Use of Information Parameters as Criterion for Determination of Biological Activity of Hepatoprotective Preparations

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Abstract: Possibility of use of the information parameters characterizing adaptational and regenerative opportunities of tissue system of an organ as potential criteria for an assessment of biological activity of hepatoprotective preparations is investigated in this research. Influence of enzymatic hydrolyzate of *Chlorophytum comosum (L.)* on a morphofunctional condition of a liver of rats at experimental toxic damage of organ and in norm was studied. The assessment of morphofunctional condition of a liver under the influence of a preparation was carried out as with use of traditional morphological, biochemical and histologic parameters, and by means of information parameters, which were earlier used for an evaluation of the adaptative and regenerative opportunities of organs of mammals. As a result of research the hepatoprotective effect of enzymatic hydrolyzate of Chlorophytum comosum (L.) is confirmed both by dynamics of change of results of traditional techniques of an assessment and by informational parameters, that allows to draw a conclusion on possibility of use of information parameters as criterion for assesment of effectiveness of biostimulation.

Keywords: Liver, hepatoprotector, biological activity, entropy.

INTRODUCTION

Prevention and treatment of liver diseases of various etiology is permanently the matter of current interest [1-6]. The general pattern of epidemiologic transition from communicable to no communicable diseases is also observed for gastrointestinal and liver diseases (GILD), which constitute a heterogeneous array of causes of death and disability [7].

Liver diseases are one of the most pressing public health problems around the world, because the liver is one of the central organs ensuring homeostasis of an organism. Hepatic injury is associated with distortion of various metabolic functions. Because of these, liver reacts with change of its morphofunctional state in response to almost any influences both from external, and from the internal environment of an organism [8-12]. These facts define emergence of an increasing number of preparations and biologically active substances of hepatoprotective action.

Therapy of diseases of hepatobiliary system, depending on their etiology and pathogenesis, includes hepatoprotective preparations of various actions [13]:

1. the agents having impact on tissue homeostasis (vitamins, amino acids, peptides, anabolic steroids, adaptogens);
2. agents stimulating antitoxic function of a liver (antidotes, adsorbents);
3. cholagogues;
4. antimicrobial,antiviral, antiparasitic agents;
5. immunomodulatory agents;
6. anti-inflammatory agents;
7. antioxidants;
8. inhibitors and inductors of microsomal systems, carrying out metabolism of xenobiotics.

The full range of drugs necessary for carrying out therapy of various diseases of a liver may be provided with use of bioactive agents of plant origin [14-15].

Herbal medicines always took an important place in therapy of various diseases. The year-by-year increasing amount of researches devoted to new groups of plant preparations may be explained with their great potential bioactivity. The wide range of bioactive molecules containing in the remedies made of plants provides them applicability in various branches of biology, medicine and veterinary. Plants may serve

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as a subsidiary source of the major nutrients, antioxidants, immunomodulatory, anti-inflammatory and antimicrobial agents and also the vitamins and minerals for an organism [16-20].

Phytotherapy of liver diseases is a long continuous course of treatment with periodic change of the used herb mixtures. Depending on an etiology and the state of a disease, therapy involves the consecutive or complex appointment of preparations represented with combinations of plants with anti-inflammatory, choleretic, reparative effects. So, the *Berberis vulgaris* renders hepatoprotective effect at acute intoxication of with direct liver toxin carbon tetrachloride, preventing development of a necrosis, steatosis, fibrosis and internucleosomal DNA fragmentation, and also normalizes the level of hepatic enzymes, triglycerides and cholesterol at non-alcoholic fatty liver disease [21-22]; stinging nettle (*Urtica dioica*) attenuates cholestatic liver injury, bile duct proliferation and fibrosis induced by biliary obstruction [23].

