

STUDY OF CHRONIC TOXICITY OF THE DRUG PHYTOFERON

Tashkent State Pharmaceutical Institute

Kh. O. Darmanov

e-mail: khakim.darmanov@mail.ru

tel: +998994624052

The chronic toxicity of the tincture made from the collection "phytoferon" was studied in white rats in the experiment. The results showed that the drug is harmless to the body in amounts of 10 ml/kg and 25 ml/kg. The drug does not adversely affect peripheral blood-shaped elements, biochemical indicators and the histomorphological structure of internal organs in the amounts studied when administered for 30 days.

Base phrases: phytoferon, aggregate, tincture, white rat, peripheral blood, hepatocyte, enzyme, hemoglobin, erythrocyte, leukocyte, histomorphological, narcosis.

UNTERSUCHUNG DER CHRONISCHEN TOXIZITÄT DES ARZNEIMITTELS PHYTOFERON

Die chronische Toxizität der Tinktur aus der Sammlung "Phytoferon" wurde im Experiment an weißen Ratten untersucht. Die Ergebnisse zeigten, dass das Medikament in Mengen von 10 ml/kg und 25 ml/kg für den Körper unschädlich ist. Das Arzneimittel beeinträchtigt periphere blutförmige Elemente, biochemische Indikatoren und die histomorphologische Struktur innerer Organe in den untersuchten Mengen bei Verabreichung über 30 Tage nicht nachteilig.

Basisphrasen: Phytoferon, Aggregat, Tinktur, weiße Ratte, peripheres Blut, Hepatozyten, Enzym, Hämoglobin, Erythrozyten, Leukozyten, histomorphologisch, Narkose.

Synthetic drugs make up the majority of the drugs currently used in the treatment of patients in the world. Judging by the analyzes, drugs obtained by the synthetic method cause various unpleasant complications in patients. Herbal remedies are of great importance in medicine. Natural remedies have the property of selectively affecting the body. The pharmaceutical industry of our republic pays great attention to the production of medicines based on raw materials of natural medicinal plants [1]. Of the more than four and a half thousand plants found in our country, one thousand one hundred and fifty varieties are medicinal plants. It is known that tubule-leaved bullfinch (**flores Achilleae filipendulinae**), bird taron (**herba polygoni avicularis**), sweet brainstem (**radisex Glycyrrhizae**), water pepper (**herba polygoni hydropiperis**) and



medicinal chamomile (**Flores Shamomillae**) plants are common in the territory of the Republic. They are used in folk medicine on a large scale in anti-inflammatory, pus-driven, accelerating blood clotting, enhancing substance metabolism, reducing blood sugar levels, and other diseases [2,3]. The creation of domestic modern medicines from them is one of the pressing issues of today (1).

The purpose of the work: to study in experimental animals the effect of Phytopheron tincture on chronic administration to the body - a collection of tubule-leaved bullfinch, bird taron, sweet brain root, water pepper and medicinal chamomile medicinal plants.

Experimental method: the experiment was carried out in 30 laboratory white rats weighing 140 – 156 g. Phytoferon tincture was administered orally for 1 month at doses of 10 ml/kg (1 ml/100 g) and 25 ml/kg (2.5 ml/100 g weight). Laboratory animals in the control group, on the other hand, were given distilled water, respectively. During the experiment, changes in the condition, weight of animals were observed [4].

To study the chronic toxicity of the drug, at the beginning of the experiment, blood tests were carried out on the 15th, 30th and 60th days after the administration of the tincture. Blood analysis was studied in a hematological analyzer (VC-3000), using colorimetric methods using serum aspartate-aminotransferase (ACaT) and alaninaminotransferase (ALaT) Raitman-Frankel, and glucose levels glucosooxidase enzyme in a biochemical analyzer (VA-88) [5]. At the end of the experiment, laboratory animals were decapitated and histomorphological tests were carried out [4]. The statistical significance of the obtained indicators was determined by calculating the probability of error (R) in the examination of the distribution norm (according to the ecstasy criterion) and the equality of general dispersions (F – Fisher criterion) by the Styudent (t) criterion, comparing the average quantitative indicators.

Results of the experiment: in both groups that received Phytopheron tincture, the general cases of animals control group did not differ from that of white rats. However, the drug had a positive effect on the weight of experimental animals. In particular, on the 60th day of the experiment, the amount of 10 ml/kg increased by 16.2% compared to the initial indication (before Administration of the drug) and 17.5% respectively in 25 ml/kg.

