IMPORTANT ADVANTAGES OF PHENOLIC COMPONENTS OF PLANT ORIGIN FOR PHARMACOCORRECTION OF PATHOLOGICAL STATES

Kuznetsova V.Yu., Kravchenko V.M., Seniuk I.V.
National University of Pharmacy, Kharkiv, Ukraine
kuznetsova.victoria@ukr.net

Abstract. Phenolic compounds and flavonoids are potential substitutes for bioactive agents in pharmaceutical and medicinal sections to promote human health and prevent and cure different diseases. The most common flavonoids found in nature are anthocyanins, flavones, flavanones, flavonols, flavanonols, isoflavones, and other sub-classes. The impacts of plant flavonoids and other phenolics on human health promoting and diseases curing and preventing are antioxidant effects, antibacterial impacts, cardioprotective effects, anticancer impacts, immune system promoting, anti-inflammatory effects, and skin protective effects from UV radiation. Phenolic acids contain a carboxylic acid group in addition to the basic phenolic structure and are mainly divided into hydroxybenzoic and hydroxycinnamic acids. Hydroxybenzoic acids are based on a C_6-C_1 skeleton and are often found bound to small organic acids, glycosyl moieties, or cell structural components. Common hydroxybenzoic acids include gallic, syringic, protocatechuic, p-hydroxybenzoic, vanillic, gentistic, and salicylic acids. Hydroxycinnamic acids are based on a C_6-C_3 skeleton and are also often bound to other molecules such as quinic acid and glucose. The main hydroxycinnamic acids are caffeic, p-coumaric, ferulic, and sinapic acids.

Keywords: phenolics, curcumin, protocatechuic, quinones, stilbenes, curcuminoids.

Introduction. Medicinal plants are very important worldwide, both when used alone and as a supplement to traditional medication [1-5]. For many years, humans have employed plants as a source of food, flavoring, and medicines [6-10]. Various parts of medicinal plants such as seeds, leaves, flowers, fruits, stems, and roots are rich sources of bioactive compounds [11-13]. Bioactive compounds should be considered as important dietary supplements [14-19]. Polyphenols are a group of secondary metabolites involved in the hydrogen peroxide scavenging in plant cells [20]. Phenolic compounds are second only to carbohydrates in abundance in higher plants, and they display a great variety of structures, varying from derivatives of simple phenols to complex polymeric materials such as lignin [21-26]. Phenolic compounds are known for their notable potential activity against various human viruses, and phenolic compounds also have immunomodulatory and anti-inflammatory activity [27]. The most abundant phenolic compounds are phenolic monoterpenes (carvacrol and thymol) and diterpenes (carnosol, carnosic acid, and methyl carnosate), hydroxybenzoic acids (p-hydroxybenzoic, protocatechuic, gallic, vanillic, catechol, and ellagic), phenylpropanoic acids (p-coumaric, caffeic, rosmarinic, chlorogenic, ferulic, cryptochlorogenic, and neochlorogenic), phenylpropenes (eugenol), coumarins (herniarin and coumarin), flavanoes (naringenin, eriocitrin, naringin, and hesperidin), flavones (apigenin, apigetrin, genkwanin, luteolin, luteolin 7-glucuronide, cynaroside, scolymoside, salvigenin, and cirsimaritin), and flavanols (catechin, astragalin, kaempferol, methyl ethers, quercetin, hyperoside, isoquercetin, miquelianin, and rutin) [28, 29].

Plant phenolics are considered promising antibiofilm and antifungal agents [30, 31]. Diaz also reported that the levels of phenolic and flavonoid compounds were correlated with the anti-inflammatory and antioxidant activities of medicinal plants [32]. Tukun reported that phenolic content is significantly connected to antioxidant activity, and halophytes have high content of nutrients and phenolic metabolites [33]. Some of the most important phenolic compounds recognized from medicinal plants are syringic acid and gallic acid from *Moringa oleifera* [34]; gallic acid, vanillic acid, 4-hydroxybenzoic acid, and syringic acid from *Peganum harmala* [35]; rosmarinic acid from *Rosmarinus officinalis L.* and Mentha canadensis L. [36]; vanillin from *Thymus vulgaris* [37]; caffeic acid and p-coumaric acid from *Ocimum basilicum L.*, *Thymus vulgaris L.*, *Salvia officinalis L.*, and *Origanum vulgare L.* [36]; piceatannol glucoside, resveratroloside, and piceid from Polygonum cuspidatum [38]; trans-rhapontin, cis-rhapontin, and trans-desoxyrhaponticin from *Rheum tanguticum* [39]; herniarin from *Matricaria chamomilla* [40]; kayeassamin I, mammeasin E, and mammeasin E from *Mammea siamensis* [41]; scopoletin, fraxetin, aesculetin, fraxin, and aesculin from *Fraxinus rhynchophylla* [42]; phyllanthin, niranthin, hypophyllanthin, nirtetralin, virgastusin, heliobuphthalmin lactone, and bursehernin from *Phyllanthus amarus* [43]; schisanchinin A, schisanchinin B, schisanchinin C, and schisanchinin D from *Schisandra chinensis* [44]; 7-methyljuglone from *Drosera rotundifolia* [45], rhein, physcion, chrysophanol, emodin, and aloe-emodin from *Rheum palmatum* and *Rheum hotaoense* [46]; curcumin, demethoxycurcumin, and bis-demethoxycurcumin from *Curcuma longa* [47]; luteolin, apigenin, orientin, apigenin-O-glucuronide, and luteolin-O-glycoside from *Origanum majorana* [48]; glycitein, genistein, formononetin, daidzein, prunetin, biochanin A and daidzin, and genistin from *Medicago spp.* [49]; kaempferol 3-O-glucoside and isorhamnetin 3-O-galactoside from *Tephrosia vogelii* [50]; rutin, kaempferol 3-O-rhamnoside, and quercetin 3-O-glucoside from M. oleifera [34]; gallocatechin and catechin from *Mentha pulegium*

[48]; taxifolin, taxifolin methyl ether, and dihydrokaempferide from Origanum majorana [48]; hesperidin, naringenin-O-rhamnoglucoside, and isosakuranetin-O-rutinoside from *Mentha pulegium* [48]; and punicalagin, pedunculagin I, granatin A, ellagic acid, ellagic acid pentoside, ellagic acid glucoside, and punigluconin from *Punica granatum* [51]. Phenolic phytochemicals include flavonoids, flavonols, flavanols, flavanones, flavones, phenolic acids, chalcones, isoflavones, tannins, coumarins, lignans, quinones, xanthones, curcuminoids, stilbenes, cucurmin, phenylethanoids, and several other plant compounds, owing to the hydroxyl group bonded directly to an aromatic hydrocarbon group [52].

