Republic of Azerbaijan

On the rights of manuscript

ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

EXPERIMENTAL AND PRIMARY CLINICAL STUDY OF THE HEPATOPROTECTIVE ROLE OF HERBAL-ORIGIN COMPONENTS IN NON-VIRAL ORIGIN HEPATITIS TREATMENT

Specialty: 3205.01 -Internal diseases
3209.01 - Pharmacology, clinical pharmacology

Field of Science: Medicine

Applicant: **Sevinj Arif Abasova**

Baku 2024

The work was performed at the Department of Internal diseases I of Azerbaijan Medical University, Scientific Research Center, Baku Health Center and Diagnoz Medical Center.

Scientific Supervisor: Doctor of Philosophy in Medicine, Assoc.Professor
Khumar Islam Gurbanova

Scientific Advisor: Doctor of Biological Sciences
Rana Anvar Jafarova

Official opponents: Doctor of Medical Sciences, professor
Azer Alijabbar Karimov

Doctor of Medical Sciences, Assoc. Professor
Eldar Mursel Hatamzada

Doctor of Medical Sciences
Novruz Ahmed Hasanov

Doctor of Philosophy in Medicine, Assoc.Professor
Gulbaniz Asif Huseynova

İMZANI TƏSDİQ EDİRƏM
Azərbaycan Tibb Universitetinin
ELMİ KATİBİ
Tibb üzrə fəlsəfə doktoru, dosent
Rəşad Səməddin oğlu Tağıyev
04.11.2024-ci il

BFD 2.27 Dissertation Council of the Supreme Attestion Comission under the President of the Republic of Azerbaijan operating at Azerbaijan Medical University

Chairman of the Dissertation council: Doctor of Medical Sciences, professor
Vasadat Ali Azizov

Scientific Secretary of the Dissertation council: Doctor of Philosophy in Medicine, Assoc.Professor
Tora Akif Sadıgova

Chairman of the scientific seminar: Doctor of Medical Sciences, professor
Alihuseyn Alishan Hidayatov

GENERAL ASPECTS OF THE RESEARCH

Relevance of the research. Despite the achievements of medical science in the prevention, diagnosis and treatment of hepatobiliary system injuries, the share of this pathology in the structure of internal diseases is increasing year by year. A special place among the pathologies of the hepatobiliary system is occupied by hepatitis of non-viral origin. Non-viral hepatitis is a disease characterized by inflammation of the liver tissue, most often caused by alcohol abuse and toxic effects of drugs. A number of works of world-renowned scientists have been devoted to the study of the pathogenesis, possible prevention and treatment of this pathology [1,2]. The following have been noted as etiological factors in the development of these pathologies: toxic agents in the environment contaminated by technogenic factors, and the entry of chemical substances and food additives into the body from household use. The number of patients with liver damage due to medication intake based on vital indicators is increasing[3]. Drug-induced hepatitis mainly occurs as a result of the intake of hepatotoxic medications[4,5]. Such diseases are primarily diagnosed in a chronic form. The damage is characterized by inflammatory-dystrophic features and is accompanied by mild fibrosis[6]. Considering that over 90% of medications have hepatotoxic side effects, one can

---

[1] Kimura, H. Liver injury after methylprednisolone pulse therapy in multiple sclerosis is usually dŞV to idiosyncratic drug-induced toxicity rather than autoimmune hepatitis / H. Kimura, A. Takeda, T. Kikukawa [et al.] // Mult Scler Relat Disord., - 2020. Jul; 42:102065.

[2] Weber, S. Challenges and Future of Drug-induced liver injury Research-laboratory Tests / S. Weber, L.A. Gerbes // J. Mol.Sci., - 2022.23(11), - p. 6049

[3] Wang, Q. Chronic Drug-Induced Liver Injury: Updates and Future Challenges / Q. Wang, A. Huang, J.B. Wang [et al.] // Front Pharmacol., - 2021. Mar 8; 12, - 627133.

[4] Ahmad, J. Liver injury associated with kratom, a popular opioid-like product: Experience from the U.S. drug induced liver injury network and a review of the literature / J. Ahmad, J.A. Odin, P.H. Hayashi [et al.] // Drug and Alcohol Dependence, - 2021. 218 (1): 108426.

[5] Aithal, G.P. HLA- A*33:01 is strongly asso-ciated with drug-induced liver in- jury (DILI) dŞV to terbinafine and several other unrelated compounds / G.P. Aithal, P. Nicoletti, E. Björnsson [et al.] // Hepatology, - 2015. 65(1), - p. 325–6.

[6] Cullen, J.M. Liver and Biliary System / J.M. Cullen, M.J. Stalker // Jubb, Kennedy & Palmer's Pathology of Domestic Animals, - 2016. vol. 2. – p. 258–352

get an idea of the seriousness of the problem[7]. Another cause for serious concern is the increasing prevalence of hepatobiliary system pathologies among young people, especially women of reproductive age, due to the rising consumption of alcoholic beverages.

Studies show that despite the similarities in morphological and pathophysiological signs of hepatitis of different etiology, they differ in the structure and development mechanism of damage to hepatocytes. Therefore, considering the pathological development mechanisms, an individualized approach is required in the treatment strategies for non-viral hepatitis of different origins. Medications, dietary therapy, and traditional medicine are used for treatment purposes.[8] Some herbal remedies used in traditional medicine play a role in reducing the activity of inflammatory processes in the liver and aiding in its recovery.

Currently, hepatoprotectors are extensively used in the treatment of hepatitis, and their positive role has been confirmed in several studies.[9] However, other studies and practical results show that these medications do not always provide the expected effect in the treatment of non-viral hepatitis of various etiologies. Therefore, considering the impact of oxidative stress, cholestasis, and other factors on hepatocytes and their regeneration, studying the pathological mechanisms of liver damage and developing effective treatment schemes for these pathologies remain current issues in medical science[10].

The aim of the Research: To investigate the effects of ursodeoxycholic acid, alpha-tocopherol acetate, and the Azhepofit phytocomplex (PC) on the course of non-viral hepatitis in an

---

[7] Rao, A. Secular Trends in Severe Idiosyncratic Drug-Induced Liver Injury in North America: An Update From the Acute Liver Failure Study Group Registry / A. Rao, A. Rule Jody, B. Hameed // American Journal of Gastroenterology, – 2022. 117 (4), - p. 617–626.

[8] Hey-Hadavi, J. Overview of Causality Assessment for Drug-Induced Liver Injury (DILI) in Clinical Trials / J. Hey-Hadavi, D. Seekins, M. Palmer [et al.] // Drug Saf., - 2021. 44(6), - p. 619-634.

[9] Chen, Q. Effectiveness of Prophylactic Use of Hepatoprotectants for Tuberculosis Drug-Induced Liver Injury: A Population-Based Cohort Analysis Involving 6,743 Chinese Patients / Q. Chen, A. Hu, A. Ma [et al.] // Front Pharmacol., - 2022. Apr 20;13, - 813682.

[10] Лекарственные поражения печени (клинические рекомендации для врачей) / В.Т. Ивашкин, А.Ю. Барановский, К.Л. Райхельсон [и др.], - Москва: - 2019. – 57 с.

experimental setting, and to develop a new treatment scheme by adding these plant-based treatments to standard therapy.