In the blood analysis, the amounts of certain shaped elements of peripheral blood (1 mm³) were examined. The results obtained showed that from the 15th day of the experiment, the amount of hemoglobin in the peripheral blood under the influence of the drug phytoferon increased compared to the indicators of intactus and the control group. Given phytoferon in 10 ml/kg and 25 ml/kg, it was noted that the hemoglobin



content in the peripheral blood of white rats increased by 0.5 and 0.6 g % compared to intact indicators, and 0.8 g% respectively compared to the control group. No change in the number of erythrocytes and leukocytes in the peripheral blood was detected in the level of mathematical accuracy. On the 30th day of the experiment, the amount of hemoglobin in the blood of white rats under the influence of the drug phytoferon in both quantities and the number of erythrocytes by 0.9-1.1 g % compared to the control group indicators, as well as 0.3-0.6 mln.ga increased was observed. Almost the same situation was noted on the 60th day of the experiment. Changes in the number of leukocytes in the peripheral blood were also detected during the experiment. But these indicators did not differ from the results of the control group in the level of mathematical accuracy. In particular, the number of leukocytes in the blood was around the physiological norm during the experiment. When chronic administration of phytoferon tincture in amounts of 10 ml/kg and 25 ml/kg, it was noted that the experiment increased the weight of white rats relative to intactness indicators. But the control group did not differ in the level of mathematical accuracy from its indicators (Table 1).

Table 1.

Effect of phytoferon tincture on indicators of peripheral blood elements when chronically administered to white rats (M±m; n=10)

Specification	Peripheral blood indications after administration of phytoferon						
	Intact	Day 15		Day 30		Day 60	
		10 ml/kg	25 ml/kg	10 ml/kg	25 ml/kg	10 ml/kg	25 ml/kg
Hemoglobin, g/%	12,1±0,1	<u>13,3±0,3</u> 5*x	<u>13,3±0,3</u> 7* x	<u>13,5±0,3</u> 5*x	<u>13,7±0,4</u> 0* x	<u>13,35±0,3</u> 9* x	<u>13,5±0,3</u> 7
		12,5±0,3 6	12,5±0,3 6	12,6±0,2 7	12,6±0,2 7	12,4±0,36	12,4±0,3 6
Erythrocytes, million/ml	6,1±0,23	<u>6,2±0,30</u> 5,9±0,25	<u>6,27±0,2</u> 7 5,9±0,25	<u>6,3±0,25</u> 6,0±0,35	<u>6,6±0,35</u> * x 6,0±0,35	<u>6,4±0,20*</u> x 5,95±0,25	<u>6,5±0,29</u> * x 5,95±0,25
Leukocytes, thousand/ml	9,7±1,9	<u>10,5±2,0</u> 10,5±2,1	10,2±2,1 10,5±2,1	<u>10,7±1,6</u> 11,5±2,1	<u>10,3±1,7</u> 11,5±2,1	<u>10,4±0,50</u> 10,5±0,42	<u>10,2±0,3</u> 2



							10,5±0,4 2
--	--	--	--	--	--	--	---------------

Note: experimental group results in the photo; control group results in the denominator

- * - level of reliability relative to the control group;
- X-degree of reliability relative to the intact indicator

This means that phytoferon tincture, when administered chronically, also stimulates the process of blood formation in normal white rats to a certain extent. In addition phytoferon tincture in both quantities increased the separation of the forehead by 19.2 - 21.0% and 21.3 - 22.3% on the 15th and 30th days of the experiment, it was noted that the color of the forehead is clear, the pH indicator is in the norm. On the 30th day of the experiment, biochemical analyzes in the blood were examined (Table 2). Based on the results obtained, the control group of levels of Alat and Asat in the blood under the influence of phytoferon tincture did not differ at all from that of white rats. So the drug under study does not affect the activity of liver enzymes.

Table 2

The effect of phytoferon tincture on biochemical indicators in the blood in chronic administration (M±m; n=6)

Pointers	Results		
	In the control group	In the group that took 5 ml/kg of tincture	In the group that took 10 ml/kg of tincture
ALAT mmol.ch.l	140,6±2,03	141,7±2,07	142,6±1,63
ACAT mmol.ch.l	143,0±1,87	144,5±2,56	145,1±1,57
Proteins g./l.	59,6±1,66	63,2±1,64*	64,0±1,36*
Cholesterol, mmol/l	1,72±0,01	1,76±0,041	1,75±0,067
Sugar content, mmol/l	4,85±0,41	5,36±0,65*	5,31±0,83*

Note: * - level of reliability relative to the control group.

