Prospective directions for searching new medicines of plant origin, effective in infections of different etiology

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The global community is concerned about the COVID-19 pandemic. Existing capacities are mobilized and new ways to counter the growing threat are actively sought. The scientific development of traditional medicine is a promising way of solving this problem. Information on the use of medicinal plants by different peoples is fragmented and largely unavailable to the world scientific community. The flora of Azerbaijan including almost 1600 species of medicinal plants with antiviral, anti-inflammatory, immunomodulatory, vitamin, general tonic and other properties are distributed in the Flora of Azerbaijan. Modern protocols for the treatment of infection caused by COVID-19, along with other therapeutic agents, will include drugs with the above properties. The article contains information about a computer database of medicinal plants in Azerbaijan, developed by the author in the frame of the doctoral thesis in the 2006 year. These data enable us to distinguish species with a set of biologically active substances that determine their required necessary physiological activity from the total number of medicinal plants. Therefore, the intensification of work on the study of traditional medicine and the creation of a worldwide information platform on medicinal plants can become the basis for the search and development of new antiviral drugs, including those effective and against COVID-19.

Keywords: Flora of Azerbaijan, medicinal and food plants, database, biologically active substances, physiological activity, COVID-19

INTRODUCTION

The raging global pandemic caused by the COVID-19 virus has completely changed the way of life of human civilization and showed that the arsenal of modern medicine is not as extensive as we would like to successfully resist this virus. Today, all the forces of the global medical community are mobilized to search for and develop new effective drugs to combat the COVID-19 virus. All possible search directions with at least some prospect of positive conclusion are being developed. Countless scientific organizations are involved in both the synthesis of chemical and the search for natural biologically active substances.

Millennia of traditional healing experience shows that medicines for many diseases are found in nature itself, including in plants that are consumed as food, or used in the form of drugs obtained on their basis. At the same time, modern data indicate that about 20 thousand plant species have been studied for medical purposes, i.e. about 6.5% of all 320 thousand described (Ших и др., 2015). There is no doubt that among the unexplored species there are many plants that can help fight many diseases, including even those that are still considered incurable. The advantage of medicines of natural origin is their gentle effect and relative harmlessness, in comparison with synthetic medicines. In recent decades, synthetic chemistry has become more and more pervasive in all spheres of human life. At present, it is impossible to imagine industry and everyday life without synthetic products - plastics, various dyes, preservatives, flavor enhancers, medical supplies, synthesized drugs, etc.

Of course, synthetic chemistry has greatly expanded the possibilities of mankind to meet its needs, primarily related to the production of food and medicines, and has improved the quality of life of people. At the same time, it has long become obvious that food products and medicines obtained or processed using the capacities of synthetic chemistry are overwhelmingly inferior to natural products and medicines of natural origin in terms of their environmental purity and human safety.

Therefore, it is not at all surprising that in the modern world the interest of people and the need of medicine for drugs derived from plants and plant materials have greatly increased. However, unfortunately, the modern scientific community does not have wide access to information about plant remedies used in some regions of the world at the local level. And this is mainly due to the fact that today such information is fragmented and still remains out of sight at the global level.

Earlier it was indicated that about 800 species of plants used for medicinal purposes grow in the flora of Azerbaijan (Əliyev, 1998; Дамиров и др., 1988; Dəmirov və b., 1992; etc.). In addition, information about these plants was limited and scattered. Recent studies have established that there are much more such plants and their number reaches almost 1600 species (Ethnobotany of the Caucasus, 2017).

Some chemicals or their natural combinations which are part of medicinal plants are so unique that, despite the achievements of modern science, they cannot be synthesized artificially. Meanwhile, medicinal plants in their natural form and their derived preparations continue to play an important role in health care and their use is part of integrative medicine. Therefore, it is essential to bring this traditional knowledge to the attention of scientists and medical practitioners around the world.

Great opportunities for solving this problem are revealed by modern computer technologies that allow accumulating, storing and ensuring the worldwide availability of such information. In a way, this also solves a certain cultural and historical problem, as it helps prevent the possibility of irrevocable loss of invaluable folk experience.

