in piglets of the second experimental group by 14.0% (P < 0.05) compared to the control group after treatment (Fig. 7).

A similar trend was established with activity of aspartate aminotransferase in the blood serum of the control piglets, which was (P < 0.001) decreased by 22.3% (Fig. 8). In piglets of the first and second experimental groups, its activity was (P < 0.001) decreased by 26.9% and 31.3%, compared to before treatment, and by 11.7% (P < 0.05) and 13.9% (P < 0.05) compared to the control group after treatment and reached the level of clinically healthy animals. The use of probiotics and phytobiotics contributed to a decrease in activity of alanine aminotransferase and aspartate aminotransferase in the blood serum of experimental piglets, indicating the stabilization of cellular structures of hepatocytes, in particular, mitochondrial and cytosolic.

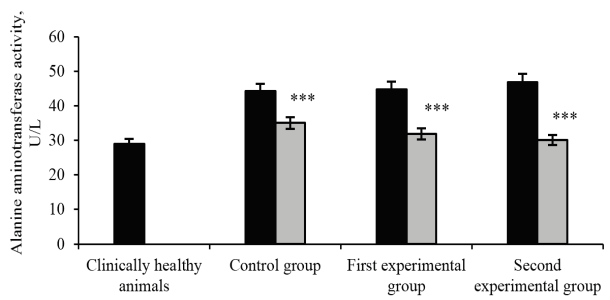

Fig. 7. Influence of different treatment regimens on alanine aminotransferase activity in the blood serum of weaned piglets with gastroenteritis: black – before treatment, grey – after treatment (U/L, x ± SE, n = 10)

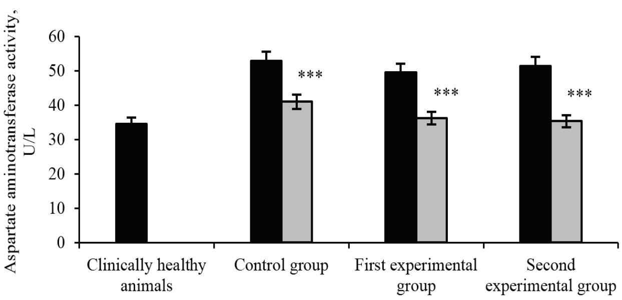

Fig. 8. Influence of different treatment regimens on aspartate aminotransferase activity in the blood serum of weaned piglets with gastroenteritis: black – before treatment, grey – after treatment (U/L, x ± SE, n = 10)

Increased activity of alkaline phosphatase in blood serum before treatment may indicate the development of intestinal diseases and intrahepatic biliary tract damage. After treatment, alkaline phosphatase activity was (P < 0.001) decreased by 30.7% in the control, 32.7% in the first and 36.9% in the second experimental group compared to piglets before treatment (Fig. 9). In animals of the second experimental group, alkaline phosphatase activity was significantly lower by 6.5% (P < 0.05) compared to the control group and reached the level of clinically healthy piglets.

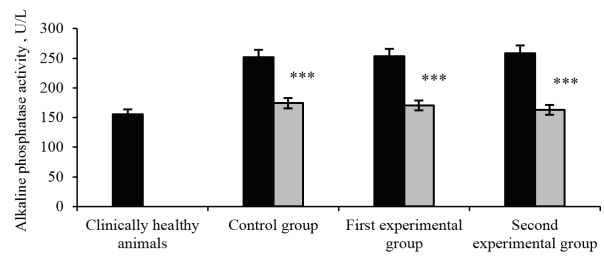

Fig. 9. Influence of different treatment regimens on alkaline phosphatese activity in the blood serum of weaned piglets with gastroenteritis, black – before treatment, grey – after treatment (U/L, x ± SE, n = 10)

Increased activity of gamaglutamiltranspeptidase activity in piglets with gastroenteritis can be explained by the development of intrahepatic cholestasis. It was established that after treatment, the gamaglutamiltranspeptidase activity in the blood serum of the control group weaned piglets was significantly lowered by 19.9% (Fig. 10).

In the first and second experimental groups, its activity was significantly lowered by 25.0 (P < 0.01) and 30.0% (P < 0.001), compared to before treatment rates and reached the level of clinically healthy piglets. Also, this parameter was significantly lower in piglets of the second experimental group by 17.0% (P < 0.05) compared to the control group after treatment. Thus, the use of probiotics and phytobiotics had a positive effect on the functional capacity of the liver and biliary tract, as indicated by the decrease in blood serum gamaglutamiltranspeptidase and alkaline phosphatase activity to the level of clinically healthy animals.

