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长花龙血树茎中抗氧化活性的木脂素类成分研究

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摘要 从长花龙血树的茎中分离得到一个新的木脂素化合物, 命名为 angudracanolide A (**1**), 以及三个已知的木脂素 **2**～**4** 和三个已知的苯基丙酸类化合物 **5**～**7**. 通过对光谱数据的分析和量子化学计算, 阐明了新化合物的绝对构型. 与作为阳性对照的 trolox 相比(IC_{50} 值为 0.45 mmol/L), 化合物 **1**～**4** 显示出明显的抗氧化活性, IC_{50} 值分别为 15, 19, 25, 30 mmol/L.

关键词 长花龙血树; 木脂素; 抗氧化活性

Lignanolides with Antioxidant Activity from the Stems of *Dracaena angustifolia*

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Abstract A new lignanolide given a trivial name angudracanolide A (**1**), together with three known lignans **2**～**4** and three known phenylpropanoids **5**～**7**, was isolated from the stems of *Dracaena angustifolia*. The complete structure of new compound was elucidated by analysis of spectroscopic data and quantum chemistry calculations. Compounds **1**～**4** showed obvious antioxidant activity with IC_{50} values of 15, 19, 25, 30 mmol/L, respectively by comparing the standard trolox with a IC_{50} value of 45 mmol/L.

Keywords *Dracaena angustifolia*; lignan; antioxidant activity

1 Introduction

Dracaena angustifolia was composed of more than 40 species and mainly found in Hainan, Taiwan and Yunnan provinces, in China, as well as Australia, India, Malaysia, and Philippines.[1] *D. angustifolia* is also regarded as one of the Li-nationality medicinal plants for treatment of endemic arthralgia and myalgia on Hainan Island, China. Hitherto

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there are few research reports about the chemical constitutes of *D. angustifolia*. Our previous phytochemical studies on the species of *D. angustifolia* had led to the discovery of a type of phenolic compounds.[2] Recently, investigation of the ethyl acetate extract from *D. angustifolia* afforded seven compounds, including a new lignanolide angudracanolide A (**1**), and three known lignans (−)-syringaresinol (**2**),[3] de-4'-*O*-methyl-yangambin (**3**),[4] (+)-isolariciresinol (**4**),[5] along with three known phenylpropanoids zhebeiresinol (**5**),[6] *β*-hydroxypropio-vanillone (**6**),[7] erythro-7*R*,8*S*-7-*O*-ethylguaiacyl glycerol (**7**)[8] (Figure 1). Meanwhile, the antioxidant activity of all compounds above was also evaluated.

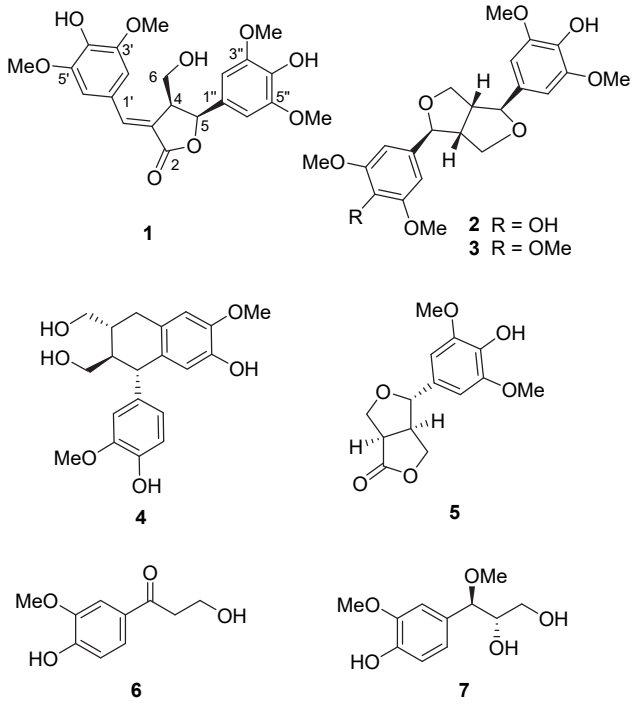

Figure 1 Chemical constituents from *Dracaena angustifolia*

2 Results and discussion

2.1 Structure elucidation

Compound **1** was obtained as a white amorphous powder with a molecular formula of $C_{22}H_{24}O_9$ by high resolution electrospray ionization mass spectroscopy (HRESIMS) spectrum showing $[M+H]^+$ ion at *m/z* 433.1495 (calcd for 433.1493), suggesting eleven degrees of unsaturation.

