New Phenylethanoid Glycosides from *Veronica pectinata* var. *glandulosa* and Their Free Radical Scavenging Activities

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A known phenylethanoid glycoside, ehrenoside (1), was isolated together with three new phenylethanoid glycosides, verpectoside A (2), B (3) and C (4) from the aerial parts of *Veronica pectinata* var. *glandulosa*. On the basis of spectral analysis (UV, FAB-MS, ^{1}H-, ^{13}C- and 2D-NMR), compounds 2—4 were determined to be 2-(3,4-dihydroxyphenyl)ethyl-*O*-α-L-arabinopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→3)]-(4-*O*-*trans*-feruloyl)-β-D-glucopyranoside, 2-(3,4-dihydroxyphenyl)ethyl-*O*-β-D-glucopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→3)]-(4-*O*-*trans*-caffeoyl)-β-D-glucopyranoside and 2-(3,4-dihydroxyphenyl)ethyl-*O*-β-D-glucopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→3)]-(4-*O*-*trans*-feruloyl)-β-D-glucopyranoside, respectively. Isolated phenylethanoid glycosides exhibited potent radical scavenging activity against the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical.

Key words *Veronica pectinata* var. *glandulosa*; Scrophulariaceae; phenylethanoid glycoside; antioxidant; DPPH

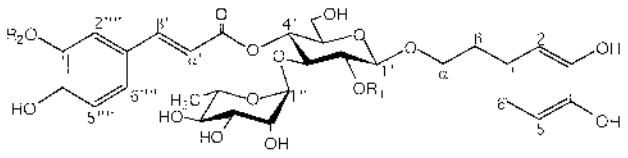
In the flora of Turkey, genus *Veronica* L. (Scrophulariaceae) is represented by 79 species, 26 of which are endemic.[1)] Some of the *Veronica* species are used as diuretics and for wound healing in traditional Turkish medicine.[2)] Several *Veronica* species are used for the treatment of cancer, influenza, hemoptysis, laryngopharyngitis, hernia, and against cough, and respiratory diseases plus as an expectorant and antiscorbutic in different countries.[3—5)] *Veronica* species contain mainly iridoid glucosides, especially benzoic and cinnamic acid esters of catalpol, some phenylethanoid and flavonoid glycosides.[6—11)] Previously, we noted that the water soluble portion of the MeOH extract of *Veronica pectinata* L. var. *glandulosa* RIEK ex M.A. Fisher showed a suppressive effect on nitric oxide production in lipopolysaccharide-stimulated mouse peritoneal macrophages.[12)] As part of the continuation of this work, we report here the isolation and structural elucidation of phenylethanoid glycosides, as well as their free radical scavenging activities, from the active fraction of *Veronica pectinata* var. *glandulosa*.

Results and Discussion

Compound **1** was obtained as an amorphous powder with negative optical rotation ($[\alpha]_D^{23}$ −58°, MeOH). Its structure was identified as ehrenoside by comparison of its spectral data with those reported in literature.[13)]

Compound **2** was isolated as an amorphous powder with negative optical rotation ($[\alpha]_D^{23}$ −59°, MeOH). The molecular formula of **2**, $C_{35}H_{46}O_{19}$, was established by high resolution (HR)-FAB-MS. Its ^{1}H- and ^{13}C-NMR spectra closely resembled those of **1**, except for the presence of a methoxy group (δ_H 3.88, s; δ_C 56.46 q) and signals due to the acyl moiety. The location of the methoxy group of **2** was determined by the NMR spectral comparison (Tables 1, 2) of **2** and **1**, and by nuclear Overhauser effect spectroscopy (NOESY) correlation between δ 3.88 and the H-2‴′ signal [δ 7.20, (1H d, J=2.1 Hz)]. These indicated that compound **2** contained (*E*)-feruloyl instead of (*E*)-caffeoyl as an acyl ester moiety. Furthermore, the above deduction was supported by a heteronuclear multiple bond correlation (HMBC) experiment (Fig. 2). From the above results, compound **2** was determined to be 2-(3,4-dihydroxyphenyl)ethyl-*O*-α-L-arabinopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→3)]-(4-*O*-*trans*-feruloyl)-β-D-glucopyranoside, and was termed verpectoside A.

