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## Biochemical Indicators Of Physiological Systems Of Animals At Using The Tylosin Compounds.

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### ABSTRACT

To study the physiological and biochemical changes in the body of farm animals under the influence of technological stress factors (transportation and rearrangement) to stress and after 1, 10, 15, 30, 35 and 60 days blood was taken from the blood vessels of animals, in which the content of red blood cells and leukocytes, hemoglobin, hematocrit, ESR, leukogram, activity: bactericidal, complementary, lysozyme, phagocytic activity of leukocytes, phagocytic index and phagocytic number, total protein content, serum protein fractions, quantitative determination of classes of immunoglobulins, the content of total immunoglobulins were investigated. Tylosin compounds (tylosin tartrate, phosphate, highly active fradizin-50 polytilosincaroxylate) have a stimulating effect on the basic physiological functions of digestion in the dose of 5 mg/kg of body weight; they increase within the physiological boundaries of the secretion of the stomach and intestines. Tylosin-containing compounds have the ability to increase the blood content of red blood cells, hemoglobin, total protein and albumin, bactericidal and lysozyme activity. Tylosin compounds contribute to the acceleration of the use of microbiological protein (experiments on the growth-stimulating effect) and thereby increase the energy of growth of animals by 5-10%. When using tylosin compounds in doses, multiplicities and terms three times higher than recommended, there are no signs of their toxic effect on the main physiological systems of the animal body: cardiovascular (electrophysiological activity of the heart muscle), digestive, urinary (biochemical tests in urine and feces). The study of the biochemical composition of the muscles and organs of animals killed by the use of tylosin compounds found that on the content of protein, fat, minerals, the amount of amino acids and quality tests for freshness they were more biologically valuable than in intact animals.

**Keywords:** tylosin compounds, birds, rats, calves, piglets, lambs, gastric and intestinal juice.

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## INTRODUCTION

The basis for the successful development of animal husbandry is the productive health of animals. At the same time, industrial farming methods are inevitably accompanied by stresses of different origin. In addition, the habitat of animals on large farms and complexes is characterized by their high concentration in small areas, the circle-logical stall content, sometimes with complete isolation from the environment, which does not always meet the biological needs of the body. Natural properties of farm animals, formed over many centuries, can not change quickly. In this regard, often there are inconsistencies between the biological nature of the body, its physiological capabilities and the environment in the form of various stresses that can significantly reduce their natural resistance and productivity, and sometimes cause death, especially of young animals.

Numerous studies of domestic and foreign authors are aimed at solving the problem of the relationship between the body of farm animals and the environment in large complexes for the production of milk and meat.

These circumstances necessitate the use of various means, cyclicity and rotation in their application, the development of new schemes of treatment of animals, increasing their general nonspecific resistance.

In the scientific literature, there are data indicating the possibility of increasing the natural resistance and reducing the stress load on the animal organism through the targeted use of some pharmacological drugs-adaptogens, especially of natural origin [1-9]. At the same time, the theoretical basis of the mechanism of their action on the body of young farm animals at low and high temperatures of the environment has not been sufficiently studied; there are few recommendations on the use of other biological and chemical substances as adaptogens.

Therefore, further study of various compounds and their degree of influence on the indicators of general nonspecific resistance is an urgent problem.

Promising for further development in this direction are the tylosin compounds.

Tylosin is produced in the form of three salts: tartaric (tartrate), phosphorus (phosphate) and adipine (adipinate). Structural formula of its salts have the general structure: 16-calanolide membered ring, and each, besides, has in its composition a high-energy sugar mycinose, mycaminose and mycarose.

In addition, there is prolonged modification of tylosin – polytilosincarboxylate and technical - different activity types of fradizins (0.5; 1; 2 and 4(5)%).

Fradizin, is a tylosin-containing compound, and in addition to the active substance - tylosin, contains phospholipid fractions, essential amino acids (except tryptophan), as well as aspartic and glutamic acids, serine, glycine, alanine, tyrosine, protein, sugar, phosphorus, calcium, iron, zinc, copper, cobalt, vitamin B2, nicotine, folic and fatty acids, wax, mono-, di - and triglycerides capable of having an etiotropic, pathogenetic and substitutive effect.

