into the common bile duct. The degree of choleretic activity of the phenolic compound complex isolated from hexaphyte was estimated by the secretion rate and by the total amount of bile secreted, which was collected every hour for 4 hours, as well as by the content of bile acids in bile.

The antioxidant activity of the complex of phenolic compounds isolated from hexaphyte was determined by its intragastric course application in the indicated doses one time per day for 10 days. The medicine was applied to rats suffering from tetrachloromethane (CCl4) hepatitis, starting from 2 days after the first injection of the damaging agent. Liver damage was induced by intragastric administration to rats of a 50% oil solution of carbon tetrachloride in a volume of 0.4 ml/100g of an animal weight, one time per day for 4 days [2]. The control group rats received water purified in an appropriate volume according to a similar scheme. The analysis were carried out after 7, 14 and 21 days from the start of the experiment. To assess the free radical lipid oxidation, the method of lipid chemiluminescent analysis was used. Spontaneous chemiluminescence of liver lipids, as well as induced luminescence of homogenate from this organ was recorded on a special quantum-meter installation designed to measure weak light fluxes [3]. Lipids were extracted from liver tissue according to the method of Folch J. et al. [10] with a chloroform-methanol mixture freshly prepared in a 2:1 ratio by volume.

The results of the studies were processed statistically using Microsoft Office Excel 2007, Statistica 6.0. Arithmetic mean (M), arithmetic mean error (m) were calculated. The normality of the distribution of variables was determined based on distribution histograms, asymmetry values and excesses. The Student's parametric t-criterion was used to evaluate the validity of the differences in samples close to the normal distribution. Differences between the compared values considered significant at the level of the probability of 95% and more ($p < 0.05$) [1].

Results and discussion. In order to clarify the mechanism of hexaphyte action, special experiments were carried out with the introduction of a complex of phenolic compounds isolated from it to rats.

Primary, the rats were arranged into following groups: the control (8 rats), experimental 1 (8 rats), and experimental 2 (8 rats) ones. The complex of hexaphyte phenolic compounds was administered to intact rats of the experimental groups once per os in doses of 100 mg/kg or 500 mg/kg. The rats of the control group were injected in equivolume amounts of purified water according to a similar regimen.

The effect of the phenolic compound complex isolated from hexaphyte on the bile secretion in intact rats has been studied (Table 1).

Table 1

The effect of the hexaphyte phenolic compound complex on bile secretion in intact rats

Group of animals	Dose, mg/kg	Bile secretion rate, mg/min per 100.0g				
		1 hour	2 hour	3 hour	4 hour	5 hour
Control	-	4.1±0.3	4.3±0.4	3.9±0.4	3.2±0.1	2.8±0.2
Experimental 1	100	3.6±0.2	4.9±0.4	5.6±0.5*	4.7±0.4*	3.4±0.2
Experimental 2	500	4.2±0.2	5.9±0.5*	6.4±0.5*	6.4±0.5*	5.2±0.3*

Note. In the Tables 1-3 * - p-values <0.05 represented significant differences.

The results presented in the Table 1 show that the administration of above indicated phenolic compound complex to intact rats was accompanied by an acceleration in bile secretion. This specific pharmacological effect of the phenolic compound complex applied at a dose of 500 mg/kg was more pronounced than at a dose of 100 mg/kg. The choleretic reaction under these conditions was longtime; it took 4-5 hours. Thus, the choleretic action of the phenolic compound complex isolated from hexaphyte is established.

The effect of the phenolic compound complex isolated from hexaphyte on bile acid content in bile in intact rats was studied (Table 2).

Table 2

The effect of the hexaphyte phenolic compound complex on the bile acid content in the bile of intact rats

Group of animals	Dose, mg/kg	Bile acid content per 1 hour, mg/100.0g				Total cholate per 4 hours, mg/100.0g
		2 hour	3 hour	4 hour	5 hour	
Control	-	1.50±0.4	1.35±0.3	0.80±0.4	0.61±0.1	4.26±0.3
Experimental 1	100	1.80±0.4	2.80±0.6*	2.19±0.5*	1.25±0.4*	8.04±0.5*
Experimental 2	500	2.46±0.4	2.56±0.5*	2.77±0.5*	2.08±0.2*	9.87±0.5*

The administration of above indicated phenolic compound complex to intact rats was accompanied by increase in bile acids biosynthesis, due to this, their content in the secreted bile increased by almost 2 times compared with the data in the control. The established pharmacological effect of the phenolic compound complex at 500 mg/kg was also more pronounced than when used at 100 mg/kg. As a result of the experiments carried out, the cholate-forming and cholate-releasing effects of the amount of phenolic compound complex studied were determined.

