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A New Phenolic Amide from *Lycium chinense* Miller

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A new phenolic amide, dihydro-*N*-caffeoyltyramine (**1**) was isolated from the root bark of *Lycium chinense* Miller, along with known compounds, *trans*-*N*-caffeoyltyramine (**2**), *cis*-*N*-caffeoyltyramine (**3**), and lyoniresinol 3α-*O*-β-D-glucopyranoside (**4**). Their structures were determined by spectroscopic analysis. A NBT superoxide scavenging assay revealed that three phenolic amides showed potent antioxidative activity.

Key words: *Lycium chinense*, *Solanaceae*, Phenolic amides, Dihydro-*N*-caffeoyltyramine, NBT superoxide scavenging assay

INTRODUCTION

Lycii Radicis Cortex, the root bark of *Lycium chinense* Miller (Solanaceae) is used in oriental medicine as a tonic and is reported to exhibit hypotensive, hypoglycemic, and antipyretic activity (Funayama *et al.*, 1980; Morota *et al.*, 1987). A number of acyclic diterpene glycosides (Terauchi *et al.*, 1998), cyclic peptides (Yahara *et al.*, 1993), sesquiterpenes (Sannai *et al.*, 1982), spermine alkaloid (Funayama *et al.*, 1995), flavonoids (Terauchi *et al.*, 1997), and cerebrosides were reported (Kim *et al.*, 1997).

In an ongoing investigation into antioxidative compounds from natural products, an ethyl acetate soluble fraction of *L. chinense* was found to inhibit superoxide radical generation significantly *in vitro*. By means of a bioassay-directed chromatographic separation technique, a new (**1**), and three known compounds (**2-4**) were isolated. Three known compounds have been isolated from this plant for the first time. The antioxidative activities of the four compounds were tested by a NBT superoxide scavenging assay according to an established method (Kirby and Schmidt 1997). Among these compounds, dihydro-*N*-caffeoyltyramine (**1**), *trans*-*N*-caffeoyltyramine (**2**), and *cis*-*N*-caffeoyltyramine (**3**) showed similar antioxidative activity, while lyoniresinol 3α-*O*-β-D-glucopyranoside (**4**) was inactive. This paper reports the isolation and characterization of a new phenolic amide and its antioxidative activity.

MATERIALS AND METHODS

General procedure

The melting point was obtained with a Fisher Scientific melting point apparatus and uncorrected. UV spectra were obtained on a Shimadzu UV/Visible Spectrophotometer. IR spectra were recorded on a IMS 85 (Bruker). NMR spectra were recorded on a Varian Unity Inova 500 (500 MHz) spectrometer. ^{1}H-^{1}H COSY, DEPT, HMQC, and HMBC NMR spectra were obtained with the usual pulse sequences. HR-FABMS were determined on a JMS 700 (JEOL). Preparative HPLC was performed on a Waters Delta 4000 with Photodiode Array Detector (Waters model 996) using a Radialpak (type: 8NVC186, 8 mm×200 mm, Waters) column. TLC and column chromatography were carried out on precoated Si Gel F_{254} plates (Merck, art. 5715), RP-18 F_{254} plates (Merck, art. 15389), and Si gel 60 (Merck, 230-400 mesh).

Plant material

The root bark of *L. chinense* (Solanaceae) was purchased from local Korean herb drug market in Kwang-ju, Korea, and was authenticated by Department of Pharmacognosy, Chosun University. Voucher specimens were deposited in the Herbarium of College of Pharmacy, Chosun University (893-16).