Based on this, we have planned and conducted studies on the effect of various compounds of tylosin on the main physiological and biochemical parameters of the organism of farm animals, including determining its general nonspecific resistance.

The purpose of these studies was: monitoring of physiological and biochemical changes in the body of farm animals at using tylosin compounds, the definition of the main indicators of general nonspecific resistance in the application of prolonged and technical forms and the study of their safety at different biological levels: biochemical, histomorphological, physiological.

To achieve this goal, it was necessary to solve the following tasks: - to study the hematological parameters of animals under technological stresses and the use of tylosin compounds;

- to determine the main functions of physiological systems under the influence of tylosin compounds;

- to give a physiological and biochemical justification for the safety of the use of tylosin compounds in animal husbandry.

### CONDITIONS, MATERIALS AND METHODS

To study the physiological and biochemical changes in the body of farm animals under the influence of technological stress factors (transportation and rearrangement) to stress and after 1, 10, 15, 30, 35 and 60 days from the blood vessels of animals the blood was taken, in which the content of red blood cells and leukocytes on the Coulter Kaunter counter of particles (France), hemoglobin- with hemometer Sali and hemoglobin-cyanide method, hematocrit on spiral centrifuge MPV - 310 (Poland), ESR-by Panchenkov, leukogram – by the method of counting 200 cells, stained by Romanovsky-Gimza, with calculation the percentage of each species, the bactericidal activity of blood serum by the method of O.V. Smirnova and T.A. Kuzmina (1966), complementary activity – by O.V. Bukharin, N.V. Vasilyev (1974), lysozyme activity on K.A. Kagramanova and Z.V. Ermolyeva (1966), phagocytic activity of leucocytes, phagocytic index and phagocytic number – on V.S. Gostev (S.I. Plyaschenko, V.G. Sidorov, 1979), the total protein content - refractometrically, protein fractions of blood serum - by the method of All and McCord in the Karpyuk modification (1962), quantitative determination of classes of immunoglobulins by the radial reaction of Mancini precipitation (1983), the content of total immunoglobulins - by A.D. Mak Yuan and co-authors (1970).

Evaluating the safety of tylosin compounds was carried out in accordance with GFC on white outbred rats with an average body weight of 160-250 g. Tested drugs were injected in doses and timing, in three times exceeding therapeutic ones.

The complex of physiological-biochemical and pharmaco-toxicological studies included the definition of chronic toxicity, teratogenic, embryotoxic (A.P. Shitskov a et al., A.M. Makashenko et al., 1967), allergenic (O.L. Alekseeva et al., 1978) and irritant action (G.P. Trubetskaya, 1976).

In the beginning, middle and end of the experiment in blood and serum the above morphological and immunobiochemical indicators of carbohydrate, lipid, mineral and protein metabolism were determined by: glucose - enzymatic method, total lipids - sulfurospirillum reagent, a urea by reaction with diacetylmonooxime, beta-lipoproteins - turbidimetrically method, cholesterol - according to Ilk, amino acids and other biologically active compounds: hydroxyproline, serine, threonine, beta-aminoizobutylic acid, arginine, tryptophan, 3-methylhistidine, histidine, 1-methylhistidine, lysine, ornithine, alanine, phenylalanine – on automatic amino acid analyzer AAA-339 (France). The activity of alkaline phosphatase was determined by the hydrolysis of beta-glycerophosphate (on Boansky), and alanin aminotransferase and aspartate aminotransferase on Raytman and Frenkel (1957) using kits of company “Lachema”.

The studies were aimed at studying changes in physiological and biochemical parameters under the action of tylosin compounds on model animals (birds, laboratory animals (rats), calves) and the main animals (pigs and lambs) in the structure of this work. In studying the effect of tylosin compounds on the secretory function of the digestive system of pigs the animals with fistulas of the stomach and the small intestine (duodenum) were used. The experiment used 15 pigs of three months of age divided into three equal groups. Animals of the first group received radisin, the second – formazin and the third one served as a control.

