ORIGINAL ARTICLE

# EFFECT OF DRY EXTRACT FROM REISHI MUSHROOMS ON THE STATE OF ANTIOXIDANT SYSTEM IN RATS WITH DMH-INDUCED COLON CARCINOGENESIS

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## ABSTRACT

**The aim:** To study pro- and antioxidant systems indicators in rats with chemically induced colon carcinogenesis on the background of the reishi mushrooms dry extract use.

**Materials and methods:** The study was performed on 120 white male rats. Chronic oncogenic intoxication was modeled by administering 1,2-dimethylhydrazine (DMH) hydrochloride for 30 weeks (1 time per week). A dry extract from the reishi mushrooms was administered intragastrically daily at a dose of 100 mg/kg of the animal's body weight. Blood and liver samples were taken for research monthly. The state of the pro- and antioxidant systems was studied by the content of oxidative modification of proteins products, superoxide dismutase and catalase activity, contents of reduced glutathione and ceruloplasmin.

**Results:** An increase in the activity of free radical oxidation processes after DMH-induced colon carcinogenesis in rats is evidenced by a decrease in the superoxide dismutase activity, catalase activity, content of reduced glutathione, an increase in the content of ceruloplasmin and products of oxidative modification of proteins in the blood serum and liver of animals. The effectiveness of the dry extract of reishi mushrooms and its positive effect on the state of pro- and antioxidant systems was experimentally proved.

**Conclusions:** The use of the dry extract of reishi mushrooms under conditions of DMH-induced colon carcinogenesis in rats led to normalization of the antioxidant protection system state and the reduction of oxidative stress.

**KEY WORDS:** colorectal cancer, dry extract, oxidative stress, reishi mushroom, dimethylhydrazine

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## INTRODUCTION

Oncological diseases are one of the main causes of mortality worldwide. It is known about cancer that it is not one disease, but at least 200 – and each of them has its own symptoms, methods of diagnosis and treatment. For many years, cancer has been one of the main components of non-infectious morbidity, disability and mortality of the population in the world, which lead to significant losses of the labor and life potential of society [1, 2]. The onco-epidemiological situation in Ukraine is characterized by high morbidity. Over the past 10 years, the number of cancer patients has increased by 25%. The dynamics of the morbidity and mortality rates of the population of Ukraine over the past 10 years, the characteristics of oncology service, indicate the need to improve all aspects of the anti-cancer fight [3, 4].

The nomenclature of natural drugs with an oncoprotective effect on the pharmaceutical market of Ukraine is insufficient, therefore the search for appropriate raw materials and the creation of new medicinal products based on them is urgent [1, 5, 6].

Reishi mushrooms have a lot of useful properties and are widely used in oriental medicine as drugs that have antibacterial, antiviral, anti-inflammatory, anti-allergenic, antioxidant and anti-tumor effects. Reishi mushrooms are usually used as oncoprotectors together with shiitake and maitake mushrooms. They have been proven to have a beneficial effect on the cardiovascular system, the ability to thin the blood, reduce the blood clotting rate and blood sugar level, expand the coronary vessels of the heart, prevent the development of coronary heart disease, thrombophlebitis and heart attacks, effectiveness in hypertension, arrhythmias, tachycardia, gastritis, ulcers stomach and duodenum, hemorrhoids, diseases of the thyroid gland and liver, respiratory and mental diseases, epilepsy [1, 7, 8]. The advantage of using reishi mushrooms as oncoprotectors is their easy assimilation by the human body, the possibility of long-term use without the risk of side effects, the mildness and reliability of the pharmacological action [9, 10].

## THE AIM

The aim of our research was to study pro- and antioxidant systems indicators in rats with chemically induced colon carcinogenesis on the background of the reishi mushrooms dry extract use.

## MATERIALS AND METHODS

Experiments were performed on white outbred male rats weighing 190-210 g, which were kept on the standard ration of the vivarium of I. Horbachevsky Ternopil National Medical University. All studies were conducted in compliance with Good Laboratory Practice (GLP) and bioethics in accordance with the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" [11]. The study was approved by the Ethical Committee of I. Horbachevsky Ternopil National Medical University (Excerpts from the protocol №70, from 01.08.2022).