In the part concerning medicinal plants growing in our country, this problem is partially solved and automated "Electronic Database of Medicinal Plants of Azerbaijan" has been created (Мехтиева, 2006).

This study aims to provide the scientific community with an overview of the research results on the study of the biodiversity of the medicinal flora of Azerbaijan and the prospects for using its capabilities in the search for new therapeutic agents effective for various infections of various etiologies.

MATERIALS AND METHODS

The object of the study was medicinal plants of the flora of Azerbaijan. Analytical information on medicinal plants was obtained through the implementation of the capabilities of the "Electronic Database of Medicinal Plants of Azerbaijan" (Mehdiyeva, 2010). On the basis of the technical assignment prepared by the author, together with the relevant specialists in the Access using DELPHI computer language programming, the Applied Computer program was developed and the electronic database "Medicinal plants of the flora of Azerbaijan" was created. The information array of the Database was formed on the basis of data from almost 500 literary sources on medicinal plants, including monographs, official reference publications, scientific periodicals (peer-reviewed publications), regulatory documents, as well as the results of our own research (Мехтиева, 2015).

RESULTS AND DISCUSSION

As a result of the analysis, it was found that about 1600 plant species with the described medicinal properties, belonging to 742 genera and 179 families, grow in the flora of Azerbaijan. Of these, 274 species are official medicinal plants, 6 species are endemic to Azerbaijan, 77 - endemic to the Caucasus, 44 - relict, and 112 - rare and endangered.

Among the studied medicinal plants of Azerbaijan, many species that contain such biologically active substances (BAS) as flavonoids, alkaloids, vitamin C, essential and fatty oils, anthocyanins, carotenoids, tannins, phenol carboxylic acids, saponins, terpenoids, coumarins, glycosides and lactones have been identified. Moreover, the form and direction of the physiological effects of these and other biologically active substances have been established by experimental and clinical studies.

Such data for some biologically active substances are given in Table 1.

It is the presence of natural biologically active substances in plants that determine their high physiological activity and its direction, including antiviral, antibacterial, antifungal, antioxidant, antihistamine, anti-inflammatory, immunomodu-latory and other effects. Ultimately, only the physiological activity of the substances contained in plants forms their medicinal properties, has a positive effect on metabolic processes, strengthens the immune system, improves the overall state of the organism and mobilizes it to fight the disease (Мехтиева, 2014).

The results of the analysis show that among the medicinal plants of Azerbaijan, there are quite a number of species with medicinal properties in demand in medicine (Fig. 1).

In the context of the considered problem of combating COVID-19, plants exhibiting antiviral, antimicrobial, restorative, anti-inflammatory, immunomodulating and other activity are of particular interest.

Table1. Medicinal plants with predominant groups of biologically active substances and the direction of their physiological activity.

