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EFFECT OF INTENSIFICATION OF SELENIUM-PROTECTION PROPERTIES IN LABORATORY ANIMALS DRINKING "FLINT" WATER DUE TO THE INCREASE IN THE COEFFICIENT OF DIFFUSION OF SELENIUM IN ORGANS AND TISSUES

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The influence of "flint" water on the development of biochemical processes which cause the accumulation of selenium in the body of laboratory animals has been studied experimentally. A decrease in the bond energy of the molecule of "flint" water with the anion SeO_3^{2-} in relation to the bond energy of the molecule of ordinary water and an increase in the coefficient of diffusion of this anion in bone and muscular tissues in filtration of "flint" water have been substantiated.

Lack of attention to the problem of microelements is obvious against the background of numerous investigations on evaluation of the available vitamin supply and measures of therapeutic and preventive character [1–3]. Most developed countries have governmental or parliamentary complex programs in the field of nutrition. This kind of state policy is absent in the Republic of Belarus at present.

Recent years have seen an increased interest among researchers in selenium, i.e., a microelement essential for normal vital functions of the body.

Selenium is required for normal functioning of the thyroid and the nervous system. Its deficiency produces weakness, higher-than-average fatigability, and dizziness; dystrophy changes in muscles, disseminated sclerosis, and a delay of growth and development occur. It is precisely selenium that protects every living thing against lead, cadmium, mercury, alcohol, tobacco-smoke, and carbon-monoxide poisonings [4].

In studying the mechanism of action of selenium, it has been found that it belongs to the group of antioxidants, i.e., substances stabilizing cell membranes owing to their capacity for protecting the unsaturated fatty acids of the membranes against overoxidation, destroying peroxides, and suppressing the formation of free radicals [5]. It has been proved that the activity of selenium in tissues is 50 to 100 times higher than the activity of another very powerful antioxidant — vitamin E [6].

The higher the content of selenium in the blood, the smaller the chance of developing cancer since, when malignant tumors grow, there is a reduction in the content of selenium in internal organs and a simultaneous increase in it in the tumor itself [7–9]. An increased affinity of tumor tissue to selenium is a consequence of the deep rearrangements in the metabolism of malignant cells associated with the necessity of maintaining, at an extremely high level, the activity of selenium-dependent glutathione peroxidase that contributes to the preservation of the high rate of multiplication of tumor cells [10].

Thus, it may be inferred that one promising microelement for improving the protective potential of the body and preventing the development of a number of diseases is selenium.

Following the recommendations of the World Health Organization, 150 μg of selenium per kg of weight must enter the body a day. Belorussians receive only 12 μg/kg, since more than 50% of the Republic belongs to a region in which the level of selenium on soil is lower than the critical level (0.1 mg/kg) and the areas of soil in the Minsk, Grodno, and Vitebsk Regions contain selenium in concentrations no higher that 0.05 mg/kg. Drinking water in which selenium amounts to just 3.5 to 8.5% of the level of the so-called fully adequate water cannot be used as the source of this microelement for the human body.

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TABLE 1. Basic Calculated Parameters of the Molecules of Ordinary and "Flint" Water and the Bond Energy of the Anion SeO_3^{2-} with Them

Type of water	r, Å	α, deg	d, Å	Atomic terms (energy levels) in H_2O, eV		Energy of bond of the anion with H_2O, kcal/mole
				hydrogen ε_s^c	oxygen ε_p^a	
Ordinary	0.9700	99.900	2.1379	9.1338	11.9441	0.4677
"Flint"	0.9700	101.500	2.2348	8.6980	11.7526	0.3023

Balancing food intake with respect to microelement composition is one of the main problems of rational nutrition. It is a thankless task to persuade people to take tablets throughout their lives in order to compensate for a deficiency in vitamins and microelements. Experts believe that it is easier to solve the problem gradually: by adding the required substances to foodstuffs. Thus, it is common practice to enrich milk with vitamins C, A, and D and useful microflora and to enrich fats and oils with the fat-soluble vitamins A, D, and E and betacarotene.

