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Effective Use of Medicinal Plants in Fatty Liver Dystrophy

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Annotation

Obesity is currently one of the most common metabolic disorders in the body. Experimental alimentary obesity leads to changes in the structural and functional organization of the liver, including disorders of blood circulation and lymph flow, the development of fatty degeneration in the parenchyma of the organ. The central links in the metabolism of proteins, lipids and carbohydrates take place in the liver, and it is also a barrier to all foreign substances entering the body. The problem of studying morphological changes in organs in obesity based on the effective use of medicinal plants as a means for the treatment and prevention of diseases is urgent. To assess the morphological changes in the liver in obesity, a natural medicinal plant "Frangula alnus" was used in the experiment. Changes in the structural organization of the liver are reflected in its functional state and the process of lipid metabolism. The article studies pathological changes in the activity of liver cells, which lead to a decrease in the detoxification function of the liver and destructive changes. Feeding rats with fatty food in combination with powder from the bark of the medicinal plant buckthorn "Frangula alnus" showed that the use of such a combination in the diet contributes to the normalization of morphological processes and restoration of the structural and functional organization of the rat liver.

Keywords: Organs; Destruction; Histology; Morphology; Necrosis; Pathology

Introduction

Obesity is widespread among the population of the whole world and is often accompanied by an increase in the incidence of chronic endocrine, inflammatory and oncological diseases - type 2 diabetes mellitus, colon cancer, biliary tract, endometrium, breast

cancer and others. Diseases associated with fatty liver cause irreversible disturbances in the functioning of all body systems. According to the WHO, from 1980 to 2019, the number of obese people around the world more than doubled, and currently in European countries more than 35% of the population is overweight, and 10 to 30% are obese [1 -4]. Excessive accumulation of triglycerides in adipose tissue in obesity develops with a combination of factors such as a high-calorie diet that exceeds the body's energy expenditure, physical inactivity, and a genetic predisposition. With obesity in adipose tissue and other organs, activation of immune and inflammatory reactions is observed. The mechanisms of obesity are intensively studied, and a large number of works devoted to this problem have been carried out on experimental animals. Literature data on morphological, functional and molecular biological changes in the liver in obesity are few and fragmentary [5-8]. In this regard, the study of morphological changes in the regulation of the functional activity of the liver and its metabolic adaptation to the effects of various factors on the basis of treatment with medicinal plants remains an important task of modern science. The search for new effective herbal preparations is an important area of experimental and clinical hepatology. Increasingly, modern medicine is turning to herbal remedies, which are used as a semi-functional agent for the treatment and prevention of various diseases. It is known that the task of all phytocomplexes containing biologically active substances polyphenols, saponins and others have an adaptogenic effect on a living organism, mobilizing its homeostatic mechanisms [9-11]. Despite the fact that significant success has been achieved in the fight against obesity, the search for new effective and low-toxic therapeutic agents for the body of animals is always relevant. Based on the above, we conducted an experiment to study the morphological changes in the liver of rats with obesity against the background of the use of the natural origin of the medicinal properties of the plant "Frangula alnus". The main pharmacological activity of buckthorn is shown by anthraglycosides, glucofrangulins A and B, emodin, frangulins A and B and others. The chemical composition of buckthorn includes a large number of biologically active substances with a highly active process, these include anthracides 8% and alkaloids 0.15%. Anthracids are responsible for the production of frangulin and glucofrangulin. The buckthorn also contains essential oils, sugar, organic acids and tannins [12-15].

