Polyesters with main and side chain phosphoesters as structural motives for biocompatible electrospun fibres

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Experimental procedures

Synthesis of poly(ω-pentadecalactone). The homopolymer poly(ω-pentadecalactone) was prepared following a procedure adapted from literature. The ω-pentadecalactone monomer was enzymatically polymerised under the presence of Novozym 435 (10 wt.% in relation to monomer). Reaction was conducted for 3 h at 70 °C using toluene as solvent. After polymerisation, the enzyme was removed by filtration, the obtained product was precipitated in ice-cold methanol and characterised by size exclusion chromatography (SEC). The polymer resulted in a number average molecular weight (M_n) of 21,700 g mol^{-1} (dispersity ($Đ_M$) of 1.8). Yield = 90 %. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 4.10-4.00 (m, $CH_2O(C=O)$), 2.30-2.20 (m, $CH_2(C=O)O$), 1.70-1.60, 1.60-1.50 (m, $CH_2(C=O)$), 1.25 (m, CH_2).

Synthesis of poly(ω-pentadecalactone) with one thiol end. The procedure for the functionalisation of pentadecalactone with 6-mercapto-1-hexanol was adapted from literature.[1] Briefly, the monomer (4.0 g, 16.64 mmol) and the initiator, 6-mercapto-1-hexanol

(0.223 g, 1.664 mmol), were transferred with a syringe to a flask containing 10 wt.% in relation to the monomer of dried enzyme. The flask was then purged with argon, the temperature was set to 80 °C and the reaction proceeded for 24 h until being stopped by filtering off the enzyme. The crude product was then precipitated in ice-cold methanol. The polymer was dried before being analysed by nuclear magnetic resonance (NMR), size exclusion chromatography (SEC), and differential scanning calorimetry (DSC). ^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm)): 4.10 - 4.04 (t, $CH_2O(C=O)$), 3.69 - 3.61 (t, CH_2OH) 2.57 - 2.50 (q, CH_2SH), 2.33 - 2.28 (t, $CH_2(C=O)O$), 1.69 - 1.54 (m, CH_2), 1.50 - 1.25 (m, CH_2).

Synthesis of phenyl di(undec-10-en-1-yl) phosphate. Phenyl dichlorophosphate was esterified with 10-undecen-1-ol in the presence of triethylamine according to a procedure adapted from literature.[2] A 250 mL Schlenk flask equipped with a dropping funnel was purged with argon and then charged with phenyl dichlorophosphate (7.08 mL, 0.047 mol) and with 40 mL of dried dichloromethane. The solution was cooled to 0 °C. Triethylamine, (1.8 eq), 10-undecen-1-ol (1.8 eq) and dried dichloromethane (20 mL) were added by the dropping funnel. After complete addition, the mixture was stirred at room temperature for 12 h, concentrated under reduced pressure, and the product was finally purified by neutral alumina chromatography using dichloromethane as eluent. The final yield was 70% and the obtained product was characterized by ^{1}H NMR and stored under refrigeration until use. ^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm)): 7.32 (t, J = 7.7 Hz = 2H), 7.21 (d, J = 7.7 Hz, 2H), 7.16 (t, J = 7.7 Hz, 1H), 5.83 - 5.77 (ddt, J = 16.8Hz, J = 10Hz, J = 3.5 Hz, 2H), 5.00 - 4.97 (ddt, J = 10Hz, J = 3.5 Hz, J = 1.4 Hz, 2H), 4.93 - 4.91 (ddt, J = 10Hz, J = 1.4 Hz, 2H), 4.16 - 4.09 (m, 4H), 2.04 - 2.01 (m, 2H), 1.69 - 1.65 (m, 4H), 1.39 - 1.32 (m, 8H), 1.26 (m, 18H).

Synthesis of poly(globalide). The synthesis was conducted in toluene using a globalide:toluene mass ratio of 1:2 (10 g of globalide:20 g of dried toluene) and 6 wt.% of Novozym 435 in relation to monomer. The reaction proceeded for 4 h at 60 °C. Then, dichloromethane was added, and the final solution was filtered and precipitated in cold methanol. The precipitate was dried under vacuum at room temperature to result in a polymer with a number average molecular weight (M_n) of 20,000 g mol^{-1} (dispersity ($Đ_M$) of 3.5). Yield: 80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 5.55-5.30 (m, CH=CH), 4.10-4.02 (m, $CH_2O(C=O)$), 2.32-2.25 (m, $CH_2(C=O)O$), 2.12-1.92, 1.72-1.55, 1.38-1.20 (m, CH_2).

