

## MOLECULAR AND CELLULAR MECHANISMS OF ACTION OF SORBENTS USED IN MEDICINE

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### ABSTRACT

The article provides an overview of the literature data on the effectiveness of the use of sorbents of various origins in diarrhea with various etiological causes. Enterosorbents, despite their very ancient use in medicine, are still relevant drugs. The use of this group of drugs has gone far beyond gastroenterology and makes it possible to effectively help patients with various diseases, including such "diseases of civilization" as cardiovascular pathology, disorders of lipid and carbohydrate metabolism. It is very valuable that the natural and safe composition of drugs, especially of domestic production, is also useful for healthy people in order to prevent diseases of the digestive system and prevent metabolic disorders: it allows achieving a higher quality of life - a priority task of medicine.

**Key words:** intoxication, diarrhea, sorbents, diagnosis, treatment, pathobiochemistry.

### INTRODUCTION

Intestinal intoxication is poisoning that occurs when the body is unable to cope with the influence of toxic substances on its own. With intestinal intoxication, the body continues to secrete enzymes that are incompatible with the normal operation of its systems. The symptoms of intoxication are very extensive and have different expressions. Their manifestations are due to the nature of the toxic substance, physical and chemical properties, affinity to certain organs, systems of physiology, subcellular structures, body tissues, enzymes produced and available receptors. It can be stated that infectious diseases still occupy a significant place among the causes of mortality of the population worldwide [1]. Intoxication can

be exogenous, when toxins enter the human intestine from the outside, and endogenous - when toxins appear as a result of a violation of the organ itself. The degree of intoxication depends on how much of the toxic substance has entered the human body. At the same time, it is important not so much how much of the toxin was absorbed, but what dose of it was absorbed and distributed through the body through the blood.

Common causes of intoxication are poisoning:

- medicines;
- alcohol, tobacco, narcotic substances;
- due to the release of decay products by parasites.

Clinical manifestations are determined by the gastrointestinal tract (GT) lesion syndrome: dyspepsia, vomiting, diarrhea, abdominal pain of various localization [2]. Each toxin causes specific symptoms, but the leading symptoms in this condition are most often diarrhea (diarrhea).

Diarrhea (diarrhea or loose stools) is a rapid emptying of the intestine, usually with an increase in the amount of feces and a change in their consistency (dilution), sometimes with the appearance of pathological impurities (mucus, blood). Diarrhea can be acute or chronic [3].

Acute diarrhea is a sudden increase in stool up to 3 times / day, usually accompanied by a change in its consistency. Only E.coli has six pathological species that can cause acute diarrhea [4].

Chronic diarrhea - frequent stools more than 3 times / day, lasting longer than 1 month.

The causes of acute and chronic diarrhea can be different conditions:

Causes of acute diarrhea:

- Acute intestinal infections (viral, bacterial, parasitic)
- Food toxicoinfections
- Poisoning with certain substances or medications
- Neuropsychiatric disorders ("bear disease")
- Intoxication caused by internal factors (uremic diarrhea)

Causes of chronic diarrhea

- Inflammatory bowel diseases (ulcerative colitis, Crohn's disease)
- Taking certain medications (laxatives, antibiotics, iron preparations, etc.)
- Malignant tumors of the gastrointestinal tract
- Hyperthyroidism, AIDS
- Infections (giardiasis)
- Variants of the syndrome of impaired absorption (celiac disease, pancreatic diseases, etc.)

- Functional motor disorders (irritable bowel syndrome).

Based on the features of pathogenetic mechanisms, four types of diarrhea are distinguished: secretory, hyperexudative, hyperosmolar, hyper- and hypokinetic.

Secretory diarrhea is caused by increased secretion of sodium and water into the intestinal lumen. A classic example is diarrhea in cholera, the causative agent of which, cholera vibrio, multiplies only on the surface of the epithelium of the small intestine, but the cholera toxin disrupts intracellular regulation, as a result, the intestinal epithelium begins to actively secrete water with electrolytes into the lumen. Hypersecretion of water and electrolytes is also caused by toxins of other bacteria (*Salmonella*, *Escherichia*, *klebsiella*), enteropathogenic viruses, bile acids, prostaglandins and other biologically active substances. The secretory form is characterized by painless, abundant water diarrhea, calculated in liters per day.

Hyperexudative diarrhea is characteristic of inflammatory bowel diseases. It develops with bacterial OCI caused by shigella, salmonella, clostridium, *Escherichia*, etc. bacteria. In this case, they are also called invasive (English invasion - invasion, invasion). The stool is liquid, often with pathological impurities (mucus, blood, pus). Similar diarrhea is also observed in non-infectious diseases: ulcerative colitis, Crohn's disease, malignant intestinal tumors.

