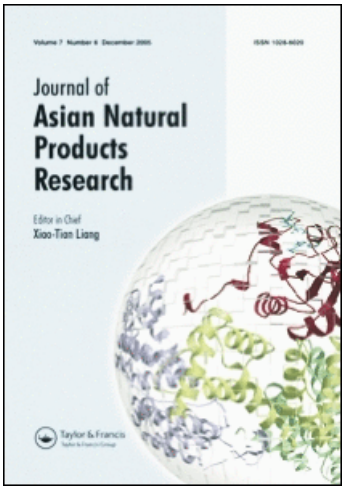

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Sesquiterpenoids from *Valeriana tangutica*

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A new guaiane-type sesquiterpenoid ethoxyvalerianol (**1**) and one known sesquiterpenoid valeranone (**2**) together with selina-4,7(11)-diene (**3**) and selinene (**4**), which were obtained from (+)-maaliol (**5**) by decyclization and dehydration, were isolated from *Valeriana tangutica*. Their structures were elucidated by 1D- and 2D-NMR spectroscopic data and HR-ESI-MS analysis.

Keywords: Valerianaceae; *Valeriana tangutica*; sesquiterpenoids; ethoxyvalerianol

1. Introduction

In search for bioactive agents from folk medicines used by Yugu nationality in northern region of Gansu province of China, we were attracted by the species of *Valeriana tangutica* Batal., locally known as 'Xiang-Mao-Cao', because of the strong fragrance [1]. *V. tangutica* has a long history of use in Yugu nationality folk medicine and it is one of the most frequently used herbal remedies in Yugu nationality. The whole plants of *V. tangutica* were utilized to treat haemorrhage [2]. *V. tangutica* belonging to the genus *Valeriana* (Valerianaceae) is a highly respected medicinal plant described in many pharmacopeia monographs [3]. The major active compounds present in *Valeriana* are fragrant monoterpenoids, sesquiterpenoids, and valepotriates [4–10]. A new sesquiterpenoid, ethoxyvalerianol (**1**) (Figure 1), and a known sesquiterpenoid valeranone (**2**) were isolated from petroleum ether extract of *V. tangutica,* together with selina-4,7(11)-diene (**3**) and selinene (**4**), which were obtained from (+)-maaliol (**5**) by decyclization and dehydration.

2. Results and discussion

Compound **1** was obtained as yellow gum. Its molecular formula was determined as $C_{19}H_{34}O_4$ on the basis of the $[M + Na]^+$ peak at *m/z* 349.2354 in its HR-ESI-MS, which was supported by the evidence from the ^{13}C NMR analysis combined with the DEPT experiment (Table 1). The NMR spectrum indicated the presence of two ethoxyl groups at δ_H 3.36 (2H, q), 1.04 (3H, t), 3.33 (2H, q), and 1.09 (3H, t) and δ_C 56.4, 15.9, 55.9, and 16.0, in the compound **1**. The ^1H NMR spectrum of **1** clearly indicated that there were four methyl groups at δ 1.31 (3H, s), 1.16 (3H, s), 1.09 (3H, s), and 0.93 (3H, d, $J = 6.4$ Hz). Both the ^1H- and ^{13}C NMR spectra showed the presence of several other typical functions, such as one C=C double bond at δ_C 146.6(C), 133.8 (CH) and δ_H 5.95 (d, $J = 4.0$ Hz, 1H); three oxygenated quaternary carbons at δ 83.5, 86.3, and 76.3, as well as one oxygenated CH group at δ_C 78.7 and δ_H 3.81 (br d, $J = 3.6$ Hz, 1H). Those structural features described above suggested that compound **1** was a sesquiterpene with two ethoxyl groups.

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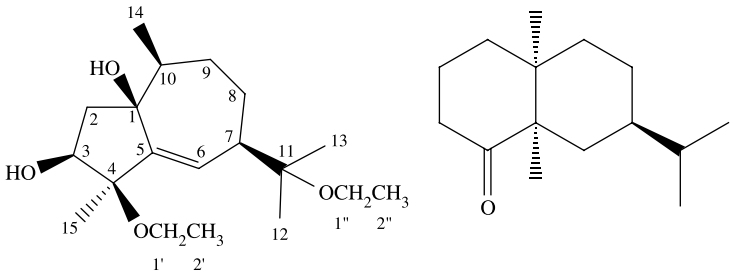
Table 1. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectral data of **1** ($CDCl_3$, TMS, δ ppm, J Hz).

