Supporting Information to:
Alkyl Phloroglucinol Derivatives from *Syzygium levinei* and their Differentiation-Inducing Activity

Jian Zou¹,²,⁴
Yi Mi²,³,⁴
Wenliang Chen¹,²
Qunfäng Liu¹
Jian Wang¹
Liguang Lou³
Weimin Zhao¹

**Affiliation**
¹ Department of Natural Products Chemistry, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, P. R. China
² Graduate School of the Chinese Academy of Sciences, Shanghai, P. R. China.
³ Department of Pharmacology, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, P. R. China
⁴ These authors contribute equally to this work

**Correspondence**
Weimin Zhao
Department of Natural Products Chemistry
Shanghai Institute of Materia Medica
Shanghai Institutes for Biological Sciences
Chinese Academy of Sciences
Shanghai 201203
People’s Republic of China
E-mail: wmzhao@mail.shcnc.ac.cn

Liguang Lou
Department of Pharmacology
Shanghai Institute of Materia Medica
Shanghai Institutes for Biological Sciences
Chinese Academy of Sciences
Shanghai 201203
People’s Republic of China
Phone: +86-21-5080-6600
Fax: +86-21-5080-7088
E-mail: lglou@mail.shcnc.ac.cn
Extraction and Isolation of known compounds

Powdered air-dried whole plants of *Syzygium javanense* (3.0 kg) were percolated with 95% ethanol at room temperature with 95% ethanol thrice (10 L × 3). The filtrate was concentrated to dryness *in vacuo* and then suspended in 20% ethanol overnight. After filtration of the precipitated chlorophyll and evaporation of ethanol in the filtrate, the aqueous residue (1 L) was extracted with petroleum ether, ethyl acetate, and *n*-butanol (1.0 L × 3), successively, to give petroleum ether fraction (5.5 g), and ethyl acetate fraction (23.0 g), and *n*-butanol fraction (41.5 g), respectively. The ethyl acetate fraction (23.0 g) was subjected to chromatography over a silica gel H60 column (10 cm i.d. × 25 cm) with a chloroform-methanol gradient (20:1, 10:1, 5:1, 1.0 L; 3:1, 1.0 L; 1:1, 500 mL; 0:1, 500 mL) to give Fr.B1 (between 0-1000 mL, 4.35 g). Fr.B2 (between 1000-1650 mL, 2.25 g), Fr.B3 (between 1650-2850 mL, 3.45 g), Fr.B4 (between 2850-4000 mL, 5.45 g), Fr.B5 (between 4000-5000 mL, 5.12 g). Fr.B2 (2.25 g) was subjected to a Sephadex LH-20 column (2.0 cm i.d. × 70 cm) eluted with 95% ethanol to give Fr.B2A (between 95 and 169 mL, 246 mg), Fr.B2B (between 169 and 238 mL, 883 mg), Fr.B2C (between 238 and 316 mL, 452 mg), Fr.B2D (between 316 and 367 mL, 389 mg) and Fr.B2E (between 367 and 515 mL, 251 mg). Fr.B2C (452 mg) was chromatographed over a silica gel H60 column (2.0 cm i.d. × 25 cm) eluted with a chloroform-methanol gradient (20:1, 10:1, 5:1, 3:1 each 100 mL) to give Fr.B4 (5.45 g) was separated by a silica gel H60 column (3.5 cm i.d. × 25 cm), eluted with chloroform-methanol gradient (10:1, 5:1, 3:1, 2:1, 1:1, 0:1, each 500 mL) to give Fr.B4A (between 0 and 600 mL, 354 mg), Fr.B4B (between 600 and 1160 mL, 1.08 g), Fr.B4C (between 1160 and 1700 mL, 780 mg), Fr.B4D (between 1700 and 2500 mL, 950 mg), Fr.B4E (between 2500 and 3000 mL, 1.75 g). Fr.B4C (780 mg) was separated over a LiChroprep RP-18
Lobar column eluted with methanol-water (40%, 60%, 80%, each 200 mL) to give 6 (240-290 mL, 56.5 mg) and 7 (305-378 mL, 43.2 mg). Fr.B4D (850 mg) was subjected to a Sephadex LH-20 column (1.0 cm i.d. × 70 cm) eluted with 95% ethanol to give 8 (130-185 mL, 26.8 mg). The n-butanol extract (41.5 g) was separated by a silica gel H60 column (10 cm i.d. × 25 cm) eluted with a chloroform-methanol gradient (10:1, 1.5 L, 5:1, 1.5 L, 3:1, 1.0 L, 2:1, 1.0 L, 1:1, 1.0 L, 0:1, 500 mL) to give Fr.C1 (between 0 and 1100 mL, 2.65 g), Fr.C2 (between 1100 and 1900 mL, 4.90 g), Fr.C3 (between 1900 and 3100 mL, 5.62 g), Fr.C4 (between 3100 and 4200 mL, 5.15 g), Fr.C5 (between 4200 and 5500 mL, 6.30 g), and Fr.C6 (between 5500-6500 mL, 11.5 g). Fr.C4 (5.15 g) was separated by a silica gel H60 column (3.5 cm i.d. × 20 cm), eluted with chloroform-methanol gradient (8:1, 5:1, 3:1, 1:1, 0:1, each 400 mL) to give Fr.C4A (between 0 and 450 mL, 320 mg), Fr.C4B (between 450 and 850 mL, 550 mg), Fr.C4C (between 850 and 1250 mL, 1.02 g), Fr.C4D (between 1250 and 1600 mL, 750 mg), Fr.C4E (between 1600 and 2000 mL, 1.02 g), Fr.C4B (550 mg) was separated over a LiChroprep RP-18 Lobar column eluted with methanol-water (30%, 50%, and 70%, each 150 mL) to give 9 (between 190-245 mL, 36.9 mg), Fr.C4C (between 1000 and 1450 mL, 1.02 g) was separated by a silica gel H60 column (3.0 cm i.d. × 25 cm), eluted with chloroform-methanol (3:1, 500 mL) to give 10 (between 205 mL and 380 mL, 35.0 mg). Fr.C4D (750 mg) was subjected to a LiChroprep RP-18 Lobar column eluted firstly with H2O (200 mL) to remove the sugar, and then with methanol-water (20%, 500 mL) to afford 11 (between 150-185 mL, 12.8 mg).