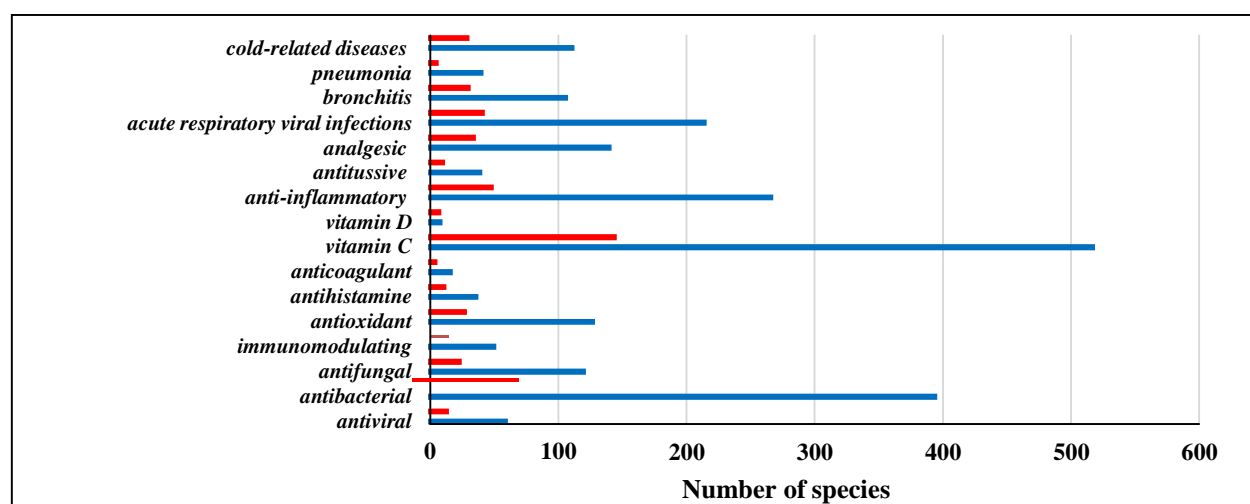| BAS	The number of species with these BAS	Physiological activity, properties	BAS	The number of species with these BAS	Physiological activity, properties
Flavonoids	930	anti-bacterial, antioxidant	Tanning agent	452	bactericide
Alkaloids	597	antifungal	Phenolcarbonic acids	375	antimicrobial, fungistatic, immunomodulating
Vitamin C	518	antioxidant	Saponin	323	anti-bacterial, antivirus, antifungal
Essential oil	468	antimicrobial, antifungal, antivirus	Terpenoids	317	antimicrobial, antifungal, antivirus
Fatty oil	454	anti-bacterial, antivirus, antifungal, immunemodulating	Coumarine	299	antimicrobial, antivirus
Anthocyanin	249	antioxidant, bactericide	Glycoside	139	cardioactive
Carotenoids	220	immunomodulating	Lacton	34	antifungal, antivirus

Fig. 1. Quantitative distribution of medicinal and food plants by biological activity and disease.

Table 2. Plants and their derivatives exhibiting physiological activity against certain viral strains.

Virus	Species name	Used parts	Extracts
Herpes types 1 and 2	*Viburnum opulus,* *Verbascum thapsus,* *Melissa officinalis* *Prunella vulgaris*	bark, aerial parts and leaves aerial parts aerial parts	aqueous extract, methanol and alcohol extract aqueous, aqueous-alcoholic extract and essential oil aqueous extract, polysaccharide
Immunodeficiency HIV	*Melissa officinalis*	aerial parts	aqueous extract
Influenza A and B	*Sambucus nigra,* *Verbascum thapsus*	fruit, aerial parts and leaves	aqueous extract, methanol and alcohol
Influenza A2 and B	*Verbascum phlomoides*	flower	decoction
Strains A/PR/8 and A/Hong Kong, FIV, H1N1	*Sambucus nigra*	flower	aqueous extract
Epstein-Barr	*Glechoma hederaceae*		ursolic and olein acid
Ortho- and para-myxoviridae	*Salvia sclarea*	aerial parts	essential oil
Hepatitis C	*Solanum nigrum,* *Lamium album*	seeds aerial parts	methanol and chloroform extract, monoterpene lamiridozin
Tobacco mosaic	*Rubia tinctorum,* *Lonicera captifolium*	aerial part	ethereal extract

Out of the total number of medicinal plants in Azerbaijan, 59 species have been identified for their antivirus activity. It has been established that this activity is manifested mainly in relation to herpes viruses type 1 and 2, HSV-1, HIV immunodeficiency, influenza virus A and B, A2 and B strains, A/PR/8 and A / Hong Kong strains, FIV virus, hepatitis C virus, Epstein-Barr virus, ortho- and para-mixoviruses, Koksaki A18 and A21, and tobacco mosaic virus (Liu et al., 2002; Zakay-Rones et al., 2004; Nolkemper et al., 2006; Mazzanti et al., 2008; Roschek et al., 2009; Javed et al., 2011, etc.). Data on the antiviral activity of some of these species are given in Table 2.

