Research Article **Open Access**

Phytomineral complexes as elements of functional nutrition to enhance the protective function of the lymphatic system in aging

Vladimir Gorchakov[1,2*], Kirill Nicolaychuk[1], Olga Gorchakova[2], Georgi Demchenko[3], and Bayan Nurmakhanova[3]

[1]Novosibirsk State University, Novosibirsk, Russia; [2]Research Institute of clinical and experimental Lymphology – branch of Institute of Cytology and Genetics of SB RAS, Novosibirsk, Russia; [3]Republic Governmental Enterprise «Institute of Genetics and Physiology» Science Committee Ministry of Education and Science of Republic Kazakhstan, Almaty, Kazakhstan.

***Corresponding Author**: Vladimir Gorchakov, Novosibirsk State University, 1, Pirogova str., Novosibirsk, 630090, Russia

Submission Date: September 6th, 2023; **Acceptance Date:** January 5th, 2024; **Publication Date:** January 15th, 2024

Please cite this article as: Gorchakov V., Nicolaychuk K., Gorchakova O., Demchenko G., Nurmakhanova B. Phytomineral complexes as elements of functional nutrition to enhance the protective function of the lymphatic system in aging. *Bioactive Compounds in Health and Disease* 2024; 7(1): 1-16. DOI: doi.org/10.31989/bchd.v7i1.1289

ABSTRACT

Background: The problem of aging remains relevant in the modern world, with a notable connection between aging and nutrition. It is important to find a way to slow down aging. Integration lymphology with functional food theory (or phytodietetics) is the most promising idea. Detection of lymphotropic properties in bioactive food ingredients will increase the lymphatic system activity in aging. Our task is to improve the protective status of lymph nodes by taking a phytomineral product in aging.

Objective: The research purpose is to provide evidence of the use of a plant-mineral complex to activate the lymph system (lymph nodes) in aging. Participants in the experiment are 160 Wistar rats divided into groups of old and young animals. Half of the aging animals took an additional food plant-mineral complex "IQdetoxSORB". The basis of the food complex is physiologically acting substances such as flavonoids, trace elements, food fibers, and others.

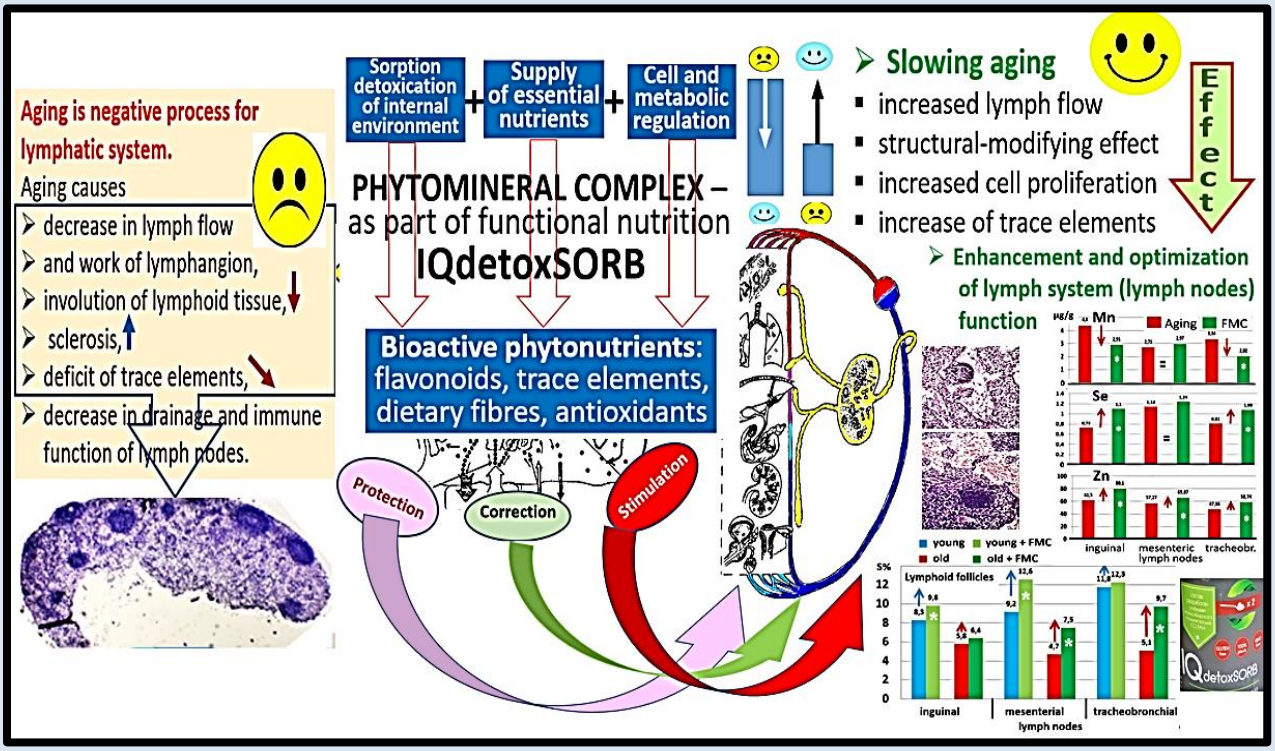
Methods: Different methods have been applied to study systems forming components of lymph nodes. The system of lymph node compartments was examined by a histological method. The liquid component of the organ is evaluated by a thermogravimetric method. Lymph node trace elements (Mn, Fe, Cu, Zn, Se) were determined by X-ray fluorescence analysis using synchrotron radiation (RFA SR). The StatPlus Pro license program and statistical analysis of dynamic series were used to process digital data.

Results: We first presented data on the effect of functional nutrition on the lymphatic system and proved the

lymphotropic properties of the plant-mineral complex. The bioactive ingredients of the complex (flavonoids, trace elements, food fibers) are useful and influence the lymphatic system, improving health in old age. The increase in lymphatic system activity occurs through the implementation of a lymphosanation mechanism due to the stimulating and protective effects of plant ingredients. Intake of the phytomineral complex accelerates lymph flow, modifies lymph node compartments, and restores trace element balance. The positive effect depends on the formation of an association of bioelements with lymphoid compartments. A plant-based diet corrects and increases the protective status of lymph nodes. The result is a slowdown in age-induced changes in peripheral lymphoid organs.

Conclusion: As an element of functional nutrition, the plant-mineral complex contains bioactive ingredients - flavonoids, trace elements, and food fibers. These bioactive substances alter the existing status of the lymphatic system, increasing protective potential. Increased activity of the lymph system (lymph nodes) is an argument for slowing aging and preventing age-associated pathology. The information presented is the basis for recommending plant-mineral complexes for wellness programs of anti-aging.

Keywords: lymphatic system; lymph nodes; compartments; trace elements; gerontology, phytotherapy, nutrition.



