

## Research Article

**Phytomodification Effects of Visceral Lymph Node Aging**

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**Abstract**

Lymph nodes are prioritized in protecting and ensuring endoecological safety at different periods of life, especially in retirement age. It destabilizes the structure and function of the lymphatic system and organs when aging increases the risk of comorbid conditions. This is a sign of age-related pathology. Improving lymph node function is an essential task in integrating gerontology and lymphology. The solution to this problem is possible with the help of a phytotherapeutic agent, which involves the evaluation of efficacy with effect on intranodular functional systems - compartments, hydration, and trace elements. Phytotherapy weakens (slows) the intensity of the old lymph node changes. Phytotherapy has a modifying effect on structures with increased hydration and trace element concentration.



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Phytotherapy prevents age-dependent changes in the lymph node and increases the reliability of lymph node operation in old age.

### **Keywords**

Lymph nodes; compartments; hydration; trace elements; gerontology; phytotherapy

## **1. Introduction**

The progress of medicine increases life expectancy. There is a demographic situation where the number of older people increases. The problem of aging and the issue of health and quality of life of older persons remain relevant to date. Older people suffer from many diseases due to pathological changes in the organs and systems of the body [1-3]. Changes in organs depend directly on the state of the lymphatic system. Lymph nodes are prioritized in protecting and ensuring endoecological safety at different periods of life, especially in retirement age. Many organs are susceptible to aging, and peripheral lymphoid organs are no exception. Lymphoid tissue involution reduces immune protection and interstitial drainage in the lymphatic region [4-7]. Destabilization of the lymphatic system increases the risk of age-induced organ pathology [1, 8]. One of the main directions of morphological aging studies remains the prognosis of change of lymph node compartments about drained organs [1, 3]. The state of water and trace balance is inextricably related to the features of the structure and function of lymph nodes [4]. There is no data on the composition of water and trace elements compared to the functional morphology of lymph nodes in old age. Obtaining such data determines the originality of the approach to assessing the condition of lymph nodes. Aging is accompanied by dehydration of the organism's internal environment [5]. There is no permanent association of hydration with age, and it significantly does not bind it to the morphofunctional state of the lymph nodes. The lymph system, including lymph nodes, is vital to body fluid homeostasis. This requires additional study in aging [1, 6]. Age changes in trace element balance [9, 10] are accompanied by peripheral lymphoid organs disrupting the immune response mechanism. The trace element content is a leading mechanism for limiting homeostatic processes in the body, which concerns lymph nodes [10]. It seems appropriate to determine the range of trace elements in lymph nodes. Otherwise, it is impossible to understand the mechanisms of the regulatory role of trace elements and justify the need for phytocorrection of an aging organism.

Age-induced disorders of the organs and lymphatic system require some correction. There is an urgent need to affect the aging organism through the functions of the lymphatic system. The phenomenon of the lymphatic system remains not thoroughly studied in providing drainage, detoxification of endoecological space, and reversibility of changes in aging. The wonder of the lymphatic system remains not thoroughly researched in providing drainage, detoxification of endoecological space, and reversibility of changes in aging [8]. Older people are a convenient object to improve health and quality of life through the management of the main functions of the lymphatic system. Older people should understand that improving the lymphatic system is vital in ensuring active longevity. It is necessary to increase the workability of the lymphatic system and non-specific resistance of the organism [1, 4]. How can this be done? Lymphotropic technologies of restorative medicine are what the elderly need in terms of the endoecological concept of countering

aging [4, 8]. Non-drug treatments, among them phytotherapy, are of interest. Phytotherapy has found widespread application in medicine [11, 12]. The lymphatic component of the mechanism of action of phytotherapy remains beyond the attention of researchers. It is necessary to justify the feasibility of phytotherapy to correct age changes in the lymphatic (lymphoid) system. The result is of practical importance for optimizing rehabilitation at the stage of late ontogenesis.

The work aims to study the effect of phytotherapy on the structure and function of the lymph node, which has undergone age changes.

## 2. Materials and Methods

### 2.1 Materials

The experiment was performed on 160 white rats of different ages from the Institute of Cytology and Genetics vivarium. We adhered to the version of periodization proposed by O.A. Gelashvili [13] for rats with a life expectancy of 2 years. We used a coefficient of 1.7 in determining the age of rats and humans [13]. This approach allowed us to classify animals aged 3-5 months as youthful human age (16-20 years) and animals aged 18-20 months to be defined as old (over 74 years). The animals were conventionally divided into two groups, young and old. Age corresponds to the primary and final periods compared to the dynamics of the study. Animals received a standard diet with free access to water. Mesenteric and tracheobronchial lymph nodes were chosen as the object.

