Poly(malic acid) copolymers as degradable rheology modifiers in aqueous formulations

Supporting Information

Materials

(2S)-2-Hydroxypropanoic acid (L-lactic acid, cat# 094601) was procured from Fluorochem. D-L Malic acid (cat# 125255000) and tetrahydrofuran (cat# 268290025) were purchased from ThermoScientific. Tin(II) chloride, anhydrous (cat# 10512991) and glycolic acid (cat# 154511000) were bought from Acros Organics. Sodium nitrate (cat # s5506) and sodium hydroxide (cat# S5881) were purchased from Sigma-Aldrich, Monosodium phosphate (cat# 106370) was obtained from Merck. Methanol (cat# 34860) was purchased from Honeywell. Easivial polystyrene standards (cat# PL2010-0401) and Easivial poly(ethylene glycol) standards (cat# PL2070-0201) were both purchased from Agilent Technologies. Shampoo ingredients were donated by Unilever.

Aqueous GPC buffers were prepared in house at either pH 6 or pH 9. Both systems comprised 30% MeOH; 70% deionised water containing sodium nitrate (0.2 M) and monosodium phosphate (0.01 M) and were adjusted to desired pH by addition of aqueous NaOH (1M).

Instruments

All NMR spectroscopy experiments were performed at 298 K on either a 400MHz Bruker AVIII spectrometer or a 500 MHz Bruker AVIII HD spectrometer. Chemical shifts are reported as δ in parts per million (ppm) and referenced to the chemical shift of the deuterated solvent used ($CDCl_3$ ^1H: δ=7.26 ppm, ^{13}C: δ=77.16 ppm; DMSO-$δ^6$ ^1H: δ=2.50 ppm, ^{13}C: δ=39.52 ppm; MeOD ^1H: δ=3.31 ppm, ^{13}C: δ=49.00 ppm) The resonance multiplicities are described as s (singlet), d (doublet), t (triplet), q (quartet) or m (multiplet).

Aqueous Gel permeation chromatography (GPC) was performed at 30 ℃ on an Agilent 1260 Infinity II Multidetector equipped with a viscometer, refractive index and light scatterer. Aqueous buffers were used as eluent at either pH6 or pH9. The pH 6 system used 2x PLAquagel-OH40 columns at 35 ℃ running at a flow rate of 1 $mLmin^{-1}$. For the pH 9 system 2x PLAquagel-OH Mixed M columns were used at 35 ℃ running at a flow rate of 0.6 $mLmin^{-1}$. Both systems were calibrated with poly(ethylene glycol) standards. Samples were dissolved in the chosen eluent and filtered using 0.2 µm nylon syringe filters (cat # 5190-5269, Agilent Technologies). Universal calibration was employed for the calibration method and molecular weights of samples were obtained by triple detection.

Organic GPC was performed on an Agilent 1260 Infinity II Multidetector equipped with 2 x PLGel Mixed C column, a viscometer, refractive index and light scatterer and used tetrahydrofuran as eluent at 35 ℃ at a flow rate of 1 $mLmin^{-1}$. The system was calibrated with polystyrene standards to a universal calibration method. Samples were dissolved in THF, filtered through PTFE syringes (cat # 5191-5913, Agilent) and molecular weights were obtained using triple detection.

Thermogravimetric analyses of the specimens were performed on a TA SDT650 model thermogravimetric analyser using alumina pans, at a heating rate of 10 K/min), from ambient temperature to 600 °C, under nitrogen atmosphere. Differential Scanning Calorimeter measurements were employed to determine the glass transition temperatures (T_g), which were conducted on a DSC 2500 model (TA Instruments, USA), under a nitrogen atmosphere. The samples (3-8 mg) were heated in aluminium T zero pans with pierced hermetic lids at 10 °C min^{-1} from - 80 to 120 °C, then cooled to −80 °C, and repeated with three total heat cycles.

The rheological properties of the shampoo formulations were measured using Discovery HR-2 (TA Instruments, New Castle, DE, USA), fitted with 60 mm, 2° stainless steel cone top geometry and a Peltier plate. Oscillatory tests were performed at 25 °C and included a 180 second soak prior to testing. Solutions (2.5 mL) were added by spoon to the Peltier plate. Frequency sweeps were run from 0.1 to 100 rad s^{-1} using a strain of 4%. Amplitude sweeps were conducted at 100 rad s^{-1} from 1 to 1000 %. Oscillation stress was calculated using the following equation and plotted as a function of Oscillation strain:

$$Oscillation\ Stress = \frac{Storage\ Modulus\ x\ Oscillation\ Strain}{100}$$

Methods

Malic acid thermal degradation to fumaric acid: Malic acid (1 g, 7.5mmol) with and without stannous chloride (1%) was added to four vials and each vial heated to 100, 120, 140 °C for 24 hours. The total contents of the vial were dissolved in DMSO-δ^6 and analysed by ^{1}H NMR spectroscopy. Ratio of degradation was determined by integration of the fumaric and malic acid resonances and calculation using the following equation.

$$Ratio\ of\ Degradation = \frac{I_{Fumaric\ acid}}{I_{Malic\ acid}}$$

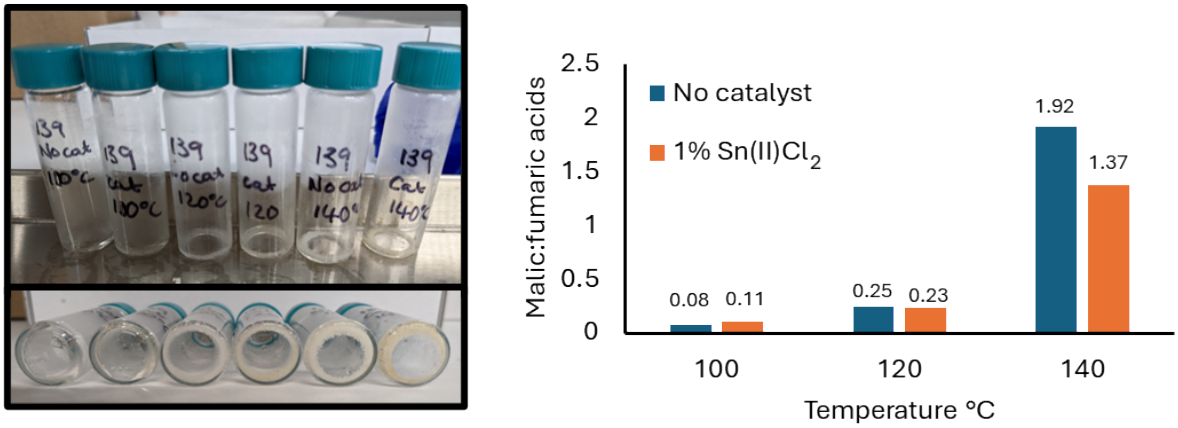

Figure S1. Left: Vials of malic acid heated for 16 hours at 100, 120 and 140 °C, with and without 1 wt% tin(II) chloride. Right: Plot of the ratio of fumaric acid formed for each malic acid, as determined by ^{1}H NMR spectroscopy analysed in deuterated dimethylsulfoxide.