Compound **3** was obtained as an amorphous powder ($[\alpha]_D^{23}$ +135°, MeOH) and assigned the molecular formula $C_{35}H_{46}O_{20}$ by HR-FAB-MS. The ^{1}H- and ^{13}C-NMR spectra of **3** resembled those of **1**. The ^{13}C-NMR spectrum of **3**, however, lacked signals for the α-L-arabinopyranosyl moiety in **1**, and instead showed signals of a characteristic hexosyl moiety in **3**. In the ^{1}H-NMR spectrum, the coupling constant of the anomeric proton of the hexosyl moiety was 7.6 Hz (δ 4.59 d). These data suggested that compound **3** had two β-D-glucose and one α-L-rhamnose as sugar units. The complete assignment of all proton and carbon resonances was based on the results of ^{1}H–^{1}H shift correlation spectroscopy (^{1}H–^{1}H-COSY), ^{1}H–^{13}C-heteronuclear multiple quantum coherence (^{1}H–^{13}C-HMQC) and HMBC experiments. HMBC correlations between δ_C 102.85 d (H-1′)/δ_H 3.74 t (H-2′), δ_C 102.85 d (H-1′)/δ_H 4.00 t (H-3′) and δ_C 103.76 d (H-1‴)/δ_H 3.43 dd (H-3‴) to differentiate the inner and terminal glucose, and δ_H 4.59 d (H-1‴)/δ_C 82.29 d (C-2′) and δ_H 5.19 d (H-1″)/δ_C 81.42 d (C-3′) to determine the sequence, confirmed the suggested structure. Furthermore, the caffeoyl group was positioned at C-4′ of the glucose on the basis of strong deshielding on the H-4′ proton of the inner glucose unit (δ 4.94 t,



1 R_1 = α-L-arabinopyranose, R_2 = H
2 R_1 = α-L-arabinopyranose, R_2 = CH_3
3 R_1 = β-D-glucopyranose, R_2 = H
4 R_1 = β-D-glucopyranose, R_2 = CH_3

Fig. 1. The Chemical Structures of Isolated Compounds (**1**—**4**)

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Table 1. ^{1}H-NMR Spectral Data of Compounds **1**—**4** (500 MHz, CD_3OD)

