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Short communication

Plebeins A-F, sesquiterpenoids and diterpenoids from *Salvia plebeian*

Cheng-Gang Zhang[a,b,1], Min-Rong Jin[a,b,1], Gui-Xin Chou[a,b,*], Qing-Shan Yang[c,**]

[a] The MOE Key Laboratory of Standardization of Chinese Medicines, SATCM Key Laboratory of New Resources and Quality Evaluation of Chinese Medicines, Institute of Chinese Materia Medica, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, People's Republic of China
[b] Shanghai R&D Center for Standardization of Chinese Medicines, Shanghai 201203, People's Republic of China
[c] College of Pharmacy, Anhui University of Chinese Medicine, Hefei 230012, People's Republic of China

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ABSTRACT

Plebein A (**1**), a sesquiterpenoid with a novel skeleton and another sesquiterpenoid, plebein B (**2**), and four new diterpenoids plebeins C-F (**4–7**), along with six known compounds were isolated from the whole plant of *Salvia plebeia* R. Br. The absolute configuration of **2** was established by an X-ray crystallographic study. In addition, compounds **4**, **6** and **9** showed anti-proliferative activity against CaCo2 and MCF-7 cell lines, with IC_{50} values ranging from 9.65 μM to 45.96 μM.

1. Introduction

The *Salvia* genus comprises nearly 1000 species worldwide, of which about 78 species are distributed in China. A variety of diterpenes were found from this genus, including abietane, clerodane, incetexane, pimarane and labdane-type (Pan et al., 2010). *Salvia plebeia* R. Br. is an annual or biennial herba, which has been used in folk medicine for the treatment of cough, hepatitis (Qu et al., 2009) and haemorrhoids. The resent studies found that the whole plant of *S. Plebeia* also had antitumor, antioxidant, and antiangiogenesis activities (Jung et al., 2009; Gu and Weng, 2001; Ren et al., 2010). Previous phytochemical studies on *S. Plebeia* were mainly flavonoids, only a few of diterpenes and sesquiterpenoids had been reported.

Herein, the isolation and structural elucidation of one sesquiterpenoid, plebein A (**1**), with a rare 5/6/3 tricyclic ring system and other five new compounds as well as the cytotoxic effects against CaCo2 and MCF-7 cells are reported.

2. Results and discussion

Compound **1** was isolated as the colorless oil. Its molecular formula was assigned to be $C_{15}H_{26}O_2$ by HRESIMS at *m/z* 261.1830 $[M+Na]^+$ (calcd. for 261.1825), indicating 3 ◦ of unsaturation. The ^1H and ^{13}C NMR data established the presence of 15 carbons, which were all sp^3 carbons. According the above data indicated that **1** had three rings. Analysis of the ^1H–^1H COSY and HSQC spectra indicated the presence of a structural fragment in the molecule: $–CH_2–CH_2–$ CH–CH–CH–CH–$CH_2–$ (C-4–C-3–C-2–C-6–C-7–C-8–C-9), as shown in Fig. 2.

The HMBCs (Fig. 2) of H-15 (δ_H 1.26) with C-4 (δ_C 43.0), C-5 (δ_C 78.8) and C-6 (δ_C 49.1), in combination with the HMBCs of H-6 (δ_H 1.05) with C-2 (δ_C 48.1), C-3 (δ_C 24.6), C-5 and C-15 (δ_C 25.9) indicated that C-2–C-3–C-4–C-5(C-15)–C-6 formed a 2-hydroxyl, 2-methyl cyclopentane moiety. In addition, the HMBCs of H-13 (δ_H 3.27) and H-14 (δ_H 0.82) with C-1 (δ_C 39.0), C-2 and C-9 (δ_C 30.1) indicated that C-1(C-13, C-14)–C-2–C-6–C-7–C-8–C-9 formed a 2-hydroxymethyl, 2-methyl cyclohexane group. The last ring was defined as 2, 2-dimethyl cyclopropane group, which was confirmed by the HMBCs of H-11 (δ_H 1.05) and H-12 (δ_H 0.99) with C-7 (δ_C 25.5), C-8 (δ_C 20.7), and C-10 (δ_C 18.5). Therefore, the planar structure of **1** was assigned as shown (Fig. 1).

