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Original Research Article

BIOCHEMICAL AND CHEMICAL PARAMETERS CHANGES IN THE BLOOD OF CHICKENS FOLLOWING TREATMENTS WITH MADURAMYCIN, MONENSIN AND DICLAZURIL

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Abstract: The aim of this study was to monitor the biochemical and chemical parameters of the blood of commercial chickens following treatment with one of three coccidiostats: maduramycin, monensin or diclazuril. Chickens received feed treated with maduramycin at concentrations of 5, 10 and 15 mg kg^{-1}, monensin at 125, 225 and 325 mg kg^{-1} or diclazuril at 1, 5 and 10 mg kg^{-1}. A control group of chickens consumed feed without the addition of coccidiostats. Following treatment, blood was sampled for 11 days and analysed for the following biochemical and chemical parameters: aspartate aminotransferase (AST), bile acid (BA), creatine kinase (CK), uric acid (UA), glucose (GLU), cholic acid (CA), total protein (TP), albumin (ALB), globulin (GLOB) and phosphorus (PHOS). Administration of different concentrations of maduramycin, monensin and diclazuril did not affect the concentration of the parameters AST, UA, GLU, BA, TP, ALB, GLOB and PHOS in experimental groups of broilers in relation to the control group. However, significant differences were observed in the concentrations of CK and CA between the experimental and control groups. Significant differences were also found in the concentrations of AST, CA and UA between experimental groups.

Key words: maduramycin; monensin; diclazuril; chickens; biochemical and chemical parameters

Introduction

Coccidiosis in chickens, caused by *coccidia* protozoan parasites, is one of the most significant issues in poultry production today. Nine species of *Eimeria spp*. have been described in chickens: *E. acervulina, E. brunetti, E. maxima, E. mitis, E. mívat, E. necatrix, E. praecox, E. tenella* and *E. hagani* (1). The disease often affects birds between 3 and 8 weeks of age. Previously, coccidiosis was treated with chemotherapy upon observation of the initial symptoms, though this was soon ceased as the treatment was found to cause more harm than good. Therefore, for virtually all poultry broilers, preventive treatment is applied by adding a coccidiostat in feed to control the growth of *coccidia* in the intestinal tract (2).

Coccidiostats can be classified into two main groups: ionophores and synthetic products that are non-natural ionophores (3). Polyether ionophores represent a large group of natural and biologically active substances. Several polyether ionophores are widely used as growth promoters in the veterinary field, and exhibit antibacterial, antifungal, antiparasitic, antiviral, and cytotoxic activity. It was recently proven that some of these substances can kill tumour cells and have been

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identified as potential new anticancer drugs. The biological activity of ionophores is strictly connected with their molecular structure (4). In general, ionophores are defined as lipophilic chelating agents that transport cations across cell membranes, including the plasma membrane cell and subcellular structures. Genuine ionophores are highly selective for specific cations and can be monovalent (monensin, narasin, salinomycin, maduramycin and semduramycin) or divalent (lasalocid) (5). Unlike antibiotics, synthetic (chemical) ionophore coccidiostats have a completely different effect. Ionophores are focused on sporozoites and act on them before they enter the host cell, while chemical coccidiostats destroy them after they invade the host cell (6). In broilers, coccidiostats are used throughout the lifetime, while their use is prohibited for laying hens (7).

All substances from the ionophore group of coccidiostats show slight differences between the therapeutic and toxic doses. Some, such as salinomycin, narasin, maduramycin, and to a lesser extent monensin, can be toxic to animals. The scale of toxicity can be represented as follows: salinomycin < lasalocid < narasin < monensin < maduramycin (8). Maduramycin is an aminoglycoside polyether derived from the bacterium *Actinomadura rubra* (9). It occurs in two structural forms, α- and β-maduramycin, whereby α -maduramycin has a greater affinity for monovalent cations and is mainly used as an additive in animal feed or for therapeutic purposes (10). A study on chickens fed with maduramycin in a concentration of 5 and 10 mg kg^{-1} for 21 days found growth disorders among chickens (9). Clinical signs included watery diarrhoea, depression, inertia, and macrocytic anaemia (increased volume of red blood cells). Leukopenia or lymphopenia was observed in the group fed 10 mg kg^{-1} maduramycin after 21 days (9). Provisional maximum residue limits (MRLs) for maduramycin residues defined for tissues of chickens for fattening are (μg kg^{-1}): 150 in liver, skin and fat; 100 in kidney; 30 in muscle (11).