The design of the experiment involved dividing animals into the following 4 groups: 1) young ones - control and 2) young ones receiving phytotherapy; 3) old and 4) old who received phytotherapy. There are 40 animals in each group. We harvested mesenteric and tracheobronchial lymph nodes for histological examination from 20 rats and assessed hydration and trace element content from the other 20 animals in each group.

In the experiment, biologically active phytocomposition was used, including medicinal plants: *Hedysarum theinum* Krasnob., *Bergenia crassifolia* L. Fritsch., *Rhodiola rosea* L., *Vaccinium myrtillus* L., *Vaccinium vitisidaea* L., *Ribes nigrum* L., *Rosa majalis* Herrm., *Thymus serpyllum* L. and food fibers. Phytocomposition is an analogue of plant preparation (biologically active additive) IQdetoxSORB (manufacturer: SPF «SIB-KRUK», Naukograd Koltsovo, Novosibirsk). The choice of specific medicinal plants is based on the principles of phytotherapy. The main bioactive substances of plants are flavonoids, food fibers, and trace elements, which have adaptogenic and lymphotropic effects [9-12]. The daily dose of phytocomposition was 0.1-0.2 g/kg when added to the main feed by animals during the month.

The work on animals was carried out following international standards (Directives of the Council of the European Communities of 24 November 1986, 86/609/EEC) and Order of the Ministry of Health of the Russian Federation No. 267 of 19.06.2003. The study was approved by the local ethical committee of NIICEL (Protocol No. 126 of 30.11.2016).

### 2.2 Methods

#### 2.2.1 Histological Method

Histological examination of lymph nodes was carried out. Lymph nodes were fixed in 10% neutral formalin. This was followed by a classic scheme for wiring and pouring the material into paraffin,

followed by the preparation of histological sections. Histological sections of lymph nodes were stained with hematoxylin and eosin, azur, and eosine, a trichromic Masson dye. The streptavidin-biotin method of lymphocyte phenotyping was used to confirm ectopically located lymphoid nodes. Morphometric analysis of the structural components of lymph nodes was carried out using a morphometric grid [14]. The grid was applied to the lymph node cut. The number of grid crossings per whole section and separately per each of the structural components of a lymph node (capsule, cortical plateau, lymphoid follicles, paracortex, medullary cords, sinuses) was calculated with recalculation into percentages.

### 2.2.2 Thermogravimetric Method

The thermogravimetric method was used to evaluate lymph node hydration [15]. Different fractions of water (total, free, and bound) and their ratio (hydration coefficient) were determined. The principle of the method is to dry lymph nodes at a constant temperature of 105°C while recording changes in their weight on analytical scales. Knowing the volume of the lymph node and the area of its structures, we calculated the volume of fluid per lymph node structure according to the principle of stereometry.

### 2.2.3 RFA SR

The work focuses on manganese, zinc, copper, selenium, and iron. These elements refer to the discharge of essential and in the form of ions and compounds with proteins. Enzymes are actively involved in the processes of general exchange and the work of the immune (lymphoid) system. X-ray fluorescence analysis using synchrotron radiation (RFA SR) on equipment of Budker's Institute of Nuclear Physics (Novosibirsk, Russia) was used to determine trace elements (Mn, Fe, Cu, Zn, Se) [16].

### 2.2.4 Statistical Method

Statistical processing of the results was carried out using the Excel program with the introduced StatFi module of the StatPlus Pro license program, AnalystSoft Inc. Mean arithmetic was calculated with determination of its standard (RMS) error, difference validity at  $p < 0.05$ . The test of membership in the normal distribution was carried out using histogram construction and for greater confidence, the Kolmogorov-Smirnov criterion and associated indicators were calculated. In the statistical analysis of dynamic rows, the growth coefficient was defined as the ratio of the finite row to the initial row. The growth coefficient ( $Cg$ ) shows the intensity of the change in indicators by comparing the «yo» as the base period (initial level, young animals), «yi» is the final row of dynamics (old animals).

$$Cg = \frac{y_i}{y_o} \quad (1)$$

The formula calculation assumes a baseline where the growth coefficient is 1. Conventionally, the baseline demonstrates no difference between the initial and final dynamic rows. The deviation of the coefficient shows the direction and intensity of changes from the baseline.