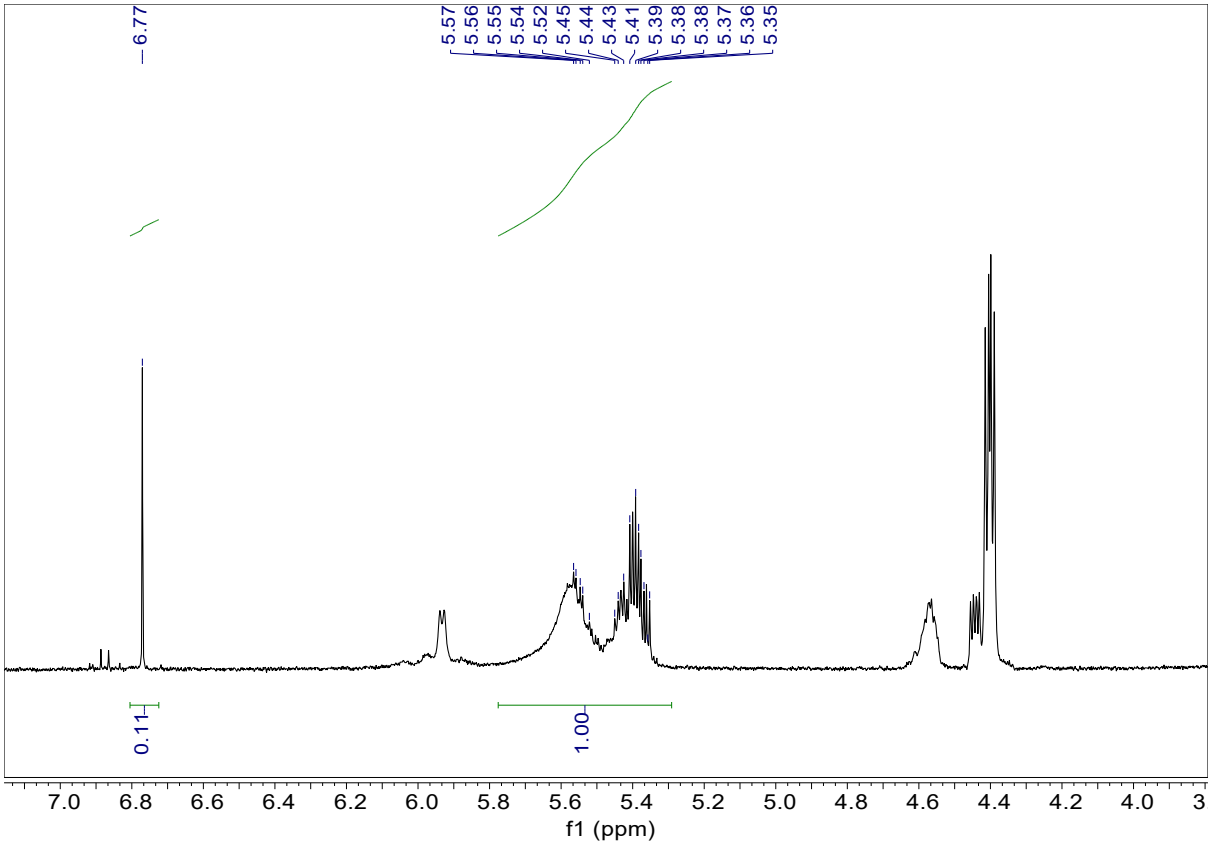

Figure S2. [1]H NMR of malic acid analysed in deuterated dimethylsulfoxide after heating at 100 °C for 16 hours in the presence of tin (ii) chloride. The ratio of the fumaric acid resonance at 6.79 ppm and the malic acid resonances between 5.30-5.68 ppm were calculated.

Entry	Sample	Scale g	Ratio MA:X	Reaction Step 1 N_2 Flow		Reaction Step 2 Vacuum <0.16 mbar		Reaction Step 3 Vacuum <0.16 mbar	
				Time hrs	Temp °C	Time hrs	Temp °C	Time hrs	Temp °C
1	PMA	40	-	24	120	6	110	-	-
2	$PMLA_{40:60}$-S	96	40:60	24	110	6	110	-	-
3	$PMLA_{40:60}$-S	36	40:60	24	110	6	110	-	-
4	$PMLA_{40:60}$-F	36	40:60	24	110	24	110	6	120
5	$PMLA_{40:60}$-F	36	40:60	24	110	24	110	6	120
6	$PMLA_{40:60}$-F	36	40:60	24	110	24	110	6	120
7	PE-$PMLA_{40:60}$-F	36	40:60	24	110	24	110	6	120
8	$PGMA_{40:60}$-F	36	40:60	24	110	24	110	6	120
9	PE-$PMGA_{40:60}$-F	36	40:60	24	110	24	110	6	120
10	$PMLA_{10:90}$-F	36	10:90	24	110	24	110	6	120

Table S1. Conditions applied for polycondensation of malic acid (MA) containing polymers. X = comonomer = lactic acid (LA) or glycolic acid (GA).