The aim of the study. To provide an overview of phenolic compounds and flavonoids as potential and important sources of pharmaceutical and medical application according to recently published studies, as well as some interesting directions for future research.

Materials and Methods. The keyword searches for flavonoids, phenolics, isoflavones, tannins, coumarins, lignans, quinones, xanthones, curcuminoids, stilbenes, cucurmin, phenylethanoids, and secoiridoids medicinal plant were performed by using Web of Science, Scopus, Google scholar, and PubMed.

Results and Discussion. Flavonoids and phenolics are commonly known as the largest phytochemical molecules with antioxidant characteristics [53]. Traditional Chinese medicinal plants that contain phenolic acids and flavonoids have shown high antioxidant activity. *Nepeta italica subsp. Cadmea* and *Teucrium sandrasicum* are rich in phenolic, tannin, and flavonoids content, which showed antioxidant and cytotoxic properties. *Bauhinia variegata L.* contained flavonoid compounds and revealed antioxidant properties against oxidative damage by radical neutralization, iron binding, and decreasing power abilities [54]. The rhizome extracts of *Polygonatum verticillatum* exhibited antioxidant activity, which is connected to the level of phenolic composition [55]. Singh and Yadav [56] have reported that, among medicinal plants, oregano, clove, thyme, and rosemary contain the highest amounts of phenolic compounds. Flavan-3-ol oligomers and monomers were potent antioxidant compounds abundantly identified in *Camellia fangchengensis* [57].

Bellis perennis L. was rich in phenolic compounds, and it can be used for wounds, cancer, inflammation, and eye diseases [58]. A total of 27 kinds of phenolic compounds were identified by HPLC-ESI-QTOF-MS/MS, and okra (*Abelmoschus esculentus*) polyphenols exhibited great antioxidant activity in vitro [59]. The Althaea officinalis extracts showed stronger antioxidant activity and excellent α-glucosidase, 5-lipoxygenase, and nitric oxide inhibitory properties [60]. Dendrobium densiflorum was rich in flavonoid, alkaloid, and antioxidant activity, *Acampe papillosa* was rich in total phenol, total tannin, and total saponin content, and *Coelogyne nitida* exhibited higher antioxidant activity because of its higher quercetin content [61]. Cirak et al. [62] showed that Achillea arabica Kotschy is an important source of natural antioxidants. The antioxidant property and bioactive constituents from the fruits of *Aesculus indica* Hook, which were quercetin and mandelic acid, were the major bioactive molecules with notable antioxidant properties to decrease oxidative stress caused by reactive oxygen species (ROS) [63]. The phytochemical compounds and biological activity of Pinus cembra L. contain higher concentration of total phenolics and flavonoids than that of needle extract, and its bark extract showed better ability as a free radical scavenger [64]. Higher antioxidant activity in normal-tannin lentil seed coats than low-tannin ones was reported; kaempferol tetraglycoside was dominant in low-tannin seed coats, and procyanidins, kaempferol tetraglycoise, and catechin-3-O-glucoside in normal-tannin has been found [65]. Zhang et al. [66] also reported that antioxidant activity and prebiotic impacts were positively correlated for oat phenolic compounds. 3,4-dihydroxybenzoic, rutin, vanillic acid, and quercetin were detected from aqueous extracts of azendjar and taamriouth figs, and a dark peel variety consisted of more phenolics and exerted a higher antioxidant capacity [67]. Although gallic acid was the most important compound in carob (*Ceratonia siliqua L.*) pulp extract, geographic origin strongly influenced the contents of bioactive compounds and antioxidant activities [68].

Asplenium nidus L. contained gliricidin 7-O-hexoside and quercetin-7-O-rutinoside that can fight against three pathogens, i.e., *Proteus vulgaris Hauser*, *Proteus mirabilis Hauser* and *Pseudomonas aeruginosa* [69]. Flavones, which were extracted from the root of *Scutellaria baicalensis*, were proven as potential antibacterial agents against Propionibacterium acnes-induced skin inflammation both in in vitro and in vivo models [70]. Kaempferol that was isolated from the *Impatiens balsamina L*. exhibited potential activity to inhibit the growth of *P. acnes* [71]. Phenolics from kernel extract *Mangifera indica L*. also showed anti-acne properties to inhibit the growth of *P. acnes* [72]. Medicinal plants such as *Albizia procera*, *Atalantia monophylla*, *Asclepias curassavica*, *Azima tetracantha*, *Cassia fistula*, *Costus speciosus*, *Cinnamomum verum*, *Nymphaea stellata*, *Osbeckia chinensis*, *Punica granatum*, *Piper argyrophyllum*, *Tinospora cordifolia*, and *Toddalia asiatica* have shown antifungal activity [73]. The strictinin isolated from the leaves of *Camellia sinensis* was a good substitute for antibacterial activities [74]. Phenolic compounds, especially flavonoids, have long been reported as chemopreventive factors in cancer therapy [75-77]. The extract of *Curcuma longa L*. rhizome has been suggested as a promising source of natural active compounds to fight against malignant melanoma due to its potential anticancer property in the B164A5 murine melanoma cell line [78]. Glircidia 7-O-hexoside and Quercetin 7-O-rutinoside, which were flavonoids isolated from the medicine fern (*Asplenium nidus*), were also proposed as potential chemopreventives against human hepatoma HepG2 and human carcinoma HeLa cells [79]. Quercetin can induce miR-200b-3p to regulate the mode of self-renewing divisions of the tested pancreatic cancer [80], and a soy isoflavone genistein inhibited the activation of the nuclear factor kappa B (NF-KB) signaling pathway that maintains the balance of cell survival and apoptosis; this soy isoflavone could also take its action to fight against cell growth, apoptosis, and metastasis, including epigenetic modifications in prostate cancer [81]. Curcumin exhibits anticancer impacts towards skin cancers, as this phenolic can influence the cell cycle by acting as a pro-apoptotic agent [82]. Curcumin acts as a non-selective cyclic nucleotide phosphodiesterase (PDE) inhibitor to inhibit melanoma cell proliferation, which is associated with epigenetic integrator UHRF1 [83]. Curcumin inhibited proliferation of the selected cell lines in prostate cancer and induced apoptosis of the cancer cells with a dose-dependent response [84].