Medicinal plants with antibacterial properties is much higher in the flora of Azerbaijan (394 species) (Fig. 1). The extracts and essential oils obtained from them are physiologically active, mainly against bacteria *Echerichia coli, Serratia marcescens*, *Klebsiella pneumonia, Staphylococcus aureus, Pseudomonas aeruginosa* and *P. hyogenicum* (Alavi et al., 2006; Mohammad et al., 2007; Цыдендамбаев и др., 2018; Manandhar et al., 2019 etc.).

There are large number of medicinal plants with antifungal properties, numbering over 120 species (Fig. 1). Antifungal activity was determined for extracts and essential oils isolated from these species, mainly against the fungi *Candida albicans*, *Aspergillus niger, Mucor circinelloides, Fusarium oxysporum, Trichoderma lignorum* and *Penicillium funicullosum* (Мустафаева и др., 2006; Sahmurova et al., 2009; Takesh et al., 2019; Giordani et al., 2020 etc.).

Since there are still no effective drugs for direct action against COVID-19, the various treatment protocols for infection caused by this coronavirus mainly consist of methods that stimulate the mobilization of the body's internal resources. For this purpose, drugs with immunomodulatory, anticoagulant, antihistamine, antioxidant and anti-inflammatory effects are used to eliminate the symptomatic manifestations of the disease.

Out of the total number of medicinal plants in Azerbaijan, more than 400 species are at the same time and edible (Мехтиева, 2014; Ethnobotany of the Caucasus, 2017; Alizade et al., 2019). Plants contain a fairly wide variety of biologically active substances with such properties and they enter the body not only in the form of drugs, but also through the direct consumption of plants as food.

For example, out of 59 speciesof medicinal plants with antiviral properties - 13 (*Rhus coriaria, Melissa oficinalis, Morus alba, Juglans regia, Mentha aquatica, Portulaca oleracea, Agrimonia eupatoria, Capsicum annuum* etc.); of 394 species with antibacterial properties - 64 (*Allium ursinum, Apium graveolens, Foeniculum vulgare, Eremurus spectabilis, Artemisia dracunculus, Armoracia rusticana, Castanea sativa, Ribes nigrum, Punica granatum, Berberis vulgaris* etc.); of 120 species

with antifungal properties - 23 (*Allium victorialis, Asparagus officinalis, Mentha longifolia, Satureja hortensis, Nigella sativa, Physalis alkekengi, Rumex crispus* etc.) are also food plants.

Food plants, which are also of medicinal importance, are widely used in the national culinary of Azerbaijan. Most of these species are used as spices and seasonings for meat and fish dishes, in marinades, for the preparation of jam, composts, soft drinks, etc., both as fresh and dried. Ultimately, all of these plant species, individually or in combination with other products, contribute, to some extent, to the fight against various diseases and strengthen immunity

Scientists are currently focusing on functional foods and biologically active compounds that support the immune system. A strong immune system is an important factor in the functioning and defense of the body against viral diseases, including those caused by coronaviruses.

To do this, the body needs a sufficient amount of various vitamins and especially C and D. Regular consumption of high-vitamin C and D foods is therefore necessary to maintain immunity.

As the analysis shows, out of 517 species of medicinal plants containing vitamin C - 144 species (*Actinidia deliciosa, Allium sativum, Anethum graveolens, Daucus sativus, Cynara cardunculus, Lactuca sativa, Berberis vulgaris, Armoracia rusticana, Raphanus sativus, Stellaria media, Atriplex hortensis, Cornus mas, Diospyros kaki, Hippophae rhamnoides, Ribes nigrum, Ocimum basilicum, Feijoa sellowiana, Olea europaea, Punica granatum* etc.), and out of 8 species of medicinal plants containing vitamin D - 7 species (*Brassica oleracea, Citrus paradisi, Helianthus annuus, Lycopersicon esculentum, Oryza sativa, Persicaria hydropiper, Spinacia oleracea*) are edible.

