Electronic Supplementary Material (ESI) for Materials Chemistry Frontiers.

Good's Buffer Based Highly Biocompatible Ionic Liquid Modified PLGA Nanoparticles for the Selective Uptake in Cancer Cells

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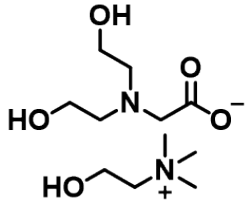
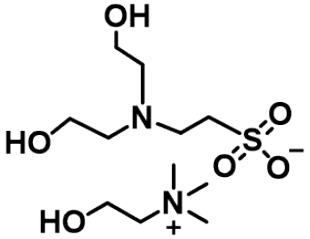
1. Characterization of the synthesized GBILs.

1. Choline N, N-bis (2-hydroxyethyl) glycinate [CBicine]



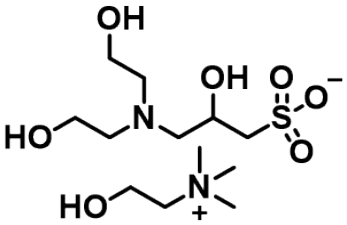
^{1}H NMR (400 MHz, d6-DMSO) δ 3.85 (dq, *J* = 5.3, 2.7 Hz, 2H), 3.46 – 3.39 (m, 2H), 3.33 (t, *J* = 5.6 Hz, 4H), 3.12 (s, 9H), 2.92 (s, 2H), 2.64 (t, *J* = 5.6 Hz, 4H). KF 0.14 %

2. Choline N, N-Bis(2-hydroxyethyl)-2-aminoethanesulfonate [CBES]



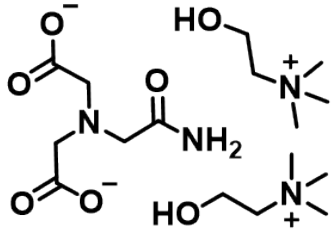
^{1}H NMR (400 MHz, DMSO) δ 5.29 (t, *J* = 4.8 Hz, 1H), 4.43 (s, 1H), 3.84 (qt, *J* = 5.1, 2.7 Hz, 2H), 3.41 (dd, *J* = 4.2, 2.4 Hz, 8H), 3.12 (s, 9H), 2.79 (t, *J* = 7.0 Hz, 2H), 2.58 (dd, *J* = 8.5, 5.9 Hz, 2H), 2.53 – 2.50 (m, 2H). KF 0.07%

3. Choline 3-(N, N-Bis[2-hydroxyethyl] amino)-2-hydroxypropanesulfonate [CDIPSO]



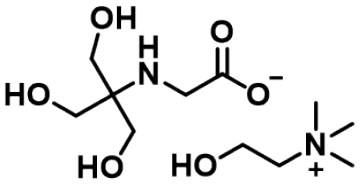
^{1}H NMR (400 MHz, DMSO) δ 5.28 (t, *J* = 4.9 Hz, 1H), 4.34 (t, *J* = 5.5 Hz, 2H), 3.84 (ddt, *J* = 7.3, 4.9, 2.4 Hz, 2H), 3.44 – 3.38 (m, 6H), 3.11 (s, 9H), 2.74 (d, *J* = 3.7 Hz, 1H), 2.71 (d, *J* = 3.7 Hz, 1H), 2.56 (t, *J* = 6.2 Hz, 4H), 2.43 (ddd, *J* = 18.3, 13.2, 7.4 Hz, 2H). KF 0.49 %

4. Choline N-(2-acetamido) iminodiacetate [CADA]



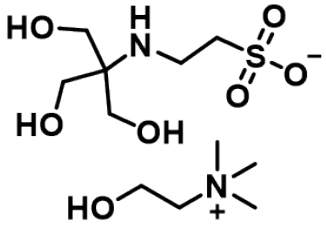
^{1}H NMR (400 MHz, d6-DMSO) δ 3.85 (dq, *J* = 5.4, 2.6 Hz, 4H), 3.45 – 3.41 (m, 4H), 3.14 (s, 18H), 3.08 (s, 2H), 2.93 (s, 4H). KF 0.54 %

5. Choline N-[tris(hydroxymethyl) methyl] glycinate [CTricine]



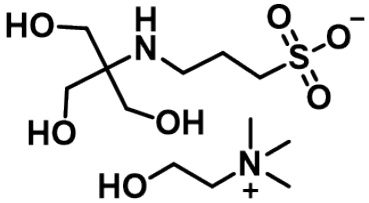
^{1}H NMR (400 MHz, DMSO) δ 3.89 – 3.81 (m, 2H), 3.43 – 3.40 (m, 2H), 3.20 (s, 6H), 3.12 (s, 9H), 2.89 (s, 2H). KF 0.32%

6. Choline 2-[(2-Hydroxy-1,1- is (hydroxymethyl)ethyl) amino] ethane sulfonate [CTES]



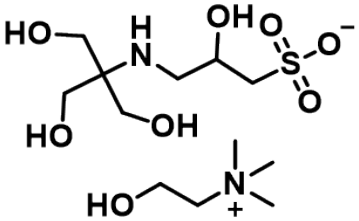
^{1}H NMR (400 MHz, DMSO) δ 5.30 (s, 1H), 4.19 (d, *J* = 5.8 Hz, 3H), 3.84 (d, *J* = 6.0 Hz, 2H), 3.42 – 3.38 (m, 2H), 3.31 – 3.25 (m, 6H), 3.11 (s, 9H), 2.79 (t, *J* = 6.4 Hz, 2H), 2.55 (d, *J* = 6.3 Hz, 2H). KF 0.57 %

7. Choline 2-Hydroxy-1,1-bis(hydroxymethyl) ethyl) amino]-1-propanesulfonate [CTAPS]



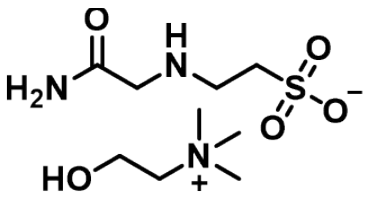
^{1}H NMR (400 MHz, DMSO) δ 5.31 (s, 1H), 4.22 (s, 3H), 3.84 (q, *J* = 4.9 Hz, 2H), 3.43 – 3.39 (m, 2H), 3.29 (s, 6H), 3.11 (s, 9H), 2.56 (t, *J* = 6.8 Hz, 2H), 2.49 – 2.46 (m, 2H), 1.71 – 1.59 (m, 2H). KF 1.10 %

8. Choline 2-Hydroxy-3-[tris(hydroxymethyl) methylamino]-1-propanesulfonate [CTAPSO]



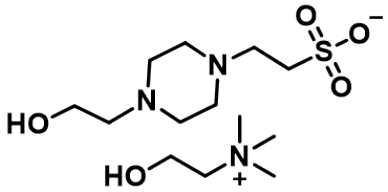
^{1}H NMR (400 MHz, DMSO) δ 5.30 (s, 1H), 4.99 – 4.93 (m, 1H), 4.22 (s, 3H), 3.84 (dq, *J* = 5.4, 2.7 Hz, 2H), 3.79 (d, *J* = 4.3 Hz, 1H), 3.44 – 3.37 (m, 3H), 3.29 (s, 6H), 3.17 (d, *J* = 2.9 Hz, 1H), 3.11 (s, 9H). KF 0.91 %

9. Choline N-(2-acetamido)-2-aminoethanesulfonate [CACES]



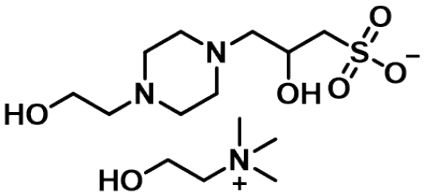
^{1}H NMR (400 MHz, DMSO) δ 7.35 (s, 1H), 7.02 (s, 1H), 3.84 (dq, *J* = 5.3, 2.6 Hz, 2H), 3.45 – 3.37 (m, 2H), 3.12 (s, 9H), 3.02 (s, 2H), 2.75 (t, *J* = 6.6 Hz, 2H), 2.59 (t, *J* = 6.6 Hz, 2H). KF 0.87%

10. Choline 4-(2-hydroxyethyl) piperazine-1-ethanesulfonate [CHEPES]



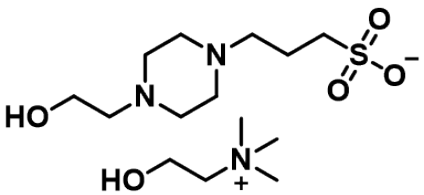
^{1}H NMR (400 MHz, DMSO) δ 4.36 (t, *J* = 5.4 Hz, 1H), 3.84 (tq, *J* = 5.1, 2.5 Hz, 2H), 3.48 (t, *J* = 5.9 Hz, 2H), 3.43 – 3.39 (m, 2H), 3.11 (s, 11H), 2.54 (s, 4H), 2.39 – 2.31 (m, 8H). KF 1.22%

11. Choline 2-Hydroxy-3-(4-(2-hydroxyethyl) piperazin-1-yl) propane-1-sulfonate [CHEPPSO]



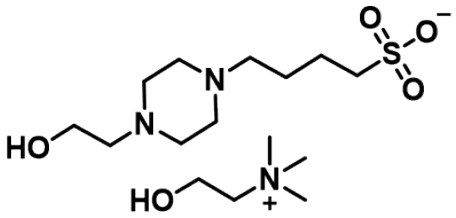
^{1}H NMR (400 MHz, DMSO) δ 4.87 (s, 1H), 3.95 (dtd, *J* = 9.1, 6.1, 2.8 Hz, 1H), 3.86 – 3.82 (m, 2H), 3.47 (t, *J* = 6.3 Hz, 2H), 3.42 – 3.39 (m, 2H), 3.11 (s, 11H), 2.71 (d, *J* = 2.8 Hz, 1H), 2.68 (d, *J* = 2.9 Hz, 1H), 2.42 – 2.32 (m, 8H), 2.28 (dd, *J* = 6.2, 4.7 Hz, 2H). KF 0.74 %

12. Choline 4-(2-Hydroxyethyl) piperazine-1-propanesulfonate [CEPPS]



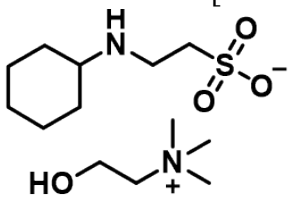
^{1}H NMR (400 MHz, DMSO) δ 3.84 (qd, *J* = 4.4, 2.4 Hz, 2H), 3.48 (t, *J* = 6.3 Hz, 2H), 3.44 – 3.40 (m, 2H), 3.12 (s, 9H), 2.49 – 2.35 (m, 10H), 2.31 (t, *J* = 7.3 Hz, 4H), 1.74 – 1.65 (m, 2H). KF 1.5%

13. Choline N-(2-Hydroxyethyl) piperazine-N′-(4-butanesulfonate) [CHEPBS]



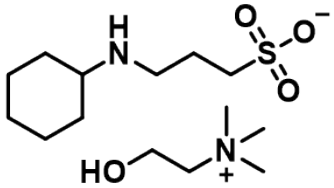
^{1}H NMR (400 MHz, d6-DMSO) δ 3.87 – 3.82 (m, 2H), 3.47 (t, *J* = 6.4 Hz, 2H), 3.44 – 3.38 (m, 2H), 3.36 (s, 3H), 3.17 (s, 1H), 3.12 (s, 9H), 2.42 – 2.33 (m, 8H), 2.20 (t, *J* = 7.2 Hz, 2H), 1.59 – 1.51 (m, 2H), 1.47 – 1.39 (m, 2H). KF 0.57%

14. Choline 2-(Cyclohexyl amino) ethane sulfonate [CCHES]



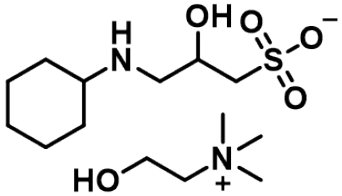
^{1}H NMR (400 MHz, DMSO) δ 5.36 (s, 1H), 3.84 (dq, *J* = 5.4, 2.6 Hz, 2H), 3.44 – 3.37 (m, 2H), 3.11 (s, 9H), 2.75 (t, *J* = 6.6 Hz, 2H), 2.53 (d, *J* = 6.6 Hz, 2H), 2.31 (tt, *J* = 10.0, 3.7 Hz, 1H), 1.74 (dt, *J* = 12.3, 3.8 Hz, 2H), 1.65 (dq, *J* = 12.7, 4.0 Hz, 2H), 1.54 (dt, *J* = 12.0, 3.8 Hz, 1H), 1.17 (ddtd, *J* = 24.1, 14.9, 11.7, 3.4 Hz, 3H), 1.02 – 0.90 (m, 2H). KF 0.66%

15. Choline 3-(Cyclohexyl amino)-1-propane sulfonate [CCAPS]



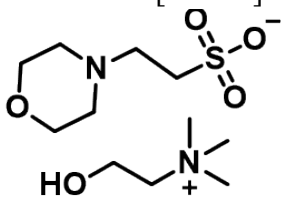
^{1}H NMR (400 MHz, DMSO) δ 3.84 (dq, *J* = 5.4, 2.6 Hz, 2H), 3.45 – 3.38 (m, 2H), 3.12 (s, 9H), 2.55 (t, *J* = 7.1 Hz, 2H), 2.46 – 2.40 (m, 2H), 2.33 (tt, *J* = 10.1, 3.7 Hz, 1H), 1.79 (dt, *J* = 12.6, 3.8 Hz, 2H), 1.70 – 1.62 (m, 4H), 1.15 (tddd, *J* = 23.7, 15.3, 11.9, 3.5 Hz, 4H), 1.03 – 0.92 (m, 2H). KF 0.97%

16. Choline 3-(Cyclohexyl amino)-2-hydroxy-1-propane sulfonate [CCAPSO]



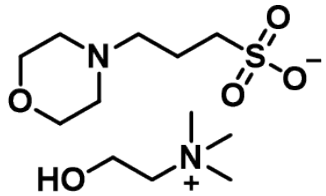
^{1}H NMR (400 MHz, D_2O) δ 4.17 – 4.07 (m, 1H), 3.98 (q, *J* = 4.7 Hz, 2H), 3.44 (t, *J* = 4.9 Hz, 2H), 3.12 (s, 9H), 3.00 (s, 1H), 2.81 (dd, *J* = 12.7, 3.7 Hz, 1H), 2.61 (dd, *J* = 12.8, 8.8 Hz, 1H), 2.46 (dq, *J* = 10.8, 5.8, 4.1 Hz, 1H), 1.81 (s, 2H), 1.65 (d, *J* = 13.0 Hz, 2H), 1.54 (d, *J* = 12.6 Hz, 1H), 1.19 (q, *J* = 12.9 Hz, 2H), 1.05 (dt, *J* = 23.6, 11.8 Hz, 4H). KF 1.97%

17. Choline 2-(N-morpholino) ethane sulfonate [CMES]



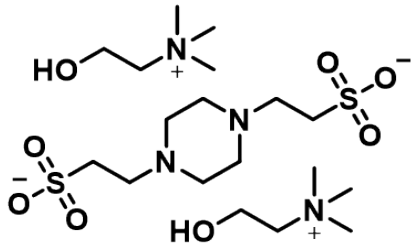
^{1}H NMR (400 MHz, DMSO) δ 3.87 – 3.81 (m, 2H), 3.54 (t, *J* = 4.7 Hz, 4H), 3.42 – 3.39 (m, 2H), 3.11 (s, 11H), 2.56 (s, 2H), 2.32 (s, 4H). KF 1.04%

18. Choline 3-(N-Morpholino) propane sulfonate [CMOPS]



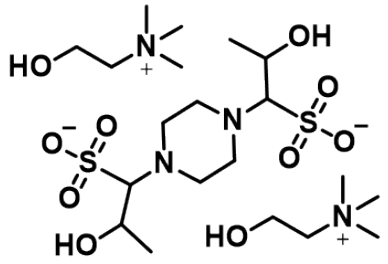
^{1}H NMR (400 MHz, DMSO) δ 3.84 (dd, *J* = 6.2, 3.5 Hz, 2H), 3.56 (t, *J* = 4.7 Hz, 4H), 3.43 – 3.40 (m, 2H), 3.12 (s, 9H), 2.46 – 2.38 (m, 2H), 2.31 (dd, *J* = 9.2, 5.5 Hz, 6H), 1.77 – 1.65 (m, 2H). KF 1.77%

19. Choline 1,4-Piperazinediethanesulfonate [CPIPES]



^{1}H NMR (400 MHz, DMSO) δ 3.84 (dq, *J* = 5.2, 2.4 Hz, 4H), 3.41 (dd, *J* = 4.2, 2.4 Hz, 4H), 3.12 (s, 22H), 2.57 (s, 8H), 2.37 (s, 4H). KF 0.78%

20. Choline Piperazine-1,4-bis(2-hydroxypropanesulfonate) [CPOPSO]



^{1}H NMR (400 MHz, DMSO) δ 3.95 (dtd, *J* = 9.0, 6.1, 2.9 Hz, 2H), 3.84 (dq, *J* = 5.3, 2.6 Hz, 4H), 3.42 – 3.39 (m, 4H), 3.09 (s, 2H), 2.39 (dd, *J* = 13.5, 9.1 Hz, 8H), 2.26 (dt, *J* = 12.6, 5.9 Hz, 6H). KF 0.84%

2. ^{1}H NMR quantification of GBIL coated PLGA NPs.