Quantification of % conversions were made by integration of ^{1}H NMR resonances using the following equations and summarised for the polymers in Table S2.

$$\%\ FA\ formed = \frac{\int_{5.57}^{5.63} FA}{\int_{5.57}^{5.63} FA + \frac{\int_{2.55}^{2.65} MA}{2} + \int_{2.89}^{3.05} PMA + \int_{2.66}^{2.89} PMA} * 100$$

$$\%\ MA\ conversion = \frac{\int_{2.89}^{3.05} PMA + \int_{2.66}^{2.89} PMA}{\frac{\int_{2.55}^{2.65} MA}{2} + \int_{2.89}^{3.05} PMA + \int_{2.66}^{2.89} PMA} * 100$$

$$\%\ LA\ conversion = \frac{\int_{1.32}^{1.56} PLA}{\int_{1.32}^{1.56} PLA + \int_{1.18}^{1.26} LA} * 100$$

$$\%\ GA\ conversion = \frac{\int_{4.72}^{4.98} PGA + \int_{4.62}^{4.68} PGA + \int_{4.54}^{4.62} PGA}{\int_{4.72}^{4.98} PGA + \int_{4.62}^{4.68} PGA + \int_{4.54}^{4.62} PGA + \int_{3.91}^{3.88} GA} * 100$$

	% FA	%MA	%GA/LA
$PMLA_{40:60}$-F	2.0	85.9	98.6
$PMLA_{40:60}$-F	1.6	94.8	95.7
$PMLA_{40:60}$-F	5.9	87.5	95.0
PE-$PMLA_{40:60}$-F	3.1	79.3	87.8
$PMGA_{40:60}$-F	0.8	98.4	99.8
PE-$PMGA_{40:60}$-F	0.7	95.8	99.4
$PMLA_{90:10}$-F	1.2	84.9	99.4
PMA-F	4.1	77.3	-

Table S2. Calculated conversions of malic acid to fumaric acid (%FA), reacted malic acid into polymeric species (%MA) and conversions of either glycolic or lactic acid comonomers into polymeric forms (%GA/LA).

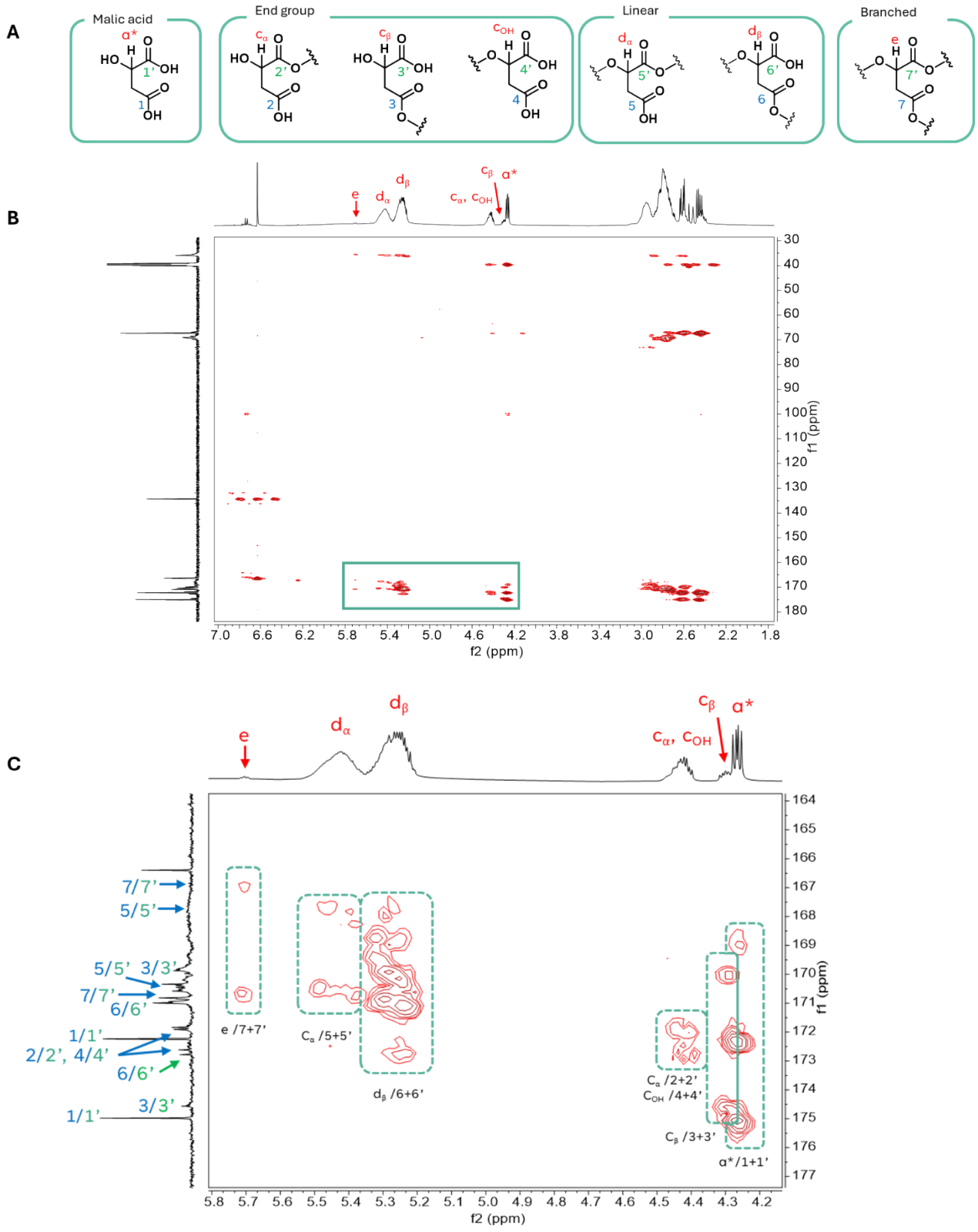

Figure S3. HMBC analysis of poly(malic acid) analysed in deuterated dimethylsulfoxide. (A) different malic acid environments within the polymer. (B) Full HMBC spectrum with highlighted region which is expanded in (C) with referenced peak regions.

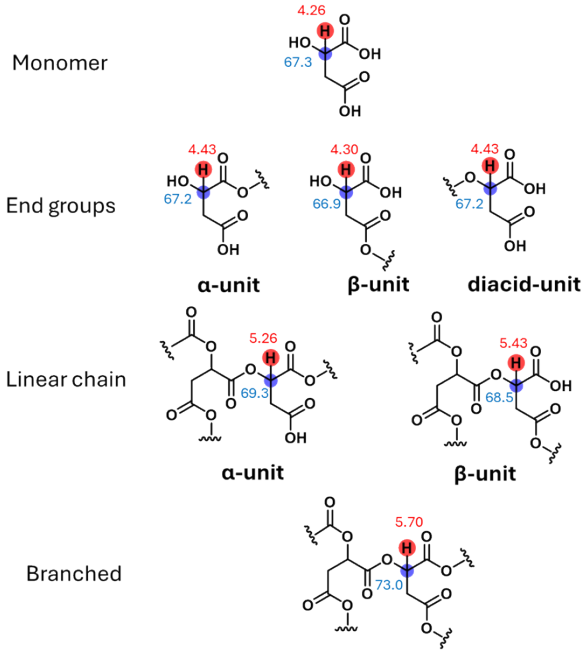

Figure S4. Assignments of methine proton and carbon in ^{1}H and ^{13}C NMR spectroscopy analysed in deuterated dimethylsulfoxide.

