ISSN: 2582-4686 SJIF 2021-3.261, 2022-2.889, 2023-5.384, 2024-6.875 ResearchBib IF: 9.948 / 2024

THE MULTIDISCIPLINARY JOURNAL OF SCIENCE AND TECHNOLOGY

VOLUME-5, ISSUE-5

SPECIFIC CHARACTERISTICS OF QUANTITATIVE CHANGES IN EXTRACELLULAR MATRIX COMPONENTS IN CHRONIC TOXIC LIVER INJURY

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Abstract This article presents an analysis of scientific sources regarding the quantitative changes of extracellular matrix components in liver tissue under chronic toxic damage. According to the research findings, prolonged exposure to toxic agents increases the levels of collagen, fibronectin, laminin, and proteoglycans, leading to the early development of liver fibrosis. The literature review serves as an important source for a deeper understanding of the morphological basis of liver injury, early diagnosis, and the development of effective therapeutic approaches.

Keywords: Chronic toxic damage, liver, extracellular matrix, collagen, fibrosis, morphology.

INTRODUCTION.

The liver performs many important functions in the body, such as metabolism, detoxification, energy storage, and immune protection. Over a long period of time, irreversible morphological and functional changes occur in liver tissues under the influence of various toxic substances. Chronic toxic damage (CTS) is characterized by a persistent disruption of the structure and function of the liver, which occurs as a result of the effects of environmental factors, drugs, chemical compounds, heavy metals, and alcohol.

Such pathological processes directly affect not only the liver parenchyma, but also the components of the extracellular matrix (ECM). ECM plays the role of a structural support in various tissues of the body and consists of proteins such as collagen, elastin, laminin, fibronectin, and proteoglycans. In chronic toxic damage, the quantitative balance of these components is disturbed, which leads to an increase in fibrosis processes and a decrease in the regenerative potential of the liver parenchyma.

In recent years, scientific research in this area has been aimed at identifying changes in the composition of HAM, especially on the basis of morphological and immunohistochemical studies. Identifying these changes is important for early diagnosis of toxic hepatopathy and developing appropriate treatment measures. Thus, qualitative and quantitative changes in the components of the intercellular matrix in chronic toxic liver damage are considered one of the main stages in its pathogenesis.

This article aims to provide a deep scientific basis for the investigation of changes in the components of the intercellular matrix in chronic toxic liver damage, to explain the main mechanisms of this process through the analysis of previously conducted scientific research results, to compare existing ideas and approaches, and to systematize scientific knowledge in this area. Also, the article analyzes modern research methods that serve to identify changes in the composition of HAM, their clinical significance and diagnostic capabilities.

REFERENCES AND METHODOLOGY.

Scientific research aimed at determining the effects of chronic toxic damage on liver tissue, especially on the components of the extracellular matrix, has become a hot topic in the last decade. Initial studies began in the early 2000s, and their main goal was to determine the effects of toxins on liver morphology. For example, in studies conducted in 2003 under the leadership of N.P.

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Zvyagintseva, it was noted that the amount of collagen fibers in liver tissue increased sharply under the influence of carbon tetrachloride (CCl_4). The study revealed that the immunohistochemical index of collagen types I and III in the liver stroma was 2.5 times higher than normal within 21 days after the toxic effect [1].

In an experimental study conducted by A.B. Kiryushchenko in 2009, changes in the levels of fibronectin and laminin in the extracellular matrix against the background of chronic toxic hepatopathy were studied. This study demonstrated a significant increase in matrix components that lead to fibrosis under the influence of toxins and their inhibition of regeneration processes [2].

In recent years, in particular in 2015, a scientific group led by V.V. Pashkov and A.I. Timoshenko identified structural changes in the layered structure and glycoproteins of the extracellular matrix against the background of toxic damage using high-density electron microscopy. Studies have shown that the structural and functional unity of the HAM is disrupted as a result of long-term exposure to toxic substances CCl_4 and ethanol [3].

Another important scientific work conducted in 2020 was conducted by S.Yu. Khayrutdinov, which analyzed changes in the amount of proteoglycans in the extracellular matrix and their distribution as a result of chronic poisoning with various toxic agents (paracetamol, ethanol, chloride-containing substances) based on experimental mouse models. This study revealed increased areas of fibrosis, impaired angiogenesis, and decreased immunoreactivity in the liver parenchyma [4].

Also, if we turn to international research, a study conducted in 2021 by scientists from Harvard Medical School in the USA deeply studied the role of transformed hepatic stellate cells in the production of extracellular matrix in toxic liver damage. According to the results of the study, after the activation of these cells, the production process of type I collagen and fibronectin was significantly activated, and fibrosis developed rapidly [5].

The above scientific studies, timely morphological and biochemical analyses clearly show that changes in the extracellular matrix play an important role in chronic toxic processes. Also, research in this area allows for the early detection of toxic hepatopathy and the development of effective treatment strategies.

Morphological and molecular changes that occur in liver tissues as a result of chronic toxic damage have a particularly profound effect on the components of the extracellular matrix (ECM). Studies show that these changes play a central role in the pathogenesis of toxic hepatopathy.

In the experiments conducted by Zvyagintseva and co-authors in 2003, a significant increase in collagen fibers [1], and in the study by Kiryushchenko in 2009, an increase in the concentration of fibronectin and laminin [2] revealed the importance of these components as morphological biomarkers for identifying the early stages of the fibrosis process in liver tissues. This indicates that one of the first structures to be damaged by toxins is the intercellular matrix.