Experimental study design comprised three groups: 1st – control (C); 2nd – animals affected by 1,2-dimethylhydrazine hydrochloride, control pathology (CP); 3rd – rats affected by 1,2-dimethylhydrazine hydrochloride, treated with a reishi mushrooms dry extract (RMDE). RMDE was administered intragastrically daily at a dose of 100 mg/kg of animal body weight during 30 weeks of the experiment. Dose 100 mg/kg in our previous studies, was found to be conditionally therapeutic for this extract [1]. 1,2-DMH was injected subcutaneously into the interscapular area at a dose of 7.2 mg/kg once a week for 30 weeks, according to the rat's body weight. Animals, which were injected subcutaneously with saline every week, were the control for experimental group of rats. There were 8 animals in the control group, which were euthanized after the first month of the experiment. The 2nd and 3rd groups included 56 animals each. 8 animals from each group were euthanized monthly. [1, 3, 12]

Liver homogenate and blood serum were tested monthly after animal euthanasia. The state of pro-oxidant system in blood serum and animal liver homogenates were evaluated by the content of oxidative modification of proteins (OMP) of neutral and alkaline character. The state of antioxidant system was evaluated by the superoxide dismutase (SOD) and catalase (CAT) activity, by the content of ceruloplasmin (CPL) and reduced glutathione (GSH) [13].

Statistical analysis of the data was performed using STATISTICA 13 (TIBCO Software Inc., 2018). For all indices, the arithmetic mean of the sample (M), lower and upper quartile were calculated. Taking into account the non-normality of the data distribution, non-parametric criteria were used to determine the reliable difference between independent and dependent indicators. The reliability of the difference between the values between the independent quantitative values was determined by the Mann-Whitney test. The difference between the values was considered probable at $p<0.05$ [14]. A significant difference between dependent indicators determined by euthanasia of experimental animals at different time points of the experiment was determined on the basis of the Friedman test.

The hypothesis of this study was the assumption of the presence of antioxidant and oncoprotective effects of reishi mushroom extract. This hypothesis is scientific, because it can be denied in the absence of reliable changes in the indicators of antioxidant protection in rats with induced carcinogenesis. To model the latter, the malignant effect of DMH on the colon of experimental animals was used, the effectiveness of which was assessed by the severity of oxidative stress.

## RESULTS

The prooxidant-antioxidant status of animals with DMH-induced carcinogenesis was assessed in blood serum and liver homogenate by the content of oxidative modification of proteins products, activity of superoxide dismutase and catalase.

The development of oxidative stress after the introduction of 1,2-DMH is evidenced by the increase in the content of products of oxidative modification of proteins in the blood serum and liver of animals. This can be explained by an excess of free radicals and active forms of oxygen, which were formed due to the negative impact of the toxicant.

When studying the parameters of OMP, it was established that in the blood serum and liver of rats with simulated carcinogenesis, there was a probable ($p<0.05$) increase in the content of neutral (370 nm) and basic (430 nm) 2,4-dinitrophenylhydrazones (2,4-DNPH ), starting from the 2nd month of the experiment (table I, II).

The content of neutral 2,4-DNPH increased by 1.9 times in the blood serum and by 1.5 times in the liver of the affected rats compared to the control on the 3rd month of the study. On the 5th and 7th month (fig 1) of the experiment, an increase of this indicator by 3.3 and 4.0 times was noted in the blood serum and by 2.3 and 2.9 times in the liver of animals with a simulated tumor process.

As can be seen from the table I, the content of 2,4-DNPH of a neutral nature was probably lower both in the serum and in the liver of animals that were injected with 1,2-DMH on the background of the use of RMDE compared to the control pathology.

**Table I.** Content of neutral 2,4-DNPH (μcmol/g protein) in blood serum and liver of rats with DMH-induced colon carcinogenesis, and after the application of reishi mushroom extract (n=120).