Hyperosmolar (osmotic) diarrhea develops due to malabsorption in the small intestine. Of the infectious agents, it is most often caused by rotaviruses, which multiply in the epithelium and disrupt the activity of enzymes of the intestinal mucosa. Because of this, disaccharides cannot split into monosaccharides and be absorbed. Disaccharides remain in the intestinal lumen and attract water. Under the influence of intestinal microflora, disaccharides ferment with the formation of gases (flatulence) and water, which leads to pain and "watery" diarrhea.

Hyperosmolar diarrhea is observed with malabsorption syndrome, with a deficiency of digestive enzymes (congenital enteropathy, chronic pancreatitis, etc.). With osmotic diarrhea, the stool is plentiful, liquid, often contains a large amount of half-digested food residues.

Hyper- and hypokinetic diarrhea occurs with an increase or decrease in intestinal motility, which is accompanied by a violation of the transit of intestinal contents. Hyperkinetic diarrhea is caused by neurogenic factors (stress), laxatives, secretin, pancreosimin, gastrin, prostaglandins and serotonin. This type of diarrhea is characteristic of patients with irritable bowel syndrome. With hyperkinetic diarrhea, the stool is liquid or mushy, frequent, but not abundant. Hypokinetic diarrhea is less common and is associated with excessive bacterial contamination of the small intestine.

## **Etiology and pathogenesis**

Various factors lead to the activation of enterocyte adenylate cyclase, further increases intracellular cAMP, which leads to disruption of the transport of Na and Cl ions through the membrane of enterocyte cells with their accumulation in the intestinal lumen. After that, there is an intense secretion of fluid into the lumen of the digestive canal, copious watery diarrhea, vomiting.

### **Mechanisms of diarrhea development:**

- increased secretion of electrolytes by the intestinal epithelium, causing massive fluid loss (secretory diarrhea);
- decreased absorption of electrolytes and nutrients from the intestinal lumen, developing due to damage to the brush border of the epithelium of the large or small intestine (exudative diarrhea);
- increased osmolarity of intestinal contents due to deficiency of saccharolytic enzymes and lactose intolerance (hyperosmolar diarrhea);
- violation of intestinal motor activity (hyperkinetic diarrhea).

Antibiotic-associated diarrhea caused by the proliferation of *Clostridium difficile* against the background of suppression of the growth of normal microflora is well known. This diarrhea is mixed – exudative and secretory.

Antibiotic-associated diarrhea is a complex of symptoms that develop against the background of quantitative and qualitative changes in the composition of the intestinal microflora during antibiotic therapy. The incidence of such a complication, according to various authors, is 5-39%. It is also known that when a patient takes six or more drugs at the same time, the probability of adverse reactions reaches 80% [5]. A decrease in the number of anaerobes against the background of antibacterial therapy leads to a violation of the metabolism of carbohydrates and fiber. Accumulating in the lumen of the large intestine, carbohydrates and fiber contribute to the secretion of water and electrolytes. As a result, osmotic diarrhea develops. Some anaerobic bacteria are involved in the metabolism of bile acids in the intestinal lumen. When antibiotics suppress such bacteria, there is a violation of the cleavage of bile acids. An excess of primary bile acids leads to secretory diarrhea. One of the mechanisms of the development of diarrheal syndrome against the background of antibiotic therapy can be attributed to the direct effect of an antibiotic on intestinal motility. Thus, macrolides are stimulators of motilin receptors. Such stimulation causes a contraction of the antrum of the stomach and duodenum and leads to such clinical manifestations: spastic abdominal pain, vomiting and diarrhea.

One of the common causes is also poisoning with ethyl alcohol. Poisoning with ethyl alcohol for a long period occupies a leading place among household poisoning by the absolute number of deaths.

Alcohol has a toxic effect on a number of human organs. Alcohol-related mortality is, according to WHO, 6.3% in men and 1.1% in women [6]. However, this is the average data for the world, whereas in a number of countries, alcohol mortality rates can reach a very high level. Disorders of the gastrointestinal tract are an indispensable attribute of acute alcohol intoxication and post-intoxication. They are manifested by acute pain in the stomach and diarrhea. Diarrhea in this condition is a consequence of a rapidly occurring lactase deficiency and the associated decrease in lactose tolerance, as well as impaired absorption of water and electrolytes from thin substances [7] substances. Alcoholic beverages worsen the absorption of nutrients from food, disrupt many links of metabolism in the body: proteins, carbohydrates, fats, mineral salts. As a result, acidic products accumulate in organs and tissues, the acid-base balance is disturbed, and this leads to serious metabolic disorders[7]. The strength of ethanol depends on the dose, tolerance to the toxicant (liver hypertrophy) and the degree of individual expression of isoenzymes, depending on the genome. With ethanol poisoning, glycogenolysis develops; nausea, vomiting and dehydration are characteristic. Thiamine deficiency is typical due to malabsorption.

