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ORIGINAL ARTICLE



# The advantages of drinking mineral water in the rehabilitation of patients with viral hepatitis C with accompanying non-alcoholic fatty liver disease after suffering from COVID-19

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## Abstract

**Introduction and Objective**. Past COVID-19 significantly worsens Chronic viral hepatitis C patients with concomitant NAFLD. The aim of the study was to assess effectiveness of including mineral water in the rehabilitation complex in patients with chronic hepatitis C with concomitant non-alcoholic fatty liver disease who contracted COVID-19.

**Materials and method**. 71 patients with chronic hepatitis C with concomitant NAFLD wo contracted COVID-19 were examined. Group I (control) – 39 patients prescribed dietary nutrition and exercise therapy. Group II (main) – 32 patients, in addition to the above, received packaged 'Shayanskaya' mineral water. Methodology comprised anamnestic, anthropometric and clinical, general clinical, biochemical, serological, and molecular genetic (markers of hepatitis C virus, HCV RNA PCR (qualitative and quantitative determination, genotyping), enzyme-linked immunosorbent assay, ultrasonographic examination of digestive organs, and statistical methods.

**Results**. Due to the treatment, there were significant improvements in carbohydrate and lipid metabolism, as well as the cytokine profile.

**Conclusions.** The effectiveness was established of the use of silicon low-mineralized bicarbonate sodium mineral water in the complex rehabilitation of patients with chronic hepatitis C and suputor NAFLD after contracted COVID-19. There was a significant improvement in the clinical course of the disease and improvement in the functional state of the liver.

## Key words

chronic viral hepatitis C, non-alcoholic fatty liver disease, COVID-19, mineral water

## INTRODUCTION

Chronic viral hepatitis C (CVHC) remains one of the most critical problems of modern medicine due to its wide distribution, progressive increase in incidence, high level of chronicity, the risk of developing liver cirrhosis and hepatocellular carcinoma [1, 2, 3]. According to various studies, liver steatosis is observed in almost 50% of patients infected with the hepatitis C virus. Non-alcoholic fatty liver disease (NAFLD) in patients with chronic hepatitis C quickly contributes to the onset and further fibrosis progression from the initial stages to liver cirrhosis. On the one hand, the hepatitis C virus itself can cytotoxically lead to direct damage to the liver or, in a genotype-specific way, to its fatty degeneration. On the other hand, the presence of such risk factors as insulin resistance (IR), diabetes mellitus, obesity, intestinal dysbiosis, and epigenomic damage, lead to the independent formation of NAFLD, which affects the development of the necrobiotic process in liver tissue, and leads to the progression of fibrosis [4]. The prevalence of NAFHP today has reached the scale of a global epidemic [5, 6]. According to the latest meta-analysis of clinical trials in 22 countries, the incidence of NAFLD in the general population is 25.24% [7, 8].

Postponed COVID-19 significantly worsens the condition of such patients and leads to a violation of the functional state of the liver [9]. Patients with COVID-19 with mild liver dysfunction are not usually prescribed anti-inflammatory and hepatoprotective drugs, but it should be considered that patients with coronavirus infection (2–11%) may experience severe hepatic complications [10]. Factors that may contribute to liver injury in COVID-19 include direct viral cytopathic effects, exaggerated immune responses/systemic inflammatory response syndrome, hypoxic changes, vascular changes due to coagulopathy, endothelitis, and cardiac congestion due to right heart failure, and drug-induced liver damage. Most symptoms of liver damage associated with COVID-19 are mild and self-limiting. Liver function tests and abdominal imaging are the preliminary investigations of

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liver injury in patients with COVID-19. The mechanisms of liver injury include SARS-CoV-2-induced hepatic steatosis, reactivation of pre-existing liver disease, mitochondrial dysfunction, hepatic congestion cardiomyopathy, immune-mediated injury, hypoxic hepatitis, direct cytotoxicity, drug-induced liver injury, ischemic hepatitis, microthrombotic disease, and extrahepatic transaminase release. The authors believe that the coronavirus disease 2019 (COVID-19) pandemic is having a variable impact on pre-existing liver disease, which range from treatment failures, liver exacerbations, and higher mortality rates, and point to the importance of studying and understanding the mechanisms of liver damage in the disease COVID-19 [11].

