Resveratrol Derivatives from the Roots of *Vitis thunbergii*

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Investigating the constituents of the roots of *Vitis thunbergii* led to the isolation of four new resveratrol derivatives, vitisinols A−D (**1**−**4**), together with (+)-ϵ-viniferin, (−)-viniferal, ampelopsin C, miyabenol A, (+)-vitisin A, and (+)-vitisin C. The structures of these 10 compounds were established by spectroscopic (NMR and MS) analyses. All of the isolated compounds, except **1**, were tested for their antiplatelet and antioxidative activities.

The roots of *Vitis thunbergii* Sieb. & Zucc. (*Vitis ficifolia* Bge.,[1,2] Vitaceae) are traditionally used for the treatment of diarrhea, fracture and injury, jaundice, and hepatitis in Taiwan.[3] Plants in the genus *Vitis* commonly contain oligomers of resveratrol.[4] It was previously reported that several polyphenols were isolated from the aerial part of *V. thunbergii*.[5] In the course of our investigation on the roots of the same species, four new and six known resveratrol derivatives were isolated. On the basis of the presence of significant antioxidative and antiplatelet activities for resveratrol found in red wine,[6] all the isolated compounds except **1** were tested for antiplatelet and antioxidative activities.

Results and Discussion

An ethanolic extract of the dried roots of *V. thunbergii* was repeatedly chromatographed on silica gel, Sephadex LH-20, and by PTLC to afford four new resveratrol derivatives, vitisinols A−D (**1**−**4**), together with six known compounds, (+)-ϵ-viniferin,[7] (−)-viniferal,[8] ampelopsin C,[7] miyabenol A,[9] (+)-vitisin A,[10] and (+)-vitisin C.[8]

Vitisinol A (**1**) was obtained as a brown powder, and its molecular formula was determined to be $C_{28}H_{20}O_6$ by HREIMS. The ^{13}C and DEPT NMR spectra of **1** showed 12 signals for 14 carbons including one oxygenated sp^3 carbon, one sp^3 methine, four sp^2-hybridized methine, three sp^2-hybridized quaternary carbons, and three oxygenated sp^2 quaternary carbons (Table 1). On the basis of the above data, compound **1** was considered to be a symmetrical dimer. The ^1H NMR spectrum of **1** showed a pair of coupled aliphatic methine signals at δ 4.49 and 5.43 (each 1H, d, J = 11.0 Hz) with related carbon signals appearing at δ 48.7 and 93.7, respectively, two *m*-coupled doublets at δ 6.12 and 6.15 (each 1H, J = 1.5 Hz) for two aromatic protons, and a pair of coupled doublets at δ 6.90 and 7.52 (each 2H, J = 8.5 Hz) for a set of AA′BB′-type aromatic protons, which suggested the presence of a tetrahydrofuran ring bearing a 4-oxyphenyl and a 3,5-dioxyphenyl group with a *trans* configuration (J = 11.0 Hz) between them.[8] In the HMBC experiment of **1** (Figure 1), the proton signals at δ 7.52 (H-2a, 6a) and 6.15 (H-14a) correlated with the methine carbon signals at δ 93.7 (C-7a) and 48.7 (C-8a), respectively. In addition, the proton signals of H-8a (δ 4.49), H-12a (δ 6.12), and H-14a (δ 6.15) all showed correlations with the quaternary carbon signal at δ 122.5 (C-10a). Thus, the structure of **1** was determined, and the compound was named vitisinol A.