Toxins have a damaging effect on membranes and receptors, in particular, affecting the subunits of G-proteins that mediate signal transmission from the receptor to the effector structures of the cell. One of the subunits of the cholera toxin penetrates into the cell and catalyzes the attachment of ADP-ribose to the GS protein, the manifestation of GTP-phosphatase activity of the  $\alpha$ S subunit is inhibited, dephosphorylation of GTP does not occur, the cycle of functioning of the GS protein stops at the stage of activation of adenylate cyclase, the increased activity of which persists for a long time. Excess cAMP accumulates in the cells of the intestinal epithelium, causing the secretion of electrolytes and water into the intestinal lumen, damage to intestinal cells occurs, dehydration of the body and death after a few hours (8).

**Antihistamines.** Histamine is a neurotransmitter capable of influencing the gastrointestinal tract (intestinal colic, stimulation of gastric secretion), smooth muscles of the intestine [9]. There is an opinion that it is antihistamines that can cause the most severe and complex form of intoxication of the body. After all, it often happens that during the course of an allergy, a person can take more pills, and sometimes even take two or more different antihistamine pills at a time that are incompatible with each other. Symptoms of antihistamine poisoning: general

weakness, severe dilation of the eyeball pupil, manifestation of hallucinations in humans, causeless mental agitation, nausea, vomiting, diarrhea. Under the action of various damaging factors, the non-selective permeability of the CPM and intracellular membranes for electrolytes and water increases, the systems of passive and active electrolyte transport are disrupted. A decrease in the activity of  $\text{Na}^+/\text{K}^+$ -ATPase leads to an increase in the intracellular content of  $\text{Na}^+$  ions and leakage of  $\text{K}^+$  ions. Stoichiometry of  $\text{Na}^+/\text{K}^+$ -ATPase under optimal conditions 3/2/1 (during hydrolysis of one ATP molecule, three  $\text{Na}^+$  ions are removed from the cell and two  $\text{K}^+$  ions enter the cell). A decrease in the potassium content in the cell leads to a decrease in this ratio to 1/1/1, the membrane potential decreases and the intracellular sodium content increases. The hydrate number of the  $\text{K}^+$  25 ion is 10.5, and the  $\text{Na}^+$  ion is 16.6 water molecules per ion, i.e.  $\text{Na}^+$  are characterized by greater hydrophilicity compared to  $\text{K}^+$ , therefore, an increase in the intracellular content of  $\text{Na}^+$  leads to cell hydration. An increase in the concentration of intracellular  $\text{Ca}^{2+}$ , associated with a decrease in the activity of  $\text{Ca}^{2+}$ -ATPase and  $\text{Na}^+/\text{Ca}^{2+}$ -ion exchange mechanism, leads to the opening of highly selective  $\text{Ca}^{2+}$ -dependent potassium channels and an increase in the rate of leakage of  $\text{K}^+$  from the cell, which is accompanied by further development of cell hydration. Hyperhydration of the cell can cause excessive stretching of the CPM and intracellular membranes, followed by their damage (osmotic cell death). Despite the widespread prevalence of OCI, many aspects of their pathogenesis in adults have been studied extremely insufficiently.

For the correction of gastrointestinal disorders developing in acute diarrheal infectious diseases, eubiotics, enzyme preparations, antispasmodics and a number of other groups of medicines are used in clinical practice, among which enterosorbents have been given increasing importance in recent years.

Enterosorbents (gr. enteron-gut; lat. sorbens - absorbing) are substances with a high sorption capacity that do not break down in the gastrointestinal tract, effectively binding and removing endogenous and exogenous toxic compounds, supramolecular structures and cells from the body, used for the treatment and prevention of diseases [10,11,12]

Enterosorbents as therapeutic agents have been known since ancient times. Even the healers of Ancient Egypt, India, Greece used charcoal, clay, crushed tuffs, burnt horn inside for the treatment of poisoning, diarrhea, jaundice and other diseases, as well as externally for the treatment of wounds. Healers of Ancient Russia used birch or bone charcoal. Avicenna (Abu Ali ibn Sina) in his Canon of Medical Science, out of the seven postulates of the art of preserving health, put the method corresponding to the modern understanding of enterosorption in the third

place. The researcher I.e. Lovitz (1785), studying the chemical properties of charcoal, justified its use for the same purposes.

The most important medical requirements for modern enterosorbents are a high sorption capacity relative to the components to be removed and the ability to sorb molecules and bacterial cells of different sizes and weights, the absence of toxic and traumatic effects on the mucous membranes of the gastrointestinal tract; they must be well evacuated from the intestine and not cause loss of useful ingredients, not have a negative effect on the secretion processes and intestinal microflora. As it passes through the intestine, the bound components should not be desorbed. Enterosorbents should not penetrate the gastrointestinal mucosa, therefore, they do not have systemic pharmacokinetics. Preparations for enterosorption should have a convenient dosage form and have good organoleptic properties [13].

