Two New Alkaloids from *Capparis himalayensis*

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Received July 17, 2007; accepted November 7, 2007; published online November 16, 2007

Two new alkaloids, Capparin A (1) and B (2), along with seven known compounds 6-methoxyindoline-2,3-dione (3), wogonin (4), oxor lyn A (5), kaempferol (6), apigenin (7), quercetin (8) and luteolin (9), were isolated from the whole plant of *Capparis himalayensis*. Their structures have been established on the basis of spectral methods and the structure of 1 was confirmed by X-ray crystallographic analysis.

Key words *Capparis himalayensis*; Capparidaceae; alkaloid; X-ray

_Capparis himalayensis_ belonging to Capparidaceae grows widely in Xinjiang Uygur Autonomous Region and Tibet of China. Its root barks, leaves and fruits are used for the treatment of rheumatism in traditional medicine. Previous investigations have led to the isolation of different chemical components showing various bioactivities from the *Capparis* genus while up to now, there is no report regarding chemical constituents of this species. In the present study, we attempted to find some bioactive components from *Capparis himalayensis* to support its development as a medicinal resource. This paper describes the isolation and structural elucidation of two new alkaloids 6-methoxyl-2-(methylthio)-1H-indole-3-carbaldehyde (1) and 6-methoxy-2-(methylthio)-1H-indole-3-carbaldehyde (2) from the ethanol extract of the plant along with seven known compounds. The known compounds were identified as 6-methoxyindoline-2,3-dione (3),12 wogonin (4),13 oxor lyn A (5),14 kaempferol (6),15,16 apigenin (7),15,16 quercetin (8)15,16 and luteolin (9)15 by comparison of spectroscopic properties (MS, 1H-NMR, 13C-NMR, HMBC and HMB). Among the known compounds, 3, 4, 5, 7, 9 were isolated from *Capparis* genus for the first time.

Results and Discussion

Compound 1 was obtained as yellow plates, and gave a positive reaction to dragendorff reagent. The molecular formula of 1 was determined to be C_{12}H_{10}N_{2}O_{5}S_{2} by HR-EL-MS (m/z 280.0341 [M]+). The IR spectrum displayed absorption bands for amide (3436 cm−1), carbonyl (1715 cm−1) and aromatic group (1615, 1505, 1463 cm−1), respectively. 1H-NMR spectrum of 1 indicated the presence of a 1,2,4-trisubstituted benzene \( \delta_H \) 7.24 (d, \( J=8.4\) Hz), 6.57 (d, \( J=8.4, 1.8\) Hz), 6.40 (d, \( J=1.8\) Hz) and a AB coupling system \( \delta_H \) 4.46, 4.36 (d, \( J=15.0\) Hz) corresponding to methylene (\( =N–CH_{2} =\)). In addition, the signal at \( \delta_H \) 10.64 (s) showed the presence of an amidocyanogen. 1H-NMR signals at \( \delta_C \) 3.74 (s) and 2.50 (s) indicated the existence of a methoxyl and a methylthio, respectively (Table 1). The 13C-NMR spectrum exhibited 12 carbon signals which revealed the existence of one carbonyl carbon atom (\( \delta_C \) 177.5), one olefinic-quinertary carbon (>C=N–) (\( \delta_C \) 161.8), and one methylene (\( \delta_C \) 73.6), one quaternary (\( \delta_C \) 64.2), one methoxyl (\( \delta_C \) 55.3), one methylthio (\( \delta_C \) 15.0), and one benzene ring (\( \delta_C \) 160.6, 142.4, 125.1, 121.4, 107.6, 96.7) (Table 1). 1H-, 13C-NMR and EI-MS data strongly suggested the feature of spiro-

brassinin derivative.17) According to the molecular formula and the structure of 1,2,4-trisubstituted benzene indicated in 1H-NMR spectrum, a methoxyl was suggested located at C-5 or C-6. In the heteronuclear multiple bond connectivity (HMBC) spectrum (Fig. 1), the long-range coupling between H-12 (\( \delta_H \) 7.74) and C-6 (\( \delta_C \) 160.6); H-4 (\( \delta_H \) 7.24) and C-3 (\( \delta_C \) 64.2), C-6 (\( \delta_C \) 160.6); H-5 (\( \delta_H \) 6.57) and C-7 (\( \delta_C \) 96.7), C-9 (\( \delta_C \) 121.4); H-7 (\( \delta_H \) 6.40) and C-5 (\( \delta_C \) 107.6), C-9 (\( \delta_C \) 121.4) indicated that the methoxyl was located at C-6. Thus 1 was identified as 6-methoxyl-2’-(methylthio)spiro[3H-indole-3,5’(4’H)thiazol]-2-one and all the 1H and 13C signals had been designed by 2D NMR. The relative structure of 1 was further confirmed by single crystal X-ray diffraction studies (Fig. 2). We named this compound Capparine A. In addition, single crystal X-ray analyses of 1 showed that it