The ^{1}H NMR spectrum of **1** showed an olefinic proton signal at δ_H 7.49 (s, 1H, H-7'), two groups of equivalent protons at δ_H 6.99 (s, 2H, H-2',6') and 6.55 (s, 2H, H-2",6"), two pairs of equivalent methoxy groups at δ_H 3.80 (s, 6H, H-3",5"-OMe) and 3.73 (s, 6H, H-3',5'-OMe), two sp^3 methine protons at δ_H 5.55 (s, 1H, H-5) and 3.63～3.66 (m,1H, H-4), and an oxygenated methylene signal with chemical shifts of δ_H 3.85～3.89 (m, 1H, H-6) and 3.60～3.64 (m, 1H, H-6). The ^{13}C NMR spectrum (Table 1) presented 22 carbon signals containing an ester carbonyl carbon at δ_C 171.9, nine sp^2 none-protonated carbons including two groups of equivalent carbons at δ_C 148.2, 148.1, five sp^2 methine carbons comprised of two suites of isovalent carbons at δ_C 108.4 and 103.2, and a carbon at δ_C 138.5, as well as two batteries of equivalent methoxyl carbons at δ_C 56.2 and 56.1, three sp^3 carbons consisted of an oxygenated methylene at δ_C 61.1, and two methines with chemical shifts of δ_C 81.0 and 49.6. Analysis of the ^{1}H NMR and ^{13}C NMR data of **1**, revealed that it was extremely similar to those of descurainolide B,[9] except for the additional appearances of a methylol group (δ_C 61.1) and a methine (δ_C 49.6) in **1**, and the absence of a methylene (δ_C 35.4) in descurainolide B.[9] Thus, it provided a speculation that the structure of **1** was an analog of descurainolide B[9] with a methylol located at C-4 (δ_C 49.6). This was supported by the observation of HMBC correlations. In the HMBC spectrum, the observed HMBC correlations from H-5 (δ_H 5.55) to C-2 (δ_C 171.9)/C-3 (δ_C 131.0)/C-4 (δ_C 49.6)/C-6 (δ_C 61.1), from H-7' (δ_H 7.49) to C-2 (δ_C 171.9)/C-4 (δ_C 49.6), from H-4 (δ_H 3.66) to C-3 (δ_C 131.0)/C-5 (δ_C 81.0)/C-6 (δ_C 61.1), ascertained that the methylene CH_2-4 in descurainolide B[9] was substituted by the methylol group (δ_H 3.87/3.63, δ_C 61.1) in **1**. The geometrical configuration of the double bond between C-3 (δ_C 131.0) and C-7' (δ_C 138.5) was determined as *E* by NOESY experiment, which showed a cross-peak between H-4 and H-2' (Figure 2). However, the establishment of the relative configuration of **1** was challenged by observation of NOESY spectrum, due to H-4 was in close proximity to H-5 in the furan ring. Thus, the relative configuration of **1** was determined by DP4+ probability analysis.[10] Structure of

Table 1 ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) data of compound **1** in DMSO-d_6

Position	**1**	
	δ_H (*J* in Hz)	δ_C
2		171.9
3		131.0
4	3.63～3.66, m	49.6
5	5.55, s	81.0
6	3.60～3.64, m; 3.85～3.89, m	61.1
1'		123.8
2',6'	6.99, s	108.4
3',5'		148.1[a]
4'		138.4
7'	7.49, s	138.5
1"		122.2
2",6"	6.55, s	103.2
3",5"		148.2[a]
4"		135.7
3',5'-OMe	3.73, s	56.1
3",5"-OMe	3.80, s	56.2

[a] Interchanged.

1 with two chiral centers afforded two possible candidate diasteroisomers **1a** (4*R**,5*S**-**1**) and **1b** (4*S**,5*S**-**1**).