H	1	2	3	4
Aglycone				
2	6.74 d (2.1)	6.74 d (2.1)	6.74 d (2.0)	6.76 d (2.1)
5	6.68 d (7.9)	6.68 d (8.0)	6.68 d (8.0)	6.68 d (7.9)
6	6.57 dd (7.9, 2.1)	6.57 dd (8.0, 2.1)	6.59 dd (8.0, 2.0)	6.58 dd (7.9, 2.1)
α	3.67 m	3.68 m	3.70 m	3.70 m
	4.07 m	4.08 m	4.10 m	4.10 m
β	2.78 t (7.1)	2.78 t (7.3)	2.78 t (7.3)	2.78 t (7.1)
Glc				
1′	4.54 d (7.6)	4.54 d (7.6)	4.59 d (7.6)	4.59 d (8.0)
2′	3.67 t (8.6)	3.67 t (9.0)	3.74 t (9.5)	3.74 t (9.5)
3′	3.98 t (9.2)	3.98 t (9.4)	4.00 t (9.0)	4.01 t (9.2)
4′	4.94 t (9.2)	4.93 t (9.4)	4.94 t (9.5)	4.93 t (9.5)
5′	3.52 t (9.5)	3.51 t (9.0)	3.54—3.57[a)]	3.54—3.58[a)]
6′	3.50 dd (12.1, 6.0)	3.49 dd (12.0, 6.0)	3.52 dd (12.0, 1.8)	3.53 br d (12.5)
	3.61 dd (12.1, 2.0)	3.63 dd (12.0, 2.0)	3.59 dd (12.0, 6.0)	3.59 dd (12.5, 6.0)
Rha				
1″	5.17 (1.5)	5.18 d (1.5)	5.19 d (2.0)	5.20 d (1.5)
2″	4.02 dd (3.3, 1.8)	4.03 dd (3.4, 1.5)	4.07 dd (3.4, 2.0)	4.06 m
3″	3.57 m	3.57 dd (9.4, 3.4)	3.58 dd (9.5, 3.4)	3.54—3.58[a)]
4″	3.28 t (9.5)	3.28 t (9.7)	3.28 t (9.5)	3.31 t (9.8)
5″	3.53—3.56[a)]	3.52—3.55[a)]	3.54—3.57[a)]	3.54—3.58[a)]
6″	1.10 d (6.1)	1.10 d (6.1)	1.10 d (6.1)	1.10 d (6.1)
Ara				
1‴	4.52 d (6.7)	4.52 d (6.7)		
2‴	3.59 t (9.4)	3.59 t (9.4)		
3‴	3.53—3.56[a)]	3.52—3.55[a)]		
4‴	3.75 br s	3.75 d (1.8)		
5‴	3.20 br d (12.5)	3.19 dd (12.0, 1.8)		
	3.81 dd (12.5, 2.9)	3.80 dd (12.0, 2.7)		
Glc				
1‴			4.59 d (7.6)	4.58 d (7.9)
2‴			3.54—3.57[a)]	3.54—3.58[a)]
3‴			3.43 dd (9.8, 3.4)	3.43 dd (9.5, 3.4)
4‴			3.80 d (3.4)	3.80 br s
5‴			3.24 t (6.4)	3.24 t (6.4)
6‴			3.72 dd (12.0, 6.0)	3.67 dd (12.0, 6.0)
			3.77 dd (12.0, 1.8)	3.78 dd (12.0, 2.0)
Acyl				
2⁗	7.05 d (2.1)	7.20 d (2.1)	7.04 d (1.8)	7.19 d (1.8)
5⁗	6.78 dd (8.2)	6.81 d (8.0)	6.77 d (8.0)	6.81 d (8.2)
6⁗	6.95 dd (8.2, 2.1)	7.08 dd (8.0, 2.1)	6.95 dd (8.0, 1.8)	7.08 br d (8.2)
α'	6.27 d (15.9)	6.37 d (15.8)	6.27 d (15.9)	6.37 d (15.9)
β'	7.58 d (15.9)	7.65 d (15.8)	7.58 d (15.9)	7.65 d (15.9)
OCH_3		3.88 s		3.89 s

a) Signal patterns are unclear due to overlappimg.

J=9.5 Hz). From the above data, the structure of **3** was determined to be 2-(3,4-dihydroxyphenyl)ethyl-*O*-β-D-glucopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→3)]-(4-*O*-*trans*-caffeoyl)-β-D-glucopyranoside and termed verpectoside B.

Compound **4** was isolated as an amorphous powder, $[\alpha]_D^{23}$ +288° (MeOH). The molecular formula of **4**, $C_{36}H_{48}O_{20}$, was established by HR-FAB-MS. ^{1}H- and ^{13}C-NMR spectra of **4** (Tables 1, 2) were closely similar to those of **3**, except for the presence of a phenolic methoxy group [δ_H 3.89 (3H, s), δ_C 56.42 q] arising from the acyl moiety. The location of the methoxy group on C-3⁗ was deduced from NOESY and HMBC correlations (δ 3.89 s and δ 7.19 d, H-2⁗; δ 3.89 s and δ 148.25 s, C-3⁗; Fig 3), and from spectral comparison of the acyl moiety of **4** with that of the *trans*-feruloyl moiety of compound **2** (Table 2). From the above data, the structure of **4** was determined to be 2-(3,4-dihydroxyphenyl)ethyl-*O*-β-D-glucopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→3)]-(4-*O*-trans-feruloyl)-β-D-glucopyranoside, and was termed verpectoside C.

