Pharmaceutical Sciences, 2020, 26(2), 198-202
doi:10.34172/PS.2020.4
https://ps.tbzmed.ac.ir/

Short Communication

Flavone Glycosides from the Aerial Parts of *Stachys lavandulifolia* Vahl

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Article Info

Article History:
Received: 11 September 2019
Accepted: 6 December 2019
ePublished: 27 June 2020

Keywords:
-*Stachys lavandulifolia* Vahl
-Flavone glycoside
-Apigenin
-Luteolin
-Chrysoeriol
-Chlorogenic acid

Abstract

Background: *Stachys lavandulifolia* Vahl is an herbaceous perennial plant which its flowering aerial parts are used traditionally as gastrotonic, spasmolytic, sedative and for the treatment of gastrointestinal disorders. In the present study the aerial parts of this medicinal plant was investigated for its flavonoid glycosides content.

Methods: *n*-butanol fraction derived from hydroalcoholic extract of *S. lavandulifolia* was subjected to phytochemical analysis using chromatography on Sephadex LH-20 and RP-18 silica gel columns. The structures of isolated compounds were identified using ^{1}H-NMR, ^{13}C-NMR and UV spectral analysis.

Results: Four flavone glycosides, chrysoeriol-7-O-β-D-glucopyranoside (**1**), apigenin-7-O-(6″-O-acetyl)-β-D-glucopyranoside (**2**), luteolin-7-O-β-D-glucopyranoside (**3**), apigenin-7-O-β-D-glucopyranoside (**4**), along with apigenin (**5**) and chlorogenic acid (**6**) were isolated from *S. lavandulifolia* aerial parts.

Conclusion: Identification of these phenolic compounds with some known biological activities in *S. lavandulifolia* explains some medicinal properties reported for this species and make scientific rationale for its traditional uses.

Introduction

Stachys lavandulifolia Vahl from Lamiaceae family is an herbaceous perennial plant distributed in Iran, Turkey, Caucasus, Iraq and central Asia.[1] In Iranian folk medicine, the infusion of flowering aerial parts of this plant is known as "Chaye-e-Koohi" and used as gastrotonic, spasmolytic, sedative and for the treatment of gastrointestinal disorders.[2,3] *S. lavandulifolia* has been mentioned as "Marv-azad" or "Marmazad" in Old Persian medicinal literature, useful in some liver and uterus diseases and as liver tonic, gastrotonic and emmenagogue.[4] This species is also used by Turkish people as a sedative and antipyretic, as well as in insomnia, cough, cold and flu.[5] Some biological and pharmacologic properties such as antioxidant, antimicrobial, gastroprotective, spasmolytic, anxiolytic, wound healing, analgesic and anti-inflammatory effects have been documented for *S. lavandulifolia*.[6-11] Moreover, the results of previous clinical trials were indicative to its beneficial effects in abnormal uterine bleeding management (caused by polycystic ovary syndrome) and in oxidative stresses.[12,13] The use of this plant, however, has been cautioned during pregnancy period because of its abortive potential and teratogenic effects.[14,15]

There are some reports in the literature on phytochemical constituents of various extracts of *S. lavandulifolia* in literature.[16-20] Four phenylethanoid glycosides including lavandulifoliosides A and B, verbascoside, and leucosceptoside A, together with one iridoid glycoside named 5-allosyloxy-aucubin have been isolated from the aerial parts of *S. lavandulifolia* by Delazar *et al.*.[16] In another study, acetyl- and butyryl-Cholinesterase and tyrosinase inhibitory activity of different extracts of *S. lavandulifolia* were assessed and monomelittoside, melittoside, stachysolone and arbutin were isolated and reported as its major compounds.[17] Recently, Delnavazi et al. reported the isolation of eight methoxylated flavonoids from chloroform extract of this species, of which chrysosplenetin, kumatakenin and viscosine were found to have higher preferential toxicity against MDA-MB-23 cells in comparison with tamoxifen.[18]

The present study was an attempt to more investigate phytochemical constituents of this medicinal species, specially its flavonoid glycosides content using various chromatographic and spectroscopic methods.

