Supplementary information

Novel Bio-friendly Thiocarbohydrate Stabilizers of Gold Nanoparticles

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Synthesis and Characterization of Compounds L1-L10

Di-(2-gluconamidoethyl) disulfide (L1)

D-(+)-Gluconic acid δ-lactone (0.51 g, 2.80 mmol), 2-aminoethanethiol (0.56 g, 2.80 mmol) and triethylamine (20.10 mmol). Yield = 82%; melting point 150-151 ^{o}C; ^{1}H NMR (D_2O, 400 MHz): δ 4.15 (d, J = 4.4 Hz, 1H, H-3), 3.88 (s, 1H, H-2), 3.62 (d, J = 12.4 Hz, 1H, H-4), 3.55 (s, 2H, H-6_a and H-6_b), 3.46 (t, J = 3.2 Hz, 1H, H-5), 3.40-3.35 (m, 2H, -NCH_2-), 2.74 (t, 2H, J = 6.0 Hz, -CH_2S-); $^{13}C\{^{1}H\}$ NMR (D_2O, 100 MHz): δ 175.4 (C-1), 74.4 (C-2), 73.2 (C-3), 72.1 (C-4), 71.3 (C-5), 63.7 (C-6), 38.8 (-NCH_2-), 37.6 (-CH_2S-). IR (neat, cm^{-1}): 1649 (C=O, amide carbonyl str.), 1099 (C-N), 1209 (O-C, 2-bands), 3220 (O-H broad), 1438 (CH_2); Raman (cm^{-1}): 2935 (CH_2), 1015 (C-C), 510 (S-S). Anal. Calcd for $C_{16}H_{32}O_{12}N_2S_2$: C, 37.79; H, 6.34; N, 5.51; S, 12.61%. Found: C, 37.58; H, 7.031; N, 5.33; S, 11.66%. HRMS (ESI): *m/z* $[M+H]^+$ Calcd 509.1390; found: 509.1010.

Di(3-gluconamidopropyl) disulfide (L2)

D-(+)-gluconic acid δ-lactone (1.75 g, 9.80 mmol) and 3-aminopropane-1-thiol (0.93 g, 9.80 mmol). Yield = 92%; melting point = 155-156 ^{o}C. ^{1}H NMR (D_2O, 400 MHz): δ 4.12 (d, J = 3.6

Hz, 1H, H-3), 3.901 (t, *J* = 2.8 Hz, 1H, H-2), 3.650 (s, 1H, H-4), 3.62 (bd, *J* = 2.0 Hz, 1H, H-6a), 3.57 (bd, *J* = 6.0 Hz, 2H, H-6b), 3.47 (dd, *J* = 5.6 and 11.6 Hz, 1H, H-5), 3.19 (t, *J* = 6.8 Hz, 2H, -NCH_2-), 2.59 (t, 2H, *J* = 7.2 Hz, -CH_2S-), 1.76 (q, *J* = 7.2 Hz, 2H, -CH_2-). $^{13}C\{^1H\}$ NMR (D_2O, 100 MHz) δ 174.3 (C-1), 73.4 (C-2) 721.2 (C-3), 71.02 (C-4), 70.3 (C-5) 62.6 (C-6), 37.6 (-NCH_2-), 35.0 (-CH_2S-), 27.9 (-CH_2-). FT-IR (neat, cm^{-1}): 1624 (C=O), 2934 (C-H), 1027-1136 (C-O, C-C and C-S), 1257 (C-N) 3294 (O-H broad), 3201 (N-H) 1445 (CH_2 str.). Raman (cm^{-1}): 2936 (CH_2), 1108 (C-C), 511 (S-S). Anal. Calcd for $C_{18}H_{36}O_{12}N_2S_2$: C, 40.29; H, 6.76; N, 5.22; S, 11.95%. Found: C, 40.35; H, 7.29; N, 5.19; S, 10.83%. HRMS (ESI): m/z $[M+H]^+$ Calcd 537.1788; found: 537.1791.

Di(4-gluconamidobutyl) disulfide (L3)

D-(+)-gluconic acid δ-lactone (1.50 g, 8.42 mmol), 4-aminobutane-1-thiol (0.89 g, 8.42 mmol). Yield = 47%; melting point = 159-160 °C. ^1H NMR (D_2O, 400 MHz): δ 4.17 (d, *J* = 3.6 Hz, 1H, H-2), 3.94 (t, 1H, *J* = 2.8 Hz, H-3), 3.67 (t, 1H, *J* = 2.8 Hz, H-4), 3.60 (q, *J* = 2.8 Hz, 2H, H-5), 3.52 (q, *J* = 5.6 Hz, 2H, H-6), 3.15 (t, *J* = 6.8 Hz, 2H, -NCH_2-), 2.64 (t, *J* = 7.2 Hz, 2H, -CH_2S-), 1.76 (m, 4H, (-CH_2CH_2-). $^{13}C\{^1H\}$ NMR (D_2O, 100 MHz): δ 174.3 (C-1), 73.4 (C-2), 721.2 (C-3), 71.0 (C-4), 70.3 (C-5), 62.6 (C-6), 37.6 (-NCH_2-), 35.0 (-CH_2S-), 27.9 (-CH_2CH_2-). FT-IR (neat, cm^{-1}) 3293 (O-H broad), 3201 (N-H), 2928 (C-H), 1623 (C=O amide carbonyl str.), 1544 (N-H), 1440 (CH_2 str.), 1257 (C-N), 1136 (C-S), 1083 (C-O). Raman (cm^{-1}): 2955 (CH_2), 1115 (C-C) 509 (S-S). Anal. Calcd for $C_{20}H_{40}O_{12}N_2S_2$: C, 42.54; H 7.14; N, 4.96; S, 11.36%. Found: C, 42.24; H, 7.73; N, 4.83; S, 10.26%. HRMS (ESI): (m/z) $[M+H]^+$ Calcd 565.2101; Found: 565.2101.

