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REVIEW OF THE LITERATURE ON THE TOXIC EFFECT OF ALCOHOL ON THE BODY OF CURRENT METHODS OF TREATMENT OF ALCOHOL INTOXICATION

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Abstract

Based on the literature review, the main risks of acute and chronic alcohol intoxication are outlined: alcohol coma, acute alcoholic hepatitis, alcoholic liver disease, cirrhosis, cancer, cardiovascular disease, alcoholic encephalopathy and psychosis, etc. The main moments of alcohol metabolism and toxicological aspects of its metabolites are highlighted, biomarkers of alcohol are noted. The main aspects of treatment of acute alcohol poisoning are considered and the list of modern drugs is indicated, their effects and mechanisms of action are studied. Based on the analysis of protocols for the provision of medical care for chronic poisoning, the main pharmacological groups used in different countries - the United States, Italy, Ukraine. The main and side effects of drugs used in the treatment of alcohol intoxication are determined. Literature data on the structure, functions, therapeutic effects and prospects of AP use in medical and pharmaceutical practice are clarified and generalized.

Keywords: *toxic effect of alcohol, alcohol intoxication, methods of treatment.*

Problems associated with alcohol abuse - is not only acute and chronic poisoning, alcohol dependence, but also the development or complication of chronic diseases of the central nervous system, heart and blood vessels, liver and gastrointestinal tract in general, endocrine system, carcinogenesis, etc.

Treatment of alcoholism and its complications can be effective in the initial stages, and long and complex, practically ineffective at the stage of addiction.

The impact of alcohol on the body and the current treatment options for alcohol intoxication, as well as the properties of our chosen for the study of apple pectin (AP) is devoted to this section.

Ethanol, C2H6O, of any origin (grain, grape, fruit, synthetic, etc.) has long been used by mankind in different concentrations and for different purposes. Alcoholic beverages of varying strengths are widely consumed around the world, and therefore the problems associated with this are global. [1]. Due to the small size of the molecule and the hydroxyl group, it dissolves well in water and lipids, which promotes its free transition from body fluids to cells.

Alcohol is mainly absorbed in the small intestine and only 20% of the consumed dose is absorbed in the stomach, where there is a presystemic metabolism of ethanol by alcohol dehydrogenase, which is produced by the microbial flora of the stomach. In healthy people, alcohol taken on an empty stomach is completely absorbed within 1 hour after a single intake. After absorption through the portal circulation from the intestine, ethanol first passes through the liver, where its bulk is metabolized. The rate of oxidation of ethanol after a single use is approximately 100 mg / kg / h for men and 85 mg / kg / h for women. When drinking alcohol at a dose of 1 g / kg (peak concentration of ethanol in the blood - about 1.0 g / l) acetaldehyde is detected in the blood for 3 hours at concentrations of 0.0001 - 0.001 g / l [2].

The oxidation process of ethanol can take place in at least three different enzymatic ways. The most important option is oxidation under the influence of cytosol ADG hepatocytes, which is activated by NAD + and converts ethanol to acetaldehyde, which is further oxidized to acetate by mitochondrial aldehyde dehydrogenase [3]. Oxidation of ethanol in the liver under the influence of ADH does not depend on its concentration. The second major route of alcohol metabolism is the microsomal ethanol oxidation system (MSOE), which includes the enzyme cytochrome P450 CYP2E1 and needs NADP. MSOE includes cytochrome activity P450, which is responsible for the oxidation of ethanol, and that this activity is different from ADH and catalase. Ethanol-induced cytochrome P450, present in MEOS, was cleaned and marked as CYP2E1. Induction of mRNA and enzymatic activity CYP2E1 varies from 4 to 10 times in the liver after alcohol consumption. Given that the pathway of ethanol metabolism in MSOE induced in chronic alcoholics, increased ethanol metabolism probably contributes to the metabolic tolerance of alcoholics to it, which in turn contributes to further alcohol consumption. Activity CYP2E1 is also important in the metabolism of several xenobiotics, especially those contained in cigarette smoke (eg benzene and nitrosamines) [3]. Thus, increased expression of this enzyme in alcoholics may have a significant effect on the production of toxic metabolites, and this is believed to contribute to ethanol-induced liver damage [4, 5, 6].

The third way of transformation is non-oxidizing, which leads to the formation of ethyl esters of fatty acids and occurs primarily in the liver and pancreas - organs very sensitive to the toxic effects of alcohol.

Another possible option is the metabolism of ethanol in peroxisomes due to catalase activity. Yes, about 2% of alcohol is broken down and it

does not play a big role in the metabolism of alcohol in people who do not abuse alcohol, but in chronic alcoholics this percentage is much higher. The oxidation of ethanol by catalase depends on its concentration in tissues [5]. The volume of distribution of ethanol in the body is 0.53 l / kg, and the rate of distribution in liquid media is directly proportional to the speed of blood flow [1, 3].

Differences in the rate of absorption, distribution and elimination of alcohol significantly contribute to the development of clinical manifestations observed in chronic alcohol consumption. These differences are explained by both genetic and environmental factors, gender, alcohol consumption patterns, starvation or nutrition, chronic alcohol consumption. [7]. Because polymorphisms ADG and aldehyde dehydrogenases play an important role in determining peak blood acetaldehyde levels and alcohol desire, they also affect sensitivity to alcohol dependence. [8]. In addition, certain proteins are particularly susceptible to the formation of complexes with acetaldehyde. These include erythrocyte membrane proteins, lipoproteins, hemoglobin, albumin, collagen, tubulin and several cytochromes, including CYP2E1 [9]. It is believed that at least 15% of circulating acetaldehyde is bound to hemoglobin, such compounds are stable and have a half-life of 5.5 days. The formation of stable complexes of acetaldehyde with hemoglobin may lead to a decrease in the ability to bind and transport oxygen, and thus to hypoxia and anemia [10, 11]. In chronic alcoholism, myelosuppression is observed, accompanied by a decrease in the number of blood cells. Alcoholics suffer from moderate anemia, decreased white blood cell count, especially neutrophils, varying degrees of platelet count [12]. In chronic alcoholism, a megaloblastic type of erythropoiesis is often observed due to cyanocobalamin and folic acid deficiency. [11, 13, 14].

Another feature of alcohol metabolism is generation AFC, which are largely regulated (and which may be exacerbated) by the family CYP2E1 [8]. These active radicals are usually produced by mitochondria, endoplasmic reticulum or Kupffer cells. They rapidly form a variety of active metabolites that can further contribute to oxidative stress in hepatocytes. [9]. In addition, acetaldehyde, the major metabolite of ethanol C_2H_4O, is a potent hepatotoxin. Numerous studies show that acetaldehyde-induced liver damage occurs through mechanisms that contribute to glutathione depletion, toxicity AFC and lipid peroxidation [9,15, 16, 17,].

Thus, ethanol metabolism can lead to direct biochemical changes in hepatocytes, including cytotoxic metabolites, AFC accumulation, and lipid peroxidation. Importantly, all of these effects can further cause complex pathological reactions that over time cause liver damage: inflammation, various types of cell death (mostly apoptosis and necrosis), steatosis, fibrogenesis, and even liver degeneration. [18, 19].

