The article discusses the role of magnesium in the body, which is one of the main intracellular elements that plays a leading role in the activity of vital organs, participates in many cellular functions including signal transmission, energy production, protein metabolism, and acts as a molecular stabilizer for RNA and DNA ribosomes. Hypomagnesemia leads to disturbances in the cardiovascular, nervous, immune, and digestive systems. Based on magnesium, mono (magnesium sulfate, magnesium citrate, etc.) and complex preparations (MagneВ6, Maalox, ATP forte, etc.) have been created and are being created. Imbalances in magnesium content are associated with the development of cardiovascular diseases such as arterial hypertension, arrhythmias, heart failure, as well as the occurrence of neurodegenerative diseases of the CNS (parkinsonism, Alzheimer’s disease, dementia), as magnesium is involved not only in nucleic acid metabolism but also in signal transmission in the CNS. Therefore, monitoring magnesium levels in the cardiovascular, nervous, and other systems may be a target for the influence of magnesium preparations. In individuals with digestive tract diseases, changes in magnesium content have also been identified in the cardiovascular system and CNS. Changes in magnesium content are associated with the occurrence of cardiovascular and digestive tract diseases in children, as well as the course of pregnancy in women. This indicates the need for further research into the properties of this trace element in normal and pathological conditions, as well as the search for new methodological approaches to determining its functional impact on the human body.

Key words: magnesium, physicochemical, biochemical, pharmacological properties.
Periodic table, was first obtained in 1809 by English scientist Humphry Davy through electrolysis and was named “magnesium” from the French word “magnifique,” which means “magnificent.” This element justifies this name, as evidenced by its involvement in improving endothelial function and its role in the metabolism of vital organs [1-2]. The total content of magnesium in the body of an average adult human is about 1000 mmol or 24 grams. Cells contain about 40-50% of the total magnesium content, while the rest is found in muscles. 96% of magnesium is intracellular. This element has become known not only due to the introduction of magnesium-containing drugs into medical practice, but also due to their wide application in various industries and agriculture [3]. The literature data presented in the review determine whether the pathogen exhibits consequences of diseases associated with changes in magnesium content in the body [4-5].

The aim of the study.

To analyze the physicochemical, biochemical, pharmacological, clinical properties of magnesium and its preparations, and the spectrum of their application in clinical practice.

Object and methods of research.

The research was conducted based on a literature review, including PubMed, Google Scholar, Scopus, on the topic of the study.

Results of the research and their discussion.

Magnesium is considered as biometal, along with potassium, calcium, zinc, cobalt, manganese, molybdenum, iron, and copper. Although the content of biometals in the body is small, they determine the coordination of processes of excitation, contraction, relaxation of muscles, transmission of impulses in the nervous and cardiovascular systems, and functioning of other vital systems [6]. Magnesium ions play an important role in the regulation of almost all organs and systems. Magnesium acts as a structural component of cells, serving as a trigger, allosteric effector, or modulator of a wide range of energy and plastic reactions.

Comparison with calcium, magnesium ions are more hydrated and have a pronounced ability to form coordination bonds with biomembrane elements, forming coordination ligands. As the concentration of magnesium increases, its ability to form complexes decreases, while for calcium, it increases. Inorganic salts and hydroxides of magnesium are well or moderately soluble in water and are strong electrolytes. Even though the four elements – potassium, calcium, sodium, and magnesium – play an important role in the body, magnesium ranks second in terms of content in organs and systems after potassium [7]. Magnesium not only competes with calcium, but also prevents the influx of sodium into cells. This may be related to the unidirectional effect of magnesium and potassium on the activity of Na+ + K+ -ATPase, as well as the magnesium-sodium antiporter. For example, the introduction of magnesium prevents cardiomyocytes from losing potassium and calcium, and from the influx of sodium. Magnesium participates in energy metabolism, specifically in the metabolism of adenosine nucleotides, the conversion of ADP to ATP with the participation of inorganic phosphorus, and the breakdown of ATP to ADP through complex formation with both adenosine nucleotides.

