Modern Issues of Medicine and Management (MIMM) 2024: 1(27)

Review

Antioxidant Properties of Some Caucasian Medicinal Plants

Giovanni N. Roviello[1], Valentina Mittova[2,3*], Zurab R. Tsetskhladze[2,3], Roza Bidzinashvili[4], Marina Jordania[5], Malkhaz Vakhania[2,3], Tornike Mindiashvili[2,3], Mariam Kobiashvili[2,3]

[1] Institute of Biostructures and Bioimaging, Italian National Council for Research (IBB-CNR), Naples, Italy
[2] Teaching University Geomedi, Tbilisi, Georgia
[3] Scientific-Research Institute of Experimental and Clinical Medicine, Teaching University Geomedi, Tbilisi, Georgia
[4] National Botanical Garden of Georgia, Tbilisi, Georgia
[5] Green movement of Georgia, Tbilisi, Georgia
* E-mail: valentina.mittova@geomedi.edu.ge

Article History

Received: May 24, 2024
Revised: Jun 5, 2024
Accepted: Jun 7, 2024

Abstract

Since antioxidants may be implicated in disease-related processes, studying these molecules is crucial. The detection of new antioxidants may result in the application of these compounds as medications. Mountain systems and long-term climate changes have contributed to the development of the Caucasus biodiversity hotspot, characterized by a great variety of plant species. For centuries many Caucasian plants were used for the treatment of different diseases, however, the scientific knowledge of the composition of natural drugs is still far from exhaustive. The present review indicates that Caucasian medicinal plants *Symphytum caucasicum* M. Bieb., *Thymus tiflisiensis* Klokov & Des.-Shost., *Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong, and *Cyclamen coum* Mill. are a valuable source of antioxidants, and extracts of these plants exhibit significant total antioxidant activity. Various classes of antioxidants were revealed in the aerial part and roots of *Symphytum caucasicum"* M. Bieb., tubers of *Cyclamen coum* Mill., petals of *Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong, and the aerial part of *Thymus tiflisiensis* Klokov & Des.-Shost. These compounds included phenolic compounds, water-soluble antioxidants, alkaloids, terpenes, and saponins. *In vitro* studies demonstrated that these antioxidants are beneficial in suppressing some biological effects related to multiple diseases. The review demonstrates the benefits of using Caucasian medicinal plants for the treatment of different disorders and offers information to scientists who are working to produce safe plant-based medications.

DOI: 10.56580/GEOMEDI44

Keywords: *Symphytum caucasicum* M. Bieb., *Thymus tiflisiensis* Klokov & Des.-Shost., *Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong, *Cyclamen coum* Mill., antioxidant activity, DPPH assay, medicinal use.

Introduction

Since antioxidants from medicinal plants are now considered promising therapeutic candidates for preventing the damage caused by free radicals, research on these compounds has grown significantly over time [1]. The great variety of climate zones and landscapes, determined by the developed mountain systems contributed to the development of the Caucasus woodland habitats and immense biodiversity [2]. Caucasian flora includes 6350 vascular plant species, out of them more than 2900 endemic species, 1000 species are used for centuries in traditional folk medicine, and 180 species are used in modern medicine [3]. The therapeutic effect of many of these species is associated with the unique composition of antioxidants since Caucasian plants contain chemical compounds of different classes that may act individually or in synergy (reviewed in [4]).

An antioxidant is any substance that, when present in low concentrations compared to those of oxidizable substrates (such as proteins, lipids, carbohydrates, and DNA) decreases or completely prevents the oxidation of such substrate [5]. Natural antioxidants can be classified as enzymatic and non-enzymatic, primary and secondary antioxidants, hydrophilic and lipophilic antioxidants (reviewed in [6]).

This review aimed to systematize the existing knowledge about the antioxidant composition of Caucasian medicinal plants. The literature search was performed in PubMed, Scopus, and Google Scholar databases, using the following search criteria: 1. "Antioxidants"; 2. "Antioxidant System"; 3. "*Symphytum caucasicum* M. Bieb.", "*Thymus tiflisiensis* Klokov & Des.-Shost.", "*Paeonia daurica* subsp. *mlokosewitschii*" (Lomakin) D. Y. Hong", *Cyclamen coum* Mill.". The choice to focus on the discussed plants in the review likely reflects their representation of diverse plant families within Caucasian medicinal flora, scientific interest in their medicinal properties, availability of data on their antioxidant activity, and practical research constraints.

