

10-3-2020

NUTRITIONAL AND BIOLOGICAL VALUE OF THE WATER FORTIFIER “MARJON”

Guli I. Shaykhova

Tashkent Medical Academy, Tashkent, 100109, Uzbekistan, guli.shayhova@gmail.com

Laziz A. Azimov

Tashkent Medical Academy, Tashkent, 100109, Uzbekistan

Shahzoda A. Zokirkhonova

Tashkent State Dental Institute, Tashkent, Uzbekistan

Follow this and additional works at: <https://uzjournals.edu.uz/tma>

Recommended Citation

Shaykhova, Guli I.; Azimov, Laziz A.; and Zokirkhonova, Shahzoda A. (2020) "NUTRITIONAL AND BIOLOGICAL VALUE OF THE WATER FORTIFIER “MARJON”," *Central Asian Journal of Medicine*: Vol. 2020 : Iss. 3 , Article 11.

Available at: <https://uzjournals.edu.uz/tma/vol2020/iss3/11>

This Article is brought to you for free and open access by 2030 Uzbekistan Research Online. It has been accepted for inclusion in Central Asian Journal of Medicine by an authorized editor of 2030 Uzbekistan Research Online. For more information, please contact sh.erkinov@edu.uz.

NUTRITIONAL AND BIOLOGICAL VALUE OF THE WATER FORTIFIER “MARJON”

Guli I. Shaykhova *¹, Laziz A. Azimov ², Shahzoda A. Zokirkhonova ³

Authors' affiliations:

1 MD, DSc, Professor, Department of Hygiene of Children, Adolescent and Nutrition of Tashkent Medical Academy, Tashkent, Uzbekistan. Email: guli.shaykhova@gmail.com

2 Independent Researcher from the Department of Hygiene of Children, Adolescent and Nutrition of Tashkent Medical Academy, Tashkent, Uzbekistan.

3 Assistant, Candidate of Medical Sciences, Department of Pediatric Dentistry, Tashkent State Dental Institute, Tashkent, Uzbekistan.

ABSTRACT

At present, the factor of healthy nutrition is recognized as one of the key components of the general strategy of the WHO, according to which 60% of the causes of death of people are directly related to nutritional problems. The food formula of the 21st century is constantly consuming the products with desired properties (functional food products) and biologically active food additives along with traditional natural food products.

The purpose of this work is to study the nutritional and biological values of the water fortifier "Marjon", in order to find the most rational ways to utilize it in human nutrition.

Materials and research methods

Materials for research were water fortifier “Marjon”, drinking water, 54 white outbred sexually mature rats of both sexes and 2 rabbits. In provided researches, the following methods were used: organoleptic, physicochemical, microbiological and toxicological methods.

Research results

Based on the results of our own research, examination of the materials of the scientific dossier and literature data, it was established that water fortifier “Marjon”, produced by “ORION SKORPION” Ltd (Uzbekistan), designed to increase the alkalinity of the medium enriched with calcium (Ca) and magnesium (Mg) ions, adsorption of heavy metals and chlorine ions of drinking water made by fractionation of crushed dolomite (microcalcite) according to Ts 25280147-14: 2017 is intended for direct use. Based on the results of toxicological studies of food products, it was found that according to the parameters of acute toxicity with the intragastric route of intake of food additives, it belongs to low-toxic substances class (class IV).

Results **hematological, biochemical and** histomorphological studies of internal organs, confirms that the water fortifier with prolonged intragastric intake does not provide a toxic effect on the organism of experimental animals.

Conclusion.

Results of nutritional and biological values allow making a conclusion about the biomedical safety of the water fortifier “Marjon” (Uzbekistan) for human health and can be approved for use in accordance with the prescriptions and in the established order.

Key words: water fortifier, “Marjon”, drinking water, distilled water, nutritional and biological value, comparative assessment, toxicology.

