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Ethnobotanical study of medicinal plants used for prevention or alleviation of symptoms of Covid-19 in Bulgaria. Part 2: The most used medicinal plants

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Abstract: *This paper is a second part of an ethnobotanical survey among phytotherapy users. The present work aimed to identify the medicinal plants used for prevention or alleviation of symptoms of COVID-19 disease in Northeastern Bulgaria. The other goal is a comparison of listed medicinal plants with the results of other ethnobotanical surveys in Bulgaria, as well with the accessible scientific data about the possibility to use listed plants in the case of Covid-19. The results revealed the significance of particular species for local people. The comparison with other ethnobotanical surveys in Bulgaria showed some peculiarities, due to the selection of the informants and to the goal of the questionnaire. Nowadays phytomedicine users rely not only to preserved traditional medicine, but also to sources as internet, mass media and specialized literature. The provided by us brief online review disclosed the existence of accessible scientific data about possibilities to use some medicinal plants for prevention or alleviation of symptoms of Covid-19 disease. The results of the survey supported folk medicine knowledge and showed the impact of the new informative sources on attitudes of the respondents. From this point of view, the responsibility of the institutions is the provision of information about safety and correct medicinal plants` utilization.*

Keywords: Phytotherapy in Bulgaria, COVID-19 pandemic, herbal medicines efficacy and safety, medicinal plants

Introduction

Symptoms of Coronavirus disease 19 (COVID-19) vary from asymptomatic to progressive and severe pneumonia [1, 2]. Recent evidence indicates multiple extrapulmonary disorders, including enteric, hepatic and neurologic diseases [3, 4]. The immune system plays a determined role in the initiation and progression of the

disease [5]. The medication treatment of Covid-19 is mainly directed to relieve the symptoms [4]. On the other hand, it is well known that medicinal plants and their derivatives have potential activities in the treatment of viral infections [6]. As described by Remali and Aizat [7] herbal medicines could be effective not only for prevention, but also at different stages of Covid infection – inhibition of viral attachment and penetration, RNA and protein synthesis, viral release and enhancement of host immunity. So, traditional remedies from different geographical locations represent a new approach for treatment of Covid-19 [8].

Traditional medicine is a part of lifestyle world widely. A lot of ethnobotanical surveys have been carried on in order to identify the medicinal plants used by local population during Covid-19 pandemic, mainly in Asia, South America, Africa and the Mediterranean. Ethnobotanical studies were provided also in Bulgaria and neighboring countries [9-12]. Folk medicine has deep traditions in this geographical region. As pointed by Grigore et al. [5] collected data could provide a bridge between tradition and science.

This paper is a second part of an ethnobotanical survey among people from Northeastern Bulgaria, who declared that used traditional remedies. The present work aimed to identify the medicinal plants used by these selected informants for prevention or treatment of COVID-19 disease in Bulgaria. The results of the first part of the survey revealed the impact of the modern lifestyle on the sources of information regarding traditional medicine – the growing influence of internet, mass media and specialized literature. So, a matter of interest is a comparison of listed medicinal plants with the results of other ethnobotanical surveys in Bulgaria, as well with the accessible scientific data about the possibility to use listed plants in the case of Covid-19.

Materials and Methods

The research was conducted by collecting information during semi-structured interviews with people, who declared that used traditional remedies. Ethnobotany Club bachelor student members (Faculty of Natural Sciences, University of Shumen, Bulgaria) carried out the survey. Questionnaires were prepared in order to document the most frequently used herbs for prevention and treatment of Covid-19 – described in the first part of the study [13]. Relative Frequency of Citation was calculated as $RFC = FC/N$ (FC - number of respondents mentioned the herb; N - number of all respondents) [14]. It represents the fraction of informants that used a given plant and the local significance of plant species [15].