Subsequently, in accordance with the objectives of the study, special experiments were conducted to evaluate the antioxidant effect of the hexaphyte phenolic compound complex. In a model of toxic hepatitis caused by the introduction of carbon tetrachloride to rats, the changes in free radical oxidation rate of liver lipids under the influence of the plant phenolic complex has been studied.

Primary, the rats were arranged into following groups: intact (24 rats); control (24 rats), experimental 1 (24 rats); experimental 2 (24 rats) ones. Animals of the first experimental group were administrated with hexaphyte phenolic compound complex into the stomach through a tube in a dose of 100 mg/kg, one time per day for 10 days, starting from 2 days after the first injection of the damaging agent. Animals of the second experimental group were administrated with hexaphyte phenolic compound complex in a dose of 500 mg/kg according to a similar regimen.

The animals of the control group were injected with purified water in equivolume amounts according to a similar regimen. Intact animals were used as an additional control group.

The parameters of liver lipid chemiluminescence under the influence of

a complex of extracted phenolic compounds in experimental (CCl4) hepatitis in rats were changed in time; it was evaluated on days 7, 14 and 21 (Table 3).

Table 3

Changes in liver lipid chemiluminescence (imp./s) under the influence of the extracted phenolic compound complex in experimental (CCl4) hepatitis in rats

Liver lipid chemiluminescence indices				
Research term	Liver lipid chemiluminescence indices in intact rats	in rats suffering from experimental hepatitis (control)	Liver lipid chemiluminescence indices in rats suffering from experimental hepatitis treated with hexaphyte phenolic compound complex at a dose of:	
			100 mg/kg	500 mg/kg
7-e	51.5±3.8	153.6±15.4	113.3±10.3*	101.0±9.5*
14-e	49.2±5.9	168.2±6.2	112.2±7.2*	96.7±12.1*
21-e	47.5±3.2	75.0±9.0	62.4±7.4	63.2±3.1

The results of the study showed that the introduction of the hexaphyte phenolic compound complex can be recognizes by pronounced glow inhibition of liver lipids. Against the background of the introduction of the total complex of phenols at a dose of 100 mg/kg, the rate of radical reactions decreases by 15.2% - 33.3% depending on the timing of the study and the development of the pathological process in the liver.

A more pronounced inhibitory effect on the processes of free radical lipid oxidation in the damaged organ was found when the phenolic complex was applied at a dose of 500 mg/kg. At the hepatitis development time on days 7, 14 and 21, a decrease in the level of weak luminescence of liver lipids was 25.5%, 42.6% and 15.8%, respectively.

Thus, the intensity of free radical lipid oxidation under the influence phenolic compound complex isolated from extract "Hexaphyte" is significantly reduced. This ability of plant phenols is due to their membrane-stabilizing effect [6].

Having a membrane-stabilizing effect, phenolic compound complex isolated from hexaphyte can increase the functional activity of hepatocytes, and mobilize the reserve capabilities of the liver. As a result, functional and structural changes occur, which are manifested by an increase in biligenic process and bile excretion, by decrease in severe metabolic disorders and prevention of gross disorders in the structure of the hepatobiliary system organs.

Conclusion. The results of successive series of experiments to determine the role of phenolic compounds in the mechanism of action of "Hexaphyte" extract, including in the manifestation of choleretic activity, concluded that the phenolic compound complex isolated from hexaphyte had a positive effect on the manifestation of choleretic, antioxidant and membrane-stabilizing activity of extract "Hexaphyte".