| Period of Affection | Index/Group of animals | | | | | |
|---|---|---|---|---|---|---|
| | C | | CP | | CP+RMDE | |
| | Serum | Liver | Serum*** | Liver*** | Serum*** | Liver*** |
| 1 month | 0,023 \|0,019; 0,029\| | 0,052 \|0,044; 0,059\| | 0,025 \|0,019; 0,031\| | 0,059 \|0,051; 0,065\| | 0,024 \|0,019; 0,028\| | 0,051 \|0,043; 0,060\| |
| 2 month | 0,023 \|0,019; 0,029\| | 0,052 \|0,044; 0,059\| | 0,035* \|0,030; 0,039\| | 0,065* \|0,060; 0,071\| | 0,029 \|0,024; 0,034\| | 0,062 \|0,057; 0,067\| |
| 3 month | 0,023 \|0,019; 0,029\| | 0,052 \|0,044; 0,059\| | 0,043* \|0,036; 0,049\| | 0,079* \|0,072; 0,085\| | 0,033** \|0,031; 0,037\| | 0,068** \|0,061; 0,075\| |
| 4 month | 0,023 \|0,019; 0,029\| | 0,052 \|0,044; 0,059\| | 0,056* \|0,050; 0,067\| | 0,102* \|0,096; 0,108\| | 0,037** \|0,029; 0,047\| | 0,079** \|0,073; 0,084\| |
| 5 month | 0,023 \|0,019; 0,029\| | 0,052 \|0,044; 0,059\| | 0,075* \|0,068; 0,079\| | 0,120* \|0,105; 0,133\| | 0,041** \|0,037; 0,046\| | 0,083** \|0,072; 0,093\| |
| 6 month | 0,023 \|0,019; 0,029\| | 0,052 \|0,044; 0,059\| | 0,083* \|0,076; 0,088\| | 0,135* \|0,126; 0,147\| | 0,042** \|0,037; 0,046\| | 0,095** \|0,084; 0,105\| |
| 7 month | 0,023 \|0,019; 0,029\| | 0,052 \|0,044; 0,059\| | 0,092* \|0,079; 0,103\| | 0,153* \|0,141; 0,167\| | 0,044** \|0,039; 0,049\| | 0,097** \|0,089; 0,106\| |

Note. Here and in the following tables * - probable changes between the index of control and dimethylhydrazine-affected animals, ** - probable changes between the index of dimethylhydrazine-affected and extract-treated animals. *** - probable difference in parameter values in dynamics.

**Table II.** Content of basic 2,4-DNPH (μcmol/g protein) in blood serum and liver of rats with DMH-induced colon carcinogenesis and after application of reishi mushroom extract (n=120).

| Period of Affection | Index/Group of animals | | | | | |
|---|---|---|---|---|---|---|
| | C | | CP | | CP+RMDE | |
| | Serum | Liver | Serum*** | Liver*** | Serum*** | Liver*** |
| 1 month | 0,015 \|0,013; 0,017\| | 0,036 \|0,033; 0,041\| | 0,018 \|0,015; 0,021\| | 0,040 \|0,034; 0,046\| | 0,016 \|0,014; 0,020\| | 0,041 \|0,038; 0,046\| |
| 2 month | 0,015 \|0,013; 0,017\| | 0,036 \|0,033; 0,041\| | 0,023* \|0,018; 0,027\| | 0,045* \|0,039; 0,051\| | 0,021 \|0,018; 0,025\| | 0,037** \|0,031; 0,041\| |
| 3 month | 0,015 \|0,013; 0,017\| | 0,036 \|0,033; 0,041\| | 0,033* \|0,026; 0,041\| | 0,056* \|0,050; 0,062\| | 0,025 \|0,022; 0,028\| | 0,040** \|0,037; 0,044\| |
| 4 month | 0,015 \|0,013; 0,017\| | 0,036 \|0,033; 0,041\| | 0,047* \|0,045; 0,051\| | 0,075* \|0,071; 0,081\| | 0,031** \|0,025; 0,038\| | 0,045** \|0,040; 0,049\| |
| 5 month | 0,015 \|0,013; 0,017\| | 0,036 \|0,033; 0,041\| | 0,060* \|0,056; 0,067\| | 0,094* \|0,088; 0,100\| | 0,035** \|0,033; 0,039\| | 0,052** \|0,046; 0,057\| |
| 6 month | 0,015 \|0,013; 0,017\| | 0,036 \|0,033; 0,041\| | 0,093* \|0,085; 0,100\| | 0,122* \|0,119; 0,129\| | 0,041** \|0,036; 0,047\| | 0,064** \|0,056; 0,076\| |
| 7 month | 0,015 \|0,013; 0,017\| | 0,036 \|0,033; 0,041\| | 0,107* \|0,098; 0,114\| | 0,144* \|0,142; 0,151\| | 0,048** \|0,042; 0,055\| | 0,070** \|0,061; 0,081\| |

When studying the content of 2,4-DNPH of a basic nature, a probable increase by 1.5 and 1.3 times was noted already on the 2nd month of the experiment in the blood serum and liver of rats with DMD pathology compared to animals of control group. On the 7th month, this indicator increased by 7.1 times in the blood serum and by 4.0 times in the liver of rats with a simulated tumor process compared to the control (fig 1).

Under the influence of RMDE, the content of 2,4-DNPH of the main character was probably lower in the blood serum and liver of rats throughout the experiment in comparison with the group of animals to which no correction was applied.