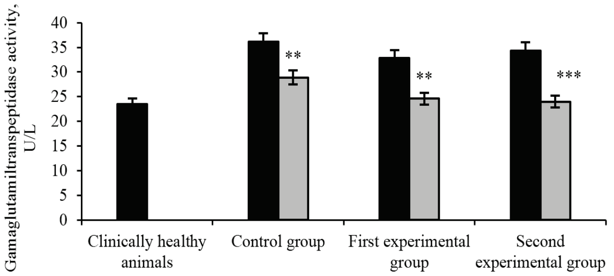

Fig. 10. Influence of different treatment regimens on gamaglutamiltranspeptidase activity in the blood serum of weaned piglets with gastroenteritis: black – before treatment, grey – after treatment (U/L, x ± SE, n = 10)

Discussion

Prevention of non-contagious diseases, in particular gastroenteritis, is a priority task of veterinary medicine specialists. This is possible with the use of effective and safe means with natural biologically active substances for preventing and treating animal diseases, that normalize the digestive processes in the body, as well as effectively correcting the qualitative composition of microflora of the digestive canal (Vondruskova et al., 2010; Slivinska & Lukashchuk, 2018; Kulyaba et al., 2019; Sobolev et al., 2019; Shcherbatyy et al., 2019). Because, the macro-organism, together with its microflora, is a united ecosystem that has been formed since birth, it is in a state of dynamic equilibrium and is a natural defense mechanism against pathological effects (Metzler et al., 2005). Ecological disbalance in the habitat of animals and equilibrium within bacterial intestinal associations, leads to decrease in colonization resistance (primarily the genera *Bifidobacterium* and *Lactobacillus*). As a result, it increases the number and spectrum of potentially pathogenic microorganisms, translocation or their toxins through the intestinal wall, leading to gastrointestinal diseases. Their development in farm animals in the first 2–3 weeks of life is not so much associated with elimination of *Bifidobacterium* and *Lactobacillus* genera as with peculiarities of intestinal normobiosis (Boyko et al., 2016; Chen et al., 2018; Kozak & Brygadyrenko, 2018; Han et al., 2019).

As noted by (Jacela et al., 2010; Ahmed et al., 2014; Fedak et al., 2018; Czech et al., 2018), most probiotics are based on different strains of lactic and bifidobacteria. Depending on the antagonistic properties of pathogenic and conditionally pathogenic microflora, appropriate strains are selected for composition of probiotic preparations. There are several types of probiotics: one-component preparations (containing one strain of bifidobacteria, lactobacilli, etc.); self-eliminating antagonists (consisting of spore bacilli and yeast fungi); combination preparations (containing several strains of bacteria); recombinant or genetically engineered probiotics (created on the basis of genetically engineered strains of microorganisms, their structural components and metabolites).

In highlighting the positive role of probiotics, it should be noted that the gastrointestinal diseases of piglets are systemic and polyetiological. Therefore, their use in various combinations with other antimicrobial agents is possible only when understanding the mechanism of their action and predicting the desired preventive effect.

Efficiency of beneficial bacterium *Bacillus cereus* var. *toyoi* spores isolated from the soil as an active substance of some probiotics is confirmed by studies of other researchers (Jadamus et al., 2000; Lodemann et al., 2008). Toyoi-spores quickly pass through the stomach and activate growth of *Lactobacillus* genus bacteria and other beneficial bacteria in the lower sections of the digestive canal. They support healthy gut microbiota by replacing pathogenic and conditionally pathogenic microorganisms, and together with the gut microbiota normalize the general condition of animals. In addition, *B. cereus* var. *toyoi* playan important role in the gut, causing an improvement in wall density and increase in intestinal space. It reduces the loss of water in the digestive canal, achieves high absorption capacity of glucose and dipeptides.

Also, an effective alternative to traditional methods for prevention and treatment of gastrointestinal diseases is use of drugs containing natural biologically active substances (Kommera et al., 2006; Lukashchuk & Slivinska, 2015; Kiczorowska et al., 2017; Boyko et al., 2018; Slivinska et al., 2019). The composition of phytobiotics may vary depending on climatic conditions and soils of plant cultivation, their species, harvest time, degree of maturity, constituents, etc. Phytobiotics are described by primary and secondary plant components. Primary constituents are the main nutrients (for example, protein, fat, etc.), while the secondary constituents are essential (esterified) and volatile oils, phenolic substances, colour pigments. Since phytobiotics do not provide a significant additive to the main nutrients of feed, the main interest is secondary components that can exhibit a wide range of biological effects. Natural herbal compounds cause a slow biological effect, which is not accompanied by abrupt changes in homeostasis and the side effects typical of most pharmacological medicines. The biological activity of herbal remedies is closely related to their chemical composition. However, a common feature of phytodrugs is that they are a complex mixture of many bioactive components.