Branching analysis by NMR spectroscopy

Having identified the different malic acid monomer environments by 2D NMR, and calculating the degree of branching, the resonance assignments were then applied to the co-polymers. The broadening of the resonances as a result of the polymerisation coupled with the overlapping peak regions meant that deconvolution of the peaks using Mestrenova 14.2.1 software was necessary. Depending on the degree of polymerisation and the copolymer, different regions required deconvolution. The areas of the peaks of interest as a fraction of the entire peak were calculated to obtain an accurate relative integration which was then used in the branching calculations.

PMLA$_{40:60}$-S: ^{1}H NMR (500 MHz, DMSO) δ 5.62 (dd, *J* = 6.0, 4.8 Hz, 1H), 5.56 – 5.36 (m, 8H), 5.34 – 5.24 (m, 6H), 5.236 – 5.149 (m, 7H), 5.15 – 5.06 (m, 6H), 5.06 – 4.87 (m, 9H), 4.53 – 4.37 (m, 7H), 4.33 – 4.29 (m, 2H), 4.27 (dd, *J* = 7.8, 4.7 Hz, 2H), 4.25 – 4.14 (m, 4H), 4.05 (q, *J* = 6.9 Hz, 2H), 3.15 – 2.66 (m, 25H), 2.66 – 2.55 (m, 4H), 2.48 – 2.36 (m, 3H), 1.58 – 1.34 (m, 46H), 1.34 – 1.20 (m, 8H).

PMLA$_{40:60}$-S: ^{1}H NMR (500 MHz, DMSO) δ 5.67 – 5.56 (m, 1H), 5.53 – 4.86 (m, 20H), 4.43 (ttd, *J* = 17.6, 8.1, 4.1 Hz, 4H), 4.27 (ddd, *J* = 17.9, 7.5, 4.8 Hz, 3H), 4.23 – 4.11 (m, 2H), 4.03 (q, *J* = 6.9 Hz, 1H), 3.15 – 2.53 (m, 17H), 2.48 – 2.32 (m, 2H), 1.42 (ddddd, *J* = 27.6, 10.4, 8.1, 4.7, 2.1 Hz, 28H), 1.32 – 1.15 (m, 7H).

PMLA$_{40:60}$-F: ^{1}H NMR (500 MHz, DMSO) δ 5.69 – 5.57 (m, 1H), 5.56 – 4.85 (m, 26H), 4.45 (dddq, *J* = 12.6, 9.1, 5.5, 3.5 Hz, 2H), 4.28 (ddd, *J* = 18.9, 7.9, 5.0 Hz, 1H), 4.2 – 4.14 (m, 1H), 4.04 (q, *J* = 6.9 Hz, 0.5H), 3.28 – 2.66 (m, 19H), 2.61 (ddt, *J* = 22.5, 13.6, 6.1 Hz, 1H), 2.47 – 2.35 (m, 1H), 1.57 – 1.31 (m, 37H), 1.25 (dd, *J* = 26.6, 6.8 Hz, 1H).

PMLA$_{40:60}$-F: ^{1}H NMR (500 MHz, DMSO) δ 5.69 – 5.55 (m, 1H), 5.54 (m, 31H), 4.43 (m, 2H), 4.35 – 4.14 (m, 2H), 4.10 – 3.98 (m, 1H), 3.21 – 2.55 (m, 28H), 2.47 – 2.34 (m, 1H), 1.42 (ddd, *J* = 29.3, 15.0, 7.2 Hz, 50H).

PMLA$_{40:60}$-F: ^{1}H NMR (500 MHz, DMSO) δ 5.79 – 5.59 (m, 1H), 5.59 – 4.85 (m, 34H), 4.42 (dddd, *J* = 20.0, 12.6, 10.4, 6.8 Hz, 3H), 4.28 (ddd, *J* = 18.0, 7.6, 4.9 Hz, 2H), 4.18 (qd, *J* = 6.8, 4.5 Hz, 1H), 4.03 (q, *J* = 6.9 Hz, 1H), 3.22 – 2.64 (m, 30H), 2.64 – 2.56 (m, 2H), 2.48 – 2.35 (m, 1H), 1.68 – 1.31 (m, 43H), 1.31 – 1.17 (m, 2H).

PMLA$_{10:90}$-F: ^{1}H NMR (500 MHz, DMSO) δ 5.62 (dd, *J* = 6.0, 4.8 Hz, 1H), 5.56 – 5.35 (m, 8H), 5.35 –5.06 (m, 18H), 5.06 – 4.86 (m, 9H), 4.54 – 4.34 (m, 7H), 4.31 (dt, *J* = 6.8, 4.5 Hz, 2H), 4.27 (dd, *J* = 7.8, 4.8 Hz, 2H), 4.24 – 4.14 (m, 4H), 4.05 (q, *J* = 6.9 Hz, 2H), 3.15 – 2.65 (m, 25H), 2.65 – 2.55 (m, 4H), 2.48 – 2.36 (m, 3H), 1.58 – 1.34 (m, 46H), 1.33 – 1.20 (m, 8H).