Additional Figures

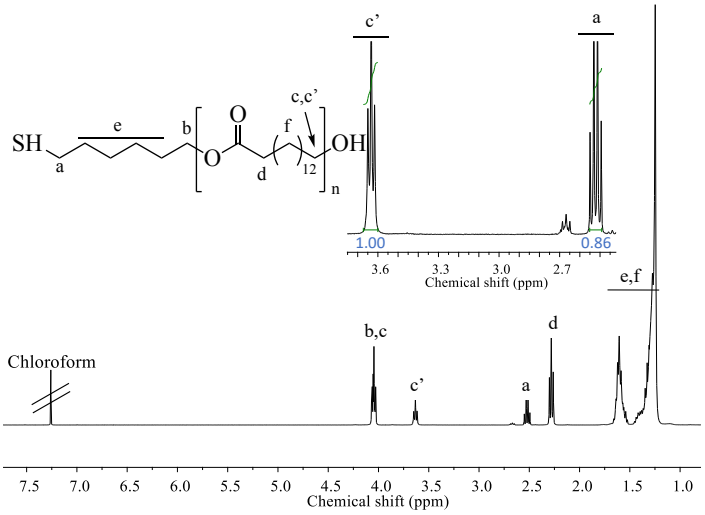

Figure S1: ^{1}H-NMR spectrum (400 MHz) of thiol-initiated ω-pentadecalactone **1** in $CDCl_3$; c' denotes the terminal CH_2-OH group.

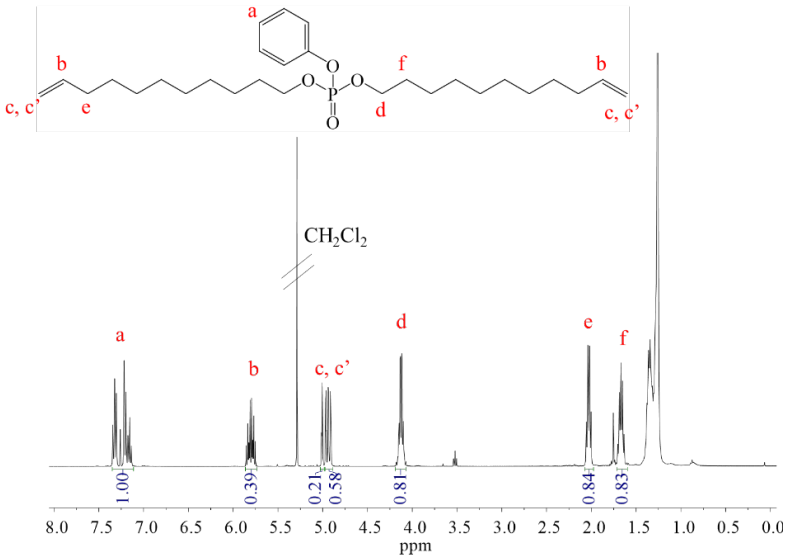

Figure S2: ^{1}H-NMR spectrum (400 MHz in $CDCl_3$) of phenyl-di(undec-10-en-1-yl) phosphate.