INTRODUCTION

The problem of demographic aging and active longevity remains relevant to date. The publication of functional nutrition theory has become a progressive moment [1, 2]. It has become apparent that physiologically active ingredients of functional products promote healthy living, reduce risk of developing pathologies, and increase quality and life expectancy [1–3]. Bioactive food

compounds affect the functioning of the body's organs and systems. These ingredients control cellular metabolism and create stable homeostasis at different periods of life. The mechanism of effect of plant food ingredients on the lymphatic system remains a secret so far. The role of the lymphatic system is intended to provide endoecological protection and safety in life, especially in retirees [4]. Homeostasis of lymphatic regions of the organism is determined by a structurally organized status of the lymphatic system [5, 6]. Lymphoid tissue involution and destabilization of the compartmental system in lymph nodes complicates detoxification of extracellular space and provokes immune inability to ensure endoecological safety [4, 6, 7]. Otherwise, the lymphatic destabilization is a sign of aging [4]. Knowing this fact, it is important to obtain confirmation of lymphatic system activation when taking physiologically active ingredients of plant food.

Studies are required to determine an indicator for occurring changes in organs after ingestion of plant food in accordance with functional food theory [1, 2]. It can be argued that such an indicator or biomarker may be a lymph node for a tissue microregion [4, 6]. The lymph node as an indicator of the internal environment allows the assessment of potential changes in aging and subsequent intake of plant nutrients. The lymph node belongs to a triune system including compartments, a liquid component, and bioelements. These systems-forming components support the operability of lymph nodes [8]. Essentially, the alteration of these three functional systems can serve as confirmation that bioactive food compounds work to their destinations. Correction of the lymphatic system is important for effective prevention of aging according to functional nutrition theory.

The lymphatic system attracts many researchers in different areas of knowledge. The creative cooperation of sciences such as lymphology, nutritiology, and pharmacology has become a progressive step in the appearance of pharmaconutritiology [9-10] and a new direction – lymphonutritiology [6]. Lymphonutritiology deals with the search and creation of lymphotropic products of functional nutrition. Aging requires a special methodology. One such approach may be phytodietetics (plant nutritive support, functional foods). The basis is plants as an element of functional nutrition [11, 12, 13]. Medicinal plants are a source of physiologically active substances of flavonoids and bioelements and other nutrients [3, 14-16]. It is not known how the lymphatic system will respond to support with plant nutrients. Formulating the task for researchers is contingent upon obtaining the solution. The research purpose is to provide evidence of the use of a plant-mineral complex with the indication of acting ingredients to activate the lymph system (lymph nodes) in aging.

MATERIALS AND METHODS

Materials: Participants in the experiment are 160 Wistar rats of different ages. We followed the age periodization for rats and humans proposed by O.A. Gelashvili [17]. This approach helped us identify groups of animals comparable to human age. We considered animals aged 3–5 months as young due to the correspondence of 16-20 human years, and animals aged 18–20 months were correlated with people over 70 years of age. Age corresponds to baseline and final periods in study dynamics. The animals had standard food with access to water. The design of the experiment included 4 groups of animals. The first group was the control and consisted of young rats. The second group is young animals treated with a food plant-mineral complex (PMC). The third group included rinse rats. The fourth group is older rats treated with phytomineral complex (PMC). There are 40 animals in each group. The object of the study is visceral mesenteric and tracheobronchial lymph nodes. We applied the original approach to lymph node evaluation. The lymph node is seen as a triune system comprising compartments, a liquid component, and trace elements.

Changing the parameters of this system makes the lymph node an indicator or biomarkers of various situations in the organism [6].

Phytomineral complex (PMC): We used food phytomineral complex IQdetoxSORB (SPF "SIB-KRUK," Koltsovo, Novosibirsk). This complex falls under the notion of functional food with bioactive ingredients in accordance with the existing definition of Functional Food Center [1, 2]. Phytomineral complex is a powder of mechanical and chemical grinding of plants. The professional IQdetoxSORB complex includes a sorption component (*Linum usitatissimum L.,* flax seeds) and plant (phyto) component (*Hedysarum neglectum or Hedysarum theinum Krasnob., Bergenia crassifolia, Rosa majalis Herrm., Ribes nigrum L., Rhodíola rosea, Vaccínium myrtíllus, Vaccinium vitis-idaea, Thymus serpyllum L.*). The principles of phytotherapy and phytodietetics guided the choice of plants [14]. The main physiologically active substances of plants are polyphenol complexes (flavonoids), dietary fibers, and bioelements. These phytochemical nutrients give us safety confidence and have positive polyfunctional effects on the organism [11, 13-16, 18]. The daily dose of the plant composition was 0.2 g/kg for a month. Microelements (Mn, Fe, Cu, Zn, Se) were determined in a sample of ground plants (phytocomposition) at the accredited Analytical Center of the Joint Institute of Geology, Geophysics and Mineralogy of SB RAS (Table 1). Error of analysis methods does not exceed 10%.

Table 1. Trace element content in food phytomineral complex, mg/kg

Sample characterization	**Se**	**Cu**	**Zn**	**Fe**	**Mn**
Plant sample (ground phytocomposition)	0,067 ± 0,014	6,11 ± 0,23	47,7 ± 2,05	317,3 ± 24,46	106,4 ± 6,28

Ethics Statement: We complied the mandatory rules of humane treatment of animals in accordance with the European Convention (Strasbourg 18.03.1986, ETS No. 123 appendix, 2010), Order of the Ministry of Health of the Russian Federation (No. 267 of 19.06.2003). The Local Ethical Committee of the Institute of Clinical and Experimental Lymphology approved biomedical studies (Novosibirsk, Protocol No. 126 of 30.11.2016). The work was carried out in the framework of the state task FWNR-2022-0012 (Russia) and the scientific project AP05133060 (Republic of Kazakhstan).

METHODS

Histological method: Histological examination of lymph nodes is the main morphological method. The lymph nodes were placed in a preservative solution of 10–12% formol. After that, we carried out a classic sequential program of moving bioobjects through alcohols-xylene-paraffin. Histological sections were made on the microtome. Histological study of sections was performed after staining with hematoxylin and eosin, a trichromic dye of C. Massson. Phenotyping of lymphocytes of ectopic lymphoid follicles was performed by streptavidin-biotin method. We applied a morphometric grid for histomorphometry of peripheral lymphoid organ compartments [19]. We considered the number of grid crossings on each compartment (capsule-trabecular base, peripheral cortex and deep paracortex, primary and secondary lymphoid follicles, medullary cords, lymphatic sinuses) and made a calculation into percentages.

Determination of lymphatic flow rate: We conducted a lifetime interstitial injection of ink to find out the state of drainage in the inguinal lymphatic region. We estimated the rate of lymph flow by recording the time of lymph passage with dye along the lymph bed, including vessels

and sinuses of the lymph node, in animals of different ages [6].

Thermogravimetric method: We determined the liquid component of lymph nodes by thermogravimetric method [20]. There is a state of matter for water bound and free in the lymph node. The bound state of water is characterized by the presence of a bond between water molecules and substances. The bound fraction cannot move freely, as it is part of biological structures. Free water has free molecules and constantly moving. An example of a free fluid may be lymph in lymph node sinuses. The ratio between the liquid fractions is the hydration coefficient. The principle of the method consists in evaporation of water from the lymph node at constant temperature 105°C with recording of weight change. Knowledge of the volume and area of lymph node structures makes it possible to calculate the volume of fluid for each immunocompetent zone on the principle of histostereometry.