Antioxidants in Caucasian Medicinal Plants

For the representatives of four families of Caucasian medicinal plants, considered in this review the data on the content and composition of antioxidants are limited. The most commonly determined parameter was the total antioxidant activity of extracts of various plant parts.

Total antioxidant activity (TAA)

The effectiveness of antioxidants depends on their chemical structure, total concentration, and location of antioxidants in

DOI: 10.56580/GEOMEDI44

the system. Many studies aiming to determine the potential application of plants in medicine are based on the determination of TAA. Currently, many methods are used to determine the antioxidant activity (reviewed in [7]), the most common and reliable methods include ABTS, FRAP, and DPPH assays. In the ABTS assay the green–blue stable radical cationic chromophore, 2,2-azinobis-(3-ethylbenzothiazoline-6-sulfonate) ($ABTS^{\cdot+}$) is produced by oxidation, the ferric reducing ability of plasma (FRAP) assay is based on the reducing power of the analyzed antioxidant and 1,1-diphenyl-2-picrylhydrazine (DPPH) method is based on the scavenging effect of stable radical DPPH through the addition of an antioxidant that decolorizes the DPPH solution (the description of methods is provided in [6]).

For Caucasian plants described in this review, TAA was assessed in various studies using the DPPH method (Table 1). Thus, the above-ground part of *Symphytum caucasicum* M. Bieb. was investigated during different vegetative stages using the DPPH method. The highest TAA was revealed in methanolic extracts of *Symphytum caucasicum* M. Bieb. and comprised from 75.48% (budding stage) to 80.81% (spring vegetation stage), ethanolic extracts – from 22.61% (blossoming stage) to 73.99% (spring vegetation stage), water extracts – from 67.46% (budding stage) to 74.45% (blossoming stage) [8]. Significant TAA was revealed for methanolic extracts of *Cyclamen coum* Mill. leaves (249.2 μg/ml) and bulbs (129.7 μg/ml) [9] and methanolic extract of the aerial part of *Thymus tiflisiensis* Klokov & Des.-Shost. [10]. TAA of *Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong was lower and comprised 32.71 μg/ml [11].

Table 1 Total antioxidant activity, determined by the DPPH method of Caucasian medicinal plants

Plant part/extractant	*Symphytum caucasicum* M. Bieb.	*Thymus tiflisiensis* Klokov & Des.-Shost.	*Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong	*Cyclamen coum* Mill.	References
Aerial part/methanol	80.81 %	1100 μg/ml	-	-	[8], [10]
Leaves/ethanol	27.5 %	-	24.81 μg/ml	164.8 μg/ml	[12], [11], [9]
Aerial part/ethanol	19.98 mg TE/g	-	-	-	[13]
Roots (tubers)/ethanol	9.00 mg TE/g	-	-	129.7 μg/ml	[13], [9]

DOI: 10.56580/GEOMEDI44

Leves/methanol	-	-	32.71 µg/ml	247.2 µg/ml	[11], [9]
Roots (tubers)/methanol	-	-	-	129.7 µg/ml 8.52 mg TE/g	[9], [14]
Leves/acetone	-	-	-	257.6 µg/ml	[9]
Roots (tubers)/acetone		-	-	336.3 µg/ml	[9]

- - was not determined

Ascorbic acid

This is the major antioxidant component in plants, with the detoxification of reactive oxygen species (OH° and O_2^{-}) by ascorbic acid occurring directly, by the removal of H_2O_2 through the water-water cycle or via the glutathione-ascorbate cycle [15]. Ascorbic acid (ASC) also participates in the xanthophyll cycle, which is needed to protect photosystem II (PSII) from photoinhibition, redox signaling, modulation of gene expression, preservation of the activities of enzymes containing prosthetic transition metal ions [15]. The high content of ascorbic acid comprising 51.81, mg% (DW) was revealed in leaves of *Symphytum caucasicum* M. Bieb. (Table 2), a perennial endemic plant inhabiting the edges and glades of the Caucasian forests (Ciscaucasia, Dagestan, and Eastern Transcaucasia) [16], Fig. 1.

