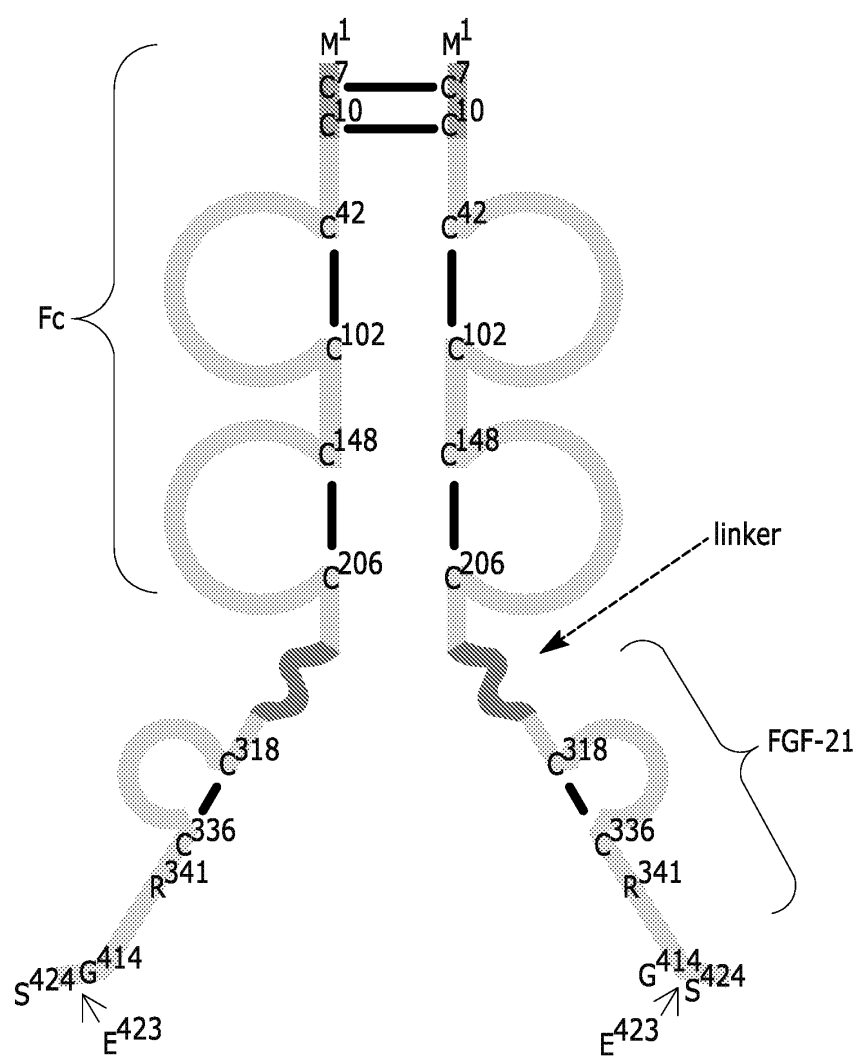


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**FIG. 1**

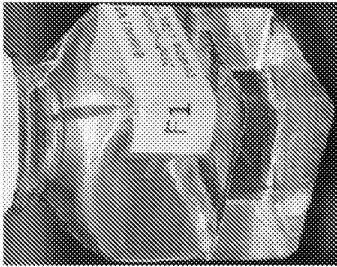
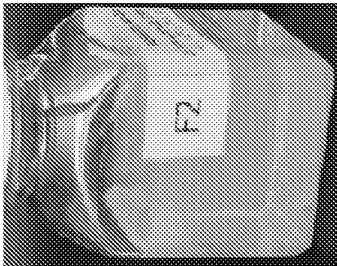
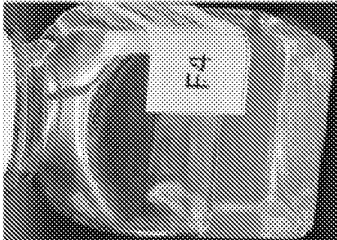
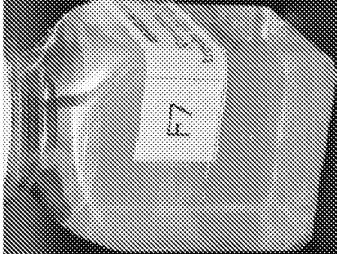
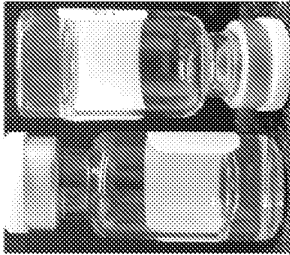
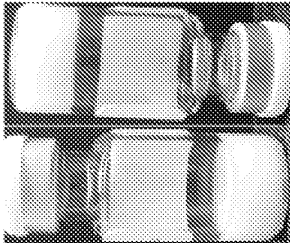
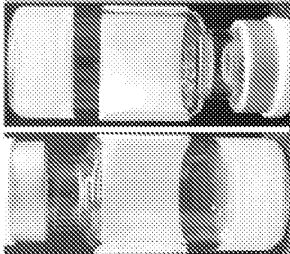
Time Point	F1	F2	F4	F7	
Before filing					Score 0/Turbid (high)
	Score 0/clear	Score 0/Turbid (high) (0.45-µm filtered)	Score 0/Turbid (medium)		
T3d_40C					

