New phenylalkanoids from the rhizome of *Cnidium officinalis* Makino

Hyoung-Geun Kim¹, Trong Nguyen Nguyen¹, Yeong-Geun Lee¹, Min-Ho Lee², Dae Young Lee³, Youn-Hyung Lee⁴* and Nam-In Baek¹*

**Abstract**

*Cnidium officinalis* rhizomes were immersed in 80% MeOH. The extract was fractionated to water, *n*-butanol, and ethyl acetate fractions (Fr). Open column chromatography was repeatedly carried out on *n*-butanol and ethyl acetate Fr using silica gel, octadecyl silica gel, and Sephadex LH-20 as the stationary phase affording five phenyl alkanoids 1–5 including two new ones. The molecular structures including stereochemistry were decided based on spectroscopic interpretation of nuclear magnetic resonance, mass spectrometry, and infrared spectroscopy as well as chemical reaction. Three known compounds, coniferyl alcohol methyl ether (1), vanillin (2), and coniferyl aldehyde (3), were reported in the beginning for this plant by authors. Two new phenyl alkanoids were named, 7-methoxyeugenol and cnidiumoside.

**Keywords:** *Cnidium officinalis*, Cnidiumoside, 7-Methoxyeugenol, Phenyl alkanoid

**Introduction**

*Cnidium officinalis* Makino (Umbelliferae) is a perennially grown herb either semi-shaded or not shaded in moist soil. It originates from China but is now extensively cultivated in Korea, Japan, and China [1]. The ground parts have been used as a medicinal, conspicuous aroma, and as condiment materials in beverages, baking, cosmetics, and the pharmaceutical industry [1]. The dried rhizomes (Cnidii Rhizoma) have been especially utilized in East-Asia countries for the treatment of female menstrual disorders and headaches through a decrease in inflammation and an improvement in blood circulation [2, 3]. Many studies have also reported the rhizomes as having anti-cancer [4], analgesic [5], antibacterial [6], anticonvulsive [7], anti-inflammatory [4, 5], febrifuge, hypotensive [8], sedative [9], and vasodilator [10] effects. The major constituents of the rhizomes were revealed to be phthalides, alkaloids, ceramides, polyphenols, and flavonoids [1]. Phthalides in particular are the most important constituents copiously contained in the essential oil [6]. Many reported biological activities of *C. officinalis* rhizomes are due to the presence of phthalides [6]. Phenols are also major constituents of rhizomes and are reported to have various pharmacological activities [11]. However, phenyl alkanoids of this plant are rarely studied. The authors isolated five phenyl alkanoids from *C. officinalis* rhizomes in this study. Among them, two compounds were revealed to be new and three others have never been reported for *C. officinalis*. This paper describes the isolation procedure for phenyl alkanoids and the structure determination including stereostructures.

**Materials and methods**

**Plant materials**

*Cnidium officinalis* rhizomes were provided and identified by Dr. J. T. Jeong, Department of Herbal Crop Research, RDA, Korea. A standard sample (NPCL-20200023) was put up at NPCL Laboratory, KyungHee University, Yongin, Korea.
General experimental procedures
The instruments and materials used for the isolation and identification of the phenyl alkanoids were the same as those in literatures [12]. The silica gel and the octadecyl silica gel (ODS) resins used for column chromatography (CC) were Kiesel gel 60 (Merck, Darmstadt, Germany) and the Lichroprep RP-18 (40–60 µm, Merck) respectively. Sephadex LH-20 was purchased from Amersham Biosciences (Uppsala, Sweden). Thin layer chromatography (TLC) was carried out using Kiesel gel 60 F254 and RP-18 F254S (Merck) TLC plates, and the spots were detected using a UV lamp Spectroline Model ENF-240 C/F (Spectronics Corporation, Westbury, NY, USA) and a 10% H2SO4 solution. Deuterium solvents were purchased from Merck Co., Ltd and Sigma Aldrich Co. Ltd (St. Louis, MO, USA). Nuclear magnetic resonance (NMR) spectra were recorded on a 600 MHz FT-NMR spectrometer (Bruker AVANCE 600, Billerica, MA, USA). Infrared (IR) spectra were obtained using a Perkin Elmer Spectrum One FT-IR spectrometer (Buckinghamshire, England). The specific rotation value was measured with JASCO P-1010 digital polarimeter (Tokyo, Japan). ESIMS spectra were recorded on an AB SCIEX Q-TOF 5600 (Framingham, MA, USA). Solvents were supplied by Burdick & Jackson (Muskegon, MI, USA).