The Tasks of the Research:

1. To create models of drug-induced, toxic, and alcoholic hepatitis and identify biochemical markers that confirm the pathological processes occurring in the liver within these models.
2. To develop different treatment strategies considering the diversity in the pathogenesis of experimental hepatitis and to evaluate the effectiveness of these treatments.
3. In the created models, under treatment with alpha-tocopherol acetate, determine the levels in blood serum of ALT, AST, γ-glutamyl transpeptidase, lactate dehydrogenase, total protein, total bilirubin, medium-molecular-weight peptides, C-reactive protein, products of lipid peroxidation (hydroperoxides, diene conjugates, malondialdehyde), the activity degree of the antioxidant system, and indicators of lipid metabolism (triglycerides, total cholesterol, low-density lipoproteins, intermediate-density lipoproteins, high-density lipoproteins).
4. To determine the above-mentioned indicators under treatment with ursodeoxycholic acid (UDCA).
5. To determine the biochemical markers of the effects of the Azhepofit Phytocomplex on the course of experimental hepatitis.
6. To determine the changes in the blood serum of animals with hepatitis models under combined treatment with the Azhepofit Phytocomplex and ursodeoxycholic acid (UDCA).
7. Clinical application of the effective treatment scheme developed in the experiment for patients with chronic alcoholic hepatitis

Research Methods:

Experimental:

- Laboratory examinations
- Visual examinations
- Statistical analysis

Clinical:

- Laboratory-clinical examinations
- Instrumental examinations

– Statistical analysis

The main arguments for the defence:

1. In the experiments conducted with 5 series of studies on models of tetracycline hepatitis, statin hepatitis, phenacetin hepatitis, toxic (CCl_4) hepatitis, and alcohol hepatitis, the best results were observed with the application of a combination of Azhepofit phytocomplex and ursodeoxycholic acid among the treatments administered, which also included placebo, alpha-tocopherol acetate, and ursodeoxycholic acid alone.

2. In the treatment of patients with chronic alcoholic hepatitis, the addition of herbal infusions to the basic therapy partially improves the liver's structural indicators (over a 3-month treatment period).

3. During liver elastography, the group that received herbal infusions in addition to the treatment regimen showed positive changes in liver tissue density before and after treatment.

Scientific novelty of the research:

- The effectiveness of the combined use of alpha-tocopherol, ursodeoxycholic acid, and the new phytocomplex (PC) in liver damage caused by hepatotoxic substances has been experimentally substantiated.
- The obtained results elucidate the theoretical foundations for explaining the pathogenetic mechanisms of non-viral hepatitis and developing treatment methods.
- The pathogenetic effects of a new phytocomplex (PC) based on Azerbaijani flora have been determined for the treatment of various types of diseases, including toxic and alcoholic hepatitis.
- The addition of herbal treatments to the therapeutic regimen for patients with chronic alcohol-related liver disease has shown a positive effect on chronic alcoholic hepatitis, as evidenced by its beneficial impact on the liver's structural indicators.

Theoretical and practical significance of the research:

In the experiment, new results were obtained regarding the effects of α-tocopherol acetate (αTocA), ursodeoxycholic acid (UA), and the phytocomplex (PC) on the pathogenesis of non-viral hepatitis. The results from the experiment have scientific and

practical significance and provide insights into the investigation of non-viral hepatitis. These findings can be incorporated into educational methodologies, allowing students and healthcare professionals to study this issue in greater detail.

The Object and the Subject of the Research: Experimental studies were conducted on 310 outbred white rats: 10 intact animals, 180 rats with drug-induced hepatitis models (tetracycline, amvastatin, phenacetin), 60 rats with a toxic (CCl_4) hepatitis model, and another 60 rats with an alcohol hepatitis model, and treatment regimens were applied.

Clinical studies were conducted on 60 patients with chronic alcoholic hepatitis: the first group received basic treatment (n=21), while the second group received basic therapy combined with a herbal infusion regimen (n=39).

Approbation of the Dissertation: The dissertation work was initially discussed in an inter-departmental meeting on October 31, 2023, and was further reviewed at the Scientific Seminar of the Dissertation Council BFD 2.27 under the Azerbaijan Medical University on May 31, 2024, during meeting number 01 (protocol №1, 31.05.2024).

The main part of the dissertation was discussed at the following scientific conferences: "Innovations and Prospects of World Science," Vancouver, June 22-24, 2022; "EuroASian Scientific Discussions," Barcelona, June 5-7, 2022; International Scientific-Practical Conference dedicated to the 270th anniversary of Shusha, May 24-25, 2022. It was also presented in the materials of the scientific conference dedicated to the 90th anniversary of Professor Z. Zeynalova (Baku, 2023); discussed in the materials of the International Scientific-Practical Congress "Təbabətin aktual problemləri – 2023(Actual Problems of Medicine – 2023)," dedicated to the 100th anniversary of Heydar Aliyev. The work was also presented at the "13th World Gastroenterology, IBD & Hepatology Conference" held from December 15-17, 2023, in Dubai.

Practical Application of the Research Results. The results of the research have been applied at the Teaching Therapeutic Clinic of the Azerbaijan Medical University (AMU) and in the

Gastroenterology Department of the Narimanov Medical Center.

Publications. On the dissertation topic, 15 scientific works have been published: 5 articles and 5 theses in national journals, 3 articles and 2 theses in international journals. Among these, 1 journal is indexed in the Belarusian Academy of Sciences (AAS), 1 journal is indexed in the Russian Academy of Sciences (RAS), and 1 journal is indexed in the Web of Science (WOS).

Organizations Where the Dissertation Work Was Conducted: The research work was carried out at the Teaching Therapeutic Clinic of the Azerbaijan Medical University, the Research Center, Baku Health Center, and Diagnosis Medical Center.

Volume and Structure of the Dissertation: The dissertation is presented in 178 pages (196,456 characters) of printed material. It includes an introduction (9,286 characters), literature review (22,724 characters), materials and methods of research (14,607 characters), research results (103,746 characters), discussion of results (41,791 characters), conclusions and practical recommendations (4,302 characters), and references. The work is illustrated with 39 tables and 42 figures. The reference list includes 169 scientific sources (4 in Azerbaijani, 27 in Russian, and 138 in foreign languages).

Materials and Methods of Research

Experimental studies were conducted at the Research Center of the Azerbaijan Medical University on 310 outbred white laboratory rats weighing between 173 and 190 grams. All animals used in the experiments, both in the main and control groups, were maintained under the same care and feeding conditions. All experiments on animals were conducted in accordance with the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986). The conduct of the experiment was authorized by the Ethics Committee of the Azerbaijan Medical University with decision No. 10 dated October 16, 2019.

The objectives and goals of the research were addressed by

dividing the animals into 6 experimental groups:

The first group consisted of 10 intact rats. The subsequent groups modeled various types of hepatitis. Specifically, the second group had the tetracycline model of drug-induced hepatitis (DIH), the third group had the statin model of DIH, the fourth group had the phenacetin model of DIH, the fifth group had the toxic (CCl_4) hepatitis model, and the sixth group had the alcohol hepatitis model. Each group (2nd to 6th) was subdivided into 6 subgroups, each consisting of 10 animals.

1. The 1st subgroup of each group consisted of animals with various models of non-viral hepatitis (model subgroup).
2. The 2nd control subgroup received a physiological solution of sodium chloride as treatment.
3. The 3rd subgroup received α-tocopherol at a dose of 50 mg/100 g.
4. The 4th subgroup received oral choludexan at a dose of 25 mg/100 g.
5. The 5th subgroup received 1 ml/100 g of a 10% aqueous extract of AZHEPOFİT PC.
6. The 6th subgroup received 1 ml/100 g of a 10% aqueous extract of AZHEPOFİT PC combined with 25 mg/100 g of choludexan.

The animals received treatment twice daily for 2 weeks, and at the end of the experiment, blood and organs were collected for research.

Modeling of Hepatitis:

Tetracycline Hepatitis Model: A 100 mg/kg dose of tetracycline (Biosintez, Russia) in an aqueous suspension was administered orally via a gavage tube to rats for 15 days.

Statin Hepatitis Model: Amvastatin (atorvastatin) produced by "Biopharma Ilaç San. ve Tic. A.Ş." (Turkey) was administered orally to the animals at a dose of 40 mg/kg for 20 days.