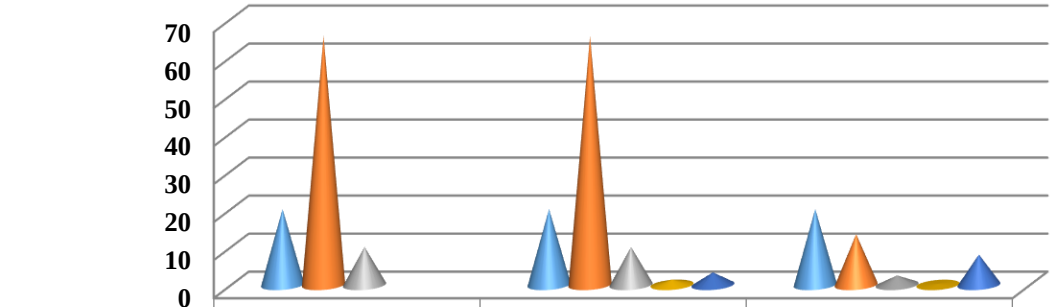
Material and research methods. The experiment used sexually mature male Wistar rats with an initial body weight of 200-220 g at the age of three months. The choice of males is due to the fact that in females at different times of the extra cycle, sensitivity to various factors can change, and it is also possible that pregnant females may enter. All animals, in the amount of 60 pieces, were divided into three groups: the first control group, intact rats that received a standard laboratory diet (Diagram 1). The second group of rats, which was created a model of nutritional obesity, by adding edible fats of animal origin to a standard laboratory diet for 30 days (Diagram 2). The third group of animals with a model of alimentary obesity received at the rate of 40 mg / kg powder of the bark of the medicinal plant buckthorn "Frangula alnus" with the basic food for 30 days, and during feeding, animal fats were not excluded from the diet.

Method of obtaining powder: pieces of bark of various shapes, weak odor, bitter taste, the outer part of the bark was dark brown, and the inner side was yellowish-orange in color, passed through a sieve with holes 7 mm in diameter. The resulting mass of powder was once again passed through a sieve with holes of 0.16 mm in size, a yellow-brown powder was formed, the smell and taste were unchanged. The healing properties of buckthorn are due to the rich biochemical composition of the bark. The bark contains: antranol, anthraquinone (frangulin, chrysarobin, emodin, etc.), organic acids, coumarins, vitamin C, pectins and alkaloids, as well as essential oil, saponins, naphthaquinones, flavonoids and tannins. Unlike

many laxatives, buckthorn bark is brittle, does not irritate the intestinal mucosa, but only enhances its peristalsis [16]. The components that make up the buckthorn bark have a beneficial effect on metabolism, cleanse the body of toxins and toxins, and also remove sand from the ureters and kidneys.

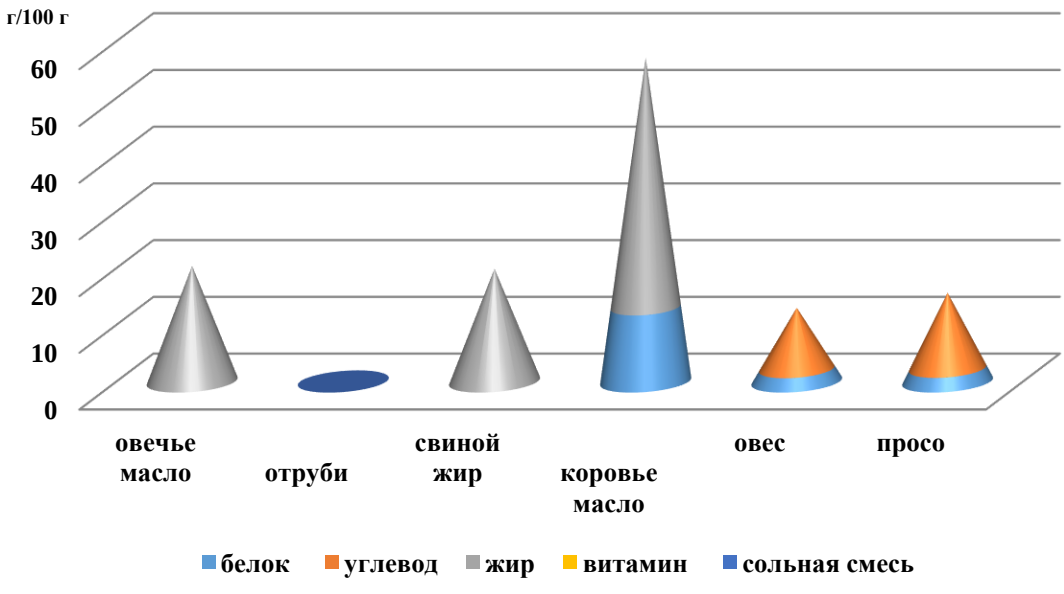
Histological processing of the material was carried out by the traditional method of microscopic technique for preparing thin sections. The rats were withdrawn from the experiment by decapitation. The studied rat livers were fixed in 10% neutral formalin, embedded in paraffin, sections with a thickness of 5-6 μm were made and stained with hematoxylin-eosin and Van Gieson. The obtained histological preparations were viewed and photographed using a Leica DMLS light microscope.

