

SUPPORTING INFORMATION | Quantification of the actual composition of polymeric nanocapsules. A quality control analysis

Supplementary Table 1. Validation of the calibration curves for each quantified substance and formulation

Formulation	Molecule	RT (min) (mean) (n=3)	Calibration range (ppb)	curve	r ² (mean ± StD) (n=3)	Precision (pooled RStD%) (%)	Accuracy (RE%) (%) (low; mid; high range)	LoQ (ppb) (mean ± StD) (n=3)
SD-/PEG-HA	Benzethonium chloride	2.6	8.0 – 80.0		0.9959 ± 0.0016	4.4	3.9; -0.3; 2.4	0.70 ± 0.38
	TPGS	4.0	64.0 – 640.0		0.9854 ± 0.0040	8.6	1.9; -1.0; 2.5	1.90 ± 0.86
	DL- α -tocopherol	4.9	216.0 – 2160.0		0.9948 ± 0.0040	4.9	-1.6; 2.6; 0.0	1.16 ± 0.47
	Hyaluronic acid (whole)	4.9	19,590.0 – 68,570.0		0.9897 ± 0.0009	4.0	3.5; 1.0; 1.0	22.51 ± 9.16
	Hyaluronic acid (supernatant)	4.9	15,670.0 – 78,370.0		0.9889 ± 0.0039	4.3	5.3; 3.6; 3.6	26.65 ± 6.62
	Hyaluronic acid (infranatant)	4.9	17,140.0 – 58,780.0		0.9840 ± 0.0056	4.8	5.6; 1.7; 1.7	34.42 ± 14.95
SD-noPEG-HA	CTAB	1.6	43.2 – 144.0		0.9985 ± 0.0009	1.0	2.0; -0.2; 1.1	0.27 ± 0.13
	C ₈ -C ₈ -C ₈ Triglyceride	1.8	881.3 – 2937.6 (*)		0.9880 ± 0.0016	3.2	5.9; -2.7; 3.4	5.99 ± 2.76
	C ₈ -C ₈ -C ₁₀ Triglyceride	1.9	881.3 – 2937.6 (*)		0.9859 ± 0.0040	3.0	6.1; -2.0; 4.3	8.22 ± 2.40
	C ₈ -C ₁₀ -C ₁₀ Triglyceride	2.0	881.3 – 2937.6 (*)		0.9852 ± 0.0031	3.7	5.6; -3.5; 3.7	8.18 ± 1.66
	C ₁₀ -C ₁₀ -C ₁₀ Triglyceride	2.0	881.3 – 2937.6 (*)		0.9792 ± 0.0036	5.0	4.2; -2.7; 3.1	1.63 ± 0.31
	Phosphatidylcholine 756.6 Da	2.0	216.0 – 720.0 (**)		0.9887 ± 0.0074	1.6	2.8; 5.4; -4.7	0.62 ± 0.44
	Phosphatidylcholine 758.6 Da	2.0	216.0 – 720.0 (**)		0.9812 ± 0.0018	3.4	4.2; 5.3; -4.1	0.14 ± 0.01
	Phosphatidylcholine 780.6 Da	2.0	216.0 – 720.0 (**)		0.9908 ± 0.0052	1.2	1.8; 4.8; -4.2	0.24 ± 0.19
	Phosphatidylcholine 782.5 Da	2.1	216.0 – 720.0 (**)		0.9880 ± 0.0086	1.2	2.6; 6.1; -4.9	0.06 ± 0.01
	Hyaluronic acid (whole)	4.9	6,120.0 – 10,200.0		0.9383 ± 0.0652	4.0	3.7; 1.3; 1.3	19.18 ± 2.49
	Hyaluronic acid (supernatant)	4.9	20,000.0 – 98,000.0		0.9876 ± 0.0039	4.8	8.1; 6.0; 6.0	32.28 ± 9.41
	Hyaluronic acid (infranatant)	4.9	10,000.0 – 29,000.0		0.9852 ± 0.0052	4.3	1.8; 2.4; 2.4	15.35 ± 1.82
	SD-noPEG-PSA	CTAB	1.6	43.2 – 144.0		0.9952 ± 0.0015	1.5	3.7; -0.2; 0.5
C ₈ -C ₈ -C ₈ Triglyceride		1.8	881.3 – 2937.6 (*)		0.9814 ± 0.0025	3.3	8.5; -1.6; 2.5	6.46 ± 1.65
C ₈ -C ₈ -C ₁₀ Triglyceride		1.9	881.3 – 2937.6 (*)		0.9801 ± 0.0017	3.8	8.4; -2.1; 2.8	9.44 ± 2.86
C ₈ -C ₁₀ -C ₁₀ Triglyceride		2.0	881.3 – 2937.6 (*)		0.9848 ± 0.0008	4.0	5.2; -0.8; 2.3	7.59 ± 1.38
C ₁₀ -C ₁₀ -C ₁₀ Triglyceride		2.0	881.3 – 2937.6 (*)		0.9697 ± 0.0165	5.9	4.6; -2.8; 3.1	1.08 ± 0.05
Phosphatidylcholine 756.6 Da		2.0	216.0 – 720.0 (**)		0.9611 ± 0.0100	2.9	7.8; 4.7; -11.6	0.91 ± 0.14
Phosphatidylcholine 758.6 Da		2.0	216.0 – 720.0 (**)		0.9552 ± 0.0114	4.7	8.1; 3.2; -11.9	0.15 ± 0.02
Phosphatidylcholine 780.6 Da		2.0	216.0 – 720.0 (**)		0.9720 ± 0.0092	1.7	7.1; 4.8; -9.1	0.31 ± 0.14
Phosphatidylcholine 782.5 Da		2.1	216.0 – 720.0 (**)		0.9628 ± 0.0116	2.2	8.0; 4.8; -11.8	0.08 ± 0.01
Polysialic acid (whole)		5.1	6,150.0 – 10,870.0		0.9788 ± 0.0115	1.4	2.4; 0.7; 0.7	86.30 ± 32.47
Polysialic acid (supernatant)		5.1	4,900.0 – 81,630.0		0.9867 ± 0.0061	2.8	3.6; 12.8; 12.8	413.54 ± 424.46
Polysialic acid (infranatant)		5.1	7,350.0 – 29,390.0		0.9929 ± 0.0054	1.7	3.6; 3.6; 3.6	245.55 ± 134.63

SUPPORTING INFORMATION | Quantification of the actual composition of polymeric nanocapsules. A quality control analysis

Supplementary Table 1. Validation of the calibration curves for each quantified substance and formulation (continuation)

Formulation	Molecule	RT (min) (mean) (n=3)	Calibration range (ppb)	curve	r ² (mean ± StD) (n=3)	Precision (pooled RStD%) (%)	Accuracy (RE%) (%) (low; mid; high range)	LoQ (ppb) (mean ± StD) (n=3)
SE- <i>b</i> -PEG-HA	Benzethonium chloride	2.5	1.0 – 9.6		0.9997 ± 0.0002	1.1	0.5; -4.7; 0.1	0.24 ± 0.03
	Macrogol-15-hydroxystearate	3.2	6.0 – 120.0 (***)		0.9992 ± 0.0001	2.0	-1.8; -0.6; -1.5	2.25 ± 1.74
	Polysorbate 80	4.4	487.2 – 2784.0		0.9990 ± 0.0002	0.8	3.9; -1.6; 1.4	11.61 ± 0.36
	C ₈ -C ₈ -C ₈ Triglyceride	8.3	849.6 – 2832.0 (*)		0.9939 ± 0.0028	2.5	3.0; -2.1; 1.1	3.32 ± 1.59
	C ₈ -C ₈ -C ₁₀ Triglyceride	8.7	849.6 – 2832.0 (*)		0.9895 ± 0.0027	3.8	3.9; -1.5; 1.0	2.51 ± 1.14
	C ₈ -C ₁₀ -C ₁₀ Triglyceride	8.9	849.6 – 2832.0 (*)		0.9895 ± 0.0030	3.7	4.8; 4.7; 0.7	2.15 ± 1.82
	C ₁₀ -C ₁₀ -C ₁₀ Triglyceride	9.0	849.6 – 2832.0 (*)		0.9889 ± 0.0046	3.6	2.5; -4.4; 2.1	1.88 ± 1.17
	Hyaluronic acid (whole)	4.9	6,730.0 – 17,140.0		0.9863 ± 0.0004	2.4	3.2; 1.7; 1.7	15.53 ± 6.42
	Hyaluronic acid (retentate)	4.9	2,450.0 – 9,180.0		0.9658 ± 0.0164	3.3	8.7; 8.4; 8.4	14.21 ± 5.29
	Hyaluronic acid (permeate)	4.9	7,000.0 – 28,000.0		0.9901 ± 0.0049	3.9	4.0; 1.1; 1.1	35.22 ± 3.82
SD-noPEG-PEG-PGA	DL- α -tocopherol	2.9	288.8 – 2,887.5		0.9958 ± 0.0009	2.5	-7.5; 2.8; -3.5	6.33 ± 0.58
	1,2-dioleoyl-3-trimethylammoniumpropane chloride	3.6	7.5 – 75.0		0.9984 ± 0.0010	1.7	-2.5; -0.3; -0.8	1.26 ± 0.49
	PEG-PGA (whole)	9.8	23,700 – 132,200		0.9978 ± 0.0012	1.1	3.8; 1.0; 1.0	432.10 ± 360.61
	PEG-PGA (supernatant)	9.8	7,700 – 184,800		0.9976 ± 0.0017	1.3	2.8; 4.6; 4.6	666.06 ± 970.38
	PEG-PGA (infranatant)	9.8	4,800 – 113,300		0.9984 ± 0.0012	1.9	2.5; 1.1; 1.1	69.37 ± 39.55

SD-*l*-PEG-HA: lineal-polyethylene glycol-containing hyaluronic acid nanocapsules formulated by solvent displacement. SD-noPEG-HA: non-PEGylated hyaluronic acid nanocapsules formulated by solvent displacement. SD-noPEG-PSA: non-PEGylated polysialic acid nanocapsules formulated by solvent displacement. SE-*b*-PEG-HA: Self-emulsifying branched-polyethylene glycol-containing hyaluronic acid nanocapsules. SD-noPEG-PEG-PGA: Solvent displacement nanocapsules not containing PEGylated surfactants and with an outer shell of polyethylene glycol polyglutamic acid. StD: standard deviation. RT: retention time. RStD%: Relative standard deviation of the responses for each concentration level. RE%: relative differences between the estimated concentrations and the actual standard concentration. LoQ: limit of quantification. TPGS: D- α -tocopherol polyethylene glycol 1000 succinate. CTAB: Hexadecyltrimethylammonium bromide. (*): C₈-C₈-C₈, C₈-C₈-C₁₀, C₈-C₁₀-C₁₀, and C₁₀-C₁₀-C₁₀ triglycerides calibration curves were built based on the amount of Miglyol® 812N. (**): Phosphatidylcholines' calibration curves were built based on the amount of Epikuron™ 145V. (***): macrogol-15-hydroxystearate calibration curves were built based on the amount of Kolliphor® HS15.

Supplementary Table 2. Chromatographic method for the analysis of non-polymeric substances

Formulation	Time (min)	A (%)	B (%)	C (%)	D (%)
SD- <i>l</i> -PEG-HA	0.00	70	30	0	0
	1.00	70	30	0	0
	1.10	0	100	0	0
	6.90	0	100	0	0
	7.00	0	0	100	0
	10.40	0	0	100	0
	10.50	70	30	0	0
	12.00	70	30	0	0
SD-noPEG-HA and SD-noPEG-PSA	0.00	90	10	0	0
	0.10	90	10	0	0
	0.11	0	40	0	60
	2.90	0	40	0	60
	2.95	0	0	100	0
	4.00	0	0	100	0
	4.05	90	10	0	0
	5.00	90	10	0	0
SE- <i>b</i> -PEG-HA	0.00	70	30	0	0
	0.20	70	30	0	0
	0.30	40	60	0	0
	5.30	24	76	0	0
	6.80	0	100	0	0
	8.50	0	30	0	70
	9.50	0	30	0	70
	9.60	0	0	100	0
	14.00	0	0	100	0
	14.10	70	30	0	0
16.00	70	30	0	0	
SD-noPEG- PEG-PGA	0.00	70	30	0	0
	1.00	70	30	0	0
	1.10	0	50	0	50
	3.00	0	50	0	50
	3.10	0	0	100	0
	4.50	0	0	100	0
	4.60	70	30	0	0
	6.00	70	30	0	0

A: 50 mM formic acid and 2 mM ammonium formate in water. B: 95 % acetonitrile and 5 % 2 mM ammonium formate aqueous solution (v/v) 50 mM formic acid. C: water. D: isopropyl alcohol. SD-*l*-PEG-HA: lineal-polyethylene glycol-containing hyaluronic acid nanocapsules formulated by solvent displacement. SD-noPEG-HA: non-PEGylated hyaluronic acid nanocapsules formulated by solvent displacement. SD-noPEG-PSA: non-PEGylated polysialic acid nanocapsules formulated by solvent displacement. SE-*b*-PEG-HA: Self-emulsifying branched-polyethylene glycol-containing hyaluronic acid nanocapsules.

Supplementary Table 3. Chromatographic method for the analysis of digested hyaluronic and polysialic acids

Time (min)	%A	%B
0.00	98	2
2.00	98	2
3.00	60	40
4.00	60	40
4.10	20	80
8.00	20	80
9.00	98	2
13.00	98	2

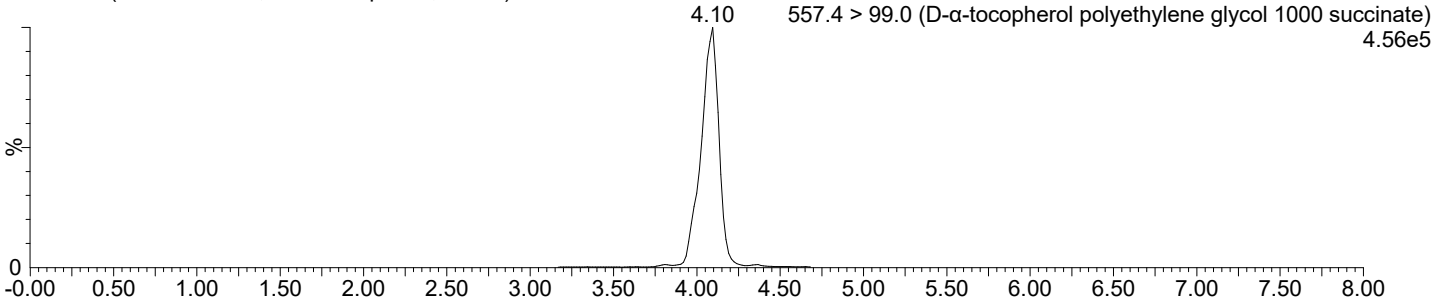
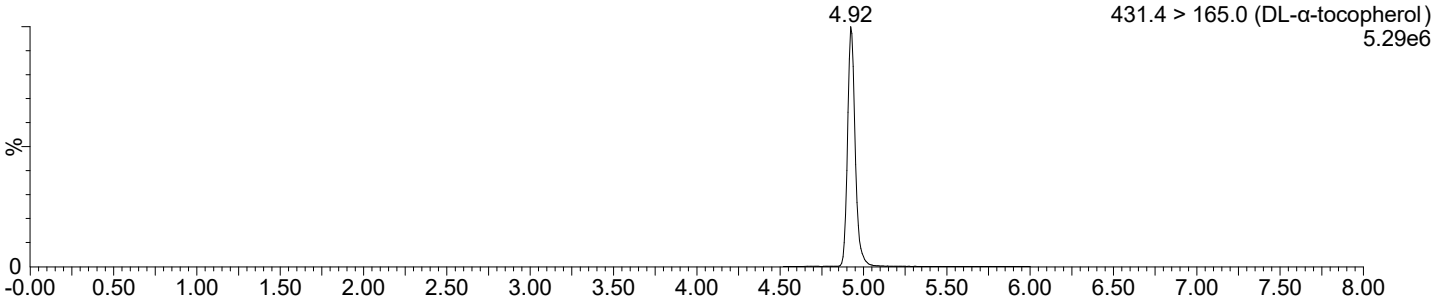
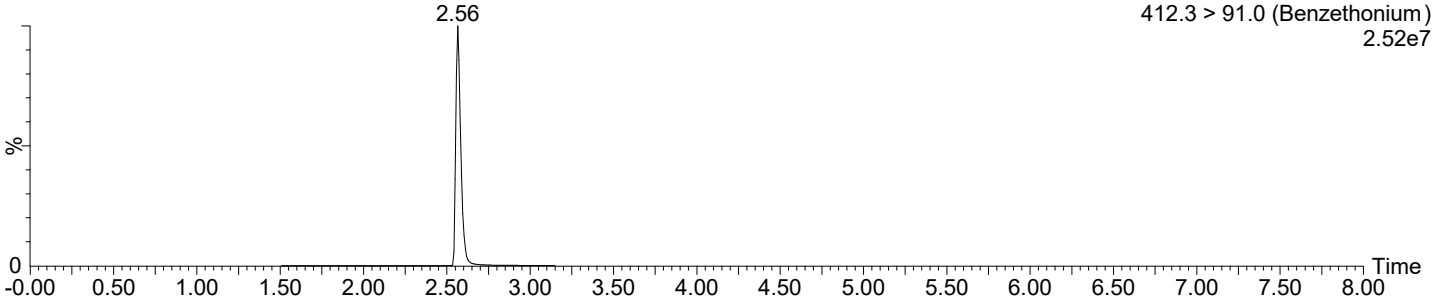
A: 50 mM formic acid and 2 mM ammonium formate in water, and B. methanol. The flow was diverted to waste from minute 0.00 to 3.90 to avoid the non-volatile salt Na₂SO₄ from entering the detector.

