Synthetic, Non-Saccharide Glycosaminoglycan Mimetics Selectively Target Colon Cancer Stem Cells

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Figure S1. Structures of NSGMs belonging to the **G1-G9** scaffolds.

Figure S2. Structures of NSGMs belonging to the **G10–G12** scaffolds.

Scheme S1. Synthesis of sulfated 5,5-*O*-flavonoid dimers G2.1-G2.6: a) K₂CO₃, dibromoalkane (0.5 equiv), DMF, rt/6 h, 85-90%, b) *p*-toluenesulfonic acid, MeOH, reflux/48 h, 55-65%, c) SO₃:Me₃N, Et₃N, CH₃CN, microwave/6 h, 75-85%.

Scheme S2. Synthesis of sulfated 3', 3'-*O*-flavonoid dimers G3.1-G3.2: a) K_2CO_3 , dibromoalkane (0.5 equiv), DMF, rt/3 h, 85-90%, b) *p*-toluenesulfonic acid, MeOH, reflux/48 h, 55-65%, c) $SO_3:Me_3N$, Et_3N , CH_3CN , microwave/6 h, 75-85%.

Scheme S3. Synthesis of sulfated 3', 5-*O*-flavonoid trimers G4.1-G4.2: a) K_2CO_3 , dibromoalkane (1 equiv), DMF, rt/3 h, 85-90%, b) **9**, K_2CO_3 , DMF, 60 °C/4 h, 85-90%, c) *p*-toluenesulfonic acid, MeOH, reflux/48 h, 55-65%, d) $SO_3 \cdot Me_3N$, Et_3N , CH_3CN , microwave/8 h, 75-85%.

Experimental Procedures and Spectral Characterization of Compounds of Schemes S1, S2, and S3.

General procedure for synthesis of methoxy methylated 5,5'; 3',3' flavonoid dimers and 5,3' flavonoid trimers 3-8, 10, 11, 14, 15. To a solution of **1** or **2** (1.0 equiv) in *N,N*-dimethylformamide was added K_2CO_3 (2.5 equiv) and stirred for two minutes. This was followed by addition of di-bromo alkane (0.5 equiv) and stirred vigorously for 12 hours. After the reaction completed as indicated from TLC the reaction mixture was diluted with EtOAc (25 mL) and water (25 mL). The organic layer was separated and the aqueous phase was extracted with EtOAc (2×25 mL), organic layer was washed with saturated NaCl solution (25 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , evaporated under reduced pressure to afford crude compounds **3-8, 10, 11, 12, 14** and **15** which were further purified using flash chromatography on silica gel (70-85% ethyl acetate in hexanes). Spectral characteristics of compounds are as follows:

5,5'-(ethane-1,2-diylbis(oxy))bis(2-(3,4-bis(methoxymethoxy)phenyl)-3,7-bis(methoxy-methoxy)-4H-chromen-4-one) (3). 1H NMR ($CDCl_3$, 400 MHz): 7.93 (d, $J = 2$ Hz, 2 H), 7.73 (d, $J = 6.6$ Hz, 2 H), 7.29- 7.26 (m, 4 H), 6.74 (d, $J = 8.1$ Hz, 2 H), 5.33 (s, 4 H), 5.32 (s, 4 H), 5.28 (s, 4 H), 5.22 (s, 4 H), 4.64 (s, 4 H), 3.56 (s, 6 H), 3.56 (s, 6 H), 3.52 (s, 6 H), 3.25 (s, 6 H). ^{13}C NMR ($DMSO-d_6$, 400 MHz): 173.60, 161.42, 159.93, 158.41, 153.33, 149.20, 146.56, 137.87, 124.94, 123.69, 117.75, 115.74, 110.46, 99.44, 97.77, 96.36, 95.70, 95.17, 94.31, 68.18, 57.58, 56.44, 56.33. MS (ESI) calculated for $C_{48}H_{54}O_{22}$, $[(M+H)]^+$, m/z 983.31, found for $[(M+H)]^+$, m/z 983.251.

5,5'-(propane-1,3-diylbis(oxy))bis(2-(3,4-bis(methoxymethoxy)phenyl)-3,7-bis(methoxy-methoxy)-4H-chromen-4-one) (4). 1H NMR ($CDCl_3$, 400 MHz): 7.88 (d, $J = 2$ Hz, 2 H), 7.66 (d, $J = 6.6$ Hz, 2 H), 7.24 (d, $J = 8.6$ Hz, 4 H), 6.63 (d, $J = 2$ Hz, 2 H), 6.53 (d, $J = 2$ Hz, 2 H), 5.29 (s, 4 H), 5.28 (s, 4 H), 5.20 (s, 4 H), 5.17 (s, 4 H), 4.45 (t, $J = 5.4$ Hz, 4 H), 3.53 (s, 6 H), 3.52 (s, 6 H), 3.46 (s, 6 H), 3.19 (s, 6 H), 2.5 (t, $J = 5.4$ Hz, 4 H). ^{13}C NMR ($DMSO-d_6$, 400 MHz): 173.63, 161.43, 160.48, 158.43, 153.18, 149.09, 146.51, 137.88, 125.03, 123.65, 117.72, 115.68, 110.09, 97.92, 97.81, 95.66, 95.18, 94.25, 94.31, 65.65, 57.54, 56.37, 56.33, 56.31, 21.5. MS (ESI) calculated for $C_{49}H_{56}O_{22}$, $[(M+H)]^+$, m/z 997.33, found for $[(M+H)]^+$, m/z 997.263.

5,5'-(ethane-1,2-diylbis(oxy))bis(2-(2,4-bis(methoxymethoxy)phenyl)-3,7-bis(methoxy-methoxy)-4H-chromen-4-one) (5). 1H NMR ($CDCl_3$, 400 MHz): 7.36 (d, $J = 8.5$ Hz, 2 H), 6.84 (d, $J = 2.2$ Hz, 2 H), 6.72 (d, $J = 6.3$ Hz, 2 H), 6.62 (d, $J = 2.1$ Hz, 2 H), 6.58 (d, $J = 2.2$ Hz, 2 H), 5.16 (s, 2 H), 5.13 (s, 2 H), 5.10 (s, 2 H), 4.95 (s, 2 H), 4.53 (s, 4 H), 3.41 (s, 6 H), 3.40 (s, 6 H), 3.39 (s, 6 H), 2.86 (s, 6 H). ^{13}C NMR ($DMSO-d_6$, 400 MHz): 173.53, 161.36, 160.11, 159.99, 159.01, 156.58, 154.32, 138.86, 132.07, 114.98, 110.95, 108.75, 103.86, 99.36, 97.50, 96.61, 94.77, 94.45, 94.35, 68.23. MS (ESI) calculated for $C_{48}H_{54}O_{22}$, $[(M+H)]^+$, m/z 983.31, found for $[(M+H)]^+$, m/z 983.281.

5,5'-(butane-1,4-diylbis(oxy))bis(2-(3,4-bis(methoxymethoxy)phenyl)-3,7-bis(methoxy-methoxy)-4H-chromen-4-one) (6). 1H NMR ($CDCl_3$, 400 MHz): 7.92 (d, $J = 2.1$ Hz, 2 H), 7.69 (d, $J = 6.6$ Hz, 2 H), 7.28 (d, $J = 2.6$ Hz, 2 H), 6.58 (d, $J = 2.1$ Hz, 2 H), 6.48 (d, $J = 2.2$ Hz, 2 H), 5.32 (s, 4 H), 5.32 (s, 4 H), 5.31 (s, 4 H), 5.21 (s, 4 H), 4.29 (s, 4 H), 3.57 (s, 6 H), 3.56 (s, 6 H), 3.5 (s, 6 H), 3.22 (s, 6 H), 2.27 (s, 4 H). ^{13}C NMR ($DMSO-d_6$, 400 MHz): 170.64, 162.40, 159.58, 158.55, 146.54, 137.92, 125.07, 123.69, 117.78, 115.74, 105.17, 97.83, 97.59, 95.69, 95.26, 95.17, 94.29, 68.07, 57.55, 56.4, 25.32. MS (ESI) calculated for $C_{50}H_{58}O_{22}$, $[(M+H)]^+$, m/z 1011.34, found for $[(M+H)]^+$, m/z 1011.296.

5,5'-(pentane-1,5-diylbis(oxy))bis(2-(3,4-bis(methoxymethoxy)phenyl)-3,7-bis(methoxy-methoxy)-4H-chromen-4-one) (7). 1H NMR ($CDCl_3$, 400 MHz): 7.91 (d, $J = 2$ Hz, 2 H), 7.71 (d, $J = 6.6$ Hz, 2 H), 7.27 (d, $J = 3.7$ Hz, 2 H), 6.68 (d, $J = 2.2$ Hz, 2 H), 6.46 (d, $J = 2.1$ Hz, 2 H), 5.31 (s, 4 H), 5.31 (s, 4 H), 5.26 (s, 4 H), 5.21 (s, 4 H), 4.15 (t, $J = 6.5$ Hz, 4 H), 3.56 (s, 6 H), 3.55 (s, 6 H), 3.52 (s, 6 H),

3.23 (s, 6 H), 2.09-2.03 (m, 4 H), 1.86-1.72 (m, 2 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 173.64, 161.35, 160.58, 158.55, 153.16, 149.12, 146.54, 137.92, 125.07, 123.69, 117.78, 115.74, 110.16, 97.83, 97.59, 95.69, 95.26, 95.17, 94.29, 69.34, 57.55, 56.4, 56.32, 28.4, 22.36. MS (ESI) calculated for $\text{C}_{51}\text{H}_{60}\text{O}_{22}$, $[(\text{M}+\text{H})]^+$, m/z 1025.36, found for $[(\text{M}+\text{H})]^+$, m/z 1025.251.

(E)-5,5'-(but-2-ene-1,4-diylbis(oxy))bis(2-(3,4-bis(methoxymethoxy)phenyl)-3,7-bis(methoxymethoxy)-4H-chromen-4-one) (8). ^1H NMR (CDCl_3 , 400 MHz): 8.02 (s, 2 H), 7.92 (d, $J = 2$ Hz, 2 H), 7.72 (d, $J = 6.6$ Hz, 2 H), 7.27 (d, $J = 8.7$ Hz, 2 H), 6.71 (d, $J = 2.1$ Hz, 2 H), 6.47 (d, $J = 2$ Hz, 2 H), 5.31 (s, 4 H), 5.31 (s, 4 H), 5.25 (s, 4 H), 5.23 (s, 4 H), 4.72 (d, $J = 3.5$ Hz, 4 H), 3.29 (s, 6 H), 3.29 (s, 6 H), 3.15 (s, 6 H), 3.02 (s, 6 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 173.65, 162.49, 161.35, 159.87, 158.55, 153.27, 149.17, 146.55, 137.92, 126.76, 124.97, 123.69, 117.76, 115.73, 110.21, 98.0, 97.78, 95.69, 95.59, 95.15, 94.37, 68.92, 57.58, 56.44, 56.32. MS (ESI) calculated for $\text{C}_{50}\text{H}_{56}\text{O}_{22}$, $[(\text{M}+\text{H})]^+$, m/z 1009.33, found for $[(\text{M}+\text{H})]^+$, m/z 1009.283.

2,2'-((propane-1,3-diylbis(oxy))bis(4-(methoxymethoxy)-3,1-phenylene))bis(5-hydroxy-3,7-bis(methoxymethoxy)-4H-chromen-4-one) (10). ^1H NMR (CDCl_3 , 400 MHz): 12.32 (s, 2 H), 7.50 (d, $J = 1.8$ Hz, 2 H), 7.43 (d, $J = 6.6$ Hz, 2 H), 7.03 (d, $J = 8.3$ Hz, 2 H), 6.40 (d, $J = 2.1$ Hz, 2 H), 6.26 (d, $J = 2.2$ Hz, 2 H), 5.06 (s, 2 H), 5.03 (s, 2 H), 4.97 (s, 2 H), 4.15 (t, $J = 4.8$ Hz, 4 H), 3.298 (s, 6 H), 3.294 (s, 6 H), 3.02 (s, 6 H), 2.25-2.22 (m, 2 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 178.56, 162.98, 161.92, 156.67, 149.22, 148.71, 135.6, 128.08, 127.39, 124.46, 122.78, 116.1, 114.29, 106.61, 99.77, 97.89, 95.25, 94.21, 94.05, 65.83, 57.75, 56.41, 56.36. MS (ESI) calculated for $\text{C}_{45}\text{H}_{48}\text{O}_{20}$, $[(\text{M}+\text{H})]^+$, m/z 909.27, found for $[(\text{M}+\text{H})]^+$, m/z 909.231.

