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Semisynthesis of apigenin and acacetin-7-O-β-D-glycosides from naringin and their cytotoxic activities

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ABSTRACT

Apigenin-7-O-β-D-glycosides **1–8** and acacetin-7-O-β-D-glycosides **9–16** were semisynthesized from 4′-*O*-benzyl apigenin **17** and acacetin **18** by glycosidation and deprotection with the corresponding α-acetylglycosyl bromide, respectively. Compounds **17** and **18** were prepared by iodination followed by base-induced elimination, 4′-O-benzylation, or 4′-O-methylation and acid hydrolysis using naringin as starting material which is readily available and cheap. Their cytotoxic potential against five human cancer cell lines (HL-60, SMMC-7721, A-549, MCF-7, and SW480) was evaluated by standard MTT method. The results show that compounds **2**, **9**, and **19** exhibit moderate cytotoxicity against HL-60, SMMC-7721, A-549, MCF-7, and SW480, while compound **3** exhibits potent cytotoxicity against MCF-7 selectively. Among the synthesized target compounds, **3**, **4**, **7**, **11**, **12**, **15**, and **16** were new compounds, the natural product **8** was the first synthesized and the synthesis of natural products **5**, **6**, **13**, and **14** was efficiently improved by the new synthetic routes.

1. Introduction

Flavonoid glycosides constitute an important class of biomolecules and are widely distributed in fruits, vegetables, and traditional medicinal plants. They exhibit a broad spectrum of biological activities.[1,2] For example, apigenin-7-O-β-D-glucoside (cosmosiin) which was isolated from *Lonicera gracilipes* var. glandulosa can inhibit the growth of various human cancer cells,[3] acacetin-7-O-β-D-galactopyranoside, a natural flavonoid isolated from flower heads of *Chrysanthemum morifolium*, was efficient to inhibit the replication of HIV in H9 cells.[4] In the past decade, the biological activities of flavonoid glycosides against cancer, anti-viral, and cardiovascular diseases have attracted increasing interest. To generate useful materials, many attempts of glycosylation of phenolic hydroxyl groups of flavonoids have been performed since 1938.[5]

During our continuous medicinal research on flavonoids to support the investigation of many important physiology processes and drug discoveries, some attempts have been made in the total synthesis of flavonoids and flavonoid glycosides starting from simple materials as well as employing many protection strategies.[6–8] However, they were achieved with very time-consuming and complicated syntheses approaches. Herein, we reported a short and effective synthesis of apigenin-7-O-β-D-glycosides **1–8** and acacetin-7-O-β-D-glycosides **9–16** from naringin which is commercially available at low cost. Furthermore, all synthesized flavoniod glycosides were evaluated for their cytotoxic potential against myeloid leukemia (HL-60), liver carcinoma (SMMC-7721), lung carcinoma (A-549), breast carcinoma (MCF-7), and intestinal carcinoma (SW480) cell lines by standard MTT method.

2. Results and discussion

Our present method provides an efficient and easy approach to access of apigenin-7-O-β-D-glycosides **1–8** and acacetin-7-O-β-D-glycosides **9–16** in just six steps from naringin, respectively as depicted in Scheme 1. This straightforward synthesis is based on the key intermediates 4′-*O*-benzyl apigenin **17** and acacetin **18** which are prepared in gram quantities in only three steps, firstly iodination followed by base-induced elimination to rhoifolin, then 4′-O-benzylation or 4′-O-methylation and acid hydrolysis of the neohesperidose residue with naringin as starting material which is readily available and cheap.

It is well known that sugar moiety could enhance water solubility and improve the targeting activity of bioactive molecules. For example, lactose can be recognized by the hepatic asialoglycoprotein receptor (ASGP-R) which localizes to liver cells providing an efficient entry point for lactose-modified molecules.[9] The modification of flavonoids with lactose may be possible to specifically target molecules to liver cells, facilitating the application of bioactive flavonoids to the treatment of hepatitis B, hepatitis C and liver cancer. On the other hand, the largely hydrophobic character of flavonoids **17**, **18** makes them poorly soluble in aqueous

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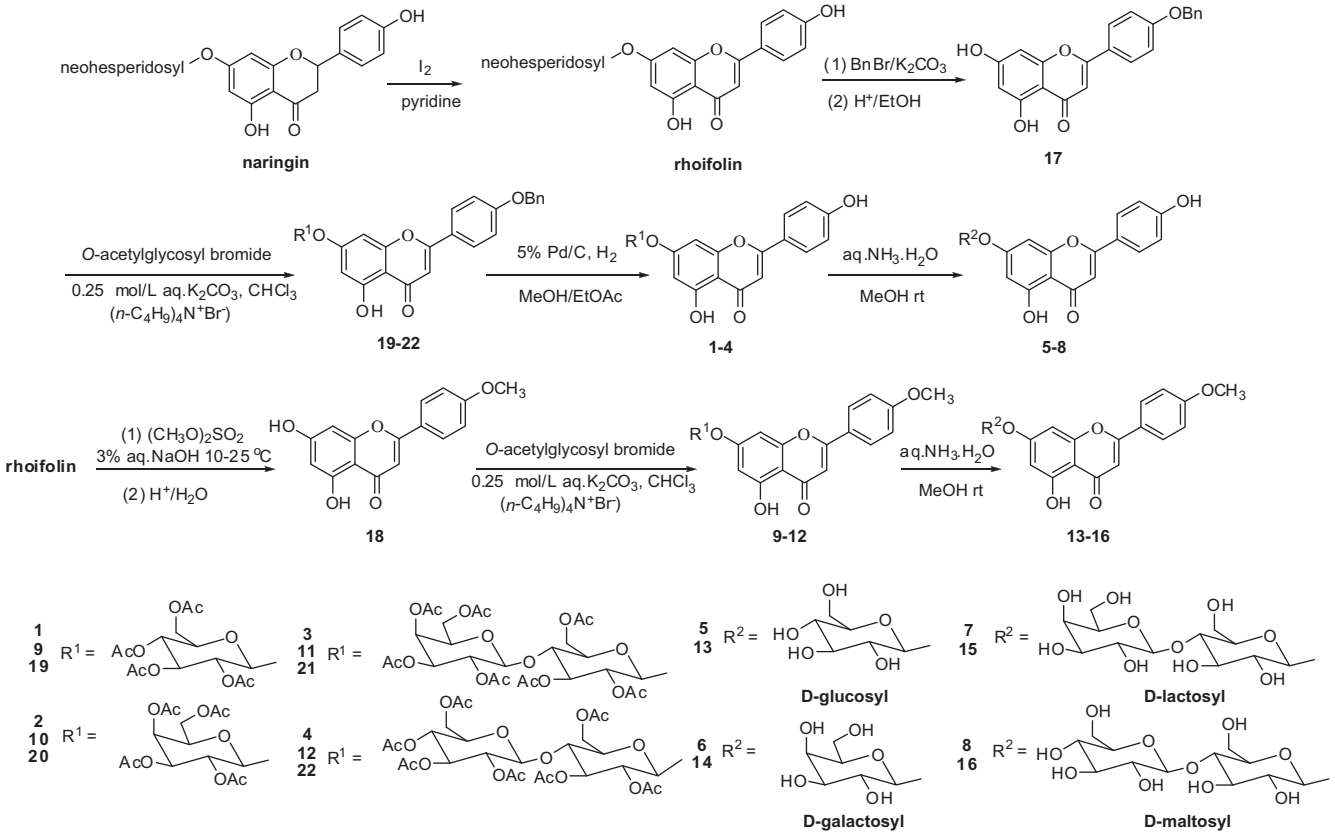