Supplementary Table 4. Chromatographic method for the analysis of digested PEG-PGA

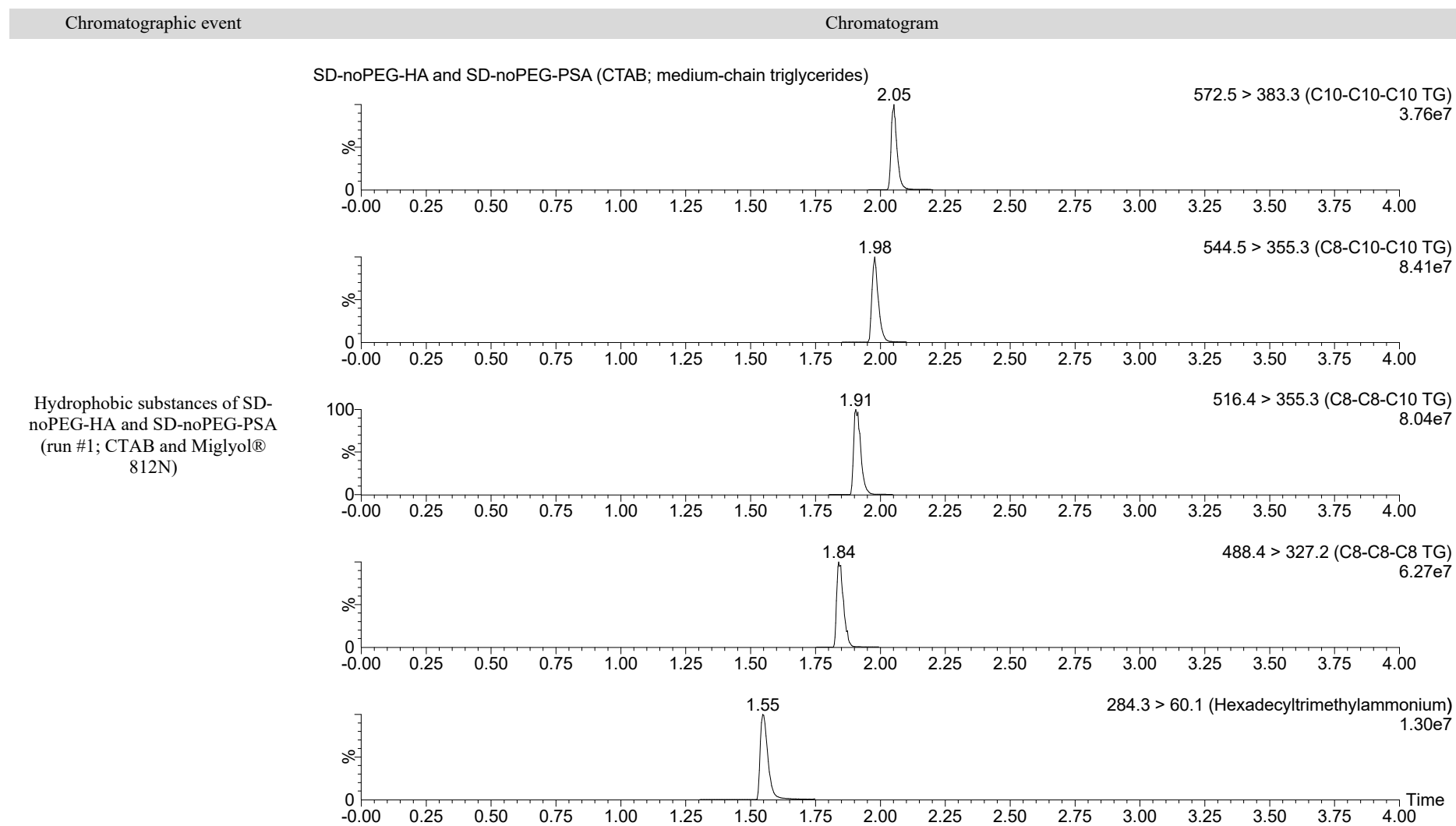
Time (min)	%A	%B
0.00	0	100
6.00	0	100
6.10	5.9	94.1
10.00	17.6	82.4
12.00	29.4	70.6
12.10	0	100
15.50	0	100

A: 75 mM formic acid and 5 mM ammonium formate in water, and B: 75 mM formic acid and 5 mM ammonium formate in acetonitrile (90 %) and water (10 %) mixture (v/v). The flow was diverted to waste from minute 0.00 to 9.00 to avoid the non-volatile salt Na₂SO₄ from entering the detector.

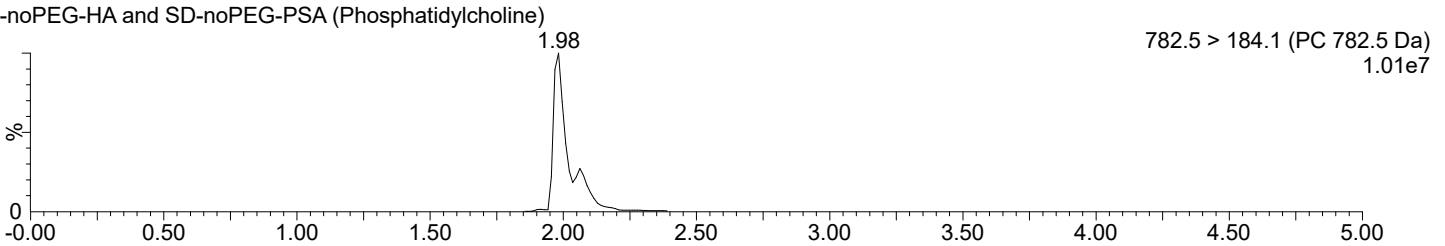
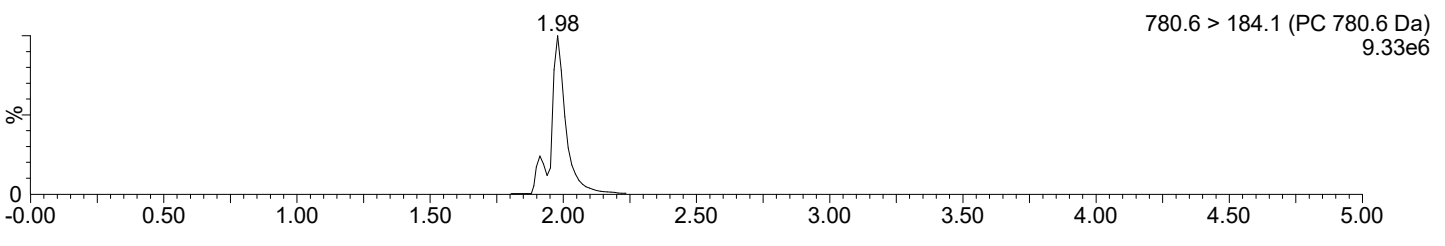
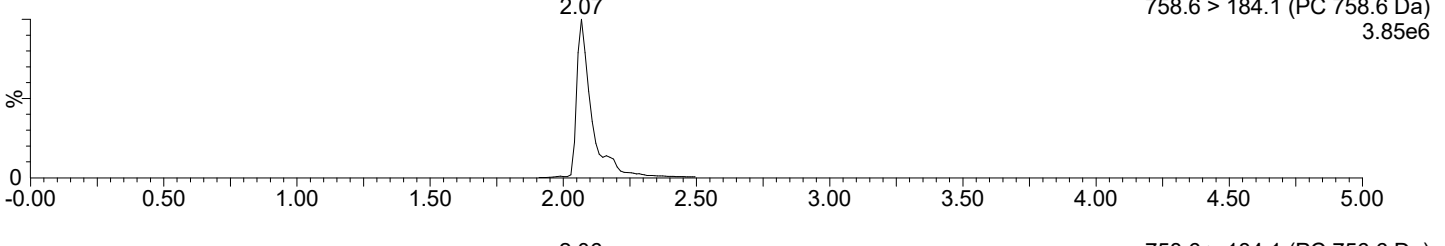
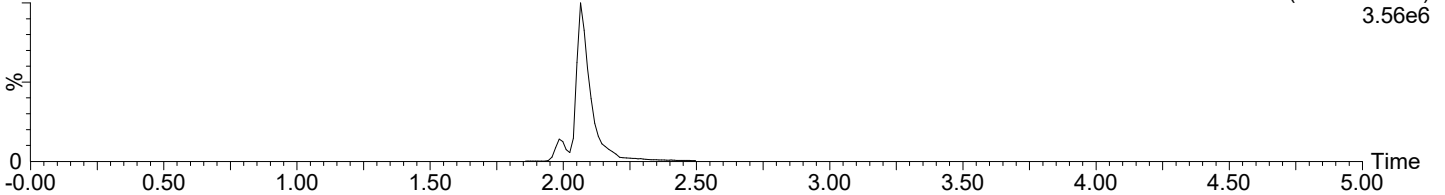
Supplementary Table 5. Chromatograms of all the chromatographic methods and quantified molecules

Chromatographic method	Chromatogram
SD- <i>I</i> -PEG-HA (Benzethonium; DL- α -tocopherol; TPGS)	 <p>557.4 > 99.0 (D-α-tocopherol polyethylene glycol 1000 succinate) 4.56e5</p>
Hydrophobic substances of SD- <i>I</i> -PEG-HA	 <p>431.4 > 165.0 (DL-α-tocopherol) 5.29e6</p>
	 <p>412.3 > 91.0 (Benzethonium) 2.52e7</p>

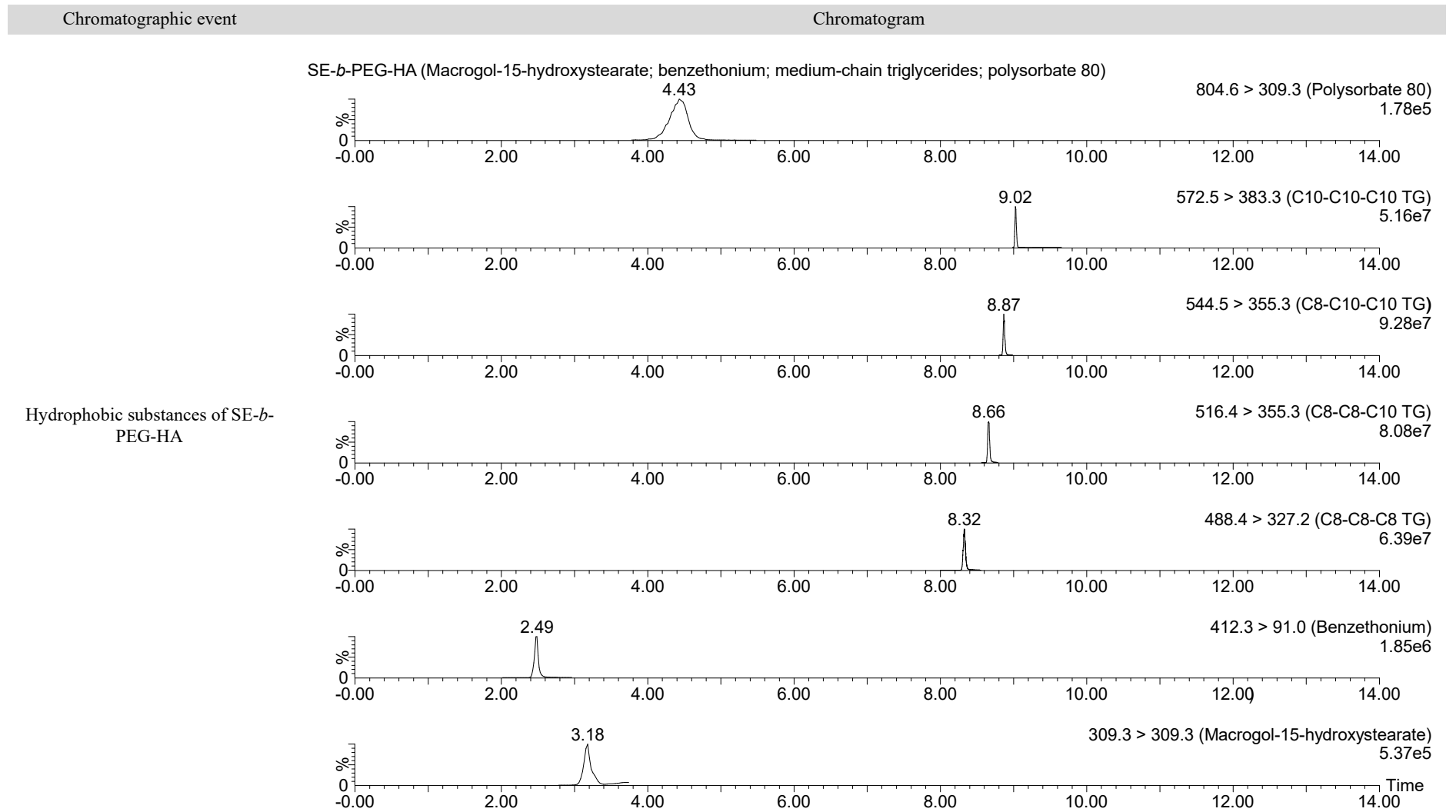
Supplementary Table 5. Chromatograms of all the chromatographic methods and quantified molecules (continuation)



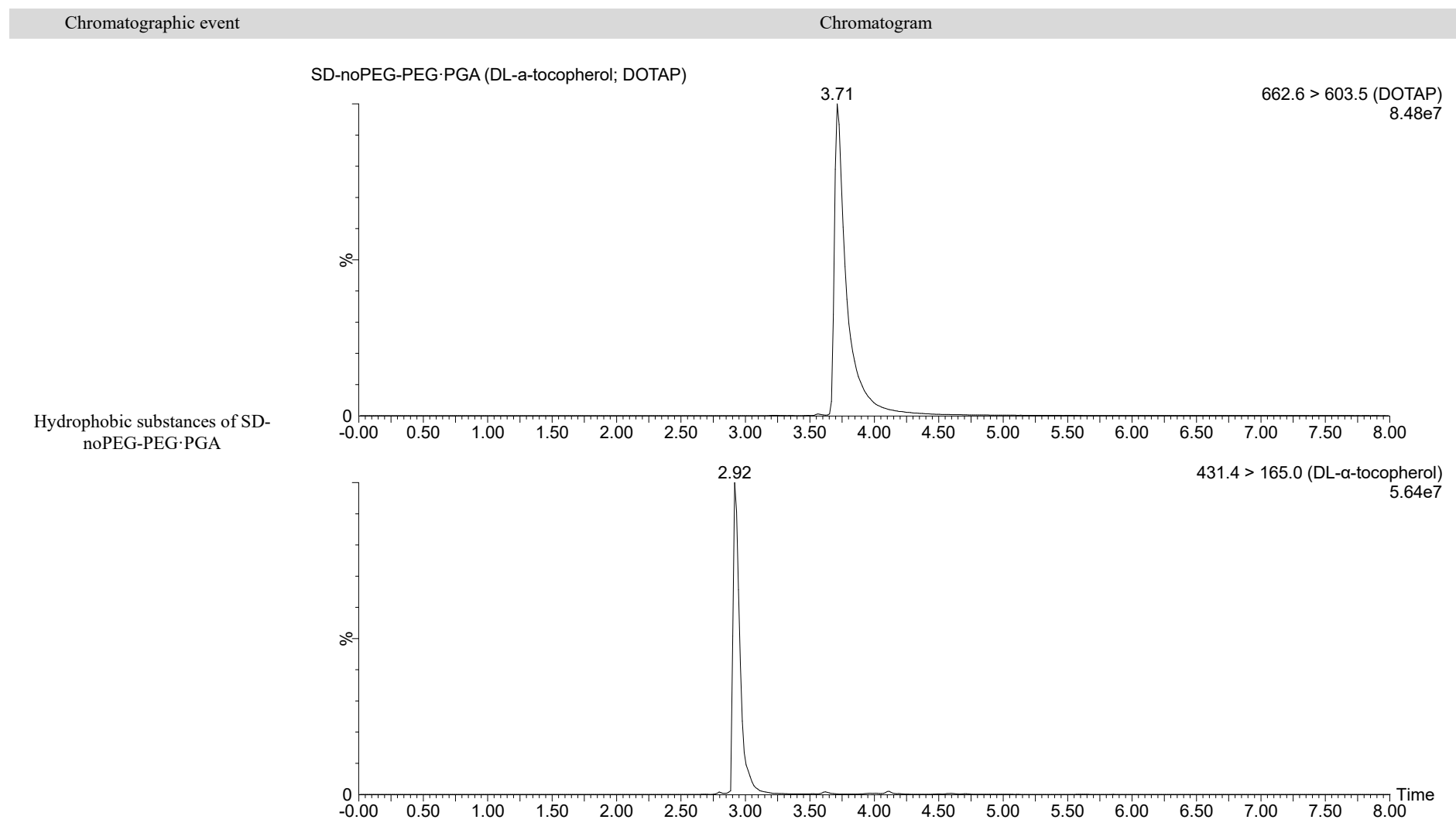
Supplementary Table 5. Chromatograms of all the chromatographic methods and quantified molecules (continuation)

Chromatographic event	Chromatogram
SD-noPEG-HA and SD-noPEG-PSA (Phosphatidylcholine)	 <p>782.5 > 184.1 (PC 782.5 Da) 1.01e7</p>
Hydrophobic substances of SD-noPEG-HA and SD-noPEG-PSA (run #2; Phosphatidylcholine)	 <p>780.6 > 184.1 (PC 780.6 Da) 9.33e6</p>
	 <p>758.6 > 184.1 (PC 758.6 Da) 3.85e6</p>
	 <p>756.6 > 184.1 (PC 756.6 Da) 3.56e6</p>

