

Influence of cadmium chloride and enterosorbents on the lymph dynamics and lymph components

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ABSTRACT

The effects of cadmium ions and sorbents on lymphatic dynamics and lymph composition were studied. Experiments showed that prolonged cadmium chloride poisoning (orally) in rats causes changes in the biochemical composition and physicochemical parameters of lymph and blood plasma. After rats were intoxicated with cadmium chloride for 30 days, an increase in the volume of the cervical and mesenteric lymph nodes was observed. They were edematous and distended, and the superficial blood vessels in the node capsule were dilated. A decrease in lymph flow from the intestinal lymphatic vessel and a decrease in blood pressure were observed. A decrease in the viscosity of the dry residue of blood plasma and lymph was observed after rat poisoning with cadmium ions. An accumulation of cadmium ions was noted in the lymph nodes, where their concentration increased by 5-7 times from the baseline. Preliminary administration of sorbents significantly reduced the negative effect of cadmium on lymphatic dynamics and lymph parameters. The natural sorbent tagan enhances the detoxifying functions of the lymphatic system, enhancing tissue drainage and the elimination of cadmium ions from the body.

Keywords: Lymph, Lymphodynamics, Blood, Plasma, Tagan sorbents.

Article type: Research Article.

INTRODUCTION

Simultaneously, a new ecological environment has emerged, to which not only humans but also flora and fauna have proven evolutionarily unadapted. All these factors lead to deteriorating human health, economic losses, and the extinction of many animal and plant species. Under these conditions, the development of scientific foundations and practical measures to enhance the body's resilience and its resistance to damaging environmental factors has become increasingly important (Sinicropi *et al.* 2010; Genchi *et al.* 2020; Chen *et al.* 2022; Charkiewicz *et al.* 2023). Large quantities of gaseous, liquid and solid waste from industrial production enter the natural environment. Various chemical substances, getting into the soil, air or water and passing along ecological links from one chain to another, eventually enter the human body (Carocci *et al.* 2014; Mezynska *et al.* 2018; Balali-Mood *et al.* 2021) and lead to poisoning with the subsequent development of various specific symptoms (Jung *et al.* 1993; Tungushbaeva *et al.* 2025). Among the wide variety of unfavorable environmental factors affecting the body, a special place is occupied by heavy metal salts, in particular cadmium (Chen *et al.* 2015; Schaefer *et al.* 2020). Exposure to heavy metals significantly disrupts the structural and functional properties of cell membranes. Lipid oxidation alters membrane fluidity, reduces the stability of the phospholipid layer, and disrupts ion channel function. These changes disrupt the ionic balance between the intracellular and extracellular spaces. Furthermore,

increased membrane permeability enhances the release of intracellular enzymes, leading to increased levels in the blood and lymph (Boujelben *et al.* 2006; Haouem *et al.* 2013; Rafati *et al.* 2017; Franzoni *et al.* 2022). When cadmium ions enter the body from the environment, they accumulate in organs and subcellular structures, primarily in the kidneys and liver of animals. It has been established that exposure to heavy metal salts in rats causes some changes in bodily functions and in the biochemical parameters of lymph and blood (Abdreshov *et al.* 2018; Abdreshov *et al.* 2021). Cadmium, entering the body of animals and humans, binds with proteins, forming strong compounds and causing long-term toxic effects on the nervous system, reproductive function, and development. It alters the blood-brain conductivity of external systems and microvessels, is absorbed by the membrane, penetrates into erythrocytes, then combines with plasma proteins and penetrates into other tissues (Hladky *et al.* 2016; Helms *et al.* 2020). Excretion from the body is carried out in various ways - through the gastrointestinal tract (15-20%), kidneys (30-5%), salivary glands (20-25%) and other organs (Satarug 2018; Davidova *et al.* 2024). In industrial workers, exposure to cadmium salts has led to cardiovascular, renal, hepatic, and other organ dysfunction. The condition of the lymphatic system in chronic cadmium ion poisoning has not been studied, although the major role of the lymphatic system in tissue drainage, fluid deposition and the body's immune responses is known. Due to the many functions that the lymphatic system performs, like the vascular system, it is of great importance for maintaining balance in the body (Abdreshov *et al.* 2019; Musaeva *et al.* 2025), has great functional significance in normal and pathological processes of the body (Borodin 2005; Sapin 2007; Abdreshov *et al.* 2024) and is generally known for its participation in lymphatic drainage in ionic, water and metabolic processes in the body during various changes. The lymphatic system, performing protective and adaptive functions, undergoes a number of changes under the influence of external environmental factors (Bridenbaugh *et al.* 2013; Gorchakova *et al.* 2021). In cases of poisoning with heavy metal salts, including cadmium salts, it is currently necessary to clarify the mechanism of the negative impact of cadmium ions on the body. At the same time, studying methods for restoring organ function after damage has become relevant in the modern era. Currently, extensive material has been accumulated on the use of enterosorbents in medicine; the mechanisms of action of enterosorbents on the body in various types of pathology have been described (Järup 2003; Mikhalevsky *et al.* 2021). In recent years, one of the new areas of medicine has been the removal of toxic substances from the body using various sorbents. Sorbents vary in nature. Natural bentonites of plant and soil origin, that is, soils containing various mineral substances in pure form, as well as artificial synthetic sorbents. That is, at present, science widely uses the removal of toxic substances from biological fluids by the body using various sorbents (Murisasco *et al.* 1986; Fatullayeva *et al.* 2021). Based on the above, it seems relevant to study the role of lymph nodes in the adaptive responses of the body to the action of heavy metals and methods for correcting the identified disorders using enterosorbents. The aim of this study is to investigate hemo- and lymphodynamics in moderate intoxication of rats with cadmium chloride and methods of detoxification of the body.