Magnesium promotes the conversion of adenosine monophosphate into cyclic adenosine monophosphate by influencing adenylate cyclase. Approximately five hundred proteins are associated with magnesium ions through the carboxyl group, and magnesium serves as a cofactor in about 350 enzymes. Magnesium interacts with membrane-polarizing groups. It also forms complexes with glucose, with the stability of magnesium-glucose complexes being greater than that of calcium, which is attributed to electrostatic interactions. For coordination compounds, the entropy contribution is higher for magnesium-glucose complexes, while the enthalpy contribution is lower for calcium-glucose complexes. Magnesium complexes with glucosamine are more stable than calcium-glucosamine complexes. Magnesium participates in glycolysis, oxidative phosphorylation, and is required for the synthesis of RNA and DNA, as well as for the functioning of mitochondria. Magnesium enzymes are involved in protein synthesis, muscle contraction, nervous function, glycemic control, ionic fluxes, especially calcium channels [8].

After magnesium intake through water and food, a person weighing 70 kg contains 25-28 grams of magnesium in various tissues: 50-53% in bones, 27-28% in muscles, 19-20% in other soft tissues, 0.5% in erythrocytes, and 0.3-0.4% in blood plasma. Like calcium, magnesium participates in enterosorption in the gastrointestinal tract, renal reabsorption and secretion, and exchange processes in various organs, forming magnesium depots (e.g., in bones) [9]. This contributes to maintaining a beneficial level of calcium in bones and supporting the crystalline lattice of tooth enamel [10]. Hypermagnesemia, a condition where the total serum magnesium level exceeds 1.2-1.3 mmol/L, is a less common phenomenon. It can occur in chronic kidney diseases, acute renal failure, excessive magnesium therapy, epilepsy, eclampsia, and prolonged stress. Adrenergic stimulation of lipolysis can increase magnesium deficiency by forming complexes of magnesium with fatty acids. Thromboxanes and endothelins, which are formed because of fatty acid metabolism, contribute to this condition.

Physical and emotional stresses increase the need for magnesium. Magnesium plays a significant role in the functioning of neurotransmitter systems. It acts as an agonist of glutamate receptors and participates in the activation of ATP-dependent potassium channels, blocking the influx of calcium through voltage-gated calcium channels. Magnesium is an agonist of GABA-A receptors and an antagonist of angiotensin II receptors, activating neurotransmission associated with protein kinase C function [11]. The use of lithium medications may lead to hypermagnesemia, where the level of magnesium in the blood increases parallel to the concentration of calcium. Hypomagnesemia is more commonly encountered in clinical practice. Hypomagnesemia is observed in severe conditions of patients, including critical illnesses and certain diseases of vital systems and organs. This primarily applies to stress situations accompanied by increased levels of catecholamines and glucocorticoids. In this case, there is an increase in magnesium excretion in urine. Stress, elevated catecholamine levels, increase the frequency of cardiovascular events, including arterial hypertension. Hypomagnesemia is observed in cases of inadequate intake of magnesium from food, exposure to pesticides in the gastrointestinal tract, decreased vitamin D levels, consumption of hard water, and alcohol. Hypomagnesemia may be caused by medications such as H1 and H2 histamine.
Magnesium is involved in cell proliferation processes, depending on the state of the nervous system and homeostasis. The magnesium content significantly decreases in severe diseases such as carcinogenesis and diabetes mellitus [2]. Studies on endothelial cells have shown that magnesium transports the TRPM7 potential receptor [15]. Magnesium content changes proportionally with changes in cognitive function [16]. The magnesium content in cerebrospinal fluid correlates with the magnesium content in erythrocytes, and the magnesium content in the pituitary gland determines the ability to memorize, which is somehow related to DNA structure. Studies focusing on determining magnesium levels in cells and intercellular fluid have established its direct influence on human health [17]. Magnesium deficiency is often associated with deficiencies in potassium, copper, zinc, and less commonly chromium, cobalt, or nickel in blood serum. It is known that a decrease in magnesium levels is accompanied by an increase in calcium concentration, which is observed in type 2 diabetes. It is important to note that magnesium deficiency contributes to potassium exchange disorders, which play a role in cardiovascular pathology. Decreased magnesium content may be associated with increased excitability of the nervous system, and in cardiomyocytes, it may lead to tachycardia and ectopic arrhythmia. Decreased magnesium concentration in smooth muscle cells leads to increased blood pressure and headaches, as well as cramps, abdominal pain, bronchospasm, and uterine hypertonicity [18]. Long-term magnesium deficiency can lead to the development of cardiovascular and cerebral pathological conditions, such as heart attack, stroke, and atherosclerosis. Magnesium deficiency not only contributes to the onset of these diseases, but also to their severe course. Currently, there are many magnesium preparations available in various doses and different pharmaceutical forms, including inorganic salts such as sulfate, chloride, hydroxide, oxide, and salts of organic acids. Inorganic magnesium salts have low bioavailability, which is why magnesium sulfate is prescribed as a laxative and detoxification agent. Organic magnesium salts have significantly higher bioavailability, making them more relevant for use, such as magnesium citrate, lactate, orotate, pyroglutamate, and others. Organic magnesium salts are better absorbed, better tolerated, and less likely to cause side effects. Treatment with magnesium will be more effective when combined with magnesium fixatives such as vitamins B1 and B6, glycine, orotic acid, and others. Different magnesium salts have their own indications, for example, magnesium citrate is used in nephrolithiasis, and magnesium hydroxide is used as an antacid.