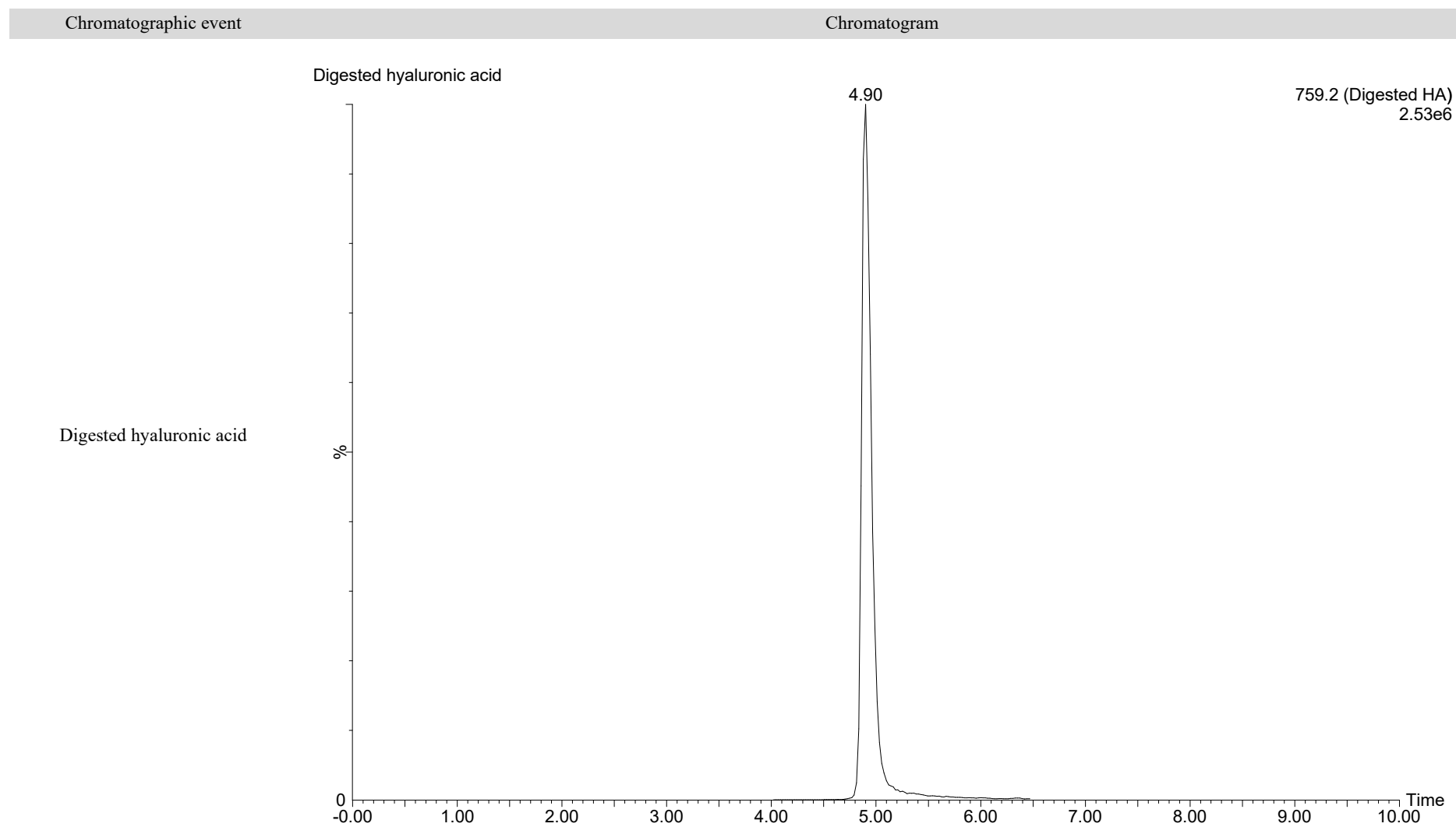
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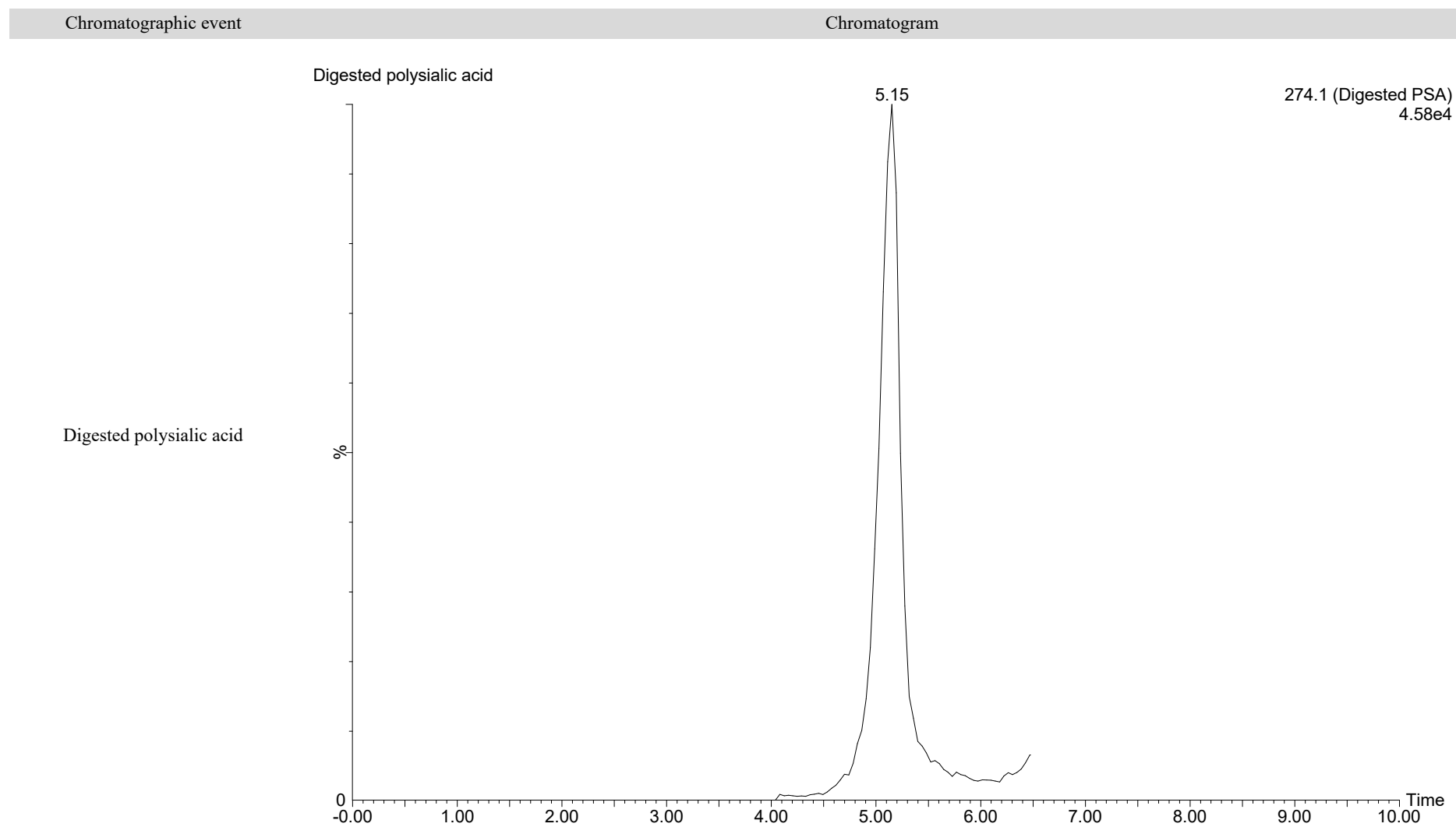
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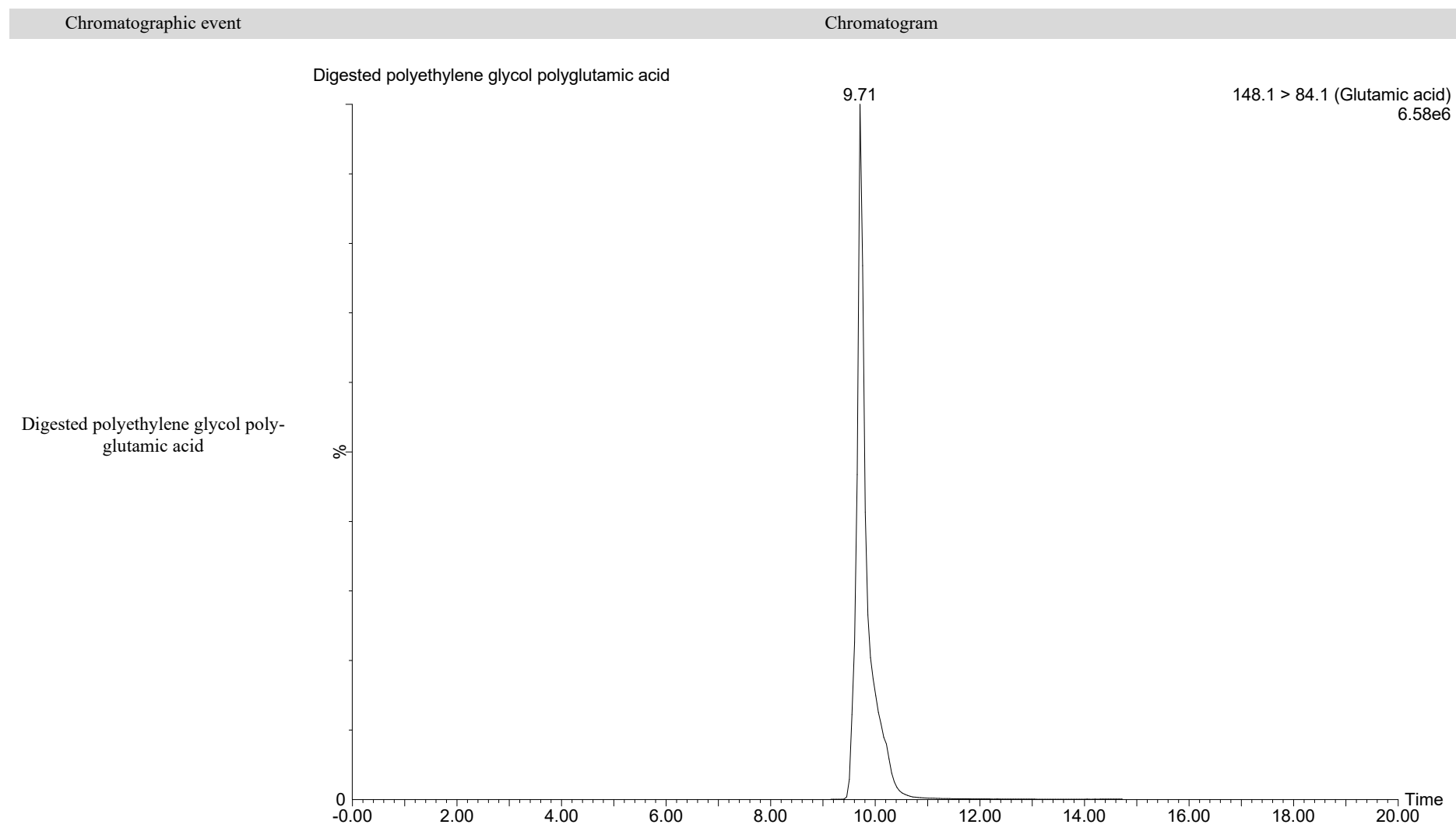
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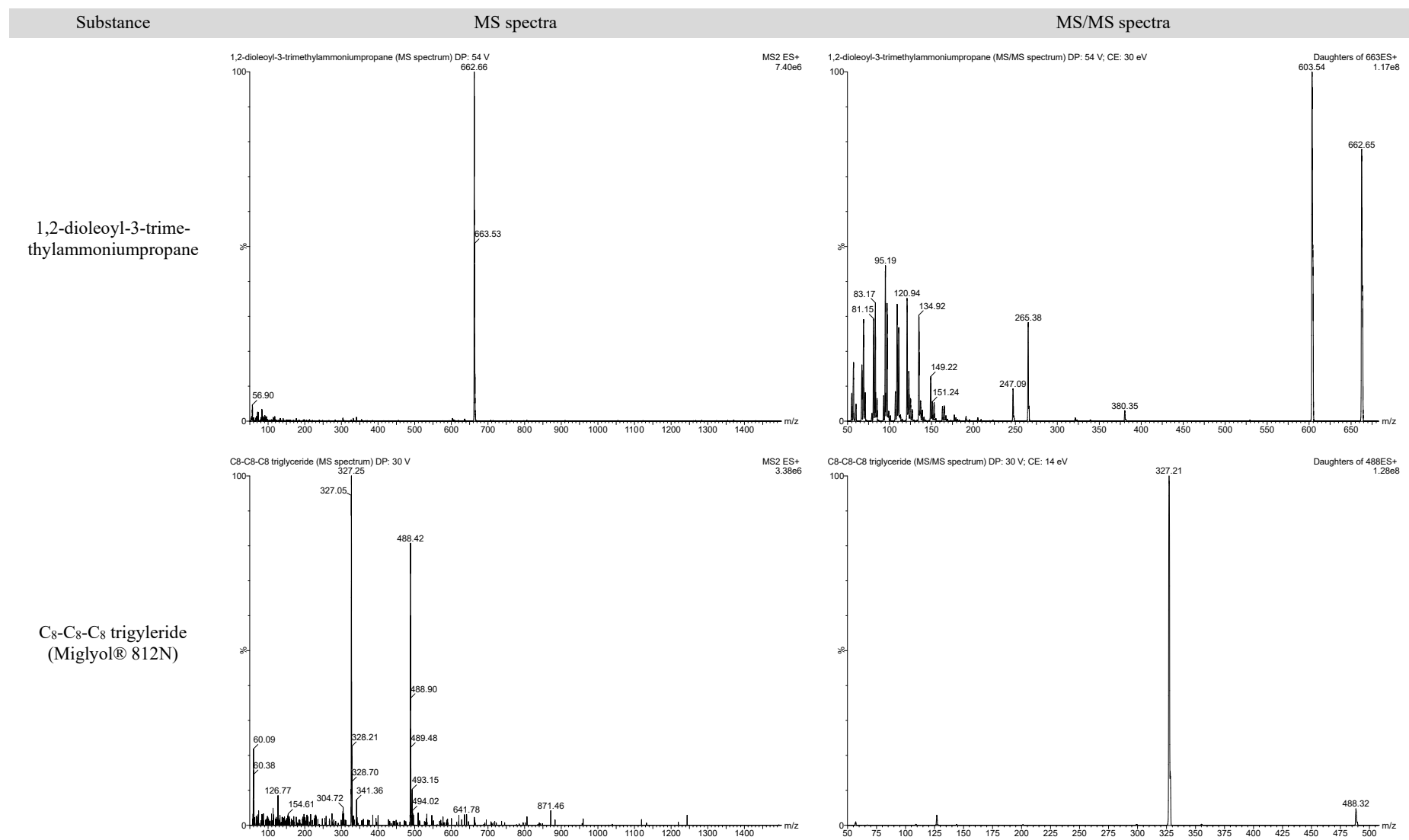
Supplementary Table 6. MS and MS/MS spectra for all the quantified substances

Substance	MS spectra	MS/MS spectra
DL- α -tocopherol	<p>D-α-tocopherol (MS spectrum) DP: 40 V</p>	<p>D-α-tocopherol (MS/MS spectrum) DP: 40 V; CE: 18 eV</p>
	MS2 ES+ 5.38e6	Daughters of 431ES+ 431.48 5.29e7
Benzethonium	<p>Benzethonium (MS spectrum) DP: 45 V</p>	<p>Benzethonium (MS/MS spectrum) DP: 45 V; CE: 44 eV</p>
	MS2 ES+ 1.10e7	Daughters of 412ES+ 91.02 1.34e8

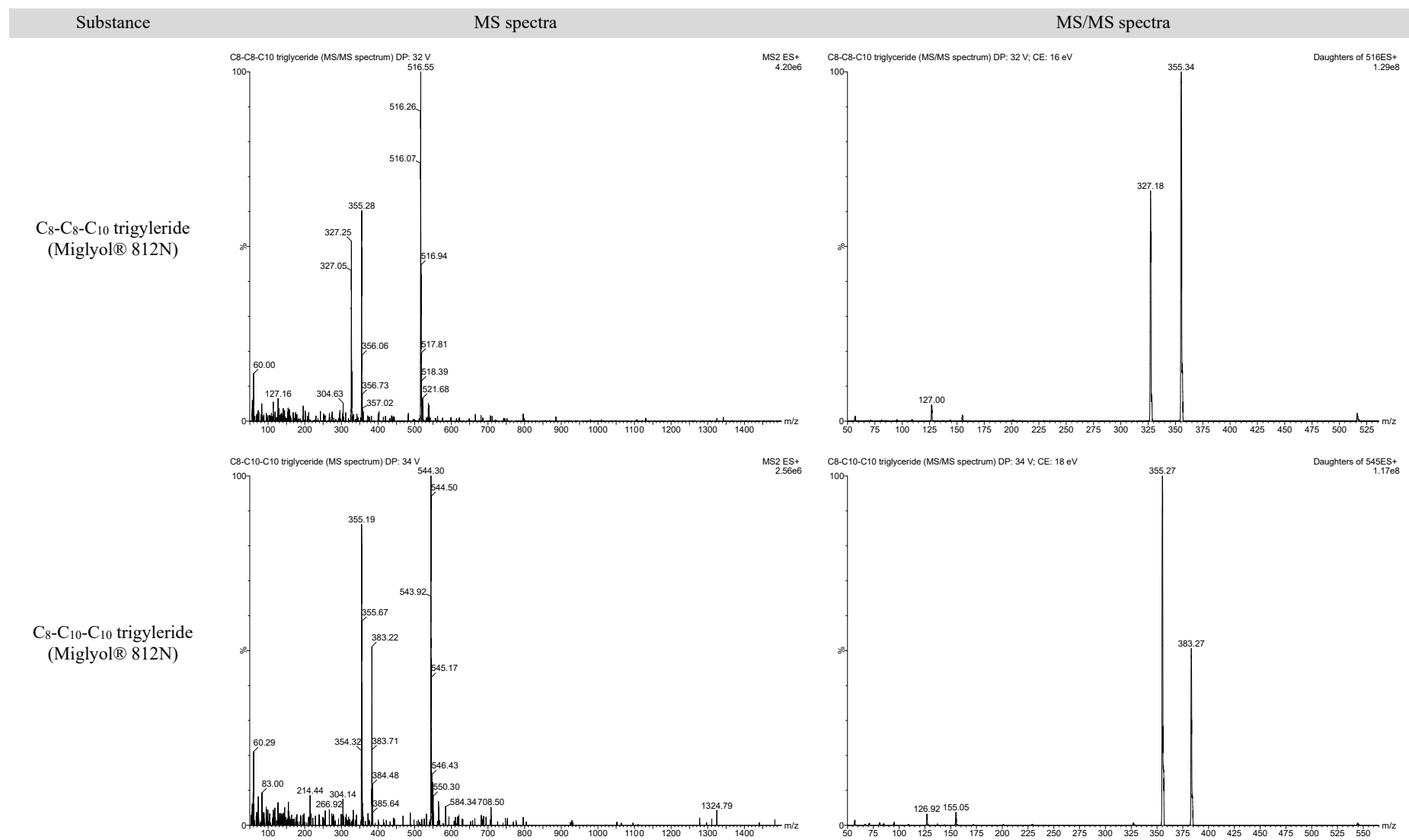
Supplementary Table 6. MS and MS/MS spectra for all the quantified substances (continuation)

Substance	MS spectra	MS/MS spectra
D- α -tocopherol polyethylene glycol 1000 succinate	<p>D-α-tocopherol polyethylene glycol 1000 succinate (MS spectrum) DP: 50 V</p> <p>MS2 ES+ 1.07e6</p>	<p>D-α-tocopherol polyethylene glycol 1000 succinate (MS/MS spectrum) DP: 50 V; CE: 30 eV</p> <p>Daughters of 557ES+ 1.99e7</p>
Hexadecyltrimethylammonium	<p>Hexadecyltrimethylammonium (MS spectrum) DP: 2 V</p> <p>MS2 ES+ 5.83e7</p>	<p>Hexadecyltrimethylammonium (MS/MS spectrum) DP: 2 V; CE: 28 eV</p> <p>Daughters of 284ES+ 1.29e8</p>

