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Nemoros
Hlavní kancelář: Rybná 716/24
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The East European Center of Fundamental Researchers
Rubna 716/24
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Vydavatel
Nemoros
Hlavní kancelář: Rybná 716/24
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CONTENTS

INVESTIGATION OF THE EFFECT OF CADMIUM AND KUPRUM ON THE DIGESTIVE SYSTEM OF LIVING ORGANISMS (LITERATURE REVIEW)

Vera Shatorna,
Doctor of Biological Sciences, Professor,
Irina Kononova,
Candidate of Biological Sciences,
Senior lecturer at the Department of Medical Biology,
Pharmacognosy and Botany,
Kateryna Rudenko,
Lecturer of the Department of Medical Biology, Pharmacognosy and Botany,
SE"Dnipropetrovsk Medical Academy of the Ministry of Health of Ukraine"

Annotation. *The article provides an overview of the literature on the problems of the accumulation and effects of cadmium and kuprum compounds on the human and experimental animals, on the digestive system. Cadmium has been shown to have toxic effects during prolonged administration of low doses, causing pathological changes in various organs and systems. The level of Kuprum in the body varies depending on age, body condition, pregnancy and more. The effects of different doses of cadmium and copper on the overall course of embryogenesis and morpho-functional status of the small intestine remain unresolved.*

Key words: *cadmium, cuprum, toxicity, environment, metallothioneins, liver, small intestine.*

Anthropogenic load to date has reached a critical level. Environmental quality has now become a vital problem. Heavy metals remain one of the priority groups of pollutants with local, regional and global distribution. A large number of chemicals entering the body of water, with industrial wastewater, can enter the human and animal body and cause morbidity. The toxicity of heavy metals depends on the concentration, duration of action, temperature, water saturation with oxygen, and many other factors. Features of toxic action of heavy metals are the versatility of their impact on living organisms as common plasma poisons and the ability to form complexes with cell components, amino acids, proteins and radicals [1].

The purpose is to analyze the results of scientific studies of biomedical guidance on the effect of cadmium and kuprum compounds on small intestinal morphogenesis in both adult and embryonic animals.

Modern researchers, biologists and physicians are increasingly paying attention to trace elements and trace elements. A new direction in medicine and ecology - medical microelementology, which studies the peculiarities of the elemental composition of the human body in various functional states and diseases and ways of increasing the adaptive-adaptive functions of the organism through the correction of trace element metabolism, has been created and is successfully developing [2]. The stability of the chemical composition is one of the most important and necessary conditions for

the normal functioning of the body. Deficiency of vital trace elements and increased concentration of toxic in the environment lead to adverse effects on human life It is known that a number of mass diseases of humans and animals are associated with man-made geochemical anomalies in the environment, and develop on the background of immunodeficiency. One of the main reasons for this is considered to be excessive content in the body of trace elements that have carcinogenic and toxic effects. Such trace elements include chromium, cobalt, nickel, zinc, cadmium, which cause the development of various pathologies, especially in the digestive system [3].

The perception of chemical stimuli, including heavy metals, is due to chemoreceptors - specialized cells, which transform the stimulus stimulus energy into signals that provide information about the active agent to the nerve centers. In the course of evolution, chemoreceptors have become sensitive to the perception of individual properties of substances, allowing mammals to subtly analyze and respond in a timely manner to chemical changes in their habitat. Changes in behavioral responses are usually the most obvious indicator of toxicity, indicating the negative effects of exposure to pollutants [4].

Cadmium (Cd) is a heavy metal classified in the second hazard class and tends to accumulate in the body. Heavy metal poisoning occurs when it enters the stomach or by inhalation. Cadmium has a gonadotropic, carcinogenic, mutagenic, embryotropic and nephrotoxic effect. Changes in the intensity of free radical reactions underlie the genotoxic action of Cadmium, lipid peroxidation with impaired DNA replication [5].

Upon admission through the gastrointestinal tract, the adsorption of Cd averages 5%, with a change in the composition of the intestinal microflora. Cadmium is much more absorbed in the digestive tract of children and young animals than in adults. The intestinal epithelium, in turn, plays a major role in the natural biological barrier, reflecting the body's ability to resist the action of various exotoxicants, including Cd. One of the risk groups for the accumulation of cadmium in the body is children, and therefore the study of the effect of this heavy metal on the developing organism is very relevant [6].

