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BIOACTIVE POWER OF LYOPHILIZED PLANT RAW MATERIALS: EVALUATION AND ASSESSMENT OF SUITABILITY FOR THE PRODUCTION OF NATURAL FOOD SUPPLEMENTS AND ANTIMICROBIAL DRUGS

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Abstract: Superior preservation and utilization of bioactive compounds (BAC) from plants, secondary or by-products of fruit and vegetable processing, can be achieved by lyophilization, witout chemicals used, so it is possible to deliver the highest level of BAC to consumers or specific groups, with environmentally friendly and effective products or dietary supplements. In this review paper, we will present the experiences of researchers worldwide and the opinion of our team on the possibilities of creating foods or dietary supplements modified by BAC from various synergistic phytocomplexes, superior bioactivity: in the lowest concentrations, proven positive effects on human health, with intact sensory and techno-functional properties of enriched food, attractive to consumers.

Keywords: lyophilisates, bioactivity, plant raw material, food supplements, antimicrobials

1.1. **Introduction**

In order to preserve and utilize BAC from bio-materials (plants, secondary or by-products of fruit and vegetable processing), certain extraction green method (GEM) and lyophilization will be applied. Obtained products (plant extracts - PE and lyophilizates - LYO) might be applied directly into the food matrix or for the production of various supplements or antimicrobial (AM)

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drugs. Vast of BAC are thermally unstable. Optimization of extraction procedure plays an important role in their preservation.

After determination of chemical composition and sterility control, LYO can be used in processing foods of plant/animal origin, heading towards the highest possible beneficial health effects, but in the lowest concentration in order to preserve sensory properties of foods. In October 2015, WHO through its International Agency for Research on Cancer (IARC) published a monograph classifying meat products as carcinogenic (Group I), and red meat as a potential carcinogen (Group IIa), based on the published results of human and animal research on the connection between meat consumption and the occurrence of colorectal and other types of cancer. Meat is a healthy food item and has quality proteins (high biological value) and high content of essential minerals and B-vitamins, but it is poor in antioxidants. The addition of phytocomplexses of LYO with antioxidant (AOX) effects to processed meat leads in healthier/functional products. Innovative approaches in preservation are needed for both conventional and organic meat products to improve sustainability and reduce potentially harmful effects of processing and meat consumption. Phytocomplexses with high contents of specific phytochemicals obtained from varied plant materials and by-products from the processing of these materials could have synergistic AM effects, prevent the growth of pathogens and bacteria that are the cause of failure in meat products, and improve their quality and safety. In fermented dry sausages, potentially toxic nitrites were replaced with PE of Serbian endemic plant (Kurćubić et al., 2014).

In Serbia and ex-Yugoslavia (due to the abundance of healthy natural resources and the development of the processing industry - intensive development of wineries and distilleries), we consider the extremely important fact, in order to promote the development of the circular economy and environmental protection: fruit processing by-products are rich in BAC, dietary fibre and unsaturated fatty acids, such as by-products of grape processing, grape pomace (GP), which contained a variety of phenolic compounds which include phenolic acids, phenolic alcohol, flavan-3-ols and flavonoids (Yu et al., 2013). Our opinion and attitude are that also important to know and apply LYO rich in BAC, used in folk and traditional medicine (weeds, medicinal plants and herbs): Wild Garlic - Ramson (*Allium ursinum* L.); Different types of buckwheat (Common buckwheat: *Fagopyrum esculentum* and Tartary buckwheat: *Fagopyrum tartaricum*); Danewort (*Sambucus ebulus*), Nettles (*Urtica dioica*). In the subsection 1.3. we will explain our opinion and support it with data from the literature.

Butkevičiūtė et al. (2021) reported that LYO of various fruits (plums, apples, peaches, pears), berries (blueberries, cranberries, strawberries), and vegetables (carrots, beets) can be applyed in the food industry for enriching and fortification of different types of meals, yogurts, ice cream, cocktails, cereals, drinks, juices. LYO fruit powder can also be added like food supplements thus increasing the content of BAC (Delpino-Rius et al., 2015; Ruszkowska et al., 2019; Bajić et al., 2020). Freeze-drying, unlike other preservation methods, effectively protects the thermolabile BAC stored in the fruit. No chemical substances are used during the freeze-drying process, which enables the delivery of the highest level of BAC to consumers through the supply of safe, environmentally friendly and effective products or dietary supplements (Butkevičiūtė et al., 2021).

The purpose of predicted goals is that food modified with BAC from a various phytocomplexes which will achieve synergy and maximize effects: strongest effects in the lowest concentrations, proven positive impacts on human health, with intact sensorial and techno-functional properties of fortified foods appealing to consumers.

1.2. ***Lyophilization*** (***freeze-drying***)

The lyophilization procedure (freeze-drying) represents the most efficient way of drying different materials by sublimation (a physical phenomenon) - a direct transition between the solid and gaseous state without passing through the liquid phase, so that the frozen product is dried under vacuum, without thawing. This procedure allows (plant) materials to be preserved without damaging the BAC in them, with minimal changes in color, smell and taste (Kittibunchakul et al., 2023).

