Supporting Information

Synthesis of Polyether-Polyoxazolidone Networks for the Design of Drug-Eluting Implants

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Synthesis of bis(α-alkylidene cyclic carbonate)s

A bis(α-alkylidene cyclic carbonate) containing a cyclic spacer (BisαCC1) was synthesized by adapting Ouhib's protocol.[1] An ethynylmagnesium bromide solution (800 mL, 0.5 M in THF, 0.4 mol, 3.1 equiv.) was first added in a 2 L two necked round-bottom flask under nitrogen atmosphere and concentrated by removal of 300 mL of THF under vacuum. 1,4-Cyclohexanedione (14.6 g, 0.13 mol, 1 equiv.) was then dissolved in a minimal amount of dry THF before being transferred in a dropping funnel and added dropwise to the solution immersed in an ice bath. After stirring for 24h at room temperature, the reaction was quenched by the addition of a saturated ammonium chloride (NH_4Cl) solution (260 mL). The formed precipitate was removed by filtration and diethylether (300 mL) was added to the filtrate. The aqueous phase was then extracted with diethylether (3x300 mL) and the combined organic phases were dried on $MgSO_4$, filtered, and dried under vacuum. The obtained 1,4-diethynylcyclohexane-1,4-diol was dissolved in diethylether (250 mL), purified by chromatography onto silica (eluent: diethylether) and collected as a white solid after evaporation of the solvent (20 g, isolated yield = 94%). 1,4-diethynylcyclohexane-1,4-diol (20 g, 0.12 mol, 1 equiv.), tetrabutylammonium phenolate (2 g, 6 mmol, 0.05 equiv., previously synthesized following Grignard's protocol[2]), CuI (1.15 g, 6 mmol, 0.05 equiv., previously purified by glacial acetic acid), and acetonitrile (40 mL) were added in a 250 ml high pressure autoclave. The reactor was heated at 40 °C and charged with a constant pressure of 100 bars of CO_2 for 24h. After depressurization of the reactor, its content was dissolved in CH_2Cl_2 (400 mL) and purified by chromatography onto silica (eluent: CH_2Cl_2). The solvent was then evaporated, and the obtained solid was dried under vacuum before being dissolved in acetonitrile (300 mL) and recrystallized at -20°C for 24h. The solid was then filtrated, washed with cold acetonitrile, and dried under vacuum to obtain a white pure product (21 g, isolated yield = 69%). The BisαCC obtained was analyzed by ^{1}H-NMR (**Figure S1.A**). Structural characterizations are identical to those reported in the initial protocol and confirm the chemical structure of the product. Given the amount of water present in the final monomers, these were subsequently freeze-dried (lyophilized) before use. BisαCC2, containing a linear spacer, was synthesized following the same protocol starting from 2,5-hexanedione (15 mL, 0.13 mol 1 equiv., previously distilled) (**Figure S2.A**).

BisαCC1: ^{1}H-NMR (400 MHz, DMSO-d_6) δ (ppm) = 4.87 (d, *J* = 4.2 Hz, 1H), 4.80 (d, *J* = 4.2 Hz, 1H), 2.20 (d, *J* = 9.7 Hz, 2H), 1.97 (d, *J* = 9.9 Hz, 2H).

BisαCC2: ^{1}H-NMR (400 MHz, DMSO-d_6) δ (ppm) = 4.89 (d, *J* = 3.9 Hz, 1H), 4.73 (d, *J* = 3.9 Hz, 1H), 1.95 (ddd, *J* = 10.6, 8.0, 5.6 Hz, 1H), 1.86 (ddd, *J* = 9.7, 7.9, 5.5 Hz, 1H), 1.62 (s, 3H).

[1] Ouhib, F. et al. *Angew. Chem. Int. Ed.* **2019**, 58 (34), 11768–11773.
[2] Grignard, B. et al. *ChemCatChem* **2018** 10, 2584–2592.