Table 1. ^{13}C NMR Data (δ) for **1**−**4**

no.	**1**[a]	**2**[b]	**3**[b]	**4**[b]
1a	131.3	130.8	136.8	129.8
2a	130.3	130.0	129.4	130.6
3a	116.6	115.9	115.7	116.1
4a	159.3	158.5	156.2	157.0
5a	116.6	115.9	115.7	116.1
6a	130.3	130.0	129.4	130.6
7a	93.7	88.5	46.4	52.1
8a	48.7	49.4	52.5	54.6
9a	137.3	142.1	148.7	147.1
10a	122.5	119.7	107.1	105.7
11a	159.7	157.8	159.1	159.8
12a	96.9	100.6	101.5	102.1
13a	160.1	157.0	159.1	159.8
14a	104.3	105.0	107.1	105.7
1b	131.3	134.9	129.4	128.5
2b	130.3	128.8	129.7	130.5
3b	116.6	115.4	116.4	116.7
4b	159.3	155.9	159.1	159.8
5b	116.6	115.4	116.4	116.7
6b	130.3	128.8	129.7	130.5
7b	93.7	40.5	135.5	138.7
8b	48.7	41.6	129.2	123.3
9b	137.3	140.6	155.1	161.6
10b	122.5	120.4	131.6	126.8
11b	159.7	160.1	201.6	195.0
12b	96.9	96.1	50.4	73.2
13b	160.1	158.8	34.6	204.2
14b	104.3	109.9		56.4
1c		133.6		
2c		160.4		
3c		115.8		
4c		129.2		
5c		128.9		
6c		135.0		
CHO		190.7		

[a] Measured in CD_3OD. [b] Measured in Me_2CO-d_6.

Compound **2** was isolated as brown-yellow powder, and the molecular formula was assigned as $C_{35}H_{26}O_8$ on the basis of its HRFABMS and ^1H and ^{13}C NMR spectra. The ^1H NMR and ^{13}C NMR spectra of **2** indicated the presence of an aldehyde group (δ_H 9.31 and δ_C 190.7). The appearance of the aliphatic proton signals at δ 4.26, 5.84 (each 1H, d, J = 11.5 Hz) and 5.47, 5.57 (each 1H, d, J = 3.5 Hz) with their related carbon signals at δ 49.4, 88.5, 40.5, and 41.6, respectively, suggested that compound **2** was a dimer of resveratrol containing a 2,3-dihydrobenzofuran moiety. The following correlations were observed in the HMBC spectrum of **2** (Figure 1): H-2a, H-6a/C-7a; H-14a/C-8a, C-10a; H-2b, H-6b/C-7b; H-8b/C-10b, C-14b; H-7a/C-9a, and

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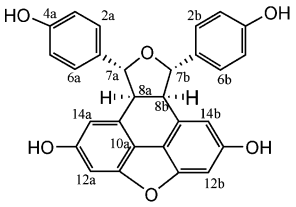

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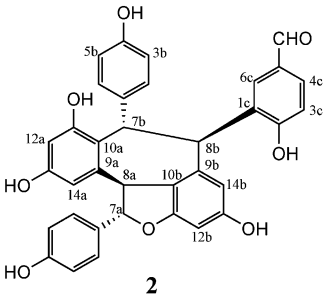

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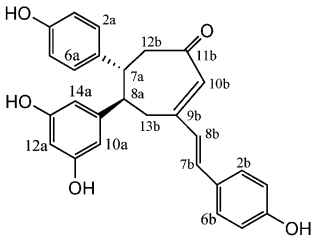

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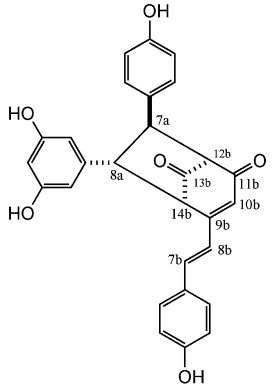

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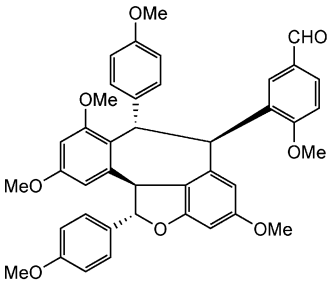

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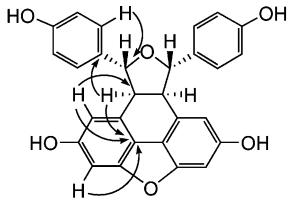

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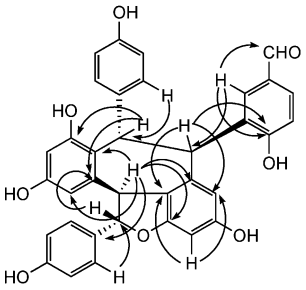

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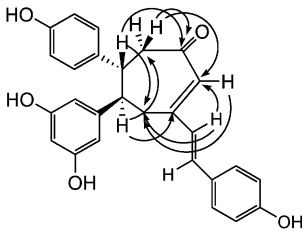

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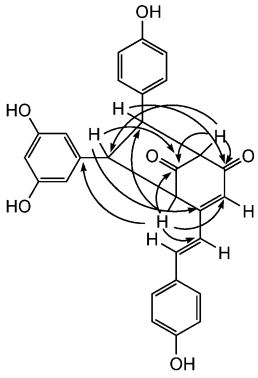

4

Figure 1. HMBC correlations of **1**−**4**.