Materials and Methods

Plant material

Aerial parts of *S. lavandulifolia* were collected from Ghotour region (Khoy, West-Azerbaijan Province, Iran) in its flowering stage. The plant voucher specimen was deposited at the herbarium of Institute of Medicinal Plants, ACECR (Academic Center for Education, Culture and Research), Karaj, Iran (Voucher no. 2014 MPIH).

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Extraction and fractionation

The shade-dried and ground plant aerial parts (0.5 kg) were macerated with methanol-water (7:3) (3×8 L each) at the room temperature. The concentrated hydroalcoholic extract was dispersed in water and fractionated successively with chloroform and *n*-butanol using liquid-liquid fractionation method. Fractions were then dried using a rotary evaporator under low pressure at 45 °C.

Isolation and purification of compounds

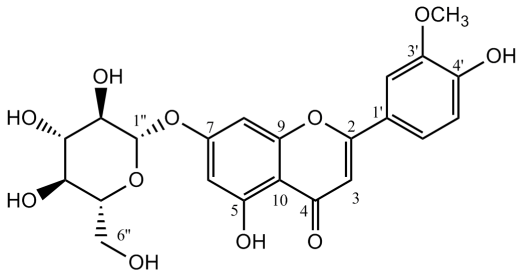
A portion of *n*-butanol fraction (3 g) was divided to nine subfractions (A-I) by column chromatography on Sephadex LH-20 (5×30 cm) using methanol as eluent. Compounds **1** (8 mg) and **2** (3 mg) were isolated from subfractions B (0.3 g) and C (0.1g), respectively, by Sephadex LH-20 column chromatography (2×80 cm) using MeOH-H_2O (8:2). Subfraction E (0.3 g) was eluted on RP18 column (2×20 cm) by MeOH-H_2O (2:8) to get compound **3** (32 mg). Compound **4** (6 mg) was obtained from subfraction G (0.5 g) by chromatography on Sephadex LH-20 column (2×70 cm) using MeOH-H_2O (8:2) as solvent system. Column chromatography of subfraction F (0.5 g) on Sephadex LH-20 column (2×70 cm) using MeOH-H_2O (8:2) resulted in isolation of compound **5** (13 mg). Subfraction F2 (35 mg) was also moved on a RP-18 column (1×20 cm) and eluted with MeOH-H_2O (2:8to 4:6) to get compound 6 (12 mg). In all chromatography steps, fractions were monitored by thin layer chromatography under 254 and 366 UV wavelengths and those with same spots were combined. NMR (Varian INOVA 500 MHz spectrometer (500 MHz for ^{1}H-NMR and 125 MHz for ^{13}C-NMR) and UV (Shimadzu UV-1800) spectral analyses were applied for structure elucidation of isolated compounds.

Results

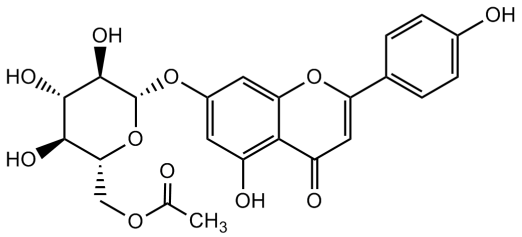
Phytochemical investigation of the hydroalcoholic extract obtained from *S. lavandulifolia* aerial parts led to the isolation and structure elucidation of four flavone glycosides; Chrysoeriol-7-O-β-D-glucopyranoside (Thermopsoside) (**1**), Apigenin-7-O-(6″-O-Acetyl)-β-D-glucopyranoside (**2**), Luteolin-7-O-β-D-glucopyranoside (Cynaroside) (**3**), Apigenin-7-O-β-D-glucopyranoside (Apigetrin) (**4**), along with Apigenin (**5**) and Chlorogenic acid (**6**) (Figure 1). The structures of compounds were established by ^{1}H-NMR, ^{13}C-NMR and UV spectral analyses comparing with those published in the literature.[19-21]

