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Igor BELENICHEV
Doctor of Biology and Medicine, Full Professor, Head of the Department of Pharmacology and Medical Formulation with Course of Normal Physiology, Zaporizhzhia State Medical and Pharmaceutical University, Stalevariv str., 31, Zaporizhzhia, Ukraine, 03057 (i.belenichev1914@gmail.com)
***ORCID:** 0000-0003-1273-5314*
***SCOPUS:** 6602434760*

Nadiya GORCHAKOVA
Doctor of Medical Sciences, Professor, Professor of the Department of Pharmacology, Bogomolets National Medical University, Beresteyskyi ave., 34, Kyiv, Ukraine, 01601 (gorchakovan1941@gmail.com)
***ORCID:** 0000-0001-7311-7347*
***SCOPUS:** 7003895729*

Tatyana HARNYK
PhD in Medicine, Professor, Professor of the Department of Physical Education, Sports and Human Health, V.I. Vernadskyi Tavria National University, John McCain str., 33, Kyiv, Ukraine, 01042 (phitotherapy.chasopys@gmail.com)
***ORCID:** 0000-0002-5280-0363*
***SCOPUS:** 6508229538*

Olena SHUMEYKO
PhD in Medicine, Associate Professor, Associate Professor of the Department of Pharmacology, Bogomolets National Medical University, Beresteyskyi ave., 34, Kyiv, Ukraine, 01601 (ashu28051972@gmail.com)
***ORCID:** 0000-0003-0655-0911*

Olena KLYMENKO
PhD in Medicine, Associate Professor, Associate Professor of the Department of Pharmacology, Bogomolets National Medical University, Beresteyskyi ave., 34, Kyiv, Ukraine, 01601 (klymenkoolena75@gmail.com)
***ORCID:** 0000-0002-2537-7029*

Oleksandra KLYMENKO
Student, Bogomolets National Medical University, Beresteyskyi ave., 34, Kyiv, Ukraine, 01601 (klymenko.sashka@gmail.com)

Yulia CHEMERYS
PhD in Medicine, Associate Professor of the Department of Disaster Medicine and Military Medicine, Zaporizhzhia State Medical and Pharmaceutical University, Stalevariv str., 31, Zaporizhzhia, Ukraine, 69035 (fpo.dekanat@gmail.com)
***ORCID**: 0000-0002-1203-131X*

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IMMUNOMODULATING EFFECT OF PHYTODRUGS

Topicality. *Today it is known that infectious diseases, cancer diseases, diseases of vital organs and systems are accompanied by violations of the indicators of the immune system, which requires the appointment of immunomodulators. It is herbal drugs that have some advantages over synthetic and biotechnological means. Despite the fact that almost all herbal drugs have a positive effect on the vital functions of the body, they, unlike synthetic and biotechnological ones, have less toxicity, a wider spectrum of action, greater benefits compared to risks, more accessible and, most importantly, more effective. Doctors of Ukraine, countries of the East, such as China, Vietnam, India and others, turn to herbal drugs as means of accompanying therapy. Therefore, it is very important to generalize information about the immunomodulatory effect of herbal drugs in order to familiarize pharmacologists and doctors with this problem in order to intensify medical care for patients in cases where a violation of the indicators of the immune system is diagnosed.*

The aim of the study *– to determine the main indicators of the activity of the immune system, which makes it possible to more purposefully prescribe herbal drugs with an immunomodulatory effect in diseases with violations of these indicators.*

Research methods. *On the basis of research data from domestic and foreign literature, SCOPUS publications, "Web of Science", Google Scholar, determine the indicators of the immune system, which allow to establish the immunoregulatory effect of herbal drugs and to identify promising herbal drugs that have immunocorrective properties in pathological conditions.*

Research results. *The analysis of literature data made it possible to distinguish non-specific and specific indicators of immunity. Non-specific indicators include such indicators of resistance as constitutional, phagocytic and lymphoid. Lymphocytes are the main cells involved in the body's immune responses. These cells are unique because they arise from hematopoietic stem cells and undergo maturation stages in primary lymphoid organs. In secondary lymphoid organs, they are separated depending on certain functions. T-lymphocytes are effector cells that play a regulatory role, and B-lymphocytes produce antibodies. The third type of lymphocytes is natural killers (cytokine lymphocytes, NK), which play a role in implementing the adaptive and innate immune response. The development of the immune response begins after the activation of lymphocytes of the immune system, which are subsequently activated by antigens. Antibodies (immunoglobulins) are the result of the activation of cells that have gone through the stages of differentiation. Immunoglobulins are glycoproteins that play an important role in antigen recognition and complement activation. Divided into IgG, IgM, IgA, IgD, IgE. These are soluble proteins that regulate the immune system, innate immunity, and the adaptive response to infection. They are considered chemical mediators (messengers) produced by various types of cells. This family includes tumor necrosis factor (TNF), interferons (IFN), chemokines, transforming growth factors (IGF), colony-stimulating factors (CST). There are interleukins, designated as IL1-IL-32.*

Unrelated interleukins meet three criteria: their genes must be cloned, they must be induced in leukocytes, and their biological activity in inflammatory processes must be consistent and catalytic.

Proteins included in the complement system are represented by cell-bound proteins whose function is to strengthen defense mechanisms against foreign proteins. Most complement proteins in blood plasma are synthesized in the liver, with the exception of C1, which is produced by epithelial cells, and factor D, which is synthesized in adipose tissue.

Additional sources of synthesis of complement proteins are monocytes and macrophages. Thus, by establishing changes in the indicators of the immune system in certain pathological conditions and under the influence of herbal drugs, it is possible to determine the areas of purpose of herbal drugs. In the literature, there are data that divide the drugs of the plant group depending on the predominant effect on certain indicators of the immune system.

Literature reviews describe the most frequently used plants, usually galenic, sometimes new galenic and biotechnological drugs, and focus on their influence on the indicators of the immune system. Thus, the immunoregulatory properties of echinacea, rhodiola rosea, ginger, garlic, soy and geranium are analyzed. As for some plant extracts, attention is indicated and emphasized on the expediency of their appointment for COVID-19, melanoma and other cancer diseases.