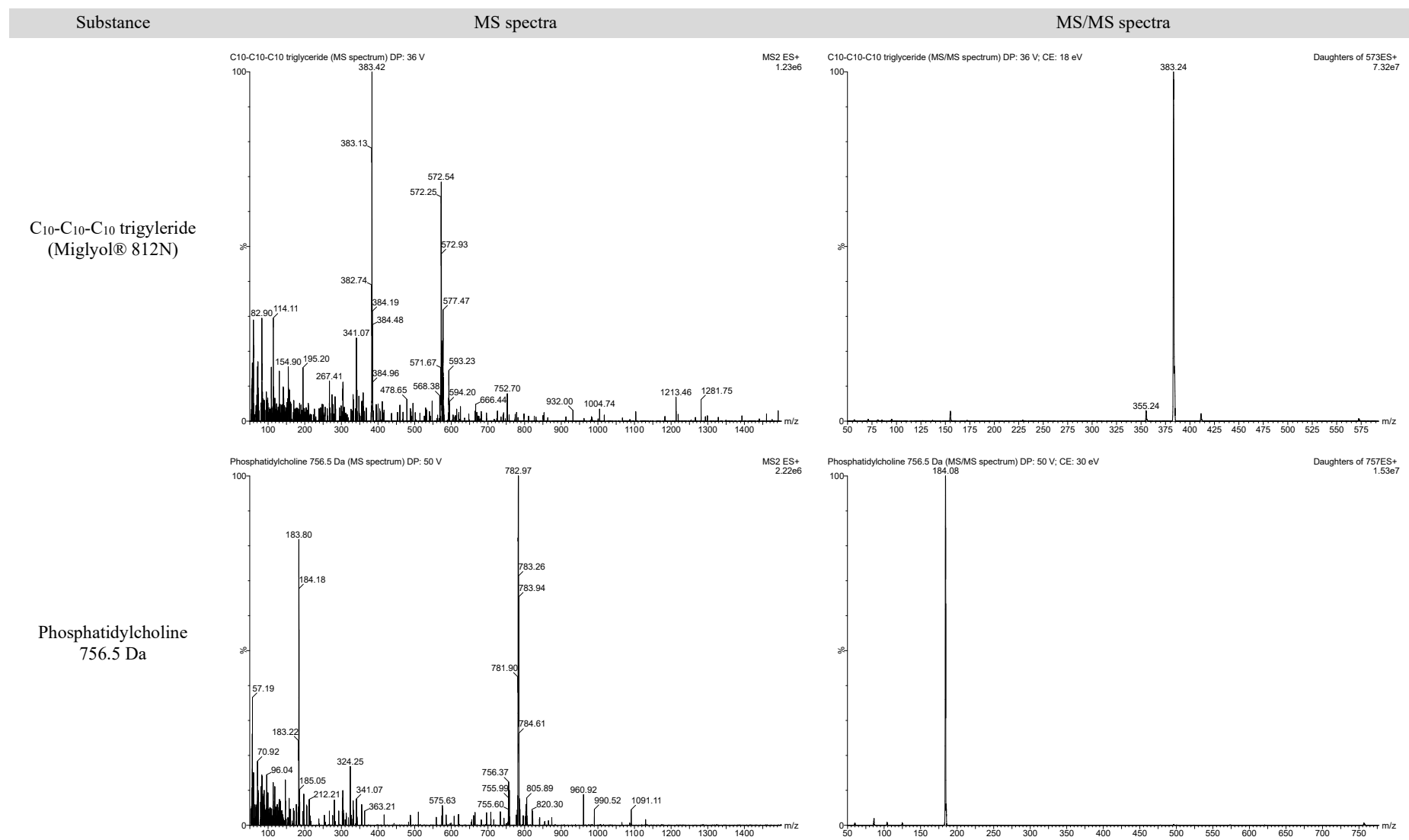
Supplementary Table 6. MS and MS/MS spectra for all the quantified substances (continuation)



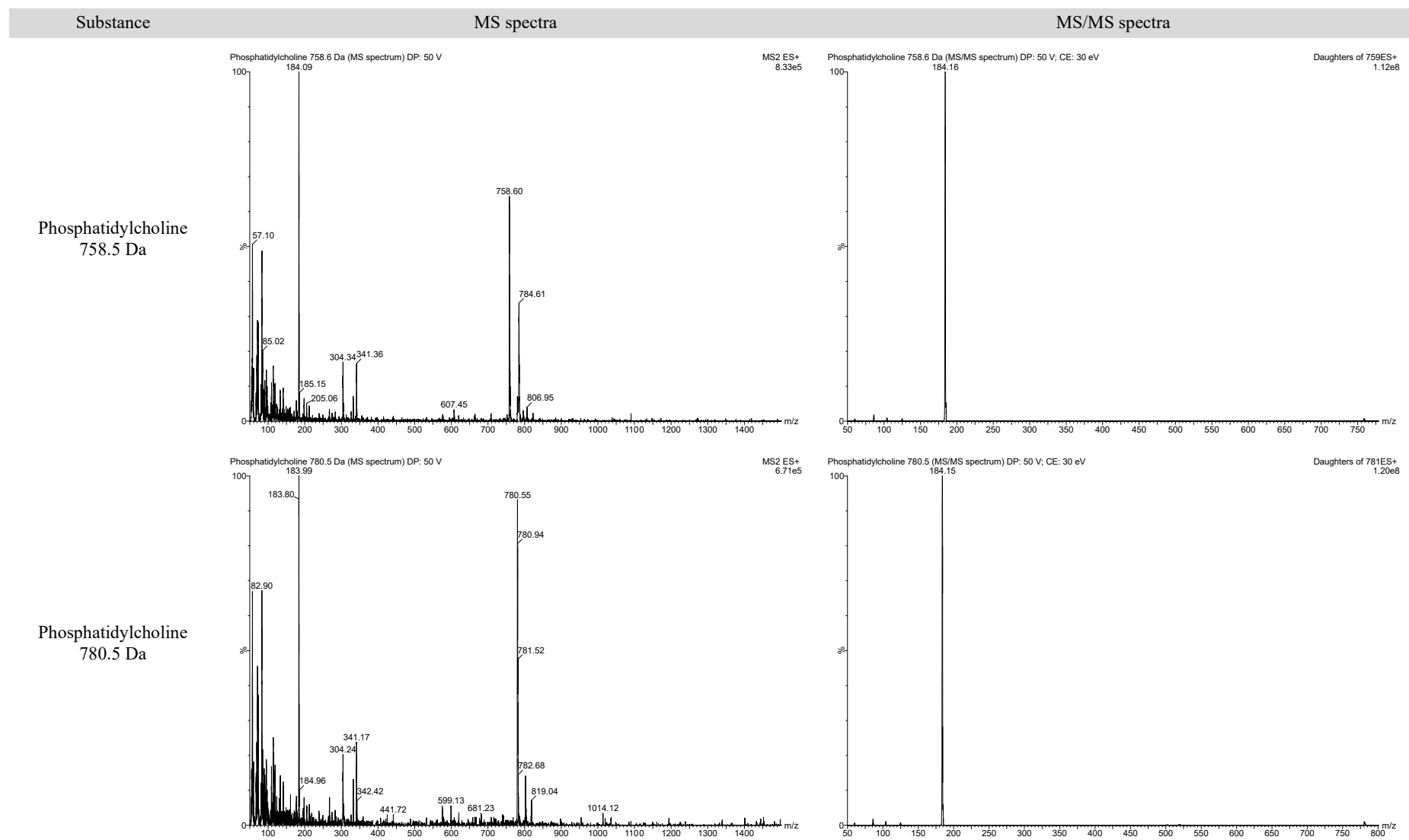
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Substance	MS spectra	MS/MS spectra
Phosphatidylcholine 782.5 Da	<p>Phosphatidylcholine 782.5 Da (MS spectrum) DP: 50 V</p> <p>MS2 ES+ 1.39e6</p>	<p>Phosphatidylcholine 782.5 Da (MS/MS spectrum) DP: 50 V; CE: 30 eV</p> <p>Daughters of 783ES+ 1.30e8</p>
Macrogol-15-hydroxys- tearate	<p>Macrogol-15-hydroxysteareate (MS spectrum) DP: 90 V</p> <p>MS2 ES+ 8.45e7</p>	N/A

Supplementary Table 6. MS and MS/MS spectra for all the quantified substances (continuation)

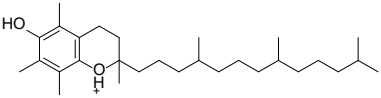
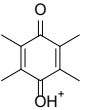
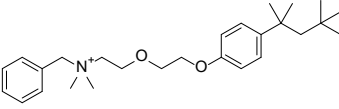

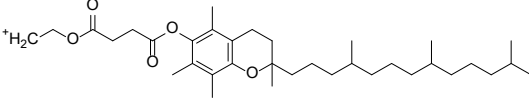
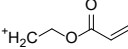
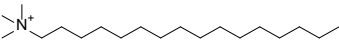

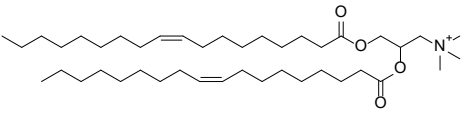
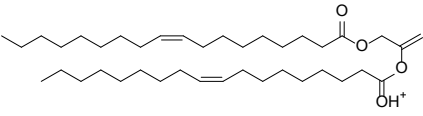
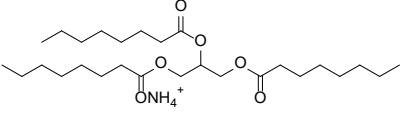
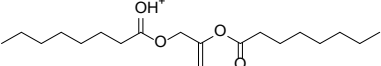
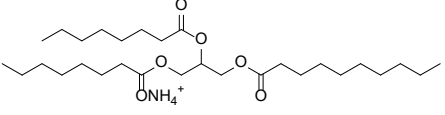
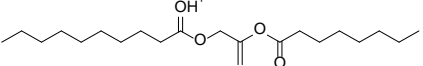
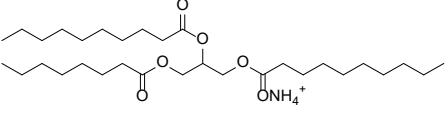
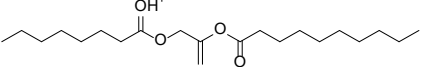
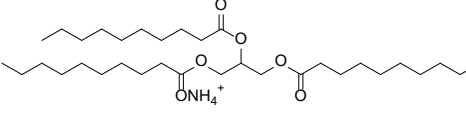
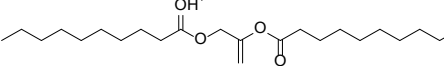
Substance	MS spectra	MS/MS spectra
Polysorbate 80	<p>Polysorbate 80 (MS spectrum) DP: 30 V</p>	<p>Polysorbate 80 (MS/MS spectrum) DP: 30 V; CE: 40 eV</p> <p>MS2 ES+ 5.67e5</p> <p>Daughters of 805ES+ 1.82e7</p>
Digested hyaluronic acid	<p>Digested hyaluronic acid (MS spectrum) DP: 100 V</p>	N/A

Supplementary Table 6. MS and MS/MS spectra for all the quantified substances (continuation)

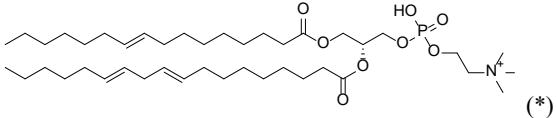
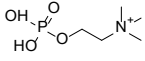
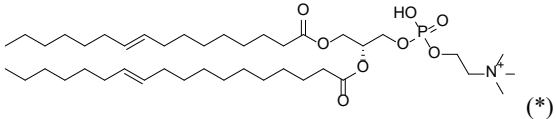

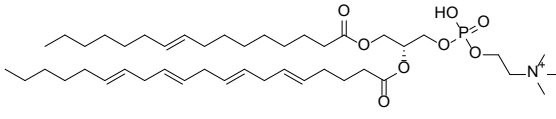

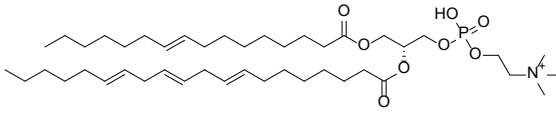

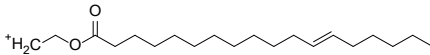
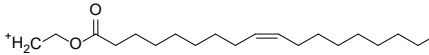
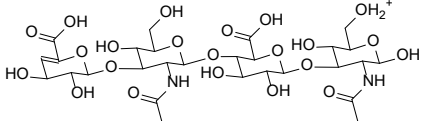
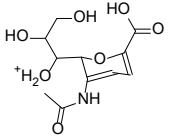
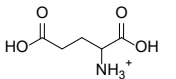
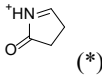
Substance	MS spectra	MS/MS spectra
Digested polysialic acid	<p>Digested polysialic acid (MS spectrum) DP: 100 V</p> <p>MS2 ES+ 1.03e6</p>	N/A
Digested polyethylene glycol polyglutamic acid	<p>Digested polyethylene glycol polyglutamic acid (MS spectrum) DP: 18 V</p> <p>MS2 ES+ 5.23e6</p>	<p>Digested polyethylene glycol polyglutamic acid (MS/MS spectrum) DP: 18 V; CE: 16 eV</p> <p>Daughters of 148ES+ 9.90e4</p>

DP: declustering potential. CE: collision energy. N/A: not applicable. MS spectra were registered with the same DP as the one in the analytical method. MS/MS spectra were registered with the same DP and CE as the ones in the analytical method.

Supplementary Table 7. Mass spectrometry methodology and fragmentation pattern of the NCs' components

Substance	Method	Parent	Daughter	Ref.
DL- α -tocopherol	MRM, m/z 431.4 \rightarrow 165.0, DP: 40 V, CE: 18 eV			1,2
Benzethonium chloride	MRM, m/z 412.3 \rightarrow 91.0, DP: 45 V, CE: 44 eV			3,4
D- α -tocopherol polyethylene glycol 1000 succinate	MRM, m/z 557.4 \rightarrow 99.0, DP: 50 V, CE: 30 eV			-
Hexadecyltrimethylammonium bromide	MRM, m/z 284.3 \rightarrow 60.1, DP: 2 V, CE: 28 eV			5
1,2-dioleoyl-3-trimethylammoniumpropane chloride	MRM, m/z 662.6 \rightarrow 603.5, DP: 54 V, CE: 30 eV			6
Miglyol® 812N	MRM, m/z 488.4 \rightarrow 327.2, DP: 30 V, CE: 14 eV			7
	MRM, m/z 516.4 \rightarrow 355.3, DP: 32 V, CE: 16 eV			7
	MRM, m/z 544.5 \rightarrow 355.3, DP: 34 V, CE: 18 eV			7
	MRM, m/z 572.5 \rightarrow 383.3, DP: 36 V, CE: 18 eV			7

Supplementary Table 7. Mass spectrometry methodology and fragmentation pattern of the NCs' components (continuation)

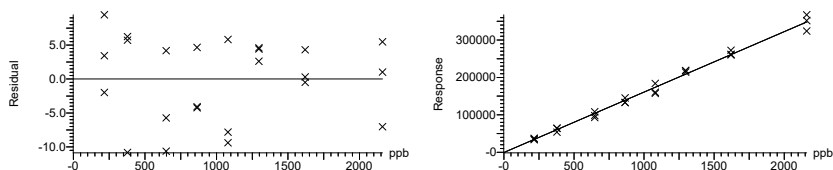
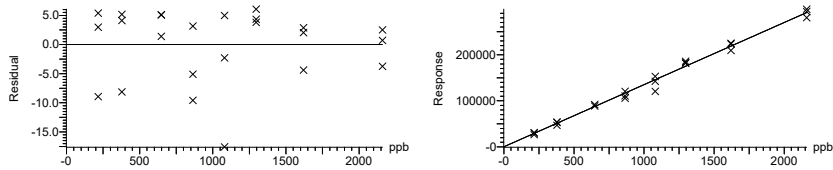
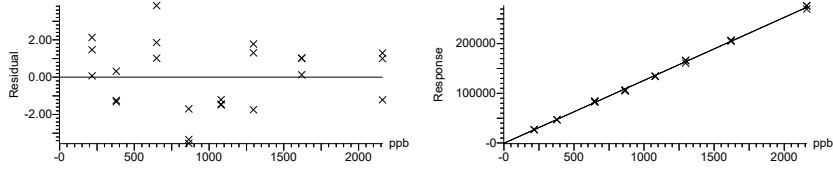
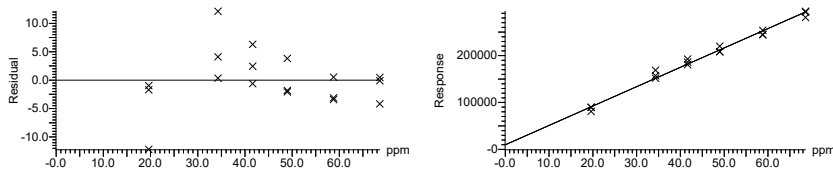
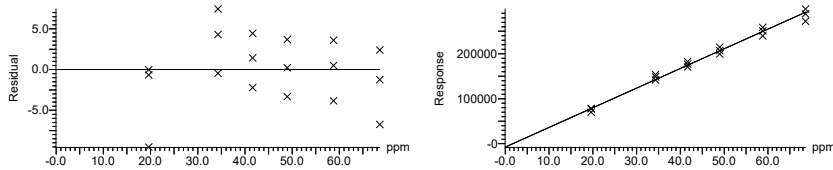
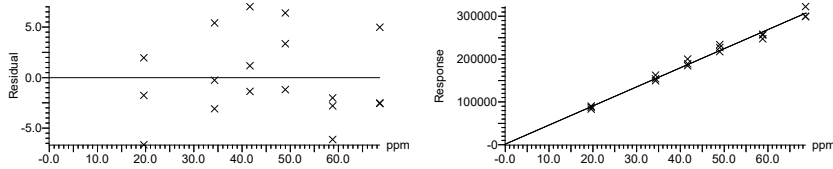
Substance	Method	Parent	Daughter	Ref.
Phosphatidylcholines (Epikuron™ 145V)	MRM, m/z 756.6 → 184.1, DP: 50 V, CE: 30 eV			8
	MRM, m/z 758.6 → 184.1, DP: 50 V, CE: 30 eV			
	MRM, m/z 780.6 → 184.1, DP: 50 V, CE: 30 eV			
	MRM, m/z 782.5 → 184.1, DP: 50 V, CE: 30 eV			
Macrogol-15-hydroxystearate (Kolliphor® HS15)	PseudoMRM, m/z 309.3 → 309.3, DP: 90 V, CE: 5 eV		N/A	9
Polysorbate 80	MRM, m/z 804.6 → 309.3, DP: 30 V, CE: 40 eV	N/D		10
Digested hyaluronic acid	SIM, m/z 759.2, DP: 100 V		N/A	11–13
Digested polysialic acid	SIM, m/z 274.1, DP: 100 V		N/A	14,15
Digested polyethylene glycol polyglutamic acid	MRM, m/z 148.1 → 84.1, DP: 18 V, CE: 16 eV			16

MRM: multiple reaction monitoring. SIM: Selected ion monitoring. DP: declustering potential. CE: collision energy. N/A: not applicable. N/D: not determined. (*): A possible structure; other molecules with the same m/z may co-exist.