Chart - 1 - *Chemical composition of the standard diet (g / 100g diet)*



	кормовая добавка	100 г	25 г
белок	20	20	20
углевод	65.5	65.5	13.37
жир	10	10	2.5
витамин		1.4	0.33
сольная смесь		3.3	8

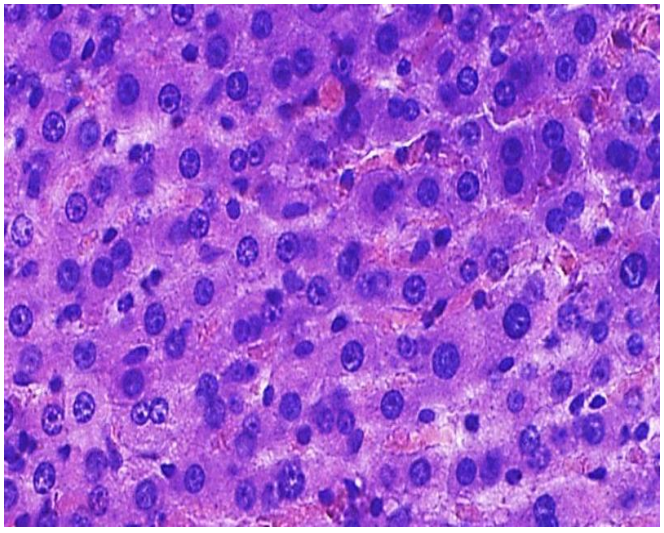
Chart - 2 - *Composition of fatty foods (g / 100g diet)*



The morphometric study of liver preparations was carried out at a magnification of 1000 times on sections with a thickness of 5 µm, stained with hematoxylin - eosin, using the method of superimposing dotted morphometric grids [17]. The relative areas of the network of sinusoids, nuclei and cytoplasm of hepatocytes, the numerical densities of sinusoidal cells, hepatocytes and binuclear parenchymal cells were determined. The nuclear-cytoplasmic ratio, the ratio of the number density of sinusoidal cells to the number density of all hepatocytes, and the ratio of the area of the network of sinusoids to the area of the parenchyma of all hepatocytes were calculated [18]. Statistical processing of the research results was carried out by the method of variation statistics using a software package using the parametric Student's test [19]. Differences between the compared values were considered statistically significant at $p < 0.05$. All experimental work was carried out in compliance with the rules of bioethics approved by the European Convention for the Protection of Vertebrate Animals used for laboratory or other purposes.

Research Results and Their Discussion

As a result of the histological study of the rat liver, it is seen that in the rats of the second group, irreversible pathomorphological disorders associated with liver obesity are visible. The liver is sensitive to food influences and the main principle, which is the observance of a balanced intake of food in proteins, fats, carbohydrates, vitamins and minerals. It is observed that with excess and artificially balanced nutrition, the body cannot cope with the excretion of the breakdown products of nutrients, and the increasing weight limits physical activity, which leads to obesity. The study of the liver of rats with experimental alimentary obesity showed that the absolute liver mass of animals of the second group increased in comparison with the control group by 25%. Such an increase in body weight corresponds to the 1st degree of obesity. Also, based on the results of light-optical and morphometric studies of the liver of rats of the second group, we have identified a number of statistically significant changes concerning, first of all, the state of the microvasculature, as well as morphometric parameters.



Picture 1.
The liver is normal.
The staining is hematoxylin and eosin. Uv.x 400

The liver of the rats of the first control group had a classic tubular structure. The organ structure and the beam structure of the hepatic lobules were preserved. Hepatocytes are hexagonal in shape, large rounded nuclei are visible, located in the center of the cell, one or

two nucleoli are visible in the nuclei. Binuclear cells were encountered. There is blood filling of the sinusoids and a slight sclerosis of the vessels. Granularity is noted in the cytoplasm of hepatocytes. Single bile ducts were found in the parenchyma. They had a regular structure in the form of a tube, covered with epithelium (Figure 1). The nuclear-cytoplasmic ratio (NCR) of hepatocytes was 0.186 ± 0.093 (at $p < 0.05$).