Scheme 1. Synthetic route of apigenin and acacetin-7-O-β-D-glycosides from naringin.

media which in some cases limits their therapeutic efficacy and this has a strong influence on their pharmacokinetic properties. Then, we turned our attention to the introduction of glucosyl, galactosyl, lactosyl and maltosyl moieties into bioactive flavonoids, so 4′-*O*-benzyl apigenin **17** and acacetin **18** were condensed with the corresponding α-acetylglycosyl bromide at more reactive hydroxyl groups on C-7 position of flavones, respectively. α-acetylglycosyl bromide had to be used immediately after preparation owing to its instability. The glycosidation procedure was modified by using potassium carbonate in a solvent mixture of $CHCl_3/H_2O$ and tetrabutylammonium bromide (TBAB) as a phase transfer catalyst leading to the desired 4′-*O*-benzyl apigenin-7-O-β-D-acetylglycosides **1–4** and acacetin-7-O-β-D-acetylglycosides **9–12** in 65–85% yields. Although the yield was moderate, the stereo- and regioselectivities were perfect with no α-glycoside, 5-O-glycoside, or 5,7-O-biglycoside being detected. Glycosylation was found to be highly regioselective with glycosylation at the hydroxyl group on C-7 predomominating over glycosylation at the hydroxyl group on C-5. This regioselectivity for hydroxyl group on C-7 can be explained by both steric and electronic effects. The hydroxyl group on C-7 is more electronically favored toward glycosylation owing to the fact that the neighboring carbonyl group at C-4 renders the hydroxyl group on C-5 less reactive toward glycosyl donors. Moreover the neighboring group participation of 2-acetyl group in proton coupling (J = 6.4–9.2 Hz) observed for the anomeric proton of glycose residue (δ 5.02–5.78) demonstrated the expected β-linkage to the apigenin or acacetin moiety.[10]

Removal of the benzyl group, which protects the apigenin 4′-hydroxyl group, by H_2 with Pd/C at room temperature furnished the compounds **19–22**. The sugar moiety was deprotected using aq $NH_3{\cdot}H_2O$ in methanol to yield apigenin-7-O-β-D-glycosides **5–8** and acacetin-7-O-β-D-glycosides **13–16**.

All the synthesized apigenin and acacetin-7-O-β-D-glycosides and their derivatives **1–16** as well as intermediates **19–22** were tested for cytotoxic activity against five human cancer cell lines (HL-60, SMMC-7721, A-549, MCF-7, and SW480). Their IC_{50} (μg/mL) values were plotted in Table 1. The results showed that compound **2** exhibits potent cytotoxicity against the HL-60, SMMC-7721, A-549, MCF-7, and SW480 cancer cell lines with IC_{50} values of 11.77, 17.60, 16.77, 10.31, and 20.71, respectively. Compound **19** exhibits potent cytotoxicity against the SMMC-7721, A-549, and

Table 1
IC_{50} values (μg/mL) of apigenin and acacetin-7-O-β-D-glycosides on the human cancer cell lines

Compound	HL-60	SMMC-7721	A-549	MCF-7	SW480
1	>40	>40	>40	>40	>40
2	11.77	17.60	16.77	10.31	20.71
3	>40	>40	>40	4.58	>40
4	>40	>40	>40	>40	>40
5	>40	>40	>40	>40	>40
6	>40	>40	>40	>40	>40
7	>40	>40	>40	4.58	>40
8	>40	>40	>40	>40	>40
9	>40	>40	28.07	16.63	16.38
10	>40	>40	>40	>40	>40
11	>40	>40	>40	>40	>40
12	>40	>40	>40	>40	>40
13	>40	>40	>40	>40	>40
14	>40	>40	>40	>40	>40
15	>40	>40	>40	>40	>40
16	>40	>40	>40	>40	>40
19	>40	14.99	29.94	27.08	>40
(DPP)[a]	2.51	14.99	13.61	18.65	18.85

[a] Cisplatin (DDP) was employed as positive control.

MCF-7 cancer cell lines with IC_{50} values of 14.99, 29.94, and 27.08, respectively. Compound **9** shows cytotoxicity against cancer cell lines A-549, MCF-7, and SW480 with IC_{50} values of 28.07, 16.63, and 16.38, respectively, while compound **3** exhibits significant selective inhibitory activity against MCF-7 cancer cell line with IC_{50} value of 4.58. Biological activities of all the compounds mentioned above are similar or even improved compared with the positive control, cisplatin (DDP).

3. Experimental

3.1. General methods

Melting points were measured on a XRC-I apparatus and were uncorrected. IR spectra were recorded on a Bruker Tensor-27 spectrometer, ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-400 instrument, using tetramethylsilane as an internal standard, chemical shifts (δ) in ppm, and coupling constants (J) in Hz. Mass spectra were determined with VG Autospec-3000 or ZAB-HS spectrometer by the FAB or EI method.

3.2. Synthesis of rhoifolin[11]

A solution of naringin (2.0 g, 3.45 mmol) and iodine (0.89 g, 3.5 mmol) in pyridine (20 mL) was heated to 95 °C for 2 h. The mixture was cooled to room temperature and poured into cold water. The resulting precipitate was filtered and washed with saturated sodium thiosulfate and water successively, and then was dried in vacuum to afford the resulting yellow solid rhoifolin 1.6 g, yield: 80%. Mp 249–252 °C. (lit. 11, 251–253 °C).