Vitamin B6 is the main regulator of magnesium in the human body, as both magnesium and B6 are important for the prevention of endothelial dysfunction in arterial hypertension, carbohydrate and lipid metabolism, and mitochondrial function. There is a correlation between the development of ischemic heart disease and these micronutrients. Therefore, Magnesium-B6, a preparation consisting of magnesium citrate and pyridoxine, is used to replenish magnesium stores [19]. Asparks (Panangin), which contains potassium and magnesium aspartates, also has high bioavailability. Aspartate anions are absorbed by the body and enter metabolic pathways (amino acid metabolism, urea cycle, Krebs cycle) without burdening the excretory systems, and intensify the detoxification of nitrogen metabolism products in the kidneys. This is important for the prevention of arterial hypertension, as increased levels of uric acid and decreased magnesium levels can trigger arterial hypertension. Therefore, magnesium and potassium ions are necessary for reducing and normalizing systolic and diastolic blood pressure in hypertension. Systematic depletion of magnesium stores contributes to the development of chronic endothelial inflammation, increased risk of cardiovascular and cerebrovascular diseases, and may also lead to insulin resistance, intolerance, and diabetes [19-23].

In this pathology, magnesium deficiency is associated with intensified free radical reactions, oxidative stress, and inflammation. Magnesium preparations are effective in blocking IL-1β, one of the main inflammatory factors. These preparations also have anti-inflammatory effects by suppressing the membrane cytoplasmic P2X7R receptor [24]. Increasing magnesium concentration in body fluids protects against oxidative stress and changes in immune competent cells [25]. In heart failure, plasma magnesium concentration is inversely correlated with the level of C-reactive protein and tumor necrosis factor (TNFα). Decreased plasma magnesium levels are associated with increased levels of monocyte chemoattractant protein-1 (MCP-1) and interleukins, such as IL-1, IL-6, TNFα, IL-8, MCP-1, in the blood.

In heart failure, several interconnected metabolic changes occur:

1. Induction of oxidative stress, as significant amounts of magnesium are consumed during stress [26].
2. Activation of the renin-angiotensin-aldosterone system.
3. Weakening of calcium channel inhibition.
4. Activation of phagocytosis.
5. Diminished antagonism of magnesium towards NMDA receptors, resulting in excitotoxicity and hyperproduction of pro-inflammatory substance P.
6. Activation of NF-kB-mediated signaling and increased transcription of cytokines and pro-inflammatory genes.
7. Reduction in the levels of anti-inflammatory media tors such as NO, lipoxins, resolvins, and protectins.

Low magnesium levels increase the oxidative activity of neutrophils, while high magnesium levels significantly reduce the production of free radicals in rats and polymorphonuclear cells in humans [27].