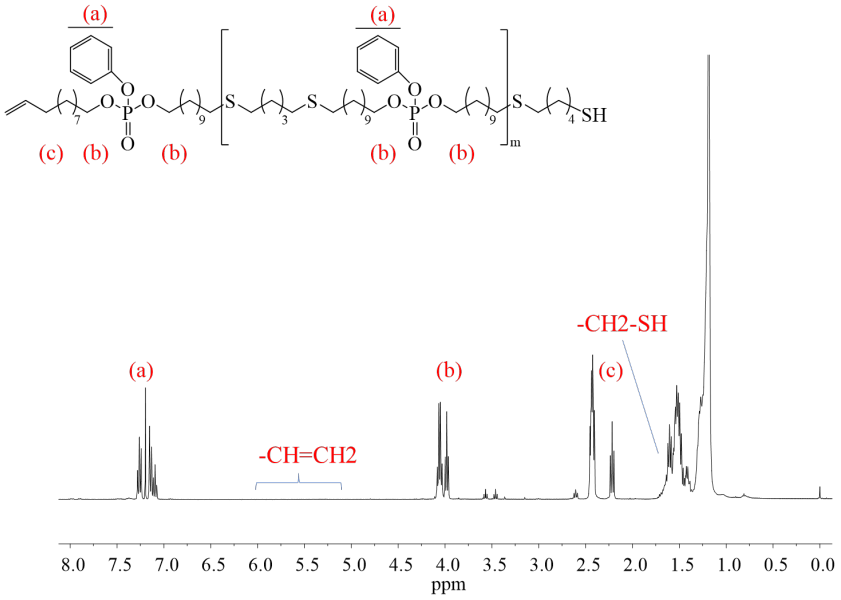

Figure S3: ^{1}H-NMR spectrum (400 MHz in $CDCl_3$) of poly(thioether-phosphoester) showing the absence of peaks in the region between 5 and 6 ppm, relative to vinyl endgroups.

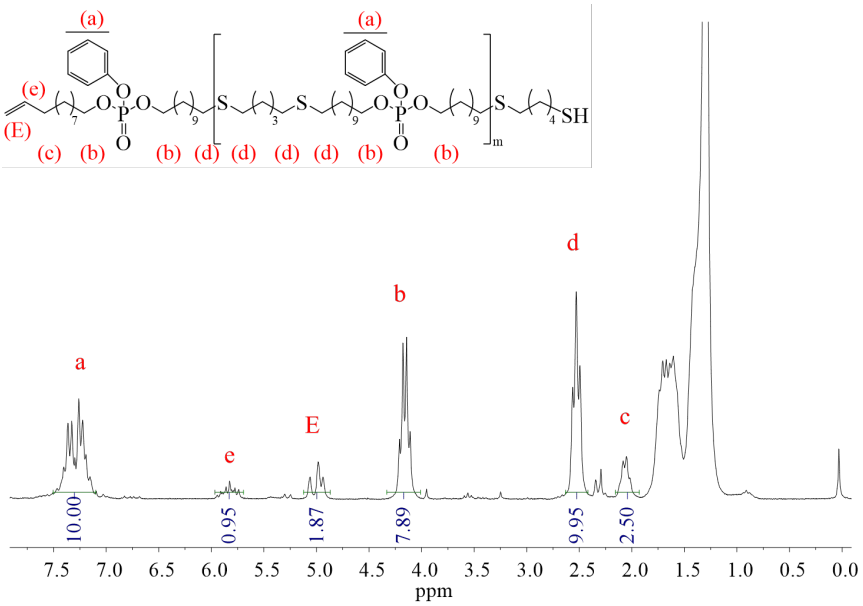

Figure S4: ^{1}H-NMR spectrum (400 MHz in $CDCl_3$) of poly(thioether-phosphoester) produced with a molar ratio of 1: 0.75 (diene to dithiol) in 30 min of reaction under UV light.

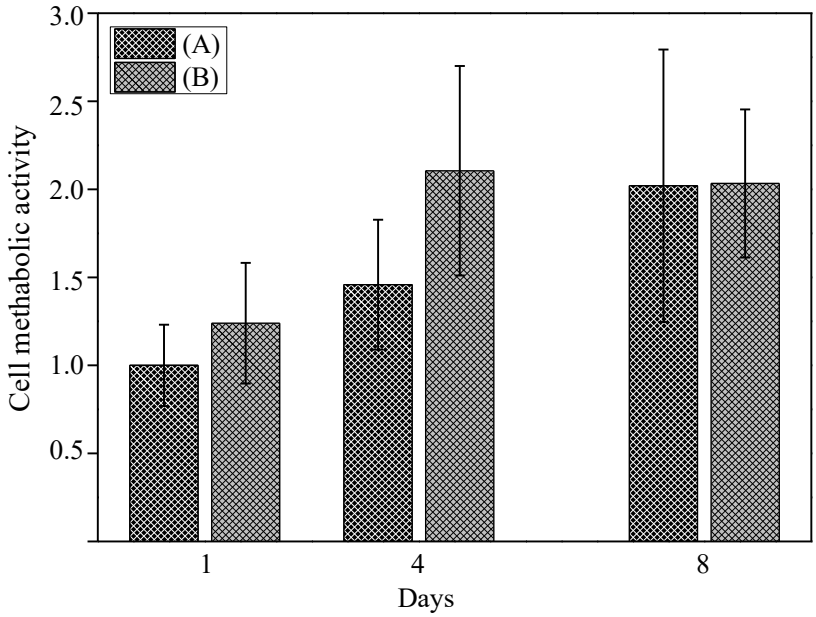

Figure S5: Metabolic activity of cells seeded on fibres produced from (A) poly(ω-pentadecalactone) and (B) poly(ω-PDL) + poly(ω-PDL-b-TEPE) after 1, 4 and 8 days of culture. Data are expressed as mean ± standard error. Even though there was no statistical significance ($p>0.05$) it is possible to see an increased cell viability in the poly(ω-PDL) + poly(ω-PDL-b-TEPE) compared to poly(ω-pentadecalactone) at day 4 of culture.

