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Selected Kazakhstani plants with possible lymphatic properties

Abstract. Search for drugs that affect the functions of the lymphatic system in normal state and under various pathologies is extremely relevant and important. Intensive research is being conducted worldwide based on the idea of influencing any pathological process through the lymphatic system. One promising strategy is the use of herbal medicines as integrative, complementary and preventive therapy. The active components in medical plants have always been an important source of clinical therapeutics and their molecular pharmacology offers a great chemical diversity with often multi-pharmacological activity. In this review, we mainly analyzed the immunomodulating/anti-inflammatory and antioxidant activity of important Kazakhstani plants (*Ribes nigrum*, *Crataegus almaatensis*, *Ziziphora bungeana*, *Alhagi kirgisorum*, *Rosa majalis*, *Hypericum perforatum*, and *Bergenia crassifolia*). These plants have industrial reserves on the territory of Kazakhstan, and they have been used in traditional medicine since ancient times and are approved for use in official medicine. They are characterized by a high content of polyphenols, polysaccharides which have a stimulating effect on the lymphatic flow and promote the activation of the synthesizing apparatus and mitochondria in lymphoid cells and macrophages in the regional lymph nodes. In addition, they have a stimulating effect on the cellular composition of the lymph node and other synergistically acting biologically active compounds necessary for treatment and prevention of lymphatic system diseases.

Key words: *Ribes nigrum*, *Crataegus almaatensis*, *Ziziphora bungeana*, *Alhagi kirgisorum*, *Rosa majalis*, *Hypericum perforatum*, *Bergenia crassifolia*.

Introduction

The immune system is the body's defense system. Without a properly functioning immune system, the body quickly succumbs to infection [1].

The lymphatic system and immune system are closely linked. The lymphatic system comprises a network of vessels and nodes that circulate immune cells and provide a site for antigen presentation and immune activation. Lymphatic vessels transport lymph, a fluid containing infection-fighting white blood cells, from body tissues into lymph ducts that drain into lymph nodes. Lymph nodes are small, oval-shaped nodes that are found in clusters on either side of the neck, collar bone, armpits and groin. Lymphatic vessels run alongside arteries and veins connecting lymph nodes throughout the body. Having several times more vessels (Figure 1), the lymphatic system in the human body plays no less important role than the circulatory system [2; 3].

Since the lymph is derived from the interstitial fluid, its composition continually changes as the blood and the surrounding cells continually exchange substances with the interstitial fluid. It is generally similar to blood plasma, which is the fluid component of blood. Lymph returns proteins and excess interstitial fluid to the bloodstream. Lymph also transports fats from the digestive system (beginning in the lacteals) to the blood via chylomicrons [4].

Bacteria may enter the lymph channels and be transported to lymph nodes, where they are destroyed. Metastatic cancer cells can also be transported via lymph. In various pathological conditions, it delivers products of metabolism, necrobiosis, and other toxic substances from tissues into the blood. [5-7].

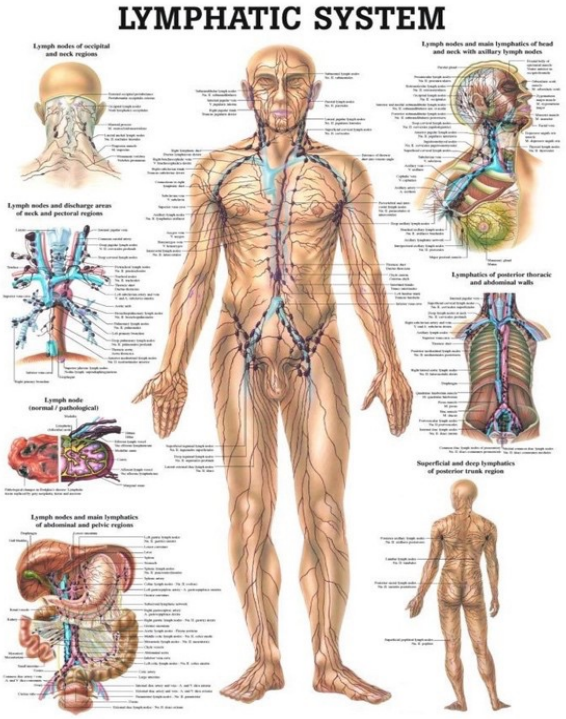

Figure 1 – The human lymphatic system

Being the first to take the products of tissue destruction, toxins and biologically active compounds under pathological processes in organs, lymph is involved in the generalization of inflammatory processes [8]. For instance, as is the case with apical periodontitis, the products of lipid peroxidation and antioxidant defense enzymes mainly enter the jugular lymph, to a lesser extent the jugular and femoral blood [9].