Spectral data for isolated flavone glycosides

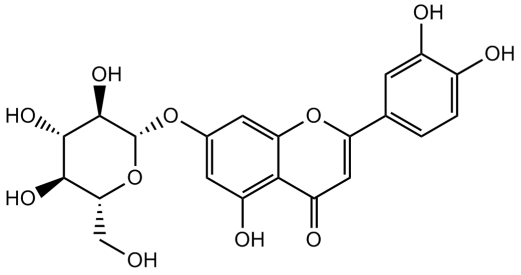
Compound **1**; *Chrysoeriol-7-O-β-D-glucopyranoside* (*Thermopsoside*), ^{1}H-NMR (DMSO-d_6, 500 MHz): δ ppm 7.60 (1H, *br d*, *J*= 8.1 Hz, H-6'), 7.59 (1H, *br s*, H-2'), 7.01 (1H, *s*, H-3),6.95 (1H, *d*, *J*= 8.1 Hz, H-5'), 6.88 (1H, *br s*, H-8), 6.46 (1H, *br s*, H-6), 5.07 (1H, *d*, *J*= 7.2 Hz, H-1"), 3.90 (3H, *s*, OCH_3), 3.1-3.8 (6H, *overlapped peaks*, H-2" to H-6"); ^{13}C-NMR (DMSO-d_6, 125 MHz): δ ppm 181.84 (C-4), 164.04 (C-2), 162.96 (C-7), 161.03 (C-5), 156.92 (C-9), 151.8 (C-4'), 146.84 (C-3'), 122.86 (C-1'), 118.73 (C-6'), 113.11 (C-5'), 112.13 (C-2'), 105.35 (C-10), 103.75 (C-3), 99.92 (C-1"), 99.54 (C-6), 94.72 (C-8), 77.12 (C-5"), 76.35 (C-3"), 73.06 (C-2"), 69.54 (C-4"), 60.58 (C-6"), 55.73 (OCH_3). UV spectrum (MeOH, λ_{max}, nm): 268, 342.[21,22]



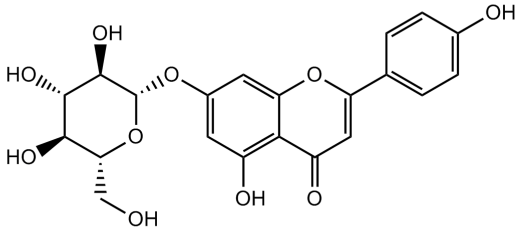
Chrysoeriol-7-O-β-D-glucopyranoside (**1**)



Apigenin-7-O-(6"-Acyl)-β-D-glucopyranoside (**2**)



Luteolin-7-O-β-D-glucopyranoside (**3**)



Apigenin-7-O-β-D-glucopyranoside (**4**)

Figure 1. Flavone glycosides isolated from the hydroalcoholic extract of S. lavandulifolia aerial parts.

Compound **2**; *Apigenin-7-O-(6″-O-Acetyl)-β-D-glucopyranoside*, ^{1}H-NMR (DMSO-d_6, 500 MHz): δ ppm 13.03 (1H, *s*, OH-5), 8.00 (2H, *d*, *J*= 8.5 Hz, H-2',6'), 6.96 (2H, *d*, *J*= 8.5 Hz, H-3',5'), 6.84 (1H, *s*, H-3),6.75 (1H, *br s*, H-8), 6.62 (1H, *br s*, H-6), 5.01 (1H, *d*, *J*= 7.5 Hz, H-1"), 4.32 (1H, *br d*, *J*= 11.7 Hz, H-6"a),4.11 (1H, *dd*, *J*= 11.7, 7.5 Hz, H-6"b), 3.73 (1H, *m*, H-5"), 3.2-3.6 (3H, *overlapped peaks*, H-2" to H-4"), 2.06 (3H, *s*, $COCH_3$); ^{13}C-NMR (DMSO-d_6, 125 MHz): δ ppm 181.95 (C-4), 172.57 ($\underline{C}OCH_3$), 167.58 (C-2), 164.43 (C-7), 162.75 (C-4",5), 156.82 (C-9), 129.58 (C-2",6"), 122.66 (C-1"), 116.04 (C-3",5"), 106.57 (C-10), 105.32 (C-3), 102.63 (C-1"), 98.51 (C-6), 94.99 (C-8), 77.10 (C-3"), 75.78 (C-5"), 74.71 (C-2"), 71.59 (C-4"), 64.00 (C-6"), 20.52 (C-CO$\underline{C}H_3$). UV spectrum (MeOH, λ_{max}, nm): 259, 335.[23,24]