3.3. Synthesis of 4′-*O*-benzyl apigenin (17)

To a mixture of rhoifolin (2.31 g, 4.0 mmol) and K_2CO_3 (0.69 g, 5.0 mmol) in DMF (20 mL) was added benzyl bromide (0.6 mL, 5.0 mmol) and the mixture was stirred under nitrogen for 8 h at 90 °C. The mixture was cooled to room temperature and poured into cold water (200 mL). The resulting precipitate was filtered and dissolved in ethanol (50 mL), and then concentrated H_2SO_4 (3 mL) was added to the mixture slowly. The mixture was heated under reflux for 2 h, and then cooled to room temperature and filtered, the resulting precipitate was washed with saturated $KHCO_3$ and water and evaporated to dryness successively, and then the crude solid was chromatographed on silica gel using petroleum ether/ethyl acetate (4:1) as eluent to afford the yellow solid 0.9 g, yield: 63%. Mp 304–306 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.92 (s, 1H, OH-5), 10.93 (s, 1H, OH-7), 8.04 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 7.33–7.49 (m, 5H, $OCH_2C_6H_5$), 7.19 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.88 (s, 1H, H-3), 6.52 (d, J = 1.6 Hz, 1H, H-8), 6.21 (d, J = 1.6 Hz, 1H, H-6), 5.23 (s, 2H, $OCH_2C_6H_5$); EIMS (m/z): 361 $(M+1)^+$.

3.4. Synthesis of acacetin (18)[12]

$(CH_3O)_2SO_2$ (2.3 mL, 24 mmol) was added dropwise to a stirred solution of rhoifolin (1.38 g, 2.4 mmol) in 3% aq NaOH (50 mL) at 10–25 °C for 30 min, then the reaction mixture was stirred for 6 h at the same temperature, and then concd H_2SO_4 (5 mL) was added to the mixture slowly. The mixture was heated under reflux for 8 h and then cooled to room temperature and filtered, the resulting precipitate was washed with saturated $NaHCO_3$ and water and evaporated to dryness successively, and then the crude solid was chromatographed on silica gel using petroleum ether/ethyl acetate (3:1) as eluent to afford the yellow solid 0.22 g, yield: 32%. Mp 262–264 °C. (lit. 12, 260–262 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.92 (s, 1H, OH-5), 10.86 (s, 1H, OH-7), 8.03 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 7.11 (d, J = 9.2 Hz, 2H, H-3′, H-5′), 6.87 (s, 1H, H-3), 6.50 (d, J = 2.0 Hz, 1H, H-8), 6.20 (d, J = 2.0 Hz, 1H, H-6), 3.85 (s, 3H, OCH_3); EIMS (m/z): 285 $(M+1)^+$.

3.5. Synthesis of 4′-*O*-benzyl apigenin-7-O-β-D-acetylglucoside (19)

A mixture of **17** (0.43 g, 1.2 mmol), TBAB (0.06 g, 0.2 mmol), and α-acetylglucose bromide (0.98 g, 2.4 mmol) in $CHCl_3$ (25 mL) was added to 0.25 mol/L K_2CO_3 (10 mL, 2.5 mmol), the mixture was stirred under nitrogen for 12 h at 45 °C, the organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2. The organic extracts were combined, washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel using petroleum ether/ethyl acetate (2:1) as eluent to afford the light yellow solid 0.7 g, yield: 85%. Mp 163–165 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.83 (s, 1H, OH-5), 7.83 (d, J = 9.2 Hz, 2H, H-2′, H-6′), 7.45–7.35 (m, 5H, $OCH_2C_6H_5$), 7.09 (d, J = 9.2 Hz, 2H, H-3′, H-5′), 6.60 (s, 1H, H-3), 6.57 (d, J = 1.2 Hz, 1H, H-8), 6.44 (d, J = 1.2 Hz, 1H, H-6), 5.32 (d, J = 6.4 Hz, 1H, H-1″), 5.30 (s, 2H, $OCH_2C_6H_5$), 5.19–5.13 (m, 3H, H-2″,3″,4″), 4.31–4.19 (m, 2H, H-6″), 3.96–3.92 (m, 1H, H-5″), 2.11–2.05 (m, 12H, 4 × CH_3CO); HRMS $[M+Na]^+$ calcd for $C_{36}H_{34}O_{14}Na$ 713.6352, found 713.6363.

3.6. Synthesis of acacetin-7-O-β-D-acetylglucoside (9)

Compound **9** was prepared from **18** and α-acetylglucose bromide as described for the preparation of **19** from **17** and α-acetylglucose bromide, yellow solid, yield: 83%. Mp 150–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.85 (s, 1H, OH-5), 7.83 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 7.03 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.60 (s, 1H, H-3), 6.58 (d, J = 2.0 Hz, 1H, H-8), 6.44 (d, J = 2.0 Hz, 1H, H-6), 5.33 (d, J = 7.2 Hz, 1H, H-1″), 5.31–5.28 (m, 1H, H-2″), 5.20–5.14 (m, 2H, H-3″,4″), 4.32–4.19 (m, 2H, H-6″), 3.98–3.95 (m, 1H, H-5″), 3.90 (s, 3H, OCH_3), 2.11–2.05 (m, 12H, 4 × CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 20.5, 20.6, 56.0, 61.3, 67.6, 71.0, 71.3, 72.1, 94.7, 96.4, 99.6, 102.6, 103.1, 105.2, 116.8, 120.2, 128.4, 156.8, 161.2, 161.3, 161.5, 164.1, 169.2, 169.5, 169.7, 169.8, 181.9; HRMS $[M+Na]^+$ calcd for $C_{30}H_{30}O_{14}Na$ 637.5394, found 637.5381.

3.7. Synthesis of 4′-*O*-benzyl apigenin-7-O-β-D-acetylgalactoside (20)

Compound **20** was prepared from **17** and α-acetylgalacotse bromide as described for the preparation of **19** from **17** and α-acetylglucose bromide, yellow solid, yield: 76%. Mp 256–258 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.76 (s, 1H, OH-5), 7.84 (d, J = 9.2 Hz, 2H, H-2′, H-6′), 7.51–7.36 (m, 5H, $OCH_2C_6H_5$), 7.09 (d, J = 9.2 Hz, 2H, H-3′, H-5′), 6.65 (s, 1H, H-3), 6.59 (d, J = 1.2 Hz, 1H, H-8), 6.45 (d, J = 1.2 Hz, 1H, H-6), 5.26 (d, J = 8.0 Hz, 1H, H-1″), 5.16 (s, 2H, $OCH_2C_6H_5$), 4.24–5.14 (m, 6H, H-2″,3″,4″,5″,6″), 2.20–2.03 (m, 12H, 4 × CH_3CO); HRMS $[M+Na]^+$ calcd for $C_{36}H_{34}O_{14}Na$ 713.6352, found 713.6338.