Isolation of phenyl alkanoids from Cnidium officinalis rhizomes
C. officinalis rhizomes were dried at room temperature and 10 kg of dried materials were powdered and soaked overnight in ethanol (70%, 54 L × 2) at room temperature. The obtained solution was evaporated using rotary vacuum evaporator at 40°C affording a brownish extract (2.1 kg). The residue was divided using systemic solvent fractionation using polarity as ethyl acetate (COE, 280 g), n-butanol (COB, 125 g), and water (COW, 1.695 kg) Fr. The column chromatography (CC) for COE (270 g) and COB (120 g) was performed as seen in Figs. 1, 2. Finally, five phenyl alkanoids (1, COE-11–5; 2, COE-13–2–3; 3, COE-13–2–5; 4, COE-13–11–12–2; 5, COB-13–9–13–2) were isolated.

Coniferyl alcohol methyl ether (1): \( R_f \) value on silica gel TLC, 0.72, n-hexane–ethyl acetate (1:1); \( R_f \) value on octadecyl silica gel TLC, 0.85, acetone–H2O (3:1); IR (LiF plates) \( \nu_{\text{max}} \) 3393, 2933, 1676, 1599, 1512, 1463 cm\(^{-1}\); 13C and 1H NMR (CMR and PMR): Tables 1 and 2. EI-MS: \( m/z \) 180 [M]+.

Vanillin (2): \( R_f \) value on silica gel TLC, 0.29, n-hexane–ethyl acetate (2:1); \( R_f \) value on octadecyl silica gel TLC, \( R_f \) 0.70, acetone–H2O (2:1); IR (LiF plates) \( \nu_{\text{max}} \) 3234, 2923, 1675, 1585, 1509 cm\(^{-1}\); CMR and PMR: Tables 1 and 2. EI-MS: \( m/z \) 152 [M]+.

Coniferyl aldehyde (3): \( R_f \) value on silica gel TLC, 0.20, n-hexane–ethyl acetate (2:1); \( R_f \) value on octadecyl silica gel TLC, \( R_f \) 0.72, acetone–H2O (2:1); IR (LiF plates) \( \nu_{\text{max}} \).
OH

3.89 (1H, dd, 11.9, 5.5, H-9a), 3.88 (3H, s,
), 5.50 (1H, d, 6.8, H-7), 4.20 (2H, dd,
′(1H, d, 8.3, H-5), 6.18 (1H, br. d, 16.0, H-7
6.79 (1H, s, H-2
6.79 (1H, s, H-2
′(1H, d, 5.3, H-5), 6.14 (1H, dt, 16.0, 5.2, H-8′) 3.50 (1H, d, 6.8, H-7), 4.20 (2H, dd, 5.2, 1.3, H-9′), 3.89 (1H, dd, 11.9, 5.5, H-9a), 3.88 (3H, s, 3-Ome or 3′-Ome), 3.81 (1H, dd, 11.9, 6.3, H-9b), 3.78 (3H, s, 3-Ome or 3′-Ome), 3.56 (1H, ddd, 6.8, 6.3, 6.5, H-8).

Results and discussion

Five phenyl alkanoins 1–5 were isolated from the C. officinalis rhizome through repeated open column chromatography using octadecyl silica gel, silica gel, and Sephadex LH-20 as the stationary phase. 1–3 were identified as coniferyl alcohol methyl ether (1) [13], vanillic (2), and coniferyl aldehyde (3) [14], respectively, from the spectroscopic data and confirmed by previously reported data.