The role of sorption materials in medicine is significant. Due to its developed porous structure, carbon materials are effectively used for detoxification of the body and are used for hemo-, enterosorption and application. They bind toxic substances on their surface and remove them from the body naturally, through wound discharge, etc. [14]. However, the use of non-selective sorbents significantly complicates their predicted use and can lead to negative consequences, in particular, due to the nonspecific sorption of substances useful for the body - hormones, vitamins, enzymes. Therefore, the development and use of selective and biospecific sorbents has become an urgent direction in the development of sorption therapy methods.

With the help of polymers with molecular imprints in biomedical research, medicinal substances (phenytoin [15], theophylline [16], propranolol [17], 7-hydroxycoumarin [18], bupivacaine [19], antibiotics (ampicillin [20], gatifloxacin [21]), acyclovir [22], celecoxib [23], berberine [24] and tizanidine [25]), biological markers (epinephrine [26], cholesterol [27], glutathione [28]), toxicants (bisphenols [29], hydroxypyrene [30]), narcotic substances (tetrahydrocannabinol and its metabolites [31]) and phytoestrogens (biohanin A, daidzein and genistein [32]).

The interaction of sorbents with the removed components is realized in four main ways: adsorption, absorption, ion exchange and complexation [33,34]. During adsorption, the interaction between the sorbent and the removed substance occurs at the interface of the media. Absorption is the process of absorption of a substance by a liquid sorbent as a result of dissolution. Ion exchange is the process of replacing ions on the sorbent surface with sorbate ions. The pathogenetic

mechanisms of enterosorption depend on the type of sorbent and the structure of the sorbed particles.

Sorbents have different properties and may differ in a number of features [35].

By dosage form and physical properties: granules, powders, tablets, pastes, gels, suspensions, colloids, encapsulated materials, food additives

According to the chemical structure, sorbents can be divided into several groups:

1. Carbon sorbents (activated carbon, Carbolong, Carbovite, Carbospherite, saturated spherical carbonite - SCN, Anthralene, etc.).

2. Silicon containing enterosorbents (Polysorb, Sillard P, white clay, Smekta, Neosmectin, etc.).

Natural and synthetic enterosorbents are distinguished among silicon-containing enterosorbents. Of the natural ones, the most famous is white clay, the suspension of which has enveloping and adsorbing properties. In addition to white clay, smectites and sodium montmorillonites, etc. are used in medicine.

Of the synthetic enterosorbents, currently the most widely used preparation is a synthesized gel of methylsilicic acid hydroxide. Having a high sorption activity, it is characterized by a selective action: binds and removes only medium-molecular toxic substances.

The main characteristics of enterosorbents are: 1) the sorption capacity indicator is the amount of substance that can absorb the sorbent per unit of its mass; 2) the ability to bind molecules of different sizes and weights, as well as bacterial agents; 3) the active surface of the enterosorbent is the total area of the adsorbing surface per unit mass of the drug [36].

The main route of administration of enterosorbents is oral, sometimes enterosorbent is administered through a probe when the patient is unable to take the drug on his own or there are obstacles due to esophageal stenosis or pyloric stomach. With probe administration, the sorbent can be withdrawn (usually with an exposure of up to 30 minutes) and a new portion of the drug is introduced. Sometimes, according to indications, enterosorbents are injected with enemas into the colon.

The mechanisms of action of enterosorbents are divided into 4 groups:

1. Intestinal absorption of exotoxins, xenobiotics, bacteria, bacterial and endogenous toxins

2. Contact effect on the structures of the gastrointestinal tract.

3. Elimination of endotoxins from the internal environment of the body into the intestinal cavity.



4. Enhancement of metabolism and elimination of endotoxins by natural detoxification organs [37].

The therapeutic effect of enterosorbents is carried out as a result of their direct and indirect effects on pathogenetic mechanisms.

The direct action of enterosorbents is aimed at binding and elimination from the gastrointestinal tract of toxic metabolic products and the inflammatory process, pathogenic bacteria and their toxins, viruses, biologically active substances, binding gases formed in excess during the putrefactive process.

The indirect effect is due to the prevention or weakening of the clinical manifestations of endotoxemia, toxic-allergic reactions, diarrheal syndrome. The use of enterosorbents reduces the metabolic load on the liver and kidneys, contributes to the normalization of the motor, evacuation and digestive functions of the gastrointestinal tract, has a positive effect on the functional state of the immune system [38].

Enterosorption is included in the group of efferent therapy means (Latin *efferens* - to remove), i.e. therapeutic measures aimed at stopping the action of toxins of various origins and their elimination from the body. Enterosorption in intestinal infectious diseases is a pathogenetically justified method of therapy.