Results and Discussion

Reported by the phytotherapy users medicinal plants

In present survey a total of 195 face to face interviews were conducted in the region of Shumen, North-eastern Bulgaria. The respondents were selected – individuals who confirmed that use medicinal plants [13]. A total of 73 medicinal plants used for prevention of Covid-19 infection were reported (Table 1). The most cited

families are Asteraceae (10 number of species), Lamiaceae (10 number of species) and Rosaceae (6 number of species). The majority of use reports are for species belonging to Lamiaceae (272 use reports), followed by Asteraceae (147 use reports). The range of Relative Frequency of Citation (RFC) was from 0.426 to 0.005 (for plants with only one-use report).

Table 1. Medicinal plants used by the respondents for prevention of COVID-19 (N=195)

Family	Scientific Name	Local Name	n	RFC
Acanthaceae	<i>Andrographis paniculata</i> (Burm.f.) Wall. ex Nees	Andrografis	1	0.005
Amaryllidaceae	<i>Allium sativum</i> L.	Chesun	12	0.062
Amaryllidaceae	<i>Allium sicutum</i> Ucria	Samardala	1	0.005
Amaryllidaceae	<i>Allium ursinum</i> L.	Levurda	4	0.021
Anacardiaceae	<i>Cotinus coggygria</i> Scop.	Tetra, smradlika	3	0.015
Araliaceae	<i>Hedera helix</i> L.	Obiknoven brushlyan	1	0.005
Araliaceae	<i>Panax ginseng</i> C.A.Mey.	Zhenshen	6	0.031
Asphodelaceae	<i>Aloe vera</i> (L.) Burm.f.	Aloe vera	1	0.005
Aspleniaceae	<i>Asplenium scolopendrium</i> L.	Volski ezik	1	0.005
Asteraceae	<i>Achillea millefolium</i> L.	Byal ravnesh	11	0.056
Asteraceae	<i>Artemisia annua</i> L.	Sladuk pelin	3	0.015
Asteraceae	<i>Calendula officinalis</i> L.	Neven	10	0.051
Asteraceae	<i>Echinacea</i> sp.	Ehinatsheya	21	0.108
Asteraceae	<i>Inula helenium</i> L.	Byal oman	1	0.005
Asteraceae	<i>Leuzea carthamoides</i> (Willd.) DC.	Levzey	1	0.005
Asteraceae	<i>Matricaria chamomilla</i> L.	Layka	83	0.426
Asteraceae	<i>Silybum marianum</i> (L.) Gaertn.	Byal trun	1	0.005
Asteraceae	<i>Taraxacum officinale</i> F. H. Wigg.	Gluharche	4	0.021
Asteraceae	<i>Tussilago farfara</i> L.	Podbel	12	0.062
Brassicaceae	<i>Capsella bursa-pastoris</i> Medik.	Ovcharska torbichka	1	0.005
Brassicaceae	<i>Lepidium meyenii</i> Walp.	Maka	1	0.005
Brassicaceae	<i>Raphanus sativus</i> var. <i>niger</i> (Mill.) J.Kern.	Cherna ryapa	1	0.005
Cannabaceae	<i>Humulus lupulus</i> L.	Hmel	1	0.005
Caprifoliaceae	<i>Valeriana officinalis</i> L.	Valeriana	1	0.005
Fabaceae	<i>Astragalus trimestris</i> L.	Astragal	2	0.010
Fabaceae	<i>Glycyrrhiza glabra</i> L.	Sladuk koren	11	0.056
Gentianaceae	<i>Centaurium erythraea</i> Rafn	Cherven kantaron	2	0.010
Geraniaceae	<i>Geranium sanguineum</i> L.	Kruven zdravetsh	1	0.005
Hypericaceae	<i>Hypericum perforatum</i> L.	Zhult kantaron	37	0.190
Lamiaceae	<i>Betonica officinalis</i> L.	Ranilist	1	0.005
Lamiaceae	<i>Lavandula latifolia</i> Medik.	Lavandula	21	0.108
Lamiaceae	<i>Melissa officinalis</i> L.	Matochina	36	0.185
Lamiaceae	<i>Mentha</i> sp. div.	Menta	69	0.354