(E)-2,2'-((but-2-ene-1,4-diylbis(oxy))bis(4-(methoxymethoxy)-3,1-phenylene))bis(5-hydroxy-3,7-bis(methoxymethoxy)-4H-chromen-4-one) (11). ^1H NMR (CDCl_3 , 400 MHz): 12.53 (s, 2 H), 7.71 (d, $J = 2$ Hz, 2 H), 7.63 (d, $J = 6.6$ Hz, 2 H), 7.24 (d, $J = 8.3$ Hz, 2 H), 6.62 (d, $J = 2.2$ Hz, 2 H), 6.48 (d, $J = 2.1$ Hz, 2 H), 6.23 (s, 2 H), 5.3 (s, 4 H), 5.25 (s, 4 H), 5.19 (s, 4 H), 4.77 (d, $J = 0.8$ Hz, 4 H), 3.55 (s, 6 H), 3.51 (s, 6 H), 3.25 (s, 6 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 178.54, 162.98, 161.91, 156.64, 156.49, 149.25, 148.15, 135.57, 128.76, 124.32, 122.73, 115.84, 114.48, 106.6, 99.77, 97.86, 95.26, 94.24, 94.06, 68.38, 57.75, 56.4. MS (ESI) calculated for $\text{C}_{46}\text{H}_{48}\text{O}_{20}$, $[(\text{M}+\text{H})]^+$, m/z 921.27, found for $[(\text{M}+\text{H})]^+$, m/z 921.241.

2-(3,4-bis(methoxymethoxy)phenyl)-5-(2-(5-(5-(2-((2-(3,4-bis(methoxymethoxy)phenyl)-3,7-bis(methoxymethoxy)-4-oxo-4H-chromen-5-yl)oxy)ethoxy)-3,7-bis(methoxymethoxy)-4-oxo-4H-chromen-2-yl)-2-(methoxymethoxy)phenoxy)ethoxy)-3,7-bis(methoxymethoxy)-4H-chromen-4-one (14). ^1H NMR (CDCl_3 , 400 MHz): 7.83-7.82 (m, 2 H), 7.71 (d, $J = 2.0$ Hz, 1 H), 7.64-7.59 (m, 3 H), 7.19-7.14 (m, 3 H), 6.68-6.55 (m, 6 H), 5.22-5.20 (m, 10 H), 5.19 (s, 4 H), 5.13 (s, 4 H), 5.09 (s, 4 H), 4.54-4.46 (m, 8 H), 3.47-3.46 (m, 18 H), 3.43 (s, 6 H), 3.16 (s, 3 H), 3.15 (s, 3 H), 3.14 (s, 3 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 173.57, 173.39, 161.45, 161.25, 160.10, 159.96, 158.46, 153.40, 153.30, 149.26, 149.0, 148.62, 146.65, 137.93, 125.20, 125.04, 124.99, 123.7, 123.09, 117.91, 116.69, 115.28, 110.72, 110.54, 99.59, 97.90, 97.82, 97.72, 96.47, 95.77, 95.63, 95.24, 94.37, 68.29, 67.89, 57.61, 57.54, 56.40, 56.30. ESI-MS calculated for $\text{C}_{71}\text{H}_{78}\text{O}_{32}$, $[(\text{M}+\text{H})]^+$, m/z 1443.36, found $[(\text{M}+\text{H})]^+$, m/z 1443.187.

2-(3,4-bis(methoxymethoxy)phenyl)-5-(3-(5-(5-(3-((2-(3,4-bis(methoxymethoxy)phenyl)-3,7-bis(methoxymethoxy)-4-oxo-4H-chromen-5-yl)oxy)propoxy)-3,7-bis(methoxymethoxy)-4-oxo-4H-chromen-2-yl)-2-(methoxymethoxy)phenoxy)propoxy)-3,7-bis(methoxymethoxy)-4H-chromen-4-one (15). ^1H NMR (CDCl_3 , 400 MHz): ^1H NMR (CDCl_3 , 400 MHz): 7.62 (d, $J = 1.0$ Hz, 2 H), 7.60-7.51 (m, 4 H), 7.19-7.09 (m, 3 H), 6.6-6.47 (m, 3 H), 6.45-6.40 (m, 3 H), 5.22-5.21 (m, 10 H), 5.15 (s, 4 H), 5.13 (s, 2 H), 5.10 (s, 2 H), 5.09 (s, 4 H), 4.38-4.23 (m, 8 H), 3.46-3.39 (m, 24 H), 3.12 (s, 6 H), 3.10 (s, 3

H), 2.44-2.38 (m, 4 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 173.37, 172.89, 162.45, 161.9, 160.25, 159.98, 158.48, 154.09, 153.25, 149.28, 148.98, 148.65, 146.86, 138.05, 125.27, 125.35, 124.28, 123.65, 123.09, 118.09, 116.89, 115.29, 110.93, 111.04, 99.78, 97.89, 97.86, 97.77, 96.57, 95.57, 95.86, 94.34, 94.38, 68.39, 67.75, 58.01, 57.58, 56.35, 56.29, 28.49. ESI-MS calculated for $\text{C}_{73}\text{H}_{82}\text{O}_{32}$ $[(\text{M}+\text{H})]^+$, m/z 1471.48, found $[(\text{M}+\text{H})]^+$, m/z 1471.162.

Synthesis of intermediates 12 and 13. To a solution of **1** (1.0 equiv) in *N,N*-dimethylformamide was added K_2CO_3 (2.5 equiv) and stirred for two minutes. This was followed by addition of di-bromo alkane (1.5 equiv) and stirred vigorously for 6 hours. After the reaction completed as indicated from TLC the reaction mixture was diluted with EtOAc (25 mL) and water (25 mL). The organic layer was separated and the aqueous phase was extracted with EtOAc (2×25 mL), organic layer was washed with saturated NaCl solution (25 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , evaporated under reduced pressure to afford crude **12** and **13**, which were further purified using flash chromatography on silica gel (70-85% ethyl acetate in hexanes). Spectral characteristics of compounds are as follows:

2-(3,4-bis(methoxymethoxy)phenyl)-5-(2-bromoethoxy)-3,7-bis(methoxymethoxy)-4H-chromen-4-one (12). ^1H NMR (400 MHz, CDCl_3): 7.69 (d, 1 H, $J = 2.0$ Hz), 7.55-7.52 (m, 1 H), 7.09 (d, 1 H, $J = 8.6$ Hz), 6.54 (d, 1 H, $J = 2.1$ Hz), 6.27 (d, 1 H, $J = 2.1$ Hz), 5.13 (s, 2 H), 5.09 (s, 2 H), 5.05 (s, 2 H), 5.04 (s, 2 H), 4.37 (t, 2 H, $J = 2.8$ Hz), 3.51 (t, 2 H, $J = 2.8$ Hz), 3.39 (s, 3 H), 3.37 (s, 3 H), 3.34 (s, 3 H), 3.30 (s, 3 H). ^{13}C NMR (100 MHz, CDCl_3): 173.80, 161.47, 161.08, 158.57, 153.19, 149.03, 147.02, 137.75, 124.73, 123.28, 115.82, 115.48, 109.93, 97.58, 96.59, 95.33, 95.25, 94.36, 78.30, 76.04, 57.67, 57.10, 56.44, 56.41, 55.93. ESI-MS calculated for $\text{C}_{25}\text{H}_{29}\text{BrO}_{11}$ $[(\text{M}+\text{H})]^+$, m/z , 585.07 found m/z 585.026.

2-(3,4-bis(methoxymethoxy)phenyl)-5-(3-bromopropoxy)-3,7-bis(methoxymethoxy)-4H-chromen-4-one (13). ^1H NMR (400 MHz, CDCl_3): 7.68 (d, 1 H, $J = 2.0$ Hz), 7.55-7.52 (m, 1 H), 7.07 (d, 1 H, $J = 8.6$ Hz), 6.54 (d, 1 H, $J = 2.1$ Hz), 6.28 (d, 1 H, $J = 2.1$ Hz), 5.13 (s, 2 H), 5.1 (s, 2 H), 5.08 (s, 2 H), 5.05 (s, 2 H), 4.37 (t, 2 H, $J = 2.9$ Hz), 3.5 (t, 2 H, $J = 2.9$ Hz), 3.39 (s, 3 H), 3.37 (s, 3 H), 3.34 (s, 3 H), 3.30 (s, 3 H), 2.02 (2 H, m). ^{13}C NMR (100 MHz, CDCl_3): 173.65, 162.07, 161.08, 158.57, 153.19, 149.03, 146.92, 137.75, 124.73, 123.28, 114.92, 115.48, 109.93, 97.58, 96.59, 95.33, 95.25, 94.36, 78.30, 76.04, 57.67, 57.10, 56.44, 56.41, 55.93, 38.25. MS (ESI) calculated for $\text{C}_{26}\text{H}_{31}\text{BrO}_{11}$ $[(\text{M}+\text{H})]^+$, m/z , 599.10 found m/z 599.038.

General procedure for synthesis of polyphenolic 5,5; 3',3' flavonoid dimers and 5,3' flavonoid trimers 3a-8a, 10a, 11a, 14a, and 15a. The methoxy methyl groups present in the compounds **3-8**, **10**, **11**, **14**, **15** were completely deprotected using following procedure. To a solution of methoxy methylated compound in methanol was taken in a flask attached to a reflux condenser and *p*-Toluenesulfonic acid (catalytic) was added to it. The reaction mixture was stirred at reflux temperature, the extent of deprotection was monitored using UPLC-MS and continued until complete deprotection of all OMOM groups. After completion of the reaction EtOAc (25 mL) was added to precipitate the mixture. The precipitate was filtered, washed with excess EtOAc to remove *p*-toluenesulfonic acid and dried to obtain pure polyphenolic compounds **3a-8a**, **10a**, **11a**, **14a**, and **15a**. Spectral characteristics of compounds are as follows:

5,5'-(ethane-1,2-diylbis(oxy))bis(2-(3,4-dihydroxyphenyl)-3,7-dihydroxy-4H-chromen-4-one) (3a). ^1H NMR (DMSO- d_6 , 400 MHz): 10.64 (bs, 2 H), 9.7-8.2 (bs, 5 H), 7.57 (d, $J = 2.2$ Hz, 2 H), 7.41 (d, $J = 6.2$ Hz, 2 H), 6.80 (d, $J = 2.4$ Hz, 2 H), 6.44-6.40 (m, 4 H), 4.37 (s, 4 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 170.80, 162.33, 159.47, 157.86, 146.92, 145.03, 141.87, 137.11, 122.23, 119.08, 115.57,

114.46, 105.46, 97.55, 95.12, 67.77. ESI-MS calculated for $C_{32}H_{22}O_{14} [(M+Na)]^+$, m/z 653.52, found $[(M+H)]^+$, m/z 631.197.

5,5'-(propane-1,3-diylbis(oxy))bis(2-(3,4-dihydroxyphenyl)-3,7-dihydroxy-4H-chromen-4-one) (4a). 1H NMR (DMSO- d_6 , 100 MHz): 10.6 (bs, 2H), 8.4-9.0 (bs, 3H), 7.55 (d, $J = 2.1$ Hz, 2 H), 7.41 (d, $J = 2.1$ Hz, 2 H), 6.80 (d, $J = 8.4$ Hz, 2 H), 6.38 (d, $J = 1.9$ Hz, 2 H), 6.30 (d, $J = 2$ Hz, 2 H), 4.29 (t, $J = 5.8$ Hz, 4 H), 2.26-2.22 (m, 2H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 171.04, 162.36, 159.74, 157.87, 146.90, 145.01, 141.88, 137.15, 122.28, 119.09, 115.56, 114.48, 105.21, 96.32, 94.54, 64.82, 28.54. ESI-MS calculated for $C_{33}H_{24}O_{14} [(M+Na)]^+$, m/z 667.54, found $[(M+H)]^+$, m/z 645.213.

5,5'-(ethane-1,2-diylbis(oxy))bis(2-(2,4-dihydroxyphenyl)-3,7-dihydroxy-4H-chromen-4-one) (5a). 1H NMR (DMSO- d_6 , 400 MHz): 9.1-10.5 (bs, 5 H), 7.14 (d, $J = 8.4$ Hz, 2 H), 6.40 (d, $J = 1.9$ Hz, 2 H), 6.31 (d, $J = 1.9$ Hz, 4 H), 6.26 (d, $J = 6.3$ Hz, 2 H), 4.36 (s, 4 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 173.72, 160.81, 159.76, 156.47, 156.13, 155.68, 154.34, 137.46, 131.07, 116.34, 113.46, 112.04, 110.35, 101.83, 100.74, 68.45. ESI-MS calculated for $C_{32}H_{22}O_{14} [(M+Na)]^+$, m/z 653.32, found $[(M+H)]^+$, m/z 631.197.

5,5'-(butane-1,4-diylbis(oxy))bis(2-(3,4-dihydroxyphenyl)-3,7-dihydroxy-4H-chromen-4-one) (6a). 1H NMR (DMSO- d_6 , 400 MHz): 10.58 (bs, 2 H), 9.34-8.64 (bs, 6 H), 7.57 (d, $J = 2.2$ Hz, 2 H), 7.42 (d, $J = 6.4$ Hz, 2 H), 6.80 (d, $J = 8.5$ Hz, 2 H), 6.37-6.32 (m, 4 H), 4.06 (s, 4 H), 2.05 (s, 4 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 170.96, 162.40, 159.90, 157.88, 146.88, 145.02, 141.72, 137.13, 122.30, 119.05, 115.56, 114.45, 105.17, 96.45, 94.41, 68.07, 25.37. ESI-MS calculated for $C_{34}H_{26}O_{14} [(M+Na)]^+$, m/z 681.56, found $[(M+H)]^+$, m/z 659.261.

