Sugar Esters from *Globularia orientalis*

İhsan Çaliş[a,*], Hasan Kirmizibekmez[a], Deniz Tasdemir[a], Otto Sticher[b] and Chris M. Ireland[c]

[a] Department of Pharmacognosy, Faculty of Pharmacy, Hacettepe University, TR-06100 Ankara, Turkey. Fax: 90-312-3114777. E-mail: icalis@hacettepe.edu.tr
[b] Department of Applied Biosciences, Institute of Pharmaceutical Sciences, Swiss Federal Institute of Technology (ETH) Zurich, CH-8057 Zürich, Switzerland
[c] Department of Medicinal Chemistry, University of Utah, Salt Lake City, Utah 84112, USA

* Author for correspondence and reprint requests

Z. Naturforsch. **57c,** 591–596 (2002); received March 12/April 14, 2002

Globularia orientalis, Sugar Esters, Iridoid and Phenylethanoid Glycosides

From the methanolic extract of the underground parts of *Globularia orientalis*, a new antioxidant sugar ester was isolated. The structure of the new compound, globularitol (**1**), was identified as 6-*O*-feruloyl-β-D-glucopyranosyl-(1→6)-glucitol by spectroscopic methods (1D and 2D NMR, ESI- and FAB-MS) and confirmed by chemical means.

Introduction

The genus *Globularia* (Globulariaceae) is represented by eight species in Turkish flora (Davis, 1982), some members of which (*G. alypum*, *G. trichosantha*) are well known in Anatolian folk medicine (Baytop, 1984; Sezik, 1991). As part of our continuing search for bioactive new natural products from Turkish *Globularia* species (Calis *et al*., 1999 and 2001), we investigated *Globularia orientalis*. Methanolic extracts of both aerial and the underground parts of this plant exhibited significant antioxidant effects, based on the scavenging activity of the stable 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical. Bioactivity-guided isolation of the underground parts afforded a new sugar ester, globularitol (**1**), along with the known sucrose esters 6-*O*-caffeoyl-β-D-fructofuranosyl-(2→1)-α-D-glucopyranoside (**2**) and 6-*O*-feruloyl-β-D-fructofuranosyl-(2→1)-α-D-glucopyranoside (**3**), 10-*O*-benzoylcatalpol and geniposide. Activity-directed fractionation of the aerial parts, using the same antioxidant assay, furnished an acetophenone glycoside (picein), eight iridoid glycosides; asperuloside, alpinoside, aucubin, catalpol, geniposidic acid, 10-*O*-benzoylcatalpol, globularin, melampyroside and three phenylethanoid glycosides (calceolarioside A, verbascoside, leucosceptoside A). In this report, we describe isolation and structure elucidation of globularitol (**1**). The antioxidant activity of the isolates will also be presented.

Material and Methods

General experimental procedures

Optical rotations were measured on a Rudolph autopol IV Polarimeter using a sodium lamp operating at 589 nm. UV spectra were recorded on a Shimadzu UV-160A spectrophotometer. IR spectra (KBr) were measured on a Perkin Elmer 2000 FT-IR spectrometer. A Varian instrument (500 MHz for ^{1}H and 125 MHz for ^{13}C) with a Nalorac MDBG 3 mm probe was used to acquire NMR data. Negative and positive mode ESIMS were recorded on a Finnigan TSQ 7000 instrument. FABMS measurements were performed on a Finnigan MAT95 spectrometer. TLC analyses were carried on silica gel 60 F_{254} precoated plates (Merck, Darmstadt); detection by 1% vanillin/H_2SO_4. For MPLC separations, a Lewa M5 pump, a LKB 17000 Minirac fraction collector, a Rheodyne injector, and a Büchi column (column dimensions 2.6 × 46 cm, and 1.8 × 35 cm) were used. Silica gel 60 (0.063–0.200 mm; Merck, Darmstadt) and polyamide (Woelm; Eschwege, Germany) were utilized for open CC. MPLC separations were performed over LiChroprep C-18 (Merck)

0939–5075/2002/0700–0591 $ 06.00

material. Gentiobiose and isomaltitol were purchased from Merck and Fluka, respectively.