At the same time, there are quite a lot of food plants among medicinal plants, which have other medicinal properties. For example, as food products are used:

out of a total of 50 species of medicinal plants with immunomodulatory - 14 species (*Cichorium intybus, Silybum marianum, Salicornia europaea, Panicum miliaceum, Polygonum aviculare, Urtica dioica* etc.);

out of 16 species of medicinal plants with anticoagulant properties - 4 species (*Petasites albus,*

P. hybridus, Filipendula ulmaria and *Punica granatum*);

out of 266 species of medicinal plants with anti-inflammatory properties - 48 species (*Allium cepa, Rhus coriaria, Coriandrum sativum, Arctium lappa, Brassica rapa, Salicornia europaea, Spinacia oleracea, Cucurbita maxima, Prunus spinosa, Rubus caesius, Sambucus ebulus, Viola arvensis* etc.);

out of 140 species of medicinal plants with analgesic effect - 34 species (*Pastinaca sativa, Eremurus spectabilis, Crocus sativus, Mentha longifolia, Morus nigra, Nigella sativa, Urtica dioica* etc.);

out of 39 species of medicinal plants with antitussive properties - 10 species (*Cydonia oblonga, Diospyros lotus, Ficus carica, Ocimum basilicum, Morus alba, Thymus transcaucasicus, Hordeum vulgare* etc.);

out of 36 species of medicinal plants with antihistamine properties - 11 species (*Apium graveolens, Berberis vulgaris, Cyperus longus, Lamium album, Mentha piperita, Solanum nigrum* etc.).

Food plants, which are also medicinal, are used for a variety of diseases and their manifestations (Киселева и др., 2007). They are also used as food for:

acute respiratory viral infections - 41 species (*Brassica juncea, Raphanus sativus, Origanum vulgare, Satureja hortensis, Fragaria vesca, Rosa canina, Sorbus aucuparia, Laurus nobilis*, etc.) out of 214 species of medicinal plants;

cold-related diseases - 29 species (*Capsella bursa-pastoris, Capparis herbacea, Beta vulgaris, Crocus speciosus, Rosmarinus officinalis, Rumex confertus, Citrus limon*, etc.) out of 111 species of medicinal plants;

bronchitis - 30 species (*Foeniculum vulgare, Pimpinella saxifraga, Artemisia dracunculus, Helianthus annuus, Fagus orientalis, Thymus kotschyanus, Ziziphus jujube, Citrus unshiu, Vitis vinifera*, etc.) out of 106 species of medicinal plants;

pneumonia - 5 species (*Iris pseudacorus, Rosa canina, Tilia begoniifolia, T. cordata, Viola odorata*) out of 40 species of medicinal plants.

Many of these plants are firmly entrenched in the diet of the population of Azerbaijan and are seasonally, almost daily, used for food, both in natural form and as part of various dishes. According to the available data, some of them are quite effectively

used both as a prophylactic agent for the prevention of diseases and as a drug for the treatment of the disease itself (Franco and Bussmann, 2020). Therefore, it can be assumed that a large plant diversity of the diet of the population of Azerbaijan to a certain extent helps to maintain people's immunity and is one of the elements of the comparatively successful fight against the coronavirus pandemic in our country.

In this context, we believe that one of the main and urgent tasks is the further expansion of research on the study of medicinal plants of the Republic of Azerbaijan. To further saturate the food ration of our people with useful substances, it is necessary to intensify scientific and practical activities for the development and production of new biologically active dietary supplements of plant origin.

CONCLUSIONS

Modern research shows that the spread of certain diseases is often influenced by regional factors, the diet of the population, preferences in tastes and smells, methods and technologies for processing products and, which is very important, but still little studied - genetics and consumer characteristics, for example, the presence of detoxifying enzymes (Rivera et al., 2007; Unnikrishnan et al., 2016; Franco and Bussmann, 2020). Ultimately, understanding the statistics and the nature of the issues associated with these factors will help to better understand how to deal with COVID-19 and other similar viruses.

Summarizing the above, it can be argued that, beyond any doubt, the plant world of Azerbaijan is an inexhaustible source of useful substances, including those that have not yet been identified, and this source probably has a remedy against COVID-19. The pandemic caused by this virus is a global problem and the entire world community is actively seeking means to address it. The key to this question is the basic information platform for the search. However, unfortunately, the vast amount of information about medicinal plants used in some regions of the world at the local level remains largely invisible to scientists worldwide.