Acetylated di(2-gluconamidoethyl)disulfide (L5)

Compound **L1** (0.10 g, 0.20 mmol) and acetic anhydride (0.74 mL). Yield = 83%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.68 (t, *J* = 5.7 Hz, 1H, N-H), 5.59 (t, *J* = 5.4 Hz, 1H, H-3), 5.39 (t, *J* = 6.0Hz, 1H, H-4), 5.23 (t, *J* = 4.8 Hz, 1H, H-2), 4.98 (q, *J* = 5.6 Hz, 1H, H-5), 4.3 (dd, *J* = 4.00 and 12.3 Hz, 1H, H-6a), 4.10 (dd, *J* = 5.70 and 12.3 Hz, 1H, H-6b), 3.56 (q, *J* = 6.8 Hz, 2H, -NC$\underline{H}_2$-), 2.76 (t, 2H, ^{3}J = 6.3 Hz, -C$\underline{H}_2$S-), 2.19 (s,-OCOC$\underline{H}_3$), 2.09 (s,-OCOC$\underline{H}_3$), 2.07 (s,-OCOC$\underline{H}_3$), 2.05 (s,-OCOC$\underline{H}_3$), 2.03 (s, -OCOC$\underline{H}_3$). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 170.7 (-O$\underline{C}$OCH$_3$), 169.9 (-O$\underline{C}$OCH$_3$), I69.8 (-O$\underline{C}$OCH$_3$), I69.3 (-O$\underline{C}$OCH$_3$), 166.5 (C-1), 71.8 (C-2), 69.5 (C-3), 68.7 (C-4), 69.0 (C-5), 61.6 (C-6), 38.1 (-NCH_2-), 37.3 (-CH_2S-), 20.6 (-OCO$\underline{C}$H$_3$) 20.7 (-OCO$\underline{C}$H$_3$), 20.7 (-OCO$\underline{C}$H$_3$), 20.7 (-OCO$\underline{C}$H$_3$), 20.5,(-OCO$\underline{C}$H$_3$). FT-IR (neat, cm^{-1}): 1744 (C=O, ester carbonyl str.), 1677 (C=O, amide carbonyl str.), 1528 (N-H); 1207 (C-N) 1038 (O-C). Anal. Calcd for $C_{36}H_{52}O_{22}N_2S_2$: C, 46.55; H, 5.64; N, 3.02; S, 6.90%. Found: C, 46.04; H, 5.28; N, 2.86; S, 5.93%. HRMS (ESI): *m/z* $[M+H]^+$ Calcd 929.2531; found: 929.2538.

Acetylated di(3-gluconamidopropyl) disulfide (L6)

Compound **L2** (0.40 g, 0.74 mmol) and acetic anhydride (0.71 mL). Yield = 84%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.35 (t, *J* = 6 Hz, 1H, N-H), 5.65 (t, *J* = 5.2 Hz, 1H, H-3), 5.41 (q, *J* = 4.8 Hz, 1H, H-4), 5.25 (d, *J* = 5.2 Hz, 1H, H-2), 5.02 (quintet, *J* = 4.0 Hz, 1H, H-5), 4.28 (dd, *J* = 4.0 and 12.4 Hz, 1H, H-6a), 4.10 (dd, *J* = 5.6 and 12.4 Hz, 1H, H-6b), 3.34 (q, *J* = 6.8 Hz, 2H, -NCH_2-), 2.64 (q, *J* = 7.2 Hz, 2H, -CH_2S-), 1.87 (t, *J* = 7.2 Hz, 2H, -CCH_2C-), 2.02 (s, 3H, -OCOCH$_3$), 2.04 (s, 3H, -OCOCH$_3$), 2.06 (s, 3H, -OCOCH$_3$), 2.07(s, 3H, -OCOCH$_3$), 2.08 (s, 3H, -OCOCH$_3$), 2.17 (s, 3H,-OCOCH$_3$). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 170.7 (-

O<u>C</u>OCH$_3$), I69.9 (-O<u>C</u>OCH$_3$), I69.8 (-O<u>C</u>OCH$_3$), 169.3 (-O<u>C</u>OCH$_3$), 166.3 (C-1), 71.7 (C-2), 69.4 (C-3), 69.0 (C-4), 68.8 (C-5), 61.6 (C-6), 53.4(-NHCH$_2$-), 38.2(-CH$_2$<u>C</u>H$_2$CH$_2$-), 35.8 (-<u>C</u>H$_2$S-), 28.7, 20.8 (2×-OCO<u>C</u>H$_3$), 20.7 (2×-OCO<u>C</u>H$_3$), 20.5 (-OCO<u>C</u>H$_3$). FT-IR (neat, cm^{-1}): 2941 (C-H str.), 1743 υ(C=O), 1673 (C=O, amide carbonyl str.), 1535 (N-H), 1370 (CH$_2$ bend), 1205 (C-N), 1033 (O-C). Anal. Calcd for $C_{38}H_{56}O_{22}N_2S_2$: C, 47.69; H, 5.90; N, 2.93; S, 6.70%. Found: C, 47.39; H, 6.46; N, 2.80; S, 5.60%. HRMS (ESI): *(*m/z) [M+H]$^+$ Calcd 957.2844; found: 957.2842.