Phenacetin Hepatitis Model: According to the method of A.O. Revyakin and colleagues (2013), rats were given an aqueous suspension of paracetamol at a dose of 2500 mg/kg daily for 7 days, along with 1 ml of 40% alcohol orally. For this purpose, the "Paracetamol sopharma" 500 mg preparation from SOPHARMA (Bulgaria, Sofia) was used.

Toxic Hepatitis Model: Toxic hepatitis was induced by administering a 4% carbon tetrachloride solution in 1 ml of olive oil intraperitoneally every other day for 3 times.

Alcohol Hepatitis Modeling: Alcohol hepatitis was induced by oral administration of 1 ml of 40% ethanol solution per 100 g of body weight twice daily for one month.

After confirming the development of hepatitis through laboratory data, the animals were treated with α-tocopherol (Treatment 1), choludexan (Treatment 2), AZHEPOFİT PC (Treatment 3), and a combination of AZHEPOFİT PC and choludexan (Treatment 4).

To evaluate the treatment outcomes, the results of the model subgroup and control subgroups receiving placebo (physiological solution) were used.

Visual and biochemical research methods were employed during the study.

Blood Tests Conducted: The levels of AST, ALT, ALP, γ-GTP, LDH, total bilirubin (TB), direct bilirubin (DB), MMWP, C-reactive protein (CRP), catalase (CAT), superoxide dismutase (SOD) activity, and TAS (total antioxidant status) were determined using BIOSKREM MS 2000 microanalyzer and reagent kits from the company "HUMAN" (USA).

Lipid peroxidation (LPO) products: Hydroperoxides (HP), concentration of dien conjugates (DC) were determined using the method of A.M. Goryachkovski (1998), and malondialdehyde (MDA) was determined using the method of L.I. Andreeva and co-authors (1988).

The levels of total cholesterol (TC), triglycerides (TG), LDL (low-density lipoprotein), VLDL (very-low-density lipoprotein), and HDL (high-density lipoprotein) were determined using a chemical reagent

kit from the German company "Human" and the enzymatic colorimetric method. The analyses were conducted using the FP-9019 analyzer from Finland.

Clinical studies were conducted on 60 male patients with chronic alcoholic hepatitis at the Gastroenterology Department of Baku Health Center and the "Diagnoz" Medical Center. The participants' ages ranged from 30 to 73 years, with an average age of 49.0 ± 1.1 years. Their weights ranged from 54 to 145 kg, with an average weight of 93.0 ± 2.3 kg. The following conditions were excluded from the study: infectious hepatitis, autoimmune hepatitis, oncological damage, Wilson's disease, primary biliary cirrhosis, and other chronic diseases in the decompensated stage.

The clinical study was approved by the Ethics Committee of Azerbaijan Medical University with decision No. 19 dated July 16, 2021. According to the study's objectives, patients were divided into 2 groups based on the treatment principle: Group 1 (the main group) consisted of 39 patients receiving basic therapy (adenomethionine 400 mg twice daily, ursodeoxycholic acid 10 mg/kg/day, and herbal teas (Hypericum perforatum -GOST 15161-93, Dandelion-GOST 34221-2017, Flaxseed-GOST-10582-76, Horseweed-GOST 6677-80, Herbaflora; Celery seeds L/A 12.01.2021, Turmeric L/A 06.02.2021 Fitoklub) along with the base therapy. Group 2 (the control group) included 21 patients who only received basic therapy. Both groups were prescribed a 3-month treatment course.

At the beginning of the study, comparative data on age, height, body weight, and body mass index (BMI) were provided for patients in both groups.

In the subsequent phase of the study, both groups of patients underwent liver ultrasound examination and elastography. Both examinations were performed before and after the treatment.

In blood serum, the activities of AST, ALT, ALP, γ-GTP enzymes, total protein (TP), total bilirubin (TB) and their fractions, C-reactive protein (CRP), glucose, triglycerides (TG), and cholesterol (CH) levels were measured using the ROCHE Cobas Integra 400 Plus device with ROCHE reagents.

The complete blood count was performed using the SYSMEX XT-2000i device from Germany.

The ultrasound examination of internal organs and liver elastography were performed using the Mindray Resona 7 model device, manufactured in China. This device is Zst platform-based and has high resolution capability. The elastography method used in this study is Shear-Wave Elastography.

The experimental study utilized a phytocomplex (PC) prepared based on Azerbaijani flora, developed by Dr. R.A. Jafarova, a Doctor of Biological Sciences. The composition of PC is as follows: 2 parts of common dandelion seed, 1 part of horseweed herb, 1 part of common hypericum perforatum, 1 part of fragrant celery, 2 parts of flaxseed, and 1 part of turmeric root.

Research findings revealed that the herbal complex (PC) contains biologically active compounds from the groups of flavonoids, alkaloids, triterpene esters, and isoquinoline derivatives. Toxicological and pharmacological studies identified the acute toxicity of the phytocomplex as having an LD50 of 10,000 mg/kg, and according to the Hodge and Stermer scale, it is practically non-toxic.

When preparing the herbal complex (PC), the availability of sufficient raw material of these plants in the republic was also taken into account. The PC, made primarily from plants collected in the Gadabay, Khachmaz, and Absheron districts, was used to prepare an aqueous infusion at a 1:10 ratio according to the standards of the USSR State Pharmacopoeia (XI edition, 2nd release).

Statistical analyses were performed using variation, discriminant, and correlation methods. Descriptive statistics for quantitative indicators included mean (M, ±m, 95% CI (confidence interval)) and median (Me, Q1, Q3) values, while qualitative indicators were described using absolute and relative measures. The statistical significance of differences between groups in cross-sectional studies was assessed using t-Student-Bonferroni and U-Mann-Whitney criteria, while longitudinal studies employed W-Wilcoxon criteria. Calculations were carried out using IBM Statistics SPSS-26 software.

Results and Discussion

Experimental Part.

After creating the intended models in the experiment, blood was collected from the model, control, and main group animals. Biochemical indicators in the blood plasma were determined and the results were analyzed. Since the control indicators were only slightly different from those of the model, the results were compared with the model results when describing the outcomes of various therapeutic schemes.

In the tetracycline hepatitis model, the levels of ALT and AST in the model group were increased by 3.2 times ($p < 0.001$) and 96.3% ($p < 0.001$), respectively. The amounts of γ-GTP, LDH, and ALP were increased by 1.6 times ($p < 0.001$), 79.7% ($p < 0.001$), and 89.5% ($p < 0.001$), respectively. The level of TB was 2.3 times higher ($p < 0.001$), MMWP decreased by 42.4% ($p < 0.001$), and CRP increased by 2.5 times ($p < 0.001$). TP decreased by 2.1 times ($p < 0.001$). The levels of lipid peroxidation products in the blood increased sharply—HP by 2.2 times ($p < 0.001$), DC by 2.5 times ($p < 0.001$), MDA by 113.5% ($p < 0.001$). The activity of the antioxidant system (TAS, CAT, SOD) was weakened, and lipid metabolism was disrupted. Thus, the cholestatic model of drug-induced hepatitis has been confirmed Thus, the formation of the DIH cholestatic model has been confirmed. In the experimental groups, treatment schemes were applied, and the following results were obtained. **Under Treatment 1,** ALT and AST – decreased by 6.6% (p=0,045) and 5.4% (p=0,384), respectively; Ritis ratio treatment = 1.15. γ-GTP, LDH, ALP – increased by 1.0% (p=0,426), 6.3% (p=0.384), and 12.2% (p=0.089), respectively. TB decreased by 2.6% (p=0.705), TP increased by 9.4% (p=0.120), MMWP decreased by 22.5% (p=0.002) and CRP decreased by 10.0% (p=0.090). The amount of lipid peroxidation products – HP, MDA, and DC – decreased by 41.8% (p<0.001), 51.7% (p<0.001), and 47.0% (p<0.001), respectively. AOS values changed as follows: TAS increased by 33.3% (p<0.001), CAT increased by 6.8% (p=0,462), SOD increased by 12.4% (p=0.149). Lipid metabolism indicators – LDL decreased

by 6.1% (p=0.473), VLDL decreased by 4.1% (p=0.402), HDL decreased by 8.1% (p=0.472), TC decreased by 5.7% (p=0.383), TG decreased by 6.5% (p=0.237).