Lamiaceae	<i>Ocimum basilicum</i> L.	Bosilek	7	0.036
Lamiaceae	<i>Origanum vulgare</i> L.	Rigan	22	0.113
Lamiaceae	<i>Rosmarinus officinalis</i> L.	Rozmarin	2	0.010
Lamiaceae	<i>Salvia officinalis</i> L.	Salviya	22	0.113
Lamiaceae	<i>Sideritis scardica</i> Griseb.	Mursalski chay	12	0.062
Lamiaceae	<i>Thymus</i> sp. div.	Mashterka	80	0.410
Laminariaceae	<i>Laminaria</i>	Laminariya	1	0.005
Lauraceae	<i>Cinnamomum verum</i> J.Presl	Kanela	8	0.041
Lauraceae	<i>Laurus nobilis</i> L.	Dafinov list	1	0.005
Lythraceae	<i>Punica granatum</i> L.	Nar	1	0.005
Malvaceae	<i>Althaea officinalis</i> L.	Lechebna ruzha	1	0.005
Malvaceae	<i>Tilia</i> sp.	Lipa	58	0.297
Moraceae	<i>Ficus carica</i> L.	Smokinya	1	0.005
Myrtaceae	<i>Eucalyptus globulus</i> Labill.	Evkalipt	3	0.015
Myrtaceae	<i>Melaleuca alternifolia</i> (Maiden & Betcher) Cheel	Chaeno durvo	1	0.005
Myrtaceae	<i>Myrtus communis</i> L.	Mirta	1	0.005
Myrtaceae	<i>Syzygium aromaticum</i> (L.) Merr. & L.M.Perry	Karamfilche	1	0.005
Orobanchaceae	<i>Euphrasia officinalis</i> L.	Ochanka	1	0.005
Phormidiaceae	<i>Spirulina platensis</i>	Spirulina	2	0.010
Pinaceae	<i>Pinus sylvestris</i> L.	Byal bor	2	0.010
Plantaginaceae	<i>Plantago</i> sp.	Zhivovlyak	5	0.026
Polygonaceae	<i>Rumex acetosa</i> L.	Kiseletsh	1	0.005
Rosaceae	<i>Crataegus monogyna</i> Jacq.	Glog	9	0.046
Rosaceae	<i>Geum urbanum</i> L.	Omayniche	2	0.010
Rosaceae	<i>Potentilla reptans</i> L.	Petoprustnik	3	0.015
Rosaceae	<i>Rosa canina</i> L.	Shipka	47	0.241
Rosaceae	<i>Rosa</i> sp.	Bulgarska roza	1	0.005
Rosaceae	<i>Rubus idaeus</i> L.	Malina	1	0.005
Rubiaceae	<i>Uncaria tomentosa</i> (Willd. ex Schult.) DC.	Koteshki nokut	3	0.015
Rutaceae	<i>Citrus limon</i> (L.) Osbeck	Limon	15	0.077
Santalaceae	<i>Viscum album</i> L.	Byal imel	2	0.010
Solanaceae	<i>Withania somnifera</i> (L.) Dunal	Ashvaganda	1	0.005
Theaceae	<i>Camellia sinensis</i> (L.) Kuntze	Zelen chay	4	0.021
Theaceae	<i>Camellia sinensis</i> (L.) Kuntze	Cheren chay	1	0.005
Urticaceae	<i>Urtica dioica</i> L.	Kopriva	7	0.036
Viburnaceae	<i>Sambucus ebulus</i> L.	Trevist buz	18	0.092
Viburnaceae	<i>Sambucus nigra</i> L.	Durvesen buz	27	0.139
Zingiberaceae	<i>Zingiber officinale</i> Roscoe	Dzhindzhifil	47	0.241
Zygophyllaceae	<i>Curcuma longa</i> L.	Kurkuma	12	0.062
Zygophyllaceae	<i>Tribulus terrestris</i> L.	Babini zubi	1	0.005