The drugs were tested in doses of 1.5, 2.5 and 5 mg (by AS - tylosin) per 1 kg of weight – with a single and multiple (five-fold) prescription.

Gastric and intestinal juice was collected an hour after giving a trial breakfast (barley porridge), which, depending on the experiment, was prescribed with or without the tested drugs. In the collected gastric juice, the pH, digesting activity, the content of free, bound and total hydrochloric acid, and in the intestinal juice, the pH, the content of trypsin and amylase were investigated by conventional methods. These background indicators of all animals before giving the drug served as a control. In addition, they were examined and before each prescription of the drug (before 1 hour).

The resulting digital material was subjected to mathematical processing using the methods of mathematical statistics, adopted in biology and medicine (E.K. Merkurjev, 1964; G.F. Lakin, 1973; E.V. Gulber, 1978) and Microsoft Excel 97 application software package.

## RESULTS AND DISCUSSION

Single prescription of fradizin and formazin at a dose of 20 mg/kg on AS – tylosin - 1 hour after their injection slowed gastric secretion and stimulated intestinal one. After 24 hours, gastric secretion increased and continued to increase further. In the secretion of the small intestine, the reverse pattern was observed. Its normalization occurred for 3 days.

The dose of 25 mg / kg had a similar effect, which was characterized first by some inhibition of gastric secretion and excitation of the intestinal, and then the reverse phenomena. At a dose of 10 mg/kg stimulation of gastrointestinal secretion occurred immediately after its prescription and lasted for 24-48 hours, followed by normalization. With repeated use of compounds in a dose of 20 mg / kg inhibition of secretory activity and gastric digestion was noted during the entire period of drug prescription. In this case, the pH of the gastric juice shifted to the acidic side. its recovery occurred after 3 to 4 days after the last injection. Changes in the enzymatic activity of the small intestine were characterized by stimulation at the beginning of the experiment and weak oppression at the end. Five-time appointment of tylosin compounds at a dose of 5 and 10 mg / kg steadily increased the secretion of hydrochloric acid and total acidity, as well as the secretion of trypsin and amylase by the intestine, the pH of the latter shifted to the alkaline side. The restoration occurred in 3 to 4 days.

Studies of the motor function of the gastrointestinal tract found that tylosin in a concentration of 0.005 µg / ml increases the functional activity of the intestines, which is expressed in the increase in rhythm and lengthening the amplitude of contractions. Increasing the concentration to 50, 100, 400 and 800 µg/ ml slightly inhibited the work of isolated intestines, and its inhibition remained within 10-20 %. This action in some cases alternated with a temporary increase in their activity, which was expressed by an increase in the amplitude of oscillations or an increase in their rhythm. In the concentration of 1000 µg/ml, the motor activity of the intestine was also suppressed, although its complete suppression did not occur. Lavage of the intestines, as a rule, restored their work.

Thus, the tylosin compounds weakly inhibit the work of segments of isolated intestines of animals, mainly reversibly slow down the rhythm of their contractions, which is restored after the termination of the use of tylosin. This property of tylosin-containing compounds is important in the treatment of gastrointestinal diseases.

Based on the foregoing, we can conclude that fradizin and formazin in small doses increase the secretion of hydrochloric acid and reduces the secretion of pepsin. In large doses, they inhibit stomach function.

Influence of fradizin and farmazin on basic metabolic processes in the liver were studied in 18 piglets with a body weight of 22-23 kg, which were divided into 3 groups. Animals of the first group (control) received normal diet, the second and third groups for 30 days - in addition, fradizin and farmazin at a dose of 10 mg/kg (for AS components). Before and on 15<sup>th</sup> day of the experiment, studies were carried out, the results of which indicate a negative reaction to bilirubin, the absence of protein structure disorders (Weltman coagulation test) and the presence of coarse globulins in the serum. Quantitative content of bilirubin, catalytic activity of ALAT and ASAT enzymes (Frenkel and Reitman method) in piglets of control and experimental groups also did not differ significantly. This indicates that the studied drugs in the prescription of therapeutic doses do not have a negative effect on liver function: protein-synthesizing, pigment - and enzyme-forming, i.e drugs do not have a toxic effect on this body.