(1) [CACES 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (s, 4H), 3.50 (t, *J* = 5.2 Hz, 4H), 3.40 (s, 4H), 3.19 (s, 19H), 3.11 (t, *J* = 6.7 Hz, 4H), 3.04 (d, *J* = 6.7 Hz, 4H), 2.06 (s, 218H).

(2) [CADA 2:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (dt, *J* = 7.3, 3.3 Hz, 10H), 3.64 (dd, *J* = 11.7, 4.2 Hz, 10H), 3.53 (dd, *J* = 19.3, 6.4 Hz, 20H), 3.35 (d, *J* = 7.6 Hz, 9H), 3.19 (d, *J* = 2.9 Hz, 48H), 2.09 – 2.05 (m, 837H).

(3) [CBES 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (d, *J* = 5.4 Hz, 6H), 3.76 (d, *J* = 5.8 Hz, 4H), 3.71 (t, *J* = 6.0 Hz, 12H), 3.64 (dd, *J* = 11.4, 4.0 Hz, 7H), 3.58 – 3.52 (m, 7H), 3.50 (d, *J* = 5.2 Hz, 6H), 3.19 (s, 26H), 3.12 (s, 13H), 2.78 (s, 11H), 2.06 (d, *J* = 1.7 Hz, 650H).

(4) [CBicine 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (dd, *J* = 6.3, 3.4 Hz, 11H), 3.71 (d, *J* = 5.8 Hz, 20H), 3.51 (d, *J* = 6.0 Hz, 10H), 3.36 (s, 11H), 3.19 (s, 53H), 2.91 (t, *J* = 5.9 Hz, 21H), 2.08 – 2.05 (m, 1163H).

(5) [CCAPS 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.04 (dd, *J* = 6.6, 3.6 Hz, 5H), 3.77 (h, *J* = 4.8, 4.1 Hz, 6H), 3.64 (dd, *J* = 11.7, 4.4 Hz, 11H), 3.59 – 3.54 (m, 9H), 3.53 – 3.48 (m, 7H), 3.19 (s, 23H), 2.98 – 2.93 (m, 5H), 2.87 (t, *J* = 7.6 Hz, 5H), 2.06 (s, 512H), 1.27 (q, *J* = 13.4, 12.8 Hz, 6H), 1.20 – 1.07 (m, 8H).

(6) [CCAPSO 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (d, *J* = 5.5 Hz, 5H), 3.76 (td, *J* = 6.4, 3.0 Hz, 6H), 3.59 – 3.53 (m, 11H), 3.50 (d, *J* = 4.7 Hz, 5H), 3.19 (s, 24H), 3.07 (d, *J* = 6.0 Hz, 5H), 2.06 (s, 732H), 1.74 (d, *J* = 13.2 Hz, 6H), 1.33 – 1.21 (m, 6H), 1.20 – 1.08 (m, 8H).

(7) [CCHES 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.09 – 4.02 (m, 3H), 3.68 – 3.61 (m, 3H), 3.56 (d, *J* = 6.7 Hz, 2H), 3.52 – 3.48 (m, 3H), 3.19 (d, *J* = 2.0 Hz, 19H), 2.88 – 2.81 (m, 2H), 2.09 – 2.04 (m, 362H), 2.01 – 1.94 (m, 4H), 1.78 (s, 3H), 1.63 (d, *J* = 13.0 Hz, 2H), 1.25 (tt, *J* = 21.1, 8.5 Hz, 9H).

(8) [CDIPSO 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.25 (s, 2H), 4.05 (d, *J* = 5.5 Hz, 3H), 3.72 (s, 7H), 3.51 (d, *J* = 5.1 Hz, 3H), 3.19 (s, 15H), 3.11 – 3.05 (m, 2H), 2.88 (s, 7H), 2.10 – 2.05 (m, 241H).

(9) [CEPPS 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (dq, *J* = 5.4, 2.8 Hz, 4H), 3.74 (d, *J* = 5.9 Hz, 4H), 3.52 – 3.48 (m, 4H), 3.22 – 3.17 (m, 19H), 2.90 (t, *J* = 7.6 Hz, 5H), 2.64 (t, *J* = 5.9 Hz, 8H), 2.59 (d, *J* = 7.7 Hz, 6H), 2.06 (dd, *J* = 3.7, 1.8 Hz, 703H), 1.95 (d, *J* = 6.8 Hz, 6H).

(10) [CHEPBS 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.08 – 4.03 (m, 4H), 3.73 (t, *J* = 6.0 Hz, 4H), 3.50 (t, *J* = 5.0 Hz, 4H), 3.18 (s, 18H), 2.92 (t, *J* = 7.4 Hz, 4H), 2.67 – 2.56 (m, 11H), 2.06 (d, *J* = 2.1 Hz, 633H).

(11) [CHEPES 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (dq, *J* = 4.9, 2.8 Hz, 5H), 3.74 (t, *J* = 6.1 Hz, 5H), 3.50 (dd, *J* = 5.9, 4.0 Hz, 5H), 3.18 (s, 20H), 3.14 – 3.08 (m, 5H), 2.86 – 2.80 (m, 6H), 2.64 (t, *J* = 6.2 Hz, 8H), 2.06 (s, 561H).

(12) [CHEPPSO 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (d, *J* = 5.4 Hz, 3H), 3.77 (d, *J* = 6.0 Hz, 2H), 3.51 (d, *J* = 5.1 Hz, 3H), 3.19 (s, 14H), 2.72 (s, 5H), 2.64 (s, 3H), 2.06 (d, *J* = 1.9 Hz, 391H).

(13) [CMES 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (t, *J* = 5.0 Hz, 3H), 3.79 – 3.73 (m, 6H), 3.50 (t, *J* = 4.9 Hz, 3H), 3.19 (s, 13H), 3.16 – 3.10 (m, 3H), 2.85 (s, 3H), 2.62 (s, 5H), 2.06 (d, *J* = 2.0 Hz, 382H).

(14) [CMOPS 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (dd, *J* = 6.1, 3.4 Hz, 5H), 3.77 (t, *J* = 4.6 Hz, 12H), 3.55 (d, *J* = 6.8 Hz, 3H), 3.50 (q, *J* = 4.8, 3.7 Hz, 5H), 3.18 (s, 23H), 2.91 (t, *J* = 7.7 Hz, 6H), 2.61 (d, *J* = 20.7 Hz, 16H), 2.06 (d, *J* = 2.0 Hz, 725H).

(15) [CPIPES 2:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (s, 4H), 3.50 (t, *J* = 5.1 Hz, 4H), 3.19 (s, 20H), 3.12 (t, *J* = 7.8 Hz, 5H), 2.87 (s, 5H), 2.06 (s, 413H).

(16) [CPOPSO 2:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (tt, *J* = 5.3, 2.6 Hz, 4H), 3.64 (dd, *J* = 11.5, 4.0 Hz, 2H), 3.56 (dd, *J* = 7.3, 3.9 Hz, 2H), 3.52 – 3.49 (m, 4H), 3.22 – 3.17 (m, 19H), 3.05 (q, *J* = 5.0 Hz, 3H), 2.64 (s, 4H), 2.10 – 2.03 (m, 454H).

(17) [CTAPS 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.07 – 4.02 (m, 7H), 3.62 (d, *J* = 3.0 Hz, 21H), 3.55 (d, *J* = 6.8 Hz, 4H), 3.50 (q, *J* = 4.8, 3.9 Hz, 8H), 3.18 (d, *J* = 2.8 Hz, 32H), 2.96 (t, *J* = 7.6 Hz, 7H), 2.87 (t, *J* = 7.6 Hz, 6H), 2.06 (d, *J* = 3.5 Hz, 896H).

(18) [CTAPSO 1:1]

^{1}H NMR (400 MHz, D_2O) δ 4.05 (dd, *J* = 6.1, 3.5 Hz, 6H), 3.59 (d, *J* = 2.4 Hz, 18H), 3.50 (d, *J* = 5.3 Hz, 6H), 3.18 (s, 29H), 3.09 (dd, *J* = 5.9, 3.1 Hz, 6H), 2.95 (d, *J* = 12.2 Hz, 3H), 2.78 (s, 3H), 2.06 (d, *J* = 2.1 Hz, 916H).

(19) [CTES 1:1]

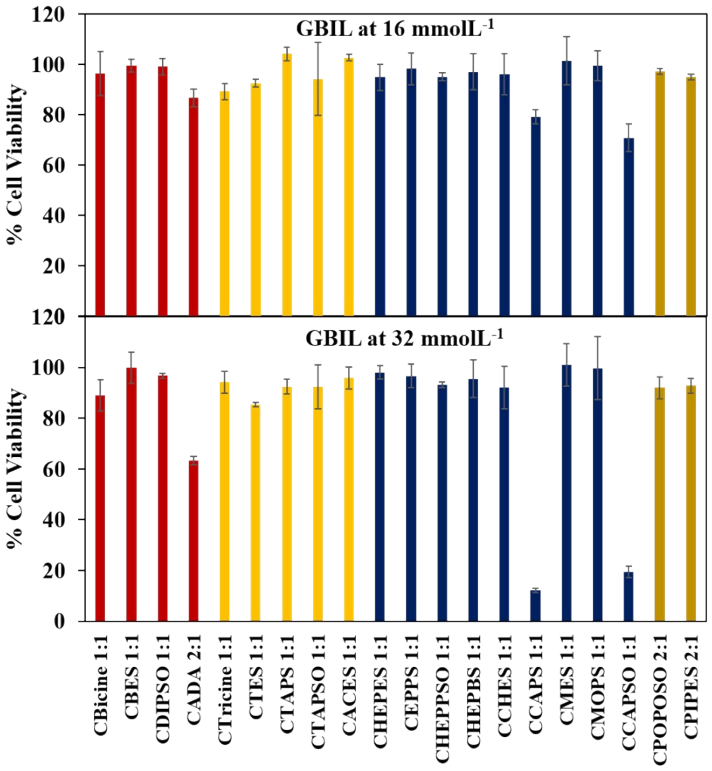
^{1}H NMR (400 MHz, D_2O) δ 4.07 – 4.02 (m, 7H), 3.60 (s, 21H), 3.52 – 3.48 (m, 6H), 3.18 (s, 34H), 3.08 (s, 13H), 2.06 (d, *J* = 2.3 Hz, 834H).

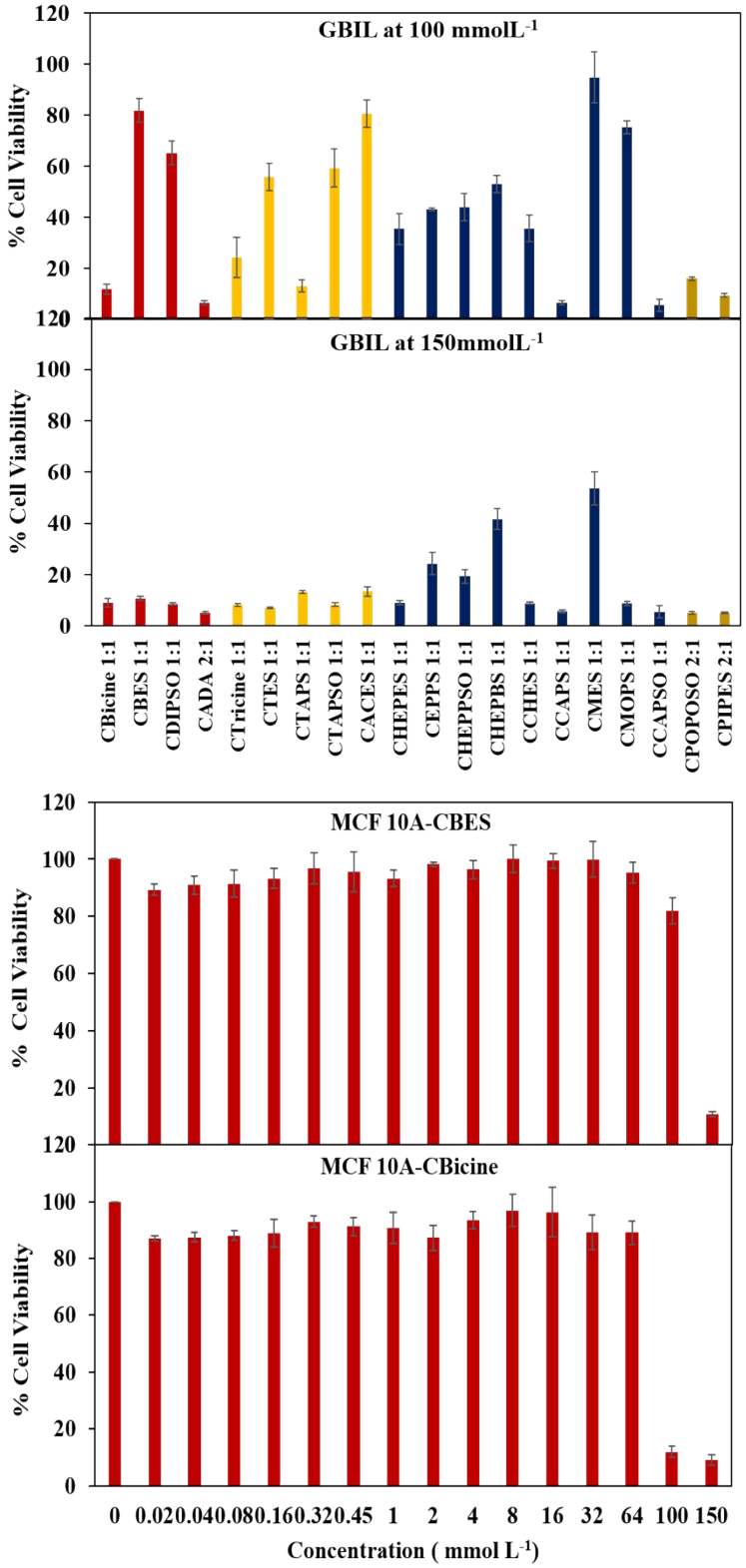
(20) [CTricine 1:1]

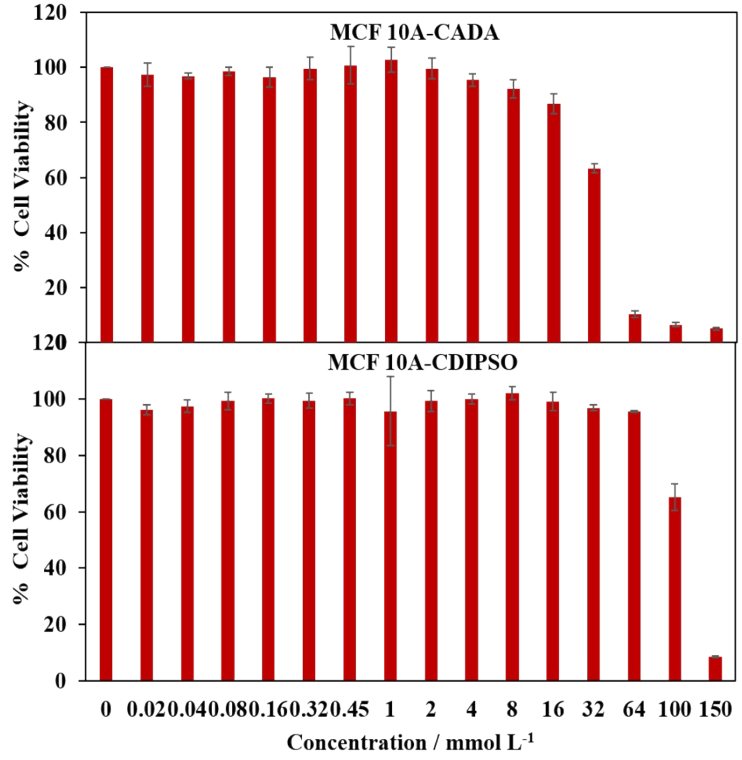
^{1}H NMR (400 MHz, D_2O) δ 4.09 – 4.02 (m, 4H), 3.58 (s, 13H), 3.50 (t, J = 5.1 Hz, 4H), 3.36 (s, 4H), 3.19 (s, 18H), 2.06 (s, 288H).