INTRODUCTION

The problems of maintaining and strengthening health, increasing human life expectancy have always been and continue to be among the most important and urgent issues in medicine and biology. At present, the factor of healthy nutrition is recognized as one of the key components of the general strategy of the WHO, according to which 60% of the causes of death of people are directly related to nutritional problems. [13,14]. Moreover, it has been shown that 80% of unfavorable environmental factors affect the human body through food and water. It is the food substances that are transformed during the digestion process into structural and energy substrates, provides physical and mental performance, and determines the duration and quality of life. Meantime, significant changes in the lifestyle of people in recent decades have caused changes in the particularity of diseases, the predominance of increasing of alimentary-dependent, i.e. food related diseases. Unfortunately, currently there is no sufficient scientific evidence to indicate that the available actual diet meets the basic requirements for energy and essential nutrients. Therefore, the food formula of the 21st century is constantly consuming the products with desired properties (functional food products) and biologically active food additives along with traditional natural food products. [9,10,11,15].

The purpose of this work is to study the nutritional and biological values of the water fortifier “Marjon”, in order to find the most rational ways to utilize it in human nutrition.

Materials and research methods

Materials for research were water fortifier “Marjon”, drinking water, 54 white outbred sexually mature rats of both sexes and 2 rabbits.

In provided researches, the following methods were used: organoleptic, physicochemical, microbiological and toxicological methods. In the study of the water fortifier “Marjon”, the data of the chemical composition of drinking water widely used by the population, served as a control.

The Research have been conducted at the Department of Hygiene of Children, Adolescents and Food Hygiene of Tashkent Medical Academy (TMA), at the Interuniversity Research Laboratory (IURL) of TMA; at the testing center of the Institute of Chemistry of Plant Substances named after academician “S.Yu. Yunusov” of the Academy of Sciences of the Republic of Uzbekistan (ICPS AS Rep.Uz).

On the physical characterization of the studied samples of the “Marjon” water fortifier and drinking water, the following indicators were studied: humidity and acidity of ash formed after the combustion of composition of the “Marjon” water enrichment in a muffle furnace (A.P. Ermakov, 1972); (15113.4-91, 15113.5-91;

Experimental studies of possible toxic properties are consisted of the following stages: study of the general toxic effect of the “Marjon” water fortifier with an assessment of the possible irritating effect on mucous membrane of the eyes, as well as its possible cumulative effect; study of possible allergenic and immunological activity [2,3,4,5,6,7,8,16].

Acute toxicity study of the water fortifier “Marjon” was carried out on 24 sexually mature white rats of both sexes with an initial body weight of 141-160 g. Experimental animals were divided into 3 groups of 6 animals. The control group is consisted of 6 animals.

The determination of the acute toxicity parameters of the substance was conducted in the conditions of a single intragastric injection of food additives at doses of 1000, 2500 and 5000 mg / kg.

For testing under acute toxicity conditions:

1. For animals of first group, when testing a dose of 1000 mg/kg, 0.1 ml/100g of body weight was injected once.
2. For animals of the second group, when testing a dose of 2500 mg / kg, 0.25 ml/100 g of body weight was injected once.
3. For animals of the third group, when testing the dose of 5000 mg / kg, 0.5 ml / 100 g of body weight was injected once.

Observation of the experimental animals was conducted during 14 days. The Symptoms of intoxication in animals has not been identified. Study animals responded adequately to the external stimuli. The hair cover is shiny and smooth, baldness areas or ulcers are not found. Visible mucous membranes are pale pink, unchanged. The death of animals was not detected when exposed to the maximum dose of 5000 mg/kg. Due to the absence of death of animals, it was not possible to calculate the average lethal dose (DL₅₀).

The skin-resorptive and local-irritating effect of the “Marjon” water fortifier has been conducted in two ways:

Method 1, a single exposure of 2/3 of the tails of white rats in food supplements. Method 2, a single 4-hour exposure of food additives to the clipped areas of the back of the animals.

To assess the effect on the mucous membranes of the eyes of rabbits, 2 drops of the “Marjon” water fortifier were added once to the conjunctival sac of the left eye of two rabbits. The right eye served as a control.

Cumulative properties water fortifier "Marjon" **studied by Lim on 12 white rats.**

Study of the immunological activity of the "Marjon" water fortifier. The concentration of immunoglobulin of the IgG and IgM classes in the blood serum was determined by the method of enzyme-linked immunosorbent assay. Serum samples from rat peripheral blood were obtained after exposure to food supplements at doses of 15 mg / kg, 150 mg / kg, and 300 mg / kg.