Compound **3**; *Luteolin-7-O-β-D-glucopyranoside* (*Cynaroside*), ^{1}H-NMR (DMSO-d_6, 500 MHz): δ ppm 13.00 (1H, *s*, OH-5), 7.45 (1H, *dd*, *J*= 8.3, 1.6 Hz, H-6'), 7.43 (1H, *d*, *J*= 1.6 Hz, H-2'), 6.90 (1H, *d*, *J*= 8.3 Hz, H-5'), 6.80 (1H, *d*, *J*= 1.2 Hz, H-8), 6.76 (1H, *s*, H-3), 6.45 (1H, *d*, *J*= 1.2 Hz, H-6), 5.09 (1H, *d*, *J*= 7.5 Hz, H-1"), 3.0-3.8 (6H, *overlapped peaks*, H2" to H6"); ^{13}C-NMR (DMSO-d_6, 125 MHz): δ ppm 181.76 (C-4), 164.52 (C-2), 162.89 (C-7), 161.09 (C-5), 156.88 (C-9), 150.36 (C-4'), 145.87 (C-3'), 120.98 (C-1'), 119.09 (C-6'), 116.00 (C-5'), 113.31 (C-2'), 105.30 (C-10), 103.00 (C-3), 99.97 (C-1"), 99.55 (C-6), 94.76 (C-8), 77.12 (C-5"), 76.37 (C-3"), 73.08 (C-2"), 69.58 (C-4"), 60.63 (C-6"). UV spectrum (MeOH, λ_{max}, nm): 256, 267 (sh), 346.[21,25]

Compound **4**; *Apigenin-7-O-β-D-glucopyranoside* (*Apigetrin*), ^{1}H-NMR (DMSO-d_6, 500 MHz): δ ppm 12.99 (1H, *s*, OH-5), 7.89 (2H, *d*, *J*= 8.5 Hz, H-2',6'), 6.90 (2H, *d*, *J*= 8.5 Hz, H-3',5'), 6.82 (1H, *s*, H-3), 6.79 (1H, *br s*, H-8), 6.41 (1H, *br s*, H-6), 5.06 (1H, *d*, *J*= 7.4 Hz, H-1"), 3.1-3.7 (6H, *overlapped peaks*, H-2" to H-6"); ^{13}C-NMR (125 MHz, DMSO-d_6): δ ppm 182.3 (C-4), 164.2 (C-7), 163.1 (C-2), 161.7 (C-9), 153.1 (C-5), 150.1 (C-4'), 128.4 (C-2',6'), 121.4 (C-1'), 116.2 (C-3',5'), 105.6 (C-10), 103.1 (C-3), 101.1 (C-1"), 99.3 (C-6) 95.2 (C-8), 76.8 (C-5"), 75.8 (C-3"), 73.2 (C-2"), 69.6 (C-4"), 60.7 (C-6"). UV spectrum (MeOH, λ_{max}, nm): 268, 332.[25,26]

Discussion

Thermopsoside (**1**), Apigenin-7-O-(6″-O-Acetyl)-β-D-glucopyranoside (**2**), Cynaroside (**3**), Apigetrin (**4**), Apigenin (**5**) and Chlorogenic acid (**6**) are the compounds isolated from *S. lavandulifolia* in the present study. Although phytochemical constituents of *S. lavandulifolia* aerial parts have been investigated in some previous studies,[16-20] this is the first report on isolation of four flavone glycosides (**1**-**4**) and chlorogenic acid (**6**) from this medicinal species. A literature review on isolated compounds showed that some of them have been documented to possess pharmacological activity and health promoting effects.[27-36] Apigenin-7-O-glucoside (apigetrin) and luteolin-7-O-glucoside (cynaroside) have been shown to have protective activity against carbon tetrachloride-induced hepatic injury, possibly through their antioxidant properties as ROS scavengers.[27,28] Moreover, significant protective effects of luteolin-7-O-glucoside and its aglycon have been demonstrated against oxidative damage induced by *t*-butyl hydroperoxidein HepG2 cultured cells.[29] In 2013, Chung and Young-Sun showed luteolin and luteolin-7-O-glucoside inhibit lipopolysaccharide-induced inflammatory responses through modulation of NF-κB/AP-1/PI3K-Akt signaling cascades in RAW 264.7 cells.[30] Luteolin was found more potent than its glucoside for anti-inflammatory activity in former study. In another study, productions of nitric oxide and prostaglandin E2 (PGE2) were significantly suppressed by luteolin-7-O-glucoside (20 μM) in bacterial lipopolysaccharide activated-mouse macrophage RAW264.7 cells without cytotoxic effects.[31] luteolin-7-O-glucoside has been reported to have a protective effect against cisplatin-induced kidney injury using HK-2 cell (human proximal tubule cell line) and an animal model.[32] It has also been reported that pretreatment of luteolin-7-O-glucoside (25 mg/kg, p.o.) for 4 days had significant gastroprotective effect against ethanol induced gastric injury in rats.[33]