Phenylethanoid glycosides are water soluble natural products widely distributed in the plant kingdom, most of which are isolated from traditional medicinal plants. Their significant biological activities such as enzyme inhibition, immunomodulatory, antibacterial and cytotoxic activities have been reported.[14)] Recently, some *in vitro* antioxidative assay models were demonstrated antioxidative and free radical scavenging activities for phenylethanoid glycosides.[15—17)] We determined the antioxidative activities of isolated phenylethanoids by using a 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging system by comparing 3-*tert*-butyl-4-hydroxyanisole (BHA), widely used synthetic antioxidant and *dl*-α-tocopherol, commonly used natural antioxidant. In this assay, antioxidants react with the stable free radical 2,2-diphenyl-1-picryl hydrazyl (which gives a strong absorption at 520 nm) and produce colorless 2,2-diphenyl-1-picryl hydrazine.[18)] Figure 4 shows the DPPH radical scavenging

Table 2. ^{13}C-NMR Spectral Data of Compounds **1**—**4** (125.65 MHz, CD_3OD)

C	1	2	3	4
Aglycon				
1	131.94	132.00	131.91	131.29
2	117.54	117.51	117.55	117.50
3	146.14	146.00	145.99	147.78
4	144.81	145.00	144.74	144.10
5	116.35	116.32	116.31	116.29
6	121.53	121.51	121.59	121.54
α	72.17	72.12	71.94	71.87
β	36.75	36.70	36.67	36.62
Glc				
1′	103.08	104.15	102.85	102.82
2′	82.72	82.73	82.29	82.25
3′	81.43	81.34	81.42	81.23
4′	70.94	70.96	70.95	70.97
5′	75.94	75.94	75.88	75.86
6′	62.50	62.50	62.47	62.47
Rha				
1″	103.28	103.23	103.23	103.10
2″	72.17	72.09	72.04	72.02
3″	72.06	72.03	71.98	71.97
4″	73.88	73.85	73.85	73.80
5″	70.68	70.67	70.64	70.57
6″	18.52	18.47	18.45	18.36
Ara				
1‴	104.15	102.01		
2‴	73.05	73.02		
3‴	74.56	74.56		
4‴	69.56	69.57		
5‴	66.87	67.00		
Glc				
1‴			103.76	103.72
2‴			73.19	73.14
3‴			75.19	75.18
4‴			70.39	70.36
5‴			76.48	76.44
6‴			62.52	62.48
Acyl				
1⁗	127.71	127.46	127.64	127.50
2⁗	115.27	111.79	115.18	111.78
3⁗	146.89	147.88	146.85	148.25
4⁗	149.85	151.00	149.82	152.79
5⁗	116.85	116.54	116.49	116.45
6⁗	123.24	124.40	123.21	124.29
α'	114.85	115.22	114.79	114.54
β'	148.02	147.65	147.97	147.78
C=O	168.37	168.20	168.33	168.00
OCH_3		56.46		56.42

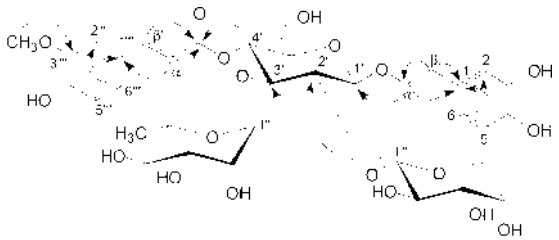

Fig. 2. Significant HMBC Correlations for **2**

Arrows point from H to C.