### 3. Results

The lymph node is a marker of the state of the drained lymph region [1, 2, 4, 17] and can be used to assess the intensity of organ changes in aging. The equivalent of adequate lymph node operation integrates three interconnected functional systems: structural organization (compartments), hydration, and trace element status. With age, the operability of lymph nodes weakens, and the morphotype of regional lymph nodes changes following the concept of lymph region [4]. Improving lymph node function is a vital task for gerontology and lymphology. A solution to this problem is possible with phytotherapy. It seems crucial to prove the effect of phytotherapeutic agents on intranodular functional systems (compartments, hydration, and trace elements) to increase lymphatic system function.

#### 3.1 Lymph Node Compartments

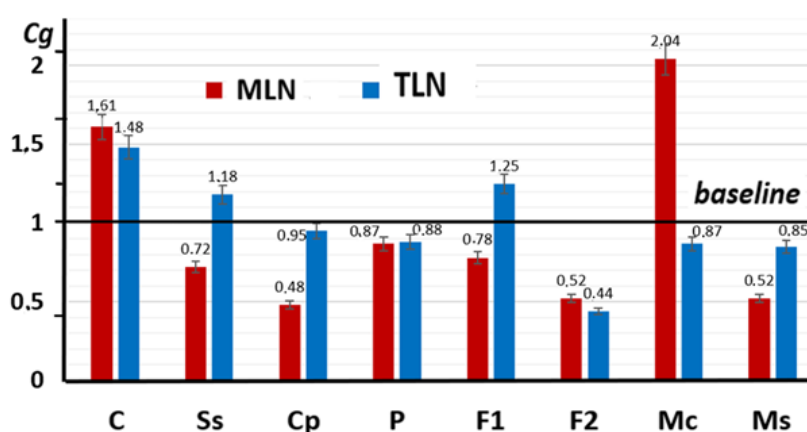
There is an uneven change in intranodular compartments in aging dynamics. The final results suggest different intensities of lymph node changes from baseline. We identified two trends with other change vectors – increasing or decreasing lymph node compartments (Figure 1, Table 1). Age-dependent changes manifest differently in the mesenteric and tracheobronchial lymph nodes. Most structures (cortical plateau, lymphoid follicles with a germinative center, paracortex, medullary sinus) are characterized by a reduction in the size of compartments. Still, their intensity is different in both lymph nodes. The mesenteric lymph node notes the most significant lag in the development of cortical plateau sizes in medullary sinuses. The reactivity of lymphoid follicles with a germinative center is reduced more in the tracheobronchial lymph node (Figure 1). The growth coefficient for lymphoid follicles with a germinative center lags far behind the baseline, indicating a decrease in lymphopoiesis function and humoral immunity. The level of reduction in paracortical area size is almost the same in both lymph nodes. Paracortex is a T-dependent zone, and a change in paracortical area indicates a decrease in the intensity of the immune response by cell type in the lymph node [4, 17]. Connective tissue growth occurs more in the mesenteric lymph node than in the tracheobronchial lymph node. This is most noticeable in the thickness of the lymph node capsule. When comparing lymph nodes, the opposite effect is noted in changing the size of structures such as subcapsular sinus, primary follicles (lymphoid follicles without a germinative center), and medullary cords. These structures are smaller except for medullary cords in the mesenteric lymph node (Figure 1, Table 1). The difference in visceral lymph nodes compartments changes suggests regional specificity of lymphoid tissue involution.

**Table 1** Area of lymph node structures in young and old animals and after phytotherapy, %.

Structures	Mesenteric lymph node (MLN)			Tracheobronchial lymph node (TLN)		
	young animals	old animals	old animals + phytotherapy	young animals	old animals	old animals + phytotherapy
	1	2	3	4	5	6
C	9.25 ± 0.14	14.9 ± 0.14*	14.7 ± 0.14*	4.78 ± 0.24	17.1 ± 0.30*	13.6 ± 0.29*

Ss	7.39 ± 0.11	5.35 ± 0.12*	7.34 ± 0.12°	4.45 ± 0.19	5.25 ± 0.23	6.87 ± 0.22°
Cp	12.5 ± 0.30	5.98 ± 0.28*	6.99 ± 0.31*°	15.2 ± 0.70	14.5 ± 0.31	12.3 ± 0.30*°
P	25.9 ± 1.08	22.6 ± 1.06	20.1 ± 0.87*	27.6 ± 1.82	24.4 ± 2.24	21.1 ± 2.17
F <sub>1</sub>	6.76 ± 0.19	5.26 ± 0.10*	7.05 ± 0.30*°	6.04 ± 0.16	7.55 ± 0.21*	5.52 ± 0.19°
F <sub>2</sub>	9.21 ± 0.27	4.79 ± 0.27*	7.54 ± 0.27*°	11.8 ± 0.46	5.18 ± 0.56*	9.79 ± 0.55*°
Mc	17.0 ± 0.52	34.8 ± 0.51*	27.1 ± 0.51*°	25.5 ± 0.86	22.1 ± 1.07	19.1 ± 1.04
Ms	11.8 ± 0.19	6.16 ± 0.38*	9.16 ± 0.19*°	4.48 ± 0.32	3.79 ± 0.40	5.72 ± 0.38°