Plant material

Globularia orientalis L. was collected from Ankara, Bala, Turkey, in June 1998. A voucher specimen (HUEF 98008) has been deposited at the Herbarium of the Department of the Pharmacognosy, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey.

Extraction and isolation

The air-dried aerial parts (200 g) of *G. orientalis* were extracted with MeOH (2 × 900 ml) at 45° C. The combined methanolic extracts were evaporated to dryness *in vacuo* (41 g, yield 20.5%). The crude extract was dissolved in H_2O and partitioned against CH_2Cl_2. The freeze-dried H_2O phase (36.7 g) was subjected ton vacuum liquid chromatography (VLC) over Si gel, using a CH_2Cl_2–MeOH–H_2O gradient system (90:10:1 to 60:40:4 v/v/v) to yield fractions A–H. Fraction C (3.1 g) was subjected to C_{18} medium pressure liquid chromatography (C_{18}-MPLC) using increasing amount of MeOH in H_2O (30–60%) to afford picein (10 mg), asperuloside (26 mg), 10-*O*-benzoylcatalpol (672 mg), a mixture (1:1) of globularin and melampyroside (786 mg) and impure calceolarioside A (148 mg). The latter was further chromatographed by Si gel CC eluting with $CHCl_3$–MeOH–H_2O (90:10:1 to 80:20:1 v/v/v) to yield 8 mg of pure calceolarioside A. Fraction D (6.2 g) was similarly separated by C_{18}-MPLC using 5 to 100% MeOH in H_2O as eluent to give catalpol (197 mg), aucubin (31 mg) and six additional fractions D_3–D_8. Fraction D_3 (59 mg) was rechromatographed on silica CC ($CHCl_3$–MeOH–H_2O, 80:20:2 to 70:30:3 v/v/v) to yield additional amounts of picein (28 mg) and geniposidic acid (11 mg). Fraction D_5 (670 mg) was applied to a Si gel column eluting with $CHCl_3$–MeOH–H_2O mixtures (80:20:1 to 61:32:7 v/v/v) and gave two fractions D_{5a} (89 mg) and D_{5b} (300 mg). Fraction D_{5b} was purified by C_{18}-MPLC using 5% stepwise gradient elution from 10% to 45% MeOH in H_2O to obtain alpinoside (42 mg), calceolarioside A (9 mg) and verbascoside (67 mg). Leucosceptoside A (38 mg) was obtained by Si gel CC of fraction D_7 (136 mg).

The air-dried underground parts (330 g) of *G. orientalis* were also extracted with MeOH (2 × 1500 ml) and filtered. The filtrate was concentrated to dryness in *vacuo* (24 g, yield 7.3%). The extract was subjected to Polyamide CC eluting with a 10% stepwise gradient from H_2O to MeOH to give fractions A–K. Fraction C (5.0 g) was subjected to C_{18}-MPLC employing H_2O–MeOH mixtures (5–50% MeOH) and yielded eight fractions, C_1–C_8. Fraction C_2 (161 mg) was rechromatographed over Si gel eluting with CH_2Cl_2–MeOH–H_2O (70:30:3 v/v/v) to give 10-*O*-benzoylcatalpol (43 mg). Fraction C_4 (73 mg) was likewise applied to a Si gel column to afford 6-*O*-caffeoyl-β-D-fructofuranosyl-(2→1)-α-D-glucopyranoside (**2**, 12 mg). Repeated chromatography of fraction C_5 (340 mg) by Si gel CC employing the same mobile phase gave 6-*O*-feruloyl-β-D-fructofuranosyl-(2→1)-α-D-glucopyranoside (**3**, 114 mg) and four additional fractions, C_{5a}–C_{5d}. Fraction C_{5a} (23 mg) afforded geniposide (9 mg) by Si gel CC (CH_2Cl_2–MeOH–H_2O, 90:10:1 v/v/v). Fr C_{5d} (30 mg) was passed through a Silica column employing an isocratic $CHCl_3$–MeOH–H_2O mixture (70:30:3 v/v/v) and afforded globulariol (**1**, 10 mg).