The cardioprotective impacts from various kinds of phenolics and flavonoids occurring in medicinal plants have been investigated in many studies [85, 86]. Many phenolic and flavonoid compounds have been studied and had reported their cardioprotective properties via different mechanisms including inhibition of ROS generation, apoptosis, mitochondrial dysfunction, NF-KB, p53, and DNA damage both in vitro and in vivo, and clinical studies [87]. Kaempferol, luteolin, rutin, and resveratrol showed their efficacy against doxorubicin-induced cardiotoxicity [88, 89]. Isorhamnetin provided a cardioprotective effect against cardiotoxicity of doxorubicin and potentiated the anticancer efficacy of this drug [90]. The total phenolic and flavonoid contents of the aqueous fraction from *Marrubium vulgare L.* have effects on ischemia-reperfusion injury of rat hearts, which proved that the aqueous fraction from M. vulgare had cardioprotective potential [91]. Aspalathin and phenylpyruvic acid-2-O-β-D-glucoside, two of the major compounds from *Aspalathus linearis* R. Dahlgren, were demonstrated as potential protective compounds to protect myocardial infarction caused by chronic hyperglycemia [92]. Puerarin is a potential isoflavone that was reported as an interesting candidate for cardioprotection by protecting myocardium from ischemia and reperfusion damage by means of opening the Ca^{2+}-activated K^{+} channel and activating the protein kinase C [93]. Quercetin, hesperidin, apigenin, and luteolin were reported as flavonoids containing potential anti-inflammatory impacts [94]. The flavonoids and phenolic compounds of Phyllanthus acidus leaves could be correlated with the analgesic, antioxidant, and anti-inflammatory activities [95]. Hydroxytyrosol and quercetin 7-O-α-L-rhamnopyranoside exhibited anti-inflammatory activity through lowering the levels of TNF-α, and hydroxytyrosol and caffeic acid showed significant anti-inflammatory activity at 100 μm by reducing the release of NO in LPS-stimulated macrophages comparable to positive control indomethacin [96].

The most important chemical compounds extracted from ethanol of *Cardiospermum halicacabum* were chrysoeriol, kaempferol, apigenin, luteolin, methyl 3,4-dihydroxybenzoate, 4-hydroxybenzoic acid, quercetin, hydroquinone, protocatechuic acid, gallic acid, and indole 3-carboxylic acid, which have shown high anti-inflammatory and antioxidant activities [97]. The most important phenolic components with antiviral effects against COVID-19 were curcumin, Theaflavin-3,3′-digallate, EGCG, Paryriflavonol A, Resveratrol, Quercetin, Luteolin, Scutellarein, Myricetin, and Forsythoside A [98]. In traditional Persian medicinal science, medicinal plants such as *Glycyrrhiza glabra L.*, *Rheum palmatum L.*, *Punica granatum L*., and *Nigella sativa L.* have been introduced for treating respiratory disorders and infections because of their phenolic compounds [99]. The anti-inflammatory activity of polyphenolic compounds in Gaillardia grandiflora Hort. Ex Van Houte and *Gaillardia pulchella* Foug from Egypt were reported [100]. Anti-inflammatory properties of two medicinal plant species, Bidens engleri O.E. Schulz from *Asteraceae* family as well as *Boerhavia erecta L.* from *Nyctaginaceae* family, were identified and reported in various fractions [101]. *Plantago subulata* has shown anti-inflammatory properties on macrophages and a protective effect against H_2O_2 injury [102]. Phenolic content changes with aromatic and medicinal plant species and extraction method used [103]. Astilbin, a dihydroflavonol, from Smilax glabra Roxb significantly inhibited nitric oxide production, tumor necrosis factor-α (TNF-α), and mRNA expression of inducible nitric oxide synthase in the tested cells [104]. Apigenin is a main flavone with skin protective impact against UV light; this flavone can be identified in various edible medicinal plants or plants-derived beverages, e.g., beer, red wine, and chamomile tea [105, 106]. Quercetin is a flavonol that can be discovered in apple peel, onion skin, and *Hypericum perforatum L.* leaves [107]. Silymarin, a standardized extract of flavonolignans from the milk thistle fruits, consists of silybin, a principle active component [108]. Genistein is a soybean isoflavone that was also reported as photoprotective molecule against photocarcinogenesis by inhibiting UV-induced DNA damage in human skin-equivalent in vitro model [109]. Equol is considered as an isoflavonoid metabolite from isoflavone daidzein or genistein produced by gut microflora. Genistein is an obvious example of an interesting choice of a flavonoid phytoestrogen for improving endothelial roles in postmenopausal women with MetS. A chrysin derivative was the most abundant flavone in *Cytisus multiflorus*, quercetin-3-O-rutinoside was the main flavonol in *Sambucus nigra*, and kaempferol-3-O-rutinoside was the main flavonol in *Malva sylvestris* [110].