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Extraction and isolation

The root bark (0.8 Kg) of *L. chinense* was extracted with MeOH at room temperature to afford 137.3 g of residue. The methanol extract was suspended in water and then partitioned by dichloromethane, ethyl acetate, and *n*-butanol in turn. 3.0 g of the EtOAc fraction were subjected to column chromatography over a silica gel (300 g, 4.8 × 45 cm) eluting with a CH_2Cl_2-MeOH-H_2O (8:1:0.1→ 6:1:0.1 → 4:1:0.1→ 2:1:0.1→ MeOH only) gradient system. The fractions were combined based on their TLC pattern to yield subfractions designated as E1-E8. Subfraction E4 (960 mg) was further purified by column chromatography over a silica gel (100 g, 2.8 × 40 cm) eluting with a $CHCl_3$-Me_2CO-MeOH-H_2O gradient system to afford seven subfractions (E41-E47). Subfraction E43 (566 mg) was purified by column chromatography over a silica gel (100 g, 2.8 × 40 cm) eluting with a $CHCl_3$-MeOH-H_2O gradient system to give twelve subfractions (E431-E4312). Subfractions E437 (195.70 mg), E438 (53.49 mg) and E439 (100.56 mg) were finally purified by prep HPLC eluting with an *i*-PrOH-MeOH-H_2O gradient system, which afforded compounds **1** (106 mg, yield 0.01325%), **2** (14.8 mg, yield 0.00185%), **3** (9.2 mg, yield 0.00115%) respectively. In addition, subfraction E6 (223 mg) was further purified by column chromatography over a silica gel (100 g, 2.8 × 44.5 cm) eluting with a $CHCl_3$-Me_2CO-MeOH-H_2O gradient system to afford eleven subfractions (E61-E611). Subfraction E69 (72 mg) was finally purified by Lichroprep RP-18 chromatography eluting with *i*-PrOH-MeOH-H_2O gradient system, which afforded compound **4** (7.40 mg, yield 0.000925 %)

Table 1. ^{1}H-, ^{13}C-NMR data and HMBC correlations of Compound **1**[a]

Position	δ ^{13}C	δ ^{1}H (m, *J* in Hz)	^{1}H-^{1}H COSY	HMBC
1	132.61(s)[b]			H-2, H-7, H -8
2	115.17(*d*)	6.63(*d*, 1.5)		H-5, H-7
3	143.45(*s*)			H-2
4	145.02(*s*)			H-5
5	115.39(*d*)	6.67(*d*, 8.5)	H-6	H-2
6	119.46(*d*)	6.50(*dd*, 8.5, 1.5)	H-5	H-2, H-5, H-7
7	31.27(*t*)	2.73(*t*, 7.5)	H-8	H-2, H-6, H-8
8	38.25(*t*)	2.37(*t*, 7.5)	H-7	H-7
9	174.26(*s*)			H-7, H-8, H-8'
1'	130.15(*s*)			H-3', H-8'
2'	129.56(*d*)	6.94(*d*, 8.5)	H-3'	H-3', H-7'
3'	115.03(*d*)	6.69(*d*, 8.5)	H-2'	H-2'
4'	155.64(*s*)			H-2', H-3'
5'	115.03(*d*)	6.69(*d*, 8.5)	H-6'	
6'	129.56(*d*)	6.94(*d*, 8.5)	H-5'	
7'	34.53(*t*)	2.60(*t*, 7.5)	H-8'	H-2', H-8'
8'	41.13(t)	3.29(*t*, 7.5)	H-7'	H-7'

[a]Spectra recorded at 500 MHz in CD_3OD, [b]Multiplicity deduced by DEPT and indicated by usual symbols

Dihydro-*N*-caffeoyltyramine (1) light yellow flakes, mp : 162-164°C; UV(MeOH) λ_{max} nm (log ε): 220 (4.44), 282 (1.18); IR ν_{max} (KBr) cm^{-1}: 3310, 2974, 1612, 1516, 1447, 1362, 1242; EIMS *m/z* (rel. int.): 301 (M^+ 1.9%), 182 (18.3), 136 (28.0), 107 (100.0); HR-FABMS *m/z*: 302.1386 (calcd. for $C_{17}H_{20}NO_4$: 302.1392); ^{1}H, ^{13}C and HMBC data: see Table 1, and Fig. 1.