Phenolic compounds

Phenolic compounds act as antioxidants by reacting with a variety of free radicals involving transfer of hydrogen atoms, single electrons, or the chelation of transition metals [17]. Phenolic compounds are usually classified into simple phenolics (hydroxyphenols or dihydroxybenzenes), phenolic acids, and polyphenols, which include flavonoids, tannins, and stilbenes. The anthocyanins, natural water-soluble pigments occurring in plants represent a particular variety of phenolic compounds.

The high content of phenolic compounds was demonstrated in Caucasian medicinal plants: thus, the content of soluble phenols was 3 mg/g DW in *Symphytum caucasicum* M. Bieb. leaves, and roots of this plant contained phenolic polymer poly[3-3,4-dihydroxyphenyl)-glyceric acid [18], (Scheme 1). The presence of phenolic compounds (C-dihexoside, quercetin-3-galactoside), flavonoids and tannins [14] was revealed in tubers of *Cyclamen coum* Mill. (Table 2), a tuberous herbaceous perennial with an extensive area from Southern and Southeastern Europe to the Mediterranean and South-West Asia [14]. The total content of anthocyanins in *Symphytum caucasicum* M. Bieb. leaves was 0.487 mg/g DW [12]. Petals of *Paeonia daurica* subsp. *mlokosewitschii*

DOI: 10.56580/GEOMEDI44

(Lomakin) D. Y. Hong contained anthocyanin peonidin-3,5-di-*O*-glucoside [19], (Scheme 1). *Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong, is a species of flowering plant native to the temperate biome of east Georgia and adjacent areas in Russia and Azerbaijan [20], (Fig. 1).

Fig. 1 Photos of medicinal Caucasian plants *Symphytum caucasicum* M. Bieb. (A) and *Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong (B)

Alkaloids

Alkaloids are a large diverse group of biologically active compounds, exhibiting antioxidant effects similar to or even more active than standard antioxidants [21]. Roots of *Symphytum caucasicum* M. Bieb. contained asperumine (Scheme 1), echimidine N-oxide, echinatine and lasiocarpine (Table 2) as the major alkaloids [22]. Alkaloids were also revealed in tubers of *Cyclamen coum,* but identification of alkaloids was not performed [14].

Terpenes

Terpenes represent a large group of hydrocarbons consisting of 5-carbon isoprene (C5H8) units as their basic building block. Terpenes were shown to inhibit ROS production and lipid peroxidation and increase the endogenous antioxidant status [23]. Nerolidol (Scheme 1), germacrene, and farnesol were shown to be the most abundant terpenes in the essential oil extracted from the aerial part of *Thymus tiflisiensis* Klokov & Des.-Shost. (Table 2) [24], a subshrub endemic

DOI: 10.56580/GEOMEDI44

to Georgia, inhabiting lower and middle mountain belts in Kakheti, Kartli, Kiziki, Gare Kakheti and Trialeti [25]

Saponins

Saponins compose a class of plant secondary metabolites, consisting of an aglycone with carbohydrate moieties. The number and type of carbohydrate moieties determine the structural diversity of the saponins. The aglycone can be a triterpene or a steroid with different substituents (–H, –COOH, $–CH_3$). The antioxidant activity of saponins was demonstrated. They have been shown to scavenge free radicals such as hydroxyl, superoxide, peroxide, and nitric oxide radicals [26]. The presence of various saponins (coumosides, cyclaminorin, deglucocyclamin, cyclacoumin (Scheme 1)) [27] was revealed in tubers of *Cyclamen coum* Mill. (Table 2).