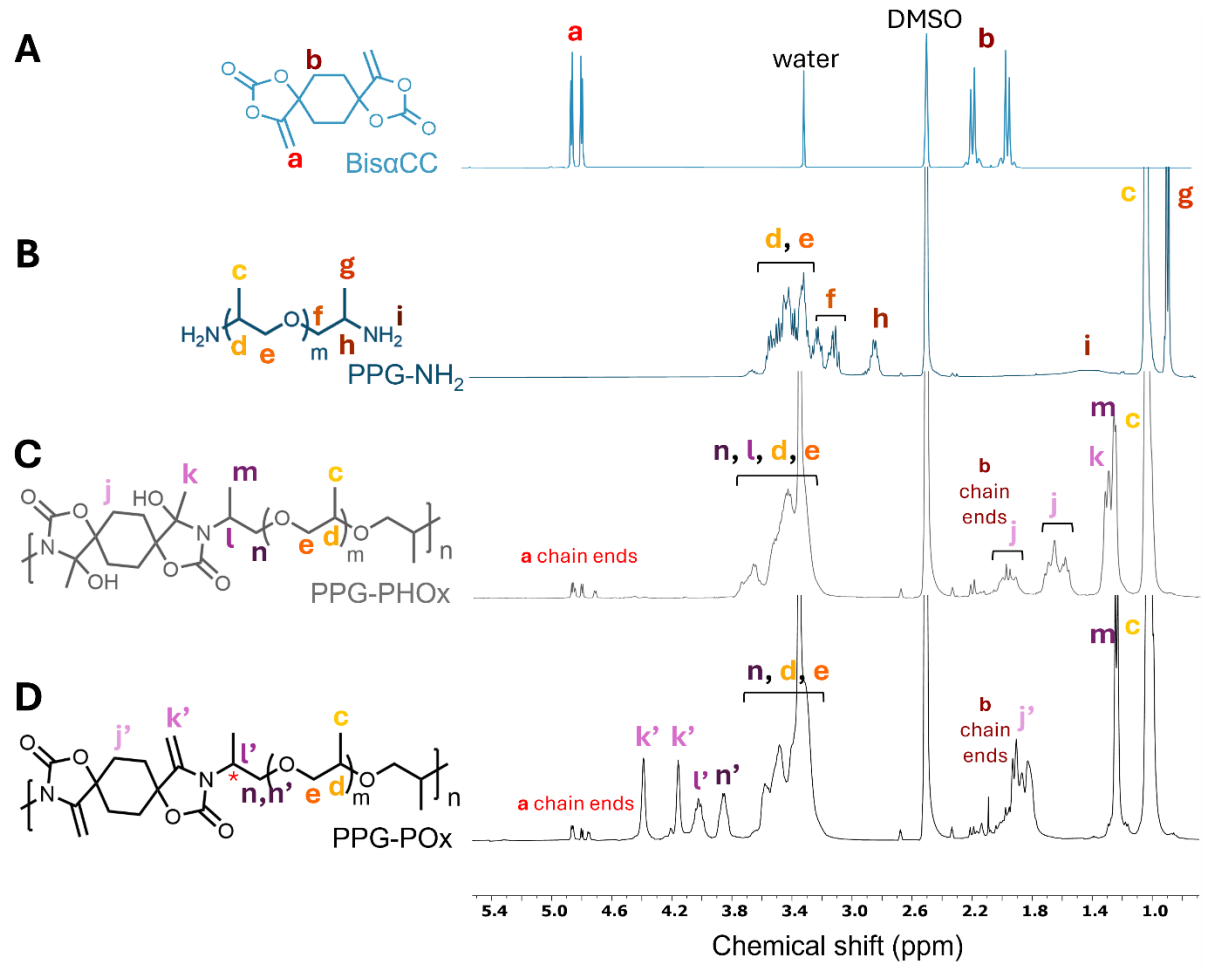

Figure S1. ^{1}H-NMR spectra of BisαCC1 (**A**), PPG-NH_2 (**B**), PPG-PHOx1 (**C**) and PPG-POx1 (**D**).

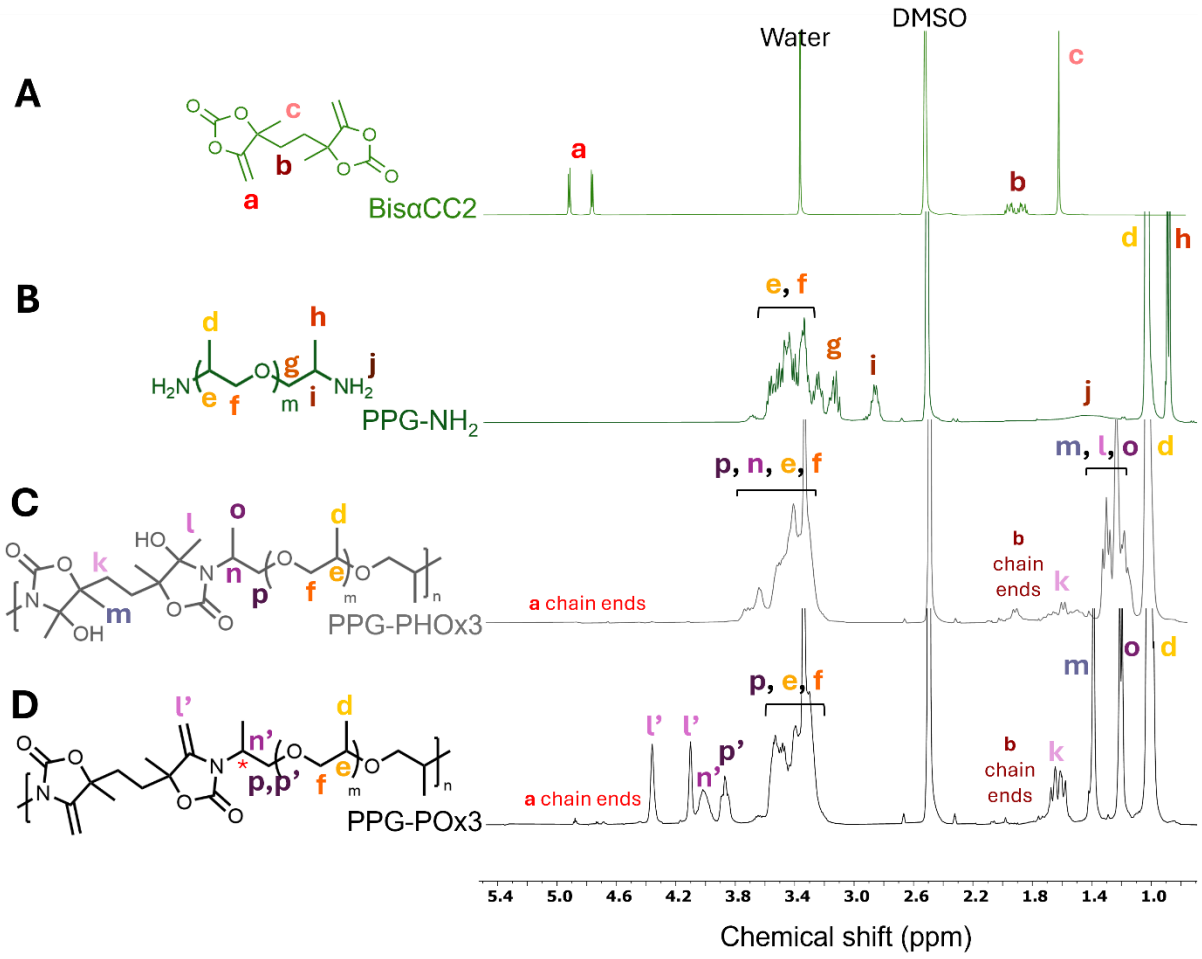

Figure S2. ^{1}H-NMR spectra of BisαCC2 (**A**), PPG-NH_2 (**B**), PPG-PHOx3 (**C**) and PPG-POx3 (**D**).

