Supplementary Information

Exploring the Utility of Hybrid Siloxane-Phosphocholine (SiPC) Liposomes as Drug Delivery Vehicles

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Syntheses

1-Capryloyl-2-hydroxy-*sn*-glycero-3-phosphocholine. A Teflon flask was charged with 0.254 g (0.988 mmol) of α-glycerophosphocholine and combined with 1.82 g (12.6 mmol) of octanoic acid and melted together at 60°C for 5 h. N435 (213.1 mg, 10 w/w%) was added and stirred for 10 min at 1000 mbar, and then the pressure was reduced to 135 mbar for 48 h with stirring. The reaction was quenched by cooling to room temperature and diluted with 10 mL of $CHCl_3$. The N435 was removed by filtering the mixture through a medium porosity, glass-fritted Büchner funnel. Solvents were removed *in vacuo* to give a viscous oil that was further purified by column chromatography on silica gel. The column was loaded with 20 g of silica gel suspended in chloroform. The column was preconditioned with 10 mL of 9:1 $CHCl_3$:MeOH before loading the crude mixture and eluting with an isocratic elution solvent of 65:25:4 $CHCl_3$:MeOH:H_2O to give 0.097 g (0.253 mmol, 26%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.878 (t, 3H, ^{3}J=6.3 Hz), 1.274 (br, 12H), 1.587 (m, 2H), 2.304 (t, 2H, ^{3}J=7.5 Hz), 3.338 (s, 9H), 3.803 (br, 3H), 3.930 (br, 2H), 4.062 (br, 2H), 4.318 (br, 2H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 14.1, 22.7, 24.9, 29.26, 29.31, 29.4, 29.5, 31.9, 34.1, 54.2. 59.4, 65.2, 66.1, 67.0, 68.7, 71.91, 173.9; ^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ -0.31; ESI+MS (m/z): $[M+H]^+$ 412.2, $[M+Na]^+$ 434.2, $[M+K]^+$ 450.2.

1-Caproyl-2-hydroxy-*sn*-glycero-3-phosphocholine. A Teflon flask was charged with 0.198 g (0.769 mmol) of α-glycerophosphocholine and combined with 1.51 g (8.80 mmol) of decanoic acid and melted together at 65°C. N435 (182.7 mg, 10 w/w%) was added and stirred for 10 min after which time the pressure

was reduced to 75 mbar for 48 h with stirring. The reaction was quenched by cooling to room temperature and diluting with 15 mL of $CHCl_3$. The N435 was removed by filtering the mixture through a medium porosity, glass-fritted Büchner funnel. Solvents were removed *in vacuo* to give a viscous oil that was further purified by column chromatography on silica gel. The column was loaded with a silica gel-chloroform slurry and preconditioned with 10 mL of 9:1 $CHCl_3$:MeOH before loading the crude mixture and eluting with an isocratic elution solvent of 65:25:4 $CHCl_3$:MeOH:H_2O to give 0.118 g (0.276 mmol, 36%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.014 (s, 6H), 0.032 (s, 9H), 0.482 (m, 2H), 0.852 (t, 3H, ^{3}J=4.8 Hz), 1.236 (br, 16H), 1.564 (m, 4H), 2.249 (t, 2H, ^{3}J=6 Hz), 2.274 (t, 2H, ^{3}J=6 Hz), 3.368 (s, 9H), 3.384 (br, 4), 4.102 (m, 1H), 4.293 (br, 2H), 4.367 (m, 1H), 5.157 (m, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 0.31, 1.97, 14.09, 18.07, 22.65, 22.95, 24.86, 28.52, 29.15, 29.27, 29.30, 29.45, 31.85, 34.08, 34.10, 54.38, 59.29, 63.03, 63.37, 66.33, 70.49, 173.19, 173.57; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ -0.77; ESI+MS (m/z): $[M+H]^+$ 642.3, $[M+Na]^+$ 664.3.

1-Myrsitoyl-2-hydroxy-*sn*-glycero-3-phosphocholine. A Teflon flask was charged with 0.232 g (0.904 mmol) of α-glycerophosphocholine and combined with 2.10 g (9.21 mmol) of myristic acid and melted together at 70°C. When the myristic acid was melted, N435 (241 mg) was added and stirred for 10 min at 1000 mbar, after which time the pressure was reduced to 135 mbar for 48 h with stirring. The reaction was quenched by cooling to room temperature and diluting with 10 mL of 7:3 $CHCl_3$:MeOH. The enzyme beads were removed by filtration through a medium porosity, glass-fritted Büchner funnel. The solvents were removed by rotary evaporation to give a viscous gel that was further purified by column chromatography on silica gel. The column was loaded with a silica gel-chloroform slurry and was preconditioned with 10 mL of 9:1 $CHCl_3$:MeOH before loading the crude mixture and eluting with an isocratic elution solvent of 65:25:4 $CHCl_3$:MeOH:H_2O to give 0.13 g (0.28 mmol, 31%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.854 (t, 3H, ^{3}J=6.3 Hz), 1.254 (br, 20H), 1.567 (m, 2H), 2.300 (t, 2H, ^{3}J=7.5 Hz), 3.320 (s, 9H), 3.781-4.314 (br, 9H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 14.1, 22.7, 24.9, 29.3, 29.4, 29.5, 29.7, 29.7, 29.8, 31.9, 34.1, 54.2. 59.4, 65.2, 66.1, 67.0, 68.6, 173.9; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ -0.15; ESI+MS (m/z): $[M+H]^+$ 468.3, $[M+Na]^+$ 490.2, $[M+K]^+$ 506.2.

1-Lauroyl-2-hydroxy-*sn*-glycero-3-phosphocholine. A Teflon flask was charged with 0.128 g (0.495 mmol) of α-glycerophosphocholine and combined with 1.09 g (5.44 mmol, 11 eq.) of lauric acid and melted together at 65 °C. When the lauric acid was melted Novozym-435 (120 mg (10 w/w%) was added and stirred for 10 min at 1 atmosphere, and then the pressure was reduced to 120 mbar for 48 h with stirring. The reaction was quenched by cooling to room temperature and diluting with 10 mL of 9:1 $CHCl_3$:MeOH. The immobilized enzyme was removed by filtering the mixture through a medium porosity, glass-fritted

Büchner funnel. Solvents were removed *in vacuo* to give a viscous oil that was further purified by column chromatography on (19 g) silica gel. The column was loaded with a silica gel-chloroform slurry and preconditioned with 10 mL of 9:1 $CHCl_3$:MeOH before loading the crude mixture and eluting with 200 mL of an isocratic elution solvent 65:25:4 $CHCl_3$:MeOH:H_2O to give 0.140 g (0.317 mmol, 68%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.878 (t, 3H, ^{3}J=6.3 Hz), 1.257 (br, 16H), 1.570 (m, 2H), 2.300 (t, 2H, ^{3}J=7.5 Hz), 3.316 (s, 9H), 3.773-4.308 (br, 9H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 14.1, 22.6, 24.9, 29.2, 29.3, 29.4, 29.5, 29.6, 29.6, 31.9, 34.1, 54.1, 59.3, 65.2, 66.0, 67.1, 68.6, 173.3, 173.8; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ -0.23.