References

1. Боровиков В.П. Популярное введение в современный анализ данных в системе STATISTICA. М.: Горячая линия. Телеком, 2014:288. [Borovikov VP. A popular introduction to modern data analysis in the STATISTICA system. M.: Goryachaya liniya, Telekom, 2014:288 (In Russ.)]

2. Буеверов А.О. Лекарственные поражения печени. *Российский медицинский журнал*. 2012; 3: 107-110 [Bueverov AO. Liver damage with drugs. *Rossijskij medicinskij zhurnal.* 2012; 3: 107-110 (In Russ.)]

3. Владимиров Ю.А. Свободные радикалы и антиоксиданты. *Вестник РАМН*. 1988; 7: 43-50. [Vladimirov YuA. Free radicals and antioxidants. *Vestnik RAMN*. 1988; 7: 43-50 (In Russ.)]

4. Государственный реестр лекарственных средств – URL https://grls.rosminzdrav.ru/ (дата обращения: 07.01.2020). [State Register of Medicines (In Russ.) – URL https://grls.rosminzdrav.ru/ (accessed on 07.01.2020)]

5. Лубсандоржиева П.-Н.Б. Разработка и стандартизация фитосредств для лечения и профилактики заболеваний органов пищеварения. Улан-Удэ: Изд-во БНЦ СО РАН, 2016:280. [Lubsandorzhieva P-NB. Development and standardization of herbal medicines for the treatment and prevention of digestive diseases. Ulan-Udeh: Izd-vo BNC SO RAN, 2016:280 (In Russ.)]

6. Николаев С.М. Фитофармакотерапия и фитофармакопрофилактика заболеваний. Улан-Удэ: Изд-во БГУ, 2012:286. [Nikolaev SM. Phytopharmacotherapy and disease phytopharmacoprophylaxis. Ulan-Udeh: Izd-vo BGU, 2012:286 (In Russ.)]

7. Руководство по проведению доклинических исследований лекарственных средств. Ч.1. М.: Гриф и К, 2012:944. [Guidelines for preclinical studies of drugs. Part 1. M.: Grif i K, 2012:944 (In Russ.)]

8. Ферубко Е.В., Николаев С.М., Даргаева Т.Д. Средство, обладающее желчегонной активностью, и способ его получения. Патент №2700681 Российской Федерации МПК A61K 36/185, A61K 36/28, A61K 36/738 A61K 36/534, A61K 36/484, A61P 1/16. Опубл. 19.09.2019, Бюллетень № 26. [Ferubko EV, Nikolaev SM, Dargaeva TD. Agent with choleretic activity, and method for its preparation. Patent No. 2700681 of the Russian Federation, IPC Codes A61K 36/185, A61K 36/28, A61K 36/738 A61K 36/534, A61K 36/484, A61P 1/16. Published 19.09.2019, Bulletin №26 (In Russ.)]

9. Циммерман Я.С. Нерешенные и спорные проблемы современной гастроэнтерологии. М.: МЕДпресс-информ, 2013:224. [Cimmerman YaS. Unresolved and controversial issues of modern gastroenterology. M.: MEDpress-inform, 2013:224 (In Russ.)]

10. Folch J [et al.] A simple method for the isolation and purification of total lipids from animal tissues. *J Biol Chem.* 1957; 226: 497–509.

11. Hirschfield GM [et al.]. Pathogenesis of cholestatic liver disease and therapeutic approaches. *Gastroenterology*. 2010; 139: 1481-1496. DOI: 10.1053/j.gastro.2010.09.004.

12. Samani MA [et al.] Medicinal plants with hepatoprotective activity in Iranian folk medicine. *Asian Pac J Trop Med*. 2015; 5(2): 146-157. DOI: https://doi.org/10.1016/S2221-1691(15)30159-3

13. Valero A [et al.] Natural products: Perspectives in the pharmacological treatment in gastrointestinal anisakiasis. *Asian Pac J Trop Med.* 2015; 8(8): 612-617. DOI: 10.1016/j.apjtm.2015.07.017

14. Zhang A [et al.] Recent advances in natural products from plants for treatment of liver diseases. *Eur J Med Chem.* 2013; 63:570-577. DOI: https://doi.org/10.1016/j.ejmech.2012.12.062