***trans*-*N*-caffeoyltyramine (2)** an amorphous powder, mp : 215-217°C; IR ν_{max} (KBr) cm^{-1}: 3316, 1650; HR-FABMS $[M+H]^+$ 300.1223 (calcd. 300.1236 for $C_{17}H_{18}NO_4$); ^{1}H-NMR (CD_3OD, 500 MHz) δ_H : 7.00 (*d*, *J* = 1.5 Hz, H-2), 6.76 (*d*, *J* = 8.5 Hz, H-5), 6.90 (*dd*, *J* = 8.5, 1.5 Hz, H-6), 7.34 (*d*, *J* = 16.0 Hz, H-7), 6.33 (*d*, *J* = 16.0 Hz, H-8), 6.72 (*d*, *J* = 8.5 Hz, H-3'/5'), 7.05 (*d*, *J* = 8.5 Hz, H-2'/6'), 2.75 (*t*, *J* = 7.5 Hz, H-7'), 3.45 (*t*, *J* = 7.5 Hz, H-8'); ^{13}C-NMR (CD_3OD, 125 MHz) δ_C : 127.15 (*s*, C-1), 113.90 (*d*, C-2), 145.56 (*s*, C-3), 147.61 (*s*, C-4), 115.30 (*d*, C-5), 120.92 (*d*, C-6), 141.00 (*d*, C-7), 117.24 (*d*, C-8), 168.13 (*s*, C-9), 130.18 (*s*, C-1'), 115.10 (*d*, C-3'/5'), 129.56 (*d*, C-2'/6'), 155.72 (*s*, C-4'), 34.24 (*t*, C-7'), 41.14 (*t*, C-8').

***cis*-*N*-caffeoyltyramine (3)** a yellow oil; IR ν_{max} (KBr) cm^{-1}: 3316, 1616, 1510; ^{1}H-NMR (CD_3OD, 500 MHz) δ_H :

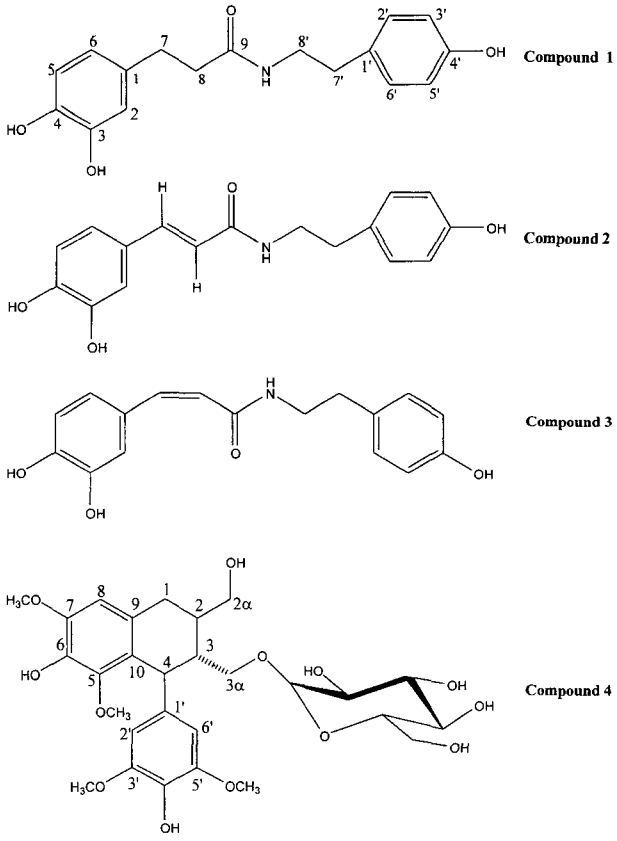

Fig. 1. Structures of Compound (1-4) isolated from *Lycium chinense*

7.04 (*d*, *J* = 1.5 Hz, H-2), 6.71 (*d*, *J* = 8.0 Hz, H-5), 6.84 (*dd*, *J* = 8.0, 1.5 Hz, H-6), 6.56 (*d*, *J* = 12.5 Hz, H-7), 5.78 (*d*, *J* = 12.5 Hz, H-8), 6.69 (*d*, *J* = 8.5 Hz, H-3'/5'), 6.99 (*d*, *J* = 8.5 Hz, H-2'/6'), 2.70 (*t*, *J* = 7.5 Hz, H-7'), 3.38 (*t*, *J* = 7.5 Hz, H-8'); ^{13}C-NMR (CD_3OD, 125 MHz) δ_C : 127.39 (*s*, C-1), 114.80 (*d*, C-2), 144.80 (*s*, C-3), 146.21 (*s*, C-4), 116.24 (*d*, C-5), 120.60 (*d*, C-6), 136.73 (*d*, C-7), 121.98 (*d*, C-8), 169.33 (*s*, C-9), 130.07 (*s*, C-1'), 115.08 (*d*, C-3'/5'), 129.55 (*d*, C-2'/6'), 155.68 (*s*, C-4'), 34.24 (*t*, C-7'), 41.14 (*t*, C-8').