Betulin and betulinic acid extracted from bark of trees of genus *Betula* stimulate work of antioxidant system of a liver, protecting the organ from development of damages and fatty dystrophy, in particular, at alcoholic intoxication, while derivatives of betulinic acid show cytotoxic effect against a hepatocellular carcinoma [24-25]. Methanolic extract of leaves of *Viburnum tinus (L.)* promotes normalization of levels alanine aminotransferase (ALT), aspartate aminotransferase (AST), lipid peroxide and nitric oxide levels at CCl_4-induced hepatotoxicity in rats [26]. *Vitis vinifera* dried seeds at experimental animals with paracetamol-induced hepatotoxicity provides lipid-lowering and hepatoprotective effects which may be attributed to its total phenols and antioxidant contents [27]. *Vitis vinifera* ethanolic extract also normalizes the level of enzymes of a liver and reduces expressiveness the histopathological changes in organ, reducing the level of an oxidative stress against the streptozocin-induced diabetes and alcoholic injury of a liver [28-29].

Preparations containing *Silybum marianum* fruit extracts, a herb and a root of *Chelidonium majus*, a herb of *Helichrysum arenarium* provide hepatoprotective, membrane-stabilizing, anti-toxic, analgesic, spasmolytic, anti-inflammatory, reparative action [30-33]. Curcumin, the main active ingredient of a rhizome of plants of genus *Curcuma*, has the regulating effect on a metabolism of hepatic stellate cells and interferes with development of fibrosis of a liver at experimental toxic influence by carbon tetrachloride. Also curcumin and its derivatives reduce the level of an oxidative stress in a liver, interfering as to development of damages of this organ, and of the phenomena of renal vasoconstriction interconnected to development of hepatorenal syndrome [34].

Due to the wide range and constantly growing number of the studied preparations of plant origin possessing potential hepatoprotective activity, the matter of criteria of determination of efficiency of their action is quite important now.

Determination of efficiency of biologically active substances and biological products may be carried out with quite wide range of methods and techniques.

Traditionally, tests of drugs are carried out on laboratory animals [35]. Actually, speaking about influence of some bioactive agent on the studied target, we estimate the level of adaptational and regenerative opportunities of the studied system, but the uniform integrative criteria of an assessment of these opportunities are not present.

At all wide range of approaches to a question of determination of level of adaptational and regenerative processes in norm, at pathologies, as a result of biostimulation [36-49], it isn't possible to mark out an only one adequate criteria of an assessment of intensity of these processes which wouldn't demand confirmation by any other methods, reflecting unity of a structure and functions of the studied systems.

One of the methods applied to an assessment of intencity of adaptational and regenerative processes in living tissue is use of information parameters. In particular, this method finds application in medicine. So, entropy is used for definition of violations in cardiac activity at fetuses at the last stages of prenatal ontogenesis [50]. Also entropy is applied to the description of regularities of secretion of hormones [51-52]. Very active information parameters are used at researches of cardiovascular system [53-54], in neurophysiology [55-56], and also in various areas of science studying cellular, tissue and organ structures of living organisms [57-65].

Research of possibility of an assessment of information parameters as the criterion displaying an effect of application of a tissue biostimulator seemed to us actual.

For confirmation of possibility of use of information parameters as criterion of efficiency of biostimulation

we conducted research of influence of an enzymatic hydrolyzate of the Chlorophytum comosum on morphofunctional condition of a liver of rats with experimental toxic hepatitis. Thus, determination of efficiency of biostimulation was made with application of traditional morphological, biochemical and histologic techniques, and also with use of information parameters.

The choice of the enzymatic hydrolysate of *Chlorophytum comosum (L.)* is caused by its hepatoprotective effect shown by earlier conducted researches [66]. Also it was shown that the information parameters used in research reflect the level of adaptational and regenerative abilities of organ [67].

MATHERIALS AND METHODS

Animals

Male Wistar Albino rats at the age of 6 months of body weights ranging from 170 g to 200 g were used in the study. The animals were fed with standard pellet diet and water ad libitum. They were maintained in controlled environment (12:12 h light/dark cycle) and temperature (30±2ºC). All the animal experiments were performed according to the compliance with the EC Directive 86/609/EEC and with the Russian law regulating experiments on animals.