Today, there has yet to be a consensus on the possibility of using natural factors in treating patients of this category, despite extensive experience in their use in treating diseases of the gastroenterological profile and metabolic disorders [12, 13, 14]. However, it is known that natural and preformed physical factors have a sanogenetic effect and a preventive effect, the ability to modify the impact on the processes of hormonal regulation of carbohydrate and lipid metabolism [15, 16]. Therefore, it is considered expedient to use natural mineral waters in the complex treatment of CVHC patients with concomitant NAFLD who have undergone COVID-19, which can improve the effectiveness of therapy in this category of patients, while avoiding undesirable effects of drug treatment.

The proposed rehabilitation treatment of patients with COVID-19 using a course of drinking mineral waters (MW), which have a pronounced biological and therapeutic potential, can be sufficiently reasonable and effective in this situation. When taken internally, mineral waters act on various human organs and systems without side-effects, are simple to use and inexpensive. The mechanism of action of medicinal waters has been sufficiently studied [17, 18].

The mineralization of water, ionic composition, and the presence of biologically active components are essential for implementing the therapeutic effect of mineral waters (MW). Thus, due to the autochthonous microflora contained in mineral water, antibacterial and hormone-like substances are produced that implement the therapeutic effect of MW [19, 20].

The study was carried out within the framework of funding by the Ministry of Health of Ukraine for the budgetary research work: 'Development of differentiated personalized complexes for the rehabilitation of patients after the transferred coronavirus infection at the sanatorium-resort stage' (State Registration No. 0122U001261).

## OBJECTIVE

The aim of the study was toi assess the effectiveness of including mineral water in the rehabilitation complex in patients with chronic hepatitis C with concomitant non-alcoholic fatty liver disease who contracted COVID-19.

## MATERIALS AND METHOD

A total of 71 patients with chronic hepatitis C with concomitant NAFLD were examined, all of whom had suffered confirmed COVID-19 1–2 months ago. The diagnosis of chronic viral hepatitis C (CVHC) was established according to the international classification of ICD-10 and the international classification of liver diseases (Los Angeles, 1994), which was confirmed by the detection of total anti-HCV in the blood of the examined patients, and determination of the absence of HCV RNA by the PCR method in the blood serum. The diagnosis of NAFLD was established based on a comprehensive examination following the Order of the Ministry of Health of Ukraine dated 06.11.2014 No. 826 'On the approval and implementation of medical and technological documents for the standardization of medical care for chronic non-infectious hepatitis', recommendations of the European Association for the Study of the Liver, the European Association for the Study of Diabetes, and the European Association for the Study of Obesity, 2016.

All studies were carried out at the Polyclinic of the Ukrainian State Research Institute of Medical Rehabilitation and Resort Therapy of Ministry of Health of Ukraine in Odesa.

*Inclusion criteria:* CVHC patients with genotype 1b, without fibrosis or with its initial stages (F0-F2) and concomitant NAFLD with a persistent and prolonged virological response, 6–12 months from the end of antiviral therapy with a modern direct-acting antiviral drug velpatasvir) transferred COVID-19 1–2 months previously. The patients included in the study consumed less than 20 g of ethanol per day and had no signs of chronic viral hepatitis B, D, E, or G, autoimmune liver damage, liver cirrhosis, drug and alcohol addiction (at the time of the examination and in history), signs of toxic or drug-induced hepatitis, which they and also denied taking in the last 6 months, and drugs with hepatoprotective or hepatotoxic properties. Patients were without concomitant diabetes mellitus and other somatic diseases.