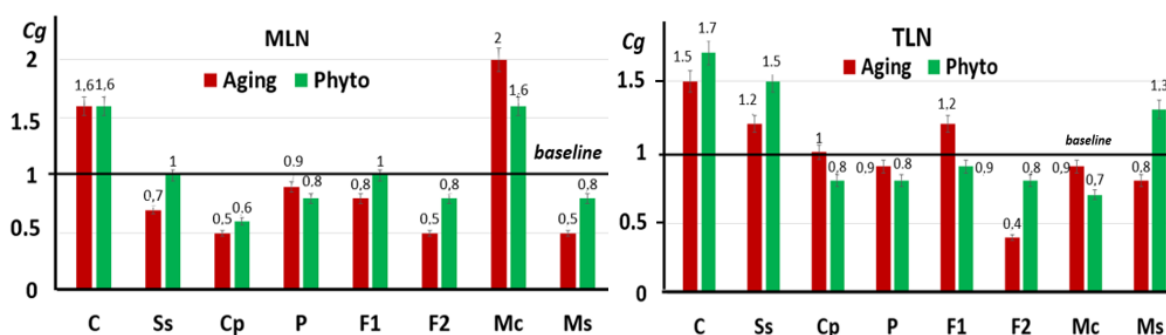
Note to the table: C - capsule; Ss - subcapsular sinus; Cp - cortical plateau; P - paracortex; F<sub>1</sub> - lymphoid follicle without germinative center; F<sub>2</sub> - lymphoid follicle with germinative center; Mc - medullary cords; Ms - medullary sinus \*P<sub>1-2,3; 4-5,6</sub> < 0.05; °P<sub>2-3; 5-6</sub> < 0.05 - statistically significant difference between different groups.



**Figure 1** Growth coefficient for mesenteric (MLN) and tracheobronchial (TLN) lymph node structures in aging. The tracheobronchial lymph node is subject to fewer changes and differs from the mesenteric one by a higher growth coefficient value for intranodal forms in aging, except for medullary cords, secondary follicles, and capsule-trabecular base. K is a capsule; Ss is subcapsular sinus; Cp is a cortical plateau; P is paracortex; F<sub>1</sub> is a primary follicle without a germinative center; F<sub>2</sub> is a secondary follicle with a germinative center; Mc is medullary cords; Ms is a medullary lymphatic sinus.

Intake of phytonutrients alters the intensity of changes in aging lymph nodes. We identified a difference between the size of lymph node compartments when aging and after phytonutrient support (Figure 2). There is a particular pattern in the direction of compartment changes after taking phytocomposition. It is noted that phytocorrection changed the response rate of compartments to aging (Figure 2). The area of bins increases after phytocorrection if there is a preceding decline in structures in aging. This is most typical of most mesenteric lymph node compartments. Conversely, if the forms retain significance when aging, these structures' area decreases after phytocorrection.