Treatment Design

In experiment 200 animals divided into 4 groups were used:

1. intact control –intact animals (n=50);
2. control group - animals, subjected to inhalation with carbon tetrachloride for 2 min. per day for 6 days (n=50);
3. I experimental group- animals, feeded by drinking with enzymatic hydrolyzare of *Chlorophytum comosum (L.)* in a dosage of 6 mg/kg.bw (n=50);
4. II experimental group – animals, subjected to inhalationwith carbon tetrachloride for 2 min a day for 6 days, but at the same time feeded by drinking with enzymatic hydrolyzate of *Chlorophytum comosum (L.)*in a dosage of 6 mg/kg.bw (n=50)

200 animals (Male Wistar Albino rats) were randomized and divided into four groups by fifty animals in each group. First group served as intact control. Animals in the second group were subjected to inhalation with carbon tetrachloride (CCl_4) for 2 min. per day for 6 days (control group). Rats in I experimental group were feed by drinking with enzymatic hydrolyzare of *Chlorophytum comosum (L.)* in a dosage of 6 mg/kg.bw (n=50) (experimental group). Animals in the II experimental group were subjected to inhalation with carbon tetrachloride for 2 min a day for 6 days, but at the same time feed by drinking with enzymatic hydrolyzate of *Chlorophytum comosum* (L.) in a dosage of 6 mg/kg.bw (n=50). On the7th day of research animals were sacrificed in carbon dioxide chamber.

Selection of carbon tetrachloride as an hepatotoxic agent is caused by the fact that this substance is a direct liver poison, widely used in experimental medicine and biology. Selecting of the liver-toxic and exposure method is determined by the fact that the use of carbon tetrachloride under this scheme provides the appearance and development of reversible changes in liver at tissue and organ level.

Carbon tetrachloride (CCl_4), or tetrachloromethane, is toxic substanse traditionally used as a model to study hepatotoxic effects. This halogenated alkane causes toxical damage of liver through a number of mechanisms. First of all, CCl_4 can induce liver damage through the formation of reactive free radicals that can bind covalently to cellular macromolecules (nucleic acids, proteines, lipids), initiating lipid peroxidation, forming nucleic acid, protein and lipid adducts and impairing critical cellular processes, including lipid metabolism, potentially leading to fatty degeneration (steatosis) [68]. CCl_4 can also affect hepatocellular calcium homeostasis that results in the loss of cellular calcium sequestration [69]. The induction of hypomethylated ribosomal RNA caused by use of carbon tetrachloride results in inhibition of protein synthesis in hepatocytes. As a whole, treatment with carbon tetrachloride can result in centrilobular steatosis, inflammation, cancer initiation, apoptosis and necrosis. If the volume of tissue damage exceeds the repair capacity of the liver, the organ will progress to fibrosis and cirrhosis [70].

Weight Measurements

All rats were weighed in grams. Weighing was made at the beginning and at the end of research in each group. At the end of experiment it was measured absolute (in grams) and relative mass of a liver of rats.

Biochemical Analyses

Level of total protein, albumin, total bilirubin, of an alanine aminotransferase (ALT) and aspartat aminotransferase (AST) in blood serum were investigated by means of the biochemical StatFax3300 analyzer (USA) with sets of Spinreact firm (Spain).

Histopathological Analysis

Small portions of liver were taken and fixed in 10% formaldehyde. After several treatments for dehydration in alcohol, sections having 5μm thickness were cut. Sections were subjected to stain with hematoxylin and eosin, and then the histopathological analysis was carried, including determination of mitotic, apoptotic, necrotic and binuclear cells indexes in liver. At hematoxylin and eosin stained sections were determined mitotic and necrotic cells. Apoptotic cells were determined at sections stained by methylene blue-azure II with after-staining by fuchsine. Visualization was performed using a light microscope Nikon Eclipse 80i at 900 × magnification. Study was made at 5 fields of view on each section.

Apoptotic index was calculated by the formula:

$$AI=Na/N\times100\%,$$

where N_a - the number of apoptotic cells; N - total number of cells in the test population.

The mitotic index was calculated by the formula:

$$MI=N_m/N\times100\%,$$

where N_m - number of mitosis; N - total number of cells in the test population.

Necrotizing index calculated by the formula:

$$NI=N_n/N\times100\%,$$

where N_n- number of necrotic cells; N - total number of cells in the test population. All studies was made for 10 fields of view on each section.

Morphometric Studies

All measurements were taken with use of image analyzer "Videotest" at hematoxylin and eosin stained sections. Study was made for 10 fields of view on each section.

