

## Apicin, A New Flavonoid from *Artemisia apiacea*

Sung-Jin Lee,<sup>†</sup> Hye Min Kim, Sanghyun Lee,<sup>†</sup> Hyun Young Kim,<sup>‡</sup> Byung-Hun Um,<sup>§</sup> and Young-Hee Ahn

<sup>†</sup>Gyeonggi Regional Research Center, Hankyong National University, Anseong 456-749, Korea  
 Department of Applied Plant Science, College of Industrial Science, Chung-Ang University, Anseong 456-756, Korea  
 E-mail: slee@cau.ac.kr

<sup>‡</sup>College of Pharmacy, Seoul National University, Seoul 151-742, Korea

<sup>§</sup>KIST Gangneung Institute, Gangneung 210-340, Korea

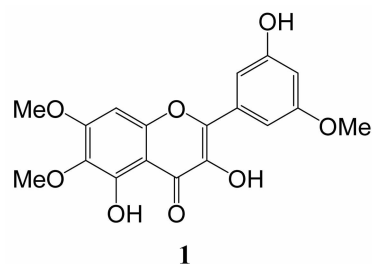
Received April 10, 2006

**Key Words :** *Artemisia apiacea*, Compositae, Flavonoid, Apicin

*Artemisia* species spreads widely in nature and are genus of the family Compositae consisting of more than 350 species. *A. apiacea* is distributed at wasteland and river beaches of Korea, Japan and China, and has been used as traditional medicine to treat eczema and jaundice.<sup>1</sup> Investigations on the compounds from *A. apiacea* have revealed the presence of campesterol, stigmasterol,  $\beta$ -sitosterol, 7-methoxycoumarin, 7,8-dimethoxycoumarin and 7,8-methylenedioxy-coumarin,<sup>2</sup> scopoletin, protocatechualdehyde and ethyl and methyl caffeates,<sup>3</sup> daphnetin, 7-hydroxy-8-methoxycoumarin and 7-isopentenyl-8-methoxycoumarin,<sup>4</sup> volatile constituents like  $\alpha$ -pinene and artemisia ketone<sup>5,6</sup> and artemicapin C, apigenin, daucosterol, cacticin, hyperin,  $\alpha$ -amyrin,  $\beta$ -amyrin,  $\beta$ -sitosterol and 5,6,7-trimethoxycoumarin.<sup>7,9</sup> During the course of our continued studies on the compounds from *A. apiacea*, a new flavonoid (**1**) was isolated and identified. Compound **1** is described here for the first time as a naturally occurring compound.

Compound **1** was obtained as yellow crystals from MeOH. It responded positively to the Shinoda test. In the EI-MS of

**1**, the molecular ion peak showed at  $m/z$  360 corresponding to the molecular formula  $C_{18}H_{16}O_8$ . The characteristic fragment ion peaks at  $m/z$  153 showed the *retro* Diels-Alder fragmentation of flavonoids.<sup>10</sup> The IR spectrum of **1** showed absorption bands for hydroxyl at  $3383\text{ cm}^{-1}$ ,  $\alpha,\beta$ -unsaturated C=O at  $1612\text{ cm}^{-1}$  and C-O at  $1015\text{ cm}^{-1}$ . In the  $^1\text{H-NMR}$  spectrum of **1**, the typical flavonoid signals were observed. The singlets of aromatic 5-OH at  $\delta$  13.03 and three -OMe signals at  $\delta$  3.91, 3.80 and 3.71 were observed. The singlets of H-8, -2', -4', and -6' were observed at  $\delta$  6.95, 7.09, 6.55 and 7.44, respectively.<sup>11</sup> Its  $^{13}\text{C-NMR}$  spectrum of **1** showed C=O at  $\delta$  183.1 and three -OMe at  $\delta$  57.3, 57.6 and 60.9. In the homonuclear COSY spectrum, the correlation of proton signals is not indicated. The assignments of the  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR signals derived hetero nuclear direct and long-range correlations on **1** are listed in Table 1. Accordingly, compound **1** was assigned as a new flavonoid and named apicin (3,5,3'-trihydroxy-6,7,5'-trimethoxyflavone).



### Experimental Section

**General Procedures.** MS spectrum was measured with a Jeol JMS-AX505WA mass spectrometer.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra were recorded with a Varian 400 NMR spectrometer using TMS as an internal standard. Chemical shifts were reported in parts per million ( $\delta$ ), and coupling constants ( $J$ ) were expressed in hertz. TLC analysis was performed on Kieselgel 60 F<sub>254</sub> (Merck) plates (silica gel, 0.25 mm layer thickness), with compounds visualized by spraying with 20%  $\text{H}_2\text{SO}_4$  followed by charring at  $100\text{ }^\circ\text{C}$ . Silica gel (Merck, 200-400 mesh ASTM) was used for column chromatography. All other chemicals and reagents were analytical grade.