Position	^{13}C NMR	HMQC (δ_H)	$^{1}H-^{1}H$ COSY	HMBC(H → C)
1	83.5 (C)			
2α	45.1 (CH_2)	2.23 (dd, $J = 14.0, 3.6$)	3	1, 3, 4, 5, 10
2β		1.76 (d, $J = 14.0$)		
3	78.7 (CH)	3.81 (br d, $J = 3.6$)	2	1, 5
4	86.3 (C)			
5	146.6 (C)			
6	133.8 (CH)	5.95 (br d, $J = 4.0$)	7	1, 4, 11, 8
7	44.7 (CH)	2.77 (dd, $J = 4.0, 10.8$)	6, 8	5, 6, 8, 9, 10, 11, 12, 13
8α	30.4 (CH_2)	1.78 (m)	7, 9	6, 7, 9, 10, 11
8β		1.22 (m)		
9α	34.8 (CH_2)	1.88 (m)	8, 10	1, 7, 8, 10
9β		1.67 (m)		
10	40.8 (CH)	1.42 (m)	14, 9	
11	76.3 (C)			
12	22.9 (CH_3)	1.16 (s)		7, 11, 13
13	23.0 (CH_3)	1.09 (s)		7, 12, 13
14	17.7 (CH_3)	0.93 (d, $J = 6.4$)	10	1, 9, 10
15	16.1 (CH_3)	1.31 (s)		3, 4, 5
1′	56.4 (CH_2)	3.36 (q, $J = 6.8$)	2′	2′, 4
2′	15.9 (CH_3)	1.04 (t, $J = 6.8$)	1′	1′
1″	55.9 (CH_2)	3.33 (q, $J = 6.8$)	2″	11, 2″
2″	16.0 (CH_3)	1.09 (t, $J = 6.8$)	1″	1″

The structure of **1** could be further confirmed as a guaiane-type sesquiterpene by comparison of the spectral data with those reported for structurally related compounds [11–17] and intensive $^{1}H-^{1}H$ COSY, HMQC, and HMBC experiments (shown in Table 1), respectively. The planar structure of **1** was established on the basis of HMBC correlations (Table 1; Figure 2), and the two ethoxyl groups could be linked at C-4 and C-11 by correlation from H-1′ (δ_H 3.36) to C-4 (δ_C 86.3) together with H-1″ (δ_H 3.33) to C-11 (δ_C 76.3). The relative configuration of **1** was further determined by NOE correlations observed between H-15 with H-3, H-3 with H-2α (δ_H 2.23), H-2α with H-10, and H-2β (δ_H 1.76) with H-14, shown the OH-1, OH-3, and CH_3-10 were β-orientation when CH_3-4 was α-orientation. The NOE correlations between H-15 with H-6, H-6 with H-7 and H-12, H-7 with H-9α (δ_H 1.88), and H-9α with H-10 indicated that the substitute at C-7 was β-orientation (Figure 3). Thus, the structure of **1** was elucidated as shown in Figure 1, and it was named as ethoxyvalerianol (Figures 2 and 3).



1 **2**

Figure 1. The structures of compounds **1** and **2**.

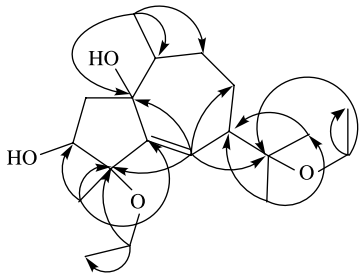


Figure 2. The significant HMBC correlations (H → C) of **1**.

The known sesquiterpene **2**, which was obtained from the plant for the first time, was elucidated as valeranone on the basis of NMR spectral data together with the database of gas chromatography–mass spectrometry (GC–MS) [18]. In our previous studies, (+)-maaliol (**5**) has been isolated from the essential oil of *V. tangutica* [19]. Herein, selina-4,7(11)-diene (**3**) and selinene (**4**) were obtained from **5** by decyclization and dehydration (Figure 4) to study the structure–activity relationship between (+)-maaliol (**5**) and selinene (**4**). The structures of **3** and **4** were identified on the basis of spectral data involving comparison with values reported in the literature [20]. Antibacterial activities against *Pseudomonas aeruginosa* of **4** and **5** (Table 2) indicate that the tricyclic and hydroxyl substructures may be the important activity functions in compound **5**.