Studies of the Information Condition of the System of the Organs

To determine the information status at focal lesions of the liver, pieces of tissue were taken from the least altered areas on the border of macroscopically distincted lesions. In case of visual homogenity of organ material for research was taken from any part of it.

Based on the concept of information in a tissue system as the displaying of the diversity of morphology and function of the process for assessing the information status of organs and tissues have been proposed and tested the such indicators - information morphological capacity (H_{max}), information morphological entropy (H), information morphological organization (S), the relative morphological entropy (h) and redundancy (R) [71-72]. The baseline characteristics, which are used to calculate these parameters, can vary widely (the linear dimensions of the structures, their quantity, etc.). In our study we defined the volume of the nuclei of hepatocytes.

Information morphological capacity H_{max}, which means the maximum structural diversity, was calculated by formula [71-72]:

$$H_{max}=\log_2 n,$$

where n - number of classes.

Next, we made the calculation of the real structural diversity H. Real structural diversity is the parameter that clearly illustrates the degree of determinism of morphofunctional system in time and space [71-72]. The calculation was made using the formula:

$$H=-\Sigma P_i \log_2 P_i,$$

where ΣP_i is the sum of probabilities of staying of the measured parameter of cells in a one of existing classes; $\log_2 P_i$ - logarithm of the probability of staying in one of the possible classes. In this case, the value of P_i is defined as the classical probability.

Knowing the maximum and actual structural diversity, we can calculate the organization of the system (S), the difference between the maximum possible and the real structural diversity (implemented structural diversity). This parameter, in our opinion, displays the state of the system adaptability to date. To determine the value of this parameter we used the formula [71-72]:

$$S=H_{max}-H.$$

It is necessary to consider that when $H = H_{max}$, the system is deterministic, but such relation to the vast majority of permissible is possible only in theory.

Then we determined the coefficient of relative entropy of the system (or the coefficient of compression of information) h by formula [71-72]:

$$h=H/H_{max}.$$

High levels of relative morphological entropy provide evidence of the disorder of the system and of significantly reduction of its structural integrity.

The coefficient of the relative organization of the system (redundancy factor) R is given by [71-72]:

$$R=(S/H_{max})\times 100\%.$$

With these data, the researcher have the opportunity to calculate the equivocation of the system(the value of reliability) ***e***:

$$\boldsymbol{e}=(H_p-H_n),$$

where H_n - real structural diversity in normal, H_p - real structural diversity in pathology.

Statistical Analysis

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 11.0 packed program. Data were presented as mean ± standard deviation unless noted as different. Difference between the control and experimental groups was analyzed using Mann-Whitney U test. $P < 0.05$ was considered statistically significant.

RESULTS

Effect on Body and Liver Mass

By results of the conducted research it is revealed that experimental toxic injury of a liver leads to decrease in body weight in control group of animals in comparison with intact rats. At the same time these animals have an increase in both absolute, and relative mass of a liver. At the same time at application of an enzymatic hydrolyzate of *Chlorophytum comosum (L.)* both at toxic influence of CCl_4, and without that, there are not observed changes of body weight and mass of a liver concerning parameters of intact animals (Table **1**).

Histopathologic Findings

As a result of histologic researches it is revealed that application of enzymatic hydrolyzate of *Chlorophytum comosum (L.)* doesn't cause any morphological changes of a liver, the structural patterns of an organ in the I experimental group and in intact control are identical and comply with norm (Figures **1**, **2**).

At research of a liver of rats of control group essential differences from norm are found. Color of organ of these animals is various: a liver is henna-red or light brown with multiple hemorrhages, at 30% of animals light gray sites alternate with the dark red. On structure a liver in most cases is friable, in some cases with the scirrhous sites. At the majority of rats liver on a section is dry, doesn't bleeding, at some cases bleeding moderately. At microscopic research at animals of control group some violations of structure of a hepatic parenchyma are noted, and the lobular structure is also violated. The connective tissue layers forming spurious lobules are noted. Among cells there are a large number of leukocytes, macrophages. In hepatocytes there is observed a large number a vacuoles, including lipidic ones. Some cells are very large and actually represent a continuous vacuoles. In 70% of cases the multiple centers of necroses of the different sizes in which structural elements of separate cells aren't visualized are found, in 30% of cases extensive necroses are noted. Blood vessels (the central veins, capillaries) in a liver of these animals are expanded, permeability of walls of vessels for blood cells is increased, focal hemorrhages are also noted.