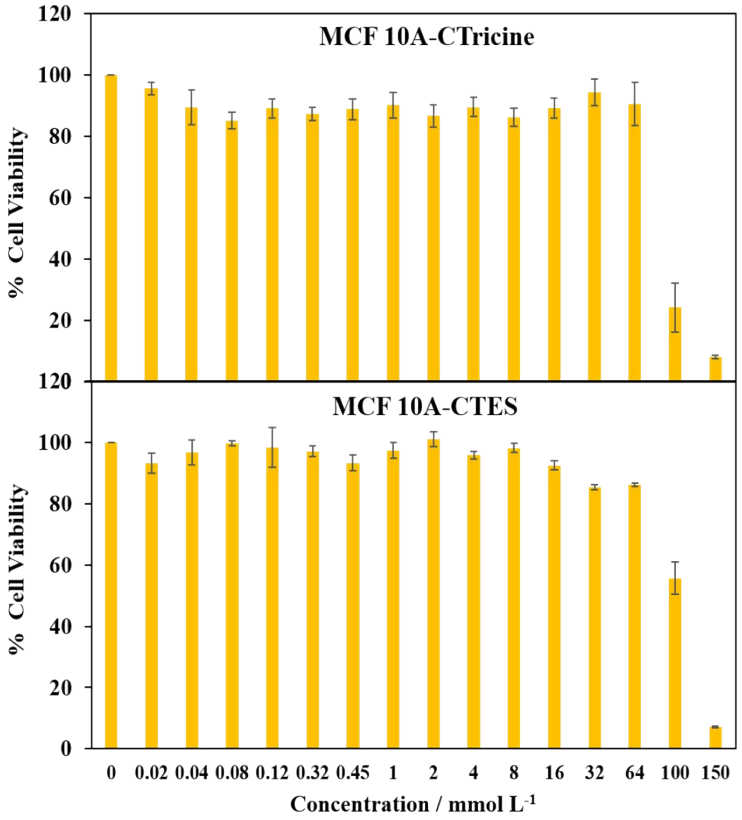
Table S1: Quantification of GBILs in GBIL-coated PLGA NPs with NMR measurements along with percentage of DiD encapsulation efficiency in PLGA NPs.

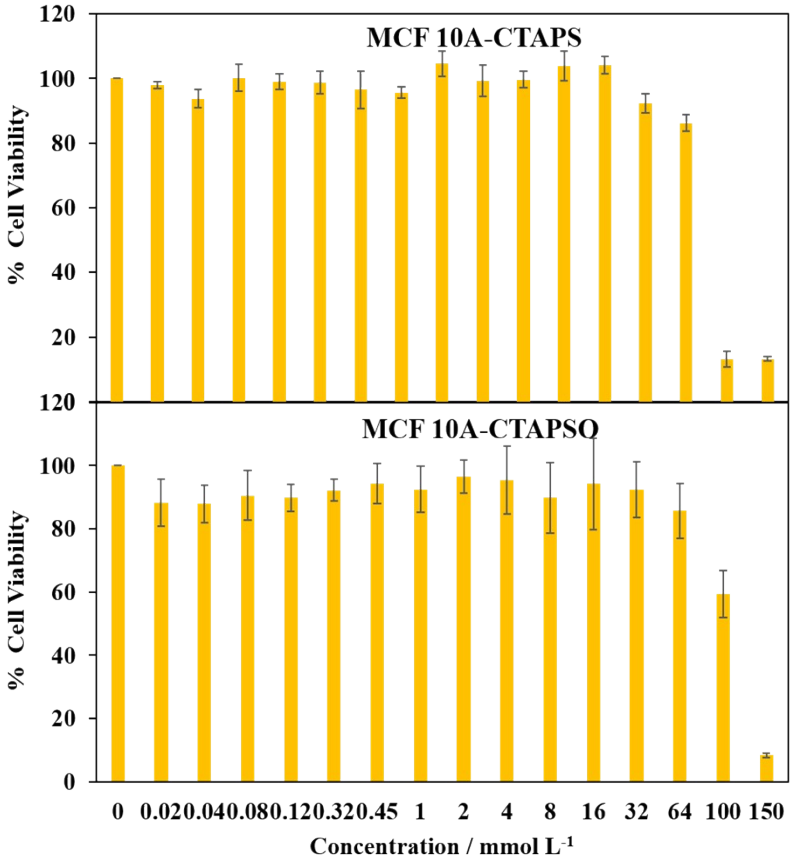
Name of NPs	CATION SIGNAL	CATION (H+)	ANION SIGNAL	ANION (H+)	TOTAL IL per NP ($x10^{-20}$)	CAPPING RATIO	Percentage Dye Loading
Bare PLGA							27.57 ± 0.71
Group 1							
CBicine 1:1	53	9	20	4	14.5	1.18:1.00	9.26 ± 1.86
CBES 1:1	26	9	11	4	7.33	1.05:1.00	19.07 ± 0.43
CDIPSO 1:1	15	9	7	4	4.46	0.95:1.00	13.77 ± 2.54
CADA 2:1	48	9	20	4	13.5	1.07:1.00	15.98 ± 2.11
Group 2							
CTricine 1:1	18	9	13	6	6.15	0.92:1.00	10.38 ± 0.28
CTES 1:1	34	9	21	6	10.9	1.08:1.00	13.79 ± 1.20
CTAPS 1:1	32	9	21	6	10.5	1.02:1.00	10.68 ± 0.38
CTAPSO 1:1	29	9	18	6	9.32	1.07:1.00	12.30 ± 2.26
CACES 1:1	19	9	4	2	4.56	1.06:1.00	24.99 ± 4.35
Group 3a							
CHEPES 1:1	20	9	8	4	5.55	1.11:1.00	9.79 ± 0.29
CEPPS 1:1	19	9	8	4	5.36	1.06:1.00	11.13 ± 0.13
CHEPPSO 1:1	14	9	5	4	3.76	1.24:1.00	7.12 ± 0.62
CHEPBS 1:1	18	9	4	2	4.36	1.00:1.00	10.41 ± 0.09
Group 3b							
CCHES 1:1	19	9	9	4	5.55	0.94:1.00	0.29 ± 0.01
CCAPS 1:1	23	9	8	4	6.15	1.28:1.00	0.05 ± 0.01
CCAPSO 1:1	24	9	8	4	6.35	1.33:1.00	0.44 ± 0.01
Group 3c							
CMES 1:1	13	9	6	4	3.77	0.96:1:00	12.27 ± 0.25
CMOPS 1:1	23	9	16	6	7.73	0.96:1:00	17.52 ± 0.27
Group 4							
CPIPES 2:1	20	9	5	2	4.95	0.89:1.00	12.48 ± 0.16
CPOPSO 2:1	19	9	4	2	4.56	1.06:1.00	11.32 ± 0.25

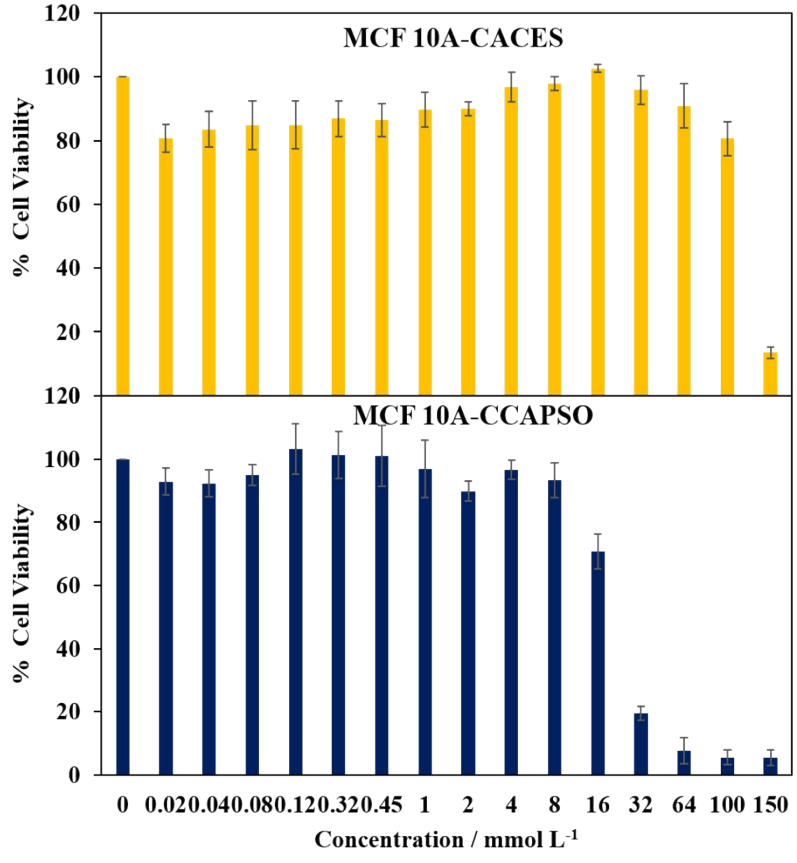

GBIL at 16 mmolL-1
% Cell Viability
120
100
80
60
40
20
GBIL at 32 mmolL-1
% Cell Viability
120
100
80
60
40
20
0
CBicine 1:1
CBES 1:1
CDIPSO 1:1
CADA 2:1
CTricine 1:1
CTES 1:1
CTAPS 1:1
CTAPSO 1:1
CACES 1:1
CHEPES 1:1
CEPPS 1:1
CHEPPSO 1:1
CHEPBS 1:1
CCHES 1:1
CCAPS 1:1
CMES 1:1
CMOPS 1:1
CCAPSO 1:1
CPOPOSO 2:1
CPIPES 2:1

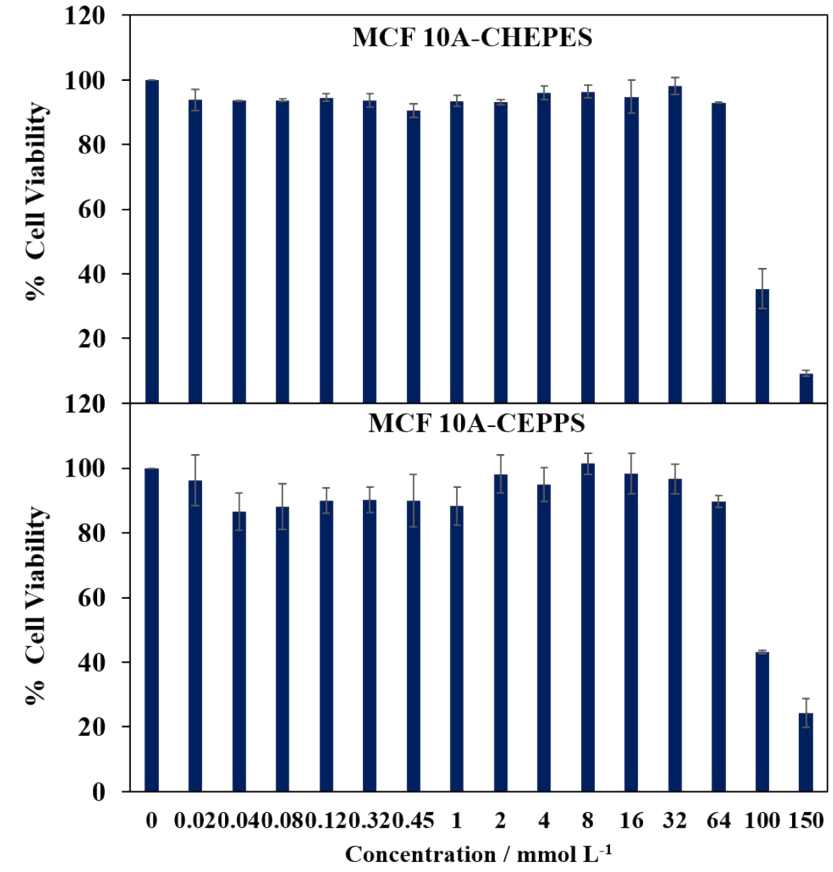

GBIL at 100 mmolL-1
GBIL at 150mmolL-1
% Cell Viability
120
100
80
60
40
20
0
CBicine 1:1
CBES 1:1
CDIPSO 1:1
CADA 2:1
CTricine 1:1
CTES 1:1
CTAPS 1:1
CTAPSO 1:1
CACES 1:1
CHEPES 1:1
CEPPS 1:1
CHEPPSO 1:1
CHEPBS 1:1
CCHES 1:1
CCAPS 1:1
CMES 1:1
CMOPS 1:1
CCAPSO 1:1
CPOPOSO 2:1
CPIPES 2:1
MCF 10A-CBES
MCF 10A-CBicine
0 0.02 0.04 0.08 0.16 0.32 0.45 1 2 4 8 16 32 64 100 150
Concentration (mmol L-1)

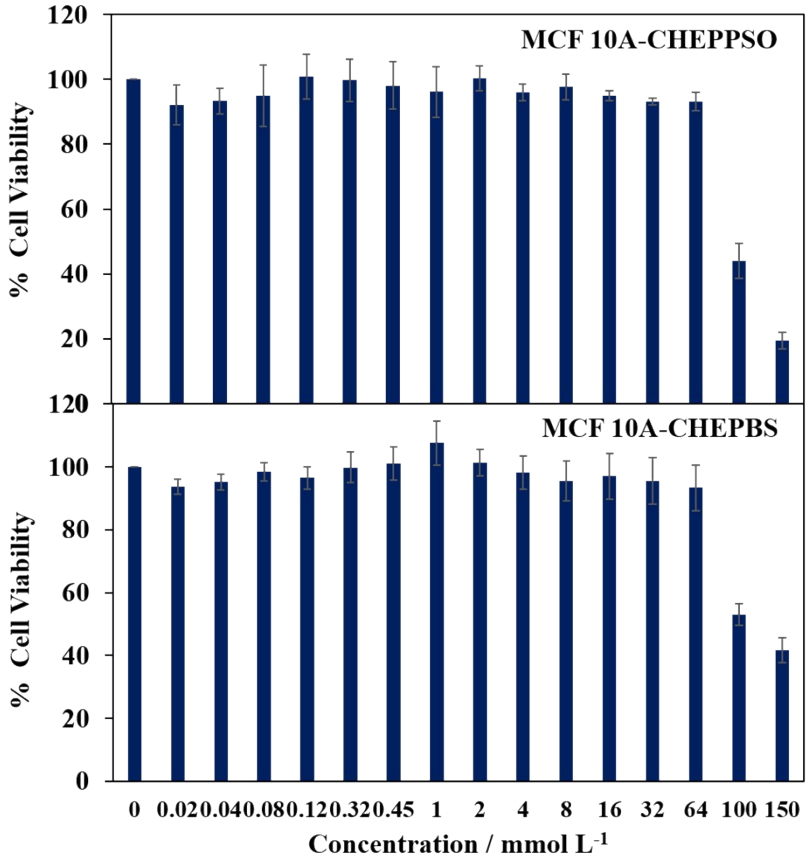

MCF 10A-CADA
MCF 10A-CDIPSO
% Cell Viability
0 20 40 60 80 100 120
0 0.02 0.04 0.08 0.16 0.32 0.45 1 2 4 8 16 32 64 100 150
Concentration / mmol L-1