It is speculated that lyophilization is a superior non-convective drying technique compared to other preservation techniques (Gaidhani et al., 2015). Properly preserves BAC present in plants and spices. Several studies have been carried out to prove this position, primarily that lyophilization properly protects the quality and quantity of BAC and volatile substances originating from raw plant material (Abascal et al., 2005; Özcan et al., 2005; Kittibunchakul et al., 2023). Due to the low preservation (operating) temperature and a shorter processing time, several research findings indicate lyophilization as the optimal drying method to preserve the fresh aroma of spices (Antal, 2010). Lyophilized and hot-air dryed at 50 °C were promising approachs to obtain fruits revealed higher retention of predominant BAC, especially for AOX substances

(Butkevičiūtė et al., 2021). There are also studies in which the results revealed certain negative effects of freeze drying (Chang et al., 2006).

Salamon (2021) reports that it is important to find optimal methods and procedures for their preservation for BACs that have been proven to prevent the progression of viruses and their spread from the host cell, so that the preparations created from them could be patented and applied in different forms and different ways of drug application (administration).

1.3. *Various applications of lyophilisate in the preparation of healthier and functional food*

The purpose of predicted goals is that food modified with BAC from a phytocomplexes which will achieve synergy and maximize effects: strongest effects in the lowest concentrations, proven positive impacts on human health, with intact sensorial and techno-functional properties of fortified foods appealing to consumers. The global market for dietary supplements is growing exponentially (9.1% annualy) and is expected to reach $327.4 billion by 2030 (Grand View Research, Inc., 2023). Consumers are becoming more aware and interested in health and wellness issues, so in an effort to improve their overall well-being, they are choosing nutritional supplements as a convenient and affordable means to meet their nutritional needs.

Grape pomace (GP) has the potential to serve as a functional food ingredient. Bread and pasta could be enriched with up to 5-20% dried and milled GP flour - AOX potential of bread increases (Tolve et al., 2021). The new snack, bar, or porridge, which includes GP, supported with buckwheat and other grains, could be used in a formulation of new healthier foods (Santiago-Ramos et al., 2022). The addition of GP powder significantly improved the content of free phenolics, highly bioavailable, that are scarce in grains, and thus the nutritional value of biscuits (Nakov et al., 2022) and storability in terms of higher shelf life. Chocolate and chocolate spreads can be enriched with many different BACs using minimally processed GP. The AOX activity of aqueous extracts of GP increases after intestinal digestion. These inhibited the growth of the tested pathogens, maintained shelf life, and improved the safety of ready-to-eat food products (Caponio et al., 2022).

Dried GP could be used as a supplement in chocolate spread formulations at a maximum of 10% without a bitterness effect (Acan et al., 2021).

More recently, Baj et al. (2016) developed a cream formulation with potential AOX properties, with a LYO of *Ligusticum mutellina* as a source of

BAC. The recipe for the composition of the cream provided a good profile of the release of polyphenolic compounds, which indicates that the examined PE (due to the retained high content of phenolic acids) can play a key role in the creation and production of AOX creams.

Kurćubić et al. (2023a) examined the chemical properties of freshly squeezed wild garlic extract (FSWGE) in burgers (BU). Technological and sensory properties of such fortified burgers (BU) were determined. LC-MS/MS analyses identified thirty-eight volatile BAC. Allicin prevalence (11.375 mg/mL) is the key parameter determining the amount of FSWGE added in raw BU (PS-I 1.32 mL/kg, PS-II 4.40 mL/kg, and PS-III 8.79 mL/kg). MIC and MBC values of the FSWGE and evaporated FSWGE (EWGE) were determined against the 6 microorganisms. FSWGE usage resulted in a reduced risk of *Listeria monocytogenes* (MIC = MBC = 90 mg/mL), *Escherichia coli* and *Staphylococcus aureus* (MIC = 90 mg/mL; MBC $\geqslant$ 100 mg/mL), and *Salmonella enteritidis* and *Enterococcus faecium* (MIC = 100 mg/mL; MBC > 100 mg/mL) in BU. Reformulation of BU with FSWGE did not negatively affect the technological and physico-chemical properties during both cold and freeze storage. Modified BU received mostly higher sensory scores compared to control (color, texture, taste and general acceptability were evaluated with higher grades), revealed the great potential of FSWGE usage in the creation of safe meat products with prolonged shelf life. Addition of FSWGE reduced weight loss after grilling, without alter the proximate composition.

Buckwheat, common (*Fagopyrum esculentum*) and Tartary buckwheat (*Fagopyrum tartaricum*) has attracted research interest due to high efficiency as a functional food. Various Tartary buckwheat food products, such as alcoholic beverages, vinegar, tea, noodles, porridge, biscuits, cakes, and sprouts, become commercially available in China (Zhu, 2016). Both species have excellent quantity of phenolic compounds, rutin and quercetin. Rutin, quercetin, and kaempferol could eliminate the DPPH radical effectively (Zhong et al., 2022).