3.8. Synthesis of acacetin-7-O-β-D-acetylgalactoside (10)

Compound **10** was prepared from **18** and α-acetylgalactose bromide as described for the preparation of **19** from **17** and α-acetylglucose bromide, yellow solid, yield: 75%. Mp 152–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.82 (s, 1H, OH-5), 7.84 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 7.02 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.60 (s, 1H, H-3), 6.59 (d, J = 2.0 Hz, 1H, H-8), 6.45 (d, J = 2.0 Hz, 1H, H-6), 5.50 (d, J = 8.0 Hz, 1H, H-1″), 5.42–5.49 (m, 1H, H-2″), 5.19–5.13 (m, 2H,

H-3″,4″), 4.26–4.20 (m, 1H, H-5″), 4.17–4.08 (m, 2H, H-6″), 3.90 (s, 3H, OCH_3), 2.20–2.03 (m, 12H, 4 × CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 20.1, 20.3, 56.1, 61.4, 67.5, 71.1, 71.2, 72.5, 94.3, 96.4, 99.7, 102.5, 103.3, 105.4, 116.9, 120.1, 128.5, 156.9, 161.1, 161.2, 161.5, 164.2, 169.5, 169.6, 169.9, 169.4, 182.5; HRMS $[M+Na]^+$ calcd for $C_{30}H_{30}O_{14}Na$ 637.5394, found 637.5377.

3.9. Synthesis of 4′-*O*-benzyl apigenin-7-O-β-D-acetyllactoside (21)

Compound **21** was prepared from **17** and α-acetyllactose bromide as described for the preparation of **19** from **17** and α-acetylglucose bromide, yellow solid, yield: 70%. Mp 158–160 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 12.82 (s, 1H, OH-5), 7.83 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 7.50–7.38 (m, 5H, $OCH_2C_6H_5$), 7.09 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.60 (s, 1H, H-3), 6.55 (d, J = 2.0 Hz, 1H, H-8), 6.42 (d, J = 2.0 Hz, 1H, H-6), 5.38 (d, J = 7.2 Hz, 1H, H-1″), 5.31 (t, J = 8.8 Hz, 1H, H-2″), 5.20 (t, J = 9.2 Hz, 1H, H-3″), 5.18 (s, 2H, $OCH_2C_6H_5$), 5.17–5.13 (m, 4H, H-4″,5″,6″), 4.50 (d, J = 8.0 Hz, 1H, H-1‴), 4.15–4.10 (m, 3H, H-2‴, 3‴, 4‴), 3.91–3.87 (m, 3H, H-5‴, 6‴), 2.17–1.98 (m, 21H, 7 × CH_3CO); HRMS $[M+Na]^+$ calcd for $C_{48}H_{50}O_{22}Na$ 1001.8852, found 1001.8865.

3.10. Synthesis of acacetin-7-O-β-D-acetyllactoside (11)

Compound **11** was prepared from **18** and α-acetyllactose bromide as described for the preparation of **19** from **17** and α-acetylglucose bromide, yellow solid, yield: 65%. Mp 98–100 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 12.85 (s, 1H, OH-5), 7.81 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 7.00 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.58 (s, 1H, H-3), 6.54 (d, J = 2.4 Hz, 1H, H-8), 6.40 (d, J = 2.4 Hz, 1H, H-6), 5.38 (d, J = 7.2 Hz, 1H, H-1″), 5.32 (t, J = 8.8 Hz, 1H, H-2″), 5.22 (t, J = 9.2 Hz, 1H, H-3″), 5.17–5.11 (m, 4H, H-4″,5″,6″), 4.56 (d, J = 8.0 Hz, 1H, H-1‴), 4.20–4.10 (m, 3H, H-2‴, 3‴, 4‴), 3.96–3.90 (m, 3H, H-5‴, 6‴), 3.89 (s, 3H, OCH_3), 2.18–1.99 (m, 21H, 7 × CH_3CO) 2.17–1.98 (m, 21H, 7 × CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 20.3, 20.4, 21.3, 21.5, 21.8, 22.0, 58.9, 61.2, 64.6, 67.3, 68.7, 71.1, 72.2, 72.3, 73.2, 75.2, 76.4, 96.2, 96.3, 99.5, 102.8, 104.6, 104.7, 115.9, 123.1, 127.3, 157.8, 159.4, 163.5, 163.8, 165.7, 169.1, 169.2, 169.3, 169.5, 169.7, 170.5, 170.7, 181.3; HRMS $[M+Na]^+$ calcd for $C_{42}H_{46}O_{22}Na$ 925.7894, found 925.7880.

3.11. Synthesis of 4′-*O*-benzyl apigenin-7-O-β-D-acetylmaltoside (22)

Compound **22** was prepared from **17** and α-acetylmaltose bromide as described for the preparation of **19** from **17** and α-acetylglucose bromide, yellow solid, yield: 68%. Mp 176–178 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 12.84 (s, 1H, OH-5), 7.84 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 7.50–7.42 (m, 5H, $OCH_2C_6H_5$), 7.09 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.60 (s, 1H, H-3), 6.57 (d, J = 2.4 Hz, 1H, H-8), 6.44 (d, J = 2.4 Hz, 1H, H-6), 5.44 (d, J = 8.4 Hz, 1H, H-1″), 5.42 (s, 2H, $OCH_2C_6H_5$), 5.41–5.33 (m, 2H, H-2″,3″), 5.26–5.03 (m, 4H, H-4″,5″,6″), 4.52 (d, J = 9.6 Hz, 1H, H-1‴), 4.30–4.24 (m, 2H, H-2‴, 3‴), 4.11–3.97 (m, 4H, H-4‴, 5‴ 6‴), 2.12–2.02 (m, 21H, 7×CH_3CO); HRMS $[M+Na]^+$ calcd for $C_{48}H_{50}O_{22}Na$, 1001.8852, found 1001.8868.

3.12. Synthesis of acacetin-7-O-β-D-acetylmaltoside (12)

Compound **12** was prepared from **18** and α-acetylmaltose bromide as described for the preparation of **19** from **17** and α-acetylglucose bromide, yellow solid, yield: 71%. Mp 118–120 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 12.82 (s, 1H, OH-5), 7.84 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 7.02 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.61 (s, 1H, H-3), 6.57 (d, J = 2.0 Hz, 1H, H-8), 6.44 (d, J = 2.0 Hz, 1H, H-6), 5.44 (d, J = 7.6 Hz, 1H, H-1″), 5.40–5.33 (m, 2H, H-2″,3″), 5.16–5.03 (m, 4H, H-4″,5″,6″), 4.52 (d, J = 8.4 Hz, 1H, H-1‴), 4.31–4.24 (m, 2H, H-2‴, 3‴), 4.09–4.06 (m, 2H, H-4‴,5‴), 4.00–3.92 (m, 2H, H-6‴), 3.90 (s, 3H, OCH_3), 2.12–2.02 (m, 21H, 7 × CH_3CO) 2.17–1.98 (m, 21H, 7 × CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 20.2, 20.5, 21.2, 21.5, 21.7, 22.0, 59.7, 61.5, 64.7, 67.8, 69.6, 72.3, 72.4, 72.7, 73.1, 75.2, 76.5, 96.1, 96.2, 99.4, 102.5, 104.2, 104.4, 115.5, 123.1, 127.2, 157.4, 157.3, 163.1, 164.2, 166.6, 169.1, 169.3, 169.6, 169.8, 169.7, 170.1, 170.4, 182.1; HRMS $[M+Na]^+$ calcd for $C_{42}H_{46}O_{22}Na$ 925.7894, found 925.7883.

