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DETERMINATION OF ACUTE TOXICITY OF THE CAPSULE OBTAINED ON THE BASIS OF GOJI DRY EXTRACT

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ABSTRACT

The calculation of acute toxicity indicators due to the absence of dead animals after oral administration of the drugs turned out to be impossible, which indicates the absence of toxicity in the dose range of 2000-6000 mg / kg, therefore LD50 is assumed to be> 6000 mg / kg. Based on the data obtained on the average lethal dose, we determined the hazard class according to GOST 12.1.007-76 (the classifier contains four levels of classification, according to the safety of substances), for the infusion of the drug, which is for oral administration, corresponds to the fourth hazard class (low hazard substances). The results obtained indicate that it is inappropriate to further study of acute toxicity for oral administration of the drug, since the maximum administered dose corresponds to the last hazard class. We also assessed the obtained data on acute toxicity according to the toxicity classifier (the classifier contains six levels of toxicity classification), described in the methodological manual for preclinical research of drugs, edited by A.V. Stefanov. According to this classifier, the drug when administered orally belongs to the fifth toxicity class (Practically non-toxic).

KEYWORDS: *Goji, Toxic Effect, Dose, Toxicity Class, Non –Toxic, Death of Animals.*

INTRODUCTION

Goji berries are rich in minerals of natural origin, which are adequately absorbed by the body for 100% (zinc, calcium, selenium, phosphorus, copper, iron) and are necessary for the prevention of prostatitis and prostate adenoma, other changes in organs and systems that men are especially susceptible to. Goji berries consist of:

• 19 amino acids necessary for the normal functions of the genitourinary system in men and the production of high-quality ejaculate and sperm; for psychological satisfaction and normalization of psycho-emotional status;

• 21 trace elements (minor minerals), including germanium which is necessary to prevent the formation of tumor cells;

• 6 fatty acids that are necessary for proper functioning of the cardiovascular system, prevention of changes in the liver;

• Vitamins B1, B2, B6, C, E, which help to improve the functioning of the genitourinary system in men;

• 20 times more beta-carotene than in carrots, which directly and effectively restores potency (virility);

• The maximum amount of antioxidants that prevent changes in the body caused by age and aging;

• 500 times more vitamin C than in oranges, which is necessary in most biochemical processes in the body for immunity, endurance, physical and sexual activity;

• 4 unique polysaccharides, not found in any other food product, which "instruct" the cells of our body, adjusting them to health;

• linoleic acid, which greatly contributes to natural weight loss;

• 15 times more iron than in spinach.

Purpose of the study: To study the acute toxicity of the "Goji" capsule preparation based on dry extract.

EXPREMENTAL PART

Materials and research methods: All studies were performed on healthy animals quarantined for at least 10-14 days.

The study of acute toxicity was carried out according to the generally accepted method, on white outbred mice (both sexes) weighing 18-22 g, 6 animals per group, 36 animals were used in total.

To conduct a preclinical study, an infusion was prepared from the collection according to SPh XI, in a ratio of 1: 3 (water was poured without taking into account the water absorption coefficient; the degree of grinding was set at the release of finished products).

Since the pharmacological effect of the extracts is determined by the content of extractives (dry residue), then for the study, and the exact calculation of the selected doses, we determined the dry residue of the infusion. The dry residue content in the aqueous extract was determined by the method described in SPh XI. The resulting infusion contained 4% of the dry residue (extractive substances), and the infusion obtained by this technology was used to set all the studied parameters.

The test drug was administered to experimental animals once orally as a 4% aqueous infusion, at doses: 2000 mg / kg (1.0 ml / 20 g), 3000 ml / kg (1.5 ml / 20 g), 4000 mg / kg (2.0 ml / 20 g), 5000 mg / kg (2.5 ml / 20 g) and 6000 mg / kg (3.0 ml / 20 g).

Since, according to the literature, the maximum volume for a single oral administration is 0.5 ml / 20 g, so we used the method of fractional administration. When a dose of 2000 mg / kg was administered, a volume of 0.5 ml / 20 g was first injected, then after 1.5 hours 0.5 ml / 20 g was injected. When a dose of 3000 mg / kg was administered, a volume of 0.5 ml / 20 g, an hour later, and 0.5 ml / 20 g was injected, and then an hour later, 0.5 ml / 20 g was injected. When a dose of 4000 mg / kg was administered, a volume of 0.5 ml / 20 g was first injected, after 0.5 hours 0.5 ml / 20 g was injected, after 0.5 hours another 0.5 ml / 20 g, then 0.5 ml / 20 g was injected afteran hour. When a dose of 5000 mg / kg was administered, a volume of 0.5 ml was injected first / 20 g, after 0.5 hour 0.5 ml / 20 g was injected, after 0.5 hour another 0.5 ml / 20 g, then after 0.5 hours 0.5 ml / 20 g was injected, and after an hour 0.5 ml / 20 g was injected, when a dose of 6000 mg / kg was administered, a volume of 0.5 ml / 20 g was first injected, 0.5 ml / 20 g was injected after 0.5 hours, another 0 after 0.5 hours, 5 ml / 20 g, after 0.5 hour another 0.5 ml / 20 g, after 0.5 hour another 0.5 ml / 20 g, then after an hour 0.5 ml / 20 g was injected.

