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CYTOTOXIC ROTENOIDS FROM *Mirabilis jalapa*

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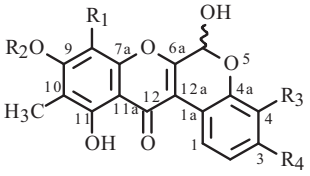
Mirabilis jalapa L. is a plant belonging to the family Nyctaginaceae, which is used as a traditional folk herb in China to treat acute arthritis, inflammation, irregular menstruation, cancerous growths, and so on, and also as an anesthetic [1]. The plant extract was found to exhibit various bioactivities, including hypoglycemic, anti-plant viral, and antiviral properties, and has an inhibitory effect on experimental prostatic hyperplasia in mice [2–4]. Chemical investigations of *M. jalapa* have led to the isolation of isoflavones, alkaloids, terpenoids, polysaccharides, rotenoids, steroids, fatty acids, volatile compounds, peptides, and proteins [5–13]. Some of the compounds showed antifungal properties, cleave DNA, inhibit HIV-1 reverse transcriptase, are cytotoxic to Hela and Raji cell lines, and possess antimicrobial and anti-plant activities [5, 6, 12, 13]. We investigated *M. jalapa* to find further antitumor principles from the plant.

The roots of *M. jalapa* were collected from Kunming, Yunnan, China in September 2003. The air-dried and chopped roots of *M. jalapa* (5.0 kg) were exhaustively extracted with 95% EtOH at room temperature, and the EtOH extract (200 g) was separated by column chromatography over silica gel, eluting with petroleum ether, $CHCl_3$, Me_2CO, and MeOH successively to give four fractions. The Me_2CO fraction (50 g) was subjected to column chromatography over silica gel (200–300 mesh), eluting with $CHCl_3$–MeOH (10:1–0:1) to give six subfractions. Subfraction 2 (20 g) was repeatedly subjected to column chromatography over silica gel (200–300 mesh), eluting with $CHCl_3$–MeOH (10:1), and over Sephadex LH-20, eluting with MeOH–H_2O (9:1) to yield compounds **1** (30 mg), **2** (27 mg), **3** (23 mg), **4** (33 mg), and daucosterol (15 mg).

Compound **1**, $C_{17}H_{12}O_6$, yellow amorphous powder. $[\alpha]_D^{23}$ –2.44° (*c* 0.00285 g/100 mL, MeOH). The mass spectrum exhibited peaks for ions at *m/z* 312 (M^+, 55), 295, 283 (100), and 267. The PMR spectrum [$(CD_3)_2CO$, δ, ppm, J/Hz] displayed signals of six protons at 8.83 (1H, dd, J = 7.9, 1.5, H-1), 7.30 (1H, ddd, J = 7.9, 7.9, 1.5, H-3), 7.13 (1H, ddd, J = 7.9, 7.9, 1.5, H-2), 7.06 (1H, dd, J = 7.9, 1.5, H-4), 6.57 (1H, s, H-8), and 6.24 (1H, s, H-6), a hydroxyl [13.19 (1H, s, 11-OH)], and a methyl group [2.26 (3H, s, 10-CH_3)]. The ^{13}C NMR and DEPT spectra [$(CD_3)_2CO$, ppm] had signals at 181.2 (C-12), 163.3 (C-9), 160.6 (C-11), 157.8 (C-6a), 155.6 (C-7a), 149.9 (C-4a), 129.5 (C-3), 127.6 (C-1), 122.9 (C-2), 118.2 (C-4), 117.9 (H-1a), 109.8 (C-12a), 108.8 (C-10), 105.7 (C-11a), 93.9 (C-8), 89.4 (C-6), and 7.5 (10-Me). Based on NMR (^1H NMR, ^{13}C NMR, COSY, HMBC, HSQC, and NOESY) and mass spectral data, **1** contains a methyl, a carbonyl, and three hydroxyls. Comparison of the spectral data with those reported in the literature showed that **1** was boeravinone B [14].



1 - 4

1: $R_1 = R_2 = R_3 = R_4 = H$
2: $R_1 = R_2 = R_3 = H$, $R_4 = OH$
3: $R_1 = R_4 = H$, $R_2 = CH_3$, $R_3 = OH$
4: $R_1 = CH_3$, $R_2 = R_4 = H$, $R_3 = OH$

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TABLE 1. Cytotoxicity of Compounds **1–4** Isolated from *Mirabilis jalapa*

Compound	IC_{50} value, μg/mL				
	K562	HL-60	A549	BEL-7402	SGC-7901
Boeravinone B (**1**)	0.92	>100	9.62	2.16	>100
Boeravinone E (**2**)	31.52	4.00	7.66	3.25	12.43
9-*O*-Methyl-4-hydroxyboeravinone B (**3**)	>100	82.31	5.00	–	2.49
Mirabijalone B (**4**)	8.73	1.26	4.44	1.94	3.55
Cisplatin	0.08	0.70	0.44	0.18	0.21

–: Not tested.

Compound **2**, $C_{17}H_{12}O_7$, yellow amorphous powder. $[\alpha]_D^{21}$ –1.51° (*c* 0.00432 g/100 mL, MeOH). The mass spectrum exhibited peaks for ions at *m*/*z* 328 (M^+, 63), and 299 (100). The NMR spectra displayed signals similar to those of **1**. The only difference is that there was one more hydroxyl group at C-3 in **2**. Comparison of the spectral data with those reported in the literature showed that **2** was boeravinone E [15].

Compounds **3** and **4** were identified as 9-*O*-methyl-4-hydroxyboeravinone B and mirabijalone B respectively, which were previously isolated from the plant [5, 6]. Compounds **1** and **2** were isolated from the plant for the first time.

Compounds **1**–**4** were evaluated for the first time for their inhibitory ability against the growth of human leukemia cell lines K562 and HL-60, human lung adenocarcinoma A549, human hepatoma BEL-7402, and human stomach cancer SGC-7901 by microculture tetrazolium (MTT) assay, with minor modifications [16, 17]. All the tested compounds displayed significant cytotoxic activity against the tested cell lines (Table 1). Mirabijalone B (**4**) was the most active compound; it exhibited IC_{50} values of 1.26–8.73 μg/mL against five cell lines, whereas boeravinone B (**1**) showed selective cytotoxicity against K562 and BEL-7402 with IC_{50} values of 0.92 and 2.16 μg/mL respectively. Boeravinone E (**2**) exerted selective activity against HL-60 and BEL-7402 with IC_{50} values of 4.00 and 3.25 μg/mL. 9-*O*-Methyl-4-hydroxyboeravinone B (**3**) showed selective cytotoxicity against SGC-7901 with IC_{50} values of 2.49 μg/mL.

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