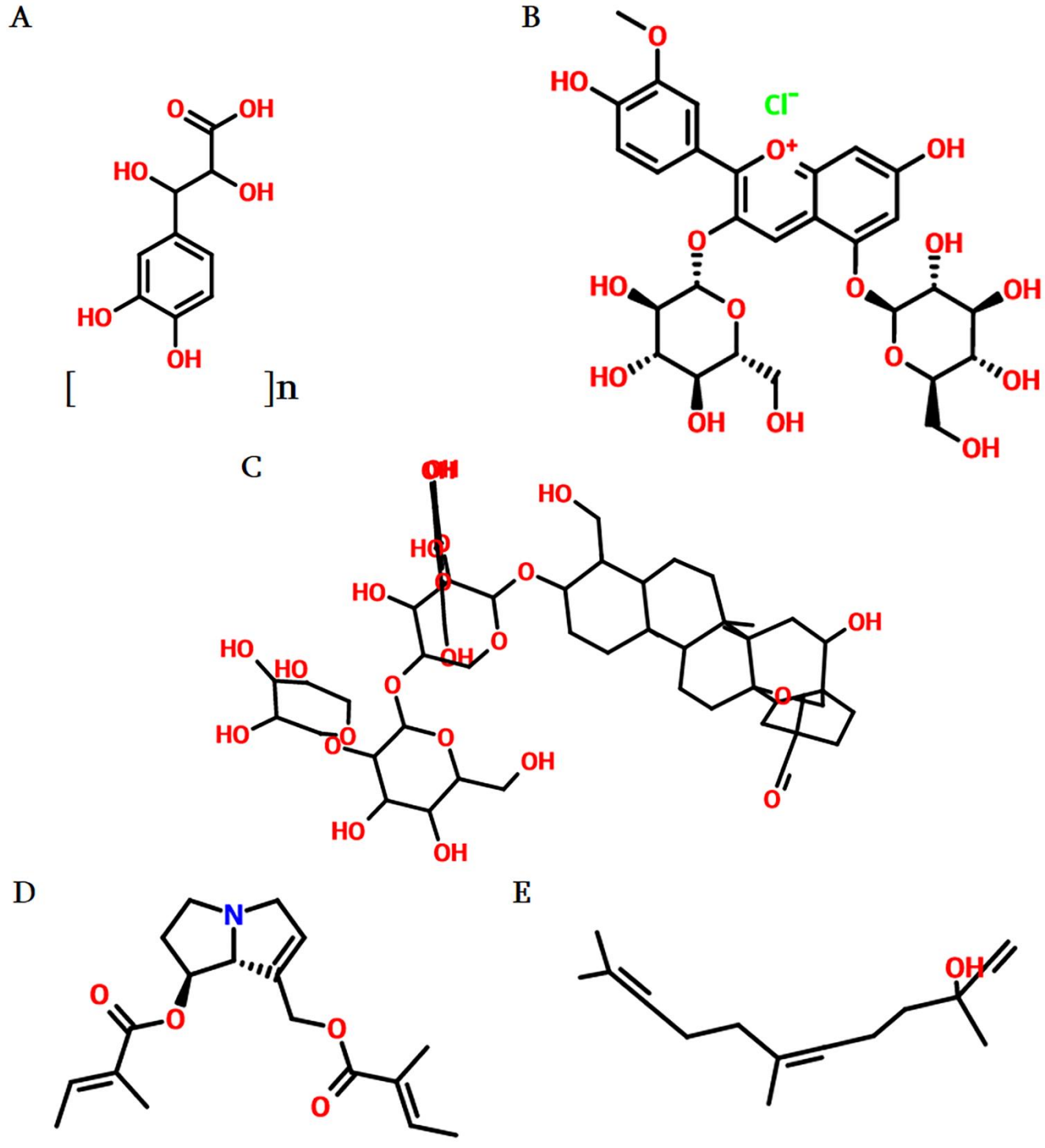
Table 2 Antioxidants revealed in Caucasian medicinal plants

Family	Plant species	Part of plant	Class of antioxidants	Antioxidant	References
Boraginaceae	***Symphytum caucasicum* M. Bieb.**	Aerial part, roots	Phenolic compounds	Poly[3-(3,4-dihydroxyphenyl)glyceric acid]	[18]
		Leaves	Water-soluble antioxidants Phenolic compounds	Ascorbic acid Anthocyanins	[12]
		Roots	Alkaloids	Asperumine, echimidine N-oxide, echinatine and lasiocarpine	[22]
Lamiaceae	***Thymus tiflisiensis* Klokov & Des.-Shost.**	Aerial part	Terpenes	Nerolidol, germacrene, farnesol, amphene, sabinene, endo-borneol, nerol, citral, bornyl acetate, terpinyl acetate, muurolene, bisabolene, E-bisabolene,	[24]

DOI: 10.56580/GEOMEDI44

				caryophyllene oxide, and epi-cubenol	
Paeoniaceae	***Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong**	Petals	Phenolic compounds	Anthocyanins peonidin-3,5-di-*O*-glucoside	[19]
Primulaceae	***Cyclamen coum***	Tubers	Saponins	Coumoside A, coumoside B, cyclaminorin, deglucocyclamin, cyclacoumin, mirabilin lactone	[27], [14]
			Phenolic compounds	Flavonoids Tannins Phloretin C-dihexoside, quercetin 3-galactoside,	
			Alkaloids	catechin,	

DOI: 10.56580/GEOMEDI44



Scheme 1 Chemical representation of some representative compounds mentioned in Table 2. Poly[3-(3,4-ihydroxyphenyl)glyceric acid] (A); peonidin-3,5-di-O-glucoside (B); cyclacoumin (C); asperumine (D); nerolidol (E).