Under Treatment 2, ALT and AST decreased by 17.1% ($p < 0.001$) and 8.5% ($p = 0.069$), respectively, with the Ritis coefficient being 1.24. γ-GTP decreased by 24.6% ($p < 0.001$), LDH by 31.8% ($p < 0.001$), and ALP by 39.9% ($p < 0.001$). TB decreased by 16.6% ($p = 0.111$), and other indicators also showed positive dynamics.

Under Treatment 3, ALT and AST decreased by 36% ($p < 0.001$) and 22.9% ($p = 0.011$), respectively, with the Ritis coefficient being 1.36. γ-GTP decreased by 18.6% ($p < 0.001$), LDH by 38.4% ($p < 0.001$), and ALP by 33.7% ($p < 0.001$). TB decreased by 12.3% ($p = 0.272$), with a more pronounced improvement observed.

Under Treatment 4, ALT and AST decreased by 59.5% ($p < 0.001$) and 44.8% ($p < 0.001$), respectively. The Ritis coefficient was 1.57. The amounts of γ-GTP, LDH, and ALP in the blood decreased by 35.4% ($p < 0.001$), 44.3% ($p < 0.001$), and 37.7% ($p < 0.001$), respectively. TB decreased by 28.2% ($p < 0.001$), TP increased by 60.9% ($p < 0.001$), and MMWP and CRP decreased by 24.4% ($p = 0.001$) and 27.5% ($p < 0.001$), respectively. Lipid peroxidation products HP decreased by 46.4% ($p < 0.001$), MDA and DC decreased by 56.6% ($p < 0.001$) and 53.5% ($p < 0.001$), respectively. TAS increased by 26.8% ($p < 0.001$), CAT by 4.2% ($p = 0.520$), and SOD by 8.7% ($p = 0.248$). Lipid metabolism indicators showed LDL decreased by 70.0% ($p < 0.001$), VLDL by 33.5% ($p < 0.001$), TC by 58.8% ($p < 0.001$), and TG by 34.0% ($p < 0.001$). HDL increased by 18.3% ($p = 0.362$). [5].

The DIH mixed type was created using statins (amvastatin). In the serum of the animals with the model, the levels of ALT and AST increased by 3.2 and 1.6 times, respectively, and the Ritis coefficient decreased by 2.1 times to 0.89. Simultaneously, γ-GTP, LDH, and ALP increased by 41.5%, 17.5%, and 114.8%, respectively. The levels of TB, MMWP, and CRP in the blood increased by 3.1, 1.4, and 2.4 times, respectively, while TP decreased by 43%. HP, DC, and MDA increased by 2.3, 2.6, and 2.2 times, respectively. TAS, CAT, and SOD decreased by 47.7%, 38.3%, and 33.6%,

respectively. LDL, VLDL, TC, and TG increased by 5.8, 3.7, 3.7, and 1.8 times, respectively, while HDL decreased by 1.6 times. The results are statistically significant ($p < 0.001$, $p < 0.01$) and confirm the development of hepatitis in the animals.

In animals receiving **Treatment 1**, the levels of ALT decreased by 8.9% ($p = 0.069$), AST decreased by 11.7% ($p = 0.226$), and the Ritis coefficient was 0.86. The level of γ-GTP in the blood decreased by 5.8% ($p = 0.472$), LDH by 2.9% ($p = 0.170$), ALP by 15.7% ($p = 0.033$), TB by 1.2% ($p = 0.623$), MMWP by 15.6% ($p = 0.011$), and CRP by 10.3% ($p = 0.057$). The amount of TP increased by 2.1% ($p = 0.492$). LDL decreased by 4.9% ($p = 0.273$), VLDL by 10.0% ($p = 0.384$), TC by 5.9% ($p = 0.172$), and TG by 8.3% ($p = 0.211$), while HDL increased by 2.5% ($p = 0.787$). The amount of HP in the blood decreased by 40.3% ($p < 0.001$), MDA by 48.8% ($p < 0.001$), and DC by 29.6% ($p < 0.001$). Simultaneously, TAS increased by 5.7% ($p = 0.405$), while CAT decreased by 4.8% ($p = 0.733$) and SOD by 3.0% ($p = 0.311$).

Under Treatment 2, ALT decreased by 18.3% ($p=0.003$) and AST by 0.8% ($p=0.970$). The Ritis ratio was 1.07. γ-GTP decreased by 7.0% ($p=0.017$), LDH by 7.1% ($p=0.008$), ALP by 47.3% ($p<0.001$), and TB by 27.3% ($p<0.001$). HP decreased by 14.6% ($p<0.001$), and MDA and DC decreased by 32.3% ($p<0.001$) and 16.7% ($p<0.001$), respectively. TAS increased by 5.1% ($p=0.425$), while CAT decreased by 11.8% ($p=0.224$) and SOD by 8.3% ($p=0.065$).

Under Treatment 3, ALT decreased by 43.5% ($p<0.001$) and AST by 60.1% ($p<0.001$), with the Ritis ratio being 0.62 ± 0.02. γ-GTP decreased by 22.2% ($p<0.001$), LDH by 25.8% ($p<0.001$), ALP by 35.1% ($p<0.001$), and TB by 34.5% ($p<0.001$). Other indicators showed more active positive dynamics.

Under Treatment 4, ALT decreased by 54.4% ($p<0.001$) and AST by 23.4% ($p=0.003$). The Ritis ratio was 1.49 ± 0.05. γ-GTP decreased by 24.0% ($p<0.001$), LDH by 15.3% ($p<0.001$), ALP by 50.1% ($p<0.001$), and TB by 58.4% ($p<0.001$). HP decreased by 45.0% ($p<0.001$), and MDA and DC decreased by 52.5% ($p<0.001$) and 37.1% ($p<0.001$), respectively. TAS increased by 92.0%

($p<0.001$), CAT by 19.7% ($p=0.0119$), and SOD by 32.1% ($p<0.001$).

The creation of the Phenacetin model has been confirmed by the increase in liver damage markers—ALT and AST—by 2.8 and 1.5 times, respectively, and the increases in γ-GTP, LDH, and ALP by 43.8%, 79.4%, and 81.0%, respectively. LPO indicators—HP, MDA, and DC—increased by 1.9, 1.6, and 1.9 times, respectively. The activity indicators of the antioxidant defense system decreased, with TAS down by 36.9% and CAT down by 33.1%, while SOD increased by 3.7% ($p = 0.650$). The following changes were observed under ongoing treatment schemes:

In animals receiving **Treatment 1**, ALT levels decreased by 36.7% ($p<0.001$), AST by 27.8% ($p<0.001$), γ-GTP by 10.8% ($p=0.028$), LDH by 6.9% ($p=0.040$), and ALP by 4.7% ($p=0.340$). The level of HP in the blood decreased by 39.2% ($p<0.001$), and MDA and DC decreased by 52.9% ($p<0.001$) and 27.7% ($p<0.001$), respectively. At the same time, TAS in the blood increased by 44.6% ($p=0.001$), CAT activity increased by 0.3% ($p=0.880$), and SOD activity increased by 2.6% ($p=0.703$). TB levels decreased by 18.8% ($p<0.001$).

During **Treatment 2**, positive results were achieved: ALT levels decreased by 13.9% ($p=0.081$), AST by 6.1% ($p=0.470$), γ-GTP by 9.4% ($p=0.002$), LDH by 6.3% ($p=0.023$), and ALP by 9.0% ($p=0.196$). Blood levels of HP decreased by 26.4% ($p<0.001$), and MDA and DC decreased by 18.4% ($p<0.001$) and 27.7% ($p<0.001$), respectively.