H-8a/C-1a, C-10a, C-14a, C-9b, C-11b. In the ^{1}H spectrum of **2**, a set of ABX-type aromatic protons at δ 6.95 (1H, d, J = 8.5 Hz), 7.42 (1H, dd, J = 2.0, 8.5 Hz), and 6.66 (1H, d, J = 2.0 Hz) were assigned to H-3c, H-4c, and H-6c, respectively. Furthermore, HMBC correlations were observed between 4c, 6c-protons and the aldehyde carbon; this aldehyde group was thus suggested to be at C-5c. The presence of key correlations between H-7b (δ 5.47) and C-9a (δ 142.1), C-11a (δ 157.8) indicated that two stilbene units formed a seven-membered ring with a *trans* H-7a/H-8a (J = 11.5 Hz) configuration. Accordingly, the structure of **2** was established and it was named vitisinol B. The hexamethyl ether of **2** was produced by the ozonolysis of (+)-decamethyl vitisin A, and its absolute configuration was determined and represented as **5**.[10] The CD spectrum of **2** was analogous to that of **5**. Thus, the absolute configuration of **2** was determined as shown.

Compound **3** had a molecular formula of $C_{27}H_{24}O_5$ as established by HREIMS and ^{1}H and ^{13}C NMR analyses. Its IR spectrum showed absorption bands at 3423, 1602, 1571, 1445, and 1167 cm^{-1}, which were closely similar to those of longusone A,[11] an analogue of **3** with a hydroxyl group at C-3a. In the ^{1}H NMR spectrum of **3**, the presence of a pair of multiplets at δ 3.16 (H-8a) and 3.31 (H-7a) due to two aliphatic methine protons, the signals at δ 6.62 (2H,

d, J = 8.5 Hz, H-3a, 5a) and 6.90 (2H, d, J = 8.5 Hz, H-2a, 6a) attributed to a set of AA′BB′-type aromatic protons, and the signals at δ 6.10 (1H, d, J = 2.0 Hz, H-12a) and 6.12 (2H, d, J = 2.0 Hz, H-10a, 14a) attributed to a set of AA′M-type aromatic protons suggested that compound **3** was a derivative of resveratrol. The remaining signals included a pair of aliphatic methylene signals at δ 3.00 (2H, d, J = 6.0 Hz, H-12b) and 3.15 (2H, m, H-13b), a pair of coupled olefinic methine (H-7b and H-8b) signals at δ 6.74 and 6.88 (each 1H, d, J = 17.0 Hz), an olefinic methine singlet at δ 6.16 (H-10b), and one set of AA′BB′-type aromatic proton signals at 6.79 (2H, d, J = 8.5 Hz, H-3b, 5b) and 7.36 (2H, d, J = 8.5 Hz, H-2b, 6b). The ^{13}C NMR and DEPT-NMR spectra of **3** showed that compound **3** contained two methylene (δ 34.6, 50.4) and one carbonyl (δ 201.6) carbons. In the HMBC spectrum of **3** (Figure 1), the proton signal at δ 3.31 (H-7a) showed correlations with a methylene carbon signal at δ 34.6 (C-13b) and the carbonyl signal at δ 201.6 (C-11b), which also correlated to one methylene proton signal at δ 3.00 (H-12b). The proton signal at δ 3.16 (H-8a) exhibited correlations with a methylene carbon signal at δ 50.4 (C-12b) and an olefinic carbon signal at δ 155.1 (C-9b, quaternary), which correlated to another olefinic proton signal at δ 6.74 (H-7b). Meanwhile, the proton signal at δ 6.88 (H-8b) displayed correlations with an olefinic carbon signal at δ 131.6 (C-10b, methine) and C-13b signal, and the signal of H-10b at δ 6.16 correlated with the signals of C-12b and C-13b. The sequence of H-12b, H-7a, H-8a, and H-13b was further confirmed by a TOCSY experiment. In an NOE experiment, the effect was observed between H-7a (δ 3.31) and H-10a (H-14a, δ 6.12), indicating a *trans* configuration between H-7a and H-8a. The NOE effect was also present between H-8b and H-10b. The *trans* configuration between H-7b and H-8b was determined from their coupling constant (J_{7b-8b} = 17.0 Hz). On the basis of the above data, the structure of **3** was established and the compound was named vitisinol C. Its absolute configuration has not been determined.