Lyoniresinol 3α-*O*-β-D-glucopyranoside (4) an amorphous powder, $[\alpha]_D^{24}$ +26.0° (MeOH; c 0.5). UV (MeOH) λ_{max} nm (log ε): 276 (3.70); IR ν_{max} (KBr) cm^{-1}: 3400, 1570; FAB-MS *m/z* (rel. int.): 605.05 ([M+Na]$^+$, 86.73 %), 581.22 ([M-H]$^+$, 13.65 %); ^{1}H-NMR (CD_3OD, 500 MHz) δ_H : 1.71 (*m*, H-2), 2.09 (*m*, H-3), 2.59-2.74 (*m*, H-7'), 3.25 (*m*, H-2α), 3.32 (*s*, -OCH_3), 3.30-3.84 (*m*, sugar H), 3.75 (*s*, -OCH_3), 3.76 (*m*, H-3α), 3.83 (*m*, H-2α), 3.86 (*s*, -OCH_3), 3.89 (*m*, H-3α), 4.28 (*d*, *J* = 8.0 Hz, anomeric H), 4.42 (*d*, *J* = 6.0 Hz, H-4), 6.43 (s, H-2',6'), 6.58 (s, H-8); ^{13}C-NMR (CD_3OD, 125 MHz) δ_C : 147.80 (*s*, C-3',5'), 147.45 (*s*, C-7), 146.40 (*s*, C-5), 138.17 (*s*, C-6), 137.74 (*s*, C-4'), 133.28 (*s*, C-1'), 128.99 (*s*, C-9), 125.26 (*s*, C-10), 106.64 (*d*, C-8), 105.71 (*d*, C-2',6'), 103.67 (*d*, C-1"), 77.06 (*d*, C-3"), 76.78 (*d*, C-5"), 74.00 (*d*, C-2"), 70.48 (*d*, C-4"), 70.23 (*t*, C-3α), 65.02 (*t*, C-2α), 61.65 (*t*, C-6"), 58.97 (*q*, OCH_3-5), 55.65 (*q*, OCH_3-3'/5'), 55.39 (*q*, OCH_3-7), 45.53 (*d*, C-3), 41.62 (*d*, C-4), 39.40 (*d*, C-2), 32.67 (*t*, C-8').

NBT superoxide scavenging assay

The NBT superoxide-scavenging assay was carried out using a slight modification of an established method (Kirby and Schmidt 1997). The reaction mixture, which was equilibrated at 25°C, contained 20 μL of a 15 mM Na_2EDTA solution in a buffer (50 mM KH_2PO_4/KOH pH 7.4 in ionized water), 50 μL of 0.6 mM NBT in a buffer, 30 μL of a 3 mM hypoxanthine in 50 mM KOH solution, 50 μL of xanthine oxidase solution in a buffer (1 units in 10 mL buffer) and 100 μl of the sample. The plate reader (Molecular Devices Vmax) took readings every 20 *s* for 5 min at 570 nm. The control was 100 μl of 5% DMSO solution instead of the sample. Results were expressed as relative percentage inhibition to control, given by [(rate of control-rate of sample reaction)/rate of control] × 100. Allopurinol was used as a reference compound.

RESULTS AND DISCUSSION

An EtOAc soluble fraction of the MeOH extract of *L. chinense* was chromatographed on columns of silica gel, reversed phase C-18, followed by prep. HPLC, afforded four compounds (**1-4**) (Fig. 1).