Acetylated di(4-gluconamidobutyl) disulfide (L7)

Compound **L3** (0.40 g, 0.71 mmol) and acetic anhydride (0.68 mL). Yield = 84%. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 6.17 (t, *J* = 6.0 Hz, 1H, N-H), 5.64 (t, *J* = 5.2 Hz, 1H, H-2), 5.42 (q, *J* = 5.2 Hz, 1H, H-3), 5.26 (t, *J* = 4.8 Hz, 1H, H-4), 5.01 (m, 1H, H-5), 4.29 (dd, *J* = 4.0 and 12.4 Hz, 1H, H-6a), 4.11 (dd, *J* = 5.6 and 12.4 Hz, 1H, H-6b), 3.25 (q, 2H, ^{3}*J* = 5.6 Hz, -CH$_2$S-), 2.64 (q, 2H, *J* = 7.2 Hz, -NCH$_2$-), 1.62 (m, 4H, -CH$_2$CH$_2$-), 2.18 (s, 3H, -OCOCH$_3$), 2.08 (s, 3H, -OCOCH$_3$), 2.06 (s, 3H, -OCOCH$_3$), 2.03 (s, 3H, -OCOCH$_3$), 2.02 (s, 3H, -OCOCH$_3$). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 170.6 (-O<u>C</u>OCH$_3$), 169.8 (-O<u>C</u>OCH$_3$), 169.8 (-O<u>C</u>OCH$_3$), 169.7 (-O<u>C</u>OCH$_3$), 169.2 (-O<u>C</u>OCH$_3$), 166.1 (C-1), 71.6 (C-2), 69.3 (C-3), 69.0 (C-4), 68.7 (C-5), 61.5 (C-6), 38.7, 30.6, 28.3, 26.8, 20.7 (-OCO<u>C</u>H$_3$), 20.7 (-OCO<u>C</u>H$_3$), 20.4 (-OCO<u>C</u>H$_3$), 20.4 (-OCO<u>C</u>H$_3$), FT-IR (neat, cm^{-1}): 2941(C-H str.), 1744 (C=O), 1685 υ(C=O, amide carbonyl str.), 1535 (N-H), 1370 (CH$_2$ bend), 1204 (C-N), 1033 (O-C). Anal. Calcd for $C_{40}H_{60}O_{22}N_2S_2$: C, 48.77; H, 6.14; N, 2.84; S, 6.51%. Found: C, 48.63; H, 6.81; N, 2.73; S, 5.56%. HRMS (ESI): m/z [M+H]$^+$ Calcd 986.0350; found: 986.0179.

Acetylated 2-gluconamidoethyl thiol (L8)

Compound **L5** (0.45 g, 0.48 mmol), Zn (1.0 g, 15.30 mmol), 5% acetic acid (10 mL). Yield = 91%. ^{1}H NMR ($CDCl_3$, 400, MHz): δ 6.64 (d, *J* = 5.2 Hz, 1H, N-H), 5.64 (t, *J* = 4.4 Hz, 1H, H-4), 5.43 (t, *J* = 6.4 Hz, 1H, H-3), 5.27 (d, *J* = 4.8 Hz, 1H, H-2), 5.03 (q, *J* = 5.2 Hz, 1H, H-5), 4.30 (dd, *J* = 3.6 and 12.4 Hz, 1H, H-6a), 4.10 (dd, *J* = 5.6 and 12.4 Hz, 1H, H-6b), 3.55 (m, *J* = 6.4 Hz, 2H, -NCH_2-), 2.76 (t, *J* = 6 Hz, 2H, -CH_2SH), 2.02 (s, 3H,-$OCOCH_3$), 2.04 (s, 3H, -$OCOCH_3$), 2.06 (s, 3H, -$OCOCH_3$), 2.09 (s, 3H,-$OCOCH_3$), 2.18 (s, 3H, -$OCOCH_3$). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 170.8 (-O<u>C</u>OCH_3), 169.9 (-O<u>C</u>OCH_3), I69.9 (-O<u>C</u>OCH_3), 169.8 (-O<u>C</u>OCH_3), 165.4 (-O<u>C</u>OCH_3), 169.4 (C-1), 71.8 (C-2), 69.5 (C-3), 69.2 (C-4), 68.9 (C-5), 61.6 (C-6), 37.5 (-NCH_2), 38.3 (-CH_2SH), 20.5 (-OCO<u>C</u>H_3), 20.7 (-OCO<u>C</u>H_3), 20.7 (-OCO<u>C</u>H_3), 20.8 (-OCO<u>C</u>H_3). FT-IR (neat, cm-1): 1744 υ(C=O), 1673 (C=O, amide carbonyl str.), 1531 (N-H), 2954 (C-H str.) 1433 (CH_2), 1206 (O-C), 1045 (C-N). Anal. Calcd for $C_{18}H_{27}O_{11}NS$: C, 46.40; H, 5.85; N, 3.01; S, 6.89%. Found: C, 45.53; H, 4.99; N, 2.86; S, 6.32%. HRMS (ESI): m/z $[M+H]^+$ Calcd 466.1383; found: 466.1390.