MATERIAL AND METHODS

Animal use

The experiments were conducted on mature laboratory rats weighing 250 ± 5 g. The rats were fed according to the standard vivarium diet. Three groups of rats were formed: Group 1 - control (12 rats), Group 2, which received cadmium chloride (CdCl_2) per os at a dose of 1.5 mg kg^{-1} with drinking water for 30 days (20 rats), Group 3, which received cadmium chloride with drinking water and additionally a natural tagan-sorbent at a dose of 1 g kg^{-1} (20 rats). All experiments with animals were conducted in strict accordance with the rules developed and approved by the local Ethical Committee of the Institute of Genetics and Physiology, Protocol No. 12-314 of November 11, 2022, as well as in accordance with the rules of bioethics approved by the European Convention for the Protection of Vertebrates (Strasbourg, 1986) and the guidelines outlined in the European Union Directive 2010/63/EU of September 22, 2010, "On the protection of animals used for scientific purposes". At the end of the experiment, on the 30th day, lymph, blood, and urine samples were collected from the rats under ether anesthesia while they were still alive. Lymph was recorded and obtained from the intestinal lymphatic vessel using a graduated microcannula, and lymph, blood, and urine samples were collected for analysis.

Rheological property analysis and biochemical blood test

In all groups of animals, the determination of the viscosity of whole blood, lymph and concentrated erythrocyte suspensions was studied using a capillary viscometer (Baskurt *et al.* 2003); the clotting time of blood and lymph was determined using the generally accepted method according to Sukharev. Measurement of blood and lymph

viscosity was determined with the capillary tube viscosimeter and compared to LS300 (KSP V-4, Rehomed GmbH, Aachen, Germany). Viscosity was determined by estimating the flow time of a known volume of liquid under the influence of applied pressure in a horizontal capillary with a working mouth radius of about 0.3 mm and thermostatically controlled at 37 °C. Determination of hematocrit index (Ht) was determined by the generally accepted method: hematocrit capillaries were filled with whole blood and centrifuged for 7 minutes at 12,000 g. Determination of osmotic pressure of lymph, blood plasma and urine was measured using an OMCK-01 osmometer (Russia). The operating principle of the device is based on changing the freezing temperature of a bio fluid depending on the concentration of soluble compounds contained in it. Physical and chemical parameters of blood, lymph and its morphological composition were studied on a hematological analyser SMEX KX-219 9 (Japan) and oxygen tension and pH of blood and lymph on an OPTI CCA-TS2 Blood Gas and Electrolyte Analyser (USA). In animals, the ion content was determined in the blood, lymph and urine electrolytes using an ABL 615/625 analyzer from Radiometer (Germany). Rats were placed in exchange cages with a wire floor to collect 24-hour urine. Determination of biochemical parameters and urine cells was carried out using a CL-50Urine Analyser High Technology (USA). In lymph and blood samples, the level of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), the content of total protein, alkaline phosphatase, urea, creatinine were determined using a standard test system (Abdreshov *et al.* 2015), in accordance with the attached instructions with further processing of the results obtained on the analyser "COBOS INTEGRA 400" (USA). The content of cadmium ions in the blood, liver tissue and lymph nodes was determined by emission spectral analysis using an SFAA S3 atomic absorption spectrophotometer (Japan). The homeostasis disorders caused by CdCl₂ were corrected by tagan adsorbent (1 g kg⁻¹). Tagan adsorbent is a natural substance, a kind of bentonite. It consists of montmorillonite of the aluminosilicate class (90-95%) and is characterized by high swelling capacity, dispersion, and exchange complex. Tagansorbent has a microporous structure, contains hydrophilic and hydrophobic centers, due to which it firmly sorbs microbial cells, their toxins and other compounds. Tagansorbent is a pink variety of bentonite from the Taganskoye deposit. It is alkaline in chemical composition and consists of 90-95% montmorillonite, an aluminosilicate. It is 98% Na-montmorillonite and exhibits high swelling properties, fine dispersion, and an exchange complex. This therapeutic and preventive preparation was registered as a drug in the Republican List approved by the Public Health Committee of the Republic of Kazakhstan (December 30, 1998; Sapargaliev *et al.* 2001).