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1. **Table 1.** 1H- and 13C-NMR Spectral Data of Compounds 1 and 2

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<td>( \delta_C )</td>
<td>( \delta_H ) (J in Hz)</td>
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<td>12.11, s</td>
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<tr>
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<td>156.5</td>
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<td>7</td>
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<tr>
<td>13</td>
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Fig. 1. Key HMBC Correlation of 1

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The molecular formula was determined to be C_{11}H_{11}NO_{2}S by IR (cm^\text{-1}) and H-11/H-7 (Fig. 4). Thus compound 2 was identified as 6-methoxy-2-(methylthio)-1H-indole-3-carbaldehyde and all the 1^H and 13C signals had been designated by 2D NMR. We named this compound Capparin B.

Compound 2 was obtained as white amorphous powder. The molecular formula was determined to be C_{11}H_{11}NO_{2}S by HR-EI-MS (m/z 221.0518 [M]+). The IR spectrum displayed absorption bands for carbonyl (1618 cm\textsuperscript{-1}) and C-6, respectively by correlations of H-1/H-12, H-11/H-5 (Table 1) indicated the presence of 1,2,4-trisubstituted benzene (\(\delta_{\text{H}} 7.87 (d, J=9.0\,\text{Hz}), 6.83 (dd, J=9.0, 2.4\,\text{Hz}), 6.90\) (d, \(J=2.4\,\text{Hz})\), a methoxyl (\(\delta_{\text{H}} 3.80,\,\text{s}\)), a methylthio (\(\delta_{\text{H}} 2.66,\,\text{s}\)), an amidoacyanogen (\(\delta_{\text{H}} 12.11,\,\text{br\,s}\)) and an aldehyde group (\(\delta_{\text{H}} 10.01,\,\text{s}\)). 13C-NMR spectrum (Table 1) exhibited 11 carbon signals. In the HMBC spectrum (Fig. 3), the correlations between H-1 (\(\delta_{\text{C}} 12.11\)) and C-3 (\(\delta_{\text{C}} 115.9\)), C-9 (\(\delta_{\text{C}} 119.4\)); H-4 (\(\delta_{\text{C}} 143.9\)) indicated a methylthio connected with C-2. Furthermore, the NOESY spectrum confirmed the methylthio and the methoxy connected with C-2 and C-6, respectively by correlations of H-1/H-1-12, H-11/H-5 and H-11/H-7 (Fig. 4).

Experimental

General Experimenting Melting points were determined on Fisher-Johns and are uncorrected. UV spectra were taken on a Philips PYE Unican Pu 8800 Spectrophotometer. IR spectra were measured with a Nicolet 5700 of Thermo. NMR spectra were measured in DMSO-d_6 on a VARIAN INOVA 600 spectrometer with chemical shifts being represented in parts per million (ppm) and tetramethylsilane (TMS) as an internal standard. EI-MS and HR-EI-MS were measured on a Zabspec E spectrometer at an ionization voltage of 70 eV. The TLC and HPTLC employed precoated silica gel plates (Qingdao Haiyang Chem. Co., Ltd.). For the column chromatography, silica gel (Qingdao Haiyang) and Sephadex LH-20 (Pharmacia) were used. X-Ray crystallographic data collection for 1 was carried on a MAC DIP-2030K single crystal X-ray diffractometer.

Plant Material The plant of Capparis himalayensis was collected in Xingjiang Uygur Autonomous Region of China, in September, 2004 and identified by Doctor Guo-qiang Li. Voucher specimen (XC-04-0912) was deposited in the Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College.