Danewort (Dwarf Elder, *Sambucus ebulus*) fruit has multiple uses and its roles as an immunological stimulator, anti-inflammatory processes, antioxidative and anticarcinogenic. Danewort is rich in health-promoting phytochemical such as polyphenols and anthocyanins, with significant AOX activity. Comparing with other *Sambucus* species, danewort contain the highest levels of beneficial phenolics (Senica et al., 2019).

The lyophilized nettle PE (in the amount of 2%) enriched the chocolate in total polyphenolic content, chlorogenic acid, and flavonoid derivatives showed more intense bitterness and astringency (Belščak-Cvitanović et al., 2015).

1.4. *Antimicrobial (AM) activity of lyophilized or GEM obtained plants - preservation of public health*

In the following section, we will present findings on the AM activity of lyophilized plants.

Antimicrobial (AM) resistance is considered a significant threat to the public health systems not just in developing countries but throughout the world (Prestinaci et al., 2015; Founou et al., 2017). Due to occurrence of multidrug-resistant (MDR) bacterial strains, attention is now being shifted towards BACs isolated from plant species communing used as herbal medicine, as they may produce a new potent source of antibacterial and antifungal activities (Maiyo et al., 2010; Erfan and Marouf, 2019). The AM properties of plants related to their ability to give several secondary metabolites of relatively complex structures possessing AM activities (Souza et al., 2005; Matasyoh et al., 2009). At the moment, the demand for medicinal plants for the isolation of natural BAC has increased rapidly (Cameron et al., 2005; Rai and Carpinella, 2006).

Kurćubić et al. (2023b) were screening the AM activity of an ethanolic extract of *Kitaibelia vitifolia* against 30 MDR bacterial strains isolated from healthcare-associated infections. Minimum inhibitory concentrations (MICs) of the samples against the tested bacteria were determined using the microdilution method. MDR bacterial strains were characterized using standard biochemical tests and the commercial identification systems API 20 NE and API 20 E. The highest level of sensitivity to *K. vitifolia* PE was confirmed in 88.89% of *Klebsiella* spp. isolates, *E. coli* ATCC 25922, two strains of MRSA (1726, 1063), *Acinetobacter* spp. strain 1578, and VRE strain 30, like *Enterococcus faecalis* ATCC 29212 (MIC =< 2.44 μg/mL). The lowest sensitivity was exhibited by 75.00% of *Acinetobacter* spp. (strains 1577 and 6401), where the highest values for MICs were noted (1250 μg/mL). *K. vitifolia* PE could be a potential basis for designing and creating a new, superior, and natural AM drugs to combat infections caused by MDR strains of bacteria originating from hospital or public environments.

The AM activity assays of the methanol extract of Tartary buckwheat sprouts showed excellent activity toward most of the tested fungi and bacteria. Quercetin presents the main active component for contributing to AM activity. Tartary buckwheat exhibits anticancer, anti-hypertension, antidiabetic, cholesterol-lowering, and cognition-improving activities (Zhu, 2016). Doctors-clinicians call buckwheat a "smart bioactive supplement", it has proven positive

effects when (according to precise recommendations) it forms the basis of meals for oncology patients.

Cvetkovic et al. (2023) investigated the AM activity of lyophilized fruit juice (RPJL—Redpoll juice lyophilizate) and waste (RPWL—Redpoll waste lyophilizate) obtained from red currant (*Ribes rubrum* L.) variety Redpoll on different G+ and G– bacteria and yeast (*Candida albicans*). Several studies have found that they have various biological effects, such as antiproliferative, anticancer, AM, antiinflammatory, antidiabetic, and antioxidant (Tsuda et al., 2003; Aneta et al., 2013; Folmer et al., 2014; Dey et al., 2016). Berries rich in phenolics also exhibit AM action against pathogenic bacteria (Heinonen, 2007). Tested RPJL and RPWL showed moderate AM activity. Cvetkovic et al. (2023) revealed that red currant RPJL did not inhibit G– bacteria (*E. coli*, *P. aeruginosa*, *S. enteritidis*, *P. mirabilis*, and *E. aerogenes*), while was effective on all G+ bacteria (*B. cereus*, *S. aureus*, *E. faecalis*), except *L. monocytogenes*. Red currant RPWL inhibited activity of both G+ and G– bacteria, except *E. coli*. RPWL shown stronger AM effects compared to RPJL, especially on G– bacteria. The significance of the bacteriostatic activity of RPJL and RPWL against *B. cereus* is that they can stop this causative agent of alimentary infections accompanied by nausea and vomiting (Kotiranta et al., 2000). AM power of RPWL against *L. monocytogenes* may prevent listeriosis, which causes food contamination (Ramaswamy et al., 2007). RPJL and RPWL might be used as a potential preservative in the food industry (Cvetković et al., 2023).