FIG. 2A

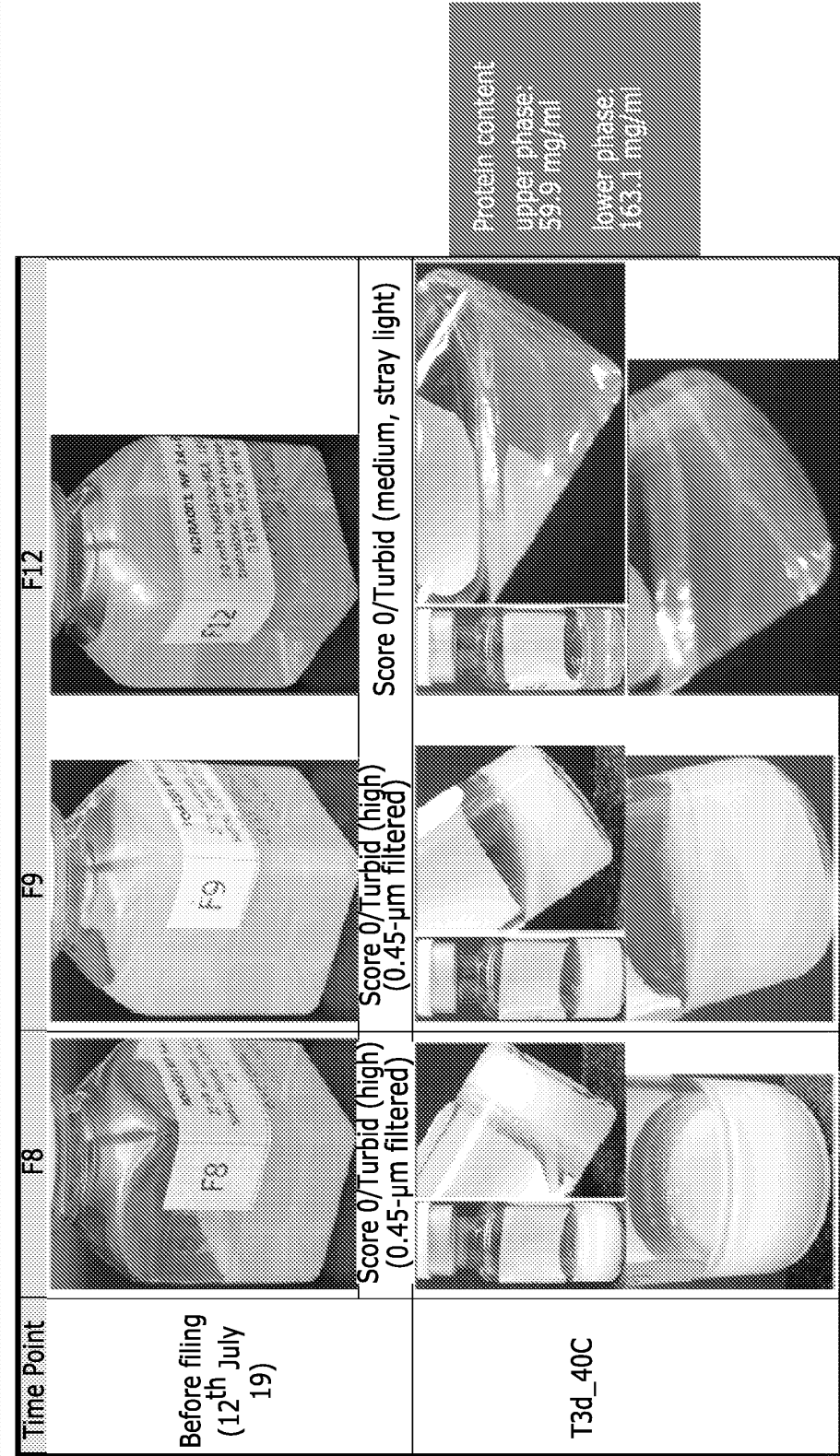


FIG. 2B

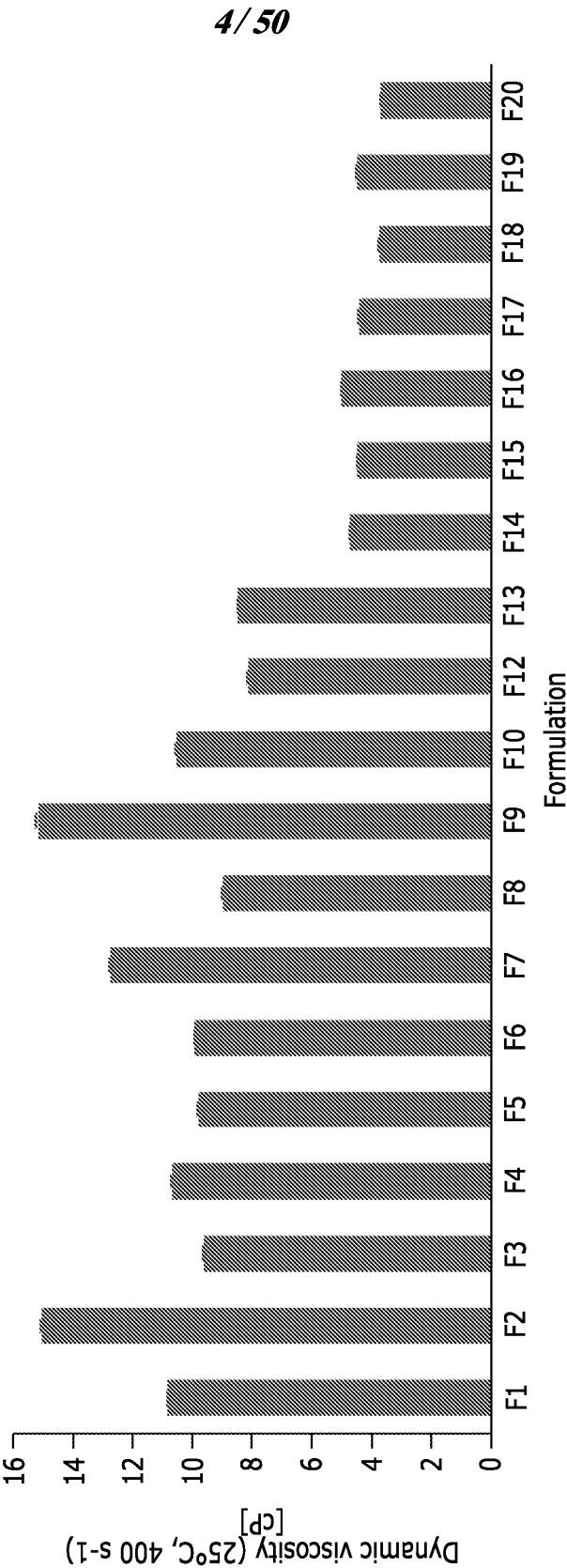