Anxiolytic potential of apigenin-7-O-glucoside isolated from *Stachys tibetica* Vatke was evaluated by Kumar and Bhar using Elevated plus-maze test in rat.[34] The results showed oral administration of apigenin-7-O-glucoside (2.5 and 5 mg/kg) had a significant anxiolytic activity, comparable to apigenin (5 mg/kg) and diazepam (1 mg/kg).[34] Modulation of $GABA_A$ receptors has been considered as a mechanism for anxiolytic activity of apigenin and its derivatives.[34] Interestingly, Apigenin has been identified as a anxiolytic principle of *S. lavandulifolia* in a bioactivity guided isolation approach by Rabbani *et al.*[35]

Chlorogenic acid (5-O-Caffeoylquinic acid) is a most caffeoylquinic acid derivative in natural resources.[30] This polyphenol compound has lately received special attention by researchers due to its beneficial health effects in cardiovascular disease (CVD), diabetes, obesity, cancer prevention, and hepatic steatosis, which are related to antioxidant and anti-inflammatory effects, as well as its potential in regulation of glucose and lipid metabolism.[36]

Conclusion

The result of this study introduce *Stachys lavandulifolia* as valuable source of natural phenolic compounds. The presence of mentioned bioactive compounds (**1**-**6**) in *S. lavandulifolia* may be correlated with some biological activities such as gastroprotective, antioxidant, anti-inflammatory and anxiolytic effects reported in literature for this species and also provide scientific rationales for some traditional uses of *S. lavandulifolia* as liver tonic, sedative and in treatment of gastrointestinal conditions.

Conflict of Interests

The authors claim that there is no conflict of interest.