Changes in antioxidant system of the rat body after the introduction of the toxicant are evidenced by a significant decrease in SOD activity in the blood serum and liver of animals relative to the control, which can be caused by an increase in concentration of hydrogen peroxide and accumulation of compounds that affect the degree of enzyme recovery (table III).

The introduction of a dry extract from reishi mushrooms into the affected body led to a probable increase of SOD

**Table III.** Superoxide dismutase activity in blood serum and liver (mcat/g protein) of rats with DMH-induced colon carcinogenesis and after the use of reishi mushroom extract (n=120).

| Period of Affection | Index/Group of animals | | | | | |
|---|---|---|---|---|---|---|
| | C | | CP | | CP+RMDE | |
| | Serum | Liver | Serum*** | Liver*** | Serum*** | Liver *** |
| 1 month | 60,81 \|55,94; 65,44\| | 45,96 \|42,77; 49,18\| | 58,72 \|55,81; 61,66\| | 47,46 \|43,68; 50,94\| | 59,06 \|55,50; 63,81\| | 44,87 \|41,21; 48,80\| |
| 2 month | 60,81 \|55,94; 65,44\| | 45,96 \|42,77; 49,18\| | 56,47 \|52,90; 59,13\| | 45,04 \|42,73; 49,10\| | 59,11 \|57,41; 60,48\| | 43,75 \|40,16; 47,04\| |
| 3 month | 60,81 \|55,94; 65,44\| | 45,96 \|42,77; 49,18\| | 53,06* \|49,10; 56,00\| | 40,03* \|38,08; 42,30\| | 58,23** \|56,08; 58,86\| | 42,51 \|40,51; 44,46\| |
| 4 month | 60,81 \|55,94; 65,44\| | 45,96 \|42,77; 49,18\| | 47,46* \|44,19; 51,87\| | 35,75* \|32,47; 38,73\| | 55,22** \|54,12; 56,55\| | 40,19 \|38,85; 42,85\| |
| 5 month | 60,81 \|55,94; 65,44\| | 45,96 \|42,77; 49,18\| | 41,66* \|36,90; 46,38\| | 32,56* \|30,92; 35,08\| | 53,84** \|51,31; 55,72\| | 38,90** \|38,08; 40,95\| |
| 6 month | 60,81 \|55,94; 65,44\| | 45,96 \|42,77; 49,18\| | 38,22* \|33,21; 41,87\| | 27,99* \|24,86; 32,13\| | 50,01** \|48,34; 53,20\| | 37,88** \|34,74; 40,48\| |
| 7 month | 60,81 \|55,94; 65,44\| | 45,96 \|42,77; 49,18\| | 31,86* \|28,30; 36,83\| | 24,56* \|20,00; 28,97\| | 48,47** \|45,89; 49,82\| | 36,65** \|34,09; 38,65\| |

**Table IV.** Catalase activity in blood serum (mcat/l) and liver (mcat/kg) of rats with DMH-induced colon carcinogenesis and after application of reishi mushroom extract (n=120).

| Period of Affection | Index/Group of animals | | | | | |
|---|---|---|---|---|---|---|
| | C | | CP | | CP+RMDE | |
| | Serum | Liver | Serum*** | Liver*** | Serum*** | Liver*** |
| 1 month | 3,79 \|3,47; 4,10\| | 5,93 \|5,50; 6,32\| | 3,46 \|3,21; 3,80\| | 5,87 \|5,53; 6,18\| | 3,95** \|3,81; 4,22\| | 6,04 \|5,88; 6,25\| |
| 2 month | 3,79 \|3,47; 4,10\| | 5,93 \|5,50; 6,32\| | 3,22 \|2,78; 3,67\| | 5,66 \|5,36; 5,90\| | 3,72 \|3,48; 3,97\| | 5,88 \|5,66; 6,00\| |
| 3 month | 3,79 \|3,47; 4,10\| | 5,93 \|5,50; 6,32\| | 3,07* \|3,01; 3,21\| | 4,75* \|4,36; 5,09\| | 3,64** \|3,47; 3,91\| | 5,46** \|5,10; 5,70\| |
| 4 month | 3,79 \|3,47; 4,10\| | 5,93 \|5,50; 6,32\| | 2,68* \|2,39; 2,97\| | 4,07* \|3,87; 4,30\| | 3,44** \|3,30; 3,67\| | 5,29** \|5,11; 5,64\| |
| 5 month | 3,79 \|3,47; 4,10\| | 5,93 \|5,50; 6,32\| | 2,23* \|1,97; 2,49\| | 3,80* \|3,58; 4,09\| | 3,29** \|3,23; 3,53\| | 5,12** \|4,85; 5,39\| |
| 6 month | 3,79 \|3,47; 4,10\| | 5,93 \|5,50; 6,32\| | 1,99* \|1,80; 2,21\| | 3,15* \|3,02; 3,38\| | 3,21** \|3,00; 3,44\| | 4,99** \|4,78; 5,23\| |
| 7 month | 3,79 \|3,47; 4,10\| | 5,93 \|5,50; 6,32\| | 1,74* \|1,50; 1,87\| | 2,77* \|2,52; 3,07\| | 2,98** \|2,80; 3,16\| | 4,69** \|4,58; 4,86\| |