The cell regulates the number AFC through a system of antioxidant protection, including various antioxidant compounds (for example, glutathione, GSH). As acetaldehyde binds SH-glutathione group and thus reduces the amount of reduced glutathione in the cell, thereby limiting the activity and function of glutathione peroxidase, which is involved in the catabolism of hydrogen peroxide. During the oxidation of ethanol production AFC increases sharply due to induction CYP2E1 and activation of Kupffer cells in the liver. The accumulation of free radicals induces activation POL of membranes and disturbance of structure of a lipid layer [20]. Both acute and chronic alcohol consumption can increase ROS production and lead to oxidative stress [21]. In the initial stages of alcoholism, the oxidation of acetyl-CoA in the Krebs cycle is the main source of energy for the cell In the initial stages of alcoholism, the

oxidation of acetyl-CoA in the Krebs cycle is the main source of energy for the cell [3]. In the cytoplasm begins the synthesis of fatty acids and triacylglycerols, hypertriacylglycerolemia develops. In chronic alcoholism, a decrease in the synthesis of phospholipids and proteins in the liver causes the accumulation of triacylglycerols in hepatocytes and liver obesity [22]. Acute alcohol intoxication increases the synthesis of ketone bodies, increases the concentration of lactate and acetoacetic acid, which is the cause of metabolic acidosis [3, 19]. In addition, the metabolism of ethanol in chronic intoxication leads to a decrease in fatty acid oxidation and conversion of carbohydrates into lipids, an increase in triacylglycerols, causes fatty infiltration and liver failure [5, 23, 24]. Disruption of energy processes is also associated with an increase in the formation of ammonia, which distracts 2-oxyglutarate from the Krebs cycle. Mitochondria in this regard are deficient in succinate - the most powerful energy source among all substrates of the tricarboxylic acid cycle. Acetaldehyde, due to the high reactivity of its carbonyl group, hardly circulates freely. Its ability to direct, non-enzymatic interaction extends primarily to proteins and is determined by the ability to covalently interact with their amino and sulfhydryl groups. [25]. By interacting with structural and functional proteins of plasma and blood cells, cellular elements of vascular endothelium and other tissues, acetaldehyde disrupts their structural organization and functional activity. [9,17].

Inhibition of protein metabolism is important. At chronic alcohol intoxication disturbance of protein-synthesizing function of a liver which is shown by decrease in levels of albumin, globulin, blood coagulation factors by disturbance of reparative processes and development of dystrophic processes in various bodies develops. [26, 27, 28] .

Although ethanol metabolism occurs predominantly in hepatocytes, enzymes involved in the oxidative metabolism of alcohol are also present in the intestinal mucosa, and intestinal bacteria also produce acetaldehyde in GIT [29, 30, 31]. In addition, less often non-oxidative metabolism of alcohol occurs in the intestine due to reactions with membrane phospholipids and / or free fatty acids. This alternative route may be especially relevant when intestinal damage occurs after chronic alcohol consumption [9]. Both the small and large intestines can be damaged by alcohol and its metabolites due to oxidative and non-oxidative metabolism. Alcohol metabolism in the gastrointestinal tract can lead to disruption of tissue homeostasis and chronic inflammation of the intestinal mucosa [20, 22]. The main mechanisms of intestinal damage under the influence of alcohol are bacterial dysbiosis, excessive growth of bacteria, increased permeability of the intestinal wall, suppression of local immunity [32, 34].

Studies show that alcohol promotes both dysbacteriosis and bacterial growth, which in turn leads to increased release of endotoxins produced by gram-negative bacteria. Endotoxins activate proteins and immune cells that promote inflammation [32]. Increased intestinal permeability consists in disruption of the epithelial cells themselves (transepithelial permeability) and changes in the intervals between them (paraclitic permeability), which consist of close compounds, cytoskeleton and several associated proteins. Trans-epithelial permeability is due to direct cell damage [33]. It is believed that alcohol-induced inflammation of the intestines contributes to the development of cancer and inflammatory bowel disease, and outside the gastrointestinal tract in the form of liver disease and neuroinflammation [34, 35].

In recent years, the idea of "intestinal-brain axis" has gained popularity. While it is not surprising that the brain can control bowel function, there is already ample evidence that the gut can interact with brain function. The main driver of this intestinal behavior to control

the human brain is the result of the activity of the intestinal microbiome [32, 34]. Convincing evidence of changes in the gut that lead to changes in the brain is the treatment of hepatic encephalopathy, which develops as a result of the liver's failure to filter ammonia molecules produced by gut bacteria, leading to the accumulation of these small molecules in the brain, causing astrocytic edema. . Hepatic encephalopathy is treated with lactulose, laxative and oral rifaximin, an antibiotic that initially remains in the intestinal lumen and is poorly absorbed. [32]. By treating only the intestines, it is possible to treat the pathology of the central nervous system. More direct evidence of this is the result of two independent studies, where the transplantation of intestinal contents from one animal to another could repeatedly cause behavioral changes. [32, 34].

There is also a post-intoxication condition that occurs when drinking alcohol in doses exceeding 1.0 g / kg, and develops after reducing the concentration of ethanol in the blood to 0.2 g / l and below. The severity of this condition directly depends on the amount of alcohol consumed and the severity of intoxication [6,36,37]. The severity of the course in different individuals with the same dose of ethanol varies greatly. This is due to ethnic, age and individual characteristics of alcohol metabolism, which determine the intensity of production and oxidation of acetaldehyde in the liver. With age, the severity of the post-intoxication condition increases. Characteristic signs of this syndrome are headache, dyspeptic disorders, problems with concentration, suppression of psychomotor and behavioral reactions, which can create problems in the performance of official duties or driving. [19, 38, 39, 40].

Chronic ethanol abuse contributes to a range of metabolic disorders that are common in alcoholics. These disorders include alcoholic liver disease, hyperlipidemia, lactic acidosis, ketoacidosis, and hyperuricremia. The first stage of liver damage after chronic alcohol consumption is the appearance of fatty liver disease, accompanied by inflammation, apoptosis, fibrosis and, finally, cirrhosis [5, 24, 37, 41].

The liver and brain interact in different ways to ensure the normal functioning of the brain. The liver also removes toxic substances from the blood, including substances formed in the brain and other tissues and must be excreted from the body, including neurotoxic. Thus, impaired liver detoxification function can cause brain dysfunction and even contribute to brain damage.

Liver dysfunction of varying severity is a frequent complication of chronic alcohol abuse. When the liver becomes fibrous and cirrhotic, the number of functional hepatocytes decreases and the liver loses the ability to remove toxic substances from the blood. Researchers have identified several toxins that are normally excreted in the liver but are found in patients with alcoholic cirrhosis, including ammonia, manganese, and chemicals called mercaptans, all of which are easily absorbed into the brain and are neurotoxic. Thus, brain function in patients with severe alcoholic liver disease is impaired, leading to a condition known as hepatic encephalopathy or portal systemic encephalopathy. [10, 19, 21, 42, 43].

It is known that chronic alcohol consumption significantly increases the risk of cancer of the esophagus and mouth, kidneys and pancreas, and also plays an important role in the development of liver cancer [8,44,45]. As mentioned above, ethanol metabolism leads to increased production of acetaldehyde and AFC, and complexes of acetaldehyde with proteins contribute to the development of cancer [25, 46, 47]. In addition, induction CYP2E1 AFC and all related cellular disorders, including cancer [44, 45].

Numerous multicenter studies in Europe and North America confirm the significant impact of

alcohol abuse on the course and mortality of cardiovascular disease [48, 49, 50,51]; increasing complications of diabetes [69]; increase in the frequency of complications in people with CNS pathology, increase in the incidence of infectious diseases (including sexually transmitted diseases), gastrointestinal disorders [25]. Alcohol use and abuse during pregnancy are especially dangerous.

Alcohol consumption is one of the most common causes of fatal road accidents in the world and in Ukraine in particular, as well as domestic violence, crime and occupational injuries. [7].