Monensin is an antibiotic product formed as a by-product of the fermentation of *Streptomyces cinnamonensis*. There are two forms A and B, which are produced in approximately equal amounts. Monensin A shows stronger biological activity against *Bacillus subtilis* than monensin B and is used as a coccidiostat. Oral administration of monensin leads to absorption, metabolism and excretion through bile, and elimination via faeces. The optimum (therapeutic) dose of monensin in chickens is 100–125 mg kg^{-1} and the lowest level at which the first toxic effects may occur in chickens is 121–150 mg kg^{-1} (12). MRLs for monensin residues in the chicken tissues are (μg kg^{-1}): 25 in skin and fat, 8 in liver, kidney and muscle (13).

Diclazuril is a derivative of benzeneacetonitrile, a broad spectrum synthetic compound against *E. acervulina, E. maxima, E. necatrix*, *E. brunetti* and *E. tenella*. It may be added to feed for the treatment of coccidiosis in broiler chickens and laying hens as of the age of 16 weeks in maximal authorised concentration of 1 mg/kg (14). Diclazuril has a very low acute toxicity and is not mutagenic, genotoxic, carcinogenic, embryotoxic, foetotoxic or teratogenic (5). MRLs for diclazuril in the chicken tissues are (μg/kg): 500 in muscle, skin and fat; 1 500 μg/kg in liver; 1 000 in kidney (15).

Chemical analysis of blood serum is used in the diagnosis and characterization of diseases, especially those diseases with poorly known pathogenesis, and to assess the general health of humans and animals (16, 17). However, due to the relatively low economic value of poultry animals, these techniques are used less often. Therefore, there are few studies reporting the concentrations of these parameters in the blood of healthy broilers or hens. The interpretation of laboratory results of these parameters is performed according to reference intervals and normal (reference) values set out for healthy animals of a given species (18). The reference values are dependent on various parameters, such as age, sex, species and natural diet, which greatly affect biochemical parameters (19).

There are few studies reporting the influence of coccidiostat application on changes in biochemical parameters, and these primarily use the therapeutic dose. The aim of this study was to examine the impact of the coccidiostats maduramycin, monensin and diclazuril at different concentrations in broiler chickens on the biochemical and chemical parameters of serum.

Material and methods

Experiment and blood sampling

The experimental chickens, a total of 315 healthy broiler chickens (*Gallus gallus*) of both sex

were purchased from commercial breeding age one day. They were housed in cages, supplied with water *ad libitum* and fed on a balanced ration free from any anticoccidial for 30 days. Chickens aged 30 days were divided into experimental groups. The control group consisted of 25 chickens and was not treated with coccidiostats. A total of 315 chickens were divided into 9 experimental groups of 35 animals each. Broiler groups Mad1, Mad2 and Mad3 received feed enriched with maduramycin in concentrations of 5, 10 and 15 mg kg^{-1}, respectively. The groups Mon1, Mon2 and Mon3 received feed with monensin at concentrations of 125, 225 and 325 mg kg^{-1}, respectively. The groups Dicl1, Dicl2 and Dicl3 received feed enriched with diclazuril at levels of 1, 5 and 10 mg kg^{-1}, respectively. All experimental groups received the treated feed for 21 days. The prescribed concentrations of coccidiostats for chickens are: 5 mg kg^{-1} for maduramycin (11), 60-125 mg kg^{-1} for monensin (13) and 1 mg kg^{-1} for diclazuril (14). Therefore, in the present design of the experiments the first experimental group of chickens received standard dose of coccidiostat while other 2 groups received overdose concentrations. Defined withdrawal periods before slaughter of chickens for fattening for three coccidiostats are: maduramycin at least 3 days (11); monensin 1 day (13); diclazuril 5 days (20).

After completion of the 21-day treatment period, on post-treatment days 1, 3, 5, 7, 9 and 11, three chickens in each group were sacrificed and their blood sampled. Serum was extracted by centrifugation at 3000 rpm for 10 min and then transferred to Eppendorf tubes and stored at -20°C until analysis.

The protocol of this study was approved by the Ministry of Agriculture of the Republic of Croatia.

Analysis of biochemical and chemical parameters

Biochemical and chemical parameters in the blood serum of chickens were determined using the biochemical analyser VetScan VS2 (ABAXIS, Union City, CA, USA). The following parameters were determined: aspartate aminotransferase (AST), creatinine kinase (CK), bile acid (BA), cholic acid (CA), uric acid (UA), total protein (TP), albumin (ALB), globulin (GLOB), glucose (GLU) and phosphorus (PHOS). The analyser performed photometric measurements on the principle of absorption of laser light. Measurement were performed using commercial rotors Avian/ Reptilian Profile Plus (ABAXIS, Union City, CA, USA), which contain all the necessary reagents. A total of 0.1 mL serum was pipetted and added to the rotor, which was then inserted into the analyser to automatically read the "rotor" default parameters.