Extraction and Isolation The air-dried plant material (18 kg) was powdered and extracted with 95% EtOH and 50% EtOH respectively. The alcohol extract was concentrated under reduced pressure and successively extracted with petroleum ether, CHCl_3, EtOAc and n-BuOH. The CHCl_3-soluble extract (60.8 g) was subjected to a silica gel column chromatography and eluted with petroleum ether/EtOAc (gradient, 1:0→1:0) to yield 26 fractions. Fr. 6-8 (3.7 g) were further separated with silica gel column using petroleum ether/EtOAc (gradient, 1:0→0:1) to yield 43 portions, and portion 27 was purified by Sephadex LH-20 to afford 4 (18 mg). Fr. 9-11 (1.5 g) were further separated with silica gel column using petroleum ether/EtOAc (gradient, 1:0→0:1) and Sephadex LH-20 to yield 2 (12 mg) and 5 (5 mg). Fr. 12-13 (5 g) were applied to silica gel column eluted with a gradient of petroleum ether/EtOAc and Sephadex LH-20 to give 1 (13 mg) and 3 (9 mg). EtOAc-soluble extract (116.3 g) was subjected to a silica gel column eluted with CHCl_3/MeOH (gradient, 1:0→0:1) to yield 28 fractions. Fr. 9 (4 g) was further separated with silica gel using petroleum ether/actone (gradient, 1:0→0:1) and Sephadex LH-20 to yield 6 (14 mg) and 7 (23 mg). Fr. 10-11 were separated with Sephadex LH-20 to yield 8 (25 mg) and 9 (10 mg) respectively.

Compound 2: Pale yellow plates crystal (CHCl_3–CH_3OH, mp 170—173°C; \([\alpha]_{\text{D}}^{28}= -9.88°\) (c=0.16, MeOH). UV \(\lambda_{\text{max}}\) (MeOH) nm (log e): 224 (3.34), 198 (2.86); HR-EI-MS m/z 280.0341 [M]+ (Caled for C_{11}H_{11}NO_{2}S, 280.0340; EI-MS %: 280 (M+, 73), 233 (22), 207 (100),175 (51), 162 (16). IR (cm\textsuperscript{-1}): 3436, 3169, 3057, 2926, 2835, 1715, 1587, 1505, 1463, 1344, 1281, 1159; \(^1^H\)-NMR (DMSO-d_6, 600 MHz) and \(^1^3^C\)-NMR (DMSO-d_6, 150 MHz) see Table 1.

Single-Crystal X-Ray Structure Determination Crystals of 1 were crystallized from CHCl_3–CH_3OH (1:1). Crystal data: C_{11}H_{11}NO_{2}S, MW = 280.38, triclinic, space group P\text{-}\text{I}, a = 5.750(1)\,\text{Å}, b = 10.189(2)\,\text{Å}, c = 11.988(2)\,\text{Å}, \alpha = 106.96°, \beta = 96.97°, \gamma = 102.59°, V = 642.6(3)\,\text{Å}^3, Z = 2, D_{calc} = 1.449\,\text{g/cm}^3, T = 283\,\text{K}. Crystal size: 0.05×0.30×0.60 mm. Single-crystal analysis of 2 was made on a MAC DIP-2030K diffractometer with monochromated MoK\alpha radiation (50 kV, 60 mA). A total of 1647 unique reflections were recorded, of which 1545 were considered observed on the basis \(R_p = 0.070\) and \(R_w = 0.1756.\) The structure was solved by direct methods with the use of the SHELX-97 program, and all hydrogen atoms were located from a difference Fourier map. Final R-factors were \(R_p = 0.0700\) and \(R_w = 0.1756.\)

Compound 2: White amorphous powder (CHCl_3–MeOH), mp 202—204°C (dec); UV \(\lambda_{\text{max}}\) (MeOH) nm (log e): 333 (2.83), 284 (2.97), 247 (3.17), 223 (3.17), 192 (3.29); HR-EI-MS m/z: 221.0518 [M]+ (Caled for C_{11}H_{11}NO_{2}S, 221.0511); EI-MS %: 221 (M+, 100), 206 (68), 178 (18); IR (cm\textsuperscript{-1}): 3092, 2949, 1618, 1581, 1515, 1453, 1349, 1146, 1092, 828.
726; 1H-NMR (DMSO-d$_6$, 600 MHz) and 13C-NMR (DMSO-d$_6$, 150 MHz) see Table 1.

Acknowledgments We would like to express our gratitude to Professor Y. Lu (Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, People’s Republic of China) for the X-ray crystallography.

References