Diagnosis of acute and chronic poisoning is based on appropriate history, determination of alcohol content in biological fluids - blood, urine and hair by various methods [36, 52, 53], including the method of gas-liquid chromatography [54, 55, 56], as well as indicators of biomarkers of alcoholism [36, 55, 57, 58]. Direct biomarkers of alcohol intoxication valid for acute alcohol intoxication include: blood alcohol content; ethylglucuronide and ethyl sulfate, which are detected up to 36 hours in the blood and up to 5 days in the urine after alcohol consumption, but the sensitivity of these methods is significantly reduced after 24 hours and at low doses [59]. In conditions of chronic intoxication, specific and highly sensitive markers are carbohydrate-deficient transferrin and phosphatidylethanol [58]. Non-specific biomarkers include indicators of ALT, AST, gamma-glutamyltransferase activity [60], and the average volume of molecules [72]. The positive point in the definition of these biomarkers is that alcohol consumption can be detected by their changes within 3-6 weeks after that, and the negative - that these changes are not specific only to the effects of alcohol and may be increased in other pathological or physiological conditions [106].

The degree of alcohol poisoning is determined by the alcohol content in the blood. Treatment of acute alcohol poisoning worldwide is carried out according to standard medical care protocols [61].

The degree of acute intoxication is determined by the blood alcohol content. According to the accepted classification, the following degrees of intoxication are distinguished:

mild - the concentration of ethanol in the blood from 1 to 1.5 ‰;

medium degree - the concentration of ethanol in the blood from 1.5 to 3 ‰;

severe - the concentration of ethanol in the blood from 3 to 5 ‰;

alcoholic coma - the concentration of ethanol in the blood from 5 ‰ and more.

The lethal dose of 96% ethanol ranges from 4 to 12 g / kg body weight.

A blood ethanol concentration greater than 6 ‰ is lethal [24, 62].

Treatment depends on the degree of intoxication - as a rule, mild degree does not require medical intervention, moderate, severe and alcoholic coma require non-pharmacological and pharmacological measures. [63].

According to the Protocol of medical care, correction of dehydration, hypoglycemia, water-electrolyte balance, administration of vitamins B and C is necessary. In order to remove unabsorbed alcohol, gastric lavage and sorbents are administered [63]. Recommended use of drugs that reduce the concentration of alcohol and acetaldehyde in the blood - metadoxin, and restore respiratory depression and normalize blood pressure due to blockade of opiate receptors - naloxone [24, 57, 63]. Naloxone affects opiate receptors, which are thought to be directly related to the development of alcoholism through genetic mechanisms. Naloxone is used in acute alcohol poisoning, and a drug from the same group - naltrexone - is used in the treatment of alcohol dependence in chronic alcohol intoxication.

Metadoxin increases the activity of alcohol dehydrogenase and acetaldehyde dehydrogenase, thereby accelerating the oxidation of alcohol and its metabolites, reducing blood concentrations and reducing toxicity [57, 64].

Metadoxin is a selective antagonist of the subtype 5-HT2B serotonin receptors, which has a high affinity for gamma-aminobutyric acid and acts as a monoamine-independent modulator of GABA. Does not affect dopamine, norepinephrine or serotonin levels [65]. In animal studies, metadoxin increased the activity of the enzyme acetaldehyde dehydrogenase, prevented decreased ADH activity in animals with chronic alcohol intoxication, accelerated plasma and renal clearance of ethanol, reduced the formation of triacylglycerols, prevented the development of hepatic steatosis and POL [65]. Metadoxin is included in treatment protocols for acute and subacute alcohol intoxication in the United States and some European countries [57, 64, 65].

The next drug approved for the treatment of chronic alcoholism was acamprosate. First approved as a treatment for alcohol dependence in Europe in 1989, acamprosate was later registered and approved for use in the United States, Canada and Japan. Although the exact mechanisms of action of acamprosate have not yet been fully studied, there is evidence that it modulates hyperactive glutamatergic states, possibly by acting as an agonist of the N-methyl-D-aspartate receptor. [57, 64].

Enterosorption is recommended throughout the acute period of intoxication. Of the sorbent preparations, methyl silicic acid hydrogel, activated carbon, or other sorbents are recommended. [52, 61, 62, 63].

In the treatment of chronic alcoholism (chronic alcohol intoxication) use drugs of different chemical groups, which are divided by pharmacodynamic effects and origin, but the basis of the drug is the ability to form a negative conditioned reflex to alcohol, based on changes in ethanol metabolism. The most common method of treatment of alcohol dependence is the use of disulfiram (antabus). Disulfiram blocks the oxidation of ethanol during the formation of acetaldehyde and increases its concentration in the blood by 5-10 times, which causes the development of unpleasant symptoms with the use of even a small amount of alcohol. Disulfiram does not affect the rate of excretion of alcohol, it does not develop tolerance [66].

In Ukraine, according to the "Clinical Protocol for the provision of medical care to patients with mental and behavioral disorders due to alcohol consumption" [52] such groups of drugs as psycholeptics, antiepileptic drugs, vitamins, hepatoprotectors, peripheral vasodilators, means to reduce endotoxicosis and encephalopathy, pro- and prebiotics are used in treatment.

Prolonged alcohol abuse leads to the development of alcoholic liver disease [67], which can transform into cirrhosis or cancer. The problem of alcoholic hepatitis and fibrosis requires appropriate treatment, and therefore drugs from the group of hepatoprotectors, vitamins and pre- and probiotics are necessary components of a comprehensive treatment that has been proven experimentally and clinically [5,13,16,37,42].

Since the metabolism of almost 95% of alcohol occurs in the liver, it is the target organ of its toxic effects. As liver damage is the most common complication of chronic alcohol abuse, the development of alcoholic hepatitis and cirrhosis in Ukraine was the cause of death in 51.6% of men and 58.4% of women out of the total number of people with similar pathology of other origins. [7] It is investigated that ethanol and products of its metabolism inhibit the protein-synthesizing function of the liver [28, 68] and significantly affect lipid metabolism [17, 41].

Alcohol abuse is considered one of the possible factors in the development of metabolic syndrome, which is manifested by a complex of metabolic disorders and is accompanied by abdominal obesity, high blood pressure, increased triacylglycerols and low levels of high-density lipoprotein, resistance to resistance and resistance to resistance. [69, 70]. These symptoms contribute to the development of complications of diabetes and cardiovascular disease. Given the above, there is no doubt about the feasibility of introducing into pharmacotherapy of alcohol intoxication of lipid-lowering drugs.

A group of intestinal sorbents should be singled out, which includes a number of drugs that have the ability to bind endogenous and exogenous substances in the intestinal lumen, which significantly reduces their absorption and bioavailability. According to the literature, it is known that the group of intestinal sorbents consists of different drugs, which are divided by origin, chemical structure, dosage form and physicochemical properties, the mechanism of sorption and selectivity. The following groups are distinguished by chemical structure: carbon, silicon-containing, natural organic and combined [71, 72,73].

According to the mechanism of sorbing action, the following are distinguished: absorbents, adsorbents, ion exchange substances, sorbents with combined mechanisms and with catalytic properties [72].

In Ukraine, sorbents of all these groups are registered, but most often used for detoxification of carbon -CA, of silicon-containing - silica gel or "white coal" -SD [74,75,76,77].

Adsorption of xenobiotics CA in the digestive tract is based on the balance between the free xenobiotic and the CA / xenobiotic complex. CA possible desorption of xenobiotics from CA. But the use of adequate doses CA shifts the equilibrium towards the complex CA / xenobiotic. This type of interaction is the rationale for dosing: the ratio of CA: xenobiotic 10: 1 [77].

Best adsorbs xenobiotics in their non-ionized forms CA. Due to pharmacodynamics CA, non-polar, poorly water-soluble organic xenobiotics are best absorbed, and polar, water-soluble molecules are less adsorbed [72]. Some drugs have reduced systemic absorption in the presence of CA, such as acetaminophen, aspirin, barbiturates, tricyclic antidepressants, theophylline, phenytoin and most inorganic and organic materials. It is investigated that CA very weakly adsorbs alcohols, metals (iron and lithium), electrolytes, and also acids or alkalis due to polarity of these substances. [72].

