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AUT-M ENTEROSORBENT STABILIZES GLUTATHIONE SYSTEM IN VINCRISTINE-TREATED RATS WITH DIMETHYLHYDRAZINE-INDUCED COLON CANCER

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Colorectal cancer is one of the leading causes of mortality in the world. The search for new methods of therapy for this disease that could correct the state of oxidative stress during the development of neoplasms is up to date. The aim of this work was to study the level of reduced glutathione and the activity of glutathione-dependent enzymes in the development of 1,2 dimethylhydrazine-induced colon cancer in rats while treated with vincristine and the use of enterosorbent. To induce carcinogenesis, dimethylhydrazine was administered to male rats subcutaneously for 30 weeks at a dose of 7.2 mg/kg of body weight. The rats with induced colon cancer received entorosorbent per os at a dose of 0.2 g per 100 g of body weight daily for 21 days. After detoxification therapy, the rats were administered cytostatic vincristine daily at a dose of 0.23 mg/kg for 14 days. A decrease in the content of reduced glutathione, the activity of glutathione reductase and glutathione peroxidase in the blood and liver tissue of rats with colorectal cancer was established. The use of enterosorbent AUT-M was shown to be effective in stabilizing the indicators of the glutathione system in rats with induced colon cancer. Cytostatic vincristine did not significantly affect the change of the studied indicators, confirming the effectiveness of previous sorption measures.

K e y w o r d s: colorectal cancer, vincristine, entorosorbent, glutathione, glutathione reductase, glutathione peroxidase, blood, liver.

The development of the oncological process is accompanied by multiple pathological manifestations. Due to the presence of mutations and intensive growth, cancer cells belong to highly metabolically active and hypoxic cells that generate an increased amount of reactive oxygen species (ROS). An excess amount of ROS has a powerful destructive effect on cells and the body in general, causing the development of oxidative stress [1, 2]. ROS plays a key role in the process of DNA damage, which is outlined as a disproportion between the production of ROS and reactive nitrogen species (RNS) and the efficiency of enzymatic and nonenzymatic antioxidant protection [3, 4].

The glutathione system plays an important role in providing antioxidant protection of cells [4]. Its consists of reduced (GSH) and oxidized (GSSG) forms of glutathione and three enzymes (glutathione peroxidase, glutathione transferase and glutathione reductase) [4, 5]. Glutathione is a tripeptide, which includes the amino acids cysteine, glycine and glutamic acid. It is found in relatively high concentrations in many body tissues and plays a key role in reducing oxidative stress, maintaining redox balance, enhancing metabolic detoxification, and regulating the immune system [5-7]. Depletion of the glutathione system is accompanied by significant cell damage and, as a result, leads to disease progression. Therefore, the study of changes in the indicators of the glutathione system is quite relevant for the search for new methods of therapy that could correct the state of oxidative stress during the development of neoplasms.

It is known that one of the main methods of treatment of oncological diseases is chemotherapy. On the other hand, toxic side effects of chemotherapy components can cause additional generation of ROS, oxidative stress, and antioxidant collapse. That is why enterosorption methods occupy a special place in the problem of reducing the toxic manifestation of chemotherapy components [4, 8, 9]. It is known from literary sources that AUT-M is one

of the enterosorbents with high adsorption action. This sorbent is a macroporous preparation, consists of carbon fibers and has a specific pore surface area of about 2000–2500 m^2/g [8-11].

The objective of the study The aim of our work was to study the content of reduced glutathione and the activity of glutathione-dependent enzymes in the tissues of rats during chemically induced colorectal cancer and the use of cytostatic after enterosorbent.

Materials and Methods

The study was performed on 77 white male rats (weigh 200–250 g). Laboratory animals were kept on a standard diet of the vivarium of I. Horbachevsky Ternopil National Medical University in compliance with the rules of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (Strasbourg, 1986). The study was approved by the Ethical Committee of I. Horbachevsky Ternopil National Medical University (Excerpts from Minutes N61, dated 13.11.2020).

The experimental study design comprised four groups: I – control animals, which received saline subcutaneously into the interscapular area once a week for 30 weeks; II – animals with induced adenocarcinoma of the colon; III – animals with induced adenocarcinoma of the colon and 21-day extracorporeal detoxification with the sorbent AUT-M; IV – animals with induced carcinogenesis of the colon, which after 21 days of entorosorption correction were administered for 14 days cytostatic Vincristine.