Acetylated 3-gluconamidopropyl thiol (L9)

Compound **L6** (0.50 g, 0.52 mmol), 5% acetic acid (10 mL) and zinc (1.00 g, 15.30 mg). Yield = 96%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.34 (t, *J* = 6.0 Hz, 1H, N-H), 5.67 (t, *J* = 5.2 Hz, 1H, H-2), 5.43 (t, *J* = 5.6 Hz, 1H, H-3), 5.27 (q, *J* = 7.6 Hz, 1H, H-4), 5.01 (q, *J* = 5.2 Hz, 1H, H-5), 4.29 (dd, *J* = 4.2, and 12.4 Hz, 1H, H-6a), 4.11 (dd, *J* = 5.4 and 12.2 Hz, 1H, H-6b), 3.37 (m, *J* = 6.8 Hz, 2H, -NCH_2-), 2.66 (t, *J* = 7.2 Hz, 1H, -CHaS-), 2.53 (t, 1H, *J* = 7.2 Hz, -CH_bS-), 2.18 (s, 3H, -$OCOCH_3$), 2.09 (s, 3H, -$OCOCH_3$), 2.07 (s, 3H, -$OCOCH_3$), 2.04 (s, 3H, -$OCOCH_3$), 2.03

(s, 3H, -OCOCH$_3$), 1.87 (t, 1H, J = 7.2 Hz, -CH$_a$-), 1.80 (tt, J = 2.4 and 6.8 Hz, 1H, -CH$_b$-), 1.44 (t, J = 8.0 Hz, 1H, SH). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ I70.7 (-O<u>C</u>OCH$_3$), 169.9 (-O<u>C</u>OCH$_3$), I69.8 (-O<u>C</u>OCH$_3$), 169.8 (-O<u>C</u>OCH$_3$), 169.3 (-O<u>C</u>OCH$_3$), 166.3 (C-1), 71.7 (C-2), 69.4 (C-3), 69.0 (C-4), 68.8 (C-5), 61.6 (C-6), 38.2 (-NCH$_2$-), 35.8 (-CH$_2$S-), 28.7 (-CH$_2$-), 20.8 (-OCO<u>C</u>H$_3$), 20.7 (-OCO<u>C</u>H$_3$), 20.7 (-OCO<u>C</u>H$_3$), 20.5 (-OCO<u>C</u>H$_3$). FT-IR (neat, cm^{-1}): 1743 (C=O), 1672 (C=O, amide carbonyl str.), 1535 (N-H) 2936 (C-H str.), 1434 (CH$_2$ bend), 1204 (O-C), 1033 (C-N). Anal. Calcd for C$_{19}$H$_{28}$O$_{11}$NS**.**0.5CH$_2$Cl$_2$: C, 45.50; H, 5.73; N, 2.65; S, 6.07%. Found: C, 45.83; H, 6.36; N, 2.77; S, 4.06%. HRMS (ESI): m/z [M+H]$^+$ Calcd 480.1540; found: 480.1513.

Acetylated 4-gluconamidobutyl thiol (L10)

Compound **L7** (0.40 g, 0.041 mmol), 5% acetic acid (7.0 mL) and Zn (0.64 g, 9.79 mmol). Yield = 90%. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 6.10 (t, J = 5.2 Hz, 1H, N-H), 5.65 (t, J = 5.2 Hz, 1H, H-4), 5.41 (t, J = 5.6 Hz, 1H, H-3), 5.25 (t, J = 4.0 Hz, 1H, H-2), 5.02 (m, H-5), 4.29 (dd, J = 4.0 and 12.4 Hz, 1H, H-6a), 4.10 (dd, J = 5.4 and 12.2 Hz, 1H, H$_b$), 3.24 (t, J = 4.0 Hz, 2H, -NCH$_2$-), 2.64 (t, J = 6.8 Hz, 1H, -CH$_a$S-), 2.53 (t, J = 7.2 Hz, 1H, -CH$_b$S-), 2.18 (s, 3H, -OCOCH$_3$), 2.09 (s, 3H, -OCOCH$_3$), 2.07 (s, 3H, -OCOCH$_3$), 2.04 (s, 3H, -OCOCH$_3$), 2.03 (s, 3H, -OCOCH$_3$), 1.57 (m, 4H, -CH$_2$CH$_2$-), 1.33 (t, J = 7.6 Hz, 1H, S-H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 170.6 (-OCOCH$_3$), I69.9 (-OCOCH$_3$), 169.9 (-OCOCH$_3$), I69.7 (-OCOCH$_3$), 169.2 (-OCOCH$_3$), 166.1 (C-1), 71.6 (C-2), 69.4 (C-3), 69.1 (C-4), 68.8 (C-5), 61.6 (C-6), 38.9 (-NCH$_2$-), 30.9 (-CH$_2$S-), 28.0 (-CH$_2$-), 24.1 (-CH$_2$-), 20.7 (2×(-OCO<u>C</u>H$_3$)), 20.7 (2×(-OCO<u>C</u>H$_3$)), 20.4 (-OCO<u>C</u>H$_3$). FT-IR (neat, cm^{-1}): 1743 (C=O), 1665 (C=O, amide carbonyl str.), 1531 (N-

H), 1434 (CH_2 bend), 1370 (C-H) 1202 (O-C), 1033 (C-N). Anal. Calcd for $C_{20}H_{31}O_{11}NS$: C, 48.67, H, 6.33, N, 2.84, S, 6.50%. Found: C, 48.35; H, 7.05; N, 2.71; S, 5.44. HRMS (ESI): *m*/*z* $[M+H]^+$ Calcd 494.1696; found: 494.1703.