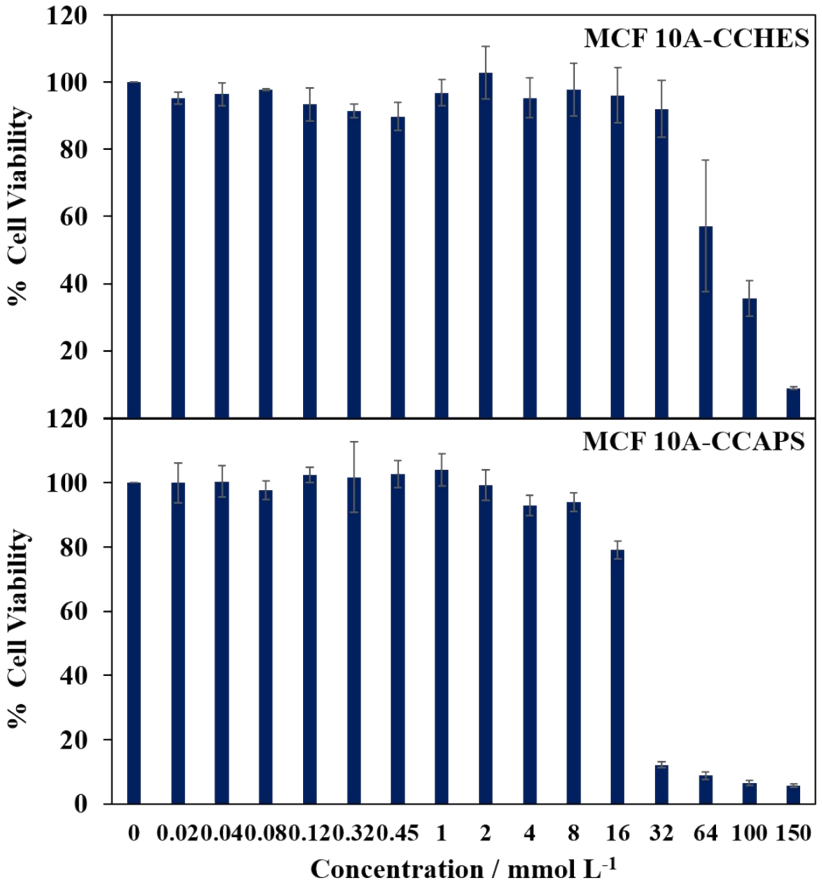

MCF 10A-CTricine
MCF 10A-CTES
% Cell Viability
0 20 40 60 80 100 120
0 0.02 0.04 0.08 0.12 0.32 0.45 1 2 4 8 16 32 64 100 150
Concentration / mmol L-1


MCF 10A-CTAPS
MCF 10A-CTAPSO
% Cell Viability
120
100
80
60
40
20
0
0 0.02 0.04 0.08 0.12 0.32 0.45 1 2 4 8 16 32 64 100 150
Concentration / mmol L-1


MCF 10A-CACES
MCF 10A-CCAPSO
% Cell Viability
120
100
80
60
40
20
0
0 0.02 0.04 0.08 0.12 0.32 0.45 1 2 4 8 16 32 64 100 150
Concentration / mmol L-1


MCF 10A-CHEPES
% Cell Viability
120
100
80
60
40
20
MCF 10A-CEPPS
% Cell Viability
120
100
80
60
40
20
0
0 0.02 0.04 0.08 0.12 0.32 0.45 1 2 4 8 16 32 64 100 150
Concentration / mmol L-1


MCF 10A-CHEPPSO
% Cell Viability
120
100
80
60
40
20
MCF 10A-CHEPBS
% Cell Viability
120
100
80
60
40
20
0
0 0.02 0.04 0.08 0.12 0.32 0.45 1 2 4 8 16 32 64 100 150
Concentration / mmol L-1


MCF 10A-CCHES
MCF 10A-CCAPS
% Cell Viability
% Cell Viability
120
100
80
60
40
20
120
100
80
60
40
20
0
0 0.02 0.04 0.08 0.12 0.32 0.45 1 2 4 8 16 32 64 100 150
Concentration / mmol L-1

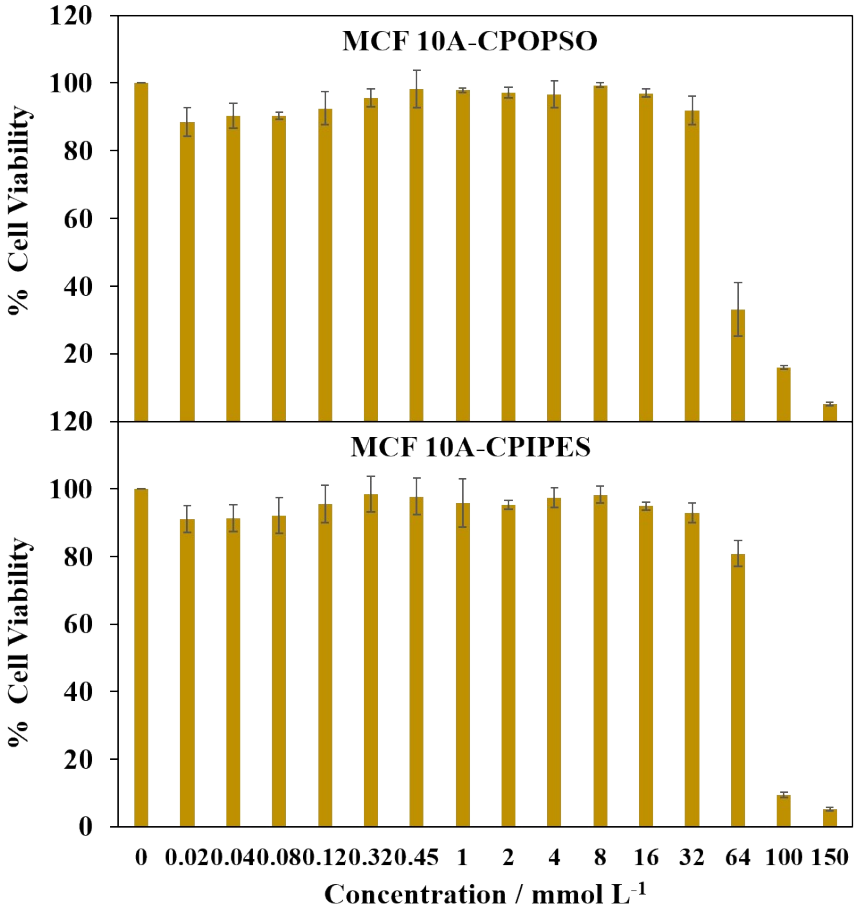
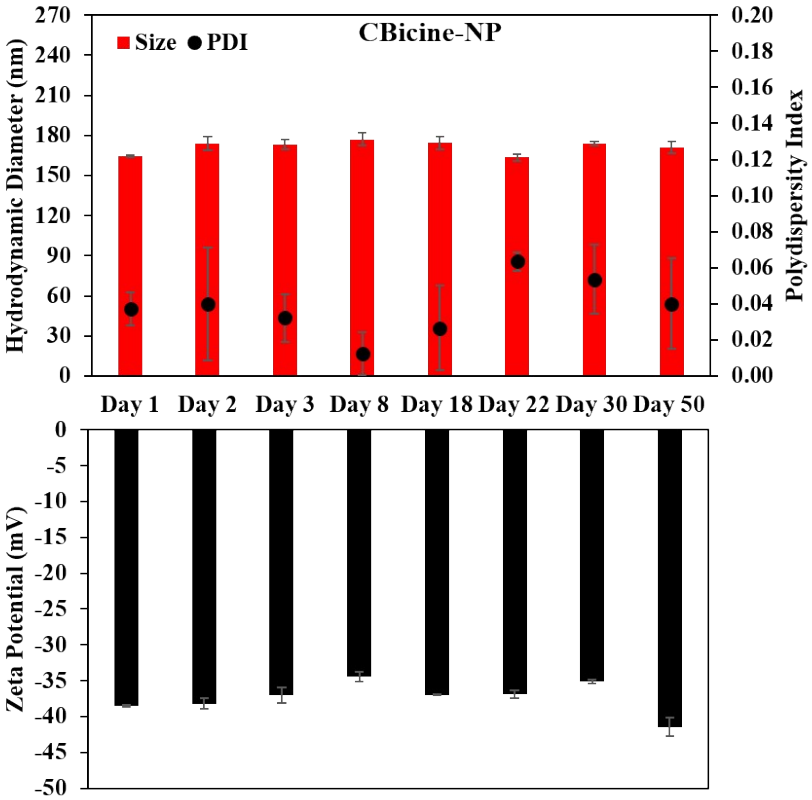
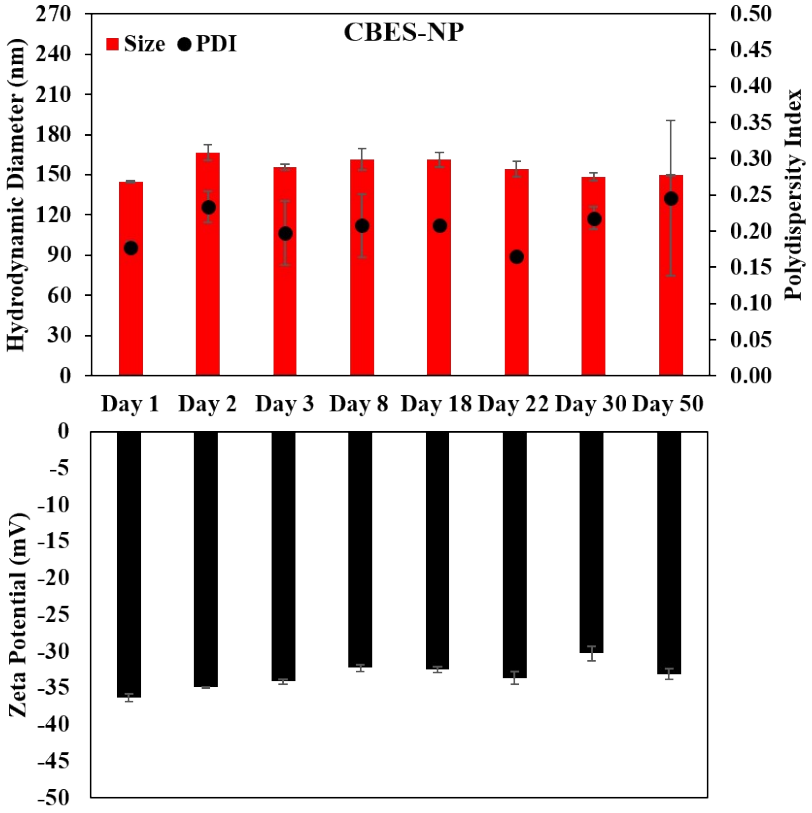
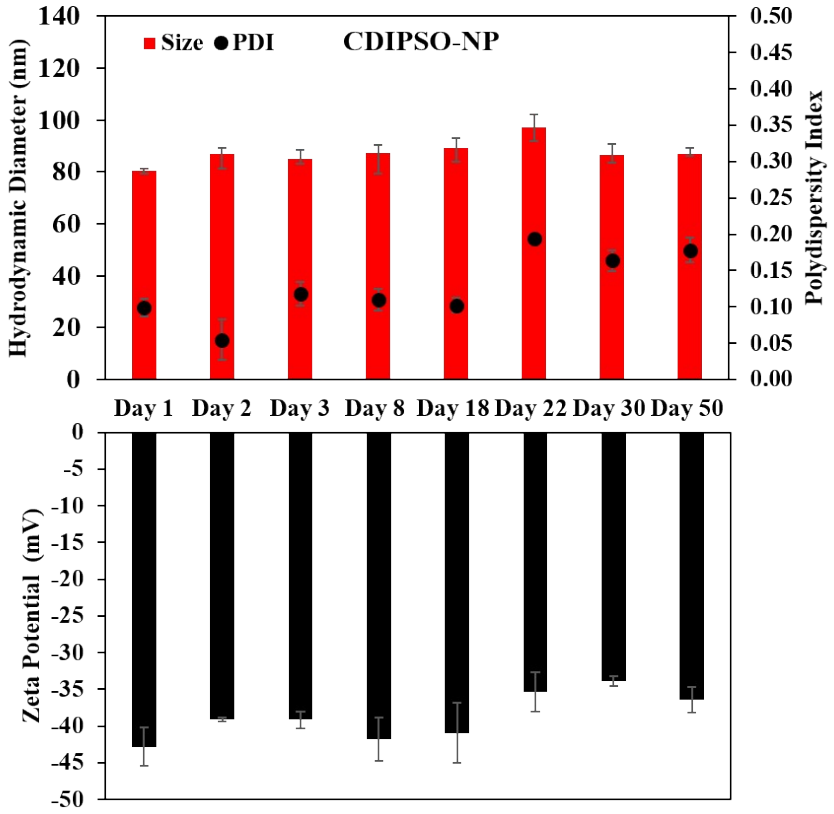
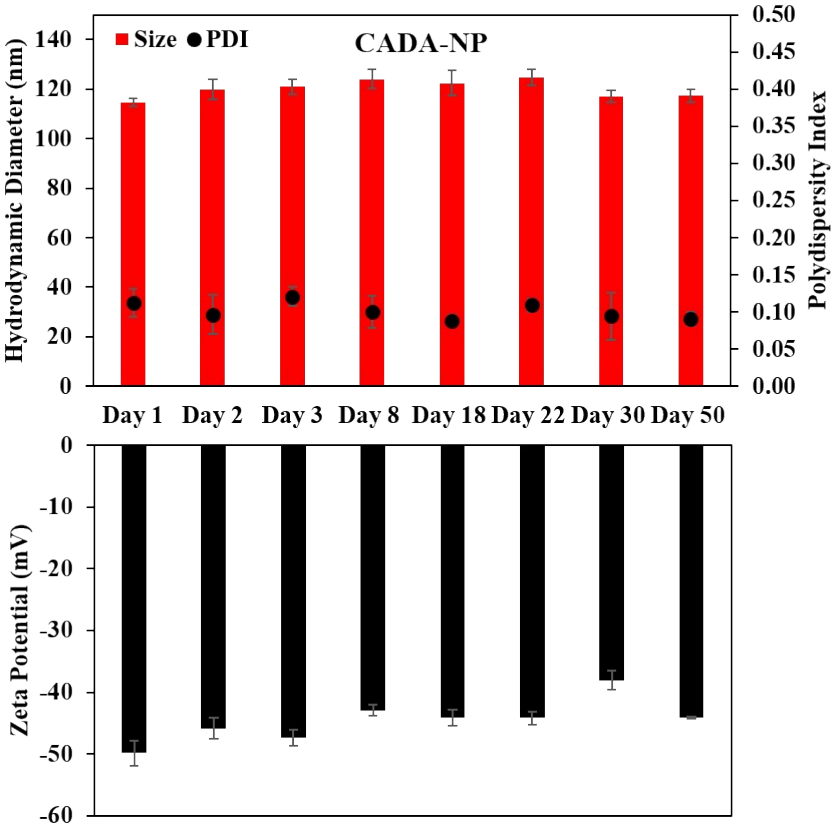


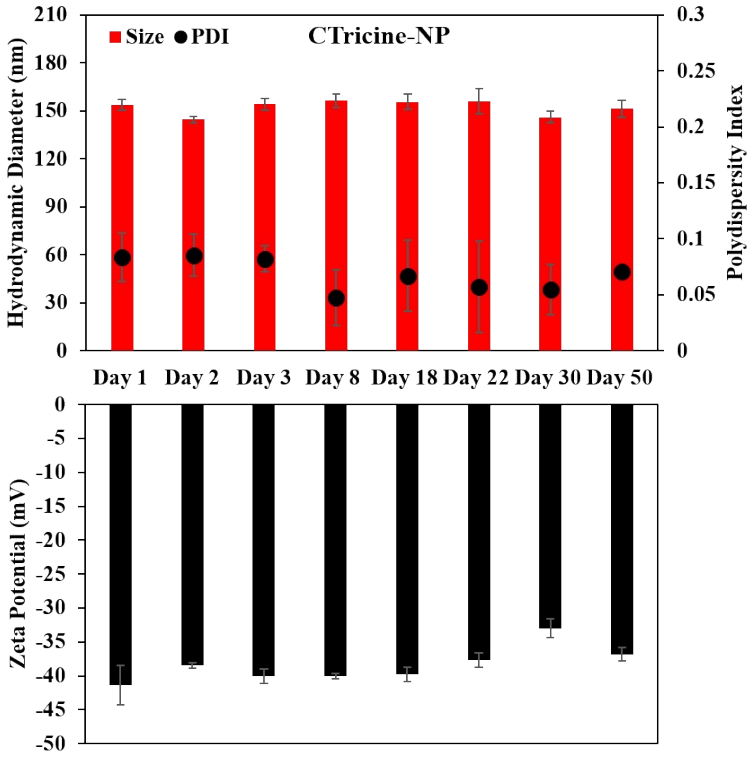
Figure S1. Cytotoxicity evaluation of GBILs towards MCF-10A at different concentration under standard conditions