Conclusions. *Awareness of markers of immune system indicators that change in infectious, oncological diseases, diseases of vital organs and the mechanisms of effect of herbal drugs in these conditions will contribute to increasing the effectiveness of treatment of widespread diseases.*

Key words: *immunomodulating effect, herbal drug, increasing the effectiveness and safety of treatment.*

Ігор БЄЛЕНІЧЕВ
доктор біологічних наук, професор, завідувач кафедри фармакології та медичної рецептури з курсом нормальної фізіології, Запорізький державний медико-фармацевтичний університет, вул. Сталеварів, 31, м. Запоріжжя, Україна, 69035 (i.belenichev1914@gmail.com)
ORCID: *0000-0003-1273-5314*
SCOPUS: *6602434760*

Надія ГОРЧАКОВА
доктор медичних наук, професор, професор кафедри фармакології, Національний медичний університет імені О.О. Богомольця, просп. Берестейський, 34, м. Київ, Україна, 01601 (gorchakovan1941@gmail.com)
ORCID: *0000-0001-7311-7347*
SCOPUS: *7003895729*

Тетяна ГАРНИК
доктор медичних наук, професор, професор загальновузівської кафедри фізичного виховання, спорту і здоров'я людини, Таврійський національний університет імені В.І. Вернадського, вул. Джона Маккейна, 33, м. Київ, Україна, 01042 (phitotherapy.chasopys@gmail.com)
ORCID: *0000-0002-5280-0363*
SCOPUS: *6508229538*

Олена ШУМЕЙКО
кандидат медичних наук, доцент кафедри фармакології, Національний медичний університет імені О.О. Богомольця, просп. Берестейський, 34, м. Київ, Україна, 01601 (ashu28051972@gmail.com)
ORCID: *0000-0003-0655-0911*

Олена КЛИМЕНКО
кандидат медичних наук, доцент кафедри фармакології, Національний медичний університет імені О.О. Богомольця, просп. Берестейський, 34, м. Київ, Україна, 01601 (klymenkoolena75@gmail.com)
***ORCID:** 0000-0002-2537-7029*

Олександра КЛИМЕНКО
студентка, Національний медичний університет імені О.О. Богомольця, просп. Берестейський, 34, м. Київ, Україна, 01601 (klymenko.sashka@gmail.com)

Юлія ЧЕМЕРИС
кандидат медичних наук, доцент кафедри медицини катастроф та військової медицини, Запорізький державний медико-фармацевтичний університет, вул. Сталеварів, 31, м. Запоріжжя, Україна, 69035 (fpo.dekanat@gmail.com)
***ORCID**: 0000-0002-1203-131X*

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ІМУНОМОДУЛЮЮЧА ДІЯ ФІТОПРЕПАРАТІВ

Актуальність. *Нині відомо, що інфекційні, онкозахворювання, хвороби життєво важливих органів і систем супроводжуються порушеннями показників імунної системи, що потребує призначення імуномодуляторів. Саме рослинні препарати мають деякі переваги перед синтетичними і біотехнологічними засобами. При тому, що практично всі рослинні препарати володіють позитивним впливом на життєво важливі функції організму, вони, на відміну від синтетичних і біотехнологічних, володіють меншою токсичністю, більш широким спектром дії, більшою користю порівняно з ризиками, більш доступні та найважливіше – більш дієві. До рослинних препаратів як засобів супроводжуючої терапії звертаються лікарі України, країн Сходу, таких як Китай, В'єтнам, Індія тощо. Тому дуже важливим є узагальнення відомостей про імуномодулюючу дію фітопрепаратів для ознайомлення фармакологів і лікарів з цією проблемою з метою інтенсифікації медичної допомоги хворим у випадках, коли діагностується порушення показників імунної системи.*

Мета дослідження *– визначити головні показники діяльності імунної системи, що дозволяє цілеспрямовано призначати фітопрепарати з імуномодулюючою дією у разі захворювань з порушеннями цих показників.*

Методи дослідження. *На підставі цих досліджень вітчизняної та зарубіжної літератури, видань SCOPUS, "Web of Science", Google Scholar варто визначити показники імунної системи, що дозволяють встановити імунорегулюючу дію рослинних препаратів, та зазначити перспективні фітопрепарати, які володіють імунокорегуючою властивістю у разі патологічних станів.*

Результати досліджень. *Аналіз даних літератури дозволив виділити неспецифічні та специфічні показники імунітету. До неспецифічних показників належать такі показники резистентності, як конституційний, фагоцитарний та лімфоїдний. Лімфоцити є основними клітинами, які беруть участь у імунних відповідях організму. Ці клітини є унікальними, оскільки виникають з гемопоетичних стовбурових клітин і проходять етапи дозрівання у первинних лімфоїдних органах. У вторинних лімфоїдних органах вони відокремлені залежно від певних функцій. Т-лімфоцити є ефекторними клітинами, які виконують регулюючу роль, а Б-лімфоцити продукують антитіла. Третій тип лімфоцитів – натуральні кілери (цитокінні лімфоцити, NK), які відіграють роль у реалізації адаптивної та вродженої імунної відповіді. Розвиток імунної відповіді розпочинається після активації лімфоцитів імунної системи, що надалі активуються антигенами. Антитіла (імуноглобуліни) – це результат активації клітин, які пройшли етапи диференціації. Імуноглобуліни є глікопротеїнами, які відіграють важливу роль у розпізнаванні антигенів та активації комплементу. Поділяють на IgG, IgM, IgA, IgD, IgE. Це розчинні білки, які регулюють імунну систему, вроджений імунітет та адаптивну відповідь на інфекцію. Їх вважають хімічними посередниками (месенджерами), що продукуються різними типами клітин. До цієї родини належать фактор некрозу пухлин (ФНП), інтерферони (ІФН), хімокіни, трансформуючі ростові фактори (IGF), колонієстимулюючі фактори (CST). Мають місце інтерлейкіни, що позначаються як IL1-IL-32.*

Інтерлейкіни, які не пов'язані між собою, відповідають трьом критеріям: їхні гени повинні бути клоновані, вони повинні бути індуковані у лейкоцитах, а їхня біологічна активність під час запальних процесів повинна бути послідовною та каталітичною.