At the same time, on the basis of our study of many years of the properties of "flint" water, it has been assumed that an intensification of the selenium-protection properties in the body can be effected in the case of drinking this kind of water. To prove this proposition we carried out investigations in two different directions. At the first stage, they involved both determination of the coefficients of diffusion and distribution of the anion SeO_3^{2-} dissolved in ordinary and "flint" water in bone and muscular tissues and calculation of the bond energy of this anion with the molecules of ordinary and "flint" water. The procedure of determination of the diffusion and distribution coefficients has been described in [11]. Below we present the empirical dependences establishing a relationship between the relative values of the diffusion and distribution coefficients in bone and muscular tissues and the concentration of selenium in "flint" and ordinary water:

for bone tissue

$$\frac{D}{D_0} = A \exp(\alpha C) = 1.18 \exp(-0.0082C), \quad \frac{\beta}{\beta_0} = B \exp(kC) = 0.42 \exp(-0.0146C);$$

for muscular tissue

$$\frac{D}{D_0} = A \exp(\alpha C) = 1.2 \exp(-0.0028C), \quad \frac{\beta}{\beta_0} = B \exp(kC) = 0.85 \exp(-0.0008C).$$

These dependences yield that the coefficient of diffusion of selenium in bone flour increases 1.18 times while the coefficient of its distribution decreases 2.4 times in filtration of "flint" water compared to the filtration of ordinary water. The coefficient of diffusion of selenium in muscular tissue increases 1.2 times, while the coefficient of its distribution decreases 1.18 times.

This experimental fact is attributable to the decrease in the bond energy of the anion SeO_3^{2-} with the molecule of "flint" water. The theory of calculation of the binding energy has also been described in [11]. Here we present results of the calculation (Table 1). As follows from the table, the bond energy of the anion SeO_3^{2-} with a molecule of ordinary water is equal to 0.4677 kcal/mole and that of the anion SeO_3^{2-} with a molecule of "flint" water is equal to 0.3023 kcal/mole, i.e., it is 1.5 times lower.

The results obtained enabled us to assume that in drinking "flint" water selenium will selectively accumulate in the bone and muscular tissues, which will decrease its content in the aqueous medium of the body and in waste products.

To prove this proposition we carried out experimental investigations on 300 non-thoroughbred white rats, 210 of which were intracutaneously reinoculated with a tumor — alveolar hepatocarcinoma (PC-1). According to the type of action, we subdivided the animals into five groups with 60 rats in each:

I) monitoring (healthy animals drinking ordinary water);

II) monitoring (healthy animals drinking "flint" water);

TABLE 2. Dynamics of the Indices of Lipid Peroxidation, the Antioxidant System, and Endogenic Intoxication in Healthy Animals and Tumor Carriers after Drinking Ordinary and "Flint" Water

Investigated indices	Investigation periods, days	Group				
		I	II	III	IV	V
Dienic conjugates, conv. units/ml	10	1.1±0.22	0.66±0.06	0.92±0.15*	0.86±0.17	0.34±0.16*
	90	0.9±0.14	0.56±0.20	2.60±0.40	1.38±0.24**	0.50±0.06**
Dieneketones, conv. units/ml	10	0.29±0.04	0.11±0.01*	0.24±0.06	0.03±0.004*	0.01±0.003*
	90	0.30±0.03	0.18±0.05	0.36±0.06	0.18±0.06**	0.18±0.08
Malonic dialdehyde, conv. units/ml	10	1.98±0.16	1.76±0.23	4.44±0.75	3.68±0.38	2.8±0.31
	90	2.10±0.18	1.36±0.48	6.20±0.62	3.0±0.2**	3.1±0.30**
Schiff bases, conv. units/ml	10	0.45±0.09	0.34±0.13	0.36±0.03*	0.33±0.08*	0.31±0.3*
	90	0.50±0.07	0.26±0.04**	1.80±0.60	0.76±0.36	0.60±0.3**
Vitamin A, μmole/liter	10	0.30±0.04	0.38±0.07*	0.59±0.07*	0.68±0.09*	0.26±0.06
	90	0.32±0.03	0.58±0.22	0.16±0.06	0.32±0.05	0.39±0.04**
Vitamin E, μmole/liter	10	1.09±0.22	0.90±0.23*	1.08±0.12*	1.12±0.10*	1.48±0.11
	90	1.31±0.14	2.40±0.18**	0.5±0.3	1.8±0.25**	1.9±0.5**
Medium-molecular-weight peptides, conv. units	10	0.32±0.01	0.19±0.01	0.26±0.01*	0.25±0.01	0.22±0.01*
	90	0.30±0.02	0.22±0.08	0.64±0.08	0.32±0.02**	0.30±0.05**
Sorption capacity of erythrocytes, % of the absorbed dye	10	43.22±1.45	40.33±1.77	57.83±2.73*	57.33±0.32*	46.37±1.42
	90	45.83±1.83	36.00±4.60	80.60±2.80	40.2±2.2**	40.2±2.6**

*) $P < 0.05$, differences between the investigation periods are statistically reliable;

**) $P < 0.05$, differences between the investigated groups are statistically reliable ($I \rightarrow II$; $III \rightarrow IV$; $III \rightarrow V$).

III) tumor-carrier animals drinking ordinary water from the first day after the reinoculation of the tumor and to their death;

IV) tumor-carrier animals drinking "flint" water from the first day after the reinoculation of the tumor and to their death;

V) animals drinking "flint" water for 30 days; thereafter they were reinoculated with the tumor and drank "flint" water to their death.