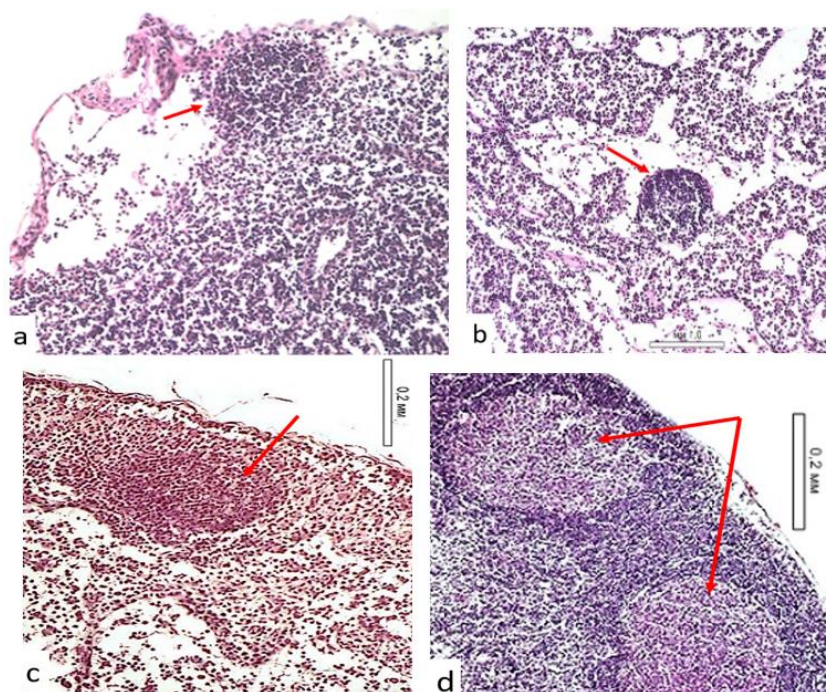
At the same time, the dimensions of structural-functional zones do not always reach baseline values. Common to both lymph nodes is the stimulation of secondary follicles with a germinative center after phytotherapy. The area of lymphoid follicles with a germinative center increases after phytotherapy. This fact is confirmed by approximating the growth ratio to the baseline (Figure 2). The formation of lymphoid follicles with a germinative center is associated with the stimulation of proliferation and differentiation of lymphocytopoietic cells. It suggests an increase in the immune status of aging lymph nodes after photo correction.



**Figure 2** Growth coefficient for mesenteric (MLN) and tracheobronchial (TLN) lymph node structures at aging and after phytocorrection. Phytotherapy has a positive effect on lymph node structures altered by aging. If growth coefficients have high values when aging, these coefficients decrease after phytotherapy. If growth coefficients have low aging values, these coefficients increase after phytotherapy. 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 sinus.

Ectopia of lymphoid follicles is detected (Figure 3). The atypical location of lymphoid follicles should be considered a compensatory response to restoring immune defense while enhancing lymphoproliferative processes and changing lymphatic flow conditions due to phytotherapy. Phytotherapy has a structural-modifying effect on lymph nodes. The results of biologically active phytotherapy travel compensate for signs of aging and increase the functional activity of lymph nodes in aging.





**Figure 3** Ectopia of lymphoid follicle formation in the subcapsular zone (a) and in the medullary substance (b) of the mesenteric lymph node of old animals after phytotherapy. Lymphoid follicles with and without a germinal center (d, c) are located in a typical location within the lymph node cortex of young animals. Hematoxylin and eosin stain. Magnification 240x.

### 3.2 Lymph Nodes Hydration

Most scientists note that tissue dehydration also comes with age [4-6]. There is no exception for lymph nodes either. The intensity of dehydration affects the transformation of lymph node structures (Figure 4, Table 2). Dehydration is most seen in the mesenteric lymph node. The growth coefficient showed a decrease in total water and free fraction. The tracheobronchial lymph node responds by reducing a predominantly free fraction of water. This fact is comparable to the mesenteric lymph node. The free fraction of water is nothing more than lymph in the sinus system of lymph nodes. The volume of free fluid in the lymph node is directly related to the reduction in the size of the sinus system in aging [4].

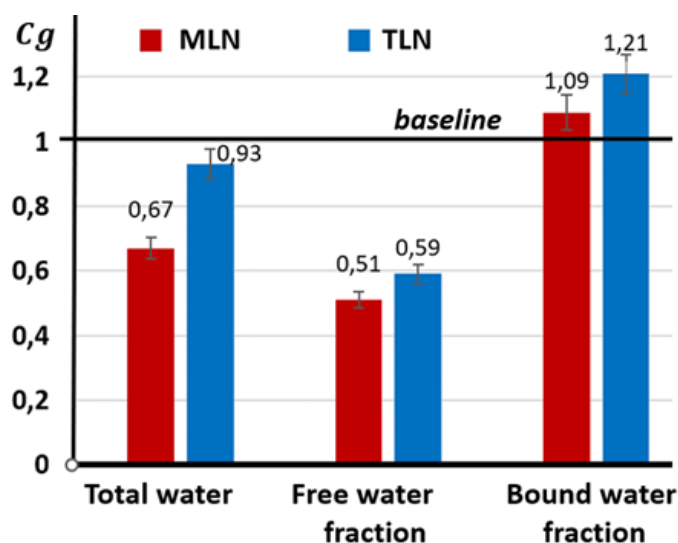
**Table 2** Total water and water fractions of visceral lymph nodes of young and old animals and after phytotherapy, %.