Compound **4** had a molecular formula of $C_{28}H_{22}O_6$ as established by HREIMS and ^{1}H and ^{13}C NMR analyses. The IR absorption bands at 1713 and 1640 cm^{-1} indicated the presence of isolated and conjugated carbonyl functions.[12] The NMR data of **4** were similar to those of **3**. The ^{13}C NMR and DEPT spectra of **4** showed a pair of methine signals (δ 56.4 and 73.2) instead of a pair of methylene signals for C-12b and C-14b (C-13b in **3**) and one more carbonyl signal (δ 204.2) compared to **3**. In the ^{1}H NMR spectrum of **4**, these two methine signals appeared at δ 3.64 (1H, br d, J = 9.0 Hz, H-12b) and 3.86 (1H, br s, H-14b). The ^{1}H−^{1}H COSY correlations of H-7a (δ 3.76)/H-8a (δ 3.41) and H-7a/H-12b were observed. In the HMBC spectrum (Figure 1), the H-8a (δ 3.41), H-12b, and H-14b signals showed correlations with one carbonyl signal at δ 204.2 (C-13b), and both H-7a and H-12b signals correlated to the other carbonyl signal at 195.0 (C-11b). In addition, the H-12b signal correlated to C-8a (δ 54.6), and the H-14b signal correlated to C-7a (δ 52.1), C-9a (δ 147.1), C-8b (δ 123.3), and C-10b (δ 126.8) signals. The sequence of H-12b, H-7a, H-8a, and H-14b was further confirmed by a TOCSY experiment. The NOE effects were present between H-2a (δ 7.06) and H-8a, H-7a and H-12b, H-14b and H-10a (δ 6.17), and H-7b (δ 7.26) and H-14b. Thus, the relative stereostructure of **4** was deduced as *rel*-(7a*S*,8a*S*,12b*S*,-14b*S*).[12] The coupling constant (J_{7b-8b} = 16.0 Hz) indicated a *trans* configuration between H-7b and H-8b. From the above data, the structure of **4** was established and it was named vitisinol D. Its absolute configuration has not been determined.

Table 2. Effect of Compounds Isolated from *V. thunbergii* on the Platelet Aggregation Induced by Arachidonic Acid (AA) and 9,11-Dideoxy-11α,9α-epoxy-methanoprostaglandin $F_{2\alpha}$ (U46619)[a]

sample	IC_{50} (μM)	
	AA	U46619
vitisinol B (**2**)	>100	7.8 ± 2.2
vitisinol C (**3**)	13.4 ± 2.2	10.5 ± 3.4
vitisinol D (**4**)	15.0 ± 4.8	5.7 ± 1.4
(+)-ε-viniferin	>100	>100
(−)-viniferal	7.0 ± 2.9	3.1 ± 2.5
ampelopsin C	8.1 ± 1.1	5.9 ± 0.9
miyabenol A	9.0 ± 1.6	7.5 ± 2.0
(+)-vitisin A	10.3 ± 1.2	13.3 ± 2.1
(+)-vitisin C	5.7 ± 1.3	3.9 ± 0.7
aspirin[b]	32.7 ± 6.4	n.d.[c]

[a] Platelet suspensions were preincubated with various concentrations of each compound or solvent (0.5% DMSO, control) at 37 °C for 2 min, and the activity of antiplatelet aggregation (%) was calculated by the following equation: antiplatelet aggregation (%) = [1 − (platelet aggregation percentage of sample/platelet aggregation percentage of control)] × 100%. Then, the IC_{50} value of each compound was calculated and shown as mean ± SD (n = 4). [b] Positive control. [c] Not detected.