Every 10 days from the beginning of the experiment and for 90 days we took blood (by the decapitation method) in 5 to 6 rats of each group to study the following parameters of the blood:

(a) levels of primary and final products of lipid peroxidation (dienic conjugates, dieneketones, malonic dialdehydes, and Schiff bases);

(b) antioxidant status (natural antioxidants — tocopherol (vitamin E) and retinol (vitamin A)).

We used the sorption capacity of erythrocytes and the level of the most toxic metabolites, i.e., medium-molecular-weight peptides, as the integral indices of endogenic intoxication of the animals' body.

The selection of these indices was motivated by the fact that numerous and diverse human diceases are based on a comparatively small number of disfunctions of organs, tissues, and cells; it is common practice to call these disfunctions standard pathological processes. The most significant of them is peroxidation of the lipids of membrane cell structures. It has been proved by experimental and clinical investigations that the development of a malignant tumor in the body occurs against a background of the intensification of lipid-peroxidation processes which are aggravated with increase in the tumor mass. Lipid peroxidation is maintained at a certain stationary level using complex and diverse

regulation mechanisms required for the body's vital functions; these mechanisms have been called antioxidant ones. Antioxidants protect membrane structures against free-radical oxidation and inhibit the process of lipid peroxidation in them. The state of the available antioxidant supply of the body is the governing factor preventing the uncontrolled lipid peroxidation from developing. Thus, the basic criterion of evaluation of new preparations synthesized at present and of their prospects for increasing the available energy supply of the body is their capacity to influence the level of lipid peroxidation by improving the antioxidant status of the body.

Table 2 gives the investigated parameters of the blood of the animals in the five groups at the beginning (10th day) and at the end (30th day) of the experiment.

Analyzing the data obtained, we should primarily note that drinking of "flint" water had no adverse effects on the body of both the healthy animals and the tumor carriers. The differences observed in a number of biochemical processes in the case of the drinking of ordinary and "flint" water by the healthy animals (groups I and II) are related to the development of selenium-protection properties in the body of the latter. Thus, in the healthy animals drinking "flint" water, we observed a reduction in the level of medium-molecular-weight peptides and an activation of the antioxidant system contributing to the blocking of the processes of free-radical oxidation. This is demonstrated by the reduction in the levels of dienic conjugates, dieneketones, malonic dialdehydes, and Schiff bases and the increase in the protective role of the antioxidant vitamins A and E.

Drinking of "flint" water by the tumor-carrier animals (group IV) reduced the level of endogenic intoxication caused by the tumor growth; the indices of the medium-molecular-weight peptides and the values of the sorption capacity of erythrocytes decreased substantially. In these animals, the indices of peroxidation of lipids (dienic conjugates, dieneketones, malonic dialdehydes, and Schiff bases) were substantially lower, while the activation of the antioxidant vitamins A and E was higher than in the tumor carriers drinking ordinary water (group III).

The positive action of "flint" water on the body of the laboratory animals was the most pronounced when the period of drinking was long. Drinking it for 30 days before the reinoculation of the tumor (group V) accelerated the processes of blocking of the initiation of lipid peroxidation to the largest extent and increased the levels of antioxidant vitamins A and E. The processes of endogenic intoxication also turned out to be decelerated in these animals. Metabolic rearrangements in the body of the tumor carriers which occurred in this series of experiments reduced the influence and duration of the general action of the tumor process on the body; this, finally, had a positive effect on the course of the disease in the form of reliable retardation of the tumor growth and an increase in the average life compared to the control group (group III).

Theoretical calculations show that about 80% of all oncological diseases are caused by one's lifestyle and the environment. According to the data of the World Health Organization, a poor diet and drinking water of poor quality are among the factors influencing the number of cancer cases. It is precisely for this reason that International Water Day is celebrated worldwide on March 23 every year — in this field of research, there are still unused opportunities for correction of living conditions and neutralization of the action of carcinogenic environmental factors.

The results obtained give grounds to recommend that population of the Republic of Belarus drink "flint" water as a general strengthener for increasing the antioxidant status of the body.

NOTATION

D and D_0, coefficients of diffusion of the ion in bone and muscular tissues in filtration of "flint" and ordinary water; d, hydrated radius of the ion; r, valence bond length; α, valence angle; β and β_0, coefficients of distribution of the ion in bone and muscular tissue in filtration of "flint" and ordinary water; C, running concentration of the ion in the filtrate; ε_s^c, atomic term of the cation of the s state; ε_p^a, atomic term of the anion of the p state. Superscripts and subscripts: c, cation; a, anion; s and p, electron states; 0, initial value.

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