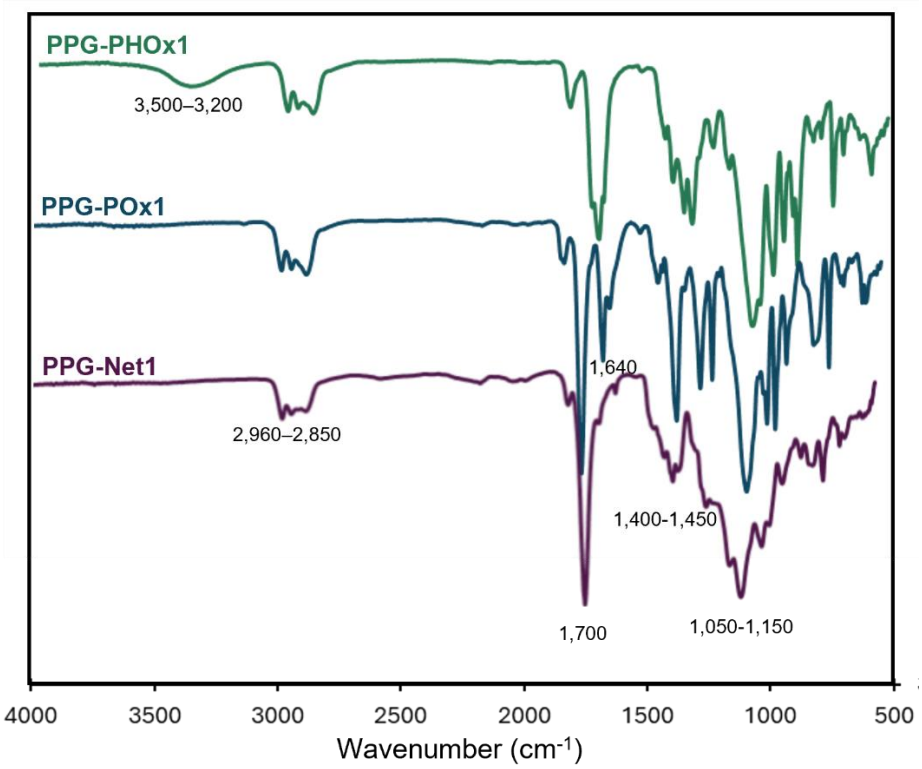

Figure S3. FTIR-ATR spectra of PPG-PHOx1, PPG-POx1 and PPG-Net1.

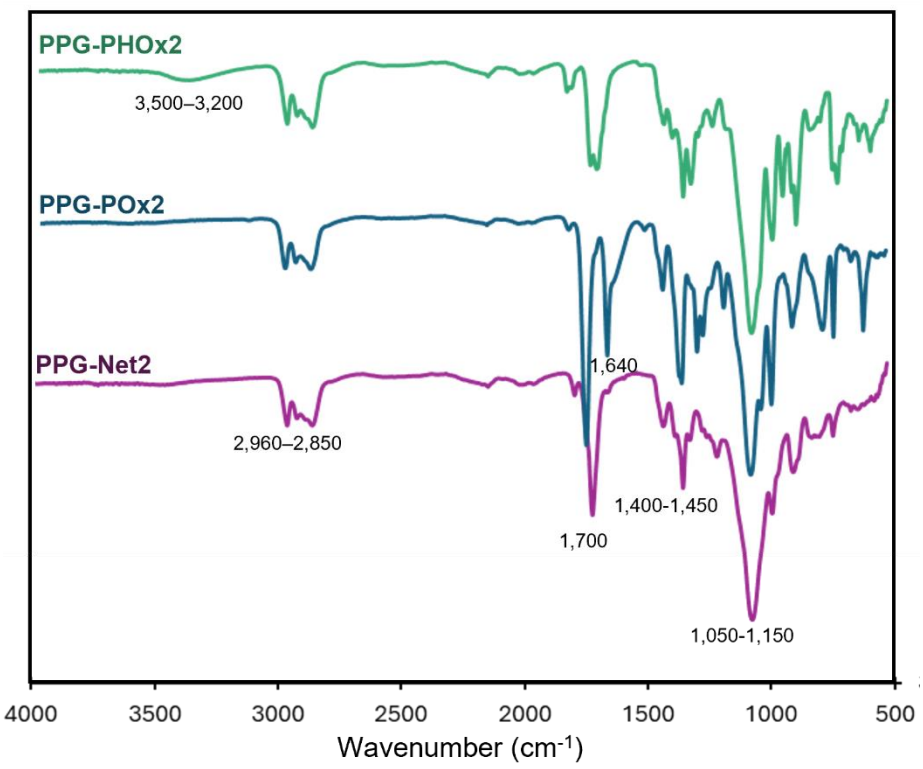

Figure S4. FTIR-ATR spectra of PPG-PHOx2, PPG-POx2 and PPG-Net2.

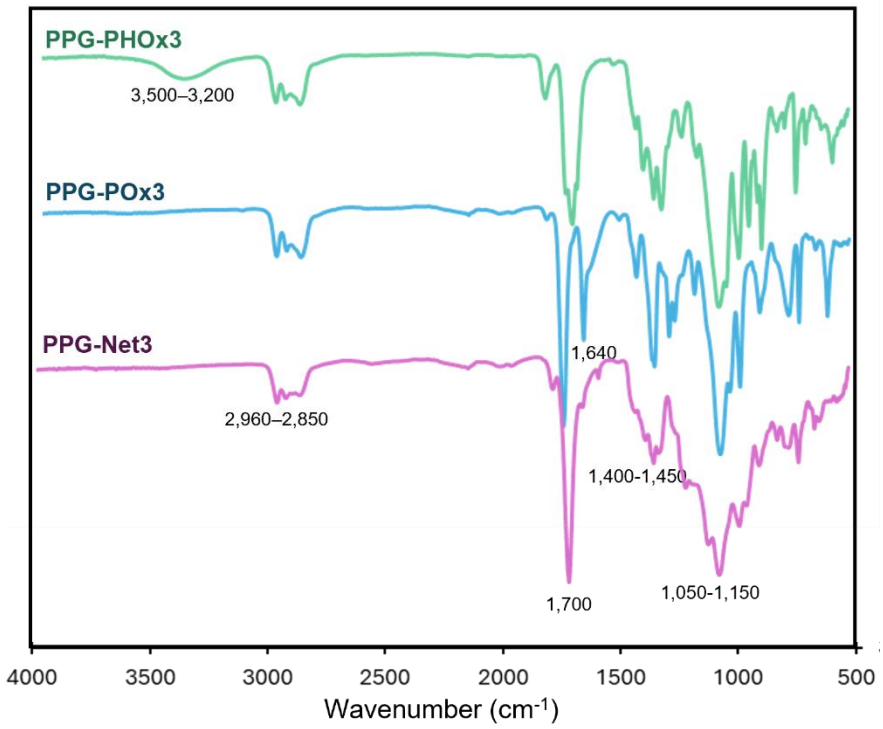

Figure S5. FTIR-ATR spectra of PPG-PHOx3, PPG-POx3 and PPG-Net3.