DOI: 10.56580/GEOMEDI44

The involvement of oxidative stress in the pathogenesis of insulin resistance, cancer, diabetes mellitus, cardiovascular diseases, and aging was demonstrated and WHO identified medicinal plants as one of the possible sources of new pharmaceuticals [28]. Antioxidants of medicinal plants can be used for both the prevention and repair of cellular damage. The effect of antioxidants is due to the prohibition of the formation of ROS and their scavenging and due to the restoration of the activities of enzymes involved in cellular development. The use of antioxidants, extracted from Caucasian medicinal plants for the treatment of various diseases was demonstrated. Thus, the bioactive poly[3-3,4-dihydroxyphenyl)glyceric acid] isolated from aerial parts and roots of *Symphytum caucasicum* M. Bieb. exhibited significant antioxidant activity, affecting ROS formation by polymorphonuclear neutrophils [18]. Essential oils from aerial parts of *Thymus tiflisiensis* Klokov & Des.-Shost. exhibited moderate cytotoxic activity against human colon cancer cell lines [24]. The most abundant phenolic compound quercetin-3-galactoside in tuber extracts of *Cyclamen coum* Mill. was attributed to the anti-tyrosinase activities exhibited by the extracts of this plant [14]. Saponin extracts of *Cyclamen coum* Mill. inhibited growth of *Pseudomonas aeruginosa, Staphylococcus aureus, Salmonella typhi, Klebsiella pneumonia,* and *Enterococcus faecalis* [29].

Conclusions

The present review indicates that Caucasian medicinal plants are a valuable source of hydrophilic and hydrophobic antioxidants that confer high ROS-scavenging ability. The analysis of the literature also demonstrated that extracts of *Symphytum caucasicum* M. Bieb., *Thymus tiflisiensis* Klokov & Des.-Shost., *Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong, and *Cyclamen coum* Mill. possess significant total antioxidant activity. The highest total antioxidant activity was revealed for the aerial part of *Thymus tiflisiensis* Klokov & Des.-Shost. Various phenolic compounds were detected in the aerial part and roots of *Symphytum caucasicum* M. Bieb., tubers of *Cyclamen coum* Mill. and petals of *Paeonia daurica* subsp. *mlokosewitschii* (Lomakin) D. Y. Hong. Aerial part of *Thymus tiflisiensis* Klokov & Des.-Shost. Also contained various terpenes. *In vitro* studies demonstrated that these compounds are beneficial in suppressing some biological effects related to multiple diseases. The identified antioxidant compounds from Caucasian medicinal plants, discussed in this review, hold great promise for developing novel therapeutic agents and represent valuable reservoirs for drug discovery efforts. The decision to concentrate on the above three plants in the review likely indicates their representation of various plant families within Caucasian medicinal flora, scientific curiosity regarding their medicinal attributes, the accessibility of data concerning their antioxidant properties, and practical limitations in research. However, in the

DOI: 10.56580/GEOMEDI44

future, the review should be extended to encompass other plants within the Caucasian medicinal flora to provide a more comprehensive understanding of antioxidant properties across a broader spectrum of species.