The physicochemical data of known compounds (4-11)

1-(2, 6-dihydroxy-4-methoxyphenyl)-hexan-1-one (4): amorphous white powder, UV (MeOH): λ
2α, 3β, 19α, 24-tetrahydroxyurs-12-en-28-oic acid (S): amorphous white powder. [α]D20 = +20.0° (c 0.05, MeOH) (lit. [α]D = +18.02° (c 0.22, MeOH)) [8]; ESI-MS: m/z 527.3 [M+Na]⁺, m/z 1031.5 [2M+Na]⁺; 1H-NMR (CDCl₃, 400 MHz): δH 5.14 (t, J = 3.8 Hz, H-12), 3.89 (1H, d, J = 12 Hz, H-24a), 3.65 (1H, t, J = 10 Hz, H-2p), 3.22 (1H, d, J = 12 Hz, H-24b), 2.91 (1H, d, J = 10 Hz, H-3α), 2.40 (1H, t, J = 13.4 Hz, H-5α), 2.35 (1H, s, H-18b), 1.20, 1.10, 1.03, 0.85, 0.63 (3H each, s, H-23, 25-29), 0.78 (3H, d, J = 6 Hz, Me-30); 13C-NMR (CDCl₃, 100 MHz): δC 45.8 (t, C-1), 67.3 (d, C-2), 83.8 (d, C-3), 42.1 (s, C-4), 52.9 (d, C-5), 17.6 (t, C-6), 32.1 (t, C-7), 40.3 (s, C-8), 46.2 (d, C-9), 38.8 (s, C-10), 24.3 (t, C-11), 126.8 (d, C-12), 137.8 (s, C-13), 40.7 (s, C-14), 28.1 (t, C-15), 25.0 (t, C-16), 47.1 (s, C-17), 54.9 (d, C-18), 71.5 (s, C-19), 41.0 (d, C-20), 27.2 (t, C-21), 36.8 (t, C-22), 22.3 (q, C-23), 63.9 (t, C-24), 21.5 (q, C-25), 14.3 (q, C-26), 22.0 (q, C-27), 180.3 (s, C-28), 22.7 (q, C-29), 15.4 (q, C-30) [9].