3.13. Synthesis of apigenin-7-O-β-D-acetylglucoside (1)[13]

A solution of **19** (0.345 mg, 0.5 mmol) and 5% Pd/C (20 mg) in dry methanol/ethyl acetate (1:1, V/V, 20 mL) was stirred under H_2 at room temperature overnight. TLC indicated that the starting material disappeared. After being filtered, the mixture was evaporated under reduced pressure to afford a residual yellow solid which was chromatographed on silica gel using petroleum ether/ethyl acetate (1:1) as eluent to afford the yellow solid 256 mg, yield: 85%. Mp 207–209 °C. (lit. 13, 207–208 °C). ^1H NMR (400 MHz, DMSO-d_6) δ 13.04 (s, 1H, OH-5), 10.46 (s, 1H, OH-4′), 7.97 (d, J = 8.4 Hz, 2H, H-2′, H-6′), 6.94 (d, J = 8.4 Hz, 2H, H-3′, H-5′), 6.90 (s, 1H, H-3), 6.80 (d, J = 2.0 Hz, 1H, H-8), 6.45 (d, J = 2.0 Hz, 1H, H-6), 5.76 (d, J = 8.0 Hz, 1H, H-1″), 5.40 (t, J = 9.6 Hz, 1H, H-2″) 5.10 (t, J = 13.2 Hz, 1H, H-3″) 5.02 (t, J = 10.0 Hz, 1H, H-4″), 4.37–4.10 (m, 3H, H-5″, 6″), 2.03–1.98 (m, 12H, 4 × CH_3CO); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.1, 20.4, 20.5, 61.4, 67.7, 70.3, 71.2, 71.8, 95.1, 96.4, 99.2, 103.2, 105.3, 116.2, 120.1, 128.2, 156.5, 161.3, 161.5, 161.7, 164.0, 169.1, 169.4, 169.6, 169.8, 182.1; HRMS $[M+Na]^+$ calcd for $C_{29}H_{28}O_{14}Na$ 624.2996, found 624.2982.

3.14. Synthesis of apigenin-7-O-β-D-acetylgalactoside (2)

Compound **2** was prepared from **20** as described for the preparation of **1** from **19**, yellow solid, yield: 83%. Mp 207–209 °C. ^1H NMR (DMSO-d_6, 400 MHz) δ 13.05 (s, 1H, OH-5), 10.48 (s, 1H, OH-4′), 7.77 (d, J = 8.0 Hz, 2H, H-2′, H-6′), 6.98 (d, J = 8.0 Hz, 2H, H-3′, H-5′), 6.58 (s, 1H, H-3), 6.56 (d, J = 2.4 Hz, 1H, H-8), 6.45 (d, J = 2.4 Hz, 1H, H-6), 5.49 (d, J = 7.6 Hz, 1H, H-1″), 5.17–5.15 (m, 2H, H-2″, 3″), 4.31–4.15 (m, 4H, H-4″,5″, 6″), 2.20–2.04 (m, 12H, 4 × CH_3CO); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.2, 20.4, 20.6, 61.6, 68.0, 70.4, 71.6, 71.8, 95.3, 96.4, 99.4, 103.2, 105.1, 116.0, 120.9, 128.4, 156.8, 161.3, 161.4, 161.5, 164.2, 169.1, 169.3, 169.5, 169.7, 182.0; HRMS $[M+Na]^+$ calcd for $C_{29}H_{28}O_{14}Na$ 624.2996, found 624.2985.

3.15. Synthesis of apigenin-7-O-β-D-acetyllactoside (3)

Compound **3** was prepared from **21** as described for the preparation of **1** from **19**, yellow solid, yield: 78%. Mp 116–118 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 12.96 (s, 1H, OH-5), 10.26 (s, 1H, OH-4′) 7.87 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 6.93 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.76 (s, 1H, H-3), 6.69 (d, J = 1.2 Hz, 1H, H-8), 6.41 (d, J = 1.2 Hz, 1H, H-6), 5.60 (d, J = 8.0 Hz, 1H, H-1″), 5.32 (t, J = 9.2 Hz, 1H, H-2″), 5.27–5.16 (m, 2H, H-3″,4″), 5.08–4.77 (m, 3H, H-5″,6″), 4.43 (d, J = 11.2 Hz, 1H, H-1‴), 4.23–4.05 (m, 5H, H-2‴, 3‴, 4‴, 6‴), 3.92 (t, J = 9.2 Hz, 1H, H-5‴), 2.54–1.92 (m, 21H, 7 × CH_3CO); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.0, 20.1, 20.4, 21.2, 21.3, 21.7, 21.8, 59.9, 65.8, 68.3, 69.6, 71.2, 72.3, 72.5, 73.1, 75.0, 76.4, 96.5, 96.8, 99.4, 102.9, 104.5, 104.6, 115.8, 123.0, 127.8, 157.7, 159.3, 163.4, 163.7, 165.4, 169.2, 169.3, 169.6, 169.7, 169.8, 170.1, 170.2, 182.3; HRMS $[M+Na]^+$ calcd for $C_{41}H_{44}O_{22}Na$ 911.7629, found 911.7645.

3.16. Synthesis of apigenin-7-O-β-D-acetylmaltoside (4)

Compound **4** was prepared from **22** as described for the preparation of **1** from **19**, yellow solid, yield: 74%. Mp 138–140 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.82 (s, 1H, OH-5), 10.30 (s, 1H, OH-4′) 7.80 (d, J = 7.2 Hz, 2H, H-2′, H-6′), 6.97 (d, J = 7.2 Hz, 2H, H-3′, H-5′), 6.62 (s, 1H, H-3), 6.54 (d, J = 2.0 Hz, 1H, H-8), 6.42 (d, J = 2.0 Hz, 1H, H-6), 5.45 (d, J = 8.4 Hz, 1H, H-1″), 5.32 (t, J = 8.8 Hz, 1H, H-2″), 5.20–5.14 (m, 2H, H-3″,4″), 5.04–4.75 (m, 3H, H-5″,6″), 4.50 (d, J = 13.2 Hz, 1H, H-1‴), 4.27–4.06 (m, 5H, H-2‴, 3‴, 4‴, 6‴), 3.96 (t, J = 8.8 Hz, 1H, H-5‴), 2.12–2.02 (m, 21H, 7×CH_3CO); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.2, 20.3, 20.5, 21.3, 21.4, 21.6, 21.8, 59.7, 65.4, 68.3, 69.6, 72.2, 72.3, 72.5, 73.3, 75.1, 76.4, 96.0, 96.2, 99.1, 102.3, 104.1, 104.2, 115.8, 123.2, 127.5, 157.7, 158.3, 164.1, 164.2, 165.5, 169.0, 169.4, 169.5, 169.7, 169.7, 170.3, 170.6, 182.0; HRMS [M+Na]$^+$ calcd for $C_{41}H_{44}O_{22}Na$, 911.7629, found 911.7641.