Water	Mesenteric lymph node (MLN)			Tracheobronchial lymph node (TLN)		
	young animals	old animals	old animals + phytotherapy	young animals	old animals	old animals + phytotherapy
	1	2	3	4	5	6
Total water	85.92 ± 3.44°	57.79 ± 2.48*	62.55 ± 3.02*	10.71 ± 0.55	9.93 ± 1.03	8.55 ± 1.38
Free water fraction	61.90 ± 1.99°	31.66 ± 1.65*	37.18 ± 1.27*°	4.88 ± 0.47°	2.90 ± 0.36*	4.21 ± 0.64°



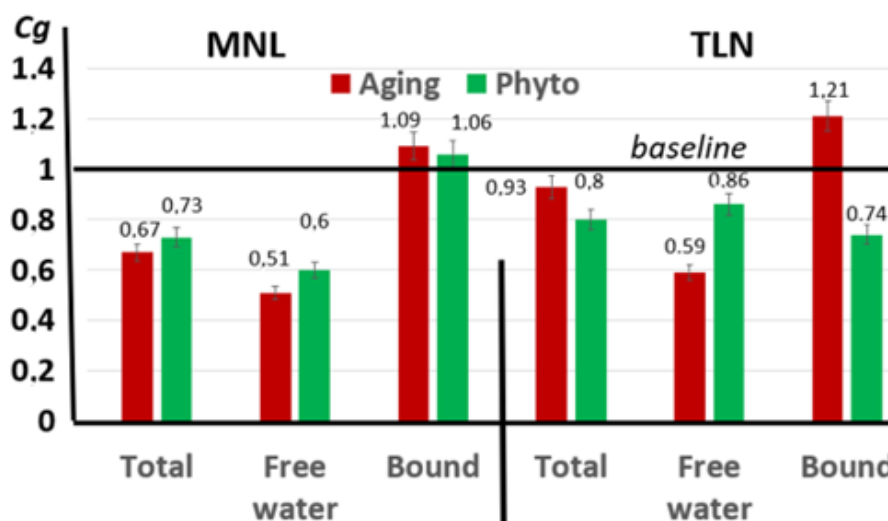
Bound water fraction	24.01 ± 1.91°	26.12 ± 2.38	25.38 ± 1.47	5.83 ± 0.28°	7.03 ± 0.73*	4.34 ± 0.64°
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\*P<sub>1-2,3; 4-5,6</sub> < 0,05; °P<sub>2-3; 5-6</sub> < 0.05.



**Figure 4** Growth coefficient for total water, free and bound water fractions of mesenteric (MLN) and tracheobronchial (TLN) lymph nodes in aging. The tracheobronchial lymph node differs from the mesenteric one by a higher degree of retained hydration in aging based on the magnitude of growth coefficients.

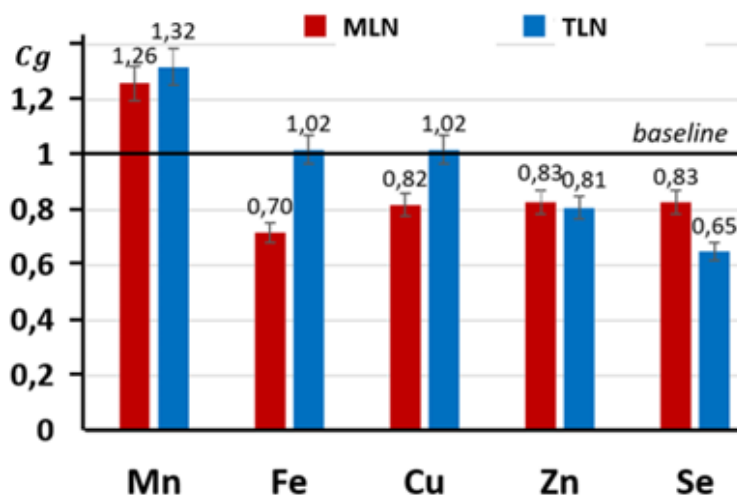
Taking phytocomposition increases the aqueous component of the lymph node. Plant flavonoids enhance lymph flow and contribute to lymph bed filling, including lymphatic sinuses of lymph nodes [2, 3]. The value of baseline indicators determines the change in the degree of lymph node hydration (Figure 5, Table 2). Phytocorrection slows down age-induced lymph node dehydration. This is achieved by redistributing the liquid fractions. The mesenteric lymph node is characterized by increased hydration due to a free bit of water without changing the bound fraction of water. There is an increase in the free water fraction (the index approaches the baseline) and a decrease in the tracheobronchial lymph node's total and bound water fraction after phytocorrection (Figure 5, Table 2). The free fraction of water is nothing more than lymph concentrated in the sinus system of the lymph node. We assume that hydration is a prerequisite for operability in activating lymph node drainage weakened due to age-induced dehydration.



