



# International Journal for Innovative Engineering and Management Research

A Peer Reviewed Open Access International Journal

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IJIEMR Transactions, online available on 19th April 2021.

Link: <https://ijiemr.org/downloads/Volume-10/Issue-4>

**DOI: 10.48047/IJIEMR/V10/I04/67**

Title: **Investigation of Rutan's choleric activity in drug hepatitis**

Volume 10, Issue 04, Pages: 275-278

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## Investigation of Rutan's choloretic activity in drug hepatitis

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**Abstract:** The experiment established a high hepatoprotective and choloretic activity of Rutan polyphenol in paracetamol hepatitis. It is believed that Rutan can be recommended in practical medicine as a means of pathogenetic treatment of hepatitis of various etiologies, including infectious toxic pathologies of the hepatopancreatobiliary system.

**Keywords:** paracetamol, legalon, bile secretion.

### Introduction

One of the important problems of modern medicine is to increase the effectiveness of treatment of diseases of the hepatobiliary system because acute and chronic hepatitis is a serious problem, due to their widespread distribution and an increase in the incidence rate. Today, this pathology has acquired great social significance, causing significant damage to society, and their wide spread threatens the health of the population and future generations (WHO Information Bulletins, 2014,2015). The problem of prevention and treatment of diseases of the hepato-biliary system still remains completely unsolved [2]. In solving this problem, the leading role belongs to pharmacotherapy. However, the therapeutic efficacy of the drugs used in modern practical medicine for the prevention and treatment of hepatitis is insufficient [3]. In accordance with the modern principles of the treatment of liver diseases, the program of complex therapy for this pathology corresponds to pathogenetic therapy aimed at adequate pharmacological correction of the universal links of the pathogenesis of the disease. In recent years, the arsenal of modern hepatoprotective drugs has expanded both due to the emergence of synthetic drugs and new natural remedies. In general, the range of medicines used in the complex therapy of liver and biliary tract diseases includes more than a hundred names. However, among such a variety of drugs, there is a relatively small group of hepatoprotectors that have a selective effect on the liver [2,3]. Taking into account the

prevalence of drug-induced liver disease, it seems important to study the effectiveness of hepatoprotectors in the correction of liver dysfunction in drug-induced hepatitis.

**The aim of this work was a comparative study of the effect of Legalon and Rutan on the biliary function of the liver in acute hepatitis induced by paracytamol.**

### Material and methods.

The choice of paracytamol in the amount of hepatotoxin was due to the fact that it is a drug that often causes liver damage. [V.T. Ivashkin and employees 2019].

The experiments were carried out on 24 sexually mature male rats with an initial weight of 180-220 g. The animals were kept in standard vivarium conditions with free access to food and water. The experiments were carried out in accordance with the "Rules for Conducting Work with the Use of Experimental Animals", as well as the rules adopted at the European Convention for the Protection of Vertebrate Animals used for Experimental Research or for Other Scientific Purposes (ETS No. 123) Strasbourg, 18.03.1986. The experiment was carried out in 4 groups of animals, 6 individuals in each. The first group consisted of healthy animals, while in the rest the model of drug-induced hepatitis was reproduced by introducing paracytamol into the body at a dose of 1500 mg / kg. [Pashko, Buniatia]. A day after the last injection of

hepatotoxin, one group received Legalon at a dose of 100 mg / kg for six days, and the other Rutan at a dose of 25 mg / kg. An untreated group of rats received an adequate amount of boiled water. In 24 hours after the last administration of the drugs, the external secretory function of the liver and the chemical composition of bile were studied in all groups of animals using the methods described by us earlier. [12,13,14]. The results of the experimental studies were processed statistically using the standard StatPlus 2009 software package according to well-known methods of variation statistics with an assessment of the significance of indicators ( $M \pm m$ ) and the differences of the samples under consideration by the Student's t-test. The difference was considered significant at a probability level of 95% or more ( $p < 0.05$ ).

### **The result of their discussion**

The results and experimental studies have shown that the investigated drugs have a distinct positive effect on the biliary function of the liver in acute drug-induced hepatitis induced by paracytamol. So, if in control (untreated) animals the volume of excreted bile for 4 hours of the experiment in terms of 100 g of the body weight of animals decreases by 31%, compared with healthy animals, then in rats treated with Legalon, it increases by 41%. We noted such a change in direction, as can be seen from the data given in the table, and in animals treated with Rutan.

It is noteworthy that after the treatment with the latter, the value of the exocrine function of the liver does not statistically significantly differ from that of healthy rats. A clear positive effect is observed when studying the influence of Rutan in comparison with Legalon on the content of the main components of bile in acute medicinal hepatitis.