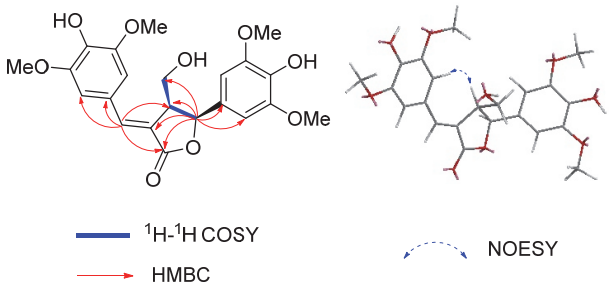

Figure 2 Key HMBC 1H-1H COSY and NOESY correlations for compound **1**

Subsequently, diasteroisomers **1a** and **1b** were employed for systematic conformational analysis by Spartan' 14 software with molecular mechanic force field (MMFF94) method, respectively. The yielded conformations for **1a** and **1b** were performed structural optimizations and single-point energy calculations. The conformations with Boltzmann Gibbs energy distributions above 1% were used for calculations of NMR data, respectively. As a result, diasteroisomer **1b** with 4*S**/5*S** configuration was in high confidence with a DP4+ probability value of 100% relative to **1a**. Therefore, the relative configuration of **1** was assigned as 4*S**,5*S**-**1**. Further the absolute configuration of **1** was established by comparison of its calculated electrostatic circular dichroism (ECD) spectra with the experimental one. Finally, a com- prehensive ECD spectrum for 4*S*,5*S*-**1** was calculated on the PBE1PBE/6-311g(d) (SMD) level of theory, while a mirrored ECD spectrum for the enantiomer 4*R*,5*R*-**1** was also afforded. And the absolute configuration of **1** was regarded as 4*S*/5*S* because the calculated curve of 4*S*,5*S*-**1** matched the experimental spectrum well (Figure 3).

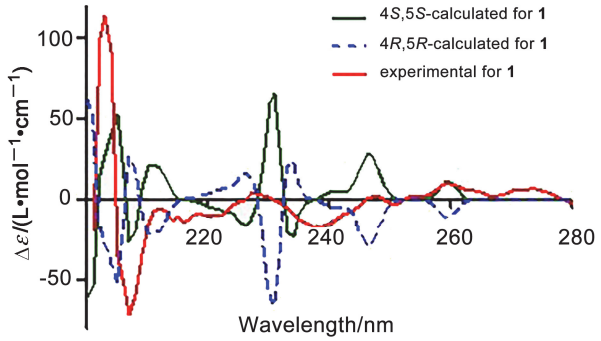

Figure 3 Comparison of the calculated and experimental ECD spectra for compound **1**

Based on above, the complete structure of **1** was established as 4*S*,5*S*,3*E*-(4-hydroxy-3,5-dimethoxy-benzylidene)-4-methylol-5-(4-hydroxy-3,5-dimethoxy-phenyl)-2(2*H*)-furanone, and was given a trivial name angudracanolide A, as depicted in Figure 1.

Other six known (−)-syringaresinol (**2**),[3] de-4'-*O*-methylyangambin (**3**),[4] (+)-isolariciresinol (**4**),[5] zhebeiresinol (**5**),[6] *β*-hydroxypropiovanillone (**6**),[7] erythro-7*R*,8*S*-7-*O*-ethylguaiacylglycerol (**7**)[8] (Figure 1) were identified by comparing their physical and spectroscopic data with those of compounds in literatures.

2.2 Antioxidant activity

Compounds **1**～**7** were evaluated for antioxidant activity, while trolox was used as a positive control. Among them, compounds **1**～**4** showed obvious antioxidant activity with IC_{50} values of 0.15, 0.19, 0.25 and 0.30 mmol/L, respectively, relative to positive control trolox with a IC_{50} value of 0.45 mmol/L (Table 2).

Table 2 Antioxidant activity of compounds **1**～**7**

Compd.	IC_{50}/(mmol•L^{-1})
1	15
2	19
3	25
4	30
5	>50
6	>50
7	>50
Trolox	45

3 Conclusions

In this study, a new lignanolide named angudracanolide A (**1**), and three known lignans **2**～**4**, along with three known phenylpropanoids **5**～**7** were isolated from the stems of *D. angustifolia*. It was noted that compounds **4**～**6** were got from the species of *D. angustifolia* for the first time. In addition, compounds **1**～**4** showed obvious antioxidant activity with respect to the positive control trolox. This investigation enriches the structural diversity of *D. angustifolia* and provides good molecular templates for the development of new drug lead compounds.

4 Experimental section

4.1 General experimental procedures

IR spectra were recorded on a Nicolet 6700 spectrophotometer. Optical rotations were measured on a JASCO P-1020 digital polarimeter. ECD spectra were obtained at room temperature on a Jasco J-815 circular dichroism spectrometer. NMR spectra were recorded on a Bruker AV spectrometer (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR). Tetramethylsilane (TMS) was used as a reference. HRESIMS spectra were measured on a Q-TOF Ultima Global GAA076 LC mass spectrometer. Semi-preparative high performance liquid chromatography (HPLC) was performed on an Agilent 1260 LC series with a DAD detector using an Agilent Eclipse XDB-C_{18} column (9.4 mm×250 mm, 5 μm). Silica gels (Qing Dao Hai Yang Chemical Group Co.; 100～200, 200～300 mesh) were

used for open column chromatography (CC). Pre-coated silica gel plates (Yan Tai Zi Fu Chemical Group Co.; G60, F-254) were used for thin-layer chromatography (TLC). Microplate spectrophotometer (BD, Bioscience U. S. A.) was used as a template reader for testing antioxidant activity.

