SMIRNOV, I., NASIBULLIN, B. and GUSHCHA, S. Assessment of the state of synergies between the structural and functional characteristics of the kidneys and liver during external use of a seaweed product Laminaria algae. Journal of Education, Health and Sport. 2024;52:215-228. eISSN 2391-8306. https://dx.doi.org/10.12775/JEHS.2024.52.108
https://apcz.umk.pl/JEHS/article/view/48770
https://zenodo.org/records/10666676

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 28.11.2023. Revised: 06.01.2024. Accepted: 29.01.2024. Published: 31.01.2024.

Assessment of the state of synergies between the structural and functional characteristics of the kidneys and liver during external use of a seaweed product Laminaria algae

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Abstract

The authors conducted studies to study the relationship between the functional activity of the kidneys, the detoxification activity of the liver and the structural features of the parenchymatous tissue of these organs under normal conditions and with external use of the laminar algae product “Lamidan”. The

work was performed on 164 white outbred Wistar rats weighing 180-200 g. The work was carried out in accordance with current standards for working with laboratory animals. The results of many years of research have shown that normally the indicators of detoxification activity of the liver and functional activity of the kidneys practically do not change, and they correspond to the structural organization of the parenchymatous tissue of these organs, corresponding to the descriptions given in well-known manuals on the activities of these organs. The use of "Lamidan" activates the detoxification function of the liver by 28 % and the functional activity of the kidneys by 28.5 %, i.e. changes are unidirectional and proportionate. In the parenchyma of both organs, changes in the structural organization are recorded, characteristic of an increase in functional activity. Thus, there is a strictly interrelated set of stereotypical changes in the indices of the two organs under study, reflecting between the organs interrelations of functional systems.

Keywords: liver; kidney; structural-functional continuum; Laminaria algae.

Introduction

In recent years, researchers have shown interest in the issues of integrative medicine, in particular in its theoretical aspect - pathological physiology. This is due to the fact that the deepening of knowledge about the structural and biochemical aspects of the processes of vital activity of organism systems

distances us from the sick person as a holistic object, which contradicts the classical approach to the need to treat the patient, not the disease manifestations [1, 2, 3, 4]. Over the past decades, two integrative concepts have emerged in medicine: the concept of the emergency system [5], and the concept of the neurogenicity of the adaptation-trophic system, based on the role of the vegetative nervous system and stress in life support [6]. An earlier integrative concept of organism activity is the concept of homeostasis. Homeostasis is understood as the stability of the internal environment of the organism. It is achieved by strict and precise regulation of extracellular and intracellular fluid parameters, parameters of intensity of metabolic reactions, functions of organs and systems [7, 8, 9]. In addition, the balance of activity of different mechanisms of homeostasis is maintained; however, all these changes are possible only in conditions of appropriate substrates - structural and functional organisation of the parenchyma of the corresponding organs.Today, one of the popular directions of valeology is naturopathy, i.e. the use of natural healing resources for the correction of homeostasis disorders in the human body. This is due to the fact that most of these resources are considered as non-specific modulators [10 - 14].

Seaweeds occupy a special place among natural plant resources, as compared to terrestrial plants they contain more macro- and microelements, bioactive compounds, iodine, selenium and alginic acid [15, 16]. Alginic acid, having properties to bind heavy metals and radionuclides, actively contribute to detoxification and excretion of xenobiotics [17, 18, 19].

Our previous study was devoted to the evaluation of the effect of external application of the brown kelp algae product "Lamadin" on the structural-functional continuum of the liver of healthy animals [20]. However, the concept of structural-functional continuum extends to the state of many organs and systems of the organism, i.e. the whole organism.

Based on the above, the aim of the work is to determine the effect of the kelp algae product "Lamidane" at its external application on the renal-hepatic continuum of healthy white rats.The term used is structural-functional continuum defines the integrative relationship between function, metabolism of human or animal body systems [21].