Table 3. Effect of Compounds Isolated from *V. thunbergii* on $ABTS^{\bullet+}$ Scavenging[a]

sample	free radical scavenging activity EC_{50} (μM)
vitisinol B (**2**)	3.6 ± 0.1
vitisinol C (**3**)	4.5 ± 0.1
vitisinol D (**4**)	4.1 ± 0.1
(+)-ε-viniferin	2.8 ± 0.1
(−)-viniferal	4.4 ± 0.1
ampelopsin C	5.4 ± 1.2
miyabenol A	6.6 ± 1.2
(+)-vitisin A	13.8 ± 2.7
(+)-vitisin C	4.8 ± 0.1
trolox[b]	28.4 ± 5.2

[a] $ABTS^{\bullet+}$ was produced from 7.5 mM ABTS and 2.5 mM $K_2S_2O_4$. Various concentrations of vehicle, drugs, and Trolox were applied to an EIA plate and then reacted with the same volume of diluted $ABTS^{\bullet+}$ solution for 6 min. The remained $ABTS^{\bullet+}$ was measured by the absorbance at 734 nm. The EC_{50} value of each compound was calculated and shown as mean ± SD (n = 6). [b] Positive control.

All the isolated compounds except **1** were tested for their antiplatelet and antioxidative activities. The inhibitory effects on arachidonic acid (AA)- and 9,11-dideoxy-11α,9α-epoxy-methanoprostaglandin $F_{2\alpha}$ (U46619, TXA_2 analogous)-induced platelet aggregation are shown in Table 2. All compounds, with the exception of vitisinol B (**2**) and (+)-ε-viniferin, showed potent activities. (+)-Vitisin C was the most effective against aggregation induced by AA, with an IC_{50} value of 5.7 ± 1.3 μM, and (−)-viniferal was the most effective against aggregation induced by U46619, with an IC_{50} value of 3.1 ± 2.5 μM. The results of the antioxidative test using the 2,2′-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) assay are shown in Table 3. The free-radical scavenging activities of all the tested compounds were more potent than Trolox.

It was reported that the antioxidative activity played an important part in the hepatoprotective[13] or antihepatotoxic effect.[14] The traditional use of *V. thunbergii* to treat hepatitis may be supported by the potent antioxidative activities of its isolated compounds.

Experimental Section

General Experimental Procedures. IR spectra were taken on a Nicolet Avatar 320 FT-IR spectrometer. Optical

rotations were measured on a JASCO DIP-370 digital polarimeter. The CD spectrum was recorded on a JASCO J-715 spectrometer. UV spectra were taken on a Hitach U-3200 UV/vis spectrometer. EIMS spectra were obtained using a JEOL JMS-D100 or Finnigan MAT GCQ spectrometer. FABMS spectra were acquired on a JEOL SX-102A spectrometer. ^{1}H NMR and ^{13}C NMR spectra were measured with a Varian Unity Inova 500 spectrometer.

Plant Material. The roots of *Vitis thunbergii* were purchased in Taipei, Taiwan, in July 1998 and identified by Mr. Jun-Chih Ou, a taxonomist retiring from our institute. A voucher specimen (NRICM-98-010) is deposited at the Herbarium of National Research Institute of Chinese Medicine, Republic of China.

Extraction and Isolation. The dried roots of *V. thunbergii* (3 kg) were extracted with EtOH. After evaporation of the solvent, the concentrated EtOH extract (120 g) was partitioned between EtOAc and H_2O, and the EtOAc fraction was chromatographed on a silica gel column eluting with gradient solvent systems of *n*-hexane−EtOAc (10:1, 5:1) and CH_2Cl_2−MeOH (15:1, 10:1, 5:1, 0:1) to yield 13 fractions. Fraction 4, CH_2Cl_2−MeOH (10:1) eluate, was further separated by a Sephadex LH-20 column (MeOH−H_2O, 3:1) and preparative silica-TLC (CH_2Cl_2−MeOH, 5:1) to afford vitisinol A (**1**, 3.2 mg). Fractions 7−12 were derived from the portion eluted with CH_2Cl_2−MeOH (5:1), and fraction 7 was purified over a silica gel column eluting with CH_2Cl_2−MeOH (10:1) to give a mixture of vitisinol C (**3**) and vitisinol D (**4**). Vitisinol C (**3**, 6.3 mg) was further purified by preparative silica-TLC (CH_2Cl_2−MeOH, 7:1), and vitisinol D (**4**, 6.7 mg) was purified by Sephadex LH-20 (MeOH−H_2O, 1:1). Fraction 9 was rechromatographed over a silica gel column eluting with CH_2Cl_2−MeOH (10:1) and then Sephadex LH-20 (MeOH−H_2O, 3:1) to afford vitisinol B (**2**, 5.2 mg). Moreover, fractions 11 and 12 were separated individually by a silica gel column eluting with CH_2Cl_2−MeOH (10:1) and Sephadex LH-20 (MeOH−H_2O, 3:1) to give (+)-ϵ-viniferin (3.5 mg), ampelopsin C (52.6 mg), and (−)-viniferal (6.4 mg) from fraction 11 as well as miyabenol A (64.7 mg), (+)-vitisin A (68.2 mg), and (+)-vitisin C (8.2 mg) from fraction 12.