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD-/PEG-HA	Benzethonium	1	<p>Compound name: benzethonium Correlation coefficient: $r = 0.998880$, $r^2 = 0.997761$ Calibration curve: $20062.6 * x + 84251.2$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: benzethonium Correlation coefficient: $r = 0.997675$, $r^2 = 0.995356$ Calibration curve: $20667.3 * x + 109777$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: benzethonium Correlation coefficient: $r = 0.997362$, $r^2 = 0.994731$ Calibration curve: $18278.7 * x + 118770$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		1	<p>Compound name: D-α-tocopherol polyethylene glycol 1000 succinate Correlation coefficient: $r = 0.990478$, $r^2 = 0.981047$ Calibration curve: $181.548 * x + 1133.68$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: D-α-tocopherol polyethylene glycol 1000 succinate Correlation coefficient: $r = 0.993116$, $r^2 = 0.986279$ Calibration curve: $190.369 * x + -843.895$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: D-α-tocopherol polyethylene glycol 1000 succinate Correlation coefficient: $r = 0.994383$, $r^2 = 0.988797$ Calibration curve: $398.723 * x + -2160.03$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>

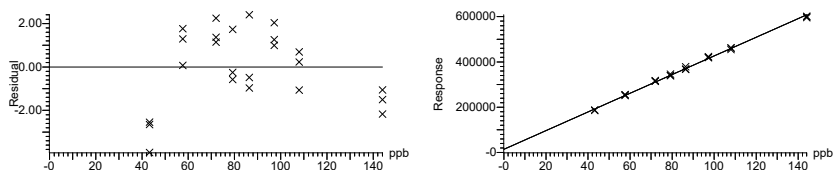
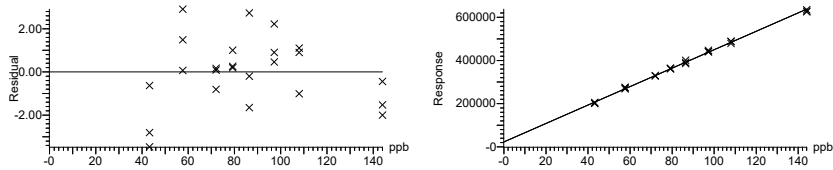
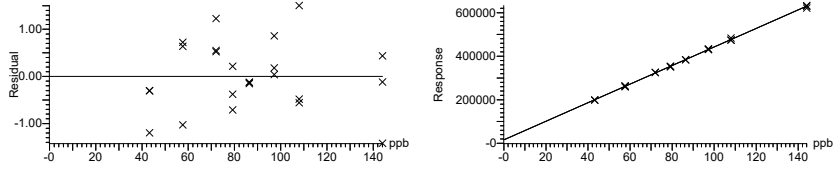
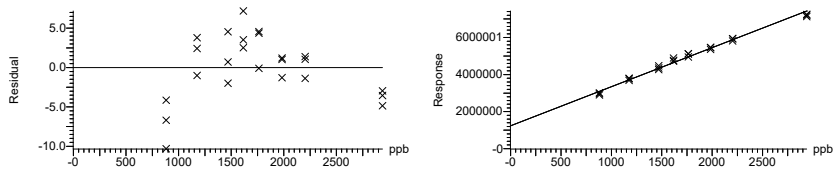
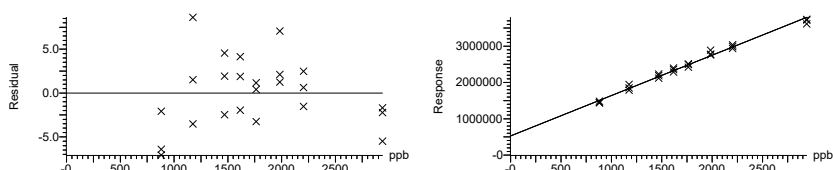
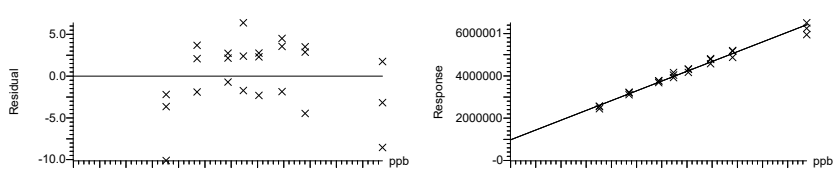
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves	
SD- <i>l</i> -PEG-HA (continuation)	D- α -tocopherol	1	Compound name: DL- α -tocopherol Correlation coefficient: $r = 0.996368$, $r^2 = 0.992749$ Calibration curve: $161.6 * x + -621.845$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 	
		2	Compound name: DL- α -tocopherol Correlation coefficient: $r = 0.996091$, $r^2 = 0.992198$ Calibration curve: $134.842 * x + 259.387$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 	
		3	Compound name: DL- α -tocopherol Correlation coefficient: $r = 0.999656$, $r^2 = 0.999312$ Calibration curve: $126.766 * x + -621.553$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 	
	Hyaluronic acid (whole)	1	1	Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.994386$, $r^2 = 0.988803$ Calibration curve: $4130.13 * x + 9837.9$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 
			2	Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.995225$, $r^2 = 0.990474$ Calibration curve: $4373.25 * x + -7479.95$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 
			3	Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.994960$, $r^2 = 0.989945$ Calibration curve: $4461.42 * x + 1376.84$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 

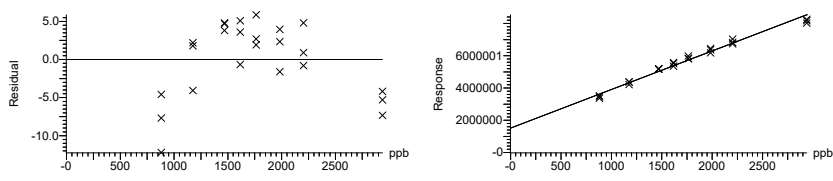
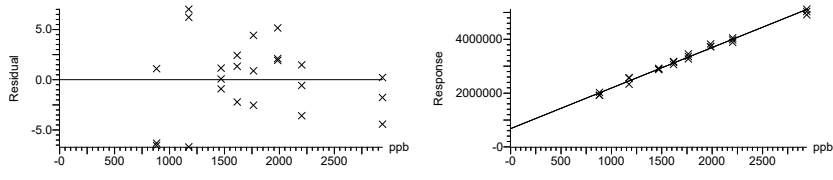
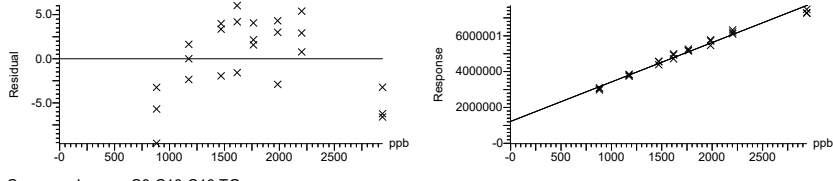
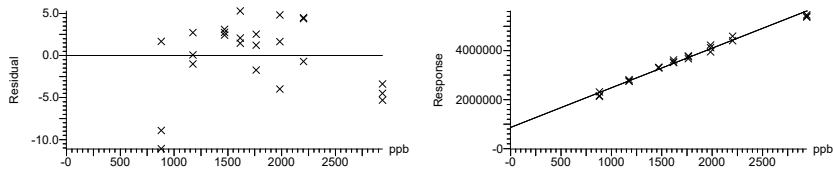
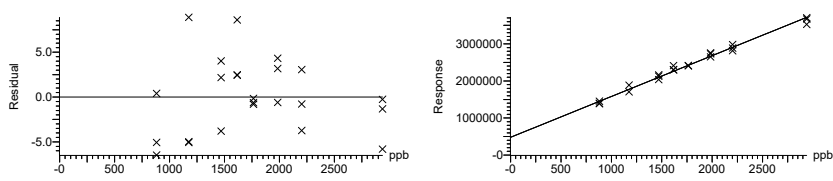
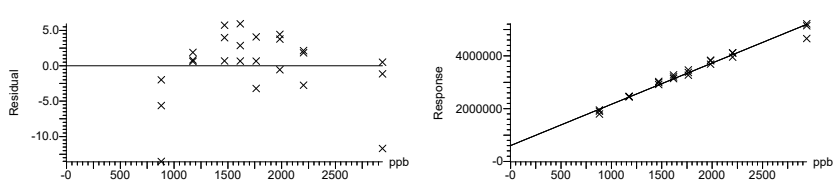
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD- <i>l</i> -PEG-HA (continuation)	Hyaluronic acid	1	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.992396$, $r^2 = 0.984849$ Calibration curve: $4199.58 * x + 6712.82$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.994621$, $r^2 = 0.989270$ Calibration curve: $4207 * x + -11030.1$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.996289$, $r^2 = 0.992591$ Calibration curve: $4373.41 * x + -583.121$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		1	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.995210$, $r^2 = 0.990444$ Calibration curve: $4956.23 * x + 2094.75$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.990110$, $r^2 = 0.980318$ Calibration curve: $4668.12 * x + 1446.87$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.990600$, $r^2 = 0.981288$ Calibration curve: $4955.03 * x + -8467.49$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>

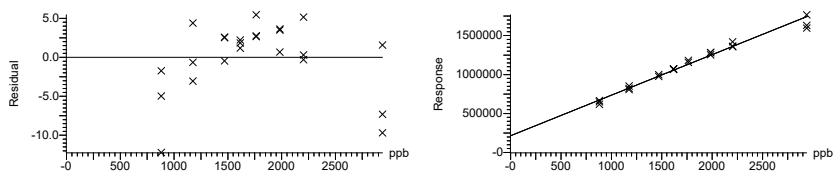
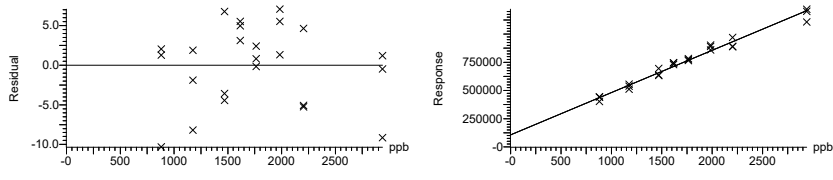
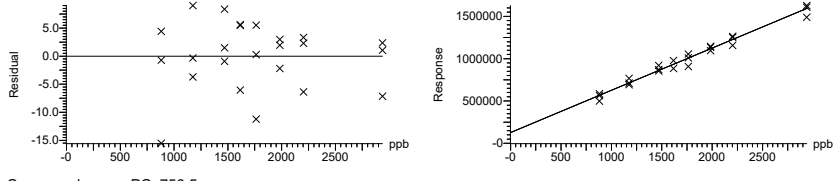
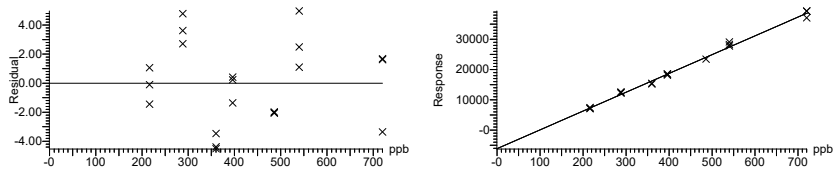
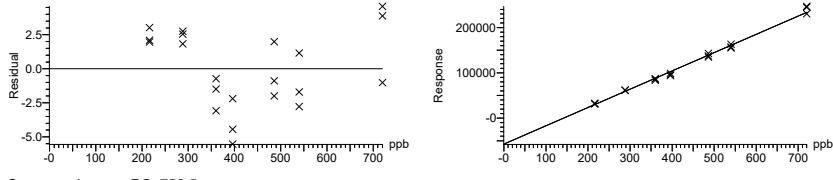
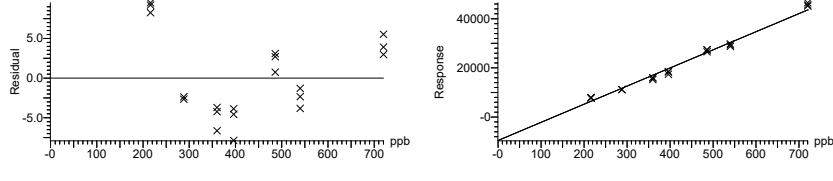
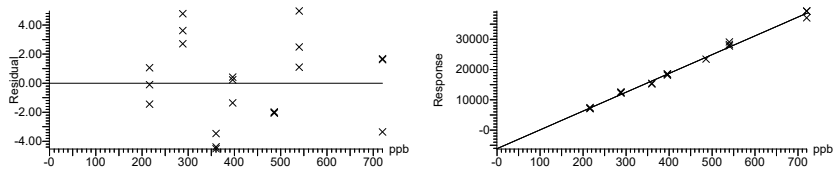
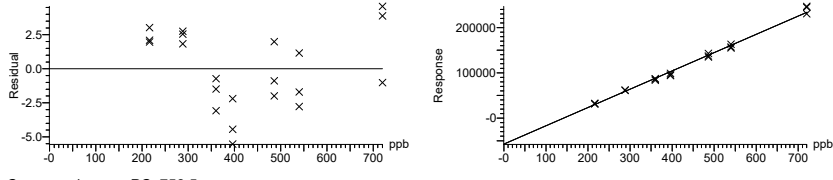
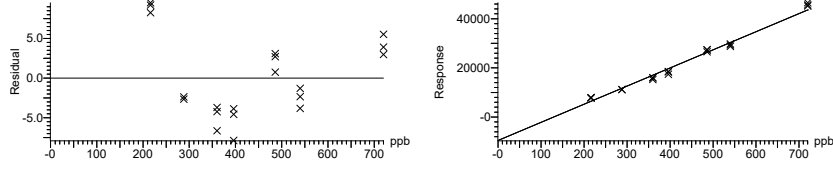
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves		
SD-noPEG-HA	CTAB	1	<p>Compound name: hexadecyltrimethylammonium Correlation coefficient: $r = 0.998943$, $r^2 = 0.997887$ Calibration curve: $4126.68 * x + 13983.3$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		2	<p>Compound name: hexadecyltrimethylammonium Correlation coefficient: $r = 0.999078$, $r^2 = 0.998157$ Calibration curve: $4266.63 * x + 22962.8$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		3	<p>Compound name: hexadecyltrimethylammonium Correlation coefficient: $r = 0.999769$, $r^2 = 0.999538$ Calibration curve: $4265.8 * x + 15844.5$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		C8-C8-C8 Triglyceride	C8-C8-C8 Triglyceride	1	<p>Compound name: C8-C8-C8 TG Correlation coefficient: $r = 0.994379$, $r^2 = 0.988791$ Calibration curve: $2109.29 * x + 1.23567e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				2	<p>Compound name: C8-C8-C8 TG Correlation coefficient: $r = 0.994465$, $r^2 = 0.988961$ Calibration curve: $1111.31 * x + 527248$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				3	<p>Compound name: C8-C8-C8 TG Correlation coefficient: $r = 0.993040$, $r^2 = 0.986129$ Calibration curve: $1850.95 * x + 977854$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

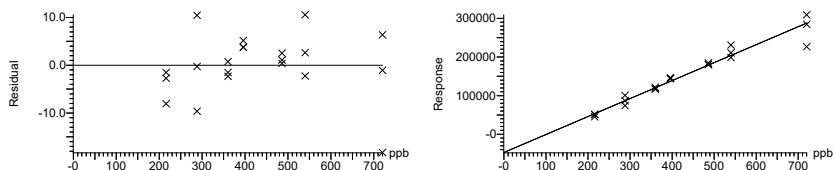
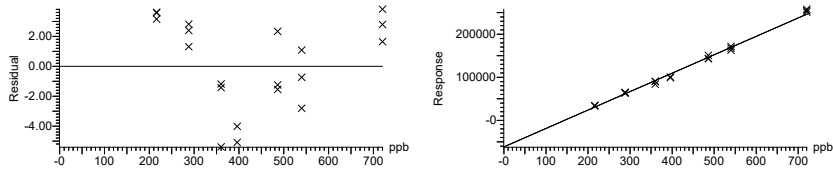
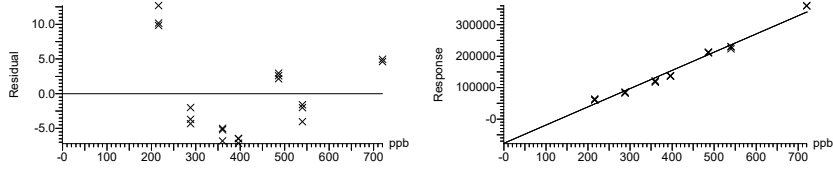
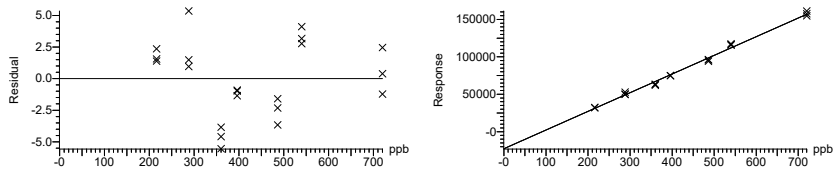
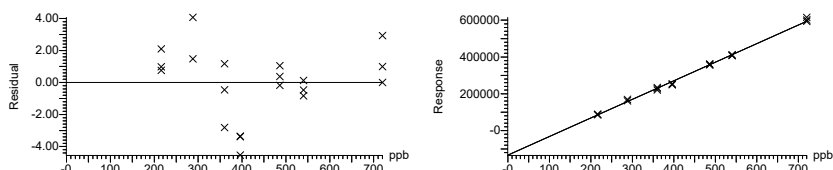
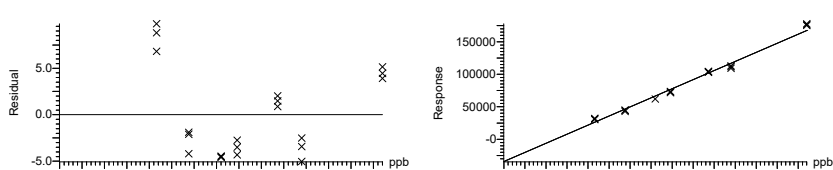
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD-noPEG-HA (continuation)	C ₈ -C ₈ -C ₁₀ glyceride	1	<p>Compound name: C₈-C₈-C₁₀ TG Correlation coefficient: $r = 0.991232$, $r^2 = 0.982542$ Calibration curve: $2391.65 * x + 1.51379e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: C₈-C₈-C₁₀ TG Correlation coefficient: $r = 0.995155$, $r^2 = 0.990334$ Calibration curve: $1508.44 * x + 679958$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: C₈-C₈-C₁₀ TG Correlation coefficient: $r = 0.992451$, $r^2 = 0.984958$ Calibration curve: $2200.96 * x + 1.22044e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		1	<p>Compound name: C₈-C₁₀-C₁₀ TG Correlation coefficient: $r = 0.993350$, $r^2 = 0.986744$ Calibration curve: $1618.69 * x + 866952$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: C₈-C₁₀-C₁₀ TG Correlation coefficient: $r = 0.993628$, $r^2 = 0.987296$ Calibration curve: $1101.43 * x + 479398$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: C₈-C₁₀-C₁₀ TG Correlation coefficient: $r = 0.990811$, $r^2 = 0.981706$ Calibration curve: $1562.36 * x + 603095$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