RFA SR: Bioelements (zinc, iron, copper, manganese, selenium) are one of the main groups of nutrients vital to the work of the immune system [18]. Trace elements are involved in the form of ions, co-factors of enzymes and compounds with proteins. The concentration of bioelements as chemical elements is determined in lymph nodes by X-ray fluorescence analysis using synchrotron radiation (RFA SR, Budker's Nuclear Physics Institute, Russia) [21].

Statistical analyses: We used the StatPlus Pro license program package for statistical data analysis technology. The arithmetic average and standard error were calculated with the accepted difference reliability at $p < 0.05$. The Kolmogorov-Smirnov criterion was the basis for testing for the membership of normal distribution. We further applied the methodology of using the dynamic rows method to imagine the aging occurring, comparing the initial or basic ("yo") and final ("yi") data series. The index (growth coefficient, Cg) shows an intensity of changes relative to the baseline (Fig. 1, 2).

$$\mathbf{Cg} = \frac{\mathbf{yi}}{\mathbf{yo}} \quad (1)$$

RESULTS

Aging and lymphatic system (lymph nodes): Aging is closely related to the modification of lymphatic system structures and development of immune failure with low interstitial drainage activity; but there is no complete understanding of the complementarity of intranodal components, that is, between compartments, the liquid component, and trace element balance. What happens in the lymphatic region when old age comes? We assessed the movement of the dye across the lymphatic vessels after intra interstitial injection. Lymph with ink flowed faster in young rats than in older animals (Table 2). In older rats, there was a 1.6–2 times slowdown in lymph flow across efferent lymph vessels and through the lymph node (Table 2). Most scientists note lymphatic network reduction, tissue dehydration, and, as a result, a decrease in lymphatic flow rate in older animals [4, 6, 7]. Water is a mandatory part of peripheral lymphoid organs, being in free and bound form. Large changes concern the free form of water when aging. The lack of free water is manifested by dehydration of both lymph nodes, resulting in weakened natural protection of peripheral lymphoid organs. Age dehydration also concerns lymph nodes (Fig. 1). Age reduction of lymph flow and the sinus system is associated with a decrease of free-flowing fluid (lymph) volume in aging [6].

Aging is accompanied by inversion of all peripheral lymphoid organs. Immunocompetent areas of lymph nodes are affected. Cortical and medullary regions are no exception. Age transformation of lymphoid tissue has its differences in lymphatic system organs (Fig. 2). Lymphoid follicles are the most reactive structures. Lymphoid follicles decrease up to disappearance in aging. Secondary lymphoid follicles are most indicative in their

response to aging. There is an onset of immune depression due to low cellular proliferation in lymphoid follicles. The most significant attenuation of the immune response occurs when secondary lymphoid follicles of the tracheobronchial lymph node are involved. The germinative centers were relatively small in size. The growth coefficient lags far behind the baseline for secondary follicles (Fig. 2). The value of the coefficient for secondary follicles does not reach the baseline, indicating an age-induced decrease of lymphocytopoiesis and, as a result, humoral immunity. There is a certain decrease in the paracortical area (T-zone) (Fig. 2). The immune response of the T compartment is associated with a size reduction due to weak saturation by lymphoid cells [5, 8]. The increase in connective tissue replaces the normal lymphoid structure in the lymph nodes of older animals. Aging enhances the process of lymph node sclerosing. This is particularly concerning the capsular-trabecular base and perivascular spaces. Sclerosing occurs most in the mesenteric lymph node. Local changes in lymph nodes are associated with age and drainable tissue microregion. There is a regional specificity of lymph node aging with a decrease in immune status in the lymph region.

Aging is one of the reasons for the development of trace element imbalance. There is a correlation of lymphoid tissue morphology with trace elements in the pathogenesis of age-induced changes. Immune group trace elements are co-factors of enzymes that provide metabolism, cell proliferation, and create a certain dimension of compartments in lymph nodes. Aging alters the concentration of minerals to form a bioelement profile in lymph nodes. The bioelement profile is individual when monitoring each lymph node (Fig. 3). There is a profile with an increase of Mn and a decrease of Zn, Se, Fe, Cu, and Se when monitoring the mesenteric lymph node. There is a profile with an increase of Mn, a decrease of Zn, Se, and Se, and no change of Fe and Cu after tracheobronchial lymph node monitoring. Research proves that destabilization of trace element balance is an important element in the etiology of age-associated lymph node involution. It is likely that age causes a certain loss of protective function of lymph nodes [22, 23] and the present results encompass this phenomenon. Understanding age changes in lymph nodes can help determine correction methods to enhance lymph node activity.

Table 2. Rate of lymph flow with ink by lymphatic vessels and through lymph node at animals of different ages and after taking plant-mineral complex (PMC), mm/sec.

V, mm/sec	**young animals (n=20)**	**young animals + PMC (n=20)**	**old animals (n=20)**	**old animals + PMC (n=20)**
	1	2	3	4
Afferent lymphatic vessels	0.65±0.05	0.68±0.04 $P_{1-2} > 0.05$	0.42±0.048 $P_{1-3} < 0.01$	0.44±0.08 $P_{3-4} > 0.05$ $P_{2-4} < 0.05$
Lymph node	0.08±0.007	0.09±0.005 $P_{1-2} > 0.05$	0.04±0.004 $P_{1-3} < 0.01$	0.06±0.004 $P_{3-4} < 0.01$ $P_{2-4} < 0.001$

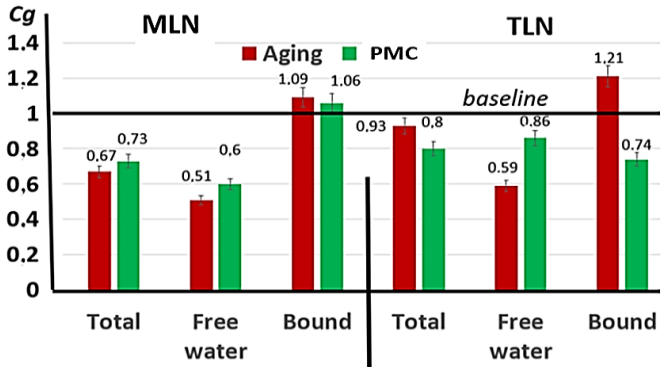


Figure 1. Growth coefficient for liquid components of mesenteric (MLN) and tracheobronchial (TLN) lymph nodes in aging and after plant-mineral support (PMC). Plant-mineral support brings the coefficient closer to baseline as proven lymph node hydration (free water fraction).