RFC (Relative Frequency of Citation) = FC/N (FC – number of respondents mentioned the herb; N- number of all respondents; n – number of use reports)

The most cited herbs used for prevention of Covid-19, declared by more than 20% of the respondents (“Top 6” herbs in this survey) are *Matricaria chamomilla* (RFC 0.426) and *Thymus* sp. div. (RFC 0.410), followed by *Mentha* sp. div. (RFC 0.354) and *Tilia* sp. div. (RFC 0.297). Species reported by around one-fourth of respondents are *Zingiber officinale* (RFC 0.241) and *Rosa canina* (RFC 0.241).

In present survey 77 medicinal plants were specified in the case of Covid-19 disease (Table 2). The most frequently cited families are Asteraceae and Lamiaceae – 13 number of species. The majority of use reports are for species belonging to Lamiaceae (251 use reports), followed by Asteraceae (130 use reports). Similarly, to data in Table 1, RFC ranged from 0.426 to 0.005.

Table 2. Medicinal plants used by the respondents for alleviation of symptoms of COVID-19 (N=195)

Family	Scientific Name	Local Name	n	RFC
Acanthaceae	<i>Andrographis paniculata</i> (Burm.f.) Wall. ex Nees	Andrografis	1	0.005
Amaryllidaceae	<i>Allium sativum</i> L.	Chesun	13	0.067
Amaryllidaceae	<i>Allium sicutum</i> Ucria	Samardala	2	0.010
Amaryllidaceae	<i>Allium ursinum</i> L.	Levurda (Div chesun)	2	0.010
Anacardiaceae	<i>Cotinus coggygria</i> Scop.	Tetra, smradlika	2	0.010
Apiaceae	<i>Anethum graveolens</i> L.	Kopur	4	0.021
Araliaceae	<i>Hedera helix</i> L.	Brushlyan	5	0.026
Araliaceae	<i>Panax ginseng</i> C.A.Mey.	Zhenshen	1	0.005
Asphodelaceae	<i>Aloe vera</i> (L.) Burm.f.	Aloe vera	1	0.005
Asteraceae	<i>Achillea millefolium</i> L.	Byal ravnesh	8	0.041
Asteraceae	<i>Artemisia absinthium</i> L.	Byal pelin	2	0.010
Asteraceae	<i>Artemisia annua</i> L.	Sladuk pelin	1	0.005
Asteraceae	<i>Calendula officinalis</i> L.	Neven	6	0.031
Asteraceae	<i>Cichorium intybus</i> L.	Sinya zhlichka	4	0.021
Asteraceae	<i>Echinacea</i> sp.	Ehinatsheya	8	0.041
Asteraceae	<i>Inula helenium</i> L.	Byal oman	1	0.005
Asteraceae	<i>Leuzea carthamoides</i> (Willd.) DC.	Levzeyia	1	0.005
Asteraceae	<i>Matricaria chamomilla</i> L.	Layka	83	0.426
Asteraceae	<i>Onopordum acanthium</i> L.	Magareshki bodil	2	0.021
Asteraceae	<i>Silybum marianum</i> (L.) Gaertn.	Byal trun	1	0.005
Asteraceae	<i>Taraxacum officinale</i> F. H. Wigg.	Gluharche	6	0.031
Asteraceae	<i>Tussilago farfara</i> L.	Podbel	7	0.036
Boraginaceae	<i>Pulmonaria officinalis</i> L.	Mecha pita	1	0.005
Brassicaceae	<i>Armoracia rusticana</i> G.Gaertn., B.Mey.	Hryan	1	0.005
Burseraceae	<i>Boswellia</i> sp.	Tamyan	1	0.005
Campanulaceae	<i>Lobelia inflata</i> L.	Loubeliya	1	0.005
Ericaceae	<i>Arctostaphylos uva-ursi</i> (L.) Spreng.	Mecho grozde	1	0.005
Ericaceae	<i>Vaccinium</i> sp.	Borovinka	1	0.005