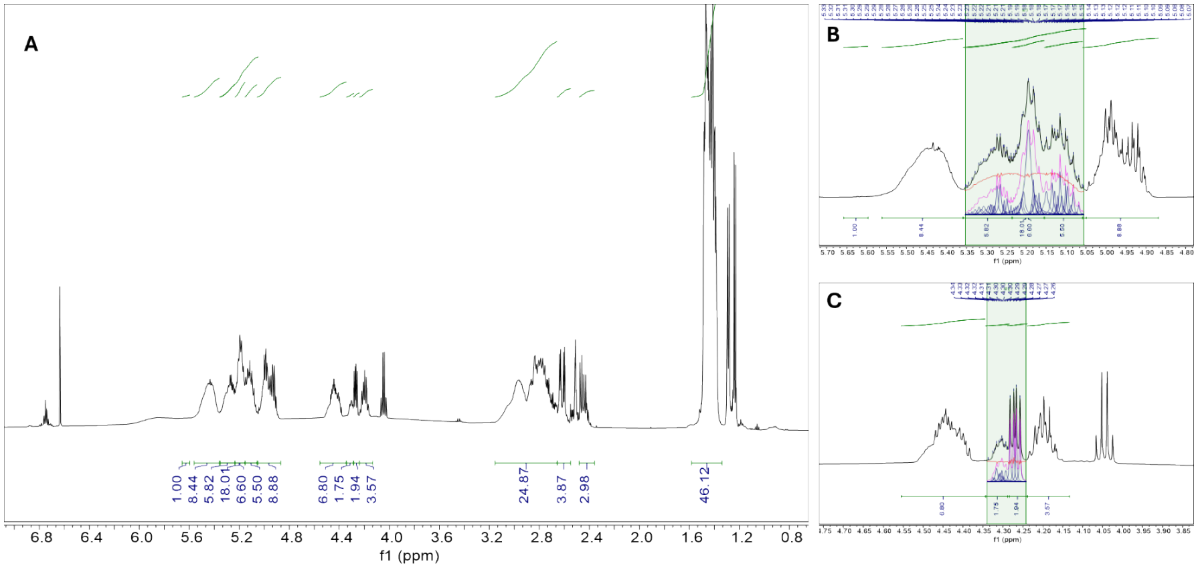

Figure S5. Quantitative ^{1}H NMR spectra of poly(malic-co-lactic acid)$_{40:60}$-S analysed in deuterated dimethylsulfoxide showing (A) full spectra and integrations used, (B) and (C) deconvolution regions to quantify different monomer environments of malic acid.

PE-PMLA$_{40:60}$-F: ^{1}H NMR (500 MHz, DMSO) δ 5.73 – 5.58 (m, 1H), 5.57 – 4.75 (m, 21H), 4.54 – 4.35 (m, 3H), 4.33 – 3.94 (m, 6H), 3.18 – 2.65 (m, 15H), 2.65 – 2.56 (m, 2H), 2.49 – 2.36 (m, 1H), 1.55 – 1.33 (m, 25H), 1.26 (dd, *J* = 26.5, 6.8 Hz, 3H).

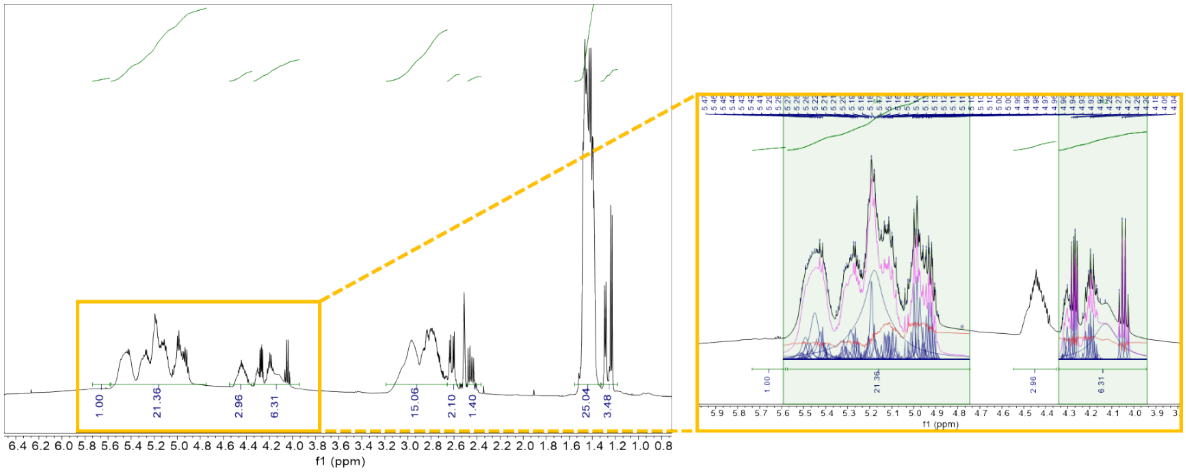

Figure S6. Quantitative ^{1}H NMR spectra of pentaerythritol-poly(malic-co-glycolic acid)$_{40:60}$-F analysed in deuterated dimethylsulfoxide showing integrations used and deconvoluted peaks in the expanded region.

PMGA$_{40:60}$-F: ^{1}H NMR (500 MHz, DMSO) δ 5.74 (dq, *J* = 36.8, 5.9 Hz, 1H), 5.65 – 5.04 (m, 21H), 4.96 – 4.38 (m, 60H), 4.32 (dt, *J* = 7.9, 3.9 Hz, 1H), 3.29 – 2.54 (m, 39H).

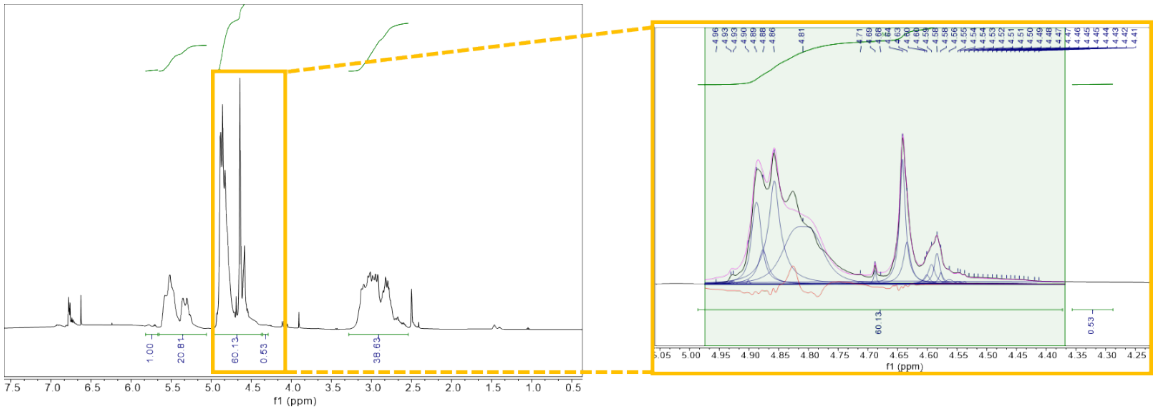

Figure S7. Quantitative [1]H NMR spectra of poly(malic-co-glycolic acid)$_{40:60}$-F analysed in deuterated dimethylsulfoxide showing integrations used.