Білки, які входять у систему комплементу, представлені клітинно-зв'язаними білками, функція яких полягає у посиленні механізмів захисту проти чужорідних білків. Більшість білків комплементу у плазмі крові синтезуються у печінці, за виключенням С1, який продукується епітеліальними клітинами, а також фактора D, що синтезується у жировій тканині.

Додатковими джерелами синтезу білків комплементу є моноцити та макрофаги. Таким чином, встановлюючи зміни показників імунної системи у разі певних патологічних станів та під впливом фітопрепаратів, можна визначити сфери призначення рослинних препаратів. У літературі є дані, які поділяють препарати рослинної групи залежно від переважного впливу на ті чи інші показники імунної системи.

В оглядах літератури надається характеристика частіше галенових, іноді новогаленових та біотехнологічних препаратів, найбільш часто застосованих рослин, та акцентується увага на їх впливі на показники імунної системи. Так, аналізуються імунорегулюючі властивості ехінацеї, родіоли рожевої, імбиря, часнику, сої та герані. Щодо деяких рослинних екстрактів, то вказується і акцентується увага на доцільності їх призначення при COVID-19, меланомі та інших онкозахворюваннях.

Висновки. *Обізнаність щодо маркерів показників імунної системи, які змінюються у разі інфекційних, онкозахворювань, хвороб життєво важливих органів та механізмів впливу рослинних препаратів при цих станах, сприятиме підвищенню ефективності лікування широко поширених захворювань.*

Ключові слова: *імуномодулююча дія, фітопрепарат, підвищення ефективності, безпечності лікування.*

Introduction. Actuality. Medicines that correct the activity of the immune system are more correctly called immunomodulators. In the literature, their names are more often found as immunostimulants, and therefore the pharmacology of these agents is described together with autogens. At the same time, it is known that some of them, along with the immunomodulatory effect, can have a calming effect on the nervous system. An example is the ashwagandha plant (lat. *Withania somnifera*).

The immune system is a natural self-defense mechanism that discriminates between protective and non-protective molecules (Cingi et al., 2023). The determination of the effect of herbal drugs on the performance indicators of the immune system will help to make a new contribution to the treatment regimens for diseases accompanied by changes in the main indicators of its activity.

The aim of the study – to determine the main indicators of the activity of the immune system, which makes it possible to more purposefully prescribe herbal drugs with an immunomodulatory effect in diseases with violations of these indicators.

Research methods. On the basis of research data from domestic and foreign literature, SCOPUS publications, "Web of Science", Google Scholar, determine the indicators of the immune system, which allow to establish the immunomodulatory effect of herbal drugs and identify promising herbal drugs that have immunocorrective properties in pathological conditions.

Research results and their discussion. Phytodrugs have immunoregulatory properties in pathological conditions (Rosales & Uribe-Querol, 2017; Striz et al., 2014).

The immune system has several stages of creating resistance, including the skin, hematopoietic, digestive, urinary, and other systems. Factors of non-specific immunity such as constitutional, phagocytic and lymphoid systems are released in the body.

Phagocytosis, which begins with physiological contact between the functioning of leukocytes and a foreign cell and the formation of a phagosome after displacement, is important in determining the adaptive effect. After displacement of cytoplasmic granules, phagosome is formed. The latter connects to the outer shell of bacteria and helps prepare it for phagocytosis. Phagocytes have receptors for immunoglobulins and complement components that help phagocytosis (Abbas & Lichtman, 2019).

Leukocytes, among which eosinophils, basophils, neutrophils, monocytes, and lymphocytes, can take part in cellular defense mechanisms.

Lymphocytes form the basis of acquired immunity. Lymphocytes, which arise in hematopoietic cells and mature in primary lymphoid organs, then enter secondary organs: spleen, lymph nodes, adrenal glands, tonsils, appendix, lymphoid tissue associated with mucous membranes. In the effector organs, T-lymphocytes are released, which as effector cells perform a regulatory role. B-lymphocytes produce antibodies. Lymphocytes, natural killer and cytotoxic NK lymphocytes, are very important for the immune response. The thymus is capable of producing T-lymphocytes, even when it is reduced in size. After lymphocyte differentiation is complete, T-lymphocytes leave the thymus and B-lymphocytes leave the bone marrow.

The immune system is regulated by soluble proteins and cytokines. They are produced by various cells and regulate both the immune and hematopoietic systems. Induction of cytokines occurs as a response to stimuli: bacteriological, lipoproducers, bacterial proteins and others, with the help of a cell adhesion molecule, as well as through the recognition of foreign antigens by lymphocytes. Cytokines include tumor necrosis factor (TNF), interferons (IFN), chemokines, transforming growth factors (TGF), colony-stimulating factors (CSF), and interleukins (IL), of which there are currently 32, from IL-1 to IL-32 .

Cytokines have a pleiotropic effect, acting not only on cells of the immune system, but also on other cells. Transforming growth factor includes three isoforms: TGF-β1, TGF-β2, TGF-β3. TGF-β is a regulator of cell growth, differentiation, apoptosis, migration and inflammatory response. Complement is a complex series of bound proteins. The complement system must be controlled so as not to cause tissue damage. Most complement proteins are synthesized in the liver, with the exception of protein C1, which is synthesized by intestinal cells, and factor D, which is synthesized in adipose tissue. Other cells, such as monocytes and macrophages, are additional sources of early complement components: C1, C2, C3.

