The effect of sumedazole (hexaaquagexaimidazole copper (II) sulfate) on the functional state of the liver

Kenzhekan Isakova[1*], *Momun* Arzybaev[2], *Nazira* Shiytyeva[3], *Ainura* Malabaeva[3], *Erkinbek* Isakov[4], and *Noomanbek* Djaparov[5]

[1]Osh State University, Osh, Kyrgyz Republic
[2]K.I.Scriabin Kyrgyz National Agrarian University, Bishkek, Kyrgyz Republic
[3]Institute of Chemistry and Phytotechnologies of the National Academy of Sciences of the Kyrgyz Republic, Bishkek, Kyrgyz Republic
[4]I.K. Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyz Republic
[5]I. Arabaev Kyrgyz State University, Bishkek, Kyrgyz Republic

Abstract. The effect of sumedazole (hexaaquagexaimidazole copper (II) sulfate) on excretory and neutralizing liver functions in rabbits and white mice was studied by phenolphthalein loading and hexanal assay methods. It was found that the drug sumedazole (hexaaquagexaimidazole copper (II) sulfate) does not have a significant harmful effect on the physiological function of the liver.

1 Introduction

The liver is a large lobular gland of the animal body, involved in the processes of digestion, metabolism, blood circulation, and maintaining the constancy of the internal environment of the body [1-20]. Liver weight varies depending on the type of animal: cows 3.2—3.4 kg, sheep up to 800 g, pigs up to 1.5 kg, horses 1.5—3.5 kg [6].

The liver performs a variety of functions in the body, the most important of which are barrier, homeostatic, synthetic, neutralizing, depositing, metabolic, excretory. In liver diseases, especially of infectious and toxic origin, significant metabolic disorders, immune response, detoxification and antimicrobial protection develop. In addition, most drugs are metabolized in the liver, which has a set of universal enzyme systems for this purpose. In this regard, it can be assumed that there are no drugs that, under certain conditions, would not cause damage to this organ [8].

Along with the most important metabolic processes in the liver, various foreign substances (xenobiotics) are detoxified, including allergens, poisons, toxins and medicines. This process occurs through the mechanisms of oxidation, reduction, methylation, acetylation and conjugation with other compounds. As a result, non-toxic and more easily excreted products are formed [13].

* Corresponding author: esenbekbelekuulu@gmail.com

All medicines are biologically active substances that have a therapeutic effect. The effect of chemical and medicinal substances on individual body systems is due to the chemical structure of drugs, their pharmacokinetics and metabolism, as well as various other patterns underlying the variability of effects.

Like no other organ, the liver is closely connected with metabolism, being a large chemical laboratory of the body. The liver performs a number of functions: protective, barrier, neutralizing and excretory. The process of neutralization of chemicals in the liver is carried out by oxidation, reduction, hydrolysis, deamination, decarboxylation and other chemical transformations. In turn, the neutralizing function of the liver depends on its excretory function [5].

In addition, liver function is closely related to other organs and systems: lungs, gastrointestinal tract, pancreas, kidneys, spleen, etc. Impaired liver function entails various disorders of the above-mentioned systems. In addition, the metabolism of drugs takes place in the liver.

The mechanism of action of drugs on the liver can be different depending on their chemical nature. Some drugs have an effect on the membrane of liver cells [18], others on transmembrane transfer of substances in the cell [19], and others on cell division [12]. All these processes ultimately lead to a change in the functional state of the liver.

Based on this, we conducted experiments to study the effect of the new anthelmintic drug sumedazole on the excretory and neutralizing function of the liver [11].

2 Materials and methods

The excretory function of the liver under the influence of sumedazole was studied by the method of intravenous bromosulfalein loading (BSF), proposed for the first time in 1925. The principle of the method is based on the fact that the paint bromosulfalein (sodium tetrabromophenolphthalein disulfonate) is secreted by the liver into bile, and under the influence of hepatotoxic drugs, the release of paint slows down and its content in the blood increases. The method is simple in technique and accurate in the results obtained. The experiments were carried out on 16 white rabbits with a live weight of 1.6-2.0 kg, which were divided into 3 experimental and 1 control groups of 4 heads each. The drug was administered orally to experimental animals in doses of 100, 300 and 500 mg / kg of live weight. BSF was injected into the right ear vein of experimental and control rats at a dose of 20 mg / kg in the form of a 5% solution 3 hours after giving sumedazole.