Myricitrin (6): amorphous yellow powder. [α]D20 = -103.0° (c 0.08, MeOH) (lit. [α]D = +152.816° (c 0.89, MeOH)) [10]; ESI-MS: m/z 465.1 [M+H]⁺; 1H-NMR (CD₃OD, 400 MHz): δH 6.20 (1H, d, J = 1.9 Hz, H-6), 6.39 (1H, d, J = 1.9 Hz, H-8), 6.98 (2H, s, H-2'; H-6'), 5.34 (1H, d, J = 1.5 Hz, H-3').
H₂O, d) 4.25 (1H, dd, J = 1.5, 3.3 Hz, H₃(18α-β)), 3.82 (1H, dd, J = 3.3, 9.5 Hz, H₃(19β-α)), 3.36 (1H, t, J = 9.5 Hz, H₃(19α-α)), 3.54 (1H, dd, J = 9.5, 6.2 Hz, H₃(19β-α)), 1.08 (3H, d, J = 6.2 Hz, H₃(19β-α)) [11].

Quercitrin (7): amorphous yellow powder; [α]D⁰ -132.0° (c 0.11, MeOH) (lit. [α]D²¹ -156.7167° (c 0.67, MeOH)) [10]. ESIMS: m/z 470.9 [M+Na]+, 1H-NMR (CD₃OD, 400 MHz): δH 6.20 (1H, d, J = 2.0 Hz, H-6), 6.39 (1H, d, J = 2.0 Hz, H-8), 7.36 (1H, d, J = 2.3 Hz, H-2), 6.90 (1H, d, J = 8.2 Hz, H-5), 7.31 (1H, dd, J = 8.2, 2.3 Hz, H-6), 5.37 (1H, d, J = 1.6 Hz, H₃(18α-β)), 4.30 (1H, dd, J = 1.6, 3.0 Hz, H₃(19β-α)), 3.80 (1H, dd, J = 3.0, 9.5 Hz, H₃(18α-β)), 3.34 (1H, t, J = 9.5 Hz, H₃(19α-α)), 3.60 (1H, dd, J = 9.5, 6.2 Hz, H₃(19β-α)), 0.90 (3H, d, J = 6.0 Hz, H₃(19β-α)) [11].

2, 4, 6-trimethoxyphenyl-1-O-β-D-(6-O-galloyl)-glucopyranoside (8): amorphous white powder; [α]D⁰ -41.0° (c 0.11, MeOH) (lit. [α]D²¹ -36.8° (c 0.62, MeOH)) [12]. ESIMS: m/z 521.4 [M+Na]+, 1019.6 [2M+Na]+, 1H-NMR (CD₃OD, 400 MHz): δH 6.40 (2H, s, H-3, H-5), 7.10 (2H, s, H₃(16α-β)), 3.68 (3H, s, 4-OMe), 3.69 (6H, s, 3-OMe, 5-OMe), 4.90 (1H, d, J = 7.8 Hz, H₃(15α-β)), 3.40-4.90 (4H, m, H₃(14α), H₃(14β), H₃(15α), H₃(15β)), 4.41 (1H, dd, J = 11.6, 6.6 Hz, H₃(16α-β)), 4.62 (1H, dd, J = 11.6, 1.5 Hz, H₃(16β-β)), 13C-NMR (CD₃OD, 100 MHz): δC 56.8 (q, 3-OMe, 5-OMe), 61.6 (q, 4-OMe), 67.0 (t, C(14β)), 72.1 (d, C(15α)), 75.3 (d, C(15β)), 76.2 (d, C(16α)), 76.3 (d, C(16β)), 95.6 (d, C-3), 103.6 (d, C(13β)), 110.5 (d, C(13α)), 121.7 (t, C(12β)), 135.0 (t, C-1), 140.2 (s, C(12α)), 147.0 (s, C(14α)), 155.1 (s, C-2), 156.2 (s, C-4), 168.6 (s, C(11β)) [12].