Adenocarcinoma of the colon in rats was induced by subcutaneous injection of the carcinogen DMH (Sigma-Aldrich Chemie, Japan), prediluted with saline into the interscapular area at a dose of 7.2 mg/kg [12]. DMH was administered once a week for 7 months.

In the next step of the experiment, enterosorben AUT-M was administered (*per os*) daily for 21 days to rats with simulated carcinogenesis. The daily dose of the sorbent was 1 ml of suspension (corresponding to 0.2 g of the net weight of the drug) per 100 g of the animal's body weight.

After the enterosorption correction, the animals were corrected with the cytostatic Vincristine. The drug was administered for 14 days at a dose of 0.23 mg/kg daily [13].

The rats were euthanized under deep thiopental-sodium anesthesia by cardiac puncture once per month for 7 months, and on the 14th and 21st day of the administration of the enterosorbent AUT-M.

Blood and liver samples were used for further investigations. To obtain blood serum (plasma), blood samples were allowed to clot (at room temperature for 30 min), then they were centrifuged for 15 min at 1200 g and room temperature. To prepare 10% homogenate liver samples were taken immediately after euthanasia, were cooled to 1–3°C in saline, dried with filter paper and homogenized in 0.05 M Tris-HCl buffer (pH 7.4) using a magnetic homogenizer SilentCrusher S, (Heidolp, Germany).

The state of the glutathione system was assessed in blood serum and liver homogenate by the content of reduced glutathione (GSH) and the activity of glutathione peroxidase (GPX) and glutathione reductase (GR) enzymes [14]. Enzyme activity was determined by the turbidimetric method on a semi-automatic biochemical analyzer Humalyzer 2000 using a colorimetric set of reagents Human (Germany).

Morphological study of the colon. For histological studies, the colons of experimental DMH-affected animals were taken every month for 30 weeks of the lesion, as well as on the 14th and 21st days of enterosorption therapy, as well as on the 14th day of cytostatic correction. Colon fragments were fixed in a 10% solution of neutral formalin. Further, the studied samples were dehydrated in alcohols of increasing concentration and embedded in paraffin. Sections of the examined blocks in paraffin were stained with hematoxylin and eosin. The micropreparations were studied under a Mikros 400 microscope. Microscopic images were photodocumented using a Nikon COOL Pix 4500 digital camera.

Statistical data analysis has been performed using STATISTICA 13 (TIBCO Software Inc., 2018). Parametric and nonparametric methods of evaluation of the obtained data were used for statistical processing of the results. For all indices, the arithmetic mean of the sample (M) and the error of the arithmetic mean (m) were calculated. The reliability of the difference between the independent quantitative values was determined by the normal distribution by the Student's *t*-test, in other cases – by the Mann-Whitney test. The difference between the values was considered significant at $P < 0.05$.

Results

We established that in animals with DMH-induced colon carcinogenesis, there is an increase in the content of reduced glutathione in the examined

tissues. Thus, the content of GSH in blood serum increases significantly ($P \leq 0.05$) during the first months of the experiment and exceeds the control values by 60% (3 months of DMH administration). In the following periods of modeling of carcinogenesis, there is a deficiency of GSH and a corresponding significant decrease in the content of the studied indicator in blood serum by 36% (5th month of DMH administration) and 41% (7th month of DMH administration) compare to the control (Table 1).

Since the synthesis of GSH takes place in the liver, it was expedient to determine the content of this indicator in this organ. The content of GSH increases significantly ($P \leq 0.05$) starting from the 1st month of the experiment. The maximum increase in the content of GSH in the liver tissue was established on the 3rd month of DMH administration, which exceeds the control values by 66%. In the following stages of carcinogenesis modeling, the content of GSH in the liver decreased by 53% (5th month of DMH administration) and 43% (7th month of DMH administration) relative to the control.

In the conditions of DMH-induced carcinogenesis and the corresponding changes in the content of GSH in the examined tissues, the introduction of enterosorbent contributed to the positive dynamics of the restoration of the level of GSH. Thus, on the 14th day of the sorbent action, this indicator in blood serum increased significantly ($P \leq 0.05$) by 13%, on the 21st day by 28% relative to the group of DMH-affected animals. In the liver homogenate, this indicator increased by 18%, and after 21 days – by 26% compared to the group of animals where carcinogenesis was modeled.