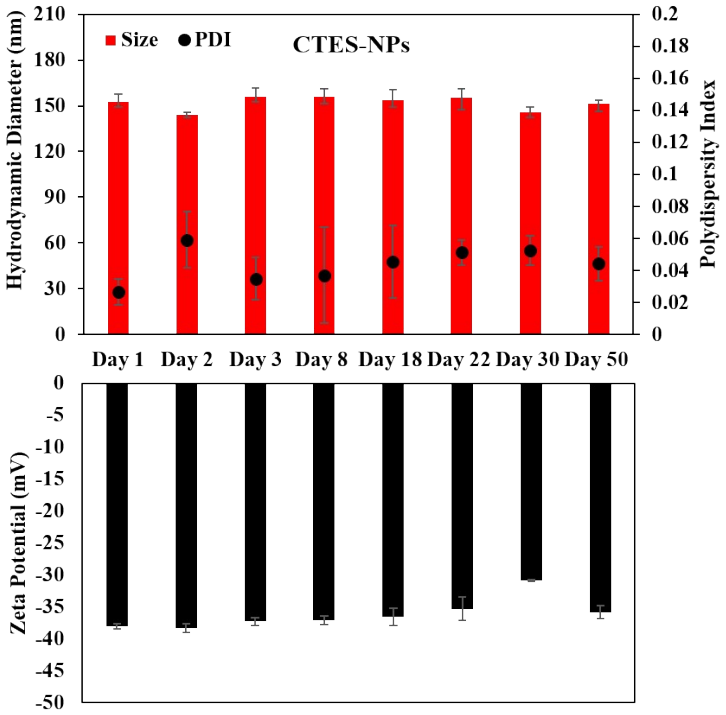

CBicine-NP
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Zeta Potential (mV)
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50

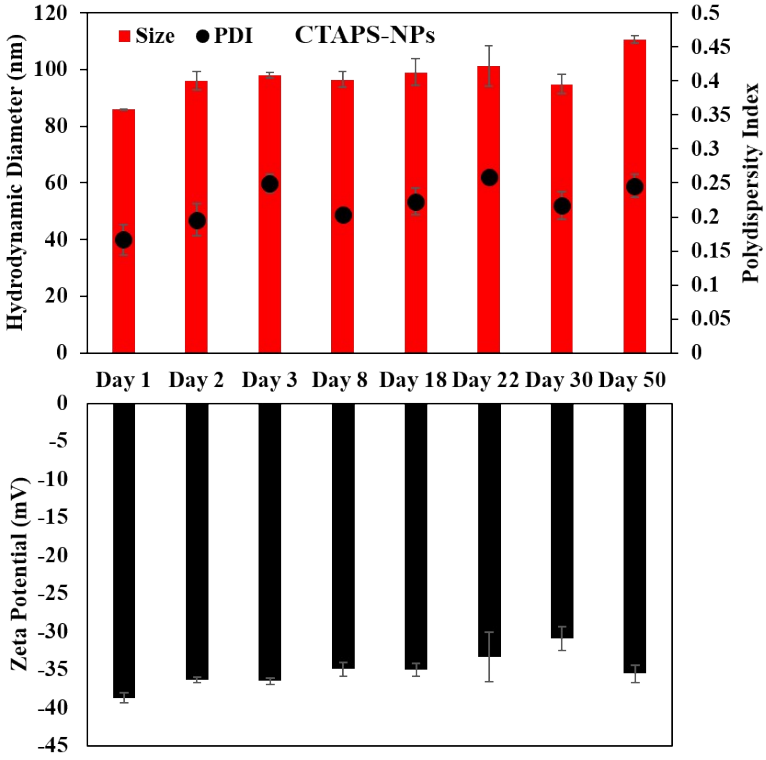

CBES-NP
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Zeta Potential (mV)
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50

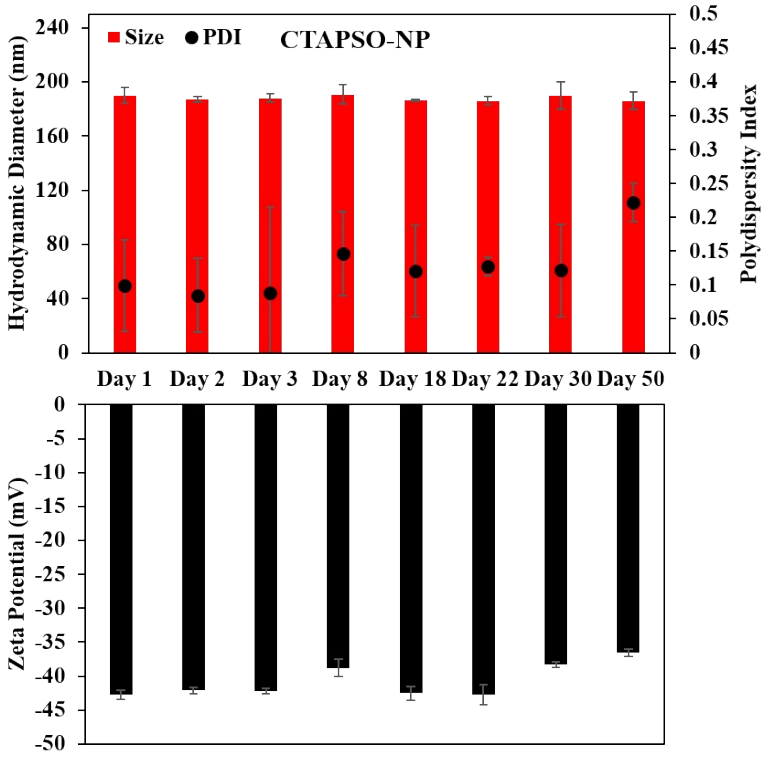

Size
PDI
CDIPSO-NP
Hydrodynamic Diameter (nm)
Polydispersity Index
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential (mV)

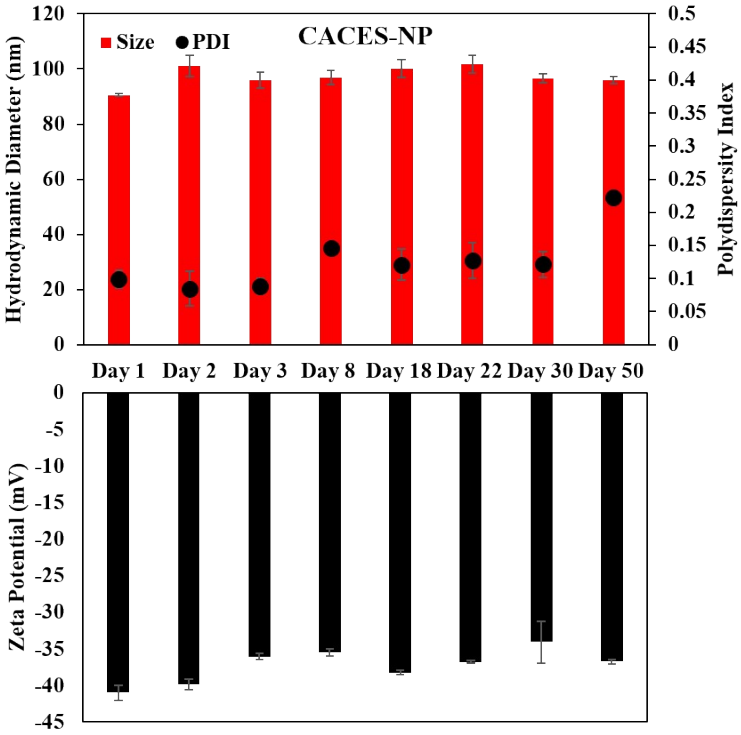

Size
PDI
CADA-NP
Hydrodynamic Diameter (nm)
Polydispersity Index
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential (mV)

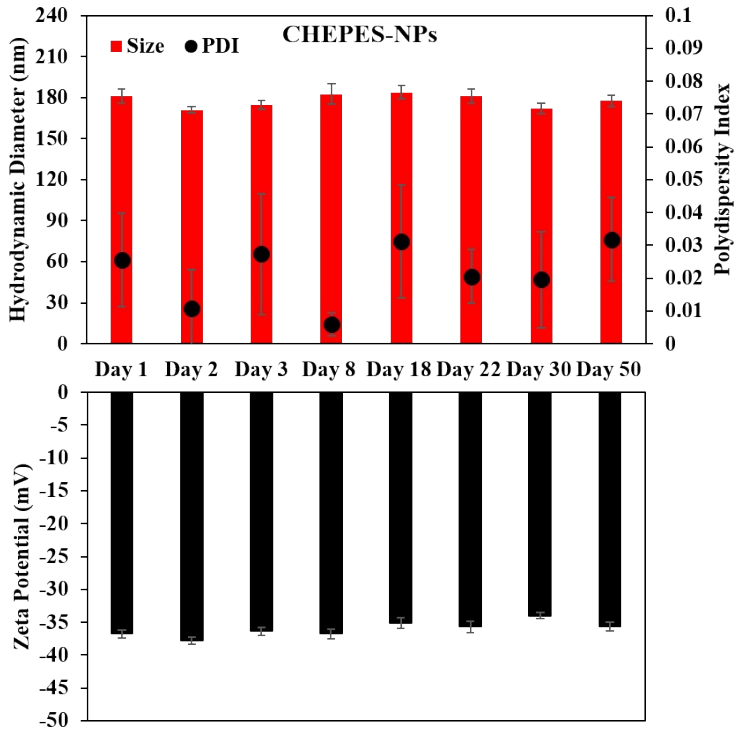

Size
PDI
CTricine-NP
Hydrodynamic Diameter (nm)
Polydispersity Index
210
180
150
120
90
60
30
0
0.3
0.25
0.2
0.15
0.1
0.05
0
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential (mV)
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50

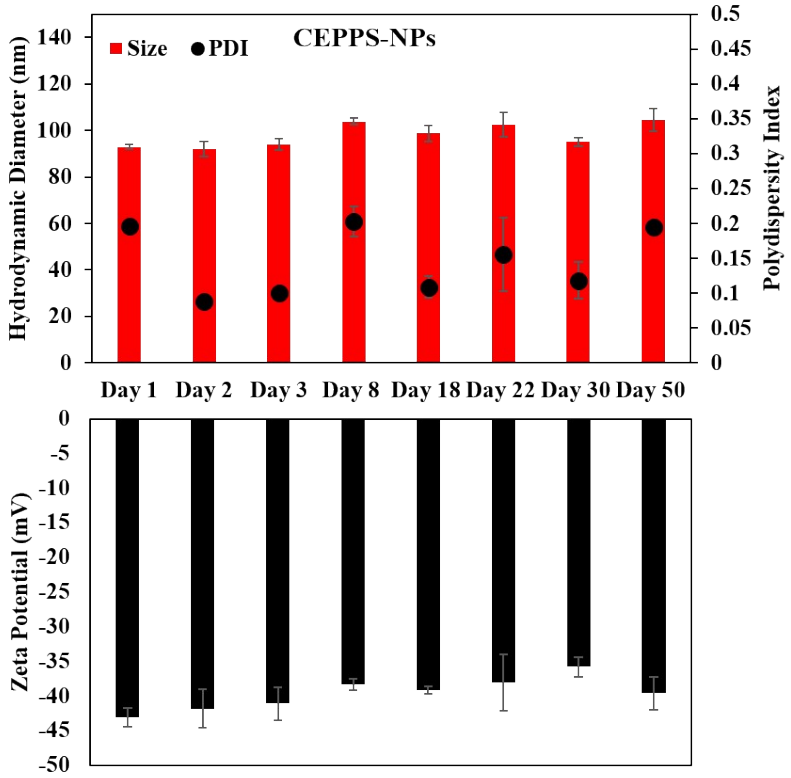

Size
PDI
CTES-NPs
Hydrodynamic Diameter (nm)
Polydispersity Index
210
180
150
120
90
60
30
0
0.2
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential (mV)
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50

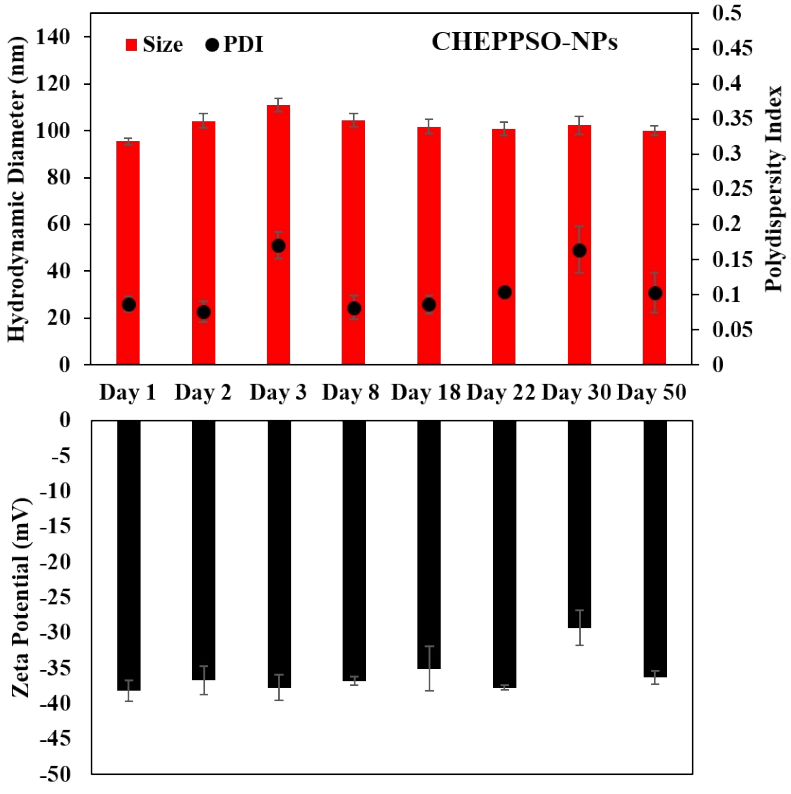

Size
PDI
CTAPS-NPs
Hydrodynamic Diameter (nm)
Polydispersity Index
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential (mV)

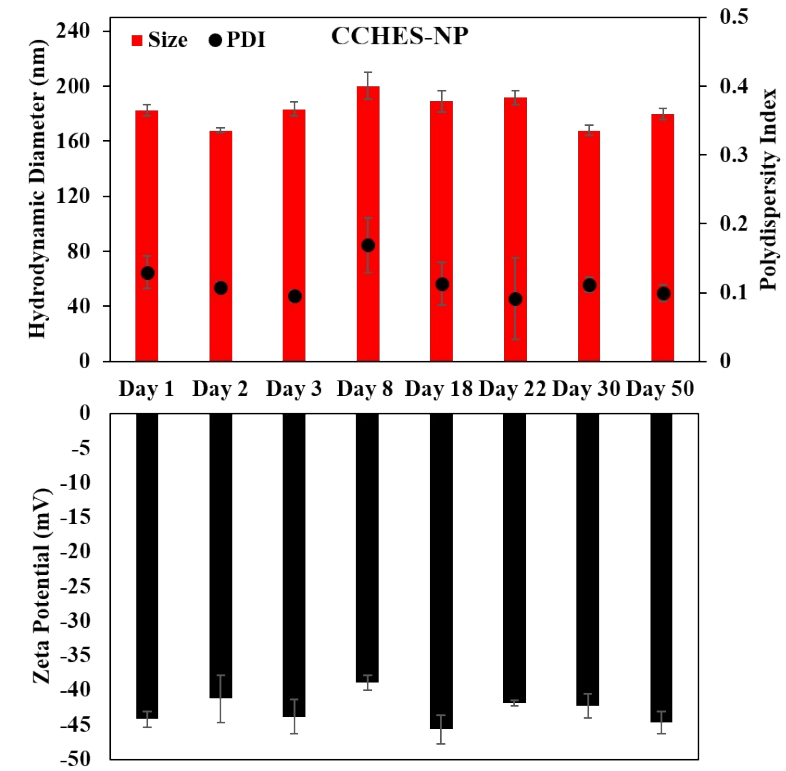

Size
PDI
CTAPSO-NP
Hydrodynamic Diameter (nm)
Polydispersity Index
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential (mV)