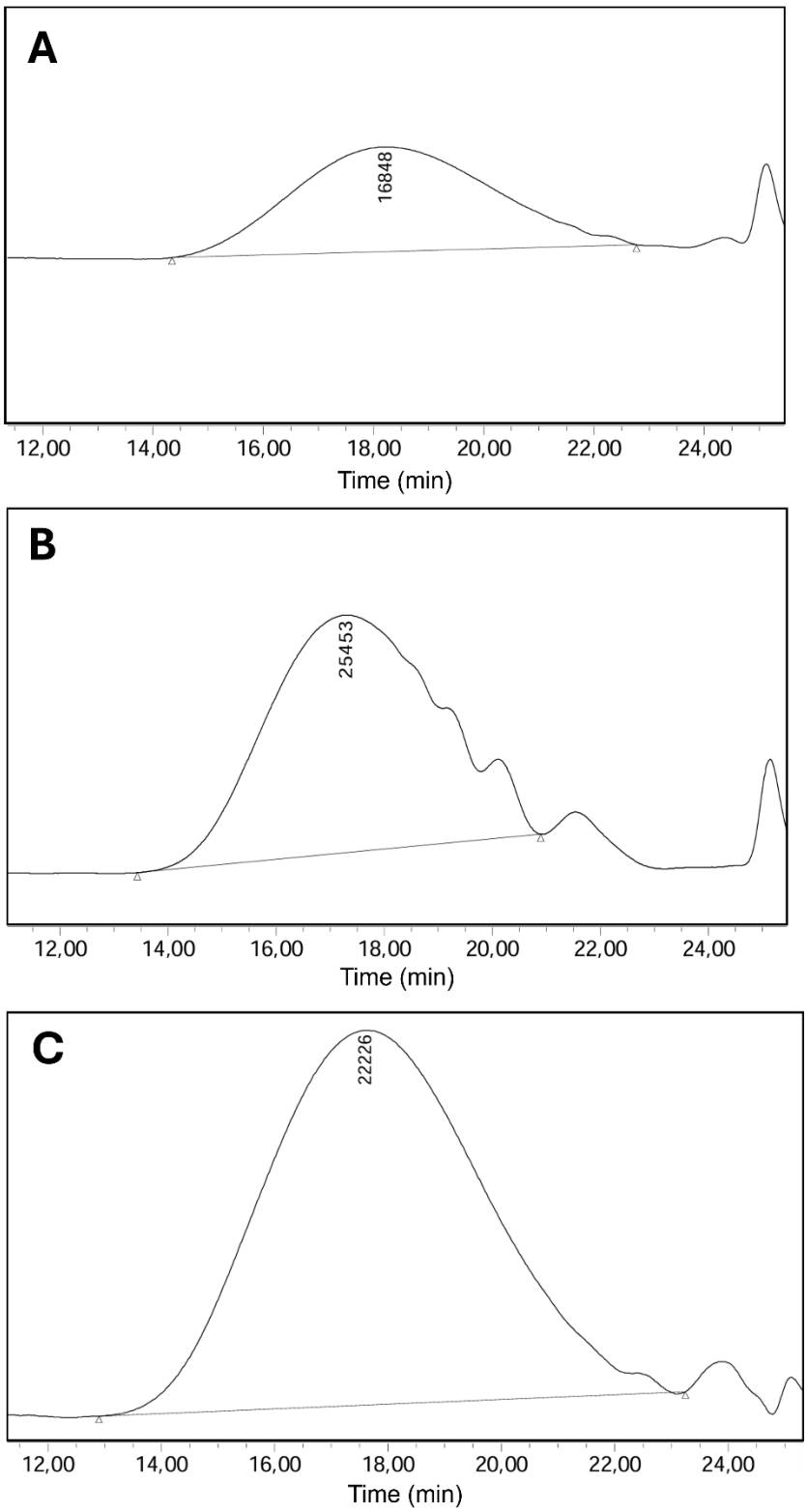

Figure S6. GPC chromatograms of PPG-PHOx1 (M_n = 11,100 g/mol, M_w = 18,800 g/mol, M_w/M_n = 1.70 (PS calibration) (**A**), PPG-PHOx2 (M_n = 18,700 g/mol, M_w = 27,000 g/mol, M_w/M_n = 1.44 (PS calibration) (**B**) and PPG-PHOx3 (M_n = 13,700 g/mol, M_w = 25,100 g/mol, M_w/M_n = 1.83 (PS calibration) (**C**).

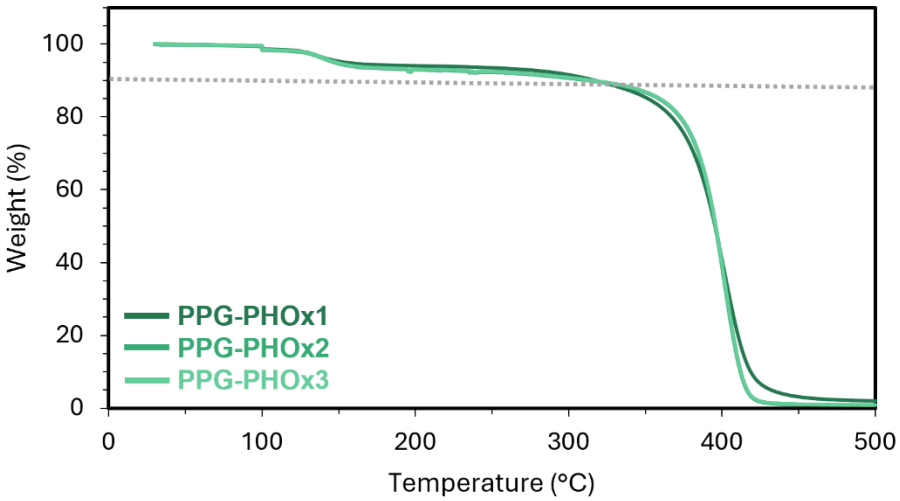

Figure S7. TGA curves of PPG-PHOx1, PPG-PHOx2 and PPG-PHOx3.