Under normal physiological conditions, entry into the lymphatic system is via the initial lymphatic capillaries in the interstitium. From lymphatic capillaries, lymph flows through progressively larger pre-collecting and collecting (afferent) lymphatic vessels, through the lymph nodes via lymphatic sinuses and then to post-nodal (efferent) lymphatic vessels. The collecting and post-nodal lymphatic vessels are segmented frequently by semilunar valves and are surrounded by smooth muscle cells that facilitate unidirectional lymph flow. In disease, there are substantial changes to the lymphatic system compared with normal physiological conditions (Figure 2, a).

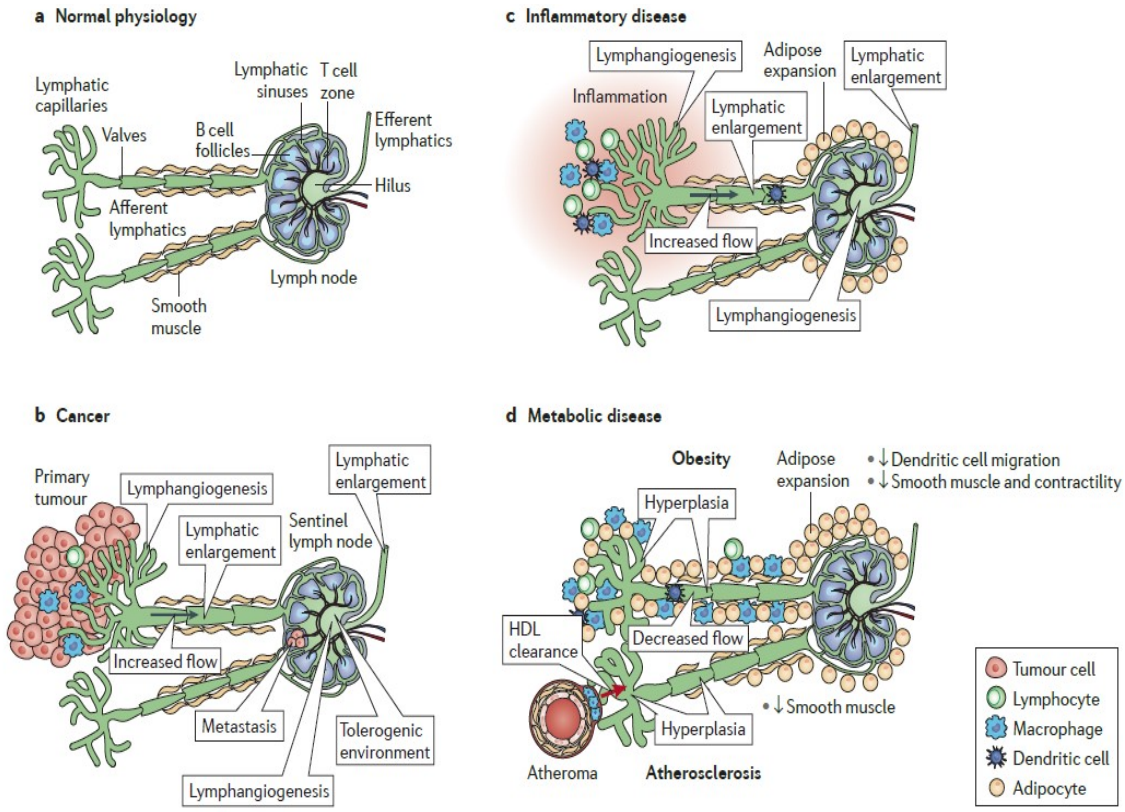

Figure 2 – Lymphatic function in health and disease [10]

In cancer, metastatic dissemination from the primary tumors often occurs via lymph vessels to the sentinel (first draining) lymph node. Tumor cells and associated macrophages induce lymph angiogenesis at the tumor site and in the draining lymph nodes via the release of pro-inflammatory and lymphangiogenic factors. Lymph angiogenesis, lymph vessel dilation and increased interstitial pressure modulate lymph flow from tumors and therefore alter immunity. Tumors may also release factors that promote immune tolerance (Figure 2, b).

