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DETERMINATION OF THE EFFECT OF RUTAN ON DRUG BIOTRANSFORMATION AND GLUCURONIDATION IN A MODEL OF ACUTE TOXIC HEPATITIS

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ABSTRACT

As a result of the experiment, in acute toxic hepatitis with SsL4 (tetrachloromethane), Rutan polyphenol isolated from the tannin plant Rhus coriaria L. is shown to reduce barbituric sleep due to its effect on drug biotransformation and glucuronidation. These results restore the functional activity of monooxygenase enzyme systems of hepatocytes, which is the basis of the beneficial effect of legalon and rutan on the bile production function of the liver in acute toxic hepatitis.

***Keywords**: tetrachloromethane, biotransformation, glucuronidation, barbituric sleep*

АННОТАЦИЯ

Эксперимент натижасида CcL_4 (тетрахлорметан)ли ўткир токсик гепатитда танинли ўсимлик Rhus coriaria L. дан ажратилган Рутан полифенолининг дорилар биотрансформацияси ва глюкуронизациясига таъсири туфайли барбитурик уйқуни қисқартиришида намоён бўлади. Бу натижалар ўткир токсик гепатитда легалон ва рутаннинг жигарнинг сафро ҳосил қилиш функциясига фойдали таъсирининг асосини ташкил этувчи гепатоцитларнинг моноксигеназа фермент тизимларининг функционал фаоллигини тиклайди.

***Калит сўзлар**: тетрахлорметан, биотрансформация, глюкуронизация, барбитурик уйқу.*

INTRODUCTION

In the world, pharmacotherapy of chronic liver diseases, especially treatment of viral hepatitis and liver cirrhosis, prevention of their consequences remains a medical and social problem. Despite the development of prevention and diagnosis of liver diseases, and the development of treatment methods, the death rates from these diseases are taking the leading places. According to the World Health Organization, "liver disease is the tenth leading cause of death among all diseases." Despite the development of a number of recommendations worldwide in recent years, there is a

sharp difference between the drugs used in the pharmacotherapy of liver diseases and the drugs specified in the treatment standards.

The scientific and research work conducted in the field of pharmacotherapy of hepatobiliary system diseases in our republic shows the following shortcomings: different approaches to treatment, low level of provision of antiviral and hepatotropic drugs, different dosage of drugs, short-term treatment, lack of dynamic monitoring of treatment, polypharmacy and lack of correction of risk factors. Uzbekistan belongs to the hyperendemic region due to the different levels of virus infection in the region due to the medical and social conditions (uniqueness of the number of family members, age structure) and the ethnic identity of the local population. In screening studies conducted by a number of authors, it was found that 5.6% of healthy population tested in our country have anti-HCV and 8.3% have HBsAg.

In Uzbekistan, as in other post-Soviet countries, it was found that there is a constant financial disparity between the use of new innovative methods, including expensive modern treatment methods and drugs, and the financing of the health care system. Therefore, analysis of the economic feasibility of using hepatotropic and antiviral drugs belonging to different clinical pharmacological groups, taking into account the effectiveness and safety of these drugs, remains a very urgent issue.

The purpose of the work: to determine the duration of chloral hydrate sleep and etaminal sodium sleep in animals treated with legalon and rutan in the model of acute toxic hepatitis.

MATERIALS AND RESEARCH METHODS

In the experiment, 24 white male rats were isolated and divided into 4 groups. SsL4 (tetrachloromethane) was injected into the body for 4 days and the hepatitis model was called. The 1st group was the control group, the 2nd group was the hepatitis model, and the untreated group, the 3rd group was treated with legalon capsules at a dose of 100ml/kg, and the 4th group was treated with rutan drug at a dose of 25mg/kg orally for 6 days. 24 hours after treatment, chloral hydrate sleep duration and ethaminal sodium sleep duration were determined in animals. For this purpose, chloral hydrate solution in a dose of 300 mg/kg, aqueous solution of ethaminal sodium in a dose of 50 mg/kg was injected into the abdominal cavity. The duration of recovery of the lateral position and turning reflex in rats was determined and the results were studied.

All experiments were conducted in compliance with the requirements of the European Convention for the Protection of Vertebrate Animals Used for

Experimental or Other Scientific Purposes (Strasbourg 1986). The results obtained from the study were statistically processed using the Biostat 2009 software package, and the data were presented as the mean (M) and the error of the mean (μ). A difference at a probability level of 95% and above ($p < 0.05$) was considered as statistically significant change.

RESEARCH RESULTS AND THEIR DISCUSSION

In order to assess the intensity of the biotransformation processes of xenobiotics in the liver using the monooxygenase system in vivo, experimental studies, for example, using test drugs such as sodium ethaminal, the duration of sleep depends on the intensity of its metabolism. Taking this situation into account, we studied the effects of legalon and rutan on the duration of sleep with etaminal sodium during therapeutic use in a series of separate experiments in a comparative aspect. The results of this series of experiments showed that in the group of rats with acute toxic hepatitis, barbiturate sleep was 178.2 ± 15.23 minutes, and in healthy rats it was 82.4 ± 3.74 minutes, that is, compared with acute hepatitis, the duration of the hypnotic effect of ethaminal sodium was 116.3% (more than twice) extended. Therefore, it can be assumed that the intensity of biotransformation of this barbiturate slows down significantly in acute toxic hepatitis.

The effect of rutan on the biotransformation and glucuronidation of drugs was determined in the model of acute toxic hepatitis

Group	Ethaminal sodium sleep (min)	Chloral hydrate sleep (min)
Healthy	82,4±3,74	75,7±3,41
Hepatitis	178,2±15,23*	168,2±13,77*
Hepatitis+Legalon	119,1±6,15*#	98,7±4,10*#
Hepatitis+Rutan	96,5±5,98#	82,5±4,49#

Note:*-differentiation compared to the indicators of a healthy group is reliable; # difference of hepatitis+Legalon and hepatitis+Rutan groups compared to other group indicators is reliable

This fact is consistent with the results of other researchers. Conversely, after experimental therapy, sleep duration was reduced: 33.2% in the group of rats treated with legalon, and 45.8% in the group treated with rutan. At the same time, the duration of the hypnotic effect of etaminal sodium does not differ statistically significantly from the value of healthy rats. These data allow us to conclude that the hepatoprotector "Legalon" and especially in rats with acute toxic hepatitis, rutan clearly restores the functional activity of the monooxygenase system, which is manifested in the reduction of barbituric sleep due to the acceleration of the drug's biotransforma. These results fully confirm the assumption that the functional activity of monooxygenase enzyme systems of hepatocytes is the basis of the beneficial effect of legalon and rutan on the bile production function of the liver in acute toxic hepatitis caused by tetrachloromethane.

CONCLUSION

1. Acute toxic hepatitis caused by tetrachloromethane is accompanied by a significant decrease in the exocrine function of the liver and the main components of bile.

2. Rutan exhibits clear choleretic activity in acute toxic hepatitis caused by tetrachloromethane.

3. During the therapeutic use of legalon and rutan, the duration of barbituric sleep decreased. This allows us to conclude that rutan clearly restores the functional activity of the monooxygenase system in rats with acute toxic hepatitis, which is manifested in the reduction of barbituric sleep due to the acceleration of the drug's biotransform

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