1-Palmitoyl-2-hydroxy-*sn*-glycero-3-phosphocholine. A Teflon round-bottomed flask was charged with 0.107 g (0.416 mmol) of α-glycerophosphocholine and 1.13 g (4.41 mmol) of palmitic acid and melted together at 80 °C for 10 min with stirring. An immobilized lipase (N435) (0.118g, 10 wt%) was added and the reaction was further stirred for 10 min under atmospheric pressure after which time the pressured was reduced to 120 mbar for 48 h. The reaction mixture was cooled to room temperature and diluted with 10 ml of 9:1 $CHCl_3$:MeOH, filtered through a medium porosity glass-fritted Büchner funnel to remove the N435, and the solvents were removed under reduced pressure. The crude residue was purified by column chromatography on 20 g of silica gel equilibrated with $CHCl_3$, pre-conditioned with 10 mL of 9:1 CHCl3:MeOH, and eluted with 300 mL 65:25:4 $CHCl_3$:MeOH:H_2O to give 59 mg (0.119 mmol, 29%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H, ^{3}J=6.3 Hz), 1.25 (br, 26H), 1.56 (m, 2H), 2.23 (t, 2H, ^{3}J=7.5 Hz), 3.37 (s, 9H), 3.792-4.051 (br, 7H), 4.37 (br, 2H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 14.12, 22.69, 24.94, 29.29, 29.38, 29.44, 29.61, 29.68, 29.74, 31.93, 34.17, 54.32, 59.50, 65.18, 66.28, 67.21, 67.89, 68.67, 173.88; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ -0.21; ESI+MS (m/z): $[M+H]^+$ 496.4, $[M+Na]^+$ 518.3.

1-Stearoyl-2-hydroxy-*sn*-glycero-3-phosphocholine. A Teflon round-bottomed flask was charged with 0.200 g (0.779 mmol) of α-glycerophosphocholine and 2.56 g (9.02 mmol) of stearic acid that were melted together at 85°C for 10 min with stirring. Immobilized lipase (N435, 0.272 g, 10 wt%) was added and the mixture was stirred for an additional 10 min under atmospheric pressure after which time the pressured was reduced to 135 mbar for 72 h. The reaction mixture was cooled to room temperature and diluted with 10 mL of $CHCl_3$:^{i}PrOH, filtered through a medium porosity glass-fritted Büchner funnel to remove the N435 and the solvents were removed under reduced pressure. The crude residue was purified by column chromatography on silica gel equilibrated with $CHCl_3$, pre-conditioned with 10 mL of 9:1 $CHCl_3$:MeOH, and eluted with 65:25:4 $CHCl_3$:MeOH:H_2O to give 81.0 mg (0.095 mmol, 20%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.868 (t, 3H, ^{3}J=6.3 Hz), 1.244 (br, 32H), 1.555 (m, 2H), 2.291 (t, 2H, ^{3}J=7.5 Hz),

3.322 (s, 9H), 3.792-4.051 (br, 7H), 4.310 (br, 2H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 14.10, 22.67, 22.94, 29.33, 29.38, 29.49, 29.68, 29.78, 31.93, 34.14, 54.29, 59.37, 65.25, 66.10, 67.17, 68.66, 173.89; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ -0.18.

1-Capryloyl-2-((5-(1,1,3,3,3-pentamethyldisiloxanyl)pentanoyl)-*sn*-glycero-3-phosphocholine. (**1**, Cap-ValDS-PC): An oven-dried flask was cooled under a nitrogen atmosphere and charged with 192 mg (0.772 mmol) of 1-(4-carboxybutyl)-1,1,3,3,3-pentamethyldisiloxane and dissolved into 1 mL of $CHCl_3$. To this solution were added 170 mg (0.823 mmol) of DCC and 10.9 mg (0.089 mmol) of DMAP and the mixture was stirred at room temperature for 10 min. A solution of 8:0 LPC (0.097 g, 0.253 mmol) in 5 mL of $CHCl_3$ was added and the reaction mixture was stirred for 48 h. A white precipitate was filtered from the reaction mixture and the solvent was removed under reduced pressure. The crude residue was purified by column chromatography using 200-400 mesh silica gel (20 g) after being suspended in $CHCl_3$. The column was preconditioned with 10 mL of 9:1 $CHCl_3$:MeOH and the eluted with 65:25:4 $CHCl_3$:MeOH:H_2O to give 32.8 mg (54 μmol, 21%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.033 (s, 6H), 0.051 (s, 9H), 0.508 (m, 2H), 0.873 (t, 3H, 3J=6.3 Hz), 1.267 (br, 12H), 1.594 (m, 2H), 2.727 (t, 2H, ^{3}J=7.5 Hz), 2.298 (t, 2H, 3J=7.5 Hz), 3.349 (s, 9H), 3.8799 (br, 2H), 3.900 (br, 2H), 4.115 (m, 1H), 4.300-4.417 (br, 2H), 5.178 (m, 1H); ^{13}C {^{1}H } NMR (75 MHz, $CDCl_3$): δ 0.15, 1.81, 14.05, 18.06, 22.58, 22.94, 24.58, 28.50, 28.93, 29.07, 31.66, 34.06, 34.09, 54.34, 59.36, 62.99, 63.37, 66.33, 70.51, 173.16, 173.55; ^{31}P {^{1}H } NMR (121 MHz, $CDCl_3$): δ -0.76; ^{29}Si {^{1}H } NMR (59.6 MHz, $CDCl_3$): δ 7.2, 7.3; ESI+MS (m/z): [M+H]+ 614.3, [M+Na]+ 636.3, [M+K]+ 652.2.