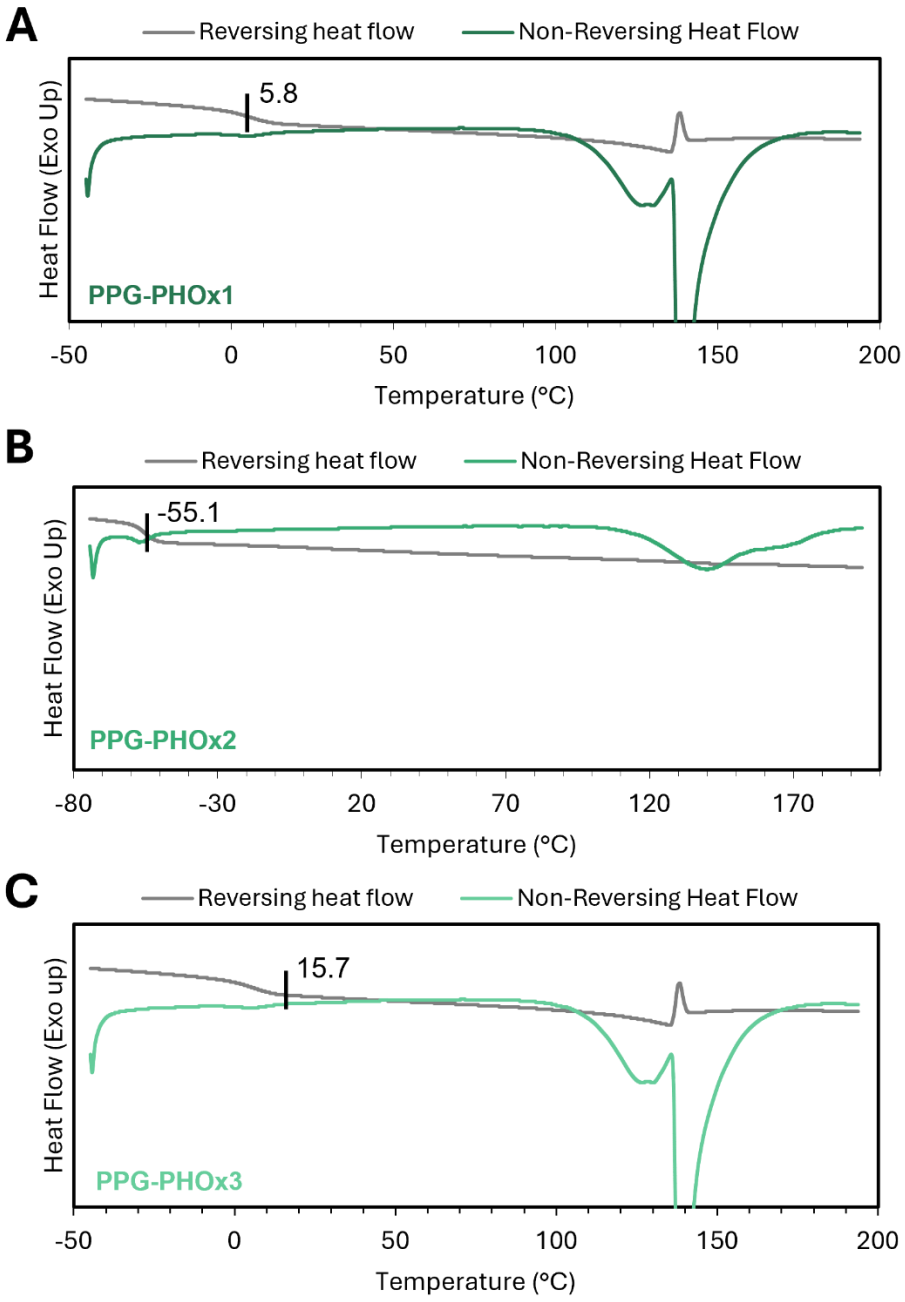

Figure S8. Modulated DSC thermograms of PPG-PHOx1, PPG-PHOx2 and PPG-PHOx3.

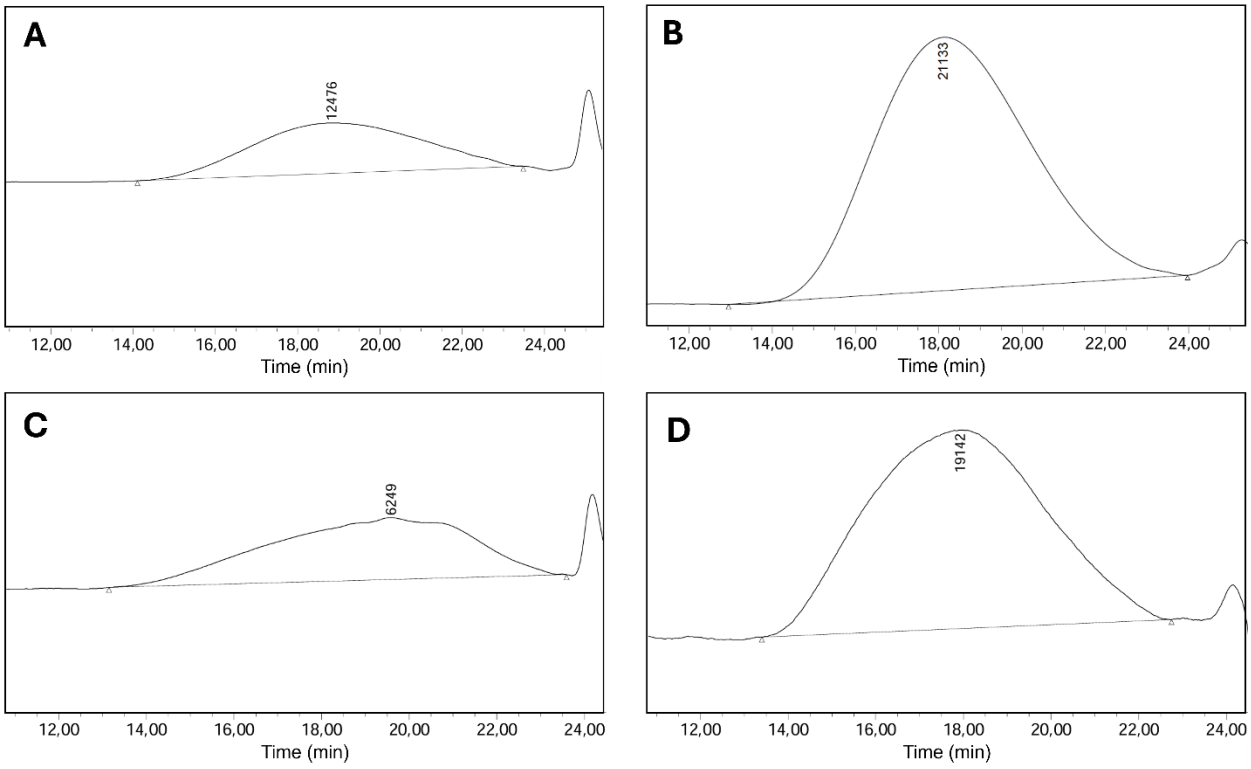

Figure S9. GPC chromatograms of PPG-POx1 (M_n = 7,900 g/mol, M_w = 15,300 g/mol, M_w/M_n = 1.95)(**A**), PPG-POx1$_{67\%}$ (M_n = 12,900 g/mol, M_w = 23,300 g/mol, M_w/M_n = 1.81) (**B**), PPG-POx2 (M_n = 5,300 g/mol, M_w = 13,800 g/mol, M_w/M_n = 2.63 (**C**) and PPG-POx3 (M_n = 12,900 g/mol, M_w = 24,100 g/mol, M_w/M_n = 1.87 (**D**) (PS calibration).

