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A Furan Derivative from *Cornus officinalis*

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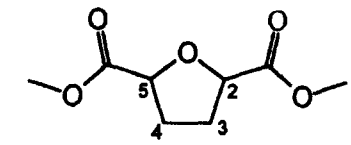
Dimethyltetrahydrofuran *cis*-2,5-dicarboxylate a furan derivative has been isolated from the fruits of *Cornus officinalis*, and it was isolated for the first time in the nature. The structure was elucidated by NMR spectroscopic techniques.

Key words : *Cornus officnalis*, Cornaceae, Dimethyltetrahydrofuran cis-2,5-dicarboxylate, Kaempferol, Quercetin

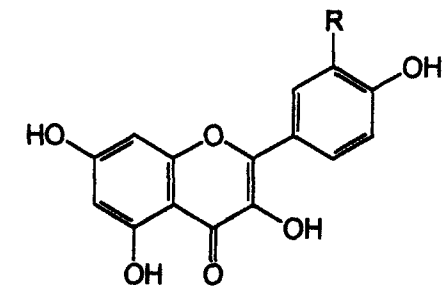
INTRODUCTION

Fruits of *Cornus officinalis* Sieb. et Zucc. (Cornaceae) is a well-known traditional medicine for its tonic, analgesic and diuretic properties in Korea, Japan and China, and this plant is widely distributed in Korea (Yook, 1981; Lee, 1989).

Previous phytochemical studies on fruits of this plants have afforded iridoids (Endo *et al.*, 1973), tannins (Okuda *et al.*, 1984; Hatano *et al.*, 1989; Lee *et al.*, 1989), volatile flavor components (Miyazawa *et al.*, 1989), and an ursolic acid (Yamahara *et al.*, 1981; Kim *et al.*, 1996). Further investigation of fruits of this plant afforded a furan derivative, dimethyltetrahydrofuran *cis*-2,5-dicarboxylate, together with two common flavonoids, kaempferol and quercetin (Fig. 1). This paper reports their isolation and structural elucidation.



Compound I



Compound II R=H
Compound III R=OH

Fig. 1. Compounds isolated from *Cornus officinalis*.

MATERIALS AND METHODS

Melting points were obtained on Gallenkamp melting point apparatus (uncorr.). IR spectra were recorded on a Nicolet model 205 FT-IR spectrophotometer. UV spectra were obtained on a Shimadzu UV_{240} UV-Visible recording spectrophotometer. ^1H- and ^{13}C-NMR spectra were determined on a Brucker AMX 400 spectrophotometer. MS was recorded on a VG70-VSEQ instrument. Analytical TLC was carried out on Merck aluminium plates precoated with Si gel 60 F_{254}. Chromatography was performed on Merck Si gel 60 (230~400 mesh) and Sephadex LH 20. LPLC was carried out on Duramat 80 equipped with a Merck Lichroprep Si 60 (240×10 mm) column.

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Plant materials

The fruits of *Cornus officinalis* were collected at Suwon, Kyungkido, Korea in 1994. A voucher specimen is deposited in the herbarium of College of Pharmacy, Woosuk University (WSU-94-006).

Extraction and isolation

Fresh fruits (4 kg) of *Cornus officinalis* were extracted twice with MeOH at room temperature. The resulting MeOH extract (257 g) was subjected to successive solvent partitioning to give CH_2Cl_2 (35 g), EtOAc (30 g), n-BuOH (65 g) and water (130 g) soluble fractions. The EtOAc extract was applied over silica gel using gradient solvent system of EtOAc:MeOH (1:0 → 0:1)

as an eluent to give five sub-fractions (E1~E5). The first sub-fraction (20 g) was chromatographed on silica gel eluted with n-hexane:EtOAc:MeOH (10:10:1) to give five fractions. Fraction 4 (300 mg) was rechromatographed on LPLC (Chloroform:MeOH, 4.5:1) to yield 100 mg of compound **I**. Fractions 3 (30 mg) and 4 (20 mg) were applied over Sephadex LH 20 column chromatography (MeOH) to yield compounds **II** (15 mg) and **III** (10 mg).