1-Caproyl-2-((5-(1,1,3,3,3-pentamethyldisiloxanyl)pentanoyl)-*sn*-glycero-3-phosphocholine (**2**, Cpc-ValDS-PC). An oven-dried flask was cooled under a nitrogen atmosphere and charged with 1-(4-carboxybutyl)-1,1,3,3,3-pentamethyldisiloxane (151.7 mg, 0.610 mmol) and dissolved into 2 mL $CHCl_3$. To this solution were added 164.3 mg (0.796 mmol) of DCC and 11.0 mg (0.082 mmol) of DMAP and the mixture was stirred at room temperature for 10 min. A solution of 10:0 LPC (0.118 g, 0.276 mmol) in 3 mL of $CHCl_3$was added and the reaction mixture was stirred for 48 h. A white precipitate was filtered from the reaction mixture and the solvent was removed *in vacuo*. The crude residue was purified by column chromatography using 20 g of 200-400 mesh silica gel suspended in $CHCl_3$. The column was preconditioned with 10 mL of 9:1 $CHCl_3$:MeOH and eluted with 300 mL of 65:25:4 $CHCl_3$:MeOH:H_2O to give 69.8 mg (109 μmol, 39%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.014 (s, 6H), 0.032 (s, 9H), 0.482 (m, 2H), 0.852 (t, 3H, ^{3}J=4.8 Hz), 1.289 (br, 16H), 2.25 (t, 2H, ^{3}J=6.0 Hz), 2.27 (t, 2H, ^{3}J=6.0 Hz), 3.37 (s, 9H), 3.84-3.909 (br, 4H), 4.10 (m, 1 H), 4.29 (br, 2H), 4.37 (m, 1H), 5.16 (m, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 0.31, 1.97, 14.09, 18.07, 22.65, 22.95, 24.86, 28.52, 29.15, 29.27, 29.30, 29.45,

31.85, 34.08, 34.10, 54.38, 59.29, 63.03, 63.37, 66.33, 70.49, 173.19, 173.57 ppm; ^{29}Si {^{1}H} NMR (59.6 MHz, $CDCl_3$): δ 7.2, 7.3 ppm; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ -0.72 ppm; ESI+MS (m/z): $[M+H]^+$ 642.4 m/z, $[M+Na]^+$ 664.3 m/z.

1-Lauroyl-2-((5-(1,1,3,3,3-pentamethyldisiloxanyl)pentanoyl)-*sn*-glycero-3-phosphocholine. (**3**, Lau-ValDS-PC). An oven-dried flask was cooled under a nitrogen atmosphere and charged with 540 mg (2.17mmol) of 1-(4-carboxybutyl)-1,1,3,3,3-pentamethyldisiloxane and dissolved into 5 mL of $CHCl_3$. To this solution were added 449 mg (2.18 mmol) of DCC and 13.3 mg (0.109 mmol) of DMAP and the mixture was stirred at room temperature for 5 min. A solution of 12:0 LPC (0.320 g, 0.728 mmol) in 5 mL of $CHCl_3$ was added and the reaction mixture was stirred for 24 h. A white precipitate was filtered from the reaction mixture and the solvent was removed *in vacuo*. The crude residue was purified by column chromatography using 200–400 mesh silica gel (22 g) suspended in hexanes. The column eluted with 50 mL of a 9:1 mixture of hexanes:ethyl acetate and then eluted with 200 mL of 65:25:4 $CHCl_3$:MeOH:H_2O to give 40 mg (58.3 μmol) of an opaque gel. Impure fractions were collected and purified again by column chromatography using 200–400 mesh silica gel (15 g) suspended $CHCl_3$. The column was preconditioned with 10 mL of 9:1 $CHCl_3$:MeOH and the eluted with 200 mL 65:25:4 $CHCl_3$:MeOH:H_2O to give 209 mg (305 μmol) of an opaque gel to yield a total of 249 mg (363 μmol, 50%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.054 (s, 6H), 0.072 (s, 9H), 0.528 (m, 2H), 0.892 (t, 3H, ^{3}J=6.3 Hz), 1.272 (br, 20H), 1.626 (m, 4H), 2.289 (t, 2H, ^{3}J=7.8 Hz), 2.315 (t, 2H, ^{3}J=7.8 Hz), 3.375 (s, 9H), 3.674-4.436 (br, 9H), 5.200 (m, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 0.4, 2.0, 14.1, 18.1, 22.7, 23.0, 24.9, 28.5, 29.2, 29.3, 29.5, 29.6, 31.9, 34.1, 54.4, 59.3, 63.0, 66.3, 70.5, 173.2, 173.6; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ -0.82; ^{29}Si {^{1}H} NMR (59.6 MHz, $CDCl_3$): δ 7.2, 7.3. ESI+MS (m/z): $[M+H]^+$ 670.4 m/z, $[M+Na]^+$ 692.4 m/z.

1-Myristoyl-2-((5-(1,1,3,3,3-pentamethyldisiloxanyl)pentanoyl)-*sn*-glycero-3-phosphocholine (**4**, Myr-ValDS-PC). An oven-dried flask was cooled under a nitrogen atmosphere and charged with 118 mg (0.479 mmol) of 1-(4-carboxybutyl)-1,1,3,3,3-pentamethyldisiloxane and dissolved into 4 mL of $CHCl_3$. To this solution were added 101 mg (0.491 mmol) of DCC and 5.0 mg (0.041 mmol) of DMAP and the mixture was stirred at room temperature for 5 min. A solution of 14:0 LPC (0.075 g, 0.161 mmol) in 4 mL of $CHCl_3$ was added and the reaction mixture was stirred for 48 h. A white precipitate was filtered from the reaction mixture and the solvent was removed *in vacuo*. The crude residue was purified by column chromatography using 200-400 mesh silica gel (20 g) suspended in $CHCl_3$. The column was pre-conditioned with 10 mL of 9:1 $CHCl_3$:MeOH and the eluted with 65:25:4 $CHCl_3$:MeOH:H_2O to give 51.1 mg (73 μmol, 46%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.032 (s, 6H), 0.050 (s, 9H), 0.506 (m, 2H), 0.870 (t, 3H, J=6.3 Hz), 1.246 (br, 20H), 1.604 (m, 2H), 2.267 (t, 2H, ^{3}J=8.1 Hz), 2.293 (t, 2H,