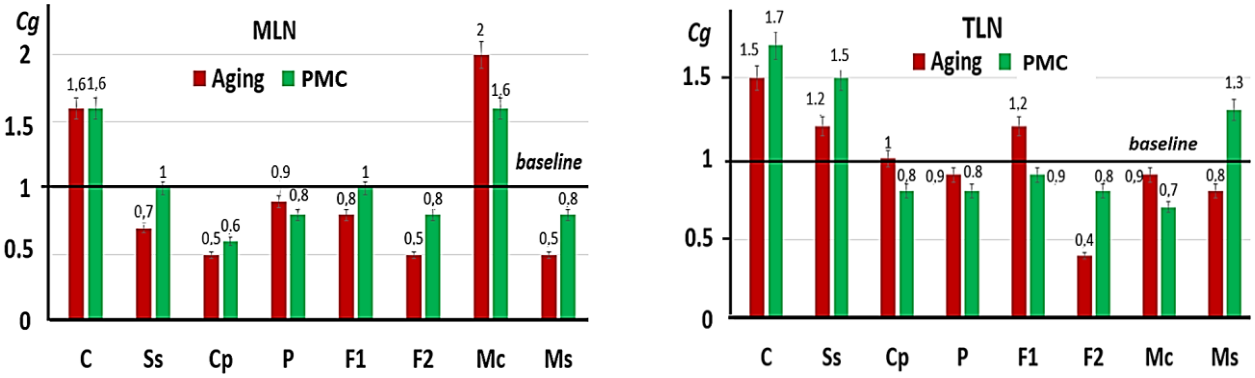


Figure 2. Growth coefficient for lymph node compartments in aging and after taking plant-mineral complex (PMC). Plant-mineral support modifies lymph nodes (MLN and TLN), previously subjected to aging.

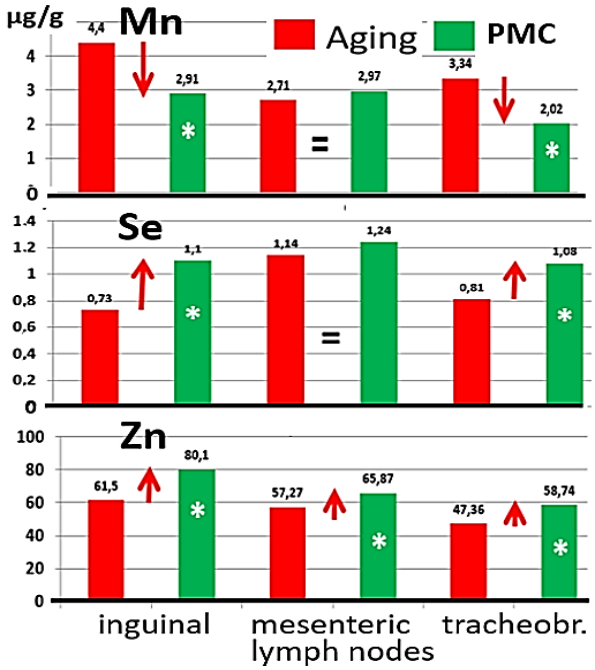


Figure 3. Bioelements of lymph nodes subjected to aging and after taking of plant-mineral complex.

*P < 0.05 – statistically significant difference; PMC – bioactive plant-mineral complex

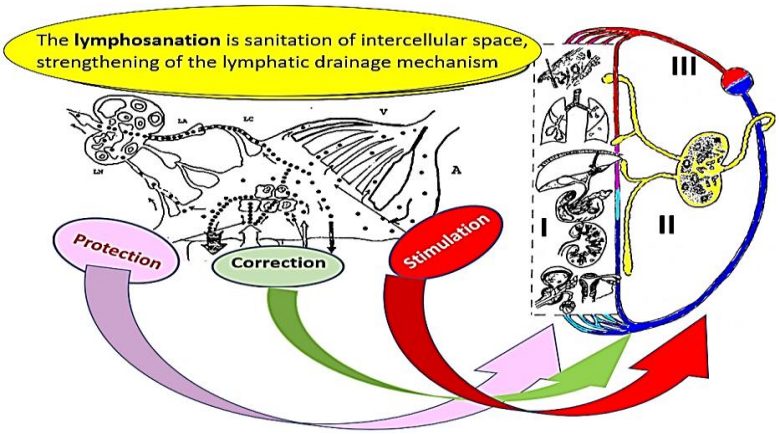


Figure. 4. Principles of plant-nutrient support lymphosanation at different levels of lymphatic region organization.

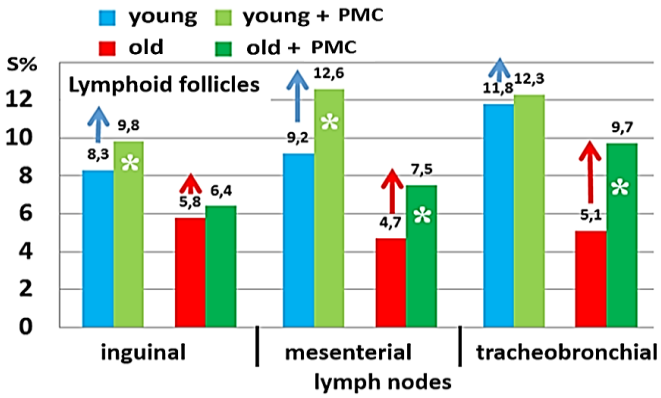


Figure 5. Size of lymphoid follicles at rats of different ages after plant-nutrient support (phytomineral complex, PMC). Arrows indicate the effect of phytostimulation.

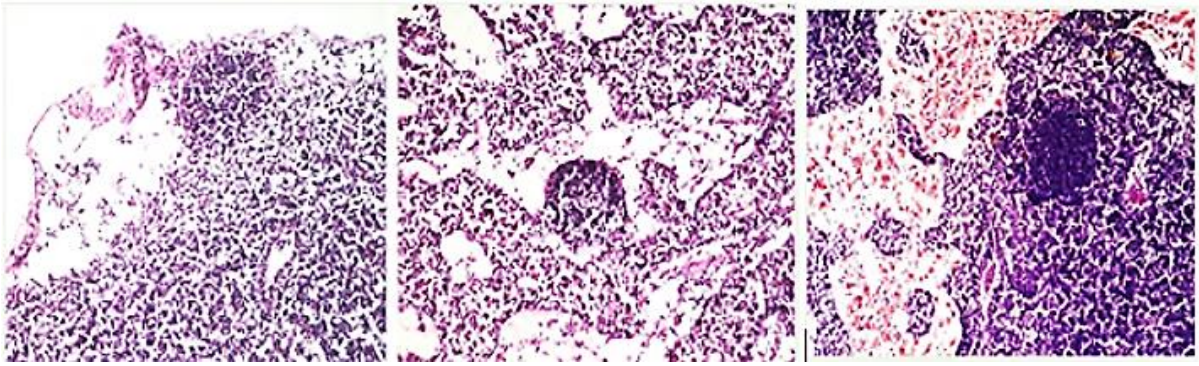


Figure 6. "Tertiary follicles" are in the peripheral sinus near the cortex (at the left), among medullary cords in the medullary substance (in the center), inside paracortical area (at the right) of lymph nodes. Phytostimulation effect in older animals. Hematoxylin and eosin stain. Magnification: microscope ocular 7 and objective 20.