2α, 3α, 19α-24-tetrahydroxyurs-12-en-oic acid 28-O-β-D-glucopyranosyl ester (9): amorphous white powder; [α]D²¹ -4.0° (c 0.11, MeOH) (lit. [α]D⁰ -4.5° (c 0.10, MeOH)) [8]. ESIMS: m/z
689.4 [M-Na]^+; 665.2 [M-H]^+. 1H-NMR (d_6-pyridine, 400 MHz): δ_H 6.21 (d, 1H, J = 7.6 Hz, H_{\text{chol}}), 5.39 (br, s, 1H, H-12), 3.75 (m, 1H, H-28), 3.47 (bs, s, 1H, H-38), 4.02-4.60 (m, 7H, Me-24, H_{\text{chol}}-2, H_{\text{chol}}-3), 2.81 (s, 1H, H-18), 1.60, 1.52, 1.30, 1.12, 0.98 (s, 3H each, Me-23, 25, 26, 27, 29), 0.99 (d, 3H, J = 6.4 Hz, Me-30). 13C-NMR (d_6-pyridine, 100 MHz): 41.6 (t, C-1), 55.5 (d, C-2), 78.3 (d, C-3), 44.5 (s, C-4), 49.0 (d, C-5), 18.7 (t, C-6), 33.3 (t, C-7), 40.2 (s, C-8), 47.1 (d, C-9), 38.1 (s, C-10), 23.6 (t, C-11), 127.8 (d, C-12), 138.8 (s, C-13), 41.5 (s, C-14), 28.7 (t, C-15), 25.4 (t, C-16), 48.0 (s, C-17), 53.9 (d, C-18), 72.1 (s, C-19), 41.5 (d, C-20), 26.1 (t, C-21), 37.0 (t, C-22), 23.8 (q, C-23), 64.8 (s, C-24), 16.9 (q, C-25), 16.7 (q, C-26), 24.0 (q, C-27), 176.3 (s, C-28), 26.5 (q, C-29), 16.1 (q, C-30), 95.6 (d, C_{\text{chol}}), 73.8 (d, C_{\text{chol}}), 78.9 (d, C_{\text{chol}}), 71.3 (d, C_{\text{chol}}), 78.2 (d, C_{\text{chol}}), 62.0 (t, C_{\text{chol}}) [13].

2, 4, 6-trimethoxyphenyl-\(\beta\)-D-glucopyranoside (10): amorphous white powder; [\alpha]_D^20 \text{c} 0.03 (c 0.03, H_2O) (lit. [\alpha]_D^20 \text{c} 0.10 (c 0.10, H_2O)) [14]. ESIMS: m/z 369.1 [M-Na]^+; 1H-NMR (CD_3OD, 400 MHz): δ_H 6.40 (2H, s, H-3, H-5), 3.66 (3H, s, 4-OMe), 3.69 (6H, s, 2-OMe, 6-OMe), 4.90 (1H, d, J = 7.8 Hz, H_{\text{chol}}), 3.40-4.90 (4H, m, H_{\text{chol}}-2, H_{\text{chol}}-3, H_{\text{chol}}-4, H_{\text{chol}}-5), 4.41 (1H, dd, J = 11.6, 6.5 Hz, H_{\text{chol}}), 4.62 (1H, dd, J = 11.6, 1.5 Hz, H_{\text{chol}}) [15].

n-butyl-\(\beta\)-D-fructopyranoside (11): amorphous white powder; [\alpha]_D^20 \text{c} 0.07 (c 0.07, MeOH) (lit. [\alpha]_D^20 \text{c} -135.0° (MeOH)) [16]. ESIMS: m/z 259.0 [M-Na]^+, 494.7 [2M-Na]^+. 1H-NMR (CD_3OD, 400 MHz): 0.91 (3H, t, J = 7.2 Hz, H-4), 1.40 (2H, m, H-3), 1.55 (2H, m, H-2), 3.50 (2H, m, H-1), 3.62 (1H, d, J = 11.5 Hz, H_{\text{chol}}), 3.68 (1H, d, J = 11.5 Hz, H_{\text{chol}}), 3.60-3.90 (5H, m, H_{\text{chol}}-2, H_{\text{chol}}-3, H_{\text{chol}}-4, H_{\text{chol}}-5), 13C-NMR (CD_3OD, 100 MHz): 14.8 (q, C-4), 20.9 (t, C-3), 32.8 (t, C-2), 62.1 (t,
C-1, 64.0 (t, C\textsubscript{Cl}\textsubscript{h\textsubscript{2}O\textsubscript{2}}), 102.0 (s, C\textsubscript{Cl}\textsubscript{h\textsubscript{2}O\textsubscript{2}}), 71.1 (d, C\textsubscript{Cl}\textsubscript{h\textsubscript{2}O\textsubscript{2}}), 72.0 (d, C\textsubscript{Cl}\textsubscript{h\textsubscript{2}O\textsubscript{2}}), 71.6 (d, C\textsubscript{Cl}\textsubscript{h\textsubscript{2}O\textsubscript{2}}), 84.6 (t, C\textsubscript{Cl}\textsubscript{h\textsubscript{2}O\textsubscript{2}})

[16].

Fig. 1. $^1$H-$^1$H COSY (---) and main $^1$H-$^{13}$C long-range correlation signals in the HMBC spectra of 1-3.