On the 14th day of cytostatic therapy, the content of GSH in blood serum slightly decreased relative to animals with induced carcinogenesis after 21 days of correction with an enterosorbent, but exceeded the level of rats affected by DMH for 30 weeks by 21% (Table 1). Also, carrying out cytostatic therapy contributed to a slight decrease in the content of GSH in the liver homogenate. Thus, on the 14th day of Vincristine administration, significant ($P \leq 0.05$) changes in the studied indicator were recorded, the content of GSH decreased by 16% compared to the group of experimental animals on the background of enterosorption therapy (21 days).

It is known that the enzyme glutathione peroxidase GPX is involved in the inactivation of the toxic effect of free radicals due to the oxidation of glutathione [15]. Under the conditions of modeling colon carcinogenesis, the activity of this enzyme

Table 1. The content of reduced glutathione in the blood serum and liver homogenate of rats affected by dimethylhydrazine under the conditions of simulated carcinogenesis against the background of the use of enterosorbent AUT-M and cytostatic Vincristine (M ± m, n = 7)

Group of animals/period of affection	Liver homogenate, mmol/kg protein	Blood serum (plasma), mmol/l
Control	1.40 ± 0.03	1.21 ± 0.03
1 month	1.70 ± 0.09*	1.35 ± 0.04*
2 month	1.87 ± 0.04*	1.42 ± 0.06*
3 month	2.33 ± 0.08*	1.94 ± 0.06*
4 month	1.12 ± 0.05*	1.04 ± 0.05*
5 month	0.65 ± 0.06*	0.77 ± 0.06*
6 month	0.74 ± 0.04*	0.72 ± 0.04*
7 month	0.79 ± 0.05*	0.71 ± 0.04*
7 months of DMH+AUT-M (14 days)	1.04 ± 0.03**	0.87 ± 0.05**
7 months of DMH+AUT-M (21 days)	1.15 ± 0.04***	1.05 ± 0.06***
7 months of DMH + AUT-M (21 days) + Vincristine (14 days)	0.92 ± 0.07***	0.97 ± 0.06#

Note: *significant changes between the indicators of animals of the control group and those affected by DMH; ***significant changes between the rates of carcinogenic animals after enterosorption therapy (21 days) and; *** animals receiving cytostatics (14 days); #significant changes between animals affected by the carcinogen (7 months) and animals treated with a cytostatic (14 days) in the background of enterosorption therapy (21 days)

in blood serum increased up to the 5th month of the experiment and exceeded the control indicators by 52%. The final terms of the study (7th month of DMH administration) were accompanied by a decrease in GPX activity by 48% relative to the parameters of unaffected animals. In the liver tissues, we established the maximum increase in GPX activity during the 4 months of modeling the oncoprocess, the indicator exceeded the control values by 58%. However, in the following periods of damage, a decrease in the activity of the enzyme under study was established by 62% (month 7) (Table 2).

In animals that underwent a course of extracorporeal detoxification, an increase in GPX activity was noted in the studied samples (Table 2). Within 21 days after the introduction of AUT-M in rats, there was a tendency to a significant ($P \leq 0.05$) increase in the activity of the enzyme in blood serum by 14%, in the liver by 8% relative to the group of animals with simulated carcinogenesis.

After detoxification correction with the AUT-M sorbent, the animals underwent chemotherapy with the cytostatic Vincristine. We established that in the group of animals where cytostatic correction was performed after previous detoxification, less pronounced changes in the glutathione system were detected. Thus, on the 14th day of the action of cytostatics and against the background of the use of the AUT-M sorbent, the activity of GPX increased significantly ($P \leq 0.05$) by 27% in the blood serum and by 15% in the liver tissue, compared to the indicators of experimental animals, which were injected sorbent daily, for 21 days.