Phytonutrients and lymph nodes: The lymphatic system is one of the few natural protective systems of our organism. The lymphatic system efficiency is reduced when aging. Age-induced changes need to be corrected. We assume that plant dietary technology will strengthen the protective mechanisms of the lymphoid system to combat aging and disease. Lymphosanation technology is most suitable for correction according to the principles of functional food and "background" therapy. The most interesting plant product is IQdetoxSORB as an element of functional nutrition. This plant-mineral complex is intended to affect target organs, including lymphatic

system structures [6]. Wellness lymphosanation suggests several clusters to affect and reduce the tension caused by aging (Fig. 4). The first cluster contains boundary membranes between internal and external environments of the organism. Boundary structures are relevant to the skin, intestinal tract, lungs, kidneys, and other organs in contact with the external environment. The second cluster provides effects on lymphatic region components (interstitial, lymph vessels, lymph nodes). We paid more attention to the second cluster. The third cluster includes a blood vessel system. All these clusters determine the main directions of exposure for the plant-food complex: I – excretory organs in contact with the external environment; II – lymphatic (lymphoid) system and circulating lymph; III – blood vessels and hemocirculation (Fig. 4). Information about lymphatic region clusters serves as a basis for directed use of plant food ingredients. Most preferred are polyphenol complexes (or flavonoids), minerals, dietary fibers, and other physiologically active nutrients. Bioactive substances affect all clusters of the lymphatic region, and plant nutrients are a driving force in lymphosanation mechanisms against aging. Strategic understanding of the role of bioactive food substances in lymphosanation should be based on scientific principles--lymphostimulation, lymphoprotection, and lymphocorrection.

Lymphostimulation: Bioflavonoids are considered promising bioactive components of many functional foods important for health [13–15, 24–26]. Bioactive substances have a positive effect on many metabolic parameters of organs and systems of the body [15, 16, 26, 27]. The plant product IQdetoxSORB is no exception. The effect of lymphostimulation is associated with plant bioflavonoids. Table analysis showed acceleration of lymph flow after plant nutrient support. The lymph passage rate with ink increased 1.5 times through the lymph node in elderly animals (Table 2). Obviously, plant flavonoids stimulate lymph flow and improve extracellular humoral transport and the drainage system of aged lymph nodes.

Intake of phytocomposition enhances the liquid component of lymphatic bed with change of lymph flow [4–6]. There is a change in hydration parameters in the lymph nodes (Fig. 1). Plant flavonoids slow down age-induced dehydration of lymph nodes. Plant-nutrient support brings closer the growth coefficient to baseline as evidence of an increase of hydration. The value of the coefficient is related to the change in volume of different forms of water (Fig. 1). The free form of water depends on the hydration of the organ. Typically, an increase of free water volume is a water-retaining feature for both lymph nodes after taking of plant functional food. The accumulation of free-flowing fluid (lymph) leads to the expansion of the sinus system. There was a release of excess immobilized (bound) water to replenish the volume of free water in the tracheobronchial lymph node (Fig. 1). Hydration is a condition for ensuring the effective work of lymph nodes weakened by age dehydration. There is an effect of fluid saturation of lymph nodes to provide protective function. Intake of phytonutrients is important for the purpose of preventing and overcoming dehydration in aging.

Lymphoprotection: The lymphatic system serves not only as a protective mechanism but also requires continuous, lifelong protection itself. It is the theory of functional nutrition that provides protection of the lymphatic system by taking bioactive compounds of the plant-mineral complex IQdetoxSORB. It is important to establish how plant food ingredients affect the excretory organ system. These organs are responsible for detoxifying the internal environment and getting rid of metabolic waste and toxic substances from the organism. The target focus of the function converges functionally the excretion organs and the lymphatic system. Plant flavonoids are multifunctional to many organs. The point

of application of flavonoids action is the excretory organs belonging to the first lymphosanation cluster (Fig. 4). Plant composition enhances the function of excretory organs [6, 11, 14] and as a result, weakening toxic pressure at the level of lymphatic cluster. Ground flax seeds are part of the plant-mineral complex. Flax (*Linum usitatissimum L.*) seeds are nothing less than a sorption compound of dietary fibers. Food fibers, entering the body, transit and along the way adsorb and remove useless substances, toxins. In other words, fibers are an enterosorbent of natural origin [6]. Food fibers prevent toxic substances from entering the internal environment of the organism due to their adsorption by the fibers. This mechanism of dietary fibers contributes to the active cleansing of the lymphatic system (Fig. 4). Lymph node protection is reached by enterosorption and exposure to the system of excretion organs by taking functionally acting components of IQdetoxSORB product at the level of the first and second lymphosanation clusters (Fig. 4). Such lymph node actively responds to plant bioflavonoids. Lymph node structure is modified under conditions of implementation of correcting principle of lymphosanation.

Lymphocorrection: Lymphocorrection is an important principle of lymphosanation in preventing age-induced changes in lymph nodes. The lymph node contains compartments relating to immunoactivity T- and B-areas. These special areas take an active part in the mechanism of adaptive immune response. Analysis of changes in immunoactivity compartments allows us to assess functional sufficiency of lymph nodes after taking plant-mineral complex. The impact of phytonutrient support is showing by lymph node restructuring. There is a selective modification of compartments depending on the initial level after plant-nutrient support. For example, the B-area of secondary lymphoid follicles increases 1.2–1.8 times following nutritional plant support in older rats (Fig. 5). Phytonutrient support slows down and compensates for age-induced changes in lymphoid tissue according to the "age standard".

Bioflavonoids of the plant-mineral complex cause proliferation of lymph node lymph cells. Phytonutrient support distributes T- and B- lymphocytes that play a key role in immunoactivity compartments. There is a reactive response with cell proliferation and differentiation in lymphoid follicles and paracortex. There is an increase in the number of plasmocytes in the medullary cords. Plasmocytes produce antibodies to destroy pathogens. Cell proliferation and differentiation in compartments allows effective control and destruction of pathogens and forming immune memory for future protection. Phytostimulation triggers cell proliferation with local formation of "tertiary follicles." Lymphoid follicles were observed in the peripheral sinus near the cortex, among medullary cords in the medullary substance, inside the paracortical area of lymph nodes (Fig. 6) These follicles appear temporarily as compensation for immune (lymphoid) failure. Lymphotropic wellness technology using a food phytomineral complex improves cytoarchitectonics and leads to lymphatic system activity.

Plant nutritional support influences trace elements and allows the elimination of their deficiency in aging-altered lymphoid tissue. Plants are a source of trace elements. Trace elements have pronounced biological activity. Plant trace elements act as a substrate for biochemical (metabolic) reactions or enzyme cofactors. The intake of trace elements from plant food eliminates the imbalance of bioelements by increasing some and reducing others in the lymph node profile at aging animals (Fig. 3). Zinc concentration increases in all lymph nodes. Selenium increases in the tracheobronchial lymph node, and selenium supports a tendency to increase in the mesenteric one. Copper content rises 1.4 times to 7.22 ± 0.22 μg/g (in older animals 5.29 ± 0.35 μg/g) in the mesenteric lymph node and decreases to 4.89 ± 0.16 μg/g (in elderly animals 5.37 ± 0.14 μg/g) in the tracheobronchial one. Iron content increased 1.3 times

to 241.2 ± 22.57 μg/g (in older animals 182.5 ± 14.33 μg/g) in the mesenteric lymph node. Iron concentration remains at the same level in the tracheobronchial node.