All data obtained in the study were subjected to statistical processing on a Pentium - IV processor personal computer, using the Microsoft Office Excel - 2003 software package by using the built-in statistical processing functions. The Methods of variational parametric and non-parametric statistics were used, with the calculation of the arithmetic mean of the studied indicator (M), standard deviation (G), standard error of the mean (m), relative values (frequency,%). The statistical significance of the obtained measurements, when comparing the mean values, was determined by the Student's test (t), with the calculation of the error probability (P) when checking the normality of the distribution (by the kurtosis criterion) and the equality of general variances (F - Fisher's criterion). The level of reliability $P < 0.05$ was taken as statistically significant changes (1).

Results and discussion

The water fortifier "Marjon" (hereinafter referred to as the product), made by fractionation of crushed dolomite, is designed to increase the alkaline environment, to enrich the drinking water with calcium (Ca) and magnesium (Mg) ions intended for direct consumption. Specifications and Technological instructions have been developed for this product (approved Ministry of Health and the "Uzstandart" Agency (Ts-25280147-26.2017)) (12).

For the production of manufactured products, the following raw materials are used:

- crushed dolomite according to the current regulatory documentation;
- potato starch according to GOST 7699;
- calcium stearate in accordance with the current regulatory document;

- talc according to GOST 21235 or imported product;
- distilled water in accordance with GOST 6709.

Water fortifier "Marjon" is available in tablets, granules and powders.

Mode of application: 1 sachet (package) weighing 1 g is dissolved in 1 liter of water. A tablet (0.3 g) is dissolved in 250 ml of water (1 glass). The resulting solution is poured into a clean glass through a sieve. Duration of admission is 1 month.

Shelf life: 36 months if stored in original, undamaged packaging. Store away from heat sources and out of direct sunlight.

Release form: tablets, granules or powder of 0.3, 0.35, 0.4, 0.45, 0.5, 0.6 grams in a bottle made of polymer (PET) material.

The technological process for the production of the "Marjon" water fortifier includes the following stages: acceptance and storage of raw materials; preparation of raw materials; preparation of a mixture (emulsion); fractionation process; grinding and sieving, packaging.

We have studied the organoleptic and physicochemical characteristics of the "Marjon" water fortifier. The control was a drinking water that meets the GOST standard.

The study of organoleptic indicators revealed that drinking water is colorless and odorless, has a neutral taste and contains many useful substances necessary for the human body. Along with the liquid, which is important for regulating the water balance, the minerals come with water - selenium, magnesium, calcium, iodine, fluorine and other substances. Water fortifier "Marjon" is somewhat different from drinking water in terms of organoleptic characteristics; however, we did not find any negative properties in the water fortifier "Marjon" (Table 1).

Table 1

Organoleptic indicators of the "Marjon" water fortifier.

The indicators	"Marjon" water fortifier	Drinking water
Appearance	Fine powder, granules, tablets. With vigorous stirring, it partially dissolves in water, forming a precipitation.	Absent
Colour	From light cream to gray-cream.	Has no color
Taste	Neutral, without foreign taste and smell.	Neutral, has no foreign taste and smell

According to the investigated physical and chemical parameters, the "Marjon" water fortifier has more positive properties. The "Marjon" water fortifier

is produced in the form of tablets and powder, has a higher ash content, and contains a mass fraction of magnesium and calcium ions. The total mineralization is higher, since it dissolves in drinking water and due to the fortifying of drinking water by the fractionation of crushed dolomite, the mass fraction of magnesium and calcium ions increases (Table 2).

Table 2

Physicochemical parameters of the "Marjon" water fortifier and drinking water

Indicator name	"Marjon" water fortifier	
	powder	tablet
1. Mass fraction of moisture, %, no more	3.0 ± 0.29	12.0 ± 0.61
2. Hydrogen exponent	from 0.6 ± 0.01 to 9.0 ± 0.02	
3. Mass fraction of Mg ions, mg / dm ³ , not less	14.0 ± 0.75	14.0 ± 0.94
4. Mass fraction of Ca ions, mg / dm ³ , not less	35.0 ± 2.26	35.0 ± 3.18
5. Water hardness 0.1% solution mg-equi. / dm ³ , no more	4.5 ± 0.32	
6. Total mineralization (dry residue) mg / dm ³	1000 ± 50.87	

The presence of toxic elements in water fortifier "Marjon" should not exceed according to the provided indicators in Table 3.