Under **Treatment 3**, ALT decreased by 21.3% ($p=0.012$) and AST by 23.5% ($p=0.006$). The Ritis coefficient was 0.97±0.09. The level of TB decreased by 34.5% ($p<0.001$), and other indicators improved.

During **Treatment 4**, ALT decreased by 51.0% ($p<0.001$) and AST by 35.7% ($p<0.001$). The Ritis coefficient was 1.29±0.07. Blood γ-GTP decreased by 28.3% ($p<0.001$), LDH by 45.2% ($p<0.001$), ALP by 42.8% ($p<0.001$), HP by 45.0% ($p<0.001$), MDA by 26.7% ($p<0.001$), and DC by 37.2% ($p<0.001$). TAS increased by 64.8% ($p<0.001$), CAT increased by 20.8% ($p=0.005$), and SOD activity decreased by 2.8% ($p=0.467$). TB decreased by 37.2% ($p<0.001$), with other indicators showing positive dynamics.

In the toxic hepatitis model, the levels of ALT and AST increased by 3.7 and 2.1 times, respectively, and the Ritis coefficient decreased by 1.9 times. γ-GTP increased by 83.1%, LDH by 105.7%, ALP by 91.9%, TB by 3.2 times, MMWP by 8.7%, and CRP by 2 times. TP decreased by 47.7%. LPO products HP, DC, and MDA increased by 2.2, 2.1, and 2.1 times, respectively. At the same time, TAS and CAT activity decreased by 27.9% and 42.9%, respectively, while SOD activity increased slightly by 2%. Lipid metabolism was disrupted.

In the context of **Treatment 1**, ALT levels decreased by 21.6% ($p<0.001$) and AST by 15.1% ($p = 0.021$). The Ritis coefficient was 1.15. The level of γ-GTP decreased by 17.5% ($p<0.001$), LDH by 17.1% ($p<0.001$), ALP by 11.4% ($p=0.024$), and TB by 45.2% ($p<0.001$).

In the context of **Treatment 2**, ALT levels decreased by 16.8% ($p=0.015$) and AST by 12% ($p=0.031$). The Ritis coefficient was 1.05. The level of γ-GTP decreased by 25.9% ($p<0.001$), LDH by 16.3% ($p<0.001$), ALP by 30.3% ($p<0.001$), showing positive dynamics.

In the context of **Treatment 3**, ALT levels decreased by 34.5% ($p<0.001$) and AST by 46.4% ($p<0.001$). The Ritis coefficient reached 1.24±0.06. The level of γ-GTP decreased by 40.9% ($p<0.001$), LDH by 44.8% ($p<0.001$), ALP by 48.6% ($p<0.001$), and TB by 37.4% ($p<0.001$).

In the context of **Treatment 4**, ALT levels decreased by 60.3% ($p<0.001$) and AST by 42.3% ($p<0.001$). The Ritis coefficient was 1.47±0.07. γ-GTP decreased by 41.6% ($p<0.001$), and TB by 55.8% ($p<0.001$), with significant improvement in the indicators.

Based on Table 1, in the alcohol hepatitis model, the levels of ALT and AST in the blood serum of the animals increased by 2.3 and 1.4 times, respectively, while the Ritis coefficient decreased by 1.7 times. γ-GTP increased by 26%, LDH by 7.2%, ALP by 61.6%, TB by 3.1 times, MMWP by 1.4 times, and CRP by 2.3 times. TP decreased by 39.8%. HP, DC, and MDA increased by 1.9, 1.8, and 1.9 times, respectively. TAS level, CAT, and SOD decreased by 30.9%, 44.0%, and 2.4% ($p=0.733$), respectively. LDL, VLDL, TC,

and TG increased by 5.8 times, 2.5 times, 3.4 times, and 1.2 times, respectively, while HDL decreased by 2.8 times. Except for the decrease in SOD activity ($p>0.05$), other indicators are statistically significant ($p<0.001$ and $p<0.01$).).

Table 1: Levels of Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) in Blood, and Ritis Ratio in the Alcoholic Hepatitis Model

Indicator	Stat. indic.	Intact (n=10)	model (n=10)	control (n=10)	treatment1 (n=10)	treatment2 (n=10)	treatment3 (n=10)	treatment4 (n=10)
ALT (CU)	M	15,4	35,4	34,7	36,3	24,9	26,8	17,5
	±m	1,0	1,6	1,8	1,6	0,3	0,8	0,6
	Me	14,9	37,4	37,3	37,5	25,0	27,3	17,0
	Q_1	12,7	30,0	28,0	30,2	24,0	25,0	17,0
	Q_3	18,1	40,0	39,0	40,7	25,0	28,0	18,0
p			<0,001*	<0,001*	<0,001*	<0,001*	<0,001*	0,118
pm				0,570	0,623	<0,001*	0,001*	<0,001*
pk					0,384	<0,001*	0,003*	<0,001*
AST (CU)	M	27,8	39,4	39,0	39,8	32,4	31,7	28,7
	±m	0,7	1,7	1,6	2,1	0,9	1,2	0,9
	Me	27,9	39,4	38,5	41,0	31,5	31,5	30,0
	Q_1	26,5	37,5	37,0	34,0	30,0	27,0	25,0
	Q_3	29,7	44,0	44,0	46,0	35,0	35,0	31,0
p			<0,001*	<0,001*	0,001*	0,002*	0,030*	0,471
pm				0,732	0,705	0,008*	0,005*	0,001*
pk					0,704	0,005*	0,006*	0,001*
AST/ ALT	M	1,88	1,12	1,14	1,12	1,30	1,19	1,66
	±m	0,14	0,06	0,08	0,09	0,04	0,06	0,09
	Me	1,83	1,06	1,07	1,09	1,28	1,13	1,76
	Q_1	1,61	0,98	0,98	0,93	1,20	1,09	1,50
	Q_3	2,25	1,18	1,13	1,20	1,40	1,24	1,77
p			0,001*	<0,001*	0,001*	0,001*	0,006*	0,256
pm				0,704	0,791	0,019*	0,140	<0,001*
pk					0,970	0,028*	0,212	0,001*

Note:The statistical significance of the differences between the groups' indicators (according to the U-Mann-Whitney criterion):

1. p – compared with the indicators of the intact group
2. pm – compared with the indicators of the model
3. pk – compared with the indicators of the control subgroup
4. * – “null” hypothesis is rejected

Under **Treatment 1**, the ALT level increased by 2.3% (p=0.623) and the AST level increased by 1% (p=0.705). The Ritis coefficient was 1.12. γ-GTP increased by 0.7% (p=0.939), LDH decreased by 22.5% (p=0.001), and ALP increased by 14.6% (p=0.028). The TB level increased by 45.7% (p<0.001), while TP decreased by 13.1% (p=0.008). MMWP increased by 5.8% (p=0.381) and CRP by 8.1% (p=0.067). The level of HP decreased by 28.6% (p<0.001), MDA by 11.2% (p=0.110), and DC by 21.4% (p=0.001). TAS increased by 49.1% (p<0.001). CAT activity remained unchanged, and SOD activity increased by 5.3% (p=0.088). The LDL level increased by 12.8% (p=0.011), while VLDL decreased by 8.1% (p=0.127), TC by 12.4% (p=0.006), and TG by 1.9% (p=0.647). The amount of HDL in blood plasma increased by 7.1% (p=0.560).

Under **Treatment 2**, the ALT level decreased by 29.7% (p<0.001) and the AST level decreased by 17.8% (p=0.008), with a Ritis coefficient of 1.30. The γ-GTP level decreased by 13.2% (p=0.003), LDH increased by 15.0% (p=0.002), and ALP decreased by 7.9% (p=0.092). The TB level decreased by 44.4% (p<0.001), and other indicators showed improvement.