Conclusions. Phenolic compounds are one of the most important types of compounds with an important role in growth and reproduction, providing protection against pathogens and predators, and they could be the main determinant of antioxidant potential of foods. Phenolics are a heterogeneous collection of compounds generated as secondary metabolites in plants. Phenolic compounds are aromatic or aliphatic compounds with at least one aromatic ring to which one or more OH groups are connected. They are subdivided into different groups depending on the number of phenolic rings that they possess and the structural elements joined to them. They are naturally occurring compounds present in several foods such as cereals, fruits, vegetables, and beverages. Polyphenols can also be found in dried legumes and chocolate. The distribution of phenolic compounds in plant tissues and cells change considerably according to the type of chemical compound. They also contribute towards the color and sensory characteristics of fruits and vegetables. Different classes of phenolic compounds in plants are simple phenolics, benzoquinones, hydroxybenzoic acids, acetophenones, phenylacetic acids, hydroxycinnamic acids, phenylpropanoids, naphthoquinones, xanthones, stilbenes, anthraquinones, flavonoids, isoflavonoids, lignans, neolignans, biflavonoids, lignins, and condensed tannins. Hydroxybenzoic acids are gallic acid and Protocatechuic acid. Hydroxycinnamic acids are p-coumaric acid, caffeic acid, ferulic acid, sinapic acid, and other components such as coumarins (umbelliferone, esculetin, scopoletin, resveratrol, piceatannol, pterostilbene), curcuminoids (curcumin, demethoxycurcumin, bisdemethoxycurcumin), condensed tannins or proanthocyanidins and lignan (sesamin). From a human physiological viewpoint, phenolic compounds are important in defense responses such as antioxidant, anti-aging, antiproliferative, and anti-inflammatory. High phenolic activity in many species could prove to be beneficial towards human health if included as part of food designs for a healthy diet.

Flavonoids are the largest group of natural phenolic compounds, and, based on the differences in the pyran ring, flavonoids can be divided into flavones, isoflavones, flavanonols, flavonols, flavanones, flavan-3-ols, and anthocyanidins. They can be subdivided into different subgroups on the basis of the carbon of the C ring on which the B ring is attached and the degree of unsaturation and oxidation of the C ring. Flavonoids in which the B ring is linked in position 3 of the C ring are called isoflavones. Those in which the B ring is linked in position 4 are called neoflavonoids, while those in which the B ring is linked in position 2 can be further subdivided into several subgroups on the basis of the structural characteristics of the C ring. The most prominent health benefits of phenolic compounds are antioxidant activity, anti-inflammatory properties, antifungal activity, antimicrobial activity, antibacterial properties, anti-coronavirus activities, neuroprotective potential, appropriate for skin health, suitable for wound healing, and anticancer activities. Flavonoids, a group of natural substances with variable phenolic structure, are found in vegetables, fruits, grains, bark, stems, roots, flowers, wine, and tea. Flavonoids are considered as an important constituent in different pharmaceutical, medicinal, nutraceutical, and cosmetic applications. They belong to a class of low-molecular-weight phenolic compounds that are extensively distributed in the plant kingdom. Future research is needed to determine the pharmaceutical benefits of phenolic and flavonoid compounds of medicinal plants, especially traditional Chinese medicinal plants, and to gain a better understanding of these chemical compounds in medicinal plants and herbs. It is also important to increase analytic techniques to allow the collection of more data on excretion and absorption.

References

1. Marmitt D., Shahrajabian M.H. Plant species used in Brazil and Asia regions with toxic properties. Phytother. Res. 2021;35:4703–4726.
2. Shahrajabian M.H., Sun W., Cheng Q. Clinical aspects and health benefits of ginger (Zingiber officinale) in both traditional Chinese medicine and modern industry. Acta Agric. Scand. B Soil Plant Sci. 2019;69:546–556.
3. Shahrajabian M.H., Sun W., Shen H., Cheng Q. Chinese herbal medicine for SARS and SARS-CoV-2 treatment and prevention, encouraging using herbal medicine for COVID-19 outbreak. Acta Agric. Scand. B Soil Plant Sci. 2020;70:437–443.
4. Shahrajabian M.H., Sun W. Using sumac (Rhus coriaria L.), as a miraculous spice with outstanding pharmacological activities. Not. Sci. Biol. 2022;14:11118
5. Shahrajabian M.H., Sun W. Medicinal plants, economical and natural agents with antioxidant activity. Curr. Nutr. Food. Sci. 2022;18:1.
6. Shahrajabian M.H., Sun W., Cheng Q. Product of natural evolution (SARS, MERS, and SARS-CoV-2); deadly diseases, from SARS to SARS-CoV-2. Hum. Vaccines Immunother. 2020;17:62–83.
7. Shahrajabian M.H., Sun W., Soleymani A., Cheng Q. Traditional herbal medicines to overcome stress, anxiety and improve mental health in outbreaks of human coronaviruses. Phytother. Res. 2020;35:1237–1247