PE-PMGA$_{40:60}$-F: [1]H NMR (500 MHz, DMSO) δ 5.85 – 5.68 (m, 1H), 5.65 – 5.40 (m, 8H), 5.40 – 5.19 (m, 5H), 4.84 (ddd, *J* = 42.6, 16.2, 9.1 Hz, 27H), 4.68 – 4.55 (m, 12H), 4.55 – 4.41 (m, 4H), 4.41 – 3.98 (m, 10H), 3.75 (d, *J* = 14.2 Hz, 1H), 3.44 (q, *J* = 7.0 Hz, 1H), 3.25 – 2.63 (m, 25H).

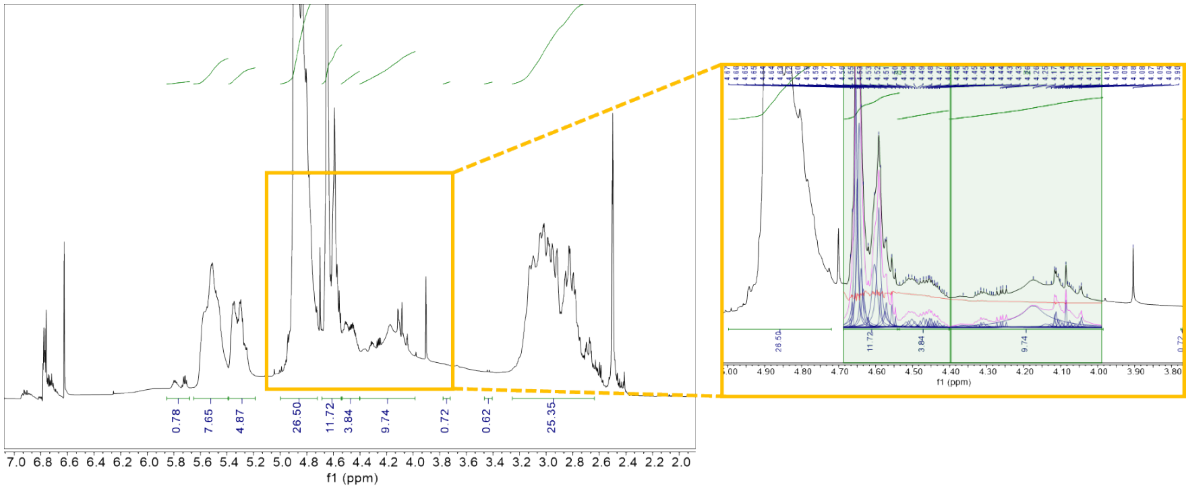

Figure S8. Quantitative [1]H NMR spectra of pentaerythritol-poly(malic-co-glycolic acid)$_{40:60}$-F analysed in deuterated dimethylsulfoxide showing integrations used and deconvoluted peaks in the expanded region.

PMA-F: [1]H NMR (500 MHz, DMSO) δ 5.77 – 5.64 (m, 1H), 5.56 – 5.13 (m, 7H), 4.42 (dtd, *J* = 14.5, 7.7, 3.6 Hz, 1H), 4.32 – 4.21 (m, 1H), 3.13 – 2.89 (m, 4H), 2.889 – 2.670 (m, 8H), 2.60 (dt, *J* = 15.7, 4.6 Hz, 2H), 2.48 – 2.37 (m, 1H).

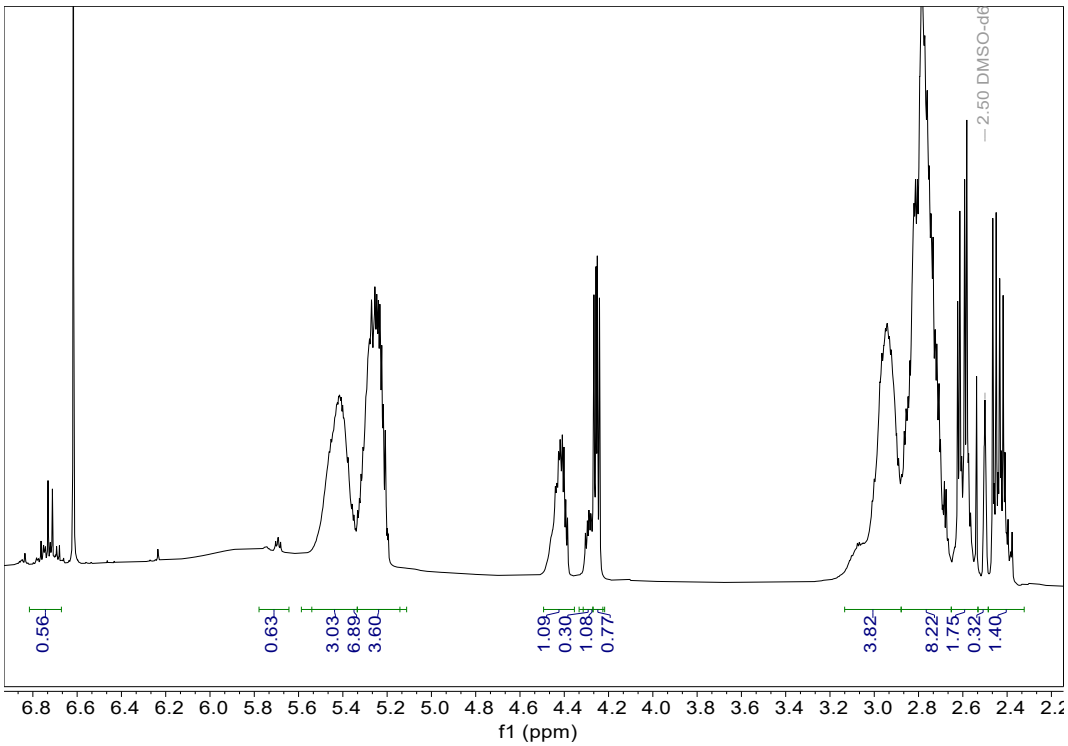

Figure S9. Quantitative ^{1}H NMR spectra of poly(malic acid)-F analysed in deuterated dimethylsulfoxide.

