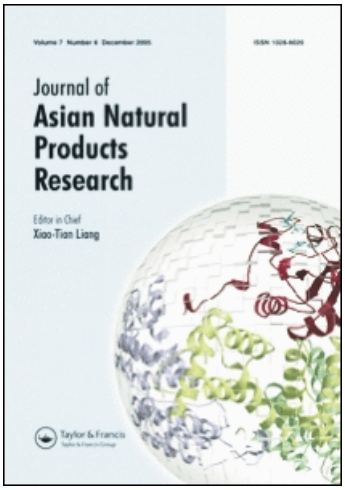

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Two new monoterpenoid glycosides from *Mentha spicata* L.

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Note

TWO NEW MONOTERPENOID GLYCOSIDES FROM *MENTHA SPICATA* L.

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Two new monoterpenoid glycosides, spicatoside A and spicatoside B, were isolated from the whole herbs of *Mentha spicata* L. which have anti-inflammatory and hemostatic activities. Their structures have been determined on the basis of spectral and chemical analysis. They are (+)-5-[1-(β-D-glucopyranosyloxymethyl)ethenyl]-2-methyl-2-cyclohexen-1-one (**1**), and (−)-5-{[2-(β-D-glucopyranosyloxy)-1-hydroxy-1-methyl]ethyl}-2-methyl-2-cyclohexen-1-one (**2**).

Keywords: *Mentha spicata* L; Spicatoside A; Spicatoside B; (+)-5-[1-(β-D-Glucopyranosyloxymethyl)ethenyl]-2-methyl-2-cyclohexen-1-one (**1**); (−)-5-{[2-(β-D-Glucopyranosyloxy)-1-hydroxy-1-methyl]ethyl}-2-methyl-2-cyclohexen-1-one (**2**)

INTRODUCTION

Mentha spicata L. belongs to the genus *Mentha* (*Lamiaceae*) which is one of the most well known oil-producing plants. It was originally grown in South Europe and the former Soviet Union. In China, it was also cultivated in many places. The fragrant oils from *Mentha spicata* L. are mainly used as spices in candies or toothpaste and also used as an aromatic stimulant. Recently, we found that the substance in the nonvolatile portion of its extract has anti-inflammatory, hemostatic and pain-relieving properties. To our knowledge, little work has previously been carried out on this substance. In this paper, we describe the isolation and structural elucidation of two new monoterpenoid glycosides, spicatoside A (**1**) and spicatoside B (**2**) (Fig. 1) from the nonvolatile portion.

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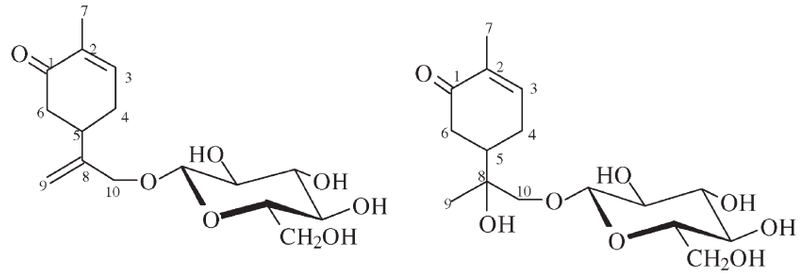

1 **2**

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

RESULTS AND DISCUSSION

Spicatoside A (**1**) was obtained as a white amorphous powder (MeOH), having $[\alpha]_D^{20}$ +39.6 (*c* 1.1, MeOH), and it responded positively to the Molish test. Acid hydrolysis carried out on TLC yielded only glucose. HR-FABMS gave an $[M-1]^-$ peak at *m/z* 327.1444 corresponding to a molecular formula of $C_{16}H_{24}O_7$. The ^{13}C-NMR spectra of the aglycone moiety exhibited 10 carbon signals which demonstrated the presence of 5 sp^2 hybridized carbons, one sp^3 hybridized oxygen-linked carbon and a carbonyl carbon signal at δ 198.9. Comparison with its IR, ^{1}H-NMR data (Table I) suggested the presence of monoterpadienone.

In the HMBC spectrum, the long-range correlation between a proton signal at δ 1.68 (H-7) and three carbon signals at δ 134.2 (C-2), 145.5 (C-3), 198.9 (C-1) could be observed, respectively. A proton signal at δ 6.85 (H-3) correlated with three carbon signals at δ 15.6

TABLE I NMR data of compound **1** (DMSO)