According to the data of scientists (Neil et al., 2006; Michiels et al., 2010), the positive effect of feeding oregano extracts (corvacrol) on fermentation processes with the formation of volatile fatty acids (VFAs) at a certain ratio of them was established. Oregano extract promotes the activation of butyric acid synthesis, which leads to inhibition of pathogenic microflora and stimulation of lactobacilli. The additional synthesis of butyrate changes the ratio of individual groups of gastrointestinal canal bacteria. Butyrate directly inhibits the development of pathogenic bacteria (salmonella, clostridia and *Escherichia coli*). On the other hand, the effect of butyric acid on enhancing the growth of lactobacilli – antagonists of pathogenic microflora, creates the additional effect of normalizing the microbial status of the gastrointestinal canal. Consequently, corvacrol can be considered as a typical natural stabilizer of lactobacilli growth and factor in inhibiting the development of pathogenic microflora in pigs.

One of the most effective among phytobiotics is extract of Mexican pepper (capsaicin), which stimulates the production of its own enzymes in animals' bodies (Frankic et al., 2010; Vondruskova et al., 2010). Capsaicin acts by directing, enhancing the activity and production of most important digestive enzymes of the pancreas and duodenum. It was established that in parallel with the increase of main enzymes activity, capsaicin increases the activity of parietal digestion enzymes, which makes the digestion process as efficient as possible. This extract begins to show its activity in the oral cavity, significantly increasing salivation. That is, capsaicin acts as natural stimulant of enzymatic activity of the gastrointestinal canal and can significantly compete with use of exoenzyme medicines, widely used in recent years in pig production.

According to the literature (Frankic et al., 2010; Gheisar & Kim, 2018), cinnamon extract (cinnamaldehyde) promotes an increase in the amount of absorbable nutrients by activating the action of mucosal antioxidant enzymes: superoxide dismutase, catalase, glutathione S-transferase. Dysmutase and glutathione transferase activate parietal digestion and facilitate the uptake of cleaved metabolites into the bloodstream. Catalase in the absorption zone acts as a factor in the utilization (cleavage) of peroxides that accumulate on the marginal epithelium of the mucous crypt (Gutyj et al., 2017b). Through active work of catalase, mucous membranes are cleansed of non-absorbable metabolic products and the intensity and volume of absorption are increased. In general, it can be said that cinnamaldehyde acts as an effective factor in preventing feed malabsorption in animals. Together with the effect of antioxidant enzymes stimulation, cinnamaldehyde in physiologically justified norms gently lowers the pH of small intestine, which stimulates the development of beneficial microflora. Due to this, it synergistically interacts with carvacrol, enhancing the effect of stimulating the growth of lactic acid bacteria at the expense of pathogenic microflora.

Therefore, the analysis of the literature sources indicates the urgency of development and use, as well as the further study of effective and safe veterinary medicines, in particular pro- and phytobiotics, which can replace existing imperfect means of preventing and treating diseases of the gastrointestinal tract in pigs.

Conclusions

In piglets with gastroenteritis, there are violations of the processes of absorption of protein in the intestine, protein synthesis and pigment-forming functions of the liver and development of dystrophic processes in hepatocytes with the appearance of hepatic cholestasis.

The use of probiotic Toyocerin 10^9 with antibiotic in the treatment of weaned piglets (first experimental group) had a positive impact on protein synthesis and pigment-forming liver functions, as indicated by the decrease of albumins, total bilirubin and an increase of serum urea; decrease of enzymes' activity. These parameters reached the level of clinically healthy animals.

It was established that use of phytobiotic Extract™ 6930 with antibiotic in treatment of weaned piglets (second experimental group) positively influenced: protein synthesis, carbohydrate and pigment-forming liver functions, as well as on functionality of the kidneys, indicating a decrease of total protein, albumins, total bilirubin, increase of serum urea and glucose; decrease of enzymes' activity. These parameters reached the level of clinically healthy animals.

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