Compound 4 showed a molecular ion peak at m/z 194.0940 [M]+ in the high resolution EI-MS, establishing the molecular formula as C_{11}H_{14}O_{3} (Calcld. for C_{11}H_{14}O_{3} 194.0937). The IR data exhibited the absorbing bands due to hydroxyl (3153 cm⁻¹) and olefin (1673, 1594 cm⁻¹) groups. CMR spectrum (150 MHz, CDCl₃) showed 11 signals including two methoxy signals (δ_C 56.06, OMe-3; 56.40, OMe-7) suggesting 4 to be a phenylpropanoid. Two oxygenated olefin quaternaries (δ_C 145.36, C-4; 146.84, C-3), one olefin quaternary (δ_C 132.99, C-1), four olefin methines (δ_C 109.14, C-2; 114.24, C-5; 120.32, C-6; 139.00, C-8), one exomethylene (δ_C 116.21, C-9), and one oxygenated methine (δ_C 84.64, C-7) were detected. PMR spectrum (600 MHz, CDCl₃) included the olefin signals due to a 1,2,4-trisubstituted benzene moiety (δ_H 6.81, dd, J = 1.8, 7.8 Hz, H-6 (δ_H′ coupling pattern, J in Hz), H-5; 6.86, d, 1.8, H-2; 6.88, d, 7.8), the signals derived from a vinyl moiety (5.20, br. d, 10.2, H-9a; 5.26, br. d, 17.4, H-9b; 5.93, ddd, 6.6, 10.2, 17.4, H-8), an oxygenated methine (4.55, d, 6.6, H-7), and two methoxies (3.31, s, OMe-7; 3.90, s, OMe-3) signals. The NMR data described above were almost identical to eugenol [15] excluding an oxygenated methine and a methoxy moieties instead of a methylene moiety, suggesting that an additional methoxy moiety was linked to C-7. The HMBC spectrum confirmed it; a methoxy proton (δ_H 3.31, OMe-7) correlated with an oxygenated methine carbon (δ_C 84.64, C-7), which also correlated with three olefin methine protons (δ_H 5.93, H-8; 6.81, H-6; 6.86, H-2) and an exomethylene proton (δ_H 5.20, 5.26, H-9). As a result, the planar structure of compound 4 was decided as a 2-methoxy-4-(1-methoxy-2-propen-1-yl) phenol, 7-methoxyugenol. The stereostructure of chiral center, C-7, could be determined as 5 by comparison of a specific rotation value, [α]D + 23.2, with a previously reported value for 7-hydroxyugenol [16, 17]. Compound 4 was identified to be 7S-7-methoxyugenol.

Compound 5 exhibited a molecular ion peak at m/z 845.3072 [M + H]⁺ in the high resolution ESI–MS, established the molecular formula as C_{38}H_{52}O_{21}

Acid hydrolysis of cnidiumoside (5)

The solution of 10 mg of 5 in 5 mL of 1N HCl was refluxed for 2 hrs. 15 mL of HCl was added and treated with ethyl acetate (20 mL × 2). The ethyl acetate phase was concentrated in vacuo and purified via open silica gel CC (2 × 8 cm) using n-hexane-ethyl acetate (2:1) as the eluting solution to give a dehydroconiferyl alcohol (5a, 4 mg).

Dehydroconiferyl alcohol (5a): [α]D -49 (c 0.18, CHCl₃); PMR (600 MHz, CDCl₃, δ_H coupling pattern, J in Hz) 6.84 (1H, d, 1.9, H-2), 6.82 (1H, s, H-2′ or H-6′), 6.79 (1H, s, H-2′ or H-6′), 6.50 (1H, dd, 1.9, 8.3, H-6), 6.46 (1H, d, 8.3, H-5), 6.18 (1H, br. d, 16.0, H-7′), 6.14 (1H, dt, 16.0, 5.2, H-8′), 5.50 (1H, d, 6.8, H-7), 4.20 (2H, dd, 5.2, 1.3, H-9′), 3.89 (1H, dd, 11.9, 5.5, H-9a), 3.88 (3H, s, 3-Oe or 3′-Oe), 3.81 (1H, dd, 11.9, 6.3, H-9b), 3.78 (3H, s, 3-Oe or 3′-Oe), 3.56 (1H, ddd, 6.8, 6.3, 6.5, H-8).