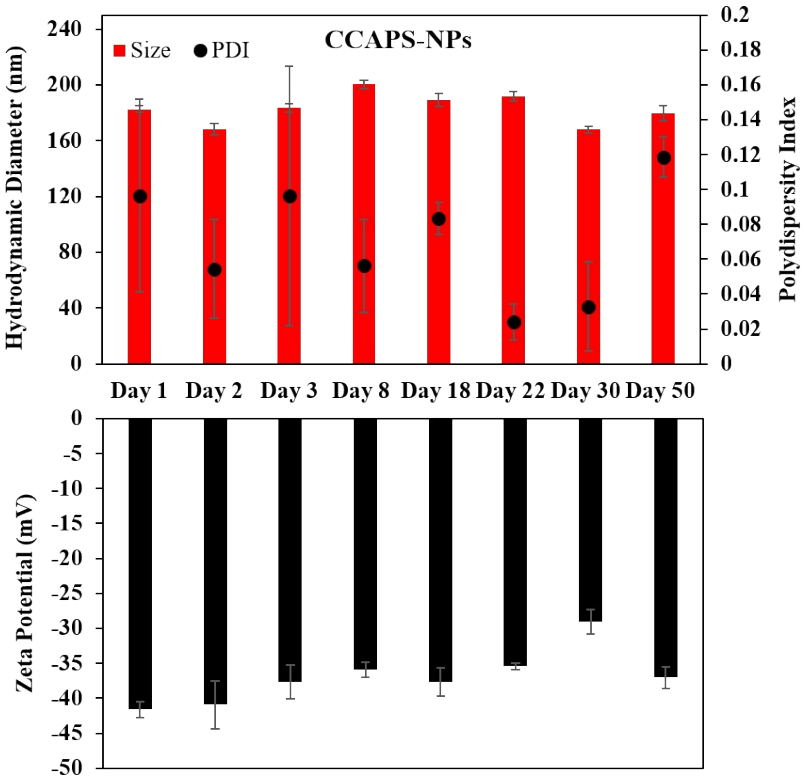

CACES-NP
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Zeta Potential (mV)
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50

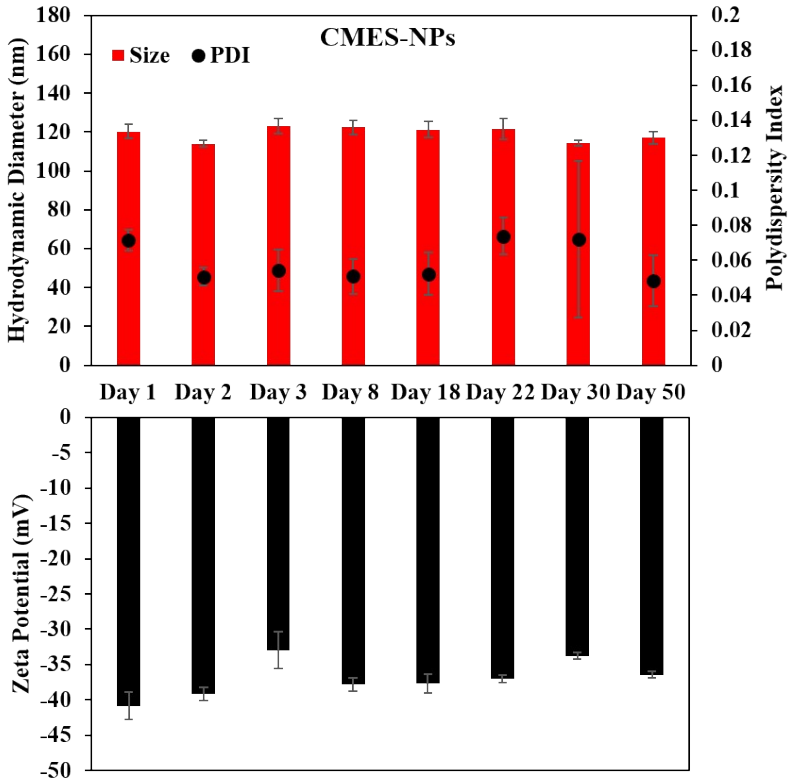

CHEPES-NPs
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Zeta Potential (mV)
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50

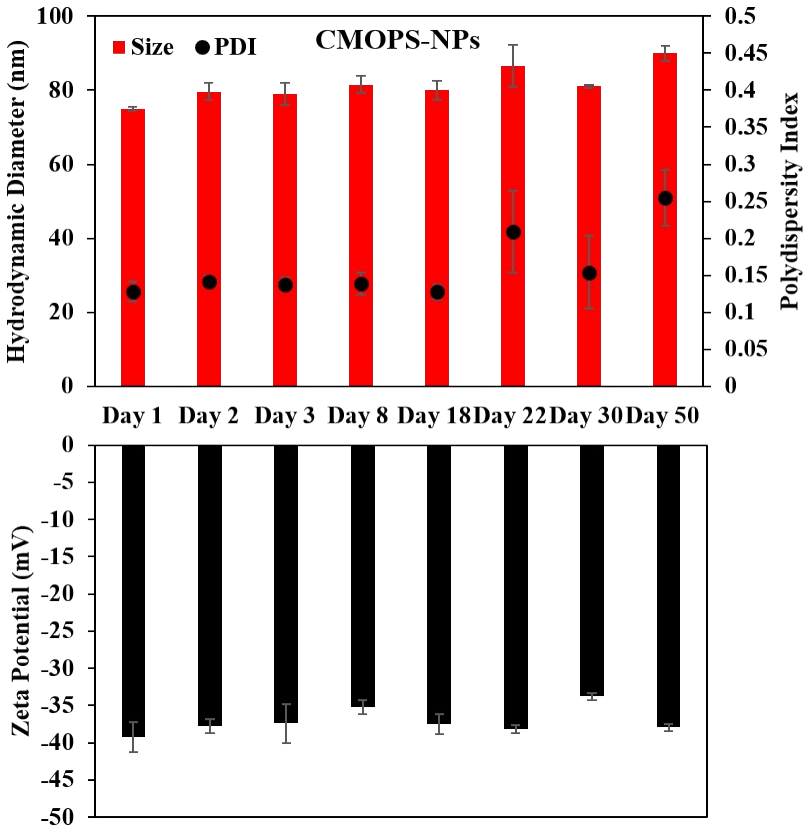

CEPPS-NPs
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Zeta Potential (mV)
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50

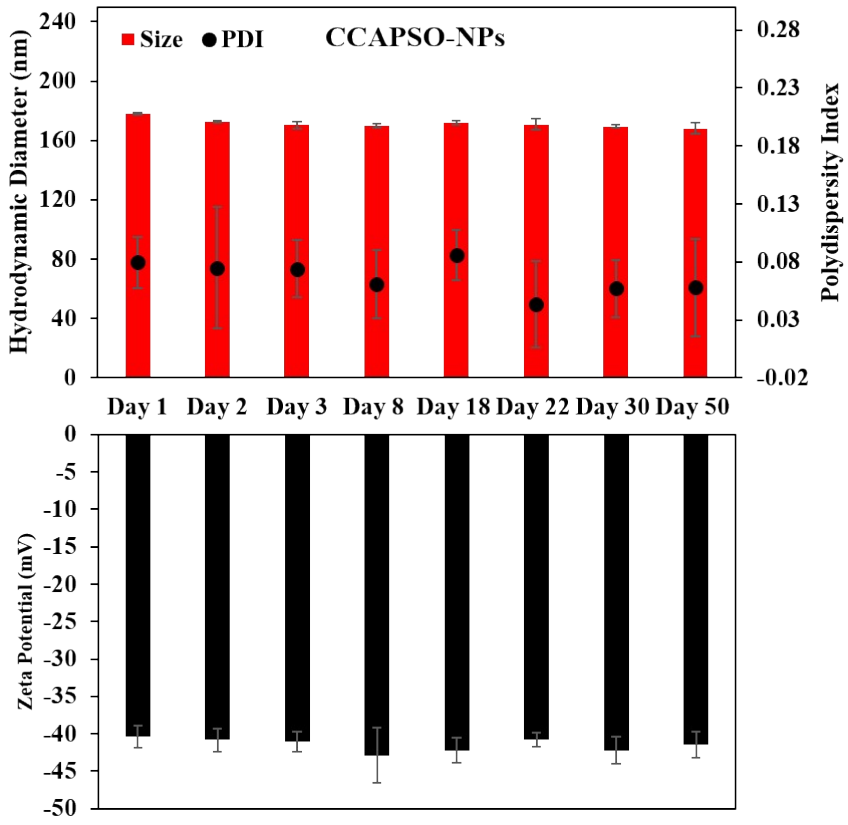

CHEPPSO-NPs
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Zeta Potential (mV)
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50

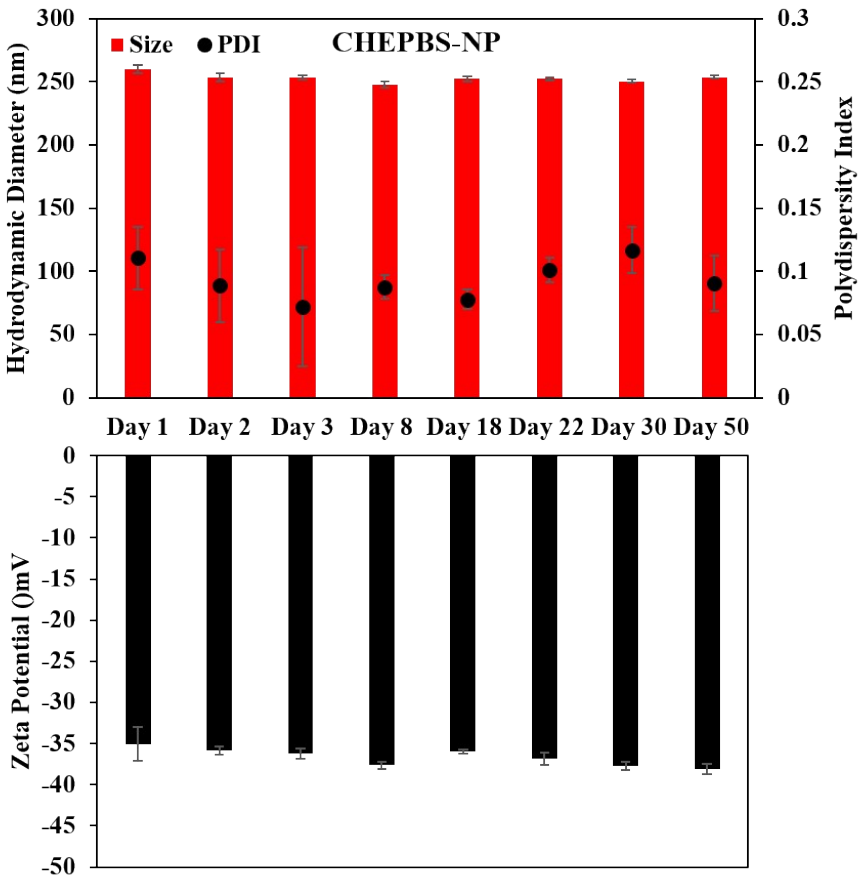

CCHES-NP
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential (mV)


CCAPS-NPs
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential (mV)


CMES-NPs
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Zeta Potential (mV)
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50


CMOPS-NPs
Size
PDI
Hydrodynamic Diameter (nm)
Polydispersity Index
Zeta Potential (mV)
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50


Size
PDI
CCAPSO-NPs
Hydrodynamic Diameter (nm)
Polydispersity Index
240
200
160
120
80
40
0
0.28
0.23
0.18
0.13
0.08
0.03
-0.02
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential (mV)
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50


Size
PDI
CHEPBS-NP
Hydrodynamic Diameter (nm)
Polydispersity Index
300
250
200
150
100
50
0
0.3
0.25
0.2
0.15
0.1
0.05
0
Day 1
Day 2
Day 3
Day 8
Day 18
Day 22
Day 30
Day 50
Zeta Potential ()mV
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50

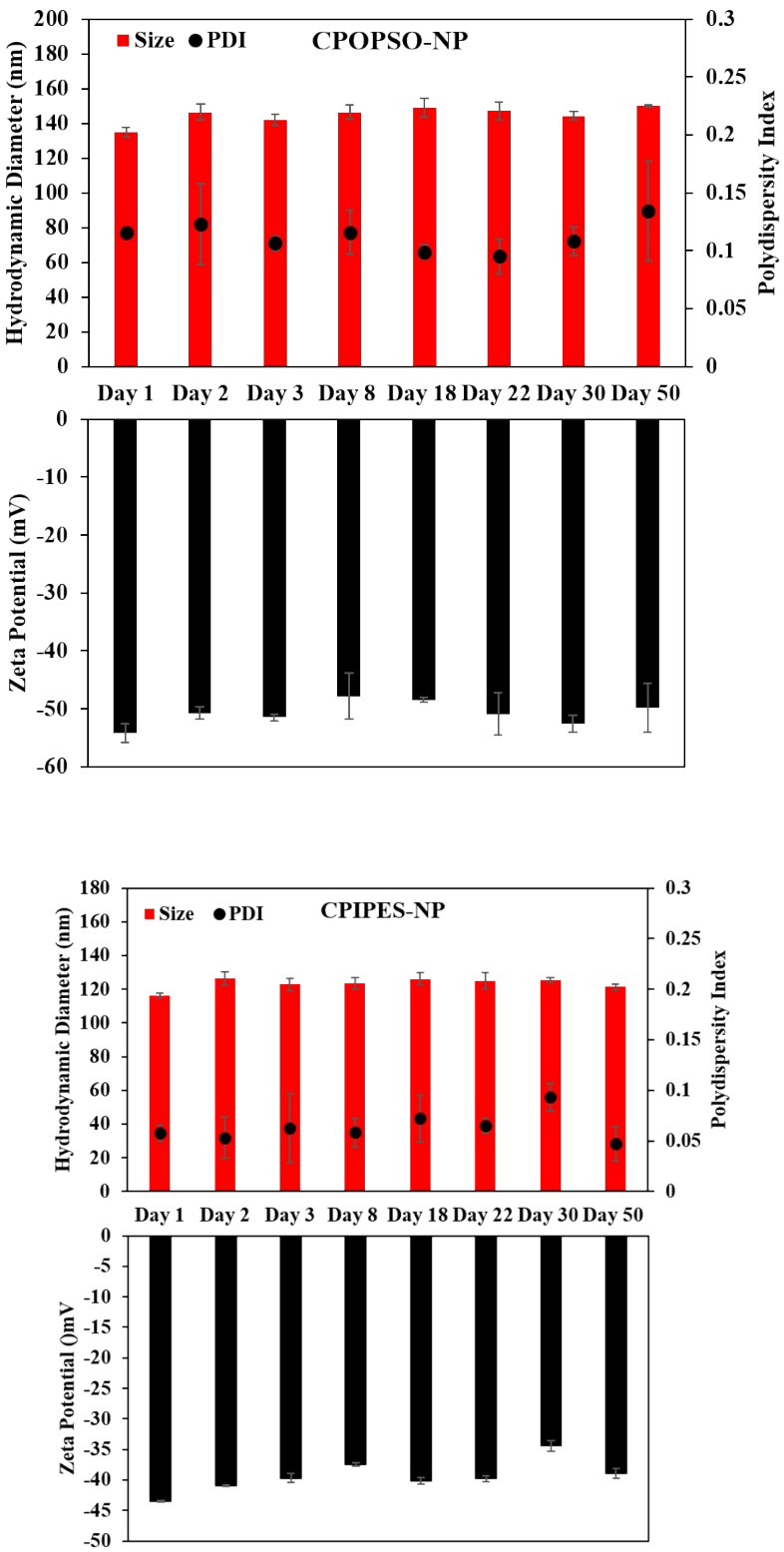


Figure S2. DLS profile showing stability of their size and zeta potential of GBIL-NPs as a function of time.

