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Research Article

STUDY THE ANTIFIBROUS EFFICACY OF PLANT PROANTHOCYANIDIN IN RATS WITH CHRONIC HELIOTRINE LIVER DAMAGE

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ABSTRACT

Under experimental conditions, the effect of plant proanthocyanidin – yantacin isolated from a camel thorn plant (Alhagi pseudalhagi) – Yantacin, when administered orally at a dose of 100 mg / kg, on possible changes in the early stages of liver fibrosis that occurred against the background of chronic heliotrine hepatitis was studied. The studies were conducted on male rats with a body weight of 100 ±10 g. The effect of yantacin on the general and biochemical parameters of the blood, as well as the amount of NO – nitrates (in connection with lipoproteins), proteins in the blood against the background of heliotrine liver damage was studied. At the same time, yantacin demonstrated a significant protective effect compared to the control group on the detected fibrosis, according to which certain indicators, against the background of chronic toxic liver damage. In this regard, a more extensive in-depth study of the effect of the studied substance plant proanthocyanidin on normal and impaired liver activity is carried out.

KEYWORDS

Heliothrin, fibrosis and cirrhosis of the liver, hepatoprotective, antifibrotic, proanthocyanidins, toxic hepatitis, yantacin.

INTRODUCTION

Currently, chronic liver diseases, including diseases of viral etiology of viral etiology, occupy one of the leading places in the structure of pathologies with steadily increasing morbidity and mortality. According to the World Health Organization report, the incidence of chronic infection caused by various types of hepatitis virus is increasing in the world [1]. At the same time, the most common cause of the development of chronic diffuse liver diseases is its defeat by the hepatitis B, C, D virus, etc. especially chronic hepatitis C (HCV) and about 399 thousand die annually. a person as a result of the development of cirrhosis of the liver (CP) and hepatocellular

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carcinoma (HCC) in the outcome of chronic hepatitis C [2, 3]. There are complications of this pathology in patients with chronic hepatitis of various etiologies, which developed liver fibrosis does not have a specific clinical picture, as well as symptoms, and since this condition does not cause much concern in patients, the expediency of their assessment still raises questions among practitioners [4, 5]. Therefore, in the first stage, it is important to determine the presence of this pathology in the early stages, as well as to start treatment of chronic hepatitis in a timely manner in order to prevent the development of liver fibrosis. In recent years, numerous clinical and experimental studies have been conducted on the early diagnosis, treatment and prevention of liver fibrosis, measures have been taken to standardize the rules for managing patients with progressive fibrosis and cirrhosis of the liver, as well as the tactics of using a number of drugs to influence the pathogenesis of liver diseases. The treatment of liver diseases accompanied by the formation of fibrosis is an extremely important task, while the prevention of the development of the occurrence of this condition remains quite relevant and justified. Despite numerous studies in this direction, currently there are no specific drugs for the treatment and prevention of fibrosis. Thus, the most rational approach to the treatment of liver pathologies is the use of natural and less harmful drugs, especially those obtained on the basis of plant origin that can prevent the occurrence, development and progression of these diseases. Currently, there are many drugs that are used to treat liver diseases, however, when most of them are used for diseases associated with liver fibrosis, there is no clear mechanism of action that allows us to discuss the occurrence and progression of fibrosis in prevention. And at the same time, almost none of these drugs show such ability in clinical trials [1, 4, 5].

Thus, improving the diagnosis of liver fibrosis in the early stages, assessing the rate of its development and developing methods to eliminate the processes of fibrogenesis in the liver are very important tasks not only for hepatology, but also for internal diseases in general.

In connection with this, extensive pharmacological and toxicological and chemical-technological studies of Yantacin – plant proanthocyanidin, isolated from the camel thorn plant (Alhagi pseudalhagi), widely distributed in Central Asia and Kazakhstan, were carried out in the laboratories of the Research Institute of

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Pediatrics and IHRV of the Academy of Sciences of the Republic of Uzbekistan [6, 7].

The object of the research. Evaluate the effect of plant proanthocyanide on the early stage of liver fibrosis of antifibrotic activity in relation to control.

