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FLAVONOIDS FROM *Dracaena cambodiana*

Hui Wang, Jian Liu, Jiao Wu, Wen-Li Mei*, and Hao-Fu Dai*

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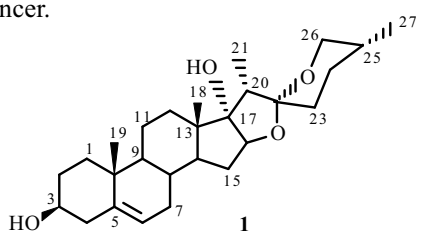
Dracaena cambodiana Pierre ex Gagnep (Liliaceae), known as one of the Dragon′s blood trees, is endemic to Hainan island of China, Cambodia, and Laos [1]. Previous studies have led to the isolation of four steroidal saponins from the fruits of *D. cambodiana* [2]. In addition, we have also isolated seven flavanes and one homoisoflavonoid from the stem of *D. cambodiana* [3, 4].

In continuation of the search for bioactive constituents, ten compounds were isolated from this plant, and their structures were identified by ^{1}H and ^{13}C NMR, as well as comparisons with the literature data. They are (25*R*)-spirost-5-ene-3β,17α-diol (**1**) [5], 3,4-dihydroxyallylbenzene (**2**) [6], 7,4′-dihydroxy-8-methoxyhomoisoflavane (**3**) [7], 7,4′-dihydroxyhomoisoflavane (**4**) [8], *p*-hydroxy-benzaldehyde (**5**) [9], 4,4′-dihydroxy-2-methoxydihydrochalcone (**6**) [10], 4,4′-dihydroxy-3,2′-dimethoxychalcone (**7**) [11], 4,2′,4′-trihydroxychalcone (**8**) [10], 4,4′-dihydroxy-2′-methoxychalcone (**9**) [10], and 8-methylsocotrin-4′-ol (**10**) [12]. Although all the identified isolates are known compounds, this is the first report of their isolation from *D. cambodiana*.

The cytotoxic activities of all the compounds against chronic myelogenous leukemia cells (K562), human hepatoma cells (SMMC-7721), and human gastric cancer cells (SGC-7901) were evaluated using MTT assay as described by Mosmann [13]. Compounds **6–10** exhibited cytotoxic activity, as demonstrated in Table 1. Compounds **7–9** are chalcones, and compound **6** is a dihydrochalcone. Compound **6**, with a single bond between C-α and C-β only, showed much lower cytotoxic activities against human hepatoma cells, while compound **7**, with a double bond between C-α and C-β and two methoxylated aromatic carbons, exhibited the highest activities against the three cell lines, with IC_{50} 2.5, 4.3, and 4.4 μg/mL, respectively, suggesting that the double bond between C-α and C-β, as well as the methoxylated aromatic carbons, contribute to its cytotoxic activities. Compound **10**, a biflavonoid, demonstrated weak cytotoxic activity, while compounds **1–5** showed no activity. In conclusion, the findings of this study suggest that some flavonoids isolated from *D. cambodiana* may prove useful for the treatment of human cancer.



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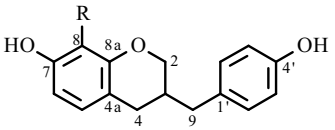
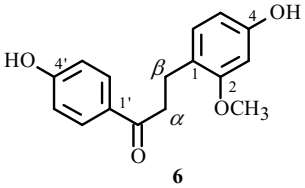


3, 4

3: R = OCH_3; **4:** R = H



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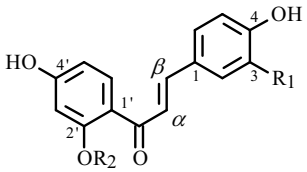
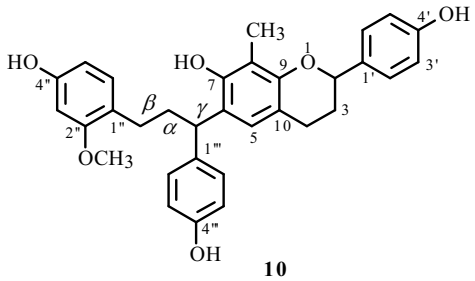


7 - 9

7: R_1 = OCH_3, R_2 = CH_3
8: R_1 = R_2 = H; **9:** R_1 = H, R_2 = CH_3



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Key Laboratory of Tropical Crop Biotechnology, Ministry of Agriculture, Institute of Tropical Bioscience and Biotechnology, Chinese Academy of Tropical Agricultural Sciences, Haikou 571101, Hainan, P. R. China, fax: 86 898 66988061, e-mail: hfdai2001@yahoo.com.cn; meiwenli@yahoo.com.cn. Published in Khimiya Prirodnykh Soedinenii, No. 4, pp. 551–552, July–August, 2011. Original article submitted April 22, 2010.