Statistical analysis

The experimental results were processed by the method of variation statistics on a computer (Microsoft Corporation, Washington, DC, USA) using Student's t-test. The mean ± standard deviation (SD) was calculated and expressed as a percentage. Significance testing was performed using Fisher's t-test and Student's t-test to evaluate differences in mean values. The results were considered significant at $p < 0.01$, $p < 0.05$.

RESULTS

After intoxication of rats with cadmium chloride for 30 days (Group 2), an increase in the volume of cervical and mesenteric lymph nodes was detected. For example, the average cervical lymph node length in control rats was 2 ± 0.1 mm, while in Group 2 it ranged from 5 ± 0.1 to 6 ± 0.1 mm, with isolated cases reaching 10 ± 0.1 to 12 ± 0.1 mm. The mesenteric nodes also increased in size by 2-2.5 times. They were edematous, distended, and hyperemic, with dilated superficial blood vessels within the node capsule. A 22% decrease in lymph flow from the intestinal lymphatic vessel and a 10% decrease in blood pressure were observed (Table 1). A decrease in the viscosity of the dry residue of blood plasma and lymph was found after poisoning rats with cadmium ions. A slight increase in blood plasma volume (according to hematocrit) was observed. It should be noted that the addition of sorbent to the food of rats contributed to the restoration of the ratio of plasma and red blood cell volumes. Fig. 1 shows that the blood plasma volume, measured by hematocrit, decreased in rats in Group 3 compared to Group 2, reaching the control group level. The volume of the red blood cell portion of the blood increased accordingly. A study of hematological parameters showed that blood counts in laboratory rats at day 30 after cadmium salt poisoning and after sorbent correction were statistically significantly different from those in the corresponding control group. Red blood cell and hemoglobin counts decreased by 20% and 13%, respectively. White blood cell and lymphocyte counts by day 30 were 15-15.5% higher than baseline values. Neutrophil, basophil, and eosinophil counts showed a tendency to increase, and by day 30 were 22-24.7% higher than baseline values. According to the data presented in Table 2, it is evident that the level of leukocytes in the blood of rats receiving Tagan-sorbent increased by 7.5%, and in the lymph by 9.3%. After correction of changes in blood composition with Tagan-

sorbent by the 30th day, the content of erythrocytes and hemoglobin was characterized by a decrease of 15 and 8.1%, respectively, compared to the experimental group.

Table 1. Indicators of lymph flow and physico-chemical parameters of lymph and blood before and after feeding rats with cadmium chloride and sorbents.

Indicators	Control group (12 rats)	Cadmium poisoning (20 rats)	Cadmium poisoning + tagan-sorbent (20 rats)
Blood pressure (mmHg)	100 ± 3	92 ± 4	100 ± 4
Lymph flow (mL min ⁻¹)	0.53 ± 0.001	0.42 ± 0.001**	0.45 ± 0.001**
Hematocrit (%)	48.2 ± 0.02	56.8 ± 0.01**	45.6 ± 0.05**
Blood pH	7.40 ± 0.05	7.29 ± 0.03	7.33 ± 0.03
Lymph pH	7.56 ± 0.08	7.42 ± 0.02	7.49 ± 0.02
Osmotic pressure, blood plasma (mosm L ⁻¹)	280 ± 4.5	290 ± 5.1	295 ± 6.7
Osmotic pressure, lymph (mosm L ⁻¹)	275 ± 8.9	284 ± 7.3	281 ± 3.8
Blood coagulation (time, s)	250 ± 2.4	290 ± 3.8**	263 ± 1.6*
Lymph coagulation (time, s)	337 ± 4.9	276 ± 6.2**	298 ± 7.7*
Blood viscosity (mPa s ⁻¹)	4.3 ± 0.6	3.2 ± 0.7*	3.8 ± 0.7
Lymph viscosity (mPa s ⁻¹)	1.7 ± 0.04	1.2 ± 0.02*	1.6 ± 0.03

Notes: Reliable in comparison with the control group, *p < 0.05, **p < 0.01.