Materials and methods of research

The material of the work was the data obtained in the study of 164 female white rats of the Wistar line, outbred breeding, weighing 180-200 g. Experimental studies were conducted in accordance with the rules establishedby 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" [22, 23]. The experiment was conducted in vivarium conditions. The animals were kept in standard laboratory conditions: photoperiod - light /darkness 12:12; air temperature - 22 ± 2 ° C; humidity - 55 ± 10 %. According to the task of the work, the animals were divided into 2 groups. Group 1 - rats were kept in vivarium conditions and not exposed to the effects.

In this group, 144 intact rats were included, in which renal function and structure, liver detoxification activity and liver structure were investigated in autumn-summer and autumn-winter seasons between 2017 and 2022. The studies were conducted in 12 rats in each season. The data obtained in each season of each year were summarised and an average norm result was formed, which was further used as a control.

Group 2 - 20 rats exposed to the skin-resorptive action of an aqueous solution of "Lamidan" with an active substance concentration of 300 mg/dm^3. For a course of external procedures with "Lamidan", 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 "Lamidan" consisted of 6 procedures every other day.

After the final procedure, rats were placed in cages, and daily urine was collected.The obtained urine was used to assess the renal functional activity (RFA) by the effect on the function of urine formation (glomerular filtration rate, tubular reabsorption, daily diuresis), excretory function (by creatinine, urea and chloride excretion).

Another 10 rats of the second 2 group of rats after the final procedure were subjected to a study on determining the detoxification function of the liver using a metabolic test. 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) [24, 25]. Animals sleep time was taken into account after entering the barbiturates, which is an integral test of the "Lamidan" 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 amanifestation of "Lamidan" sedative influence on central nervous system, and increased sleep time – as an exciting effect of "Lamidan". 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 rase of stimulation of its functional state. The animals were injected with sodium thiopental at a dose of 80 mg/kg.

After completing of the course of procedures with "Lamidan", the animals were withdrawn from the experiment by decapitation under ether anaesthesia. Kidneys and livers wereremoved from the animals and fixed for 48 hours in10 % formaldehyde solution. Kidney and livers parts (1 cm^3) werepassed through alcohols of increasing concentrationand embedded in celluloid according to the usual method. Histological sections of 7-9 μm thickness were madefrom the obtained blocks and stained with haematoxylin-eosin. The obtained preparations were examinedunder a light microscope. The content of total bilirubin and its fractions was determined in the blood serum using biochemical methods.

Statistical processing of the data obtained in the seriesof experiments was performed using the Statistica10.0 statistical package. Significant shifts were consideredto be within the range of probability for all meansof processing statistical material according to Student'stables $p<0.05$.

Results and discussion

Changes in detoxification function of the liver under the influence of a course of external application of the drug "Lamidan" are reflected in Table 1.

Table 1. The effect of "Lamidan" on the detoxification activity of the liver of rats according to the data of the metabolically (thiopental) test

Indicators	1st group	2nd group
Time to fall asleep, min	2,60 ± 0,33	3,00 ± 0,24
Durationofsleep, min	116,20 ± 1,53	33,12 ± 3,07*
Totalbilirubin, mkmol/l	8,44 ± 0,28	4,26 ± 0,29*
Directbilirubin, mkmol/l	3,07 ± 0,15	1,67 ± 0,14*
Bilirubinindirect, mkmol/l	5,38 ± 0,17	2,59 ± 0,22*

Notes: * – probability of changes in groups between groups 1 and 2 ($p<0.05$).

According to the data of Table 1, no significant change in the time of falling asleep in rats that received "Lamidan" was found, which may indicate the invariability of the fast component of detoxification activity of the liver. At the same time, the duration of medicated sleep in experimental rats decreased 3.5 times, which is possible only with a sharp intensification of the slow component of detoxification function of the liver. At the same time a significant decrease in the content of total bilirubin and its fractions in blood serum is determined. It should be emphasised that if in norm the content of indirect bilirubin is 1.76 times higher than direct bilirubin (control group index), then when using "Lamidan" it decreases and makes 1.55 times. That is, the efficiency of detoxification reaction increases, it is higher than in the control group.