In inflammatory disease, immune cells (for example, macrophages and lymphocytes) release pro-inflammatory and lymphangiogenic factors that promote lymphatic hyperplasia. These changes stimulate alterations in the flow of fluid, inflammatory mediators and dendritic cells from inflamed tissue to lymph nodes and therefore modulate immunity and inflammation. In chronic inflammation, there is also expansion of the adipose tissue surrounding the lymph node (Figure 2, c).

In metabolic disease, lymphatic function is markedly altered by high-fat diets and hypercholesterolemia. High-fat diets and/or obesity alter lymph node structure, promote lymphatic vessel hyperplasia and dilatation, reduce lymphatic smooth muscle coverage and contractility, and reduce lymph transport of fluid and dendritic cells. The lymphatics are surrounded by adipose, and impairments in lymphatic function typically increase lipid deposition in adipose, promoting obesity. Mice with hypercholesterolemia exhibit lymphatic vessel hyperplasia in the skin and loss of smooth muscle coverage. Recent data also suggest that lymphatic vessels facilitate high-density lipoprotein (HDL)-mediated cholesterol clearance from atheroma's. In this way, the lymph and lymphatics are broadly implicated in the development and progression of metabolic disease (Figure 2, d) [11].

In general, without restoration of the drainage function of the lymphatic apparatus, for which complete decongestive physiotherapy (which is a combination of four methods: manual lymphatic drainage, lymphedema rehabilitation exercises, compression therapy, skin care), a complete rehabilitation of the morphological and functional parameters of each organ is impossible [12].

The possibility of a drug effect on the lymphatic channel in order to correct violations of the homeostasis of the whole organism has been considered for a long time [13], but only with the development of clinical lymphology has this method been put into the practice. Drugs that stimulate lymph circulation and, thereby, activate the drainage function of the lymphatic system (drugs with an osmotic effect – mannitol, polyglucin, hemodes, glucose, isotonic sodium chloride solution and others) are widely used in treatment of various pathological processes [14]. In chemical terms, the structure of drugs of natural origin is close to the structure of metabolites produced by the human body, and, accordingly, is accessible to the action of its enzymatic systems, which makes drugs based on plant materials not only more effective, but also safer.

Due to its unique anatomy and physiology, potential exists to exploit the lymphatic system as a means of drug delivery. Targeting drugs into the lymph has certain advantages arising mainly from the unique anatomy and physiology of the lymphatic system (Figure 3). These advantages include avoidance of first pass metabolism, direct delivery of drugs to particular regions of the lymphatic circulation, e.g., in the treatment of disease states, and the possibility of regulating the rate of drug delivery into the systemic circulation.

The lymphatic system consists of a network of lymphatic vessels, tissues and nodes. Fluid, immune cells, macromolecules and molecules packaged into carriers such as lipoproteins, vesicles or exosomes enter the initial lymphatic capillaries to form lymph fluid. From here, lymph flows through a network of progressively larger collecting (afferent) lymphatic vessels, lymph nodes and post-nodal (efferent) lymphatic vessels to converge at either the left (or right) thoracic lymph duct. Lymph empties from the major lymph ducts directly into the venous system. Therapeutics can be targeted to the lymphatic system via mucosal, intestinal or parenteral routes. Mucosal delivery of particulate materials leads to their absorption across the epithelium into mucosa-associated lymphoid tissue (Figure 3, a). Intestinal or oral delivery of lipophilic drugs (typically logP values >5) leads to their incorporation into the process of intestinal lipoprotein assembly and transport into the intestinal lymphatics (Figure 3, b). Parenteral or interstitial delivery of macromolecular materials leads to their entry into lymphatic capillaries as these materials are too large to access the blood capillaries draining the injection site (Figure 3, c) [11].

Complications associated with the lymphatic system span a wide spectrum, including congenital disorders, cancer and side-effects of cancer treatments, cardiovascular disease, diabetes, and parasitic infections [15]. According to some estimates, 140-250 million people across the globe are affected by lymphedema [16]. While some lymphatic disorders are genetically related, lymphatic complications most

often arise as a secondary complication following cancer, cardiovascular disease, and immunological disorders [17]. For example, patients undergoing radiation therapy or surgery for breast cancer treatment are at a high risk of developing lymphedema [18]. Breast cancer is the most commonly observed cancer among women and is the second-most common type of cancer. According to the World Cancer Research Fund, an estimated 2 million cases of breast cancer were reported in 2018 across the world [19]. Another interesting aspect is that tumors may engage the lymphatic system in order to invade and metastasize [20].