The redistribution of trace elements resulted in the formation of a different new microelement profile in both lymph nodes after taking the plant-mineral complex. The profile of visceral lymph nodes differs from each other. There is a smaller content of iron, copper, and zinc in the tracheobronchial lymph node. The mesenteric lymph node has the highest copper content (7.22 ± 0.22 μg/g). Manganese and selenium have almost the same concentrations in both lymph nodes. Plant-mineral food supplements make up for age-induced shortage of necessary trace elements. Plant-nutrient support brings trace element concentration closer to the level of lymph nodes of young animals. This fact is important for ensuring stability of operation of immunocompetent compartments and resistance to dehydration factors. Phytonutrients activate protective and adaptive mechanisms, enhance the effective work of lymph nodes to cope with age changes and try to prevent the development of immune failure in the lymphatic region.

DISCUSSION

Gerontology is expected to be another reasonable way to combat the negative effects of population aging. Many researchers are skeptical about this, despite compelling evidence from experiments [4, 6]. There is every reason to believe that only cooperation between scientists of different specialties is a solution to the problem of aging. It would be progressive to integrate gerontologists, lymphologists and nutritiologists. Such symbiosis of scientists provides a new methodology for aging. The trajectory of health and aging is associated with the notion of endoecological safety in internal and external exposures [4, 7]. The aging of organs and systems depends largely on the work of the lymphatic system. Lymph nodes are a tool for assessing senile changes. Recent advances confirm the etiology of the lymphatic system with aging and development of age-induced pathology [4, 6–8, 15]. It becomes clear to choose the lymphatic system as a target for therapeutic exposure and to develop an effective strategy to decelerate aging, expanding the range of an active, healthy lifestyle without disease.

Nutrition specialists pay special attention to functional food with bioactive ingredients in preserving health and active longevity without disease [1–3, 9, 10]. Signs of aging in lymphoid organs can be used to assess the effectiveness of the food diet. This approach extends the field of application of functional products to alter the activity of the lymphatic system to overcome aging and pathology. Many publications appear on the topic of the significant role of plant raw materials as a basis for functional foods in the scientific literature. This is one of the most important directions of modern nutritiology. The development of a plant product should follow the methodology of functional food science using biologically active substances as a health optimization tool [1, 2]. Studies confirm the role of "functional foods" with a plant-mineral basis in the prevention and therapy of age-associated diseases [28, 29]. Functional products become "nutraceutical" means [29]. Therefore, functional food science is a new discipline with a primary sphere to stimulate the study of bioactive substances [30, 31]. Phytotherapy and nutraceutical approaches can be a promising way to fight aging.

The plant product IQdetoxSORB as an element of functional food is intended for systematic consumption. Our research has shown that the phytomineral complex increases the protective level of lymphatic region clusters to improve health and quality of life in old age. The effect is related to the presence of physiologically functional ingredients in the composition. Functional foods are a very effective way to deliver beneficial nutrients for health and reduce the risk of disease [1, 2, 28]. The development of such foods is related to bioactive

ingredients such as flavonoids, trace elements, nutrients, and others, all of which are found in plants.

The composition of the plant complex is original. Phytocomposition has two components. The first is a compound of dietary fibers; the second is a complex of plants in Siberia. Dietary fibers (flax seeds) are classified as physiologically active food ingredients. The addition of dietary fibers is a common practice for the promotion of healthy food [32]. Dietary fibers are natural sorbents with respect to a wide class of substances. The sorption potential of dietary fibers reduces pressure on the lymphatic system. The phytocomponent of the IQdetoxSORB complex exhibits lymphotropic properties. Unfortunately, supplies of bioactive substances are insufficient when consuming traditional products, so it is important to offer a specialized IQdetoxSORB product. Various natural food systems such as vegetables, fruits, and plants contain compounds to promote health and prevent disease [33].

Bioflavonoids are a large group of phytochemical compounds (e.g. catechins, flavonols, flavones, anthocyanins, phenolic acids, and polyphenols). Bioflavonoids and various secondary metabolites in plant extract have antioxidant, anti-inflammatory activity and restrain aging of body cells and tissues [34–36]. The food supplement IQdetoxSORB is advertised as a sorption-detoxification agent of the organism's internal environment [37]. Detoxification of the internal environment depends on the function of the lymphatic system [4, 7]. Our studies have shown that flavonoids have an effect on constituent clusters of the lymphosanation mechanism. We recorded an active response of the lymphatic (lymphoid) system, which made it possible to claim the presence of lymphotropic properties of plant polyphenols. Along with this, as our studies show, flavonoids influence the structures of the lymphatic system. Lymphotropic properties of phytomineral complex are associated with implementation of mechanisms of protection, stimulation, and correction according to the lymphosanation program. The structural-modifying effect of plant bioflavonoids has been proven.

The growing interest in the use of plant polyphenols is supported by the results of studies proving the efficacy and safety of use. Bioflavonoids effectively act not only on the affected organ, but also on integrated organism systems [6, 11, 15-16]. It is most important to consider the presence of lymphoid-microelement integration. Plants are a donator of chemical elements (minerals) and can eliminate age-induced trace element deficiency. Plants are a source of trace elements and can eliminate age-induced trace element deficiency. The action of bioflavonoids and trace elements is combined, and they contribute to the proliferation of immunocompetent cells and the formation of an immune response [34, 36]. We created a pathogenetic scheme with a leading role of trace elements (Fig. 7). Trace elements are a co-factor for many enzymes involved in the metabolism of proliferating cells.

This scheme justifies the formation of a certain immune morphotype of the node when trace elements interact with enzymes, immunocompetent cells, and compartments. The following moments prove this [6]. First, immune sufficiency is determined by the development of compartments, where T- and B-lymphocytes interact; secondly, bioelements are part of enzyme co-factors and are involved in the activation and proliferation of lymphoid cells; thirdly, trace elements, also as bioflavonoids, can be targeted to correct the mechanism of immune response. A functional plant food containing flavonoids, trace elements and other nutrients exhibits biological activity against the lymphatic system and provides confirmed health benefits. And, eventually, we got information about the ingredients of the phytomineral complex capable of affecting the lymphatic system (lymphotropic effect).