The purpose of CA has a number of contraindications, namely:

- in patients with unprotected airways without endotracheal intubation;
- at high risk of gastrointestinal perforation or bleeding;
- if necessary, endoscopy, as CA may interfere with endoscopic imaging;
- in the presence of intestinal obstruction;
- under conditions of poisoning by metals, acids, alkalis, electrolytes or alcohols, which are poorly adsorbed by CA[72,77].

As a drug, SD is used in various dosage forms containing particles of silicon dioxide of different sizes, including nanoparticles. It has been investigated that adsorption is observed only for deprotonated molecules and is irreversible, since surface structures with strong coordination bonds between silicon atoms and adsorbate anions are formed. [75]. The increase in adsorption occurs with increasing molecular weight, decreasing polarity of the adsorbate, and others. It is believed that the basis of the biological activity of SD is its physicochemical properties, determined by the structure and reactivity of the adsorption centers of the surface, namely: high hydrophilicity of the surface; ability to sorb proteins; active binding of pathogenic microorganisms and viruses and

adsorption of low molecular weight polar substances [80]. The drug containing SD nanoparticles (Silix) acts as an enveloping agent due to the interaction with glycoproteins of the intestinal mucosa. The result of this interaction is to create an obstacle to the diffusion of pathogenic substances through the mucosa and reduce their absorption and protection of mucosal receptors from the adhesion of microorganisms and exposure to microbial toxins. Given that the intestinal mucosa throughout the pH from 6.0 to 9.0 has a negative charge, such an interaction for SD should occur with the overcoming of electrostatic repulsion. This means that the enveloping ability of SD will be weaker than that of drugs based on alumina, which are positively charged in the intestine. [75, 78, 79]. In general, the absorbing mechanism as the main for the manifestation of the therapeutic effect can be used only in the case of highly porous sorbents: activated carbon, zeolites, silica gel,Syloid® 244FP and others. [71, 73, 81].

Other drugs of the group of enterosorbents (anthralen, smecta, enterosgel, mycoton, polyfepan, polysorb, pectins, alginates, etc.) are more often prescribed for outpatient treatment or self-treatment of intestinal disorders, diarrhea in children, food poisoning. Given the structure, physicochemical, chemical and pharmacological properties AP and virtually no toxicity, we were interested in the possibility of its study for ethanol intoxication.

Pectins are high molecular weight heteropolysaccharides that make up about 1/3 of the cell wall composition of higher plants in terms of dry matter. Sources of pectin are apples, citrus fruits, sugar beets, soybeans and others.[82].

Depending on the structure and degree of polymerization, pectins are divided into pectic acids (products of polymerization of alpha-D-galacturonic acid residues, bound by 1,4-bonds, in linear chains, soluble in water and are the basis for other groups of pectin substances) , pectic acids (higher molecular weight compounds containing 100-200 units of alpha-D-galacturonic acid, the carbonyl groups of which can be methoxylated to varying degrees), pectates, pectinates (salts of pectic and pectic acids), protopectins - high molecular weight polymers of methoxylated polyglylate galactan and arabinan of the cell wall, which is sometimes interrupted by the remains of rhamnose, insoluble in water).

Empirical formula: $(C_6H_8O_6)_n \cdot (OCH_3)_m$, n about 50; m = 30-80 % from n. [50].

Pectins are obtained from wastes from the production of fruit juices (apple, lemon, lime, orange, tangerine), sometimes from wastes from the production of beet sugar or sunflower oil by acid extraction and precipitation by alcohol. Pectins are classified by the degree of methoxylation (esterification), namely by the ratio of the number of methoxyl groups $-OCH_3$ to all acid residues in the molecule [83].

Highly methoxylated pectin forms a gel in the presence of acid (within pH about 3) and sugars. When the pH decreases, the dissociation of free carboxyl groups slows down, and the number of negatively charged ions in pectin decreases accordingly. This in turn reduces the attraction between pectin molecules and water molecules and reduces the repulsive force between the molecules of the high molecular weight substance. Sugar further reduces the hydration of pectin, competing for water. These conditions reduce the ability of pectin to be in a dispersed state. Therefore, at low temperatures, less hydrated pectin forms a gel - a continuous network of pectin, which holds an aqueous solution.

Low methoxylated pectin requires divalent metals to form a gel. Calcium and magnesium ions are present in the composition AP. [84, 85]. Highly methoxylated pectins with a degree of esterification of more than 50% have a high molecular weight and are capable of forming gems. In order for the gems to be stable, there must be certain conditions, namely - an acid

reaction (pH about 3.0) and the presence of sugar [86, 87].

Low-methoxylated pectins are able to form chelated compounds in the body by demethoxylating pectin and converting it into polygalacturonic acid, which binds to some heavy metals and radionuclides, and remove them from the body with feces. [88,89]. Molecular weight and degree of esterification affect the activity of pectins in the formation of complexes with metals: pectin more strongly than CA adsorbs lead, radioactive cobalt, strontium, cesium, ruthenium and other metals by forming pectates and pectinates [89,90,91,92]. Different extraction methods, the types of plants from which it is obtained, different fragmentation methods and complex structure make the characterization of the active pectin molecule complex.

Highly esterified pectins, with a degree of methoxylation of 50% or more, are readily soluble in water. Known properties of pectin to form chelated compounds with metal salts - pectinates that are insoluble in water and not adsorbed in the intestine [93]. These properties are due to the presence of carboxyl and hydroxyl groups in the pectin molecule [94]. It has also been investigated that low-esterified pectins, which have more carboxyl groups than high-esterified ones, form metal chelates more easily. Highly esterified pectin envelops the intestinal wall and reduces the contact of food and other components of chyme with its surface, and through the mechanism of gel filtration reduces the absorption of small molecules [95,96,97].

Researchs in vitro, conducted Dongovski G. and co-authors [62], showed that under conditions that mimic the lumen of the gastrointestinal tract, slightly reduced the degree of esterification of pectin in the small intestine of rats without microflora and normal rats and additionally in the cecum and colon of rats in the absence of microflora. Pectin passes through the small intestine in the form of a macromolecule. The molecular weight distribution of pectins, measured by gel chromatography with viscosity detection, was almost unchanged. However, during the in vitro fermentation of pectin with human fecal flora, unsaturated oligogalacturonic acids were detected as intermediates in variable concentration and composition within approximately 8 hours. [96]. Pectin reduces the rate of digestion due to the immobilization of food components in the intestine. This leads to less absorption of food. The thickness of the pectin layer affects absorption, limiting contact between digestive enzymes and food, thus reducing its availability [98]. Pectin reduces the absorption of water and glucose in the small intestine at different dosages [99,100,101,102,103].

Prebiotic properties of pectin are associated with the ability of individual members of the normal intestinal microflora to ferment pectin and dispose of it for the growth and development of microbiota colonies [29,30,31,104].

Pectin is not absorbed in the human body. In the upper gastrointestinal tract, pectin is not digested and can protect cells from mutagenic attacks. In the colon, bacteria ferment pectin into butyrate, which suppresses inflammation of the colon and prevents carcinogenesis.

Pectin is not absorbed in the human body. In the upper gastrointestinal tract, pectin is not digested and can protect cells from mutagenic attacks. In the colon, bacteria ferment pectin into butyrate, which suppresses inflammation of the colon and prevents carcinogenesis. [46].

In medical practice, the properties of pectin have been used in several fields and for different indications. The ability of pectin to agglutination of microorganisms is used to treat wounds and burns in surgery and combustiology [106, 107]. he ability to reduce the absorption of glucose and fats in the intestine by the use of pectin is used in the

complex treatment of diabetes and hyperlipidemia.