Statistical analysis

Statistical analyses were performed using STATA® 13.1 (StataCorp LP®, USA). The concentrations of biochemical and chemical parameters were expressed as mean ± standard deviation (SD). The Shapiro-Wilk test was applied to determine the distribution of the data. One-way ANOVA test and the Kruskal-Wallis test were used to test differences in the concentrations of parameters between experimental groups. Differences were compared for statistical significance at the level $P < 0.05$ and $p < 0.01$.

Results and discussion

Enzymes AST and CK

Aspartate aminotransferase (AST) belongs to the class of enzymes present in the cytoplasm and mitochondria and various types of tissue, though high concentrations are primarily found in liver and muscles (21, 22). Creatine kinase (CK) is an enzyme that is also present in high concentrations in skeletal and cardiac muscle, smooth muscle and brain, and in smaller amounts in organs such as the intestine, liver and spleen. It is also found free in the cytoplasm of muscle cells. Four isoenzymes have been identified: brain, heart, muscle and mitochondrial isoforms. The enzymes AST and CK are used to assess injuries, as the post-injury muscle activity of AST increases at a significantly slower rate than that of CK. An increase in CK activity suggests an acute muscle injury, while increase in activity of both AST and CK indicates an active or current injury, while growth of only AST indicates muscle injury (22). These two enzymes are localized in the cytoplasm and are released during cell damage (23).

The concentrations of AST and CK in the experimental and control groups of chickens

are shown in Figure 1. Concentrations were determined in the ranges (U L^{-1}): control group AST 173–307 and CK 2023–6033; experimental groups AST 146.5–362.5 and CK 1502–6929. AST concentrations determined were in the range of the reference values 131–486 IU L^{-1} (24) and similar to previously presented values for healthy control group of broilers of 176.5 and 227.17 U L^{-1} (17, 25). However, CK values were significantly higher than defined normal plasma CK activity ranges for the most bird species from 100 to 500 IU/L (22). It has been concluded that increased plasma CK activity can result from muscle cell injury. Severe skeletal muscle injury often results in marked increases of the plasma CK activity and moderate increases of the plasma AST activity (22).

In this study AST concentrations in the experimental groups were not significantly different compared to the control group throughout the observation period. Also, there were no differences in AST and CK concentrations between the first experimental group chickens received so called standard dose (Mad1) and other 2 groups received overdose concentrations (Mad2 and 3). In the experiment with maduramycin, significantly lower concentrations were found in the group treated with a concentration of 10 mg k^{-1} (Mad2) than in the group treated with 15 mg kg^{-1} (Mad3) on post-treatment days 3 and 9 ($p<0.01$, both). Significant differences in CK concentrations were found between the Mad1 and Mad2 groups and control group on day 11 ($p<0.05$ and $p<0.001$).

A recent study using maduramycin in a concentration of 5 mg kg^{-1} determined increased activity of the enzyme AST (25). A similar study on broilers treated with maduramycin at a concentration of 5 to 8 mg kg^{-1} for 6 weeks found that animals treated with 8 mg kg^{-1} of maduramycin also had increased AST levels (26). On the other hand, the group treated with 5 mg kg^{-1} showed no significant changes in AST concentrations. Research conducted in cattle fed with hen litter with the addition of maduramycin in the concentration of 4.8 and 12 mg kg^{-1} showed elevated AST and CK levels (28). Increased AST activity in animals has been explained as the general degeneration of liver, muscle and soft tissue (25). In birds, increases of plasma AST activity are suggested when it is greater than 275 IU/L and is result from either hepatic or muscle injury. Markedly increased AST activity is considered when is above 800 IU/L (22).

In this study with monensin, AST concentrations showed variations between groups on days 7 and 9. On day 7, broilers treated with authorised monensin level of 125 mg kg^{-1} (Mon1) had significantly lower concentrations of AST (173 U L^{-1}) than those treated with 225 (Mon2) and 325 mg kg^{-1} (Mon3) of monensin (270 and 274 U L^{-1}, respectively) ($p<0.01$, both). Also, the Mon3 group had significantly lower CK levels than the control group on day 7 ($p<0.05$). However, the Mon2 and Mon3 groups showed significantly higher CK values than the control group on days 9 and 11 ($p<0.01$, all). Studies at higher doses to investigate the effects of monensin in chickens and turkeys showed increased activity of AST, indicating its undesirable effects in the body. Visibly increased activity of CK, and to a lesser extent of AST in serum indicated progressive structural muscle damage (27).

In the diclazuril experiments, on post-treatment day 9, first standard group received dose of diclazuril at level of 1 mg kg^{-1}, Dicl1 had a significantly lower AST concentration of 146.5 U L^{-1} than other two overdose groups Dicl3 and Dicl2, with values of 262.0 and 223.5 U L^{-1}, respectively ($p<0.01$, both). Significantly lower CK concentrations compared to the control group were found only for the Dicl1 group on post-treatment day 7 ($p<0.05$). However, significantly higher values were determined for group Dicl2 than the control group on days 9 and 11 ($p<0.01$, both).