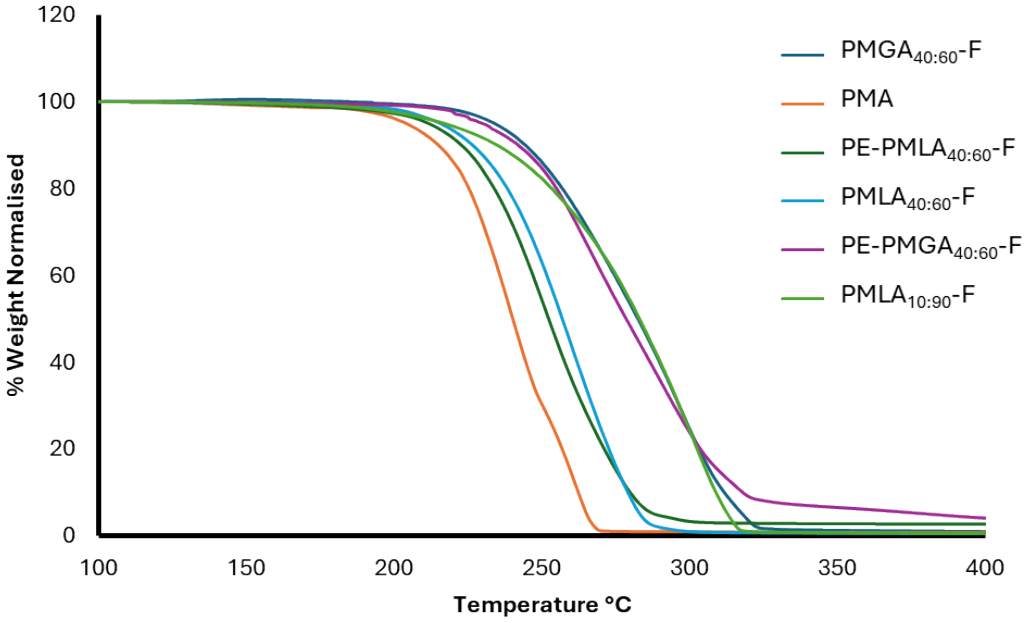

Figure S10. Thermal gravimetric analysis traces of malic acid containing polyesters.

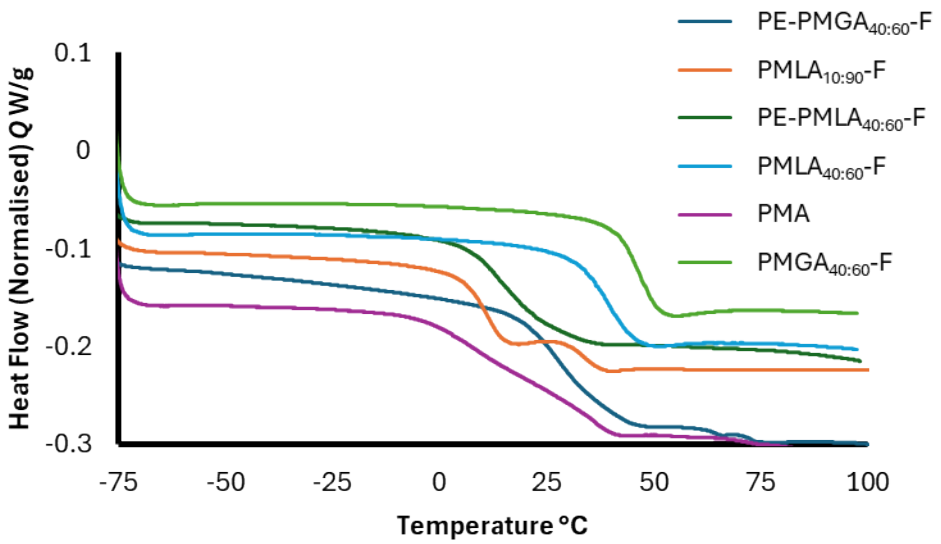

Figure S11. Differential scanning calorimetry analysis showing glass transition profiles of poly(malic acid) copolymers on a second heating ramp.

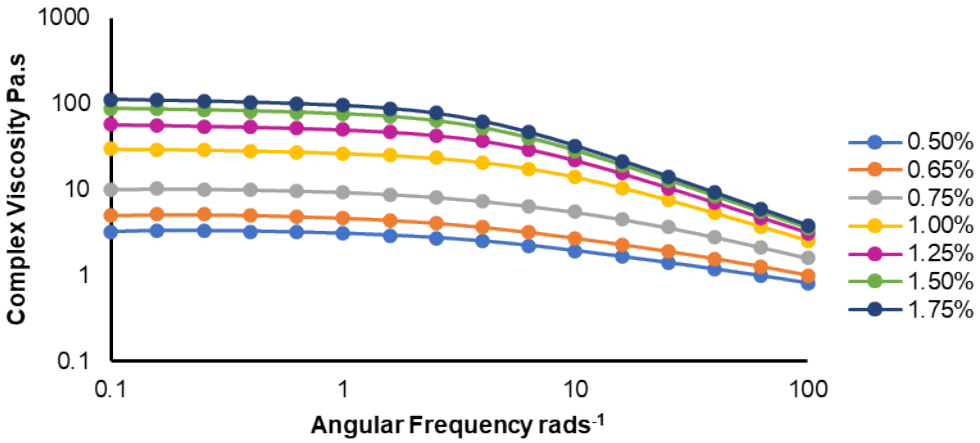

Figure S12. Complex viscosity profiles as a function of angular frequency for carbomer formulated shampoos containing differing percentages of sodium chloride.

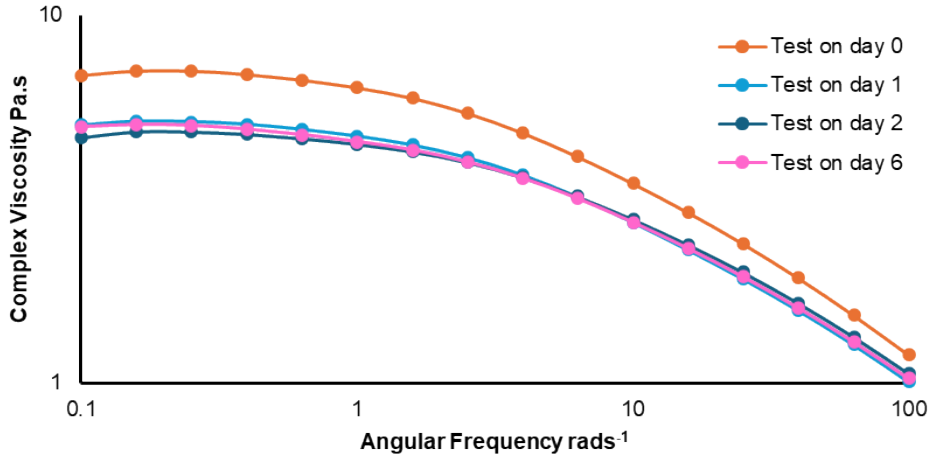

Figure S13. Rheological analysis of carbomer-formulated shampoo showing complex viscosity as a function of angular frequency when analysed on different days after initial formulation.