Fig. 2 Chemical structure of phenyl alkanoids from the rhizome of Cnidium officinalis. 1, coniferyl alcohol methyl ether; 2, vanillin; 3, coniferyl aldehyde; 4, 7S-7-methoxyugenol; 5, cnidiumoside.
(Calcd. for C_{38}H_{53}O_{21}, 845.3072). The IR data showed the absorption bands due to hydroxyl (3153 cm\(^{-1}\)) and phenyl (1673, 1594 cm\(^{-1}\)) moieties. Though CMR spectrum (150 MHz, CD\(_3\)OD) showed about 50 carbon signals, some of them were revealed from those of impurities included in compound 5. Among them, 38 carbon signals were defined as those of the compound. The 20 signals including two methoxy signals as those of the aglycone moiety and 18 carbon signals due to three hexoses were detected, suggesting that 5 was a lignan triglyceride. CMR spectrum showed two hemiacetals (\(\delta_C\) 102.89, C-1\(^{16}\); 104.71, C-1\(^{16}\)) and one hemiketal (\(\delta_C\) 99.34, C-2\(^{16}\)) carbon signals as well as PMR spectrum showed only two hemiacetal proton signals (4.37, d, 7.8, H-1\(^{16}\); 4.89, d, 7.8, H-1\(^{16}\)), indicating that three sugars in compound 5 were composed of two aldohexoses and one ketohexose. CMR chemical shifts of three sugars confirmed the presence of one terminal \(\beta\)-d-galactopyranosyl (\(\delta_C\) 62.65, C-6\(^{16}\)); 64.69, C-1\(^{16}\)); 71.42, C-3\(^{16}\)); 71.79, C-4\(^{16}\)); 83.46, C-5\(^{16}\)); 99.34, C-2\(^{16}\)) moieties as well as one \(\beta\)-d-glucopyranosyl (\(\delta_C\) 71.49, C-4\(^{16}\)); 75.05, C-2\(^{16}\)); 78.23, C-5\(^{16}\)); 78.35, C-3\(^{16}\)); 104.71, C-1\(^{16}\)) with a downshifted oxygenated methylene signal (\(\delta_C\) 66.06, C-6\(^{16}\)) due to a glycosidation shift [18] indicating a terminal sugar to be connected to the hydroxyl group at C-6\(^{16}\) of a glucopyranosyl moiety. The coupling constants of two hemiacetal protons were 7.8 and 7.8 Hz confirming the anomeric hydroxyl groups of both aldohexose moieties to have a \(\beta\)-configuration. The carbon signals of the aglycone moiety included four oxygenated olefin quaternaries (\(\delta_C\) 145.71, C-3\(^{16}\)); 147.74, C-4; 149.29, C-4\(^{16}\)); 151.04, C-3), three olefin quaternaries (\(\delta_C\) 129.89, C-5\(^{16}\)); 132.91, C-1\(^{16}\)); 138.22, C-1\(^{16}\)), seven olefin methines (\(\delta_C\) 111.50, C-2; 112.37, C-2\(^{16}\)); 116.92, C-6\(^{16}\)); 118.13, C-5; 119.62, C-6; 127.86, C-8\(^{16}\)); 132.05, C-1\(^{16}\)); one oxygenated methine (\(\delta_C\) 89.01, C-7), two oxygenated methylenes (\(\delta_C\) 63.99, C-9\(^{16}\)); 72.57, C-9\(^{16}\)), two methoxys (\(\delta_C\) 56.92 × 2), and one methine (\(\delta_C\) 53.39, C-8) signals. The