In the NOESY spectrum, H-6 was correlated with H-12, H-14 and H-15, H-13 was correlated with H-2 and H-8, H-7 was correlated with H-2 and H-11 was correlated with H-8, suggesting H-6, H-12, H-14 and H-15 were α-oriented, while H-2, H-7, H-8, H-11 and H-13 were β-oriented. Based on the above analyses, the structure of compound **1**, plebein A, was characterized as shown.

* Corresponding author at: The MOE Key Laboratory of Standardization of Chinese Medicines, SATCM Key Laboratory of New Resources and Quality Evaluation of Chinese Medicines, Institute of Chinese Materia Medica, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, People's Republic of China.
** Corresponding author.
E-mail addresses: chouguixinzyb@126.com (G.-X. Chou), yqssyx2008@163.com (Q.-S. Yang).
[1] These authors contributed equally to this work.

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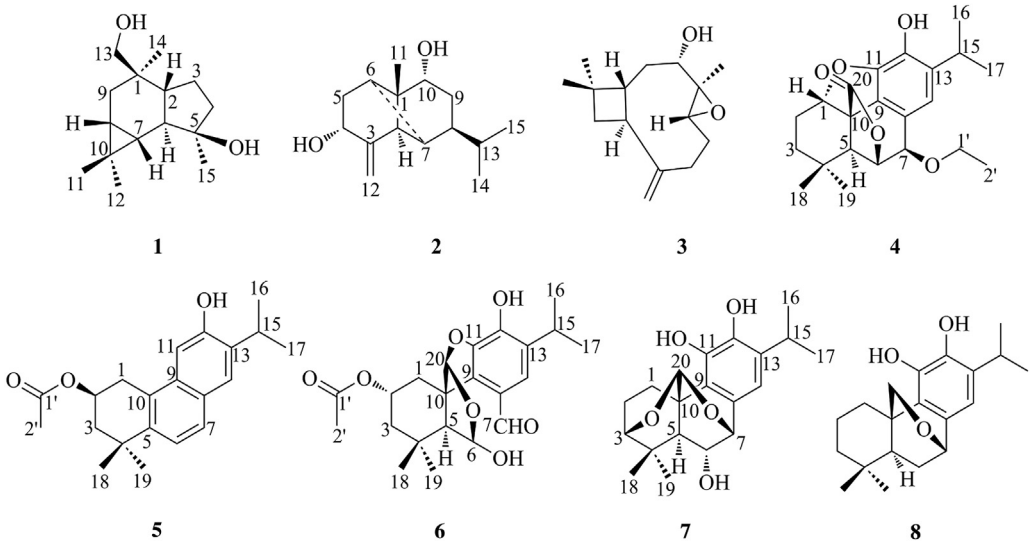

Fig. 1. Compounds from the whole plant of *Salvia plebeia*.