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TABLE 1. *In vitro* Cytotoxic Activity of the Compounds against Three Cancer Cell Lines (IC_{50}, μg/mL)

Compound	K562	SMMC-7721	SGC-7901	Compound	K562	SMMC-7721	SGC-7901
6	–	34.0	–	**9**	32.5	12.5	11.0
7	2.5	4.3	4.4	**10**	28.5	39.5	16.8
8	40.5	19.0	–	Mitomycin C*	7.1	2.2	8.8

*Mitomycin C (MMC) was used as the positive control.

Melting points were obtained on a Beijing Taike X-5 stage apparatus and were uncorrected. The NMR spectra were recorded on a Bruker AV-400 spectrometer, using TMS as an internal standard. Column chromatography was performed with silica gel (Marine Chemical Industry Factory, Qingdao, China) and Sephadex LH-20 (Merck). TLC was preformed with silica gel GF254 (Marine Chemical Industry Factory, Qingdao, China).

Plant Material. The stems of *D. cambodiana* were collected in Haikou, Hainan province, China (July, 2007), dried immediately, and crushed into pieces. The specimen was identified by Associate Professor Dai Zheng-Fu of the Institute of Tropical Bioscience and Biotechnology, Chinese Academy of Tropical Agricultural Sciences, where a voucher specimen (No. 20070701) of *D. cambodiana* was deposited.

Isolation of the Constituents. The dried and crushed stems of *D. cambodiana* (13.3 kg) were extracted three times with 95% EtOH at room temperature. The extract was evaporated under reduced pressure to dryness and then partitioned in succession between H_2O and petroleum ether, EtOAc, and then *n*-BuOH. The EtOAc fraction (150.0 g), which showed cytotoxic activities against several cancer cell lines, was separated into 10 fractions on a silica gel column using step gradient elution of $CHCl_3$–MeOH (v/v, 100:1–0:1).

Fraction 2 (18.0 g) was subjected to chromatography on a silica gel column with petroleum ether–acetone (7:1, v/v) as eluent, and yielded 11 subfractions. Subfraction 4 (0.9 g), subfraction 5 (1.6 g), subfraction 10 (0.79 g), and subfraction 11 (1.3 g) were subjected to repeated column chromatography on silica gel with $CHCl_3$–MeOH (50:1–30:1, v/v) as eluent and Sephadex LH-20 with EtOH as eluent, yielding compounds **1** (62.4 mg), **2** (116.6 mg), **3** (13.6 mg), and **4** (8.3 mg), respectively.

Fraction 3 (20.0 g) was subjected to column chromatography on silica gel with step gradient elution of $CHCl_3$–MeOH (v/v, 50:1–0:1), yielding 10 subfractions. Subfraction 4 (1.3 g), subfraction 5 (4.3 g), subfraction 6 (1.7 g), and subfraction 7 (3.2 g) were subjected to repeated column chromatography on silica gel and Sephadex LH-20, yielding compounds **5** (9.8 mg), **6** (178.7 mg), **7** (26.5 mg), **8** (15.5 mg), and **9** (57.7 mg), respectively.

Fraction 4 (51.0 g) was subjected to column chromatography on silica gel with step gradient elution of $CHCl_3$–MeOH (v/v, 50:1–0:1), yielding 8 subfractions. Subfraction 4 (6.2 g) was subjected to repeated column chromatography on Sephadex LH-20 and silica gel to yield compound **10** (55.8 mg).

***In vitro* Cytotoxic Activities Assay**. All the compounds were examined for their cytotoxic activities against chronic myelogenous leukemia (K562), human gastric cancer (SGC-7901), and human liver cancer (SMMC-7721) cell lines. Cancer cells were incubated at 37°C for 3 days in the presence of various concentrations of compounds from DMSO-diluted stock solutions. The growth inhibitory property was determined using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay as described by Mosmann [13].

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