activity in the blood serum already on the 3rd month of the experiment by 1.1 times compared to the control pathology. When investigating the effect of RMDE on SOD activity in the liver of animals with DMH-induced carcinogenesis, it was established that a probable increase in the activity of the enzyme by 1.2 times relative to the affected rats occurred on the 5th month of the experiment.

White rats' affection with a carcinogen caused a decrease in catalase activity in the blood serum and liver of animals (table IV). Due to insufficient CAT activity, hydrogen peroxide accumulates, which leads to the appearance of lipid hydroperoxides and oxidative modification of proteins.

The activity of the enzyme in blood serum decreased by 19%, in the 5th month this indicator decreased by 41%, in the 7th month – by 54% compared to the control on the 3rd month after the injury. Catalase activity in the liver of rats under the influence of DMH decreased by 20%, 36%, and 53% on the 3rd, 5th, and 7th months of the study, respectively, relative to animals of control group (figure 2).

A positive trend was observed after the correction with RMDE with regard to catalase activity, which already was probably by 1.2 times higher in blood serum and by 1.1 times higher in the liver of animals compared to the control pathology on the 3rd month of the experiment (table IV).

**Table V.** Content of CPL (mg/l) in the blood serum of rats with DMH-induced colon carcinogenesis and after application of reishi mushroom extract (n=120).

| Period of Affection | Index/Group of animals | | |
|---|---|---|---|
| | C | CP*** | CP+RMDE *** |
| 1 month | 3,46<br>\|3,22; 3,80\| | 3,35<br>\|3,12; 3,64\| | 3,63<br>\|3,19; 3,80\| |
| 2 month | 3,46<br>\|3,22; 3,80\| | 4,10<br>\|3,18; 5,24\| | 3,79<br>\|3,36; 4,03\| |
| 3 month | 3,46<br>\|3,22; 3,80\| | 4,59*<br>\|3,73; 5,24\| | 3,95<br>\|3,42; 4,40\| |
| 4 month | 3,46<br>\|3,22; 3,80\| | 5,50*<br>\|5,28; 5,71\| | 4,18**<br>\|3,85; 4,57\| |
| 5 month | 3,46<br>\|3,22; 3,80\| | 6,04*<br>\|5,65; 6,44\| | 4,32**<br>\|3,97; 4,92\| |
| 6 month | 3,46<br>\|3,22; 3,80\| | 7,14*<br>\|6,69; 7,69\| | 4,70**<br>\|4,25; 5,07\| |
| 7 month | 3,46<br>\|3,22; 3,80\| | 7,90*<br>\|7,56; 8,25\| | 4,80**<br>\|4,57; 4,98\| |

**Table VI.** GSH content (mmol/g protein) in serum and liver of rats with DMH-induced colon carcinogenesis and after application of reishi mushroom extract (n=120).