MATERIALS AND METHODS

The experimental part was performed on white mongrel male rats. An experimental model of chronic liver pathology was obtained in male rats weighing 100±10 g. The hepatotoxicity of heliotrin has been shown by us in rats before, therefore, the model of heliotrin-induced hepatitis or liver fibrosis is the most suitable model of toxic liver damage. The chronic form of experimental hepatitis was caused by the administration of heliotrin in decreasing doses: according to the scheme: 10 mg/100 g of mass, 7 mg/100 g of mass, 5 mg/100 g of mass, 3 mg/ 100 g of mass [8]. Chronic intoxication, confirmed morphologically, was obtained on the 35th day of the experiment [1]. The mortality rate was 30%.

To characterize the degree of fibrosis of liver tissue, a general and biochemical blood analysis and a morphological examination of the liver were simultaneously performed. The total content of NO - nitrites and nitrates of proteins in the blood serum was determined by the EIA method.

On the 35th day of the experiment, the animals were taken out of the experiment under ether anesthesia, the liver was fixed and poured into paraffin according to the standard procedure.

RESEARCH RESULTS AND DISCUSSION

The liver in the mammalian body performs complex and multifaceted functions aimed at preserving homeostasis. It actively participates in all types of metabolism – protein, carbohydrate, fat, pigment, vitamin, etc. The first task of our study was to study the blood pattern of experimental animals. Modeling of toxic liver damage in rats caused by the introduction of heliotrin led to the development of disorders of the functional state of liver cells.

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Table 1. Peripheral blood parameters of rats with ChHH and after administration yantacin

The name of the indicator	Intact animals	Control + ChHH	Yantacin + ChHH
Hematocrit index, %	44,46±1,01	40,7±0,88	43,6±1,2
Hemoglobin, g/l	145,2±0,16	138,75±3,6	151,8±0,44
Red blood cells, T/l	8,85±0,24	7,98±0,29	8,7±0,21
Average volume of red blood cells, fl	50,24±0,44	54,56±0,76	49,86±0,55
Average hemoglobin content in erythrocyte, pg.	16,42±0,34	19,0±0,25	16,20±0,28
The average concentration of Hemoglobin in the erythrocyte, g/ dl	32,7±0,53	34,86±0,25	34,46±0,35
Leukocytes, G/l	13,38±0,84	14,32±1,94	19,40±2,07
Lymphocytes, G/l	10,64±0,73	9,7±0,44	14,43±1,40
Lymphocytes, %	79,6±1,33	73,75±2,29	72,80±1,87
Average cells, G/l	1,66±0,11	2,94±1,49	3,93±0,51
Platelets, G/l	663,8±35,07	589,0±53,36	553,20±47,4

Notes: - differences with intact ones are significant ($p<0.05$).

With the introduction of heliotrin in the blood of experimental animals, a change in the content of erythrocytes was detected, not only qualitative, but also quantitative indicators of erythropoiesis change: the hematocrit index decreases. This fact is associated with an increase in tissue hypoxia, which leads to necrosis and apoptosis of cells.

On the part of white blood cells, the most pronounced changes are observed in the blood of rats with chronic heliotrin hepatitis (HCG), when the number of hepatocytes and medium cells increases in peripheral blood, which reflects the exudative phase of inflammation in response to damage to functional cells in the organ. This also reflects the proliferative phase aimed at phagocytosis of destructively altered hepatocytes of the liver. The decrease in platelets in the blood is apparently associated with a decrease in the functional activity of poorly differentiated

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hepatocytes. The concentration of hemoglobin and the content of erythrocytes in the group of rats treated with yantacin is almost restored.

In rats with chronic GH, the activity of transaminases (AST and ALT) in the blood serum was 264.8% and 318.3%, respectively, compared with the level of these indicators in the control ($p<0.05$). The administration of anthracene to experimental animals reduced the activity of these enzymes in comparison with similar indicators of rats who did not receive the drug, while remaining significantly more than in control group rats. The de Ritis coefficient was lowered in the control and experimental groups. (Table 2). The activity of the antioxidant enzyme - GGTP increased by 7.3 times. In the experimental group of rats, it decreased to 75.4±0.86, remaining above the control value. The activity of the alkaline phosphatase remained within the normal range.

Table 2. Activity of excretory and indicator enzymes of blood serum of rats with ChHH and under the action of Yantacin

Исследуемый показатель	Intact animals	Control + ChHH	Yantacin + ChHH
AsAT, E / l	8,78±0,27	23,25±0,31	15,41±0,34
AlAT, E / l	8,62±0,25	27,44±0,13	18,32±0,21
De Ritis Coefficient(AST/ALT)	1,01±0,01	0,84±0,02	0,84±0,02
Glutamyltranspeptidase (γ-GTP), U/l	16,60±0,48	121,45±0,71	75,4±0,86
Alkaline phosphatase (alkaline phosphatase), U/l	87,51±0,49	96,49±6,12	90,01±4,08

Notes: - differences with intact ones are significant ($p<0.05$).