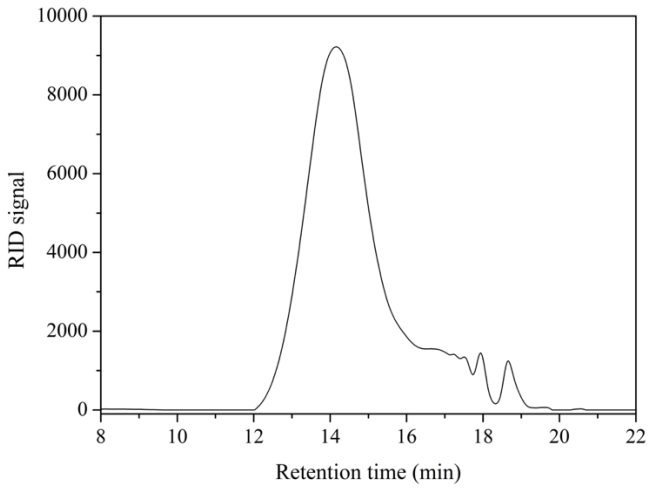

Figure S6: SEC trace of poly(globalide) homopolymer.

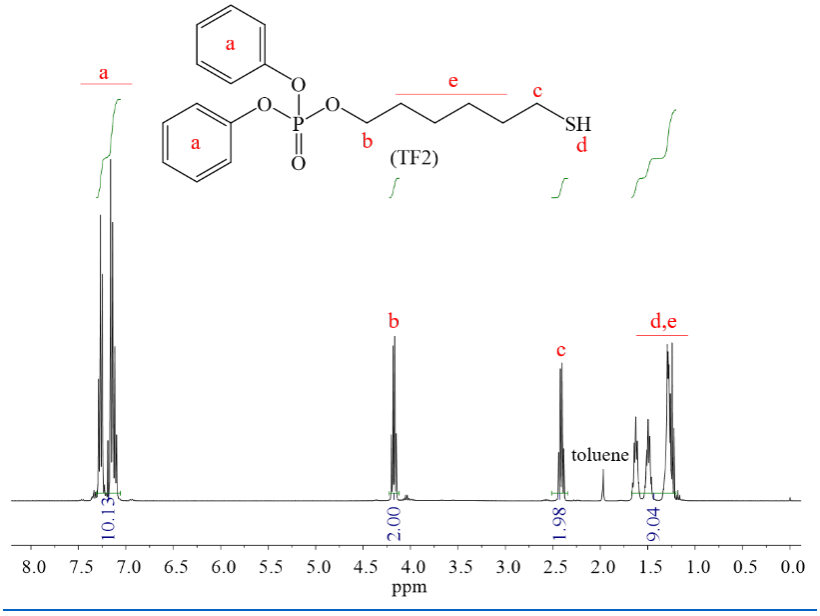

Figure S7: ^{1}H-NMR spectrum (400 MHz in $CDCl_3$) of diphenyl 6-mercapto-1-hexyl phosphate - TF2.

