ORIENTALOLS A, B, AND C, SESQUITERPENE CONSTITUENTS FROM CHINESE ALISMATIS RHIZOMA, AND REVISED STRUCTURES OF ALISMOL AND ALISMOXIDE

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Three new sesquiterpenes named orientalols A, B, and C were isolated from Chinese Alismatis Rhizoma, the dried rhizome of *Alisma orientale* JUZEPCZUK, together with two known sesquiterpenes, alismol and alismoxide. On the basis of the chemical and physicochemical evidence, the structures of orientalols A (**3**), B (**4**), and C (**5**) were determined and those of alismol and alismoxide were revised from **1'** and **2'** to **1** and **2**, respectively.

KEYWORDS Alismatis Rhizoma ; *Alisma orientale* ; Alismataceae ; orientalol A ; orientalol B ; orientalol C ; alismol ; alismoxide ; aquatic plant

Alismatis Rhizoma (Takusha in Japanese), the dried rhizome of *Alisma orientale* JUZEPCZUK (Alismataceae), is known as an important Chinese crude drug used for diuretic and antiinflammatory purposes and has been extensively investigated in search of its biologically active principles.[1,2] In regard to sesquiterpene constituents of this crude drug, guaiane-type sesquiterpenes, alismol and alismoxide, were isolated, and their structures were respectively proposed as **1'** and **2'**.[3] During the course of our chemical studies on bioactive constituents of natural occurring crude drug originating from aquatic plants,[4] we have isolated three new sesquiterpenes, orientalols A (**3**), B (**4**), and C (**5**) containing the 1,5-*trans* guaiane skeleton from Chinese Alismatis Rhizoma together with alismol and alismoxide. Furthermore, there was some ambiguity about the 1,5-*cis* junction in the reported structure of alismol (**1'**) and alismoxide (**2'**). Detailed reinvestigation of the structures of alismol and alismoxide revealed that their structures should be revised from **1'** and **2'** to **1** and **2**, respectively. This paper deals with the structures of orientalols A-C (**3-5**) and the structure revision of alismol and alismoxide.

The MeOH extract of Chinese Alismatis Rhizoma was partitioned into AcOEt and water. Repeated separation of the AcOEt soluble portion by normal and reversed phase column chromatography furnished alismol (**1**, 0.010% from the crude drug), alismoxide (**2**, 0.012%), orientalols A (**3**, 0.0006%), B (**4**, 0.0002%) , and C (**5**, 0.0002%).

Orientalol A (**3**),[5] a colorless oil, $[\alpha]_D^{20}$ ± 0° (c= 0.83, MeOH), IR (KBr): 3600,1460,1040 cm^{-1}, had the molecular formula of $C_{15}H_{26}O_3$ determined by the high resolution FAB-MS (HR-FAB-MS). The ^1H- and ^{13}C-NMR spectra of **3** showed the presence of a primary hydroxyl [δ 3.64, 3.80 (ABq, *J*=11Hz) ; δc 63.7] and two tertiary hydroxyl (δc 77.3, 81.2) groups together with an isopropyl, a tertiary methyl and a trisubstituted olefin moieties. These spectral features suggested **3** to be a guaiane-type sesquiterpene.[6] Treatment of **3** with Ac_2O-pyridine afforded a monoacetate (**3a**),[7] while oxidation of **3** with $NaIO_4$ gave the ketone **6**.[8] The chemical conversions indicated an exocyclic vicinal diol moiety in **3**. Furthermore, the NOE correlations were observed in the pairs of protons (1-H and 14-H_3; 5-H and 15-H_2) of **3** and in the pairs of protons (1-H and 14-H_3; 14-H_3 and 6-H; 6-H and 12-H_3) of **6** in their NOESY spectra. Consequently, orientalol A was shown to be **3** possessing the 1,5-*trans* guaiane skeleton.

Intense analysis of ^1H- and ^{13}C-NMR (Table I) data disclosed that orientalols B (**4**)[9] and C (**5**)[10] had the same guaiane-type skeleton as orientalol A (**3**). The ^{13}C-NMR data of **4** were fairly analogous to those of **3** except for the carbon signals due to C-1 and C-15. This finding presumed that orientalol B (**4**) was an epimer of **3** at C-10. Observation of NOEs in the following pairs of protons (1-H and 14-H_3; 1-H and 15-H_2) confirmed the above presumption and established orientalol B as depicted in Chart 1.