References

1. Jamzad Z. Flora of Iran: Lamiaceae. Tehran:Research Institute of Forests and Rangelands; 2012. p. 213-9.
2. Amin GR. Popular medicinal plants of Iran. Tehran: Iranian Research Institute of Medicinal; 1991. p.126.
3. Zargari A. Medicinal herbs. Vol. 4. Tehran: University of Tehran Press; 1987. p.123.
4. Aghili M. Makhzan-al-Advia. In: Rahimi R, Shams-Ardekani MR, Farjadmand F, editors. Tehran: Tehran University of Medical Sciences Press; 2009. p. 737.
5. Polat R, Cakilcioglu U, Satil F. Traditional uses of medicinal plants in Solhan (Bingöl-Turkey). J Ethnopharmacol. 2013;148(3):951-63. doi:10.1016/j.jep.2013.05.050
6. Işcan G, Demirci B, Demirci F, Göger F, Kirimer N, Köse Y, et al. Antimicrobial and antioxidant activities of *Stachys lavandulifolia* subsp. *lavandulifolia* essential oil and its infusion. Nat Prod Commun. 2012;7(9):1241-4. doi:10.1177/1934578x1200700937
7. Nabavizadeh F, Alizadeh AM, Adeli S, Golestan M, Moloudian H, Kamalinejad M. Gastroprotective effects of *Stachys lavandulifolia* extract on experimental gastric ulcer. Afr J Pharm Pharmacol. 2011;5(2):155-9. doi:10.5897/ajpp10.296
8. Naseri MKG, Adibpour N, Namjooyan F, Rezaee S, Shahbazi Z. Spasmolytic Effect of *Stachys lavandulifolia* Vahl. Crude Methanolic Extract and Fractions on Rat Ileum. Iran J Pharm Res. 2011;10(2):307-12.
9. Rabbani M, Sajjadi SE, Zarei HR. Anxiolytic effects of *Stachys lavandulifolia* Vahl on the elevated plus-maze model of anxiety in mice. J Ethnopharmacol. 2003;89(2-3):271-6. doi:10.1016/j.jep.2003.09.008
10. Pirbalouti AG, Koohpyeh A. Wound Healing Activity of Extracts of *Malva sylvestris* and *Stachys lavandulifolia*. Inter J Biol. 2010;3(1):174-9. doi:10.5539/ijb.v3n1p174
11. Hajhashemi V, Ghannadi A, Sedighifar S. Analgesic and anti-inflammatory properties of the hydroalcoholic, polyphenolic and boiled extracts of *Stachys lavandulifolia*. Res Pharm Sci. 2007;1:92-8.
12. Jalilian N, Modarresi M, Rezaie M, Ghaderi L, Bozorgmanesh M. Phytotherapeutic management of polycystic ovary syndrome: role of aerial parts of wood betony (*stachys lavandulifolia*). Phytother Res. 2013;27(11):1708-13. doi:10.1002/ptr.4921
13. Rahzani K, Malekirad AA, Zeraatpishe A, Hosseini N, Seify SMR, Abdollahi M. Anti-Oxidative Stress Activity of *Stachys lavandulifolia* Aqueous Extract in Human. Cell J. 2013;14(4):314-7.
14. Jafarzadeh L, Asgari A, Golshan-Iranpour F, Kheyri S, Parvin N, RafieianM, et al. Abortificient effects of *Stachys lavandulifolia* Vahl in mice. J Shahrekord Univ Med Sci. 2010;11(4):26-31.
15. Golshan Iranpoor F, Jafarzadeh L, Asgari A. Teratogenic effects of hydroalcoholic extract of *Stachys lavandulifolia* Vahl on the skeletal system and fetal growth in Balb/c mice. J Shahrekord Univ Med Sci. 2012;14(4):21-9. Persian
16. Delazar A, Delnavazi MR, Nahar L, Moghadam SB, Mojarab M, Gupta A, et al. Lavandulifolioside B: a new phenylethanoid glycoside from the aerial parts of *Stachys lavandulifolia* Vahl. Nat Prod Res. 2011;25(1):8-16. doi:10.1080/14786411003754330
17. Tundis R, Bonesi M, Pugliese A, Nadjafi F, Menichini F, Loizzo MR. Tyrosinase, acetyl- and butyryl-cholinesterase inhibitory activity of *Stachys lavandulifolia* Vahl (Lamiaceae) and its major constituents. Rec Nat Prod. 2015;9(1):81-93.
18. Delnavazi MR, Saiyarsarai P, Jafari-Nodooshan S, Khanavi M, Tavakoli S, Yassa N. Cytotoxic Flavonoids from the Aerial Parts of *Stachys lavandulifolia* Vahl. Pharm Sci. 2018;24(4):332-9. doi:10.15171/PS.2018.47
19. Sajjadi SE, Ghanadian SM, Rabbani M, Tahmasbi F. Isolation and identification of secondary metabolites from the aerial parts of *Stachys lavandulifolia* Vahl. Iran J Pharm Res. 2017;16:58-63.
20. Khoigani SR, Rajaei A, Goli SA. Evaluation of antioxidant activity, total phenolics, total flavonoids and LC-MS/MS characterisation of phenolic constituents in *Stachys lavandulifolia*. Nat Prod Res. 2017;31(3):355-8. doi:10.1080/14786419.2016.1233410
21. Harput US, Calis I, Saracoglu I, Donmez A, Nagatsu A. Secondary metabolites from *Phlomis syriaca* and their antioxidant activities. Turk J Chem. 2006;30(3):383-90.
22. Heshmati Afshar F, Delazar A, Nazemiyeh H, Khodaie L, Bamdad Moghaddam S. Phenolic derivatives of *Artemisia spicigera* C Koch growing in Iran. Iran J Pharm Res. 2015;14(4):1241-6.
23. Svehlikova V, Bennett RN, Mellon FA, Needs PW, Piacente S, Kroon PA, et al. Isolation, identification and stability of acylated derivatives of apigenin 7-O-glucoside from chamomile (*Chamomilla recutita* [L] Rauschert). Phytochemistry. 2004;65(16):2323-32. doi:10.1016/j.phytochem.2004.07.011
24. Venditti A, Frezza C, Guarcini L, Foddai S, Serafini M, Bianco A. Phytochemical study of a species with Ethnopharmacological Interest: *Sideritis romana* L. Eur J Med Plants. 2016;12(3):1-9. doi:10.9734/ejmp/2016/23809
25. Guvenalp Z, Ozbek H, Unsalar T, Kazaz C, Demirezer LO. Iridoid, flavonoid, and phenylethanoid glycosides from *Wiedemannia orientalis*. Turk J Chem. 2006;30(3):391-400.
26. Güvenalp Z, Özbek H, Kuruüzüm-Uz A, Kazaz C, Demirezer LÖ. Secondary metabolites from *Nepeta heliotropifolia*. Turk J Chem. 2009;33(5):667-75.
27. Qiusheng Z, Xiling S, Xubo W, Meng S, Changhai W. Protective effects of luteolin-7-glucoside against liver injury caused by carbon tetrachloride in rats. Pharmazie. 2004;59(4):286-9.
28. Zheng QS, Sun XL, Xu B, Li G, Song M. Mechanisms of apigenin-7-glucoside as a hepatoprotective agent. Biomed Environ Sci. 2005;18(1):65-70.
29. Lima CF, Fernandes-Ferreira M, Pereira-Wilson