Targeted clinical studies on the effectiveness of domestic enterosorbents were started in the mid-80s of the last century [39]. At that time, only carbon sorbents were used in practice, which, along with positive properties, had a relatively small sorption capacity and side effects and a number of contraindications. The creation of new drugs derived from other groups of sorbents has expanded the possibilities of using enterosorption in the complex treatment of OCI. The first of them was Enterodesis, a drug of low molecular weight polyvinylpyrrolidone, which was used in the complex therapy of 144 patients with OCI (men - 71, women - 73), 124 of whom were diagnosed with food toxicoinfection, 20 - shigellosis. In 105 (72.9%), the course of the disease was of moderate severity, in 37 (25.9%) — mild, in 2 (0.015%) — severe. The drug was prescribed, as recommended by the manufacturer, in dissolved form (5 g in 100 ml of water) 2-4 doses per day for 3 days. The therapeutic effect was registered in all patients: abdominal pain, flatulence, nausea, vomiting were stopped; after 6-12 hours from the start of treatment, body temperature normalized in 75.6% of patients. Parenteral rehydration was not required in all patients treated with enterodesis on the first or second day of the disease. The pronounced clinical effect, the absence of adverse reactions (also controlled by laboratory biochemical studies) made it possible to include this drug in the complex of remedies for the treatment of patients with acute diarrheal infections.

According to infectious disease doctors and pediatricians, timely, i.e. early use of enterosorbents in acute infectious diarrheal diseases of an invasive type has a rapid and pronounced detoxification, hypothermic and antidiarrheal clinical effect [40].

Such results were obtained with the combined use of enterosorbents with antibacterial drugs or probiotics in the treatment of OCI. According to some authors, the clinical efficacy of enterosorbents in mild and moderate forms of OCI is not inferior to antibacterial drugs widely used in clinical practice [41,42].

A. A. Novokshonov et al. (2002) used enterosorbent for the treatment of 60 children with mild and moderate forms of OCI, of which 40 patients received the drug as a means of etiotropic monotherapy (20) or in combination with furazolidone (20). It has been established that "etiotropic" monotherapy with enterosorbent is more effective than treatment with furazolidone, and significantly increases when they are used together in the treatment of moderate forms of acute bacterial etiology of an invasive type of diarrhea. Along with the rapid and pronounced detoxification clinical effect, the sanitizing effectiveness of combination therapy also increased markedly: repeated seeding of the causative agents of AKI was not registered, while with furazolidone monotherapy, a third of patients had repeated seeding of salmonella and *Pseudomonas aeruginosa* at the end of the 5-day course. The authors note that "the high antibacterial activity of enterosorbents not only contributes to the rehabilitation of the gastrointestinal tract from pathogens, but also can have an indirect immunomodulatory effect due to detoxification and prevention of antigenic overload of the immune system, which creates favorable conditions for the relief of the infectious process [43].

In the complex treatment of 63 patients aged 19 to 34 years who were admitted to the hospital with a diagnosis of "food toxicoinfection", we also used enterosorbent. As a control, a group of 23 patients who met the age and other criteria of the first group, received detoxification and rehydration therapy, was observed. Due to the fact that according to the clinical and epidemiological characteristics confirmed by laboratory studies, the etiological agents were opportunistic bacteria or rotaviruses (in 14), antibacterial drugs were not prescribed to patients. All patients were admitted in a state of moderate severity. Enterosorbent treatment was carried out in accordance with the manufacturer's recommendation: 2-3 tab. 3 times a day an hour before meals and taking other medications. The duration of use of the drug averaged  $4 \pm 0.3$  days. As a result, in patients receiving enterosorbent, a decrease in the duration of fever and manifestations of intoxication was registered to  $2.3 \pm 0.4$  days, in the control group this indicator was  $3.2 \pm 0.3$  days ( $p > 0.05$ ), the duration of diarrhea decreased,

which in the groups under consideration was  $1.6 \pm 0.5$  and  $2.8 \pm 0.7$  days, respectively ( $p > 0.05$ ). The use of enterosorbent contributed to an earlier cessation of pain syndrome - after  $1.4 \pm 0.2$  days ( $p < 0.05$ ), which in patients of the control group lasted up to  $2.6 \pm 0.3$  days, the time of disappearance of such manifestations as flatulence was less -  $1.9 \pm 0.2$  days ( $p < 0.05$ ), in the control group - up to  $3.7 \pm 0.4$  days, lethargy and anorexia  $1.8 \pm 0.3$  and  $3.1 \pm 0.4$  days ( $p < 0.05$ ), respectively. The tolerability of the drug was good, no adverse reactions were noted. Thus, the inclusion of enterosorbent in the complex treatment of patients with food toxicoinfections had an obvious therapeutic effect, expressed in a reduction in the time of disappearance of manifestations of intoxication and functional disorders of the gastrointestinal tract.

The given examples of the use of the drug indicate the good effectiveness of an enterosorbent based on hydrolysis lignin - a polymer of plant origin with a high sorption capacity, capable of removing toxins, pathogenic microorganisms, and their waste products from the body, as well as contributing to the restoration of microflora and normalization of intestinal motility. Drugs of this group are actively being introduced into medical practice, especially in pediatrics, because they can be prescribed to children starting from infancy.