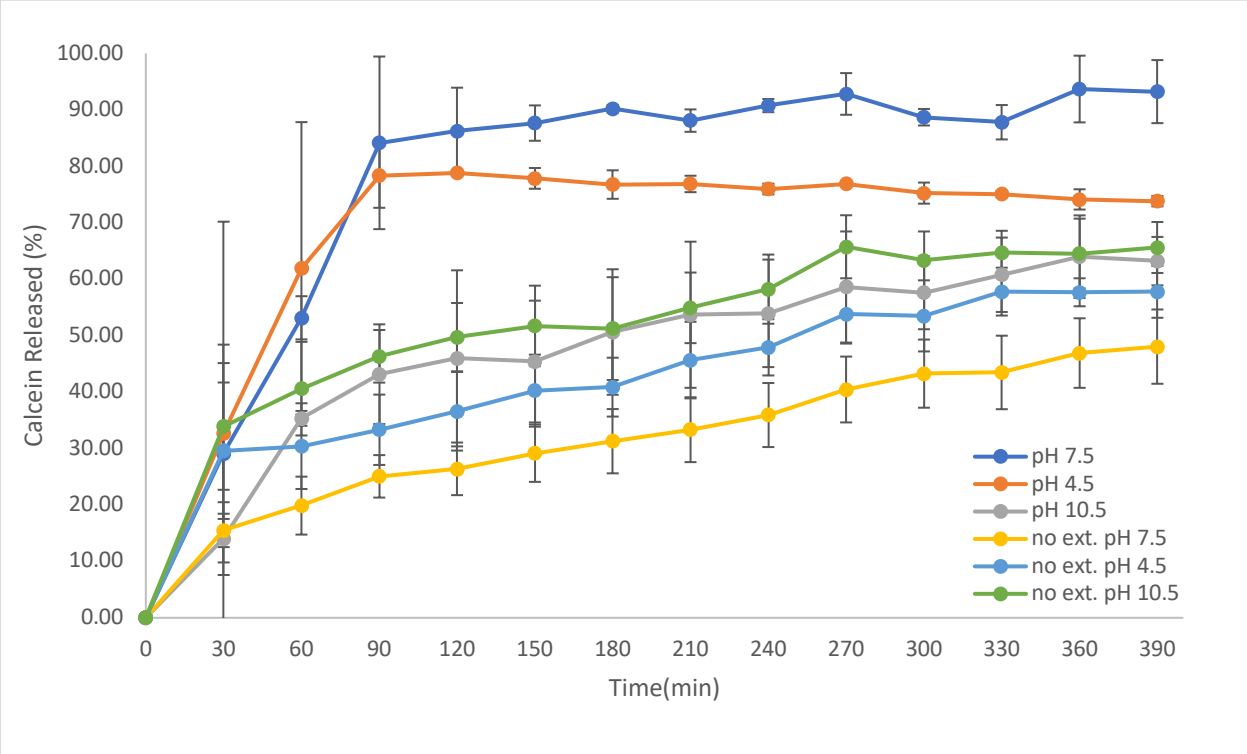
^{3}J=7.5 Hz), 3.347 (s, 9H), 3.808-4.408 (br, 9H), 5.175 (m, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 0.3, 2.0, 14.1, 18.1, 22.7, 23.0, 24.9, 28.5, 29.2, 29..4, 29.6, 29.7, 31.9, 34.1, 54.4, 59.4, 63.0, 66.4, 173.2, 173.6; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ -0.84, 16.5; ^{29}Si {^{1}H} NMR (59.6 MHz, $CDCl_3$): δ 7.2, 7.3. ESI+MS (m/z): [M+H]+ 698.4 m/z, [M+Na]+ 720.4 m/z.

1-Palmitoyl-2-((5-(1,1,3,3,3-pentamethyldisiloxanyl)pentanoyl)-*sn*-glycero-3-phosphocholine (**5**, Pal-ValDS-PC) An oven-dried flask was cooled under a nitrogen atmosphere and charged with 131 mg (0. 527 mmol) of 1-(4-carboxybutyl)-1,1,3,3,3-pentamethyldisiloxane and dissolved into 5 mL of $CHCl_3$. To this solution were added 96.7 mg (0.469 mmol) of DCC and 3.2 mg (0.026 mmol) of DMAP. After stirring for 10 min, a solution of 16:0 LPC (0.078 g, 0.157 mmol) in 5 mL of $CHCl_3$ was added and the reaction mixture was stirred for 24 h. The crude residue was purified by column chromatography using 200–400 mesh silica gel (20 g) suspended in hexanes. The column eluted with 50 mL of a 9:1 mixture of hexane:ethyl acetate and then eluted with 250 mL of 65:25:4 $CHCl_3$:MeOH:H_2O to give 22 mg (30.5 μmol, 19%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.039 (s, 6H), 0.057 (s, 9H), 0.512 (m, 2H), 0.876 (t, 3H, 3J=6.3 Hz), 1.251 (br, 28H), 1.602 (m, 4H), 2.276 (t, 2H, ^{3}J=8.4 Hz), 2.301 (t, 2H, ^{3}J=8.4 Hz), 3.400 (s, 9H), 3.820 (br, 2H), 3.910 (br, 4H), 4.10 (m, 1H), 4.338-4.423 (br, 3H), 5.183 (m, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 0.31, 1.98, 14.11, 18.06, 22.68, 22.95, 24.88, 28.50, 29.20, 29.35, 29.56, 29.66, 29.71, 31.92, 33.87, 34.07, 34.11, 54.36, 59.34, 63.00, 66.36, 70.45, 173.19, 173.57; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ -0.38; ^{29}Si {^{1}H} NMR (59.6 MHz, $CDCl_3$): δ 7.2, 7.3; ESI+MS (m/z): $[M+H]^+$ 726.5, $[M+Na]^+$ 748.4.