The next link in the glutathione system is the glutathione reductase enzyme (GR). In the conditions of the oncological process, the activity of this enzyme increases in blood serum by 19% within 2 months. In the following periods of the experiment (5 and 7 months of DMH administration), this indicator, relative to the control, decreased by 36% and 48%, respectively. Similar changes were found in the liver tissues of experimental rats, for 1 month of administration of DMH, the activity of GR increased by 13%. Starting from the 2nd month of the experiment, the studied indicator decreased by 14%, 5th month – 27%, 7th month – 59% relative to the GP indicators in the group of control animals (Table 3).

Administration of the AUT-M enterosorbent within 21 days from the moment the animals were exposed to the carcinogen showed an increase in the

Table 2. Dynamics of changes in glutathione peroxidase enzyme activity in blood serum and liver homogenate of rats affected by dimethylhydrazine under conditions of simulated carcinogenesis against the background of the use of enterosorbent AUT-M and cytostatic Vincristine (M ± m, n = 7)

Index/Group of animals, period of affection	Blood serum (plasma), Mmol/(min l)	Liver homogenate, mmol/kg protein
Control	0.366 ± 0.014	0.413 ± 0.017
1 month	0.441 ± 0.021*	0.472 ± 0.014*
2 month	0.452 ± 0.019*	0.474 ± 0.013*
3 month	0.470 ± 0.016*	0.485 ± 0.017*
4 month	0.482 ± 0.018*	0.654 ± 0.018*
5 month	0.557 ± 0.015*	0.517 ± 0.022*
6 month	0.240 ± 0.020*	0.173 ± 0.011*
7 month	0.189 ± 0.012*	0.158 ± 0.011*
7th month DMH+AUT-M (14 days)	0.217 ± 0.012	0.177 ± 0.005
7th month DMH+AUT-M (21 days)	0.239 ± 0.013**	0.191 ± 0.005**
7 months DMH +AUT-M (21 days) + Vincristine (14 days)	0.142 ± 0.011***	0.127 ± 0.005***

Note: *significant changes between the indicators of animals of the control group and those affected by DMH; ***significant changes between the rates of carcinogenic animals after enterosorption therapy (21 days) and ; *** animals receiving cytostatics (14 days); #significant changes between animals affected by the carcinogen (7 months) and animals treated with a cytostatic (14 days) in the background of enterosorption therapy (21 days)

activity of GR. Thus, the activity of this enzyme increased by 13% in blood serum, and by 14% in the liver (Table 3).

The use of cytostatic vincristine led to a slight decrease in GR activity. In the blood serum of experimental animals, this indicator decreased by 28%, in the liver by 22% relative to the indicators of experimental animals with induced carcinogenesis.

To confirm the development of experimental carcinogenesis and the influence of corrective factors on the morpho-physiological state of the colon, we conducted histological studies. Thus, it was established that as a result of 7-month administration of DMH, severe dysplasia of the epithelium of the crypts of the large intestine is observed, which is characterized by the presence of hyperchromic nuclei and a violation of the orderliness of epitheliocytes. The nuclei of epithelial cells are hyperchromic, of different shapes and sizes, the nuclear-cytoplasmic ratio is shifted towards the nucleus, which indicates manifestations of cellular atypism. The integrity of the basement membrane is broken. These morphological changes indicate the development of adenocarcinoma in situ in the colon (Fig. 1).

As a result of enterosorption correction, an improvement in the morpho-functional state of the colon was recorded in the studied animals with induced carcinogenesis. On the 14th day of administration of enterosorbent AUT-M, after administration of DMH, desquamation of cells of single-layer cylindrical epithelium is observed at the microscopic level, pyknotic nuclei are present in a significant number of enterocytes.

In the lamina propria of the mucous membrane and the submucosal base, congestion in lymphatic vessels and capillaries was detected. The lymph nodes are somewhat hyperplastic, and there is edema around the vessels (Fig. 2).

At the optical level, it was established that on the 21st day of enterosorption therapy, under the conditions of simulated colon carcinogenesis, the state of its structural components improves. In the mucous membrane, the integrity of the epithelial lining of the crypts is preserved, hyperplasia of goblet cells is visible in some places. There is slight lymphocytic infiltration in the lamina propria (Fig. 3). Perivascular edema is observed around the vessels in the submucosal base.