The lectin pathway is one of the means of activation of the complement system that does not require the presence of antibodies. One of the key ways of lectin binding is its interaction with lactose, that is, with the help of sugar, in the presence of glycoproteins (MDL). The development of the immune response in the body, in particular the activation of lymphocytes, occurs with the participation of substances called immunogens or antigens. At the same time, an immune response is formed, which includes the synthesis of antibodies (immunoglobulins). Currently, several classes of immunoglobulins are known, which are determined by the electrophoresis method: IgG, IgA, IgM, IgD, IgE. Immunoglobulins belong to the humoral link of the immune system.

The immunomodulating effect is aimed at the indicators listed above (Nicholson, 2016; El-Radhi, 2018; Dinarello, 2017; Yazdani et al., 2015; McNab et al., 2015).

The interest in herbal remedies that can be used in diseases to support the activity of the immune system as part of complex treatment is related to their lower toxicity, availability, low cost and influence on the indicators of the immune system (Deva et al., 2023).

Some herbal medicines continue to be prepared according to Ayurvedic recipes. Immunomodulatory properties of plants determine their constituent components. Herbal remedies are conditionally distributed according to their effect on one or another link of the immune system.

Thus, the synthesis of interferon can be influenced by medicinal argan, aloe tree, Icelandic moss and others; geranium, anise and others increase the content of lysocin; the complement system is affected by wild mallow, basil and others; horsetail, St. John's wort and others increase the activity of phagocytosis; activate phagocytosis of celandine, black elderberry; T-lymphocytes are affected by stinging nettle, garden marjoram and others; licorice root affects B-lymphocytes (Mishchenko et al., 2020).

One of the medicinal plants whose bark has immunomodulatory activity is patala (*Sweet-smelling stereosperm*) or stereospermum. There are galenic drugs from the leaves of this plant, which have a wide range of action. The effect of galenic drugs of leaves on colds, diseases of the intestine, liver and respiratory system has been established experimentally. Experimental studies have shown its anti-inflammatory and immunomodulatory effects. The active substances of the root are N-triacontanol, dehydrotectanol and lopagon (affects cell growth). Galen drugs from the root of the plant have an immunomodulatory effect, affecting phagocytosis and increasing the level of neutrophils and T- and B-lymphocytes. Due to these properties, they are prescribed in the complex treatment of diseases of the respiratory tract and digestive tract.

Galen drugs are prepared from the branches and leaves of the plant. The roots contain such active substances as N-triacontanol, dehydrotectanol, dehydrolopagon and lapagon. Galen drugs from the root have immunomodulatory properties. They have non-specific immunomodulatory activity and can affect phagocytosis. It was later established that the galenic preparation from the root can also affect erythropoiesis and leukopoiesis. In various in vivo studies, it was established that the plant extract has an immunomodulatory effect.

Tinospora sinensis (Chinese Tinospora, Tinospora heart-shaped) is a herb whose galena drugs have immunomodulatory activity. Later, it was established that the alpha-glucan isolated from the herb has immunomodulatory activity, which is manifested due to the content of 11-hydroxymastakone, N-methyl-1,2-pyrrolidone, N-formylammonium, N-formylalonium, sortiloside and other compounds that affect 11 -hydroxymastacon, N-methyl-2-pyrrolidone, N-formylalonium and tinocordizide. These components contribute to an increase in the level of nitric oxide, reactive oxygen radicals and phagocytosis.

Atractylodes lancea (Chinese atractyla, flat atractyla) – the active substances culmesmol and atractylodine were studied for their ability to prevent the death of animals with cholangiocarcinoma. In addition, the immunomodulatory properties of galena drugs of the plant were determined. *Atractylodes lancea* – bioactive compounds were identified in the extract, in particular culmesmol and atractylodine, which showed activity in an experiment in cholangosarcoma. The above-mentioned active compounds determined the immunomodulatory effect of the plant extract, as well as the effect on the size of cholangiocarcinoma.

Its therapeutic properties were proven in the first phase of clinical trials, which also confirmed its immunomodulatory properties due to the presence of atractylodin, which blocks interleukin-6. At a dose of 1000 mg, the drug increased the production of cytokines (TNF-α, IL-7, IL-2, IL-4) and decreased the production of IL-10 and IFN-γ compared to placebo. In capsules, the extract lowered the content of all cytokines and inhibited IL-17A, increased the subpopulation of lymphocytes: B-lymphocytes, CD8+ cytotoxic T-lymphocytes, CD4+ T-helpers, and NK cells.

Stevia rebaudiana (stevia honey). Stevoside is a diterpenoid glycoside with various pharmacological properties. Stevoside is effective in liver damage due to its antioxidant, anti-inflammatory, anti-tumor and anti-diabetic effects. Against the background of administration of thioacetamide to rats, stevoside eliminated histological and structural changes in the liver. Stevoside prevented thioacetamide-induced changes in the content of glycolysis products and also improved liver function. Thioacetamide increased the level of p65 mRNA, but this effect was less pronounced under the influence of stevozide, which is confirmed by Western studies. Stevozid showed a prophylactic effect in in vivo experiments.

Bamboo-shaped leaf weeder *(Phyllostachys bambusoides)* is a source of flavonoids, glycosides, and antioxidants. The active fraction of the plant contains flavonoids orientin and isorientin. The immunomodulatory activity of these fractions was shown in experiments on mice. The

active substances stimulate the proliferation of epitheliocytes and improve the function of macrophages. The drug regulates the formation of nitric oxide, increases the synthesis of cytokines TNF-γ and IL-4, as well as the expression of CD80 and CD86 in mice.

Cassia fistula (*Cassia fistula*) is considered one of the most famous plants used in Ayurveda and is used to treat many ailments, including pruritus, vitiligo, diabetes, and hemoptysis. An extract is prepared from the leaves and shavings, which has an immunomodulatory effect, increases the density of the skin, and also activates the proliferation of T- and B-lymphocytes.