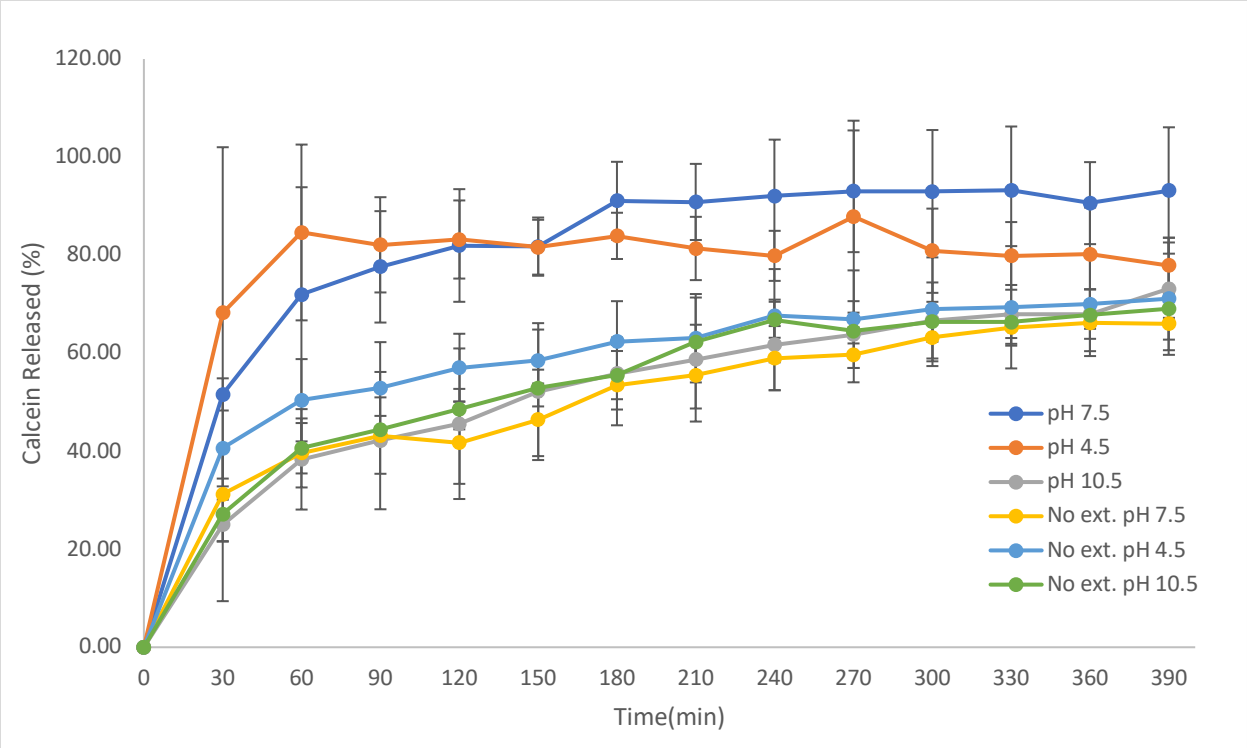
1-Stearoyl-2-((5-(1,1,3,3,3-pentamethyldisiloxanyl)pentanoyl)-*sn*-glycero-3-phosphosphocholine (**6**, Ste-ValDS-PC). A 2-necked round-bottomed flask was cooled under dry nitrogen and charged with 1-(4-carboxybutyl)-1,1,3,3,3-pentamethyldisiloxane (119.9 mg, 0.484 mmol) and dissolved into 5 mL of $CHCl_3$. DCC (99.8 mg, 0.484 mmol) and DMAP (2.7 mg, 0.022 mmol) were added and stirred at room temperature for 5 min. A solution of 18:0 LPC (51.6 mg, 0.095 mmol) dissolved in 5 mL of $CHCl_3$ was added and the reaction mixture was stirred at room temperature for 48 h. A white precipitate was removed by filtration through a medium-porosity glass-fritted Büchner funnel and the solvents were removed in vacuo. The crude residue was purified by column chromatography on silica gel equilibrated with $CHCl_3$. The column was preconditioned with 10 mL of 9:1 $CHCl_3$:MeOH and then eluted with 65:25:4 $CHCl_3$:MeOH:H_2O to give 21.8 mg (0.034 mmol, 19%) of an opaque gel. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.034 (s, 6H), 0.053 (s, 9H), 0.509 (m, 2H), 0.872 (t, 3H, ^{3}J=6.3 Hz), 1.274 (br, 32H), 1.61 (m, 4H), 2.270 (t, 2H, ^{3}J=8.4 Hz), 2.294 (t, 2H, ^{3}J=8.4 Hz), 3.361 (s, 9H), 3.820 (br, 2H), 3.902 (br, 2H), 4.115 (m, 1H), 4.367-4.414 (br, 3H), 5.178 (m, 1H); ^{13}C {^{1}H} NMR (75 MHz, CDCl3): δ 0.32, 1.99, 14.11, 18.07, 22.68, 22.95, 24.90, 28.51, 29.21.

29.36, 29.58, 29.72, 31.92, 34.08, 54.41, 59.34, 63.01, 63.45, 173.21, 173.59; ^{31}P {^{1}H} NMR (121 MHz, CDCl3): δ -0.75: ^{29}Si {^{1}H} NMR (59.6 MHz, CDCl3): δ 7.2, 7.3.