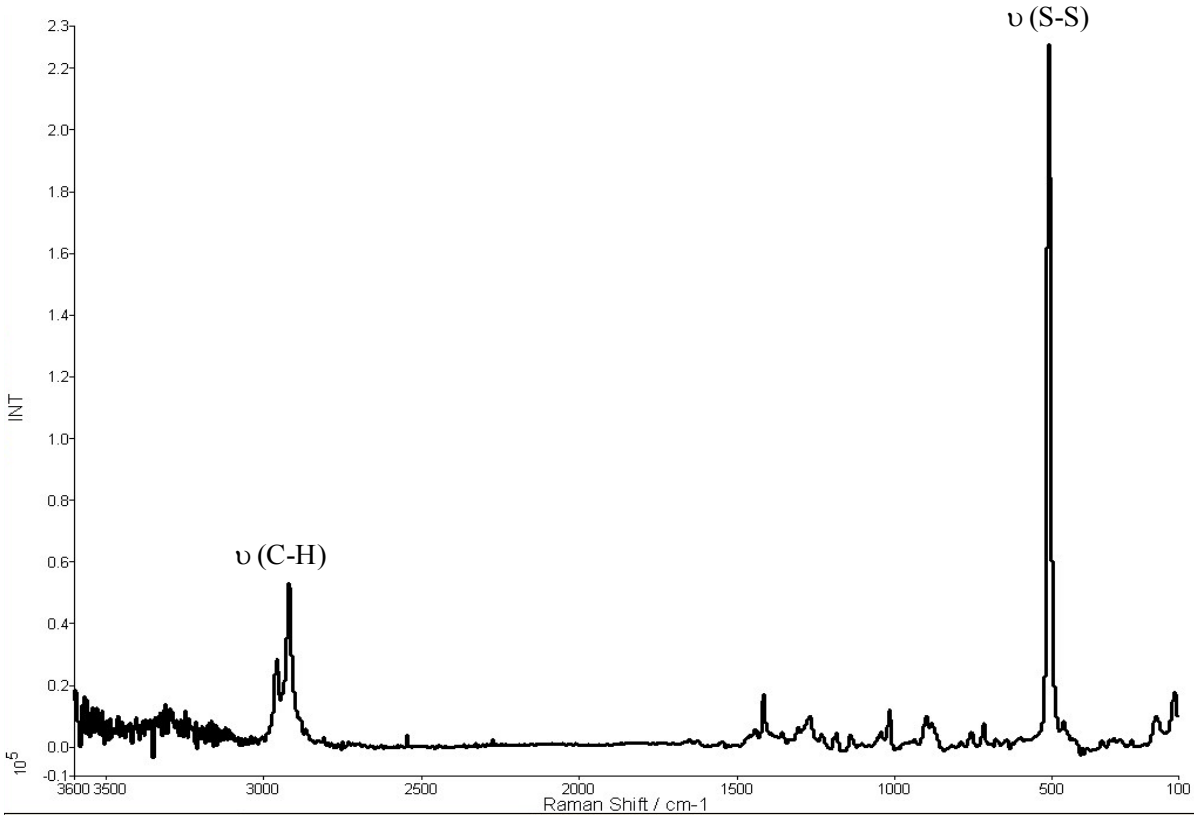

Figure S1. Raman spectrum of **L1**

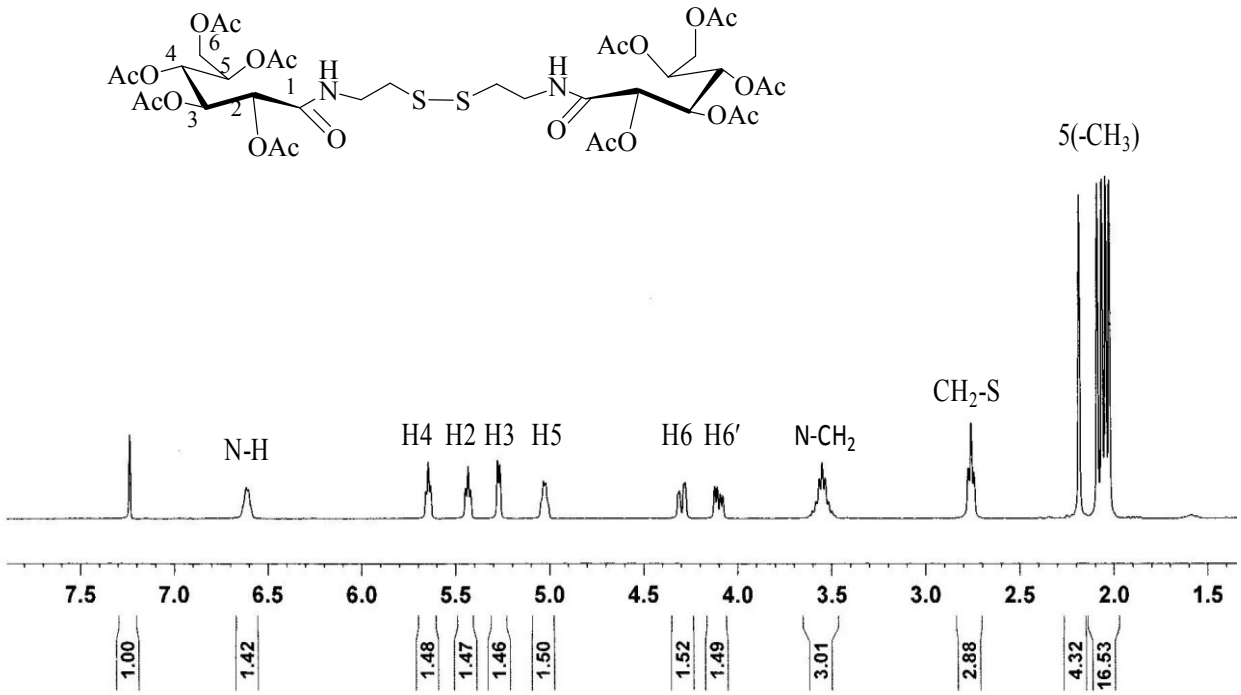

Figure S2. ^{1}H NMR spectrum of **L5**

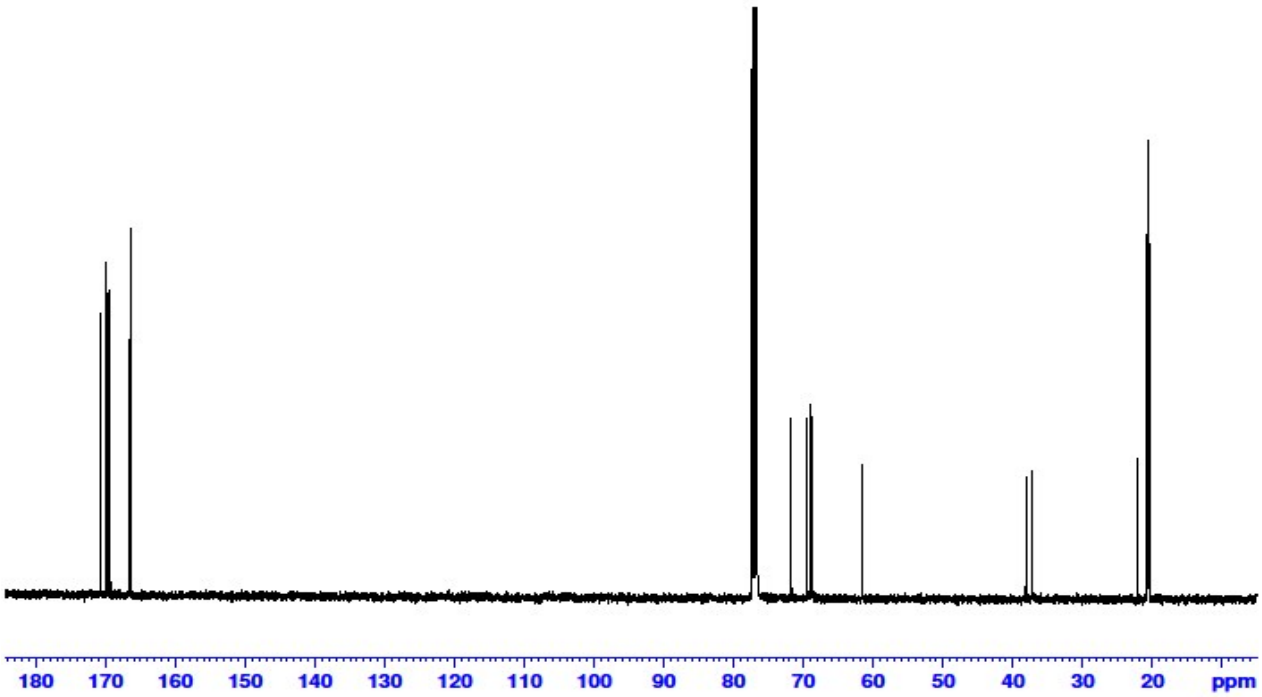