Tinospora crispata (*Tinospora crispa*). Plant extracts contain phenols and flavonoids, such as catechin, metheolin, murine, rutin, which have significant antioxidant properties. These phenolic components are responsible for the antioxidant activity. There are studies that confirm that this plant is a source of antioxidants. The plant has also been found to have eicosanoid properties, as well as cardiotonic compounds such as cardioside, boldin and quercetin.

Dendrobium catenatum (orchid of peace). The active substances of the plant have immunomodulatory properties and are a trigger for NF-κB, transmitting signals from Janus kinase, which activates transcriptional signaling pathways. The effects of leaf and stem extracts have immunomodulatory properties. The extract affects the activity of NK cells and increases the formation of NO, which dose-dependently stimulates the activity of macrophages. The extract can increase the production of IL-2 and IL-4. The drug increases the content of NO, IL-4, IL-1β, TNF-α.

Chlorophytum borivilianum (Safed Musli). The plant extract has immunomodulatory properties. Thanks to plant polysaccharides, the content of NK cells increases, and an increase in the level of immunoglobulin G is also noted.

Spock is spotted. Immunomodulatory activity of the extract is manifested due to polysaccharides. In the experiment, this galena preparation showed antiviral activity, increased the level of immunoglobulin, and also increased the content of IL-6 and TNF-α cytokines.

Clerodendrum splendens (clerodendrum brilliant). The volatile oil of this plant was isolated and studied, which made it possible to establish its immunomodulatory activity. This oil was used against *Staphylococcus aureus* and *Shining white*. The investigated plant extract increased the content of NO, IL-12, IL-1β, IL-6, IL-10, TNF-α, as well as granulocyte-macrophage immunostimulators. An increase in the level of growth factor in lymph nodes and a decrease in TNF-α, IL-13, IL-17, and interferon γ were also noted.

Glycyrrhiza uralensis (sweet Chinese). Polysaccharides isolated from the plant had an effect on proliferation in vitro, which indicates the presence of immunomodulatory activity. Further experiments on rats confirmed the effect on the immune system, showing changes in the spleen and thyroid gland. Blood analysis showed changes in the levels of TNF-α and other indicators of immunogenesis.

The paws of the Arctic L. (big burdock). Fructoliposaccharides are the active substances of the root of the plant, which lower the level of sugar in the blood, regulate metabolism and promote the sorption of minerals. The immunomodulatory activity of compounds has been proven in experiments *alive* and *in vitro*; they affect the activity of macrophages and increase the level of nitric oxide.

Lepidium meyenii (Peruvian poppy). The plant is a natural source of polysaccharides, which determine its biological activity and immunomodulatory properties. The antioxidant properties of the active substances have been established experimentally.

Eurycoma longifolia (Eurekama long-leaved). A small series of experiments on the effect of polysaccharides revealed that their immunomodulatory activity is associated with the effect on phagocytosis.

Ligustrum vicaryi Rehder (Vicari hybrid violet). The phenotype and properties of plants are determined by the content of chlorophyll. Plant polysaccharides have the ability to show immunomodulating and adaptive effects. Later, it was established that they improve the expression of IL-10, TNF-α, dose-dependently.

Stachytarpheta cayennensis. The plant leaf extract has analgesic, antimalarial and anti-inflammatory effects. This year, the plant was found to have an immunomodulatory effect.

Aegle marmelos. plant The plant contains a number of biologically active substances: carotenoids, phenols, alkaloids and flavonoids, due to which its extracts show effectiveness in chronic diarrhea and other conditions associated with digestive tract disorders.

Gentiana olivieri Griseb. Galenic drugs of plants are prescribed for many diseases in the East, in particular in the Southeast, where they were mentioned in Ayurveda. In the form of aqueous solutions of flowers, they are taken under increased pressure. Thanks to alkaloids, terpenoids and other active substances, the immunomodulating activity of the plant is manifested. Alcoholic extract increases phagocytosis. It is believed that the plant extract affects both cellular and humoral immunity.

Rhaphidophora korthalsii Schott. Plant extracts have traditionally been used to treat tumors, as they had a cytotoxic effect on cancer cells. Experiments proved the

presence of immunomodulatory activity, the ability to influence NK cells, Gamma immunoglobulins and the level of IL-2.

Amorphophallus changed. The plant is used in cooking, for the treatment of toxic diseases, as an antidote for snake bites, and also to relieve itching. Galen drugs from this plant have antibacterial and hepatoprotective activity. Toxicological studies indicate low toxicity of the extract, which allows its use for long-term treatment. *In vitro* the ability of the plant to influence the proliferation of endothelial cells was established. Due to the content of concanavalin, the drug can affect the cells of the spleen, increase the production of antibodies and dose-dependently affect the processes of hemolysis.

Momordica charantia (Chinese bitter gourd). The extract of the fruits of this plant can show both immunostimulating and immunosuppressive properties. It stimulates phagocytosis and activity of splenocytes. The effect on phagocytosis was confirmed by experiments on white mice that were injected *Salmonella typhi*. Violation of the function of T-lymphocytes is associated with a violation of their proliferation, which includes macrophages. In patients with impaired T-lymphocyte function, impaired proliferation and immunosuppression are observed. The drug affects the level of nitric oxide, free oxygen radicals and lysosomal phosphatase, with a change in the number of neutrophils and macrophages. Recent data confirm the immunostimulating effect of the extract.

Moringa oleifera Lam. – a herbal plant containing micro- and macroelements that contribute to its medicinal properties. It is used to treat asthma, bronchitis, mastitis, skin diseases and infections, including HIV/AIDS. The ability of plant extracts to treat various diseases is due to its multicomponent antioxidant properties. The antioxidant effect of the plant was found in many organs. Treatment improves biochemical and hematological parameters.

Trichopodium zeylanicum (Gaertn.) Thwaites. In experiments on rats, the immunomodulatory effect of the plant extract was established, which helps to increase the content of neutrophils and the level of hemoglobin in the peripheral blood. The plant extract can increase the tone of the body, has rejuvenating properties.