Loss of magnesium content in the myocardium has been observed in myocardial infarction and acute heart failure in the area of necrosis formation. It has been noted that magnesium prevents the occurrence of arrhythmias, whereas magnesium deficiency can lead to fatal arrhythmias. Magnesium can strengthen the potential of ventricular myocardium, as low magnesium levels in cardiomyocytes lead to membrane destabilization, while high magnesium levels stabilize the membranes. Therefore, there is accumulating evidence that magnesium preparations can prevent arrhythmias. They are effective in various types of tachyarrhythmias, including those caused by digoxin, multifocal atrial tachycardia in-
Levels in the body. In addition, inadequate magnesium content is associated with mitochondrial dysfunction [33]. Deficiency of magnesium has been shown to play a role in the survival of patients with cardiomyopathy and heart failure [32]. It has also been shown that patients with mitral valve prolapse have magnesium deficiency, which is associated with reduced magnesium content in lymphocytes, leading to induction of fibrosis and depletion of glycogen stores.

Magnesium is a natural anti-stress factor that inhibits the development of excitatory processes in the central nervous system (CNS) and reduces the sensitivity of the body to external influences. While calcium and glutamate are excitatory substances and can be toxic in excess, magnesium protects NMDA receptors from toxin action and ensures activation of the neuroprotective agent glycine [34]. The recommended daily intake of magnesium is 400 mg for men and 500 mg for women. Magnesium deficiency is more common in women, and the need for magnesium increases during pregnancy and lactation. Special attention should be paid to magnesium supplementation in pregnant women, as this mineral is essential for stabilizing the processes of mitosis and meiosis, which contribute to the formation of a healthy embryo. Magnesium is found in significant amounts in the heart, brain, muscles, but its highest concentration is in the placenta [33]. Therefore, magnesium deficiency in pregnant women results in placental pathology, inhibition of physiological apoptosis leading to embryonic developmental defects, alkaline phosphatase activity alteration in the placenta negatively affecting phosphate metabolism and transport of class G globulins. In addition, pregnant women with magnesium deficiency may experience seizures, more commonly in calf muscles, arrhythmias, and increased excitability. Moreover, it has been observed that magnesium deficiency in pregnancy leads to an increase in the level of cascade apoptosis [34]. At the same time, mice that received magnesium acetate at all doses showed an increase in magnesium levels in brain tissue and skeletal muscles. Moreover, the increase in magnesium levels was more pronounced after a single administration of the preparation compared to twice-daily administration. The mechanisms of magnesium transport were found to be dependent on electrochemical gradient, transmolar transport, and the soluble form of magnesium. Symptoms of magnesium deficiency and stress are very similar and are accompanied by dizziness, anxiety, uncontrollable weakness, and headache. Magnesium penetrates very well through the blood-brain barrier, controls membrane excitability, and is present in significant amounts in the extracellular space and cerebrospinal fluid, playing a significant role in brain homeostasis. In cerebrospinal fluid, magnesium exists in a soluble form of magnesium. Symptoms of magnesium deficiency and stress are very similar and are accompanied by dizziness, anxiety, uncontrollable weakness, and headache. Magnesium penetrates very well through the blood-brain barrier, controls membrane excitability, and is present in significant amounts in the extracellular space and cerebrospinal fluid, playing a significant role in brain homeostasis. In cerebrospinal fluid, magnesium exists in a soluble form of magnesium. Symptoms of magnesium deficiency and stress are very similar and are accompanied by dizziness, anxiety, uncontrollable weakness, and headache.
may require magnesium supplementation, especially in combination with vitamin B6 [36-38].

Research has shown that magnesium ions block NMDA-associated channels in a voltage-dependent manner and, by engaging in non-competitive antagonism with glutamate, inhibit its release, thereby reducing excitotoxicity [38]. Hypomagnesemia leads to genetic disorders of the central nervous system (CNS) that require magnesium therapy from childhood [39-40]. The neuroprotective effects of magnesium are associated with its role in genome repair and interaction with phosphate groups of DNA [41]. Magnesium deficiency can damage dopamine receptors and alter the sensitivity of NMDA and AMPA receptors [42]. Magnesium deficiency contributes to the development of Parkinson’s disease, Alzheimer’s disease, and dementia [43-44]. Genetic defects in the synthesis of dopamine transporters due to magnesium deficiency (TRPM7 and SCLA1) promote the development of Parkinson’s disease [43-44]. In the pathogenesis of Alzheimer’s disease, it has been noted that magnesium may prevent the formation of beta-amyloid and influence the NKB factor [43-44].