FIG. 3

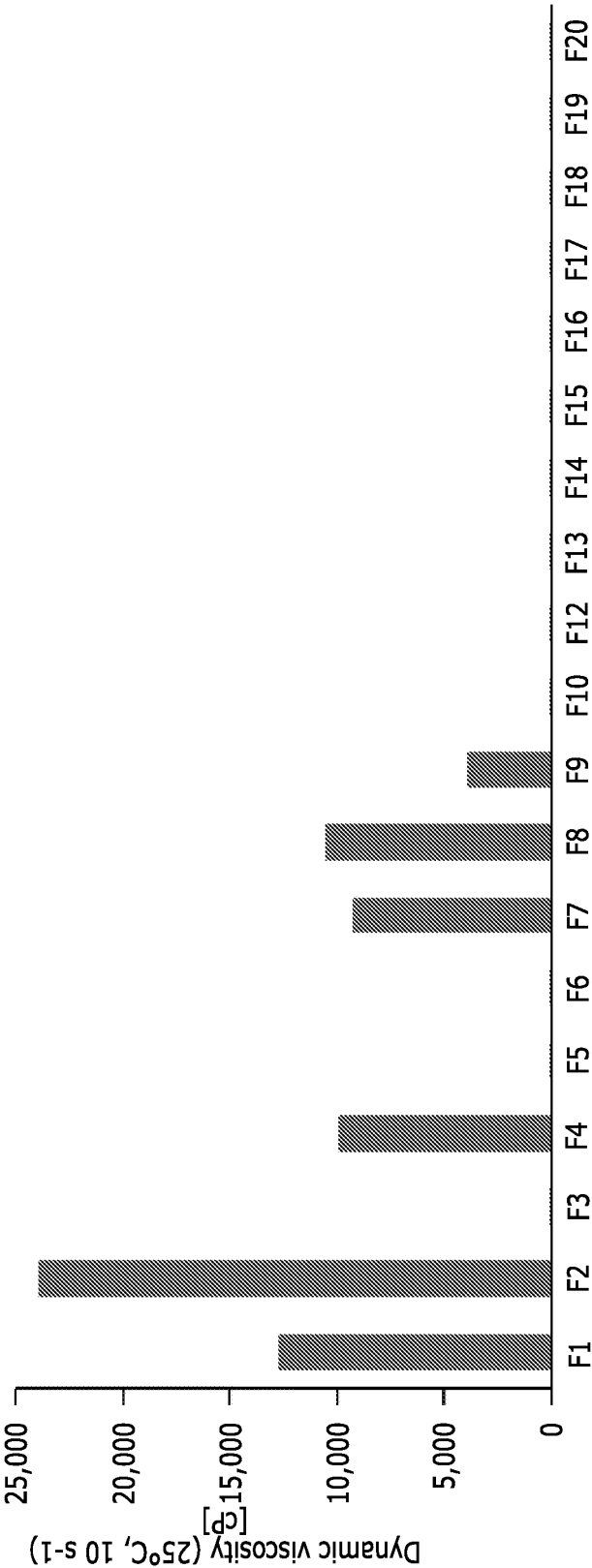


FIG. 4A