But the process of synthesis of proteins in the liver has intensified a little. In this, the amount of proteins in the blood increased by 6% and 7.8%, respectively, compared



to the control group, in the group of white rats, who received 5 ml/kg and 10 ml/kg of tincture.

At the end of the experiment, white rats were decapitated against the background of mild narcosis and histomorphological examinations of their internal vital organs were carried out. Based on histological analysis, the boundaries of the liver sections in the liver of animals in the control group are not clearly visible. The trabecular structure of hepatocytes is clearly visible, and one branch of it is surrounded by septa. The central vein of the liver is empty, the intercalary space is narrowed, the triad is well visible. Hepatocytes located in all sections of the liver are of almost the same structure, their nuclei are clearly visible.

The liver capsule of the animals that received the tincture under study was very thin, as in the trabecular control group of hepatocytes, the Triads are well visible, the process of proliferation in the hepatocytes around the triad and septa pathway, 2 nuclei were recorded in some hepatocytes.

Renal parenchaemia is in a simple structure and it is made up of central brain and peripheral bark substances. The capsule is very thin, the parenchyma stroma is in a thin structure, the clublets are the same size, round or oval in shape, the petlya capillaries are thin and in an empty position. Shumlyansky-Bauman capsules are free of pathological fluids. In the cavity of the nephron ducts, protein weights of the eye progenitor, pink color were recorded.

Animals that receive phytoferon tincture have a kidney that looks like a histostructure control group. Shumlyansky-Bauman capsules in a hollow state, while in the kidneys of some animals, noticeable tumors and metachromasias are visible. Stromani klubochk recorded a state of proliferation in fibroblasts in some of its lands etilgan.Me in the wall, the mucous, sub-mucous, muscular and serous floors look normal. The structure of the intestinal walls is also simple, lying on the muscular floor and recorded in the form of a circular floor. The mucous membrane of the intestine is full-blooded, the vorsinkae are well developed, its epithelial floor protoplasm is basophilic, the nucleus is plasmatic in appearance. on the floor of the mucosa, fat groups are assembled, which are made up of porous cytoplasmic cells with a boccal foam.

The intestinal mucosa of some of the animals that received the tincture is well preserved, the vorsinkae are made up of a plasmatic epithelium, the stroma of which is in a fine structure, the mucous membrane of the intestinal glands is partially swollen, the cell cytoplasm is vacuolated. The intestinal lymphoid apparatus is well developed. Sometimes very small volumes of tumors have been recorded on the mucous membrane.



Cardiac histostructure is normal, the heart is saturated with muscle layer - myocardial blood, cardiomyocytes are full-blooded, the core is oval. Muscle capillaries are significantly hypertrophied, vacuoles have been recorded in their cytoplasm.

Histological structure of other vital internal organs in animals in the control and experimental group it was found that Dearness appears the same.

In conclusion, the histological structures of the vital internal organs of white rats in the control and experimental group did not differ from each other. So phytoferon tincture does not adversely affect the histological structures of internal organs.

Conclusions.

1. Phytoferon tincture affects peripheral blood-shaped elements when administered for 1 month in amounts of 10 ml/kg and 25 ml/kg.

2. Phytoferon tincture does not affect the activity of liver enzymes in the amounts studied when administered chronically. Accelerates the breakdown of proteins in the liver.

3. Phytoferon tincture does not affect the histological structure of internal organs when chronically administered to experimental white rats in amounts of 10 ml/kg and 25 ml/kg.

Bibliography:

1. Шарипов А.Т. Разработка и стандартизация серосодержащих лекарственных средств на основе местного сырья.- Автореф. дисс. ... докт.фарм. наук. - Ташкент, 2016. - С.75

2. Холматов Ў. Х., Дўсчанов Б. О., Собиров Р. С. Абу Али ибн Сино ишлатган доривор ўсимликлар. - Урганч, 2003, - 179 б.

3. Эгамбердиева М.Н., М.Ж.Аллаева, Муллажанова М.Т. Тубулғибаргли буймадорон ва қашқарбеда ўсимлиги ва унинг экстрактини конкуюклашиш жараёнига таъсири /Ibn Sino ilmiy-amaliy xalqaro jurnal. - 2005. - №3/4. - С. 84-85.

4. Руководство по экспериментальному (доклиническому) изучению новых фармакологических веществ. -Москва, 2005.- 289 с.

5. Макаров В.Г. и соавт. СПРАВОЧНИК. Физиологические, биохимические и биометрические показатели нормы экспериментальных животных. СПб.: Изд-во «ЛЕМА», 2013. -116 с.