Globulariol (**1**): Amorphous yellowish solid; $[\alpha]_D^{20}$ −22° (*c* = 0.1, MeOH); ESI-MS *m/z*: 519 $[M-H]^-$; FAB-MS *m/z*: 543 $[M+Na]^+$, HR-FAB-MS *m/z*: calcd for $C_{22}H_{32}O_{14}Na$: 543.1690. Found: 543.1725; UV λ_{max} (MeOH, nm): 217, 235, 295 (sh), 323; υ_{max} (KBr, cm^{-1}) 3372 (OH), 1698 (C=O), 1635 (C=C), 1600 and 1519 (aromatic ring), 1020 (C–O–C); ^{1}H-NMR (500 MHz, CD_3OD): Table I; ^{13}C-NMR (CD_3OD, 125 MHz): Table I.

Alkaline Hydrolysis of **1**. Compound **1** (2 mg) was treated with 5% KOH in MeOH at 80 °C for 2 h. After neutralization with methanolic HCl (1%), the reaction mixture was evaporated to dryness. The residue was dissolved in H_2O and extracted three times with *n*-BuOH. The combined *n*-BuOH extracts were concentrated and compared with gentiobiose (β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside), isomaltitol (α-D-glucopyranosyl-(1→6)-glucitol) and the reduction product of gentiobiose (β-D-glucopyranosyl-(1→6)-glucitol (**4**) by TLC, using two solvent systems (CH_2CI_2–MeOH–H_2O, 60:40:4 and 50:50:5) and metaperiodate (sodium)-benzidine as spray reagent (Stahl, 1969).

Preparation of β-D-glycopyranosyl-(1→6)-glucitol (**4**). Gentiobiose (20 mg) was dissolved in H_2O.

50 mg of $NaBH_4$ was added to this mixture and was kept overnight at room temperature. After neutralization with methanolic HCI (1%), the reaction mixture was evaporated to dryness. The residue was dissolved in H_2O and extracted three times with *n*-BuOH. Evaporation of the *n*-BuOH phase yielded **4**.

β-D-glycopyranosyl-(1→6)-glucitol (**4**). $[\alpha]_D^{20}$ −2° (*c* = 0.1, H_2O). ^{1}H-NMR (300 MHz, D_2O) δ: 4.53 (1H, d, *J* = 7.2 Hz, H-1), 4.14 (1H, br d, *J* = 10.2, H-6′a), 3.92 (1H, br d, *J* = 12.0 Hz, H-6a), 3.75 (overlapped, H-6′b), 3.70 (overlapped, H-6b), 3.85–3.60 (6H, overlapped, H_2-1′–H-5′), 3.50 (overlapped, H-5), 3.49 (1H, t, *J* = 9.2 Hz, H-3), 3.42 (1H, t, *J* = 9.2 Hz, H-4), 3.32 (1H, dd, *J* = 9.2, 7.2 Hz, H-2). ^{13}C-NMR (75 MHz, D_2O) δ: 105.7 (d, C-1), 78.7 (d, C-5), 78.4 (d, C-3), 76.1 (d, C-2), 75.7 (d, C-5′), 74.2 (t, C-6′), 73.6 (d, C-4′), 72.6 (d, C-2′), 72.5 (d, C-4), 72.4 (d, C-3′), 65.2 (t, C-1′), 63.5 (t, C-6).

Reduction of DPPH radical. Methanolic solutions (0.1%) of all isolates were chromatographed on a Si gel TLC plate using a $CHCI_3$–MeOH–H_2O (61:32:7) solvent system. After drying, TLC plates were sprayed with a 0.2% DPPH (Fluka) solution in MeOH. Compounds showing a yellow-on-purple spot were regarded as antioxidant (Cuendet *et al.*, 1997).

Table I. ^{13}C- and ^{1}H-NMR (CD_3OD, 125 MHz for ^{13}C and 500 MHz for ^{1}H NMR) data and HMBC correlations for **1***.