5,5'-(pentane-1,5-diylbis(oxy))bis(2-(3,4-dihydroxyphenyl)-3,7-dihydroxy-4H-chromen-4-one) (7a). 1H NMR (DMSO- d_6 , 400 MHz): 7.64 (d, $J = 2.1$ Hz, 2 H), 7.51-7.47 (m, 2 H), 7.13 (d, $J = 7.9$ Hz, 1 H), 6.88 (d, $J = 8.1$ Hz, 2 H), 6.46-6.37 (m, 3 H), 4.05 (t, $J = 5.5$ Hz, 4 H), 2.05-2.01 (m, 4 H), 1.89-1.85 (m, 2 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 170.78, 163.25, 158.89, 157.76, 146.97, 145.28, 141.82, 136.95, 122.48, 119.35, 115.86, 113.98, 105.16, 98.35, 94.35, 68.37, 25.38, 22.24. ESI-MS calculated for $C_{35}H_{28}O_{14} [(M+Na)]^+$, m/z 695.59, found $[(M+H)]^+$, m/z 673.213.

(E)-5,5'-(but-2-ene-1,4-diylbis(oxy))bis(2-(3,4-dihydroxyphenyl)-3,7-dihydroxy-4H-chromen-4-one) (8a). 1H NMR (DMSO- d_6 , 400 MHz): 10.73 (s, 1 H), 9.45-8.6 (bs, 6 H), 7.68 (d, $J = 3.5$ Hz, 2 H), 7.51-7.51 (m, 2 H), 6.90-6.87 (m, 3 H), 6.62-6.43 (m, 5 H), 4.75 (d, $J = 3.5$ Hz, 4 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 170.89, 163.45, 158.94, 157.69, 147.78, 145.82, 142.07, 138.15, 124.67, 123.49, 122.15, 119.28, 115.58, 113.95, 105.18, 98.34, 95.47, 56.35. ESI-MS calculated for $C_{34}H_{24}O_{14} [(M+Na)]^+$, m/z 679.55, found $[(M+H)]^+$, m/z 657.181.

2,2'-((propane-1,3-diylbis(oxy))bis(4-hydroxy-3,1-phenylene))bis(3,5,7-trihydroxy-4H-chromen-4-one) (10a). 1H NMR (DMSO- d_6 , 400 MHz): 12.38 (s, 2H), 10.82-10.42 (bs, 2H), 9.8-9.2 (bs, 4H), 7.73-7.61 (m, 4 H), 6.89 (d, $J = 9.2$ Hz, 2 H), 6.39 (d, $J = 2.1$ Hz, 2 H), 6.12 (d, $J = 1.9$ Hz, 2 H), 4.20 (t, $J = 5.4$ Hz, 4 H), 2.23-2.20 (m, 2H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 175.83, 163.88, 160.64, 156.13, 148.95, 146.56, 146.51, 135.78, 121.99, 121.79, 115.64, 112.93, 102.99, 98.17, 93.56, 65.36, 28.85. ESI-MS calculated for $C_{33}H_{24}O_{14} [(M+Na)]^+$, m/z 667.54, found $[(M+H)]^+$, m/z 645.149.

(E)-2,2'-((but-2-ene-1,4-diylbis(oxy))bis(4-hydroxy-3,1-phenylene))bis(3,5,7-trihydroxy-4H-chromen-4-one) (11a). 1H NMR (DMSO- d_6 , 400 MHz): 12.46 (bs, 2 H), 10.75 (s, 2 H), 9.77 (bs, 2 H), 9.33 (bs, 2 H), 7.85 (d, $J = 2$ Hz, 2 H), 7.68 (d, $J = 6.3$ Hz, 2 H), 6.97 (d, $J = 8.7$ Hz, 4 H), 6.47 (d, $J = 2$ Hz, 2 H), 6.25 (d, $J = 2$ Hz, 2 H), 4.70 (s, 4 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 175.83, 163.85,

160.64, 156.12, 149.07, 146.53, 146.18, 135.77, 128.58, 121.91, 115.76, 113.58, 103.0, 98.16, 93.57, 68.38. ESI-MS calculated for $C_{34}H_{24}O_{14} [(M+Na)]^+$, m/z 679.55, found $[(M+H)]^+$, m/z 657.124.

14a. 1H NMR (DMSO- d_6 , 400 MHz): 10.69 (bs, 3 H), 9.53-8.7 (bs, 6 H), 7.83 (d, $J = 0.1$ Hz, 1 H), 7.70-7.64 (m, 3 H), 7.49 (d, $J = 9.0$ Hz, 2 H), 6.98 (d, $J = 8.6$ Hz, 1 H), 6.87 (d, $J = 8.5$ Hz, 2 H), 6.59 (d, $J = 1.9$ Hz, 1 H), 6.51-6.44 (m, 5H), 4.45-4.40 (m, 8 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 170.92, 170.81, 162.38, 162.34, 159.47, 157.94, 157.89, 148.61, 146.95, 146.26, 145.04, 141.98, 141.92, 141.63, 137.24, 137.24, 137.12, 137.09, 127.99, 125.47, 122.42, 121.49, 119.11, 115.58, 114.51, 113.50, 105.52, 105.44, 97.71, 95.20, 95.10, 67.84, 67.72, 59.69. ESI-MS calculated for $C_{49}H_{34}O_{21} [(M+H)]^+$, m/z 958.16, found $[(M+H)]^+$, m/z 958.187.

15a. 1H NMR (DMSO- d_6 , 400 MHz): 10.65 (bs, 3 H), 9.54-8.9 (bs, 6 H), 7.75 (d, $J = 0.4$ Hz, 1 H), 7.72-7.66 (m, 3 H), 7.5 (d, $J = 8.9$ Hz, 2 H), 6.96 (d, $J = 8.7$ Hz, 1 H), 6.88 (d, $J = 8.6$ Hz, 2 H), 6.58 (d, $J = 1.7$ Hz, 1 H), 6.52-6.43 (m, 5H), 4.48-4.37 (m, 8 H), 2.39-2.27 (m, 4 H). ^{13}C NMR (DMSO- d_6 , 400 MHz): 171.92, 170.61, 162.37, 161.35, 158.47, 157.93, 157.85, 148.81, 147.85, 146.28, 144.04, 142.97, 141.98, 142.68, 137.28, 137.26, 137.13, 137.09, 126.98, 125.45, 122.35, 122.09, 119.19, 114.98, 114.48, 113.25, 105.35, 105.09, 97.61, 95.52, 95.23, 67.74, 67.62, 59.80, 29.13. ESI-MS calculated for $C_{51}H_{38}O_{21} [(M+H)]^+$, m/z 987.19, found $[(M+H)]^+$, m/z 987.462.

General Procedure for Synthesis of Sulfated Flavonoid Dimers and Trimers. Sulfation of phenolic precursors was achieved using microwave-assisted chemical sulfation as described earlier. Briefly, to a stirred solution of polyphenol in anhydrous CH_3CN (1–5 mL) at room temperature, Et_3N (10 equiv per $-OH$ group) and Me_3N/SO_3 complex (6 equiv per $-OH$) were added. The reaction vessel was sealed and microwaved (CEM Discover, Cary, NC) for 4 to 6 h at 90 °C. The reaction mixture was cooled and transferred to a roundbottom flask, and the volume was reduced as much as possible under low pressure conditions at 25 °C. The reaction mixture was then directly loaded on to a flash chromatography column and purified using a dichloromethane and methanol solvent system (5–30%) to obtain the sulfated flavonoid dimers and trimers. The samples were concentrated and reloaded onto a SP Sephadex C-25 column for sodium exchange. Appropriate fractions were pooled, concentrated in vacuo, and lyophilized to obtain a white powder. Spectral characteristics of all the sulfated compounds G-2.1–G-2.6, G-3.1, G-3.2, G-4.1 and G-4.2, are listed below.

G2.1. 1H NMR (DMSO- d_6 , 400 MHz): 8.19-8.09 (m, 4 H), 7.66 (d, $J = 9$ Hz, 2 H), 7.1 (d, $J = 2$ Hz, 2 H), 6.87 (d, $J = 2.0$ Hz, 2 H), 4.55 (s, 4 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 174.14, 158.66, 156.91, 154.16, 146.72, 142.98, 135.13, 124.6, 123.27, 119.90, 118.83, 109.70, 99.78, 68.21. ESI-MS calculated for $C_{32}H_{14}Na_8O_{38}S_8 [(M+Na)]^+$, m/z 1469.87, found $[(M-8Na+8 HxA)+2HxA]^{2+}$, m/z 1142.812.

G2.2. 1H NMR (DMSO- d_6 , 400 MHz): 8.07-7.99 (m, 4 H), 7.56 (d, $J = 9$ Hz, 2 H), 6.98 (d, $J = 1.6$ Hz, 2 H), 6.66 (s, 2 H), 4.2 (s, 4 H), 2.28 (s, 2 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 159.07, 157.02, 146.44, 142.92, 135.31, 124.50, 123.56, 119.81, 109.56, 66.37, 42.41. ESI-MS calculated for $C_{33}H_{16}Na_8O_{38}S_8 [(M+Na)]^+$, m/z 1483.90, found $[(M-8Na+8 HxA)+2HxA]^{2+}$, m/z 1149.085.

G2.3. 1H NMR (DMSO- d_6 , 400 MHz): 7.60 (d, $J = 9$ Hz, 2 H), 7.35 (d, $J = 2$ Hz, 2 H), 7.09-7.06 (m, 4 H), 6.97 (d, $J = 1.8$ Hz, 2 H), 4.55 (s, 4 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 174.62, 158.61, 158.46, 157.47, 156.13, 155.68, 152.14, 136.26, 131.07, 116.34, 113.46, 112.04, 110.35, 101.83, 100.74, 68.65. ESI-MS calculated for $C_{32}H_{14}Na_8O_{38}S_8 [(M+Na)]^+$, m/z 1469.87, found $[(M-8Na+8 HxA)+2HxA]^{2+}$, m/z 1142.588.

G2.4. ^1H NMR (DMSO- d_6 , 400 MHz): 8.15-8.07 (m, 4 H), 7.64 (d, $J = 9$ Hz, 2 H), 7.04 (d, $J = 1.8$ Hz, 2 H), 6.72 (s, 2 H), 4.15 (s, 4 H), 2.11 (s, 4H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 173.0, 159.41, 158.31, 157.01, 153.27, 146.41, 142.92, 135.30, 124.50, 123.59, 119.80, 118.77, 109.42, 100.02, 98.85, 68.81, 25.5. ESI-MS calculated for $\text{C}_{34}\text{H}_{18}\text{Na}_8\text{O}_{38}\text{S}_8[(\text{M}+\text{Na})]^+$, m/z 1497.95, found $[(\text{M}-8\text{Na}+8\text{HxA})+2\text{HxA}]^{2+}$, m/z 1156.367.

G2.5. ^1H NMR (DMSO- d_6 , 400 MHz): 8.14-8.05 (m, 4 H), 7.63 (d, $J = 9$ Hz, 2 H), 7.03 (d, $J = 1.8$ Hz, 2 H), 6.72 (s, 2 H), 4.1 (s, 4 H), 1.94 (s, 4H), 1.74 (s, 2H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 173.6, 159.21, 158.21, 157.01, 153.17, 146.21, 142.52, 135.30, 124.4, 123.95, 119.79, 118.76, 109.45, 100.32, 98.65, 67.81, 25.5, 23.8. ESI-MS calculated for $\text{C}_{35}\text{H}_{20}\text{Na}_8\text{O}_{38}\text{S}_8[(\text{M}+\text{Na})]^+$, m/z 1511.95, found $[(\text{M}-8\text{Na}+8\text{HxA})+2\text{HxA}]^{2+}$, m/z 1163.163.

G2.6. ^1H NMR (DMSO- d_6 , 400 MHz): 8.07(d, $J = 2.2$ Hz, 2 H), 8.0 (d, $J = 6.7$ Hz, 2 H), 6.98 (d, $J = 1.9$ Hz, 2 H), 6.63(d, $J = 1.9$ Hz, 2 H), 6.39 (s, 2H), 4.64 (s, 4 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 173.24, 158.43, 158.25, 157.08, 154.28, 148.43, 143.82, 134.31, 123.50, 123.28, 119.84, 118.78, 108.45, 100.05, 98.87, 75.81. ESI-MS calculated for $\text{C}_{34}\text{H}_{16}\text{Na}_8\text{O}_{38}\text{S}_8[(\text{M}+\text{Na})]^+$, m/z 1495.91, found $[(\text{M}-8\text{Na}+8\text{HxA})+2\text{HxA}]^{2+}$, m/z 1155.620.

