Apicin, A New Flavonoid from *Artemisia apiacea*

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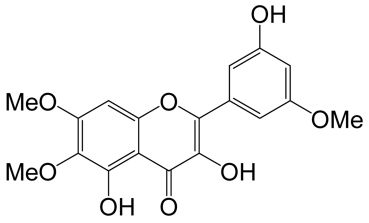
Artemisia species spreads widely in nature and are genus of the family Compositae consisting of more than 350 species. *A. apiacea* is distributed at wasteland and river beaches of Korea, Japan and China, and has been used as traditional medicine to treat eczema and jaundice.[1] Investigations on the compounds from *A. apiacea* have revealed the presence of campesterol, stigmasterol, β-sitosterol, 7-methoxycoumarin, 7,8-dimethoxycoumarin and 7,8-methylenedioxycoumarin,[2] scopoletin, protocatechualdehyde and ethyl and methyl caffeates,[3] daphnetin, 7-hydroxy-8-methoxycoumarin and 7-isopentenyloxy-8-methoxycoumarin,[4] volatile constituents like α-pinene and artemisia ketone[5,6] and artemicapin C, apigenin, daucosterol, cacticin, hyperin, α-amyrin, β-amyrin, β-sitosterol and 5,6,7-trimethoxycoumarin.[7-9] 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.[10] The IR spectrum of **1** showed absorption bands for hydroxyl at 3383 cm^{-1}, α,β-unsaturated C=O at 1612 cm^{-1} and C-O at 1015 cm^{-1}. In the ^{1}H-NMR spectrum of **1**, the typical flavonoid signals were observed. The singlets of aromatic 5-OH at δ 13.03 and three -OMe signals at δ 3.91, 3.80 and 3.71 were observed. The singlets of H-8, -2', -4', and -6' were observed at δ 6.95, 7.09, 6.55 and 7.44, respectively.[11] Its ^{13}C-NMR spectrum of **1** showed C=O at δ 183.1 and three -OMe at δ 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}H- and ^{13}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).

Table 1. NMR chemical shifts and correlations of **1** in DMSO-d_6

Position	δ_H	δ_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*	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*	CH	C-2, C-3, C-3', C-5'
5-OH	13.03 (s)	–	–	–
6-OMe	3.71 (s)	60.9	CH_3	C-6
7-OMe	3.92 (s)	57.3	CH_3	C-7
5'-OMe	3.80 (s)	57.6	CH_3	C-5'

*The carbon signals were reciprocally overlapped.



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Experimental Section

General Procedures. MS spectrum was measured with a Jeol JMS-AX505WA mass spectrometer. ^{1}H- and ^{13}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 (δ), and coupling constants (J) were expressed in hertz. TLC analysis was performed on Kieselgel 60 F_{254} (Merck) plates (silica gel, 0.25 mm layer thickness), with compounds visualized by spraying with 20% H_2SO_4 followed by charring at 100 °C. Silica gel (Merck, 200-400 mesh ASTM) was used for column chromatography. All other chemicals and reagents were analytical grade.

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 × 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_2Cl_2 (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 $CHCl_3$-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 ν_{max} (KBr): see text; ^{1}H-NMR (400 MHz, DMSO-d_6) and ^{13}C-NMR (100 MHz, DMSO-d_6): see Table 1; EI-MS (70 eV, rel. int., %): *m/z* 360 $[M]^+$ (100), 345 (67), 331 (12), 314 (16), 285 (6), 181 (21), 165 (11), 153 (9), 137 (5).

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