Compound **1** responded positively to Dragendorff's reagent. Its molecular formula was found to be $C_{17}H_{19}NO_4$ by HR-FAB mass spectrometry ([M+H]$^+$ found 302.1386, calcd 302.1392). The UV maxima at 282 nm, the IR bands at 3310 cm^{-1}, 1612 cm^{-1}, and a signal appearing at δ 174.26 (*s*) in the ^{13}C-NMR spectrum suggested that hydroxyl groups and an amide group might be present. The ^{1}H-NMR spectrum of **1** displayed signals at δ 6.67 (1H, *d*, *J* = 8.5 Hz, H-5), δ 6.63 (1H, *d*, *J* = 1.5 Hz, H-2), and δ 6.50 (1H, *dd*, *J* = 8.5, 1.5 Hz, H-6), which were assigned to three aromatic protons of an ABX system. Two coupled triplets of the methylene protons at δ 2.73 (2H, *t*, *J* = 7.5 Hz, H-7) and 2.37 (2H, *t*, *J* = 7.5 Hz, H-8) suggested that an olefinic proton of a *cis*- or *trans*-caffeoyl moiety was replaced by a pair of methylene in **1**. In addition, the signals at δ 6.94 (2H, *d*, *J* = 8.5 Hz, H-2',6') and 6.69 (2H, *d*, *J* = 8.5 Hz, H-3',5') assignable to four aromatic protons of an AA'BB' system, two coupled triplets corresponding to the methylene protons at δ 3.29 (2H, *t*, *J* = 7.5 Hz, H-8') and 2.60 (2H, *t*, *J* = 7.5 Hz, H-7') revealed the presence of a tyramine moiety in **1**. The ^{13}C-NMR and DEPT spectrum showed seventeen signals consisting of four methylenes, seven methines, and six quaternary carbons. The ^{1}H-^{1}H COSY spectrum showed that two coupled triplets corresponding to the methylene protons at δ 2.73, and δ 2.60 were coupled with the methylene protons at δ 2.37, and δ 3.29 each other. These results were further supported by HMBC spectrum. In the HMBC spectrum, the methylene carbon signals at δ 31.27 (C-7) and δ 34.53 (C-7') showed a ^{1}H-^{13}C long range correlation with H-2/H-6, and H-8 signals, and with H-2'/H-6', and H-8' signals, respectively. Moreover, the carbonyl signal at δ174.26 (C-9) showed a ^{1}H-^{13}C long range correlation with H-7, H-8, and H-8', respectively. In addition, acid hydrolysis of **1** gave a dihydro-caffeic acid and tyramine, which were identified by a direct comparison with authentic samples on TLC, HPLC, and ^{1}H-NMR spectra (data were not shown here). A structurally related compound, dihydro-*N*-feruloyltyramine was previously isolated from *Annona cherimola* (Chen *et al.*, 1998). On the basis of the foregoing observations, compound **1** was determined to be dihydro-*N*-caffeoyltyramine. A complete assignment of the proton and carbon shifts aided by

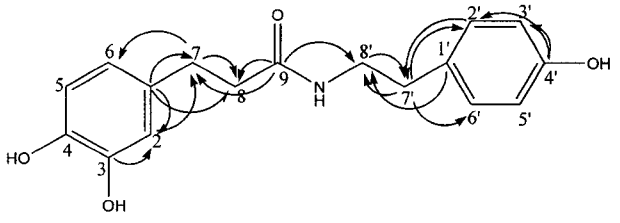

Fig. 2. Important HMBC correalations for Compound 1 (arrows are indicated C→H)

DEPT, HMQC, and HMBC experiments are shown in Table 1 and Fig. 2.