G3.1. ^1H NMR (DMSO- d_6 , 400 MHz): 12.33 (s, 2 H), 8.01 (s, 2 H), 7.64-7.56 (m, 4 H), 6.95 (d, $J = 1.9$ Hz, 2 H), 6.58 (d, $J = 2.0$ Hz, 2 H), 4.17 (t, $J = 2.0$ Hz, 4 H), 2.13-2.11 (m, 2 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 177.97, 160.11, 159.60, 155.32, 148.52, 145.74, 133.29, 124.47, 121.16, 119.64, 115.11, 106.08, 101.93, 97.75, 65.50, 52.77. ESI-MS calculated for $\text{C}_{33}\text{H}_{18}\text{Na}_6\text{O}_{32}\text{S}_6[(\text{M}+\text{Na})]^+$, m/z 1279.81, found $[(\text{M}-6\text{Na}+6\text{HxA})+\text{HxA}]^+$, m/z 1833.882.

G3.2. ^1H NMR (DMSO- d_6 , 400 MHz): 12.34 (s, 2H), 8.03(d, $J = 2$ Hz, 2 H), 7.64-7.58 (m, 4 H), 6.92 (d, $J = 1.8$ Hz, 2 H), 6.57 (d, $J = 1.8$ Hz, 2 H), 6.10 (s, 2H), 4.61 (s, 4 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 177.97, 160.14, 159.60, 156.40, 155.30, 148.29, 145.65, 133.35, 128.69, 124.35, 119.46, 114.92, 106.10, 101.96, 97.75, 68.41, 52.78. ESI-MS calculated for $\text{C}_{34}\text{H}_{18}\text{Na}_6\text{O}_{32}\text{S}_6[(\text{M}+\text{Na})]^+$, m/z 1291.82, found $[(\text{M}-6\text{Na}+6\text{HxA})+\text{HxA}]^+$, m/z 1845.498.

G4.1. ^1H NMR (DMSO- d_6 , 400 MHz): 8.18-8.06 (m, 5 H), 7.79-7.63 (m, 4 H), 7.31-7.14 (m, 3 H), 6.92-6.74 (m, 3 H), 4.52 (s, 6 H), 4.42 (s, 2 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 170.92, 170.81, 162.38, 162.34, 159.47, 157.94, 157.89, 148.61, 146.95, 146.26, 145.04, 141.98, 141.92, 141.63, 137.24, 137.12, 137.09, 127.99, 125.47, 122.42, 122.26, 121.49, 119.11, 115.84, 115.58, 114.51, 113.50, 105.52, 105.44, 97.71, 95.20, 95.10, 67.84, 67.72, 59.69. ESI-MS calculated for $\text{C}_{49}\text{H}_{23}\text{Na}_{11}\text{O}_{54}\text{S}_{11}[(\text{M}+\text{Na})]^+$, m/z 2104.28, found $[(\text{M}-11\text{Na}+11\text{HxA})+2\text{HxA}]^{2+}$, m/z 1578.349.

G4.2. ^1H NMR (DMSO- d_6 , 400 MHz): 8.14-8.06 (m, 5 H), 7.68-7.62 (m, 4 H), 7.16-7.05 (m, 3 H), 6.79-6.63 (m, 3 H), 4.32 (s, 6 H), 4.24 (s, 2 H), 2.35-2.27 (m, 4 H). ^{13}C NMR (DMSO- d_6 , 100 MHz): 171.92, 170.29, 162.48, 162.64, 159.67, 157.85, 157.19, 149.81, 145.85, 146.86, 144.04, 140.68, 141.82, 140.73, 137.64, 137.32, 137.19, 127.88, 124.48, 123.41, 122.26, 121.49, 119.11, 115.84, 115.58, 114.51, 113.50, 105.52, 105.44, 97.71, 95.20, 95.10, 66.94, 66.68. ESI-MS calculated for $\text{C}_{49}\text{H}_{23}\text{Na}_{11}\text{O}_{54}\text{S}_{11}[(\text{M}+\text{Na})]^+$, m/z 2132.33, found $[(\text{M}-11\text{Na}+11\text{HxA})+2\text{HxA}]^{2+}$, m/z 1592.727.

Scheme S4. Structures and synthesis of side chains. *a)* BnBr (3-4 eq.) K₂CO₃ (3-4 eq.), DMAP (Cat.), CH₂Cl₂, rt, 24 hrs, 87%. *b)* LiOH.H₂O (5 eq.), CH₃OH, H₂O, rt, 8 hrs, 71%. *c)* BnBr (1.5 eq.), K₂CO₃ (1.5 eq.), DMAP (Cat.), CH₂Cl₂, rt, 4 hrs, 92%. *d)* Oxone[®] (2 eq.), DMF, rt, 24 hrs, 78%.

Scheme S5. Synthesis of *penta*-substituted glycosides. *a)* 5, 6, 7, or 10 (5 eq.), DCC (5 eq.), DMAP (5 eq.), CH₂Cl₂, reflux, 24 hrs, 75%. *b)* H₂ (g) (50 psi), Pd(OH)₂/C (20%), CH₃OH/THF, rt, 6 hrs, 95%. *c)* SO₃-N(CH₃)₃ (5 eq./OH), CH₃CN (2 mL), MW, 90 °C, 8 hrs, 55-70%.

Scheme S6. Synthesis of *tetra* and *tri*-substituted glycosides. *a)* 5 (3-4 eq.), DCC (3-4 eq.), DMAP (3-4 eq.), CH₂Cl₂, reflux, 24 hrs, 80-85%. *b)* H₂ (g) (50 psi), Pd(OH)₂/C (20%), CH₃OH/THF, rt, 6 hrs, 90%. *c)* SO₃-N(CH₃)₃ (5 eq./OH), CH₃CN (2 mL), MW, 90 °C, 8 hrs, 65-72%.

Scheme S7. Synthesis of *di*-substituted glycosides. *a*) **5** (2 eq.), DCC (2 eq.), DMAP (2 eq.), CH₂Cl₂, reflux, 24 hrs, 91%. *b*) H₂ (g) (50 psi), Pd(OH)₂/C (20%), CH₃OH/THF, rt, 8 hrs, 83%. *c*) SO₃-N(CH₃)₃ (5 eq./OH), CH₃CN (2 mL), MW, 90 °C, 8 hrs, 65%.

Scheme S8. Structures and synthesis of substituted inositol derivatives. *a)* **5** (6 eq.), DCC (6 eq.), DMAP (6 eq.), CH_2Cl_2 , reflux, 24 hrs, 70%. *b)* H_2 (g) (50 psi), $\text{Pd}(\text{OH})_2/\text{C}$ (20%), $\text{CH}_3\text{OH}/\text{THF}$, rt, 6 hrs, 90%. *c)* $\text{SO}_3\text{-N}(\text{CH}_3)_3$ (5 eq./OH), CH_3CN (2 mL), MW, 90 °C, 8 hrs, 60-65%.

Synthesis of Sulfated Tetrahydroisoquinolines (THIQs) G10.1–G10.8, Sulfated Glycosides G11.1–G11.7, and Sulfated Inositols G12.1–G12.5.

Polyphenolic 1,2,3,4-tetrahydroisoquinolines (THIQs) were chemically synthesized as reported earlier.^{2,3} Briefly, synthesis of polyphenolic THIQ derivatives was achieved starting from the corresponding aldehydes by Horner–Wadsworth–Emmons reaction, followed by catalytic hydrogen and *N*-Boc deprotection. The resulting amino esters were subjected to formaldehyde/TFA-mediated Pictet–Spengler reaction, EDCI-mediated amidation, and BBr₃-assisted deprotection to afford the desired polyphenolic derivatives as yellowish white solids in yield of >75%.

Polyphenolic glycosides (**13a–c**, **16**, **19**, **22**) and polyphenolic substituted inositols (**27** and **28**) were obtained in two steps, esterification and catalytic hydrogenation. In esterification step, a substituted benzoic acid (4-benzyloxy benzoic acid, 3,5-dibenzyloxy benzoic acid (**5**), 3,4,5-tribenzyloxy benzoic acid (**6**), or 4-benzyloxycarbonyl benzoic acid (**10**)) was treated with DCC and DMAP in anhydrous CH₂Cl₂. The resulting activated acids were further treated with the desired polyalcohols (β -*D*-glucopyranose, α , β -*D*-glucopyranose, 1-*O*-methyl- α -*D*-mannopyranose, 4, 6-*O*-ethylidene- α -*D*-glucopyranose, 4, 6-*O*-benzylidene-1-*O*-methyl- α -*D*-glucopyranoside, myo-inositol, and *D*-(+)-chiro-inositol) and refluxed 24 hrs to afford the corresponding protected esters (**12a–d**, **15**, **18**, **21**, **25**, or **26**) as white solids in yield of 70–91%. In catalytic hydrogenation (deprotection of benzyl group), a solution of benzylated benzoyl derivatives in CH₃OH/THF solvent mixture was hydrogenated over 20% of 10% Pd(OH)₂/C with H₂ (gas) (50 psi) at RT for 6–8 hrs. After purification, the desired polyphenolic intermediates were obtained as yellow–white solids in yield of 83–95%. Importantly, the polyalcohols along with 4-benzyloxy benzoic acid used in the esterification step were commercially available whereas benzoic acid derivatives (**5**, **6**, and **10**) were chemically synthesized. Briefly, benzyl bromide-mediated protection of methyl 3,5-dihydroxy benzoate and methyl 3,4,5-trihydroxy benzoate followed by LiOH-promoted ester hydrolysis afforded intermediates **5** and **6**, respectively, in overall yield of 61–65%. Intermediate **10** was quantitatively obtained in overall yield of about 70% by benzyl bromide treating of 4-formyl benzoic acid in CH₂Cl₂ in presence of K₂CO₃ and catalytic amount of DMAP, followed by Oxone® oxidation in DMF (Scheme 1).

Sulfated molecules were synthesized by microwave-assisted synthesis followed by size exclusion and sodium exchange chromatographies. All sulfated molecules (*penta*-substituted glycosides: **G11.1–G11.3** (Scheme 2), *tetra*-substituted glycoside **G11.5** and *tri*-substituted glycoside **G11.6** (Scheme 3), *di*-substituted glycoside **G11.7** (Scheme 4), and inositol derivatives **G12.1–G12.3**, and **G12.5** (Scheme 5)) were quantitatively obtained in yield of 55–70% as white fluffy powder. Briefly, the polyphenolic precursors (**13a–c**, **16**, **19**, **22**) and trimethylamine–sulfur trioxide (5 equivalents/–OH group) were mixed in anhydrous CH₃CN (2 mL) under nitrogen in microwave tube. The reaction tube was sealed and microwaved for 2–8 at 90–100 °C. Sulfated chlorogenic acid (**G12.5**) was obtained by the same sulfation protocol for its commercially available polyphenolic precursor, chlorogenic acid. The only phosphorylated molecule in this series, sodium phytate (**G12.4**), was commercially available and was used in relation to sulfated myo-inositol (**G12.3**).

Experimental Section

General procedure for benzylation. To a stirring solution of methyl 3,5-dihydroxyl benzoate (**1**), methyl 3,4,5-trihydroxy benzoate (**2**), or 4-formyl benzoic acid (**8**) (1.0 mmol) in anhydrous CH₂Cl₂ (10 mL), K₂CO₃ (1.5–4.0 mmol) and DMAP (cat.) were added at 0 °C. The resulting mixture was kept stirring until it became clear solution. A solution of benzyl bromide (1.5–4.0 mmol) in CH₂Cl₂ was then added dropwise and temperature brought back to RT. The solution was kept stirring

for 4–24 hrs and the reaction was then stopped as TLC indicated the completion of reaction. The organic phase was then diluted (10 mL), washed with HCl (1 N, 15 mL) and brine solution (15 mL). The organic phase was dried over anhydrous Na₂SO₄, concentrated *in vacuo*, and purified by flash chromatography using hexanes/EtOAc mobile phase as described above. 20 mL fractions containing the desired product (**3**, **4**, or **9**) were pooled together and concentrated *in vacuo* to afford the desired products as colorless oil (87–92%).

Methyl 3,5-(dibenzyloxy)benzoate (3). ¹H NMR (CDCl₃, 400 MHz): 7.36–7.30 (m, 7 H), 7.27 (d, 2 H, *J* = 6.68 Hz), 7.23 (s, 2 H), 6.73 (s, 1 H), 5.0 (s, 4 H), 3.83 (s, 3 H). ¹³C NMR (CDCl₃, 100 MHz): 166.75, 159.85, 136.54, 132.13, 128.61, 128.09, 127.54, 108.50, 107.35, 70.35, 52.20. MS (ESI) calculated for C₂₂H₂₀O₄, [M + H]⁺, *m/z* 349.4, found for [M + H]⁺, *m/z* 349.419.

