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EFFECT OF THE BIOLOGICALLY ACTIVE SUPPLEMENT (M-1) ON A MODEL OF MICE WITH TOXIC HEPATITIS

Fayzullaeva N.Ya.[1]; Kayumov A.A.[1], Raufov A.A.[1], Baratov K.R.[2]
[1]Institute of immunology and human genomics,
[2]Institute of Bioorganic Chemistry at the Academy of Sciences of the Republic of Uzbekistan

XULOSA

Jigar kasalliklari, ayniqsa toksik gepatit, yuqori tarqalishi va samarali davolash usullarining cheklanganligi sababli dolzarb sog'liqni saqlash muammosi bo'lib qolmoqda. Ushbu tadqiqotda M-1 biofaol qo'shimchasining CCl4 yordamida chaqirilgan o'tkir toksik gepatit modelida gepatoprotektiv ta'siri o'rganildi. Turli dozalarda M-1 qo'llangandan so'ng sichqonlarning yashovchanlik darajasi, jigar og'irligi koeffitsienti va umumiy fiziologik ko'rsatkichlari baholandi. Tadqiqot natijalari shuni ko'rsatdiki, 10 ml/kg doza eng yuqori gepatoprotektiv faollikka ega bo'lib, hayotiylikni oshirish va jigar shikastlanishini kamaytirishda samaradorligini namoyon etdi. Ushbu natijalar M-1 preparatini jigar himoyasi uchun istiqbolli vosita sifatida ko'rsatmoqda, ammo uning molekulyar mexanizmlarini va klinik qo'llanilish imkoniyatlarini chuqurroq o'rganish zarur.

Kalit so'zlar: *gepatoproteksiya, biofaol qo'shimcha, toksik gepatit, jigar shikastlanishi, tetraklormetan, eksperimental model.*

РЕЗЮМЕ

Заболевания печени, в частности токсический гепатит, представляют серьезную проблему для здравоохранения из-за высокой распространенности и ограниченных методов лечения. В данном исследовании изучена гепатопротекторная активность биологически активной добавки М-1 на модели острого токсического гепатита, вызванного введением тетрахлорметана (CCl4) у лабораторных мышей. Оценивались показатели выживаемости, коэффициент массы печени и общее физиологическое состояние животных после введения различных доз М-1. Результаты показали, что доза 10 мл/кг обладает наибольшей гепатопротекторной активностью, способствуя улучшению выживаемости и снижению повреждений печени. Эти данные свидетельствуют о перспективности М-1 как потенциального средства для защиты печени, однако необходимы дальнейшие исследования его молекулярных механизмов и клинической эффективности.

Ключевые слова: *гепатопротекция, биологически активная добавка, токсический гепатит, поражение печени, тетрахлорметан, экспериментальная модель.*

Liver diseases, particularly toxic hepatitis, represent a significant global health burden, with rising incidences attributed to environmental toxins, pharmaceuticals, and lifestyle factors [2,6,9]. Carbon tetrachloride (CCl4) is widely used as an experimental hepatotoxin to study mechanisms of liver damage and hepatoprotective agents [4,8,11]. Despite advances in pharmacotherapy, there remains a critical need for safe and effective hepatoprotective agents derived from natural or bioactive compounds [5,10,13]. Various studies have demonstrated the hepatoprotective potential of bioactive supplements; however, their mechanisms and efficacy require further validation [3,7,13,15]. The M-1 bioactive supplement has shown promise in mitigating hepatic injury, yet its precise effects and optimal dosing have not been fully elucidated [4,7,14]. Animal models are essential for assessing the efficacy of hepatoprotective agents, particularly in the context of acute toxic hepatitis. Research indicates that bioactive compounds can enhance hepatocyte regeneration and modulate inflammatory responses in toxin-induced

liver injury. Histopathological evaluation remains a key method for confirming the protective effects of hepatoprotective agents [2,5,11]. The Hepatoprotective Activity Coefficient (HAC) is a useful parameter in determining the efficacy of these agents in experimental models. This study aims to evaluate the hepatoprotective properties of M-1 in a CCl4-induced acute toxic hepatitis model and determine its therapeutic potential. The findings could provide valuable insights into the development of novel hepatoprotective strategies. Further exploration of molecular mechanisms underlying the hepatoprotective effects of M-1 could pave the way for clinical applications [5,9,12].