**Table 1.** NMR chemical shifts and correlations of **1** in  $\text{DMSO-}d_6$

Position	$\delta_{\text{H}}$	$\delta_{\text{C}}$	DEPT	HMBC
2	—	162.8	C	—
3	—	154.1	C	—
4	—	183.1	C	—
5	—	161.6	C	—
6	—	132.5	C	—
7	—	159.3	C	—
8	6.95 (s)	92.5	CH	C-6, C-9, C-10
9	—	153.5	C	—
10	—	105.7	C	—
1'	—	112.8 <sup>a</sup>	C	—
2'	7.09 (s)	107.6	CH	C-2
3'	—	152.8	C	—
4'	6.55 (s)	105.2	CH	C-2', C-3', C-5'
5'	—	142.5	C	—
6'	7.44 (s)	112.8 <sup>a</sup>	CH	C-2, C-3, C-3', C-5'
5-OH	13.03 (s)	—	—	—
6-OMe	3.71 (s)	60.9	CH <sub>3</sub>	C-6
7-OMe	3.92 (s)	57.3	CH <sub>3</sub>	C-7
5'-OMe	3.80 (s)	57.6	CH <sub>3</sub>	C-5'

<sup>a</sup>The carbon signals were reciprocally overlapped.

**Plant Material.** The whole plant of *Artemisia apiacea* Hance was purchased from the Kyungdong market, and verified by Prof. Young-Hee Ahn, Chung-Ang University, Korea. A voucher specimen (No. LEE 2005-01) was deposited at the Herbarium of Dept of Applied Plant Science, Chung-Ang University, Korea.

**Extraction and Isolation.** The air-dried powders of *A. apiacea* (5 kg) were extracted with MeOH (10 liters  $\times$  3) under reflux. The resultant extracts were combined and concentrated under reduced pressure to afford 255 g of the residue. The MeOH extract (255 g) was suspended in water and then fractionated successively with equal volumes of *n*-hexane (40 g), CH<sub>2</sub>Cl<sub>2</sub> (38 g), EtOAc (56 g) and *n*-BuOH (30 g). The resulting EtOAc fraction (50 g) was chromatographed on a silica gel (600 g) column eluting with a gradient of CHCl<sub>3</sub>-MeOH (0, 10, 30, 50, 70, and 100% MeOH, each 5,000 liters) to afford six subfractions (EA1, 2, 3, 4, 5, and 6, respectively). Among them, subfraction EA3 (7.0 g) was chromatographed on a silica gel column eluting with a gradient of EtOAc-MeOH (70 : 30, 3,000 liters) to afford compound **1** (2 mg).

**Compound 1:** IR  $\nu_{\max}$  (KBr): see text; <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>) and <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): see Table 1; EI-MS (70 eV, rel. int., %): *m/z* 360 [M]<sup>+</sup> (100), 345 (67), 331 (12), 314 (16), 285 (6), 181 (21), 165 (11), 153 (9), 137 (5).

**Acknowledgement.** This work was supported by a grant from the "GRRRC" Project of Gyeonggi Provincial Government, Republic of Korea.

### References

1. Yook, C. S. *Coloured Medicinal Plants of Korea*; Academy Publishing Co.: Seoul, 1989; p 522.
2. Shimomura, H.; Sashida, Y.; Ohshima, Y. *Phytochemistry* **1979**, *18*, 1761-1762.
3. Shimomura, H.; Sashida, Y.; Ohshima, Y. *Chem. Pharm. Bull.* **1980**, *28*, 347-348.
4. Shimomura, H.; Sashida, Y.; Ohshima, Y.; Azuma, T.; Saitoh, M. *Yakugaku Zasshi* **1980**, *100*, 1164-1166.
5. Yano, K. *Flavour Ind.* **1970**, *1*, 328-330.
6. Kim, O. C.; Jang, H. J. *Hanguk Nonghwa Hakhoechi* **1994**, *37*, 37-42.
7. Lee, S.; Kim, K. S.; Jang, J. M.; Park, Y.; Kim, Y. B.; Kim, B. K. *Arch. Pharm. Res.* **2002**, *25*, 285-288.
8. Lee, S.; Kim, K. S.; Shim, S. H.; Park, Y. M.; Kim, B. K. *Arch. Pharm. Res.* **2003**, *26*, 902-905.
9. Kim, K. S.; Lee, S.; Kang, K. H.; Kim, B. K. *Nat. Prod. Sci.* **2005**, *11*, 10-12.
10. Markham, K. R. *Techniques of Flavonoid Identification*; Academic press: London, 1982; pp 87-90.
11. Lee, H.-J.; Lee, O.-K.; Kwon, Y.-H.; Choi, D.-H.; Kang, H.-Y.; Lee, H.-Y.; Paik, K.-H.; Lee, H.-J. *Bull. Korean Chem. Soc.* **2006**, *27*, 426-428.