Table 3

Presence of toxic elements of the "Marjon" water fortifier

Name of substance (element)	mg / kg, no more	
Toxic elements	Plumbum	4.0 ± 0.35
	Arsenic	3.0 ± 0.19
	Cadmium	1.0 ± 0.06
	Mercury	0.5 ± 0.01

At the next stage, we studied the acute toxicity of the "Marjon" water fortifier. Observation of the experimental animals was carried out for 14 days. Study animals responded adequately to the external stimuli. The hair cover is shiny and smooth, baldness areas or ulcers are not found. Visible mucous membranes are pale pink, unchanged. The death of animals was not detected when exposed to the maximum dose of 5000 mg/kg. Due to the absence of death of animals, it was not possible to calculate the average lethal dose (DL₅₀). Symptoms of intoxication of animals have not been identified.

In this way, the water fortifier "Marjon" according to the parameters of the toxicity degree can be classified as class IV (low-toxic substance).

The study of the skin-resorptive and local-irritating effect of the "Marjon" water fortifier carried out in two ways showed that no symptoms of intoxication and their death were revealed on white rats during the observation period for 3 weeks. The animals remained active, willingly ate food, and adequately responded to external stimuli. Therefore, the investigated nutrition product the "Marjon" water fortifier, do not have skin-resorptive and local irritating effects.

When evaluating the effect on the mucous membranes of the eyes of rabbits for 7 days, no signs of an inflammatory reaction were detected. The "Marjon" water fortifier does not irritate the mucous membrane of the eyes.

Cumulative properties of the "Marjon" water fortifier. For 3 weeks, food supplements were injected intragastrically daily at an initial dose of 300 mg. Every 5 days, the dose was increased for 1.5 times. At the maximum dose of 1518.75 mg on the day 21, the indicators of survival, general condition, activity of animals, hematological parameters of peripheral blood and biochemical parameters of blood serum did not differ from those of the control group.

In this way, water fortifier "Marjon" does not possess the properties of material and functional accumulation.

Determination of the immunological activity of the studied products in vivo is an important characteristic of the biological safety of food additives. The results of the influence of the investigated food additives on the presence of immunoglobulin IgG and IgM classes in the blood serum of rats are presented in table. 4.

Table 4

Results of the influence of food additives on the content of immunoglobulin IgG and IgM classes in the blood serum of rats

Groups	Dose of "Marjon" exposure, mg/kg	IgG concentration, mg/ml	IgM concentration, mg/ml
Water fortifier "MARJON"	15.0	3.20 ± 0.10	0.10 ± 0.01
	150.0	3.30 ± 0.15	0.12 ± 0.02
	300.0	3.30 ± 0.15	0.11 ± 0.01
The control	-	3.30 ± 0.15	0.10 ± 0.01

The research results showed that the water fortifier "Marjon" at doses of 15 mg / kg, 150 mg / kg and 300 mg / kg does not affect the content of

immunoglobulin IgG and IgM classes in the blood serum of rats. The obtained results of the presence of the investigated immunoglobulins did not statistically significantly differ from those of the control group.

Thus, the nutritional properties of the “Marjon” water fortifier with prolonged intragastric injection at doses of 15, 150 and 300 mg/kg do not have an immunostimulating or immuno-inhibitory effect on the organism of the experimental animals.

Toxicity of the water fortifier “Marjon” was studied in conditions of long-term per os administration at doses of 15, 150 and 300 mg/kg.

The results of the studies have shown that long-term intragastric injection of food additives in the studied doses is well tolerated by the experimental animals. Indicators of general condition, behavior, weight gain, hematological and biochemical parameters of the experimental animals did not differ from the control values. Thus, observation of the dynamics of changes in the body weight of animals showed that with an initial body weight of 124.0 ± 2.56 after 30 days of intragastric injection, an increase in body weight up to 158.7 ± 3.99 has been noted (in percentage terms, the increase is +27,9 %).