The influence of Cd on the human body takes place in the production of electroplating elements, in the melting of metals, in photography, in the production of batteries and batteries, x-ray screens, the manufacture of cigarettes, fertilizers, in the aircraft and automotive industries. An increased risk of acute cadmium vapor poisoning is observed in welders, soldering irons and jewelers working with alloys of this metal. Absorbed cadmium is accumulated in the kidneys and liver as a complex with metallothionein. In erythrocytes and soft tissues, Cd binds to α2-macroglobulin and albumin. Cadmium binds to sulfhydryl groups of proteins, which subsequently leads to the denaturation and inactivation of enzymes; free radical oxidation in cells increases and mitochondrial activity is inhibited [7]. The clinic for acute poisoning is characterized by headache, nausea, dizziness, epigastric pain, pallor, sweet taste in the mouth. Chronic poisoning is characterized by a decrease and loss of smell, neurasthenic, asthenoneurotic, hypothalamic syndromes with autonomic disorders. With further development of intoxication ulcers and perforations of the nasal septum, nasal bleeding, chronic obstructive pulmonary diseases, gastrointestinal disorders, liver damage appear [8].

The maximum permissible concentration of cadmium oxide in the workplace is 0.1 mg / m3 in air. At high occupational risk of cadmium poisoning, urine proteinuria is regularly analyzed. In the absence of its and other symptoms of poisoning, a concentration of 15 mcg of cadmium per 1 g of creatinine is considered acceptable, although kidney damage is sometimes observed at a concentration of 5 mcg per 1 g of creatinine. The half-life of cadmium from mammals has been estimated at more than 20 years, with the exception of impaired renal function as urinary excretion increases. In chronic poisoning Cd, its concentration in the urine, which reflects the slow release from the liver of the complex with metallothionein, better reflects the total content in the body than the concentration in the blood [2].

The intake of Cd with food into the human body can and drinking water most often occurs through vegetables, fruits, meat and fish, which can contain up to 10-20 mcg / kg of cadmium, but high Cd content is found in mushrooms and seafood (over 100 mg / kg, namely thousands of mcg) [9]. Tobacco smoke has been found to be a significant additional source of Cd in the human body: people who smoke cigarettes additionally receive 5–60 mcg of Cd per day. According to the requirements of the World Health Organization (WHO), the level of Cd in the human body from all sources should not exceed 400-500 mcg / week. Large doses of cadmium can cause embryotoxic and gonadotoxic effects, and thus affect reproductive function [10].

The most dangerous among cadmium compounds are oxide and simple cadmium salts, in particular cadmium chloride, which causes dystrophic changes in the liver and kidneys [5]. Less soluble compounds of this metal affect the respiratory tract and gastrointestinal tract (GIT), and more soluble compounds after absorption into the blood affect the central nervous system (CNS). The distribution and accumulation of Cadmium in the body and its excretion largely depend on the pathways of receipt of this element [11]. When cadmium enters the small intestine, it can disrupt its digestive function. The process of absorption of cadmium ions in the intestine is characterized by its rapid accumulation in the mucous membrane and subsequent slow flow into the circulation system [12].

The possibility of formation of cadmium complexes with metallothioneins of the small intestinal mucosa, which are released on the serous surface of the intestine and provide the flow of cadmium to the kidneys, liver and other organs, has been shown [13]. After single intraperitoneal administration of cadmium to mice after 3 hours, its maximum concentration is observed in the liver (40%), moderate in the small intestine (17%) and kidneys (12%), and low - in the heart, lungs and spleen (4%) [5].

Cadmium is found in the body in almost all animals (in terrestrial animals on average about 0.5 mg / kg in weight, and in marine animals - 0.14-3 mg / kg), although the physiological role has not been established to date. It should be noted that, depending on the geographical region, the level of Cd in the human body is different. In the countries of New Zealand, USA, Europe this figure reaches 8-30 mkg per day, and in Japan it is much higher [13]. It is obvious that cadmium affects the carbohydrate metabolism, the synthesis of hypuroic acid in the liver, the activity of some enzymes, as well as

the exchange of copper, zinc, iron and calcium in the body. Some studies suggest that microdoses of food in cadmium may contribute to mammalian growth processes, and on the basis of which some Cd is classified as an essential micronutrient, although this position is highly debatable [14].