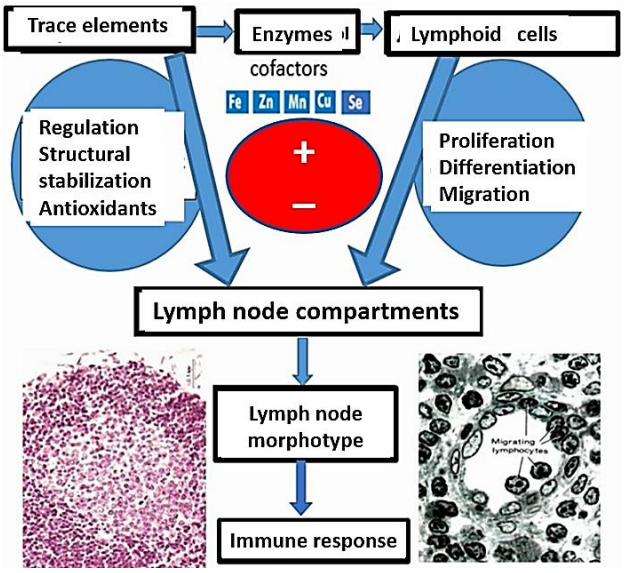


Figure. 7. Pathogenetic scheme of trace element effects on lymph nodes

Therefore, use of the phytomineral complex can have a protective effect against aging and age-induced diseases with increased activity of the lymph system (lymph nodes). The health and aging study reported significant depletion of immune defenses in older adults compared to younger people with the same dietary history. The paradigm of the need to accept plant specialized foods by older people is being implemented [9, 10, 12]. Functional foods do not undergo special clinical studies. This is the main difference between plant food and medicine. This determines the need for scientific research to identify new properties and their use in wellness and preventive nutrition in anti-aging programs. The results of the experiment demonstrate the prospect of using plant products as an element of functional food to increase the effective functioning of the lymphatic system in old age. The prospect of using functional nutrition allows activation of the lymphatic system and the likelihood that healthy individuals will remain healthy with age, and aging and disease will be effectively delayed or slowed down.

This idea was confirmed in the implementation of the lymphosanation and endoecological rehabilitation program in sanatorium and resort practice. One of the main stages of the program is food with the definition of dietary tables and specifically functional food. The implementation of plant functional products into practice is intended to improve the effectiveness of therapy and rehabilitation of a particular disease rather than intervene against "unhealthy" aging as such. If we supplement the diet with functional foods, we focus on improving health through the lymphatic system with age-associated pathology. One of the most effective ways to improve the health of the population is the widespread use of natural stimulants for the functions of organs and systems of the human organism. Currently, natural stimulants are food ingredients, and they are represented by a wide range of so-called biologically active additives, functional foods, nutraceuticals, and others. The food product IQdetoxSORB has a plant-mineral base, and this complex has found application in improving the nutritional structure of the elderly resting in the sanatorium. The approbation of plant-mineral complexes has shown the effectiveness of their use for restoration of health in sanatorium and resort rehabilitation [6]. Functional food in the rehabilitation complex allowed to improve quality of life, reduce intoxication, increase remission period in chronic

diseases, and reduce dose and number of preparations of basic therapy. More research is required to find out how long the effects are caused by eating a plant-mineral complex as an element of functional food.

CONCLUSION

Aging is a situation that requires an increase in the operability of the lymphatic system. The food plant mineral complex IQdetoxSORB with lymphotropic properties offers a new direction of lymphonutritiology in functional food science. A non-drug method of functional nutrition (phytodietetics) is positioned as a hero protection factor. Efficacy is due to functional food ingredients such as flavonoids, trace elements, dietary fibers, and others. If the lymphatic system is activated, the trajectory of aging can be changed. Bioactive plant compounds allow additional correction of lymphatic system structure and function in aging. The effects of stimulation, protection, and correction with respect to the lymphatic system (lymph nodes) are implemented. There is an increase in lymph flow, an increase in cell proliferation, optimization of hydration and balance of trace elements, and modification of lymph node structure in old age. We have made sure that the active functioning of the lymphatic (lymphoid) system stands as a crucial element in antiaging, increasing nonspecific resistance, and preventing polymorbidity. General biological laws allow the idea of experimental research to extrapolate to humans and plan the implementation of plant-mineral complexes as an element of functional food into the practice of rehabilitation of aging populations.

List of Abbreviations: PMC, plant(phyto)mineral complex; MLN, mesenteric lymph node; TLN, tracheobronchial lymph node; RFA SR, X-ray fluorescence analysis using synchrotron radiation; C, capsule; Ss, subcapsular sinus; Cp, cortical plateau; P, paracortex; F1, lymphoid follicle without germinative center; F2, lymphoid follicle with germinative center; Mc, medullary cords; Ms, medullary lymphatic sinus.

Competing interests: The authors declare that they have no competing interests.

Authors' contributions: All authors contributed to this study.

Acknowledgments: We thank scientific workers of the Institute of Nuclear Physics (Novosibirsk, Russia) for their help in determining trace elements of X-ray fluorescence analysis using synchrotron radiation.

REFERENCES

1. Martirosyan, D.M., Lampert T., Ekblad M. Classification and regulation of functional food proposed by the functional food center. Functional Food Science 2022; 2(2): 25–46. DOI: https://www.doi.org/10.31989/ffs.v2i2.890
2. Martirosyan, D., Kanya H., Nadalet C. Can functional foods reduce the risk of disease? Advancement of functional food definition and steps to create functional food products. Functional Foods in Health and Disease 2021; 11(5): 213–221. DOI: https://www.doi.org/10.31989/ffhd.v11i5.788
3. Kussmann, M., Cunha D. H. A., Nature has the answers: Discovering and validating natural bioactives for human health. Bioactive Compounds in Health and Disease 2022; 5(10): 222-234. DOI: https://www.doi.org/10.31989/bchd.v5i10.1000
4. Borodin, Yu. Lymphatic system and aging. Fundamental research 2011; 5: 11–15. [https://fundamental-research.ru/ru/article/view?id=21252]. Retrieved on January 12, 2024
5. Cakala-Jakimowicz, M., Kolodziej-Wojnar P., Puzianowska-Kuznicka M. Aging-Related Cellular, Structural and Functional Changes in the Lymph Nodes: A Significant Component of Immunosenescence? An Overvie. Cells 2021; 10: 3148. DOI: https://www.doi.org/10.3390/cells10113148
6. Borodin, Yu., Gorchakova O., Suhovershin A., Gorchakov V., Fartukov A., Kolmogorov Yu., et al. The concept of lymphatic region in preventive lymphology. Beau Bassin: LAP LAMBERT Academic Publishing. 2018; 1–74.
7. Toporova, S. Features of the system near cellular humoral transport in aging. Almanac Gerontology and Geriatrics 2003, 2: 90–94.
8. Hadamitzky, C, Spohr H., Debertin A.S. Age-dependent histoarchitectural changes in human lymph nodes: an

underestimated process with clinical relevance? J. Anat. 2010; 216: 556–562. DOI: https://www.doi.org/10.1111/j.1469-7580.2010.01213.x