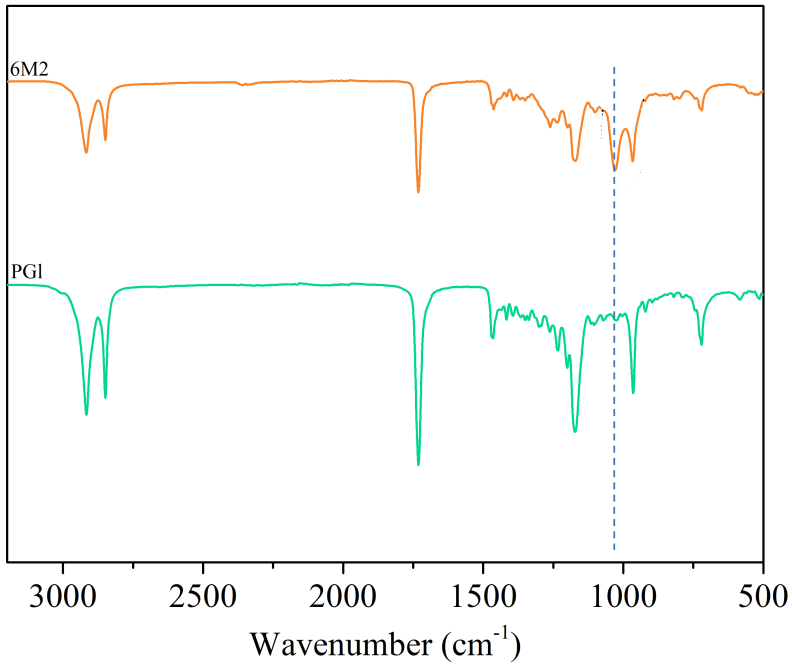

Figure S8: FTIR spectra of 6M2 and PGL. Characteristic signals oringinating from the P-O-C groups at around 1028 cm^{-1} (circled) are detectable for sample 6M2.

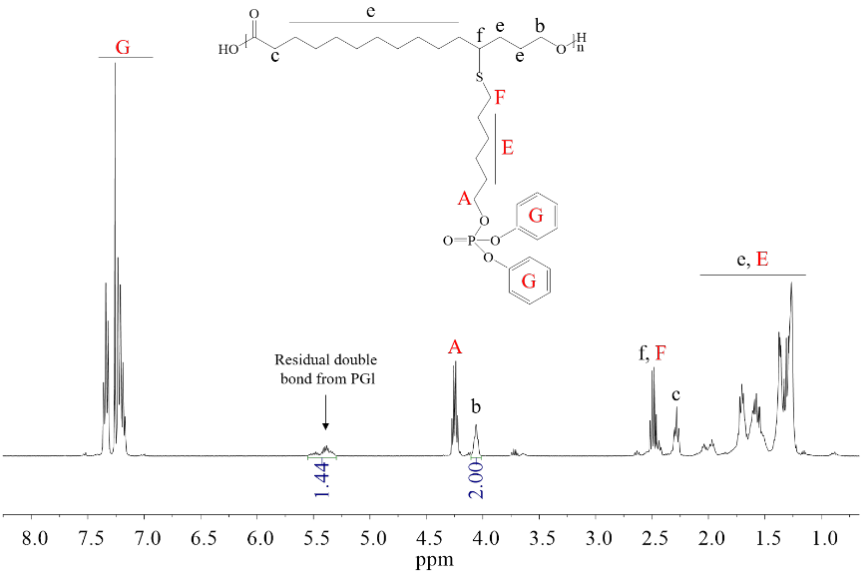

Figure S9. ^{1}H-NMR spectrum (400 MHz in $CDCl_3$) of PGl-TF2 (entry Ph6).

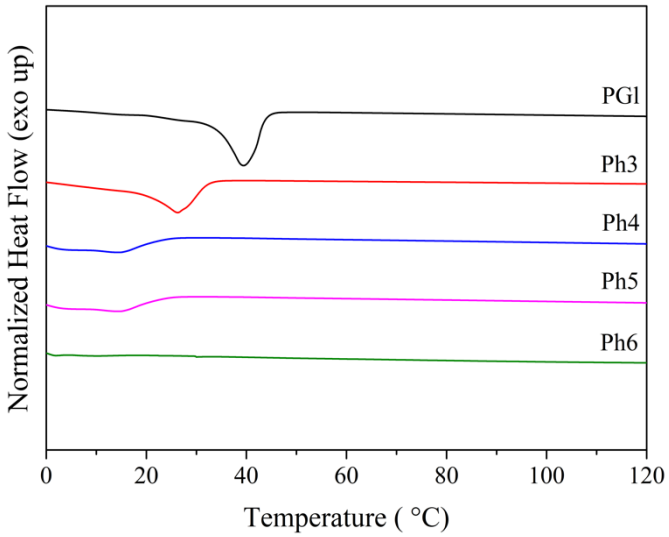

Figure S10. Differential scanning calorimetry (DSC) thermograms (second heating curve) before and after post-polymerisation modification of PGl with TF2.

[1] M. Takwa, N. Simpson, E. Mcilmsitröm, K. Hult, M. Martinelle, *Macromol. Rapid Commun.,* 2006, **27**, 1932–1936.

[2] F. Marsico, M. Wagner, K. Landfester, F. R. Wurm, *Polym. Chem.,* 2012, **45**, 8511.