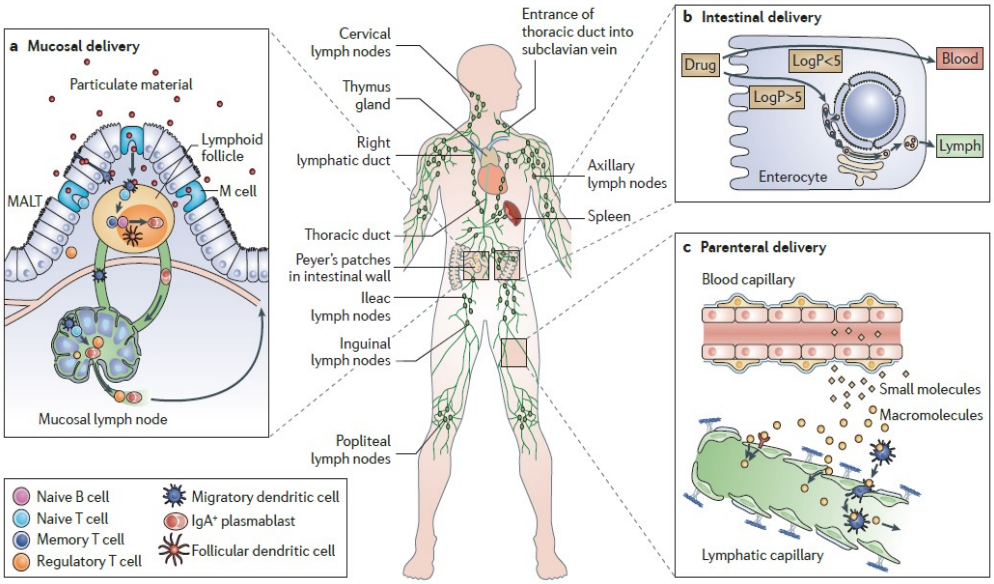

Figure 3 – Access routes to the lymphatics after oral and parenteral delivery [11]

Ongoing research for the development of novel therapies for the treatment of lymphedema is another driver of the global lymphedema treatment market. The emergence of a new direction in prophylactic lymphology, so-called lymphophytonutriciology, served as basis for the proposal to use phytocomposites with the realization of the effect of their action through the lymphatic system. The active ingredients of phlebotonic drugs with known lymphotropic effect, such as Antistax (Switzerland) and Ginkor Fort (France) are extracts of red grapes (*Vitis vinifera*) and Ginkgo bilobate (*Ginkgo bilobae*), obtained from plant materials of their own region [21; 22].

Alternative systemic approaches to development of a lymphedema-reversing pharmacology, including targeted anti-inflammatory therapy, are beginning to show promise. According to a new study conducted at the Stanford University School of Medicine, a new molecular mechanism primarily responsible for causing lymphedema, along with a drug (bestatin) that has the potential for hindering the process, was uncovered in May 2017. Bestatin is currently undergoing clinical trials for the treatment of secondary lymphedema. Positive outcome from the trials is expected to be a step forward toward developing new treatment options for the management of lymphedema [23]. Two early-stage clinical trials led by Stanford researchers have shown that ketoprofen, a nonsteroidal anti-inflammatory drug, or NSAID, can improve skin damage in patients with lymphedema. The researchers found that the buildup of lymph fluid is actually an inflammatory response within skin tissue. Thus, it is not merely a "plumbing" problem within the lymphatic system, as previously thought. They discovered that the naturally occurring inflammatory molecule LTB4 is elevated in both animal models of lymphedema and in humans with the disease, and that at elevated levels it causes tissue inflammation and impaired lymphatic function. Further research in mice showed that using ketoprofen to target LTB4 induced lymphatic repair and reversed the disease processes. This indicated that perhaps other therapies could reverse the negative impact of inflammation on lymphatic repair by targeting LTB4 [24].

The Institute of Human and Animal Physiology of the National Academy of Sciences of the Ministry of Education and Science of the Republic of Kazakhstan is the leading Institution of the

Kazakh Physiological Society, key organization in the Republic of Kazakhstan engaged in detailed studies of the activity of the lymphatic system, its morphofunctional state and direct relationship with various pathologies of metabolism, cardiovascular system, digestive tract, as well as the effects of weightlessness on the structure and function of lymphoid organs. A number of studies are conducted with leading organizations of near and far abroad, in particular with the Scientific Research Institute of Clinical and Experimental Lymphology SB RAMS [25; 26].