Schwartzia brasiliensis (Choisy) Bedell ex Gir. Dengue virus damages various dendritic cells, monocytes, hepatocytes, and endothelial cells. When rats were infected, the content of TNF-α, IL-6, and IL-8 increased, indicating damage to the vascular endothelium. On the other hand, this indicates the activation of defense mechanisms. Monocytes also intervene in the defense response by increasing interferon-γ and reducing the effect of inflammatory cytokines, in particular TNF-α.

Phyllanthus mellerianus. The plant extract helps with diarrhea, dysentery and tuberculosis. The drug is useful in many diseases due to its immunomodulatory properties, including antioxidant, immunomodulatory and antitumor effects. It improves hematological and biochemical parameters. In experiments on rats, the drug restored indicators against the background of cyclophosphamide.

Alstonian scholar. Alkaloids and terpenes isolated from the plant have immunomodulatory properties (Vijay, 2018).

In Indian medicine, a herb with leaves resembling a heart was used – *Tinospora cordifolia*, which also had the name Giloy/Guduchi (Roy et al., 2021).

Galen drugs increased the activity of macrophages when pathogens entered the body during infectious diseases and increased the activity of the immune system. This plant was mentioned in Ayurveda, where it intensified the immune defense. It had hypolipidemic, anti-inflammatory, anticarcinogenic and antimutagenic properties that actively participated in detoxification processes. These drugs activated T- and B-lymphocytes, as well as natural killer lymphocytes. They are used to treat conditions when there is resistance to gram-positive and gram-negative microorganisms. In infectious diseases, galenic drugs of toxins showed an antitoxic effect.

Tulasi *(holy basil)*. Galenic drugs of this plant improve mental and physical activity. The grass and leaves contain vitamin C, which explains their immunomodulatory effect and ability to form resistance to diseases. The juice of the plant is used for fever, diseases of the respiratory system and asthma. Galen drugs have anti-stress and anesthetic properties. Extracts from the plant are used for liver diseases and cardiovascular diseases. Antiviral, antimicrobial and antiallergic effects were confirmed in experiments. The drugs reduce the level of substances that cause hypersensitivity due to the content of antioxidants. The plant contains zinc and vitamin C. The drug has antioxidant and antiviral properties, is effective for colds and sore throats, can be used as an antiseptic for hand treatment due to its antimicrobial properties. In India, tea or balm is made from this plant to treat colds. The plant extract is useful for immunomodulatory and antimicrobial effects in respiratory diseases. The plant is involved in detoxification processes, which is important along with its antimicrobial and antiviral activity in respiratory diseases, including asthma. In addition, galenic drugs of this plant are recommended for diarrhea, gastritis, diseases of the cardiovascular system. Recently, these drugs are used for increased excitability, disorders of the nervous system, diseases of the liver and digestive tract, as well as in gynecolog-

ical practice. The active components of the leaves are sesquiterpenes, monoterpenes, bornyl acetate, beta-element, ursulic acid, biolin, antigenin 7-D-glucuronide, methionine, 7-O-glucuronide, orientin and molludistin. The plant contains many sequiterpenes, monoterpenes, bornyl acetate, beta-element, camnestyrol, cholesterol and beta-sitosterol. Modern medicine also pays attention to the unique properties of Tulasi (Sharma et al., 2017).

Garlic *(Allium sativum)*. It is a component of food. Antioxidants in garlic help with diseases that are accompanied by oxidative stress. Thanks to biologically active components, garlic has immunomodulatory and anti-inflammatory activity. The main active substances are alliin and allicin, into which alliin is transformed. However, allicin is unstable and quickly turns into other sulfur-containing compounds. In recent years, substances such as disulfide, S-allylcysteine, and diethyl sulfide have also been identified in garlic. Garlic has antibacterial, antiviral, antidiabetic, antihypertensive, cardioprotective and hepatoprotective properties. Currently, the biological components of garlic that provide its immunomodulatory activity are being studied. Garlic affects both gram-positive and gram-negative microorganisms. He shows activity about *Shigella spp.*, *Klebsiella spp.*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. In recent years, the effectiveness of its components has been confirmed in relation to *Streptococcus mutans* and *Streptococcus faecalis*. Garlic also helps reduce respiratory symptoms in COVID-19. The specific activity is mainly due to alliin. The active substances of this plant have been known since Ayurveda. Among them are sequiterpenes, monoterpenes, metheolin and other biologically active components.

Turmeric. A plant better known as turmeric. Turmeric extracts have been found to have antimicrobial and antioxidant properties due to the presence of polyphenols. Turmeric drugs have the ability to show antioxidant activity and increase immunity (Nakhostin-Roohi et al., 2016).

It should be recognized that all the mentioned active substances of plants have immunomodulatory, anti-inflammatory and antimicrobial effects. Some of them also affect other organs and systems, showing antimicrobial, antifungal and antitumor activity (Sherly et al., 2023).

The antioxidant properties of turmeric are due to polyphenolic components that provide an antimicrobial effect. These substances reduce the content of malondialdehyde and free oxygen radicals. Although curcumin may slightly reduce the activity of antioxidant enzymes such as catalase, superoxide dismutase and others, this does not affect its value and properties in general. It provides antimicrobial activity and acts as a scavenger of oxygen radicals. Due to biologically active compounds, turmeric has a wide spectrum of pharmacological activity. Its effects include anti-inflammatory, anti-mutagenic and antioxidant effects.

Antimutagenic activity has been determined in plants along with their ability to protect the structure and function of important organs.

Ginger (Ginger). Ginger has antioxidant, antitumor and anticoagulant properties. The plant contains polysaccharides, polyphenols and other biologically active compounds. Ginger also has significant antimicrobial and immunomodulatory properties. Its extract or tea is often prescribed for inflammatory processes and tumors. Ginger extract exhibits pronounced immunomodulatory and antioxidant effects.