3.17. Synthesis of apigenin-7-O-β-D-glucoside (5)

Compound **1** (150 mg, 0.25 mmol) was added to a solution of 30% aq $NH_3{\cdot}H_2O$ (5 mL) in CH_3OH (20 mL) with stirring. After stirring for 12 h at room temperature, the solvent was removed under reduced pressure. The residual was chromatographed on silica gel using ethyl acetate/MeOH (3:1) as eluent to afford the yellow solid 78 mg, yield: 72%. Mp 234–236 °C. (lit. 13, 238–239 °C); IR (KBr, cm^{-1}) 3440, 2918, 1615, 1563, 1452, 1346, 1273, 1245, 1146, 1103, 1072, 1024, 895; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.97 (s, 1H, OH-5), 10.48 (s, 1H, OH-4′), 7.96 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 6.94 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.87 (s, 1H, H-3), 6.83 (d, J = 1.6 Hz, 1H, H-8), 6.45 (d, J = 1.6 Hz, 1H, H-6), 5.42 (d, J = 8.0 Hz, 1H, H-1″), 5.15 (s, 1H, OH-2″), 5.08 (s, 1H, OH-3″), 5.06 (s, 1H, OH-4″), 4.63 (s, 1H, OH-6″), 3.72–3.70 (m, 1H, H-2″), 3.49–3.18 (m, 5H, H-3″,4″,5″, 6″); ^{13}C NMR (100 MHz, DMSO-d_6) δ 60.6, 69.6, 73.1, 76.5, 77.2, 94.8, 99.6, 99.9, 103.1, 105.4, 116.0, 121.1, 128.6, 156.9, 161.1, 161.4, 163.0, 164.3, 180.1; HRMS [M+Na]$^+$ calcd for $C_{21}H_{20}O_{10}Na$ 455.3665, found 455.3649.

3.18. Synthesis of acacetin-7-O-β-D-glucoside (13)[14]

Compound **13** was prepared from **9** as described for the preparation of **5** from **1**, yellow solid, yield: 70%. Mp 262–264 °C. (lit. 14, 260–262 °C); IR (KBr, cm^{-1}) 3343, 2961, 1623, 1505, 1444, 1220, 1144, 1081, 886; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.93 (s, 1H, OH-5), 8.07 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 7.13 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.96 (s, 1H, H-3), 6.86 (d, J = 1.6 Hz, 1H, H-8), 6.46 (d, J = 1.6 Hz, 1H, H-6), 5.33 (d, J = 7.4 Hz, 1H, H-1″), 5.16 (s, 1H, OH-2″), 5.08 (s, 1H, OH-3″), 5.07 (s, 1H, OH-4″), 4.64 (s, 1H, OH-6″), 3.87 (s, 3H, OCH_3), 3.74–3.70 (m, 1H, H-2″), 3.49–3.18 (m, 5H, H-3″,4″,5″, 6″); ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.0, 61.5, 68.7, 72.3, 75.7, 78.3, 95.8, 98.5, 99.7, 102.4, 105.6, 116.1, 122.3, 127.5, 157.6, 162.0, 162.4, 163.1, 164.3, 182.4; HRMS [M+Na]$^+$ calcd for $C_{22}H_{22}O_{10}Na$ 469.3930, found 469.3946.

3.19. Synthesis of apigenin-7-O-β-D-galactoside (6)[15]

Compound **6** was prepared from **2** as described for the preparation of **5** from **1**, yellow solid, yield: 65%. Mp 206–208 °C. (lit. 15, 208–210 °C); IR (KBr, cm^{-1}) 3377, 2924, 1627, 1509, 1497, 1152, 1071, 897; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.97 (s, 1H, OH-5), 10.40 (s, 1H, OH-4′), 7.96 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 6.94 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.87 (s, 1H, H-3), 6.82 (d, J = 2.0 Hz, 1H, H-8), 6.45 (d, J = 2.0 Hz, 1H, H-6), 5.25 (d, J = 8.0 Hz, 1H, H-1″), 5.02 (d, J = 7.6 Hz, 1H, OH-2″), 4.92 (d, J = 5.6 Hz, 1H, OH-3″), 4.70 (t, J = 5.6 Hz, 1H, OH-6″), 4.55 (d, J = 4.4 Hz, 1H, OH-4″), 3.72–3.68 (m, 2H, H-2″,3″), 3.60–3.32 (m, 4H, H-4″,5″,6″); ^{13}C NMR (100 MHz, DMSO-d_6) δ 60.5, 69.3, 73.2, 76.6, 77.0, 94.3, 99.3, 100.1, 103.2, 105.2, 116.8, 121.4, 128.1, 156.3, 161.4, 162.3, 163.2, 164.5, 180.3; HRMS [M+Na]$^+$ calcd for $C_{21}H_{20}O_{10}Na$ 455.3665, found 455.3677.

3.20. Synthesis of acacetin-7-O-β-D-galactoside (14)[16]

Compound **14** was prepared from **10** as described for the preparation of **5** from **1**, yellow solid, yield: 67%. Mp 252–254 °C. (lit. 16, 251–254 °C); IR (KBr, cm^{-1}) 3437, 2951, 1557, 1524, 1466, 1134, 1041, 896; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.93 (s, 1H, OH-5), 8.07 (d, J = 9.2 Hz, 2H, H-2′, H-6′), 7.13 (d, J = 9.2 Hz, 2H, H-3′, H-5′), 6.98 (s, 1H, H-3), 6.85 (d, J = 2.0 Hz, 1H, H-8), 6.46 (d, J = 2.0 Hz, 1H, H-6), 5.28 (d, J = 6.4 Hz, 1H, H-1″), 5.03 (d, J = 7.6 Hz, 1H, OH-2″), 4.95 (d, J = 5.6 Hz, 1H, OH-3″), 4.72 (t, J = 5.2 Hz, 1H, OH-6″), 4.58 (d, J = 4.8 Hz, 1H, OH-4″), 3.87 (s, 3H, OCH_3), 3.72–3.68 (m, 2H, H-2″, 3″), 3.57–3.43 (m, 4H, H-4″,5″, 6″); ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.2, 60.3, 69.3, 73.1, 76.5, 77.6, 95.2, 98.4, 101.2, 104.3, 105.2, 117.8, 121.2, 128.5, 156.7, 161.8, 162.3, 164.2, 165.6, 181.5; HRMS [M+Na]$^+$ calcd for $C_{22}H_{22}O_{10}Na$ 469.3930, found 469.3947.