Methyl 3,4,5-(tribenzyloxy)benzoate (4). ¹H NMR (CDCl₃, 400 MHz): 7.41–7.16 (m, 17 H), 5.09 (s, 1H), 5.08 (s, 1 H), 5.05 (s, 3 H), 5.03 (s, 1 H), 3.79 (s, 3 H). ¹³C NMR (CDCl₃, 100 MHz): 166.62, 152.60, 151.12, 149.47, 142.52, 138.61, 137.49, 136.69, 136.36, 128.73, 128.68, 128.59, 128.54, 128.26, 128.18, 128.02, 127.93, 127.69, 127.55, 125.82, 125.25, 110.15, 109.19, 107.01, 75.46, 75.14, 71.29, 71.13, 52.20. MS (ESI) calculated for C₂₉H₂₆O₅, [M + H]⁺, *m/z* 455.52, found for [M + Na]⁺, *m/z* 477.210.

Benzyl 4-formyl benzoate (9). ¹H NMR (CDCl₃, 400 MHz): 10.02 (s, 1 H), 8.15 (d, 2 H, *J* = 8.24 Hz), 7.87 (d, 2 H, *J* = 8.36 Hz), 7.39–7.28 (m, 5 H), 5.32 (s, 2 H). ¹³C NMR (CDCl₃, 100 MHz): 191.50, 165.38, 139.26, 135.58, 135.14, 130.30, 129.48, 129.07, 128.68, 128.61, 128.49, 128.32, 67.31. MS (ESI) calculated for C₁₅H₁₂O₃, [M + H]⁺, *m/z* 241.26, found for [M + Na]⁺, *m/z* 263.24.

Methyl ester hydrolysis. To a stirred solution of methyl ester, methyl 3,4-(dibenzyloxy)benzoate (**3**) or methyl 3,4,5-(tribenzyloxy)benzoate (**4**), (1.0 mmol) in CH₃OH:H₂O (18:2 mL) was added LiOH·H₂O (5.0 mmol) at RT. Water (5 mL) was added after 8 hrs to the reaction mixture which was kept stirring for further 30 min. The reaction mixture was then concentrated *in vacuo* to about 10 mL and acidified by HCl (1 N, 5 mL). The mixture was extracted with EtOAc (2 × 20 mL). The organic extracts were combined, dried over anhydrous Na₂SO₄, filtered, and finally concentrated by rotary evaporation. The corresponding carboxylic acid derivative, 3,5-(dibenzyloxy)benzoic acid (**5**) or 3,4,5-(tribenzyloxy)benzoic acid (**6**), was obtained as yellowish white solid in 70% yield.

3,5-(dibenzyloxy)benzoic acid (5). ¹H NMR (acetone-*d*₆, 400 MHz): 7.53 (s, 2 H), 7.51 (s, 2 H), 7.44–7.35 (m, 4 H), 7.30 (t, 3 H, *J* = 1.36 Hz), 6.95 (s, 1 H), 5.20 (s, 4 H). ¹³C NMR (acetone-*d*₆, 100 MHz): 171.48, 165.25, 142.34, 137.81, 133.62, 133.03, 132.76, 113.70, 111.94, 75.16. MS (ESI) calculated for C₂₁H₁₄O₆, [M + H]⁺, *m/z* 363.34, found for [M + H]⁺, *m/z* 386.086.

3,4,5-(tribenzyloxy)benzoic acid (6). ¹H NMR (acetone-*d*₆, 400 MHz): 7.56 (d, 4 H, *J* = 7.28 Hz), 7.48–7.36 (m, 10 H), 7.30–7.28 (m, 3 H), 5.25 (s, 4 H), 5.16 (s, 2 H), 2.84 (s, br, 1 H). ¹³C NMR (acetone-*d*₆, 100 MHz): 171.38, 157.86, 147.55, 143.18, 142.44, 133.59, 133.46, 133.22, 133.03, 132.90, 132.82, 130.89, 114.28, 79.82, 76.08. MS (ESI) calculated for C₂₈H₂₄O₅, [M + H]⁺, *m/z* 441.5, found for [M + Na]⁺, *m/z* 463.236.

Aldehyde oxidation. To a stirring solution of the aldehyde, benzyl-4-formyl benzoate (**9**), (1 mmol) in DMF (10 mL), Oxone® (2 mmol) was added in one portion and stirred at RT for 12 hrs. After the reaction completion (as indicated by TLC), diluted solution of HCl (1 N, 5 mL) was used to dissolve the salts. The reaction mixture was then diluted with EtOAc (30 mL) and again washed with HCl (1 N, 2 × 10 mL) and brine solution. The organic phase was then dried over anhydrous Na₂SO₄ and EtOAc was removed under reduced pressure. The resulting organic residue was purified by flash

chromatography using hexanes/EtOAc mobile phase as described above. 20 mL fractions containing the desired product, 4-benzyloxycabonyl benzoic acid (**10**), were pooled together and concentrated under reduced pressure to afford the desired product as white solid in 78% yield.

4-Benzyloxycabonyl benzoic acid (10). ^1H NMR (acetone- d_6 , 400 MHz): 8.03 (s, 4 H), 7.39 (d, 2 H, $J = 7.16$ Hz), 7.31–7.23 (m, 3 H). ^{13}C NMR (acetone- d_6 , 100 MHz): 171.88, 166.77, 165.99, 137.19, 135.46, 134.93, 132.13, 130.59, 130.36, 129.42, 129.35, 129.08, 128.98, 67.59. MS (ESI) calculated for $\text{C}_{15}\text{H}_{12}\text{O}_4$, $[\text{M} + \text{H}]^+$, m/z 257.26, found for $[\text{M} + \text{Na}]^+$, m/z 279.24.

General procedure for Esterification of Polyalcohols. To a stirring solution of benzoic acid derivative (**5**, **6**, **7**, or **10**) (1.0 mmol/OH of polyalcohol) and DMAP (1.0 mmol/OH of polyalcohol) in anhydrous CH_2Cl_2 (20 mL), DCC (1.0 mmol/OH of polyalcohol) was added and the resulting mixture was stirred for 30 min at RT. A properly protected saccharide (**11**, **14**, **17**, or **20**) or psudosaccharide (**23** or **24**) (1.0 mmol) was then added and the resulting reaction mixture was refluxed 24 hrs. After that, the reaction was cooled to RT and filtered through a pad of Celite. The organic phase was then washed with HCl (1 M, 15 mL), brine solution (15 mL), and H_2O (15 mL). The organic phase was dried over anhydrous Na_2SO_4 , concentrated *in vacuo*, and purified by flash chromatography using hexanes/EtOAc mobile phase as described above. 20 mL fractions containing the desired product (**12a–d**, **15**, **18**, **21**, **25**, or **26**) were pooled together and concentrated *in vacuo* to afford the desired products as white solid in yield of (70–91%).

1, 2, 3, 4, 6-Penta-O-(3, 4, 5-tri-O-benzylgalloyl)- β -D-glucopyranose (12a). ^1H NMR (CDCl_3 , 400 MHz): 7.38–7.08 (m, 85 H), 6.15 (d, 1 H, $J = 8.12$ Hz), 5.98 (t, 1 H, $J = 9.68$ Hz), 5.78–5.74 (dd, 1 H, $J_1 = 9.80$ Hz, $J_2 = 8.20$ Hz), 5.66 (t, 1 H, $J = 9.64$ Hz), 5.08–4.77 (m, 30 H), 4.71–4.68 (dd, 1 H, $J_1 = 11.68$ Hz, $J_2 = 2.32$ Hz), 4.39–4.35 (m, 1 H), 4.35–4.28 (dd, 1 H, $J_1 = 11.8$ Hz, $J_2 = 5.88$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz): 165.67, 165.61, 165.07, 165.01, 164.22, 152.67, 152.62, 152.54, 143.36, 143.30, 143.23, 142.74, 137.56, 137.38, 136.78, 136.51, 136.46, 136.37, 128.57, 128.55, 128.53, 128.48, 128.46, 128.41, 128.39, 128.31, 128.24, 128.17, 128.13, 128.05, 127.65, 127.60, 127.58, 124.62, 123.75, 123.64, 123.40, 109.56, 109.51, 109.43, 109.31, 109.27, 106.51, 93.08, 75.14, 73.36, 73.30, 71.47, 71.34, 71.26, 71.16, 71.11, 69.88, 63.23. MS (ESI) calculated for $\text{C}_{146}\text{H}_{122}\text{O}_{26}$, $[\text{M} + \text{H}]^+$, m/z 2293.53, found for $[\text{M} + \text{H} - \text{C}_{28}\text{H}_{23}\text{O}_5]^+$, m/z 1852.975.

1,2,3,4,6-Penta-O-(3, 5-di-O-benzyloxybenzoyl)- α,β -D-glucopyranose (12b). ^1H NMR (CDCl_3 , 400 MHz): 7.34–7.09 (m, 60 H), 6.78 (d, 1 H, $J = 3.6$ Hz), 6.70–6.69 (m, 1 H), 6.66–6.64 (m, 2 H), 6.63–6.62 (m, 2 H), 6.20 (t, 1 H, $J = 9.92$ Hz), 5.69 (t, 1 H, $J = 10.12$ Hz), 5.59–5.56 (dd, 1 H, $J_1 = 10.16$ Hz, $J_2 = 3.76$ Hz), 4.95–4.71 (m, 20 H), 4.63–4.59 (m, 1 H), 4.55–4.52 (m, 1 H), 4.37–4.33 (dd, 1 H, $J_1 = 12.36$ Hz, $J_2 = 4.76$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz): 165.72, 165.66, 165.11, 164.95, 164.23, 159.98, 159.88, 159.85, 159.80, 136.58, 136.30, 131.47, 130.89, 130.69, 130.54, 128.63, 128.59, 128.54, 128.14, 128.06, 127.64, 127.59, 127.55, 108.76, 108.71, 108.55, 108.39, 108.19, 107.96, 90.33, 70.91, 70.74, 70.56, 70.34, 70.30, 70.25, 70.17, 69.43, 62.86. MS (ESI) calculated for $\text{C}_{111}\text{H}_{92}\text{O}_{21}$, $[\text{M} + \text{H}]^+$, m/z 1761.91, found for $[\text{M} + \text{Na}]^+$, m/z 1784.975.

1,2,3,4,6-Penta-O-(4-O-benzyloxybenzoyl)- α,β -D-glucopyranose (12c). ^1H NMR (CDCl_3 , 400 MHz): 7.99–7.96 (dd, 4 H, $J_1 = 6.88$ Hz, $J_2 = 1.6$ Hz), 7.87–7.64 (dd, 4 H, $J_1 = 8.84$ Hz, $J_2 = 3.88$ Hz), 7.82 (d, 2 H, $J = 8.8$ Hz), 7.41–7.32 (m, 25 H), 6.96 (s, 2 H), 6.94 (s, 2 H), 6.90–6.83 (m, 6 H), 6.22 (d, 1 H, $J = 8.0$ Hz), 5.94 (t, 1 H, $J = 9.44$ Hz), 5.78–5.71 (m, 2 H), 5.10 (s, 2 H), 5.09 (s, 2 H), 5.07 (s, 2 H), 5.04 (s, 2 H), 5.03 (s, 2 H), 4.62–4.59 (dd, 1 H, $J_1 = 12.32$ Hz, $J_2 = 2.84$ Hz), 4.46–4.43 (dd, 1 H, $J_1 = 7.36$ Hz, $J_2 = 4.88$ Hz), 4.35–4.31 (m, 1 H). ^{13}C NMR (CDCl_3 , 100 MHz): 165.77, 165.29, 164.77, 164.75, 164.25, 163.20, 162.94, 162.88, 162.80, 162.64, 136.37, 136.23, 136.19, 136.15, 132.40,

132.02, 131.98, 131.92, 129.09, 128.66, 128.10, 127.47, 127.41, 127.34, 122.39, 121.54, 121.49, 121.22, 114.78, 114.68, 114.57, 114.54, 114.47, 92.69, 73.30, 72.72, 70.80, 70.15, 70.12, 69.07, 62.68. MS (ESI) calculated for $C_{76}H_{62}O_{16}$, $[M + H]^+$, m/z 1232.30, found for $[M + Na]^+$, m/z 1254.484.

1,2,3,4,6-Penta-O-(4-O-benzyloxycarbonybenzoyl)- α,β -D-glucopyranose (12d). 1H NMR ($CDCl_3$, 400 MHz): 8.23–7.88 (m, 20 H), 7.59–7.29 (m, 25 H), 6.85 (d, 1 H, $J = 8.0$ Hz), 6.26 (t, 1 H, $J = 8.84$ Hz), 5.84 (t, 1 H, $J = 10.04$ Hz), 5.70–5.67 (m, 1 H), 5.42 (s, 1 H), 5.39 (s, 3 H), 5.35 (s, 2 H), 5.32 (s, 4 H), 4.67–4.63 (m, 2 H), 4.53–4.51 (m, 1 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 165.48, 165.24, 165.18, 165.03, 164.42, 164.34, 163.56, 135.72, 135.60, 135.09, 134.72, 134.66, 134.59, 134.30, 133.24, 132.49, 132.22, 132.17, 132.09, 131.90, 130.13, 129.95, 129.92, 129.74, 128.71, 128.66, 128.50, 128.41, 128.28, 128.24, 126.48, 90.29, 70.74, 70.58, 70.47, 68.97, 67.33, 67.14, 67.07. MS (ESI) calculated for $C_{81}H_{62}O_{21}$, $[M + H]^+$, m/z 1371.35, found for $[M + Na]^+$, m/z 1394.529.