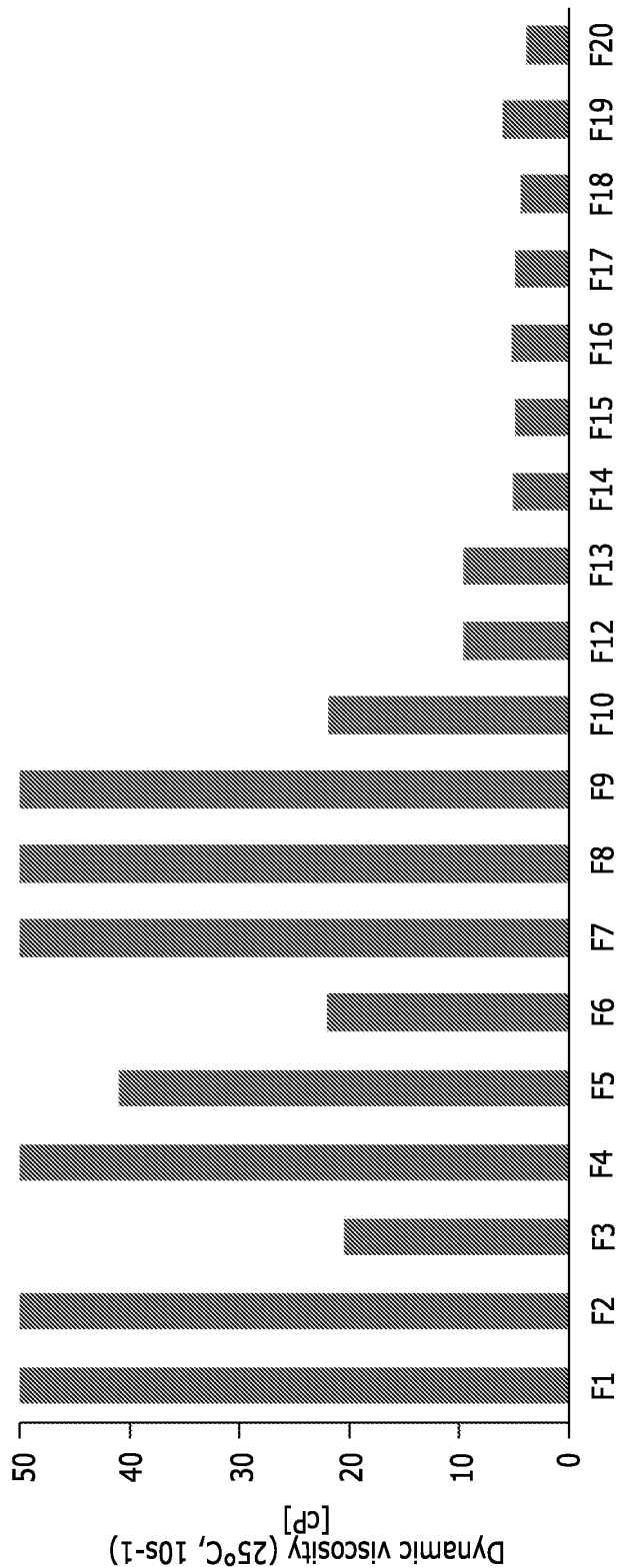
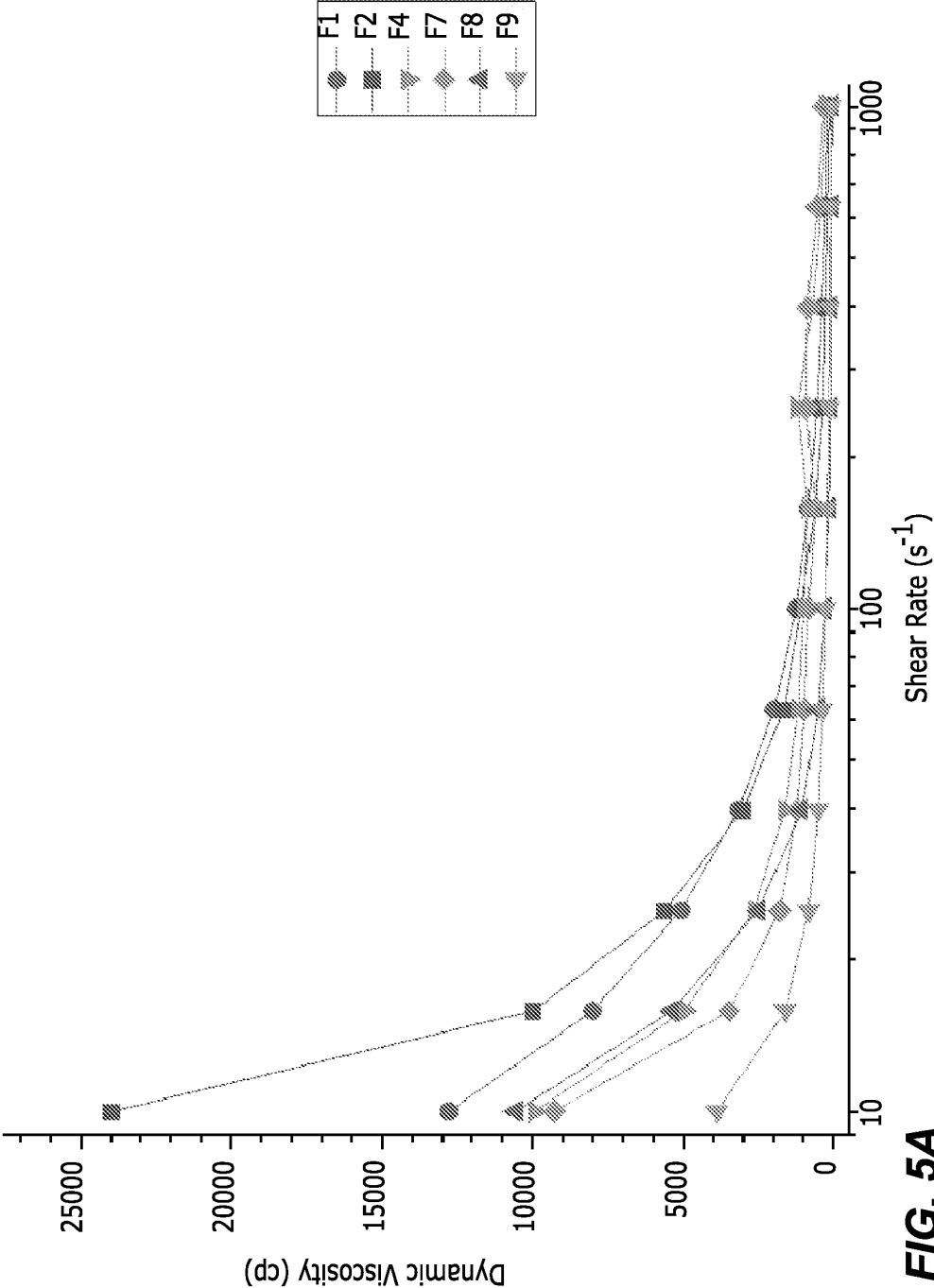