Fabaceae	<i>Astragalus trimestris</i> L.	Astragal	2	0.021
Fabaceae	<i>Glycyrrhiza glabra</i> L.	Sladuk koren	15	0.077
Fabaceae	<i>Trigonella foenum-graecum</i> L.	Sminduh	2	0.010
Gentianaceae	<i>Centaurium erythraea</i> Rafn.	Cherven kantaron	5	0.026
Geraniaceae	<i>Geranium sanguineum</i> L.	Kruven zdravetsh	1	0.005
Hypericaceae	<i>Hypericum perforatum</i> L.	Zhult kantaron	26	0.133
Lamiaceae	<i>Agastache rugosa</i> Kuntze	Koreyska menta	1	0.005
Lamiaceae	<i>Betonica officinalis</i> L.	Ranilist	1	0.005
Lamiaceae	<i>Clinopodium vulgare</i> L.	Koteschka stupka	1	0.005
Lamiaceae	<i>Lavandula latifolia</i> Medik.	Lavandula	16	0.082
Lamiaceae	<i>Melissa officinalis</i> L.	Matochina	44	0.226
Lamiaceae	<i>Mentha</i> sp. div.	Menta	57	0.292
Lamiaceae	<i>Nepeta cataria</i> L.	Kocha bilka	1	0.005
Lamiaceae	<i>Ocimum basilicum</i> L.	Bosilek	13	0.067
Lamiaceae	<i>Origanum vulgare</i> L.	Rigan	17	0.087
Lamiaceae	<i>Rosmarinus officinalis</i> L.	Rozmarin	1	0.005
Lamiaceae	<i>Salvia officinalis</i> L.	Salviya	26	0.133
Lamiaceae	<i>Sideritis scardica</i> Griseb.	Mursalski chay	10	0.051
Lamiaceae	<i>Thymus</i> sp. div.	Mashterka	63	0.323
Laminariaceae	<i>Laminaria</i>	Laminariya	1	0.005
Lauraceae	<i>Cinnamomum verum</i> J.Presl	Kanela	1	0.005
Malvaceae	<i>Althaea officinalis</i> L.	Lechebna ruzha	5	0.026
Malvaceae	<i>Tilia</i> sp.	Lipa	63	0.323
Moraceae	<i>Ficus carica</i> L.	Smokinya	3	0.015
Myrtaceae	<i>Eucalyptus globulus</i> Labill.	Evkalipt	2	0.010
Myrtaceae	<i>Myrtus communis</i> L.	Mirta	1	0.005
Myrtaceae	<i>Syzygium aromaticum</i> (L.) Merr. &	Karamfilche	1	0.005
Papaveraceae	<i>Papaver</i> sp.	Mak	2	0.010
Phormidiaceae	<i>Spirulina platensis</i>	Spirulina	2	0.010
Pinaceae	<i>Pinus sylvestris</i> L.	Byal bor	3	0.015
Plantaginaceae	<i>Plantago</i> sp.	Zhivovlyak	8	0.041
Primulaceae	<i>Primula veris</i> L.	Iglike	1	0.005
Ranunculaceae	<i>Nigella sativa</i> L.	Cheren kimion	1	0.005
Rosaceae	<i>Crataegus monogyna</i> Jacq.	Glog	8	0.041
Rosaceae	<i>Potentilla reptans</i> L.	Petoprustnik	4	0.021
Rosaceae	<i>Rosa canina</i> L.	Shipka	36	0.185
Rosaceae	<i>Rubus idaeus</i> L.	Malina	3	0.015
Rubiaceae	<i>Uncaria tomentosa</i> (Willd. ex Schult.)	Koteschki nokut	3	0.015
Rutaceae	<i>Citrus limon</i> (L.) Osbeck	Limon	13	0.067
Santalaceae	<i>Viscum album</i> L.	Byal imel	2	0.010
Solanaceae	<i>Withania somnifera</i> (L.) Dunal	Ashvaganda	6	0.031
Theaceae	<i>Camellia sinensis</i> (L.) Kuntze	Zelen chay	6	0.031
Theaceae	<i>Camellia sinensis</i> (L.) Kuntze)	Cheren chay	2	0.010
Urticaceae	<i>Urtica dioica</i> L.	Kopriva	10	0.051