Morphological study at the light-optical level in the parenchyma of the liver of rats of the second group, there is a violation of cell contacts, extensive areas with signs of fatty degeneration of hepatocytes in the form of numerous lipid droplets of various sizes were found. The multiple lipid droplets tended to coalesce and form large fat droplets. The nuclei are small, pushed back to the periphery of the cells, and are deformed in places. Some vessels are deformed, there is an uneven blood filling of large vessels. Due to fatty degeneration, there is a sharp narrowing and blood filling of the sinusoids and stagnation of plasma in the capillaries, as well as hardening of large vessels (Figure 2-3). The liver NCR of this group is 0.282 ± 0.18 (with $p < 0.05$).

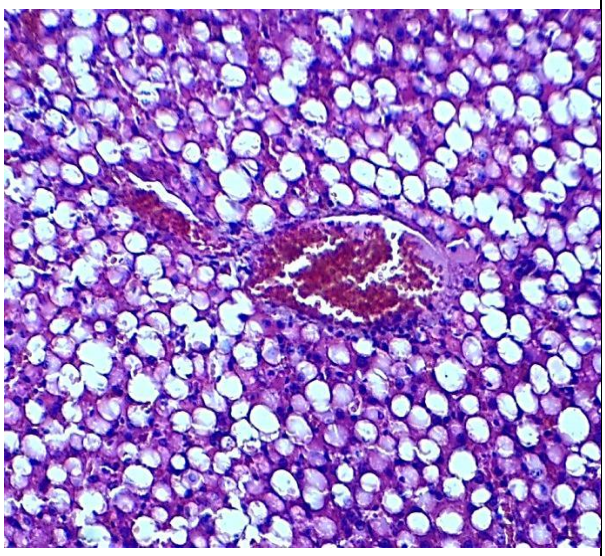


Figure 2.
Fatty degeneration of the liver.
The staining is hematoxylin and eosin.
Uv.x400

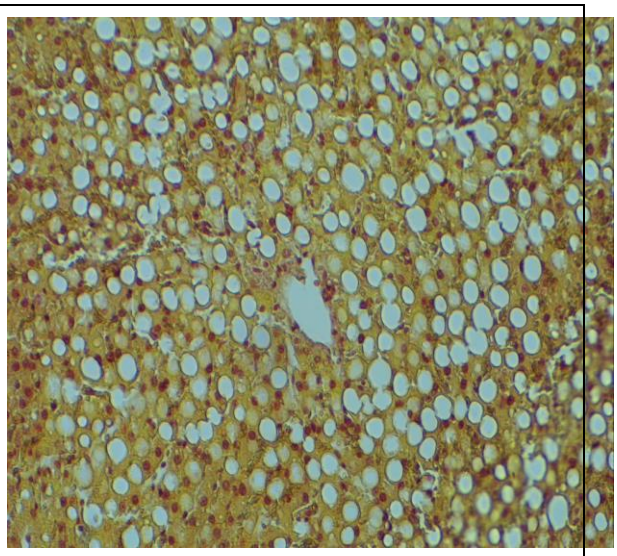


Figure 3
Fatty degeneration of the liver.
Painting by Van Gieson. Uv. x200

It was morphometrically established that in rats of the second group, the structural and functional parameters of the cells of the parenchyma and stroma, as well as the microvasculature, have significant statistically significant changes, the relative area of the parenchyma increased by 13%, where the proportion of hepatocytes with signs of fatty degeneration was 71% of all parenchymal cells in the study area. The average size of the hepatocyte increased by 8.3%, the increase in the relative area of the nuclei of parenchymal cells by 53% compared to the control, exceeded the growth in the relative size of their cytoplasm by 13% compared to the control of parenchymal cells and, as a consequence, the nuclear-cytoplasmic ratio increased significantly by almost by 1.5 times (table 1). The observed changes in the parenchymal cells of the liver indicate the activation of metabolic processes both between the nucleus and the cytoplasm, and between the cell and the extracellular environment, which is usually accompanied by a high functional tension of the capillary-connective tissue structures.

The study of the liver of rats of the third group and received at the rate of 40 mg / kg powder of the bark of the medicinal plant "Frangula alnus" with the basic food showed that the structure was preserved, there were areas with stromal edema. Hepatocytes are hexagonal in shape; the cell membrane is expressed heterogeneously. The nuclei are polymorphic, located in the center of the cell.