The antidiarrheal effect of pectin is used in the treatment of intestinal failure and as a symptomatic remedy for diarrhea in pediatric practice [72, 111]. The gastroprotective properties of pectin with the use of aspirin and alcohol have also been studied [100].

Numerous experimental studies have shown the effectiveness of pectin use in colon cancer and reduce metastasis. It has been experimentally proven that pectin has the ability to inhibit tumor growth, induce apoptosis through fragmentation DNA in HT29 colon cancer cells, inhibit metastasis and modulate immune responses [34,113].

Chelation with heavy metal salts and radionuclides was an indication for the use of pectin for prevention and treatment of intoxications in people living in areas contaminated with salts of heavy metals and radionuclides. [32].

Properties of pectin as an absorbent, used for therapeutic purposes in endogenous and exogenous toxicosis [72]. Pectin shortens blood clotting time and can be used to stop bleeding locally. Pectin slows down the motility of the stomach, gives a feeling of satiety, used in the treatment of obesity and overeating. [99,110].

Prebiotics are used to alter the intestinal microbiota through the selective stimulation of bacteria in the intestinal tract that are considered positive for human health. Prebiotics, such as inulin and galacto-oligosaccharides (pectins), are often targeted to the genus Bifidobacterium. his is due to the size and molecule structure of these prebiotics. Investigation of the product of hetero-oligosaccharides, which is made by the method of reverse synthesis β- galactosidase from enzymes Bifidobacterium bifidum NCIMB 41 171 showed that this mixture of Bimuno-GOS supports the growth of bifidobacteria in young, overweight people and in patients with irritable bowel syndrome. In addition, animal models have shown that the mixture demonstrates antimicrobial mechanisms against Salmonella enterica Typhimurium, and there was a positive effect on the immune response in overweight elderly people[15].

Pectin is used as a sorbent in the form of a monopreparation and in various combinations for the treatment of poisoning by salts of heavy metals. [92,101,102].

In the pharmaceutical industry, pectin is widely used as a stabilizer, an excipient in the manufacture of drugs: capsules of pectin, which is not destroyed by digestive enzymes in the upper gastrointestinal tract [99], allow to deliver medicinal substances to the destination - in the colon [114,115,116], than enhance the effect or reduce the toxic effects of drugs.

The combination of cisplatin with pectin significantly reduces the toxicity of this antitumor drug [117], and the introduction of pectin to the nasal spray with fentanyl improves the pharmacokinetic properties of the latter without changing the bioavailability [118].

Pectins are used in the pharmaceutical and food industries as gelling agents, adsorbents, emulsifiers, stabilizers, thickeners, water-retaining agents, clarifiers, substances that facilitate filtration, encapsulating agents, production of nutrient media [82,90]. They have the ability to prolong the action of drugs.

Given the sorption and prebiotic properties of pectin, it is logical to assume that alcohol intoxication is likely to have a positive detoxifying effect.

Thus, the literature data on alcohol metabolism and its effect on the human body were analyzed. According to the results of the analysis conducted by WHO experts in 2016, it was found that the amount of alcohol consumption per capita is one of the highest in Europe and is 13.8 litres.

Based on the literature review, the main risks of acute and chronic alcohol intoxication are outlined: alcohol coma, acute alcoholic hepatitis, alcoholic liver disease, cirrhosis,

cancer, cardiovascular disease, alcoholic encephalopathy and psychosis, etc. The main moments of alcohol metabolism and toxicological aspects of its metabolites are highlighted, biomarkers of alcohol are noted. The main aspects of treatment of acute alcohol poisoning are considered and the list of modern drugs is indicated, their effects and mechanisms of action are studied. Based on the analysis of protocols for the provision of medical care for chronic poisoning, the main pharmacological groups used in different countries - the United States, Italy, Ukraine. The main and side effects of drugs used in the treatment of alcohol intoxication are determined. Literature data on the structure, functions, therapeutic effects and prospects of AP use in medical and pharmaceutical practice are clarified and generalized.

References

1. Thompson W., Randon S.W. Alcoholism. Overview. [Internet]. Доступно з: www. http://emedicine.medscape.com/article/2859 13- Updated: Nov 14, 2016. Accessed September 26, 2017.
2. Ethanol Metabolism. [Інтернет]. Доступно з: https://themedical biochemistrypage.org/ethanol-metabolism.php. Last modified: Dec.13, 2018.
3. Severin.S., editor. Biochemistry. Textbook for universities.2- is ed. M: Geotar-Med;2019:768.
4. Alexandrova KV, Skoda OS, Vasiliev DA, Yurchenko DM, Levich SV Determination of enzyme activity in biological media. Units of enzyme activity. Enzymopathy. Medical enzymology. Zaporozhye: Zaporozhye State Medical University.2015. 45c.2015. 45c.
5. Baryshnikova H.V. Alcoholic liver disease: features of diagnosis and treatment. Gastroenterology. Supplement to the journal Consilium Medicum.2014; 2: 16-18.
6. Jonas D.E., Amick H.R., Feltner C., et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. JAMA.doi:10.1001/jama.2014.3628.
7. Global status report on alcohol and health 2018. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO. Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.
8. Jelski W., Szmitkowski M. Alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) in the cancer diseases. Clin Chim Acta. 2008;3(95):1–5.
9. Jensen N.S., Canale-Parola E. Bacteroides pectinophilus sp. nov. and Bacteroides galacturonicus sp. nov.: two pectinolytic bacteria from the human intestinal tract. Appl Environ Microbiol. 1986;52:880–887.
10. Frakes Vozzo C, Welch N., Romero-Marrero C., Fairbanks K.D. Alcoholic Liver Disease. Інтернет: http://www.clevelandclinicmeded.com/ medicalpubs/disease management/hepatology/alcoholic-liver-disease/. Published: June 2018.
11. Lee S.Y., Park H.J., Best-Popescu C., Jang S., Park Y.K. The Effects of Ethanol on the Morphological and Biochemical Properties of Individual Human Red Blood Cells. PLoS ONE. 2015; 10(12): e0145327. https://doi.org/10.1371/journal.pone.0145327
12. Elanchezhian, Yoganandh T., Mayilsamy S., Radhakrishnan S. Comparison of haematological parameters between alcoholics and non-alcoholics. Int J Res Med Sci. 2017;5(11):5041-5047.
13. Alende-Castro V, Alonso-Sampedro M, Vazquez-Temprano N, Tuñez C, Rey D, García-Iglesias C.et al. Factors influencing erythrocyte sedimentation rate in adults. New evidence for an old test. Medicine: August 2019,98(34):p e16816. doi: 10.1097/MD.0000000000016816.
14. Mutlag S., A Abdulhussein A.J., Mustafa S., Taher M.A., Hawi A.J. The assessment of alcohol effects on red blood cell indices in rats. Drug Invention Today. 2018; 10(special issue 3):3153-3158.
15. Chandini, Mathai P.J. Haematological Parameters in Patients with Alcohol Dependence Syndrome. Journal of Dental