C/H Atom		δ_C ppm	δ_H ppm, *J* (Hz)	HMBC (H→C)
Glucose				
1	CH	105.0	4.36 d (7.8)	C-6′
2	CH	75.2	3.27 dd (7.8, 9.0)	C-1, C-3
3	CH	77.7	3.39 t (9.0)	C-4
4	CH	71.7	3.37 t (9.0)	C-3, C-6
5	CH	75.6	3.54 ddd (9.0, 5.5, 2.0)	C-4
6	CH_2	64.6	4.52 dd (12.1, 2.0)	C-4
			4.30 dd (12.1, 5.5)	C=O, C-5
Glucitol				
1′	CH_2	65.2	3.79†	C-2′, C-3′
			3.61†	C-2′, C-3′
2′	CH	71.1	3.77†	C-1′
3′	CH	70.9	3.76†	C-1′
4′	CH	71.6	3.77†	
5′	CH	72.9	3.66†	C-3′
6′	CH_2	73.7	4.15 dd (10.5, 2.3)	
			3.72 dd (10.5, 6.3)	C-1
Ferulic acid				
1″	C	127.7		
2″	CH	111.7	7.19 d (2.0)	C-β, C-4″, C-6″
3″	C	149.5		
4″	C	151.0		
5″	CH	115.1	6.80 d (8.2)	C-1″, C-3″, C-4″
6″	CH	124.2	7.07 dd (8.2, 2.0)	C-β, C-2″, C-4″
α	CH	116.6	6.39 d (16.0)	C=O, C-1″
β	CH	147.2	7.64 d (16.0)	C=O, C-2″, C-6″
C=O	C	169.2		
OCH_3	CH_3	56.5	3.89 s	C-3″

* The ^{13}C and ^{1}H NMR assignments were based on gCOSY, gHSQC and gHMBC experiments.
† Multiplicity of the signal is unclear due to overlapping.

Results and Discussion

The methanolic extract of the air-dried stocks of *G. orientalis* was fractionated by polyamide column chromatography (CC) followed by C_{18}-MPLC and Si gel CC. Globularitol (**1**) was obtained as a yellowish amorphous powder. The positive- and negative ion FAB- and ESI mass spectra exhibited pseudomolecular ion peaks $[M+Na]^+$ and $[M-H]^-$ at *m/z* 543 and *m/z* 519, respectively. This observation, combined with the ^{1}H- and ^{13}C-NMR data (see Table I), indicated the molecular formula of $C_{22}H_{32}O_{14}$, thus, the presence of seven degrees of unsaturation. UV absorption bands at λ_{max} 217, 235, 295 (sh) and 323 nm indicated the phenolic nature of **1**. The IR spectrum revealed absorption bands for hydroxyl (3372 cm^{-1}), α,β-unsaturated ester carbonyl (1698 cm^{-1}), olefinic (1635 cm^{-1}), aromatic (1600 and 1519 cm^{-1}) and ether (1020 cm^{-1}) functionalities. The ^{13}C-NMR spectrum exhibited 22 distinct resonances. When taken together with the ^{1}H-NMR, the DEPT-135 and proton-detected gHSQC spectral data, the presence of one methoxy, three methylene and fourteen methine resonances could be assigned for **1**. The remaining quaternary carbons were assignable to a carbonyl (δ 169.2) and three quaternary aromatic carbons two of which are oxygenated (δ 127.7, 149.5, 151.0). The ^{1}H-NMR spectrum of **1** exhibited signals for three aromatic protons at δ 7.19 (d, *J* = 2.0 Hz), 7.07 (dd, *J* = 2.0, 8.2 Hz) and 6.80 (d, *J* = 8.2 Hz) as an ABX system, and two olefinic protons at δ 7.64 and 6.39 as an AX system (J_{AX} = 16.0 Hz). These signals, plus the methoxy singlet at δ 3.89 were consistent with the presence of a *trans*-ferulic acid moiety. Since the feruloyl moiety accounts for six degrees of unsaturation, **1** had to have one additional ring. An an-