Studying dynamics hematological parameters of peripheral blood after exposure to the substance did not reveal statistically significant differences in animals of the experimental groups in comparison with the control data (Table 5). The results of studying the biochemical parameters of the blood serum of experimental and control animals after exposure to food additives are presented in table 6. Analysis of the obtained data showed that in experimental animals the indices of total protein, total bilirubin, direct and indirect bilirubin, urea, cholesterol, ALT, AST, gamma-glutamyltransferase (γ GT) and glucose in blood serum did not differ significantly from the control values.

Thus, the “Marjon” water fortifier with prolonged intragastric injection to the experimental animals in the studied doses doesn't have a toxic effect on hematological and biochemical parameters.

In a histomorphological study, carried out 1 month after intragastric injection of a water fortifier at doses of 15, 150 and 300 mg / kg, in animals of the control and experimental groups, the anatomical location and structure of internal organs corresponded to the normal conditions. The appearance, size and macroscopic structure of internal organs did not visually differ from the normal condition.

On histological sections of the stomach, there is an integumentary epithelium protruding to different depths of its own submucosa, which creates dimples of different sizes. The cylindrical glandular epithelium are built in one

layer, without signs of atypia and distortion in the architectonics of the structure. The mucous cells alternate with the lining cells. In the area of the bottom of the gland, the main zymogenic cells are unchanged (Fig. 1-3).

Table 5.
Hematological parameters of rat blood after prolonged per os administration of the “Marjon” water fortifier in doses of 15, 150 and 300 mg/kg.

Groups, doses	Leukocytes, 10 ⁹ /l WBC	Color indicator, %	Hemoglobin, g/l	Erythrocytes, g/l RBC	Stab cells, %	Segmented %	Platelets in absolute numbers, 10 ⁹ /l PLT	Eosinophils %	Lymphocytes %	Monocytes, %	ESR, mm / hour
Control (intact)	8.4 ± 1.96	0.9 ± 1.96	180 ± 1.96	5.1 ± 1.96	1.9 ± 0.3	51 ± 6.97	284 ± 20.15	4 ± 0.8	68 ± 11.70	1.9 ± 0.4	5.2 ± 0.07
15 mg/kg	7.1 ± 0.36	0.8 ± 0.21	160.8 ± 4.62	4.80 ± 0.09	1.8 ± 0.317	37.8 ± 4.24	247.8 ± 11.21	2.7 ± 0.42	55.5 ± 4.06	1.8 ± 0.31	3.8 ± 0.48
150 mg/kg	6.8 ± 0.44	0.9 ± 0.21	168.3 ± 3.68	4.9 ± 0.08	2.0 ± 0.26	47.8 ± 2.88	230.8 ± 13.60	2.2 ± 0.31	45.2 ± 2.76	2.5 ± 0.34	3.5 ± 0.56
300 mg/kg	7.1 ± 0.38	0.9 ± 0.22	168.7 ± 5.65	4.9 ± 0.07	1.8 ± 0.32	48.3 ± 4.78	238.2 ± 15.65	25 ± 0.22	44.4 ± 4.98	2.5 ± 0.43	3.9 ± 0.64

Table 6.
Biochemical parameters of the blood of rats after prolonged per os administration of the “Marjon” water fortifier in doses of 15, 150 and 300 mg/kg.

Groups, doses	Alanine aminotransferase activity, ALT, U/L (at 37°C)	Activity of aspartate aminotransferase, AST, U/L (at 37°C)	Alkaline phosphatase activity, ALP, U/l (at 37°C)	Total protein, TP, g/dl (at 37°C)	Urea, Mmol/l	Glucose, Glu, Mmol/l
Control (intact)	76.63 ± 4.22	330.83 ± 20.70	584.47 ± 93.82	90.72 ± 5.86	5.68 ± 0.51	2.42 ± 0.23
15 mg/kg	68.17 ± 2.35	329.50 ± 20.17	474.13 ± 78.34	86.03 ± 6.25	4.56 ± 0.37	2.20 ± 0.26
150 mg/kg	88.63 ± 2.09	323.67 ± 23.46	531.35 ± 96.75	83.83 ± 4.95	5.07 ± 0.26	2.86 ± 0.32
300 mg/kg	64.38 ± 3.45	321.17 ± 29.04	594.85 ± 64.35	90.65 ± 6.66	4.71 ± 0.50	2.88 ± 0.31