Fireweed (*Chamaenerion angustifolium* L.) is a well-known medicinal plant due to its anti-inflammatory, AOX, antibacterial, analgesic, and anti-cancer properties (Kuznetsova et al., 2020; Sõukand et al., 2020). Fireweed herb contains about 1–2% of flavonoids (aglycones myricetin, kaempferol, 8-methoxykaempferol, quercetin, and their glycosides (Hevesi Tóth et al., 2009; Karasiewicz et al., 2011). Gram-positive flora (G+: *Staphylococcus aureus*, *Bacillus cereus*) as evidenced by the bactericidal effect was the most sensitive to the native L.

The neuraminidase enzyme is found on the surface of the virus and allows it to leave the host cell. Neuraminidase is blocked by natural substances (e.g. flavonoid anthocyanin - cyanidin-3 sambubiocid, in the amount of 8200 ng.ml-1, isolated from the fruits of *Sambucus nigra* L.) (Swaminathan et al., 2013; Wu et al., 2015). An antiviral preparation can be a LYO of anthocyanins, isolated from elderberry fruits. Anthocyanins are unstable under different conditions, and lyophilization stabilizes them for a long time by removing water or other components from the solution, which are thermolabile and sensitive to pH,

light or structural changes. Final anthocyanin product has the potential to be used as a food supplement, gelatin tablets, but also to be administered by injection. The berries contain a coloring agent that can be added to confectionary spreads and creams, sweets, dough, jams, and marmalades, as well as in liqueurs and wine products to give color (Burak, 2020). The listed LYO are useful for the prevention or therapy of cardiovascular and neurodegenerative diseases, eye, muscle and sarcopenia disorders, even for the possible dietary treatment of Duchenne muscular dystrophy (Wicks et al., 2018). Several scientific experiments (ZakayRones et al., 1995; Wilks et al., 2012) have shown that natural components (anthocyanin flavonoids) extracted from the fruits of the elderberry (*Sambucus nigra* L.) prevent the spread of swine flu infection by preventing its entry into the H1N1 virus from entering the lung host cell. *In vitro* experiments have shown that these flavonoids are able to prevent the entry of various parasitic strains of influenza viruses into human cells (Ishiguro et al., 2018). Anthocyanin flavonoids extracted from the fruits of elderberry have ability to increase the production of interferons (IFN-β) (Barak et al., 2001; Frokiaer et al., 2021).

According to the scientific literature, *Philadelphus coronarius* possesses AM properties. It has been previously studied by the microdilution method for G+ and G– bacteria as well. It was confirmed that the extract had a strong antibacterial effect (Nagy et al., 2000). In experiments of Peto et al. (2022), the antibacterial properties of the lyophilized flower and leaf were studied, followed by antifungal investigations. First, microdilution was carried out. In this investigation, the *P. coronarius* flower reduced the viability of *E. coli* and the leaf decreased the cell viability of *S. aureus* and *E. coli*. AM testing was continued with the *in vitro* time-kill test, whereby the effect of *P. coronarius* was studied on the growth of microbes over time. The growth of *S. aureus* and *C. albicans* was delayed by the leaf, while the flower did not elicit any changes. However, these results are not consistent with the results of the microdilution, since it is obvious that the leaf has AM potential. The time-kill test is considered to be the more accurate of the two methods, because it includes time as an important factor in the experiment. Previous chemical studies have revealed the flavonoid, triterpene, coumarin and phenolic-acid content of the herb (Klecáková et al., 2004). *P. coronarius* is said to exhibit antibacterial effects, which is confirmed by the experience of folk medicine using it in the treatment of different gynecological illnesses (Egészségtér, 2022).

Dinslage et al. (2002) reported about the greater intraocular bioavailability of fluorescein from an innovative water free, lyophilized drug delivery system

for use in ophthalmology compared to conventional fluorescein eye drops (preservative-free), and implies that such an approach may be useful for supplying the eye with BAC. It was confirmed by the existence of findings that several plant species can be used for treatment of the ophthalmological problems (Calvo and Cavero, 2016; Alghamdi et al., 2023). Salazar-Gómez et al. (2023) systematized and published literature data on medicinal plants in the prevention and treatment of eye diseases in Mexico.

Conclusion

This new concept of implementation and processing of plant material can lead to new ideas for its application to other plant species or by-products of plant processing (weeds, herbs, fruits, vegetables, cereals, etc.). It also offers the possibility of cooperation between researchers of different scientific profiles: technologists, microbiologists, veterinarians, IT experts, and chemists. Results achieved through this approach may become a ground base for future projects in different research institutions and teams concerning the transformation of plant raw materials into final products (food) with strong bioactive potentials.

A major practical benefit of the applying of LYO will be new recipes for fortified/enriched food and modeling the most appropriate GEM and a combination of animal and plant materials for a specific food. The similar projects may attract also other end-users such as interested institutions.