3. Experimental

3.1 General experimental procedures

Optical rotations were measured with a Perkin–Elmer 241 polarimeter. IR Spectra were recorded using an FTS165-IR instrument (Bio-Rad, Boston, MA, USA). NMR spectra were run in $CDCl_3$ on a Varian INOVA-400 FT-NMR spectrometer (USA) with TMS as internal standard. HR-ESI-MS data were obtained on Bruker APEX II spectrometer. GC–MS was performed in Agilent 6890N GC/5973 MSD (NIST02 library). About 200–300 mesh silica gel used for column chromatography and GF_{254} silica gel for TLC were supplied by the Qingdao Marine Chemical Factory in China. Spots were detected on the TLC by visualization under UV light, or by spraying with H_2SO_4/EtOH 5:95 (v/v) and heating at 110°C. All the chemicals were of analytical grade.

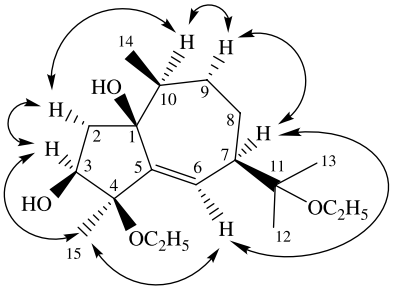


Figure 3. Key NOESY correlations of **1**.

3.2 Plant material

Valeriana tangutica was collected in Sunan County, Gansu province, in April 2005 and identified by Prof. Ji Ma, Faculty of Pharmacy, First Military Medical University of PLA, Guangzhou, China. A voucher specimen (No. 2005008) has been deposited at Key Laboratory for Natural Medicine of Gansu province, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, China.

3.3 Extraction and isolation

The air-dried *V. tangutica* (800 g) was extracted seven times with 95% EtOH (each for 7 d) at r.t. The crude extract (220 g) was suspended in water and extracted successively with petroleum ether, EtOAc, and BuOH. The extract of petroleum ether (35 g) was subjected to column chromatography (silica gel; petroleum ether/EtOAc 40:1, 30:1, 20:1, 15:1, 10:1, 7:1, 5:1, 3:1, 2:1 (v/v)) to give nine fractions (A–I), which were examined by TLC. Fraction D was separated by column chromatography (silica gel; petroleum ether/$CHCl_3$ 20:1, 15:1, 10:1, 5:1, 3:1, 2:1, 1:1, 0:1 (v/v)) to give eight fractions (D1–D8). Fraction D1 was afforded to GC–MS to identify the sesquiterpenoids and was further separated by column chromatography (silica gel; petroleum ether/EtOAc 15:1 (v/v)) to

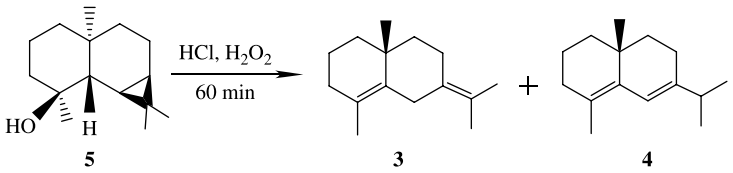


Figure 4. The change of compound **5** to **3** and **4**.

Table 2. The results of minimum inhibitory concentration (MIC; mg/ml) for compounds **4** and **5**.

Samples	*Pseudomonas aeruginosa* (ATCC 27853)
Selinene (**4**)	3.725
(+)-Maaliol (**5**)	0.40
Berberine hydrochloride*	2.00

* Positive control. Each test was performed in duplicate and repeated twice.

produce **1** (11 mg). Fraction D4 was isolated by column chromatography (silica gel, using petroleum ether/acetone 6:1 (v/v)) to give compound **2** (9 mg).

*3.3.1 Ethoxyvalerianol (**1**)*

Yellow gum. $[\alpha]_D^{20}$ +10 (*c* 0.64, $CHCl_3$). IR (KBr) υ_{max}: 3414, 2974, 2925, 2876, 2853, 1715, 1459, 1384, 1144, 1110, 1066, 757 cm^{-1}. UV ($CHCl_3$) λ_{max}: 228 nm. ^1H and ^{13}C NMR spectral data, see Table 1. HR-ESI-MS: *m/z* 349.2354 $[M + Na]^+$ (calcd for $C_{19}H_{34}O_4Na$, 349.2349).