**Table 1** \(^{13}\)C-NMR data of phenylalkanoids from the rhizome of Cnium officinalis Makino (125 MHz, \(\delta_C\))

| No of C | Phenylalkanoids* | 1 (CDCl\(_3\)) | 2 (CDCl\(_3\)) | 3 (CDCl\(_3\)) | 4 (CDCl\(_3\)) | 5 (CD\(_3\)OD) |
|---------|------------------|----------------|----------------|----------------|----------------|--------------|
| 1/1’    | 129.48           | 130.20         | 126.95         | 132.99         | 138.22         | 132.91       |
| 2/2’    | 108.49           | 109.07         | 109.76         | 109.14         | 111.50         | 112.37       |
| 3/3’    | 146.81           | 147.39         | 147.21         | 146.84         | 151.04         | 145.71       |
| 4/4’    | 145.77           | 151.91         | 149.19         | 145.36         | 147.74         | 149.29       |
| 5/5’    | 114.61           | 114.62         | 115.19         | 114.24         | 118.13         | 129.89       |
| 6/6’    | 120.56           | 127.70         | 124.28         | 120.32         | 119.62         | 116.92       |
| 7/7’    | 132.87           | 191.03         | 153.20         | 84.64          | 89.01          | 132.05       |
| 8/8’    | 123.73           | -              | 126.73         | 139.00         | 53.39          | 127.86       |
| 9/9’    | 73.41            | -              | 193.76         | 116.21         | 72.57          | 63.99        |
| 3/-3’-OMe | 56.05          | 56.38          | 56.26          | 56.06          | 56.92          | 56.92        |
| 7/-9-OMe | 58.07           | -              | -              | -              | -              | -            |

1, coniferyl alcohol methyl ether; 2, vanilline; 3, coniferyl aldehyde; 4, 75-7-methoxyegenolen; 5, ligusticoside F

*Gal, \(\beta\)-D-galactopyranosyl; *Glc, \(\beta\)-D-glucopyranosyl, *All, \(\beta\)-D-allulofuranosyl, *Exchangeable
oxygenated methylene carbon was shifted down-field compared to the usual one, confirming it to be linked to a sugar. PMR spectrum exhibited proton signals due to one 1,2,4-trisubstituted benzene ring (6.98, br. d, 8.4, H-6; 7.08, br. s, H-2; 7.14, d, 8.4, H-5), one 1,2,3,5-tetrasubstituted benzene ring (6.85, br. s, H-2; 7.01, br. s, H-6; 7.08, br. s, H-2; 7.14, d, 8.4, H-5), one oxygenated methylene (5.70, d, 8.0, H-7), two oxygenated methylenes (4.20, d, 5.0, H-9′; 3.77, overlapped, H-9a; 4.24, dd, 4.0, 10.2, H-9b), two methoxies (3.84, s, OMe-3; 3.89, s, OMe-3′), and one methine (δ_H 3.64, H-8) correlated with the carbon signals due to one oxygenated olefin quaternary (C-4′), one olefin quaternaries (C-1 and C-5′), one olefin methine (δ_C 116.92, C-6′), and one oxygenated methylene (C-9) moieties. Therefore, the two phenylpropanoid moieties of neolignan were linked at C-7 and C-4′ through an ether bond and at C-8 and C-5′. The anomer proton signals of one β-D-galactopyranosyl and one β-D-glucopyranosyl moieties (δ_H 4.37, H-1″′ and 4.89, H-1′′′) showed correlations with the oxygenated olefin quaternary (δ_C 147.74, C-4) and the oxygenated methylene (C-9) carbon signals, respectively, as well as the anomer carbon signal of a β-D-glucopyranosyl moiety (δ_C 104.71, C-1″′) correlated with the proton signals of an oxygenated methylene moiety (δ_H 3.77 and 4.24, H-9). Long-range coupling between the anomer carbon signal of the β-D-allulopyranosyl moiety (δ_C 99.34, C-1′) and the oxygenated methylene proton signals (δ_H 3.47 and 3.65, H-6) of the β-D-glucopyranosyl moiety in the HMBC spectrum were detected. The HMBC correlations described above concluded the linkage position of three sugars as seen in Fig. 1. The relative stereostructure