კავკასიაში გავრცელებული ზოგიერთი სამკურნალო მცენარის ანტიოქსიდანტური თვისებები

ჯოვანი ნ. როვიელო[1], ვალენტინა მიტოვა[2,3*], ზურაბ რ. ცეცხლაძე[2,3], როზა ბიძინაშვილი[4], მარინა ჟორდანია[5], მალხაზ ვახანია[2,3], თორნიკე მინდიაშვილი[2,3], მარიამ კობიაშვილი[2,3]

[1] ბიოსტრუქტურებისა და ბიოიმიჯინგის ინსტიტუტი, იტალიის კვლევების ეროვნული საბჭო, ნეაპოლი, იტალია
[2] სასწავლო უნივერსიტეტი გეომედი, თბილისი, საქართველო
[3] ექსპერიმენტალური და კლინიკური მედიცინის სამეცნიერო-კვლევითი ინსტიტუტი, სასწავლო უნივერსიტეტი გეომედი, თბილისი, საქართველო
[4] საქართველოს ეროვნული ბოტანიკური ბაღი, თბილისი, საქართველო
[5] საქართველოს მწვანეთა მოძრაობა, თბილისი, საქართველო
* ელ. ფოსტა: valentina.mittova@geomedi.edu.ge

აბსტრაქტი

ვინაიდან ანტიოქსიდანტური თვისების მქონე ნაერთებს შეუძლიათ გავლენა მოახდინონ ადამიანის სხვადასხვა დაავადებების მიმდინარეობაზე, აქედან გამომდინარე, ამ ტიპის მოლეკულების შესწავლას დიდი მნიშვნელობა ენიჭება. ახალი ანტიოქსიდანტური თვისების მქონე ნაერთების აღმოჩენა იძლევა იმის იმედს, რომ ისინი მომავალში სამკურნალო პრეპარატების სახით იქნება გამოყენებული. კავკასიის უნიკალურმა მთათა სისტემამ და კლიმატურმა თავისებურებამ ჩამოაყალიბა მცენარეთა სახეობათა სიმრავლით გამორჩეული სამყარო. საუკუნეების მანძილზე კავკასიის ტერიტორიაზე არსებული მცენარეები გამოიყენებოდა და გამოიყენება სხვადასხვა დაავადებების სამკურნალოდ. თუმცა, თანამედროვე კვლევის მეთოდებით, მათ შემადგენლობაში არსებული ბიოლოგიურად აქტიური ნაერთების მოქმედებების მექანიზმების გარკვევა, ჯერ კიდევ არის არის კარგად შესწავლილი. მოცემულ მიმოხილვაში ნაჩვენებია კავკასიის სამკურნალო მცენარეების: *Symphytum caucasicum* M. Bieb. (ლაშქარა); *Thymus tiflisiensis* Klokov & Des.-Shost. (თბილისური ბეგქონდარა), *Paeonia daurica subsp. mlokosewitschii (Lomakin) D. Y. Hong* (მლოკოშევიჩის იორდასალამი) და *Cyclamen coum* Mill. (კავკასიური ყოჩივარდა) ექსტრაქტების ანტიოქსიდანტური თვისებები, რაც იმაზე მიუთითებს, რომ ისინი მეტად მნიშვნელოვანი წყაროა ამ ტიპის ნაერთების მისაღებად.

DOI: 10.56580/GEOMEDI44

მცენარეების - *Symphytum caucasicum* M. Bieb-ის (ლაშქარა) მიწისზედა ორგანოებიდან და ფესვებიდან; *Cyclamen coum* Mill-ის (კავკასიური ყოჩივარდა) გორგლებიდან; *Paeonia daurica subsp*-ის *mlokosewitschii* (Lomakin) D. Y. Hong-ის (მლოკოშევიჩის იორდასალამი) ფოთლებიდან და *Thymus tiflisiensis* Klokov & Des.-Shost-ის (თბილისური ბეგქონდარა) მიწისზედა ორგანოებიდან, გამოყოფილია სხვადასხვა ანტიოქსიდანტური თვისების მქონე ნაერთები, მაგალითად; ფენოლური მოლეკულები, წყალში ხსნადი ანტიოქსიდანტები, ალკალოიდები, ტერპენები და საპონინები. In vitro კვლევებმა აჩვენა, რომ აღნიშნული ანტიოქსიდანტური თვისების მოლეკულები თრგუნავენ სხვადასხვა დაავადებებთან დაკავშირებულ ბიოლოგიურ ეფექტებს. მიმოხილვაში წარმოდგენილია კავკასიის ტერიტორიაზე გავრცელებული სამკურნალო მცენარეების გამოყენება სხვადასხვა დაავადებებთან მიმართებაში. ასევე წარმოდგენილია მასალები იმ მკვლევარებისათვის, რომლებიც იკვლევენ და ქმნიან მცენარეების საფუძველზე დამზადებულ უსაფრთხო სამკურნალო საშუალებებს.