omeric proton signal appeared at δ 4.36 (d, H-1) and the resonances in the region of δ 3.27–4.52 along with the corresponding carbon signals inferred from the gHSQC spectrum, suggested the presence of a glucopyranose unit. The β position of the glucose was judged from the large coupling constant value ($J_{1,2}$ = 7.8 Hz) of H-1. This left six ^{13}C signals to be assigned. The DEPT-135 spectrum contained signals for two methylene and four methines in the region of δ 65.2–73.7, but no anomeric carbon resonance around δ 100, indicating the second sugar to be an acyclic hexitol. From this data, associated with the interpretation of the gCOSY spectrum, the hexitol was identified as glucitol (Colson *et al.*, 1975). The gHMBC (J = 8 Hz) experiment (see Table I) permitted the determination of the glycosidic linkages. The feruloyl group was positioned at C-6 of the glucose on the basis of obvious deshielding of both H_2-6 and C-6 (δ_H 4.52 dd, J = 12.1, 2.0 Hz, δ_H 4.30 dd, J = 12.1, 5.5 Hz; δ_C 64.6) and the observed long range correlations between H_2-6 and the carbonyl resonance (δ 169.2). The cross-peaks observed between the anomeric proton of glucose (δ 4.36) and the C-6′ (δ 73.7) of the glucitol unit led to the identification of carbohydrate portion of **1** as β-D-glucopyranosyl-(1→6)-glucitol. In order to confirm the proposed sugar moiety, compound **1** was subjected to alkaline hydrolysis (5% methanolic KOH). The adduct was co-TLCed with gentiobiose (β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside), isomaltitol (α-D-glucopyranosyl-(1→6)-glucitol) and β-D-glucopyranosyl-(1→6)-glucitol (**4**), which was prepared by reduction of gentiobiose. The alkaline hydrolysis product of **1** gave a spot which had the same R_f value with that of **4** in two different TLC solvent systems. Furthermore, the ^1H- and ^{13}C-NMR data of **4** were found to be identical with the carbohydrate chain of **1** (see Material and Methods). Hence, the structure of compound **1** was established as 6-*O*-feruloyl-β-D-glucopyranosyl-(1→6)-glucitol.

Additionally, the underground parts of *G. orientalis* yielded two known sucrose esters, 6-*O*-caffeoyl-β-D-fructofuranosyl-(2→1)-α-D-glucopyranoside (**2**) (Wang *et al.*, 1999), 6-*O*-feruloyl-β-