8. Marmitt D., Shahrajabian M.H., Goettert M.I., Rempel C. Clinical trials with plants in diabetes mellitus therapy: A systematic review. Expert Rev. Clin. Pharmacol. 2021;14:735–747.
9. Sun W., Shahrajabian M.H., Cheng Q. Barberry (Berberis vulgaris), a medicinal fruit and food with traditional and modern pharmaceutical uses. Isr. J. Plant Sci. 2021;68:61–71.
10. Sun W., Shahrajabian M.H., Cheng Q. Fenugreek cultivation with emphasis on historical aspects and its uses in traditional medicine and modern pharmaceutical sciences. Mini Rev. Med. Chem. 2021;21:724–730.
11. Sun W., Shahrajabian M.H., Cheng Q. Anise (Pimpinella anisum L.), a dominant spice and traditional medicinal herb for both food and medicinal purposes. Cogent Biol. 2019;5:1673688.
12. Barragan-Zarate G.S., Lagunez-Rivera L., Solano R. et al. Validation of the traditional medicinal use of a Mexican endemic orchid (Prosthechea karwinskii) through UPLC-ESI-qTOF-MS/MS characterization of its bioactive compounds. Heliyon. 2022;8:e09867.
13. Shahrajabian M.H. Medicinal herbs with anti-inflammatory activities for natural and organic healing. Curr. Org. Chem. 2021;25:2885–2901.
14. Shahrajabian M.H., Sun W., Cheng Q. Exploring Artemisia annua L., artemisinin and its derivatives, from traditional Chinese wonder medicinal science. Not. Bot. Horti Agrobot. 2020;48:1719–1741.
15. Shahrajabian M.H., Sun W., Cheng Q. Chemical components and pharmacological benefits of Basil (Ocimum basilicum): A review. Int. J. Food Prop. 2020;23:1961–1970.
16. Shahrajabian M.H., Sun W., Cheng Q. Traditional herbal medicine for the prevention and treatment of cold and flu in the autumn of 2020, overlapped with COVID-19. Nat. Prod. Commun. 2020;15:1431.
17. Shahrajabian M.H., Sun W. Sustainable approaches to boost yield and chemical constituents of aromatic and medicinal plants by application of biostimulants. Recent Adv. Food Nutr. Agric. 2022;13:72–92.
18. Shahrajabian M.H., Sun W. Importance of thymoquinone, sulforaphane, phloretin, and epigallocatechin and their health benefits. Lett. Drug Des. Discov. 2022;19.
19. Shahrajabian M.H., Sun W. Survey on medicinal plants and herbs in traditional Iranian medicine with antioxidant, antiviral and antimicrobial, and antiinflammation properties. Lett. Drug Des. Discov. 2022;19.

20. Supritha P., Radha K.V. Estimation of phenolic compounds present in the plant extracts using high pressure liquid chromatography, antioxidant properties, and its antibacterial activity. Indian J. Pharm. Educ. Res. 2018;52:321–326.
21. Amessis-Ouchemoukh N., Madani K., Fale P.L.V. et al. Antioxidant capacity and phenolic contents of some Mediterranean medicinal plants and their potential role in the inhibition of cyclooxygenase-1 and acetylcholinesterase activities. Ind. Crop. Prod. 2014;53:6–15.
22. El-Haci I.A., Bekkara F.A., Mazari W., Gherib M. Phenolic content and antioxidant activity of some organic extracts of endemic medicinal plant Anabasis aretioides Coss. & Moq. From Algerian Sahara. Pharmacogn. J. 2013;5:108–112.
23. Subedi L., Timalsena S., Duwadi P. et al. Antioxidant activity and phenol and flavonoid contents of eight medicinal plants from Western Nepal. J. Tradit. Chin. Med. 2014;34:584–590.
24. Skotti E., Anastasaki E., Kanellou G. et al. Total phenolic content, antioxidant activity and toxicity of aqueous extracts from selected Greek medicinal and aromatic plants. Ind. Crop. Prod. 2014;53:46–54.
25. Jimenez N., Carrillo-Hormaza L., Pujol A. et al. Antioxidant capacity and phenolic content of commonly used anti-inflammatory medicinal plants in Colombia. Ind. Crop. Prod. 2015;70:272–279.
26. Cisneros H.S., Bertiller M.B., Furlong J.J.P., Carrera A.L. Similar structural complexity of phenols in plant morphotypes with contrasting soluble phenol concentration and richness in arid rangelands of Patagonia. Flora. 2022;295:152134.
27. Tirado-Kulieva V.A., Hernandez-Martinez E., Choque-Rivera T.J. Phenolic compounds versus SARS-CoV-2: An update on the main findings against COVID-19. Heliyon. 2022;8:e10702.
28. Sun W., Shahrajabian M.H., Cheng Q. Natural dietary and medicinal plants with anti-obesity therapeutics activities for treatment and prevention of obesity during lock down and in post-COVID-19 era. Appl. Sci. 2021;11:7889.
29. Sun W., Shahrajabian M.H., Lin M. Research progress of fermented functional foods and protein factory-microbial fermentation technology. Fermentation. 2022;8:688.
30. Macharia J.M., Mwangi R.W., Rozmann N. et al. Medicinal plants with anti-colorectal cancer bioactive compounds: Potential game-changers in colorectal cancer management. Biomed. Pharmacother. 2022;153:113383.
31. Jaiswal N., Kumar A. HPLC in the discovery of plant phenolics as antifungal molecules against Candida infection related biofilms. Microchem J. 2022;179:107572.