In the domestic manuals on infectious diseases, manuals for doctors and special scientific literature of recent years, recommendations on the use of enterosorbents in the complex treatment of acute infectious diarrheal diseases are constantly present [44].

However, it should be noted that the list of recommended drugs is relatively small. There is little information about their use in intestinal infectious diseases of a viral nature, which, as many researchers have shown, occupy a significant share among diarrheal diseases. Thus, compared to the previous year, the incidence of rotavirus gastroenteritis increased by more than 50%, the Norwalk virus was registered 1.8 times more often [45]. In this regard, more studies have been conducted by infectious diseases pediatricians, which is quite natural given the wider spread of viral diarrheal diseases among children. Currently, specific immunoglobulins, interferon inducers and immunomodulatory drugs are used as etiotropic therapy agents for these diseases, and probiotics and enterosorbents are used for etiopathogenetic therapy. It should be borne in mind that not all known enterosorbents are effective enough for viral diarrheal diseases, but some of them have a noticeable etiotropic effect, which is due to the ability to sorption and elimination of viruses and opportunistic bacteria from the intestine. A number of enterosorbents (dioctahedral smectite, preparations based on hydrolysis lignin) prevent the introduction of viruses through the protective intestinal mucosal

barrier, absorb excess disaccharides, intestinal gases, reduce flatulence and abdominal pain caused by it; normalize the absorption of water and electrolytes, the composition of the intestinal microflora; have a pronounced detoxification and antidiarrheal clinical effect.

N. Mazankova et al. [46] noted a noticeable positive effect when using an enterosorbent of natural and artificial origin in the treatment of OCI in children, where the etiological agents were bacteria and rotaviruses. Enterosorbents were prescribed to patients from the moment of admission against the background of oral rehydration and diet therapy. Already from the first days of treatment, a positive effect of sorbents on general toxic and local OKA syndromes was noted in the form of fever relief, reduction in the frequency or complete cessation of vomiting, improvement of appetite, elimination of abdominal pain and flatulence, reduction of the frequency of defecation and improvement of the general condition of patients. According to V. F. Uchaykin et al. (2008), the inclusion of another well-known enterosorbent drug (dioctahedral smectite) in the complex therapy of AKI of viral (osmotic) and viral-bacterial etiology (invasive osmotic type of diarrhea) in children, it contributes to the faster disappearance of symptoms of intoxication and exicosis, fever, relief of flatulence, abdominal pain and diarrheal syndrome.

Most modern enterosorbents are known to practitioners of various specialties. However, many registered enterosorbents have not yet found wide application due to various reasons: due to insufficient awareness of doctors of medical institutions about the role of enterosorbents in the treatment of infectious and non-infectious diseases of the gastrointestinal tract, ignorance of the advantages and disadvantages of certain sorbents in a particular pathology and the actually existing skeptical attitude of doctors to enterosorption. In one of the conclusions of Academician of the Russian Academy of Sciences V.F. Uchaykin et al. [47], who have extensive experience in the use of enterosorbents, it is said that "in gastroenterological pathology, including acute respiratory infections, enterosorbents are a means with multifaceted effectiveness, determined not only by their pathogenetic (detoxification, antidiarrheal, etc.), but also etiotropic action against both pathogenic bacteria and viruses."

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Thus, enterosorbents, despite their very ancient use in medicine, are still relevant drugs. The use of this group of drugs has gone far beyond gastroenterology and makes it possible to effectively help patients with various diseases, including such "diseases of civilization" as cardiovascular pathology, disorders of lipid and carbohydrate metabolism. It is very valuable that the natural and safe composition of drugs is also useful for healthy people in order to prevent diseases of the digestive system and prevent metabolic disorders: it allows achieving a higher quality of life - a priority task of medicine.

## REFERENCES

1. National guidelines: infectious diseases, edited by N.,D.Yushchuk, Yu.Ya. Vengerov 2009 - 25c.
2. Yushchuk N. D., Rosenblum A. Yu. Gastrointestinal tract lesion syndrome in infectious diseases. In: Infectious Diseases: National Guidelines. Edited by N. D. Yushchuk. Yu. Ya. Vengerov. M.: GEOTAR-Media. pp. 276-282
3. Mukhin N.A., Moiseev V.S. Propaedeutics of internal diseases: textbook. - 2nd ed., add. And pererab. - M.: GEOTAR-Media, 2012.-848s.
4. McFarland L.V., 1998.-847s.
5. N.I. Shvets, T.M. Benz, P.L. Shupik National Medical Academy of Postgraduate Education, Kiev, 2009.-43s.
6. Rehm J, Mathers C, Povova S, Thavorncharoensap M, Teerawattananon Y, Patra J. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. National Center for Biotechnology