Magnesium relaxes smooth and skeletal muscles by inhibiting calcium-dependent channels, leading to the relaxation of myocytes. A comparison was made between the absorption of inorganic magnesium salts (magnesium citrate, magnesium malate) and organic salts (magnesium acetyl taurate, magnesium glycinate), with attention to magnesium transport, bioavailability, and impact on the immune system [42]. All compounds were administered in three different doses: 45 mg, 135 mg, and 405 mg of elemental magnesium per 70 kg of body weight. The highest dose was divided into 202.5 mg/70 kg and taken twice a day.

It is known that magnesium deficiency can occur due to inadequate intake from food, improper food preparation, certain diseases, or the use of certain medications. Magnesium galenic preparations were prepared and administered to mice, and magnesium levels were determined in brain, muscle tissues, and serum after one day [42]. Magnesium, along with vitamin supplements B, C, D, E, omega-3 polyunsaturated fatty acids, and manganese, may boost immunity. The mechanism of action of magnesium may be effective in patients with mutations in interleukin 2 and inducible forms of nitric oxide, as magnesium controls membrane excitability and can influence inflammation and immunity processes associated with these conditions. Therefore, it is considered that magnesium, along with the aforementioned vitamin supplements, can be prescribed in the treatment of viruses, infections, including influenza and COVID-19 [45-47]. Due to the association between psychoemotional and endocrine disorders with magnesium deficiency in the body, children with signs of chronic gastritis and arterial hypertension were additionally prescribed magnesium lactate with vitamin B6 according to the protocol, based on existing hypomagnesemia. This resulted in a reduction of abdominal and headaches, alleviation of stomach discomfort, improvement in sleep quality, and a decrease in daily systolic arterial tension (SAT) over the course of one month [48].

Magnesium plays a significant role in the detoxification process by promoting the elimination of toxic substances from the body. It is known that magnesium is necessary for the elimination of mercury, lead, zinc, and arsenic from the body. Magnesium protects the body from the toxic effects of calcium, lead, mercury, nickel, and prevents the penetration of toxic metals into brain cells [49-51].

It is known that type 2 diabetes is a risk factor for the development of heart failure. In patients with type 2 diabetes, metabolic syndrome, and a history of ischemic heart disease, who had low levels of magnesium and zinc in their blood, zinc and magnesium supplements were added to the standard therapy. After receiving traditional therapy along with zinc and magnesium supplements, the overall condition of the patients improved, and the levels of magnesium, zinc, C-reactive proteins, LDL cholesterol, and markers of prooxidant-antioxidant homeostasis normalized. The obtained results indicated the effectiveness of the prescribed therapy [51-52].

Thus, magnesium actively regulates the state of the cellular membrane, facilitates the transfer of calcium and sodium ions, and is involved in metabolic reactions, including energy production. 80-90% of magnesium is complexed with ATP, which facilitates its accumulation in the body. Magnesium is necessary for nerve-muscle conduction, reduces anxiety, inhibits the release of catecholamines and aldosterone during stress states. Additionally, magnesium promotes reactions such as DNA synthesis, glycolysis, oxidative phosphorylation, as it is a component of guanosine triphosphatase, phosphofructokinase, Na-K-ATPase, Ca-ATPase, adenylate cyclase, and plays an important role in the transmission of genetic information, as it participates in nucleotide production [53]. Magnesium is crucial for the functioning of the cardiovascular system as it maintains myocardial function and exerts a hypertensive effect. Balanced magnesium levels are necessary for the functioning of the immune system and the support of B and T lymphocyte functions [53-55]. Considering the influence of magnesium on the immune system, magnesium supplements are recommended to be included in the treatment regimens of bronchial asthma in children [56].

In recent years, it has been determined that magnesium preparations can have an antinociceptive effect, which is associated with their influence on NMDA receptors, specifically inhibiting their activity. This allows for the use of these preparations in children and pregnant women [57, 58].

The data provided indicate that there is no system in the body that does not involve the participation of magnesium ions in the functioning of metabolic and genomic processes of organs and systems.

Conclusions.