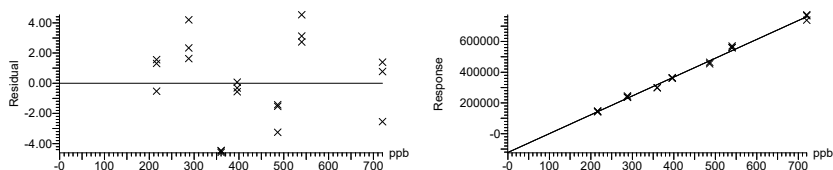
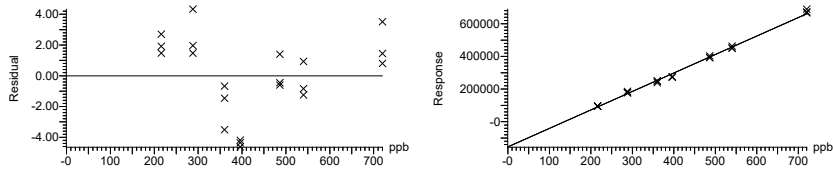
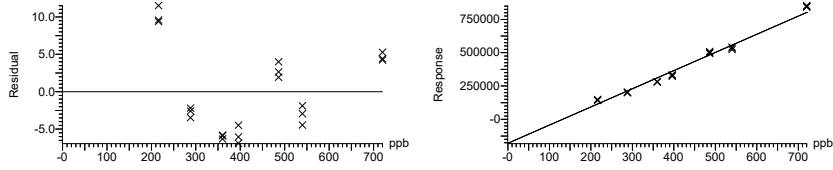
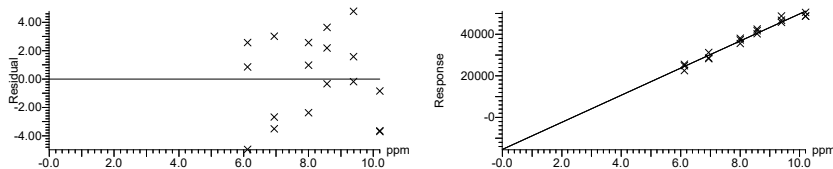
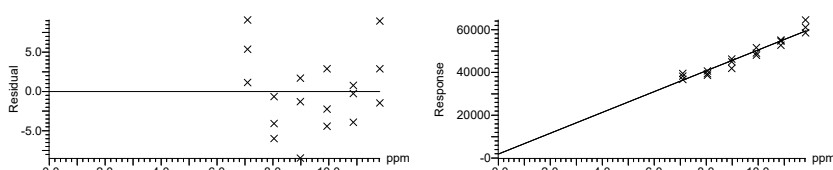
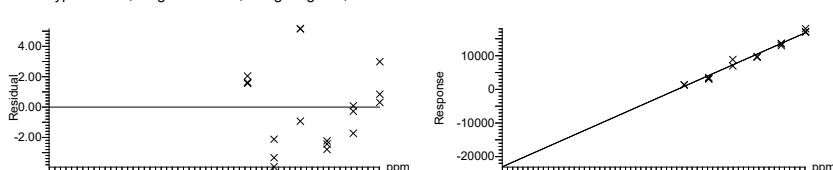
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves		
SD-noPEG-HA (continuation)	C ₁₀ -C ₁₀ -C ₁₀ glyceride	1	<p>Compound name: C10-C10-C10 TG Correlation coefficient: $r = 0.991252$, $r^2 = 0.982581$ Calibration curve: $520.173 * x + 215015$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		2	<p>Compound name: C10-C10-C10 TG Correlation coefficient: $r = 0.989802$, $r^2 = 0.979709$ Calibration curve: $374.753 * x + 106561$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		3	<p>Compound name: C10-C10-C10 TG Correlation coefficient: $r = 0.987630$, $r^2 = 0.975413$ Calibration curve: $498.949 * x + 127026$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		1	<p>Compound name: PC_756.5 Correlation coefficient: $r = 0.997083$, $r^2 = 0.994175$ Calibration curve: $62.1519 * x + -6144.89$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		2	<p>Compound name: PC_756.5 Correlation coefficient: $r = 0.996890$, $r^2 = 0.993789$ Calibration curve: $403.916 * x + -57356.6$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		3	<p>Compound name: PC_756.5 Correlation coefficient: $r = 0.992193$, $r^2 = 0.984448$ Calibration curve: $73.7867 * x + -9540.06$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		Phosphatidylcholine 756.6 Da		1	<p>Compound name: PC_756.5 Correlation coefficient: $r = 0.997083$, $r^2 = 0.994175$ Calibration curve: $62.1519 * x + -6144.89$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				2	<p>Compound name: PC_756.5 Correlation coefficient: $r = 0.996890$, $r^2 = 0.993789$ Calibration curve: $403.916 * x + -57356.6$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				3	<p>Compound name: PC_756.5 Correlation coefficient: $r = 0.992193$, $r^2 = 0.984448$ Calibration curve: $73.7867 * x + -9540.06$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD-noPEG-HA (continuation)	Phosphatidylcholine 758.6 Da	1	<p>Compound name: PC_758.5 Correlation coefficient: $r = 0.981541$, $r^2 = 0.963422$ Calibration curve: $465.7 * x + -47279.4$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: PC_758.5 Correlation coefficient: $r = 0.996625$, $r^2 = 0.993262$ Calibration curve: $427.877 * x + -61715.9$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: PC_758.5 Correlation coefficient: $r = 0.989484$, $r^2 = 0.979078$ Calibration curve: $579.431 * x + -77046.3$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		1	<p>Compound name: PC_780.5 Correlation coefficient: $r = 0.996934$, $r^2 = 0.993877$ Calibration curve: $249.502 * x + -22763.5$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: PC_780.5 Correlation coefficient: $r = 0.998443$, $r^2 = 0.996889$ Calibration curve: $1010.34 * x + -133621$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: PC_780.5 Correlation coefficient: $r = 0.993020$, $r^2 = 0.986089$ Calibration curve: $279.912 * x + -34205.1$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD-noPEG-HA (continuation)	Phosphatidylcholine 782.5 Da	1	<p>Compound name: PC_782.5 Correlation coefficient: $r = 0.997218$, $r^2 = 0.994443$ Calibration curve: $1226.51 * x + -122120$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: PC_782.5 Correlation coefficient: $r = 0.997761$, $r^2 = 0.995526$ Calibration curve: $1131.64 * x + -154034$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: PC_782.5 Correlation coefficient: $r = 0.990150$, $r^2 = 0.980398$ Calibration curve: $1362.81 * x + -179537$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		1	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.986828$, $r^2 = 0.973829$ Calibration curve: $6523.57 * x + -15392.9$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.967398$, $r^2 = 0.935858$ Calibration curve: $4864.8 * x + 1886.82$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.988969$, $r^2 = 0.978060$ Calibration curve: $3370.43 * x + -22997$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

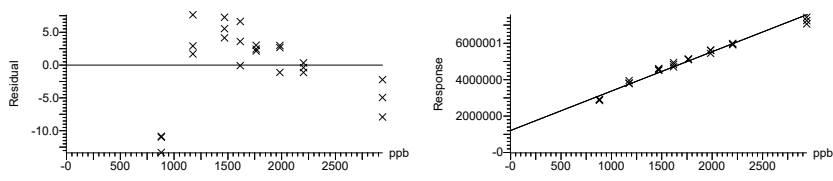
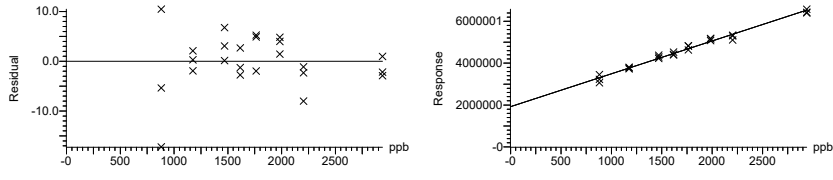
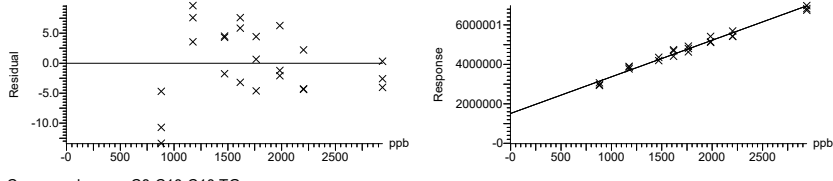
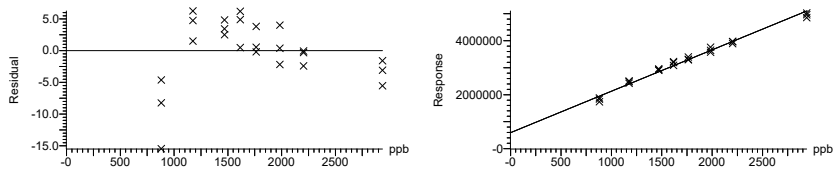
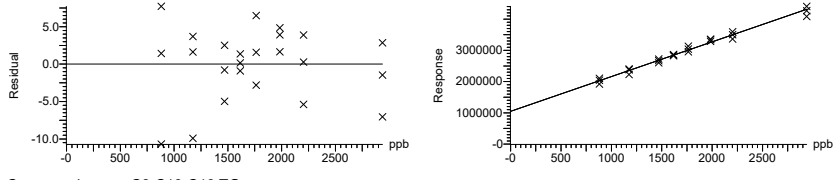
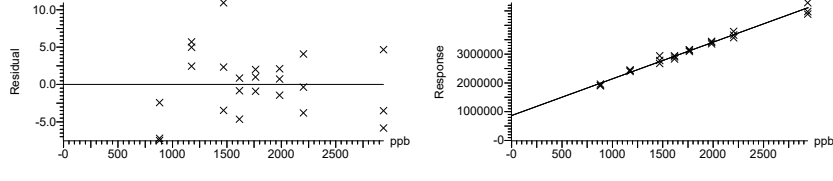
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD-noPEG-HA (continuation)	Hyaluronic acid	1	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.992565$, $r^2 = 0.985185$ Calibration curve: $4404.76 * x + -14916.4$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.996035$, $r^2 = 0.992085$ Calibration curve: $4135.47 * x + -31361.2$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.993772$, $r^2 = 0.987583$ Calibration curve: $3391.73 * x + -39008.5$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		1	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.993810$, $r^2 = 0.987659$ Calibration curve: $5893.24 * x + 1224.65$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.994331$, $r^2 = 0.988695$ Calibration curve: $4370.09 * x + -9223.01$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.991640$, $r^2 = 0.983349$ Calibration curve: $4115.71 * x + -21346.5$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>

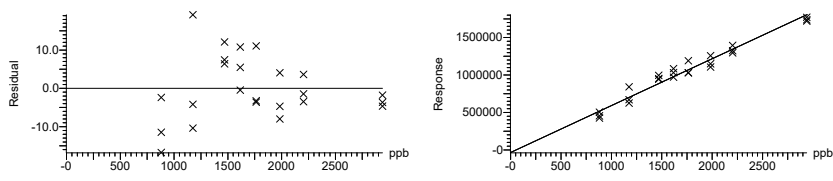
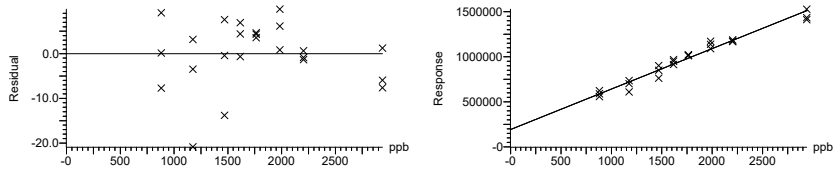
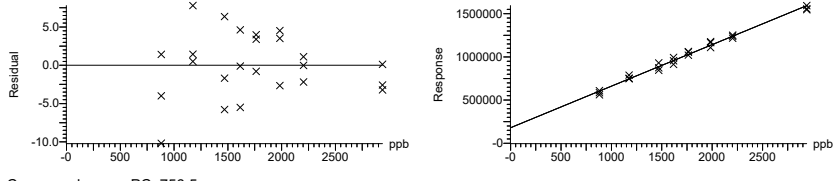
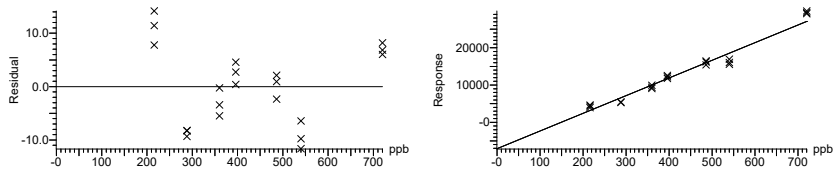
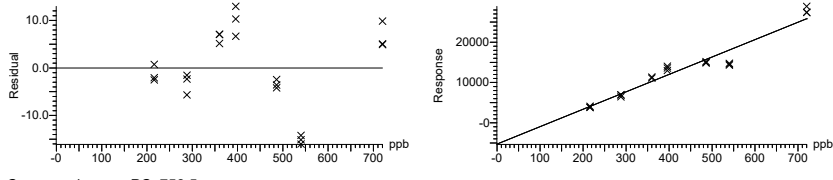
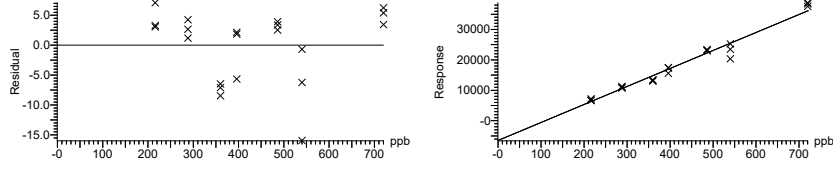
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves		
SD-noPEG-PSA	CTAB	1	<p>Compound name: hexadecyltrimethylammonium Correlation coefficient: $r = 0.997990$, $r^2 = 0.995984$ Calibration curve: $3657.04 * x + 2984.29$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>		
		2	<p>Compound name: hexadecyltrimethylammonium Correlation coefficient: $r = 0.998108$, $r^2 = 0.996219$ Calibration curve: $3114.3 * x + 39261.4$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>		
		3	<p>Compound name: hexadecyltrimethylammonium Correlation coefficient: $r = 0.996723$, $r^2 = 0.993458$ Calibration curve: $3447.94 * x + 20029.8$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>		
		C8-C8-C8 Triglyceride	C8-C8-C8 Triglyceride	1	<p>Compound name: C8-C8-C8 TG Correlation coefficient: $r = 0.989550$, $r^2 = 0.979210$ Calibration curve: $1951.37 * x + 1.00607e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
				2	<p>Compound name: C8-C8-C8 TG Correlation coefficient: $r = 0.990411$, $r^2 = 0.980914$ Calibration curve: $1452.6 * x + 1.77029e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
				3	<p>Compound name: C8-C8-C8 TG Correlation coefficient: $r = 0.992065$, $r^2 = 0.984193$ Calibration curve: $1676.78 * x + 1.24921e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>

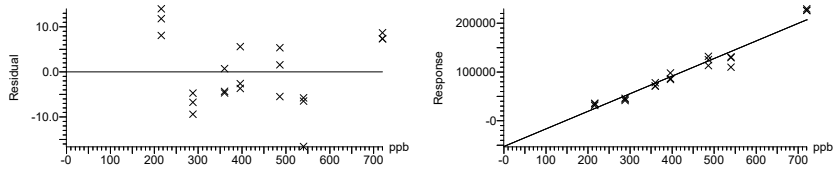
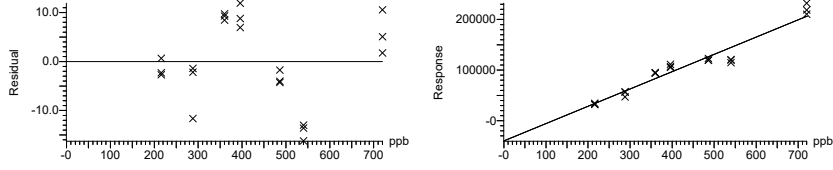
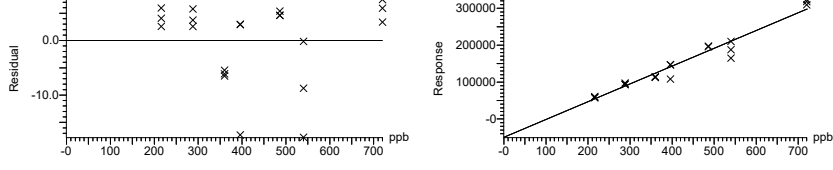
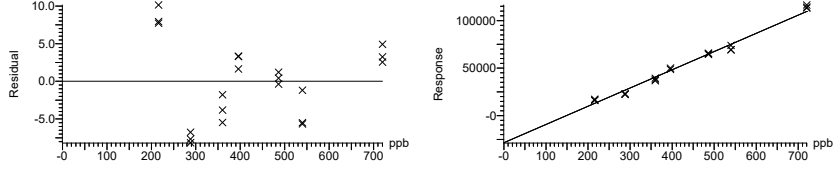
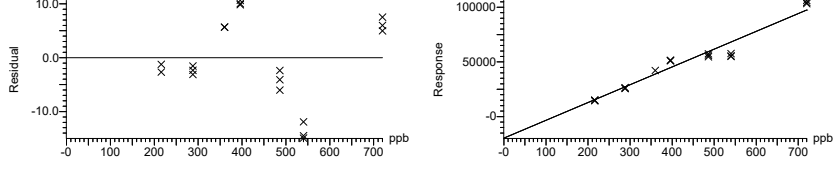
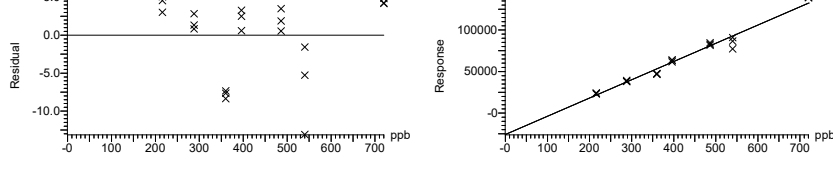
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves	
SD-noPEG-PSA (continuation)	C ₈ -C ₈ -C ₁₀ glyceride	1	Compound name: C ₈ -C ₈ -C ₁₀ TG Correlation coefficient: $r = 0.989462$, $r^2 = 0.979035$ Calibration curve: $2163.78 * x + 1.20952e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 	
		2	Compound name: C ₈ -C ₈ -C ₁₀ TG Correlation coefficient: $r = 0.990996$, $r^2 = 0.982073$ Calibration curve: $1569.23 * x + 1.92218e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 	
		3	Compound name: C ₈ -C ₈ -C ₁₀ TG Correlation coefficient: $r = 0.989581$, $r^2 = 0.979271$ Calibration curve: $1854.36 * x + 1.51298e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 	
	C ₈ -C ₁₀ -C ₁₀ glyceride	Tri-	1	Compound name: C ₈ -C ₁₀ -C ₁₀ TG Correlation coefficient: $r = 0.992471$, $r^2 = 0.984999$ Calibration curve: $1534.99 * x + 593742$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 
			2	Compound name: C ₈ -C ₁₀ -C ₁₀ TG Correlation coefficient: $r = 0.991897$, $r^2 = 0.983860$ Calibration curve: $1112.18 * x + 1.04842e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 
			3	Compound name: C ₈ -C ₁₀ -C ₁₀ TG Correlation coefficient: $r = 0.992729$, $r^2 = 0.985511$ Calibration curve: $1274.23 * x + 866565$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None 