Discussion

During previous research, we recognized that DMH-induced colon carcinogenesis in rats is accompanied by disturbances in the antioxidant defense system (significant decrease in the activity of

Table 3. Glutathione reductase activity in the blood serum and liver of rats in the dynamics of DMH lesions and against the background of the use of enterosorbent AUT-M and the cytostatic Vincristine (M ± m, n = 7)

Index/Group of animals, period of affection	Blood serum (plasma), Mmol/(min l)	Liver homogenate, mmol/kg protein
Control	0.381 ± 0.019	0.476 ± 0.019
1 month	0.435 ± 0.013*	0.540 ± 0.018*
2 month	0.454 ± 0.018*	0.411 ± 0.015*
3 month	0.304 ± 0.025*	0.290 ± 0.023*
4 month	0.283 ± 0.022*	0.311 ± 0.020*
5 month	0.242 ± 0.018*	0.348 ± 0.025*
6 month	0.225 ± 0.017*	0.211 ± 0.022*
7 month	0.196 ± 0.010*	0.193 ± 0.010*
7 month DMH+AUT-M (14 days)	0.224 ± 0.006*	0.234 ± 0.012*
7 month DMH+AUT-M (21 days)	0.246 ± 0.013**	0.256 ± 0.015**
7 months DMH + AUT-M (21 days) + Vincristine (14 days), *n* = 7	0.140 ± 0.013***	0.150 ± 0.015***

Note: *significant changes between the indicators of animals of the control group and those affected by DMH; ***significant changes between the rates of carcinogenic animals after enterosorption therapy (21 days) and ; *** animals receiving cytostatics (14 days); #significant changes between animals affected by the carcinogen (7 months) and animals treated with a cytostatic (14 days) in the background of enterosorption therapy (21 days)

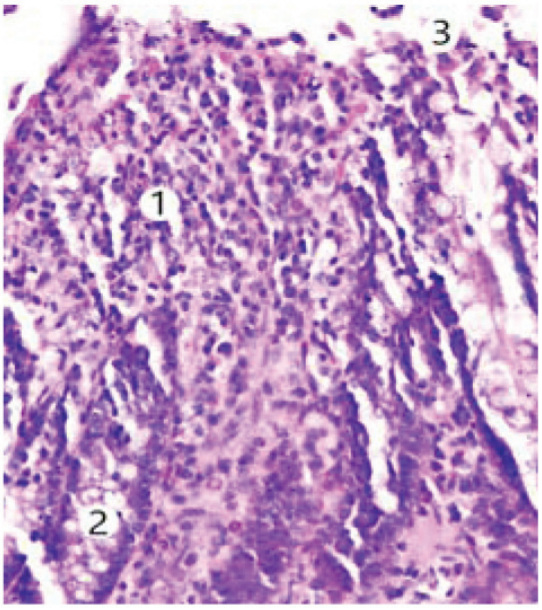

Fig. 1. Microscopic changes in the large intestine of an animal 7 months after chronic DMH exposure. Dysplasia of the epithelium of the mucous membrane (1), crypt (2), erosion of the epithelium of the mucous membrane (3). Staining with hematoxylin and eosin (×400)

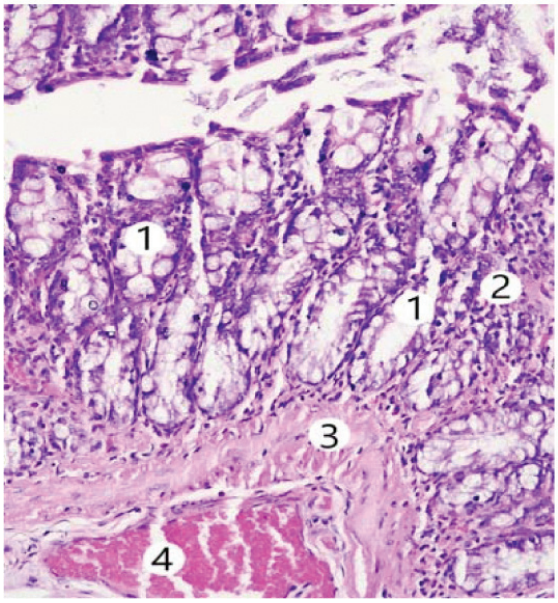

Fig. 2. Histological changes in the large intestine of an animal on the 14th day of AUT-M application after 7 months of chronic DMH exposure. Crypts (1), lymphocytic infiltration of the lamina propria (2), muscular lamina of the mucous membrane (3), vein (4). Staining with hematoxylin and eosin (×200)

SOD, CAT) and activation of free radical oxidation processes (significant increase in OMP) in blood serum and liver homogenate [16, 17]. Taking into account that the above indicators of antioxidant system (AOS) are involved in the neutralization of ROS at the beginning of the genesis of the free radical chain, it was reasonable to study the content of GSH and glutathione-dependent enzymes in rats with induced colon carcinogenesis and under conditions of cytostatic correction against the background of enterosorption.