Compound **2** responded positively to Dragendorff's reagent. Its molecular formula was found to be $C_{17}H_{18}NO_4$ by HR-FAB mass spectrometry ($[M+H]^+$ found 300.1223, calcd 300.1236). The ^{1}H-NMR spectrum of **2** displayed signals at δ 7.00 (1H, *d*, *J* = 1.5 Hz, H-2), δ 6.76 (1H, *d*, *J* = 8.5 Hz, H-5), and δ 6.90 (1H, *dd*, *J* = 8.5, 1.5 Hz, H-6), corresponding to three protons on caffeoyl moiety. In addition, the signals at δ 7.05 (2H, *d*, *J* = 8.5 Hz, H-2',6') and δ 6.72 (2H, *d*, *J* = 8.5 Hz, H-3',5') assignable to four aromatic protons of an AA'BB' system, two coupled triplets corresponding to the methylene protons at δ 3.45 (2H, *t*, *J* = 7.5 Hz, H-8') and δ 2.75 (2H, *t*, *J* = 7.5 Hz, H-7') revealed the presence of a tyramine moiety in **2**. A downfield doublet at δ 7.34 (*J* = 16.0 Hz) was assigned to the C-7 olefinic proton of the caffeic acid moiety showed *trans*-coupling with the C-8 olefinic protons, which appeared as a doublet δ 6.33 (*J* = 16.0 Hz). The ^{13}C-NMR and DEPT spectrum showed seventeen signals consisting of two methylenes, nine methines, and six quaternary carbons. Based on the ^{13}C-NMR, DEPT, HMQC, and HMBC spectral data, compound **2** was determined to be *trans-N*-caffeoyltyramine, which was previously isolated from *Annona montana* (Sakakibara *et al.*, 1991; Wu *et al.*, 1995; Lajide *et al.*, 1995; Santos *et al.*, 1996).

Compound **3** was obtained as a yellow oil. A comparison of the spectral data with **2** and **3** revealed that both of the compounds were much similar, except for the olefinic proton of C-7 and C-8 were different. The signals at δ 6.56 (1H, d, *J* = 12.5 Hz), and δ 5.78 (1H, d, *J* = 12.5 Hz) indicated that the olefinic protons of C-7 and C-8 were *cis*-coupling. Furthermore, the ^{13}C-NMR showed a good agreement with reported data of *cis-N*-caffeoyltyramnine (Chen *et al.*, 1998). Therefore, compound **3** was determined to be *cis-N*-caffeoyltyramnine, which was previously isolated from *Annona cherimola*.

Compound **4**, an amorphous powder, $[\alpha]_D^{24}$ +26.0° (MeOH; c 0.5), FAB-MS *m/z* 605.05 ($[M+Na]^+$), 581.22 ($[M-H]^+$) exhibited carbon signals ascribable to the glucopyranosyl residue and four aromatic methoxyl groups, and twelve carbon signals ascribable to two substituted benzene ring, and two carbinol carbons, in the ^{13}C-NMR spectrum. In addition, compound **4** displayed signals at δ 6.43 (s, H-2', 6'), 6.58 (s, H-8) 1.71 (*m*, H-2), 2.09 (*m*, H-3), 2.59-2.74 (*m*, H-1), 4.42 (*d*, *J* = 6.0 Hz, H-4) in the ^{1}H-NMR spectrum, The above evidence was reminiscent of a 4-aryltetralin type lignan monoglucopyranoside for **4**. Based on the ^{1}H-, ^{13}C-NMR, DEPT, HMQC, and HMBC data, compound **4** was determined to be (+)-lyoniresinol-3α-*O*-β-D-glucopyranoside, which was previously isolated from *Cinnamomum cassia* (Miyamura *et al.*, 1983).

The antioxidative activity of the isolated compounds was examined. Among these compounds, dihydro-*N*-caffeoyltyramine (**1**), *trans-N*-caffeoyltyramine (**2**), and *cis-N*-caffeoyltyramine (**3**) showed similar antioxidative activity, while lyoniresinol 3α-*O*-β-D-glucopyranoside (**4**) was inactive at high concentration (IC_{50}>200 μg/mL). The IC_{50} values for compound **1**, **2**, and **3** were 8.49 ± 0.50 μg/mL, 16.19 ± 1.05 μg/mL, and 12.66 ± 1.53 μg/mL, respectively. Moreover, no clear difference in antioxidative activity was observed between the *cis*- and *trans*- isomers of *N*-caffeoyltyramine. These results suggest that the *ortho*-dihydroxy (catechol) structure and aromatic nuclei of these structurally related phenolic amides also play an important role in the antioxidative function as exhibited in flavonoids (Pietta 2000; Akdemir *et al.*, 2001).