		Correlated protons	
No.	δ_c	*HMQC*	*HMBC*
1	198.9		5-H,6-H,7-H
2	134.2		4-H,7-H
3	145.5	6.85 (1H, s)	4-H,5-H,7-H
4	30.9	2.50 (1H, m) 2.33 (1H,m)	3-H,5-H,6-H
5	37.6	2.80 (1H, m)	3-H, 4-H,6-H,9-H,10-H
6	42.7	2.45 (2H, m)	4-H, 5-H
7	15.6	1.68 (3H, s)	3-H,4-H
8	147.5		5-H,6-H,9-H,10-H
9	111.9	4.96 (1H, s) 5.16 (1H, s)	5-H,10-H
10	69.6	4.04 (1H, d, J = 13.0 Hz) 4.28 (1H,d, J = 13.0 Hz)	5-H,9-H,1′-H
1′	101.9	4.11 (1H, d, J = 7.7 Hz)	10-H,2′-H
2′	73.6	2.98 (1H, m)	3′-H
3′	77.1	3.11 (1H, m)	1′-H,2′-H,5′-H
4′	70.3	3.05 (1H, m)	3′-H,5′-H
5′	76.9	3.02 (1H, m)	4′-H,6′-H
6′	61.3	3.67 (1H, d, J = 11.0 Hz) 3.45 (1 Hz, m)	5′-H

(C-7), 30.9 (C-4), 37.6 (C-5), whereas a proton signal at δ 2.45 (H-6) correlated with the signals of δ 198.9 (C-1), 37.6 (C-5), 30.9 (C-4). The above results indicated the presence of the 2-methyl-2-cyclohexen-1-one moiety.

In the HMQC experiment, the carbon signal at δ 69.6 (C-10) showed the correlation with the proton signals at δ 4.04 (1H, d, $J = 13.0$ Hz), 4.28 (1H, d, $J = 13.0$ Hz) and the carbon signal at δ 111.9 (C-9) gave the correlation with δ 5.16 (1H, s), 4.96 (1H, s). These indicated the carbon signal at δ 69.6 was due to an oxygen-substituted methene carbon, whereas the signal at δ 111.9 was from the carbon of a terminal double bond. Furthermore, from the HMBC spectrum we found that the proton at δ 2.80 (H-5) was correlated with the carbon signal at δ 147.5 (C-8) and δ 111.9 (C-9), and this suggested the double bond attached to position 5. A pair of protons of the same carbon at δ 4.04 and 4.28 showed cross-peaks to the carbon at δ 111.9 (C-9) and 147.5 (C-8) which indicated C-10 was attached to the double bond. Therefore, we could infer the presence of a 10-*O*-carvone aglycone moiety [1].

The glycosidic linkage was determined to be at the C-10 position based on the cross-peaks due to ^3J long range coupling between the anomeric proton (δ 4.11, H-1′) and C-10 (δ 69.6) in the HMBC spectrum. Furthermore, the anomeric configuration of the sugar moiety was determined to be the β form on the basis of the coupling constant for H-1′ ($J = 7.7$ Hz). From the above evidence, the structure of compound **1** was concluded to be (+)-5-[1-(β-D-glucopyranosyloxymethyl)ethenyl]-2-methyl-2-cyclohexen-1-one, named spicatoside A.

Spicatoside B (**2**) was obtained as a white amorphous powder (MeOH), having $[\alpha]_D^{20} - 0.8$ (*c* 1.1, MeOH) and it also responded positively to the Molish test. Acid hydrolysis carried out on TLC yielded only glucose. HR-FABMS showed an $[M - 1]^-$ peak at *m/z* 345.1558 corresponding to a molecular formula of $C_{16}H_{26}O_8$. The ^{13}C-NMR spectrum of **2** showed 16 carbon signals. Comparison of the ^{13}C-NMR data with those of **1** showed an additional oxygen-linked carbon, whereas a methyl carbon and two olefinic carbons were absent.

On the basis of the assigned protons, an HMQC experiment gave the corresponding carbon assignments which were further confirmed by HMBC. In the HMBC spectrum, correlations were observed from the resonance at δ 1.65 (H-7) with signals of δ 134. 2 (C-2), 146.2 (C-3) and 200.2 (C-1), the resonance at δ 6.82 (H-3) with signals at δ 15.6 (C-7), 41.4 (C-5), the proton signal at δ 2.20 (H-6) with signals at δ 200.2 (C-1), 41.4 (C-5). From the above data, we could deduce the presence of the 2-methyl-2-cyclohexen-1-one unit. Furthermore, the carbon signal at δ 41.4 (C-5) correlated with the proton signal at δ 3.66, 3.24 (H-10) and 1.00 (H-9), and in turn the proton signal at δ 1.00 (H-9) correlated with δ 41.4 (C-5), 72.0 (C-8) and 75.3 (C-10). This indicated the carbon at δ 72.0 (C-8) was attached to position 5. The protons at δ 3.66, 3.24 (H-10) have correlation with the anomeric carbon (δ 103.9) of glucose, so C-10 was attached to glucose and the OH group was located at C-8 (δ 72.0). The above data showed the presence of hydroxydihydrocarvone [2].