*Exclusion criteria:* patients with concomitant viral, autoimmune, toxic, or drug-induced liver damage, confirmed by the results of serological and immunological studies, liver cirrhosis of various origins, patients who were approved the use of ethanol at a dose of more than 20 g per day, patients with drug or alcohol concomitant diabetes mellitus and other somatic diseases (acute, chronic in the stage of exacerbation or decompensation); patients in the period of pre-, menopause and post-menopause who needed hormone replacement therapy.

The number of men and women among the studied patients was almost identical: women – 36 (50.70%) and men – 35 (49.30%). The age of the patients varied from 32–58 years, average – 42.13±8.64 years.

All patients were divided into 2 groups, randomized by gender, age, stage of underlying disease, and metabolic and post-coagulant disorders.

Group I (control) – 39 patients prescribed dietary nutrition and exercise therapy. Meals included a Mediterranean diet supplemented with Atherodinol, a safe, natural complex for cholesterol control and vascular protection, based on red fermented rice extract, Bergamot extract and folic acid.

Group II (main) – 32 patients, in addition to the above, received packaged 'Shayanskaya' mineral water at the rate of 3 ml per 1 kg of body weight, 30, 40 and 60 minutes before meals, depending on stomach acidity, and the same dose three times in a day after meals.

'Shayanska' mineral water (MW) is designated as silicon low-mineralized bicarbonate sodium water from Well No. 242 in Shayan village, Khust district of the Transcarpathian region (Ukraine). The formula for the chemical composition of the water is as follows:

$$H_2SiO_3 \quad M_{2.76} \quad 0.063 \quad \frac{HCO_3\ 91\ Cl\ 7\ SO_3\ 2}{(Na+K)\ 97\ Ca\ 3\ Mg\ 2}$$

Total mineralization in the water – 2.76 g/l, content of sodium and potassium ions – 0.617 g/l, calcium ions – 0.010 g/l, magnesium ions – 0.009 g/l, bicarbonate ions – 1.453 g/l, chloride ion – 0.121 g/l, and sulfate ions – 0.043 g / l. The MW additionally contains biologically-active components: silicon in the form of metasilicic acid (H2SiO3) 63.4 mg/l (with a balneological norm for silicon waters from 50 mg/l) and boron in the form of orthoboric acid (H3O3) 29.13 mg/lIn, while the balneologicalcriterion for boron waters is 35 mg/l.

Physiotherapy exercises were prescribed individually, taking into account the age, capabilities, and comorbidities of patients. Physical activity was increased gradually, from 30 minutes 3 times a week to 45 minutes 3–5 times a week. The treatment was carried out on an outpatient basis, and the duration of treatment was 2 months.

All patients underwent the following examinations:
- anthropometry with the subsequent calculation of the body mass index and the ratio of waist-hip circumferences;
- biochemical parameters of blood serum assessed the functional state of the liver:
- pigment function of the liver was studied by determining unconjugated and conjugated bilirubin; the activity of indicator enzymes determined cytolysis syndrome: alanine aminotransferase (ALAT) and aspartate aminotransferase (AST);
- protein-synthetic function of the liver was assessed by determining the total protein;
- cholestasis syndrome was evaluated by alkaline phosphatase (LF) and gamma-glutamyltranspeptidase (GGTP) activity;
- lipid metabolism was studied by the content of total cholesterol (TC), β-lipoproteins, low-density lipoproteins (LDL), high-density lipoproteins (HDL), triglycerides (TG) and atherogenic coefficient (CA) (according to Goryachkovsky A. M., 2005) [21].

To determine insulin resistance (IR), a homeostatic model assessment of the HOMA-IR was used (according to Matthews D. R., 1985) [22].

To diagnose the level of viral load and the genotype of HCV infection, serological markers of viral hepatitis C were used (HCV RNA PCR, quantification and genotyping).