In general, at the vast majority of rats of control group the picture of acute toxic hepatitis with rather

Table 1: Effect of Enzymatic Hydrolyzate of *Chlorophytum comosum (L.)* on Weight Parameters of Rats

Groups	Body weight, g	Absolute mass of liver, g	Reliable mass of liver, %
Intact control group, (n=50)	205.28±7.15	7.94±0.32	3.87±0.30
Control group, (n=50)	178.52±9.90*	10.57±0.51*	5.91±0.41*
I group, (n=50)	207.60±8.40▲	7.78±0.41▲	3.73±0.32▲
II group, (n=50)	201.67±6.88▲	8.44±0.35▲	4.19±0.44▲

Hereinafter: Intact control group – intact animals; Control group – animals subjected to inhalation with CCl_4; I group – animals, feeded by drinking with enzymatic hydrolyzate of *Chlorophytum comosum (L.)*, II group – animals, subjected to inhalation with CCl_4 and at the same time feeded withenzymatic hydrolyzate of *Chlorophytum comosum (L.)*.

*P≤0,05 – in comparison with intact control, ▲P≤0,05 – differences from control, ▼ - P≤0,05 – differences of parameters of the II group from the I group.

high intensity of tissue damage (alterant hepatitis) is noted. At part of animals is defined hepatosis with the expressed necrotic component (Figures **3**, **4**, **5**, **6**).

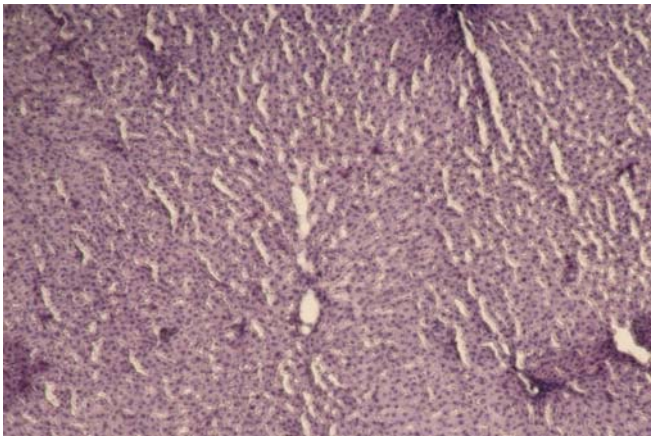

Figure 1: Liver of intact rat. ×100, H&E.

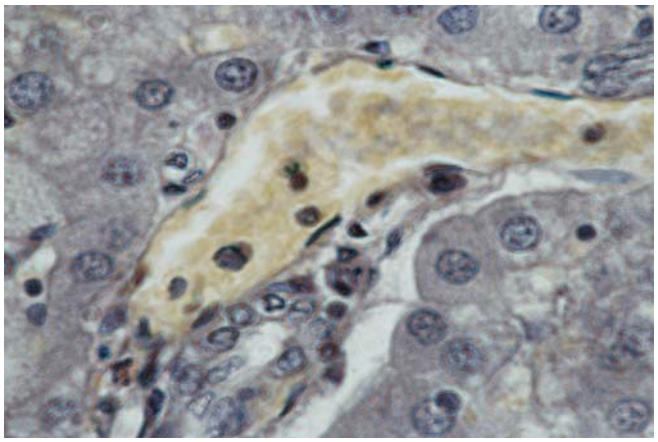

Figure 2: Liver of rat of I experimental group. ×1000, H&E.

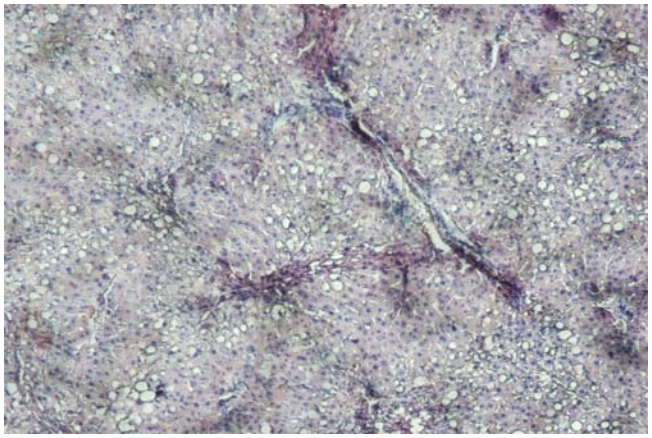

Figure 3: Liver of animals of control group. ×100, H&E.