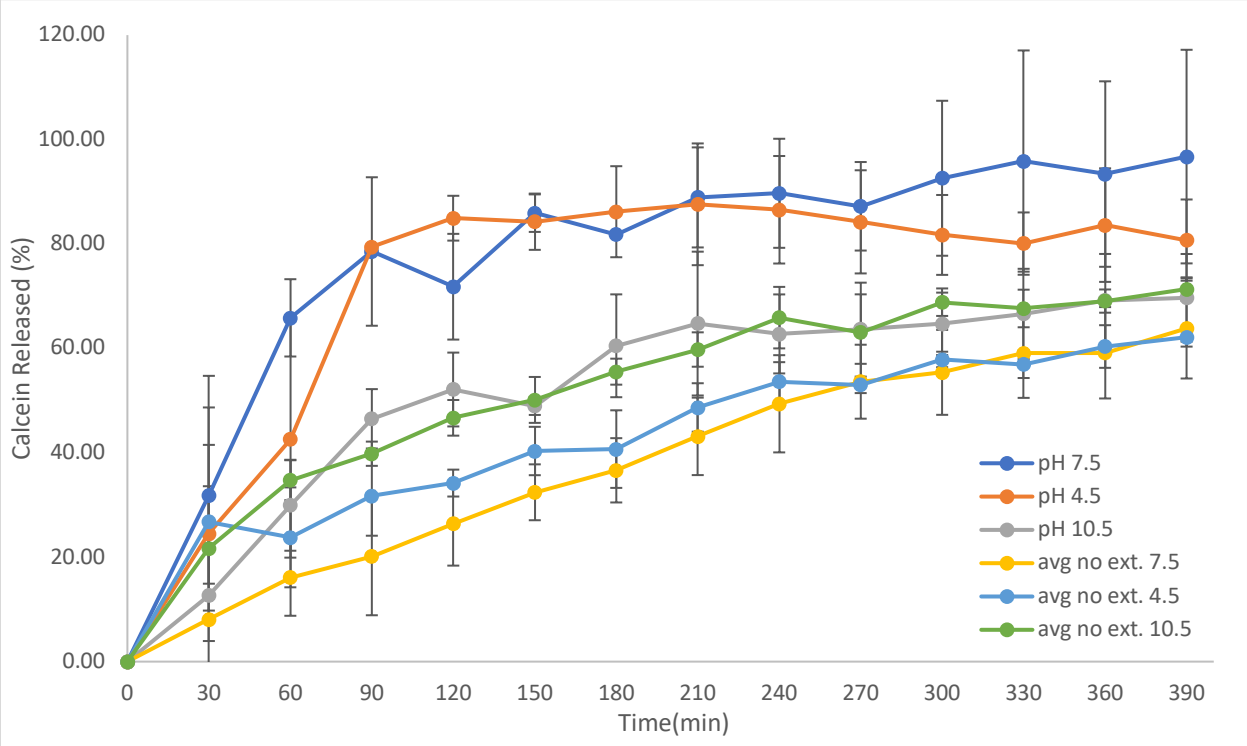
Supplementary Figures



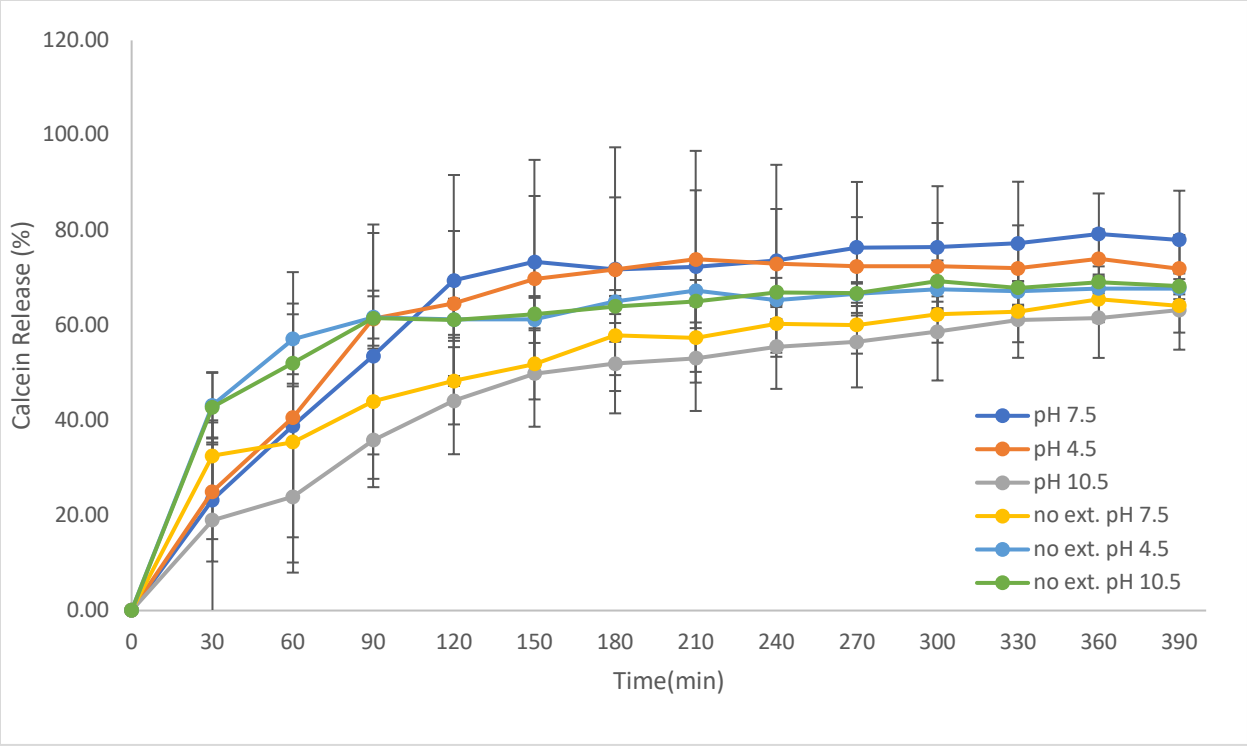
Supplementary Figure 1. Release of calcein from Cap-ValDS-PC liposomes (n = 5-10). Error bars represent the standard deviations in the measurements.



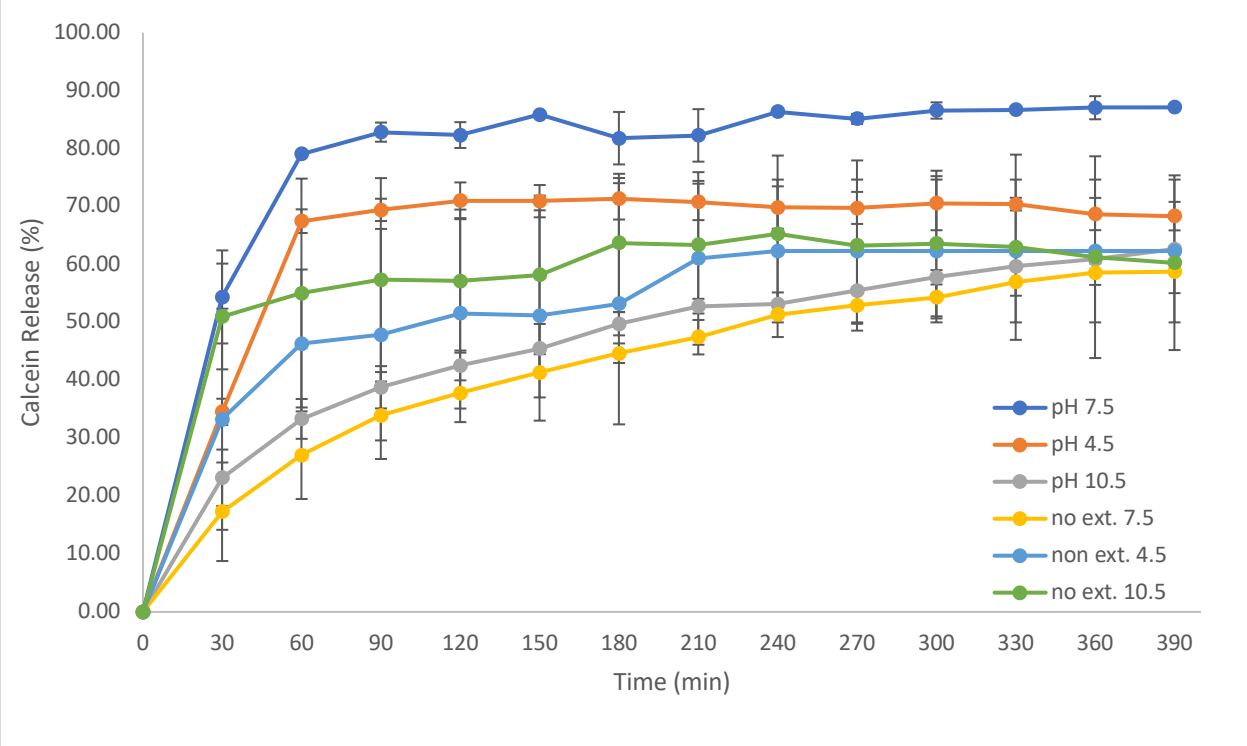
Supplementary Figure 2. Calcein release from Cpc-ValDS-PC liposomes (n = 5-10). Error bars represent the standard deviations in the measurements.