### Table 2 1H-NMR data of phenyl alkanoids from the rhizome of Cnidium officinalis Makino (600 MHz, δ_H, coupling pattern, J in Hz)

| No of C | Phenylalkanoids* |
|---------|------------------|
|         | 1 (CDCl3) | 2 (CDCl3) | 3 (CDCl3) | 4 (CDCl3) | 5 (CD3OD) |
| 2/2′′   | 6.91, br.s | 7.40, d, 1.8 | 7.05, d, 1.8 | 6.86, d, 1.8 | 7.08, br.s |
| 5/5′′   | 6.83, d, 8.4 | 7.02, d, 8.4 | 6.94, d, 8.4 | 6.88, d, 7.8 | 7.14, d, 8.4 |
| 6/6′′   | 6.86, br.d, 8.4 | 7.41, dd, 1.8, 8.4 | 7.09, dd, 1.8, 8.4 | 6.81, dd, 1.8, 7.8 | 6.98, br.d, 8.4 |
| 7/7′′   | 6.50, d, 15.6 | 9.81, d | 7.38, d, 16.2 | 4.55, d, 6.6 | 5.70, d, 8.0 |
| 8/8′′   | 6.10, dt, 7.0, 15.6 | 6.57, dd, 1.8, 16.2 | 5.93, ddd, 6.6, 10.2, 17.4 | 3.64, overlapped | 6.23, dt, 15.6, 5.0 |
| 9/9′′   | 4.05, d, 7.0 | 9.63, d, 7.8 | 5.26, br, d, 17.4 | 5.20, br, d, 10.2 | 3.77, overlapped |
| 3-3′-OMe | 3.87, s | 3.93, s | 3.90, s | 3.84, s | 3.89, s |
| 7-9-OMe| 3.36, s | | | | |
| 1″″/1″′| 4.89, d, 7.8 | 3.78, overlapped | 3.23, dd, 7.8, 7.8 | 3.48, overlapped | 3.39, overlapped |
| 2″″/2″′| 3.78, overlapped | 3.45, overlapped | 3.38, overlapped | 3.86, overlapped | 3.65, overlapped |
| 3″″/3″′| 3.83, overlapped | 3.48, overlapped | 3.37, overlapped | 3.85, overlapped | 3.67, overlapped |
| 4″″/4″′| 3.28, overlapped | 3.86, overlapped | 3.65, overlapped | 3.47, overlapped | |
| 5″″/5″′| 3.73, overlapped | 3.85, overlapped | 3.65, overlapped | 3.47, overlapped | |
| 6″″/6″′| 3.67, overlapped | 3.85, overlapped | 3.65, overlapped | 3.47, overlapped | |

1, coniferyl alcohol methyl ether; 2, vanilline; 3, coniferyl aldehyde; 4, 7-methoxyeugenol; 5, ligusticoside F. δ_H, β-D-glucopyranosyl; δ_C, β-D-galactopyranosyl. All, β-D-allulofuranosyl. Exchangeable

*In Cnidium officinalis rhizomes, coniferyl alcohol methyl ether, coniferyl aldehyde, 7-methoxyeugenol, ligusticoside F, β-D-glucopyranosyl, β-D-galactopyranosyl, and β-D-allulofuranosyl moieties were identified.
between H-7 and H-8 was determined to be a trans configuration because the cross peak was not observed between H-7 (δH 5.70) and H-8 (δH 3.64) but was observed between H-7 and H-9 (δH 3.77 and 4.24) in the NOESY spectrum. The glycoside, compound 5, was treated with 1 N HCl and refluxed at 90°C for two hours to finally yield the aglycone, dehydrodiconiferyl alcohol (5a). The dehydrodiconiferyl alcohol moiety with two chiral carbons, C-7 and C-8, has four stereoisomers, that showed typical specific rotation value [19]. 5a had an erythro-configuration between C-7 and C-8 and the specific rotation value was measured to be -49, confirming the absolute stereostructure of C-7 and C-8 to be R and S, respectively. Finally, the chemical structure of compound 5 was determined to be (2R,3S)-4-O-β-d-galactopyranosyl-9-[6-O-β-d-allulofuranosyl-β-d-gucopyranosyloxy] dehydrodiconiferyl alcohol as seen in Fig. 1. It was revealed to be a new compound, named cnidiumoside.

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s13765-021-00650-1.