3.4 Reactions

To a solution of 35 mg of (+)-maaliol (**5**) in 4.5 ml of ethanol was added 0.85 ml of concentrated aqueous HCl solution and 0.5 ml H_2O_2 (30%). The mixture was heated at reflux for 60 min [21]. The aqueous solution was extracted with petroleum ether. The petroleum ether part was subjected to column chromatography (silica gel; petroleum ether and petroleum ether/EtOAc 50:1 (v/v)) to give **3** (5 mg) and **4** (8 mg), respectively.

3.5 Antibacterial activity against Pseudomonas aeruginosa

The minimum inhibitory concentration method was employed for the determination of antibacterial activity against *Pseudomonas aeruginosa* (ATCC 27853), which was obtained from the Test Center of Clinical Disease in Jiangxi, China.

Acknowledgements

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References

[1] State Administration of Flora Reipublicae Popularis Sinicae, *Flora Reipublicae Popularis Sinicae*, **73**(1) (Science Press, Beijing, 1986), p. 27.
[2] L. Qi and D.S. Luo, *Collection of Chinese Minorities Medicine* (Inner Mongolia Science Press, Inner Mongolia, 2000), p. 1330.
[3] S.M. Chandra, S.C. Chandan, S.S. Subhash, K.P. Anil, and P. Siddharth, *Chem. Biodivers.* **2**, 1174 (2005).
[4] F. Sebastián, W. Cristina, C.P. Alejandro, and M. Mariel, *Pharmacol. Biochem. Behav.* **77**, 399 (2004).
[5] P.W. Thies, *Tetrahedron Lett.* **7**, 1163 (1966).
[6] R. Baranauskiene, *Chem. Nat. Compd.* **43**, 331 (2007).
[7] X.Q. Gao and L. Bjork, *Fitoterapia* **71**, 19 (2000).
[8] C. Paul, W.A. König, and H. Muhle, *Phytochemistry* **57**, 307 (2001).

[9] C.S. Mathela, C.S. Chanotiya, S. Sati, S.S. Sammal, and V. Wray, *Fitoterapia* **78**, 279 (2007).
[10] K. Nishiya, T. Kimura, K. Takeya, and H. Itokawa, *Phytochemistry* **31**, 3511 (1992).
[11] H. Oh, J.S. Kim, E.K. Song, H. Cho, D.H. Kim, S.E. Park, H.S. Lee, and Y.C. Kim, *Planta Med.* **68**, 748 (2002).
[12] K. Kasahara, S. Nomura, Subeki, H. Matsuura, M. Yamasaki, O. Yamato, Y. Maede, K. Katakura, M. Suzuki, Trimurningsih, Chairul, and T. Yoshihara, *Planta Med.* **71**, 482 (2005).
[13] F. Bohlmann and N. Borthakur, *Phytochemistry* **21**, 1160 (1982).
[14] F. Bohlmann, C. Zdero, R.M. King, and H. Robinson, *Phytochemistry* **22**, 1201 (1983).
[15] C. Zdero, F. Bohlmann, R.M. King, and H. Robinson, *Phytochemistry* **25**, 2873 (1986).
[16] N. Osaki, T. Koyano, T. Kowithayakorn, M. Hayashi, K. Komiyama, and M. Ishibashi, *J. Nat. Prod.* **68**, 447 (2005).
[17] H.S. Al-Easa, A.F.M. Rizk, and A.A. Ahmed, *Phytochemistry* **43**, 423 (1996).
[18] A. Srikrishna, R. Viswajanani, and C. Dinesh, *J. Chem. Sect. B* **43**, 1265 (2004).
[19] H.-Y. Qi and Y.-P. Shi, *2006 Proceedings of the Seminar on Fragrance and Flavor China*, 49 (2006).
[20] H.H. Sun and K.L. Erickson, *J. Org. Chem.* **43**, 1613 (1978).
[21] H.J.M. Gijsen, J.B.P.A. Wijnberg, C.V. Ravenswaay, and A.D. Groot, *Tetrahedron* **50**, 4733 (1994).