FIG. 4B



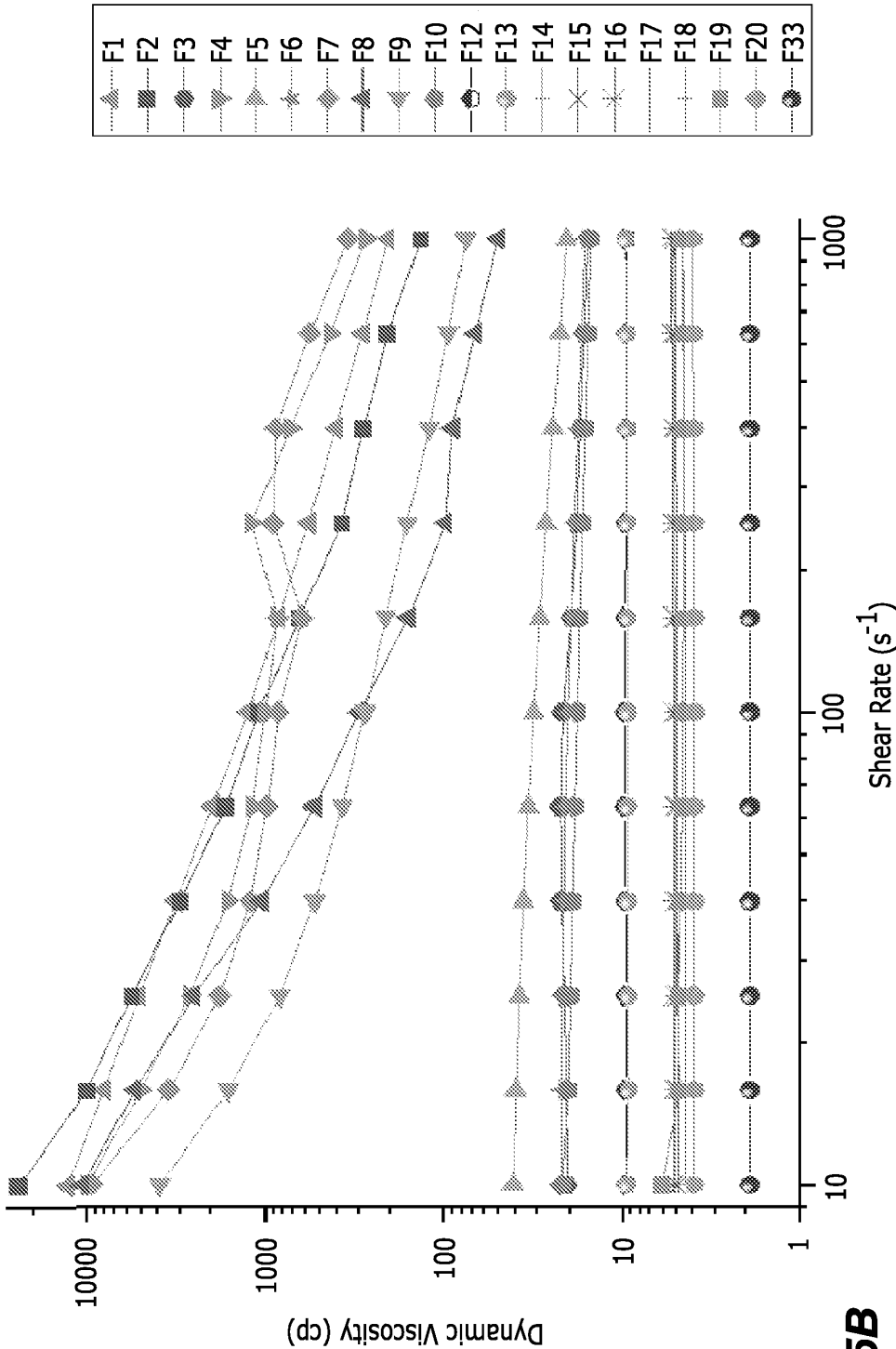


FIG. 5B