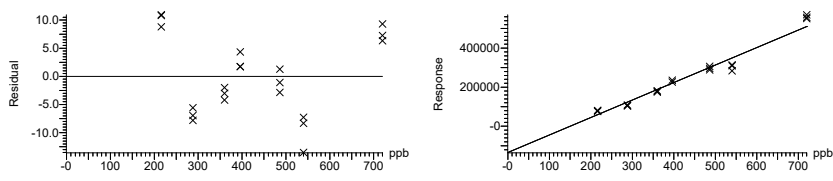
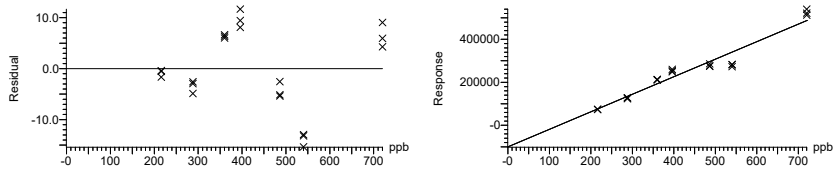
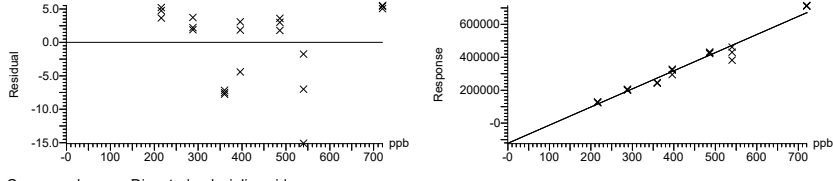
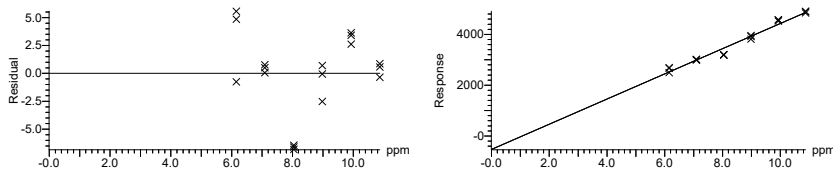
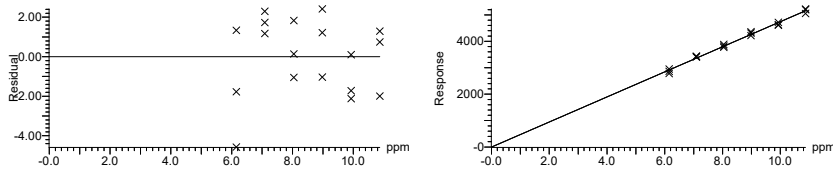
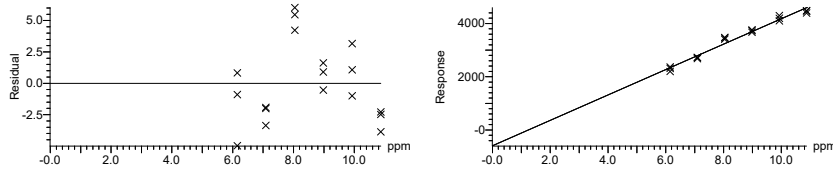
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves		
SD-noPEG-PSA (continuation)	C ₁₀ -C ₁₀ -C ₁₀ Tri-glyceride	1	<p>Compound name: C10-C10-C10 TG Correlation coefficient: $r = 0.978117$, $r^2 = 0.956712$ Calibration curve: $626.111 * x + -34775.9$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		2	<p>Compound name: C10-C10-C10 TG Correlation coefficient: $r = 0.981912$, $r^2 = 0.964152$ Calibration curve: $448.743 * x + 192818$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		3	<p>Compound name: C10-C10-C10 TG Correlation coefficient: $r = 0.994138$, $r^2 = 0.988311$ Calibration curve: $480.788 * x + 180271$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		Phosphatidylcholine 756.6 Da	PC_756.5	1	<p>Compound name: PC_756.5 Correlation coefficient: $r = 0.981717$, $r^2 = 0.963769$ Calibration curve: $47.4852 * x + -7090.4$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				2	<p>Compound name: PC_756.5 Correlation coefficient: $r = 0.971896$, $r^2 = 0.944581$ Calibration curve: $43.2079 * x + -5281.14$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				3	<p>Compound name: PC_756.5 Correlation coefficient: $r = 0.986049$, $r^2 = 0.972293$ Calibration curve: $59.1599 * x + -6493.77$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD-noPEG-PSA (continuation)	Phosphatidylcholine 758.6 Da	1	<p>Compound name: PC_758.5 Correlation coefficient: $r = 0.978454$, $r^2 = 0.957372$ Calibration curve: $360.953 * x + -52734.3$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: PC_758.5 Correlation coefficient: $r = 0.971378$, $r^2 = 0.943575$ Calibration curve: $341.841 * x + -39868.1$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: PC_758.5 Correlation coefficient: $r = 0.978576$, $r^2 = 0.957611$ Calibration curve: $482.411 * x + -49778.1$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		1	<p>Compound name: PC_780.5 Correlation coefficient: $r = 0.991907$, $r^2 = 0.983880$ Calibration curve: $191.822 * x + -28502.3$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: PC_780.5 Correlation coefficient: $r = 0.975548$, $r^2 = 0.951693$ Calibration curve: $162.687 * x + -19690.5$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: PC_780.5 Correlation coefficient: $r = 0.989517$, $r^2 = 0.979145$ Calibration curve: $219.467 * x + -25771.8$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves		
SD-noPEG-PSA (continuation)	Phosphatidylcholine 782.5 Da	1	<p>Compound name: PC_782.5 Correlation coefficient: $r = 0.982009$, $r^2 = 0.964341$ Calibration curve: $895.531 * x + -134281$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		2	<p>Compound name: PC_782.5 Correlation coefficient: $r = 0.974672$, $r^2 = 0.949985$ Calibration curve: $815.527 * x + -100263$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		3	<p>Compound name: PC_782.5 Correlation coefficient: $r = 0.986556$, $r^2 = 0.973292$ Calibration curve: $1101.46 * x + -122320$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		Polysialic acid (whole)	acid	1	<p>Compound name: Digested polysialic acid Correlation coefficient: $r = 0.984542$, $r^2 = 0.969323$ Calibration curve: $495.967 * x + -528.657$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				2	<p>Compound name: Digested polysialic acid Correlation coefficient: $r = 0.995783$, $r^2 = 0.991583$ Calibration curve: $474.707 * x + -2.33855$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				3	<p>Compound name: Digested polysialic acid Correlation coefficient: $r = 0.987737$, $r^2 = 0.975625$ Calibration curve: $477.285 * x + -592.32$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

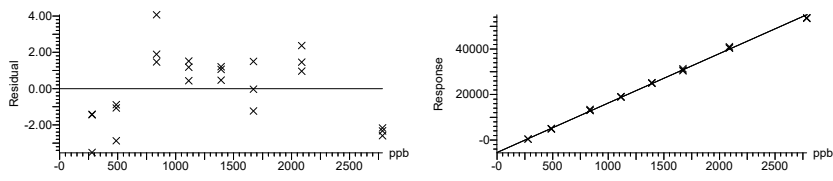
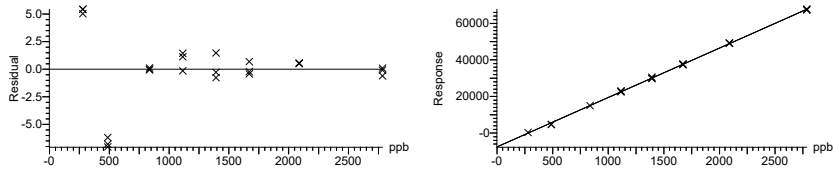
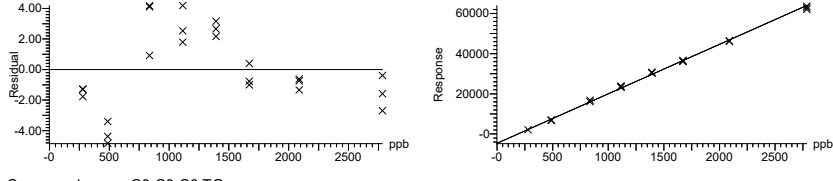
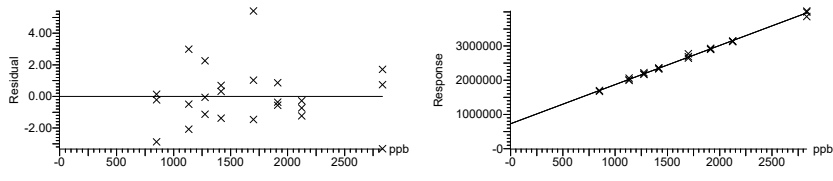
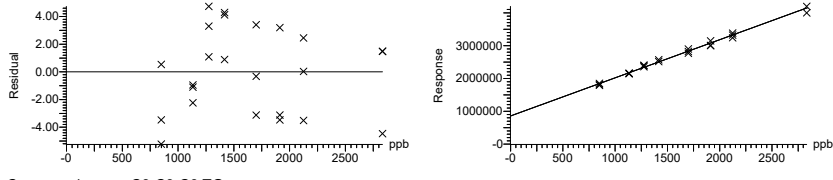
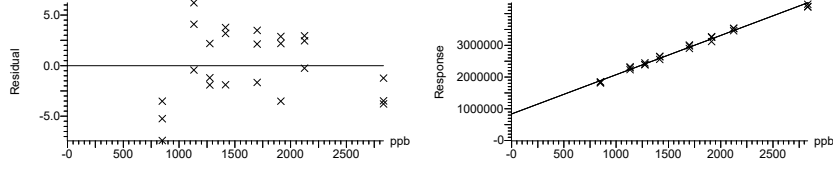
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD-noPEG-PSA (continuation)	Polysialic acid (supernatant)	1	<p>Compound name: Digested polysialic acid Correlation coefficient: $r = 0.996813$, $r^2 = 0.993635$ Calibration curve: $215.458 * x + -41.1843$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested polysialic acid Correlation coefficient: $r = 0.991058$, $r^2 = 0.982196$ Calibration curve: $336.608 * x + -508.845$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested polysialic acid Correlation coefficient: $r = 0.992138$, $r^2 = 0.984337$ Calibration curve: $278.905 * x + -449.887$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		1	<p>Compound name: Digested polysialic acid Correlation coefficient: $r = 0.998050$, $r^2 = 0.996104$ Calibration curve: $328.803 * x + 27.6584$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested polysialic acid Correlation coefficient: $r = 0.997997$, $r^2 = 0.995998$ Calibration curve: $441.915 * x + -248.6$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested polysialic acid Correlation coefficient: $r = 0.993285$, $r^2 = 0.986614$ Calibration curve: $352.887 * x + 329.055$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>

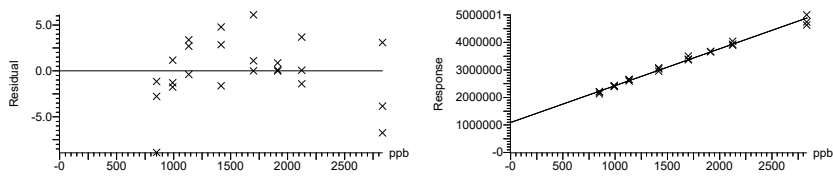
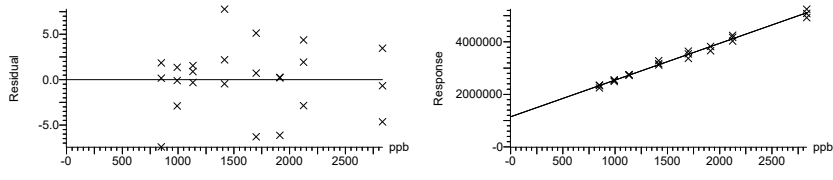
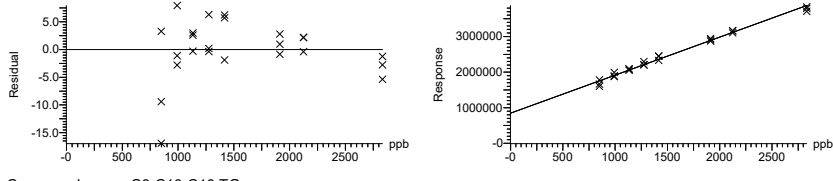
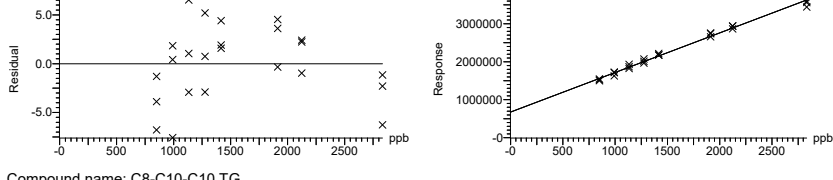
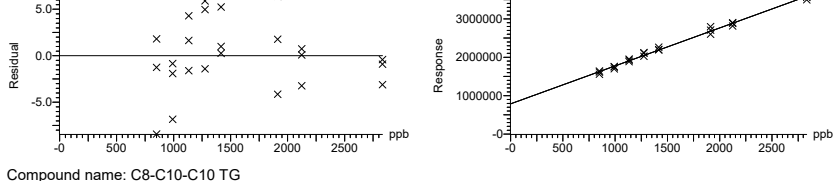
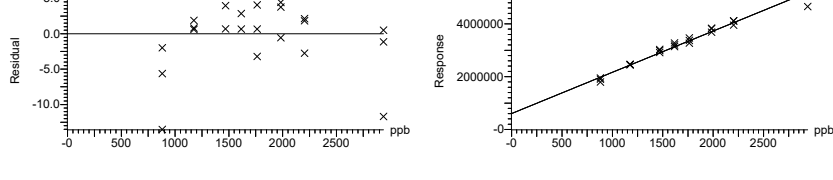
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves		
SE- <i>b</i> -PEG-HA	Benzethonium	1	<p>Compound name: benzethonium Correlation coefficient: $r = 0.999809$, $r^2 = 0.999617$ Calibration curve: $20837.2 * x + 8846.54$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>		
		2	<p>Compound name: benzethonium Correlation coefficient: $r = 0.999915$, $r^2 = 0.999830$ Calibration curve: $28497.7 * x + 9350.55$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>		
		3	<p>Compound name: benzethonium Correlation coefficient: $r = 0.999769$, $r^2 = 0.999538$ Calibration curve: $21075.3 * x + 18948$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>		
		Macrogol-15-hydroxystearate		1	<p>Compound name: macrogol-15-hydroxystearate Correlation coefficient: $r = 0.999616$, $r^2 = 0.999233$ Calibration curve: $490.537 * x + 621.962$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
				2	<p>Compound name: macrogol-15-hydroxystearate Correlation coefficient: $r = 0.999613$, $r^2 = 0.999226$ Calibration curve: $552.297 * x + 1523.58$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
				3	<p>Compound name: macrogol-15-hydroxystearate Correlation coefficient: $r = 0.999533$, $r^2 = 0.999066$ Calibration curve: $492.173 * x + 1525.34$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>