activity of compounds **1**—**4**. The results confirmed that the DPPH radical scavenging activities of compounds **1** and **3** were more than that of BHA and comparable to that of *dl*-α-tocopherol, while compounds **2** and **4** had more moderate activities. In a comparison of compounds **1** and **3** with **2** and **4**,

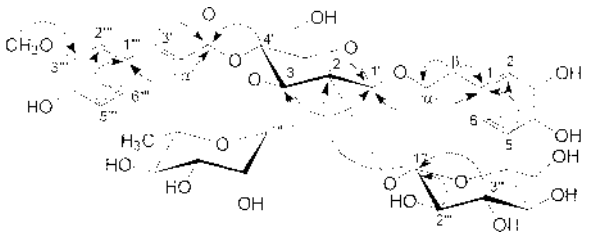

Fig. 3. Significant HMBC Correlations for **3**

Arrows point from H to C.

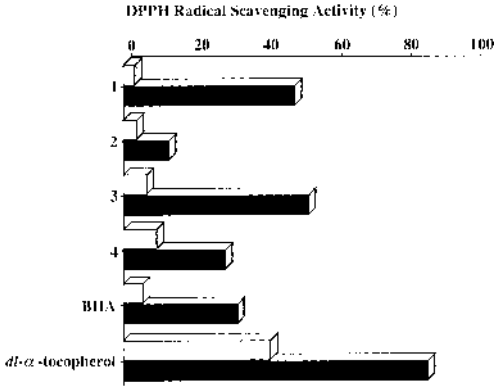

Fig. 4. Scavenging Activity of Compounds **1**—**4**, BHA and *dl*-α-Tocopherol on DPPH Radicals (1.5×10^{-4} M)

□, 1×10^{-4} M; ■, 5×10^{-4} M. Each value is the average of duplicate determinations. The inhibitory ratio of each compound is expressed as follows: Inhibition %$=100\times[(Abs_{blank}-Abs_{samp.})/Abs_{blank})$. Blank: in the absence of sample.

the antioxidative effects of these compounds was potentiated by an increase in the number of phenolic hydroxyl groups in the molecule. The free radical scavenging effects of these phenylethanoids proven here may play an important role in the actions of the *Veronica* species, and partly explain the mechanisms of the activities of phenylethanoids against neoplasm,[19,20] inflammation[21] and nephritis,[22] in which free radicals are seriously involved.

Experimental

General Experimental Procedures Optical rotations were measured on a JASCO-DIP 140 digital spectrometer using a sodium lamp operating at 589 nm. UV (λ_{max}) was recorded on a Shimadzu UV-240 spectrometer. NMR spectra were recorded on a JEOL JNM-A 500 spectrometer in methanol-d_4 with tetramehylsilane (TMS) as an internal standard. FAB-MS and HR-FAB-MS were recorded in an NBA matrix in the positive ion mode on a JEOL JMS-DX300 spectrometer. TLC plates, Silica gel 60 F_{254} and RP18 F_{254s} were obtained from Merck (Darmstadt, Germany). DPPH was purchased from Aldrich Chem. Co. (Milw., WI, U.S.A.). BHA and *dl*-α-tocopherol were obtained from Nacalai Tesque Co. (Kyoto, Japan).

Plant Material *Veronica pectinata* L. var. *glandulosa* Riek ex M.A. Fisher was collected from Beypazari-Turkey. A voucher specimen (HUEF 99014) is deposited in the herbarium of the Faculty of Pharmacy, Hacettepe University.