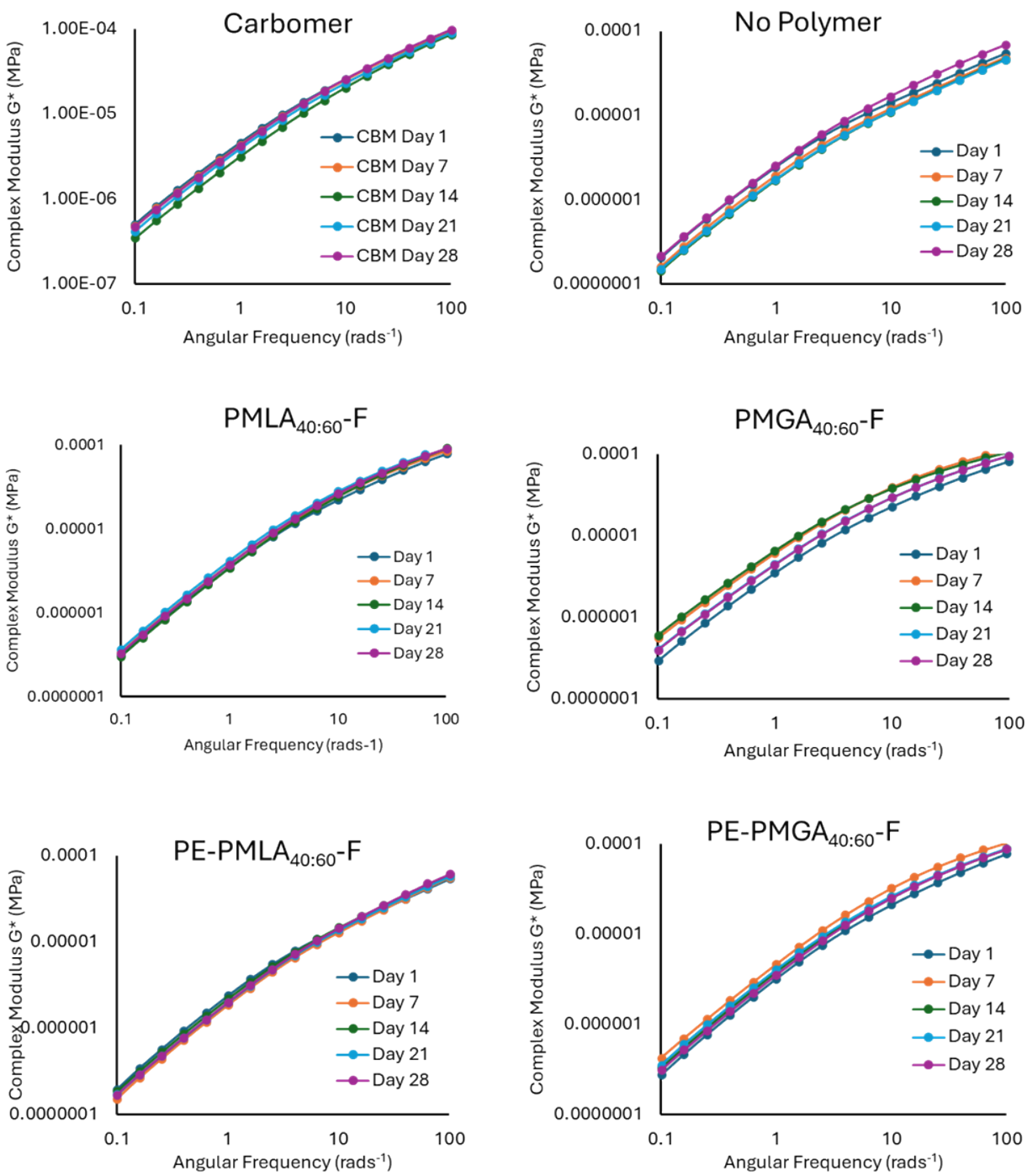

Figure S14. Complex modulus of shampoo formulations as a function of angular frequency over time.

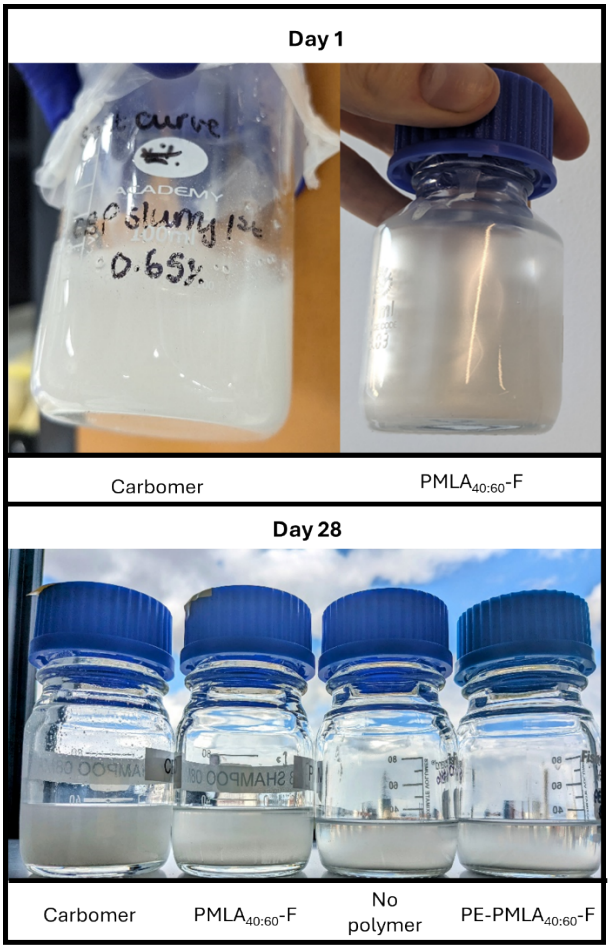

Figure S15. Top: Incorporation of mica in carbomer shampoo (left) and $PMLA_{40:60}$-F (right) one day 1. Bottom: sedimentation of mica in shampoo formulations over time.