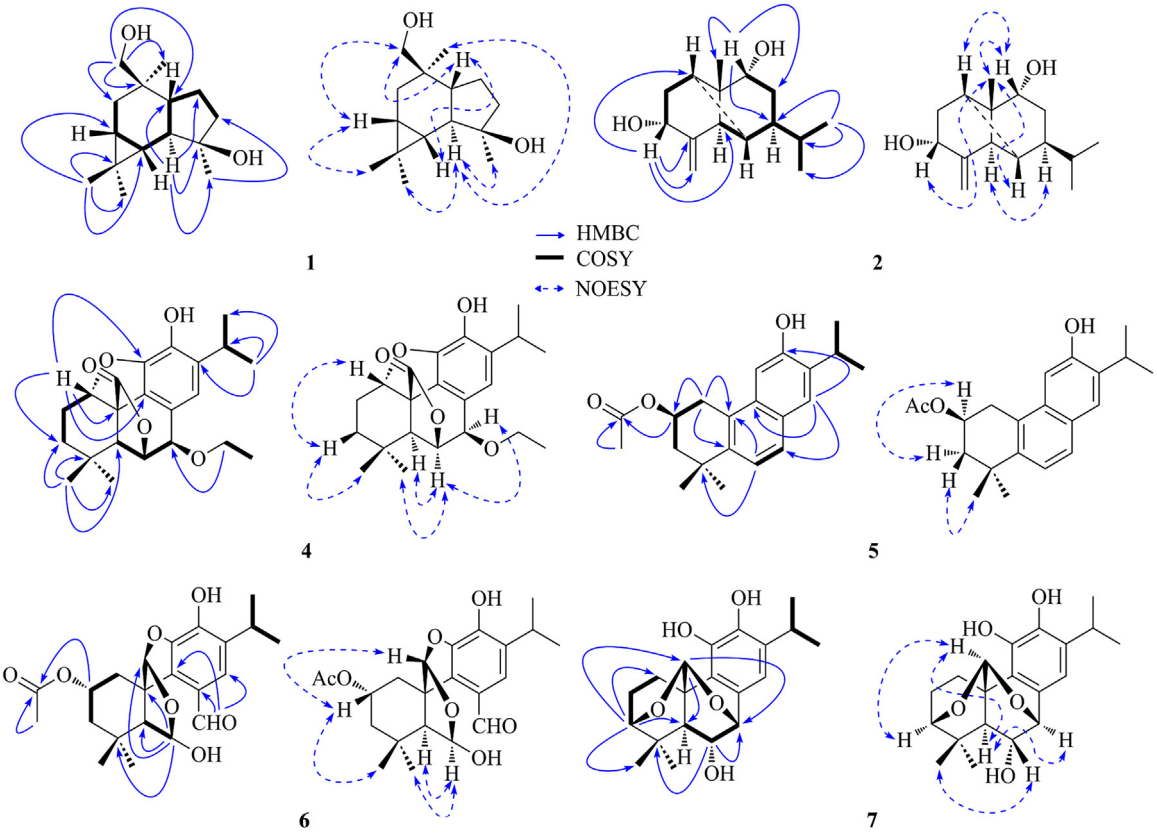

Fig. 2. Key HMBC, COSY and NOESY correlations of compounds **1**–**2**, **4**–**7**.

Compound **2** had a molecular formula of $C_{15}H_{24}O_2$ as established by the sodium adduct (+)-HRESIMS ion and ^{13}C NMR data. The ^{1}H and ^{13}C NMR data (Tables 1 and 3) of **2** were very similar to those of lemnalol (Kikuchi et al., 1982), a ylangene-type sesquiterpene, except for an additional hydroxyl group at C-10 in **2**. The HMBCs (Fig. 2) of H-10 to C-8, C-9 and C-11 demonstrated the hydroxyl was attached at C-10 position. In the NOESY spectrum, the correlations of H-10/H-11, H-10/H-6, H-4/H-11, H-7/H-11 revealed these protons were cofacial and were randomly assigned as β-oriented. While the H-2 was correlated with H-8, suggesting they were α-oriented. Additionally, the absolute configurations of 2 was further determined as 1*R*, 2*R*, 4*S*, 6*S*, 7*S*, 8*S* and 10*R* by an X-ray diffraction (Fig. 3) study. Thus, the structure of **2** was elucidated as 10*R*-hydroxyllemnalol and named plebein B.

Compound **4** was isolated as a colorless crystal. Its molecular formula was assigned as $C_{22}H_{28}O_5$ by HRESIMS [a molecular ion peak $[M+Na]^+$ at m/z 395.1859 (calcd. for 395.1834)] and ^{1}H and ^{13}C NMR spectroscopic data, suggesting 9 ° of unsaturation. The ^{1}H and ^{13}C NMR data (Tables 2 and 3) resembled those of 7-ethoxyr-osmanol (Ahmed et al., 1995), except for the loss of one methylene