4.2 Plant material

Dracaena angustifolia was collected in July 2017 from Changjiang city, Hainan province, China. The species was authenticated as *Dracaena angustifolia* by Dr. Yu-Kai Chen (Hainan Normal University, Hainan, China). The specimens (No C17-L07) were deposited at the Key Laboratory of Tropical Medicinal Resource Chemistry of Ministry of Education, Hainan Normal University (Hainan, China).

4.3 Extraction and isolation

The powdered air-dried stems (10 kg) of *D. angustifolia* were extracted with 75% ethanol (20 L×4, 5 d each) at room temperature. The filtered solution was evaporated in vacuum to give a crude extract. Subsequently, the extract was partitioned with petroleum ether and ethyl acetate solvent, respectively. The extract (90 g) derived from ethyl acetate layer was separated using a normal phase silica gel column chromatography (CC) [petroleum ether/ethyl acetate and chloroform/methanol, step gradient], affording ten major fractions (Fr.1～Fr.10). Frs.8 (9.9 g) was subjected to silica gel column chromatography (CC) (petroleum ether/ethyl acetate and chloroform/methanol, step gradient), attaining nine sub-fractions (Frs.8.1～Frs.8.9). Frs.8.2 (1.1 g) was further purified using semi-preparative HPLC (MeCN/H_2O, V∶V=30∶70) to obtain **5** (2.4 mg) and **6** (9.7 mg). Frs.8.6 (2.6 g) was prepared through semi- preparative HPLC (MeCN/H_2O, V∶V=15∶85, ULTRON ES-OVM column) to obtain **1** (13.4 mg) and **4** (17.4 mg). Frs.8.7 (5.0 g) was subjected to CC (chloroform/methanol from 30% to 100%) to yield three sub-fractions (Fr.8.7.1～Fr.8.7.3). Fr.8.7.1 (2.1 g) was purified by CC (petroleum ether/acetone, V∶V=7∶3～1∶1) to afford compound **7** (3.81 mg). Frs.8.7.2 (2.5 g) was performed by reverse-phase (RP) CC and eluted with methanol/water (from 10% to 100%), obtaining three subfractions (Fr.8.7.2.1 ～ Fr.8.7.2.3). Fr.8.7.2.2 (200 mg) was separated by repeated semi-preparative HPLC (MeOH/H_2O, V∶V=30∶70) to obtain **2** (5.1 mg). Fr.8.7.2.3 (1.4 g) was purified by semi-preparative HPLC (MeCN/H_2O, V∶V=10∶90, ULTRON ES-OVM column) to collect **3** (12.4 mg).

4.4 Physical properties of compound **1**

Compound **1**: White amorphous powder; $[\alpha]_D^{25}$ −3.5 (*c* 0.1 MeOH); UV (MeOH) λ_{max} [log ε/(L•mol^{-1}•cm^{-1})]: 338.0 (0.810), 242.0 (0.837), 208.0 (2.21) nm; IR (KBr) ν_{max}: 3554, 3437, 2939, 2846, 1734, 1629, 1605, 1516, 1461, 1334, 1213, 1157, 1114, 1043, 831, 735, 681, 624, 565, 527 cm^{-1}; ECD (*c* 1.16 mmol/L, MeOH) λ_{max} [$\Delta\varepsilon$/(L•mol^{-1}•cm^{-1})]: 203 (114.06), 212 (−5.11), 227 (3.27) nm. HR-ESI-MS calcd for $C_{22}H_{25}O_9$ $[M+H]^+$ 433.1495, found 433.14934.

4.5 Assay of antioxidant activity

The antioxidant capacity was measured using T-AOC assay kit.[11-12] Firstly, an 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonicacid) (ABTS) working mother solution with equal volumes of ABTS solution and oxidant solution was prepared. Then the radical cation (ABTS+•) solution was prepared (7 mmol/L ABTS in water) with potassium persulfate (2.45 mmol/L) and incubated at room temperature for 12～16 h, to achieve a stable oxidative state in a space without light. The ABTS+• solution was diluted with phosphate-buffered saline (PBS) (pH 7.4) to obtain a solution with an absorbance of (0.700±0.01) at 734 nm. A portion of 10 μL of sample mixed with an aliquot of 200 μL of ABTS solution reacted for 2～6 min in the dark apace at room temperature. And the accumulations of oxidation products were measured by the absorption spectrum of 734 nm with a UV-spectrophotometer. The absorbance of ABTS+• blank and trolox as a positive control was also measured at the paralleled approach. Percentage inhibitions of ABTS were calculated according to the following equation: Inhibition of $A_{734}(\%) = (1 - A_S/A_b) \times 100\%$, where A_S=absorbance of sample, A_b=absorbance of blank.

Supporting Information 1D NMR and 2D NMR, HR-ESI-MS spectra of compound **1**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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