The aim of the work of M-1 biologically active additiveThe study consists of studying its activity against acute toxic hepatitis induced by CCl4 (tetrachloromethane) in mice.

THE AIM OF THE STUDY

Biologically active supplement M-1 has a specific smell and was presented in the form of oil for the experiment.

RESEARCH METHOD AND OBJECTS

Experimental animals were kept in the vivarium of the Institute of Bioorganic Chemistry and provided with generally accepted daily food and water.

Acute toxic hepatitis. It is characterized by liver damage caused by certain toxic substances and is caused by a number of hepatotoxins. The hepatoprotective activity experiment was conducted to comprehensively evaluate the effectiveness of the biologically active supplement M-1 and select the most promising dose with hepatoprotective activity. For this purpose, the obtained M-1 sample was tested in a CCl4-induced acute toxic hepatitis model in mice.

The experiments were conducted on healthy, male white laboratory mice with a body weight of 20±2.0 g, which had passed the quarantine period for 10-14 days. Six mice were taken for each group, totaling 30 mice. To create an acute toxic hepatitis environment, the LD50 dose of CCl4, which causes necrosis of hepatocytes, was used. According to the experiment conducted on mice on the acute poisoning properties of the studied sample, it was 2.7 ml/kg of animal body weight. In order not to cause damage (burns) to the animal, CCl4 was introduced into it mixed with olive oil, maintaining the appropriate dose in a 1:1 ratio [3.4].The results obtained were compared with intact and control mice, which were divided into the following groups:

The experimental groups consisted of I - intact (healthy), II - control group (CCl4 + water); III - (CCl4 + 5 ml / kg of M-1 sample); IV - (CCl4 + 10 ml / kg of M-1 sample), V - (CCl4 + 15 ml / kg of M-1 sample). 1 hour after the introduction of tetrachloromethane into the abdominal cavity of mice at a dose of 2.7 ml / kg, M-1 sample was administered in doses of 5, 10 and 15 ml / kg, and the control group animals were given purified water in an equivalent volume (10 ml / kg) for 5 days using a special probe. After 5 days, its hepatoprotective effect was evaluated by the following parameters: survival (%), life expectancy (in days), liver weight ratio (relative to body weight) and the dynamics of body weight of animals. For the comparative evaluation of the obtained results, the coefficient of hepatoprotective activity (GFK) was determined as follows:

$$GFC = (N - T)/(N - I)$$

where: I – intact group (healthy), T – experimental group animals, N – control group (untreated) animals results.

General GFK was determined by four parameters as follows:

$$GFCum. = \sum GFC/4.$$

According to the level of hepatoprotective activity: GFK>0.7 high level; GFK>0.40-0.69 medium level; GFK>0.20 - 0.39 is a relatively low level; GFK>0.20 has no hepatoprotective activity.

On the 6th day of the experiment, the animals were anesthetized with chloroform, decapitated, and examined to determine the differential efficacy and mechanisms of pathological changes. The results of the study were statistically processed using Microsoft Excel using conventional methods to determine the mean value (M) and the standard error of the mean (m); differences according to the Student’s test (t) were considered statistically significant at the $p<0.05$ level.

OBTAINED RESEARCH RESULTS

In mice the effect of the M-1 sample on CCl4-induced toxic hepatitis was studied by treating it with doses of 5 ml/kg, 10 ml/kg, and 15 ml/kg for 5 days.

The obtained results are presented in table below.