2,3,4,6-Tetra-O-(3, 5-di-O-benzyloxybenzoyl)-1-O-methyl- α -D-mannopyranose (15). 1H NMR ($CDCl_3$, 400 MHz): 1H NMR ($CDCl_3$, 400 MHz): 7.26–7.02 (m, 48 H), 6.63–6.57 (m, 4 H), 5.88 (dt, 1 H, $J_1 = 9.96$ Hz, $J_2 = 2.32$ Hz), 5.80 (dd, 1 H, $J_1 = 10.04$ Hz, $J_2 = 2.44$ Hz), 5.63 (d, 1 H, $J = 1.4$ Hz), 4.99–4.61 (m, 20 H), 4.54–4.51 (m, 2 H), 4.39–4.37 (m, 1 H), 3.45 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 165.83, 165.36, 165.10, 159.93, 159.85, 159.73, 136.51, 136.44, 136.39, 136.34, 131.63, 131.21, 131.08, 130.99, 128.64, 128.55, 128.49, 128.09, 128.01, 127.69, 127.62, 127.48, 127.41, 108.95, 108.62, 108.53, 108.40, 108.24, 108.05, 107.81, 107.62, 98.75, 70.85, 70.31, 70.13, 68.61, 68.08, 64.0, 55.50. MS (ESI) calculated for $C_{91}H_{78}O_{18}$, $[M + H]^+$, m/z 1460.59, found for $[M + Na]^+$, m/z 1482.763.

1,2,3-Tri-O-(3, 5-di-O-benzyloxybenzoyl)-4,6-O-ethylidene- α -D-glucopyranose (18). 1H NMR ($CDCl_3$, 400 MHz): 7.34–7.19 (m, 32 H), 7.18–7.16 (m, 2 H), 7.08 (d, 1 H, $J = 2.28$ Hz), 7.04 (d, 1 H, $J = 2.28$ Hz), 6.71–6.60 (m, 3.5 H), 6.03–5.41 (m, 2.5 H), 4.98–4.88 (m, 8 H), 4.84 (s, 2 H), 4.75–4.65 (m, 3 H), 4.26–3.69 (m, 3 H), 3.59–3.52 (m, 1 H), 1.30–1.26 (dd, 3 H, $J_1 = 13.28$ Hz, $J_2 = 4.96$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): 165.39, 165.28, 165.10, 164.31, 159.93, 159.89, 159.84, 159.81, 159.77, 136.42, 136.41, 136.37, 136.36, 136.31, 131.43, 131.28, 130.77, 130.69, 130.53, 130.36, 128.70, 128.61, 128.57, 128.53, 128.13, 128.10, 128.08, 127.69, 127.61, 127.44, 127.30, 108.75, 108.62, 108.49, 108.31, 108.21, 107.88, 107.53, 107.43, 100.08, 99.98, 93.32, 90.68, 78.32, 78.15, 72.14, 71.83, 71.05, 70.35, 70.30, 70.14, 70.01, 68.09, 67.96, 67.48, 65.44, 20.29, 20.23. MS (ESI) calculated for $C_{71}H_{62}O_{15}$, $[M + H]^+$, m/z 1155.24, found for $[M + Na]^+$, m/z 1178.652.

2,3-Di-O-(3, 5-di-O-benzyloxybenzoyl)-4,6-O-benzylidene-1-O-methyl- α -D-glucopyranoside (21). 1H NMR ($CDCl_3$, 400 MHz): 7.20–7.40 (m, 29 H), 6.67 (s, 1 H), 6.64 (s, 1 H), 5.96 (t, 1 H, $J = 9.8$ Hz), 5.48 (s, 1 H), 5.15 (d, 1 H, $J = 3.64$ Hz), 5.05 (dd, 1 H, $J_1 = 9.88$ Hz, $J_2 = 3.64$ Hz), 5.05–4.8 (m, 8 H), 4.29 (dd, 1 H, $J_1 = 10.24$ Hz, $J_2 = 4.8$ Hz), 4.02–3.96 (m, 1 H), 3.79 (dd, 2 H, $J_1 = 20.08$ Hz, $J_2 = 9.72$ Hz), 3.36 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 165.76, 165.43, 159.86, 159.82, 136.97, 136.48, 136.40, 131.68, 131.03, 129.03, 128.61, 128.57, 128.19, 128.1, 127.66, 127.6, 126.25, 126.20, 108.70, 108.58, 108.30, 107.24, 101.69, 97.85, 79.27, 73.13, 70.32, 69.87, 68.97, 62.65, 55.59. MS (ESI) calculated for $C_{56}H_{50}O_{16}$, $[M + H]^+$, m/z 916.0, found for $[M + Na]^+$, m/z 937.401.

1,2,3,4,5,6-Hexa-O-(3,5-di-O-benzyloxybenzoyl)-myo-inositol (25). 1H NMR ($CDCl_3$, 400 MHz): 7.39 (d, 2 H, $J = 1.84$ Hz), 7.30–7.13 (m, 62 H), 7.09 (d, 4 H, $J = 2$ Hz), 7.07 (d, 4 H, $J = 2$ Hz), 6.66–6.59 (m, 6 H), 6.35 (t, 2 H, $J = 10.28$ Hz), 6.28 (t, 1 H, $J = 2.24$ Hz), 5.97 (t, 1 H, $J = 10.12$ Hz), 5.78 (t, 1 H, $J = 2.12$ Hz), 5.75 (t, 1 H, $J = 2.24$ Hz), 4.95 (s, 2 H), 4.90 (s, 4 H), 4.82 (s, 7 H), 4.76 (s, 4 H), 4.73 (dd, 7 H, $J_1 = 16.92$ Hz, $J_2 = 11.4$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): 165.61, 165.4, 164.91, 160.07, 159.87, 159.84, 159.80, 136.50, 136.43, 136.36, 131.06, 130.81, 130.79, 130.57, 128.65,

128.60, 128.58, 128.53, 128.13, 128.1, 128.06, 127.69, 127.63, 127.60, 127.44, 108.68, 108.64, 108.57, 108.41, 108.12, 108.09, 70.61, 70.32, 70.28, 70.19, 70.13, 69.90. MS (ESI) calculated for $C_{132}H_{108}O_{24}$, $[M + H]^+$, m/z 2079.26, found for $[M + H - C_{21}H_{17}O_4]^+$, m/z 1744.999.

1,2,3,4,5,6-Hexa-O-(3,5-di-O-benzyloxybenzoyl)-D-(+)-chiro-inositol (26). 1H NMR ($CDCl_3$, 400 MHz): 7.35 & 7.32 (s & s, 12 H), 7.26–7.07 (m, 60 H), 6.70 (s, 2 H), 6.60 (t, 4 H, $J = 1$ Hz), 6.27 (d, 2 H, $J = 6.48$ Hz), 6.03 (s, 2 H), 5.95 (d, 2 H, $J = 7.44$ Hz), 4.97 (s, 8 H), 4.78 (s, 8 H), 4.74–4.67 (dd, 8 H, $J_1 = 19.8$ Hz, $J_2 = 11.32$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): 165.61, 164.92, 164.79, 160.05, 159.86, 159.82, 136.43, 136.33, 130.95, 130.73, 128.67, 128.55, 128.38, 128.33, 128.15, 128.08, 127.89, 127.83, 127.70, 127.64, 127.45, 108.81, 108.56, 108.52, 108.34, 107.98, 105.62, 70.53, 70.51, 70.39, 70.30, 70.15, 68.91. MS (ESI) calculated for $C_{132}H_{108}O_{24}$, $[M + H]^+$, m/z 2079.26, found for $[M + H - C_{21}H_{17}O_4]^+$, m/z 1744.740.

General Procedure for Catalytic Hydrogenation (Debenzylation). A solution of benzylated benzoyl derivatives of saccharides and pseudosaccharides (**12a–d**, **15**, **18**, **21**, **25**, or **26**) in CH_3OH/THF solvent mixture (15 mL) was hydrogenated over 20% of 10% $Pd(OH)_2/C$ with H_2 (gas) (50 psi) at RT for 6–8 hrs. The $Pd(OH)_2/C$ catalyst was then removed by filtration over Celite and the resulting filtrate was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. A flash chromatography using hexanes/EtOAc mixture as a mobile phase was utilized to purify the reaction crude to afford the desired polyphenolic intermediates (**13a–c**, **16**, **19**, **22**, **27**, or **28**) and carboxylated final product (**G11.4**) as yellow–white solid in yield of (83–95%).

1,2,3,4,6-O-Pentagalloyl- β -D-glucopyranose (13a). 1H NMR (acetone- d_6 , 400 MHz): 8.32–7.98 (m, br, 15 H, phenolic–OH), 7.18 (s, 2 H), 7.12 (s, 2 H), 7.06 (s, 2 H), 7.02 (s, 2 H), 6.97 (s, 2 H), 6.33 (d, 1 H, $J = 8.32$ Hz), 6.01 (t, 1 H, $J = 9.68$ Hz), 5.68–5.59 (m, 2 H), 4.56–4.52 (m, 2 H), 4.43–4.39 (dd, 1 H, $J_1 = 12.68$ Hz, $J_2 = 4.68$ Hz). ^{13}C NMR (acetone- d_6 , 100 MHz): 166.40, 165.92, 165.70, 165.65, 164.98, 146.18, 146.06, 146.02, 145.98, 145.90, 139.81, 139.32, 139.04, 121.52, 120.75, 120.65, 120.04, 110.46, 110.36, 110.25, 110.20, 93.39, 74.03, 73.37, 71.82, 69.38, 62.86. MS (ESI) calculated for $C_{41}H_{32}O_{26}$, $[M + H]^+$, m/z 941.69, found for $[M + Na]^+$, m/z 963.157.

1,2,3,4,6-Penta-O-(3, 5-dihydroxybenzoyl)- α,β -D-glucopyranose (13b). 1H NMR (acetone- d_6 , 400 MHz): 8.5 (s, br, 20 H, phenolic–OH), 7.03 (d, 1 H, $J = 2.08$ Hz), 6.95 (d, 1 H, $J = 2.08$ Hz), 6.94 (d, 1 H, $J = 2.16$ Hz), 6.87 (d, 1 H, $J = 2.08$ Hz), 6.82 (d, 1 H, $J = 2.12$ Hz), 6.81 (d, 1 H, $J = 2.16$ Hz), 6.76–6.75 (m, 3 H), 6.73 (d, 1 H, $J = 2.12$ Hz), 6.69–6.29 (d & t & t & d, 2 H, $J = 3.52$ Hz & $J = 1.88$ Hz & $J = 2.08$ Hz & $J = 8.28$ Hz), 6.47–6.44 (m, 1 H), 6.42 (s, 1 H), 6.37 (s, 1 H), 6.35 (d, 1 H, $J = 1.8$ Hz), 6.10 & 5.97 (t & t, 1 H, $J = 10.04$ Hz & $J = 9.68$ Hz), 5.75 (t & m & dd, 2 H, $J = 10.04$ Hz & $J_1 = 10.28$ Hz, $J_2 = 3.64$ Hz), 4.66–4.51 (m, 1 H), 4.47–4.37 (m, 2 H). ^{13}C NMR (acetone- d_6 , 100 MHz): 166.50, 166.30, 166.10, 166.03, 165.81, 165.75, 165.06, 159.75, 159.64, 159.49, 159.46, 159.42, 159.39, 132.75, 132.72, 131.97, 131.94, 131.91, 131.86, 131.55, 131.34, 125.42, 109.16, 109.16, 109.08, 109.0, 108.91, 108.86, 108.75, 108.66, 108.41, 93.51, 90.69, 73.89, 73.7, 72.07, 71.59, 71.57, 71.24, 69.62, 69.25, 63.06, 62.86. MS (ESI) calculated for $C_{41}H_{32}O_{21}$, $[M + H]^+$, m/z 861.69, found for $[M + Na]^+$, m/z 883.225.