In a liver of animals of the II experimental group the unaltered tubular and lobular structure is noted. Thus not numerous centers of dystrophy alternate with the sites presented by the uninjured and binuclear

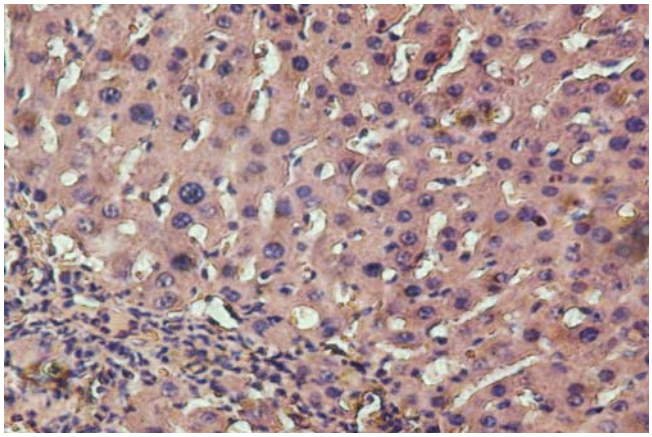

Figure 4: Liver of animals of control group. ×400, H&E.

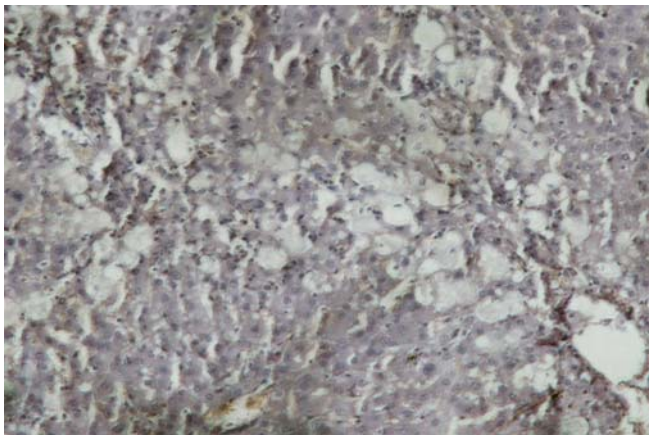

Figure 5: Liver of animals of control group. ×100, H&E.

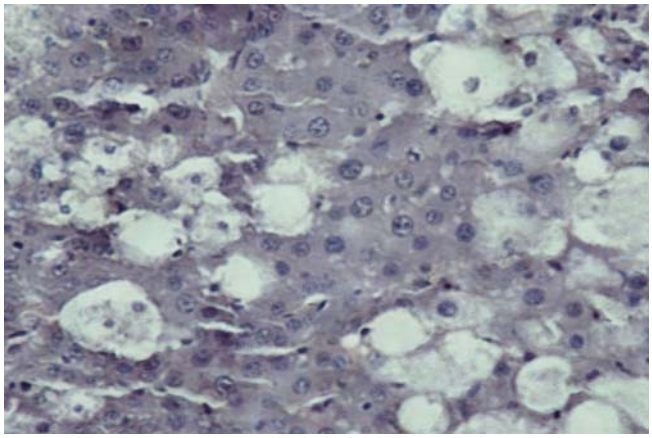

Figure 6: Liver of animals of control group. ×400, H&E.

hepatocytes (signs of regeneration) or hepatocytes in a condition of the initial stage of granular dystrophy. Fatty dystrophy meets in 20% of cases. Absence of focal hemorrhages is noted, interframe capillaries are moderately hyperemic, there are also no signs of edema. Vessels in the field of triads are moderately dilated. In 28% of hepatocytes small vacuoles are noted (Figures **7**, **8**).