Compound I (dimethyltetrahydrofuran *cis*-2,5-dicarboxylate): colorless needle in MeOH, mp. 76~78°C, $[\alpha]_D^{25}$; 0.0° (c 0.15, MeOH), IRν_{max}^{KBr}cm^{-1} 1736 (C=O), 1228, GCMS:m/z (rel. int.); 188 (M^+, 3), 59 (12), 71 (95), 89 (85), 102 (10), ^{1}H-NMR (CD_3OD, δ): 4.44 (2H, dd, *J*=7.1, 4.5 Hz, H-2,5), 3.69 (6H, s, 2×OCH_3), 2.73 (2H, dd, *J*=16.1, 4.5 Hz, H-3β, 4β), 2.59 (2H, dd, *J*=16.1, 7.1 Hz, H-3α, 4α), ^{13}C-NMR (CD_3OD, δ): 175.1 (C=O), 174.0 (C=O), 66.7 (C-2, 5), 52.6 (2×OCH_3), 39.9 (C-3, 4).

Compound II (kaempferol): yellowish needles in MeOH, Mg-HCl, Zn-HCl test, $FeCl_3$ positive, mp. 274~277°C, IRν_{max}^{KBr}cm^{-1} 3500 (OH), 1660 (C=O), 1620, 1510, 1260, UVλ_{max}^{MeOH}nm 261, 320 (sh), 370, EIMS:m/z (rel. int.); 286 (M^+, 100), 258 (21), 229 (25), 153 (19), ^{1}H-NMR (DMSO-d_6, δ): 12.60 (1H, s, 5-OH), 8.02 (2H, d, *J*=8.8 Hz, H-2', 6'), 6.86 (2H, d, *J*=8.8 Hz, H-3', 5'), 6.43 (1H, d, *J*=2.0 Hz, H-8), 6.21 (1H, d, *J*=2.0 Hz, H-6), ^{13}C-NMR (DMSO-d_6, δ): 175.9 (C-4), 163.9 (C-7), 160.7 (C-5), 156.4 (C-9), 159.2 (C-4'), 146.8 (C-2), 135.6 (C-3), 121.8 (C-1'), 128.6 (C-2', 6'), 115.0 (C-3', 5'), 103.2 (C-10), 98.2.(C-6), 93.5 (C-8).

Compound III (quercetin): yellowish powder in MeOH, Mg-HCl, Zn-HCl test, $FeCl_3$ positive, mp. 309~312°C, IRν_{max}^{KBr}cm^{-1} 3390 (OH), 1670 (C=O), 1620, 1520, 1430, UVλ_{max}^{MeOH}nm 254, 292 (sh), 370, EIMS:m/z (rel. int.); 302 (M^+, 100), 273 (12), 245 (35), 229 (18), 153 (50), ^{1}H-NMR (DMSO-d_6, δ): 12.50 (1H, s, 5-OH), 7.68 (1H, d, *J*=2.1 Hz, H-2'), 7.54 (1H, dd, *J*=8.5, 2.1 Hz, H-6'), 6.89 (1H, d, *J*=8.5 Hz, H-5'), 6.40 (1H, d, *J*=1.8 Hz, H-8), 6.18 (1H, d, *J*=1.8 Hz, H-6), ^{13}C-NMR (DMSO-d_6, δ): 175.7 (C-4), 163.9 (C-7), 160.8 (C-5), 152.4 (C-9), 147.5 (C-4'), 146.6 (C-2), 145.0 (C-3'), 135.8 (C-3), 122.0 (C-1'), 120.1 (C-6'), 115.6 (C-5'), 115.0 (C-2'), 103.2 (C-10), 98.2 (C-6), 93.4 (C-8).

RESULTS AND DISCUSSION

The furan derivative, compound **I** was obtained as colorless needles (MeOH). Its IR spectrum showed the presence of an ester (1736 cm^{-1}) group, and molecular formula was established as $C_8H_{12}O_5$ by ^{1}H-NMR (12H), ^{13}C-NMR (8C) and mass (m/z 188) spectra. The formula showed three unsaturated-bond equivalents. ^{13}C-NMR (DEPT) spectra of compound **I** exhibited the two carbonyl (δ175.1 and 174.0 ppm) signals, hence the remaining one unsaturated-bond equivalent should be a cyclic. The remaining carbon signals were revealed a methine bearing oxygen (δ66.7 ppm), a methoxy (δ 52.6 ppm) and a methylene (δ40.0), thus the structure of compound **I** was supposed to have a symmetric skeleton. From the values of chemical shifts and coupling patterns of ^{1}H-NMR (^{1}H-^{1}H COSY), AMX spin system (δ4.44, 2.73 and 2.59 ppm), and ^{13}C-NMR spectra, a remaining unsaturation was accounted for one ring suggestive of a 2,5-disubstituted tetrahydrofuran compound. Finally, compound **I** was characterized as dimethyltetrahydrofuran *cis*-2,5-dicarboxylate. The structure and stereochemistry of compound **I** was identified by comparison with the ^{1}H-NMR spectrum data of the synthesized compounds (cis δ4.59 and trans δ4.71 ppm, H-2,5 in CCl_4), those reported in the literature (Moore *et al.*, 1972).