Information, U.S. National Library of Medicine // ncbi.nlm.nih.gov (Lancet; 2009 Jun 27)

7. Interaction of drugs and the effectiveness of pharmacotherapy / L. V. Derimedved, I. M. Pertsev, E. V. Shuvanova, I. A. Zupanets, V. N. Khomenko; edited by Prof. I. M. Pertsev. - Kharkiv: Megapolis Publishing House, 2001. - 784 p— - 5000 copies. - ISBN 996-96421-0-X

8. L. N. Oskolok, G.V. Ordin Mechanisms of cell damage//Tutorial.-2016.-55c.

9. Desensitizing agents / Lukyanov S. V. // Big Russian Encyclopedia [Electronic resource]. — 2016. (Desensitisers. / L. S. V. Grigoriev — Dynamics. — M. : Big Russian encyclopedia, 2007. — P. 574. — (Great Russian encyclopedia : [in 35 t] / ed. by Y. S. Osipov ; period 2004-2017, vol. 8). — ISBN 978-5-85270-338-5.)

10. Belyakov N. A., solomennikov A. V. Enterosorption is the mechanism of therapeutic action // Efferent therapy. 1997, vol. 3, No. 2.

11. Uchaykin V. F., Novokshonov A. A., Sokolova N. V. Enterosorption is an effective method of etiopathogenetic therapy of acute intestinal infections. 2005. No. 3. pp. 39-43.

12. Uchaykin V. F., Novokshonov A. A., Sokolova N. V., Berezhkova T. V. Enterosorption - the role of enterosorbents in the complex therapy of acute and chronic gastroenterological pathology. Manual for doctors. M., 2008. 24 p.

13. Nikolaev V. G. et al. Enterosorption: the state of the issue and prospects for the future // Bulletin of Problems of Biology and Medicine. 2007. No. 4, pp. 7-17.

14. Surovikin, V. F. New hemo- and enterosorbents based on nanodisperse carbon-carbon materials / V. F. Surovikin, L. G. Pyanova, L. S. Luzyanina // Russian Chemical Journal. - 2007. -T.LI, No. 5. - pp.159-165.

15. Berezki A, Toloka'n A, Horvai G, Horva' th V, Lanza F, Hall AJ, et al. Determination of phenytoin in plasma by molecularly imprinted solid-phase extraction. J Chromatogr A 2001; 930: 31- 8

16. Mullet WM, Lai EPC. Determination of theophylline in serum by molecularly imprinted solid-phase extraction with pulsed elution. Anal Chem 1998; 70: 3636- 41

17. Martin P, Wilson ID, Morgan DE, Jones GR, Jones K. Evaluation of molecular-imprinted polymers for use in the solid phase extraction of propranolol from biological fluids. Anal Commun 1997; 34: 45- 7

18. Walshe M, Howarth J, Kelly MT, O’Kennedy R, Smyth MR. The preparation of a molecularly imprinted polymer to 7-hydroxycoumarin and its use as a solid-phase extraction material. *J Pharm Biomed Anal* 1997; 16: 319- 25

19. Andersson LI. Efficient sample pre-concentration of bupivacaine from human plasma by solid-phase extraction on molecularly imprinted polymers. *Analyst* 2000; 125: 1515- 7

20. Wu N. et al. A novel surface molecularly imprinted polymer as the solid-phase extraction adsorbent for the selective determination of ampicillin sodium in milk and blood samples // *J. Pharm. Anal.* 2016. № Lc. P. 1–8.

21. Dramou P. et al. Development of novel amphiphilic magnetic molecularly imprinted polymers compatible with biological fluids for solid phase extraction and physicochemical behavior study // *J. Chromatogr. A.* 2013. Vol. 1317. P. 110–120

22. Yan H. et al. Hybrid molecularly imprinted polymers synthesized with 3-aminopropyltriethoxysilane-methacrylic acid monomer for miniaturized solid-phase extraction: A new and economical sample preparation strategy for determination of acyclovir in urine // *J. Chromatogr. A.* 2014. Vol. 1346. P. 16–24.

23. Arabi M. et al. Synthesis and application of molecularly imprinted nanoparticles combined ultrasonic assisted for highly selective solid phase extraction trace amount of celecoxib from human plasma samples using design expert (DXB) software // *Ultrason. Sonochem.* ., 2016. Vol. 33. P. 67–76.

24. Zhang W., Chen Z. Preparation of micropipette tip-based molecularly imprinted monolith for selective micro-solid phase extraction of berberine in plasma and urine samples // *Talanta.* 2013. Vol. 103. P. 103–109.

25. Sheykhaghaei G. et al. Magnetic molecularly imprinted polymer nanoparticles for selective solid phase extraction and pre-concentration of Tizanidine in human urine // *J. Chromatogr. B.* 2016. Vol. 1011. P. 1–5.