Orientalol C (**5**) exhibited the presence of exomethylene and epoxy moieties as well as an isopropyl and a tertiary methyl group in its ^1H- and ^{13}C-NMR data. NOE examination corroborated the relative stereochemistry in **5**. Thus, the structure of olientalol C (**5**) was elucidated.

The physicochemical properties of alismol and alismoxide, isolated by us in the present investigation, were found to be the

same as those reported previously.[3] Oxidation of alismol (**1**) with OsO_4 provided orientalols A (**3**) and B (**4**) in a ratio of 1:1, while epoxidation of **1** with *m*-chloroperbenzoic acid gave orientalol C (**5**, 61%) and **7** (12%).[11] Based on this chemical evidence and the ^1H- and ^{13}C-NMR analysis of **1**, the structure of alismol was formulated as **1**. On the other hand, both the EI-MS and FAB-MS of alismoxide (**2**) showed the ion peak at *m/z* 220 ($C_{15}H_{24}O$) previously presented as the molecular ion peak **2'**, while the quasimolecular ion peak at *m/z* 261 [$(M+Na)^+$, $C_{15}H_{26}O_2Na$] was observed in its SIMS.

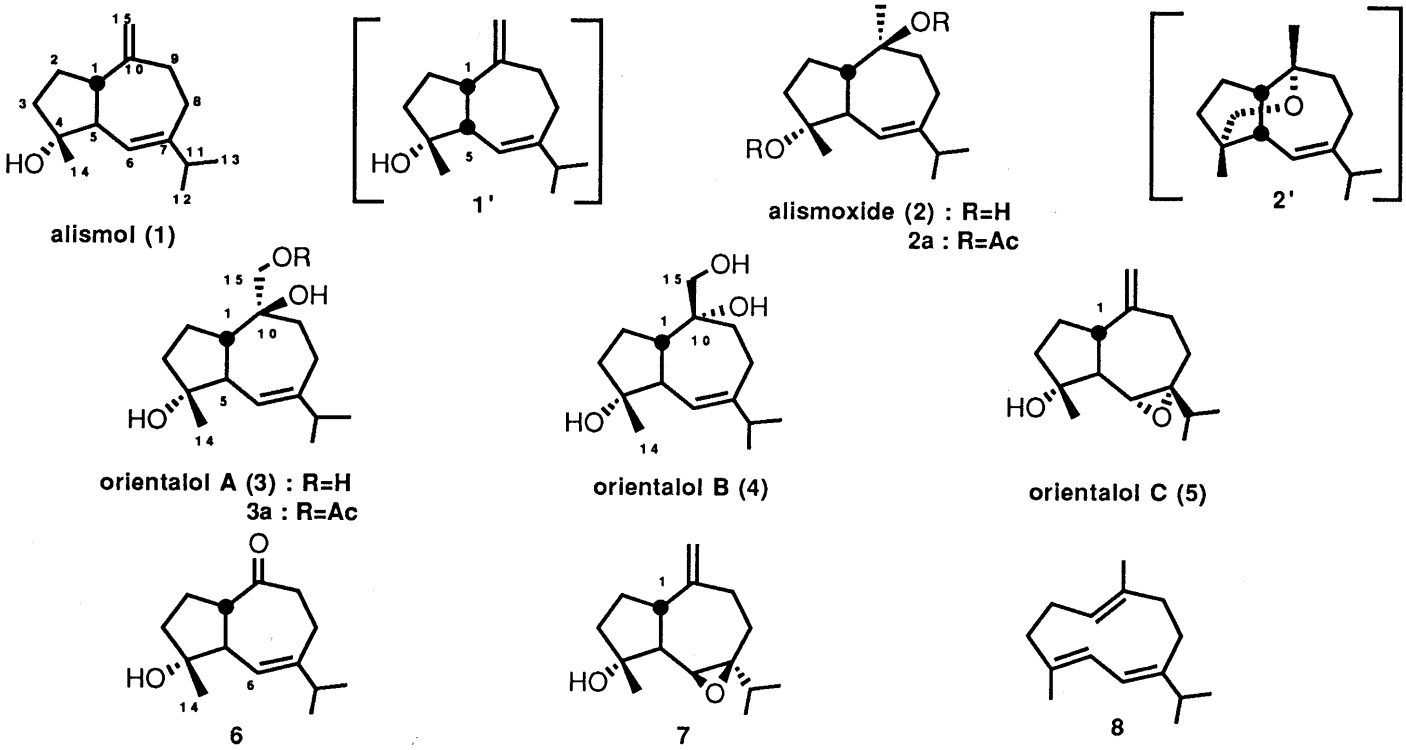

Chart 1

Table I. The ^{13}C-NMR Data for **1**, **2**, **2a**, **3**, **3a**, **4**, **5**, **6**, and **7**[a]