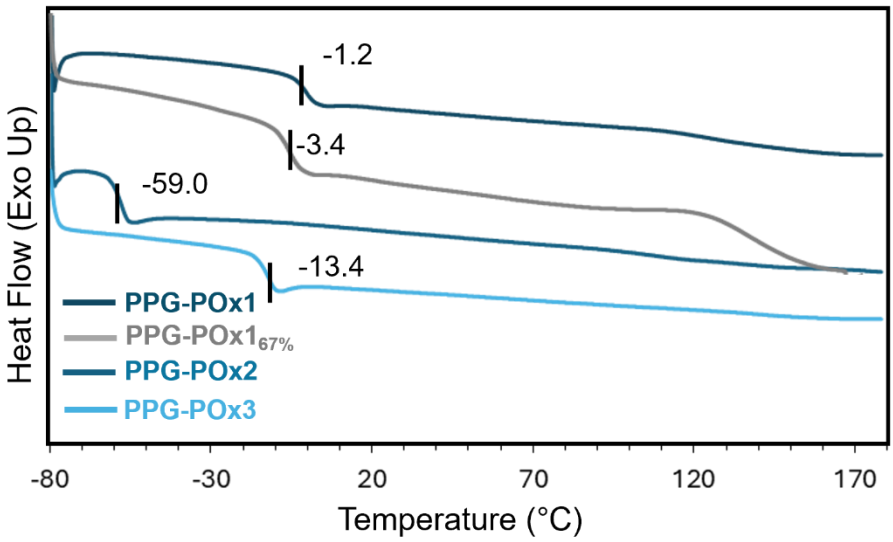

Figure S10. DSC thermograms of PPG-POx1, PPG-POx1$_{67\%}$, PPG-POx2 and PPG-POx3.

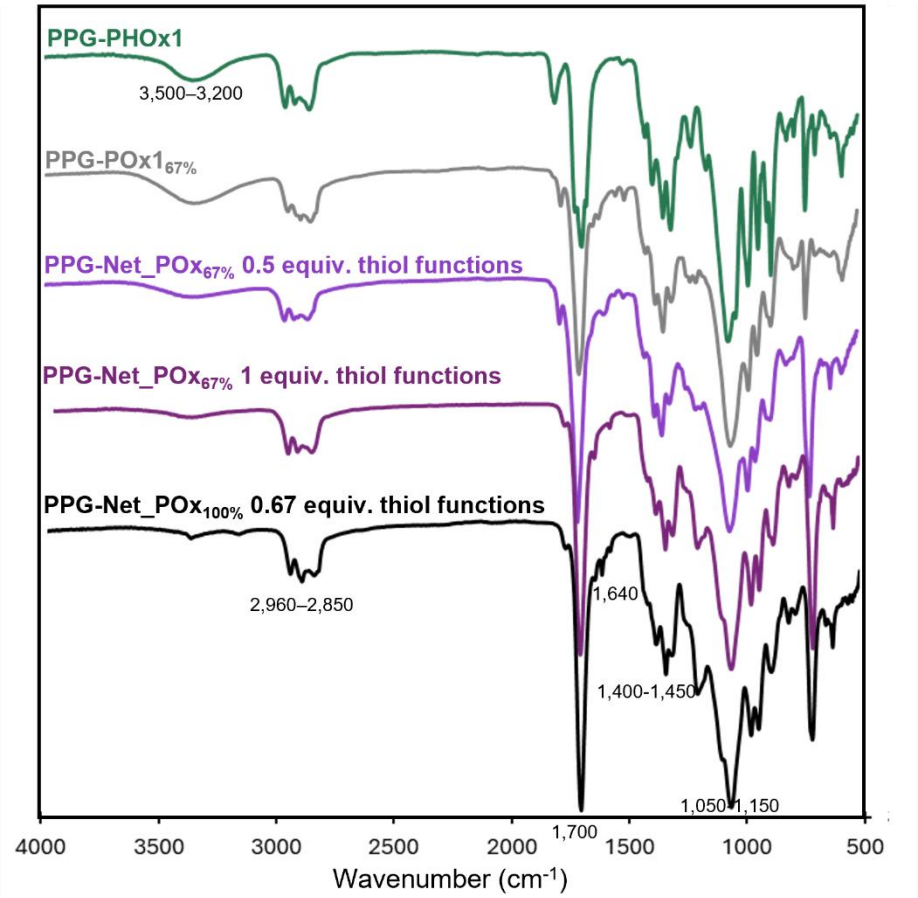

Figure S11. FTIR spectra of PPG-PHOx1 (green), PPG-POx1$_{67\%}$ (grey), PPG-Net1$_{67\%}$S$_{0.5}$ (PPG-POx1$_{67\%}$ with 0.5 equiv. of thiol functions (light purple), PPG-Net1$_{67\%}$ (PPG-POx1$_{67\%}$ with 1 equiv. of thiol functions) (dark purple) and PPG-Net1S$_{0.67}$ (PPG-POx1 with 0.67 equiv. of thiol functions) (black).