Extraction and Isolation The air-dried aerial parts of the plant (80 g) were extracted twice with MeOH at 40 °C for 12 h (×2, 2 l). The MeOH solution was evaporated under a vacuum to give a MeOH extract (16 g). The MeOH extract was dissolved in H_2O (0.1 l), and H_2O insoluble material was removed by filtration. The filtrate was fractionated with $CHCl_3$ (×5, 100 ml) and the $CHCl_3$ phase was rejected. The water fraction was lyophilized to yield 10 g dry weight. 1 g of the water fraction was separated for activity studies, and 9 g was subjected to polyamide column chromatography elution with H_2O, followed by increasing concentrations of MeOH to yield seven fractions: Frs. A—G (Fr. A, 4.90 g; Fr. B, 0.45 g; Fr. C, 0.28 g; Fr. D, 0.27 g; Fr. E, 0.41 g; Fr. F, 0.65 g; Fr. G, 0.23 g). Frs. D and E, rich in phenylethanoid glycosides, were further applied to a series of column chromatogra-

phies to yield compounds **1**—**4**. An aliquot of Fr. D (150 mg) was chromatographed over silica gel by stepwise elution with $CHCl_3$: MeOH : H_2O (95 : 5 : 0.5 to 70 : 30 : 3), and than rechromatographed over MPLC using reversed-phase material (Lichroprep RP-18, 40—63 μm). Elution with increasing amounts of MeOH (30—50%) yielded compounds **2** (2.3 mg) and **4** (2 mg) in a pure form. In addition, 45 mg of Fr. E was subjected to reverse phase medium pressure liquid chromatography (20—50% MeOH), and compounds **1** (6.5 mg) and **3** (6 mg) were isolated as pure. Frs. A, B and C, rich in iridoid glucosides, and Frs. F and G, rich in flavonoid glycosides, are still under investigation.

Ehrenoside (**1**): Amorphous powder, $[\alpha]_D^{23}$ −58° (c=0.16, MeOH). UV λ_{max} (MeOH) nm (log ε): 345 (sh, 2.7), 300 (2.8) and 217 (2.6). ^{1}H- and ^{13}C-NMR data are superimposable with those reported in the literature.[13] FAB-MS *m*/*z*: 779 $[M+Na]^+$. HR-FAB-MS *m*/*z*: 779.2410 (Calcd for $C_{34}H_{44}O_{19}Na$: 779.2374).

Verpectoside A (**2**): Amorphous powder, $[\alpha]_D^{23}$ −59° (c=0.03, MeOH). UV λ_{max} (MeOH) nm (log ε): 345 (sh, 3.0), 300 (3.1) and 217 (1.8). ^{1}H-NMR: see Table 1. ^{13}C-NMR: see Table 2. FAB-MS *m*/*z*: 793 $[M+Na]^+$. HR-FAB-MS *m*/*z*: 793.2521 (Calcd for $C_{35}H_{46}O_{19}Na$: 793.2531).

Verpectoside B (**3**): Amorphous powder, $[\alpha]_D^{23}$ +135° (c=0.08, MeOH). UV λ_{max} (MeOH) nm (log ε): 345 (sh, 2.8), 300 (2.9) and 217 (2.7). ^{1}H-NMR: see Table 1. ^{13}C-NMR: see Table 2. FAB-MS *m*/*z*: 809 $[M+Na]^+$. HR-FAB-MS *m*/*z*: 809.2521 (Calcd for $C_{35}H_{46}O_{20}Na$: 809.2480).

Verpectoside C (**4**): Amorphous powder, $[\alpha]_D^{23}$ +288° (c=0.11, MeOH). UV λ_{max} (MeOH) nm (log ε): 345 (sh, 2.7), 300 (2.8) and 217 (2.6). ^{1}H-NMR: see Table 1. ^{13}C-NMR: see Table 2. FAB-MS *m*/*z*: 823 $[M+Na]^+$. HR-FAB-MS *m*/*z*: 823.2671 (Calcd for $C_{36}H_{48}O_{20}Na$: 823.2637).

