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A Benzenoid from the Stem of *Acanthopanax senticosus*

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Seven compounds were isolated from the stem of *Acanthopanax senticosus* by repeated column chromatography. Their structures were elucidated as isovanillin (**1**), (-)-sesamin (**2**), isofraxidin (**3**), (+)-syringaresinol (**4**), 5-hydroxymethylfurfural (**5**), eleutheroside B (**6**), and eleutheroside E (**7**) by spectral analysis. Among them, isovanillin (**1**) was isolated for the first time from the family Araliaceae.

Key words: *Acanthopanax senticosus*, Araliaceae, Benzenoid, Isovanillin

INTRODUCTION

Approximately fifteen species of the genus *Acanthopanax* are known to be self-grown in the Korean peninsula. *A. senticosus*, which is distributed in northern Asia, has been traditionally used as a tonic and a sedative, as well as in the treatment of rheumatism and diabetes (Perry, 1980; Yook, 1990).

Investigations on the compounds from *A. senticosus* have revealed the presence of phenolic compounds from the stem barks (Nishibe *et al.*, 1990), eleutheroside E_2 and isomaltol 3-*O*-α-D-glucopyranoside from the roots (Li *et al.*, 2001), and chiisanoside, chiisanogenin and hyperin from the leaves (Lee *et al.*, 2003), *etc.* Recently we reported the inhibitory effect of the water extract from the stem bark of this plant on hyperlipidemia in rats (Lee *et al.*, 2001) and the isolation of constituents from this plant (Ryu *et al.*, 2003).

In this study, we elucidated the structures of constituents from *A. senticosus* stem.

MATERIALS AND METHODS

Instruments and reagents

MS spectrum was measured with a Jeol JMS-AX505WA mass spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded with a Bruker AVANCE 500 NMR spectrometer in $CDCl_3$ or DMSO 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 stem of *Acanthopanax senticosus* (Rupr. & Maxim.) Harms was collected at Jilin Province, China in Oct. 2002, and verified by Prof. S. H. Cho, Gongju National University of Education, Korea. A voucher specimen of this plant was deposited at the R & D Center for Functional Foods, Institute of Food and Culture, Pulmuone Co. Ltd., Korea.

Extraction and isolation

The air-dried powdered stem of *A. senticosus* was extracted with H_2O under reflux. The resultant extract was combined and lyophilized to afford a residue. The H_2O extract was re-suspended in H_2O and then extracted successively with equal volumes of $CHCl_3$, EtOAc, and *n*-BuOH. Each fraction was evaporated *in vacuo* to obtain $CHCl_3$ (14.82 g), EtOAc (23.55 g), *n*-BuOH (48.62 g), and H_2O (394.6 g) fractions.

A portion of the $CHCl_3$ fraction (4 g) was chromatographed on a silica gel column (7×60 cm, No. 7734) eluting with a gradient of $CHCl_3$-MeOH to afford 20 subfractions. Sub-fraction 3 (ASC-13, 100:0.1) was chromatographed on a silica gel column (No. 7729) eluting with *n*-

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hexane-EtOAc (10:2) to afford 15 sub-fractions. Sub-fraction ASC-13-8 was chromatographed by preparative TLC using $CHCl_3$-MeOH (100:1) to give compound **1** (3 mg). Sub-fraction 6 (ASC-33, 100:0.5) was chromatographed by preparative TLC using $CHCl_3$-Me_2CO (8:2) to give compounds **2** (3 mg, R_f 0.95) and **3** (5 mg, R_f 0.55). Sub-fraction 8 (ASC-53, 100:1) was chromatographed on a silica gel column eluting with a gradient of $CHCl_3$-MeOH to afford 5 sub-fractions. Sub-fraction ASC-53-20 was chromatographed by preparative TLC using *n*-hexane-EtOAc (5:8) to give compound **4** (4 mg). A portion of the EtOAc fraction (6 g) was chromatographed on a silica gel column eluting with a gradient of $CHCl_3$-MeOH to afford 25 sub-fractions. Sub-fraction 5 (ASE-25, 100:0.5) was chromatographed over a silica gel column (No. 7729) eluting with a gradient of $CHCl_3$-Me_2CO (8:2) to give compound **5** (4 mg). A portion of the *n*-BuOH fraction (10 g) was chromatographed on a silica gel column eluting with a gradient of $CHCl_3$-MeOH to afford compounds **6** (326 mg, 95:5) and **7** (697 mg, 90:10).