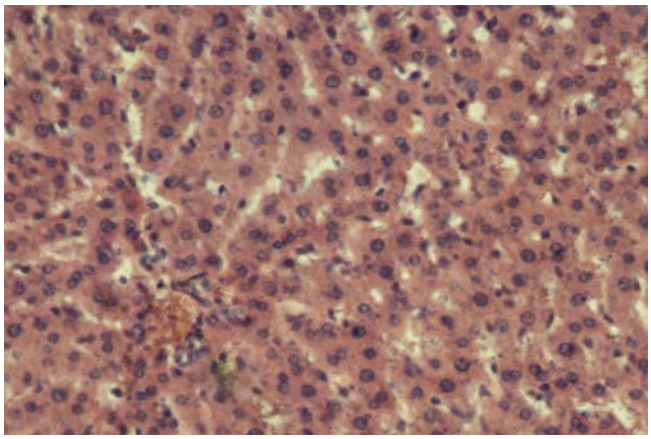

Figure 7: Liver of animals of II experimental group. ×200, H&E.

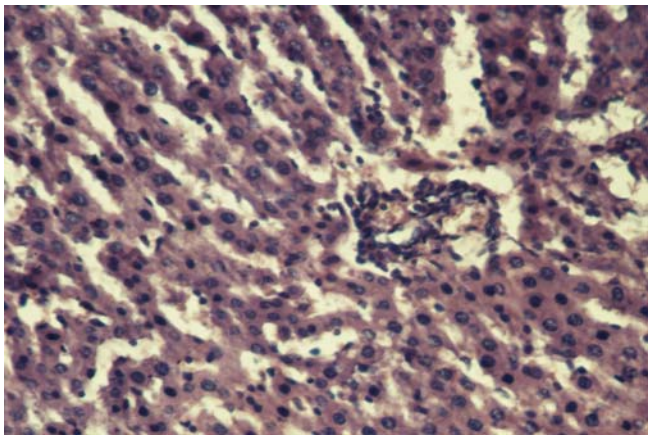

Figure 8: Liver of animals of II experimental group. ×200, H&E.

Effect on Mitotic, Apoptic and Necrotic Activity

The result of action of CCl_4 on a liver realizes in essential decrease in mitotic and apoptotic activity against significant increase of number of hepatocytes in a condition of a necrosis. Application of enzymatic hydrolyzate of *Chlorophytum comosum (L.)* at rats in norm have no essential impact on the described parameters of liver. At the same time, at simultaneous application of a hydrolyzateand toxic influence, mitotic, apoptotic and necrotic activities are increased in comparison with intact control, but at the same time the quantity the necrotic cells in this case is significantly less, than in control.

Effect on Blood Serum

Under the influence of tetrachlormethane there is an increase in the content of AST, ALT and total bilirubin and reduction of level of albumine in blood of rats. Parameters of the I experimental group don't differ from values of intact animals, and the same picture is also observed in parameters of the II experimental group

Effect on Informational Condition

At the analysis of the studied information parameters it is established that under the influence of CCl4 in a liver of rats there is an increase in values of parameters H and h and, respectively, decrease in the values of S and R. As the arisen condition of a liver isn't norm, value of parameter ***e*** is also defined.

The studied information parameters characterizing a liver of animals of the I experimental group don't differ from parameters of intact animals, except for parameter ***e***. In the analysis of parameters of the II experimental group it is revealed that H and h increase in comparison with intact control, and S and R, on the contrary, decrease. Thus the studied parameters in II

Table 2: Effect of Enzymatic Hydrolyzate of *Chlorophytum comosum (L.)* on Liver Tissue Parameters

Groups	Mitotic index, %	Apoptotic index, %	Necrotic index, %
Intact control group, (n=50)	6.56±0.20	1.72±0.09	0.41±0.05
Control group, (n=50)	2.41±0.34*	0.70±0.10*	16.38±1.35*
I group, (n=50)	7.0±0.39▲	1.51±0.12▲	0.37±0.1▲
II group, (n=50)	7.81±0.42▲*	2.51±0.18▲*	1.81±0.13*▲

Table 3: Effect of Enzymatic Hydrolyzate of Chlorophytum Comosum on Biochemical Parameters of Blood Serum