The consumption of certain complex natural substances derived from plants is widely accepted for their protective role in microvascular and lymphatic physiological functionality. Among the natural substances demonstrated to maintain microvascular and lymphatic homeostasis, our attention was focused on polyphenolic compounds, such as flavonoids, saponins and polysaccharides.

As is known, polyphenols have a stimulating effect on the lymphatic flow and promote the activation of the synthesizing apparatus and mitochondria in lymphoid cells and macrophages in the regional lymph nodes, and have a stimulating effect on the cellular composition of the lymph node [27].

Flavonoids are plant secondary metabolites to which such pharmacological functions as antioxidant, anti-mutagenic, antibacterial, anti-angiogenic, anti-inflammatory, anti-allergic, enzyme modulation, and anti-cancer are attributed. They are known as phytochemicals that exist either as free aglycones or glyosidic conjugates. Flavonoids are polyphenolic with a wide range of structures. they are categorized mainly into flavones, flavanols, isoflavones, flavanols, flavanones, flavanonols, and chalcones. The diverse structures of flavonoids have resulted in many properties including anti-cancer and anti-inflammatory effects. Recently, it has been shown that flavonoids can affect immune system response and might have immune-modulator effects [28].

Flavonoids like daflon, a combination of two flavonoids – hesperidin and diosmin, increase the intensity and frequency of lymphatic contraction and the total number of lymphatic capillaries. This results in the decrease of adhesion, migration, and activation of leukocytes, leading to lowering of prostaglandin's PGE2 and PGF2a and the reduction of radical oxygen species [29].

Rutin inhibits platelet aggregation and decreases capillary permeability, improving circulation. Among the other protective activities, rutin has anti-inflammatory and anti adipogenic activity [30].

Flavonoids possess different mechanisms of antioedemic action. It was determined that diosmin exerts a direct influence upon the functional state of the lymphatic system, activating proliferation of the lymphatic endothelium by means of gemmation, which leads to the formation of new capillary lymphatic networks with the resulting increase in both the total absorption area of the lymphatic capillary networks and the volume of lymph reabsorption. Troxerutin acts predominantly on the endothelium of blood capillaries, decreasing permeability in the arterial segment of the capillary, thus lowering the total volume of fluid in the interstitial space and accordingly the load on the lymphatic system [31].

Benzopyrones also have a variety of beneficial effects on the body. For example, they increase lymph drainage, reduce the fragility of capillaries. Of these, the first is coumarin (5,6-benzo-α-pyron). In Australia, coumarin is available on the market under the name "Lodema as 200 mg tablets, as well as 10% ointment. There are other oral forms of coumarin on the pharmaceutical market. For example, Venium (Limex containing 100 mg of coumarin) is produced in Switzerland and Liz Edem (15 mg of coumarin) is produced in France. There is also a drug known as Venalot-Depot (Germany), which contains 15 mg of coumarin and 90 mg of troxerutin. In addition, saponins (escin and horsechestnut extract), plant extracts (anthocyanosides – blueberries, proanthotonidols – preparations from grape seeds, Ginkgo extract), and synthetic drugs (calcium dobsilate, tribenoside, etc.) are used [32]. Polysaccharides also have positive effect on the circulatory and lymphatic systems [33].

In order to develop our own knowledge base, we started looking at the valuable properties of Kazakhstani plants with possible lymphatic properties. In this regard, valuable parts of seven medicinal plants (i.e. leaves of Ribes nigrum, fruits of *Crataegus almaatensis*, *Ziziphora bungeana* and *Alhagi* kirgisorum grass, fruits of Rosa majalis, *Hypericum perforatum* grass, and leaves and roots of *Bergenia crassifolia)* caught our special attention. These plants occur in abundance on the territory of Kazakhstan, and they have been used in traditional medicine since ancient times and are approved for use in official medicine (monographs on them are available in world pharmacopoeias). They are characterized by a high content of polyphenols, polysaccharides and other synergistically acting biologically active compounds necessary for treatment and prevention of lymphatic system diseases.