Additional file 1: Fig. S1. 1H and 13C NMR spectra of coniferyl alcohol methyl ether (1). Fig. S2. 1H and 13C NMR spectra of vanilline (2). Fig. S3. 1H and 13C NMR spectra of coniferyl aldehyde (3). Fig. S4. 1H and 13C NMR spectra of 7S-7-methoxyeugenol (4). Fig. S5. 1H COSY and HSQC spectra of 7S-7-methoxyeugenol (4). Fig. S6. HMBC spectrum of 7S-7-methoxyeugenol (4). Fig. S7. 1H and 13C NMR spectra of cnidiumoside (5). Fig. S8. 1H COSY and HMBC spectra of cnidiumoside (5). Fig. S9. HMBC spectra of cnidiumoside (5). Fig. S10. NOESY spectrum of cnidiumoside (5).

**Acknowledgements**

This work was supported by the “Cooperative Research Program for Agriculture Science & Technology Development” (Project no. PJ01420403), Rural Development Administration, Republic of Korea.

**Authors’ contributions**

N-IB planned the study and wrote the paper. H-GK, TNN, and Y-GL isolated and purified the compounds. DYL, MHL, and N-IB were involved in the phytochemical analysis. Y-GL, H-GK, TNN, and N-IB performed the biological tests. The data and materials used in this study are available under permission from the corresponding author on reasonable request.

**Funding**

Rural Development Administration (RDA), Republic of Korea (Project no. PJ01420403) funded this study.

**Availability of data and materials**

The data and materials used in this study are available under permission from the corresponding author on reasonable request.

**Declarations**

**Competing interests**

There are no conflicts to declare.

**Author details**

1Graduate School of Biotechnology and Department of Oriental Medicinal Biotechnology, Kyung Hee University, Yongin 17104, Republic of Korea.
2Department of Horticultural Biotechnology, Kyung Hee University, Yongin 17104, Republic of Korea.
3Department of Food Technology and Services, Eulji University, Seongnam 461-723, Republic of Korea.
4Department of Herbal Crop Research, National Institute of Horticultural and Herbal Science, RDA, Eumseong 27709, Republic of Korea.
5Department of Horticultural Biotechnology, Kyung Hee University, Yongin 17104, Republic of Korea.