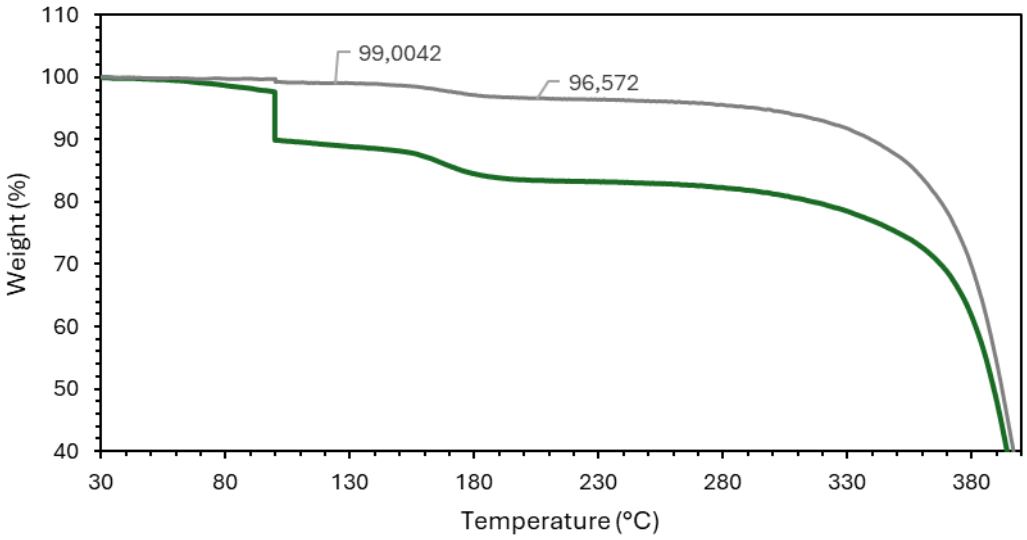

Figure S12. Zooms on the TGA curves of PPG-PHOx1 (lower curve), and PPG-POx1$_{67\%}$ (upper curve), with an isotherm step of 10 min at 100 °C.

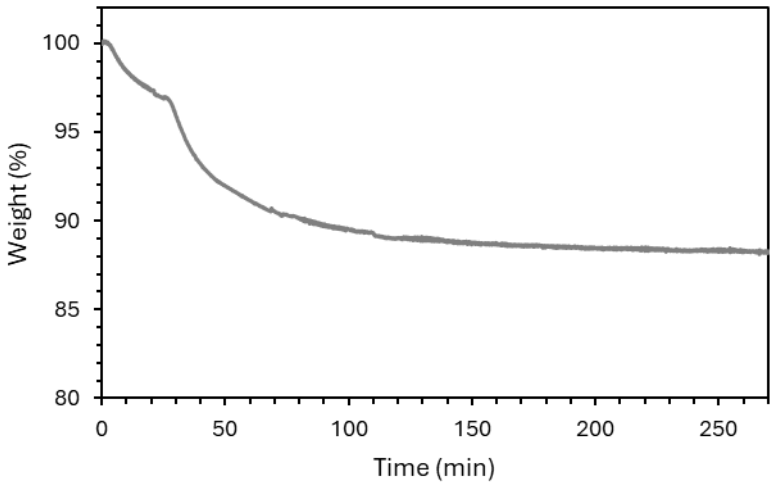

Figure S13. TGA curve of the heating ramp of 10°C/min from -80°C to 130°C followed by an isotherm step performed at 130 °C on PPG-PHOx1, showing the complete dehydration of the sample after 2h at 130°C.

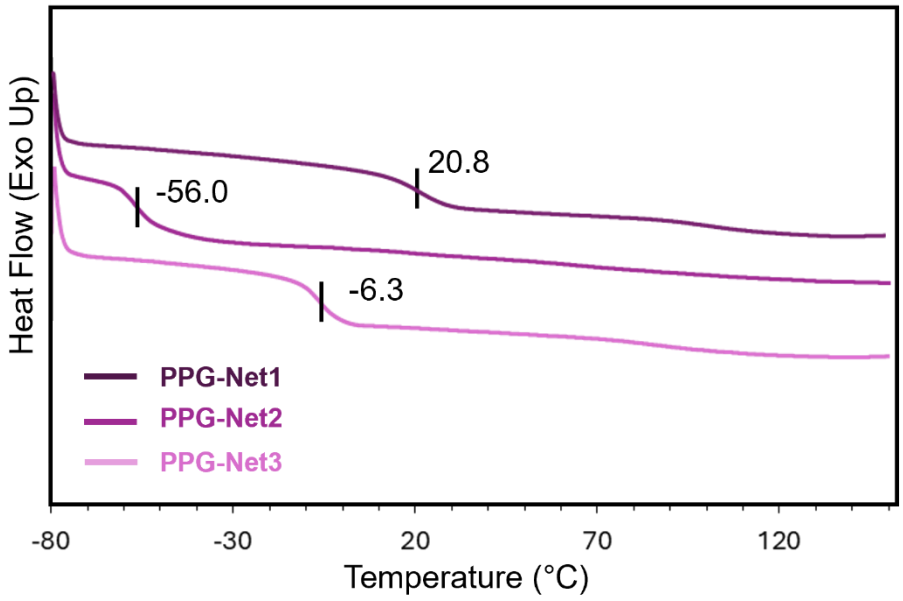

Figure S14. DSC thermograms of PPG-Net1, PPG-Net2 and PPG-Net3.

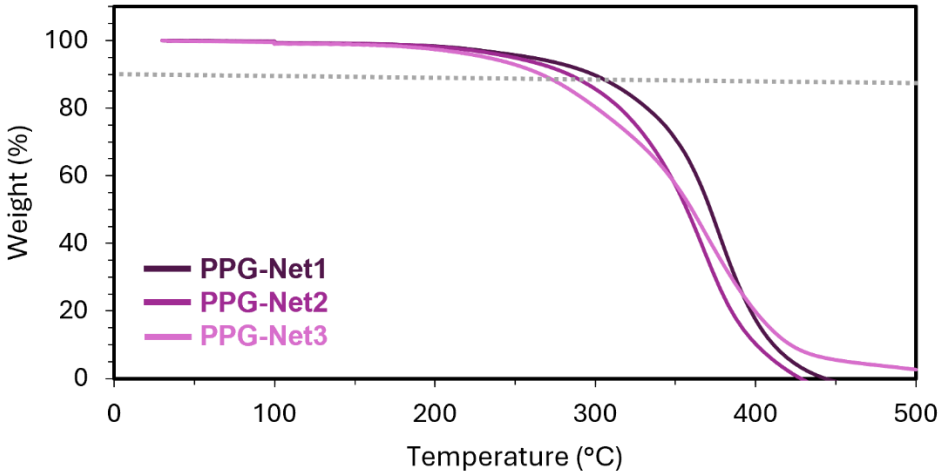

Figure S15. TGA curves of PPG-Net1, PPG-Net2 and PPG-Net3.