Blackcurrant (*Ribes nigrum*) is a berry that belongs to the family *Grossulariaceae*. It includes 150

cultivars and is one of the most common woody shrubs in the world. *Ribes nigrum* has a well-deserved demand because its fruits have dietary and medicinal properties. Blackcurrant contains a complex of significant biologically active compounds. Its leaves are rich in ascorbic acid (up to 470 mg%), carotene, polyphenols, phytoncides and essential oils. Due to its rich chemical composition, blackcurrant leaves are of much interest as a source of plant material, which, among other properties, display high antioxidant activity [34]. Experimental data show that consumption of blackcurrant juice prevents the development of oxidative stress, improves the state of vascular endothelium, and protects the erythrocyte membranes from destruction when exposed to free oxygen and ultraviolet radiation [35; 36]. Therefore, the extract obtained from the leaves of blackcurrant is a valuable component of the synthetic drug. Its sugar composition includes more fructose (4.2%), less glucose (1.5%) and sucrose (1.0%). Non-digestible carbohydrates are represented by fiber (up to 3%) and pectins (up to 1.5%). An important property of pectins is their ability to adsorb bacterial toxins, heavy metal ions, including radionuclides. In addition, pectins bind and remove cholesterol from the body, preventing the development of atherosclerosis and the oxidation of ascorbic acid and catechins in fresh fruits. Organic acids in blackcurrant fruits are mainly citric acid (2.0%); they also contain malic (0.25%) and oxalic (0.06%) acids. They have a positive effect on digestion by increasing the secretion of gastric glands and intestinal peristalsis [37].

Blackcurrant berries are rich in polyphenols, which range from 488 to 1116 mg and significantly determine their taste, nutritional and medicinal value. Ripe fruits are also a rich source of anthocyanins. The anthocyanin complex of black currant includes four main components: 3-glucosides and 3-rutinosides of delphinidine and cyanidine. These components ocur in all varieties of *R. nigrum* with black color, regardless of the variety and growing region. Anthocyanins have capillary-strengthening activity, antioxidant, antibacterial, anticarcinogenic properties and are effectively used in medicine for the treatment and prevention of a host of diseases. The beneficial properties of anthocyanins, cyanidins and their glycosides are due to their ability to scavenge free radicals, including the reactive oxygen species [38].

Almaty hawthorn (*Crataegus almaatensis* Pojark) is an endemic plant that grows only in the foothills of Zailiysky Alatau, Almaty region, Kazakhstan. Hawthorn fruits contain the flavonoids hyperoside, quercetin, vitexin, triterpene saponins, acids, proanthocyanides of various degrees of polymerization related to condensed tannins. They also contain a large number of such beneficial organic acids as ascorbic, tartaric, citric, malic, caffeic, chlorogenic, and vitamins (K, C, F, B) and trace elements (K, Ca, Mg, Fe, Mn, Zn) [39; 40]. Its extracts are used for treatment of cardiovascular disorders, such as arrhythmia, myocardial infarction, heart failure, as well as a hypotensive and diuretic drug [4].

Broad range of biological activities of Almaty hawthorn, such as anti-inflammatory, antioxidant, vasodilator, positive inotropic and cholesterol synthesis inhibiting properties has been described as being important for medical practices. These activities are significantly affected by the presence of antioxidant molecules in the extracts of hawthorn, which have the ability to absorb free radicals formed as a result of biochemical and physiological reactions in the human body. Furthemore, oligomeric procyanidins, triterpenes, flavonoids, polysaccharides and catecholamines have been identified in hawthorn extracts, and they are thought to have pharmacological potential [41; 42]. Fresh or dried fruits, flowers and leaves are used as a source of extracts for the production of various dosage forms of over-the-counter medicines or dietary supplements [43].

Ziziphora bungeana Juz. is found in meadows and highlands of Kazakhstan. Capsules obtained on its basis are used for treatment of various viral infections of the upper respiratory tract; a preparation from its flavonoid fraction is recommended for treatment of cardiovascular diseases. Its chemical composition includes monoterpene essential oil, polyphenols and triterpenes [44]. Industrial reserves and cultivation capability, experience in traditional medicine and the rich chemical composition of *Ziziphora* suggest that its extract be added to the formulae.

The antibacterial and antiseptic activities of *Ziziphora* species are determined by their content of essential oils such as thymol and carvacrol. Some components of the essential oils of *Ziziphora* (terpinolene, thymol, borneol, karyofillen, carvacrol) show antioxidant activity. Moreover, flavonoids from *Ziziphora* grass show antioxidant, anti-inflammatory and antitumor activity. Flavonoids such as chrysin, apigenin, linarin, luteolin have anti-inflammatory effects [45].