საკვანძო სიტყვები: ლაშქარა (Symphytum caucasicum M. Bieb), თბილისის ბეგქონდარა (Thymus tiflisiensis Klokov & Des.-Shost.), მლოკოშევიჩის იორდასალამი, (Paeonia daurica subsp. mlokosewitschii (Lomakin) D. Y. Hong), კავკასიური ყოჩივარდა, (Cyclamen coum Mill.,) ანტიოქსიდანტური აქტიურობა, DPPH-ანალიზი, სამედიცინო მიზნებისათვის გამოყენება.

References

1. Bhatt ID, Rawat S, Rawal RS. Antioxidants in Medicinal Plants. In: Chandra S, Lata H, Varma A, eds. Biotechnology for Medicinal Plants. Springer Berlin Heidelberg; 2013:295-326. Accessed April 27, 2023. https://link.springer.com/10.1007/978-3-642-29974-2_13

2. Nakhutsrishvili GS, Abdaladze O, Batsatsashvili K, Spehn EM, Körner C, eds. Plant Diversity in the Central Great Caucasus: A Quantitative Assessment. Springer International Publishing; 2017.

3. Mamedov, Nazim; Mehdiyeva, N.P.; Craker, Lyle E. Medicinal plants used in traditional medicine of the Caucasus and North America. Journal of Medicinally Active Plants. 2015; 4 : 42-66. doi:10.7275/R51834DS

4. Fik-Jaskółka M, Mittova V, Motsonelidze C, Vakhania M, Vicidomini C, Roviello GN. Antimicrobial metabolites of Caucasian medicinal plants as alternatives to antibiotics. Antibiotics. 2024;13(6):487. doi:10.3390/antibiotics13060487

5. Halliwell B, Gutteridge JMC. Free Radicals in Biology and Medicine. Fifth edition. Oxford University Press; 2015.

6. Pirtskhalava M, Mittova V, Tsetskhladze ZR, Palumbo R, Pastore R, Roviello GN. Georgian medicinal plants as rich natural sources of antioxidant derivatives: a review on the current knowledge and future perspectives. CMC. 2024;31. doi:10.2174/0109298673262575231127034952

7. Krishnaiah D, Sarbatly R, Nithyanandam R. A review of the antioxidant potential of medicinal plant species. Food and Bioproducts Processing. 2011;89(3):217-233. doi:10.1016/j.fbp.2010.04.008

8. Vergun O, Brindza J, Rakhmetov D. Total antioxidant activity of plants of *Symphytum* L. species. In: Klymenko S, ed. Agrobiodiversity for Improving Nutrition, Health and Life Quality. 1. ed. Slovak University of Agriculture in Nitra, Slovakia; 2017:488-492. doi:10.15414/agrobiodiversity.2017.2585-8246.488-492

9. Aydin C, Mammadov R, Davidov M. Biological activities, phenolic constituents and of various extracts of *Cyclamen coum* tubers and leaves from Turkey. JCPRM. 2023;(1):255-263. doi:10.14258/jcprm.20230111262

10. Korkotadze T., Gokadze S., Mshvildadze V., Jokhadze M., Berashvili D. Evaluation of antioxidant activity of some species of the Labiatae family, common in Georgia. In: "Chemistry - Achievements and Prospects" Collection of Scientific Works of the International Scientific Conference Dedicated to the 90th Anniversary of Givi Tsinstadze. Technical University; 2023:301-303.

11. Mittova V, Pirtskhalava M, Bidzinashvili R, Vakhania M, Mindiashvili T, Kobiashvili M. Effects of different drying, extraction methods, and solvent polarity on the antioxidant properties of *Paeonia daurica* subsp. *mlokosewitschii* leaves. MIMM. 2023;26(2):1-15. doi:10.56580/GEOMEDI39

12. Chanishvili, Sh., Chigladze, L., Kikvidze, M., et al. Content of antioxidants in leaves of some plants of Tbilisi environs. Bulletin of the Georgian National Academy of Sciences. 7:105-111.