Uric acid, bile acid, cholic acid and glucose

Bile acid (BA) is the group of water-soluble steroids produced during the catabolism of cholesterol, synthesized in hepatocytes in the liver. The products of primary bile acids are cholic acid (CA) and chenodeoxycholic acid (29). In healthy birds, bile acid is present in small amounts in the peripheral blood stream (22). Uric acid (UA) is the main end product of nitrogen metabolism in birds and is excreted via the faeces. It is relatively inert and substantially less toxic in comparison to ammonia and urea. Uric acid (the oxidized form of purine - hypoxanthine) is mainly synthesized in the liver by the metabolism of purine (21). The main metabolite of animal metabolism is glucose (GLU), which is the primary metabolic fuel and is stored as glycogen in the liver (1–5% of wet matter) and muscles (~1% of wet matter). It is also a major energy substrate used by the brain (30).

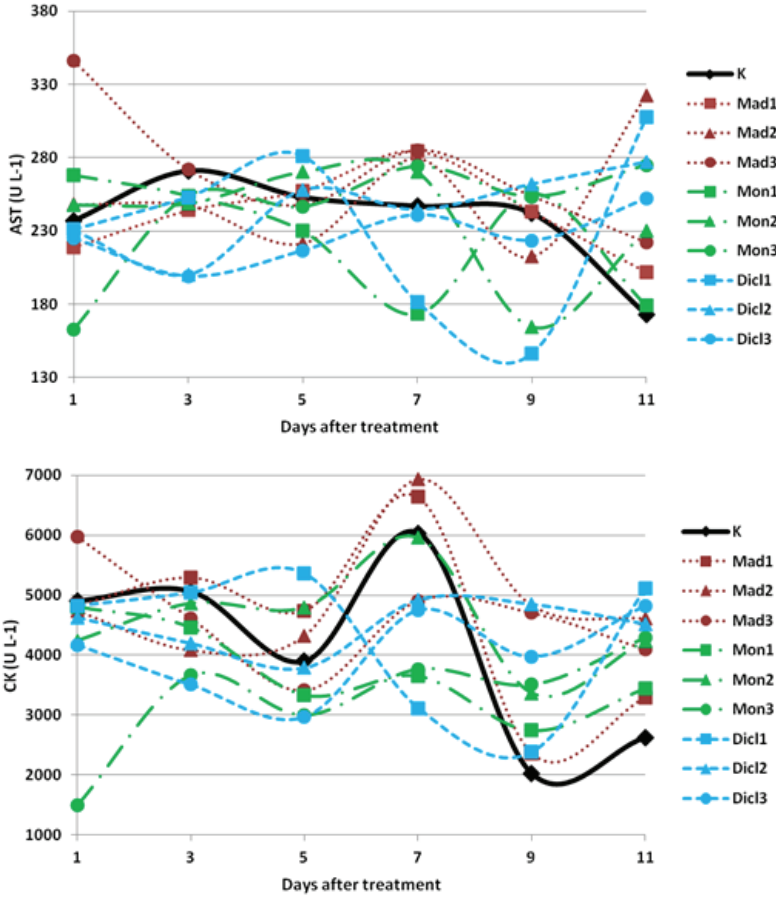

Figure 1: Concentrations of CK and AST (U L^{-1}) of the control group (K) and the experimental groups treated with maduramycin (Mad1: 5 mg kg^{-1}, Mad2: 10 mg kg^{-1}, Mad3: 15 mg kg^{-1}), monensin (Mon1: 125 mg kg^{-1}, Mon2: 225 mg kg^{-1}, Mon3: 325 mg kg^{-1}) and diclazuril (Dicl1: 1 mg kg^{-1}, Dicl2: 5 mg kg^{-1}, Dicl3: 10 mg kg^{-1}) after administration of coccidiostats

Significant differences between groups for **AST**:
day 3 and 9: Mad2-Mad3 $p<0.01$, both
day 7: Mon1-Mon2 and Mon1-Mon3 $p<0.01$, both
day 9: Dicl1-Dicl2 and Dicl1-Dicl3 $p<0.01$, both

Significant differences between groups for **CK**:
day 11: Mad1- C $p<0.05$
day 11: Mad2- C $p<0.01$
day 7: Mon3-C $p<0.05$
day 9 and day 11: Mon2-C and Mon3-C $p<0.01$, all
day 7: Dicl1-C $p<0.05$
day 9 and day 11: Dicl2-C $p<0.01$, both