Compound **1**; White crystals; mp 117°; EI-MS (70 eV, rel. int., %): *m/z* 152 $[M]^+$ (95), 151 (100), 137 (10), 123 (21), 109 (21), 108 (15), 93 (11), 81 (36); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 9.83 (1H, s, -CHO), 7.43 (1H, dd, *J* = 1.8, 8.2 Hz, H-6), 7.42 (1H, d, *J* = 1.8 Hz, H-2), 7.04 (1H, d, *J* = 8.2 Hz, H-5), 3.97 (3H, s, -OMe), 6.18 (1H, s, -OH); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 190.9 (-CHO), 129.9 (C-1), 108.7 (C-2), 151.6 (C-3), 147.1 (C-4), 114.3 (C-5), 127.5 (C-6), 56.1 (-OMe).

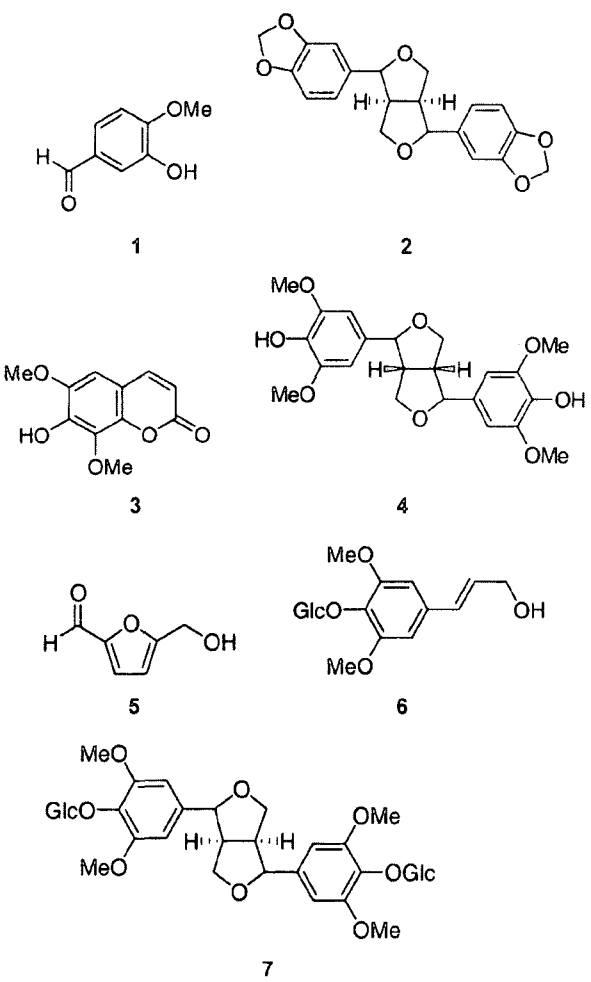

Fig. 1. Structures of compounds **1-7**

RESULTS AND DISCUSSION

Isolation of constituents from the stem of *A. senticosus* was conducted by repeated column chromatography. A chromatographic separation of the fractions from *A. senticosus* stem led to the isolation of compounds **1-7**. Their structures were elucidated as (-)-sesamin (**2**), isofraxidin (**3**), (+)-syringaresinol (**4**), 5-hydroxymethylfurfural (**5**), eleutheroside B (**6**), and eleutheroside E (**7**) by comparing their spectral analysis in the literature (Das *et al.*, 1999; Lee *et al.*, 2002; Nishibe *et al.*, 1990; Ryu *et al.*, 2003; Wagner *et al.*, 1982).

Compound **1** from the $CHCl_3$ fraction was obtained as white crystals from MeOH. The EI-MS of **1** showed an $[M]^+$ ion at *m/z* 152. The ^{1}H-NMR spectrum of **1** showed resonances for a typical aldehyde signal at δ 9.83 (s), ABX splitting proton signals at δ 7.04 (d, *J* = 8.2 Hz), 7.42 (d, *J* = 1.8 Hz) and 7.43 (dd, *J* = 1.8, 8.2 Hz), and a methoxyl signal at δ 3.97 (s), indicating that it has a 1,3,4-trisubstituted aromatic ring system. The ^{13}C-NMR spectrum of **1** showed resonances for an aldehyde signal at δ 190.9 and a methoxyl signal at δ 56.1. The position of 1,3,4-trisubstitution was confirmed by HMBC analysis. Accordingly, the structure of **1** was elucidated as isovanillin (3-hydroxy-4-methoxy-benzaldehyde) by spectral analysis.