Under **Treatment 3**, the ALT level decreased by 24.5% (p=0.001) and the AST level decreased by 19.6% (p=0.005), with a Ritis coefficient of 1.19±0.06. The γ-GTP level decreased by 16.4% (p=0.001), and the TB level decreased by 48.4% (p=0.001).

Under **Treatment 4**, the ALT level decreased by 50.6% (p<0.001) and the AST level decreased by 27.2% (p=0.003), with a Ritis coefficient of 1.66±0.09. The γ-GTP level decreased by 20.3% (p<0.001) and the TB level decreased by 64.1% (p<0.001), with statistically significant results.

In both cases, other indicators also showed improvement.

The obtained results indicate that alpha-tocopherol acetate (α-TFA) significantly reduces the severity of lipid peroxidation (LPO) and increases the level of total antioxidant status (TAS), demonstrating its potent antioxidant properties. However, the activity of catalase (CAT) and superoxide dismutase (SOD) either slightly decreases (as seen in the statin model) or increases to a statistically

insignificant degree (as in the tetracycline model). This phenomenon can be explained by the complex nature of the pathogenic mechanisms involved in liver damage, which are not solely related to LPO. Furthermore, it is known that α-tocopherol stimulates the synthesis and release of fertility hormones, which are delivered to target organs with the help of globulins. In the context of liver damage, both the synthesis of carrier globulins and the liver's metabolic function decrease, leading to an accumulation of liver-damaging metabolites in the presence of excess vitamin E. For instance, in the statin hepatitis model treated with α-tocopherol acetate, the Ritis coefficient was 0.86. A value of less than 1 indicates liver damage. The atherogenic index (AI), calculated using the formula (Total Cholesterol - HDL) / HDL, was significantly higher than the normal range of 2-3, reaching 14.65. Additionally, there was an increase in the levels of ALT, AST, MMWP, and CRP in the blood. Although this increase was not statistically significant ($p > 0.05$), the observation itself holds theoretical importance in understanding the pathogenesis of statin-induced hepatitis and in developing treatment methods.

The results show that, in the context of the cytolytic hepatitis model induced by phenacetin, treatment with α-TFA had a significantly more positive effect on liver enzyme indicators compared to the cholestatic hepatitis model induced by tetracycline and the mixed-type hepatitis model induced by statins. This positive effect is also statistically confirmed. The value of the Ritis coefficient being greater than 1 indicates a reduction in hepatocyte damage and, consequently, an improvement in the functional condition of the liver.

Treatment with α-TFA has led to worsening of liver pathology in animals with alcoholic hepatitis. This is reflected in the increase of markers such as ALT and AST in the blood. Compared to the placebo control group, the use of α-TFA was associated with an increase in ALT and AST levels. Specifically, the plasma levels of ALT increased by 4.6% ($p=0.384$) and AST by 2.1% ($p=0.704$), while the Ritis coefficient decreased by 2.2% ($p=0.970$). Compared to the control, γ-GTP levels increased by 3.4% ($p=0.481$), LDH by

23.1% (p=0.001), and ALP by 15.5% (p=0.007). Thus, α-TFA treatment has had a negative impact on the progression of the pathology regarding these indicators.

“UDCA” reduces cholestasis and simultaneously exerts an antioxidant effect."

The rich content of biologically active compounds in PC exhibits antioxidant, anti-inflammatory, choleretic, restorative, and systemic effects, which are reflected in the AO status and other indicators. Significant improvement in liver functional status is observed under PC treatment, confirmed by the positive dynamics in all indicators. The most notable result occurs in the statin model, where the atherogenic index (AI) is 3.43, practically within the normal range, and the Ritis ratio is 0.97±0.09.

During treatment with PC and UDCA together, the indicators in the models approach intact values. The synergy between PC's active ingredients and UDCA results in an enhanced pharmacological effect. For example, in the statin model, the levels of key liver damage markers, such as ALT and AST, differed from intact values by only 45.9% and 19.5%, respectively. Considering the complexity of the drug-induced liver damage pathogenesis, this result is quite satisfactory. Additionally, the Ritis ratio is 1.49 ± 0.05 and the atherogenic index (AI) is 2.29, both of which are within normal ranges, indicating a return to normal liver functional status.

In the alcohol model, the levels of key liver damage markers, such as ALT and AST, in the blood approach intact values, differing by only 14% (p=0.118) and 3.3% (p=0.471), respectively. The Ritis ratio also approaches intact values, reflecting a normal functional state of the liver.

Thus, the pathological indicators determined in the blood during modeling show a trend towards improvement with treatment. In the placebo control group, spontaneous recovery of hepatocytes leads to a slight improvement in the organ's functional status, which is reflected in a minor positive trend in laboratory indicators. Regarding the treatment regimens, it should be noted that treatment with α-TFA did not yield positive results, and the level of bilirubin (TB) continued to rise, exceeding the model indicator. In other

treatment regimens, varying degrees of positive dynamics are observed, with the highest effect seen in the combined treatment with PC and UDCA.

Clinical Part/

Based on the results obtained from the experiment, we conducted an initial clinical application involving 60 patients with chronic alcoholic hepatitis. These patients were divided into two groups: a control group and a main group. The first control group received standard therapy, while the second main group received standard therapy along with a treatment regimen including herbal extracts. The aim was to evaluate the effectiveness of these treatment regimens.

The results of some instrumental and laboratory examinations of the patients involved in the study are provided in Table 2.

Table 2. Results of Some Instrumental and Laboratory Examinations of Patients Before Treatment

Indicators	Minimum level	Maximum level	M ±m
The Density of the liver tissue (Kpa)	7,38	11,62	8,9± 0,2
Glucose (mmol/l)	4,8	17,5	6,8± 0,6
Total Protein (g/l)	55,0	82,0	66,1± 1,0
Albumin	42,0	51,0	45,8± 0,5
Globulin	13,0	26,0	18,7± 0,8
AST (v/l)	9,0	417,0	39,7±7 ,2
ALT (v/l)	7,0	488,0	65,3± 9,3
AST/ALT	0,06	1,88	0,8± 0,1
γ-GTP- (v/l)	11,0	459,0	80,4± 10,4
ALP (v/l)	56,0	135,0	79,7± 3,9
Total bilirubin (mkmol/l)	0,3	23,4	6,4 ± 0,9
Direct bilirubin	0,08	28,0	3,1± 0,7
Indirect bilirubin	0,11	16,3	3,8 ± 0,6
Chol (mg/dl)	125,0	297,0	207,8 ± 5,7
TG (mg/dl)	76,0	493,0	203,5 ± 20,0
CRP (mg/l)	0,60	15,97	3,3± 0,7

Unlike the control group, in the main group of patients, the liver thickness significantly improved after treatment. Before treatment, 13 patients (40.6%) in this group had normal liver thickness, whereas after treatment, this number increased to 19 patients (59.4%). In this group, while 9 patients (28.1%) had a significant increase in liver thickness before treatment, no patient showed a significant increase in liver thickness after treatment. The difference in liver thickness measurements before and after treatment in the main group was statistically significant ($p = 0.000$). However, despite significant improvement in liver thickness among patients in the main group compared to the control group after treatment, no statistically significant difference was detected ($p = 0.175$).

Under baseline treatment, liver size showed partial changes: after 3 months of treatment, these indicators improved slightly. However, the results were not statistically significant ($p = 0.705$).

In the main group, the number of patients with normalized liver size increased approximately threefold, from 5 (15.6%) to 14 (43.8%). This confirms the positive role of the herbal decoction.

According to Table 3, no statistically significant difference was found in liver structure and exogeneity indicators during the treatment process in the control group ($p = 0.180$ and $p = 0.317$, respectively).

In the main group, both liver structure and exogeneity indicators improved statistically significantly during treatment ($p = 0.000$ in both cases). Liver exogeneity indicators were statistically significantly different compared to the control group ($p = 0.001$).

Thus, adding herbal decoction to baseline therapy for the treatment of chronic alcoholic hepatitis partially improves liver structural indicators.