In this study, the concentration of UA, CA and GLU in chicken serum were measured in the ranges (mg dL^{-1}): control group UA 6–13.7, CA 8.35–12.5 and GLU 72.5–248; experimental groups UA 3.1–22.7; CA 8.2–14.2 and GLU 20.5–301 (Figure 2). UA and GLU levels obtained for control group in this study were similar to previously obtained values for healthy control group of broilers (mg dL^{-1}): UA 4.99 and 5.31; GLU 111.41 and 242.95 (17, 25). In general, the blood GLU concentration in normal birds ranges from 200 to 500 mg dL^{-1} (22). There were no literature reference values for CA. The BA concentration for the control and all experimental groups of chickens was less than 35 µmol L^{-1} which is in line with reference BA concentration values determined by the enzymatic method and which are generally less than 75 µmol L^{-1} (22).

In maduramycin experiment, significantly higher CA level were determined in standard dose group Mad1 compared to the control group on day 9 ($p<0.05$). In treatment with monensin significant differences were found between experimental groups. Significantly higher CA concentrations were measured for the group Mon2 compared to the groups Mon1 and Mon3 in the initial days

following treatment with monensin ($p<0.01$, both). In diclazuril treatment, significantly lower CA were found in the group Dicl1 than in the control group on day 9 ($p<0.05$). Significant differences were determined on day 9 between the group Dicl2 and the groups Dicl1 and Dicl3 ($p<0.01$ and $p<0.05$).

For the parameters UA and GLU, there were no significant differences between the experimental groups and control group of broilers. Also, no significant differences were found between experimental groups for GLU. In the maduramycin experiment, significantly lower UA values were determined in the group Mad3 compared to groups Mad1 and Mad2 on post-treatment day 9 ($p<0.05$, both). On the same day after diclazuril experiments, significantly different concentrations of UA were found between the groups Dicl3 and Dicl2 ($p<0.05$).

A previous study with maduramycin at a concentration of 5 mg kg^{-1} during 6 weeks in broilers showed increased UA levels of 9.31 mg dL^{-1} in comparison with 4.99 mg dL^{-1} measured for control group a day after the end of treatment (25). In experiments in this study, serum UA changes were determined on day 9 after the end of treatments with maduramycin and also diclazuril. Uric acid is secreted in the proximal tubules of the cortical nephrons and approximately 90% of blood uric acid is removed by the kidneys. Therefore, serum or plasma UA levels has been widely used in the detection of kidney disease and damages. In general, UA greater than 13 mg dL^{-1} suggested impaired renal function in birds (22).

Proteins - total, albumin and globulins

There are over a thousand proteins (total protein, TP) in the body, and each has one or more functions (21). Two main types of plasma proteins are albumin and globulins. Albumin (ALB) is classified as a small protein and plays a major role in the transport of free fatty acids, bile acids, bilirubin, calcium, hormones and drugs. It is synthesized in the liver before entering the bloodstream, and is catabolized in different tissues (2). It is also found in plasma, mostly outside the vascular body fluids, cerebrospinal fluid and urine. The basic function is the regulation of osmotic pressure within and outside vascular areas. Albumin values were lower in broilers than in hens (21). Globulins (GLOB) are a heterogeneous group of proteins of varying size but are generally larger than albumin. In plasma, there are over a thousand different types of globulins. Most GLOB are synthesized in the liver, with the exception of immunoglobulins (antibodies), which are produced in the lymphoid tissues. GLOB are classified as alpha (α1, α2), beta (β) or gamma (γ) according to their electrophoretic mobility (22). In birds, any plasma that is not albumin or transthyretin is classified as GLOB (21), and therefore, in this study, GLOB concentrations were calculated by subtracting the concentration of the albumin concentration from total protein.

The concentrations of TP, ALB and GLOB in the experimental and control groups of broilers are shown in Figure 3. Concentrations were determined in the ranges (g dL^{-1}): control group TP 2.45–4.65, ALB 1.71–3.15 and GLOB 0.75–1.5; experimental groups TP 2.75–4.95, ALB 1.90–3.90 and GLOB 0.25–1.75. The concentrations obtained for TP were in line with the reference values for poultry and birds, and ranged from 2.5 to 4.9 g dL^{-1} (18, 22). Also, ALB values were within the reference values from 0.8 to 2.0 g dL^{-1} (22) and previously obtained values for healthy control broilers 2.3 to 3.3 g dL^{-1} (17, 31).

In this study, there were no significant differences in the concentrations of TP, ALB and GLOB between the experimental and control groups, or between experimental groups treated with different concentrations of coccidiostats. The values of all three parameters followed the trend of the control group. Somewhat higher values were determined on post-treatment day 11 for all three parameters in the experimental groups compared to the control group. ALB concentrations were slightly higher on days 7–11 for the groups Mad2 and Mad3, and were in the ranges of 1.9–3.1 and 2.7–3.1 g dL^{-1} compared to the control group (1.70–2.25 g dL^{-1}). GLOB concentrations were slightly lower in all experimental groups than in control broilers, especially in the period of 5 to 9 days after treatment.