Evaluation of the effect of M-1 sample against acute toxic hepatitis induced in mice, (M±m, n=6)

Groups	Survival rate, (%)	Life expectancy (in days)	Weight coefficient of the liver	Dynamics of body weight, g	Σ GFC
Intact	100	6.0	50.36±1.42*	(+) 2.00 ± 0.24	1
Control	33.3	3.0	66.57± 4.9	(-) 2.17 ± 0.28	0
High level of hepatoprotective activity					
10 ml/kg	83.3	5.8	55.71±2.03*	(+)1.70±0.33	0.76
Moderate level of hepatoprotective activity					
15 ml/kg	50	5.0	58.1±4.09	(-)1.33±0.08*	0.40
Relatively low level of hepatoprotective activity					
5 ml/kg	50	4.0	58.66± 3.66	(-) 1.5 ± 0.31	0.30

Note: *$p<0.05$ significant differences compared to the control group.

During the experiment, the survival rate of mice in the intact group was 100%, while in the control group (CCl4 + water) this indicator was 33.3%, and death was recorded in 4 out of 6 animals. The average life expectancy was 3 days, and the dynamics of body weight decreased by 2.17 ± 0.28 grams, or 16.5%, compared to the initial body weight. The liver weight coefficient in the intact group was 50.36 ± 1.42, and in the control group it increased by 1.32 times compared to the intact one, to 66.57 ± 4.9, and when compared with each other, a statistically significant difference was observed ($p < 0.05$).

Model M-15 ml/kg dosed animals had 50% viability, and the average life expectancy was 4 days, 1.3 times higher than the control group. The weight coefficient of the liver at this dose is 58.66±was 3.66, decreased compared to control but no statistically significant difference was observed. When evaluated according to the dynamics of body weight, the weight of the animals was 1.5±0.31 g, which decreased compared to the initial weight, and the differences were not statistically significant compared to the control. The 5 ml/kg dose of sample M-1 was 0.30 on GFK and showed a relatively low level of hepatoprotective activity.

Model M-1the survival rate of 10 ml/kg animals was 83%, and the life expectancy was 5.8 days, which was 1.93 times higher than the control group. The weight coefficient of the liver is 55.71 at the dose of 10 ml/kg of this sample±2.03 is,achieved a statistically significant difference compared to the control,($p<0.05$). When assessed by body weight dynamics, the body weight of mice increased by 1.70±0.33 grams compared to the initial one, and the differences were statistically significant compared to the control ($p<0.05$). The level of GPC at a dose of 10 ml/kg of M-1 showed an indicator of 0.76, indicating a high level of hepatoprotective activity.

Model M-1 administered to mice at a dose of 15 ml/kg, the survival of the animals was 50%, and the life expectancy was 5 days, which was 1.66 times longer than the control group. The weight coefficient of the liver is 58.1 at this dose±It is 4.09,did not reach a statistically significant difference when compared to the control, but when assessed by the dynamics of their weight, their body weight decreased by 1.33±0.08 grams compared to the initial one, and the differences were statistically significant compared to the control ($p<0.05$). The level of GFR at a dose of 15 ml/kg of M-1 was 0.40, indicating a moderate level of hepatoprotective activity.

So, when the hepatoprotective activity of the M-1 sample was studied in the acute toxic hepatitis model induced in mice, it was found that the M-1 sample had a high level of GFK at a dose of 10 ml/kg, a medium level at a dose of 15 ml/kg, and a relatively low level of hepatoprotective activity at a dose of 5 ml/kg.

CONCLUSION

Tetrachloromethane in an acute toxic hepatitis model induced using sample M-1 was administered to mice at doses of 5, 10 and 15 ml/kg for 5 days, the highest level of GFK was recorded at the dose of 10 ml/kg. A medium level of GFK was recorded at a dose of 15 ml/kg, and a relatively low level of activity was recorded at a dose of 5 ml/kg of the sample.

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