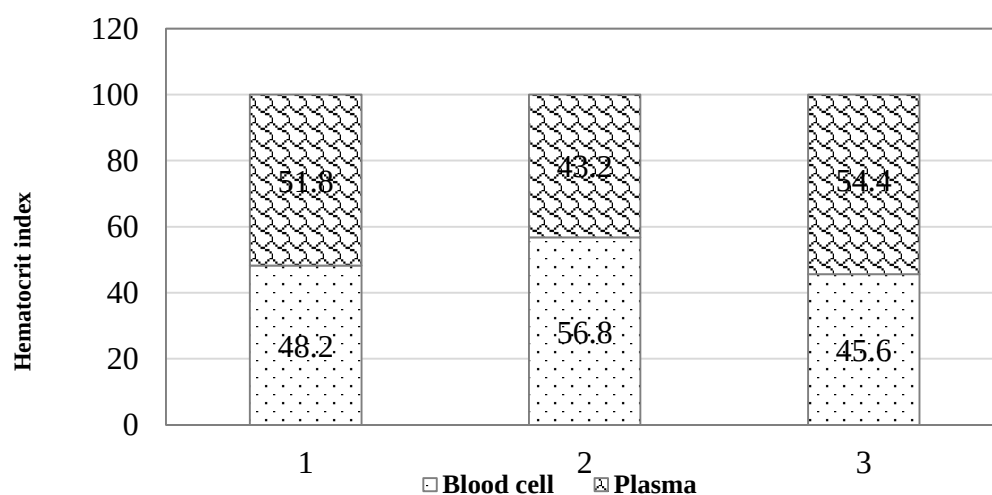


Fig. 1. Changes in the hematocrit index in cases of cadmium chloride poisoning and administration of sorbents. Designations: ordinate axis: hematocrit index. X-axis: 1 – Control group, 2 – Poisoning with CdCl₂, 3 – CdCl₂ + tagan sorbent.

The total number of basophils, eosinophils, and monocytes in the blood increased by 9% after administration of Tagan-sorbent, while the granulocyte level increased by 18%. These figures indicate that administration of Tagan-sorbent to rats after poisoning increased their body's defenses against various factors. Lymphocytes are the primary effector and regulatory cells of the immune system, as well as the cells responsible for the development of adaptive and immune responses. These indicators increased by 5.9% after the use of Tagan-sorbent, and by 23.8% in lymph.

Table 2. Peripheral blood parameters in rats with cadmium poisoning and after its correction with sorbent.

Indicators	Control group (12 rats)	Cadmium poisoning (20 rats)	Cadmium poisoning + tagan-sorbent (20 rats)
Erythrocytes (RBC; g L ⁻¹)	5.45 ± 0.12	4.38 ± 0.01*	5.03 ± 0.008
Hemoglobin (HGB; g L ⁻¹)	125.4 ± 2.5	109.6 ± 2.9**	118.1 ± 2.3**
Platelets (PLT; g L ⁻¹)	580.8 ± 4.1	526.3 ± 3.9*	569.9 ± 4.7*
Leukocytes (10 ⁹ L ⁻¹)	5.3 ± 0.002	6.1 ± 0.001**	5.7 ± 0.008*
Neutrophils (10 ⁹ L ⁻¹)	3.7 ± 0.004	4.6 ± 0.006**	4.2 ± 0.001
Lymphocytes (10 ⁹ L ⁻¹)	4.5 ± 0.04	5.2 ± 0.01***	4.9 ± 0.003**
Monocytes (10 ⁹ L ⁻¹)	1.5 ± 0.01	1.2 ± 0.01**	0.1 ± 0.003*
Basophils (10 ⁹ L ⁻¹)	0.1 ± 0.002	0.122 ± 0.003	0.11 ± 0.006
Granulocytes, (10 ⁹ L ⁻¹)	1.0 ± 0.003	0.4 ± 0.001**	0.58 ± 0.005*
Eosinophils (g L ⁻¹)	0.3 ± 0.005	0.07 ± 0.003	0.18 ± 0.007

Notes: * – p < 0.05; ** – p < 0.01; *** – p < 0.001 – reliability of distinctions between control and experienced groups.

The study showed a significant decrease in total protein levels in blood plasma and lymph (Table 3). These data indicate a decrease in the metabolic function of the lymphatic system. Total protein levels did not change significantly throughout the experiment. After using the Tagan sorbent, the total protein level in the lymph increased by 8.8% and 11.7%, in blood plasma by 10% and 10.7%, and the albumin index by 9.8% and 5.9% in the lymph and by 9.6% and 7.9% in blood plasma.

Table 3. Effect of tagan-sorbent on biochemical parameters of lymph and blood of rats.