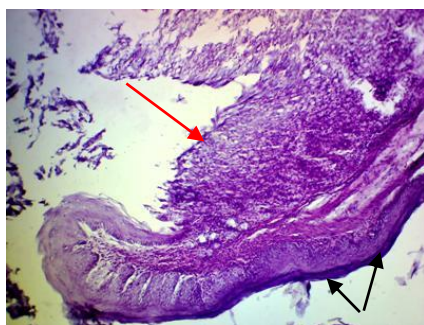


Fig. 1. Forestomach (black arrows) of white rats. Stomach (red arrow). The structure is not disturbed. HE staining. Size 10x10

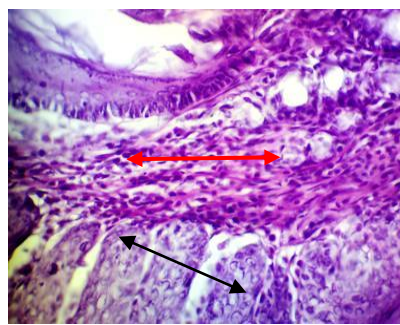


Fig. 2. The proventriculus of white rats. Mucosa - stratified squamous epithelium (black arrow), own mucous membrane (red arrow). The structure is not disturbed. HE staining. Size 10x40

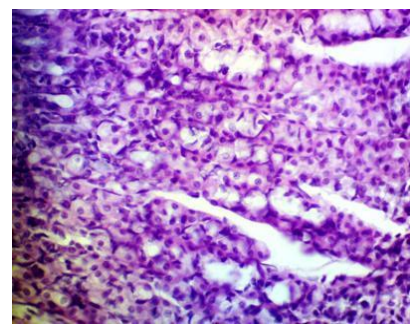


Fig. 3. The stomach of white rats. Glands. The structure is not disturbed. HE staining. Size 10x40

Macroscopically, the liver of white rats is red-brown in color, the surface is smooth, the consistency is elastic, homogeneous. Concrements and signs of bile stagnation were not found in the bile ducts. The histomorphological picture of the liver after 30-day administration of the “Marjon” water fortifier per os, regardless of the exposure dose, revealed a similar picture. On histological sections of the liver, stained with hematoxylin and eosin, the architectonics of the hepatic lobules is preserved. Their edges were determined by the location of the hepatic triads. The liver capsule is not thickened. The liver parenchyma is formed by the classic hepatic lobules. Hepatocytes are polygonal, with a centrally located nucleus. The beam structure is not damaged (Fig. 4-5).

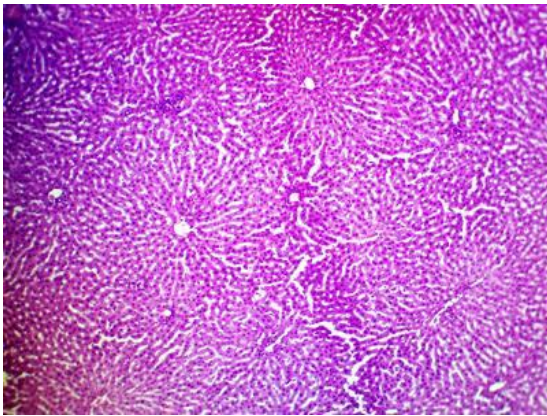


Figure: 4. Liver of white rats. The beam structure is not disturbed, there is no dystrophy or necrosis.
HE staining. Size 10x10

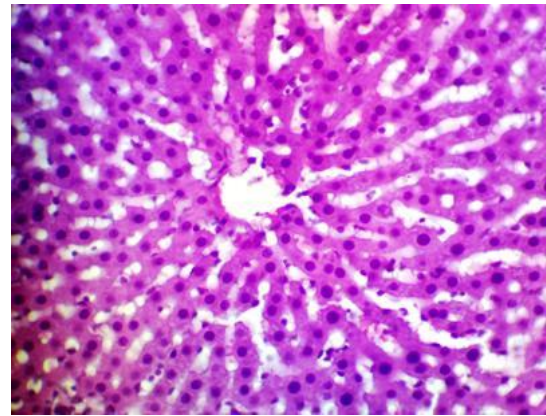


Figure: 5. Liver of white rats. The beam structure is not disturbed, there is no dystrophy or necrosis.
HE staining. Size 10x40.