The anomeric configuration of the sugar moiety was determined to be the β-form based on the coupling constant for H-1′ at δ 4.10 ($J = 7.7$ Hz). From the above evidence the structure of compound **2** was assigned as (−)-5-{[2-(β-D-glucopyranosyloxy)-1-hydroxy-1-methyl]ethyl}-2-methyl-2-cyclohexen-1-one, named spicatoside B.

EXPERIMENTAL SECTION

General Experimental Procedures

IR spectra were taken on a Bruker IFS-55 IR spectrometer; NMR spectra were run on a Bruker ARX-300 (300 MHz for ^{1}H and 75 MHz for ^{13}C) spectrometer; HR-FABMS were measured with a Bruker APEX II mass spectrometer; TLC was performed on silica gel H

(10–40 u). Separation and purification were performed by column chromatography on silica gel (200–300 mesh); HPLC was carried out on a Shimadzu LC-8A HPLC spectrometer.

Plant Material

Mentha spicata L. was obtained as whole herbs from Faku in Liaoning Province of China and identified by Professor Qi-shi Sun in the Department of Pharmacognosy of Shenyang Pharmaceutical University. The voucher specimen was deposited at the same department.

Extraction and Isolation

The whole herbs of *Mentha spicata* L. (7 kg) were extracted with water three times. The extracts were collected together and concentrated, then mixed with three times the volume of EtOH to cause precipitation. The supernatant was evaporated under reduced pressure to obtain the crude extract (550 g) which was then suspended in water and extracted with petroleum ether, chloroform, ethyl acetate successively. The water-soluble portion was submitted to a macroporous resin D101 column and eluted with water (20%) and ethanol (80%) successively. The 20% EtOH portion was subjected to column chromatography on silica gel and eluted with $CHCl_3$–MeOH (10:1). The fraction was further treated by CC over silica gel to give a fraction which was finally isolated by preparative HPLC (25% MeOH in water as mobile phase) to yield compound **1** (22.0 mg) and **2** (39.1 mg).

*Spicatoside A, (+)5-[1-(β-D-glucopyranosyloxymethyl)ethenyl]-2-methyl-2-cyclohexen-1-one (**1**).* White amorphous powder (MeOH); $[\alpha]_D^{20}$ + 39.6 (*c* 1.1, MeOH); UV (MeOH) λ_{max} (log ε) 235 (3.72) nm; IR ν_{max}^{KBr} $cm^{-1:}$ 3388, 2923, 1663, 1383, 1076, 906, 616; HR-FABMS *m/z* $[M-1]^-$ 327.1444 (calcd for $C_{16}H_{24}O_7$-1, 327.1449); ^1H, ^{13}C-NMR, HMQC and HMBC (DMSO-d_6) data, see Table I.

*Spicatoside B, (−)-5-{[2-(β-D-glucopyranosyloxy)-1-hydroxy-1-methyl]ethyl}-2-methyl-2-cyclohexen-1-one (**2**).* White amorphous powder (MeOH); $[\alpha]_D^{20}$ − 0.8 (*c* 2.0, MeOH) UV (MeOH) λ_{max} (log ε) 235 (3.88) nm; IR ν_{max}^{KBr} cm^{-1}: 3396, 2924, 1658, 1432, 1381, 1309, 1162, 1078, 906, 583; HR-FABMS *m/z*$[M-1]^-$ 345.1558 (calcd for $C_{16}H_{26}O_8$-1, 345.1555); ^1H, ^{13}C-NMR, HMQC and HMBC (DMSO-d_6) data, see Table II.

TABLE II NMR data of compound **2** (DMSO)

		Correlated protons	
No.	δ_c	*HMQC*	*HMBC*
1	200.2		6-H,7-H
2	134.2		7-H
3	146.2	6.82 (1H, d, J = 4.7 Hz)	7-H
4	27.2	2.19 (1H, m), 2.33 (1H, m)	6-H
5	41.4	2.23 (1H, m)	3-H,4-H,6-H,9-H,10-H
6	38.7	2.42 (1H, d, J = 11.0 Hz), 2.20 (1H, m)	
7	15.6	1.65 (3H, s)	3-H
8	72.0		4-H,6-H,9-H,10-H
9	21.3	1.00 (1H, s)	10-H
10	75.3	3.66 (1H, m), 3.24 (1H, d, J = 9.8 Hz)	9-H,1′-H
1′	103.9	4.10 (1H, d, J = 7.7 Hz)	10-H,2′-H
2′	73.8	3.03 (1H, t, J = 8.0 Hz)	1′-H
3′	77.1	3.01–3.14 (1H, m)	2′-H,4′-H
4′	70.3	3.01–3.14 (1H, m)	5′-H
5′	76.6	3.01–3.14 (1H, m)	4′-H
6′	61.3	3.66 (1H, m),3.40 (1H, m)	

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