3.21. Synthesis of apigenin-7-O-β-D-lactoside (7)

Compound **7** was prepared from **3** as described for the preparation of **5** from **1**, yellow solid, yield: 62%. Mp 172–174 °C; IR (KBr, cm^{-1}) 3421, 2976, 1647, 1504, 1476, 1114, 1071, 892; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.97 (s, 1H, OH-5), 10.46 (s, 1H, OH-4′), 7.97 (d, J = 8.8 Hz, 2H, H-2′, H-6′), 6.94 (d, J = 8.8 Hz, 2H, H-3′, H-5′), 6.87 (s, 1H, H-3), 6.84 (d, J = 2.0 Hz, 1H, H-8), 6.46 (d, J = 2.0 Hz, 1H, H-6), 5.57 (d, J = 9.2 Hz, 1H, H-1″), 5.17 (d, J = 8.0 Hz, 1H, OH-2″), 5.11 (d, J = 4.4 Hz, 1H, OH-3″), 4.83–4.82 (m, 1H, OH-6″), 4.80 (d, J = 5.2 Hz, 1H, OH-2‴), 4.70–4.66 (m, 2H, OH-3‴,6‴), 4.54 (d, J = 3.2 Hz, 1H, OH-4‴), 4.25 (d, J = 6.8 Hz, 1H, H-1‴), 3.60–3.43 (m, 12H, sugar-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 65.3, 65.6, 73.5, 75.5, 75.7, 76.1, 77.4, 78.5, 79.8, 81.7, 96.5, 96.8, 104.5, 104.6, 105.8, 106.9, 115.8, 123.0, 127.8, 157.7, 159.3, 163.1, 163.7, 165.4, 182.1; HRMS [M+Na]$^+$ calcd for $C_{27}H_{30}O_{15}Na$ 617.5067, found 617.5082.

3.22. Synthesis of acacetin-7-O-β-D-lactoside (15)

Compound **15** was prepared from **11** as described for the preparation of **5** from **1**, yellow solid, yield: 63%. Mp 278–280 °C; IR (KBr, cm^{-1}) 3420, 2917, 1635, 1505, 1457, 1224, 1038, 885; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.94 (s, 1H, OH-5), 8.08 (d, J = 8.4 Hz, 2H, H-2′, H-6′), 7.15 (d, J = 8.4 Hz, 2H, H-3′, H-5′), 6.98 (s, 1H, H-3), 6.87 (d, J = 1.2 Hz, 1H, H-8), 6.48 (d, J = 1.2 Hz, 1H, H-6), 5.61 (d, J = 9.2 Hz, 1H, H-1″), 5.20 (d, J = 8.0 Hz, 1H, OH-2″), 5.14 (d, J = 4.4 Hz, 1H, OH-3″), 4.85–4.83 (m, 1H, OH-6″), 4.80 (d, J = 3.2 Hz, 1H, OH-2‴), 4.70–4.68 (m, 2H, OH-3‴,6‴), 4.57 (d, J = 4.0 Hz, 1H, OH-4‴), 4.25 (d, J = 6.8 Hz, 1H, H-1‴), 3.87 (s, 3H, OCH_3), 3.80–3.31 (m, 12H, sugar-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.4, 65.2, 65.3, 74.2, 75.6, 76.3, 76.5, 78.2, 78.6, 79.4, 81.5, 95.6, 96.4, 103.5, 104.7, 105.5, 106.8, 116.3, 122.3, 125.7, 158.6, 158.9, 162.1, 164.6, 167.6, 181.3; HRMS [M+Na]$^+$ calcd for $C_{28}H_{32}O_{15}Na$ 631.5332, found 631.5348.

3.23. Synthesis of apigenin-7-O-β-D-maltoside (8)[17]

Compound **8** was prepared from **4** as described for the preparation of **5** from **1**, yellow solid, yield: 60%. Mp 252–254 °C. (lit. 17, 251–254 °C); IR (KBr, cm^{-1}) 3523, 2967, 1605, 1555, 1438, 1265, 1026, 816; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.97 (s, 1H, OH-5), 10.44 (s, 1H, OH-4′), 7.96 (d, J = 8.4 Hz, 2H, H-2′, H-6′), 6.94 (d, J = 8.4 Hz, 2H, H-3′, H-5′), 6.88 (s, 1H, H-3), 6.84 (d, J = 2.0 Hz, 1H,

H-8), 6.45 (d, J = 2.0 Hz, 1H, H-6), 5.67 (d, J = 8.4 Hz, 1H, H-1″), 5.54 (d, J = 3.2 Hz, 1H, OH-2″), 5.48 (d, J = 2.0 Hz, 1H, OH-3″), 5.15–4.13 (m, 1H, OH-6″), 5.06 (d, J = 7.6 Hz, 1H, OH-2‴), 4.97–4.92 (m, 2H, OH-3‴,6‴), 4.65 (d, J = 6.0 Hz, 1H, OH-4‴), 4.56 (d, J = 6.8 Hz, 1H, H-1‴), 3.65–3.34 (m, 12H, sugar-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 65.4, 65.6, 73.7, 75.2, 75.4, 76.5, 77.6, 78.6, 79.1, 81.2, 96.3, 96.7, 104.1, 104.2, 105.3, 106.6, 115.9, 123.1, 127.8, 157.3, 159.7, 163.2, 163.7, 165.8, 181.6; HRMS [M+Na]$^+$ calcd for $C_{27}H_{30}O_{15}Na$ 617.5067, found 617.5054.

3.24. Synthesis of acacetin-7-O-β-D-maltoside (16)

Compound **16** was prepared from **12** as described for the preparation of **5** from **1**, yellow solid, yield: 61%. Mp 266–268 °C; IR (KBr, cm^{-1}) 3456, 2939, 1623, 1508, 1371, 1226, 1057, 839; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.91 (s, 1H, OH-5), 8.06 (d, J = 9.2 Hz, 2H, H-2′, H-6′), 7.12 (d, J = 9.2 Hz, 2H, H-3′, H-5′), 6.95 (s, 1H, H-3), 6.85 (d, J = 1.2 Hz, 1H, H-8), 6.45 (d, J = 1.2 Hz, 1H, H-6), 5.66 (d, J = 8.4 Hz, 1H, H-1″), 5.54 (d, J = 5.2 Hz, 1H, OH-2″), 5.48 (d, J = 6.0 Hz, 1H, OH-3″), 5.05–4.03 (m, 1H, OH-6″), 5.01 (d, J = 5.6 Hz, 1H, OH-2‴), 4.95–4.92 (m, 2H, OH-3‴,6‴), 4.55 (d, J = 6.0 Hz, 1H, OH-4‴), 4.56 (d, J = 6.8 Hz, 1H, H-1‴), 3.62–3.35 (m, 12H, sugar-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.3, 64.5, 65.7, 73.4, 75.1, 75.4, 75.5, 78.5, 78.7, 79.2, 82.3, 95.5, 96.8, 103.5, 104.2, 105.6, 106.7, 116.8, 123.1, 128.7, 156.3, 158.8, 163.1, 165.7, 167.5, 182.0; HRMS [M+Na]$^+$ calcd for $C_{28}H_{32}O_{15}Na$ 631.5332, found 631.5317.