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REFERENCES

Akdemir, Z. Ş., Tati, İİ., Saraccoğlu, İ., İsmailoğlu, U. B., Şahin-Erdemli, İ., and Caliş, İ., Polyphenolic compounds from *Geranium pratense* and their free radical scavenging activities. *Phytochemistry,* 56, 189-193 (2001).

Chen, C.-Y., Chang, F.-R., Yen, H.-F., and Wu, Y.-C., Amides from stems of *Annona cherimola*. *Phytochemistry,* 45, 1443-1447 (1998).

Funayama, S., Yoshida, K., Konno, H., and Hikkino, H., Structure of Kukoamine A, a hypotensive principle of *Lycium chinense* root bark. *Tetrahedron Lett.*, 21, 1355-1356 (1980).

Funayama, S., Zhang, G.-R., and Nozoe, S., Kukoamine B, a spermine alkaloid from *Lycium chinense. Phytochemistry,* 38, 1529-1531 (1995).

Kim, S.Y., Choi, Y.-H., Huh, H., Kim, J., Kim, Y.C., and Lee, H.S., New antihepatotoxic cerebroside from *Lycium chinense* fruits. *J. Nat. Prod.*, 60, 274-276 (1997).

Kirby, A.J., and Schmidt, R.J., The antioxidant activity of Chinese herbs for eczema and of placebo herbs - I. *J. of Ethnopharmacology,* 56, 103-108 (1997).

Lajide, L., Escoubas, P., and Mizutani, J., Termite antifeedant activity in *Xylopia aethiopica*. *Phytochemistry,* 40, 1105-1112 (1995).

Miyamura, M., Nohara, T., Tomimatsu, T., and Nishioka, I., Seven aromatic compounds from bark of *Cinnamomum cassia*. *Phytochemistry,* 22, 215-218 (1983).

Morota, T., Sasaki, H., Chin, M., Sato, T., Katayama, N., Fukuyama, K., and Mitsuhashi, H., Studies on the crude drug

containing the angiotensin I converting enzyme inhibitors(I) on the active principles of *Lycium chinense* Miller. *Shoyakugaku Zasshi*, 41, 169-173 (1987).

Pietta, P-G., Flavonoids as antioxidants. *J. Nat. Prod.*, 63, 1035-1042 (2000).

Sakakibara, I., Katsuhara, T., Ikeya, Y., Hayashi, K., and Mitsuhashi, H., Cannabisin A, an arylnaphthalene lignanamide from fruits of *Cannabis sativa*. *Phytochemistry*, 30, 3013-3016 (1991).

Sannai, A., Fujimori, T., and Kato, K., Isolation of (–)-1,2-dehydro-α-cyperone and solavetivone from *Lycium chinense*. *Phytochemistry*, 21, 2986-2987 (1982).

Santos, L. P., Boaventura, M. A., Oliveira, A. B., and Cassady, J. M., Grossamide and *N-trans*-caffeoyltyramine from *Annona crassiflora* seeds. *Plant. Med.*, 62, 76-76 (1996).

Terauchi, M., Kanamori, H., Nobuso, M., Yahara, S., and Nohara, T., Detection and determination of antioxidative components in *Lycium chinense*. *Natural Medicines*, 51, 387-391 (1997).

Terauchi, M., Kanamori, H., Nobuso, M., Yahara, S., and Yamasaki, K., New acyclic diterpene glycoside, Lyciumoside IV-IX from *Lycium chinense* Mill. *Natural Medicines*, 52, 167-171 (1998).

Wu, Y.-C., Chang, G.-Y., Ko, F.-N., and Teng, C.-M., Bioactive constituents from the stems of *Annona montana*. *Plant. Med.*, 61, 146-149 (1995).

Yahara, S., Shigeyama, C., Ura, T., Wakamatsu, K., Yasuhara, T., and Nohara, T., Cyclic peptides, acyclic diterpene glycoside and other compounds from *Lycium chinense* Mill. *Chem. Pharm. Bull.*, 41, 703-709 (1993).