A significant outcome of the innovative technology will be a clean label product of animal and plant origin, with potentially positive effects on human health, which could be incorporated into industrial processes.

The results of the innovative technology transfer will also contribute to improve awareness of new ideas and concepts for further experiments/projects.

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References

Abascal K., Ganora L., Yarnell E. (2005). The effect of freeze-drying and its implications for botanical medicine: a review. Phytotherapy Research, 19(8), 655–660. https://doi.org/10.1002/ptr.1651

Acan B.G., Kilicli M., Bursa K., Toker O.S., Palabiyik I., Gulcu M., Yaman M., Gunes R., Konar N. (2021). Effect of grape pomace usage in chocolate spread formulation on textural, rheological and digestibility properties. LWT, 138, 110451, https://doi.org/10.1016/j.lwt.2020.110451

Alghamdi A.H., Ahmed A.A.E., Bashir M., Abdalgadir H., Khalid A., Gul S. (2023). The use of medicinal plants in common ophthalmic disorders: A systematic review with meta-analysis. Helyon, 9(4), E15340, https://doi.org/10.1016/j.heliyon.2023.e15340

Aneta W., Jan O., Magdalena M., Joanna W. (2013). Phenolic profile, antioxidant and antiproliferative activity of black and red currants (*Ribes* spp.) from organic and conventional cultivation. International Journal of Food Science and Technology, 48, 715–726. https://doi.org/10.1111/ijfs.12019

Antal T (2010). Inspection of the technological characteristics influencing the quality of dried fruits and vegetables. PhD diss., University of Debrecen, Debrecen, Hungary.

Baj T., Sieniawska E., Kubiak B., Partyka D. (2016). The use of a freeze-dried extract of *Ligusticum mutellina* in a cosmetic cream with potential antioxidant properties. Current Issues in Pharmacy and Medical Sciences, 29(4), 155-157. https://doi.org/10.1515/cipms-2016-0032

Bajić A., Pezo L., Stupar A., Filipčev B., Cvetković B.R., Tepić Horecki A., Mastilović J. (2020). Application of lyophilized plum pomace as a functional ingredient in a plum spread: Optimizing texture, colour and phenol antioxidants by ANN modelling. LWT, 130, 109588, https://doi.org/10.1016/j.lwt.2020.109588

Barak V., Halperin T., Kalickman I. (2001). The effect of Sambucol, a Black Elderberry-based, Natural Product, on the Production of Human Cytokines: I. inflammatory cytokines. European Cytokine Network, 12(2), 290–296.

Belščak-Cvitanović A, Komes D, Dujmović M, Karlović S, Biškić M, Brnčić M, Ježek D. (2015). Physical, bioactive and sensory quality parameters of reduced sugar chocolates formulated with natural sweeteners as sucrose alternatives. Food Chemistry, 167, 61-70. https://doi.org/10.1016/j.foodchem.2014.06.064

Butkevičiūtė A, Liaudanskas M, Ramanauskienė K, Janulis V. (2021). Biopharmaceutical Evaluation of Capsules with Lyophilized Apple Powder. Molecules, 26(4), 1095. http://dx.doi.org/10.3390/molecules26041095

Burak L.Č. (2020) Использование выжимок бузины в пищевой промышленности// Новые технологији, 16(5), 20–27. https://doi.org/10.47370/2072-0920-2020-16-5-20-27

Calvo M.I., Cavero R.Y. (2016). Medicinal plants used for ophthalmological problems in Navarra (Spain). Journal of Ethnopharmacology, 190, 212–218, https://doi.org/10.1016/j.jep.2016.06.002

Cameron S, Smith R, Kierstead K. (2005). Linking medicinal/nutraceutical products research with commercialization. Journal of Pharm Biol, 43(5), 425-433. http://dx.doi.org/10.1080/13880200590963736

Caponio G.R., Noviello M., Calabrese F.M., Gambacorta G., Giannelli G., De Angelis, M. (2022). Effects of Grape Pomace Polyphenols and In Vitro Gastrointestinal Digestion on Antimicrobial Activity: Recovery of Bioactive Compounds. Antioxidants, 11, 567. https://doi.org/10.3390/antiox11030567

Chang C.H., Lin H.Y., Chang C.Y., Liu Y.C. (2006). Comparisons on the antioxidant properties of fresh, freeze-dried and hot-air-dried tomatoes. Journal of Food Engineering, 77, 478–485. https://doi.org/10.1016/j.jfoodeng.2005.06.061

Cvetković M., Mihajilov Krstev T., Šavikin K., Zdunić G., Kitić D., Dušica Stojanović D., Ranđelović M., Milutinović M., Ilić D., Miladinović B. (2023). Antimicrobial Activity Evaluation of Lyophilized Juice and Waste Extract of Red Currant Variety Redpoll. Acta Medica Medianae, 62(2), 38-43. https://doi.org/10.5633/amm.2023.0205