Isovanillin (**1**) has been isolated from *Asparagus dumosus* (Khaliq-uz-Zaman *et al.*, 2000), *Hernandia sonora* (Chen *et al.*, 1995a; Chen *et al.*, 1995b), *Mondia whiteii* (Mukonyi and Ndiege, 2001) and *Stelmatocrypton khasianum* (Zhang *et al.*, 2000). To our knowledge, this is the first report on the isolation of isovanillin (**1**) from a plant of the family Araliaceae.

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REFERENCES

Chen, I. S., Chen, J. J., and Tsai, I. L., Alkaloids from *Hernandia sonora*. *Phytochemistry*, 40, 983-986 (1995a).

Chen, I. S., Chen, J. J., Tsai, I. L., Chang, Y. L., and Teng, C. M., New *p*-quinonoid aporphine alkaloids and antiplatelet aggregation constituents of *Hernandia sonora*. *Planta Med.,* 61, 537-539 (1995b).

Das, B., Venkataiah, B., and Kashinatham A., (+)-Syringaresinol from *Parthenium hysterophorus*. *Fitoterapia,* 70, 101-102 (1999).

Khaliq-uz-Zaman, S. M., Simin, K., and Ahmad, V. U., Chemical constituents from *Asparagus dumosus*. *Fitoterapia,* 71, 331-333 (2000).

Lee, S., Kim, B.-K., Cho, S. H., and Shin, K. H., Phytochemical constituents from the fruits of *Acanthopanax sessiliflorus*. *Arch. Pharm. Res.,* 25, 280-284 (2002).

Lee, S., Shin, D. S., Oh, K. B., and Shin, K. H., Antibacterial compounds from the leaves of *Acanthopanax senticosus*. *Arch. Pharm. Res.,* 26, 40-42 (2003).

Lee, Y. S., Jung, S. H., Lim, S. S., Ji, J., Lee, S., and Shin, K. H., Effects of the water extract from the stem bark of *Acanthopanax senticosus* on hyperlipidemia in rats. *Kor. J. Pharmacogn.,* 32, 103-107 (2001).

Li, X. C., Barnes, D., and Khan, I. A., A new lignan glycoside from *Eleutherococcus senticosus*. *Planta Med.,* 67, 776-778 (2001).

Mukonyi, K. W., and Ndiege, I. O., 2-Hydroxy-4-methoxy-benzaldehyde: Aromatic taste modifying compound from *Mondia whiteii* Skeels. *Bull. Chem. Soc. Ethiopia,* 15, 137-141 (2001).

Nishibe, S., Kinoshita, H., Takeda, H., and Okano, G., Phenolic compounds from stem bark of *Acanthopanax senticosus* and their pharmacological effect in chronic swimming stressed rats. *Chem. Pharm. Bull.,* 38, 1763-1765 (1990).

Perry, L. M., Medicinal plants of East and Southeast Asia. MIT press, Cambridge, Massachusetts and London, p. 41 (1980).

Ryu, J., Son, D., Kang, J., Lee, S. Y., Kim, H.-S., Shin, K. H., and Lee, S., Phytochemical constituents of *Acanthopanax senticosus* (Rupr. et Maxim.) Harms stem. *Kor. J. Med. Crop Sci.,* 11, 306-310 (2003).

Wagner, H., Heur, Y. H., Obermeier, A., Tittel, G., and Bladt, S., Die DC- and HPLC-Analyse der Eleutherococcus Droge. *Planta Med.,* 44, 193-198 (1982).

Yook, C. S., Coloured medicinal plants of Korea. Academy Book Co., Seoul, p. 377 (1990).

Zhang, Q. Y., Zhao, Y. Y., Liu, X. H., Zhang, N. X., Cui, Y. X., and Cheng, T. M., Studies on chemical constituents of *Stelmatocryptonm khasianum* (Benth.) H. Bail. *China J. Chin. Mat. Med.,* 25, 101-103 (2000).