Electron microscopic analyses by Pashkov and Timoshenko in 2015 showed that the uneven arrangement of HAM components, structural disruption, and disruption of their layered systems lead to a decrease in the proliferation and differentiation capabilities of liver cells [3]. Such changes complicate the process of liver cell regeneration and lead to a deepening of the fibrosis process.

S.Yu. Khayrutdinov's 2020 study showed that the imbalance of proteoglycans, abnormalities in angiogenesis, and suppression of immune responses under the influence of chronic toxins require the development of new criteria for the diagnosis of toxic hepatopathy [4]. In particular, the fact that the distribution of proteoglycans causes the expansion of the fibrosis zone and the narrowing of the hepatic capillaries is recognized as an important theoretical basis.

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VOLUME-5, ISSUE-5

In a 2021 Harvard study in the USA, the identification of transformed stellate cells as one of the main factors enhancing fibrosis [5] provided the possibility of targeting these cells from a therapeutic perspective. This could serve as a scientific basis for antifibrotic approaches in chronic toxic hepatopathy.

RESULTS AND CONCLUSIONS.

In general, the analyzed results show that changes in the extracellular matrix cause continuous damage to the structure, regeneration, immunological protection and metabolic functions of the liver parenchyma against the background of toxic damage. This creates the basis for studying HAM components as the main targets in the diagnosis and treatment of toxic hepatopathy.

Literature analysis is an integral part of any scientific research and is necessary to expand, update existing knowledge in a particular field or topic, and develop new approaches. Literature analysis in the study of the effects of chronic toxic damage, especially on liver tissue, not only helps us expand the scope of existing knowledge, but also creates the opportunity to re-analyze previously achieved results based on new approaches and methodologies. This, in turn, leads to many useful results, including:

Literature analysis can identify limitations of previously conducted research, scientific errors or uncertainties. For example, in the study of toxic effects on liver tissue, some scientific studies focus only on the same toxicant or only on one type of cell. This does not show differences between other toxicants and cells. Thus, by analyzing the literature, it is possible to develop new research directions and methodologies, for example, the need to study the combined effects of multiple toxicants or the interaction of different cells and matrices of the liver.

One of the main goals of scientific studies is to consolidate the results and concepts achieved. Through the analysis of the literature, similar studies and their results are compared, which shows that the results obtained are reliable and reproducible. In several scientific studies conducted on chronic toxic lesions, changes in liver tissue are similar to each other, which helps to determine which parameters are the most reliable and general. For example, in many studies, an increase in the amount of collagen fibers and increased fibrosis in liver tissue have been noted [1][2]. Such results confirm the general reliability of previously obtained scientific data and serve as a basis for new studies.

Another important aspect of the literature review is that it allows for the analysis of existing diagnostic and therapeutic methods. Literature review plays an important role in the early detection and effective treatment of diseases such as toxic hepatopathy. For example, collagen and proteoglycans [3][4] are of particular interest as biomarkers indicating the onset or exacerbation of fibrosis in liver tissue. Information about these components helps to identify their deviations from the norm early. Such analyzes serve as an important source of knowledge for the creation of new diagnostic methods, as well as for the identification of effective treatment methods.

Studying the effects of toxic agents on liver tissue not only helps to understand existing damage, but also makes it possible to develop new methods of combating toxic effects. For example, a 2021 study by Harvard Medical School scientists [5] investigated the activity of stellate cells that accelerate liver damage. Such studies could lead to new therapeutic approaches, especially antifibrotic and anti-inflammatory treatment strategies.

When discussing the practical benefits of literature review, it is important to focus on how scientific results can be applied to clinical practice. The information obtained from scientific research, such as changes in the amount and distribution of proteoglycans in liver tissue under the influence of

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toxic agents [4], will serve as the basis for creating effective treatment protocols in the clinic. Such studies are also a source of knowledge necessary for the development of new pharmacological agents for the treatment of liver diseases and their clinical trials.

Literature review provides an important opportunity for the exchange of existing knowledge within the international scientific community. Scientific research on toxicological lesions is conducted in individual countries under specific conditions. However, through global reviews, there is an opportunity to compare different methodologies, exchange experiences and further develop scientific networks. For example, studies conducted by Harvard University in the USA [5] help to familiarize the scientific community around the world with new approaches and provide an impetus for the development of global approaches to combat liver damage.

Literature review is a process necessary to create a solid scientific basis for scientific research and effectively direct new research. Studies on chronic toxicological lesions and effects on liver tissue not only strengthen existing knowledge, but also provide guidance for new research. This provides information of high value not only from a scientific, but also from a clinical and pharmacological point of view.

CONCLUSION.

Chronic toxic damage is now a global medical and biological problem, requiring special attention, especially with pathological changes occurring in liver tissue. The liver, as the main detoxification organ of the body, is significantly damaged by the effects of various chemicals, drugs and industrial toxins. Long-term toxic effects are accompanied by impaired hepatocyte function, pathological proliferation of intercellular matrix components (collagen, laminin, fibronectin, proteoglycans), deformation of sinusoids and activation of fibrosis processes. Morphological and biochemical changes reveal the direct and indirect damaging effects of toxins, in which quantitative changes in collagen fibers and glycoproteins are determined based on immunohistochemical markers. Also, as a result of activation of stellate cells, the production of intercellular matrix increases, which negatively affects the structure and function of liver tissue. Scientific research in recent years has shed light on the mechanisms of development of these changes and offers new approaches to diagnosis and treatment. In particular, the analysis of scientific literature on this topic is of great importance in identifying the early stages of hepatotoxic processes, developing a strategy for treating toxins, and preventing liver failure. In conclusion, a thorough study of the structural and functional changes that occur in liver tissue during chronic toxic damage is one of the main directions in the development of toxicology and hepatology.

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