Delpino-Rius A., Eras J., Vilaró F., Cubero M.Á., Balcells M., Canela-Garayoa R. (2015). Characterisation of phenolic compounds in processed fibres from the juice industry. Food Chemistry, 172, 575–584. https://doi.org/10.1016/j.foodchem.2014.09.071

Dey T.B., Chakraborty S., Jain K.K., Sharma A., Kuhad R.C. (2016). Antioxidant phenolics and their microbial production by submerged and solidstate fermentation process: A review. Trends in Food Science and Technology, 53, 60–74. https://doi.org/10.1016/j.tifs.2016.04.007

Dinslage S., Diestelhorst M., Weichselbaum A., Süverkrüp R. (2002). Lyophilisates for drug delivery in ophthalmology: pharmacokinetics of fluorescein in the human anterior segment. British Journal of Ophthalmology, 86, 1114-1117.

Egészségtér H.A. (2022). Jezsámennek (*Phyladelphus coronarius*) Nyár Elején Nyílnak Krémfehér Virágai, Intenzív Illatot Árasztva. Ne tévesszük Össze az Általában Kisebb Termet ˝u és Csak Igen Ritkán Látható Valódi Jázminnal. Available: https://egeszsegter.hu/cikk/1453/a-jezsamen-nem-jazmin#gsc.tab=0 (accessed on 2 February 2022).

Erfan A.M., Marouf S. (2019). Cinnamon oil downregulates virulence genes of poultry respiratory bacterial agents and revealed significant bacterial

inhibition: An *in vitro* perspective. Veterinary World, 12(11), 1707-1715. https://doi.org/10.14202/vetworld.2019.1707-1715

Folmer F., Basavaraju U., Jaspars M., Hold G., El-Omar E., Dicato M., Diederich, M. (2014). Anticancer effects of bioactive berry compounds. Phytochemistry reviews, 13(1), 295-322. https://doi.org/10.1007/s11101-013-9319-z

Founou R.C., Founou L.L., Essack S.Y. (2017). Clinical and economic impact ofantibiotic resistance in developing countries: a systematic review and metaanalysis. PloS One, 12, e0189621. https://doi.org/10.1371/journal.pone.0189621

Frokiaer H., Henningsen L., Metzdorff S.B., Weiss G., Roller M., Flanagan J. (2012). Astragalus Root and Elderberry Fruit Extracts Enhance the IFN-beta Stimulatory Effects of *Lactobacillus acidophilus* in Murine-derived Dendritic Cells. PLoS One, 7(10), 478-482. https://doi.org/10.1371/journal.pone.0047878

Gaidhani A.K., Harwalkar M., Bhambere D., Nirgude S.P. (2015). Lyophilization / freeze drying – a review. World Journal of Pharmaceutical Research, 4(8), 516–543.

Grand View Research Market Analysis, Available on: https://www.grandviewresearch.com/press-release/global-dietary-supplements-market (last access on 15 February 2024).

Heinonen M. (2007): Antioxidant activity and antimicrobial effect of berry phenolics – a Finnish perspective. Molecular Nutrition & Food Research, 51(6), 684–691. https://doi.org/10.1002/mnfr.200700006

Hevesi Tóth, B., Blazics, B., Kéry, A. (2009). Polyphenol composition and antioxidant capacity of *Epilobium* species. Journal of Pharmaceutical and Biomedical Analysis, 49(1), 26–31. https://doi.org/10.1016/j.jpba.2008.09.047 https://doi.org/10.38093/cupmap.950755

Ishiguro N., Koseki N., Kaiho M. et al. (2018). Clinical Effectiveness of Four Neuraminidase Inhibitors (Oseltamivir, Zanamivir, Laninamivir, and Peramivir) for Children with Influenza A and B in the 2014-2015 to 2016-2017 Influenza Seasons in Japan. Journal of Infection Chemotheraphy, 24(6), 449-457. https://doi.org/10.1016/j.jiac.2018.01.013

Karasiewicz M., Bartkowiak-Wieczorek J., Ożarowski M., Mrozikiewicz P., Czerny B., Kujawski R., Bogacz A., Cichocka J. (2011). Current knowledge on phytochemical profile of *Epilobium* sp. raw materials and extracts. Potential benefits in nutrition and phytotherapy of age-related diseases. Herba Polonica, 57, 33–44.

Kittibunchakul S., Temviriyanukul P., Chaikham P., Kemsawasd V. (2023). Effects of freeze drying and convective hot-air drying on predominant bioactive compounds, antioxidant potential and safe consumption of maoberry fruits. LWT, 184, 114992, https://doi.org/10.1016/j.lwt.2023.114992

Klecáková J., Chobot V., Jahodár L., Laakso I., Víchová P. (2004). Antiradical activity of petals of *Philadelphus coronarius* L. Central European Journal of Public Health, 12, S39–S40.