Indicators	Control group (12 rats)	Cadmium poisoning (20 rats)	Cadmium poisoning + tagan-sorbent (20 rats)
Lymph			
Albumin (g L ⁻¹)	10.1 ± 0.07	11.09 ± 0.09*	10.7 ± 0.11
Total protein (g L ⁻¹)	39.3 ± 4.4	42.5 ± 5.9	43.9 ± 4.8*
Glucose (mmol L ⁻¹)	9.35 ± 0.5	13.9 ± 0.8*	10.22 ± 0.9
ALT, ed/l	150.0 ± 10.8	152.5 ± 13.4	102.5 ± 12.1
AST, ed/l	80.0 ± 11.5	92.9 ± 7.1*	120.5 ± 8.4*
Cholesterol (mmol L ⁻¹)	0.39 ± 0.02	0.46 ± 0.03*	0.40 ± 0.03
Lipids LDL (mmol L ⁻¹)	0.37 ± 0.04	0.42 ± 0.06	0.38 ± 0.05
Bilirubin (μmol L ⁻¹)	1.50 ± 0.04	1.9 ± 0.05*	1.65 ± 0.05*
Creatinine (μmol L ⁻¹)	44.5 ± 3.8	59.1 ± 4.3*	55.4 ± 5.3*
Urea (mmol L ⁻¹)	3.90 ± 0.20	5.00 ± 0.6*	4.8 ± 0.4*
Triglycerides (mmol L ⁻¹)	3.7 ± 0.05	4.1 ± 0.07	3.9 ± 0.06
Alkaline phosphatase (U L ⁻¹)	180 ± 17.0*	217 ± 19.0*	194 ± 16.7
Blood plasma			
Albumin (g L ⁻¹)	23.9 ± 0.10	26.2 ± 0.08*	25.8 ± 0.09
Total protein (g L ⁻¹)	63.4 ± 2.11	69.9 ± 3.71*	70.3 ± 3.10*
Glucose (mmol L ⁻¹)	12.55 ± 0.81	16.29 ± 0.95*	15.41 ± 0.99
ALT (ed L ⁻¹)	154.7 ± 6.17	223.0 ± 8.46*	211.3 ± 9.21*
AST (ed L ⁻¹)	118.4 ± 5.27	188.7 ± 6.36*	143.2 ± 6.88*
Cholesterol (mmol L ⁻¹)	0.48 ± 0.03	0.56 ± 0.01*	0.54 ± 0.02
Lipids LDL (mmol L ⁻¹)	0.39 ± 0.01	0.46 ± 0.01*	0.45 ± 0.02*
Bilirubin (μmol L ⁻¹)	16.3 ± 0.41	20.4 ± 0.50*	17.5 ± 0.66
Creatinine (μmol L ⁻¹)	45.1 ± 4.22	56.8 ± 3.15*	55.6 ± 4.51*
Urea (mmol L ⁻¹)	3.4 ± 0.05	4.58 ± 0.05*	4.44 ± 0.06*
Triglycerides, (mmol L ⁻¹)	0.84 ± 0.03	0.93 ± 0.02*	0.88 ± 0.04
Alkaline phosphatase (U L ⁻¹)	264.2 ± 10.41	305.0 ± 12.21*	278.5 ± 11.43

Note: reliable compared to control, - $p < 0.05^*$; - $p < 0.01^{**}$.

There was an increase in the level of glucose in the lymph and blood, as well as an upraise in the level of plasma cholesterol, high-density lipoproteins (HDL) and low-density lipoproteins (LDL) compared to the control group. Biochemical indicators of the lymph were slightly reduced after taking the tagan-sorbent, but were significantly higher than in the control group. According to Table 3, after taking the sorbent, in the experimental groups, compared to the control group, ALT indicators in the lymph increased by 16.1% and 28.1%, while AST indicators by 1.7% and 3.1%. The level of ALT in the blood was 46.9% and 11.5%, while AST was 44.0% and 36.6%. The level of alkaline phosphatase in the lymph and blood increased by 15.4%-20.6% after using the sorbent. After using tagan-sorbent, the level of bilirubin in the lymph decreased by 13%, and in the blood by 10.2%, but it is observed that they are higher than in the control group. It is also possible to observe that the level of creatinine in the lymph increased by 24.5%, the level of urea by 23.1%, and the indicators in the blood plasma increased by 25.9-36.6%, respectively, compared with the experimental group (Table 3). It should be noted that after using Tagan-sorbent, the level of triglycerides in rats increased by 10.8% and 5.4% in the lymph, and by 10.7% and 4.8% in the blood. Also, the levels of ALT and AST increased, which in turn indicates an elevation in the activity of lipid metabolism and the regulatory role of the liver with an upraise in the body weight of rats (Table 3). Studies of the blood of white rats poisoned with cadmium and given Tagan-sorbent indicate less pronounced changes in hematological and biochemical parameters than in control groups of animals (Fig. 2). Cadmium ion levels in the blood and tissues of animals exposed to cadmium chloride increased sharply after poisoning. In the blood, concentrations rose from $0.05 \pm 0.001 \mu\text{g kg}^{-1}$ in the control group to $0.24 \pm 0.03 \mu\text{g kg}^{-1}$ after 30 days of exposure to cadmium chloride (Group 2). Cadmium levels were even higher in the cervical and mesenteric lymph nodes (Fig. 3). These data indicate a 5-7-fold increase in cadmium ion levels in the blood and tissues compared to baseline values after chronic cadmium chloride poisoning. The accumulation of cadmium ions in the lymph nodes leads to decreased lymphatic transport and tissue drainage. In these experiments, cadmium ion levels were

determined in the blood and several organs of rats, specifically the lymph nodes (LNs) and liver of intact rats (Group 1), after cadmium chloride poisoning (Group 2), and after administration of sorbents (Group 3).