	1	2	2a	3	3a	4	5	6	7
C-1	55.8	50.5	48.3	50.9	51.1	46.6	47.9	53.1	42.7
C-2	25.7	21.5	22.4	22.5	22.2	22.2	26.3	19.1	25.5
C-3	40.7	40.4	36.5	41.5	41.4	41.4	41.5	39.4	40.3
C-4	81.0	80.1	88.9	81.2	81.1	81.5	80.3	80.5	81.0
C-5	48.9	50.2	46.9	50.6	50.7	49.3	57.5	51.9	55.7
C-6	123.2	121.3	121.0	123.5	123.4	124.0	62.3	120.6	61.2
C-7	150.3	149.5	149.3	150.4	150.4	151.6	65.1	148.6	65.1
C-8	31.0	25.0	24.6	25.9	25.7	26.1	29.4	25.7	27.1
C-9	38.2	42.5	36.9	38.4	38.6	37.3	34.1	42.2	33.9
C-10	155.2	75.2	87.5	77.3	76.2	77.0	151.7	211.9	152.4
C-11	38.7	37.2	37.3	39.1	39.1	39.0	34.6	37.4	37.1
C-12	21.7[b]	21.3[b]	21.1[b]	22.6[b]	22.6[b]	22.5[b]	17.8[b]	21.2[b]	17.4[b]
C-13	22.0[b]	21.4[b]	21.4[b]	22.7[b]	22.7[b]	22.7[b]	18.8[b]	21.5[b]	18.0[b]
C-14	24.1	22.4	19.4	22.2	22.2	23.2	25.0	22.1	24.6
C-15	107.0	21.1	19.0	63.7	68.5	70.0	107.4		107.5

a) The spectra of **1**, **3**, **3a**, and **4** were taken in CD_3OD, and those of **2**, **2a**, **5**, **6**, and **7** were in $CDCl_3$ at 67.5MHz.

b) The assignments may be interchangeable within the same column.

Acetylation of **2** with Ac_2O-pyridine in the presence of 4-dimethylaminopyridine gave a diacetate (**2a**).[12] Comparison of the ^1H- and ^{13}C-NMR data for **2** and **2a** with those for the other sesquiterpenes involving the NOE data led us to the chemical structure of alismoxide (**2**). Consequently alismol (**1**) and alismoxide (**2**) were identified with the marine sesquiterpenes isolated from Australian soft coral *Nephthea chabrolii* and *Lemnalia africana*,[6] and Okinawan soft coral *Xenia sp.*.[13] Finally, we have comparatively analyzed the sesquiterpene constituents of various Alismatis Rhizoma and the fresh rhizome of *Alisma orientale*. The analysis showed that the fresh rhizome of *Alisma orientale* contained not alismol (**1**) and alismoxide (**2**) but germacrene C (**8**) as a major sesquiterpene constituent.[14] Taking into consideration that alismol, alismoxide, orientalols A, B, and C showed no significant optical activity in addition to the above finding, these guaiane-type sesquiterpenes would be considered to be formed from germacrene C (**8**) during the processing procedure of this crude drug.

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5) **3** : a colorless oil, $C_{15}H_{26}O_3$, FAB-MS : *m/z* 277 $(M+Na)^+$, *m/z* 261 $(M+Li)^+$, ^1H-NMR (CD_3OD, 270MHz, δ) : 1.00 (d, *J*=7Hz), 1.01 (d, *J*=7Hz) (12, 13-H_3), 1.11 (s, 14-H_3), 2.40 (br d, *J*=12Hz, 5-H), 3.64, 3.80 (ABq, *J*=11Hz, 15-H_2), 5.54 (br s, 6-H).