Viburnaceae	<i>Sambucus ebulus</i> L.	Trevist buz	20	0.103
Viburnaceae	<i>Sambucus nigra</i> L.	Durvoviden buz	35	0.180
Zingiberaceae	<i>Curcuma longa</i> L.	Kurkuma	12	0.062
Zingiberaceae	<i>Zingiber officinale</i> Roscoe	Dzhindzhifil	54	0.277
Zygophyllaceae	<i>Tribulus terrestris</i> L.	Babini zubi	4	0.021

RFC (Relative Frequency of Citation) = FC/N (FC – number of respondents mentioned the medicinal plant; N – number of all respondents; n – number of use reports)

„Top 6” medicinal plants used for treatment of symptoms of Covid-19 infection, are *Matricaria chamomilla* (RFC 0.426) and *Thymus* sp. div. (RFC 0.323). *Tilia* sp. div. (RFC 0.323) and *Mentha* sp. div. (RFC 0.292) was the second frequently used herbs. Species reported by around one-fourth of respondents are *Zingiber officinale* (RFC 0.277) and *Melissa officinalis* (RFC 0.226).

Comparison with other ethnobotanical surveys in Bulgaria

In our survey five of “Top 6” plants were pointed for both purposes – prevention and alleviation of symptoms of Covid disease. Interestingly, a foreign plant *Zingiber officinale* was pointed by one quarter of respondents. According to Cherneva et al. [9] the use of non-native medicinal plants is an evidence of influence of other cultures on the local traditional medicine, especially in contemporary societal changes. This statement is confirmed by a preliminary survey during the first phase of the pandemic in different regions of the world (five metropolises and twelve rural areas) which revealed that *Zingiber officinale* is among the “international plant favorites” [16]. This plant is known in Bulgarian society – it was pointed in our previous online study focused on the socially significant diseases to be useful in the case of malignant neoplasms and diabetes [17].

The other used for both purposes plants – *Matricaria chamomilla* L., *Thymus* sp. div., *Tilia* sp. div. and *Mentha* sp. div. are indigenous. Interestingly, two among “Top 6” plants was preferred for one purpose – *Rosa canina* for prevention and *Melissa officinalis* – for treatment of Covid-19.

We have tried to compare the results of present survey with some ethnobotanical surveys in Bulgaria. For example, a survey in Northern Black Sea Coast Region [18] reported that most used families are Asteraceae, Lamiaceae and Rosaceae, followed by Apiaceae and Fabaceae. In other study [19] the majority of respondents were a random sample of people and few people, known to be particularly interested in medicinal plants. The plants referred as “Granny’s cure” were *Hypericum perforatum*, *Cotinus coggigia*, *Plantago major*, *Sempervivum* sp. div., *Calendula officinalis*, *Melissa officinalis*, *Allium sativum*, *Aesculus hippocastanum*, *Matricaria chamomilla* and *Cornus mass.* In our previous study [20] with key informants – few people known to be particularly interested in traditional health practices, the most frequently pointed medicinal plants were *Hypericum perforatum*, *Sambucus nigra*, *Achillea millefolium*, *Thymus* sp. div., *Urtica dioica* and *Matricaria chamomilla*. In recent online pilot study about most commonly used medicinal plants using a snowball sampling

strategy [21] respondents pointed *Mentha* sp., *Thymus* sp., *Matricaria chamomilla*, *Hypericum perforatum*, and *Cotinus coggygia*. A matter of interest is comparison with recent study regarding Covid-19 pandemic with randomly selected respondents in Bulgaria [9]. The most cited plants were *Matricaria chamomilla*, *Tilia* sp., *Thymus vulgaris*, *Zingiber officinale*, *Mentha* sp., *Citrus x limon*, *Rosa canina* and *Sideritis scardica*.