32. Diaz P., Jeong S.C., Lee S., Khoo C., Koyyalamudi S.R. Antioxidant and anti-inflammatory activities of selected medicinal plants and fungi containing phenolic and flavonoids compounds. Chin. Med. 2012;7:26.
33. Tukun A.B., Shaheen N., Banu C.P. et al. Antioxidant capacity and total phenolic contents in hydrophilic extracts of selected Bangladeshi medicinal plants. Asian Pac. J. Trop. Med. 2014;7(Suppl. 1):S568–S573.
34. Manguro L.O.A., Lemmen P. Phenolics of Moringa oleifera leaves. Nat. Prod. Res. 2007;21:56–68.
35. Sodaeizadeh H., Rafieiolhossaini M., Havlik J., van Damme P. Allelopathic activity of different plant parts of Peganum harmala L. and identification of their growth inhibitors substances. Plant Growth Regul. 2009;59:227–236.
36. Shah B., Cai Y.Z., Sun M., Corke H. Antioxidant capacity of 26 spice extracts and characterization of their phenolic constituents. J. Agric. Food Chem. 2005;53:7749–7759.
37. Koksal E., Bursal E., Gulcin I. et al. Antioxidant activity and polyphenol content of Turkish thyme (Thymus vulgaris) monitored by liquid chromatography and tandem mass spectrometry. Int. J. Food Prop. 2017;20:514–525.
38. Vastano B.C., Chen Y., Zhu N.Q. et al. Isolation and identification of stilbenes in two varieties of Polygonum cuspidatum. J. Agric. Food. 2000;48:253–256.
39. Zhao X.H., Han F., Li Y.L., Yue H.L. Preparative isolation and purification of three stilbene glycosides from the Tibetan medicinal plant Rheum tanguticum Maxim. Ex Balf. by high-speed counter-current chromatography. Phytochem. Anal. 2013;24:171–175.
40. Ahmad A., Misra L.N. Isolation of herniarin and other constituents from Matricaria chamomilla flowers. Int. J. Pharmacogn. 1997;35:121–125.
41. Morikawa T., Luo F.L., Manse Y. et al. Geranylated coumarins from Thai medicinal plant Mammea siamensis with testosterone 5 alpha-reductase inhibitory activity. Front. Chem. 2020;8:199.
42. Thuong P.T., Hung T.M., Ngoc T.M. et al. Antioxidant activities of coumarins from Korean medicinal plants and their structure-activity relationships. Phytother. Res. 2010;24:101–106.
43. Singh M., Tiwari N., Shanker K.L. et al. Two new lignans from Phyllanthus amarus. J. Asian Nat. Prod. Res. 2009;11:562–568.
44. Hu D., Yang Z.Y., Yao X.C. et al. Dibenzocyclooctadiene lignans from Schisanra chinensis and their inhibitory activity on No production in lipopolysaccharide-activated microglia cells. Phytochemistry. 2014;104:72–78.

45. Baranyai B., Backer C., Reich C., Lindequist U. The production of 7-methyljuglone, plumbagin, and quercetin in wild and cultivated Drosera rotundifolia and Drosera intermedia. Mires Peat. 2016;18:1–8.
46. Tian K., Zhang H.G., Chen X.G., Hu Z.D. Determination of five anthraquinones in medicinal plants by capillary zone electrophoresis with beta-cyclodextrin addition. J. Chromatogr. A. 2006;1123:134–137.
47. Ali I., Haque A., Saleem K. Separation and identification of curcuminoids in turmeric powder by HPLC using phenyl coloumn. Anal. Methods. 2014;6:2526–2536.
48. Taamalli A., Arraez-Roman D., Abaza L. et al. LC-MS-based metabolite profiling of methanolic extracts from the medicinal and aromatic species Mentha pulegium and Origanum majorana. Phytochem Anal. 2015;26:320–330.
49. Rodrigues F., Almeida I., Sarmento B. et al. Study of the isoflavone content of different extracts of Medicago spp. as potential active ingredient. Ind. Crop. Prod. 2014;57:110–115.
50. Stevenson P.C., Kite G.C., Lewis G.P. et al. Disntinct chemotypes of Tephrosia vogelii and implications for their use in pest control and soil enrichment. Phytochemistry. 2012;78:135–146.
51. Russo M., Fanali C., Tripodo G. et al. Analysis of phenolic compounds in different parts of pomegranate (Punica granatum) fruit by HPLC-PDA-ESI/MS and evaluation of their antioxidant activity: Application to different Italian varieties. Anal. Bioanal. Chem. 2018;410:3507–3520.
52. Bravo L. Polyphenols: Chemistry, dietary sources, metabolism, and nutritional significance. Nutr. Rev. 1998;56:317–333.
53. Choudhary P., Guleria S., Sharma N. et al. Comparative phenolic content and antioxidant activity of some medicinal plant extracts prepared by choline chloride based green solvents and methanol. Curr. Res. Green Sustain. Chem. 2021;4:100224.
54. Mishra A., Sharma A.K., Kumar S. et al. Bauhinia variegata leaf extracts exhibit considerable antibacterial, antioxidant, and anticancer activities. BioMed Res. Int. 2013;2013:915436.
55. Kumar Singh S., Patra A. Evaluation of phenolic composition, antioxidant, anti-inflammatory and anticancer activities of Polygonatum verticillatum (L.) J. Integr. Med. 2018;16:273–282.
56. Singh N., Yadav S.S. A review on health benefits of phenolics derived from dietary spices. Curr. Res. Food Sci. 2022;5:1508–1523.
57. Meng X.-H., Liu C., Zhug L.Z. et al. Antioxidative Flavan-3-ol Dimers from the Leaves of Camellia fangchengensis. J. Agric. Food Chem. 2018;66:247–254.

58. Karakas F.P., Turker A.U., Karakas A. et al. I vitro cytotoxic, antibacterial, anti-inflammatory and antioxidant activities and phenolic content in wild-grown flowers of common daisy—A medicinal plant. J. Herb. Med. 2017;8:31–39.
59. Wang L., Li N., Yu S., Zhou J. Enhancing caffeic acid production in Escherichia coli by engineering the biosynthesis pathway and transporter. Bioresour. Technol. 2023;368:128320.
60. Xue T.-T., Yang Y.-G., Tang Z.-S. et al. Evaluation of antioxidant, enzyme inhibition, nitric oxide production inhibitory activities and chemical profiles of the active extracts from the medicinal and edible plant: Althaea officinalis. Food Res. Int. 2022;156:111166.
61. Natta S., Mondol S.A., Pal K. et al. Chemical composition, antioxidant activity and bioactive constituents of six native endangered medicinal orchid species from north-eastern Himalayan region of India. S. Afr. J. Bot. 2022;150:248–259.
62. Cirak C., Radusiene J., Raudone L. et al. Phenolic compounds and antioxidant activity of Achillea arabica populations. S. Afr. J. Bot. 2022;147:425–433
63. Zahoor M., Shafiq S., Ullah H. et al. Isolation of quercetin and mandelic acid from Aesculus indica fruit and their biological activities. BMC Biochem. 2018;19:5.
64. Lungu C., Tuchilus C., Aprotosoaie A.C. et al. Chemical, antioxidant and antimicrobial investigations of Pinus cembra L. bark and needles. Molecules. 2011;16:7773–7788.
65. Pathiraja D., Wanasundara J.P.D., Elessawy F.M. et al. Water-soluble phenolic compounds and their putative antioxidant activities in the seed coats from different lentin (Lens culinaris) genotypes. Food Chem. 2023;407:135145.
66. Zhang Y., Li Y., Ren X. et al. The positive correlation of antioxidant activity and prebiotic effect about oat phenolic compounds. Food Chem. 2023;402:134231.
67. Kebal L., Pokajewicz K., Djebli N. et al. HPLC-DAD profile of phenolic compounds and in vitro antioxidant activity of Ficus carica L. fruits from two Algerian varieties. Biomed. Pharmacother. 2022;155:113738.
68. Richane A., Rim B.M., Wided M. et al. Variability of phenolic compounds and antioxidant activities of ten Ceratonia siliqua L. provenances. Biochem. Syst. Ecol. 2022;104:104486.
69. Jarial R., Thakur S., Sakinah M. et al. Potent anticancer, antioxidant and antibacterial activities of isolated flavonoids from Asplenium nidus. J. King Saud. Univ. Sci. 2018;30:185–192.