1,2,3,4,6-Penta-O-(4-hydroxybenzoyl)- α,β -D-glucopyranose (13c). 1H NMR (acetone- d_6 , 400 MHz): 8.15–7.80 (m, 10 H), 7.07–6.81 (m, 10 H), 6.51 (d, 1 H, $J = 8.08$ Hz), 6.37 & 5.95 (t & t, 1 H, $J = 10$ Hz & $J = 10.04$ Hz), 6.20 & 5.88 (t & t, 1 H, $J = 9.48$ Hz, $J = 9.64$ Hz), 5.86–5.82 & 5.74–5.71 (dt & dd, 1 H, $J_1 = 8.2$ Hz, $J_2 = 1.3$ Hz & $J_1 = 10.24$ Hz, $J_2 = 3.76$ Hz), 4.89–4.64 (m, 2 H), 4.56 & 4.55–4.52 (t & dd, 1 H, $J = 4.4$ Hz, $J_1 = 8.04$ Hz, $J_2 = 3.8$ Hz). ^{13}C NMR (acetone- d_6 , 100 MHz): 166.42, 166.0, 165.69, 164.96, 163.62, 163.56, 163.22, 163.19, 163.17, 163.13, 163.03, 163.02, 162.86, 133.16,

132.97, 132.94, 132.82, 132.78, 122.07, 121.41, 121.35, 121.33, 121.29, 121.02, 120.77, 116.58, 116.42, 116.37, 116.2, 116.12, 93.56, 90.7, 73.94, 73.62, 71.97, 71.66, 71.53, 71.32, 70.06, 69.66, 63.37, 63.24. MS (ESI) calculated for $C_{41}H_{32}O_{16}$, $[M + H]^+$, m/z 781.69, found for $[M + Na]^+$, m/z 803.223.

1,2,3,4,6-Penta-O-(4-carboxybenzoyl)- α , β -D-glucopyranose (G11.4). 1H NMR (acetone- d_6 , 400 MHz): 8.29 (d, 2 H, $J = 8.36$ Hz), 8.22 (d, 2 H, $J = 8.16$ Hz), 8.10–7.92 (m, 16 H), 6.96 (d, 1 H, $J = 3.68$ Hz), 6.38 (t, 1 H, $J = 9.84$ Hz), 6.03 (t, 1 H, $J = 9.84$ Hz), 5.91 (dd, 1 H, $J_1 = 9.96$ Hz, $J_2 = 2.76$ Hz), 4.95–4.89 (m, 1 H), 4.7–4.65 (m, 2 H). ^{13}C NMR (acetone- d_6 , 100 MHz): 166.73, 166.58, 166.02, 165.90, 165.29, 134.49, 133.53, 131.16, 131.03, 130.84, 130.80, 130.78, 130.72, 130.70, 130.66, 130.63, 91.84, 72.64, 72.21, 71.78, 70.61, 64.07. MS (ESI) calculated for $C_{46}H_{32}O_{21}$, $[M + H]^+$, m/z 921.74, found for $[M + Na]^+$, m/z 943.248.

2,3,4,6-Tetra-O-(3, 5-dihydroxybenzoyl)-1-O-methyl- α -D-mannopyranose (16). 1H NMR (acetone- d_6 , 400 MHz): 8.51–8.40 (br, 8 H, phenolic–OH), 6.96 (d, 2 H, $J = 2.24$ Hz), 6.94 (d, 2 H, $J = 2.24$ Hz), 6.84 (d, 2 H, $J = 2.24$ Hz), 6.73 (d, 2 H, $J = 2.24$ Hz), 6.49 (t, 1 H, $J = 2.24$ Hz), 6.47 (t, 1 H, $J = 2.24$ Hz), 6.40 (t, 1 H, $J = 2.24$ Hz), 6.34 (t, 1 H, $J = 2.24$ Hz), 5.66 (t, 1 H, $J = 10.2$ Hz), 5.63 (dd, 1 H, $J_1 = 9.92$ Hz, $J_2 = 3.36$ Hz), 5.51 (dd, 1 H, $J_1 = 2.8$ Hz, $J_2 = 1.8$ Hz), 4.90 (d, 1 H, $J = 1.56$ Hz), 4.39 (dd, 1 H, $J_1 = 7.28$ Hz, $J_2 = 1.76$ Hz), 4.36–4.33 (m, 2 H), 3.43 (s, 3 H). ^{13}C NMR (acetone- d_6 , 100 MHz): 166.52, 166.06, 165.96, 165.79, 159.56, 159.47, 159.45, 159.38, 132.81, 132.24, 132.02, 131.97, 109.05, 108.97, 108.88, 108.83, 108.73, 108.63, 108.52, 108.33, 99.99, 71.09, 70.86, 69.68, 67.81, 64.44, 55.61. MS (ESI) calculated for $C_{35}H_{30}O_{18}$, $[M + H]^+$, m/z 739.61, found for $[M + Na]^+$, m/z 761.077.

1,2,3-Tri-O-(3, 5-dihydroxybenzoyl)-4, 6-O-ethylidene- α -D-glucopyranose (19). 1H NMR (acetone- d_6 , 400 MHz): 8.5 (s, br, 6 H, phenolic–OH), 6.99 (d, 1 H, $J = 2.28$ Hz), 6.87 (d, 1 H, $J = 2.76$ Hz), 6.85 (d, 1 H, $J = 2.6$ Hz), 6.83 (d, 1 H, $J = 2.84$ Hz), 6.74 (d, 1 H, $J = 2.24$ Hz), 6.72 (d, 1 H, $J = 2.28$ Hz), 6.55 & 6.14 (d & d, 1 H, $J = 3.76$ Hz & $J = 8.12$ Hz), 6.52 & 6.46 (t & t, 1 H, $J = 2.28$ Hz & $J = 2.28$ Hz), 6.43 (dd, 1 H, $J_1 = 4.56$ Hz, $J_2 = 2.28$ Hz), 6.36 (dd, 1 H, $J_1 = 4.60$ Hz, $J_2 = 2.28$ Hz), 5.82 & 5.68 (t & t, 1 H, $J = 9.88$ Hz & $J = 9.32$ Hz), 5.46–5.33 (m, 1 H), 4.76–4.71 (m, 1 H), 4.10–4.01 (m, 1 H), 3.95–3.88 (m, 1 H), 3.80–3.75 (m, 1 H), 3.57 (m, 1 H), 1.13–1.10 (dd, 3 H, $J_1 = 6.92$ Hz, $J_2 = 5.08$ Hz). ^{13}C NMR (acetone- d_6 , 100 MHz): 166.10, 165.97, 165.89, 165.71, 164.93, 164.88, 159.77, 159.60, 159.43, 132.44, 132.40, 131.92, 131.81, 131.51, 131.43, 109.03, 108.98, 108.92, 108.85, 108.73, 108.57, 108.42, 108.37, 100.51, 100.33, 93.75, 90.97, 78.80, 78.76, 72.79, 72.54, 71.84, 70.24, 68.44, 68.36, 67.94, 66.63, 20.83, 20.58. MS (ESI) calculated for $C_{29}H_{26}O_{15}$, $[M + H]^+$, m/z 615.52, found for $[M + Na]^+$, m/z 637.128.

2,3-Di-O-(3, 5-dihydroxybenzoyl)-1-O-methyl- α -D-glucopyranoside (22). 1H NMR (acetone- d_6 , 400 MHz): 8.8–8.2 (s, br, 2 H, phenolic –OH), 6.90 (dd, 4 H, $J_1 = 9.0$ Hz, $J_2 = 2.28$ Hz), 6.57–6.54 (m, 2 H), 5.76 (t, 2 H, $J = 9.2$ Hz), 5.07 (dd, 1 H, $J_1 = 12.4$ Hz, $J_2 = 3.56$ Hz), 3.97–3.68 (m, 5 H), 3.44 (s, 3 H). ^{13}C NMR (acetone- d_6 , 100 MHz): 166.45, 166.29, 159.35, 159.31, 159.22, 133.14, 132.26, 108.91, 108.87, 108.37, 107.93, 97.91, 74.13, 73.33, 72.88, 69.60, 62.12, 55.39. MS (ESI) calculated for $C_{21}H_{22}O_{12}$, $[M + H]^+$, m/z 467.4, found for $[M + Na]^+$, m/z 467.175.

1,2,3,4,5,6-Hexa-O-(3,5-dihydroxybenzoyl)-myo-inositol (27). 1H NMR (acetone- d_6 , 400 MHz): 8.75–8.40 (br, 12 H, phenolic–OH), 7.02 (d, 2 H, $J = 1.84$ Hz), 6.79–6.74 (m, 10 H), 6.60 (s, 1 H), 6.41 (s, 5 H), 6.21 (t, 1 H, $J = 2.72$ Hz), 6.18–6.10 (m, 3 H), 5.92–5.89 (dd, 2 H, $J_1 = 9.32$ Hz, $J_2 = 1.72$ Hz). ^{13}C NMR (acetone- d_6 , 100 MHz): 166.15, 166.02, 165.89, 159.67, 159.35, 159.29, 131.96, 131.93, 131.87, 131.66, 129.39, 129.33, 129.28, 128.77, 128.70, 128.61, 108.97, 108.84, 108.67, 108.55, 71.71,

71.08, 70.88, 70.80, 70.63, 69.74. MS (ESI) calculated for $C_{48}H_{36}O_{24}$, $[M + H]^+$, m/z 997.79, found for $[M + H]^+$, m/z 1019.250.

1,2,3,4,5,6-Hexa-O-(3,5-dihydroxybenzoyl)-D-(+)-chiro-inositol (28). 1H NMR (acetone- d_6 , 400 MHz): 8.73 (s, 4 H, phenolic-OH), 8.46 & 8.44 (s & s, 8 H, phenolic-OH), 7.21 (d, 4 H, $J = 2.12$ Hz), 6.92 (d, 4 H, $J = 2.12$ Hz), 6.88 (d, 4 H, $J = 2.12$ Hz), 6.72 (d, 2 H, $J = 2.04$ Hz), 6.52–6.50 (m, 4 H), 6.29–6.26 (m, 2 H), 6.09–6.08 (m, 2 H), 5.98–5.95 (m, 2 H). ^{13}C NMR (acetone- d_6 , 100 MHz): 166.02, 165.94, 165.28, 159.78, 159.40, 131.87, 131.73, 1329.40, 129.32, 129.27, 128.77, 128.64, 128.59, 109.14, 109.06, 108.87, 108.71, 108.60, 71.20, 70.75, 69.18. MS (ESI) calculated for $C_{48}H_{36}O_{24}$, $[M + H]^+$, m/z 997.79, found for $[M + Na]^+$, m/z 1019.259.

General Procedure for Microwave-Assisted Sulfation. To a stirring solution of polyphenolic intermediate (**13a–c**, **16**, **19**, **22**, **27**, or **28**) (1.0 mmol) in anhydrous CH_3CN (2 mL), the sulfating reagent, $N(CH_3)_3-SO_3$ complex (5 mmol/OH), was added. The resulting mixture was then microwaved at 90 °C for 8 hrs. The resulting crude product was cooled to RT and concentrated *in vacuo* at temperature less than 35 °C. All resulting polysulfated molecules were purified as described above using the size exclusion chromatography (G-10). The sodium salt form of the isolated white fluffy powder of sulfated species (**G11.1–G11.3**, **G11.5–G11.7**, **G12.1–G12.3**) was generated by the sodium exchange chromatography as described above in yield of (55–70%).

Sodium 1,2,3,4,6-penta-O-(3, 5-di-O-sulfonato-benzoyl)- β -D-glucopyranose (G11.2). 1H NMR (D_2O , 400 MHz): 7.38 (d, 2 H, $J = 1.92$ Hz), 7.36 (d, 2 H, $J = 1.96$ Hz), 7.32–7.27 (m, 9 H), 7.24 (d, 2 H, $J = 1.76$ Hz), 6.45 (d, 1 H, $J = 7.88$ Hz), 6.10 (t, 1 H, $J = 9.28$ Hz), 5.72 (t, 1 H, $J = 8.52$ Hz), 5.55 (t, 1 H, $J = 8.88$ Hz), 4.68 (s, br, 1 H), 4.32 (s, br, 2 H). ^{13}C NMR (D_2O , 100 MHz): 166.19, 165.45, 165.14, 165.01, 164.43, 152.29, 152.0, 131.35, 130.48, 130.32, 120.98, 120.61, 120.54, 120.42, 120.21, 120.11, 93.20, 73.84, 72.48, 71.97, 71.72, 70.09, 63.67. MS (ESI) calculated for $C_{41}H_{22}Na_{11}O_{51}S_{10}$ (sodium sulfates), $[M + Na]^+$, m/z 1904.12 and calculated for $C_{113}H_{214}N_{12}O_{51}S_{10}$ (*n*-hexylammonium sulfates), $[M + (CH_3(CH_2)_5NH_3)_{12}]^{+2}$, m/z 1438.815, found for $[M + (CH_3(CH_2)_5NH_3)_{12}]^{+2}$, m/z 1438.707.