3.25. Assay for cytotoxic activity

The cytotoxic assay was performed by using the (4,5-dimethylthia-zol-2-yl)-2,5-diphenyltetrazalium bromide (MTT) assay method, cisplatin (DDP, MW300) as a positive control. Five different human cancer cell lines, myeloid leukemia (HL-60), liver carcinoma (SMMC-7721), lung carcinoma (A-549), breast carcinoma (MCF-7), and intestinal carcinoma (SW480), were cultured on DMEM or RPMI-1640 medium supplemented with fetal bovine serum (10%). A suspension of the cells was added to each well (1×10^4–2×10^4 cells/well, 100 μL) of 96-microwell plates and incubated for 12 h. Test compounds were dissolved in DMSO at various concentrations (30, 10, 1, 0.1 μg/mL) and 10 μL of the test solution or DMSO (control) was added to each well. The plate was incubated to 37 °C for 48 h. After termination of the cell culture by adding 5% MTT in PBS (20 μL) to each well, the plate was kept in the incubator for 4 h. To each well was added 100 μL of 20% SDS, the formazan crystals were dissolved, and the plate was read on a microplate reader (Bio-Rad 680) at 595 nm. A dose–response curve was plotted for each compound, and the half maximal inhibitory concentration (IC_{50}) for cancer cell lines was recorded.

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References

1. Janmejaik, K. S.; Sanjay, G. *J. Agric. Food Chem.* **2007**, *55*, 9470–9478.
2. (a) Cook, N. C.; Sammam, S. *J. Nutr. Biochem.* **1996**, *7*, 66–76; (b) Harbored, J. B.; Williams, C. A. *Photochemistry* **2000**, *55*, 481–504.
3. Masao, K.; Morikco, M. *J. Nat. Prod.* **1996**, *59*, 314–315.
4. Hu, C. Q.; Chen, K.; Shi, Q.; Kilkuskie, R. E.; Cheng, Y. C.; Lee, K. H. *J. Nat. Prod.* **1994**, *57*, 42–51.
5. (a) Wagner, H.; Aurnhammer, G.; Hörhammer, L.; Farkas, L.; Nógrádi, M. *Chem. Ber.* **1969**, *102*, 785–791; (b) Wagner, H.; Budweg, W.; Hörhammer, L.; Vermes, B.; Farkas, L. *Chem. Ber.* **1971**, *104*, 2118–2123; (c) Kleine, H. P.; Weinberg, D. V.; Kaufman, R. J.; Sidhu, R. S. *Carbohydr. Res.* **1985**, *142*, 333–337; (d) Demetzos, C.; Skaltsounis, A.-L.; Tillequin, F.; Koch, M. *Carbohydr. Res.* **1990**, *207*, 131–137; (e) Li, M.; Han, X.; Yu, B. *J. Org. Chem.* **2003**, *68*, 6842–6845; (f) Zacharia, J. T.; Hayashi, M. *Carbohydr. Res.* **2012**, *348*, 90–94; (g) Soulage, C. O.; Grand, L.; Géloën, A.; Chambert, S. *Tetrahedron Lett.* **2012**, *53*, 480–483; (h) Zhu, C. S.; Peng, W. J.; Li, Y. W.; Han, X. W.; Yu, B. *Carbohydr. Res.* **2006**, *341*, 1047–1051; (i) Li, M.; Han, X. W.; Yu, B. *Tetrahedron Lett.* **2002**, *43*, 9467–9470; (j) Zhang, Y.; Wang, K. J.; Zhan, Z. L.; Yang, Y.; Zhao, Y. M. *Tetrahedron Lett.* **2011**, *52*, 3154–3157; (k) Urgaonkar, S.; Shaw, J. T. *J. Org. Chem.* **2007**, *72*, 4582–4585; (l) Maloney, D. J.; Hecht, S. M. *Org. Lett.* **2005**, *7*, 1097–1099; (m) Chen, J. L.; Huang, W.; Lian, G. Y.; Lin, F. *Carbohydr. Res.* **2009**, *344*, 2245–2249; (n) Gao, Q.; Lian, G. Y.; Lin, F. *Carbohydr. Res.* **2009**, *344*, 511–515; (o) Caldwell, S. T.; Crozierb, A.; Hartley, R. C. *Tetrahedron* **2000**, *56*, 4101–4106; (p) Du, Y. G.; Wei, G. H.; Linhardt, R. J. *J. Org. Chem.* **2004**, *69*, 2206–2209; (q) Du, Y. G.; Wei, G. H.; Linhardt, R. J. *Tetrahedron Lett.* **2003**, *44*, 6887–6890; (r) Kondo, T.; Oyama, K.; Yoshida, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 894–897.
6. Wang, Q. A.; Wu, Z.; Liu, L.; Zou, L. H.; Luo, M. *Chin. J. Org. Chem.* **2010**, *30*, 1682–1688.
7. Liao, T. G.; Wang, Q. A.; Fang, W. Q.; Zhu, H. T. *Chin. J. Org. Chem.* **2006**, *26*, 685–689.
8. Wu, Z.; Jiang, L.; Chen, H.; Wang, Q. A. *J. Chem. Res.* **2009**, 195–197.
9. Zhang, X.; Simmons, C. G.; Corey, D. R. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1269–1272.
10. Wu, Z.; Liang, Z. Y.; Li, W.; Ren, Y. M.; Wang, Q. A. *Chem. Res. Chin. Univ.* **2011**, *27*, 949–954.
11. Barreca, D.; Bellocco, E.; Caristi, C.; Leuzz, U.; Gattuso, G. *J. Agric. Food Chem.* **2010**, *58*, 3031–3036.
12. Seijas, J. A.; Vázquez-Tato, M. P.; Carballido-Reboredo, R. *J. Org. Chem.* **2005**, *70*, 2855–2858.
13. Oyama, K.; Kondo, T. *Tetrahedron* **2004**, *60*, 2025–2034.
14. Jia, L. Y.; Sun, Q. S.; Huang, S. W. *Zhongguo Yaowu Huaxue Zazhi* **2003**, *13*, 159–161.
15. Sashida, Y.; Nakata, H.; Shimomura, H.; Kagaya, M. *Phytochemistry* **1983**, *22*, 1219–1222.
16. James, T. Z.; Masahiko, H. *Carbohydr. Res.* **2012**, *348*, 91–94.
17. Veitch, N. C.; Grayer, R. J.; Irwin, J. L.; Takeda, K. *Phytochemistry* **1998**, *48*, 389–393.