Simultaneously with changes in detoxification function of the liver, rearrangements of the liver parenchyma were observed. The lobular structure of the liver parenchyma does not change with the use of "Lamidan". Interlobular layers are thin, dense. Fibrous fibres in them are of usual appearance. Triad vessels and central veins of increased blood filling. Hepatocytes in lobules around the central vein are gathered in beams. Such organisation of hepatocytes is determined approximately in the central half of the lobule. On the rest area of the lobule hepatocytes are located in a continuous array. Hepatocytes in the

overwhelming majority are of medium size, their cytoplasm is dark eosinophilic, colouring is not uniform over the cell area, darker under the shell and lighter around the nucleus. The nuclei are of medium size, moderately coloured with a visible granular fibrous pattern of chromatin. No binuclear hepatocytes were detected on the slice of the lobule. In general, it is possible to fix the presence of structural manifestations of increased functional activity of the liver parenchyma.

The state of renal function after the course of "Lamidan" is reflected in Table 2. According to the data of table 2 there is some decrease of daily diuresis due to reliable and significant increase of tubule reabsorption, despite the increase in the rate of glomerular filtration. As for the excretory function of kidneys, its structure is slightly changed - urea excretion is weakened (its excretion is significantly decreased by 1.52 times). Probably "Lamidan" inhibits the breakdown of nitrogenous compounds, as the amount of excreted creatinine decreases, although unreliably. There is also an increase in the excretion of chlorides (their excretion significantly increased by 3.2 times) and a slight shift of urine pH to acidic side.

Table 2. Effect of "Lamidan" on indicators of renal functional activity

Indicators	1st group	2nd group
Daily diuresis, ml/dm^2 of body surface area	1,10 ± 0,06	0,88 ± 0,13
Glomerular filtration rate, ml/(dm^2×min)	0,12 ± 0,009	0,15 ± 0,02
Tubular reabsorption, percentage to filtration, %	99,260 ± 0,070	99,600 ± 0,040*
Creatinineexcretion, mmol	0,012 ± 0,0009	0,015 ± 0,002
Ureaexcretion, mmol	0,87 ± 0,06	0,57 ± 0,08*
Chlorideexcretion, mmol	0,26 ± 0,040	0,85 ± 0,08*
pH of daily urine, pH units	7,63 ± 0,25	7,00 ± 0,36

Notes: * – probability of changes in groups between groups 1 and 2 ($p<0.05$).

These changes in functional activity of kidneys are accompanied by changes in the structure of their parenchyma. Swelling of endoceliocytes of capillary tubules of renal tubules was observed, small vaeocytes appeared in a part of endotheliocytes, epithelium of convoluted tubules was swollen; in renal tubules Bowman's spaces were enlarged. The lumen of the straight tubules is dilated.

Thus, the results of our studies have shown that administration of the food supplement "Lamidan" causes changes in the functional activity of kidneys and detoxification activity of the liver. These changes in function are closely related to the appearance of structural changes in the parenchyma of these organs. By their character structural changes are similar to those observed in case of strengthening of urine formation and urine excretion in kidneys and in case of activation of metabolic processes in liver. As for the changes in the state indices

of different components of the functional activity of the studied organs, they give an idea of the rearrangements in the structure of the organ functioning, but do not give an idea of the integral activity of the organ.

To determine this uncertainty, we assigned 1 conditional score to each of the studied indicators and summed them up. For functional activity of kidneys of control animals this sum made 7 points, and for functional activity of kidneys of rats receiving "Lamidan" externally - 8,94 points, i.e. increase of integral functional activity - 28 %.

The integral score of the functional activity of the liver is 2 points, and the integral score of the functional activity of the liver of experimental animals is 1.44, i.e. the changes are 28.0 %. As this change is caused by the reduction of medicated sleep, which is associated with the increase of deactivating reactions in the liver, i.e. the reduction of the integral score indicates the activation of deamination processes. The growth of functional activity in both organs occurs by the same amount and in the same direction and is accompanied by the same structural changes in the parenchyma of the studied organs. The sameness of structural changes should be considered taking into account the peculiarities of the organisation of the structure of the parenchyma of each of them.

Conclusions. Thus, the results of our research have shown that it is possible to consider structural and functional rearrangements of the liver and kidneys under external influence as a continuous set of reaction-capable indices, i.e. structural and functional continuum.

Author Contributions

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

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

Funding

This study received no specific funding

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» (1/2024, 08 January 2024).

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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