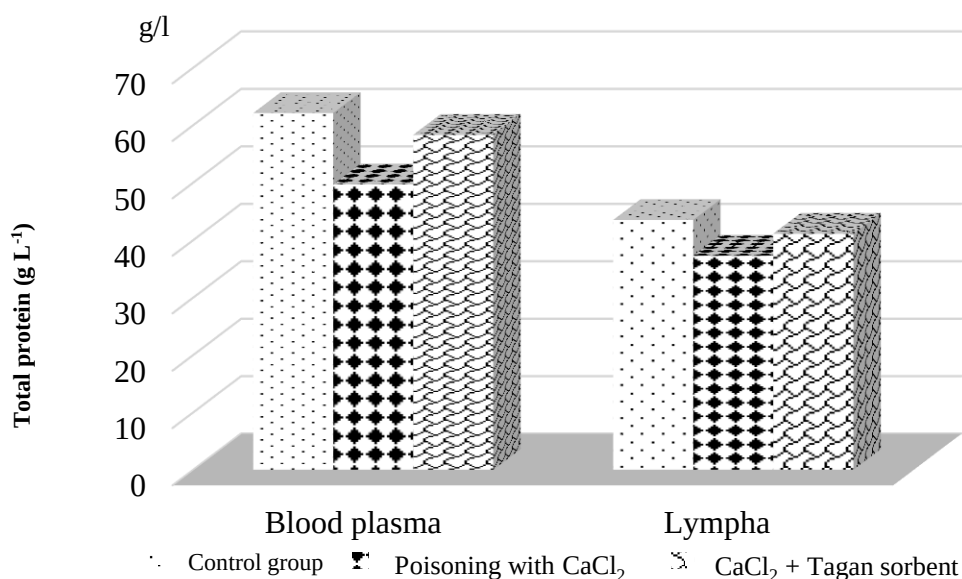


Fig. 2. Total protein content in blood plasma and lymph in the control, after poisoning with cadmium chloride and administration of enterosorbents. Designations: ordinate axis: total protein content in g L⁻¹. X-axis: 1 – control group, 2 – group receiving cadmium chloride, 3 – group receiving cadmium chloride and Tagan-sorbent.

According to the data obtained, cadmium ion levels in rats are normally low (Group 1). However, after chronic poisoning of rats with cadmium chloride (1.5 mg kg⁻¹ per os) for 30 days, cadmium ion levels in the blood, lymphoid organs, and liver increased sharply. In the blood plasma of rats in Group 2, their levels increased by 480% and in the liver by 750%, i.e., 7.5 times, 633% in the cervical lymph nodes, and 700% in the mesenteric lymph nodes compared to the intact rats. Data on cadmium ion levels in the blood and various organs of intact rats, rats poisoned with cadmium chloride, and those treated with sorbents are presented in Table 4. These data show that the lymph nodes and liver accumulate cadmium ions that enter the body, fulfilling their protective functions. The accumulation of cadmium ions in the lymph nodes leads to a decrease in lymphatic transport through the lymph nodes. The enlargement and hyperemia of the lymph nodes after cadmium ion poisoning, as noted above in this section, is caused by the accumulation of cadmium ions in their tissues, leading to tissue proliferation due to the activation of their immune defenses.