| Period of Affection | Index/Group of animals | | | | | |
|---|---|---|---|---|---|---|
| | C | | CP | | CP+RMDE | |
| | Serum | Liver | Serum*** | Liver*** | Serum*** | Liver *** |
| 1 month | 1,33<br>\|1,28; 1,39\| | 1,94<br>\|1,89; 2,01\| | 1,30<br>\|1,21; 1,39\| | 2,01<br>\|1,88; 2,19\| | 1,37<br>\|1,26; 1,46\| | 1,96<br>\|1,87; 2,06\| |
| 2 month | 1,33<br>\|1,28; 1,39\| | 1,94<br>\|1,89; 2,01\| | 1,20*<br>\|1,13; 1,27\| | 1,89<br>\|1,79; 2,05\| | 1,31<br>\|1,26; 1,39\| | 1,90<br>\|1,81; 2,00\| |
| 3 month | 1,33<br>\|1,28; 1,39\| | 1,94<br>\|1,89; 2,01\| | 1,06*<br>\|0,98; 1,15\| | 1,61*<br>\|1,43; 1,75\| | 1,24**<br>\|1,17; 1,29\| | 1,86**<br>\|1,80; 1,94\| |
| 4 month | 1,33<br>\|1,28; 1,39\| | 1,94<br>\|1,89; 2,01\| | 0,91*<br>\|0,83; 1,02\| | 1,42*<br>\|1,36; 1,46\| | 1,17**<br>\|1,09; 1,24\| | 1,79**<br>\|1,69; 1,88\| |
| 5 month | 1,33<br>\|1,28; 1,39\| | 1,94<br>\|1,89; 2,01\| | 0,74*<br>\|0,64; 0,82\| | 1,28*<br>\|1,19; 1,35\| | 1,09**<br>\|0,99; 1,18\| | 1,72**<br>\|1,58; 1,87\| |
| 6 month | 1,33<br>\|1,28; 1,39\| | 1,94<br>\|1,89; 2,01\| | 0,60*<br>\|0,52; 0,67\| | 1,09*<br>\|0,93; 1,27\| | 1,03**<br>\|0,91; 1,09\| | 1,67**<br>\|1,59; 1,76\| |
| 7 month | 1,33<br>\|1,28; 1,39\| | 1,94<br>\|1,89; 2,01\| | 0,52*<br>\|0,44; 0,61\| | 0,95*<br>\|0,84; 1,10\| | 0,97**<br>\|0,89; 1,08\| | 1,57**<br>\|1,45; 1,71\| |

It was noted a probable increase in the activity of the enzyme by 1.8 times in blood serum and by 1.7 times in the liver of rats relative to animals with DMH-induced carcinogenesis on the 7th month of the research.

The next stage of our research was to study the content of CPL in the blood serum of rats affected by DMH and after correction with RMDE (fig 3). CPL has pronounced oxidative activity, it limits the release of iron reserves, activates the oxidation of ascorbic acid, norepinephrine, serotonin and sulfhydryl compounds, inactivates reactive oxygen species, preventing the peroxidation of lipids in the cell membrane, can modulate the function of endothelial nitric oxide synthase, regulating NO-dependent relaxation vessels.

As can be seen from the data in table V, the content of CPL in the blood serum of animals after exposure to a toxic agent increased significantly ($p \leq 0.05$) starting from the 3rd month of the experiment compared to the group of control animals. The use of RMDE in a dose of 100 mg/kg of animals body weight showed a positive effect on the content of this enzyme, probably reducing it by the 4th month of the study.

Reduced glutathione (GSH) belongs to endogenous water-soluble antioxidants, is a cofactor and substrate of the enzymatic antioxidant system, and has a direct neutralizing effect on free radicals.

A probable ($p \leq 0.05$) decrease in the content of GSH in the blood serum of rats was noted from the 2nd month of the experiment by 1.1 times, respectively,

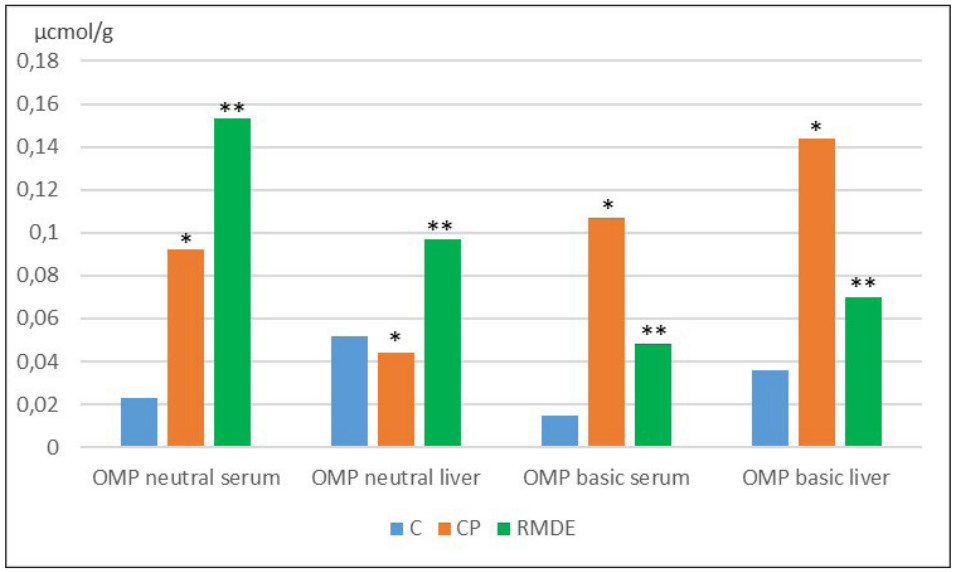


**Fig. 1.** The content of neutral and basic 2,4-DNPH in the blood serum and liver of rats with DMH-induced colon carcinogenesis and after the application of reishi mushroom extract, 7th month
Note. Here and in the following figures * - probable changes between the index of control and dimethylhydrazine-affected animals, ** - probable changes between the index of dimethylhydrazine-affected and extract-treated animals