Vitisinol A (1): brown powder; UV (MeOH) λ_{max} (log ∈) 277 (3.58), 230 (3.88), 201 (4.19) nm; IR (KBr) ν_{max} 3448 (OH), 2922, 1614, 1580, 1414, 1256, 1114 cm^{-1}; ^{1}H NMR (CD_3OD, 500 MHz) δ 7.52 (4H, d, J = 8.5 Hz, H-2a, 2b, 6a, 6b), 6.90 (4H, d, J = 8.5 Hz, H-3a, 3b, 5a, 5b), 6.15 (2H, d, J = 1.5 Hz, H-14a, 14b), 6.12 (2H, d, J = 1.5 Hz, H-12a, 12b), 5.43 (2H, d, J = 11.0 Hz, H-7a, 7b), 4.49 (2H, d, J = 11.0 Hz, H-8a, 8b); ^{13}C NMR (CD_3OD, 125 MHz), see Table 1; EIMS *m/z* 452 [M]$^+$ (66), 420 (42), 149 (90), 94 (100); HREIMS *m/z* 452.1253 (calcd for $C_{28}H_{20}O_6$, 452.1254).

Vitisinol B (2): brown-yellow powder; [α]$^{25}_D$ + 194.3° (*c* 0.35, MeOH); UV (MeOH) λ_{max} (log ∈) 282 (4.13), 228 (4.60), 204 (4.85) nm; IR (KBr) ν_{max} 3417 (OH), 2923, 1650, 1603, 1598, 1504, 1435, 1341, 1256, 1219, 1177, 1135, 1098, 836 cm^{-1}; CD (*c* 4.88 × 10^{-5} M, MeOH) Δ∈ (nm) −1.3 (202), +32.4 (212), +18.1 (222), +26.2 (232), −0.7 (268), +7.2 (289), +0.1 (365); ^{1}H NMR (Me_2CO-d_6, 500 MHz) δ 9.31 (1H, s, CHO), 7.42 (1H, dd, J = 2.0, 8.5 Hz, H-4c), 7.12 (2H, d, J = 8.5 Hz, H-2a, 6a), 7.04 (2H, d, J = 8.5 Hz, H-2b, 6b), 6.95 (1H, d, J = 8.5 Hz, H-3c), 6.76 (2H, d, J = 8.5 Hz, H-3a, 5a), 6.67 (2H, d, J = 8.5 Hz, H-3b, 5b), 6.66 (1H, d, J = 2.0 Hz, H-6c), 6.21 (1H, br s, H-14a), 6.14 (1H, d, J = 2.0 Hz, H-14b), 6.10 (1H, d, J = 2.0 Hz, H-12b), 6.02 (1H, br s, H-12a), 5.84 (1H, d, J = 11.5 Hz, H-7a), 5.57 (1H, d, J = 3.5 Hz, H-8b), 5.47 (1H, d, J = 3.5 Hz, H-7b), 4.26 (1H, d, J = 11.5 Hz, H-8a); ^{13}C NMR (Me_2CO-d_6, 125 MHz), see Table 1; negative FABMS *m/z* 573 [M − H]$^-$; HRFABMS *m/z* [M − H]$^-$ 573.1566 (calcd for $C_{35}H_{26}O_8$−H, 573.1550).