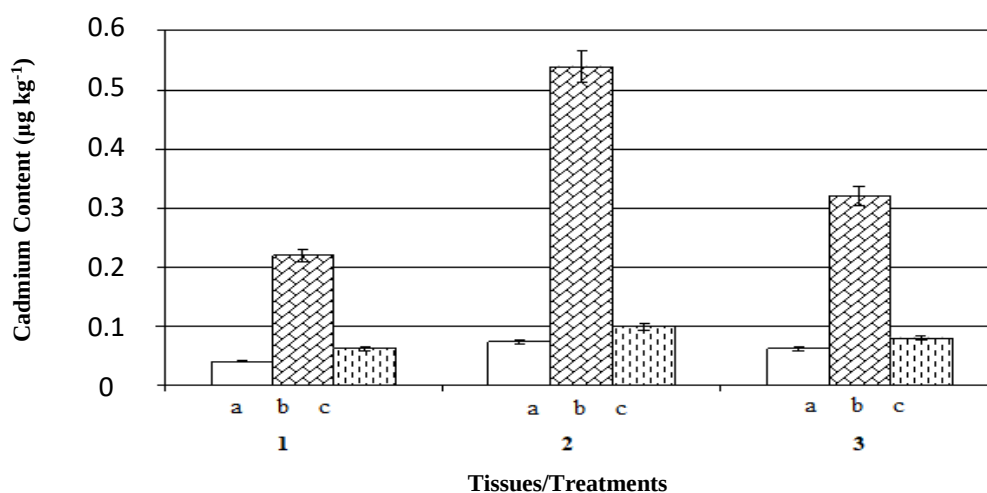


Fig. 3. Content of cadmium ions before and after 30 days of oral administration of CdCl₂ separately and in combination with enterosorbents. Designations: along the ordinate axis – concentration of cadmium ions in µg kg⁻¹, along the abscissa axis – groups of animals in the form of columns: 1 – blood, 2 – mesenteric node, 3 – cervical node, a – control group, b – after administration of cadmium chloride, c – after the use of cadmium chloride and Tagan-sorbent.

Table 4. Content of cadmium ions ($\mu\text{g kg}^{-1}$) in the blood and some organs of rats.

Name of organs	Control group (12 rats)	Cadmium poisoning (20 rats)	Cadmium poisoning + tagan-sorbent (20 rats)
Blood	0.050 ± 0.001	$0.24 \pm 0.03^{**}$	$0.10 \pm 0.001^*$
Liver	0.060 ± 0.001	$0.45 \pm 0.03^{**}$	$0.10 \pm 0.001^*$
Cervical lymph nodes	0.062 ± 0.001	$0.38 \pm 0.03^{**}$	$0.12 \pm 0.002^*$
Mesenteric lymph nodes	0.070 ± 0.002	$0.50 \pm 0.04^{**}$	$0.20 \pm 0.001^*$

Note: * - reliable compared to control, $p < 0.05$. ** - $p < 0.01$.

DISCUSSION

The above data demonstrate that moderate, long-term cadmium intoxication in animals negatively impacts the internal environment, lymphodynamics, and biochemical composition of blood and lymph. Lymph flow and arterial pressure, total protein content, dry matter, lymph and blood viscosity, and plasma ion concentrations were reduced. Blood and lymph are the main fluid systems that ensure the stability of the internal environment of the body and work in close interaction to maintain physiological homeostasis. The function of these systems is not limited to the transport function, but also ensures the harmonious functioning of metabolic, regulatory and protective processes in the body. Through blood and lymph, not only oxygen and nutrients are delivered to cells, but also metabolic products, carbon dioxide and various metabolites are removed. In this regard, the relative stability of their biochemical composition is considered an important indicator of the normal functional state of the body (Abdreshov *et al.* 2024). In rats chronically poisoned with cadmium chloride, plasma sodium levels increased slightly, by only 2% compared to Group 1. Chloride levels fluctuated within physiological limits. Plasma potassium levels decreased sharply in rats poisoned with cadmium ions. They decreased significantly by 42% compared to intact rats. Changes in blood ion composition after cadmium intoxication indicate dysfunction of the excretory system. Plasma potassium levels in rats sharply decreased after cadmium poisoning, likely due to impaired renal potassium reabsorption. A slight increase in plasma sodium and chloride levels led to water retention, i.e., it promotes water accumulation in tissues and its influx into the bloodstream and lymphatic system, increasing the plasma portion of the blood, and inhibited the elimination of cadmium ions from the body. In this regard, the decrease in viscosity, dry residue, and protein content in the lymph and blood plasma, which may be directly related to hydermia, becomes understandable. As can be seen from the data obtained, after cadmium intoxication in rats, the total protein content in plasma and lymph decreased, while the plasma fraction of the blood increased. A simultaneous decrease in blood and lymph viscosity indicates their dilution. These facts suggest a decrease in lymph formation after cadmium ion administration to animals, and consequently, a reduction in lymph flow. Blood tests in white rats, cadmium-poisoned laboratory rats, and those treated with enterosorbent after 30 days indicate less pronounced changes in hematological and biochemical parameters than in control groups. In subsequent series of experiments, rats received cadmium chloride and sorbents (Group 3 rats) to detoxify the body and rapidly remove cadmium ions. A domestically produced sorbent of natural origin, "Tagansorbent," used in Kazakhstan, generally meets these requirements. The use of the sorbent in our experiments demonstrated positive results. Tagan-sorbent has a microporous structure, which allows it to firmly adsorb toxins and other compounds. This sorbent possesses high adsorption properties and is fully suitable for use in our experiment against the background of cadmium chloride. Experiments have shown that the use of Tagan-sorbent improved lymph parameters and structural changes in lymph nodes and vessels (Abdreshov *et al.* 2009), and other researchers have shown that the use of fermented milk product had positive effects on blood biochemical parameters during cadmium intoxication (Attia *et al.* 2014; Nadirova *et al.* 2022). Protein concentrations in the lymph and blood plasma of rats in Group 3, which received the sorbent, increased but did not reach control levels (Table 1, Group 1). Physicochemical parameters were within control limits, slightly exceeding their levels in intact rats (Table 1, Group 1). Cadmium ion levels in the blood and lymph node tissue decreased sharply in rats receiving the sorbent, remaining slightly above background levels (Fig. 1). All indicators of enzymatic activity in the lymph also showed an increase of 20-25%, as well as the level of bilirubin pigment and creatinine. The elevation in bilirubin and creatinine is probably associated with the increase in body weight of animals when fed a protein-rich diet and feed additives. Lymph nodes perform numerous functions in the body, the most important of which include storage, transport, barrier, and metabolic functions. In extreme situations, lymph nodes can store significant amounts of extracellular fluid and accumulate heavy metals in cases of poisoning (Iannitti *et al.* 2010; Leong *et al.* 2022). Under normal conditions, the biochemical composition of blood plasma is a reflection of all the main metabolic processes in the body. It includes high-molecular compounds (proteins), energy metabolism