Figure S3. ^{1}H NMR spectrum of **L5**

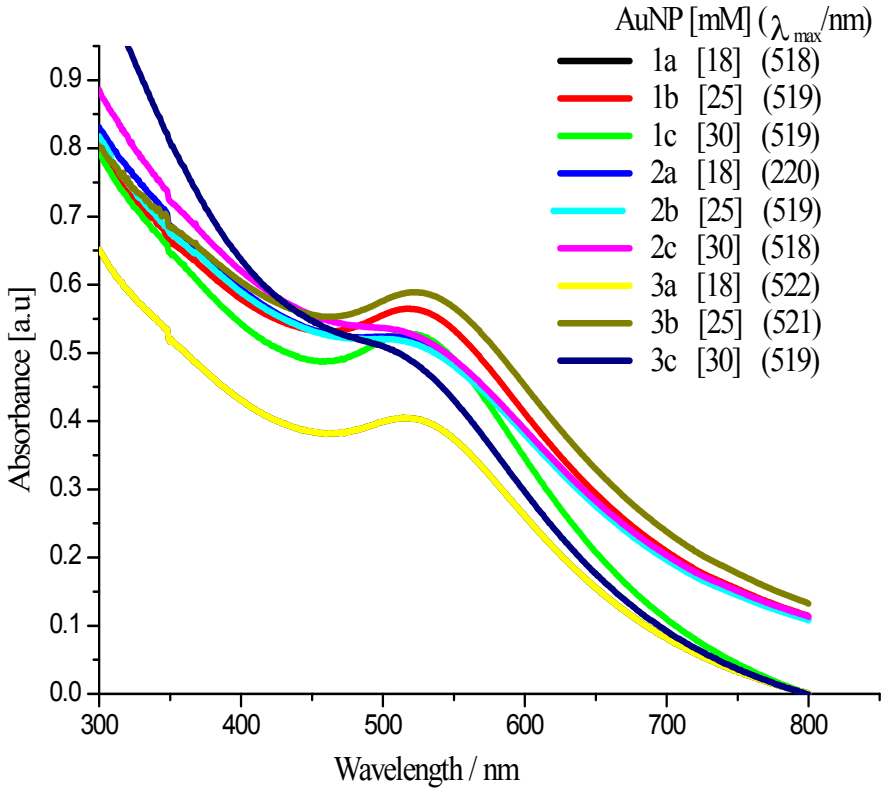

Figure S4. UV-vis spectra of **AuNP 1-3**

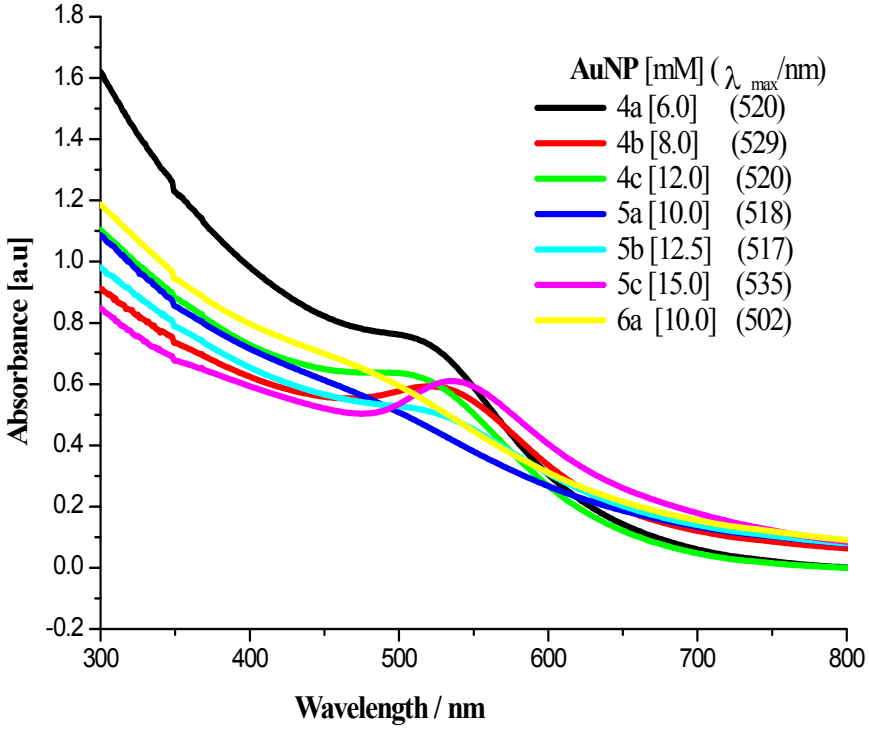