C. Phenolic compounds protect HepG2 cells from oxidative damage: Relevance of glutathione levels. Life Sci. 2006;79(21):2056-68. doi:10.1016/j.lfs.2006.06.042

30. Park CM, Song YS. Luteolin and luteolin-7-O-glucoside inhibit lipopolysaccharide-induced inflammatory responses through modulation of NF-kappaB/ AP-1/ PI3K-Akt signaling cascades in RAW 264.7 cells. Nutr Res Pract. 2013;7(6):423-9. doi:10.4162/nrp.2013.7.6.423
31. Hu C, Kitts DD. Luteolin-7-O-glucoside from dandelion flower suppress iNOS and COX-2 in RAW 264.7 cells. Mol Cell Biochem. 2004;265(1):107-13. doi:10.1023/b:mcbi.0000044364.73144.fe
32. Nho JH, Jung HK, Lee MJ, Jang JH, Sim MO, Jeong DE, et al. Beneficial effects of cynaroside on cisplatin-induced kidney injury in vitro and in vivo. Toxicol Res. 2018;34(2):133-41. doi:10.5487/tr.2018.34.2.133
33. Antonisamy P, Subash-Babu P, Baskar AA, Alshatwi AA, Aravinthan AA, Ignacimuthu S, et al. Experimental study on gastroprotective efficacy and mechanisms of luteolin-7-O-glucoside isolated from *Ophiorrhiza mungos* L. in different experimental models. J Funct Foods. 2016;25:302-13. doi:10.1016/j.jff.2016.06.003
34. Kumar D, Bhat ZA. Apigenin 7-glucoside from *Stachys tibetica* Vatke and its anxiolytic effect in rats. Phytomedicine. 2014;21(7):1010-4. doi:10.1016/j.phymed.2013.12.001
35. Rabbani M, Sajjadi SE, Karimi-Firozjai M, Ghanadian M. Bioactivity guided isolation of apigenin from *Stachys lavandulifolia* Vahl. in mice with anxiolytic effects. J Herbmed Pharmacol. 2018;7(2):74-8. doi:10.15171/jhp.2018.13
36. Tajik N, Tajik M, Mack I, Enck P. The potential effects of chlorogenic acid, the main phenolic components in coffee, on health: a comprehensive review of the literature. Eur J Nutr. 2017;56(7):2215-44. doi:10.1007/s00394-017-1379-1