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## Study of the effect of external use of a brown algae product on the structural-functional continuum

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### Abstract

The authors, in a study on 25 outbred Wistar white rats weighing 180-200 g, determined the effect of Lamidana (a product from sea brown algae) on the structural-functional continuum, that is, the correlation of the functional activity of the liver parenchyma and its structural characteristics. Methods. The detoxifying function of the liver was studied by the duration of sleep of animals due to the action of anesthesia - intraperitoneal administration of sodium thiopental (estimate the rate of metabolism of thiopental, carried out by the cytochrome-P-450-dependent monooxygenase system of hepatocytes). The structural and functional state of the liver parenchyma was assessed according to the study of histological preparations. The results of the studies showed that under the influence of the external application of "Lamidin" in the test rats, the liver's detoxification function is

enhanced (significantly significant decrease in the duration of sleep of animals). At the same time, structural signs of increased functional activity of hepatocytes are determined in the parenchyma. Conclusions. The authors believe that "Lamidán", due to the peculiarities of its chemical composition, enhances the metabolic and functional activity of hepatocytes but does not damage the correlative relationships between the structure and function of hepatocytes.

**Keywords: product from brown algae; liver; structural-functional continuum.**

### **Introduction**

Modern conditions of human existence determine the negative impact on the body of many damaging factors, which leads to the depletion of the mechanisms of regulation, energy metabolism, and antioxidant protection [1. 2]. The consequence of such negative rearrangements is a violation of the structural-metabolic continuum in various organs and systems of the body, which leads to the development of pathological reactions in them. The structural-metabolic continuum is the optimal correlation between the structural characteristics of a particular organ and the activity of metabolic processes in its cells [3]. The optimal ratio of these phenomena determines the effective stress-free activity of an organ or system and, accordingly, the optimal course of adaptation and life processes. To maintain the structural-metabolic continuum, it is necessary to supply substrates, ions, and microelements to the body to form regulatory molecules, energy supply of functions, and so on. The main source of essential substances is natural resources [4, 5, 6].

Seaweeds occupy a special place among natural resources. Seaweeds have the advantages associated with their abundance and wide distribution, significant productivity and relatively low cost. They are characterized by the richness and variety of valuable bioactive compounds, such as polyphenols, polysaccharides, proteins, peptides, amino acids, lipids, vitamins, etc [7]. Also, seaweeds are characterized by a high content of macro- and microelements, biologically active substances, and compounds [8]. In terms of the content of such essential substances as iodine, selenium, and alginic acid, brown algae have no equal [9]. The preparation of brown algae "Lamidán" is widely used in practice as a bioactive additive [10].

Given the above, our work aimed to determine the effect of the product from sea brown algae "Lamidán" with its external (transdermal) application on the structural and metabolic continuum of the liver of healthy rats.

## **Materials and methods of research**

The material of the work was the data obtained in the study of 25 female white rats of the Wistar line, outbred breeding, weighing 180-200 g.

Experimental studies were conducted in accordance with the rules established by the Directive of the European Parliament and the Council (2010/63/EU), by the order of the Ministry of Education and Science, Youth and Sports of Ukraine No. 249 of March 1, 2012 "On Approval of the Procedure for conducting scientific experiments, experiments on animals by scientific institutions" [11]. The experiment was conducted in vivarium conditions. The animals were kept in standard laboratory conditions: photoperiod - light /darkness 12:12; air temperature -  $22 \pm 2$  ° C; humidity -  $55 \pm 10$  %.

The study used "Lamidin" - a drug in the form of a powder of brown algae Japanese kelp.

According to the task of the work, the animals were divided into 2 groups:

Group 1 - 10 rats were kept in vivarium conditions and not exposed to the effects. The results obtained from their study served as controls.

Group 2 - 15 rats exposed to the skin-resorptive action of an aqueous solution of "Lamidin" with an active substance concentration of 300 mg/dm<sup>3</sup>. For a course of external procedures with "Lamidin", rats of the 2nd group were placed in a special device, where the animals were placed in individual cases. In contrast, the tails of the animals were immersed in test tubes with MB for 2/3 of the length (the tail is 5 - 7% of the body surface) . The procedure was carried out for 2 hours at T 38-40°C. The course application of "Lamidin" consisted of 6 procedures every other day.