In previous study with the maduramycin in broilers at a concentration of 8 mg kg^{-1} for 6 weeks decrease of TP, ALB and GLOB concentrations were found (26). However, there were no changes in TP and ALB levels in broilers treated with maduramycin feed concentrations of 5 mg kg^{-1} (25). However, a recent study with the application of monensin at a concentration of 13 mg kg^{-1} in goats for 5 days showed no effect on TP and ALB levels (23).

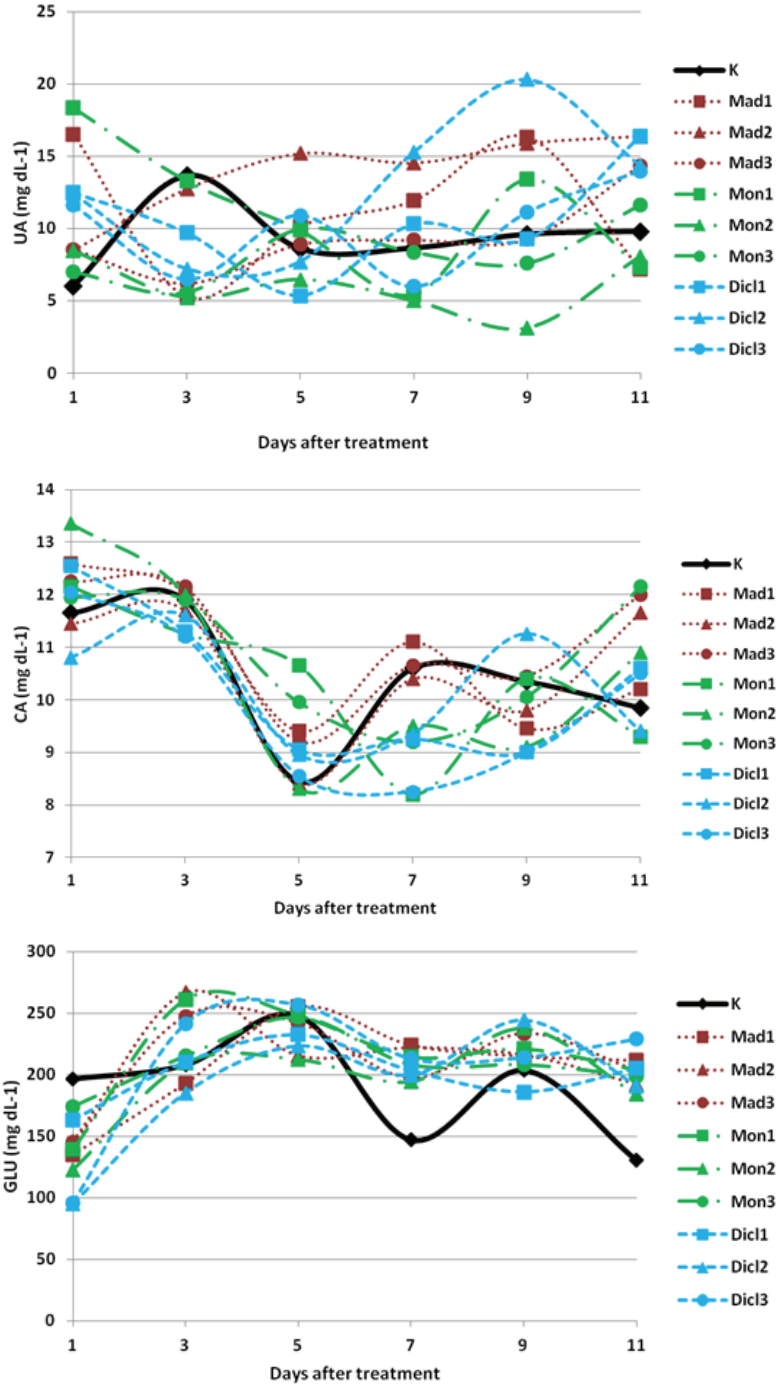

Figure 2: Concentrations of UA, CA i GLU (mg dL^{-1}) of the control group (K) and the experimental groups treated with maduramycin (Mad1: 5 mg kg^{-1}, Mad2: 10 mg kg^{-1}, Mad3: 15 mg kg^{-1}), monensin (Mon1: 125 mg kg^{-1}, Mon2: 225 mg kg^{-1}, Mon3: 325 mg kg^{-1}) and diclazuril (Dicl1: 1 mg kg^{-1}, Dicl2: 5 mg kg^{-1}, Dicl3: 10 mg kg^{-1}) after administration of coccidiostats