and Medical Sciences (IOSR-JDMS) . 2017;16(5):11-16. DOI: 10.9790/0853-1605011116.
16. Das SK, Vasudevan D.M. Monitoring oxidative stress in patients with non-alcoholic and alcoholic liver diseases. Indian J Clin Biochem. 2005; 20(2), 24-28. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3453846/
17. Gupta S., Figueredo V.M. Alcohol and lipids. OA Alcohol. 2014; 2(1):3-15. www.oapublishinglondon.com/article/1223.
18. Kim S.K., Hong S-H, Chung J-H, Cho K.B. Association Between Alcohol Consumption and Metabolic Syndrome in a Community-Based Cohort of Korean Adults. Med Sci Monit. 2017; 23: 2104–2110.Published online 2017 May 3. doi: 10.12659/ MSM.901309
19. Louvet A., Mathurin P. Alcoholic liver disease: mechanisms of injury and targeted treatment. Nature Reviews Gastroenterology & Hepatology, 2015;12:231–242.
20. Mukherjee S. Alcohol metabolism and generation of free radicals: A deep insight. OA Alcohol. 2014;2(1):10.
21. Das SK, Vasudevan D.M. Monitoring oxidative stress in patients with non-alcoholic and alcoholic liver diseases. Indian J Clin Biochem. 2005; 20(2), 24-28. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3453846/
22. Mukherjee S. Alcoholism - a deep insight to its role in various diseases: A critical review. OA Alcohol. 2013;1(2):11-17.
23. Butorova L.I. Hepatoprotective therapy of fatty liver disease of non-alcoholic and alcoholic origin. Effective pharmacotherapy.2016; 34: 12-21.
24. Rykalo N.A, Romanenko I.V. Pathomorphological changes of the liver and biochemical changes of blood serum in acute alcoholic hepatitis under experimental conditions. Experimental and clinical medicine. 2016; 2 (71): 156-160.
25. Setshedi M., Wands J.R., Monte S.M. Acetaldehyde adducts in alcoholic liver disease. Oxid Med Cell Longev. 2010;3:178–185.
26. Konopelnyuk V.V, Voitenko V.V, Savchuk O.M, Ostapchenko L.I The content of amino acids in the serum of rats in chronic alcohol intoxication. Laboratory diagnostics. 2013; 1 (63): 44-47.
27. Raksha N.G, Konopelnyuk V.V, Savchuk O.M, Ostapchenko L.I Transferrin as a potential marker for diagnosing chronic alcohol intoxication. Biological Studies / Studia Biologica. 2014; 8 (3–4): 79–86.
28. Stepanets I., Morgaenko O., Ostapchenko L. Protein composition of serum of rats under conditions of development of chronic alcohol intoxication. Visn. Lviv. University. Biologist series. 2013; 61: 30–36.
29. Dongowski G., Lorenz A., Anger H. Degradation of Pectins with Different Degrees of Esterification by Bacteroides thetaiotaomicron Isolated from Human Gut Flora. Appl Environ Microbiol. 2000; 66(4): 1321–1327.
30. Jensen N.S., Canale-Parola E. Nutritionally limited pectinolytic bacteria from the human intestine. Appl Environ Microbiol. 1985;50:172–173.
31. Jensen N.S., Canale-Parola E. Bacteroides pectinophilus sp. nov. and Bacteroides galacturonicus sp. nov.: two pectinolytic bacteria from the human intestinal tract. Appl Environ Microbiol. 1986;52:880–887.
32. Bishehsari F, Magno E, Swanson G, Desai V, Voigt RM, Forsyth CB, Keshavarzian A. Alcohol and Gut-Derived Inflammation. Alcohol Res. 2017; 38(2): 163–171.
33. de Lima M.B., Gama A., Hauschildt A.T., Dall'Agnol DJR, Corá LA, Americo MF. Gastrointestinal Motility, Mucosal Mast Cell, and Intestinal Histology in Rats: Effect of Prednisone. BioMed Research International. 2017; Article ID 4637621: 8. https://doi.org/10.1155/2017/4637621
34. Gorky J., Schwaber J. The role of the gut-brain axis in alcohol use disorders. Prog Neuropsychopharmacol Biol Psychiatry. 2016;65:234-41. doi: 10.1016/j.pnpbp .2015. 06.013.
35. Nnamdi G Nelson, Faten A Suhaidi, Ross S DeAngelis, Nu-Chu Liang. Appetite and weight gain suppression effects of alcohol

depend on the route and pattern of administration in Long Evans rats. Pharmacology Biochemistry and Behavior, 2016; 150-151: 124 DOI: 10.1016/j.pbb.2016.10.006
36. Derecha L.M., Myasoyedov V.V., Bondarenko V.V. Objectification of laboratory diagnostics of acute and chronic alcohol intoxication with the use of modern biochemical markers. Theory and practice of forensic science and criminology. 2016; 16: 406-412.
37. Lamas-Paz A., Hao F., Nelson L.J., Vázquez M.T., Canals S., Gómez del Moral M., Martínez-Naves E., Nevzorova Y.A., Cubero F.J. Alcoholic liver disease: Utility of animal models. World J Gastroenterol. 2018; 24(45): 5063-5075. DOI: https://dx.doi.org/10.3748/wjg.v24.i45.5063
38. Effects of alcohol abstinence on glucose metabolism in Japanese men with elevated fasting glucose: A pilot study. Scientific Reports, 2017; 7, Article number: 40277. Published: 09 January 2017.
39. Kim S.K., Hong S-H, Chung J-H, Cho K.B. Association Between Alcohol Consumption and Metabolic Syndrome in a Community-Based Cohort of Korean Adults. Med Sci Monit. 2017; 23: 2104–2110.Published online 2017 May 3. doi: 10.12659/ MSM.901309
40. Mukherjee S. Alcoholism - a deep insight to its role in various diseases: A critical review. OA Alcohol. 2013;1(2):11-17.
41. Hainiuk M., Sheremeta L. The apple pectin influence upon the liver histological structure and the activity of lipid peroxidation in experimental acute alcohol intoxication. The Pharma Innovation Journal. 2019; 8(2): 590-593.
42. Frazier T.H., Stocker A.M., Kershner N.A., Marsano L.S., McClain C.J. Treatment of alcoholic liver disease. Therap Adv Gastroenterol. 2011; 4(1): 63–81. doi: 10.1177/1756283X10378925.
43. Morgan T.R. Treatment of Alcoholic Liver Disease. Gastroenterology & Hepatology, 2017;13(7). Інтернет: https://www.gastroenterologyandhepatology. net/archives /july-2017/treatment-of-alcoholic-liver-disease/.
44. Bagnardi V, Rot, M, Botteri E, Tramacere I, Islami F, Fedirko V et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose–response meta-analysis. Br J Cancer 2015;112: 580–593. doi:10.1038/bjc.2014.579.
45. Seitz H.K., Stickel F. Molecular mechanisms of alcohol-mediated carcinogenesis. Nat Rev Cancer. 2007;7:599–612.
46. Hainiuk M.B. Apple pectin as a detoxifier in acute and chronic alcohol intoxication. Innovations in medicine: Abstracts of the 88th scientific-practical conference of students and young scientists with international participation, March 28-30, 2019. Ivano-Frankivsk; 2019: p.83.
47. Cao Y, Willett WC, Rimm EB, Stampfer MJ, Giovannucci EL. Light to moderate intake of alcohol, drinking patterns, and risk of cancer: results from two prospective US cohort studies. BMJ 2015;351:h4238.
48. Kiyak Y.A., Onishchuk Y.I., Bashta A.A., Peretyatko N.A., Fartushok N.A. Cardiovascular complications with excessive alcohol consumption. Experiment. and wedge. physiology and biochemistry. 2015; 3: 72-76.
49. Klatsky A.L. Alcohol and cardiovascular diseases: where do we stand today? J Intern Med. 2015; 278(3):238-250. doi: 10.1111/joim.12390. Epub 2015 Jul 8.
50. Ogunmoroti O., Osibogun O., McClelland R.L., Burke G.L., Nasir K., Michos E.D. Alcohol and ideal cardiovascular health: The multi_Ethnic study of atherosclerosis. Clin Cardiol. 2019; 42(1):151-158.
51. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. -2018. URL https://www.R-project.org/.
52. Protocols of medical narcological care (2009). Collective of authors. Kyiv. Access code: https://phc.org.ua/uploads/files/pdf.
53. Raksha N.G., Konopelnyuk V.V., Savchuk O.M., Ostapchenko L.I. Transferrin as a potential marker for diagnosing chronic alcohol intoxication. Biological Studies / Studia Biologica. 2014; 8 (3–4): 79–86.