Table 1. *Results of morphometric study of rat liver sections in the control group and experimental groups (M ± m), %*

№	Parameter, structure	"The control I group of rats "	"II group of rats"	"III group of rats"
1	Cytoplasm of hepatocytes	69,83±0,33	72,41±0,28*	68,6±0,3*#
2	Hepatocyte nucleus	8,81±0,18	12,7±0,27*	10,14±0,28*#
3	Blood sinusoidal capillaries	19,11±0,25	8,9±0,18*	16,43±0,17*#
4	Total hepatocyte count	50,53±0,93	52,21±0,84	44,37±0,90*#
5	The number of unchanged liver cells	50,53±0,93	13,67±0,4*	41,33±0,88*#
6	The number of degenerative liver cells	0	39,55±0,77*	3,03±0,26*#
7	The number of binucleated cells	1,71±0,14	5,05±0,26*	2,43±0,1*#
8	Total number of sinusoidal cells	20,3±0,59	17,25±0,56*	24,61±0,51*#
9	Nuclear-cytoplasmic ratio	0,12±0,002	0,18±0,003*	0,14±0,004*#
10	The ratio of the number of sinusoidal cells to the number of all hepatocytes	0,3±0,01	0,32±0,01*	0,54±0,02*#
11	The ratio of the number of binucleated hepatocytes to the number of all hepatocytes	0,02±0,002	0,1±0,005*	0,05±0,004*#

Note: * - *differences are reliable in comparison with the indicators of the "Control" group; # - differences are reliable compared to group indicators*

Single vacuoles are found in the cytoplasm. Single erythrocytes are noted in the vessels. Individual hepatocytes in a state of hydrolytic dystrophy, nuclei clearly contoured. The sinusoidal space is enlarged. Hepatocytes are mononuclear and multinucleated. Changes in morphological parameters in animals were less significant and at the end of the study, they approached the background values. In the liver, there is a slight dilation of blood vessels filled with plasma and erythrocytes. The liver capsule is not thickened, contains longitudinally oriented bundles of collagen fibers. The liver parenchyma is formed by the classic hepatic lobules, consisting of the hepatic tracts radially oriented to the central vein NCR = 0.198 ± 0.06 (Figure 3-4).

In our experiment, in rats with a model of obesity, structural and functional rearrangements in hepatocytes took place against the background of activation of the organ stroma, which was expressed in an increase in the relative area of sinusoidal liver cells (by 57%) and in an increase in the average size of a “sinusoidal cell” (by 88%). It should be remembered that the group of "sinusoidal cells" includes endothelial cells of sinusoidal capillaries, Kupffer cells, stellate or perisunusoidal cells, lipocyte cells. The mechanism of the protective action is associated with the restoration of the cell membranes of hepatocytes.

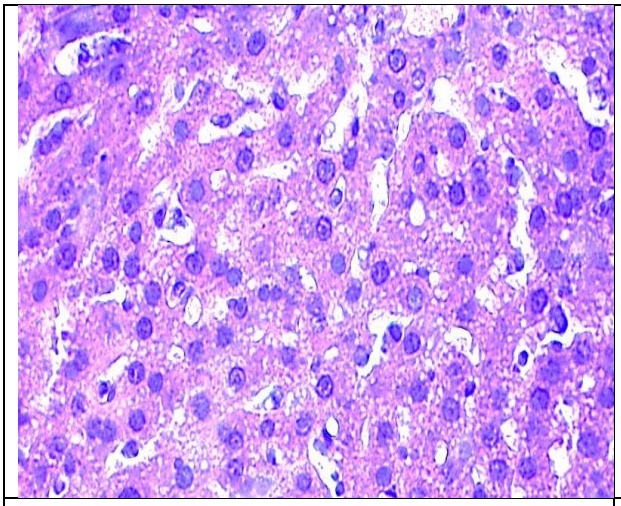


Figure 4
Individual hepatocytes in a state of hydrolytic dystrophy
The staining is hematoxylin and eosin. Uv. x 400