The study of lymphoid follicles, white and red pulp after prolonged intragastric administration of the “Marjon” water fortifier at doses of 15, 150 and 300 mg/kg established that the structure of the spleen is not disturbed (Fig. 6). The red pulp occupies 75% of the cut area; it contains a variety of blood cells. Secondary follicles appear. The follicular pattern is clearly expressed. The white pulp is represented by a periarterial lymphatic sheath around the pulp artery, in which there is a T-lymphocytic proliferation center without mitosis. In the white pulp, a large number of small lymphocytes, a decrease in blast cells, an accumulation of macrophages and plasma cells.

In kidney tissues after prolonged intragastric administration of the “Marjon” water fortifier at doses of 15, 150 and 300 mg/kg does not cause dystrophic or inflammatory changes (Fig. 7).

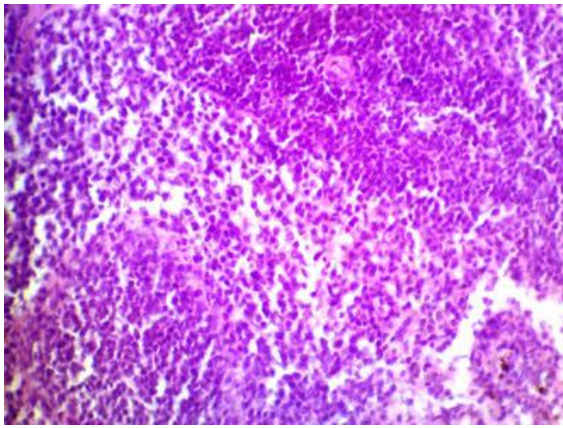


Fig. 6. Spleen of white rats. Red and white pulp. The structure is not disturbed, foci of necrosis, dystrophy are not observed. HE staining. Size 10x40.

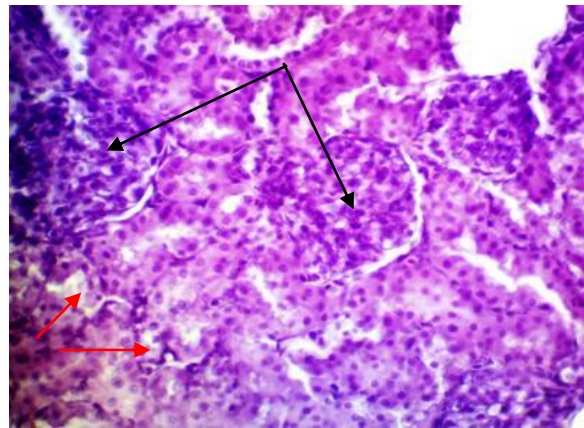


Fig. 7. Kidney of white rats after exposure to the "Marjon" water fortifier. Cortical substance. The structure is not broken. Glomeruli (black arrow), tubules (red arrow). HE staining. Size 10x40

In the histological section of the jejunum, the mucosa and submucosa layers are visible, the muscular membrane and serosa - without morphological changes. The apical surface has finger-like projections (villi) where goblet cells with mucoid secretions are visible.

On a histological section, the tissue of the colon is with short and relatively wide crypts. The crypts are much more developed than the upper gastrointestinal tract, they outnumber them and they are located very often. Between the crypts, small gaps of the own layer of the mucous membrane remain, filled with loose fibrous unformed connective tissue.

On the basis of a comparative histomorphological study of organs and tissues of control and experimental animals, it can be concluded that prolonged intragastric administration of the water fortifier "Marjon", production of the "ORION SKORPION" Ltd (Uzbekistan) in doses of 15, 150 and 300 mg/kg does not have a toxic effect on the internal organs of experimental animals.

Conclusion

Based on the expertise of the scientific dossier, literature data and the results of toxicological studies of the food product - "Marjon" water fortifier in terms of acute toxicity parameters with the intragastric route of intake of the additive to food belongs to the low toxic substances class (class IV). Food products in doses of 15, 150 and 300 mg / kg do not have a skin-resorptive and skin-irritating effect, do not irritate the mucous membranes of the eyes, and do not exhibit cumulative and allergenic properties.