Although Cd has not been considered a mutagenic agent for many years, recent studies show that Cd induces gene mutations, impairs DNA repair, and causes oxidative damage [3].

The high rate of Cd accumulation is determined by the intestinal mucosa and the low rate of diffusion transfer to the blood. Partially in the intestine and then in the liver, Cd binds to metallothioneins. The formed Cd-MTN gradually enters the proximal tubules of the kidneys, where chronic toxicity of Cd is manifested.

Cd accumulation in hepatocytes is slowed by Zn, as is the case with some other metals; calcium in this case is little effective. Also, the accumulation of cadmium in the intestine is associated with zinc. The cessation of zinc cadmium accumulation in the small intestine of rats has been shown to be independent of Cd concentration and not of a competitive nature in experimental conditions. Increased intake of Zn enterocytes after its deficiency in tissues was not accompanied by simultaneous stimulation of CD accumulation [15]. However, J.E. Hoadley and R. Cousins [14] showed that in vitro experiments on the intestine as a whole, competition between Cd and Zn persists, and not only in the segments of the small intestine. The absorption of zinc in the intestinal lumen is complex. The endogenous metallothionein formed in the intestine must penetrate the serous side of the mucous membrane and deliver Cd-MTN to other organs, facilitating the transport of Cd into the kidneys [15].

Cd in tissues of the liver, kidneys and erythrocytes binds to sulfhydryl groups of proteins - metallothioneins, which leads to their denaturation and inactivation of enzymes. MTN synthesis is induced in response to the entry of Cd into the body and increases with increasing dose [8]. This protein binds up to 80% of cadmium in the liver, and induction plays a protective role. Scientists have suggested that MTNs reduce or eliminate the toxic effects of this element. However, the formation of these complexes inhibits the release of cadmium from cells and promotes its intracellular accumulation, which leads to dystrophic intracellular changes [2, 9].

The role of metallothioneins is well known in the transport and metabolism of zinc and copper, however, the mice lines with the damaged metalothionein synthesis gene (MTN) live long enough and under normal retention conditions are quite viable [7]. In the case of cadmium poisoning, fatty liver infiltration and hepatocyte dystrophy are observed. The general structure of hepatocytes is not disturbed, but subsequently increases in size, and nuclei reach different sizes, with the duration of intoxication the depth of dystrophic processes in hepatocytes increases. Dystrophic changes in them gradually developed into destructive disorders [16].

Ukrainian researchers have studied in the liver of rats that once single parenteral administration of rodents at doses of 1.8 mg / kg and less Cd does not cause hepatotoxicity, but at injections at doses of 3.5-3.8 mg / kg reveal inflammation, necrosis and fibrosis in

the liver, and under conditions of oral admission, liver necrosis occurs only at very high doses of Cd (30–138 mg / kg per day) [17].

Scientists of Ternopil region in case of poisoning with cadmium chloride solution of experimental white rats, intraperitoneally, at the dose of 6 mg / kg of body weight, revealed structural restructuring of the vessels of the hemomicrocirculatory bed of the hollow and ileum, which significantly influenced the state of hematopoiesis. This study allowed us to establish the age-specific features of vascular remodeling of the hemomicrocirculatory bed of the small intestine of experimental animals in poisoning of the body with cadmium chloride, which make it possible to predict the likely destructive and regenerative changes of the small intestine in these pathology conditions [18].

The distribution, absorption and toxic effects of cadmium compounds in the body are influenced by the content of copper, zinc and other elements in the diet. Copper and zinc inhibit the deposition and absorption of cadmium [10, 15].

Cuprum (Cu, copper) is one of the indispensable trace elements in humans and animals, a cofactor of many enzymes and a component of Cu-containing proteins. As part of these biomolecules, it is involved in important metabolic processes. Kuprum is of great importance in phenolic, nitrogen, nucleic and auxin metabolisms. Due to the need for the functioning of the nervous, immune and hematopoietic systems, angiogenesis, hemostasis, formation of bone and cartilage tissues, maintaining the elasticity of connective tissue, keratinization and pigmentation of the skin, Kuprum cations are indispensable for the growth and development of post-organism animals ontogenesis, as well as during pregnancy and lactation [13, 20]. Copprum is of great importance in improving the immunobiological resistance and resistance of the body to the harmful effects of environmental factors.