Figure S5. UV-vis spectra of **AuNP 4-6**

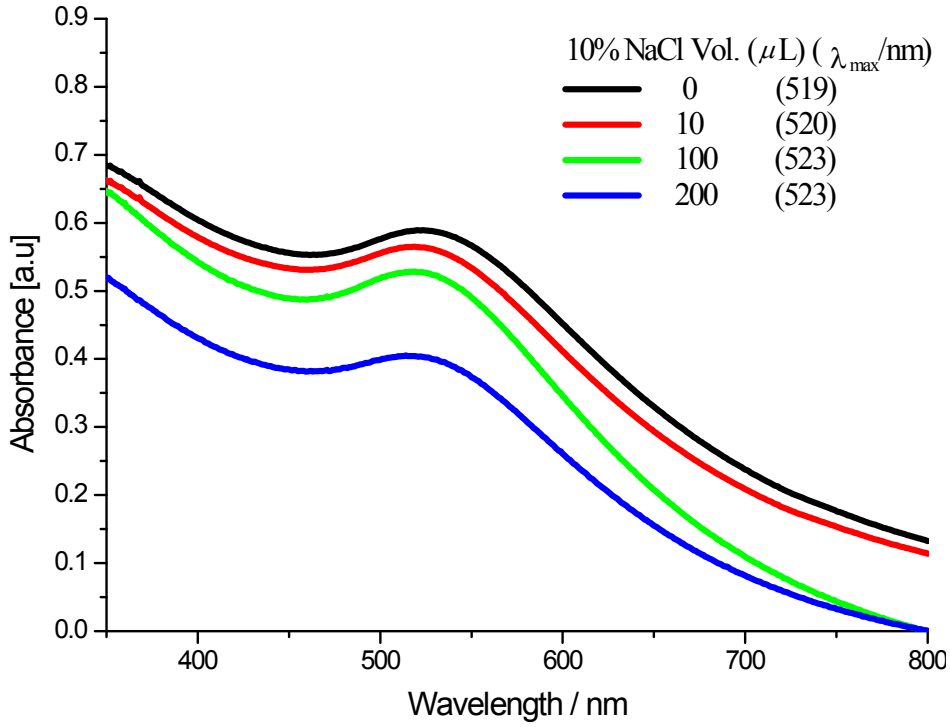

Figure S6. Stability of glyco GNPs assessed by measuring the critical flocculation concentration using 1.7 M NaCl solution.