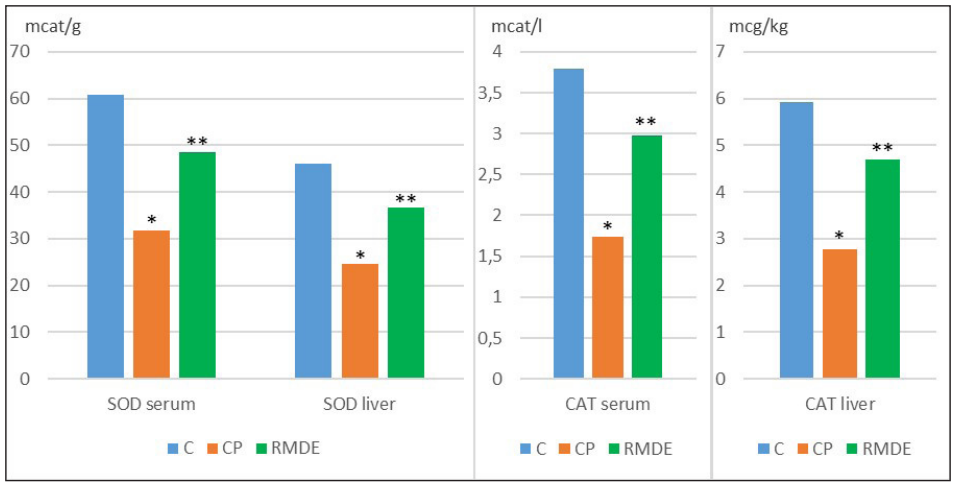


**Fig. 2.** SOD and CAT activity in serum and liver of rats with DMH-induced colon carcinogenesis and after application of reishi mushroom extract, 7th month.

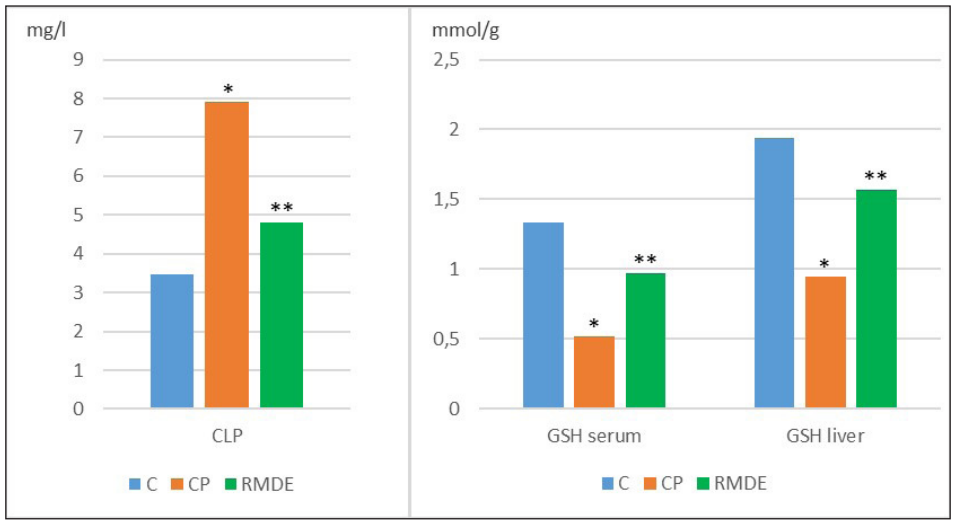


**Fig. 3.** Content of CPL in the blood serum and content of GSH in the blood serum and liver of rats with DMH-induced colon carcinogenesis and after the application of reishi mushroom extract, 7th month.

compared to the control group (table VI). By the end of the experiment, this indicator decreased by 2.6 times relative to C. A similar tendency was observed in the liver of animals with DMH pathology. Administration of SEGR to animals under the conditions of DMH-induced carcinogenesis led to a probable increase in the content of GSH in the blood serum and liver of rats as early as the 3rd month of the experiment. By the end of the study, the content of GSH in the blood serum and liver of the affected rats, which were injected with the studied extract, increased by 87% and 65%, respectively, relative to the control pathology.