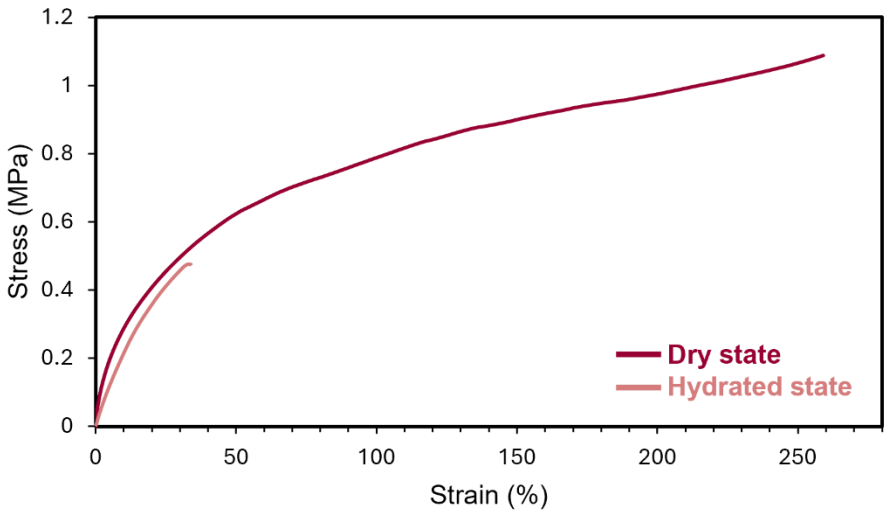

Figure S16. Stress-strain curve examples of PPG-Net1 in dry and hydrated environments.

Table S1. Weight of samples (8 mm diameter discs) in mg measured weekly to evaluate PPG-Net1 stability in PBS.

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
Medical grade PU	42.4 ±0.8	42.5 ±0.8	42.4 ±0.9	42.2 ±0.9	42.2 ±0.8	42.0 ±0.8	42.2 ±0.8	42.3 ±1.0
PPG-Net1	38.6 ± 7.0	38.8 ± 7.4	38.2 ± 7.4	38.6 ± 7.4	38.2 ± 7.1	38.9 ± 7.3	39.7 ± 7.1	38.8 ± 7.6

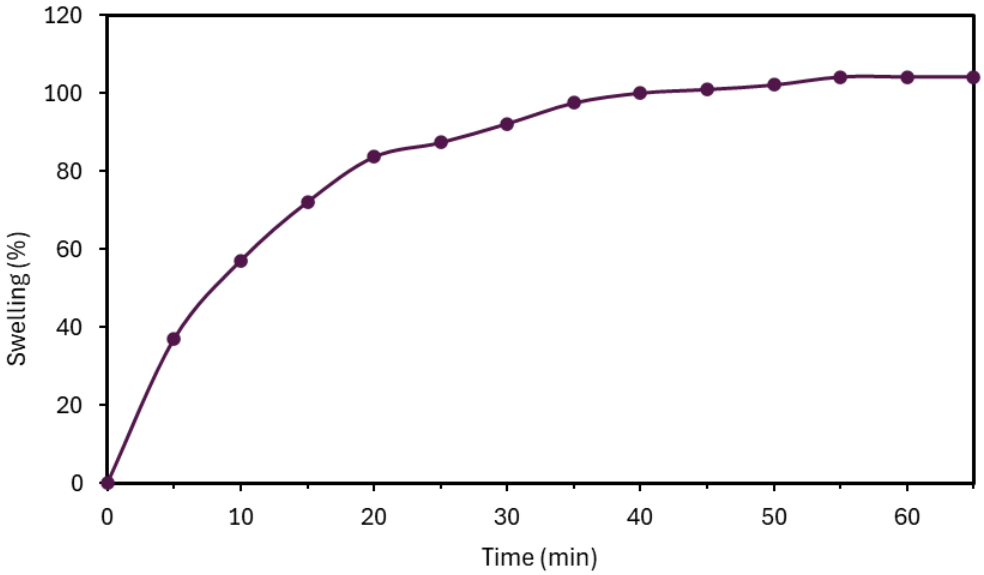

Figure S17. Swelling kinetics of PPG-Net1 in a 50:50 (v/v) EtOH:CH_2Cl_2.

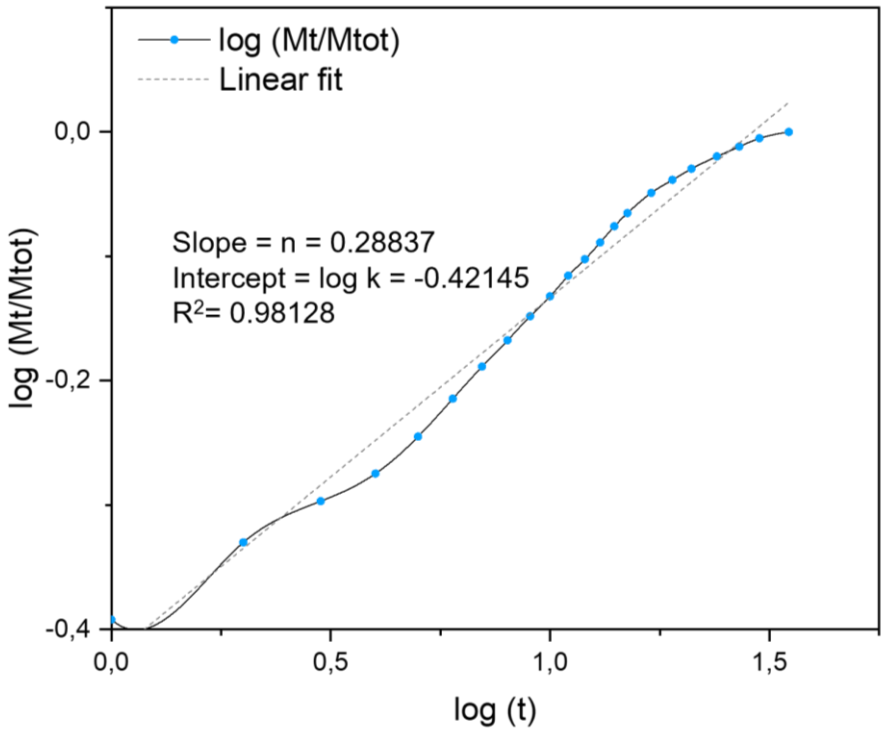

Figure S18. Korsmeyer-Peppas model for the mechanism of ASA release.