Table S1: Inhibitory concentration 50 (IC50) of thiocarbohydrate compounds (**L1-L4**) and **AuNPs 1-3** derivatives in cancer cell lines

	Cell lines / IC_{50} (μM)		
Compounds	MCF7	HCT116	PC3
Parthenolide	6.38	16.09	18.42
L1-L4	≥ 100	≥ 100	≥ 100
AuNPs-1a	88.61	151.30	179.40
AuNPs-2a	91.39	216.90	136.50
AuNPs-3a	126.8	296.50	271.50

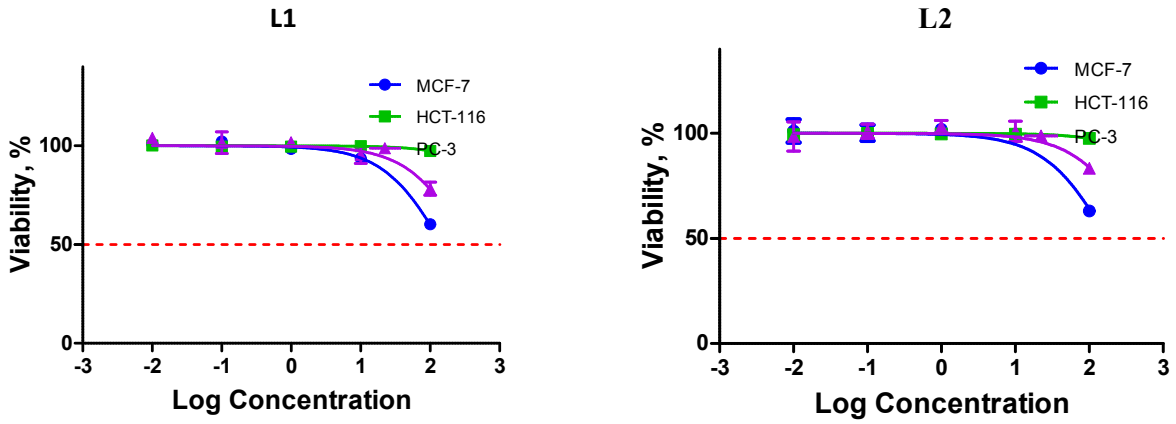

Figure S7. Growth inhibition profile of three human cancer cells of thiocarbohydrate L**1**and **L2.**

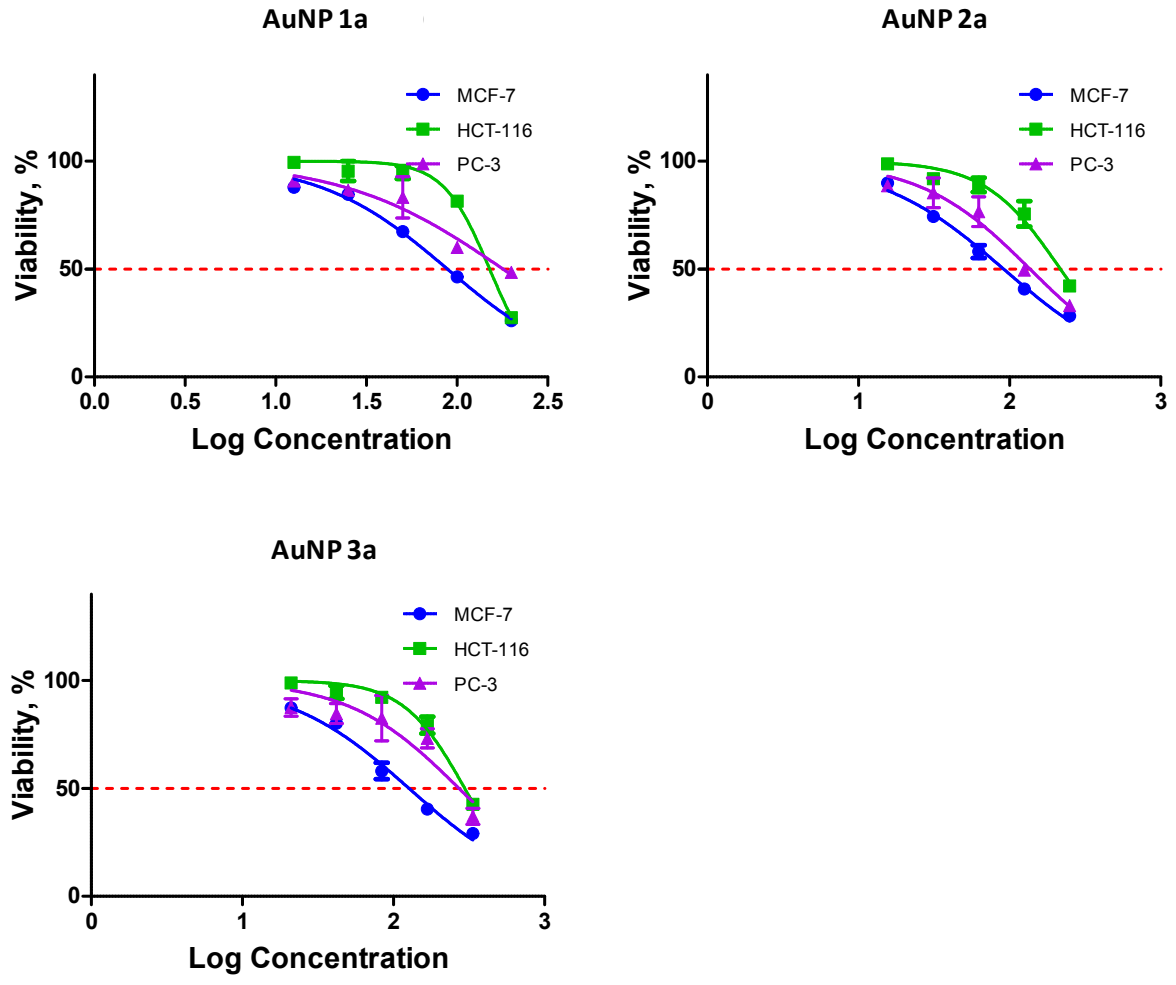

Figure S8. Growth inhibition profile of three human cancer cells of **AuNPs 1a**, **2a** and **3a**