As can be seen, all indigenous plants were reported in different ethnobotanical surveys in Bulgaria, but listed medicinal plants in our study revealed some peculiarities. This could be explained by the specificity of the survey – the respondents are selected phytotherapy users, and by the goal of the herbal utilization – during Covid-19 pandemic.

Scientific data regarding the active constituents of reported by the respondents' plants

Another goal of the present study was the comparison of the results with the accessible scientific data regarding the possibility to use listed plants in the case of Covid-19.

Matricaria chamomilla (chamomile) possess anti-inflammatory, antidepressant, anxiolytic and analgesic properties [22]. Chamomile contains numerous valuable compounds – terpenoids, phenolic acids, flavonoids and coumarins [23]. Flavonoids like apigenin and luteolin possess antiviral activity [24]. Habibzadeh and Zohalinezhad [25] proposed that *M. chamomilla* can prevent SARS-CoV-2 invasion into the human body. *In vitro* studies show a significant inhibition of the virus by crude chamomile extract [26]. Additionally, due to the anti-inflammatory effects, chamomile has beneficial effect in covid disease by reducing the level of the pro-inflammatory cytokine TNF- α [27].

Nadi et al. [28] reviewed the beneficial properties of *Thymus* sp. div. (thyme) and its valuable effects against on the complications of Covid disease. This plant is rich of bioactive compounds including phenols (thymol and carvacrol), phenolic acids (rosmarinic and caffeic acids) and flavonoids (luteolin, quercetin, and apigenin). Thyme traditionally has been used for respiratory and cardiovascular disorders. Antimicrobial, antiseptic and antiviral properties were well studied. Thyme anti-inflammatory effects could attenuate the deleterious consequences of Covid disease. Hammoudi et al. [29] summarized investigations on thyme active constituents that block virus invasion in cells and enhance the cell immunity. According to Öztürkkan et al. [30] thymol and carvacrol prevent the entrance in cells through interaction with Omicron Variant viral proteins.

Mentha sp. div. (mint) is another popular medicinal plant widely used in Bulgaria. Mint is a well-studied plant – the terpenoid compound menthol predominated in the essential oils, extracts contain valuable phenolic compounds [31]. Mint exerts different effects on respiratory and digestive systems, and possess anti-inflammatory, antiemetic, carminative, analgesic and antitussive properties [32, 33]. In the context of Covid pandemic, a survey [34] showed that menthol inhibits the coronavirus protease – a key enzyme in viral reproduction.

Tilia sp. (linden) was pointed by above 20% of respondents in our survey. The linden flower has been used in traditional medicine in different parts of the world to treat upper respiratory tract disturbances [35, 36]. Kruk et al. [36] listed the active compounds in the linden flower – volatile oil (farnesol, geraniol, eugenol etc.), flavonoids (quercetin and kaempferol glycosides), condensed tannins. *Tilia* is mentioned in some surveys in Bulgaria, but is not among the most cited herbs. According to Boycheva and Kosev [37], respondents' preferences could be due to the geographical principle – plants that are widespread in proximity to the place where they live. Really, linden is a common plant in the region of North-Eastern Bulgaria. A survey in neighbour to Bulgaria country – Turkey, revealed that linden, traditionally used by population against influenza, was among most frequently used herbs during Covid pandemic [10]. Scientific researches revealed that linden could prevent the spread of the virus by blocking its propagation in cells [38].