Before the end of the experiment, a "metabolic" test, according to Speransky, was carried out, due to which the state of the detoxic function of the liver was assessed.

The liver is the site of metabolism of chemicals and biological components. Therefore, during the study of the functional state of the liver in some cases, researchers have limited display of the earliest signs of sensory disturbances and its functions. Neurogenic and hepatotropic effect of the studied MW was found by a method of "metabolic tests" scheme Speranskii using barbiturates (thiopental sodium) [12]. Animals sleep time was taken into account after entering the barbiturates, which is an integral test of the MW impact on the functional state of the CNS. Accelerated time of animals falling asleep, compared with previously removed the source of the same background white rat is considered as a

manifestation of MW sedative influence on central nervous system, and increased sleep time – as an exciting effect of MW. Duration of sleep medication is associated with the work of the liver, its antitoxic ability, the ability of hepatocytes to reduce the concentration of sodium thiopental in the blood, from which animals wake. General mechanism of monooxygenase system provides biotransformation in the liver and the detoxification of toxins or metabolization of xenobiotics (barbiturates) with subsequent excretion of the liver. The indicators of the negative impact of the investigational product in function of the liver is to increase the effective liquid duration – due to inhibition of inactivation. Increased sleep duration indicates a decrease in detoxifying the liver, and fell – the raise of stimulation of its functional state. The animals were injected with sodium thiopental at a dose of 80 mg/kg.

Animals were taken out of the experiment under ether anesthesia by decapitation. During autopsy, 1 cm<sup>3</sup> of liver tissue was removed, which was poured into celloidin according to generally accepted methods. Prepared histological preparations were examined with a microscope.

Statistical processing of the obtained data was carried out using the statistical package Statistica 10.0. With all means of processing statistical material, significant shifts were considered within the probability according to Student's tables  $p < 0.05$ .

### **Results and discussion**

The liver of healthy rats has a smooth surface, and a sharp front edge; the color of the parenchyma is brown with a purple tint. Microscopic examination revealed the usual lobular organization of the parenchyma. The interparticle layers are thin and dense. Vessels of triads of moderate blood supply. Hepatocytes in lobules are partially assembled into beams. On the distal part, they are located in a conglomerate. The spaces between the beams are mostly like cracks, but some of them are widened. Hepatocytes are mostly of moderate size, with moderately eosinophilic, homogeneous cytoplasm. The kernels are of medium size, with moderate coloration. Individual hepatocytes are enlarged in size; their cytoplasm is of a normal appearance, with two nuclei of moderate size with granular fibrous chromatin. In the center of the lobule is the central vein; it is thin-walled, with a normal moderate blood supply. Around individual veins, lymphocytes are observed that have come out diapedesically.

Assessment of the state of the detoxification system of the liver was carried out during the thiopental test. The results of this study are presented in Table 1.

A pretty quick falling asleep of the test animals and a long drug-induced sleep (more than two hours) were established, indicating a not very high detoxification activity of the liver under normal conditions of intact test animals.

Table 1. The effect of "Lamidin" on the detoxification activity of the liver of rats according to the data of the thiopental test

Indicators	1st group	2nd group	p
Time to fall asleep, min	2,12 ± 0,15	2,85 ± 0,10	< 0.05
Duration of sleep, min	137,20 ± 2,27	22,60 ± 1,15	< 0.05

Notes: p < 0.05 - reliability of comparison between groups.

Studies of the structural characteristics of the liver parenchyma after the course of "Lamidin" determined some non-rough changes, reflecting changes in the functional activity of this organ.

On macroscopic examination, the appearance of the liver does not differ from the control data; the surface of the liver is smooth and shiny, the front edge is sharp, and the parenchyma is brown. On microscopic examination, the lobular organization of the parenchyma was unchanged. The interparticle layers are thin, dense, and consist of fibrous fibers. Vessels of triads are plethoric, and some single diapedetic lymphocytes are determined. Hepatocytes in the lobules are partially assembled into beams, but visually, the part of the lobule where it is located in a single array is wider than in the control. Interbeam spaces in some lobules are expanded. In such spaces, oval dark nuclei of Kupffer cells are observed on the walls.