**Received: 7 September 2021   Accepted: 2 November 2021**

**References**

1. Li W, Tang Y, Chen Y, Duan JA (2012) Advances in the chemical analysis and biological activities of chuanxiong. Molecules 17:10614–10651
2. Zhou J, Qu F (2009) Treating gynaecological disorders with traditional Chinese medicine: A review. Afr J Tradit Complement Altern Med 6:494–517
3. Shin HY, Lee SH, Kim HR, Kim JH, Yang SB, Cho SY, Park JM, Ko CN, Park SU (2020) A review of clinical research trends in the treatment of primary headache disorders with pharmacopuncture. J Int Complement Med 59:1191–1205
4. Lee KY, Kim JH, Kim EY, Yeom M, Jung HS, Sohn Y (2019) Water extract of Cnidii Rhizoma suppresses RANKL-induced osteoclastogenesis in RAW 264.7 cell by inhibiting NFATc1/C-Fos signaling and prevents ovariectomized bone loss in SD-rat. BMC Complement Altern Med 19:207–219
5. Cho SK, Kwon OI, Kim CJ (1996) Anti-inflammatory and analgesic activities of the extracts and fractions of Cnidii Rhizoma. Kor J Pharmacogn 27:282–287
6. Sim Y, Shin S (2014) Antibacterial activities of the essential oil from the leaves and rhizomes of Cnidium officinale Makino. J Essent Oil Res 26:452–457
7. Jeong JE, Lee YJ, Choi YI, Park JM, Lee SM, Jo NY, Lee EY, Lee CK, Roh JD (2021) Seizure after subdural hematoma treated with combination western-Korean medicine. J Acupunct Res 38:72–78
8. Jeong JB, Ju SY, Park JH, Lee JR, Yoon KW, Kwon ST, Lim JH, Chung GY, Jeong HJ (2009) Antioxidant activity in essential oils of Cnidium officinale Makino and Ligusticum chuanxiong hort and their inhibitory effects on DNA damage and apoptosis induced by ultraviolet B in mammalian cell Cancer Epidemiol 33:41–46
9. Lee JT, Park JH, Lee KH (2005) Effect of methanol extract of Cnidii Rhizoma on the function of receptors for GABA and glycine. J Korean Acad Pediatr Dent 32:55–66
10. Kim SD, Kim GW, Shin HM (2006) Effects of Cnidium officinale, Petasites japonicas, Capsis chinensis extract mixture on vasodilation. Korean J Orient Physiol & Pathol 20:1620–1624
11. Adil M, Ren X, Jeong BR (2019) Light elicited growth, antioxidant enzymes activities and production of medicinal compounds in callus culture of Cnidium officinale Makino. J Photochem Photobiol B 196:111509
12. Kim HG, Jung YS, Oh SM, Oh HJ, Ko JH, Kim DO, Kang SC, Lee YG, Lee DY, Baek NI (2020) Coreolanceolins A-E, new flavanones from the flowers of Coreopsis lanceolata, and their antioxidant and anti-inflammatory effects. Antioxidants 9:359
13. Naito T, Nittsu K, Ikeya Y, Okada M, Mitsuhashi H (1992) Synthesis of enantiopure Lanceolins A-G, hydroxychalcones, from the flowers of Cnidium officinale. Molecules 17:10614–10651
14. Naito T, Ikeya Y, Okada M, Mitsuhashi H (1992) A phthalide and their antioxidant and anti-inflammatory effects. Antioxidants 9:359
15. Zhao YX, Luo JR, Li CS, Yi TM, Zhou J (2008) Palaeophytochemical constituents of the extracts and fractions of Cnidii Rhizoma suppresses RANKL-induced osteoclastogenesis in RAW 264.7 cell by inhibiting NFATc1/C-Fos signaling and prevents ovariectomized bone loss in SD-rat. BMC Complement Altern Med 19:207–219
16. Stambasky J, Malkov VA, Kocovsky P (2008) Synthesis of 1-arylmethyl ketones. J Org Chem 73:9148–9150
17. Zhang SY, Fan CL, Huang XJ, Huang WH, Liu XH, Wang L, Ye WC (2015) A new phenylpropanoid and a new isoflavone glycoside from Shenqi Fuzheng Injection. J Asian Nat Prod Res 17:274–279
18. Kim HG, Oh HJ, Ko JH, Song HS, Lee YG, Kang SC, Lee DY, Baek NI (2019) Phenylpropanoids, hydroxychalcones, from the flowers of Cnidium officinale. Molecules 17:10614–10651
19. Lanceolins A-G, hydroxychalcones, from the flowers of Cnidium officinale. Molecules 17:10614–10651
20. Jeong JB, Ju SY, Park JH, Lee JR, Yoon KW, Kwon ST, Lim JH, Chung GY, Jeong HJ (2009) Antioxidant activity in essential oils of Cnidium officinale Makino and Ligusticum chuanxiong hort and their inhibitory effects on DNA damage and apoptosis induced by ultraviolet B in mammalian cell Cancer Epidemiol 33:41–46
21. Elfiedy EM, Khayyat SA (2008) Oxidation reactions of some natural volatile aromatic compounds: Anethole and eugenol. Russ J Org Chem 44:823–829
22. Stambasky J, Malkov VA, Kocovsky P (2008) Synthesis of enantiopure 1-arylprop-2-en-1-ols and their tert-butyl carbonates. J Org Chem 73:9148–9150
23. Zhang SY, Fan CL, Huang XJ, Huang WH, Liu XH, Wang L, Ye WC (2015) A new phenylpropanoid and a new isoflavone glycoside from Shenqi Fuzheng Injection. J Asian Nat Prod Res 17:274–279
24. Kim HG, Oh HJ, Ko JH, Song HS, Lee YG, Kang SC, Lee DY, Baek NI (2019) Phenylpropanoids, hydroxychalcones, from the flowers of Cnidium officinale. Molecules 17:10614–10651
25. Lanceolins A-G, hydroxychalcones, from the flowers of Cnidium officinale. Molecules 17:10614–10651
19. Hirai N, Okamoto M, Udagawa H, Yamamuro M, Kato M, Koshimizu K (1994) Absolute configuration of dehydrodiconiferyl alcohol. Biosel Biotech Biochem 58:1679–1684

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.