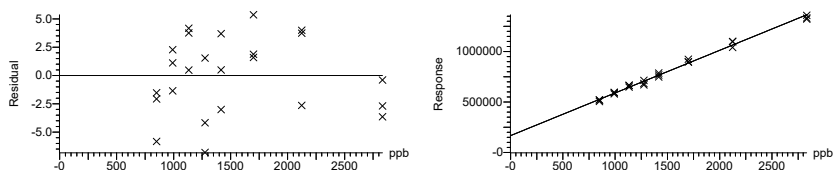
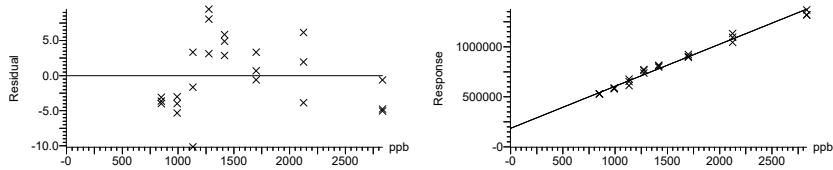
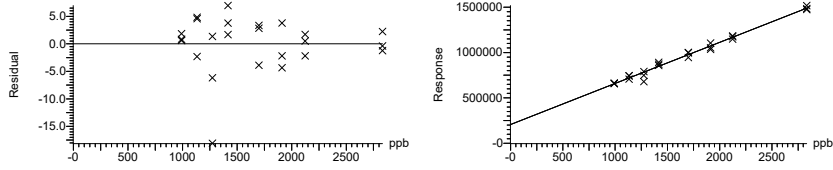
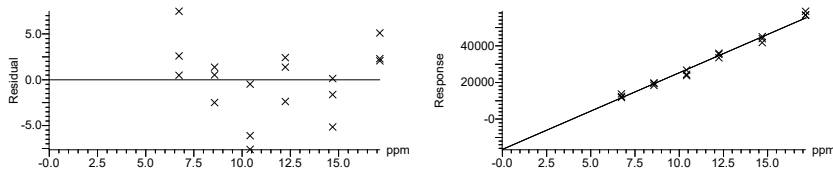
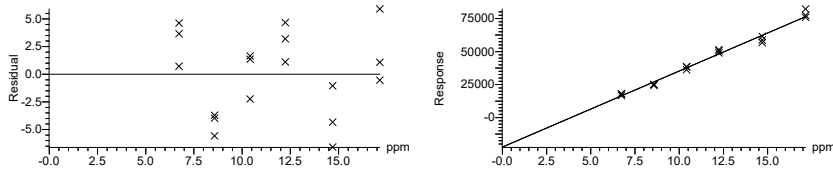
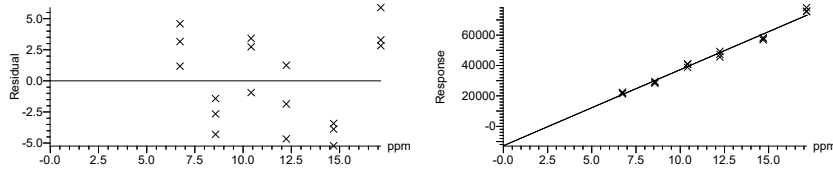
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SE- <i>b</i> -PEG-HA (continuation)	Polysorbate 80	1	<p>Compound name: polysorbate 80 Correlation coefficient: $r = 0.999571$, $r^2 = 0.999142$ Calibration curve: $21.7494 * x + -5484.45$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: polysorbate 80 Correlation coefficient: $r = 0.999600$, $r^2 = 0.999200$ Calibration curve: $27.0221 * x + -7565.95$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: polysorbate 80 Correlation coefficient: $r = 0.999386$, $r^2 = 0.998773$ Calibration curve: $24.6304 * x + -4631.83$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
	C ₈ -C ₈ -C ₈ Triglyceride	1	<p>Compound name: C8-C8-C8 TG Correlation coefficient: $r = 0.998555$, $r^2 = 0.997112$ Calibration curve: $1143.7 * x + 729914$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: C8-C8-C8 TG Correlation coefficient: $r = 0.996395$, $r^2 = 0.992802$ Calibration curve: $1161.24 * x + 857869$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: C8-C8-C8 TG Correlation coefficient: $r = 0.995926$, $r^2 = 0.991868$ Calibration curve: $1236.69 * x + 836793$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SE- <i>b</i> -PEG-HA (continuation)	C ₈ -C ₈ -C ₁₀ glyceride	1	<p>Compound name: C8-C8-C10 TG Correlation coefficient: $r = 0.995759$, $r^2 = 0.991536$ Calibration curve: $1340.75 * x + 1.08877e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: C8-C8-C10 TG Correlation coefficient: $r = 0.995234$, $r^2 = 0.990491$ Calibration curve: $1399.21 * x + 1.14637e+006$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: C8-C10-C10 TG Correlation coefficient: $r = 0.992999$, $r^2 = 0.986048$ Calibration curve: $1067.63 * x + 847138$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		1	<p>Compound name: C8-C10-C10 TG Correlation coefficient: $r = 0.995371$, $r^2 = 0.990763$ Calibration curve: $1042.33 * x + 675228$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		2	<p>Compound name: C8-C10-C10 TG Correlation coefficient: $r = 0.995793$, $r^2 = 0.991604$ Calibration curve: $987.866 * x + 787402$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
		3	<p>Compound name: C8-C10-C10 TG Correlation coefficient: $r = 0.990811$, $r^2 = 0.981706$ Calibration curve: $1562.36 * x + 603095$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

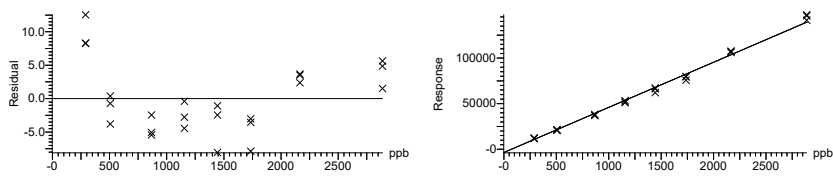
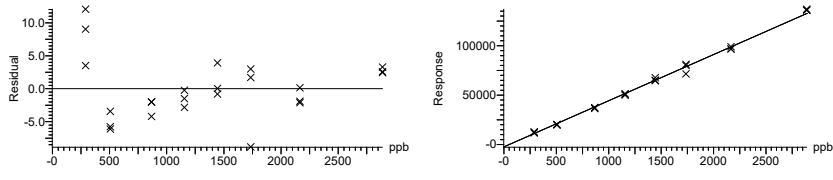
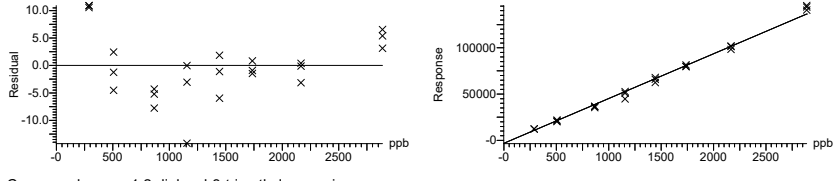
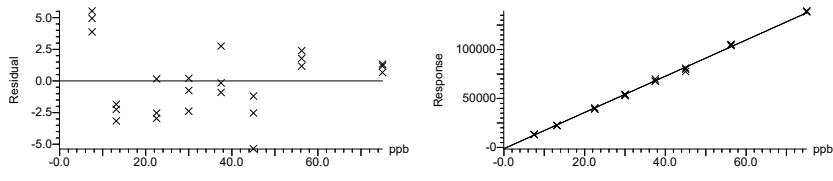
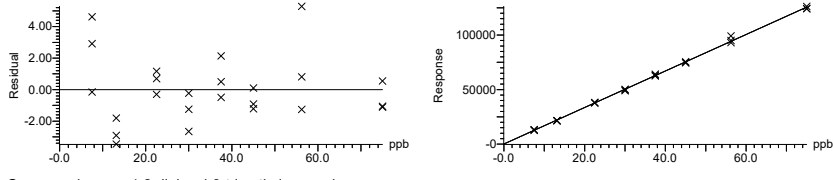
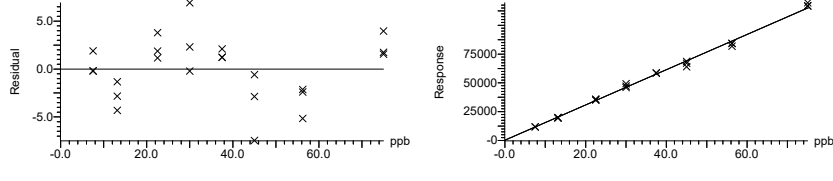
Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves		
SE- <i>b</i> -PEG-HA (continuation)	C ₁₀ -C ₁₀ -C ₁₀ glyceride	1	<p>Compound name: C10-C10-C10 TG Correlation coefficient: $r = 0.995952$, $r^2 = 0.991921$ Calibration curve: $422.591 * x + 167207$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		2	<p>Compound name: C10-C10-C10 TG Correlation coefficient: $r = 0.991788$, $r^2 = 0.983644$ Calibration curve: $420.378 * x + 185286$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		3	<p>Compound name: C10-C10-C10 TG Correlation coefficient: $r = 0.990394$, $r^2 = 0.980880$ Calibration curve: $452.742 * x + 206773$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		Hyaluronic acid (whole)	acid	1	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.993235$, $r^2 = 0.986517$ Calibration curve: $4187.56 * x + -16548$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				2	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.992919$, $r^2 = 0.985888$ Calibration curve: $5760.23 * x + -22313.5$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				3	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.993213$, $r^2 = 0.986472$ Calibration curve: $5010.39 * x + -12794.7$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SE- <i>b</i> -PEG-HA (continuation)	Hyaluronic acid (retentate)	1	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.984484$, $r^2 = 0.969209$ Calibration curve: $2948.95 * x + -7474$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.990093$, $r^2 = 0.980285$ Calibration curve: $3985.69 * x + -7849.32$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.973670$, $r^2 = 0.948034$ Calibration curve: $3972.57 * x + -8904.86$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		1	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.990870$, $r^2 = 0.981823$ Calibration curve: $2674.08 * x + -9315.04$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.996754$, $r^2 = 0.993519$ Calibration curve: $2756.76 * x + -7074.99$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested hyaluronic acid Correlation coefficient: $r = 0.996494$, $r^2 = 0.993000$ Calibration curve: $2247.5 * x + -6382.66$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves		
SD-noPEG- PEG-PGA	DL- α -tocopherol	1	<p>Compound name: DL-α-tocopherol Correlation coefficient: $r = 0.997469$, $r^2 = 0.994945$ Calibration curve: $49.4472 * x + -3461.7$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		2	<p>Compound name: DL-α-tocopherol Correlation coefficient: $r = 0.998434$, $r^2 = 0.996871$ Calibration curve: $46.7148 * x + -2340.53$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		3	<p>Compound name: DL-α-tocopherol Correlation coefficient: $r = 0.997046$, $r^2 = 0.994100$ Calibration curve: $48.3276 * x + -3138.24$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 		
		DOTAP	1,2-dioleoyl-3-trimethylammoniumpropane	1	<p>Compound name: 1,2-dioleoyl-3-trimethylammoniumpropane Correlation coefficient: $r = 0.999393$, $r^2 = 0.998787$ Calibration curve: $1851.7 * x + -1312.06$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				2	<p>Compound name: 1,2-dioleoyl-3-trimethylammoniumpropane Correlation coefficient: $r = 0.999553$, $r^2 = 0.999106$ Calibration curve: $1673.68 * x + 86.2758$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 
				3	<p>Compound name: 1,2-dioleoyl-3-trimethylammoniumpropane Correlation coefficient: $r = 0.998635$, $r^2 = 0.997271$ Calibration curve: $1530.23 * x + 253.64$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p> 

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD-noPEG- PEG-PGA (continuation)	PEG-PGA (whole)	1	<p>Compound name: Digested polyethylene glycol polyglutamic acid Correlation coefficient: $r = 0.998487$, $r^2 = 0.996977$ Calibration curve: $10575.9 * x + -30283.5$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested polyethylene glycol polyglutamic acid Correlation coefficient: $r = 0.999504$, $r^2 = 0.999009$ Calibration curve: $7449.11 * x + 22416.1$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested polyethylene glycol polyglutamic acid Correlation coefficient: $r = 0.998669$, $r^2 = 0.997340$ Calibration curve: $8812.53 * x + -7182.38$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
PEG-PGA (su- pernatant)	PEG-PGA (su- pernatant)	1	<p>Compound name: Digested polyethylene glycol polyglutamic acid Correlation coefficient: $r = 0.998201$, $r^2 = 0.996404$ Calibration curve: $9707.07 * x + 13837.7$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested polyethylene glycol polyglutamic acid Correlation coefficient: $r = 0.999767$, $r^2 = 0.999534$ Calibration curve: $7914.54 * x + 12392.4$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested polyethylene glycol polyglutamic acid Correlation coefficient: $r = 0.998509$, $r^2 = 0.997020$ Calibration curve: $7881.39 * x + 20487.5$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>

Supplementary Table 8. Calibration curves and residual plots of all the quantified substances (continuation)

Formulation	Molecule	Rep.	Residual plots and calibration curves
SD-noPEG-PEG-PGA (continuation)	PEG-PGA (in-franantant)	1	<p>Compound name: Digested polyethylene glycol polyglutamic acid Correlation coefficient: $r = 0.998736$, $r^2 = 0.997474$ Calibration curve: $11304.1 * x + 8801.48$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		2	<p>Compound name: Digested polyethylene glycol polyglutamic acid Correlation coefficient: $r = 0.999069$, $r^2 = 0.998139$ Calibration curve: $8114.2 * x + 3596.93$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>
		3	<p>Compound name: Digested polyethylene glycol polyglutamic acid Correlation coefficient: $r = 0.999902$, $r^2 = 0.999803$ Calibration curve: $8230.45 * x + 11492.7$ Response type: External Std, Area Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None</p>

SD-*l*-PEG-HA: lineal-polyethylene glycol-containing hyaluronic acid nanocapsules formulated by solvent displacement. SD-noPEG-HA: non-PEGylated hyaluronic acid nanocapsules formulated by solvent displacement. SD-noPEG-PSA: non-PEGylated polysialic acid nanocapsules formulated by solvent displacement. SE-*b*-PEG-HA: Self-emulsifying branched-polyethylene glycol-containing hyaluronic acid nanocapsules. SD-noPEG-PEG-PGA: Solvent displacement nanocapsules not containing PEGylated surfactants and with an outer shell of polyethylene glycol polyglutamic acid. Residuals were plotted as percentual relative residuals (%RRES) vs. concentration, while calibration curves, response vs. concentration. In both cases, a weighting factor of 1/x was applied. In all cases, the mean of the triplicates of the %RRES for each concentration level was found to be in the range of -20 % to 20 %, confirming the linearity of the calibration curve. In general, residuals followed a random distribution around the value %RRES = 0. Rep.: replicates.

Supplementary Table 9. Mass percentage detected in each fraction relative to the theoretical amount added to the formulation

Formulation	Substance	Recovery before isolation (%)	Supernatant / re-tentate (%)	Infranatant/perme-ate recovery (%)	Sum of the fractions' recoveries (%)
SD- <i>l</i> -PEG-HA	Benzethonium	92 ± 10	39 ± 5	56 ± 4	95 ± 9
	DL- α -tocopherol	106 ± 10	72 ± 5	30 ± 5	102 ± 10
	D- α -tocopherol polyethylene glycol 1000 succinate	103 ± 10	58 ± 6	43 ± 6	101 ± 12
	Hyaluronic acid	100 ± 5	18 ± 3	86 ± 2	104 ± 5
SD-noPEG-HA	Hexadecyltrimethylammonium	99 ± 19	35 ± 8	42 ± 9	77 ± 16
	C ₈ -C ₈ -C ₈ Triglyceride	113 ± 8	52 ± 3	24 ± 3	75 ± 6
	C ₈ -C ₈ -C ₁₀ Triglyceride	109 ± 7	53 ± 4	25 ± 4	78 ± 7
	C ₈ -C ₁₀ -C ₁₀ Triglyceride	109 ± 8	53 ± 4	24 ± 4	77 ± 7
	C ₁₀ -C ₁₀ -C ₁₀ Triglyceride	110 ± 10	54 ± 5	23 ± 4	77 ± 9
	Phosphatidylcholine 756.5 Da	96 ± 14	16 ± 3	27 ± 9	43 ± 11
	Phosphatidylcholine 758.5 Da	98 ± 18	16 ± 3	27 ± 9	43 ± 12
	Phosphatidylcholine 780.5 Da	97 ± 12	16 ± 3	25 ± 10	42 ± 13
	Phosphatidylcholine 782.5 Da	97 ± 14	16 ± 3	27 ± 9	44 ± 12
	Hyaluronic acid	105 ± 7	14 ± 2	80 ± 7	95 ± 8
SD-noPEG-PSA	Hexadecyltrimethylammonium	103 ± 11	31 ± 4	59 ± 6	90 ± 9
	C ₈ -C ₈ -C ₈ Triglyceride	101 ± 10	68 ± 8	28 ± 5	95 ± 13
	C ₈ -C ₈ -C ₁₀ Triglyceride	100 ± 12	66 ± 8	28 ± 5	94 ± 13
	C ₈ -C ₁₀ -C ₁₀ Triglyceride	99 ± 11	66 ± 8	28 ± 4	94 ± 13
	C ₁₀ -C ₁₀ -C ₁₀ Triglyceride	98 ± 12	64 ± 7	30 ± 5	94 ± 12
	Phosphatidylcholine 756.5 Da	96 ± 8	17 ± 3	40 ± 8	57 ± 11
	Phosphatidylcholine 758.5 Da	94 ± 9	18 ± 3	40 ± 8	58 ± 11
	Phosphatidylcholine 780.5 Da	98 ± 9	18 ± 2	41 ± 9	59 ± 11
	Phosphatidylcholine 782.5 Da	97 ± 7	17 ± 3	40 ± 8	58 ± 11
	Polysialic acid	103 ± 2	14 ± 1	91 ± 3	104 ± 4
SE- <i>b</i> -PEG-HA	Polyethylene glycol	103 ± 9	< 10	96 ± 13	N/A
	Benzethonium	109 ± 4	51 ± 12	51 ± 8	102 ± 20
	Macrogol-15-hydroxystearate	99 ± 6	39 ± 5	54 ± 11	93 ± 16
	Polysorbate 80	111 ± 4	24 ± 9	63 ± 6	87 ± 15
	C ₈ -C ₈ -C ₈ Triglyceride	106 ± 5	95 ± 7	< 10	N/A
	C ₈ -C ₈ -C ₁₀ Triglyceride	108 ± 6	95 ± 6	< 10	N/A
	C ₈ -C ₁₀ -C ₁₀ Triglyceride	107 ± 6	94 ± 6	< 10	N/A
	C ₁₀ -C ₁₀ -C ₁₀ Triglyceride	104 ± 10	89 ± 8	< 10	N/A
	Hyaluronic acid	91 ± 3	43 ± 4	53 ± 3	96 ± 7
	DL- α -tocopherol	96 ± 4	95 ± 6	9 ± 3	103 ± 8
SD-noPEG-PEG-PGA	1,2-dioleoyl-3-trimethylammoniumpropane	84 ± 8	89 ± 3	12 ± 3	101 ± 6
	PEG-PGA	109 ± 11	34 ± 9	67 ± 5	101 ± 15

SD-*l*-PEG-HA: lineal-polyethylene glycol-containing hyaluronic acid nanocapsules formulated by solvent displacement. SD-noPEG-HA: non-PEGylated hyaluronic acid nanocapsules formulated by solvent displacement. SD-noPEG-PSA: non-PEGylated polysialic acid nanocapsules formulated by solvent displacement. SE-*b*-PEG-HA: Self-emulsifying branched-polyethylene glycol-containing hyaluronic acid nanocapsules. N/A: not applicable. n = 3. Data are shown as mean ± standard deviation.

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