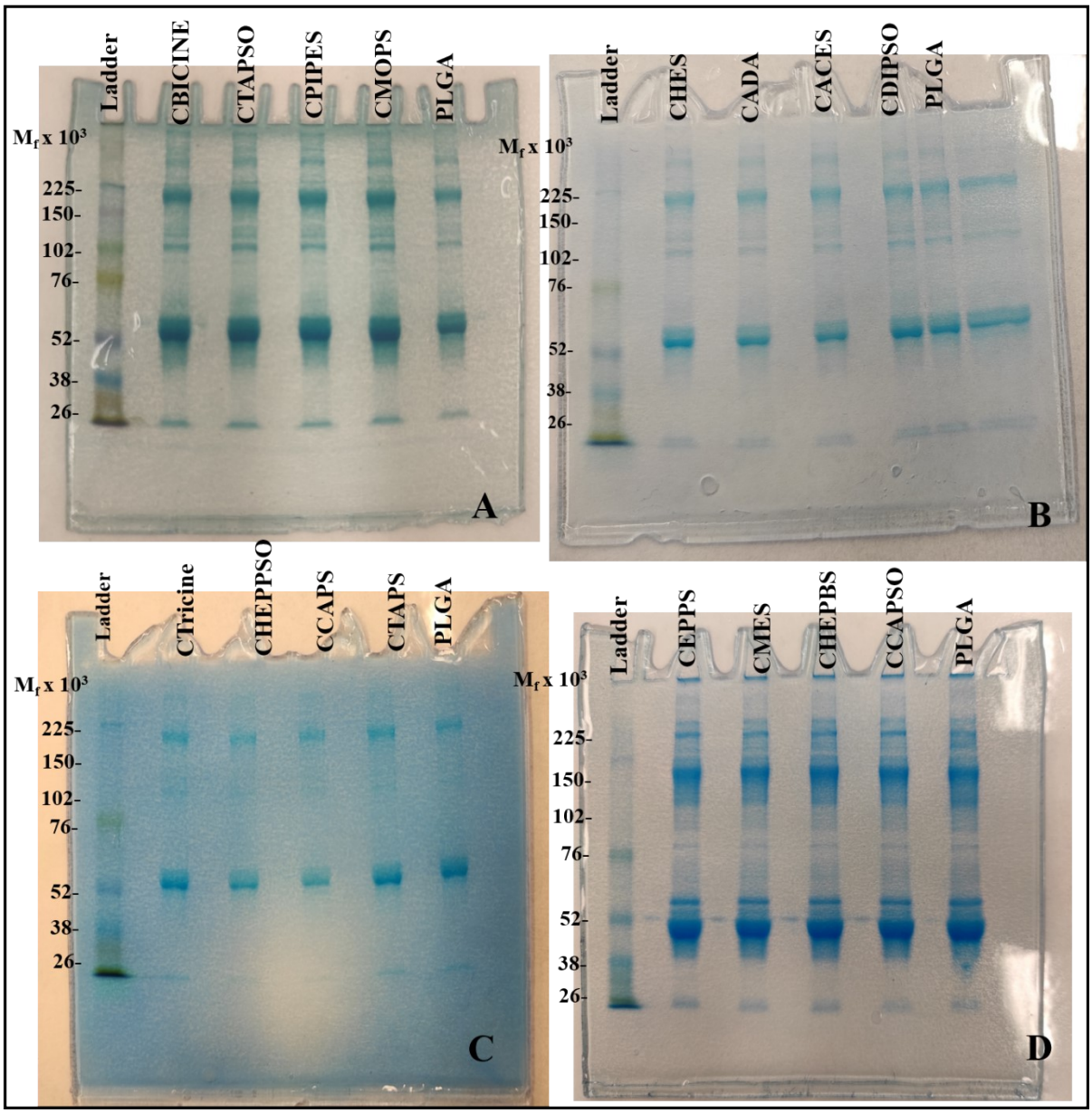


Figure S3. SDS-PAGE profile of mouse serum with GBIL-NPs.

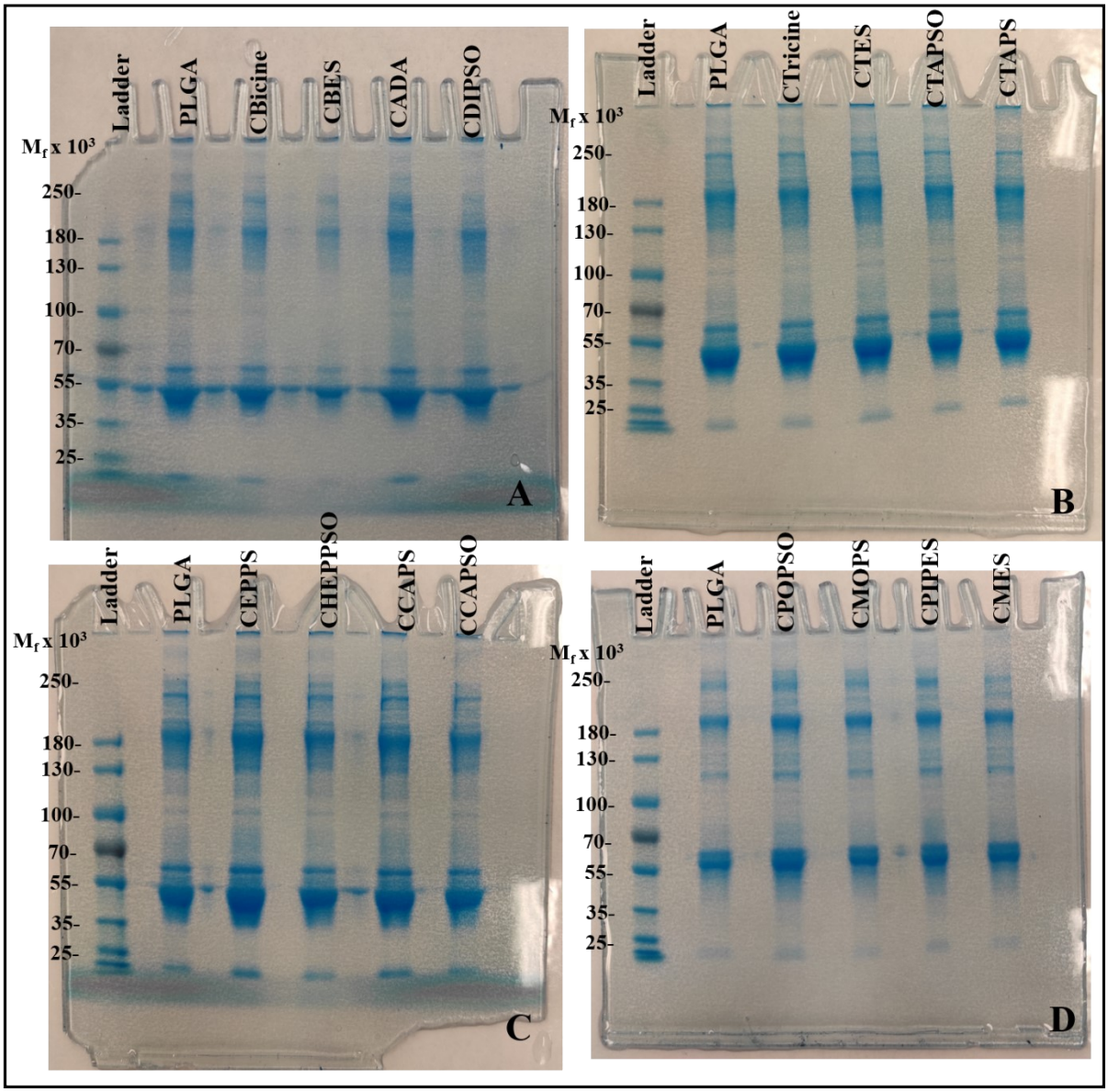
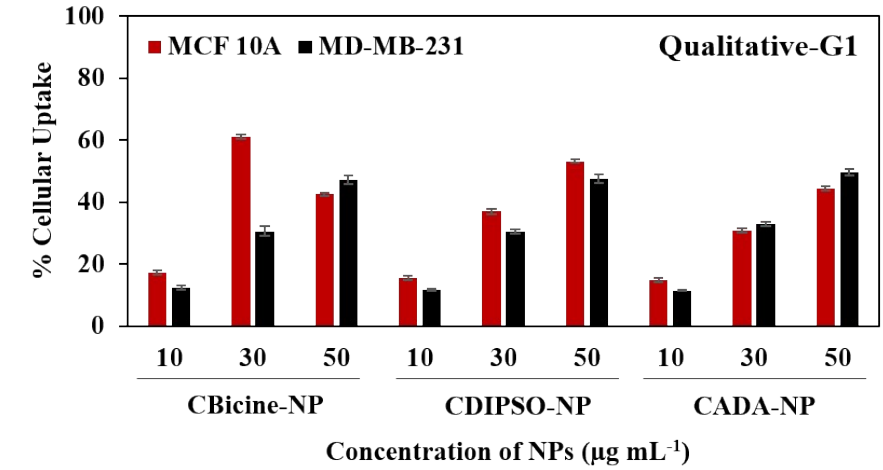
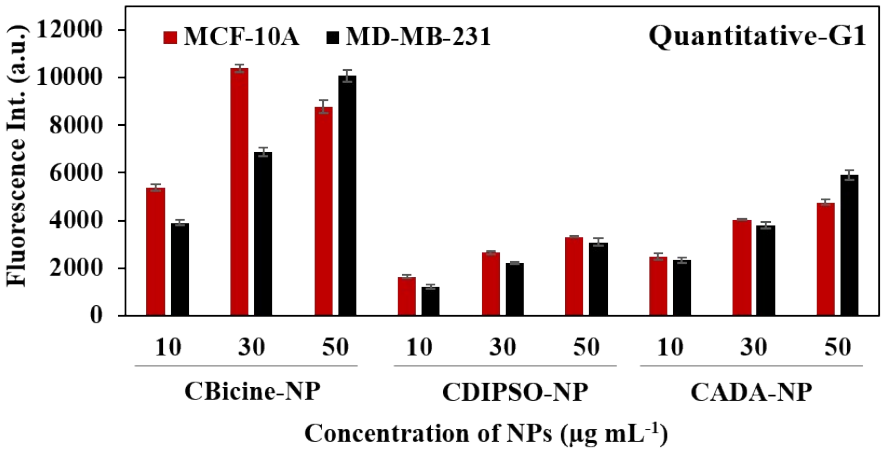
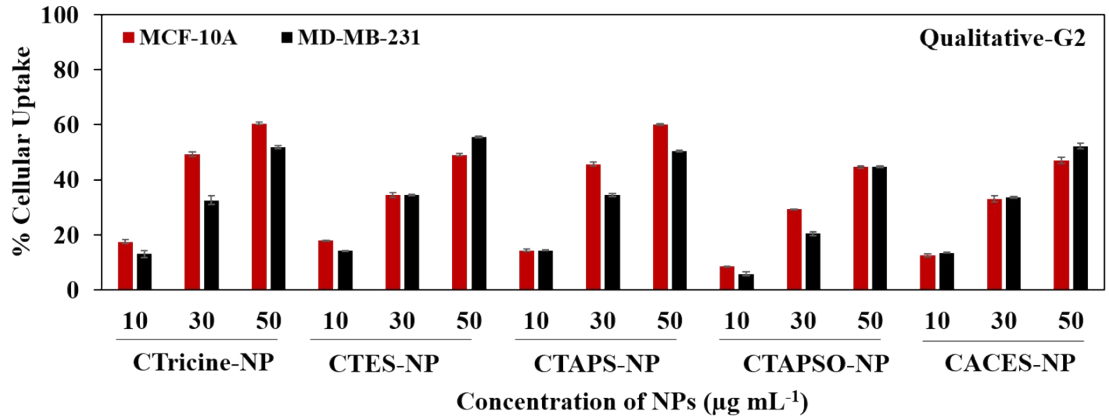
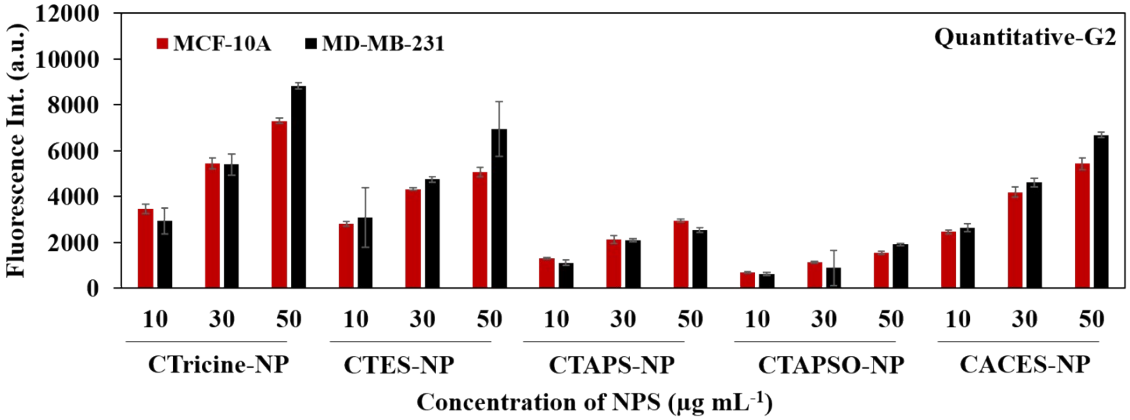


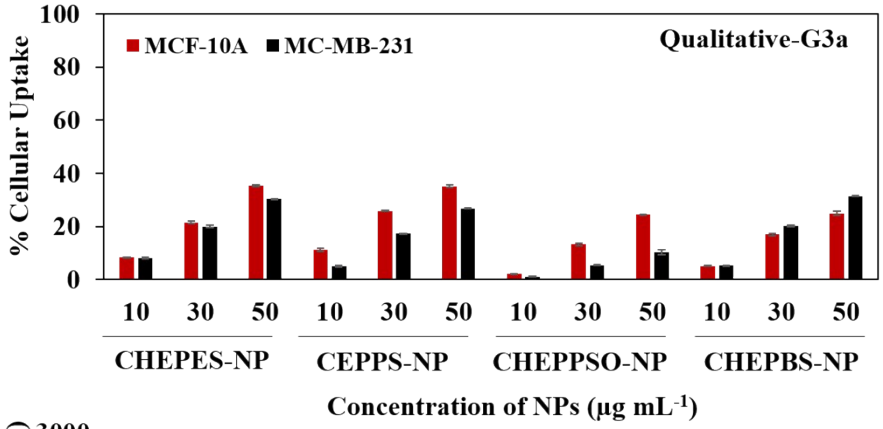
Figure S4. SDS-PAGE profile of human serum with GBIL-NPs.

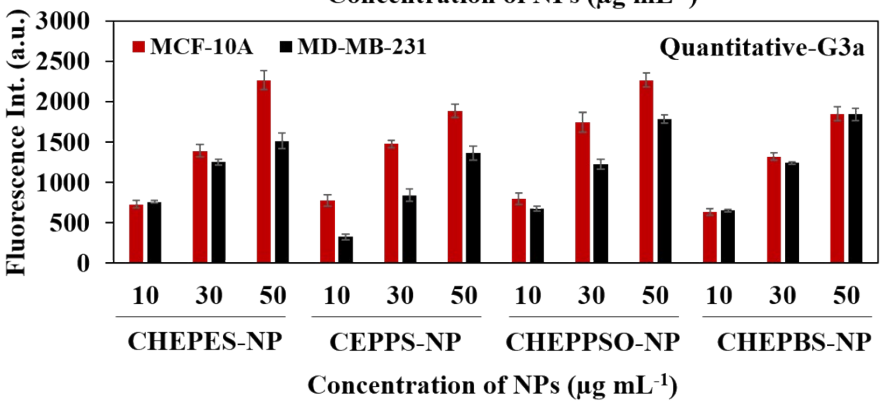

MCF 10A
MD-MB-231
Qualitative-G1
% Cellular Uptake
100
80
60
40
20
0
10
30
50
CBicine-NP
CDIPSO-NP
CADA-NP
Concentration of NPs (µg mL-1)

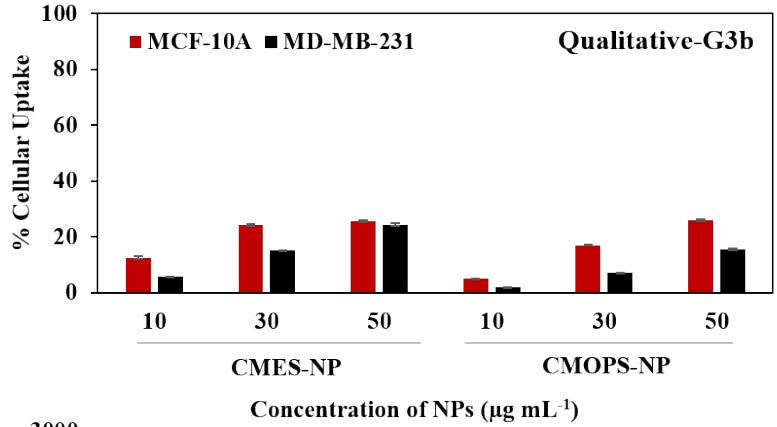

MCF-10A
MD-MB-231
Quantitative-G1
Fluorescence Int. (a.u.)
12000
10000
8000
6000
4000
2000
0
10
30
50
CBicine-NP
CDIPSO-NP
CADA-NP
Concentration of NPs (µg mL-1)