Kotiranta A, Lounatmaa K, Haapasalo M. (2000). Epidemiology and pathogenesis of *Bacillus cereus* infections. Microbes and Infection, 2(2), 189-98. https://doi.org/10.1016/S1286-4579(00)00269-0

Kurćubić V.S., Mašković P.Z., Vujić J.M., Vranić D.V., Vesković-Moračanin S.M., Okanović Đ.G., Lilić S.V. (2014). Antioxidant and antimicrobial activity of *Kitaibelia vitifolia* extract as alternative to the added nitrite in fermented dry sausage. Meat Science, 97/4: 459-467. https://doi.org/10.1016/j.meatsci.2014.03.012

Kurćubić V.S., Stajić S.B., Miletić N.M., Petković M.M., Dmitrić M.P., Đurović V.M., Heinz V., Tomasevic I.B. (2023a). Techno-Functional Properties of Burgers Fortified by Wild Garlic Extract: A Reconsideration. Foods, 12, 11, 2100. https://doi.org/10.3390/foods12112100

Kurćubić VS, Raketić SV., Mašković J.M., Mašković P.Z., Kurćubić L.V., Heinz V., Tomasevic I.B. (2023b). Evaluation of Antimicrobial Activity of *Kitaibelia vitifolia* Extract against Proven Antibiotic-Susceptible and Multidrug-Resistant (MDR) Strains of Bacteria of Clinical Origin. Plants, 12, 3236. https://doi.org/10.3390/plants12183236

Kuznetsova N., Kalle R., Belichenko O., Kolosova V., Prakofjewa J., Stryamets N., Mattalia G., Šarka P., Simanova A., Prūse B., Mezaka I., Sõukand R. (2020). Gaining momentum: Popularization of *Epilobium angustifolium* as food and recreational tea on the Eastern edge of Europe. Appetite, 150, N/A-N/A. https://doi.org/10.1016/j.appet.2020.104 638

Maiyo Z., Ngure R., Matasyoh J., Chepkorir R. (2010). Phytochemical constituents and antimicrobial activity of leaf extracts of three *Amaranthus* plant species. African Journal of Biotechnology, 9(21), 3178-3182.

Matasyoh J., Maiyo Z., Ngure R., Chepkori R. (2009). Chemical composition and antimicrobial activity of the essential oil of *Coriandrum sativum*. Food Chemistry, 113(2), 526-529. https://doi.org/10.1016/j.foodchem.2008.07.097

Nakov G., Brandolini A., Estivi L., Bertuglia K., Ivanova N., Jukić M., Komlenić D.K., Lukinac J., Hidalgo A. (2022). Effect of Tomato Pomace Addition on

Chemical, Technological, Nutritional, and Sensorial Properties of Cream Crackers. Antioxidants, 11, 2087. https://doi.org/10.3390/antiox11112087

Nagy M., Grancai D., Jantova S., Ruzekova L. (2000). Antibacterial Activity of Plant Extracts from the Families Fabaceae, Oleaceae, Philadelphaceae, Rosaceae and Staphyleaceae. Phytherapy Research, 14, 601–603. https://doi.org/10.1002/1099-1573(200012)14:8<601::aid-ptr771>3.0.co;2-b

Özcan M., Arslan D., Ünver A. (2005). Effect of drying methods on the mineral content of basil (*Ocimum basilicum* L.). Journal of Food Engineering, 69(3), 375–379. https://doi.org/10.1016/j.jfoodeng.2004.08.030

Peto Á., Kósa D., Haimhoffer Á., Nemes D., Fehér P., Ujhelyi Z., Vecsernyés M., Váradi J., Fenyvesi F., Frum A., et al. (2022). Topical Dosage Formulation of Lyophilized *Philadelphus coronarius* L. Leaf and Flower: Antimicrobial, Antioxidant and Anti-Inflammatory Assessment of the Plant. Molecules, 27, 2652. https://doi.org/10.3390/molecules27092652

Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon (2015). Pathogens and Global Health, 109(7),309. https://doi.org/10.3390/10.1179/2047773215Y0000000030

Rai M., Carpinella M.C. (2006). Naturally occurring bioactive compounds. Elsevier, 3. http://dx.doi.org/10.1016/S1572-557X(06)03021-2

Ramaswamy V., Cresence V.M., Rejitha J.S., Lekshmi M.U., Dharsana K.S., Prasad S.P., et al. (2007). Listeria-review of epidemiology and pathogenesis. Journal of Microbiology, Immunology and Infection, 40(1), 4-13.