54. Basharova R.V., Musina L.D., Khakimova A.L. Identification of acetaldehyde in biological objects by gas chromatographic method. Current issues of forensic medicine and law. Kazan. 2010; 1. [Internet] Publication in electronic media: 22.10.2011 Available from: http://journal.forens-lit.ru/node/392.
55. Trofimchuk G.E, Tishchenko G.M, Sinitska T.V Features of laboratory methods for diagnosing intoxication with psychoactive substances. Archive of psychiatry. 2009; 3 (58): 66-71.
56. Shcherbina O.M., Bedzai A.O., Mikhalichko B.M. Identification of hazards associated with poisoning of the human body by alcohol and its surrogates by chromatography. Bulletin of LSU BJD. 2012; 6: 168-175.
57. Caputo F, Agabio R, Vignoli T, Patussi V, Fanucchi T, Cimarosti P. et al. Diagnosis and treatment of acute alcohol intoxication and alcohol withdrawal syndrome: position paper of the Italian Society on Alcohol. Internal and Emergency Medicine. [Інтернет] https://doi.org/10.1007/s11739-018-1933-8; Доступно з: https://www.epicentro.iss.it /alcol/pdf/ 2018 [Caputo].pdf
58. Jastrzębska I., Zwolak A., Szczyrek M., Wawryniuk A., Skrzydło-Radomańska B., Daniluk J. Biomarkers of alcohol misuse: recent advances and future prospects. Prz Gastroenterol. 2016; 11(2): 78–89. doi: 10.5114/pg.2016.60252.
59. Andresen-Streichert H, Müller A, Glahn A, Skopp G, Sterneck M. Alcohol Biomarkers in Clinical and Forensic Contexts. Dtsch Arztebl Int. 2018; 115(18): 309–315. doi: 10.3238/arztebl.2018.0309.
60. Sosin I.K., Skvira I.M., Goncharova O.Y., Chuyev Y.F. Integrated diagnostic identification of alcohol dependence in general somatic practice. Eastern European Journal of Internal and Family Medicine. 2014; 1: 95-99.
61. Zozulya I.S., Kurdil N.V., Padalka V.M., Ivashchenko O.V. Acute alcohol poisoning in adults, alcohol coma: practical recommendations at the prehospital stage. Ukr Med Journal, 2017; 3 (119). Internet: https://www.umj.com.ua/article/110491/gostri-otruyennya-alkogolem-u-doroslih-alkogolna-koma-praktichni-rekomendatsiyi-na-dogospitalnomu-etapi.
62. The only clinical protocol for emergency medical care "acute poisoning" [Internet]. Available from: medstandart.net.
63. Unified clinical protocol of emergency medical care "acute poisoning". Order of the Ministry of Health January 15, 2014 № 34. Internet: mtd.dec.gov.ua ›index.php.
64. ATC - Classifier - State Form of Medicines [Internet]. 2018; Available from: preparaty.org/atc.
65. Shayakhmetova G.M., Karpova O.V., Voronina A.K., Golovenko M.Ya. Hepatoprotective effect of metadoxin in experimental alcoholic hepatitis in rats. Medical and clinical chemistry. 2015; 17 (4): 54-58. DOI 10.11603 / mcch.2410-681X.2015.v17.i4.5685
66. Antabuse. Internet: https://www.rxlist.com/antabuse-drug.htm#medguide.
67. Baranova I.I., Zaporozhskaya S.N. Comparative characteristics of reoparameters of gelling agents of different origin. Запорож.мед.журн. 2008; 4 (49): 81-84.
68. Kharchenko O., Savchuk O., Ostapchenko L. Analysis of protein profile changes in chronic alcohol intoxication to diagnose the development of this pathological condition of the body. Visn. KNU them. T.Шевченка. Biology. 2015; 2 (70): 11-19.
69. Schrieks I.C., Heil A.L., Hendriks H.F., Mukamal K.J., Beulens J.W. The effect of alcohol consumption on insulin sensitivity and glycemic status: A systematic review and meta-analysis of intervention studies. Diabetes Care. 2015;38:723–732.
70. Steiner J.L., Crowell K.T., Lang C.H. Impact of Alcohol on Glycemic Control and Insulin Action. Biomolecules. 2015; 5(4): 2223–2246. doi: 10.3390/biom5042223.
71. Gurina N.M., Bardakhivska K.I. Enterosorbents as a means of detoxifying

the body. [Internet]. kiulong.com.ua. http: // www. //kiulong.com.ua/ content / view / 67/1.
72. Demidova T.I, Emelyanov S.I, Demidov D.A, Bogdanov D.Yu. Enterosorption and enterosorbents in the treatment of surgical endotoxicosis. Bulletin of the Academy of Medical and Technical Sciences. 2010; 1: 29-35.
73. Komarov V.S., Ratko A.I. Adsorbents: production, structure, properties. Minsk: Belarus. Science; 2009: 256.
74. White coal: instruction UA / 16126/01/01 (23205) - Medication Control. Available from: likicontrol.com.ua/instruction/?[23205]
75. Pogorely V.K. Regularities of adsorption of natural bioactive compounds on the surface of nanodispersed silica. Surface. 2009; 1 (16): 322-349.
76. Tarasenko Yu.A., Gerashchenko II, Kartel NT Enterosorption as a method of excretion of heavy metals and radionuclides. Surface. 2014; 6 (21): 110–121.
77. Silberman J., Taylor A. Activated Charcoal. [Інтернет]. Доступно з: https://www.ncbi.nlm.nih.gov/books/NBK482294/#_article-17128_s2_Last Update: November 22, 2018.
78. Makarevich N.A., Bogdanovich N.I. Theoretical foundations of adsorption: a textbook. North (Arctic.) Feder. Univ. M.V. Lomonosov. Arkhangelsk: SAFU; 2015: 362 p.
79. Parfit D., Rochester K. Editors. Adsorption from solutions on solid surfaces. M .: Mir; 1986: 488.
80. Chuiko A.A. Editor. Medical chemistry and clinical application of silicon dioxide. Kiev. Science. Opinion; 2003: 416 p.
81. Datsko T.Ya., Zelentsov VI The dependence of the surface charge and adsorption of fluorine by γ-alumina on the temperature of the solution. Electronic Materials Processing, 2009; 5: 65–73.
82. Pectins: properties, preparation, application. [Internet]. Available from: http://newchemistry.ru/letter.php?n_id=6344.
83. Taran N.G. Adsorbents and ion exchangers in the food industry. M .: Light and food industry, 1983: 248 p.
84. Sergushchenko I.S, Kovalev V.V, Bednyak A.E, Khotimchenko S.V Comparative evaluation of metal-binding activity of low-esterified pectin from seaweed zostera marina and other sorbents. Marine biology. 2004; 1: 83-85.
85. Stabilizer E440 (Pectin) [Internet]. Available from: http://am-am.su/53-stabilizator-e440-pektin.html
86. Bilay I.M., Demchenko V.O., Bilay A.I., Krasko M.P., Ostapenko A.O. Influence of herbal medicines on lipid metabolism and lipid peroxidation in experimental hyperlipidemia. Journal of Scientific Review. 2017; 7 (39): 1-8.
87. Zozulya I.S, Kurdil N.V, Padalka V.M, Ivashchenko O.V Acute alcohol poisoning in adults, alcohol coma: practical recommendations at the prehospital stage. Ukr Med Journal, 2017; 3 (119). Internet: https://www.umj.com.ua/article/110491/ gostri-otruyennya-alkogolem-u-doroslih-alkogolna-koma-praktichni-rekomendatsiyi-na-dogospitalnomu-etapi.
88. Nesterenko V.B., Nesterenko A.V., Babenko V.I., Yerkovich T.V., Babenko I.V. Reducing the 137Cs-load in the organism of "Chernobyl" children with apple pectin. Swiss Med. Wkly. 2004; 134: 24–27. DOI: 2004/01/smw-10223.
89. Leung P.C., Siu W.S., Erik CHKO, Ko ECH, Lee HK et al. A Food Supplement with Lead A Preliminary Study. J Heavy Met Toxicity Dis. 2017, 2:1.
90. Pectin. Drugs.com. [Internet]: https://www.drugs.com/npp/ pectin.html.
91. Trakhtenberg I.M, Dmitrukha N.M, Kozlov K.P, Apikhtina O.L, Korolenko TK, Krasnokutskaya LM Modern approaches to the prevention of heavy metal intoxication. Taurian Medical and Biological Bulletin. 2012; T 15, 1 (57): 253-257.
92. Wang R., Liang R.,Dai T., Chen J., Shuai X., Liu C. Pectin-based adsorbents for heavy metal ions: A review. Trends in Food Science & Technology, 2019;91:319-329. https://doi.org/10.1016/j.tifs.2019.07.033.
93. Guo X., Meng H., Tang Q., Pan R., Zhu S., Yu S. Effects of the precipitation pH on the