The results of **hematological, biochemical and** histomorphological studies of internal organs, confirm that the "Marjon" water fortifier with prolonged

intragastric injection of 15, 150 and 300 mg/kg doesn't have a toxic effect on the organism of experimental animals.

The results of toxicological studies allow us to make a conclusion about the biomedical safety of the "Marjon" water fortifier produced by the "ORION SKORPION" Ltd (Uzbekistan) for human health and can be approved for use in accordance with the prescription and in the established order.

The Technical conditions for this product have been developed - Ts 19658570-004: 2013 "CaMaLife water fortifier. Technical conditions". Drinking water is intended for direct consumption (approved by the Ministry of Health and the "Uzstandart" Agency) [12].

REFERENCES

1. Zaitseva V.M., Lifyandsky V.G., Marinkin V.I. Applied Medical Statistics / Textbook.-SPb.-LTD "Foliant Publishing House".- 2003.- p.432.
2. Makarov V.G. et al. Manual. Physiological, biochemical and biometric indicators of the norm of experimental animals. SPB.: Publishing house "LEMA", 2013, - p.116.
3. Guidelines for experimental (preclinical) study of new pharmacological agents. Ed. Kurlyandsky B.A.- M.; 2005.- p.165.
4. SanNiR No. 0283-10 dated 05.02.10 "Hygienic requirements for food safety". T 2010. P. 48.
5. OECD Standards for Research in Chemistry No. 423 "Thorough Toxicological Evaluation - The Classic Method" dated March 22, 1996.
6. I.V. Sanotskiy. Methods for determining the toxicity and hazard of chemicals. Moscow, 1970, p. 161-163; 175-177.
7. Khabriev R.U. Guidelines for the study of the general toxic effect of pharmacological substances // Guidelines for experimental (preclinical) study of new pharmacological substances. M., 2005: p.50-100.
8. Khudayberganov A.S., Kamilova R.T., Navruzov E.B., Khegay L.N., Basharova L.M. /Methodical guidelines for conducting toxicological studies of food and biologically active food additives in an experiment on animals No. 012-3 / 0312 from 18.06. 2017
9. Tutelyan V.A. Biologically active additives in human nutrition (quality and safety assessment, efficacy, characteristics, use in preventive and clinical medicine). Textbook for postgraduate education of doctors of all specialties / - Tomsk; Publishing house NTL, 1999.- p.296.
10. Tutelyan V.A., Sukhanov B.P., Kerimova M.G. Prerequisites and factors for the formation of a regional policy in the field of healthy nutrition in Russia. - 2007. - Volume 76. - №6. - p. 39-43.
11. Tutelyan V.A., Sukhanov B.P., Vasiliev A.V. et al. Implementation of the concept of the state policy of healthy nutrition of the population of Russia at the regional level: the formation of regional policy and regional programs. Methodological aspects of the development and

implementation of programs. Part 2. Features of regional programs to improve the macro- and micronutrient security of the population // Nutrition issues. - 2005. - No. 2. - p. 3-9.

12. Specifications - Ts 19658570-004: 2013 "CaMaLife" water fortifier. Drinking water intended for direct consumption.

13. Shaikhova G.I., Odilova B.T. What is healthy eating and how can we return to it // Organization and management of health care. T. No. 7. 2019. - p.42-48.

14. Christiansen L.C., Burckhardt B., Yanofsky M.F., et al. Pod opening in soybean - isolation of potential IND1 orthodox // Soy 2002. Program and proceeding for the 9th Biennial conference of the cellular and molecular biology in Soybean. Lexington, Kentucky, 2002. p. 803.

15. Ermatov N.J., Shaikhova G.I., Salomova F.I., Azizova F.L., Rustamov B. The effectiveness of red palm oil in patients with gastrointestinal diseases. - (International Journal of Pharmaceutical Research) Oct-Dec 2019 (Vol. 11] Issue 4. p. 648-651.

16. [Parasuraman](#) S. Toxicological screening // [J. Pharmacol Pharmacother...](#) 2011 Apr-Jun; 2 (2): p.74-79.