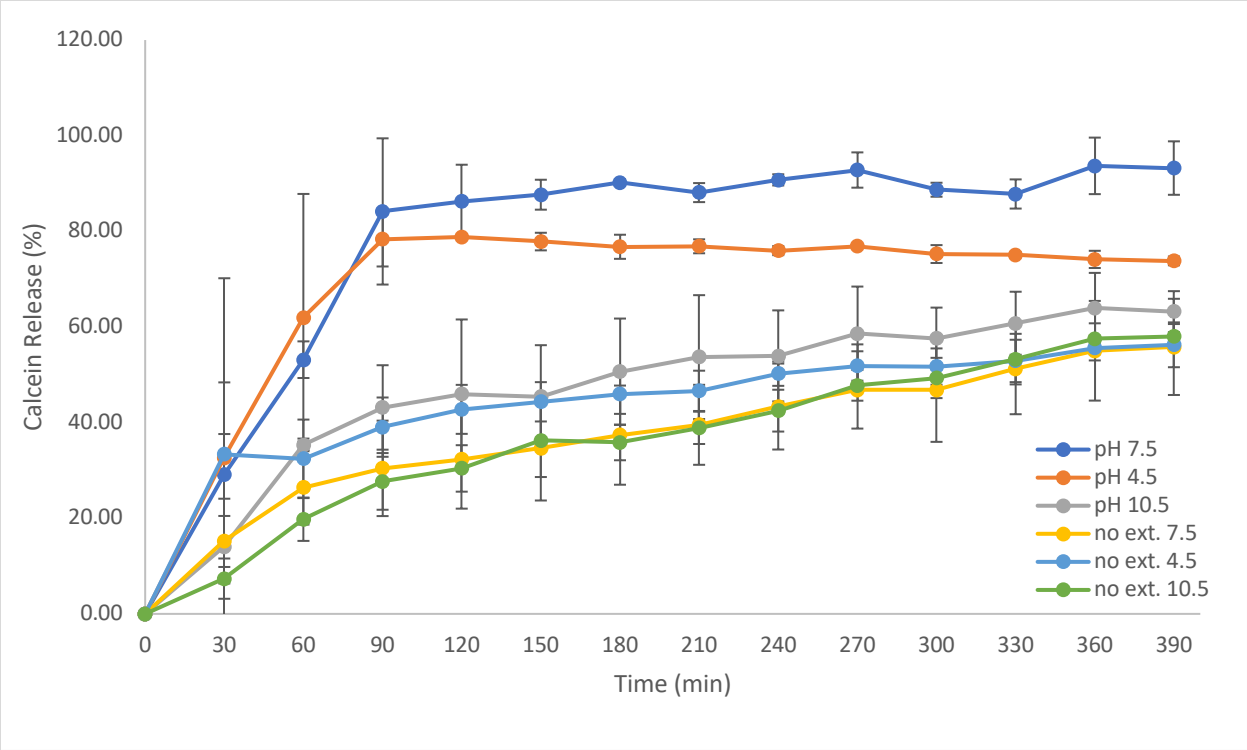
Supplementary Figure 3. Calcein release from Lau-ValDS-PC liposomes (n = 5-10). Error bars represent the standard deviations in the measurements.



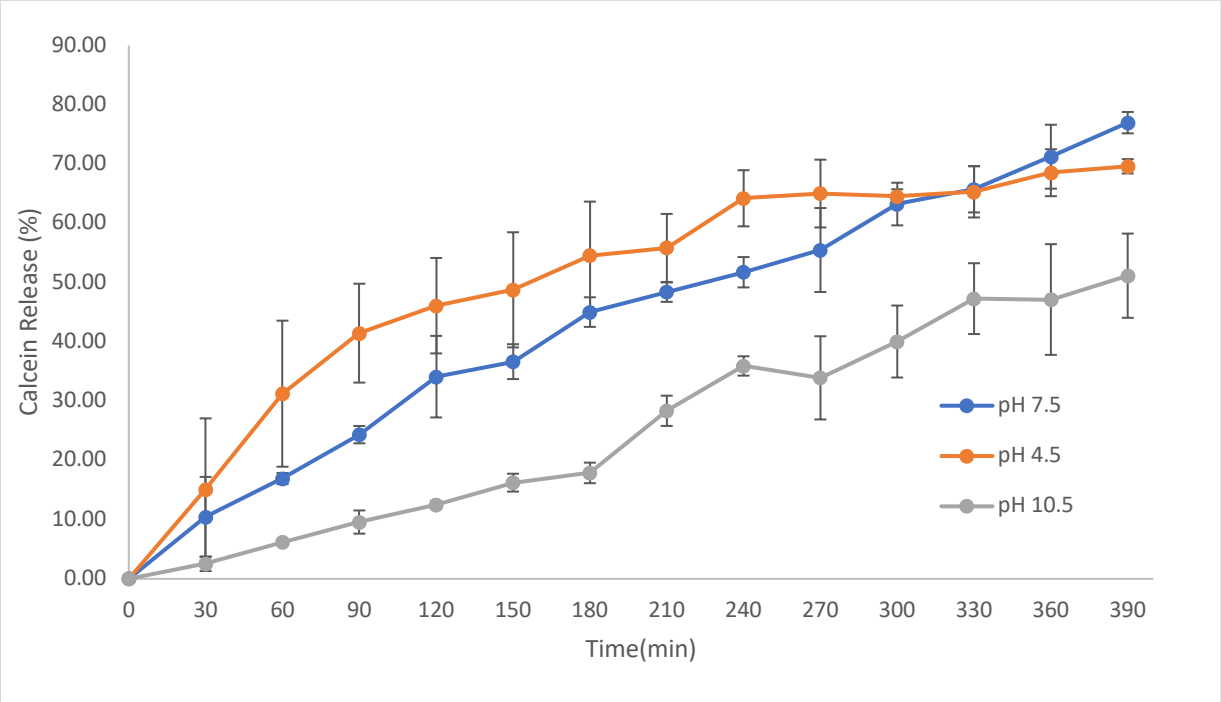
Supplementary Figure 4. Calcein release from Myr-ValDS-PC liposomes (n = 5-10). Error bars represent the standard deviations in the measurements.