The animals were placed in separate cages in groups and were continuously monitored for the first hour, then were monitored hourly, during the first day, and once a day in the next 13 days of the experiment (total observation period was 14 days). At the same time the followings were taken into account: the general condition of the animals, the features of their behavior, the intensity and nature of motor activity, the presence and nature of seizures, coordination of movements, tone of skeletal muscles, response to tactile, painful, sound and light stimuli, frequency and depth of respiratory movements ,heart rate, the condition of the coat and skin, the color of the mucous membranes, the position of the tail, the amount and consistency of fecal matter, the consumption of food and water, as well as other indicators characterizing the toxic effect. The timing of the development of intoxication and the death of animals were also recorded.

During the experiment, all animals were kept in standard vivarium conditions and were on a complete food and water diet.

RESEARCH RESULTS

After oral administration of the drug, a number of changes were observed characterizing the toxic effect of the drug (Table 1).

TABLE 1 THE RESULTS OF THE TOXIC EFFECT OF THE DRUG "GOJI" CAPSULE "TASHPHARMI" UZBEKISTAN

Dose	Result
2000 mg / kg	After administration of the drug, no significant changes in general condition, behavior, and death were observed.
3000 mg / kg	After administration of the drug, no significant changes in general condition, behavior, and death were observed.
4000 mg / kg	Thirty minutes after drug administration, disunity and decreased motor activity were observed. These symptoms lasted for about three hours
5000 mg /	Thirty minutes after drug administration, disunity and decreased motor activity

kg	were observed. These symptoms lasted for about three hours
6000 mg / kg	20 minutes after the drug was administered, disunity and decreased motor activity were observed. These symptoms lasted for about five hours

The results of the study of changes in body weight gain showed (Table 2) that after oral administration of the drug, there were no significant changes in body weight gain in any of the doses, in comparison with the intact group.

TABLE 2 RESULTS OF STUDYING CHANGES IN BODY WEIGHT OF ANIMALS, IN GRAMS

Group: Intact

№	Body weight of animals (in grams)		
	initial	after 7 days	after 14 days
1.	21	22	24
2.	18	18	20
3.	19	20	19
4.	18	20	21
5.	19	22	24
6.	20	22	24
Average	19,17 (17,94÷20,39)	20,67 (18,95÷22,38)	22,00 (19,61÷24,39)

Group: "Goji" capsules "Tashpharmi" Uzbekistan (at a dose of 2000 mg / kg)

№	Body weight of animals (in grams)		
	initial	after 7 days	after 14 days
1.	22	21	20
2.	18	18	19
3.	21	19	21
4.	20	22	23
5.	20	20	22
6.	21	20	22
Average	20,33 (18,90÷21,77)	20,00 (18,52÷21,48)	21,17 (19,62÷22,71)

Group: "Goji" capsules "Tashpharmi" Uzbekistan (at a dose of 3000 mg / kg)

№	Body weight of animals (in grams)		
	initial	after 7 days	after 14 days
1.	20	23	24
2.	18	18	20
3.	19	21	20
4.	22	23	22

5.	21	18	18
6.	20	18	20
Average	20,00 (18,52÷21,48)	20,17 (17,56÷22,77)	20,67 (18,50÷22,83)

Group: "Goji" capsules "Tashpharmi" Uzbekistan (at a dose of 4000 mg / kg)

№	Body weight of animals (in grams)		
	initial	after7 days	after 14 days
1.	20	22	22
2.	20	18	18
3.	18	15	15
4.	18	18	22
5.	21	20	23
6.	20	23	25
Average	19,50 (18,21÷20,79)	19,33 (16,24÷22,42)	20,83 (17,00÷24,67)

Group: "Goji" capsules "Tashpharmi" Uzbekistan (at a dose of 5000 mg / kg)