products (glucose, and lipids), electrolytes, enzymes, hormones, and nitrogen metabolism products. Each of these components performs a specific physiological function, and their concentration is strictly regulated. The stability of biochemical indicators in blood plasma is based on the coordinated work of neurohumoral regulatory mechanisms, and their deviations are considered an early sign of pathological changes in the body. Based on the results of these series of experiments, it can be concluded that preliminary prophylactic administration of tagan-sorbent to animals before acute poisoning with doses of CdCl_2 and their administration during and after poisoning had a positive effect on the body's resistance to the damaging effects of the toxicant, as well as on lymphodynamic indicators and biochemical indicators of lymph. The use of enterosorbents significantly reduced the negative effect of cadmium ions on lymphatic dynamics and lymph composition. After administration of Tagan-sorbent, physicochemical and biochemical parameters of blood plasma and lymph were restored to insignificant levels (Table 1). Increased lymph flow after administration of enterosorbents accelerated the removal of cadmium ions from the microcirculation zone. Cadmium ion concentrations in the blood and lymph nodes decreased to control values (Fig. 1). Tagan-sorbent, by adsorbing cadmium ions on its surface, reduces the potential for these ions to accumulate in the blood and body tissues. These data indicate that cadmium ions have a significant inhibitory and damaging effect on the transport and barrier-protective functions of the lymph nodes and vessels. Thus, prolonged moderate poisoning of rats with cadmium ions inhibits lymphatic dynamics, tissue drainage, and reduces a number of physicochemical and biochemical parameters of lymph and blood plasma. The use of enterosorbents effectively reduces the negative impact of cadmium ions on the body's homeostasis. These facts indicate that Tagan-sorbent, by adsorbing cadmium ions on its granules, permanently detoxifies tissues, enhances lymph flow, and consequently tissue drainage and the removal of toxicants from the body. According to the obtained data, the use of enterosorbents protects the function of lymphatic vessels and nodes from the damaging effects of cadmium ions. Tagan-sorbent enhances the detoxifying functions of the lymphatic system, increasing the removal of cadmium ions from the body.

CONCLUSION

The results of this study indicate that when exposed to extreme factors, the body's adaptive responses involve the lymphatic system. This involvement manifests itself in changes in lymph flow, lymph node motility, and lymph composition, which are aimed at reducing the negative impact of extreme factors on the body. Chronic cadmium chloride intoxication of animals leads to decreased lymph flow, hyperemia and hyperplasia of the lymph nodes, accumulation of high doses of cadmium ions in the lymph nodes and liver, and changes in the biochemical and physicochemical parameters of the lymph and blood plasma. After 30 days of cadmium chloride intoxication of rats, a 2-3-fold increase in the volume and linear dimensions of the cervical and mesenteric lymph nodes, edema, and swelling were observed. The use of Tagan-sorbent significantly reduced the negative effects of cadmium ions on lymphatic dynamics and lymph composition. In experiments, the use of the sorbent (1 g kg^{-1}) as a detoxifier reduced the negative effects of cadmium ions on lymph flow and lymph composition, which were disrupted by the introduction of cadmium chloride into the body with drinking water. Total protein levels in the lymph and blood plasma of rats in both groups differed slightly from the control. Cadmium ion concentrations in the blood, liver, and lymph nodes decreased several fold, exceeding control values by 12-15%. Tagan-sorbent, by adsorbing cadmium ions on its surface, reduces the potential for these ions to accumulate in the blood and body tissues. A relative restoration of osmotic pressure, dry residue, and lymph and blood viscosity was observed, along with increased lymph flow and normalization of lymph and plasma biochemical parameters. Cadmium ion concentrations in the blood, liver, and lymph nodes decreased. According to the data obtained, the use of the sorbent protects the structure and function of the lymphatic system from the damaging effects of cadmium ions. Sorbents enhance the detoxifying functions of the lymphatic system, enhancing tissue drainage, and, as detoxifiers, reduce the negative impact and facilitate the elimination of cadmium ions from the body.

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