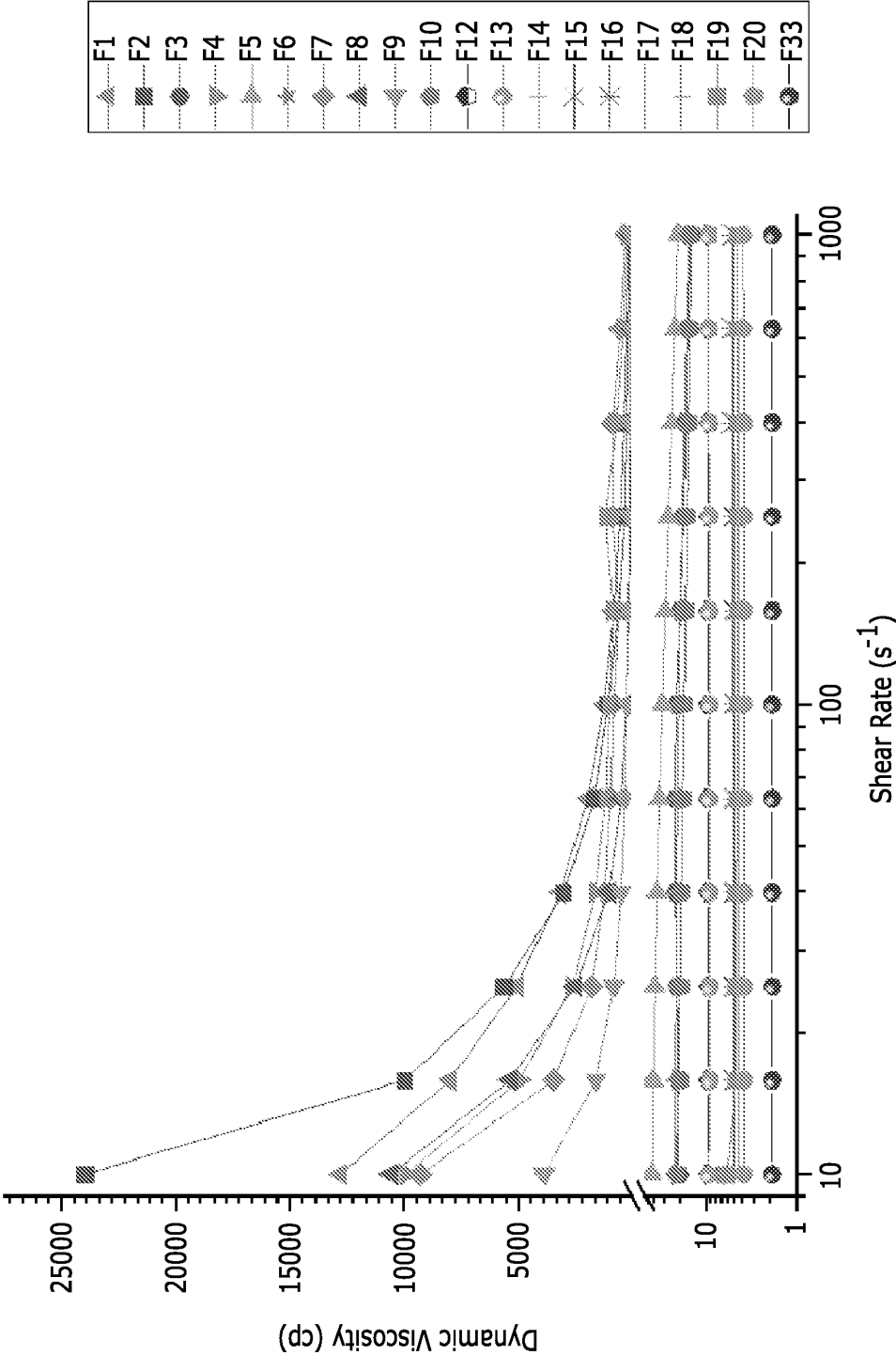


FIG. 5C

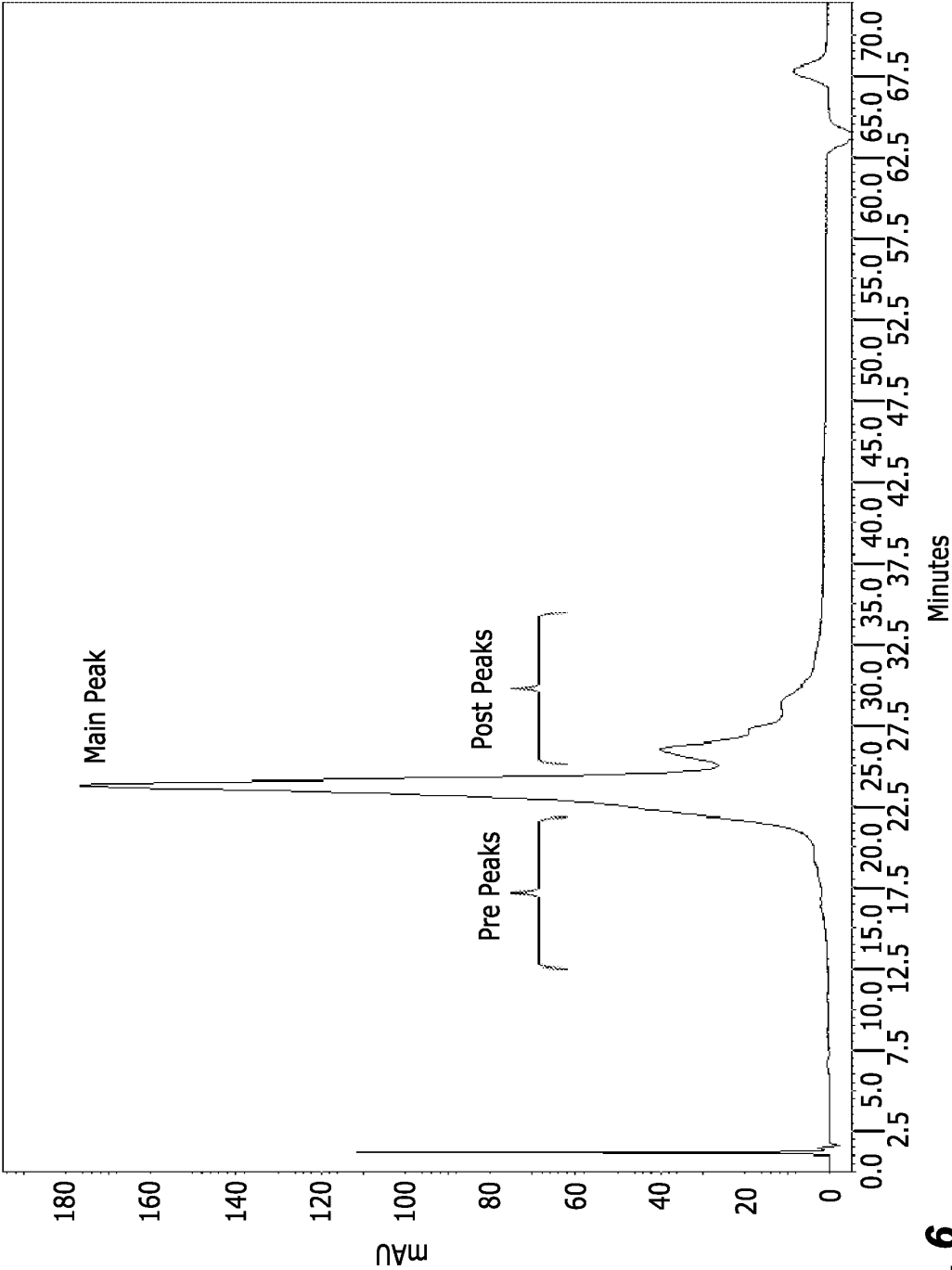


FIG. 6