Compounds **II** and **III** have very similar patterns in their UV, IR and NMR spectra. Two compounds showed positive results in $FeCl_3$, Zn/HCl, Mg/HCl tests, and UV spectra exhibited characteristic absorptions for flavonols (Mabry *et al.*, 1970). Compounds **II** and **III** were identified as well-known flavonols, kaempferol and quercetin, respectively, by comparison of IR, NMR and UV data in literature (Kim *et al.*, 1995; Do *et al.*, 1992), and finally established by comparison with authentic standards.

ACKNOWLEDGEMENT

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REFERENCES CITED

Do, J. C., Yu, Y. J., Jung, K. Y. and Son, K. H., Flavonoids from the leaves of *Polygala japonica*. *Kor. J. Pharmacong.*, 23, 9-13 (1992).

Endo, T. and Taguchi, H., Studies on the consitituents of *Cornus officinalis* Sieb. et Zucc. *Yakugaku Zasshi*, 93, 30-32 (1973).

Hatano, T., Ogawa, N., Kira, R., Yasugara, T. and Okude, T., Tannins of Cornaceous Plants I. Cornusiins A, B and C, dimeric, monomeric and trimeric hydrolyzable tannins from *Cornus officinalis*, and orientation of valoneoyl group in related tannins. *Chem. Pharm. Bull.*, 37, 2083-2090 (1989).

Kim, D. K., Kwak, J. H., Ryu, J. H., Kwon, H. C., Kang, S. S., Kwon, N. S., Lee, K. R. and Zee, O. P., A component from *Cornus officinalis* enhances hydrogen peroxide generation from macrophages. *Kor. J. Pharmacogn.*, 27, 101-104 (1996).

Kim, J. S., Kang, S. S., Lee, M, W. and Kim, O. K., Isolation of flavonoids from the leaves of *Aralia conitnentalis*. *Kor. J. Pharmacogn.*, 26, 239-243 (1995).

Lee, S.H., Tanaka, T., Nonaka, G. I., and Nishioka, I., Sedoheptulose digallate from *Corus officinalis*.

Phytochemistry, 25, 3469-3472 (1989).
Lee, T. B., *Illustrated Flora of Korea.* Hayngmoonsa, Seoul, p. 594, 1989.
Mabry, T. J., Markham, K. R. and Thomas, M. B., The *systematic identification of flavonoids.* Springer-Verlag, N. Y., New York, p. 41, 1970.
Miyazawa, M. and Kameoka, H., Volatile flavor components of Corni Fructus (*Cornus officinalis* Sieb. et Zucc.). *Agric. Biol. Chem.,* 53, 3337-3340 (1989)
Moore, J. A. and Kelly, J. E., An improved hydrogenation for the preparation of tetrahydrofuran *cis*-2,5-dicarboxylic acid. *Org. Prep. Proced. Int.,* 4, 289-292 (1972)
Okuda, T., Hatano, T., Ogawa, N., Kira, R. and Matsuda, M., Cornusiin A, a dimeric ellagitannin forming four tautomers and accompanying new tannins in *Cornus officinalis. Chem. Pharm. Bull.,* 32, 4662-4665 (1984).
Yamahara, J., Mibu, H., Sawada, T., Fujimura, H., Takino, S., Yoshikawa, M. and Kitagawa, I., Biologically active principles of crude drugs. Anti-diabetic principles of Corni Fructus in experimental diabetes induced by streptozotocin. *Yakugaku Zasshi,* 101, 86 (1981).
Yook, C. S., *Medicinal Plants of Korea.* Jinmyeong Publishing Co., Seoul, p. 268, 1981.