**Figure 5** Growth coefficient of total water, free and bound fractions in mesenteric (MNL) and tracheobronchial (TLN) lymph nodes in aging and after phytocorrection. Phytotherapy approaches the coefficient to the baseline as evidence of increased hydration due to total water and free water fraction in the mesenteric lymph node and due to free water fraction while reducing the bound water fraction in the tracheobronchial lymph node.

### 3.3 Bioelements of Lymph Nodes

Aging is associated with an imbalance of trace elements in various organs, including lymph nodes. Of most significant interest are the trace elements of the immune group related to cell proliferation in lymph nodes. The results showed heterogeneous trace element content in mesenteric and tracheobronchial lymph nodes (Figure 6, Table 3) and the blood (Table 4). Aging results in an increase in manganese concentration in both lymph nodes. Iron and copper concentrations decrease in the mesenteric lymph node and remain at baseline in the tracheobronchial lymph node. Zinc and selenium trace elements are deficient in both lymph nodes. At the same time, selenium is a greater deficiency in the tracheobronchial lymph node. The level of trace element concentration is different in visceral lymph nodes belonging to lymph regions of other organs. There is a manifestation of regional specificity of lymph nodes concerning trace element concentration in aging.



**Figure 6** Growth coefficient of trace elements concentration of mesenteric (MLN) and tracheobronchial (TLN) lymph nodes in aging. There is more Fe and Cu deficiency development in the mesenteric lymph node, Se deficiency in the tracheobronchial lymph node. There is an increase in Mn concentration and a decrease in Zn in both lymph nodes.

**Table 3** Trace element concentration in lymph nodes at aging and after phytocorrection,  $\mu\text{g/g}$ .

Trace elements, $\mu\text{g/g}$	Mesenteric lymph node (MLN)		Tracheobronchial lymph node (TLN)	
	old animals	old animals + phytotherapy	old animals	old animals + phytotherapy
	1	2	3	4
Mn	$2.71 \pm 0.14$	$2.97 \pm 0.20$	$3.34 \pm 0.25$	$2.02 \pm 0.30^{*^{\circ}}$
Fe	$182.5 \pm 14.33$	$241.2 \pm 22.57^{*}$	$226.4 \pm 14.64$	$185.5 \pm 8.67$
Cu	$5.29 \pm 0.35$	$7.22 \pm 0.22^{*}$	$5.37 \pm 0.14$	$4.89 \pm 0.16$
Zn	$57.27 \pm 1.72$	$65.87 \pm 2.09^{*}$	$47.36 \pm 2.83^{*}$	$58.74 \pm 1.46^{*}$
Se	$1.14 \pm 0.06$	$1.24 \pm 0.07$	$0.81 \pm 0.04^{*}$	$1.08 \pm 0.04^{*}$

Note:  $*P_{1-2, 3-4} < 0.05$

**Table 4** Blood trace elements of young and old rats and after phytotherapy,  $\mu\text{g/g}$ .

Trace elements	young animals	young animals + phytotherapy	old animals	old animals + phytotherapy
	1	2	3	4
Mn	$7.95 \pm 0.39$	$6.15 \pm 0.35^{\circ}$	$5.18 \pm 0.17^{*}$	$5.54 \pm 0.11$
Fe	$2034.05 \pm 96.4$	$2374.3 \pm 83.01$	$1945.7 \pm 110.7$	$2272 \pm 68.01$
Cu	$4.07 \pm 0.16$	$3.45 \pm 0.15$	$5.56 \pm 0.36$	$7.99 \pm 0.76^{\circ}$
Zn	$27.42 \pm 0.76$	$29.23 \pm 1.40$	$19.77 \pm 0.51^{*}$	$26.5 \pm 0.47^{\circ}$
Se	$2.05 \pm 0.11$	$2.26 \pm 0.11$	$1.48 \pm 0.10^{*}$	$2.17 \pm 0.06^{\circ}$

Note:  $*P_{1-3} < 0.05$ ;  $^{\circ}P_{1-2, 3-4} < 0.05$  - the statistical difference between groups.