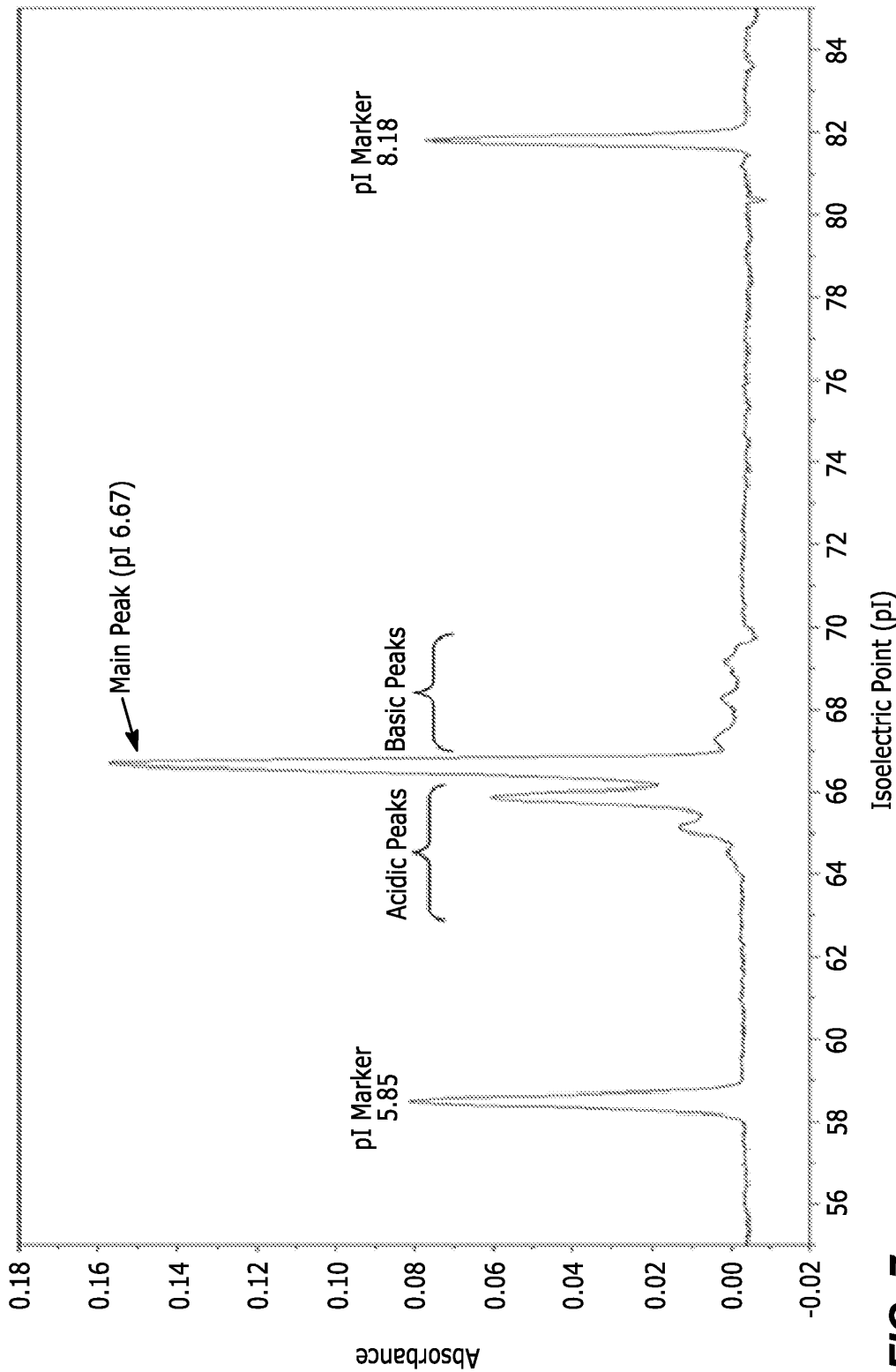
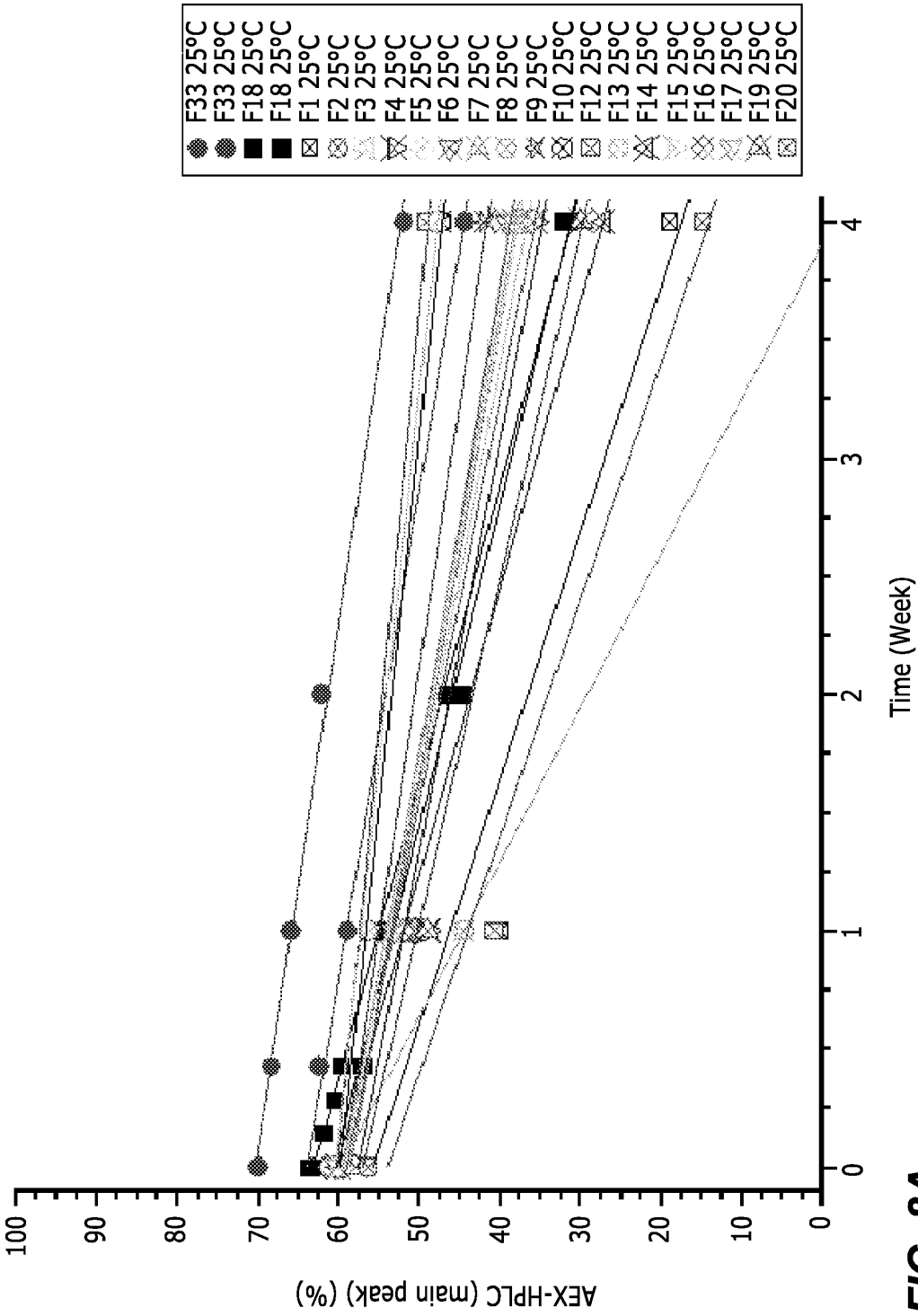