Ziziphora extracts that had a high concentration of polyphenolic substances showed vasodilator activity. The presence of a 4-hydroxy group without methyl substitution in flavonoids and the absence of constant substitution at positions 5, 6 and 7 of the

flavonoid structure are apparently responsible for the vasodilator effect [46].

The world flora includes 7 species of the genus *Alhagi,* of which 5 species grow in Central Asia: *Alhagi pseudalhagi* (M.Bieb.) Desv. ex Shap., *Alhagi sparsifolia* Shop., *Alhagi canescens* (Regel) B. Keller & Shap., *Alhagi kirghisorum* Schrenk. and *Alhagi persarum* Boiss. & Buhse. The phytochemical profile of two species (*Alhagi pseudalhagi* and *Alhagi sparsifolia)* have been most studied to date. These species of camel thorn have been shown to produce biologically active alkaloids, phenolic compounds and terpenoids. Kyrgyz camel thorn (*Alhagi* kirgisorum Schrenk.) grows in southern part of Kazakhstan. Polyphenols in the form of flavonols, their glycosides, phenolic acids, condensed tannins, and heteropolysaccharides were isolated from its aerial parts. On the basis of the substance "Alkhidin", the following dosage forms were developed: alchidin ointment, 5%, "Zhantak" syrup, introduced into the medicine [47].

For the purpose of treatment the roots of the Kyrgyz camel thorn is recommended. Infusions and decoctions of yantak are widely used in traditional medicine as a diuretic, diaphoretic, and laxative. Its extract is widely used in medicine as an anti-inflammatory and wound healing agent. The following phenolic compounds were isolated and identified from the aboveground part of *Alhagi kirghisorum*: gallic acid, (+)- catechin, narcissin and rutin. Gallic acid has strong antioxidant properties and also exhibits hepatoprotective properties when it is part of more complex substances. Catechin enhances the hepatotoxic effect of carbon tetrachloride, and it was found to increases the killer activity of T-lymphocytes. Narcissine can have an spasmolytic effects on the heart vessels, and is used in cardiological practice. Rutin is a strong antioxidant that prevents the formation of carcinogens, strengthens the walls of blood vessels, improves blood circulation, including blood circulation in the capillaries of the joints and spine, provides the flow of necessary nutrients to the joints, improving their function [45; 47].

Rose hip (*Rosa* L.) is a genus of wild plants in the family *Rosaceae*. It is an erect, large-leaved shrub, reaching a height of 1-2 m. There are more than 120 species of wild rose that are widely distributed in Europe, Asia, the Middle East and North America. Plants are resistant to harsh environmental conditions (rocky and sloping terrain, poor soil, and lack of water). It is of great scientific interest as a source of biologically active compounds and is widely used as medicinal, vitamin and food raw materials. Its positive effect has been demonstrated in reducing the risk of cardiovascular diseases, various forms of cancer, diarrhea, bladder infection, and diabetes. Rosehip preparations have a wide pharmacological spectrum of action. They have a strong antioxidant, restorative effect, stimulate nonspecific resistance of the body, reduce vascular permeability, enhance hormone synthesis and tissue regeneration, and have anti-inflammatory, immunostimulating, and choleretic properties. In traditional medicine, fruits, flowers, leaves and roots of a plant are used [48; 49].

The value of rose hips is determined by a complex of such biologically active compounds as ascorbic acid, carotenoids, flavonoids (quercetin, kempferol, isocvercetin), catechins (epigallocatechin, gallocatechin, epigallocatechin gallate), carbohydrates, organic acids, vitamins of group B, K1, Pac, E, Pol, E, Pol, E, Pol, E, Pol , pectic substances, salts of potassium, sodium, calcium, magnesium, phosphorus, iron, etc. It is considered the richest natural source of vitamin C. In this case, the biological role of vitamin C is manifested in the presence of organic acids and P-active compounds, which include anthocyanins, catechins, leucoanthocyanins and flavonols, which differ in chemical composition, but have a similar effect on the human body. Flavonoids act as antioxidants and inactivate free radicals in the presence of metals. In the fruits of the plant genus *Rosa* L., they are represented in particular by hyperoside, quercetin, rutin, astragalin, kaempferol-3-arabinoside, kaempferol-3-rhamnoglucoside, and others. Fruits *Rosa majalis* Herrm. are used as vitamin supplement [48; 49]. Fruits of May rose hips (*Rosa majalis* Herrn.) contain vitamins C, B2, K, E, provitamin A, polyphenols, a complex of higher organic acids with a predominant content of polyenes, and it is part of vitamin and multivitamin collection and Traskov's anti-asthma potion, Hepar immunostimulant. The strongest anti-scurring agent, rosehip oil and Karotolin, used as wound healing agents, Holosas syrup, used for hepatitis, cholecystitis, biliary dyskinesia, are obtained from the fruits of *Rosa majalis*. Drugs from rose hips are prescribed for disorders of carbohydrate metabolism and impaired functions of the bone marrow, liver and pancreas [49]. The immunostimulating properties of the extract from *Rosa majalis* will contribute to such in new formulation.