Thus, the results of studies of the digestive system, as well as qualitative reactions to the state of protein and pigment metabolism, confirmed by quantitative research methods, indicate the absence of toxic effects of tylosin compounds on the digestive organs and liver.

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The functional state of the kidneys under the influence of the tylosin compounds were evaluated by clinical tests and physico-chemical parameters of the urine of pigs and calves receiving mfradizin and farmazin. Urine was collected on the 1st, 15th and 30th days of the experiment.

It is established that urination acts in piglets and calves of all experimental and control (intact) groups were regular, arbitrary, painless, in a natural position. Phenomena of urinary symptoms, changes in the quantity and quality of the acts of urination, stranguria, pyuria (sample with KOH), hematuria (hemoglobin - sample Adler-Call) and erythrocyturia (attentivepersonal microscopy of sediment), and proteinuria (test with boiling, Geller, Roche and William), carbohydrates (samples Benedict, Roberts, Gaines and Nylander), indican (sample of Obeymayer and Jaffa), urobilinogen (sample Florence), urobilin (the method of Bogomolov), acetone bodies (definition by means of reagents Lange, Libena, Ross, Lestrade and Rothera), bile pigments (samples with potassium permanganate, Frank, Rosin, Kapralov) and bile acids (method Hai-Kraft) are not registered at animals. At auscultation at the site of the optimum point of the aorta of animals (4th intercostal cows, sheep and 3rd in pigs at the level of the shoulder joint), the accent and pathological sound phenomena indicating the presence of cardiovascular syndrome of kidney damage were not registered. Components of the uremic syndrome of intoxication: apathy of animals, hyporeflexia in the most labile superficial reflexes of the skin and mucous membranes are not marked. When provoking pain in the kidneys (3-4 lumbar vertebrae), no positive reaction was revealed. Urine is light-yellow, transparent (without any admixture of mucus and blood), watery consistency, peculiar smell, with hydrogen ion concentrations from 6.5 to 7.8 in piglets and 7.0 to 8.3 in calves.

Consequently, tylosin compounds do not adversely affect the functions of the urinary system and the physico-chemical properties of urine.

Our blood studies revealed the hematopoietic effect of tylosin-containing compounds and their ability to increase cellular and humoral resistance of piglets and lambs: their use was accompanied by an increase in the content of erythrocytes and hemoglobin, total protein, albumins, beta-and gamma globulin protein fractions.

Besides the fact that tylosin compounds due to their composition, including sugar (miconose, mycinose and mycaminose-tylosin and polytylosincarboxylate), most amino acids, phospholipids, vitamins, macro- and trace elements-fracdizin-40 (50), have a stimulating general nonspecific resistance of the body action, which was shown by the above experiments, we planned and conducted further research on the study of another mechanism of potentiation of nonspecific immunity, namely, the positive effect of these compounds on the basic functions of digestion, which are the main source of plastic substances and trophic function for all physiological systems of the body of farm animals, and hence its protective properties.

Form and peroxidase samples and reaction with copper sulphate, investigation of chemical composition of eggs and muscle tissue of laboratory animals (rats), hens and chickens, as well as the determination of the remaining amounts of the active substance in the tissues and organs of farm animals, for a long time receiving high doses of tylosin compounds, it was found that the meat and organs of such animals are nutritionally complete and suitable for consumption.

It is shown that under the action of tylosin-containing compounds in the muscles of laboratory and model animals (farm birds) protein content due to lysine, methionine and threonine increased.

### CONCLUSIONS

Thus, the use of tylosin-containing compounds does not cause changes in the biochemical composition of animal muscles and its qualitative composition.

The results of these studies lead to the conclusion that the various tylosin compounds (tylosin tartrate, its technical form – a highly active fradizin-50 and prolonged – polytylosincarboxylate) have properties that can improve the basic parameters of cellular and humoral resistance of farm animals and birds.



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