The level of the total content of bile acids in bile in control animals is statistically significantly reduced in comparison with the values of intact rats by 27.7%, while in rats treated with Legalon and Rutan it, on the contrary, increased by 24.4 and 27.4%.

correspondingly and practically reached the level of healthy rats. Against this background, under the influence of experimental pharmacotherapy, their excretion of cholesterol in bile was also restored. So, if in rats with acute drug hepatitis the level of the latter statistics significantly decreased by 29.5% compared with healthy rats, then in those treated with Legalon it increased by 24.5%, and in those treated with Rutan - by 32. It is noteworthy that in those treated with Rutan, the amount of released cholesterol does not statistically significantly differ from the values of intact animals. We found a similar positive effect of pharmacotherapy by Legalon and Rutan when we studied the effect of these drugs on the excretion of bilirubin in bile. From the data in the table, it can be noted that in untreated rats, in comparison with healthy rats, the content of bilirubin in the bile of the experiment carried out for 4 hours decreased by 37.1%, while in those treated with Legalon and Rutan it increased by 52.3% and 48.9% respectively. From the above experimental material, it can be seen that the experimental therapy with Rutan made it possible to fully eliminate violations of the exocrine function of the liver and the chemical composition of bile in acute drug-induced hepatitis induced by paracytamol. It can be seen that, in terms of its pharmacological activity, Rutan is not inferior to the well-known hepatoprotector Legalon (and by some indicator it even somewhat surpasses it). The positive effect of Rutan on the functional state of the liver, and in particular, on the biliary process, is probably associated with the suppression of the process of free radical oxidation of lipids of the membranes of hepatocytes, because the drug is a polyphenolic compound characterized by the presence of antioxidant properties [9]. Under these conditions, damage to membranes is eliminated and favorable conditions are created for reparative and biosynthetic processes. This assumption is in good agreement with the data of the authors investigating the effect of Rutan on the functional and metabolic parameters of rat liver mitochondria under heliotrin intoxication. Treatment with Rutan eliminated



disturbances in the functional and metabolic parameters of liver mitochondria not only during the oxidation of FAD-dependent substrates, but also of NAD-dependent substrates. At the same time, in rats treated with Rutan, protein biosynthesis is restored by 19-30.5% [11]. It can be assumed that under the influence of Rutan, the synthesis of mitochondrial proteins, including the enzymes of this organoid, is enhanced, which leads to an increase in energy production and the maintenance of a high degree of conjugation of oxidative phosphorylation processes. As you know, the process of synthesis of bile acids from cholesterol and conjugation of bilirubin with glucuronic acid occurs in the cytoplasmic reticulum of hepatocytes, where the monooxygenase enzyme system is localized.

The functional activity of the latter during intoxication with paracetamol is probably significantly inhibited, which manifests itself in a significant decrease in the externally secretory function of the liver and the content of bile acids, cholesterol and bilirubin in bile [3,4].

Considering the fact that pharmacotherapy with Rutan in rats with drug-induced hepatitis restores the biliary function of the liver, it can be argued that under the influence of Rutan, the functional and metabolic parameters of not only mitochondria, but also the cytoplasmic reticulum of hepatocytes are restored. All this ensures the functioning of the liver at the level of healthy animals. Thus, based on the results of the experimental studies, it can be concluded that Rutan has a distinct choleric property that manifests itself in conditions of significant inhibition of the functional state of the liver induced by paracetamol.

The influence of Legalon and Rutan on the biliary function of the liver in acute

toxic hepatitis induced by paracetamol

(for 4 hours per 100 g of body weight)

Group	Bile, ml	Ogk mg	Cholesterol mg	Bilirubin, mcg
Intact	1,47 ± 0,106	5,56 ± 0,42	0,278 ± 0,009	124,6 ± 4,68
Hepatitis	1,01 ± 0,087*	4,02 ± 0,25*	0,196 ± 0,007*	78,4 ± 3,67*
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Hepatitis +Legalon	1,42 ± 0,065#	5,00 ± 0,44	0,244 ± 0,012#	119,4 ± 5,50#
Hepatitis +Rutan	1,37 ± 0,081*	5,12 ± 0,31 #	0,260 ± 0,008#	116,7 ± 3,37 #

Note: \* statistically significant differences compared to intact animals

# - statistically significant differences in comparison and hepatitis.

### Conclusions:

1. Paracetamol in rats induce acute toxic hepatitis characterized by significant impairment of bile fission function of the liver.
2. Experimental therapy by Legalon and Rutan have a clear correcting effect on the excretory function of the liver and the chemical composition of bile.
3. In terms of its pharmacological activity, Rutan is not inferior to the well-known hepatoprotector Legalon.
4. Rutan can be recommended as a choleric agent for diseases of the hepatobiliary system

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