Significant differences between groups for CA:
day 9: Mad1-C $p<0.05$
day 1: Mon2-Mon1 and Mon2-Mon3 $p<0.01$, both
day 9: Dicl1-C $p<0.05$
day 9: Dicl1-Dicl2 and Dicl2-Dicl3 $p<0.01$ and $p<0.05$

Significant differences between groups for UA:
day 9: Mad1- Mad3 and Mad2- Mad3 $p<0.05$, both
day 1: Dicl2-Dicl3 $p<0.05$

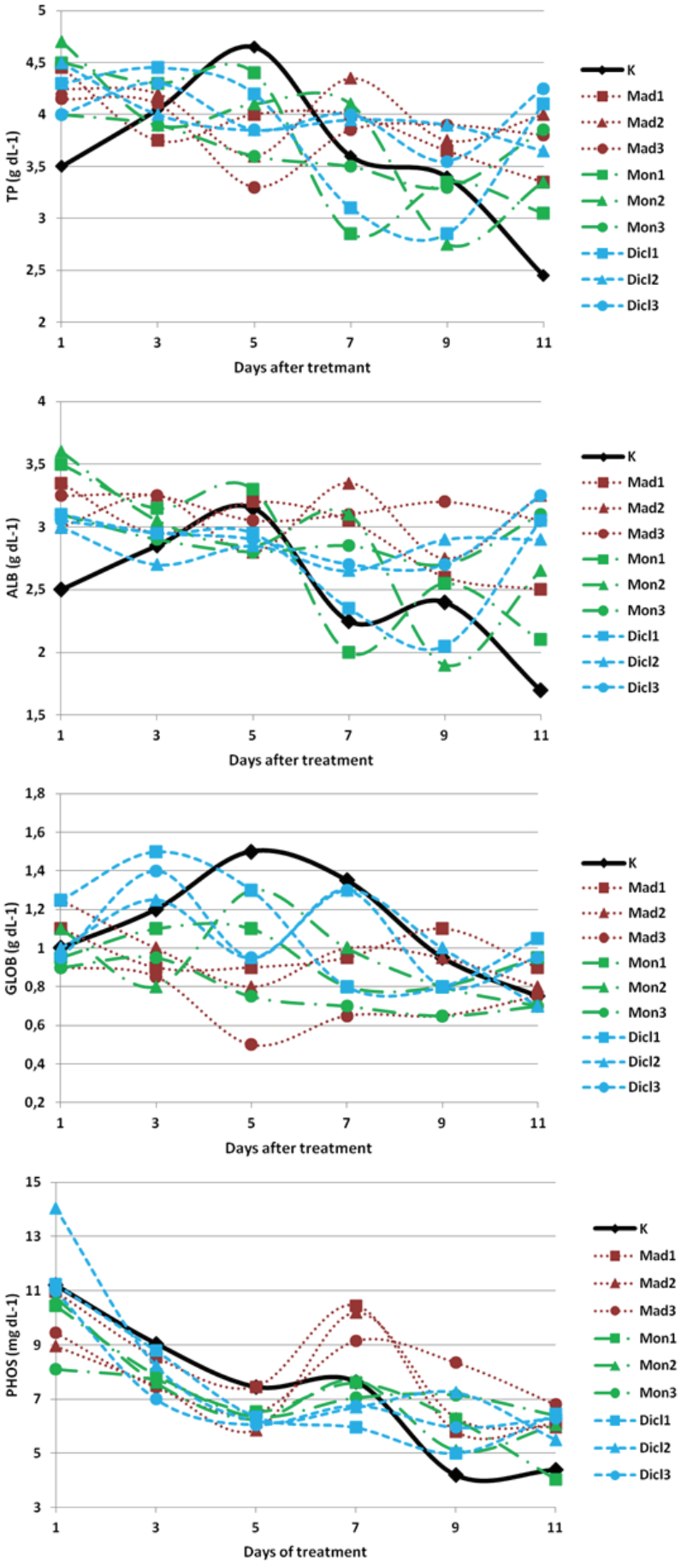

Figure 3: Concentrations of TP, ALB and GLOB (g dL^{-1}) of the control group (K) and the experimental groups treated with maduramycin (Mad1: 5 mg kg^{-1}, Mad2: 10 mg kg^{-1}, Mad3: 15 mg kg^{-1}), monensin (Mon1: 125 mg kg^{-1}, Mon2: 225 mg kg^{-1}, Mon3: 325 mg kg^{-1}) and diclazuril (Dicl1: 1 mg kg^{-1}, Dicl2: 5 mg kg^{-1}, Dicl3: 10 mg kg^{-1}) after administration of coccidiostats