13. Luca SV, Zengin G, Kulinowski Ł, Sinan KI, Skalicka-Woźniak K, Trifan A. Phytochemical profiling and bioactivity assessment of underutilized *Symphytum* species in comparison with *Symphytum officinale*. J Sci Food Agric. 2024;104(7):3971-3981. doi:10.1002/jsfa.13279

14. Mahomoodally MF, Picot-Allain MCN, Zengin G, et al. Chemical profiles and biological potential of tuber extracts from *Cyclamen coum* Mill. Biocatalysis and Agricultural Biotechnology. 2021;33:102008. doi:10.1016/j.bcab.2021.102008

15. Paciolla C, Fortunato S, Dipierro N, et al. Vitamin C in Plants: from functions to biofortification. Antioxidants. 2019;8(11):519. doi:10.3390/antiox8110519

16. Batsatsashvili K, Mehdiyeva N, Fayvush G, et al. *Symphytum caucasicum* M. Bieb. Boraginaceae. In: Bussmann RW, ed. Ethnobotany of the Caucasus. European Ethnobotany. Springer International Publishing; 2016:1-6. doi:10.1007/978-3-319-50009-6_61-1

17. Zeb A. Concept, mechanism, and applications of phenolic antioxidants in foods. J Food Biochem. 2020;44(9). doi:10.1111/jfbc.13394

18. Barbakadze VV, Kemertelidze EP, Mulkijanyan KG, et al. Antioxidant and anticomplement activity of poly[3-(3,4-dihydroxyphenyl)glyceric acid] from

Symphytum asperum and *Symphytum caucasicum* plants. Pharm Chem J. 2007;41(1):14-16. doi:10.1007/s11094-007-0004-7

19. Jia N, Shu QY, Wang DH, et al. Identification and Characterization of anthocyanins by high-performance liquid chromatography–electrospray ionization–mass spectrometry in herbaceous peony species. J Amer Soc Hort Sci. 2008;133(3):418-426. doi:10.21273/JASHS.133.3.418

20. Hong DY, Zhou SL. Paeonia (Paeoniaceae) in the Caucasus. Botanical Journal of the Linnean Society. 2003;143(2):135-150. doi:10.1046/j.1095-8339.2003.00173.x

21. Macáková K, Afonso R, Saso L, Mladěnka P. The influence of alkaloids on oxidative stress and related signaling pathways. Free Radical Biology and Medicine. 2019;134:429-444. doi:10.1016/j.freeradbiomed.2019.01.026

22. Salehi, Sharopov, Boyunegmez Tumer, et al. *Symphytum* species: a comprehensive review on chemical composition, food applications and phytopharmacology. Molecules. 2019;24(12):2272. doi:10.3390/molecules24122272

23. Kim T, Song B, Cho KS, Lee IS. Therapeutic potential of volatile terpenes and terpenoids from forests for inflammatory diseases. IJMS. 2020;21(6):2187. doi:10.3390/ijms21062187

24. Getia M, Korkotadze T, Moshiashvili G, Tabatadze N, Legault J, Mshvildadze V. Composition and cytotoxicity of essential oils from aerial parts of *Thymus tiflisiensis* and *T. collinus* growing in Georgia. Chem Nat Compd. 2022;58(5):959-961. doi:10.1007/s10600-022-03840-5

25. Miller JS, McCue K, Consiglio T, Stone J, Eristavi M, Sikharulidze S, Mikatadze-Pantsulaia T, Khutsishvili M. Endemic Medicinal Plants of Georgia (Caucasus). Missouri Botanical Garden Press; 2005. 46.

26. Tapondjou LA, Nyaa LBT, Tane P, et al. Cytotoxic and antioxidant triterpene saponins from *Butyrospermum parkii* (Sapotaceae). Carbohydrate Research. 2011;346(17):2699-2704. doi:10.1016/j.carres.2011.09.014

27. Bokov Do B, Krasikova Mk K, Sergunova Ev S, et al. Pharmacognostic, phytochemical and ethnopharmacological potential of *Cyclamen coum* Mill. PJ. 2020;12(1):204-212. doi:10.5530/pj.2020.12.31

28. Alfadda AA, Sallam RM. Reactive oxygen species in health and disease. Journal of Biomedicine and Biotechnology. 2012;2012:1-14. doi:10.1155/2012/936486

29. Saboora A, Sajjadi ST, Mohammadi P, Fallahi Z. Antibacterial activity of different composition of aglycone and glycosidic saponins from tuber of *Cyclamen coum* Miller. Industrial Crops and Products. 2019;140:111662. doi:10.1016/j.indcrop.2019.111662