ethanolic precipitation of sugar beet pectins. Food Hydrocolloids. January 2016;52:431-437. https://doi.org/10.1016/j.foodhyd.2015.07.013.
94. Jakóbik-Kolon A., Milewski A.K., Krzysztof Karoń K., Bok-Badura J. New, hybrid pectin-based biosorbents. Separation Science and Technology. 2016; 51(15-16):2604-2611. https://doi.org/10.1080/01496395.2016.1162809.
95. Dongowski G., Lorenz A., Anger H. Degradation of Pectins with Different Degrees of Esterification by Bacteroides thetaiotaomicron Isolated from Human Gut Flora. Appl Environ Microbiol. 2000; 66(4): 1321–1327.
96. Dongowski G., Lorenz A., Proll J. The Degree of Methylation Influences the Degradation of Pectin in the Intestinal Tract of Rats and In Vitro. J. Nutr. 2002;132:1935–1944.
97. Wikiera A., Irla M., Mika M. Health-promoting properties of pectin. Postepy Hig Med Dosw (Online). 2014;68:590-596. 24864109.
98. Wilson F.A, Dietschy J.M. The intestinal unstirred layer: Its surface area and effect on active transport kinetics. Biochimica et Biophysica Acta (BBA) - Biomembranes.1974;363(1): 112-126. Інтернет. https://doi.org/10.1016/ 0005-2736(74)90010-8.
99. Di Lorenzo C, Williams C.M., Hajnal F., Valenzuela J.E. Pectin delays gastric emptying and increases satiety in obese subjects. Gastroenterology. 1988 Nov;95(5):1211-5.
100. Figler M, Mozsik G. Effect of pectin application on gastric mucosal lesions induced by ethanol or aspirin in rats. Dig Dis Sci. 1998;43[abstract A13]:2342.
101. Jakóbik-Kolon A., Milewski A.K., Krzysztof Karoń K., Bok-Badura J. New, hybrid pectin-based biosorbents. Separation Science and Technology. 2016; 51(15-16):2604-2611. https://doi.org/10.1080/01496395.2016.1162809.
102. Koriem K.M., Fathi G.E., Salem H.A., Akram N.H., Gamil S.A. Protective role of pectin against cadmium-induced testicular toxicity and oxidative stress in rats. Toxicol Mech Methods. 2013;23(4):263-72. doi: 10.3109/15376516.2012. 748857. Epub 2013 Jan 22.
103. Mohnen D. Pectin structure and biosynthesis. Current Opinion in Plant Biology. 2008; 11:266–277. [Internet]: www.sciencedirect.com.
104. Caffall KH, Mohnen D. The structure, function, and biosynthesis of plant cell wall pectic polysaccharides. Carbohydrate Research.[інтернет]. 2009; Доступно з:http://plantometrics.com/files/biblio_attachments/Caffall,K (2009) Pectin-review.pdf.
105. Re-evaluation of pectin (E 440i) and amidated pectin (E 440ii) as food additives. Інтернет:https://efsa.onlinelibrary.wiley.com /doi/10.2903/j.efsa.2017.4866. First published: 06 July 2017.
106. Ermolov A.C., Lazareva EB Efficacy of pectins in the complex treatment and prevention of purulent-inflammatory infections in patients with urgent surgical pathology. Epidemiology and infectious diseases. 2006; 3: 47-51.
107. Lazareva EB Efficacy of topical application of pectins in the treatment of burn wounds. Antibiotics and chemotherapy. 2002; 9: 9-13.
108. Judd P.A., Truswell A.S. The hypocholesterolaemic effects of pectins in rats. Br J Nutr. 1985;53(3):409-425.
109. Liu Y., Dong M., Yang Z., Pan S. Anti-diabetic effect of citrus pectin in diabetic rats and potential mechanism via PI3K/Akt signaling pathway. Int J Biol Macromol. 2016 Aug;89:484-8. doi: 10.1016/j.ijbiomac.2016.05.015.
110. Miettinen T.A., Tarpila S. Effect of pectin on serum cholesterol, fecal bile acids and biliary lipids in normolipidemic and hyperlipidemic individuals. Clin Chim Acta. 1977;79(2):471-7.
111. Dvoenosova P.A, Doronin A.F, Izotova T.I Functional pectin-containing products in intestinal failure syndrome. Food industry.2009; 6: 54-55.
112. Tian L., Scholte J., Borewicz K., van den Bogert B., Smidt H., Scheurink A.J. Effects of pectin supplementation on the fermentation patterns of different structural

carbohydrates in rats. Mol Nutr Food Res. 2016;60(10):2256-2266. doi: 10.1002/mnfr.201600149. Epub 2016 Jun 8.
113. Olano-Martin E. Pectin and pectic-oligosaccharides induce apoptosis in in vitro human colonic adenocarcinoma cells. Anticancer Res. 2003; 23:341–346.
114. Rao K.P., Prabhashankar B., Kumar A, Khan A., Biradar S.S., Srishail P., Satyanath B. Formulation and roentgenographic studies of naproxen-pectin-based matrix tablets for colon drug delivery. Yale J Biol Med. 2003;76(4-6):149-54.
115. Soares G.A., de Castro A.D., Cury B.S., Evangelista R.C. Blends of cross-linked high amylose starch/pectin loaded with diclofenac. Carbohydr Polym. 2013; 91(1):135-142. doi: 10.1016/j.carbpol.2012.08.014. Epub 2012 Aug 10. https://www.ncbi.nlm.nih.gov/pubmed/23193971
116. Sundar Raj A.A., Rubila S., Jayabalan R., Ranganathan T.V. A Review on Pectin: Chemistry due to General Properties of Pectin and its Pharmaceutical Uses. Open Access Scientific Reports [Internet]. 2012;1:550 doi:10.4172/scientificreports.550.
117. Tsai S.W., Yu D.S., Tsao S.W., Hsu F.Y. Hyaluronan-cisplatin conjugate nanoparticles embedded in Eudragit S100-coated pectin/alginate microbeads for colon drug delivery. Int J Nanomedicine. 2013;8:2399-407. doi: 10.2147/ IJN.S46613. Epub 2013 Jul 3. https://www.ncbi.nlm.nih.gov/pubmed/23861585
118. Mercadante S., Prestia G., Adile C., Casuccioy A. Intranasal Fentanyl Versus Fentanyl Pectin Nasal Spray for the Management of Breakthrough Cancer Pain in Doses Proportional to Basal Opioid Regimen. The Journal of Pain. 2014;15(6): 602-607.

Figure 1. Molecular structure of pectin