70. Tsai P.J., Huang W.C., Hsieh M.C. et al. Flavones isolated from Scutellariae radix suppress Propionibacterium acnes-induced cytokine production in vitro and in vivo. Molecules. 2016;21:15.
71. Lim Y.-H., Kim I.-H., Seo J.-J. In vitro activity of kaempferol isolated from the Impatiens balsamina alone and in combination with erythromycin or clindamycin against Propionibacterium acnes. J. Microbiol. 2007;45:473–477.
72. Poomanee W., Chaiyana W., Mueller M. et al. In vitro investigation of anti-acne properties of Mangifera indica L. kernel extract and its mechanism of action against Propionibacterium acnes. Anaerobe. 2018;52:64–74.
73. Duraipandiyan V., Ignacimuthu S. Antifungal activity of traditional medicinal plants from Tamil Nadu, India. Asian Pac. J. Trop. Biomed. 2011;1:S204–S215.
74. Hsieh S.K., Xu J.R., Lin N.H. et al. Antibacterial and laxative activities strictinin isolated from Pu er tea (Camellia sinensis) J. Food Drug Anal. 2016;24:722–729.
75. Ahmed S.I., Hayat M.Q., Tahir M. et al. Pharmacologically active flavonoids from the anticancer, antioxidant, and antimicrobial extracts of Cassia angustifolia Vahl. BMC Complement. Altern Med. 2016;16:460.
76. Block V., Patterson B., Subar A. Fruit, vegetables, and cancer prevention: A review of the epidemiological evidence. Nutr. Cancer. 1992;18:1–29.
77. Brusselmans K., de Schrijver E., Heyns W. et al. Epigallocatechin-3-gallate is a potent natural inhibitor of fatty acid synthase in intact cells and selectively induces apoptosis in prostate cancer cells. Int. J. Cancer. 2003;106:856–862.
78. Danciu C., Vlaia L., Fetea F. et al. Evaluation of phenolic profile, antioxidant, and anticancer potential of two main representants of Zingiberaceae family against B164A5 murie melanoma cells. Biol. Res. 2015;48:1.
79. Nwaeburu C.C., Abukiwan A., Zhao Z., Herr I. Quercetin-induced miR-200b-3p regulates the mode of self-renewing divisions in pancreatic cancer. Mol. Cancer. 2017;16:23.
80. Adjakly M., Ngollo M., Boiteux J.P. et al. Genistein and daidzein: Different molecular effects on prostate cancer. Anticancer Res. 2013;33:39–44.
81. Dazialo M., Mierziak J., Korzun U. et al. The potential of plant phenolics in prevention and therapy of skin disorders. Int. J. Mol. Sci. 2016;17:160.
82. Abusnina A., Keravis T., Yougbare I. et al. Anti-proliferative effect of curcumin on melanoma cells is mediated by PDE1A inhibition that regulates the epigenetic integrator UHRF1. Mol. Nutr. Food Res. 2011;55:1677–1689.
83. Ide H., Lu Y., Noguchi T. et al. Modulation of AKr1C2 by curcumin decreases testosterone production in prostate cancer. Cancer Sci. 2018;109:1230–1238.

84. Dludla P.V., Joubert E., Muller C.J.F. et al. Hyperglycemia-induced oxidative stress and heart disease-cardioprotective effects of rooibos flavonoids and phenylpyruvic acid-2-O-β-D-glucoside. Nutr. Metab. 2017;14:45.
85. Garjani A., Tila D., Hamedeyazdan S. et al. An investigation on cardioprotective potential of Marrubium vulgare aqueous fraction against ischaemia-reperfusion injury in isolated rat heart. Folia Morphol. 2017;76:361–371.
86. Razvani-Azarkhiavi K., Iranshahy M., Sahebkar A. et al. The protective role of phenolic compounds against doxorubicin-induced cardiotoxicity: A comprehensive review. Nutr. Cancer. 2016;68:892–917.
87. Han X., Gao S., Cheng Y. et al. Protective effect of naringenin-7-O-glucoside against oxidative stress induced by doxorubicin in H9c2 cardiomyocytes. Biosci. Trends. 2012;6:19–25.
88. Morrison D.K. MAP kinase pathways. Cold Spring Harb. Perspect. Biol. 2012;4:a011254.
89. Sun J., Sun G., Meng X. et al. Isorhamnetin protects against doxorubicin-induced cardiotoxicity in vivo and in vitro. PLoS ONE. 2013;8:e64526.
90. Gao Q., Yang B., Ye Z.-C. et al. Opening the calcium-activated potassium channel participates in the cardioprotective effect of puerarin. Eur. J. Pharmacol. 2007;574:179–184.
91. Kumar S., Pandey A.K. Chemistry and biological activities of flavonoids: An overview. Sci. World J. 2013;2013:162750.
92. Chakraborty R., Biplab D., Devanna N., Sen S. Antiinflammatory, antinociceptive and antioxidant activities of Phyllanthus acidus L. extracts. Asian Pac. J. Trop. Biomed. 2012;2:S953–S961.
93. Kirmizibekmez H., Inan Y., Reis R. et al. Phenolic compounds from the aerial parts of Clematis viticella L. and their in vitro anti-inflammatory activities. Nat. Prod. Res. 2019;33:2541–2544.
94. Cheng H.-L., Zhang L.-J., Liang Y.-H. et al. Antiinflammatory and antioxidant flavonoids and phenols from Cardiospermum halicacabum. J. Tradit. Complement. Med. 2013;3:33–40.
95. Augusti P.R., Conterato G.M.M., Denardin C.C. et al. Bioactivity, bioavailability, and gut microbiota transformations of dietary phenolic compounds: Implications for COVID-19. J. Nutr. Biochem. 2021;97:108787.
96. Setayesh M., Karimi M., Zargaran A. Efficacy of a persian herbal medicine compound on coronavirus disease 2019 (COVID-19): A randomized controlled trial. Integr. Med. Res. 2022;11:100869.