Ruszkowska M., Kropisz P., Wi´sniewska Z. (2019). Evaluation of the stability of the storage of selected fruit and vegetables freeze-dried powder based on the characteristics of the sorption properties. SJ GMU, 19, 55–63. https://doi.org/10.26408/109.05

Salamon I. (2021). Can Medicinal Plants Help in the Treatment of the New Coronavirus? Some R&D Aspects in Slovak Republic. Current Perspectives on Medicinal and Aromatic Plants, 4(1), 58-65. https://doi.org/10.38093/cupmap.950755

Salazar-Gómez A., Velo-Silvestre A.A., Alonso-Castro A.J., Hernández-Zimbrón L.F. (2023). Medicinal Plants Used for Eye Conditions in Mexico—A Review. Pharmaceuticals 2023, 16, 1432. https://doi.org/10.3390/ph16101432

Santiago-Ramos R., Silva C.L.M., Ramos I.N. (2022). Modelling and Optimization of the Processing of a Healthy Snack Bar Made of Grape and Tomato Pomaces. Foods, 11, 2676. https://doi.org/10.3390/foods11172676

Senica M., Stampar F., Mikulic-Petkovsek M. (2019). Harmful (cyanogenic Glycoside) and Beneficial (phenolic) Compounds in Different Sambucus

Species. Journal of Berry Research, 9(3), 395-409. https://doi.org/10.3233/JBR-180369

Sõukand R., Mattalia G., Kolosova V., Stryamets N., Prakofjewa J., Belichenko O., Kuznetsova N., Minuzzi S., Keedus L., Prūse B., Simanova A., Ippolitova A., Kalle R. (2020). Inventing a herbal tradition: The complex roots of the current popularity of *Epilobium angustifolium* in Eastern Europe. Journal of ethnopharmacology, 247, 112254. https://doi.org/10.1016/j.jep.2019.112254

Souza E.L.D., Lima E.D.O., Freire K.L., Sousa C.D. (2005). Inhibitory action of some essential oils and phytochemicals on the growth of various moulds isolated from foods. Brazilian Archives of Biology and Technology, 48(2), 245-250. https://doi.org/10.1590/S1516-89132005000200011

Swaminathan K., Dyason J., Maggioni A., von Itzstein M., Kevin M. Downard K.M. (2013). Binding of a Natural Anthocyanin Inhibitor to Influenza Neuraminidase by Mass Spectrometry. Analytical and Bioanalytical Chemistry, (405), 6563–6572. https://doi.org/10.1007/s00216-013-7068-x

Tolve R., Simonato B., Rainero G., Bianchi F., Rizzi C., Cervini M., Giuberti G. (2021). Wheat Bread Fortification by Grape Pomace Powder: Nutritional, Technological, Antioxidant, and Sensory Properties. Foods, 10, 75. https://doi.org/10.3390/foods10010075

Tsuda T., Horio F., Uchida K., Aoki H., Osawa T. (2003). Dietary Cyanidin 3-O-D-Glucoside-Rich Purple Corn Color Prevents Obesity and Ameliorates Hyperglycemia in Mice. Journal of Nutrition, 133, 2125–30. https://doi.org/10.1093/jn/133.7.2125

Wicks S.M., Salamon I., Calderon A.I., de Blanco E.J.C., Mahady G.B. (2018). Sarcopenia, Diabetes, and Nutritional Intervention. In Nutritional and Therapeutic Interventions for Diabetes and Metabolic Syndrome; Elsevier Science Publishing Co. Inc.: San Diego, United States, 279–292. ISBN 978-0-12-812019-4.

Wilks S., de Graaf M., Smith D.J., Burke D.F. (2012). A Review of Influenza Hemagglutinin Receptor Binding as it Relates to Pandemic Properties. Vaccine, 30(29), 4369-4376. https://doi.org/10.1016/j.vaccine.2012.02.076

Wu H., Johnson M.C., Lu C.H., Fritsche A.L., Thomas Z.C., Greenlief C.M. (2015). Determination of Anthocyanins and Total Polyphenols in a Variety of Elderberry Juices by UPLC-MS/MS and other Methods. Acta Horticulturae, 1061, 43-51. https://doi.org/10.17660/ActaHortic.2015.1061.3

Yu J., Kim Y.H., Choi S.J. (2020). Usage-and daily intake-based cytotoxicity study of frequently used natural food additives in South Korea. Korean

Journal of Food Science and Technology, 52(5), 546-554. https://doi.org/10.9721/KJFST.2020.52.5.546

Zakay-Rones Z., Varsano N., Zlotnik M., Manor O., Regev L., Schlesinger M., Mumcuoglu M. 1995. Inhibition of Several Strains of Influenza Virus in vitro and Reduction of Symptoms by an Elderberry Extract (*Sambucus nigra* L.) during an Outbreak of Influenza B Panama. Journal of Alternative Complementary Medicine, 1(4), 361-369. https://doi.org/10.1089/acm.1995.1.361

Zhong L., Lin Y., Wang C., Niu, B., Xu Y., Zhao G., Zhao J. (2022). Chemical Profile, Antimicrobial and Antioxidant Activity Assessment of the Crude Extract and Its Main Flavonoids from Tartary Buckwheat Sprouts. Molecules 2022, 27, 374. https://doi.org/10.3390/molecules27020374

Zhu F. Chemical composition and health effects of Tartary buckwheat. Food Chemistry, 203, 231-245. https://doi.org/10.1016/j.foodchem.2016.02.050