To assess the level of fibrosis, the activity of the inflammatory process and steatosis in the studied patients, the Fibro Max panel was used, which is a combination of 5 non-invasive tests: FibroTest, ActiTest, SteatoTest, NashTest, and AshTest. FibroTest, ActiTest, and SteatoTest from this panel were used.

In order to determine the activity of lipid peroxidation (LPO) processes in the blood serum, the concentration of malondialdehyde (MDA) was determined (according to Goryachkovsky A. M., 2005) [21].

The cytokine profile was studied by determining adiponectin using the standard 'Mediagnost Adiponectin ELISA E09' equipment and leptin using the standard kit EIA-2395, Leptin (Germany).

All patients underwent transabdominal ultrasonography of the abdominal organs (TUS OCH) using PhilipsHD 3 (Korea), and Aloka 3500 (Japan) devices.

## RESULTS

Concomitant digestive system diseases in patients were primarily represented by chronic non-calculous cholecystitis – 67.6% of patients. In comparision, gall bladder cholesterosis was determined in 39.4% of patients which, to some extent, explains the development of NAFLD in these patients. Chronic pancreatitis was diagnosed in 30 (42.25%) patients.

Before the start of treatment, 100% of patients had signs of an asthenic syndrome (general weakness, rapid fatigue), less often they diagnosed signs of dyspeptic (81.69±2.51)% of persons) and painful abdominal (76.05±2.65)% syndromes. Objective examination most often revealed hepatomegaly (59.15±2.25)% and pain on palpation in the right hypochondrium (53.52±2.53)%).

The average BMI of the examined patients at the beginning of treatment was (31.97±1.32) kg/m$^2$. At the same time, overweight was diagnosed in 24 (25.35±2.32)% patients, obesity of the 1st degree in 12 (16.9±3.63)% patients, obesity of the 2nd degree in 16 (22.53±1.84)% patients. Measurement of the waist circumference/hip circumference ratio showed that most patients had an android type of distribution of adipose tissue – abdominal obesity. It is known that the abdominal type of obesity is directly related to the development of IP due to an imbalance of adipocytokines, the synthesis of pro-inflammatory cytokines, which led to the long-term consequences of COVID-19.

A biochemical study of blood serum at the beginning of treatment revealed a violation of the functional state of the liver in most patients, mainly due to the presence of a cytolytic syndrome (Tab. 1).

**Table 1.** Indicators of the biochemical composition of the blood of patients before treatment (M±m)

| Indicator | Value |
|---|---|
| AlAT, mmol/(h·l) | 58.22 ±4.08 |
| AsAT, mmol/(h·l) | 52.71±2.06 |
| Total cholesterol, mmol/l | 6.04 ± 0.16 |
| Triglycerides, mmol/l | 3.15 ± 0.43 |
| LDL, mmol/l | 3.87 ± 0.18 |
| HDL, mmol/l | 1.16 ± 0.09 |
| Coefficient of atherogenicity | 4.09 ± 0.46 |
| Adiponectin, ng/ml | 12.28 ± 1.14 |
| Leptin, ng/ml | 23.71 ± 3.36 |

To a greater extent, an increase in the level of ALT and AST activity was observed. The rise in the level of LF and GGT manifested signs of cholestatic syndrome.

An increase the TCh, β-lipoproteins, and TG concentration characterized a lipid metabolism violation. An increase in LDL and a decrease in HDL led to a sharp change in the atherogenic coefficient.

The study of the cytokine profile before the start of treatment determined the presence of hyperleptinaemia and hypoadiponectinaemia in patients (Tab. 2).

An analysis of the state of the LPO and antioxidant defense systems (Tab. 2) determined the predominance of LPO processes, which was expressed in an increase in the level of MDA and diene conjugates (DC) in all patients. The level of total antioxidant activity (TAA) as one of the indicators of the severity of the pathological process in the

**Table 2.** Indicators of the antioxidant defence system in patients before treatment (M±m)

| Indicator | Value |
|---|---|
| MDA, μmol/l | 6.98 ± 0.27 |
| DC, c.o., IO | 1.84± 0.19 |
| TAA, % | 35.17 ± 1.89 |

liver at the beginning of treatment was reduced and averaged (35.17±1.02)%.