Groups	AST, u/l	ALT, u/l	Total bilirubin, g/l	Total protein, g/l	Albumin, g/l
Intact control group, (n=50)	163.80±12.62	132.83±8.67	1.32±0.10	80.61±3.88	34.47±1.61
Control group, (n=50)	329.08±18.50*	504.20±48.55*	1.92±0.18*	93.48±5.71	28.15±2.22*
I group, (n=50)	148.27±10.94▲	148.11±10.58▲	1.43±0.12▲	82.70±4.08	33.92±2.0▲
II group, (n=50)	191.24±19.58▲	164.90±14.58▲	1.48±0.16▲	84.66±4.90	32.61±2.85▲

Table 4: Informational Parameters of Liver of Rat Satan Assessment of Biological Activity of Enzymatic Hydrolyzate of *Chlorophytum comosum (L.)*

Group	H_{max}(bit)	H(bit)	S (bit)
Intact control group, (n=50)	3.32±0.002	2.52±0.023	0.8018±0.023
Control group, (n=50)	3.32±0.002*	2.82±0.025*	0.50±0.025*
I group, (n=50)	3.32±0.002	2.55±0.020▲	0.77±0.20▲
II group, (n=50)	3.32±0.002	2.60±0.027*▲	0.72±0.027*▲
	h (bit)	**R (%)**	***e* (bit)**
Intact control group, (n=50)	0.7585±0.007	24.15±0.71	-
Control group, (n=50)	0.8494±0.012*	15.06±1.20*	0.302±0.026*
I group, (n=50)	0.7680±0.010▲	23.19±1.27▲	0.032±0.005▲
II group, (n=50)	0.7831±0.009*▲	21.69±1.0*▲	0.080±0.009*▲▼

experimental group are also authentically differ than those in control group, and value of ***e*** is higher, than in the I experimental group.

DISCUSSION AND CONCLUSION

At the analysis of results received with using of traditional morphological, histological and biochemical methods it is established that enzymatic hydrolyzate of *Chlorophytum comosum (L.)* possesses the expressed hepatoprotective action which is shown at application of preparation at experimental toxic damage of a liver.

The above-mention hepatoprotective activity is shown in the expressed normalization of the majority of the studied biochemical parameters, preservation of morphological integrity of a liver, maintenance of a tissue homeostasis of organ. It is remarkable that the leading mechanism of cellular death at toxic hepatitis and simultaneous application of the enzymatic hydrolyzate of *Chlorophytum comosum (L.)* is not the necrosis, but apoptosis, which intensity increases in a liver of animals of the II experimental group even in comparison with control.

In a liver of rats of control group the sum of obtained parameters illustrates an essential morphofunctional changes owing to use of hepatotropic toxin.

At the same time at application of a preparation on an intact liver there are not observed reliable changes of the studied parameters.

The aplying informational parameters representing the level of adaptational and regenerative opportunities of a liver allow us to trace more accurately and subtly the changes happening in the organ. So, in a liver of rats of the I experimental group information parameters don't differ authentically from intact control, in spite of some changes. The exception is made by the value of parameter ***e*** characterizing the level of reliability of tissue biosystem. Emergence of this parameter in this group is caused by influence of a biostimulator, but value of this parameter doesn't exceed 0,1 bits.

In control group and II experimental group the studied parameters change unidirectionally. But thus in control the values of H and h increase by 12% concerning to parameters of intact animals , and S and R decrease by 37% while in the II experimental group these changes make up 3.7% and 10.10% respectively. Thus value of e in control group is equal to 0.302± 0.026 bits, and in the II experimental group – to 0.080±0.009.

It is shown that fluctuations of ***e*** up to 0,1 bits testify to some tension of adaptation, but not to approach of a pathological state. In the same conditions an increasing of parameters H and h in the range up to 5% from norm and decrease in the values of S and R to 25% from norm also characterize adaptational and regenerative opportunities of tissue system as sufficient for compensation of adverse effects of the external or internal environment.

Thus, the conducted research testifies that the applied information parameters characterizing the level of adaptational and regenerative opportunities of organs reflect morphofunctional changes of organ at biostimulation and can be used as criteria of an assessment of efficiency of biostimulators.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.

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