97. Moharram F.A., El Dib R.A.E.M. et al. New apigenin glycoside, polyphenolic constituents, anti-inflammatory and hepatoprotective activities of Gaillardia grandiflora and Gaillardia pulchella aerial parts. Pharmacogn. Mag. 2017;13:244–249.
98. Compaore M., Bakasso S., Meda R., Nacoulma O. Antioxidant and anti-inflammatory activities of fractions from Bidens engleri O.E. Schulz (Asteraceae) and Boerhavia erecta L. (Nyctaginaceae) Medicines. 2018;5:53.
99. Genc Y., Harput U.S., Saracoglu I. Active compounds isolated from Plantago subulata L. via wound healing and antiinflammatory activity guided studies. J. Ethnopharmacol. 2019;241:112030.
100. Skendi A., Irakli M., Chatzopoulou P. et al. Phenolic extracts from solid wastes of the aromatic plant essential oil industry: Potential uses in food applications. Food Chem. Adv. 2022;1:100065.
101. Lu C.L., Zhu Y.F., Hu M.M. et al. Optimization of astilbin extraction from the rhizome of Smilax glabra, and evaluation of its anti-inflammatory effect and probably underlying mechanism in lipopolysaccharide-induced RAW264.7 macrophages. Molecules. 2015;20:625–644.
102. Gerhauser C. Beer constituents as potential cancer chemopreventive agents. Eur. J. Cancer. 2005;41:1941–1954.
103. McKay D.L., Blumberg J.B. A review of the bioactivity and potential health benefits of chamomile teas (Matricaria recutita L.) Phytother. Res. 2006;20:519–530.
104. Wach A., Pyrzynska K., Biesaga M. Quercetin content in some food and herbal samples. Food Chem. 2007;100:699–704.
105. Bijak M. Silybin, a major bioactive component of milk thistle (Silybum marianum L. Gaernt.) –Chemistry, bioavailability, and metabolism. Molecules. 2017;22:1942.
106. Moore J.O., Wang Y., Stebbins W.G. et al. Photoprotective effect of isoflavone genistein on ultraviolet B-induced pyrimidine dimer formation and PCNA expression in human reconstituted skin and its implications in dermatology and prevention of cutaneous carcinogenesis. Carcinogenesis. 2006;27:1627–1635.
107. Widyarini S. Protective effect of the isoflavone equol against DNA damage induced by ultraviolet radiation to hairless mouse skin. J. Vet. Sci. 2006;7:217–223.
108. Setchell K.D.R., Clerici C. Equol: History, chemistry, and formation. J. Nutr. 2010;140:1355S–1362S.
109. Irace C., Marini H., Bitto A. et al. Genistein and endothelial function in postmenopausal women with metabolic syndrome. Eur. J. Clin. Investig. 2013;43:1025–1031.

110. Shahrajabian M.H., Petropoulos S.A., Sun W. Survey of the influences of microbial biostimulants on horticultural crops: Case studies and successful paradigms. Horticulturae. 2023;9:1–24.

NATURAL BIOLOGICALLY ACTIVE COMPOUNDS - PERSPECTIVE AGENTS FOR LONGEVITY

Kravchenko V.M., Galyzinskaya L. V., Honcharov O. V., Ochkur O.V.
National University of Pharmacy, Kharkiv, Ukraine
biochem@nupn.edu.ua

Abstract. Aging is the most prominent risk factor for many diseases, which is considered to be a complicated biological process. The rate of aging depends on the effectiveness of important mechanisms such as the protection of DNA from free radicals, which protects the structural and functional integrity of cells and tissues. In any organism, not all organs may age at the same rate. Slowing down primary aging and reaching maximum lifespan is the most basic necessity. In this process, it may be possible to slow down or stabilise some diseases by using the compounds for both dietary and pharmacological purposes. Natural compounds with antioxidant and anti-inflammatory effects, mostly plant-based nutraceuticals, are preferred in the treatment of age-related chronic diseases and can also be used for other diseases. An increasing number of long-term studies on synthetic and natural compounds aim to elucidate preclinically and clinically the mechanisms underlying being healthy and prolongation of life. To delay age-related diseases and prolong the lifespan, it is necessary to take these compounds with diet or pharmaceuticals, along with detailed toxicological results.

Keywords: anti-aging compounds, caffeine, curcumin, fucoxanthin, metformin, resveratrol, spermidine, α-lipoic acid.

Introduction. Aging can be defined as the accumulation of damage over time, a loss in functional ability, adaptation difficulties to the environment and an increase in illness and mortality. The aging of the global population is posing significant issues for both industrialised and developing countries due to changes in the population pyramid [1, 2]. The percentage of persons over the age of 60 is increasing globally, and it is predicted that by 2050, it would nearly double, rising from 12 per cent in 2015 to 22 percent [3-5]. Despite the continued predicted increase in the aging population, the geriatric population's life expectancy and survival are improving significantly [4].