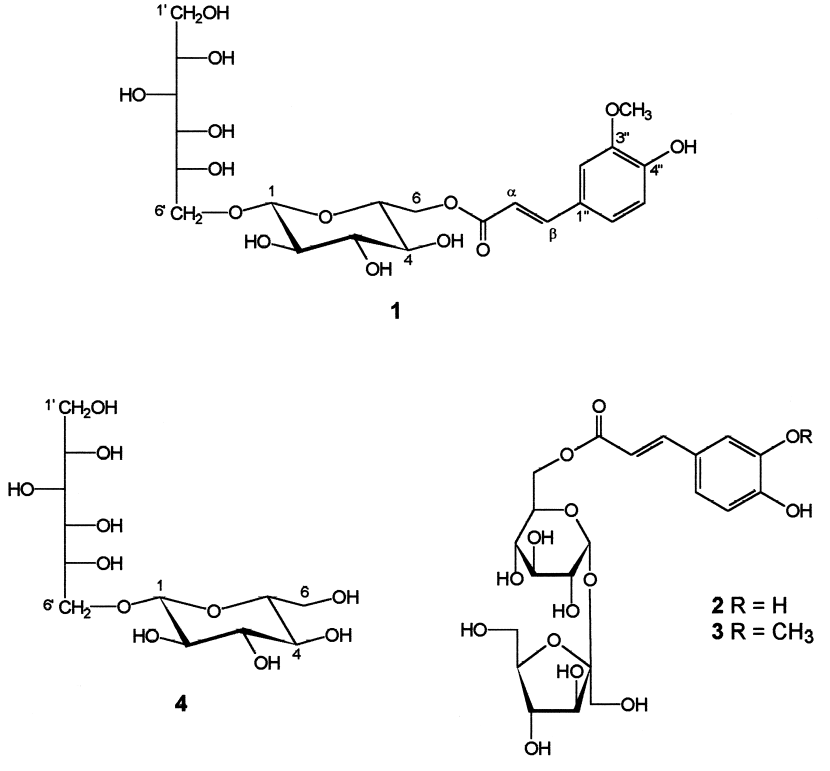

Fig. 1. Sugar esters (**1–3**) from *G. orientalis* and β-D-glucopyranosyl-(1→6)-glucitol (**4**).

D-fructofuranosyl-(2→1)-α-D-glucopyranoside (**3**) (Bokern *et al*., 1991), 10-*O*-benzoylcatalpol (Foderaro *et al*., 1992) and geniposide (Inouye *et al*., 1969) were also isolated and identified by comparison of their spectral data with published values. The aerial parts of *G. orientalis* afforded an acetophenone glycoside, picein (Junior, 1984), eight iridoid glycosides; asperuloside (Otsuka *et al*., 1991), alpinoside (Jensen *et al*., 1996), aucubin (Bianco *et al*., 1983), catalpol (Chaudhuri and Sticher, 1981), geniposidic acid (Bianco *et al*., 1983; Akdemir and Calis, 1991), 10-*O*-benzoylcatalpol (Foderaro and Stermitz, 1992), globularin (Chaudhuri and Sticher, 1981), melampyroside (Chaudhuri and Sticher, 1980) and three phenylethanoid glycosides, calceolarioside A (Nicoletti *et al*., 1986), verbascoside (Sticher and Lahloub, 1982) and leucosceptoside A (Calis *et al*., 1988).

The antioxidant property of the isolates was tested using 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical (Takao *et al*., 1994; Cuendet *et al*., 1997). Compounds **1**, **2**, **3**, calceolarioside A, verbascoside, and leucosceptoside A showed antioxidant potential (yellow-on-purple spot) indicating their ability to efficiently scavenge free radicals. Similar sucrose esters from *Polygonum lapathifolium* have recently been reported to show significant inhibitory effects on the Epstein-Barr virus early antigen activation by tumor-promoters (Takasaki *et al*., 2001).

It is interesting that the underground parts of *G. orientalis* contain only simple caffeoyl sugar esters, whereas the aerial parts contain phenylethanoid glycosides which include an additional phenylethanol moiety as aglycone. However, the ability of both type of compounds to scavenge free radicals might indicate their importance for the welfare of the plant.

Acknowledgments

The authors thank Prof. Dr. Hayri Duman, Gazi University, Ankara, for authentification of the plant material. We also acknowledge Dr. Elliot Rachlin and Dr. Vajira Nanayakkara, University of Utah, for recording mass spectra.

Akdemir Z. and Calis I. (1991), Iridoid and phenylpropanoid glycosides from *Pedicularis pontica Boiss. Doga – Tr. J. Pharmacy* **1**, 67–75.

Baytop T. (1984), Therapy with Medicinal Plants (Past and Present). Istanbul University Publications, Istanbul, No. 3255, pp. 419.

Bianco A., Passacantilli P., Polidori G., Nicoletti M. and Messana I. (1983), NMR spectroscopy of epimeric pairs of glucosidic iridoids from Rubiaceae. Gazz. Chim. Ital. **113**, 829–834.

Bokern M., Heuer S., Wray V., Witte L., Macek T., Vanek T. and Strack D. (1991), Ferulic acid conjugates and betacyanins from cell cultures of *Beta vulgaris*. Phytochemistry **30**, 3261–3265.

Calis I., Kirmizibekmez H. and Sticher O. (2001), Iridoid glycosides from *Globularia trichosantha*. J. Nat. Prod. **64**, 60–64.