The study of the state of carbohydrate metabolism, according to the HOMA-IR index, revealed signs of IR in the vast majority – 62 (87.32±2.07)% of patients, basal hyperinsulinaemia was found in 22 (38.09±7.49)% individuals, an increase in glucose levels was observed in 99 (30.98±3.97)% of the examined patients (Tab. 3).

**Table 3.** Characteristics of carbohydrate metabolism (M±m)

| Indicator | Norm | Average value |
|---|---|---|
| Blood serum glucose, mmol/l | 4.11–5.89 | 5.73±0.23 |
| Insulin, mcd/l | 2.6–18 | 19.67±0.84 |
| HOMA-IR index | < 2.77 | 5.10±0.32 |

After the treatment, patients in the control group showed an improvement in the clinical manifestations of the disease: a decrease in the signs of an asthenic syndrome in (56.75±8.08)% of persons, and pain syndrome in (48.64±8.16) patients. The dynamics of signs of the dyspeptic syndrome were unreliable (p>0.05).

In the main group, there was a significant levelling of the signs of asthenic and dyspeptic syndromes (p<0.001), and the symptoms of the abdominal syndrome also significantly decreased (p<0.05).

In both groups, the average weight of patients significantly decreased (2.95±0.36 kg) in the control group and (5.95±0.36 kg) in the main group.

As a result of the treatment, in patients of both groups, there was a decrease in the signs of cytolytic (p<0.001), mesenchymal-inflammatory (p<0.05) and cholestatic syndromes (p<0.001). According to the TUS of OCHP, in 36.58% of patients with concomitant damage to the biliary system, a decrease in the inhomogeneous content in the gallbladder was observed, in 60.97%; a reduction in echogenicity and size of the liver is likely (p<0.001).

As can be seen from Table 4, improvement in the clinical state of the liver was accompanied by the normalization of the enzyme spectrum. In both groups, there were significant changes in AST and ALT; however, in the main group, their normalization was significantly higher than in the control group (Tab. 4).

There were also changes in lipid metabolism, notably, only total cholesterol and LDL were significantly normalized in the control group. At the same time, all studied parameters significantly changed in the main group: total cholesterol, triglycerides, LDL and HDL. These changes led to a significant decrease in the coefficient of atherogenicity.

Positive changes were also observed in the study of adipokines. In both groups there was a significant decrease in the level of leptin, and in the main group, there was a significant increase in the adiponectin level.

An improvement in carbohydrate metabolism was expressed in a decrease in the level of insulin resistance due to levelling and hyperglycaemia and hyperinsulinaemia. However, these changes were significant only in the main group. Moreover, regarding Insulin and the HOMA-IR index, a significant difference was registered between the main and control groups (Tab. 5).

The treatment complex contributed to a significant restoration of the balance in the LPO/AOS system, namely, the limitation of LPO processes and the increase in TAA. From Table 6, it follows that in the main group, there was a significant decrease in the concentration of malondialdehyde compared with the control (Tab. 6).

Thus, the use of mineral water in the rehabilitation complex in patients with chronic hepatitis C with concomitant non-