Measurement of DPPH Radical-Scavenging Activity MeOH solutions of compounds **1**—**4** (1×10^{-4} M and 5×10^{-4} M, 10 μl) were each added to 1.5×10^{-5} M DPPH/MeOH solution, and the absorbance of each mixture was determined at 520 nm after 30 min. The radical scavenging activity was determined by comparing the absorbance with that of a blank (100%) containing only DPPH and solvent. BHA and *dl*-α-tocopherol were used as standards, and samples were prepared using the same dilution procedures.[23,24]

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References

1) Davis P. H., "Flora of Turkey and The East Aegean Islands," Vol. 6, University Press, Edinburg, 1978, pp. 689—753.
2) Baytop T., "Therapy with Medicinal Plants in Turkey (Past and Present)," Publications of Istanbul University, No: 3255, Istanbul, 1984, p. 423.
3) Tomassini L., Brkic D., Serafini M., Nicoletti M., *Fitoterapia*, **66**, 382 (1995).
4) Su B., Zhu Q., Jia Z., *Tetrahedron Lett.*, **40**, 357—358 (1999).
5) Graham J. G., *J. Ethnopharmacol.*, **73**, 347—377 (2000).
6) Chari V. M., Grayer-Barkmeijer R. J., Harborne J. B., Osterdahl B. G., *Phytochemistry*, **20**, 1977—1979 (1981).
7) Lahloub M. F., Zaghloul M. G., Afifi M. S., Sticher O., *Phytochemistry*, **33**, 401—405 (1993).
8) Aoshima H., Miyase T., Ueno A., *Phytochemistry*, **37**, 547—550 (1994).
9) Taskova R., Handjieva N., Peev D., Popov S., *Phytochemistry*, **49**, 1323—1327 (1998).
10) Ozipek M., Saracoglu I., Kojima K., Ogihara Y., Calis I., *Chem. Pharm. Bull.*, **47**, 561—562 (1999).
11) Taskova R., Handjieva N., Evstatieva L., Popov S., *Phytochemistry*, **52**, 1443—1445 (1999).
12) Harput U. S., Saracoglu I., Inoue M., Ogihara Y., Abstract of Papers, The 121st Annual Meeting of the Pharmaceutical Society of Japan, Sapporo, Japan, March 28—30, 2001, part 2, p. 101.
13) Lahloub M. F., Grass G. A., Sticher O., Winker T., Schulten H. R., *Planta Med.*, **52**, 352—355 (1986).
14) Jimenez C., Riguera R., *Nat. Prod. Rep.*, **11**, 591—606 (1994).
15) Li J., Wang P. F., Li J., Liu Z. M., Jia Z. J., *Planta Med.*, **59**, 315—317 (1993).
16) Xiong Q., Kadota S., Tani T., Namba T., *Biol. Pharm. Bull.*, **19**, 1580—1585 (1996).
17) Gao J., Igarashi K., Nukina M., *Chem. Pharm. Bull.*, **48**, 1075—1078 (2000).
18) Hatano T., Edamatsu R., Hiramatsu M., Mori A., Fujita Y., Yasuhara T., Okuda T., *Chem. Pharm. Bull.*, **37**, 2016—2021 (1989).
19) Petit G. R., Numata A., Takemura T., Ode R. H., Narula A. S., Schimidt J. M., Cragg G. M., Pase C. P., *J. Nat. Prod.*, **53**, 456—458 (1990).
20) Saracoglu I., Inoue M., Calis I., Ogihara Y., *Biol. Pharm. Bull.*, **18**, 1396—1400 (1995).
21) Murai M., Tamayama Y., Nishibe S., *Planta Med.*, **61**, 479—480 (1995).
22) Hayashi K., Nagamatsu T., Ito M., Hattori T., Suzuki Y., *Jpn. J. Pharmacol.*, **66**, 47—52 (1994).
23) Blosi M. S., *Nature* (London), **181**, 1199—1200 (1958).
24) Zhang H. L., Nagatsu A., Watanabe T., Sakakibara J., Okuyama H., *Chem. Pharm. Bull.*, **45**, 1910—1914 (1997).