Figure 4: Concentrations of PHOS (mg dL^{-1}) of the control group (K) and the experimental groups treated with maduramycin (Mad1: 5 mg kg^{-1}, Mad2: 10 mg kg^{-1}, Mad3: 15 mg kg^{-1}), monensin (Mon1: 125 mg kg^{-1}, Mon2: 225 mg kg^{-1}, Mon3: 325 mg kg^{-1}) and diclazuril (Dicl1: 1 mg kg^{-1}, Dicl2: 5 mg kg^{-1}, Dicl3: 10 mg kg^{-1}) after administration of coccidiostats

Phosphorus

Electrolytes are present in all inner- and extracellular body fluids, though their concentrations are only measured only in the blood, plasma or serum (22). Phosphorus (PHOS), alongside potassium and calcium, is the most abundant mineral in animals. It is an essential nutrient present in bones, where together with calcium it forms hydroxyapatite in the ratio Ca : P, 2 : 1. In the body, the phosphorus composition is about 70% organic phosphate and 30% inorganic (30). Unlike inorganic phosphorus, organic phosphate is an essential component found in membrane phospholipids and nucleic acids (21). Phosphorus plays a major role in the storage, release and transfer of energy, and is part of the acid-base metabolism (32).

PHOS concentrations in broiler serum after treatments with coccidiostats are presented in Figure 4. Concentrations were determined in the ranges (mmol L^{-1}): control group 4.2–11.2; experimental groups 4.05–14.05. There were no significant differences for PHOS levels in the experimental groups compared to the control, or between experimental groups. In the literature, PHOS levels in broiler chickens were measured in ranges from 3.0 to 6.8 mg dl^{-1} (31, 33).

In a previous study, higher PHOS values were found in heifers following the administration of maduramycin at concentrations of 4, 8 and 12 mg kg^{-1}. However, the increase was significant only in the third week after the treatment. Ultimately, an increase was observed in both groups treated with maduramycin (28). It was concluded that the application of ionophore coccidiostats in high concentrations caused the release of neurotransmitters, mainly norepinephrine. Consequently, ions such as sodium and calcium accumulate in the cell, accelerating intracellular oxidative processes and ultimately degenerative disorders in tissue and organs. The generation of active oxygen groups can lead to necrosis (25). The effect of ionophores on serum calcium levels and inorganic phosphorus can be attributed to the previous conclusion that carboxylic ionophores, such as monensin, lasalocid and salinomycin, react with certain cations to alter mineral metabolism (34, 35).

In conclusion, the administration of different concentrations of maduramycin, monensin and diclazuril did not affect the concentration of the parameters AST, UA, GLU, BA, TP, ALB, GLOB and PHOS in experimental groups of broilers in relation to the control group. Significant differences were observed only in the concentrations of CK and CA in experimental groups in comparison to the control. Significant differences were also determined in the concentrations of AST, CA and UA between experimental groups.

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SPREMEMBE BIOKEMIJSKIH IN KEMIJSKIH PARAMETROV V KRVI KOKOŠI PO ZDRAVLJENJU Z MADURAMICINOM, MONENZINOM IN DIKLAZURILOM

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Povzetek: Namen raziskave je bil spremljanje biokemijskih in kemijskih parametrov krvi industrijsko gojenih piščancev po zdravljenju z enim od treh kokcidiostatikov: maduramicinom, monenzinom ali diklazurilom. Piščanci so dobivali krmo z maduramicinom v koncentracijah 5, 10 in 15 mg/kg, monenzin v koncentracijah 125, 225 in 325 mg/kg ali diklazuril v koncentracijah 1, 5 in 10 mg/kg. Kontrolna skupina piščancev je dobila krmo brez dodatka kokcidiostatikov. Enajsti dan po zdravljenju je bila piščancem odvzeta kri in analizirani so bili naslednji biokemijski in kemijski parametri: koncentracija aspartatne aminotransferaze (AST), žolčnih kislin (BA), kreatininske kinaze (CK), sečne kisline (UA), glukoze (Glu), skupnih beljakovin (TP), albuminov (ALB), globulinov (GLOB) in fosforja (Phos). Dodajanje različnih koncentracij maduramicina, monenzina in diklazurila ni vplivalo na koncentracijo parametrov AST, UA, Glu, BA, TP, ALB, GLOB in Phos v poskusnih skupinah pitovnih piščancev v primerjavi s kontrolno skupino. Statistično značilne razlike so bile ugotovljene v koncentracijah CK in CA med poskusnimi in kontrolno skupino. Značilne razlike so bile ugotovljene tudi v koncentracijah AST, CA in UA med posameznimi poskusnimi skupinami.

Ključne besede: maduramicin; monenzin; diklazuril; piščanci; biokemijski in kemijski parametri