Ginger extract helps with coughs, runny noses, respiratory diseases, nausea, vomiting, food poisoning and arthritic pain. Ginger has antimicrobial, anti-inflammatory and anti-tumor properties. The active substance of ginger is gingerol, which includes ambicin, alin, aton, as well as allinase, peroxidase, and myosinase enzymes. The drug increases the activity of glutathione peroxidase and superoxide dismutase enzymes, which confirms its immunomodulatory and antimicrobial activity.

Immunomodulators include plant metabolites that contribute to increasing the resistance of the immune system. Metabolites of some plants have immunomodulatory properties, thanks to which they can be used as gerontological, antitumor and antimicrobial agents.

Polyphenols and phenols are active components of many herbal drugs. They contain one or more hydroxyl groups in the aromatic ring derived from phenylalanine or tyrosine. In the process of metabolism, these compounds can be transformed into other substances, for example, stilbenes, which contain two aromatic rings.

Resveratrol is a natural polyphenol of the stilbene class obtained from *Polygonum cuspidatum*. It is able to pass through the biological barrier and protect its integrity. Resveratrol promotes neuroprotection, lowers interleukins (IL) and prevents beta-amyloid accumulation. It reduces the content of inflammatory factors, stimulates the production of interleukin SIRT1, and after phosphorylation activates the transcription of proteins (Belenichev, et al., 2024).

Resveratrol affects the transcription of the IL-17A gene, regulating its activity through epigenetic mechanisms that reduce inflammation.

Hydrocinnamic acid derived from turmeric (*Turmeric is long*), has anti-inflammatory, antitumor and wound-healing properties. Its immunomodulatory activity is associated with the ability to block interleukin-2 (IL-2) and the IKKβ pathway (inhibitor of kappa-B

kinase beta), which is a key element in the regulation of the inflammatory response through the NF-κB signaling pathway.

Gingerol, the main active ingredient *Zingiber officinale* (ginger), has anti-inflammatory, antibacterial and antimicrobial properties. Ginger extract is recommended for angiogenesis and angiogenesis-dependent tumors.

Active ingredient *Bidens pilosa* (series) – centaurein – activates the production of cytokines and lymphocytes. A traditional plant of India, also known as ponarnava (*Widespread Boerhavia*), has medicinal properties, including anti-inflammatory and immunomodulatory activity.

Hydroxycinnamic acid, contained in turmeric, is often used in medicine due to its beneficial properties. Curcumin, which has immunomodulatory properties, promotes the development of spinal cord cells, increases the phagocytic activity of macrophages and has a positive effect on the proliferation of cells with α-esterase activity, is released from the root of the plant.

Turmeric has a positive effect on coronavirus, particularly effective on oxidative stress, cytokine release and apoptosis. It can interact with membrane proteins, providing protection against the virus. Curcumin also prevents the development of COVID-19 by regulating the Nrf2 signaling pathway. Due to its immunomodulatory action, this compound helps prevent the progression of COVID-19.

Ginger contains a variety of biologically active compounds, including gingerol, which is the main active ingredient. Gingerol has anti-inflammatory, anti-tumor properties and can affect the growth of tumors by regulating signaling pathways in cells.

Centaurein is a flavonoid extracted from a plant *Bidens pilosa* (hair follicle), which exhibits antiviral, anti-inflammatory and antioxidant activity. This compound is also known for its properties in reducing inflammation, which makes it promising in the treatment of inflammatory and viral diseases.

For many years, sera has been considered a remedy with immunomodulatory potential, effective in bacterial infections. It is the aqueous extracts of this plant that demonstrate the ability to improve the immune response. The main active substance is bucolitin (3-O-β-D-galactopyranoside), which belongs to the alkaloid family, affects the immune system, stimulating the production of cytokines such as interleukin-2 (IL-2) and supporting leukopoiesis. In addition, this compound is able to affect the production of nitric oxide (NO) and control the formation of leukotrienes (eg, LTA2).

Myricetin is the active substance of papaya (*Load papaya*), contains bioflavonoids and is recommended for use with tumors and acne.

Chrysanthemum indica (Indian chrysanthemum). The active substance of chrysanthemum, galena drugs of which are used for inflammation, diseases of the respiratory tract and conditions associated with suppression of the immune system. Due to the content of flavonoids, the plant has immunomodulatory properties.

Hippophae rhamnoides (common sea buckthorn). Immunomodulatory properties of the plant extract due to active flavonoids and isorhamnetin were established. The extract activates the production of interleukin-6 and stimulates the activity of intracellular killers. It has also been established that the extract suppresses the action of pro-inflammatory cytokines, such as TNF-α, and inhibits the genetic transmission factor in granulocytic diseases.

Quercetin from stinging nettle (*Stinging nettle*). Quercetin has long been used to treat arthritis due to its flavonoid content. It supports the immune response by influencing chemotaxins and killer activity.

Luteolin from *Rosaceae*. Luteolin, a flavonoid found in plants of the family *Rosaceae*, has anti-inflammatory, immunomodulatory and antitumor activity. Recently, it is also used as an anti-allergic agent. According to research, its effectiveness in some cases is not inferior to hydrocortisone. The main targets of luteolin are SRS, Syk, SOCS3, which regulate the activation of cytokines and growth factors. Luteolin affects NF-κB, AP-1, IRF-1 – transcription factors that control inflammatory processes.

Terminal chebula. Fruits *Terminal chebula* is a rich source of tannins, which determine their irritating, laxative and tonic properties. They affect cellular immunity and contribute to the improvement of humoral immunity.

Camellia green tea (*Camellia sinensis*). Epigallocatechin-3-gallate (EGCG) is a flavonoid in green tea that has been used for centuries for its antitumor, antiviral, and immunomodulatory properties. The drug reduces the level of TNF-α, IL-1β, IL-6, as well as the content of inducible NO-synthase, which regulates neural, immune and inflammatory responses. It is prescribed for inflammatory processes and cognitive disorders. The extract reduces the level of cytokines (TNF-α, IL-1β, IL-6), which helps reduce inflammatory reactions in microglia.

Buchanamine is an alkaloid, an active substance *The doubts of Cryptolepis*. The plant extract is used as an immunomodulating agent.