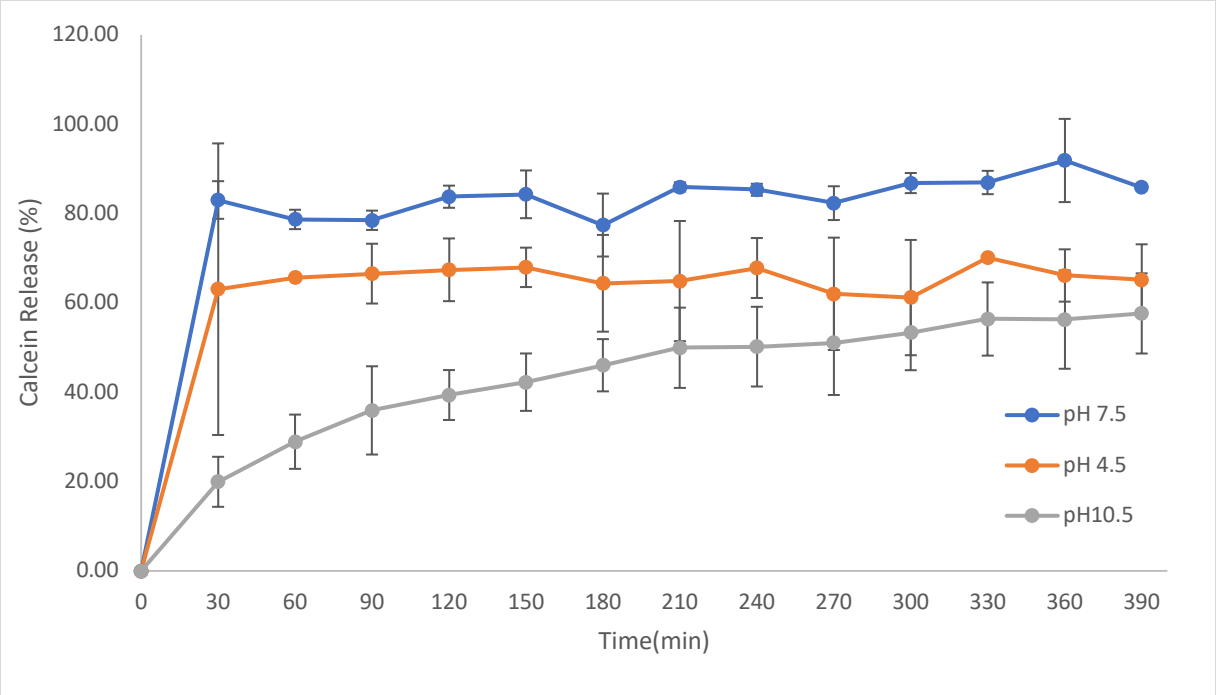
Supplementary Figure 5. Calcein release from Pal-ValDS-PC liposomes (n = 5-10). Error bars represent the standard deviations in the measurements.



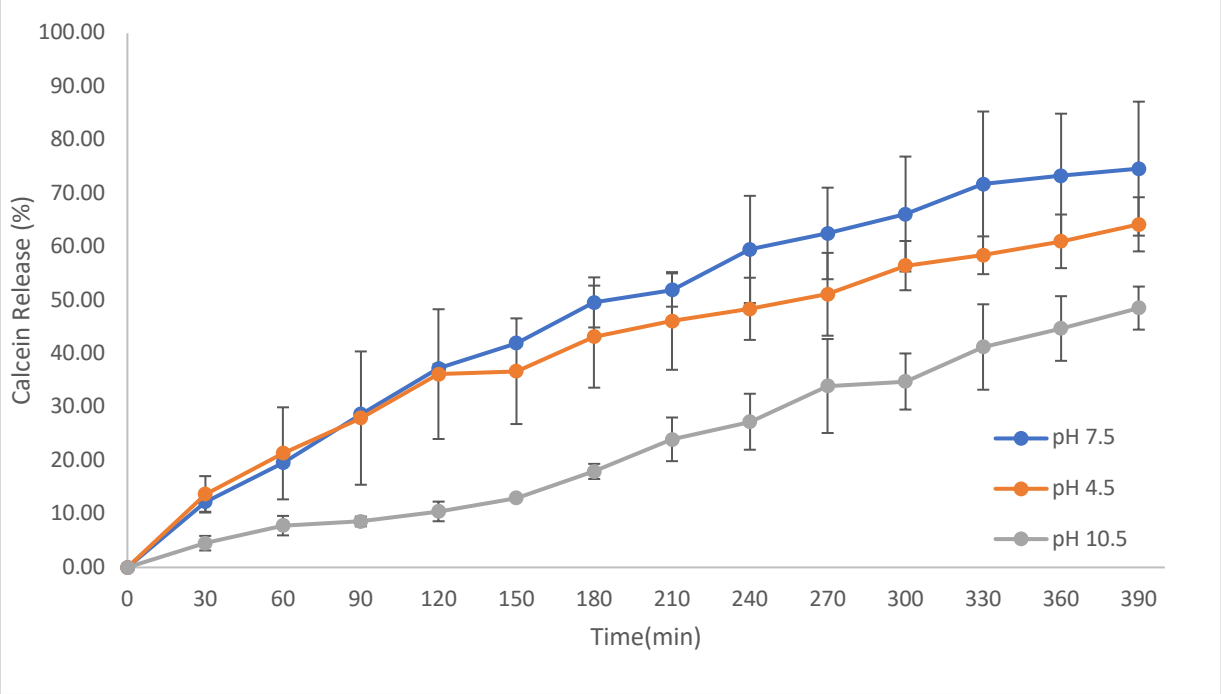
Supplementary Figure 6. Calcein release from Ste-ValDS-PC liposomes (n = 5-10). Error bars represent the standard deviations in the measurements.



Supplementary Figure 7. Calcein release from extruded POPC liposomes (n = 5-10). Error bars represent the standard deviations in the measurements.



Supplementary Figure 8. Calcein release from extruded DPhPC liposomes (n = 5-10). Error bars represent the standard deviations in the measurements.



Supplementary Figure 9. Calcein release from extruded DPPC liposomes (n = 5-10). Error bars represent the standard deviations in the measurements.