Table 3. Dynamics of liver size changes in the control and main groups before and after treatment.

Indicator	Gradation	Control (n18)				P_W	Main (n=32)				P_W	P_U
		BT		AT			BT		AT			
		Say	%	Say	%		Say	%	Say	%		
Density of the Liver	Normal Range	10	55,6	9	50	0,180	13	40,6	19	59,4	0,000	0,175
	Increased	5	27,8	4	22,2		10	31,3	13	40,6		
	Greatly Increased	3	16,7	5	27,8		9	28,1	0	0		
Size of the Liver	Normal Range	5	27,8	7	38,9	0,705	5	15,6	14	43,8	0,000	0,234
	Increased	9	50	6	33,3		17	53,1	17	53,1		
	Greatly Increased	4	22,2	5	27,8		10	31,3	1	3,1		
Margins of the Liver	Smooth	10	55,6	10	55,6	0,317	15	46,9	18	58,1	0,001	0,353
	Rough	5	27,8	3	16,7		8	25,0	13	41,9		
	Irregular	3	16,7	5	27,8		9	28,1	0	0		
Structure of the Liver	Homogeneous	10	55,6	9	50,0	0,180	12	37,5	17	53,1	0,000	0,295
	Non-homogeneous	5	27,8	4	22,2		11	34,4	15	46,9		
	Structureless	3	16,7	5	27,8		9	28,1	0	0		
Exogenity of the Liver	Norma	0	0	0	0	0,317	0	0	5	15,6	0,000	0,001
	Increased	15	83,3	13	72,2		23	71,9	27	84,4		
	Greatly Increased	3	16,7	5	27,8		9	28,1	0	0		

The results regarding liver tissue stiffness obtained before and after treatment using liver elastography are of particular interest (Table 4).

Table 4. Comparative Analysis of Liver Tissue Density Indicators Before and After Treatment in the Main and Control Groups (Based on Elastography Examination)

Indicator	Stat. parameter	Control n = 10		P_W	Main n = 15		P_W	P_U
		MƏ	MS		MƏ	MS		
The density of the Liver (kPa)	M ± m Me $Q_1 – Q_3$	8,49±0,30 8,39 8,14 - 8,76	8,65±0,34 8,58 8,12 - 8,76	0,735	9,23 ± 0,29 8,90 8,40 - 9,88	7,61±0,26 7,45 6,85 - 8,10	0,001	0,011

In the main group, the liver tissue density significantly decreased after treatment, averaging 7.61±0.26 kPa (p=0.001). The difference between the post-treatment values of the main and control group patients was also statistically significant (p=0.011).

In the control group, the difference between pre- and post-treatment values was not statistically significant (p=0.317). As shown in the table, in the main group, these indicators significantly improved after 3 months of treatment, and the difference between the indicators was statistically significant (p=0.002). Compared to the control group, treatment in the main group was more effective, and the difference between the groups was statistically significant (p=0.026).

Protein metabolism in patients was also investigated, and the results showed that the amount of globulins significantly increased in the main group after treatment. The difference between the groups after treatment was also statistically significant (p=0.030). Thus, adding herbal decoctions to the baseline therapy improves protein metabolism indicators in patients with chronic alcohol-related hepatitis.

The effect of herbal decoctions on the functional indicators of the liver in the patients involved in the study was investigated by us (Table 5)

Table 5. Comparative Analysis of Liver Functional Indicators Before and After Treatment in the Main and Control Groups

Indicator	Statistical Parameter	Control n = 21		P_W	Main n = 39		P_W	P_U
		BT	AT		BT	AT		
AST (v/l)	M ± m Me $Q_1 – Q_3$	31,5±6,1 23,0 19,0 – 37,0	27,8±2,7 28,0 16,0 – 33,3	0,262	44,4±10,7 31,0 22,7 – 45,0	24,0±1,3 23,0 18,0 – 30,0	0,000	0,244
ALT (v/l)	M ± m Me $Q_1 – Q_3$	55,4±11,7 43,0 26,0 – 56,0	48,0±8,7 36,0 25,0 – 46,0	0,889	70,7±12,9 53,8 26,9 – 92,0	34,7±2,9 34,0 18,0 – 46,7	0,000	0,535
DeRitis AST/ALT	M ± m Me $Q_1 – Q_3$	0,71±0,07 0,65 0,53 – 0,73	0,75±0,08 0,73 0,59 – 0,92	0,380	0,79±0,07 0,66 0,49 – 0,93	0,83±0,06 0,75 0,57 – 1,0	0,058	0,566
Total bilirubin (mkmol/l)	M ± m Me $Q_1 – Q_3$	7,9±1,5 6,5 3,65 – 12,4	9,1±2,7 7,9 2,5 – 10,95	0,496	8,9±1,3 5,4 0,56 – 7,9	8,5±0,7 5,9 0,5 – 9,3	0,767	0,145
Direct bilirubin (mkmol/l)	M ± m Me $Q_1 – Q_3$	3,2±0,6 2,6 2,0 – 4,35	3,3±0,7 3,0 0,99 – 4,9	0,842	3,0±1,1 2,3 0,19 – 3,4	2,0±0,3 2,8 0,17 – 3,1	0,493	0,105
Non-direct bilirubin (mkmol/l)	M ± m Me $Q_1 – Q_3$	4,7±0,9 3,9 1,65 – 7,1	5,7±1,4 4,8 1,525 – 6,3	0,320	3,3±0,7 3,3 0,36 – 4,8	3,4±0,6 3,4 0,4 – 5,9	0,954	0,228

After treatment, the levels of ALT and AST in the blood decreased in both groups (p=0.889 and p=0.000, respectively). At the end of the treatment, no statistically significant difference was found between the bilirubin (TB) indicators in the main and control group patients (p=0.145). Before treatment, the bilirubin level in the control group fluctuated between 0.17 – 8.3 μmol/l, with an average of 3.2 ± 0.6 μmol/l.

The results indicate that while the addition of herbal decoctions to the baseline therapy statistically significantly reduced the levels of AST and ALT in the blood, it did not have an additional effect on the levels of total bilirubin, direct, and indirect bilirubin. The addition of herbal decoctions to the baseline therapy did not have a significant effect on lipid metabolism (p=0.724 and p=0.959).

To determine whether the correlation between liver instrumental-laboratory indicators before and after treatment was maintained, analyses were conducted.

As before treatment, after treatment there was a direct correlation between liver thickness and the level of total protein in the blood ($p = 0.560$, $p = 0.001$), and between liver exogeneity and AST ($p = 0.299$, $p = 0.037$). Additionally, a direct correlation emerged between liver thickness ($\rho = 0.392$, $p = 0.005$) and size with AST ($\rho = 0.438$, $p = 0.002$). Furthermore, an inverse correlation was found between liver thickness and total bilirubin ($\rho = -0.524$, $p = 0.001$), and between liver structure and total bilirubin ($\rho = -0.563$, $p = 0.000$).

Thus, the use of herbal decoction in conjunction with basic therapy improves liver measurements, structural homogeneity, and exogeneity indicators. Notably, the decrease in liver tissue density and the positive dynamics observed in liver fibrosis were particularly noteworthy.

Results

1. In five experimental models of non-viral liver damage, three main types of hepatopathies were identified (cholestatic, mixed, cytolytic), and criteria confirming liver damage were established.

2. Despite the different pathogenetic developments of the created models, the biochemical diagnostic criteria for hepatitis related to hepatocyte damage were similar. [4,5].

3. In the treatment of non-viral experimental hepatitis, α-TFA significantly reduced the severity of lipid peroxidation as a strong antioxidant and increased the levels of antioxidant status. However, there was no satisfactory positive dynamic observed in the levels of biochemical markers of liver pathology, including ALT, AST, Ritis coefficient, γ-GTP, LDH, ALP, total bilirubin (TB), MMWP, CRP, and lipid metabolism indicators. Additionally, in the context of statin and alcohol hepatitis models, there was an increase in the levels of ALT, AST, MMWP, and CRP. [8].