**Table 4.** Indicators of the biochemical composition of the blood of patients after treatment M±m)

| Indicator | Before treatment | After treatment – Group 1 | After treatment – Group 2 | p |
|---|---|---|---|---|
| AlAT, mmol/(h·l) | 58.22 ±4.08 | 34.44 ±2.38* | 21.28 ±2.76* | <0.001 |
| AsAT, mmol/(h·l) | 52.71±2.06 | 31.15±2.64* | 24.74±2.06* | <0.05 |
| Total cholesterol, mmol/l | 6.04 ± 0.16 | 5,24 ± 0.21* | 5.11 ± 0.18* | >0.05 |
| Triglycerides, mmol/l | 3.15 ± 0.43 | 2.42 ± 0.33 | 2.17 ± 0.12* | >0.05 |
| LDL, mmol/l | 4.74 ± 0.18 | 4.01 ± 0.18* | 3.61 ±0.19* | <0.05 |
| HDL, mmol/l | 1.16 ± 0.09 | 1.22 ± 0.13 | 1.34 ±0.08* | >0.05 |
| Coefficient of atherogenicity | 4.09 ± 0.46 | 3.29 ± 0.23 | 2.72 ±0.18* | <0.05 |
| Adiponectin, ng/ml | 12.28 ± 1.14 | 14.75 ± 1.28 | 15.44 ± 1.23* | >0.05 |
| Leptin, ng/ml | 23.71 ± 3.36 | 16.02 ± 1.63* | 15.97 ± 1.55* | >0.05 |

* significant difference between indicators in the groups before and after treatment; p – significant difference between indicators in the main and control groups

**Table 5.** Characteristics of carbohydrate metabolism after treatment (M±m)

| Indicator | Before treatment | After treatment – Group 1 | After treatment – Group 2 | p |
|---|---|---|---|---|
| Blood serum glucose, mmol/l | 5.73±0.23 | 5.58 ± 0.22 | 5.19 ± 0.22* | >0.05 |
| Insulin, mcd/l | 19.67±0.84 | 18.83 ± 1.25 | 15.06 ± 1.20** | <0.001 |
| HOMA-IR index | 5.10±0.32 | 4.75 ± 0.34 | 3.54 ± 0.39*** | <0.001 |

* significant difference between indicators in the groups before and after treatment; p – significant difference between indicators in the main and control groups

**Table 6.** Indicators of the antioxidant defense system in patients after treatment (M±m).

| Indicator | Before treatment | After treatment – Group 1 | After treatment – Group 2 | p |
|---|---|---|---|---|
| MDA, μmol/l | 6.98 ± 0.27 | 5.62 ± 0.26* | 4.52 ±0.15* | <0.001 |
| DC, c.o., IO | 1.84 ± 0.19 | 0.96 ± 0.16* | 0.67±0.13* | >0.05 |
| TAA, % | 35.17 ± 1.89 | 39.45 ± 2.49 | 42.12±2.11* | >0.05 |

alcoholic fatty liver disease who underwent COVID-19 significantly improves the treatment results.

## DISCUSSION

According to many authors, liver damage in patients with COVID-19, is observed from 14.8%- 53.1%, but the mechanism of this is unknown [23, 24]. An increase in the activity of ALT and AST in the blood serum indicates liver inflammation. An increase in bilirubin levels is less common, and an increase in gamma-glutamyl transferase activity can be detected in 54% of patients with COVID-19. Several authors [25, 26, 27] suggest the following possible mechanisms of liver damage in COVID-19:

– direct cytopathic effect of the SARS-CoV-2 virus on the liver (penetration of the virus into the cell occurs due to the binding of the S-protein of the virus to the ACE2 receptors, a significant increase in the expression of which is manifested in cholangiocytes (59.7% of cells) and hepatocytes (2.6% of cells);
– immune inflammation (cytokine 'storm' within the systemic inflammatory response);
– drug-induced liver damage due to the use in the treatment of drugs that may potentially have a hepatotoxic effect.

More than 50% of patients with SARS-CoV have a mild, self-limiting increase in liver function tests, and a high alanine aminotransferase (ALT) level has been considered a predictor of intensive care unit admission and mortality In those who did not survive SARS-CoV-2 infection, the incidence of acute liver injury was higher than that of survivors. Hypoalbuminaemia is an independent predictor of severe MERS-CoV, and liver biopsy showed mild hydropic hepatocyte degeneration and lymphocytic infiltration.