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Müxtəlif etiologiyalı infeksiyalara qarşı effektiv olan bitki mənşəli yeni vasitələr axtarışının perspektiv istiqamətləri

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Dünya birliyi COVİD-19 virusunun doğurduğu pandemiya ilə bağlı narahatlıq keçirir. Getdikcə artan təhlükəyə əks təsir göstərmək üçün bütün mövcud imkanlar səfərbər edilmiş və yeni yolların fəal axtarışı gedir. Bu problemin həll edilməsinin perspektivi istiqamətlərindən biri xalq təbabəti təcrübəsinin elmi baxımdan işlənilməsidir. Müxtəlif xalqlar tərəfindən dərmən bitkilərinin istifadəsinə dair məlumatlar pərakəndə xarakter daşıyır və dünyanın elmi birliyi bu bilgilərdən əsasən məlumatlı deyildir. Azərbaycan florasında təqribən1600 növ dərman bitkisi yayılmışdır ki, onların arasında antivirus, antiiltihab, immun-modulləşdirici ümümmöhkəmləndirici, vitaminli və s. bu kimi xüsusiyyətlərə malik bitkilərdə kifayət qədərdir. Digər müalicə vasitələri ilə yanaşı, COVİD-19 virusunun doğurduğu infeksiyanın müasir müalicə protokollarında yuxarıda göstərilən xüsusiyyətlərə malik preparatlar da yer almışdır. Məqalədə, şəxsən müəllifin işləyib hazırladığı Azərbaycanın dərman bitkilərinin komputer bazasında toplanılmış belə bitkilər barədə məlumatlar verilir. Bu məlumatlar bütövlükdə dərman bitkiləri sırasından, zəruri fizioloji fəallığı şərtləndirən bioloji fəal maddələr tutumlu bitki növlərini seçməyə imkan verir. Ona görədə, xalq təbabəti təcrubəsinin tədqiq edilməsi üzrə işlərin fəallaşdırılması və dərman bitkilərinə dair ümumdünya informasiya platformasının yaradılması antivirus xüsusiyyətlərə, o cümlədən COVİD-19 virusuna qarşıda effektiv olan vasitələrinin axtarışı və yeni dərman preparatlarının hazırlanması üçün elmi əsas olabilər.

Açar sözlər: Azərbaycan florası, dərman və qida bitkiləri, məlumat bazası, bioloji fəal maddələr, fizioloji fəallıq, COVİD-19

Перспективные направления поиска новых средств растительного происхождения, эффективных при инфекциях различной этиологии

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Мировое сообщество обеспокоено пандемией, вызванной COVID-19. Мобилизованы существующие возможности и идет активный поиск новых путей противодействия продолжающей нарастать угрозе. Перспективным направлением решения этой проблемы является научная разработка опыта народной медицины. Информация об использовании лекарственных растений разными народами носит разрозненный характер и в массе своей недоступна мировому научному сообществу. Во флоре Азербайджана произрастает почти 1600 видов лекарственных растений, в том числе обладающих антивирусными, противовоспалительными, иммуномодулирующими, общеукрепляющими, витаминными и другими свойствами. Современные протоколы лечения инфекции, вызванной COVID-19, наряду с другими лечебными средствами включают и препараты с вышеперечисленными свойствами. В статье приводятся сведения о таких растениях, включенных в компьютерную базу данных лекарственных растений Азербайджана, разработанную лично автором. Эти данные позволяют выделять из общего числа лекарственных растений виды с набором биологически активных веществ, определяющих их требуемую физиологическую активность. Поэтому активизация работы по исследованию опыта народной медицины и создание общемировой информационной платформы по лекарственным растениям может стать основой для поиска и разработки новых антивирусных препаратов, в том числе эффективных и против COVID-19.

Ключевые слова: Флора Азербайджана, лекарственные и пищевые растения, база данных, биологически активные вещества, физиологическая активность, COVID-19