4. The results of treatment with UDCA showed varying degrees of improvement depending on the type of non-viral experimental hepatitis. The most notable results were observed in the cholestatic (tetracycline model) and mixed (statins, alcohol) types of models. [6].

5. Significant improvement in liver function was observed during treatment with PC, which is confirmed by the positive dynamics of these indicators. Lipid metabolism normalizes. The most notable result was seen in the statin model, where AI = 3.43, which is practically within the normal range. However, the Ritis ratio was 0.97±0.09, and a value < 1 indicates the continuation of pathological processes in the liver. [13].

6. The use of PC in combination with UDCA results in enhanced pharmacological activity due to the synergy between PC's active compounds and UDCA. Nearly all the studied indicators approach intact values, the process of lipid peroxidation is slowed down, and liver function is normalized. The Ritis coefficient decreases to 1.49 ± 0.05 and the Atherogenic Index (AI) to 2.29, which align with normal values and indicate a return to normal liver

function. [9]

7. In initial clinical trials, the addition of herbal infusions to standard therapy in the treatment of patients with chronic alcohol hepatitis partially improves liver structural indicators. Notably, significant improvement in liver fibrosis was observed after three months of treatment. [10,14,15].

Practical Recommendations

1. The results of modeling various types of non-viral hepatitis are recommended for investigating the pathogenetic mechanisms of hepatopathies and for the development and therapeutic application of new medicinal products.

2. The use of AZHEPOFIT PC in combination with UDCA shows more beneficial effects, with nearly all investigated indicators approaching intact values. It slows down lipid peroxidation processes and normalizes liver function, which will allow for recommending pathogenetic treatment regimens for non-viral hepatitis for future research and potential application in medical practice.

3. The obtained results have theoretical significance in explaining the pathogenetic mechanisms of non-viral hepatitis and in developing treatment methods. It is recommended that these results be included in methodological developments intended for teaching and practical use by healthcare professionals.

List of Published Scientific Works on the Dissertation Topic

1. Abasova S.A., Əzizov V.Ə., Qurbanova X.İ., Şirəliyeva G.Ş., İbadova F.Ə. / Qaraciyərin dərmanla zədələnməsinə müasir baxış // "Metabolizm Jurnalı",
- 2021, №2, səh. 3-14.
2. Abasova S.A., Qurbanova X.İ., Əzizov V.Ə. / Qaraciyərin alkoqol xəstəliyi // "Sağlamlıq", - 2021,
№2, səh. 39-44.
3. Abasova S.A., Əzizov V.Ə., Qurbanova X.İ., İbadova F.Ə, Şirəliyeva G.Ş, Muradova S.R. / Qaraciyərin alkoqol xəstəliyinin müalicəsi (problemlər və perspektivlər) // "Metabolizm Jurnalı", - 2021, №3, səh. 3-13.
4. Абасова С.А., Джафарова Р.Э. / Изучение изменения печеночных показателей на фоне различных схем лечения в экспериментальной модели тетрациклиного гепатита // "Şuşa ili"nə həsr olunmuş "Təbabətin aktual problemləri" adlı beynəlxalq elmi-praktiki konfransın materialları", - 2022, səh. 331-332.
5. Абасова С.А., Джафарова Р.Э. / Нарушенный липидный обмен в тетрациклиновой модели лекарственного гепатита и возможности его коррекции // Proceedings of V International scientific and practical conference "Eurasian scientific discussions" 5-7 june, - 2022, стр. 123-129.
6. Абасова С.А., Джафарова Р.Э. / Изучение состояния перекисного окисления липидов и активности антиоксидантной системы в тетрациклиновой модели лекарственного гепатита на фоне применения а-токоферола, урсодезоксихолиевой кислоты и фитокомплекса AZHEPOFİT // XI International scientific and practical conference "Innovations and prospects of world science" 22-24 june, - 2022, стр. 60-69.
7. Абасова С.А. / Эффективность фитотерапии на фоне фенацетиновой модели лекарственного гепатита // "Медицинские новости", - 2022, стр. 58-61.
8. Jafarova R.A., Abasova S.A. / Treatment of alcoholic liver

damage in experiment // “Вестник”, - 2022, стр. 14-21.

9. Абасова С.А. / Сравнительный анализ эффективности различных схем лечения токсическво гепатита // “Sağlamlıq”, - 2022, №2, стр. 105-113.

10. Abasova S.A. / Xronik alkoqol hepatiti olan xəstələrdə AZHEPOFİT fitokompleksinin qaraciyərin bəzi morfo-funksional göstəricilərinə təsiri // “Professor Zərifə Ağarza qızı Zeynalovanın anadan olmasının 90 illiyinə həsr olunmuş elmi konfransın materialları”, - 2023, səh. 6-12.

11. Abasova S.A. / AZHEPOFİT fitokompleksinin xronik alkoqol hepatiti olan xəstələrdə zülal mübadiləsinə təsiri // “Professor Zərifə Ağarza qızı Zeynalovanın anadan olmasının 90 illiyinə həsr olunmuş elmi konfransın materialları”, - 2023, səh. 14-15.

12. Abasova S.A. / AZHEPOFİT fitokompleksinin xronik alkoqol hepatiti olan xəstələrdə lipid mübadiləsinə təsiri // “Professor Zərifə Ağarza qızı Zeynalovanın anadan olmasının 90 illiyinə həsr olunmuş elmi konfransın materialları”, - 2023, səh. 15-16.

13. Jafarova R.A., Abasova S.A. / Effectiveness of the α-tocopherol, ursodeoxycholic asid, and AZHEPOFIT phyto-complex against the statin model of drug-induced hepatitis // “Advancements in Life Sciences”, - 2023, page 137-142.

14. Abasova S.A./AZ HE POFİT fitokompleksinin “Alkohol hepatitis olan xəstələrdə qaraciyər Fibrozuna təsiri //Təbabətin actual problemləri – 2023, Beynəlxalq elmi-praktiki konqres, -3-6 may, 2023, səh.133

15. Abasova S.A./Xronik Alkoqol hepatitli xəstələrdə bitki dəmləməsinin qaraciyərin morfo-funksional vəziyyətinə təsiri/Sağlamlıq 2023, № 4, səh. 94-99

Abbreviations

ALD - Alcoholic Liver Disease
ALT - Alanine Aminotransferase
AST- Aspartate Aminotransferase
ALP - Alkaline Phosphatase
γ-GTP - Gamma-Glutamyltranspeptidase.
TB- Total Bilirubin
CU – Conditional Unit
SG -Subgroup
LDH - Lactate dehydrogenase
EU- Effect Unit
TP – Total Protein
MMWP - Medium Molecular Weight Peptides
CRP - C-reactive protein
AI – atherogenic index
UDCA - Ursodeoxycholic Acid
PC - Phytocomplex
α – TFA - Alpha-tocopherol acetate
DIH – Drug Induced Hepatitis
TG – Triglycerides
TC – Total Cholesterol
LDL – Low-Density Lipoprotein
VLDL – Very Low-Density Lipoprotein
HDL – High-Density Lipoprotein
TAS – Total Antioxidant Status
SOD – Superoxide Dismutase
CAT – Catalase
CHOL - Cholesterol

The defense will be held on 10 december 2024 at 14^{00} at the meeting of the Dissertation council BFD 2.27 of Supreme Attestation Comission under the President of the Republic of Azerbaijan operating at Azerbaijan Medical University.

Address: AZ 1022. Baku, A.Gasımzada str., 14

You can review the dissertation at the library of Azerbaijan Medical University.

The electronic versions of the dissertation and abstract have been posted on the official website of Azerbaijan Medical University (www.amu.edu.az).

The abstract was sent on "4" november 2024.

Signed for publication:
Paper format:
Volume: 38.237
Number of hard copies: 30