Thus, magnesium is one of the key intracellular elements that plays a leading role in the activity of vital organs, participates in many cellular functions, including signal transmission, energy production, protein metabolism, and acts as a molecular stabilizer for RNA and DNA ribosomes. Hypomagnesemia leads to disruptions in the functioning of the cardiovascular, nervous, and immune systems, as well as the gastrointestinal tract. Based on magnesium, mono-preparations (such as magnesium sulfate, magnesium citrate, and others) and complex preparations (such as MagneB6, Maalox, ATP forte, and others) have been developed and continue to be developed. The development of cardiovascular diseases such as arterial hypertension, arrhythmias, heart failure, as well as neurodegenerative diseases of the central nervous system.
Cardiovascular and central nervous system. Low magnesium levels have been identified not only in the gastrointestinal tract but also in the cardiovascular system and central nervous system. Low magnesium levels are associated with the occurrence of cardiovascular and gastrointestinal diseases in children, as well as pregnancy outcomes in women. This indicates the necessity for further research into the properties of this micronutrient in health and disease, and the search for new methodological approaches to determine its impact on the human body.

Prospects for further research.

The role of metabolite-based drugs in the development of modern pharmaceuticals will be further investigated.

References


Магній є одним з головних внутрішньоклітинних елементів, який грає одну з провідних ролей в фізіо-хімічних, біохімічних, фармаکологічних властивостях. Він є компонентом багатьох ферментів, участь яких визначається в багатьох хімічних реакціях у клітині. Магній також необхідний для нормального функціонування нервової, серцево-судинної та імунної систем, органів травного каналу.

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ФІЗІКО-ХІМІЧНІ, БІОХІМІЧНІ, ФАРМАКОЛОГІЧНІ ВЛАСТИВОСТІ МАГНІЮ

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Зайченко Г. В., Горчакова Н. О., Клименко О. В., Шумейко О. В., Бабак В. В.
PHYSICOCHEMICAL, BIOCHEMICAL, PHARMACOLOGICAL PROPERTIES OF MAGNESIUM

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Abstract. Magnesium is one of the main intracellular elements that plays a prominent role in the functioning of vital organs, participating in various cellular functions, including signal transmission, energy production, protein metabolism, and acting as a molecular stabilizer of RNA and DNA ribosomes. Hypomagnesemia can lead to disruptions in the functioning of the cardiovascular, nervous, and immune systems, as well as the digestive tract organs. Based on magnesium, mono preparations (such as magnesium sulfate, magnesium citrate, etc.) and complex drugs (Magnesium-B6, Maalox, ATP Forte, etc.) have been developed and are being used.

The development of cardiovascular diseases such as arterial hypertension, arrhythmias, heart failure, as well as neurodegenerative diseases of the central nervous system (Parkinsonism, Alzheimer’s disease, dementia) is associated with magnesium deficiency, as magnesium not only participates in nucleic acid metabolism, but also in signal transmission in the central nervous system. Therefore, monitoring magnesium levels not only in the cardiovascular and nervous systems but also in other systems may be targeted for the influence of magnesium preparations. Magnesium protects the body from the toxic effects of calcium, lead, mercury, nickel, and prevents the penetration of toxic metals into brain cells. Individuals with gastrointestinal disorders have been found to have magnesium deficiency not only in the gastrointestinal tract but also in the cardiovascular system and CNS. Reduced magnesium levels have been associated with the occurrence of cardiovascular and gastrointestinal diseases in children, as well as pregnancy outcomes in women. Magnesium also plays a crucial role in the functioning of the cardiovascular system, maintaining myocardial function, and implementing a hypotensive effect. Balanced magnesium levels are necessary for the functioning of the immune system. Based on scientific data regarding the influence of magnesium on the immune system, the inclusion of magnesium preparations in the treatment regimens for childhood bronchial asthma is recommended.

The data presented indicate that there is no system in the body in which magnesium ions do not participate, as they are involved in metabolic and genomic processes of organs and systems in general. This highlights the need for further research into the properties of this trace element in normal and pathological conditions, and the search for new methodological approaches to determine its impact on the human body.

Key words: magnesium, physicochemical, biochemical, pharmacological properties.

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