Hydrastis canadensis. Berberine is the active substance of this plant. It is used to treat respiratory tract diseases and flu (Balasubramaniam et al., 2024).

Tinospora cordifolia. The extract from this plant has an immunomodulatory effect, stimulates macrophages. Recent studies devoted to this plant have shown new properties of its active substances, namely diterpenoids, lactoids, alkaloids, glycosides, steroids, substances of ali-

phatic structure. The plant exhibits immunomodulating, anti-diabetic, anti-leprosy, anti-inflammatory, anti-spasmodic, antioxidant, anti-arthritic, anti-stress, anti-carcinogenic activity. In clinical practice, the use of plant extracts has shown the presence of cardioprotective, hepatoprotective, antitumor activity (Ahsan et al., 2023).

Herbal drugs are effective when prescribed with immunosuppressants for tumors and inflammatory diseases. A plant on the background of cyclophosphamide *Rhus toxicodendron* restored the content of interleukin-γ, NF-κB, which confirms the properties of the plant as an immunomodulator (Saka et al., 2024).

A number of modern herbal remedies, which were introduced into our medicine from Ayurvedic treatises, continue to interest pharmacologists and pharmacists. Such plants as *Atropa belladonna*, *Solanum dulcamara*, *Digitalis purpurea*, *Cinchona ledgeriana*, *A sleepy poppy*.

Even galenic drugs of these plants had significant activity, an even more active effect was observed in new galenic remedies and complex drugs, which included active components of these plants. Advances in complementary medicine about the active plant sources emphasized in Ayurveda continue to be studied.

One of the plants whose extracts are widely used in Africa, India and the Mediterranean countries is *Withania somnifera* (ashwagandha). Roots, flowers and leaves serve as raw materials for creating extracts.

There is also another name for the plant – *Physalis somnifera* (physalis hypnosis). The main active substances are alkaloids, steroid lactones, saponins, flavonoids, and tachins. It is believed that the active substances of the plant can have a sedative and immunomodulating effect. The sedative and relaxing effect is manifested due to the increase in the level of GABA. In this regard, the plant extract was added to the complex therapy of patients with schizophrenia, Alzheimer's disease and dementia. Later, it was established that plant extracts can affect M1 receptors, have antioxidant mechanisms, and promote nerve growth. The drugs also reduce excitability and have anti-stress activity. At the same time, plant extracts have been shown to have immunomodulatory activity. Plant extracts can change the level of immunomodulatory cells, immune complexes and immunoglobulins. They inhibit the system of complement and mitogen, cause the proliferation of lymphocytes. In recent years, studies have shown the possibility of the influence of plant active substances on the cytokine storm observed in COVID-19. One such agent is the isoquinol alkaloid berberine, which has the ability to modulate the immune response, particularly in the context of reducing excessive inflammation associated with cytokine storm (Alarabei et al., 2023).

Plant extracts can activate and mobilize peritoneal macrophages, phagocytes, and lysosomal enzymes, stimulating lymphocyte proliferation and reducing the production of interleukin-1 (IL-1) and TNF-α.

They also have antioxidant activity, increasing the level of superoxide dismutase and catalase, which contributes to the inhibition of lipid peroxidation. Further studies have shown that extracts can increase levels of nitric oxide and antioxidants while inhibiting NF-κB activity, which is important in the regulation of inflammation (Xu & Cock, 2023).

Prospects for the use of certain plants and the isolation of active substances that can have an immunomodulatory effect and contribute to the elimination of symptoms of COVID-19, such as fever, cough, pneumonia, exacerbation. Such plants include: *Chenopodium quinoa* (quinoa), *Croton lechleri* (croton red), *Lepidium meyenii* (pain), *Maytenus macrocarpa*, *Mauritia flexuosa* (Mauritius murita), *Physalis peruviana* (physalis peruvian), *Uncaria* (Choi et al., 2024).

Green tea extract had an anti-inflammatory effect in skin diseases and acts on mucous membrane warts. In some cases, phytoimmunotherapy can complement synthetic means (Tabolacci et al., 2023).

One of the dangerous diseases, in the treatment of which the use of herbal drugs is proposed, is melanoma, which is complicated by atypical transformation of the melanin pigment under the influence of radiation. Melanoma is characterized by heterogeneity and the ability to metastasize. At the same time, BRAF kinase is activated. The target on which the drugs vemurafenib (Vemurafenib), dabrafenib (Dabrafenib) and encorafenib (Encorafenib) acted was identified.

Trimetinib, binimetinib, and colometinib are proposed for targeted therapy, which prevent the progression of melanoma. Currently, it has been established that melanoma is an immunogenic disease that is amenable to immunotherapy, but this complicates treatment. Melanoma progresses through several mechanisms, so the use of immunotherapy is considered possible. This leads to the need to find non-toxic phytoremedies for the treatment of melanoma, in particular, those with immunomodulatory properties (Behl et al., 2021).

Indeed, a number of sources indicate the presence of immunomodulatory activity of plants and their metabolites. Green tea extract has a therapeutic effect on inflammatory markers (IL-6, IL-1β) of interest. Currently, there are no phytodrugs that have therapeutic properties for melanoma. However, their use may be able to reduce the dosage of chemotherapy drugs (Tabolacci et al., 2023).

Conclusions

Awareness of markers of immune system indicators that change in infectious, oncological diseases, diseases of vital organs and the mechanisms of effect of herbal drugs in these conditions will contribute to increasing the effectiveness of treatment of widespread diseases.

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Belenichev I.F. – data collection and analysis, article corrections, conclusions;
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Harnyk T.P. – concept and design of the work, article corrections, critical review;
Shumeiko O.V. – data collection and analysis, article corrections, conclusions;
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Klymenko O.H. – data collection and analysis, participation in writing the article;
Chemerys Y.O. – data collection and analysis, participation in writing the article.

Corresponding author's email: ***gorchakovan1941@gmail.com.***