9. Martirosyan, D.M., Sanchez S.S. Establishment of dosage of bioactive compounds in functional food products. Functional Food Science 2022; 3(2): 79–93. DOI: https://doi.org/10.31989/ffs.v2i3.915
10. Tutelyan, V.A., Nikityuk D.B. Nutriciology and Clinical Dietetics. Moscow: GEOTAR-Media. 2022; 1008p. DOI: 10.33029/9704-6280-5-NKD-2021-1-1008. DOI: https://doi.org/10.2337/dc21-1512
11. Mazo, V.K., Sidorova Yu.S., Sarkisyan V.A., Kiseleva T.L., and Kochetkova A.A. The prospective of using plant polyphenols as functional food ingredients. Vopr Pitan. 2018; 87(6): 57–66. PMID: 30763491. DOI: https://doi.org/10.24411/0042-8833-2018-10067
12. Puzin, S.N., Pogozheva A.V., Potapov V.N. Optimizing nutrition of older people as a mean of preventing premature aging. Vopr Pitan. 2018; 87(4): 69–77. PMID: 30570960. DOI: https://doi.org/10.24411/0042-8833-2018-10044
13. Fedko, I.V. Medicinal plants are possible sources of main macro- and microelements. "Concept". 2013; 3: 526–530. URL: http://e-koncept.ru/2013/53107.htm
14. Korsun, V.F., E.V. Korsun: Encyclopedia of phytotherapy. Herbs of Professor Korsun's life. Moscow: Centropolligraf. 2007; 1–443.
15. Gorchakov, V., Gorchakova O., Nurmakhanova B., Demchenko G. Role of phytonutrients in delaying aging of somatic lymph node. Archiv Euromedica 2023; 13(2): DOI: https://doi.org/10.35630/2023/13/2.40611
16. Ross, J.A., Kasum C.M. Dietary flavonoids: bioavailability, metabolic effects, and safety. Annu. Rev. Nutr. 2002; 22: 19–34. DOI: https://doi.org/10.1146/annurev.nutr.22.111401.144957
17. Gelashvili, O.A. Variant of periodization of biologically similar stages of human and rat ontogenesis. Saratov J Med Sci Res. 2008; 4 (22): 125–126.
18. Koudrine, A.V., Skalny A.V., Zhavoronkov A.A., Scalnaya M.G., Gromova O.A. Immunopharmacology of trace elements. Moscow: KMK Scientific Press. 2000; 1–537.
19. Avtandilov, G.G. Medical morphometry. Moscow: Medicine. 1990; 1–178.
20. Farashchuk, N.F. Water is the structural matrix of life. Bulletin Smolensk State Medical Academy. Vestnik Smolenskoy Gosudarstvennoy Medicinskoy Akademii 2020; 19(1): 56–70.
21. Piminov, P. Synchrotron Radiation Research and Application at VEPP-4. Physics Procedia 2016; 84: 19–26. DOI: https://doi.org/10.1016/j.phpro.2016.11.005
22. Grewe, M. Chronological ageing and photoageing of dendritic cells. Clin Exp Dermatol 2001; 26(7): 608–612. DOI: https://doi.org/10.1046/j.1365-2230.2001.00898.x
23. Pahlavani, M.A., Richardson A., Cheung H.T. Age-dependent changes of the mesenteric lymph node of Fischer F344 rats: morphological and histometric analysis. Mech Ageing Dev 1987; Jul; 39(2): 137–146. DOI: https://doi.org/10.1016/0047-6374(87)90005-4
24. Devkota, H.P., Kurizaki A., Tsushiro K., Adhikari-Devkota A., Hori K., Wada M., and Watanabe T. Flavonoids from the leaves and twigs of Lindera sericea (Seibold et Zucc.) Blume var. sericea (Lauraceae) from Japan and their bioactivities. Functional Foods in Health and Disease 2021; 11(1): 34–43. DOI: https://www.doi.org/10.31989/ffhd.v11i1.769
25. Madardam, J., Wattanachant S., and Yupanqui C.T. Evaluation of the antioxidant activity and nitric oxide production effect of formulated crispy vegetables from thermal processing of Amaranthus viridis and Sauropus androgynous. Functional Foods in Health and Disease 2023; 13(9):409–423. DOI: https://www.doi.org/10.31989/ffhd.v13i9.1116
26. Hashizume, Y., and Tandia M. The reduction impact of monoglucosyl rutin on abdominal visceral fat: A randomized, placebo-controlled, double-blind, parallel-group. Journal of Food Science 2020; 85(10): 3577–3589. DOI: https://doi.org/10.1111/1750-3841.15429
27. Iriti M., Varoni E.M., Vitalini S. Bioactive Compounds in Health and Disease – Focus on Rutin. Bioactive Compounds in Health and Disease 2023; 6(10): 235-242. DOI: https://www.doi.org/10.31989/bchd.v6i10.1145
28. Martirosyan, D., Von Brugger J., Bialow S. Functional food science: Differences and similarities with food science. Functional Foods in Health and Disease 2021; 11(9): 408-430. DOI: https://www.doi.org/10.31989/ffhd.v11i9.831
29. Damian, M.R., Cortes-Perez N.G., Quintana E.T., Ortiz-Moreno A., Garfias Noguez C., Cruceno-Casarrubias C.E. [et al.] Functional Foods, Nutraceuticals and Probiotics: A Focus on Human Health. Microorganisms 2022; 10(5): DOI: https://www.doi.org/10.3390/microorganisms10051065
30. Roberfroid, M.B. Concepts and strategy of functional food science: the European perspective. Am J Clin Nutr 2000; 71(6 Suppl): 1660S–1664S, discussion 1674S–1675S. DOI: https://www.doi.org/10.1093/ajcn/71.6.1660S
31. Panwar, P., Butler G.S., Jamroz A., Azizi P., Overall C.M., Brömme D. Aging-associated modifications of collagen

affect its degradation by matrix metalloproteinases. Matrix Biol 2018; 65: 30–44. DOI: https://doi.org/10.1016/j.matbio.2017.06.004

32. Alkhamova, G.K., Mazaev A.N., Rebezov Y.M. [et al.] Functional Purpose Products. Young Scientist 2014; 12(71): 62–65. URL: https://moluch.ru/archive/71/12258/
33. Mariod, A.A., Mustafa E.M.A., Yahia M.B. A review on the health benefits of Monechma ciliatum (Black mahlab): A potential functional food. Functional Foods in Health and Disease 2022; 12(2): 70–80. DOI: https://www.doi.org/10.31989/ffhd.v12i2.879
34. Khonthun, C., Khoothiam K., Chumphukam O., Thongboontho R., Oonlao P., Nuntaboon P., Phromnoi K., Screening and characterization of antioxidant, anti-aging, and anti-microbial activity of herbal extracts in Northern Thailand. Functional Foods in Health and Disease 2023; 13(2): 52–68, DOI: https://www.doi.org/10.31989/ffhd.v13i2.1070
35. Lorenzetti, A., Osato M., He F., Aperio C., Ayala A., Rasulova S., Barbagallo M. Interim report from a 2-year double-blind rct testing fermented papaya preparation on immune enhancement, endothelial health and qol in elderly adults. Functional Foods in Health and Disease 2023; 13(2): 69–81. DOI: https://www.doi.org/10.31989/ffhd.v13i2.1050
36. Ndolo, V., Maoni M., Mwamatope B., Tembo D. Phytochemicals in Commonly Consumed Foods in Malawian Diets. Functional Foods in Health and Disease 2022; 12(10): 578–592. DOI: https://www.doi.org/10.31989/ffhd.v12i9.976
37. Gorchakov, V.N., Nikolaychuk K.M., Demchenko G.A., Nurmakhanova B.A., Gorchakova O.V. Integral evaluation of thyroid lymphatic region in phytocorrection of hypothyroidism consequences. Siberian scientific medical journal 2023; 43(6): 106–118. DOI: https://doi.org/10.18699/SSMJ20230613