26. Prasad B.B. et al. Molecularly imprinted micro solid-phase extraction technique coupled with complementary molecularly imprinted polymer-sensor for ultra trace analysis of epinephrine in real samples // *Colloids Surfaces B Biointerfaces.* 2014. Vol. 113. P. 69–76.

27. Shi Y. et al. Selective solid-phase extraction of cholesterol using molecularly imprinted polymers and its application in different biological samples. // *J. Pharm. Biomed. Anal.* 2006. Vol. 42, № 5. P. 549–555.

28. Song R. et al. Molecularly imprinted solid-phase extraction of glutathione from urine samples // *Mater. Sci. Eng. C.* 2014. Vol. 44. P. 69–75.

29. Sun X. et al. Highly class-selective solid-phase extraction of bisphenols in milk, sediment and human urine samples using well-designed dummy molecularly imprinted polymers // *J. Chromatogr. A*. 2014. Vol. 1360. P. 9–16.
30. Serrano M. et al. On-line flow injection molecularly imprinted solid phase extraction for the preconcentration and determination of 1-hydroxypyrene in urine samples // *Talanta*. 2016. P. 1–8.
31. Nestic M. et al. Molecularly imprinted solid phase extraction for simultaneous determination of tetrahydrocannabinol and its main metabolites by gaschromatography-mass spectrometry in urine samples // *Forensic Sci. Int.* 2013. Vol. 231, № 1-3. P. 317–324.
32. Chrzanowska A.M., Poliwoda A., Wieczorek P.P. Surface molecularly imprinted silica for selective solid-phase extraction of biochanin A, daidzein and genistein from urine samples // *J. Chromatogr. A*. 2015. Vol. 1392. P. 1–9.
33. Enterosorption. Edited by N. A. Belyakov. Leningrad. 1991. 329 p.
34. Khotimchenko Yu. S., Kropotov A.V. The use of enterosorbents in medicine // *Pacific Medical Journal*. 1999, No. 2, pp. 84-89.
35. Uchaykin V. F. et al. The place and significance of enterosorption in etiopathogenetic therapy of OCI // *Pediatrics*. 2007, 86 (2), pp. 44-50
36. Ursova N. I., Gorelov A.V. Modern view on the problem of enterosorption. Optimal approach to drug selection. *RMZH*. 2006; 19: 1391-1396.
37. V.N. Panfilova, T.E. Taranushenko The use of enterosorbents in clinical practice//*Pediatric Pharmacology/2012.-9.-№6.- p.36-38* .
38. Vatutina O. V., Bestev V. I., Burova S. V. The effect of enterosorbent filtrum on the level of specific endotoxemia in patients with Flexner's shigellosis / *Sat. mat. XIV Congr. "Man and medicine"*. M., 2007. p. 536.
39. Zaitseva I. A., Koshkin A. P., Levin D. Yu. The use of enterosorbent "Filtrum" in the complex therapy of acute intestinal infections in children // *Childhood infections*. 2005, No. 1, pp. 61-62.
40. Novokshonov A. A. et al. The role of enterosorbents in the complex therapy of acute intestinal infections in children // *Practice of pediatrician*. 2008, No. 5, pp. 20-26.
41. Novokshonov A. A., Portnykh O. Yu., Sokolova N. V. The study of the clinical efficacy of the oral sorbent "Filtrum" in children with OCI / *Proceedings "Application of the method of enterosorption in practical medicine"*. M., 2002. pp. 24-31.
42. Gruzdeva O. A., Maryin G. G. Features of the incidence of acute intestinal infections in the modern metropolis / *Materials of the III Annual All-Russian Congress on Infectious Diseases*. Moscow, March 28-30, 2011. p. 83.



43. Mazankova L. N., Pavlova A. A. Improvement of pathogenetic therapy of acute intestinal infections in children // *Childhood infections*. 2006, 4, pp. 67-69
44. Uchaykin V. F., Novokshonov A. A., Sokolova N. V., Berezhkova T. V. Enterosorption - the role of enterosorbents in the complex therapy of acute and chronic gastroenterological pathology. Handbook for doctors. M., 2008. 24
45. Infectious diseases: national guidelines / Edited by N. D. Yushchuk. Yu. Ya. Vengerov. M.: GEOTAR-Media, 2009. 1056 p.
46. Rational pharmacotherapy of children's diseases: Hands. for practicing doctors / Under the general editorship of A. A. Baranov, N. N. Volodina, G. A. Samsygina M.: Litterra, 2007. Vol. 1. 1088 p.
47. Handbook of infectious Diseases / Edited by Yu. V. Lobzin 3rd ed., add. And reworked . St. Petersburg: Folio Publishing House. 2003. 1040 p.
48. Zaitseva I. A., Koshkin A. P., Levin D. Yu. The use of enterosorbent "Filtrum" in the complex therapy of acute intestinal infections in children // *Childhood infections*. 2005, No. 1, p. 62.