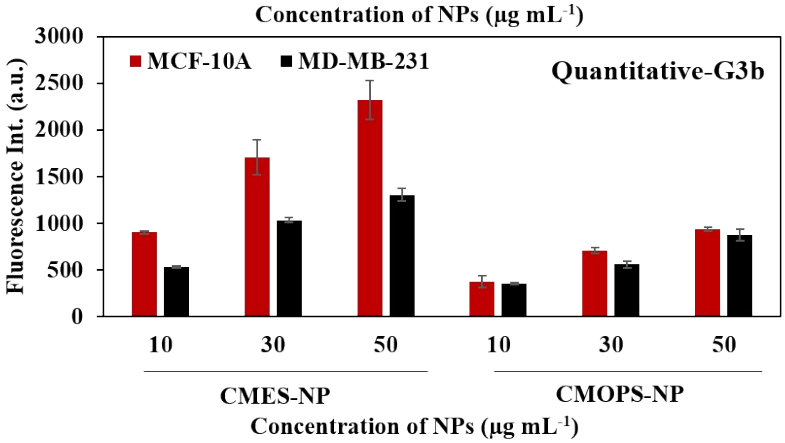

MCF-10A
MD-MB-231
Qualitative-G2
% Cellular Uptake
100
80
60
40
20
0
10
30
50
CTricine-NP
CTES-NP
CTAPS-NP
CTAPSO-NP
CACES-NP
Concentration of NPs (µg mL-1)


MCF-10A
MD-MB-231
Quantitative-G2
Fluorescence Int. (a.u.)
12000
10000
8000
6000
4000
2000
0
10
30
50
CTricine-NP
CTES-NP
CTAPS-NP
CTAPSO-NP
CACES-NP
Concentration of NPS (µg mL-1)


MCF-10A
MC-MB-231
Qualitative-G3a
% Cellular Uptake
100
80
60
40
20
0
10 30 50 10 30 50 10 30 50 10 30 50
CHEPES-NP
CEPPS-NP
CHEPPSO-NP
CHEPBS-NP
Concentration of NPs (µg mL-1)


MCF-10A
MD-MB-231
Quantitative-G3a
Fluorescence Int. (a.u.)
3000
2500
2000
1500
1000
500
0
10 30 50 10 30 50 10 30 50 10 30 50
CHEPES-NP
CEPPS-NP
CHEPPSO-NP
CHEPBS-NP
Concentration of NPs (µg mL-1)


MCF-10A
MD-MB-231
Qualitative-G3b
% Cellular Uptake
100
80
60
40
20
0
10 30 50 10 30 50
CMES-NP
CMOPS-NP
Concentration of NPs (µg mL-1)


MCF-10A
MD-MB-231
Quantitative-G3b
Fluorescence Int. (a.u.)
3000
2500
2000
1500
1000
500
0
10 30 50 10 30 50
CMES-NP
CMOPS-NP
Concentration of NPs (µg mL-1)

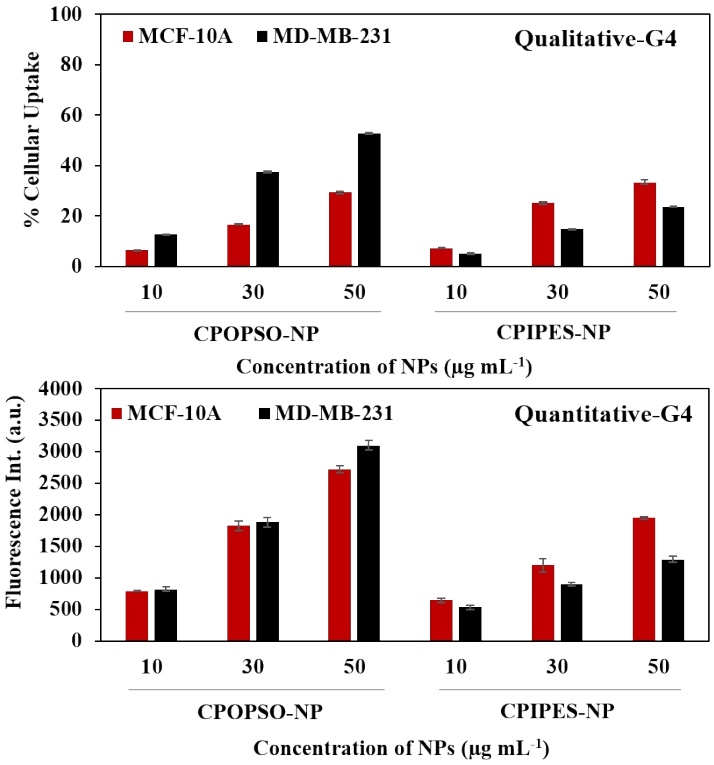


Figure S5. Qualitative and quantitative analysis of cellular uptake of GBIL-coated PLGA NPs by MCF-10A and MDA-MB-231 cell lines.

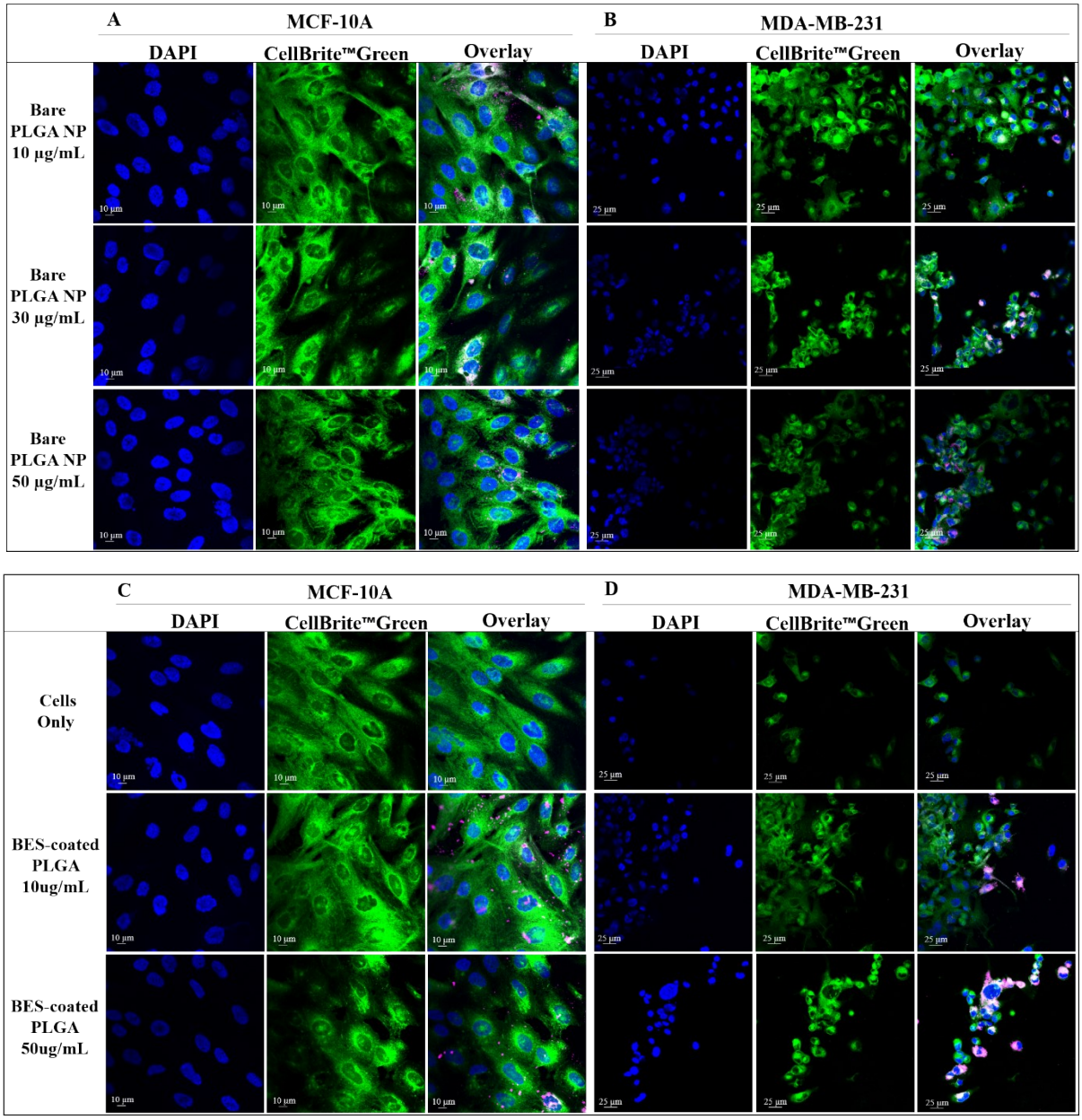


Figure S6. Confocal microscopy images showing cellular uptake of bare PLGA and CBES-coated PLGA NPs by MCF-10A and MDA-MB-231 cells at different concentrations of NPs.

Table S2: List of proteins which are common in adsorbed/depleted over all GBIL-NPs and bare PLGA NPs identified by LC-MS/MS analysis from human serum.

List of proteins found in Mouse Serum common in all GBILs coated NPs and bare PLGA NPs		
Serial Number	**UniProtID**	**Protein Name**
1	P07724	Albumin
2	Q921I1	Serotransferrin
3	Q00623	Apolipoprotein A-I
4	P01837	Immunoglobulin kappa constant
5	Q91X72	Hemopexin
6	Q61646	Haptoglobin
7	P01863	Ig gamma-2 A chain C region, Aallele
8	Q61838	Pregnancy zone protein
9	A0A0R4J038	Bradykinin
10	P07759	Serine protease inhibitor A 3K
11	P01027	Complement C3
12	A0A075B5P3	Immunoglobulin heavy constant gamma 2B (Fragment)
13	P08226	Apolipoprotein E

List of Proteins found in Human Serum common in all GBILs coated NPs and bare PLGA NPs		
Serial Number	**UniProtID**	**Protein Name**
1	P02768	Albumin
2	P02647	Apolipoprotein A-I
3	P02787	Serotransferrin
4	P00738	Haptoglobin
5	P01876	Immunoglobulin heavy constant alpha 1
6	P01834	Immunoglobulin kappa constant
7	P02652	Apolipoprotein A-II
8	P02790	Hemopexin
9	P02656	Apolipoprotein C-III
10	P04217	Alpha-1B-glycoprotein
11	P0DOY2	Immunoglobulin lambda constant 2
12	P01024	Complement C3
13	P02766	Transthyretin
14	P02765	Alpha-2-HS-glycoprotein
15	P01619	Immunoglobulin kappa variable 3-20
16	P01859	Immunoglobulin heavy constant gamma2
17	P01871	Immunoglobulin heavy constant mu
18	P01023	Alpha-2-macroglobulin

Table S2: List of all the proteins adsorbed/depleted over GBIL-NPs and bare PLGA NPs identified by LC-MS/MS analysis from human serum.

Proteins found in Mouse Serum for all GBIL coated NPs and Bare PLGA NPs		
Serial Number	**UniProtID**	**Protein Name**
1	P07724	Albumin
2	Q921I1	Serotransferrin
3	P00761	Fibrinogen alpha chain
4	Q00623	Apolipoprotein A-I
5	P01837	Immunoglobulin kappa constant
6	Q91X72	Hemopexin
7	Q61646	Haptoglobin
8	P01863	Iggamma-2A chain C region, Aallele
9	Q61838	Pregnancy zone protein
10	A0A338P7G1	Alpha-2-HS-glycoprotein
11	A0A0R4J038	Bradykinin
12	P01869	Iggamma-1chain C region ,membrane-bound form
13	P02769	Albumin
14	P07759	SerineproteaseinhibitorA3K
15	F6TQW2	Immunoglobulin heavy constant gamma 2 C(Fragment)
16	P09813	Apolipoprotein A-II
17	Q91VB8	Alphaglobin1
18	P01592	Immunoglobulin J chain
19	P01027	Complement C3
20	P01631	Ig kappa chain V-II region
21	A0A075B5P3	Immunoglobulin heavy constant gamma 2 B (Fragment)
22	A0A075B5P6	Immunoglobulin heavy constant mu (Fragment)
23	P07309	Transthyretin
24	P21614	Vitamin D-binding protein
25	E9Q8I0	Complement factor H
26	A8DUK4	Beta-globin
27	P07361	Alpha-1-acidglycoprotein2
28	P13020	Gelsolin
29	P06728	Apolipoprotein A-IV
30	A0A075B6A3	Immunoglobulin heavy constant alpha (Fragment)
31	A0A075B5V6	Immunoglobulin heavy variable V 1-42
32	P01644	Ig kappa chain V-V region HP
33	E9PZD8	Ceruloplasmin
34	P28665	Murinoglobulin-1
35	Q9QWK4	CD5antigen-like
36	P02768	Gene_Symbol=ALB
37	A0A140T8M2	Immunoglobulin kappa variable 12-44 (Fragment)
38	Q60590	Alpha-1-acidglycoprotein1
39	P19221	Prothrombin
40	A0A140T8P2	Immunoglobulin kappa variable 6-20 (Fragment)
41	P08226	Apolipoprotein E
42	Q01339	Beta-2-glycoprotein1
43	A0A075B5P5	Immunoglobulin heavy constant gamma 3 (Fragment)
44	D3Z5G7	Carboxylicester hydrolase
45	A0A338P699	Kininogen2(Fragment)
46	B8JJN0	C3/C5convertase
47	A0A0R4J039	Histidine-rich glycoprotein

48	A0A075B5K2	Immunoglobulinkappachainvariable9-124
49	P05366	SerumamyloidA-1protein
50	P34928	Apolipoprotein C-I
51	Q61129	Complement factor I
52	Q6YJU1	Fetuin-B
53	Q3UHL6	Fibronectin
54	Q06890	Clusterin
55	P20918	Plasminogen
56	A0A140T8M5	Immunoglobulinkappavariable6-15(Fragment)
57	P01898	H-2 class I histocompatibility antigen, Q10 alpha chain
58	O89020	Afamin
59	A0A0A6YX70	Antithrombin-III(Fragment)
60	Q91XL1	Leucine-rich HEV glycoprotein
61	Q00897	Alpha-1-antitrypsin1-4
62	P29788	Vitronectin
63	D3YY36	RIKENcDNA1300017J02gene
64	P01029	ComplementC4-B
65	P02070	Albumin
66	P23953	Carboxylesterase1C
67	A0A075B5M7	Immunoglobulinkappavariable5-39
68	P11680	Properdin
69	P05367	SerumamyloidA-2protein
70	P24270	Catalase
71	A0A0A6YYE7	Immunoglobulinkappavariable4-57(Fragment)

List of all the Proteins found in Human Serum for All GBIL coated NPs		
Serial Number	**UniProtID**	**Protein Name**
1	P02768	Albumin
2	P00761	alpha-1-antitrypsin (A1AT)
3	P02647	Apolipoprotein A-I
4	P02787	Serotransferrin
5	P00738	Haptoglobin
6	P01876	Immunoglobulin heavy constant alpha 1
7	P01834	Immunoglobulin kappa constant
8	P02652	Apolipoprotein A-II
9	P02790	Hemopexin
10	P02656	Apolipoprotein C-III
11	P04217	Alpha-1B-glycoprotein
12	P02649	Apolipoprotein E
13	P0DOY2	Immunoglobulinlambdaconstant2
14	P01024	ComplementC3
15	A0A024R6I7	Alpha-1-antitrypsin
16	P06727	Apolipoprotein A-IV
17	P02766	Transthyretin
18	P08519	Apolipoprotein(a)
19	P01857	Immunoglobulinheavyconstantgamma1
20	P02765	Alpha-2-HS-glycoprotein
21	K7ER74	Apolipoprotein C-II
22	A0A096LPE2	SAA2-SAA4readthrough

23	P02654	Apolipoprotein C-I
24	P01042	Kininogen-1
25	P01591	Immunoglobulin J chain
26	P00734	Prothrombin
27	P10909	Clusterin
28	P02749	Beta-2-glycoprotein1
29	P0C0L4	ComplementC4-A
30	B4E1Z4	Complement factor
31	P04114	ApolipoproteinB-100
32	P69905	Hemoglobin sub unit alpha
33	P01619	Immunoglobulinkappavariable3-20
34	P02763	Alpha-1-acid glycoprotein1
35	P01859	Immunoglobulin heavy constant gamma 2
36	P0DOY3	Immunoglobulin lambda constant 3
37	P05090	Apolipoprotein D
38	P04040	Catalase
39	P02774	Vitamin D-binding protein
40	P01871	Immunoglobulin heavy constant mu
41	P01023	Alpha-2-macroglobulin
42	P35527	Keratin, type I cytoskeletal 9
43	P01008	Antithrombin-III
44	P01860	Immunoglobulinheavyconstantgamma3
45	P02753	Retinol-bindingprotein4
46	P0CG04	Immunoglobulinlambdaconstant1