In the pathogenesis of liver damage caused first by the hepatitis C virus and NAFLD, and then by COVID-19, a vital role is played by imbalances in the LPO and AOD systems with the accumulation of toxic forms of free radicals and reactive metabolites[28, 29].

According to many researchers, carbohydrate metabolism disorders in NAFLD occur, on average, in 74% of patients with NAFLD [30, 31]. In the current study, it was diagnosed that in patients who had previously had chronic viral hepatitis C with concomitant NAFLD, and then COVID-19 infection, the presence of IR is diagnosed more often than traditional indicators, which means that HCV infection and coronavirus will aggravate carbohydrate metabolism disorders. It is known that IR (both virus-induced and metabolic) leads to hyperinsulinaemia, an essential aspect of developing liver fibrosis [32], all of which determines the criticalrole of IR in these patients as a factor influencing the course of the pathological process.

The research conducted by for the current study convincingly confirm the stimulating effect of drinking mineral waters of various compositions on the induction of digestive system hormones, many of which activate insulin production. The significance of enteroinsular hormonal relationships in the development of metabolic disorders and the realization of the biological potential of MW, has been confirmed [33]. In the mechanisms of the systemic (organismal) influence of drinking MW, a prominent role belongs to their non-specific hormone-stimulating effect, the magnitude of which largely depends on the concentration of monovalent ions (primarily hydrocarbonates and sodium) and free carbon dioxide [34].

It has been proven that, despite the relatively low concentration of ions and their spectrum, MW in the first days of its administration has a significant stress potential, which at the hormonal and biochemical level is accompanied by the activation of glucagon and the pituitary-adrenal system, with an increase in the concentration of glucose in the blood, the fastest source of ATP. In turn, these reactions initiate the formation of stress-limiting processes, the active participants of which are the enteroinsular hormonal axis, endogenous opiates, and antioxidant mechanisms [35].

It is known that insulin receptors are submerged in the thickness of the cell membrane and are inactive concerning the hormone circulating in the blood [36]. Even though several hundred receptors exist for each hormone on the cell membrane, one is enough, which, when combined with a related hormone, realizes its biological potential.

The process of 'emergence' of the receptor from the thickness of the cell membrane to meet the hormone is little studied, and the data available to date allow the consideration of 2 hypothetical mechanisms for increasing insulin receptor sensitivity after activation of the early phase of hypoglycemic hormone secretion. The first mechanism is associated with the fact that when studying the lipid peroxidation processes against the background of MW administration, a paradoxical phenomenon is revealed that contradicts many clinical and pharmacological studies. It has been established that the course use of MF is accompanied by an increase in pro-oxidant activity which, by changing the fluidity of cell membranes, provides a more effective interaction of insulin with receptors. The second mechanism is associated with neurohumoral conformational modification of the receptor, which also increases the accessibility and affinity of both receptor sites for the ligand.

The course application of MW is accompanied by inhibiting the secretion of the central mediator of the inflammatory process and allergic reactions – histamine. The studies carried out by the authors showed that the elevated concentration of this biogenic amine under conditions of chronic inflammation against the background of a course of MW intake is statistically significantly reduced by almost a third [37].

The increase in cortisol levels by 12–15% observed during course use, which, in the authors' opinion, determines the adaptive nature of the structural and functional restructuring of homeostatic processes, also testifies in favour of the anti-inflammatory effect of MW. To date, a large amount of experimental and clinical material has been accumulated, confirming the effectiveness of the use of MW in inflammatory diseases of the gastrointestinal tract and hepatobiliary system [38–41].

## CONCLUSIONS

The effectiveness of the use of silicon low-mineralized bicarbonate sodium mineral water in the complex rehabilitation of patients with chronic hepatitis C and suputor NAFLD after transferred COVID-19 has been established. There was a significant improvement in the clinical course of the disease and improvement in the functional state of the liver.

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