The system glutathione peroxidase – glutathione reductase – reduced glutathione plays the main role in the destruction of hydroperoxides formed during the activation of free radical processes [4, 5, 18]. GSH performs the function of the main modulator of the enzymatic redox system of glutathione, as well as the activity of glutathione-dependent enzymes. According to the results of our research, it was found that at the initial stages of modeling carcinogenesis, the content of GSH in the blood serum and liver of animals increases, but the following periods of the experiment are accompanied by a decrease in the studied indicator in the corresponding tissues. Also, we investigated the

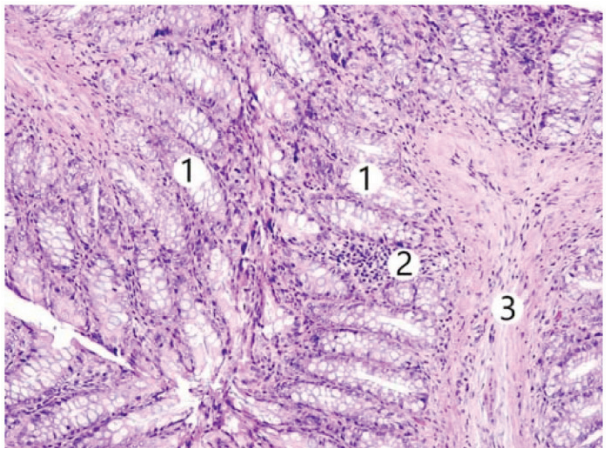

Fig. 3. Microscopic changes in the large intestine of an animal on the 21st day of AUT-M use after 7 months of chronic DMH exposure. Crypts (1), lymphocytic infiltration of the lamina propria (2), submucosal base (3). Staining with hematoxylin and eosin (×200)

decrease in the activity of glutathione-dependent enzymes glutathione peroxidase and glutathione reductase in blood serum and liver of rats with DMH-induced carcinogenesis [19, 20]. An increase in the

level of GSH in the liver and blood serum of animals in the early stages of the study is quite natural, since this is the main organ of GSH biosynthesis. Also, the obtained results may indicate the inclusion of GSH, as an antioxidant, in the process of neutralization of free radicals in the DMH-affected organism already at the initial stages of the research [21].

The deficiency of GSH content, registered in the later periods of the study, is consistent with the data given in a number of literature sources, which indicate that the decrease in the level of GSH in the later periods of induced carcinogenesis may be associated with increased vulnerability of cells to oxidative stress, inflammation, and the progression of the tumor process [1, 3, 22].

The results of our research indicate an increase in the activity of the researched enzyme in the liver and blood serum of animals during the first months of modeling the oncological process. On the other hand, at later times of the experiment, the activity of GPX decreased significantly. A decrease in the activity of the GPX enzyme may result from depletion of the GSH pool during antiradical activity, increased sensitivity to O_2^-, which can be inhibited by GPX.

At the same time, an increase in GSH activity was recognized in the first months of DMH administration. The GR enzyme maintains a high intracellular concentration of GSH due to the reduction of the oxidized disulfide form of glutathione with the involvement of NADPH, which may indicate the active involvement of the GR enzyme in the process of restoring the oxidized form of glutathione [23].

The results of our research, which indicate changes in the concentration of GSH, the activity of GR and GPX, can be used as a marker of the negative impact of many toxicants, which is confirmed by the research of scientists [5, 24].