To confirm the detected changes in biochemical indicators and the development of colorectal cancer in

animals, we conducted a histopathological study. The development of DMH-induced colon carcinogenesis in white rats was confirmed histologically. The results of this research are covered in scientific publications [5, 7].

## DISCUSSION

The process of oncopathology development is accompanied by a change in the redox balance and disturbances in the antioxidant defense system. The study of the state of the pro- and antioxidant system in the model of DMH-induced carcinogenesis in rats showed a probable increase in the content of OMP products in the blood serum and liver of animals relative to the control. This indicates the development of a pathological process in the affected body. Oxygen-dependent oxidation of proteins is an early indicator of damage to organs and tissues, and the processes of oxidative modification of proteins in all pathological conditions must be under continuous laboratory control [15-18].

Catalase and superoxide dismutase are the main components of the enzyme link of the body's antioxidant defense. SOD regulates the conversion of highly reactive superoxide anion into less active hydrogen peroxide. Catalase, in turn, inactivates the product of SOD reaction with water and molecular oxygen. As a result of the work of these enzymes, the formation of the hydroxyl radical, which is the most active oxidant, is sharply reduced [15, 19].

In the conditions of DMH-induced carcinogenesis, the activity of SOD, which is a key enzyme of antiradical protection, and CAT, which has a significant effect on the intracellular concentration of reduced glutathione and plays a decisive role in neutralizing free radicals, was investigated [12].

It has been experimentally proven that long-term administration of 1,2-DMH leads to an imbalance in the functioning of the antioxidant defense system of the blood and liver of rats, which is manifested by a decrease in SOD and CAT activities, an increase in the content of CP and a decrease in the content of GSH. A decrease in catalase and superoxide dismutase activities in blood serum and liver of experimental rats may indicate 1,2-DMH induction of oxidative stress. This is also indicated by a change in the content of GSH and CP in the blood serum and liver of affected animals, which are one of the markers of the intensity of lipid peroxidation and the development of oxidative stress [19].

Analyzing the dynamics of changes in the activity of the studied enzymes and the content of OMP products in the blood serum and liver homogenate of affected rats, which were injected with RMDE for 7 months, it was established that there was a probable increase in the activity of antioxidant protection enzymes and a decrease in the content of OMP products in all studied tissues of the affected animals. Thus, the effective influence of RMDE on the pro-oxidant-antioxidant state of the liver and blood of rats with a simulated oncological process was proven [20, 21].

In the future, it is planned to study the effect of reishi mushroom extract on the activity of glutathione peroxidase and glutathione reductase in DMH-induced colon carcinogenesis. The antioxidant effect of reishi will be investigated on models of other pathologies, which are accompanied by the activation of oxidative processes.

## CONCLUSIONS

The obtained results of the study allow us to state that the lesion of rats with 1,2-DMH leads to the activation of free radical oxidation processes and a compensatory decrease in the activity of the studied enzymes with the subsequent depression of antioxidant protection. This is evidenced by an increase in the content of 2,4-DNPH and CPL, a decrease in SOD and catalase activity, a decrease in the content of GSH in the blood serum and liver of animals with a simulated tumor process. Thus, by the end of the experiment, the following changes were observed after the introduction of 1,2-DMH: the content of neutral and basic 2,4-DNPH probably increased by 4.0 and 7.1 times, respectively, in blood serum and by 2.9 and 4.0 once in the liver of affected animals; the activity of SOD and CAT decreased by 1.9 and 2.2 times in blood serum and by 1.9 and 2.1 times in the liver of animals with DMD pathology; the content of CP and reduced glutathione in blood serum decreased by 2.3 and 2.6 times compared to the control group. This indicates the feasibility of DMH using to model oncogenesis in rats.

The introduction of RMDE for the correction of simulated pathology showed an effective positive influence on the normalization of the studied indicators, caused a gradual stimulation of the antioxidant defense system and a decrease in the content of OMP products in the body during experimental carcinogenesis. Thus, on the 7th month of the study, the content of neutral and basic 2,4-DNPH probably decreased under the influence of reishi extract by 2.1 and 2.2 times, respectively, in blood serum and by 1.6 and 2.1 times in the liver of animals . The activity of SOD and CAT increased by 1.5- and 1.7-fold, respectively, in the serum and liver of rats treated with RMDE, relative to affected animals. This is probably a consequence of the antioxidant and oncoprotective effect of the studied pharmacological drug, which can be a reasonable basis for further study of RMDE. The revealed probable positive dynamics of antioxidant protection indicators allows to confirm the assumption about the effectiveness of reishi extract.

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