Experimental studies on the neutralization (antitoxic) liver function were carried out on 24 male white mice with a body weight of 28-32 g. using the “hexanal test” [10,13]. The principle of the method is that the criterion for evaluating the effect of the drug is the duration of hexanal sleep in experimental animals. According to its duration, the degree of negative effect of the test drug on the liver is judged.

Hexanal was administered to experimental and control animals at a dose of 60 mg / kg, intraperitoneally, 3 hours after giving sumedazole at doses of 100, 300 and 500 mg / kg. The duration of hexanal sleep was taken into account minute by minute from the moment of “lateral position of the animals” to the moment of “back up” [3,4,14].

3 The results of the study

The results of experiments to study the excretory function of the liver under the influence of the drug showed (Table 1) that 3 minutes after administration of sumedazole, the concentration of BSF in animals of the control group averaged 15.12 ± 0.23 mg/%. Oral

administration of sumedazole at doses of 100 and 300 mg/kg did not cause a significant delay in BSF in the total blood flow in animals, its indicators were close to the control ones and were 15.41±0.3 and 15.53±0.48 mg/%. When a five-fold therapeutic dose (500 mg / kg) of sumedazole is administered, a slightly increased concentration of BSF is observed with a value of 16.42 ± 0.26 mg /%. The marked difference in the concentration of BSF compared with the control parameters is not statistically significant (P >0.05).

Table 1. The effect of sumedazole on the excretory function of the liver (bromsulfalein test (BSF), rabbits, n=4)

Time of taking blood, min	Concentration of BSF in blood plasma, mg/%			
	Control group	The dose of the medicine, mg / kg		
		100	300	500
3	15,35	15,15	15,30	17,19
	14,50	16,30	16,20	16,15
	15,20	14,60	15,20	16,20
	15,45	15,61	15,45	16,17
	15,12 ±0,23	15,41±0,31 P >0,05	15,53±0,48P >0,05	16,42 ±0,26 P >0,05
45	5,30	5,97	6,22	7,10
	5,32	6,04	6,19	6,40
	5,30	6,10	6,25	6,20
	5,28	6,07	6,20	6,00
	5,30±0,97	6,04±0,03 P >0,05	6,21±0,12 P	

Measurement of the concentration of BSF in the blood of control and experimental rabbits showed that it decreased significantly in all animals and in animals of the control group amounted to 5.30±0.97 mg/%, and in the experimental groups 6.04±0.03 mg/%, 6.21±0.12 mg/% and 6.42±0.26 mg/%, respectively.

As can be seen from the above data, there is also a tendency for a slight increase in BSF values in the blood of animals as the dose of the drug increases. Although the differences are statistically unreliable (P>0.05), these digital data indicate a certain effect of the studied drug on liver function in experimental animals, proving its biological activity [11].

The results of experiments on the study of the neutralizing function of the liver of animals under the action of sumedazole showed (Table 2) that with oral administration of it.

Table 2. The effect of sumedazole on the neutralization liver function (hexenal test, white mice, n=6)

Group	Dose, mg/kg	Duration of hexenal sleep, min. M ± m	P
1st	100	30,12	>0,05
		32,40	
		30,45	
		30,25	
		30,80 ±0,52	

2nd	300	30,20	>0,05
		32,45	
		32,50	
		31,15	
		31,82 ± 0,36	
3rd	500	34,35	>0,05
		32,20	
		32,45	
		31,50	
		130,5	
		32,62± 1,04	
Control group	-	29,42	
		32,35	
		30,45	
		31,32	
		30,38 ± 0,72	

When administered at doses of 100, 300 and 500 mg / kg, the sleep state in animals under the action of gesanal lasted 30.80 ± 0.52; 31.82 ± 0.36 and 32.62 ± 1.04 minutes, respectively, with a control value of 30.38 ± 0.72 minutes. In these experiments, there is also a tendency to prolong the sleepy state of mice with increasing doses of the drug. Although the difference in readings compared to the control indicators is not statistically significant (>0.05).

4 Discussion

Summarizing the results of experiments to study the effect of sumedazole on liver function, it should be noted that the drug administered orally at a therapeutic dose of 100 mg / kg and in 3 and 5 times increased doses does not significantly disrupt the neutralizing function of the liver.