Calis I., Kirmizibekmez H., Rüegger H. and Sticher O. (1999), Phenylethanoid glycosides from *Globularia trichosantha*. J. Nat. Prod. **62**, 1165–1168.

Calis I., Saracoglu I., Kitagawa S. and Nishibe S. (1988), Phenylpropanoid glycosides isolated from *Rhynchocorys stricta* (Scrophulariaceae). Doga Tu J. Med. Pharm. **12**, 234–238.

Chaudhuri R. K. and Sticher O. (1980), Globularifolin, a new acyl iridoid glucoside from *Globularia cordifolia*. Helv. Chim. Acta **63**, 117–120.

Chaudhuri R. K. and Sticher O. (1981), New iridoid glycosides and a lignan diglucoside from *Globularia alypum* L. Helv. Chim. Acta **64**, 3–15.

Colson P., Slessor K. N., Jennings H. J. and Smith I. C. P. (1975), A carbon-13 nuclear magnetic resonance study of chlorinated and polyol analogs of glucose and related oligomers. Can. J. Chem. **53**, 1030–1037.

Cuendet M., Hostettman K., Potterat O. and Dyatmiko W. (1997), Iridoid glucosides with free radical scavenging properties from *Fagraea blumei*. Helv. Chim. Acta **80**, 1144–1152.

Davis P. H. (1982), "Flora of Turkey and East Aegean Islands," University Press: Edinburgh, Vol. **7**, pp. 27–31.

Foderaro T. A. and Stermitz F. R. (1992), Iridoid glycosides from *Penstemon* species: A C-5, C-9 trans iridoid and C-8 epimeric pairs. Phytochemistry **31**, 4191–4195.

Inouye H., Saito S., Taguchi H. and Endo T. (1969), Two new iridoglucosides gardenoside and geniposide from *Gardenia jasminoide*. Tetrahedron Lett. **28**, 2347–2348.

Jensen S. R., Olsen C. E., Rahn K.and Rasmussen J. H. (1996), Iridoid Glucosides in *Plantago alpina* and *P. altissima*. Phytochemistry **42**, 1633–1636.

Junior P. (1984), Iridoidglucoside und ein acetophenonglucosid aus *Penstemon whippleanus*. Planta Med., **50**, 444–445.

Nicoletti M., Galeffi C., Messana I., Garbarino J. A., Gambaro V., Nyandat E. and Marini-Bettola G. B. (1986), New phenylpropanoid glucosides from *Calceolaria hypericina*. Gazz. Chim. Ital. **116**, 431–433.

Otsuka H., Yoshimura K., Yamasaki K. and Cantoria M. C. (1991), Isolation of 10-*O*-acyl iridoid glucosides from a Philippine medicinal plant, *Oldenlandia corymbosa* L. (Rubiaceae). Chem. Pharm. Bull. **39**, 2049–2052.

Sezik E., Tabata M., Yesilada E., Honda G., Goto K. and Ikeshiro Y. (1991), Traditional medicine in Turkey I. Folk medicine in northeast Anatolia. J. Ethnopharm. **35**, 191–196.

Stahl E. (1969), Thin-Layer Chromatography A Laboratory Handbook. Springer Publ., Berlin, Heidelberg, New York, pp. 885.

Sticher O. and Lahloub M. F. (1982), Phenolic glycosides from *Paulownia tomentosa* bark. Planta Med. **46**, 145–148.

Takao T., Kitatani F., Watanabe N., Yagi A. and Sakata K. (1994), A simple screening method for antioxidants produced by marine bacteria from fish and shellfish. Biosci. Biotech. Biochem. **58**, 1780–1783.

Takasaki M., Kuroki S., Kozuka M. and Konishima T. (2001), New phenylpropanoid esters of sucrose from *Polygonum lapathifolium*. J. Nat. Prod. **64**, 1305–1308.

Wang M., Shao Y., Li J., Zhu N., Rangarajan M., La Voie E. J. and Ho C-T. (1999), Antioxidative phenolic glycosides from sage (*Salvia officinalis*). J. Nat. Prod. **62**, 454–456.