Sodium 1,2,3,4,6-penta-O-(4-O-sulfonato-benzoyl)- α , β -D-glucopyranose (G11.3). 1H NMR (DMSO- d_6 , 400 MHz): 7.91 (d, 2 H, $J = 8.72$ Hz), 7.84 (d, 2 H, $J = 8.8$ Hz), 7.81 (d, 2 H, $J = 8.76$ Hz), 7.75 (d, 2 H, $J = 8.68$ Hz), 7.70 (d, 2 H, $J = 8.68$ Hz), 7.29 (d, 2 H, $J = 8.64$ Hz), 7.26 (d, 2 H, $J = 8.88$ Hz), 7.22 (d, 2 H, $J = 8.8$ Hz), 7.18 (d, 2 H, $J = 8.56$ Hz), 7.15 (d, 2 H, $J = 7.76$ Hz), 6.71 & 6.48 (2 $\times$ d, 1 H, $J = 8.88$ Hz & $J = 8.04$ Hz), 6.13 (d, 1 H, $J = 9.56$ Hz), 5.65 (t, 2 H, $J = 9.4$ Hz), 4.71 (d, 1 H, $J = 5.36$ Hz), 4.49–4.40 (m, br, 2 H). ^{13}C NMR (D_2O , 100 MHz): 167.12, 166.46, 166.17, 165.65, 165.32, 156.0, 155.78, 155.45, 155.15, 132.55, 132.22, 131.67, 131.53, 131.25, 131.14, 125.71, 125.36, 124.38, 121.21, 121.08, 120.28, 120.10, 119.95, 93.44, 74.24, 72.07, 71.63, 69.37, 62.08. MS (ESI) calculated for $C_{41}H_{27}Na_6O_{31}S_5$ (sodium sulfates), $[M + Na]^+$, m/z 1313.9 and calculated for $C_{83}H_{139}N_7O_{31}S_5$ (*n*-hexylammonium sulfates), $[M + (CH_3(CH_2)_5NH_3)_7]^{+1}$, m/z 1789.15 found for $[M + (CH_3(CH_2)_5NH_3)_7]^{+1}$, m/z 1789.078.

Sodium 2,3,4,6-tetra-O-(3,5-di-O-sulfonato-benzoyl)-1-O-methyl- α -D-mannopyranose (G11.5). 1H NMR (D_2O , 400 MHz): 7.91 (d, 2 H, $J = 1.52$ Hz), 7.85 (d, 2 H, $J = 1.20$ Hz), 7.81 (d, 2 H, $J = 1.60$ Hz), 7.65–7.63 (m, 3 H), 7.55–7.51 (m, 3 H), 5.97–5.85 (m, 3 H), 5.21 (br s, 1 H), 4.81–4.75 (m, 3 H), 3.64 (s, 3 H). ^{13}C NMR (D_2O , 100 MHz): 166.32, 165.98, 165.42, 152.53, 152.38, 152.20, 152.09, 152.04, 151.90, 130.91, 130.80, 130.75, 130.49, 120.74, 120.59, 120.45, 120.34, 120.24, 120.18, 120.07, 119.94, 98.41, 71.38, 70.61, 68.71, 68.20, 64.79, 55.77. MS (ESI) calculated for $C_{35}H_{22}Na_9O_{42}S_8$ (sodium sulfates), $[M + Na]^+$, m/z 1577.95 and calculated for $C_{95}H_{182}N_{10}O_{42}S_8$ (*n*-

hexylammonium sulfates), $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_{10}]^{+2}$, m/z 1196.51, found for $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_{10}]^{+2}$, m/z 1196.004.

Sodium 1,2,3-tri-*O*-(3,5-di-*O*-sulfonato-benzoyl)-4,6-*O*-ethylidene- α -D-glucopyranose (G11.6). ^1H NMR (D_2O , 400 MHz): 7.97 (s, 1 H), 7.84 (s, 1 H), 7.82 (s, 1 H), 7.80 (s, 1 H), 7.74 (s, 1 H), 7.65 & 7.53 (br 2 $\times$ s, 3 H), 7.49 & 7.46 (br 2 $\times$ s, 1 H), 6.8 & 6.42 (d & d, 1 H, $J = 3.56$ Hz & $J = 8.83$ Hz), 6.05 & 5.91 (t & t, 1 H, $J = 9.24$ Hz & $J = 9.24$ Hz), 5.84–5.575 (m, 1 H), 5.0–4.99 (t, 1 H, $J = 5.4$ Hz), 4.39–4.35 (m, 1 H), 4.32–4.21 (m, 1 H), 4.06–4.0 (m, 1 H), 3.85–3.80 (m, 1 H), 1.35 (d, 3 H, $J = 4.76$ Hz). ^{13}C NMR (D_2O , 100 MHz): 165.72, 165.61, 165.18, 164.94, 164.68, 164.35, 152.22, 152.12, 152.02, 131.10, 130.93, 130.71, 130.50, 130.43, 130.30, 121.0, 120.48, 120.33, 120.21, 120.15, 120.09, 119.92, 100.43, 93.35, 91.26, 77.27, 77.19, 73.02, 72.89, 71.41, 70.92, 67.48, 67.37, 19.29. MS (ESI) calculated for $\text{C}_{29}\text{H}_{20}\text{Na}_7\text{O}_{33}\text{S}_6$ (sodium sulfates), $[M + \text{Na}]^{+1}$, m/z 1249.77 and calculated for $\text{C}_{71}\text{H}_{132}\text{N}_7\text{O}_{33}\text{S}_6$ (*n*-hexylammonium sulfates), $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_7]^{+1}$, m/z 1804.22, found for $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_7]^{+1}$, m/z 1804.234.

Sodium 2,3-Di-*O*-(3,5-di-*O*-sulfonato-benzoyl)-1-*O*-methyl-4,6-di-*O*-sulfonato- α -D-glucopyranoside (G11.7). ^1H NMR (D_2O , 400 MHz): 7.90 (d, 2 H, $J = 2.04$ Hz), 7.81 (d, 2 H, $J = 1.84$ Hz), 7.62 (s, 1 H), 7.60 (s, 1 H), 6.0 (t, 1 H, $J = 9.76$ Hz), 5.61–5.59 (dd, 1 H, $J_1 = 3.64$ Hz, $J_2 = 10.24$ Hz), 5.39 (d, 1 H, $J = 3.56$ Hz), 4.84 (t, 1 H, $J = 9.24$ Hz), 4.66 (d, 1 H, $J = 9.68$ Hz), 4.42–4.39 (m, 2 H), 3.87 (s, 3 H). ^{13}C NMR (D_2O , 100 MHz): 166.06, 165.42, 152.39, 152.31, 152.11, 152.0, 131.50, 130.84, 120.64, 120.52, 120.32, 120.18, 96.52, 74.20, 72.17, 71.87, 68.39, 67.09, 55.89. MS (ESI) calculated for $\text{C}_{21}\text{H}_{16}\text{Na}_7\text{O}_{30}\text{S}_6$ (sodium sulfates), $[M + \text{Na}]^{+1}$, m/z 1101.65 and calculated for $\text{C}_{63}\text{H}_{128}\text{N}_7\text{O}_{30}\text{S}_6$ (*n*-hexylammonium sulfates), $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_7]^{+1}$, m/z 1656.11, found for $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_7]^{+1}$, m/z 1656.12.

Sodium 1,2,3,4,5,6-Hexa-*O*-(3,5-di-*O*-sulfonato-benzoyl)-myo-inositol (G12.1). ^1H NMR (D_2O , 400 MHz): 7.93 (d, 2 H, $J = 2.12$ Hz), 7.64 (d, 4 H, $J = 2.08$ Hz), 7.62 (d, 1 H, $J = 2.16$ Hz), 7.57 (d, 5 H, $J = 2.2$ Hz), 7.40 (t, 6 H, $J = 1.88$ Hz), 6.41–6.36 (m, 3 H), 6.25 (t, 1 H, $J = 9.8$ Hz), 6.11–6.08 (dd, 2 H, $J_1 = 10.16$ Hz, $J_2 = 2.6$ Hz). ^{13}C NMR (D_2O , 100 MHz): 165.71, 165.29, 165.15, 164.94, 152.28, 151.95, 151.88, 130.33, 130.31, 130.25, 130.19, 120.75, 120.48, 120.35, 120.07, 119.91, 71.75, 71.28, 70.44, 69.89. MS (ESI) calculated for $\text{C}_{48}\text{H}_{24}\text{Na}_{12}\text{O}_{60}\text{S}_{12}$ (sodium sulfates), $[M + \text{Na}]^{+1}$, m/z 2244.32 and calculated for $\text{C}_{132}\text{H}_{248}\text{N}_{14}\text{O}_{60}\text{S}_{12}$ (*n*-hexylammonium sulfates), $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_{14}]^{+2}$, m/z 1688.11, found for $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_{14}]^{+2}$, m/z 1688.13.

Sodium 1,2,3,4,5,6-Hexa-*O*-(3,5-di-*O*-sulfonato-benzoyl)-D-(+)-chiro-inositol (G12.2). ^1H NMR (D_2O , 400 MHz): 8.04 (d, 4 H, $J = 2.08$ Hz), 7.74 (d, 5 H, $J = 2.16$ Hz), 7.69 (d, 5 H, $J = 2.16$ Hz), 7.51 (d, 4 H, $J = 2.44$ Hz), 6.43 (d, 2 H, $J = 7.12$ Hz), 6.29–6.27 (d, br, 4 H, $J = 6.32$ Hz). ^{13}C NMR (D_2O , 100 MHz): 166.02, 165.48, 165.15, 165.05, 152.27, 152.07, 151.98, 130.59, 130.52, 130.45, 130.26, 129.0, 128.91, 128.64, 128.55, 128.06, 127.81, 120.71, 120.64, 120.58, 120.20, 120.04, 71.17, 71.10, 69.03. MS (ESI) calculated for $\text{C}_{48}\text{H}_{24}\text{Na}_{12}\text{O}_{60}\text{S}_{12}$ (sodium sulfates), $[M + \text{Na}]^{+1}$, m/z 2244.32 and calculated for $\text{C}_{132}\text{H}_{248}\text{N}_{14}\text{O}_{60}\text{S}_{12}$ (*n*-hexylammonium sulfates), $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_{14}]^{+2}$, m/z 1688.11, found for $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_{14}]^{+2}$, m/z 1688.125.

Sodium 1,2,3,4,5,6-Hexa-*O*-sulfonato-myoinositol (G12.3). ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): 5.0 (br s, 2 H), 4.77 (br s, 2 H), 4.59 (br s, 1 H), 4.50 (br s, 1 H). ^{13}C NMR (D_2O , 100 MHz): 74.71, 73.74. MS (ESI) calculated for $\text{C}_6\text{H}_6\text{Na}_7\text{O}_{24}\text{S}_6$ (sodium sulfates), $[M + \text{Na}]^{+1}$, m/z 815.42 and calculated for $\text{C}_{48}\text{H}_{118}\text{N}_7\text{O}_{24}\text{S}_6$ (*n*-hexylammonium sulfates), $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_7]^{+1}$, m/z 1368.66, found for $[M + (\text{CH}_3(\text{CH}_2)_5\text{NH}_3)_7]^{+1}$, m/z 1368.767.

LEGENDS for SUPPLEMENTARY FIGURES S3 – S10

Figure S3. Flow cytometric analysis for LGR5 expression in HT-29 colon cancer cells grown as monolayer and spheroid.

Figure S4. Primary screening studies with 53 NSGMs belonging to 12 structurally distinct scaffolds. Initial screening revealed differential growth in CSC enriched spheroid, measured by average number of spheres/100 plated cells at 120 h (**A**) vs. monolayer condition, measured by MTT assay (values derived as OD@490nm wavelength) at 72 h (**B**), by several NSGMs in HT-29 colon cancer cells. Data is presented as percent of control. Only two NSGMs from the G6 scaffold, (G6.1 and G6.9) demonstrated ~50% inhibition in monolayer but not in spheroid condition. In contrast, several compounds (12/53) belonging to four different scaffolds (G2, G4, G11 and G12, especially G2.2, G2.6, G11.1, G11.4 and G11.6) showed ≥ 50 % inhibition of spheroid growth without having any effect on growth in monolayer condition. All 53 NSGMs were screened at 100 μ M concentration.

Figure S5. Dose response profile of G2.2 treatment (0 $\rightarrow$ 500 μ M) on the growth in spheroid and monolayer conditions.

Figure S6. Effect of 100 μ M G2.2 on primary spheroid growth in additional cancer cell lines. G2.2 treatment caused similar growth inhibition in HCT-116 p53^{-/-} (p53 null) and Panc-1 (pancreatic cancer, K-RAS and p53 mutant) spheroids to that observed with HCT-116 and HT-29 colon cancer cell lines (**A**). Photomicrograph of Panc-1 spheroids at day 5 treated with vehicle or G2.2 taken at 10X resolution (**B**). *p<0.005.

Figure S7. Flow cytometric analysis of DCLK1. Flow cytometric analysis of spheroids treated with G2.2 (100 μ M) showing robust inhibition in DCLK1 expression. Vehicle or G1.4 (100 μ M) treated cells do not show this inhibition.

LGR5 Expression in Monolayer and Spheroid Culture of HT-29 Colon Cancer Cells

Figure S3

Differential Targeting of Monolayer and Spheres by NSGMs

G2.2 Dose-Response Curve- Monolayer vs. Spheroid Growth

Figure S5

G2.2 Inhibition of Growth of Two Other Colon Cancer Cell Lines

B Inhibition of Panc 1 colonospheres by G2.2

Figure S6

Flow cytometric analysis shows inhibition of DCLK1 by G2.2, but not by G1.4

Figure S7