Most of the hepatocytes are medium in size with dark eosinophilic cytoplasm and a medium-sized nucleus; in most nuclei, a fibrous pattern of chromatin is read. Some hepatocytes are enlarged with moderately eosinophilic plasma and two average-sized homogeneous nuclei. In some hepatocytes, the chromatin in the nuclei is redistributed to the zone near the karyolem.

In most cases, the central vein is thin-walled with moderate blood filling, but there are also increased blood filling.

Conducting a thiopental test in rats at the end of the course of procedures with "Lamidin" established the presence of significant changes compared to control values.

According to Table 1, the time of falling asleep in rats of the 2nd group was increased by 1.34 times, which indicates a slight excitatory effect of "Lamidin" on the state of the central nervous system. The duration of medical sleep was reduced by 6.1 times compared with the control data. The established changes may indicate a significant increase in the liver's detoxification function

Thus, the results of the conducted studies indicate that the course external application of the natural modulator "Lamidin" does not violate the structural and functional continuum in the liver parenchyma of healthy rats. This data is evidenced by changes in the parameters of the thiopental test - an extension of the period of falling asleep and a reduction in drug-induced sleep. Such restructuring is possible with a significant increase in the activity of the detoxification function of the liver. At the same time, we observed signs of structural changes in the liver parenchyma, which are characteristic of the activation of metabolic processes in hepatocytes: plethora of triad vessels, expansion of interstitial spaces, lumpy organization of the cytoplasm of a part of hepatocytes; the presence of a lumpy-fibrous pattern of chromatin in the nucleus, changes in its distribution over the volume of the nucleus. That is, changes in structural characteristics in the liver correlate with changes in its functional activity.

A specific positive effect on the structural-functional continuum is connected, in our opinion, on the one hand, with the peculiarities of the chemical composition of Lamidin - the presence of numerous biologically active substances, microelements, etc. [7 – 10, 13, 14].

On the other hand, this positive effect is associated with the peculiarities of the physicochemical properties of the skin. Numerous studies have shown that the skin of humans and animals is permeable to fat-soluble substances, lipid solvents, as well as gases and dissociated molecules of weak acids [15 - 20].

Moreover, compounds exhibiting solubility in lipids and moderate solubility in water have the maximum permeability. The composition of "Lamidin" includes a variety of active substances that meet these requirements. Quickly penetrating the skin, they, acting as regulatory molecules, cause changes in the activity of the function and the corresponding restructuring of the structure without changing the structural-functional continuum. In this aspect, the concept of hormesis and its role in hydrothermal treatments should be mentioned [21].

**Conclusions.** Thus, the product from brown algae Lamidan, when applied transdermally, changes the functional activity of the liver and causes corresponding changes

in its structural organization while maintaining the balance of these characteristics without disturbing the structural and functional continuum of the parenchyma.

### **Author Contributions**

Conceptualization, Nasibullin B.A. & Dekhtyar Yu.N. ; methodology, Gushcha S.G.; formal analysis, Gushcha S.G.; data curation, Nasibullin B.A. & Dekhtyar Yu.N.; writing—original draft preparation, Gushcha S.G. & Volyanska V.S.; writing—review and editing, Volyanska V.S.; supervision, Nasibullin B.A. & Dekhtyar Yu.N..

All authors have read and agreed to the published version of the manuscript.

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### **Institutional Review Board Statement**

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of State Institution «Ukrainian Research Institute of Medical Rehabilitation and Resort Therapy of the Ministry of Health of Ukraine» (17/2011, 22 November 2011).

### **Informed Consent Statement**

"Not applicable" for research not involving human subjects

### **Data Availability Statement**

The data presented in this study are available on request from the corresponding author.

### **Conflicts of Interest**

The authors declare no conflict of interest.

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