As can be seen from these data, the duration of hexanal sleep under the influence of therapeutic (100 mg/kg) and 3 (100 mg/kg) and 5 (100 mg/kg) times increased doses of sumedazole in both control and experimental animals did not significantly differ (>0.05). The observed tendency of BSF retention in the blood and an increase in the duration of hexanal sleep with an increase in the dose of the drug was statistically unreliable, this confirms the harmlessness of the drug on this liver function.

Similar experiments were conducted by M.T.Toimbetov [15] to study the effect of the new anthelmintic almegum [9] on the functional state of the liver of white rats. At the same time, it was found that the drug administered orally at a therapeutic dose of 50 mg/kg and in three (150 mg/kg) and eight times increased (400 mg/kg) doses did not significantly violate the excretory and neutralizing liver functions of these animals. N.A.Azhybekov [1] reports

that the anthelmintic alpemedium [10] in therapeutic (25 mg/kg) and five-fold increased (125 mg/kg) doses has no significant effect on rat liver function.

5 Conclusions

The new anthelmintic drug sumedazole in experimental conditions on laboratory animals (white mice, rabbits) in therapeutic and 3 and 5 times higher doses statically does not significantly have a harmful effect on the excretory and neutralizing functions of the liver of animals.

References

1. N.A. Azhybekov, Abstract. Dissertation of the Candidate of Veterinary Sciences. (Moscow, 2010)
2. I. T. Abasov, Klin, med. **40**, 9, 121 (1962)
3. M.A. Belousova, Tr. VIGIS. **23**. 25-31 (1977)
4. V.F. Gladkikh, H.I. Seyfula, E.V. Sazanova, Pharmacological study of new anthelmintic drugs - phenasal, dichlorophene and combination //Tez. dokl. conf. of Pharmacologists (M., I965)
5. L.M. Golber, Essays on the physiology and pathophysiology of the hepatolienal system (M. : Medicine, 1977)
6. A.P. Kostin, F.A. Meshcheryakov, A.A. Sysoev, Physiology of agricultural animals (Publishing house: M.: Kolos, 1983)
7. A.S. Loginov, V.I. Fomichev, The clinical significance of the bromosulfan test in chronic hepatitis and cirrhosis of the liver, in the book: Actual, vopr. gastroenterol., edited by V. X. Vasilenko, M., **4,** 364 (1971)
8. O.N. Minushkin, Some hepatoprotectors in the treatment of liver diseases. Lech doctor **6:** 55-58 (2002)
9. Patent No. 889. 07/31/2006. The Kyrgyz Republic. Cu (I) complex with humate and 5-(propyl-thio)-1-n-benzimidazole-2-yl-carbamate, which has anthelmintic activity. [Text]/ Zhorobekova Sh.Zh., Toimbetov M.T. et al.
10. Patent No. 1019. 02/29/2008, Kyrgyz Republic. Albendazole and copper pectinate, which has anthelmintic activity. [Text]/ Zhorobekova Sh. Zh., Koroleva R. P. Azhybekov N. A., et al.
11. Patent KG No.2280 03/31/2022 "Application of the compound hexaaquagexaimidazole copper (II) sulfate as an anthelmintic agent" [Text] / [Arzybaev M., Shytyeva N. et al.].
12. A.A. Pokrovsky, L.P. Korystev, Liver, lysasomes and nutrition. Sofia. pp.145-163 (1977)
13. T.A. Popov, A.M. Jenev, Toxicity of oleandomycin phosphate when administered by inhalation in an experimental production model (M.:1973)
14. V.A. Ryabova, Byull. VIGIS **13**. 94-101 (1974)
15. M.T. Toimbetov, *The influence of almegum on the functional state of the liver* //Mat of the scientific conference "Theory and practice of combating parasitic diseases. Issue 6. –pp. 48-49 (M., 2006)

16. Anthony L. Mescher. Junqueira's basic histology : text and atlas. (Thirteenth edition. New York, 2013)
17. T. Balazs, T,R., Marrey et al. Toxicol. appl. Phamacol. **3**, 71 (1961)
18. D. Brandes, E. Anton, B. Schofield, S. Barnard, Role of lysosomal labilizers in treatment of mammary gland carcinomas with cyclophosphamide (NSC-20271)-preliminary report. Cancer Chemother. Rep.50,47 (1966)
19. Fell H. B., J. T. Dingle. Biochem J. **87(2):** 403–408 (1963).
20. Rosentha1 S. M., White E.C. Journal of the American Medical Association**. 4,** 1112 (1925)