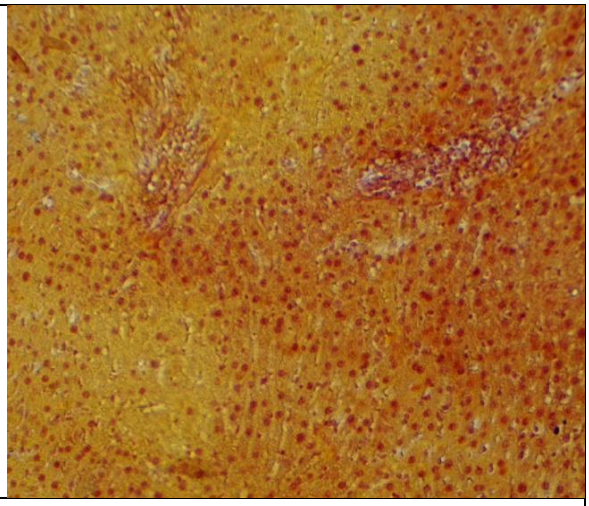


Figure 5
Slight vasodilation.
Painting by Van Gieson. Uv. x200

Analysis of histopathological preparations of the liver of rats with a model of alimentary obesity and received at the rate of 40 mg / kg powder of the bark of the medicinal plant buckthorn "Frangula alnus" with basic food, a 2.0-fold decrease in the relative area of the network of sinusoidal capillaries in the intermediate zone of the hepatic lobules was found. Based on a 2.2-fold decrease in the ratio of the specific area of sinusoids to the specific area of hepatocytes, it can be assumed that the drainage function of the regional lymph nodes of the organ will increase.

The results of morphological and morphometric studies of pathohistological preparations of the liver of rats with a model of alimentary obesity after administration showed that the use of powder from the bark of the medicinal plant buckthorn "Frangula alnus" accelerates the recovery and normalizes microcirculatory processes in the organ, which ultimately leads to a significant improvement in the structural and functional state of the liver ... The introduction to animals of a mixture from the bark of the medicinal plant buckthorn "Frangula alnus" had a pronounced effect on the studied parameters. It is noteworthy that all changes in the liver of rats of the third group are characterized by statistically significant values in comparison with the experimental groups of the first and second groups. The structure was preserved, there were small areas with stromal edema. Hepatocytes are polygonal, no special pathological changes are visible, the cell membrane is expressed heterogeneously. The nuclei are polymorphic, located in the center of the cell [20].

Conclusion. As a result of our study, it can be seen that obesity leads to significant disorders of blood circulation and lymph flow in the liver, the development of fatty degeneration in the parenchyma of the organ. In rats of the third group, in the study of histological preparations, it was shown that when using a powdery mixture from the bark of the medicinal plant buckthorn "Frangula alnus" promoted the enhancement of reparative processes in the liver, normalization of microcirculatory processes, restoration of the structural and functional organization of the organ. A less significant mosaicity of blood filling of the vessels of the hepatic lobules, a slight dilation of the vessels of the portal tracts were observed. Areas with dystrophic changes in hepatocytes were found to a lesser extent compared to the second group of experimental animals.

A morphometric study revealed an increase in the relative area of the network of sinusoidal capillaries by almost 2 times and a decrease in the relative size of the parenchyma compared with the second group. Restoration of blood circulation, lymph flow, normalization of the state of tissue non-vascular microcirculation pathways contributed to the creation of conditions for the restoration of the structural organization and normal functioning of parenchymal liver cells. The introduction of a powdery mixture from the bark of the medicinal plant buckthorn "Frangula alnus" led to almost complete disappearance of dystrophic changes in hepatocytes. At the same time, a decrease in the specific area of nuclei and cytoplasm of hepatocytes and a decrease in the nuclear-cytoplasmic ratio were noted. However, these parameters were not fully restored to the control level, which may indicate the depth and persistence of the violations we identified.

On the basis of the above obtained experimental data, it was found that the natural medicinal plant buckthorn "Frangula alnus" is not a toxic and dangerous substance for animals. The results of the study indicate that due to the content of anthracene derivatives in the buckthorn bark, mainly in the form of glycosides - anthraglycosides, the obtained research results show the therapeutic and prophylactic effect of the medicinal plant "Frangula alnus" as a stimulant of the digestive system, affecting the functional state of the body. The role of the main medicinal additives, taking into account a number of new information about the mechanisms of their therapeutic and prophylactic action, must be considered from the standpoint of a biologically significant effect on the course of metabolic processes in conditions of both healthy and sick organisms. The use of medicinal biologically active substances based on plant raw materials will increase the body's resistance in the field of preventive measures. Buckthorn bark has been collected for medicinal purposes since ancient times. An effective medicinal plant can be used as a raw material for the industrial production of pure active substances with a pronounced therapeutic effect, and is of considerable theoretical and practical interest.

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