Zingiber officinale (ginger) have been used for various health disorders worldwide from ancient times, [39, 40]. According to a literature review [41] *Z. officinale* was the most researched plant that exerts immune modulation, antioxidant, anti-inflammatory and antiviral activities. The chemical constituents of ginger predicate the possibility to prevent and cure Covid-19 [42] – the volatile oil consists mainly of sesquiterpene hydrocarbons (zingiberene, curcumene, and farnesene) and non-volatile compounds include gingerols, shogaols, paradols, and zingerone. According to these authors, preclinical studies have confirmed multipurpose therapeutic effects of ginger, including against Covid-19.

Rosa canina (rosehip) was included in the “Top 6” herbs used for prevention of Covid infection. The rosehip fruits are rich in valuable ingredients such phenolic compounds (tannins, flavonoids, phenolic acids, etc.), carotenoids and vitamins (especially ascorbic acid) [43]. A current ethnobotanical survey in Turkey [44] reported that *Rosa canina* is one of the most important species used for respiratory system disorders. Moreover, according to the same survey, *Rosa canina*, *Matricaria chamomilla*, *Thymus* sp. div. and *Tilia* sp. div. are used in multi-herbal recipes. Viral infections like Covid-19 cause oxidative stress in infected tissues, so plant antioxidants could prevent the systematic inflammatory syndrome. Current study in Bulgaria confirmed antioxidant activity of traditional Bulgarian herbs, including *Rosa canina*, *Matricaria chamomilla* and *Thymus* sp. div. [45].

Melissa officinalis (lemon balm) was pointed in our survey for treatment of the symptoms of Covid disease. This plant contains flavonoids, terpenoids, phenolic acids, tannins and volatile compounds (geranial, neral, citronellal and geraniol) [46]. Clinical trials confirmed various activities of this plant as well as its effects on mood, cognition and memory [47]. Behzadi et al. [48] summarize antiviral effects of lemon balm against a group of viruses including SARS-CoV-2. According to this review *Melissa officinalis* is a rich source of bioactive compounds with antioxidant and anti-inflammatory activity which is an alternative to treatment of viral infections.

Safety concerns

All “Top 6” medicinal plants listed above are not considered to be toxic. However, there are data about some adverse effects. Among them, rare allergic reactions have been reported.

Ginger is known as a safe compound, scarce side effects include digestive disorders [49]. Chamomile is generally safe when used in appropriate dosages [22]. As pointed by Khazaei et al. [50] because of the lack of toxicity *Rosa canina* has been considered as a valuable complementary medicine. Similarly, according to European Medicines Agency [51], data support a safe use of *Tilia* at the recommended traditional uses.

More attention should be paid on some mentioned contraindications. The long-term use or overuse of *Melissa officinalis* is not recommended. High doses of this herb can reduce thyroid hormones, so people who have thyroid problems should not take it without medical supervision [52]. Another problem could be the stopping treatment with lemon balm suddenly after long-term use – that might cause worsening of the symptoms [53]. Essential oil of *Mentha* sp. div. interacts with liver cytochrome P450 and is contraindicated in patients with bile disorders [54]. Although thyme is generally safe, there are data that its components may potentiate the general sedative effect. Additionally, thyme constituents interact with enzymes that metabolize the drugs and could influence such drugs, especially in high amounts at the same time [55].

Conclusion

The present survey indicates that medicinal plants were used in Bulgaria during new Covid pandemic. Quantitative analysis revealed the significance of particular species for local people. The comparison with other ethnobotanical surveys in Bulgaria revealed some peculiarities. To a great extent they are due to the selection of the informants – phytotherapy users, and to the goal of the questionnaire – use of medicinal plants during Covid pandemic. These data supported folk medicine knowledge, but also revealed some safety concerns. Nowadays phytomedicine users rely not only on the traditional knowledge of their relatives and friends, but also to sources as internet, mass media and specialized literature. The provided by us brief online review revealed the existence of accessible scientific data about possibilities to use some herbs for prevention and treatment of Covid-19 disease. The results of the survey showed the impact of the new informative sources on attitudes of the respondents. From this point of view, the responsibility of the institutions is the provision of information about safety and correct medicinal plants' utilization.

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