The obtained data allowed us to state that in the conditions of the experiment, the administration of yantacin to rats caused a normalizing effect. This is evidenced by the above data on the dynamics of the activity of indicator and excretory enzymes in the blood serum of rats treated with this drug.

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In addition, niacin reduces the content of NO products in both liver tissue and blood. At the same time, it is known that the hyperproduction of NO occurs due to the participation of an induced form of NO synthase (enos), the activation of which occurs only in pathological conditions. The resulting NO-products and its active derivatives have a cytodestructive effect, causing cytolysis.

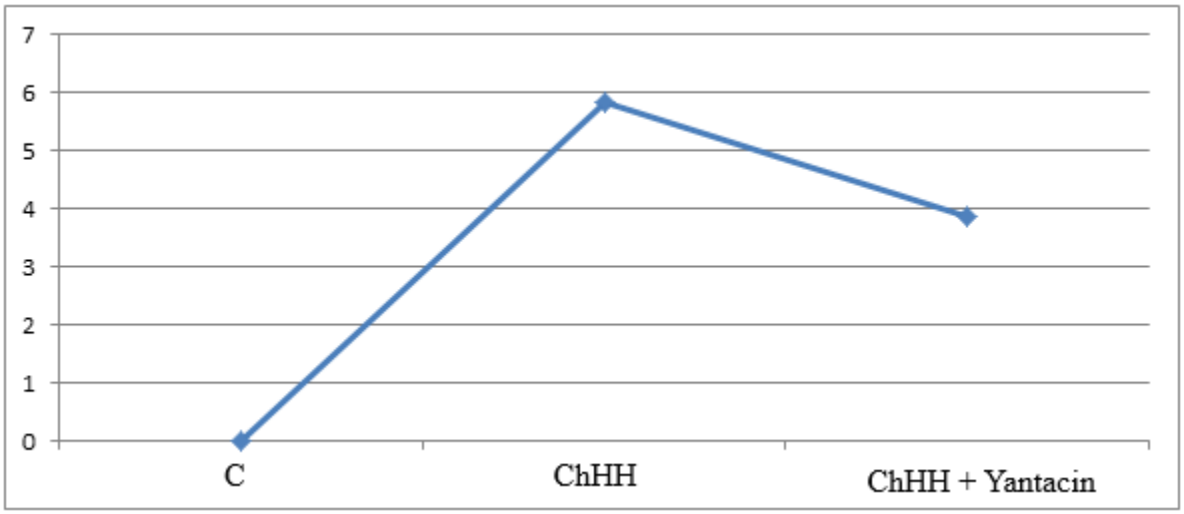

Fig.1. The effect of yantacin on the NO content (mmol/L) in the blood of rats with ChHH.

Unlike iNOS, the constitutive form of NO synthase (with NOS) functions under physiological conditions and contributes to the production of NO for the functional needs of the body. Therefore, it is believed that NO in moderate concentrations has not a cytodestructive, but a cytoprotective effect. Apparently, yantocin, influencing the NO-ergic systems of the body, contributes to the preservation of NO in moderate concentrations. However, within the framework of this study, it is not possible to say whether its influence on the NO system is direct or indirect. In addition, protein indicators in the liver of rats with chronic heliotrine intoxication and under the influence of yantacin. The development of fibrous changes in the liver is based on the imbalance between the processes of synthesis and breakdown of extracellular matrix proteins towards the predominance of the formation of extracellular matrix components. The state of the NO-ergic system was assessed by changes in the main metabolites of NO (NO2 – and NO3 –). An

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increase in the level of NO in the blood of rats with ChHH by 50.5% relative to the control value was noted. An increase in the levels of NO metabolites against the background of hypercholesterolemia is associated with the inhibitory effect of NO during high-density lipoproteins (LDL) oxidation. One of the end products of the reaction of NO with lipid radicals are nitrites, their level can increase accordingly to the intensity of free radical oxidation of LDL (Lankin V.Z. et al.2000), which also contributes to the formation of fibrous tissue in the liver. An increase in the concentration of NO was revealed with the presence of a negative correlation of NO with the level of total cholesterol and low-density lipoprotein cholesterol (LDL cholesterol).