St. John's wort (*Hypericum perforatum* L.) is a promising source of such biologically active compounds as naphthodianthrones pigments and flavonoids, widely used in traditional and scientific medicine, and it is included in the pharmacopeias of many countries. *St John's wort* (*Hypericum perforatum* L.)

is widespread in Kazakhstan in the foothills of Zailiysky and Dzhungarsky Alatau, and it has been used in the treatment of genitourinary and gastrointestinal inflammations since ancient times. Both in folk and scientific medicine, preparations from St. John's wort are used as astringents, anti-inflammatory and antiseptic agents for treatment of various wounds and burns. The chemical composition of plants of the genus *Hypericum* L. is complex and diverse in the type of structures of biologically active compounds. Lead role in the therapeutic properties of the species of this genus is played by naphthodianthrones (anthraquinones), flavonoids and derivatives of hyperforin. Vitamins C, PP, carotenoids tone up, improve brain activity; flavonoids normalize the nervous system and positively affect reproductive function, which indicates the importance of including this component in the developed phytocomposite. St. John's wort has a strong anti-inflammatory effect, including improving microcirculation and dissolves infiltrates that helps to cure serious diseases and the penetration of antibiotics to the source of infection. In homeopathic practice, the entire St. John's wort plant is used, as well as its individual parts as an analgesic, hemostatic and regenerating agent, as well as for lesions of the central and peripheral nervous systems [50; 51].

Badan thick-leaved (*Bergenia crassifolia* (L.) Fritsch) perennial herb of the family Saxifragaceae. Badan thick-leaved has industrial reserves in Eastern Kazakhstan. It contains up to 35% of mixture of pyrocatechol and pyrogall hydrolyzable tannins, gallic acid, vitamin C, carotenes, oxidized and reduced flavonoids, coumarins, mineral salts, essential oils and resins, trace elements Mn, Fe, Cu, and carbohydrates. By the content of glycoside arbutin (22%), badan is the richest plant source in the world. Infusions and decoctions from it are used to treat pulmonary tuberculosis, throat diseases, rheumatism, diseases of the gastrointestinal tract, high blood pressure, as well as in gynecological practice as a hemostatic agent and for the treatment of cervical dysplasia [52]. A complex of biologically active compounds from this plant is appropriate for inclusion in the formulated drug. Badan refers to plants that accumulate tannins. Quite large amounts of tannins accumulate in the rhizomes of badan from 6 to 30%. Simple phenols, flavonoids, and catechins found in various parts are precursors of tannins and serve as building materials for polymeric phenols [53]. Modern pharmacological studies have revealed a number of medicinal properties of preparations from the leaves of badan. Badan leaves are used for diseases of the digestive system (colitis, enterocolitis, hyposecretory gastritis), allergies, and to normalize metabolism. The decoction of leaves has an anti-hypoxic and choleretic effect, and it has antibacterial activity against gram-positive bacteria in gynecological practice to treat various bleedings. Dry leaves of badan are used for Mongolian tea, which has tonic properties, improves metabolism in the body and normalizes blood pressure [54]. Research to be continued.

Conclusion

The active components in medical plants have always represented an important source of clinical therapeutics since they offer tremendous chemical diversity that is often associated with a large number of pharmacological activities and the absence of cumulative and side effects. Their use in traditional medicine for their properties and health benefits is well recognized since ancient times. In this paper our focus was on some biologically active compounds from selected Kazakhstani plants, which might be potentially valuable for creation of drug enhancing lymphotropic activity and immune status of the human organism. Authors are thankful to Prof. Asim Esen Virginia Polytechnic Institute and State University (Blacksburg, USA) for his kind assistance in preparing the manuscript.

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