Foods (2-3 mg per day), including meat, liver, seafood, cereals, nuts and seeds, are the main sources of copper intake, and animals receive it from plant foods. The absorption processes of Kuprum cations occur mainly in the small intestine. From the portal vein, this element is transported to the liver and from there to cells of all organs and tissues. However, only a third of the total amount of Kuprum that comes into the body during the day is absorbed into the bloodstream in the gastrointestinal tract, and the rest turns into insoluble compounds and is excreted. In general, an adult contains 100-150 mg of copper, with about 10% of this amount coming from liver cells. The reserve in the liver maintains a constant level of Kuprum in the blood and supplies the trace element to other organs [21]. The decrease in the content of cuprum is most often observed as a result of an overload of its antagonists (cadmium, lead, zinc, iron, selenium, molybdenum, boron) or malabsorption syndrome [20].

Cu absorption occurs in the stomach and small intestine, the mucous membrane of which contains copper transport proteins, in particular metallothionein, which forms complex compounds with copper. Protect Cu + / Cu2 + initiated copper binding proteins from free radical reactions. The transport of copper from the cells of the mucous membrane into the portal vein occurs through ATPase p-type. Copper enters the liver through a portal vein with a blood flow. The function of transporting copper to the fetus

instead of albumin is performed by α-fetoglobulin [22].

Micronutrients play the role of regulators of the most important chemical processes in metabolism, and during pregnancy their role is significantly increased. The physiological development of mammalian pregnancy is characterized by an increase in the content of kuprum in the organs and tissues of the mother and fetus. The high content of Cu in the tissues is especially necessary to create an adequate level of synthetic processes that provide energy and growth of the tissues and organs of the fetus. To meet these needs, certain changes occur in the body of the mother, namely the absorption of kuprum is increased, instead of its excretion, on the contrary, is reduced [20]. Thus, increasing the content of kuprum in the body of pregnant rats is a natural and physiologically necessary process [21].

The transport of individual metals, in particular of copper, through the basolateral membrane of the enterocyte is an energy-dependent process. This leads to the emergence of competitive relationships during their absorption from the small intestine into the blood [9, 23].

In hepatocytes, copper binds to metallothionein. Violation of the regulation of the biosynthesis of metallothionein, which leads to an increase in its synthesis and to the accumulation of copper in liver cells, occurs primarily in some genetic diseases. The excess copper leads to impaired excretion of lysosomes, which remove the copper-thionein complex from the plasma. It should be noted that the delay in the release of copper from the cell leads to the induction of biosynthesis of metallothionein, forming a closed circle. Metallothionein-bound copper in hepatocytes is a part of Cu-containing enzymes, in particular ceruloplasmin, which contains about 75% of plasma copper, which performs the functions of amino oxidase, ferroxidase and superoxide dismutase in the body, plays the role of acute organism in the process of acute organism a protein that transfers copper to tissue enzymes, primarily to cytochrome oxidase, and protects lipid membranes from peroxidation [14, 19].

In the gastrointestinal tract, sulphurous is absorbed, which is subject to competitive inhibition by other metals, including zinc [15]. The presence of dietary proteins and amino acids, ascorbic acid, fructose, dietary fiber can affect the absorption of copper from the gastrointestinal tract. The content of kuprum in plasma is regulated by neurohumoral mechanisms. In hyperthyroidism in humans, there is an increase in the level of this trace element in the blood, and with hypofunction of the thyroid gland - a decrease. This metal has a pronounced anti-inflammatory effect, softens the manifestation of autoimmune diseases and helps maintain the normal structure of collagen and elastin [5]. Copper deficiency interferes with the formation of heme and the absorption of iron in the intestines of mammals. Accumulating in tissue and organ cells, Cd and its compounds adversely affect most systems of humans and animals. Absorption on Cd membrane transport is carried out by means of transport systems of essential divalent metals. The binding of Cd to molecules of specific proteins of metallothionein reduces the intensity of metabolism in mammals and the toxicity of cellular structures [1, 9].

Conclusions. Our analysis of recent research results shows that cadmium

compounds are highly cumulative and highly toxic substances (second toxicity class), and environmental degradation and industry development have led to increased levels of cadmium in the environment. Important role among the chemical elements is played by cuprum, the content of which often depends on the content of other elements, can normally change the quantitative indicators depending on age, health, gender. However, the data on the influence of the above microelements on the small intestine morphology and the morphogenesis of the digestive system are disparate and contradictory and need further investigation.

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