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7) **3a** : a colorless oil, $[\alpha]_D^{20}$ ± 0 ° (c=0.40, MeOH), $C_{17}H_{28}O_4$, IR (KBr) : 3450, 1740, 1460, 1040 cm^{-1}, ^1H-NMR (CD_3OD, 270MHz, δ) : 1.00 (d, *J*=7Hz), 1.01 (d, *J*=7Hz) (12, 13-H_3), 1.12 (s, 14-H_3), 2.09 (s, acetyl methyl), 2.41 (br d, *J*=11Hz, 5-H), 4.17, 4.37 (ABq, *J*=11Hz, 15-H_2), 5.54 (br s, 6-H).

8) **6** : a colorless oil, $[\alpha]_D^{20}$ ± 0 ° (c=0.45, MeOH), $C_{14}H_{22}O_2$, IR (KBr) : 3600, 1700, 1460, 950 cm^{-1}, FAB-MS : *m/z* 245 $(M+Na)^+$, *m/z* 229 $(M+Li)^+$, ^1H-NMR ($CDCl_3$, 270MHz, δ) : 1.04 (d, *J*=7Hz, 12, 13-H_3), 1.20 (s, 14-H_3), 2.88 (ddd, *J*=3, 6, 10Hz, 1-H), 5.65 (br s, 6-H).

9) **4** : a colorless oil, $C_{15}H_{26}O_3$, $[\alpha]_D^{20}$ ± 0° (c= 0.83, MeOH), IR (KBr) : 3550, 1460, 1045 cm^{-1}, FAB-MS : *m/z* 277 $(M+Na)^+$, *m/z* 261 $(M+Li)^+$, ^1H-NMR (CD_3OD, 270MHz, δ) : 0.99 (d, *J*=7Hz), 1.00 (d, *J*=7Hz) (12, 13-H_3), 1.14 (s, 14-H_3), 2.73 (br d, *J*=10Hz, 5-H), 3.28, 3.40 (ABq, *J*=11Hz, 15-H_2) , 5.55 (br s, 6-H).

10) **5** : a colorless oil, $C_{15}H_{24}O_2$, $[\alpha]_D^{20}$ +2.5 ° (c=0.56, MeOH), IR (KBr) : 3445, 1470, 1050, 900 cm^{-1}, FAB-MS : *m/z* 259 $(M+Na)^+$, *m/z* 243 $(M+Li)^+$, ^1H-NMR ($CDCl_3$, 270MHz, δ) : 0.97 (d, *J*=7Hz), 1.00 (d, *J*=7Hz) (12, 13-H_3), 1.44 (s, 14- H_3), 2.91 (d, *J*=7Hz, 6-H), 4.71, 4.73 (both s,15-H_2).

11) **7** : a colorless oil, $C_{15}H_{24}O_2$, $[\alpha]_D^{20}$ +10.0° (c=0.54, MeOH), IR (KBr) : 3330, 1360, 1100, 890 cm^{-1}, FAB-MS : *m/z* 259 $(M+Na)^+$, *m/z* 243 $(M+Li)^+$, ^1H-NMR ($CDCl_3$, 270MHz, δ) : 0.92 (d, *J*=7Hz), 1.00 (d, *J*=7Hz) (12, 13-H_3), 1.38 (s, 14-H_3), 3.03 (s, 6-H), 4.70 , 4.73 (both s,15-H_2).

12) **2a** : a colorless oil, $[\alpha]_D^{20}$ ± 0° (c=0.50, $CHCl_3$), $C_{19}H_{30}O_4$, IR (KBr) : 2900, 1730, 1470 cm^{-1}, FAB-MS : *m/z* 345 $(M+Na)^+$, *m/z* 329 $(M+Li)^+$, ^1H-NMR ($CDCl_3$, 270MHz, δ) : 0.98 (d, *J*=7Hz), 0.99 (d, *J*=7Hz) (12, 13-H_3), 1.41 (s, 14-H_3), 1.53 (s, 15-H_3), 1.96, 2.00 (both s, acetyl methyl), 5.49 (d, *J*=3Hz, 6-H).

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14) Germacrene C (**8**, 0.030%), alismol (**1**, 0.0026%), and alismoxide (**2**, 0.0031%) were isolated from the acetone extract of the fresh rhizome of *Alisma orientale* (originating in China).

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