№	Body weight of animals (in grams)		
	initial	after7 days	after 14 days
1.	20	18	20
2.	20	18	18
3.	22	23	24
4.	19	20	23
5.	19	21	24
6.	21	23	24
Average	20,17 (18,94÷21,39)	20,50 (18,13÷22,87)	**22,17 (19,48÷24,86)**

Group: "Goji" capsules "Tashpharmi" Uzbekistan (at a dose of 6000 mg / kg)

№	Body weight of animals (in grams)		
	initial	after 7 days	after 14 days
1.	20	22	20
2.	19	20	21
3.	18	17	18
4.	18	22	21
5.	20	24	25
6.	18	17	17
Average.	18,83(17,80÷19,87)	20,33 (17,32÷23,35)	20,33 (17,39÷23,28)

(M±tm; p=0,05; n=6)

Group	initial	after 7 days	after 14 days
Интакт	19,17 (17,94÷20,39)	20,67 (18,95÷22,38)	22,00 (19,61÷24,39)
"Goji" capsules "Tashpharmi" Uzbekistan			
2000 mg / kg	20,33 (18,90÷21,77)	20,00 (18,52÷21,48)	21,17 (19,62÷22,71)
3000 mg / kg	20,00 (18,52÷21,48)	20,17 (17,56÷22,77)	20,67 (18,50÷22,83)
4000 mg / kg	19,50 (18,21÷20,79)	19,33 (16,24÷22,42)	20,83 (17,00÷24,67)
5000 mg / kg	20,17 (18,94÷21,39)	20,50 (18,13÷22,87)	22, 17 (19, 48÷24, 86)
6000 mg / kg	18,83 (17,80÷19,87)	20,33 (17,32÷23,35)	20,33 (17,39÷23,28)

The calculation of acute toxicity indicators due to the absence of dead animals after oral administration of the drugs turned out to be impossible, which indicates the absence of toxicity in the dose range of 2000-6000 mg / kg; therefore LD50 is assumed to be> 6000 mg / kg (Table 3).

TABLE 3 THE RESULTS OF THE TOXIC EFFECT OF THE DRUG

Dose	Case of death of animals
2000 mg / kg	0/6
3000 mg / kg	0/6
4000 mg / kg	0/6
5000 mg / kg	0/6
6000 mg / kg	0/6
$ЛД_{50}$>6000 mg / kg	

Based on the data obtained on the average lethal dose, we determined the hazard class according to GOST 12.1.007-76 (the classifier contains four levels of classification, according to the safety of substances), for the infusion of the drug, which is for oral administration, corresponds to the fourth hazard class (low hazard substances). The results obtained indicate that it is inappropriate to further study of acute toxicity for oral administration of the drug, since the maximum administered dose corresponds to the last hazard class.

We also assessed the obtained data on acute toxicity according to the toxicity classifier (the classifier contains six levels of toxicity classification), described in the methodological manual for preclinical research of drugs, edited by A.V. Stefanov. According to this classifier, the drug when administered orally belongs to the fifth toxicity class (Practically non-toxic).

It should be admitted that according to the instructions for studying the parameters of acute toxicity described in the methodological manual for preclinical research of drugs, edited by Stefanov A.V., it is said that in the absence of animals death, upon administration, that any substance introduced in large quantities, is capable of causing toxic effects, therefore, the limiting indicator is the maximum dose of the fourth class of toxicity (low toxic substances), taking into account the route of administration. And if no death is observed with the introduction of a dose of the drug corresponding to the maximum dose of the fourth class of toxicity, then the

introduction of a larger dose is usually inappropriate. In case of death of animals due to exposure to the test substance, it is necessary to carry out tests in full.

Based on the data obtained, we can conclude that the infusion of "Goji" of the capsule "Tashpharmi" Uzbekistan has high safety, since when high doses of the infusion are administered orally; there is no death of animals.

Despite a number of symptoms of intoxication that were observed in animals after oral administration of the drug, it can be said that the drug is harmless, since with oral administration of high doses of the drug, no death of animals is observed, and no significant changes in body weight gain are observed.

Summarizing the above, we can conclude that further studies of acute toxicity after oral administration of the drug are complete.

Conclusion: The acute toxicity of the drug "Goji" of the capsule "Tashpharmi" Uzbekistan was studied, according to the results of which a high safety of the water extract from the collection was established, since no death of animals was observed at the maximum dose.

CONCLUSION:

Preclinical studies of the drug "Goji" of the capsule "Tashpharmi" Uzbekistan were carried out in terms of acute toxicity. As a result, it was found that the drug has high safety, since even the maximum dose does not cause death of animals when administered orally, and belongs to the fifth class of toxicity (Practically non-toxic).

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