Correction with AUT-M enterosorbent helps restore the functional activity of the glutathione system. A significant ($P \leq 0.05$) increase in the content of GSH in the blood serum and liver of animals with simulated carcinogenesis after the use of the sorbent was revealed. It was established that enterosorbent AUT-M provides a increase in the activity of GR and GPX enzymes both in blood serum and in the liver homogenate of rats with DMH-induced colon carcinogenesis. Our results are consistent with previously cited scientific data indicating that oral charcoal enterosorbents can repair damage caused by ROS. Such sorbents can absorb toxins of exo- and endogenous origin, including products of peroxidation of lipids and proteins [5, 24]. This process probably occurs due to osmosis or diffusion through the walls of the capillaries of the villi of the small intestine with subsequent fixation on the sorbent [20, 21].

Antitumor drug Vincristine belongs to alkaloids of pink periwinkle. However, the action mechanism of this cytostatic is associated with a number of side effects. In particular, the formation of free radicals, the development of oxidative stress, increased endogenous intoxication and toxic cell damage [25-27]. However, we found that the administration of Vincristine to rats with DMH-induced carcinogenesis after 21 days of enterosorption with AUT-M sorbent has little effect on the state of the glutathione system. In particular, the content of GSH in the liver and blood of the studied rats decreases slightly. A slight decrease in the activity of glutathione-dependent enzymes was also noted in the examined tissues of animals with a simulated tumor process against the background of extracorporeal detoxification with the AUT-M sorbent. The obtained results probably indicate the mitigation of side effects of chemotherapy, after the application of enterosorbtion correction before chemotherapy.

Histological studies of the colon of rats with simulated carcinogenesis established the development of cellular atypism and violation of the integrity of the basement membrane. These morphological changes indicate that long-term administration of the carcinogen DMH contributes to the development of adenocarcinoma in the colon. However, extracorporeal decoction with AUT-M sorbent improves the condition of the structural components of the colon.

Conclusions. Carbon enterosorbent AUT-M has a positive effect on oxidation processes in rats under conditions of induced carcinogenesis. As a result of the sorption of exo- and endogenous toxins, the activity of the glutathione system is restored, which plays an important role in the implementation of anti-radical and anti-peroxidase protection of cells.

Also, previously carried out detoxification therapy helps to restore the protective capabilities of AOS and probably increases the resistance of experimental animals to the toxic effect of cytostatics.

The received results can become the basis for further study of the possibility of using enteral sorption therapy in patients with colorectal cancer in order to reduce the side effects of chemotherapy and facilitate the course of the disease.

Conflict of interest. Authors have completed the Unified Conflicts of Interest form at http://ukr-biochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

ЕНТЕРОСОРБЕНТ АУТ-М СТАБІЛІЗУЄ СИСТЕМУ ГЛУТАТІОНУ У ЩУРІВ ІЗ ДИМЕТИЛГІДРАЗИН-ІНДУКОВАНИМ РАКОМ ТОВСТОЇ КИШКИ, ЯКІ ОТРИМУВАЛИ ВІНКРИСТИН

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Колоректальний рак є однією з провідних причин смертності у світі. На сьогоднішній день ведуться пошуки нових методів терапії цього захворювання, які могли б корегувати стан оксидативного стресу за розвитку новоутворень. Метою дослідження було вивчення рівня відновленого глутатіону та активності глутатіонзалежних ензимів за розвитку 1,2-диметилгідразин-індукованого раку товстої кишки за умов використання вінкристину і ентеросорбенту АУТ-М. Рак товстої кишки індукували введенням щурам-самцям підшкірно диметилгідразину (7,2 мг/кг) протягом 30 тижнів. Щурам із раком товстої кишки перорально вводили ентеросорбент у дозі 0,2 г на 100 г маси тіла щоденно протягом 21 дня. Після детоксикаційної терапії щурам щоденно вводили цитостатик вінкристин (0,23 мг/кг) протягом 14 днів. Встановлено зниження вмісту відновленого глутатіону, активності глутатіонредуктази та глутатіонпероксидази в крові та тканині печінки щурів із колоректальним раком. Показано ефективність застосування ентеросорбенту АУТ-М для стабілізації показників глутатіонової системи щурів з індукованим раком товстої кишки. Цитостатик вінкристин суттєво не впливав на зміну досліджуваних показників, що підтверджує ефективність попередніх сорбційних заходів.

Ключові слова: колоректальний рак, вінкристин, енторосорбент, глутатіон, глутатіонредуктаза, глутатіонпероксидаза, кров, печінка.

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