Medicinal plants are rich in trace elements and can compensate for their deficiency in the body [4, 5, 11]. Phytocorrection increases the concentration of elements such as iron (in 1.3 times), copper (in 1.4 times), zinc (in 1.2 times) with a slight tendency to increase manganese and selenium in the mesenteric lymph node (Table 1). At the same time, the growth rate is more significant than one, which is close to or higher than the baseline level and a similar indicator in aging. Phytocorrection alters the concentration of trace elements in the tracheobronchial lymph node. The concentration of manganese (in 1.6 times), and iron (in 1.2 times) decreases; increase selenium concentration (in 1.3 times), and zinc (in 1.2 times); the copper content remains unchanged. Taking phytocomposition increases the attention of all trace elements in the mesenteric lymph node and only zinc and selenium in the tracheobronchial lymph node (Table 3). The difference in trace element balance of mesenteric and tracheobronchial lymph nodes is determined by the principle of regional determinant when each lymph node is provided with its level of lymphoproliferation, antioxidant status, and compartment size [18-20].

#### **4. Discussion**

Lymph nodes have a specific localization to different organs and systems according to the concept of lymph region [4]. Lymphatic regions of the respiratory and digestive system organs have noticeable individual differences, which are associated with the functions of organs in the body and the features of contact with the external environment. The dynamics of aging of regional lymph nodes are related to the parts of lymph region drainage. The lymph region with different connections with the external environment and other antigenic loads causes accelerated aging of the mesenteric lymph node compared to the tracheobronchial lymph node. The difference in structural response to aging depends mainly on the morphophysiological features of the lymphatic region [4]. Evidence of the regional principle of aging of peripheral lymphoid organs has been obtained, which confirms the introductory provisions of the lymphoid theory of aging [1, 5, 6] and the concept of the lymphatic region [4].

The relationship of hydration trace elements with the structural-functional organization of lymph nodes and their immune function is traced. Trace element level is directly or indirectly associated with lymphoid cell proliferation enzymes [10]. Proliferation processes cause the development of lymph node compartments. A certain lymph node morphotype is formed in the proliferation and differentiation of immunocompetent cells. Aging is a factor that leads to the destabilization of structure, dehydration, and imbalance of trace elements. Copper and zinc deficiency causes impaired synthesis of non-specific T-helper factors and inhibits lymphocyte differentiation and proliferation [10]. When aging, the intensity of changes varies in the lymph nodes of different regions. Age-induced changes affect cells and their microenvironment, compartments in the lymph node, and bioelement exchange, reducing its operability [3, 6, 17-20] and reflecting the regional specificity of aging [4].

An undeniable condition of endoecological comfort is the normal functioning of the lymph node. Structural-functional unity of the lymph node can be achieved using the original phytocomposition. Phytonutrient support allows the effects of aging at the lymph node level to be alleviated or slowed down. This is achieved by the presence in phytocomposition of the acting bioactive substances - flavonoid fraction, trace elements, and other micronutrients [9, 10]. Bioactive substances solve functional focus problems, positively affecting the structure, hydration, and trace elements of lymph

nodes altered by aging. Trace elements potentiate cell-mediated protective responses of the organism. Zinc increases T-lymphocyte development and B lymphocyte maturation into Ig-secreting cells through Zn-dependent finger proteins [10]. Selenium increases the reaction of lymphocytes (blast transformation) to various mitogens through glutathione peroxidase [10]. The described structural-modifying effect of phytocomposition on lymph nodes is pathogenetically related to trace element status. The paper justifies the feasibility of using phytonutrient support to optimize lymph nodes in ensuring endoecological safety in old age.

## **5. Conclusions**

Localization is determinative in forming the morphofunctional status of lymph nodes in aging. Age changes in mesenteric and tracheobronchial lymph nodes occur at different intensities. The mesenteric lymph node changes to a greater extent than the tracheobronchial lymph node due to contact features of the lymph region with the external environment. Changes in lymph nodes suggest a decrease in drainage and immune function in aging.

Phytotherapy has a leading role in improving the operability of the lymphatic system in aging. Phytonutrients (flavonoids, elements) affect the structure, hydration, and content of trace elements in lymph nodes. Phytocorrection alters the rate and intensity of changes in lymph nodes susceptible to aging. There is a structural-modifying effect. Phytotherapy slows age changes in lymph nodes and improves the reliability of the lymph system in old age. Endoecological comfort is provided, and nonspecific resistance of the body is increased. Phytotherapy is recommended for wellness anti-aging programs.

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## **Author Contributions**

The author's contribution of each is as follows: V.N. Gorchakov is the formation of an idea, the formulation of purpose and tasks; K.M. Nicolaychuk, O.V. Gorchakova is an experiment and data collection; G. A. Demchenko, B.A. Nurmakhanova is a design development and methodology. All authors participated in the analysis, interpretation of the data obtained and preparation of the text of this article.

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## **Competing Interests**

The authors have declared that no competing interests exist.

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