In patients with chronic viral hepatitis B, as in patients with ChHH, a decrease in HDL and an increase in TG significantly increased the risks of MS and its individual components, and also contributed to the development of fibrosis. Dyslipidemia did not depend on the level of viral load

The content of prealbumin and postalbumin fraction-1 in the group of animals, with ChHH changes slightly (P>0.05). The exception is the content of postalbumin fraction-1 and post-albumin fraction-2, which they increase by 65.1%

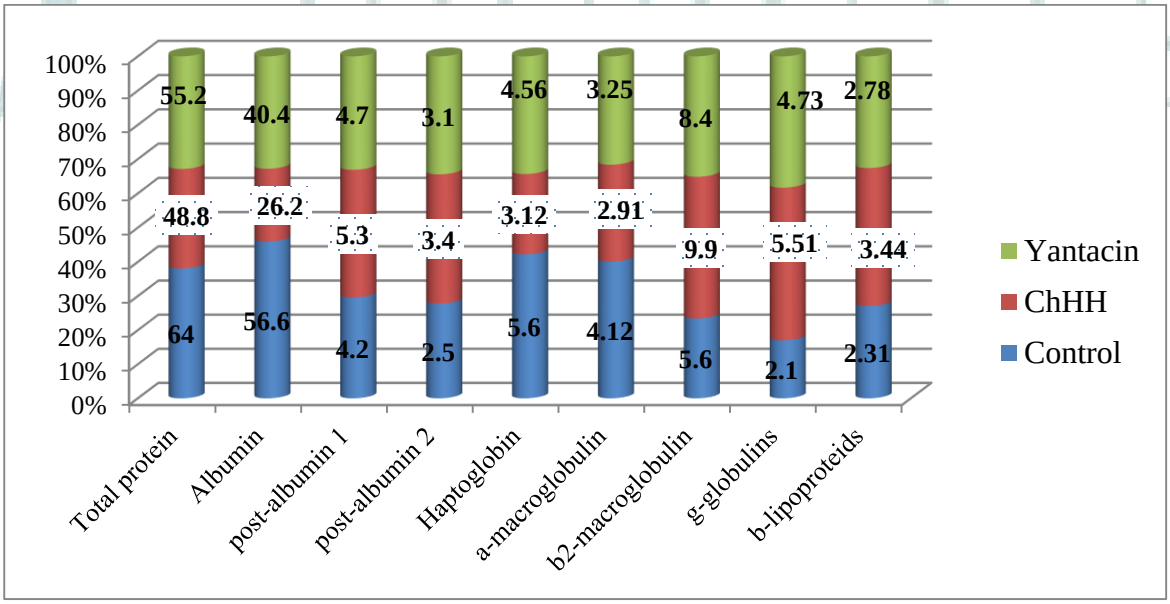

Fig.2. The effect of yantacin on blood proteins of rats with chronic heliotrine hepatitis.

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Along with shifts in the coarse fraction of blood proteins (albumins) in the conditions of the pathology under study, certain changes occur in the content of the fine fraction of blood proteins. The blood content of γ-globulin increases in the experimental group by 2 times compared to the control group similar pattern can be traced with respect to the content of β2-microglobulin.The content of alpha-macroglobulin in the blood, haptoglobin, on the contrary, decreases. At the same time, the values of beta-macroglobulin and haptoglobin become 28.8% lower than the control values.

Thus, summarizing the data obtained from the study in the liver and blood of experimental animals, it can be concluded that in conditions of chronic hepatitis there are signs of a violation of the protein-forming, lipid function of the liver, which is the main mechanism of regulation of fibrogenesis in liver tissue;

The use of anthocyanins for the treatment has a noticeable effect on the lipid parameters of the educational function of the liver. As can be seen from the presented data, against the background of the use of niacin, the level of lipoperoxidation products significantly decreases, the content of CL and TG is practically normalized.

Conclusion

Thus, the studies conducted to study the state of cellular renewal in chronic toxic hepatitis, allows us to conclude that in conditions of toxic liver damage, hepatocyte death accelerates and their renewal slows down. The substance studied in this study showed that plant proanthocyanidin significantly reduced the death of hepatocytes and accelerated their regeneration in small quantities. In this regard, a more extensive in-depth study of the effect of the studied substance plant proanthocyanide on normal and impaired liver activity is being conducted.

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