Vitisinol C (3): yellow powder; [α]$^{25}_D$ + 87.5° (*c* 0.24, MeOH); UV (MeOH) λ_{max} (log ∈) 358 (4.29), 279 (3.84), 226 (4.26), 202 (4.66) nm; IR (KBr) ν_{max} 3423 (OH), 2922, 1602, 1571, 1513, 1445, 1382, 1240, 1167, 830 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz) δ 7.36 (2H, d, J = 8.5 Hz, H-2b, 6b), 6.90 (2H, d, J = 8.5 Hz, H-2a, 6a), 6.88 (1H, d, J = 17.0 Hz, H-8b), 6.79 (2H, d, J = 8.5 Hz, H-3b, 5b), 6.74 (1H, d, J = 17.0 Hz, H-7b), 6.62 (2H, d, J = 8.5 Hz, H-3a, 5a), 6.16 (1H, s, H-10b), 6.12 (2H, d, J = 2.0 Hz, H-10a, 14a), 6.10 (1H, d, J = 2.0 Hz, H-12a), 3.31 (1H, m, H-7a), 3.16 (1H, m, H-8a), 3.15 (2H, m, H-13b), 3.00 (2H, d, J = 6.0 Hz, H-12b); ^{13}C NMR (Me_2CO-d_6, 125 MHz), see Table 1; EIMS *m/z* 428 [M]$^+$ (68), 414 (100), 310 (37); HREIMS *m/z* 428.1589 (calcd for $C_{27}H_{24}O_5$, 428.1555).

Vitisinol D (4): yellow powder; [α]$^{25}_D$ +142.9° (*c* 0.21, MeOH); UV (MeOH) λ_{max} (log ∈) 366 (4.23), 284 (3.89), 226 (4.29), 202 (4.62) nm; IR (KBr) ν_{max} 3437 (OH), 2917, 1713, 1640, 1592, 1509, 1446, 1340, 1240, 1172, 826 cm^{-1}; ^{1}H NMR (Me_2CO-d_6, 500 MHz) δ 7.54 (2H, d, J = 8.5 Hz, H-2b, 6b), 7.26 (1H, d, J = 16.0 Hz, H-7b), 7.13 (1H, d, J = 16.0 Hz, H-8b), 7.06 (2H, d, J = 8.5 Hz, H-2a, 6a), 6.86 (2H, d, J = 8.5 Hz, H-3b, 5b), 6.72 (2H, d, J = 8.5 Hz, H-3a, 5a), 6.24 (1H, s, H-10b), 6.23 (1H, d, J = 1.5 Hz, H-12a), 6.17 (2H, d, J = 1.5 Hz, H-10a, 14a), 3.86 (1H, br s, H-14b), 3.76 (1H, t, J = 9.0 Hz, H-7a), 3.64 (1H, br d, J = 9.0 Hz, H-12b), 3.41 (1H, d, J = 9.0 Hz, H-8a); ^{13}C NMR (Me_2CO-d_6, 125 MHz), see Table 1; EIMS *m/z* 454 [M]$^+$ (100); HREIMS 454.1405 (calcd for $C_{28}H_{22}O_6$, 454.1393).

Platelet Aggregation. Platelets were obtained from fresh rabbit blood according to the washing procedures described previously.[15] Aggregation was measured by a platelet aggregation chromogenic kinetic system (Helena Laboratories, Beaumont, TX) using the turbidimetric method[16] with the absorbance of platelet suspension assigned 0% aggregation and the absorbance of platelet-free Tyrode solution assigned 100% aggregation. The final concentration of the solvent DMSO was fixed at 0.5%, which did not affect the aggregation. Aspirin was used as a positive control.

Free-Radical Scavenging Activity.[17] The antioxidative activities of the pure compounds were assessed on the basis of the radical scavenging effect of the stable ABTS$^{\bullet+}$ free radical. ABTS$^{\bullet+}$ was produced from 7.5 mM ABTS and 2.5 mM $K_2S_2O_4$. Various concentrations of vehicle, drugs, and Trolox were applied to an EIA plate and then reacted with the same volume of diluted ABTS$^{\bullet+}$ solution for 6 min. The remained ABTS$^{\bullet+}$ was measured by the absorbance at 734 nm. Trolox was used as a positive control.

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