FIG. 7



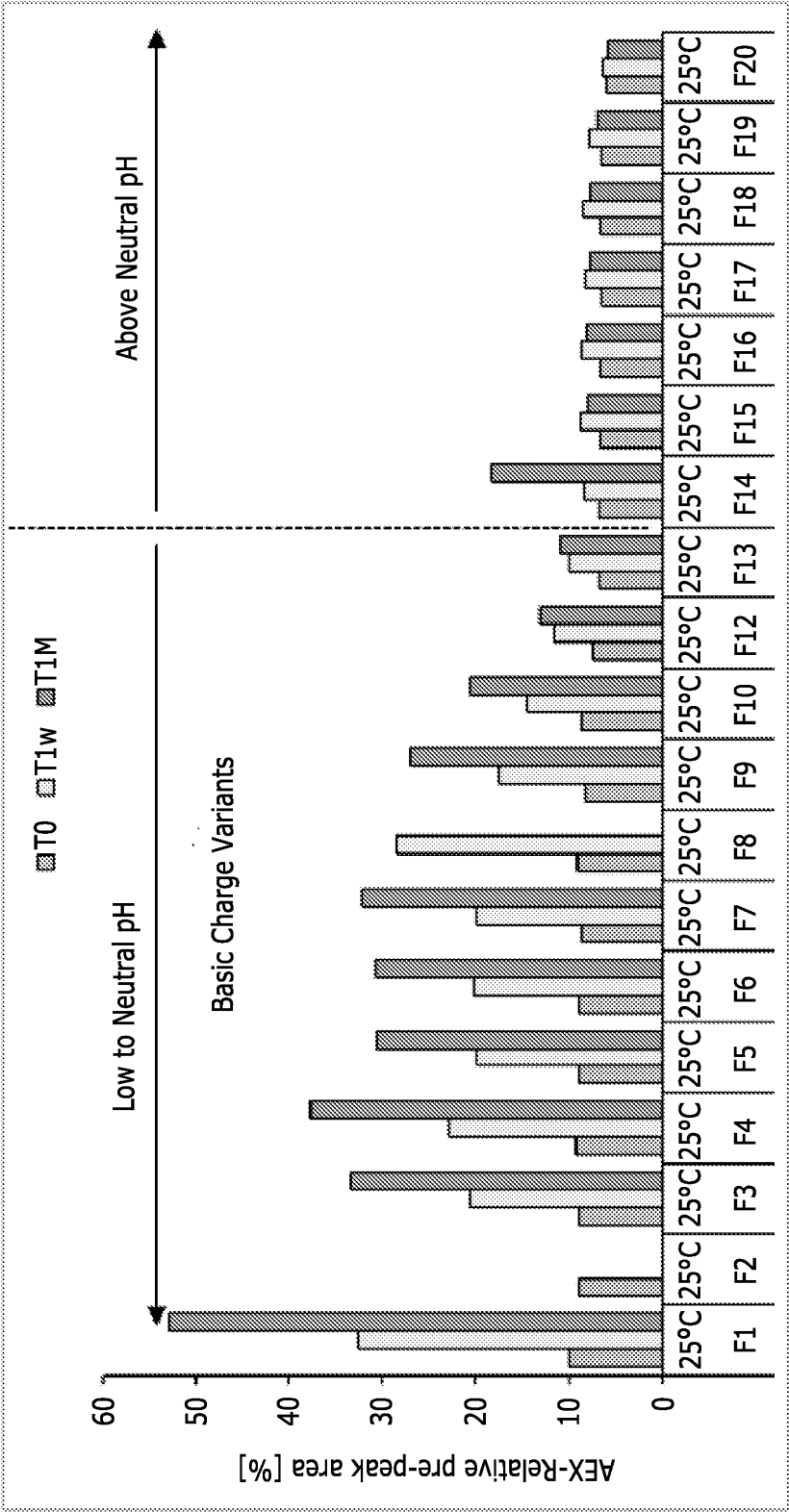


FIG. 8B

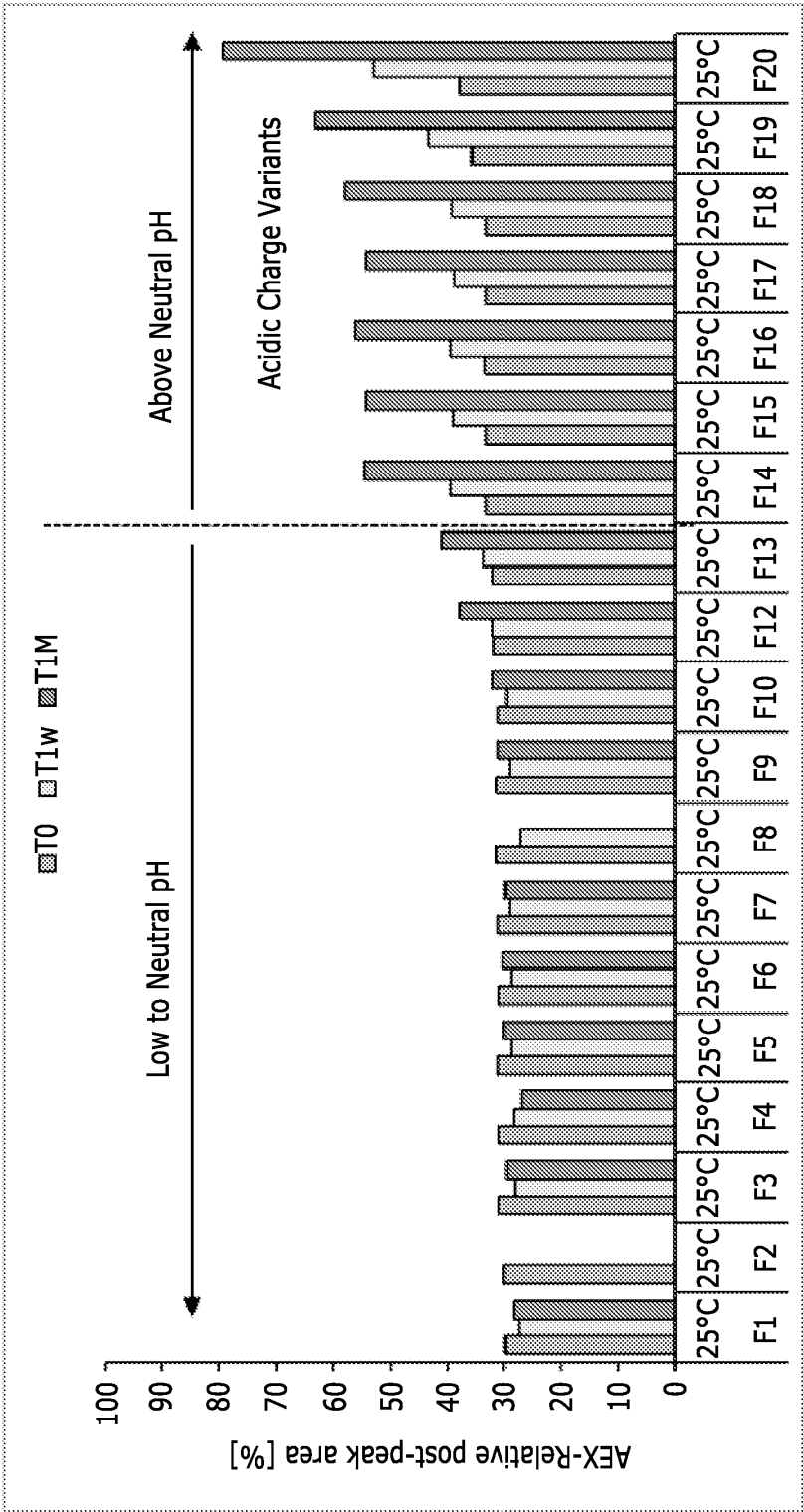


FIG. 8C

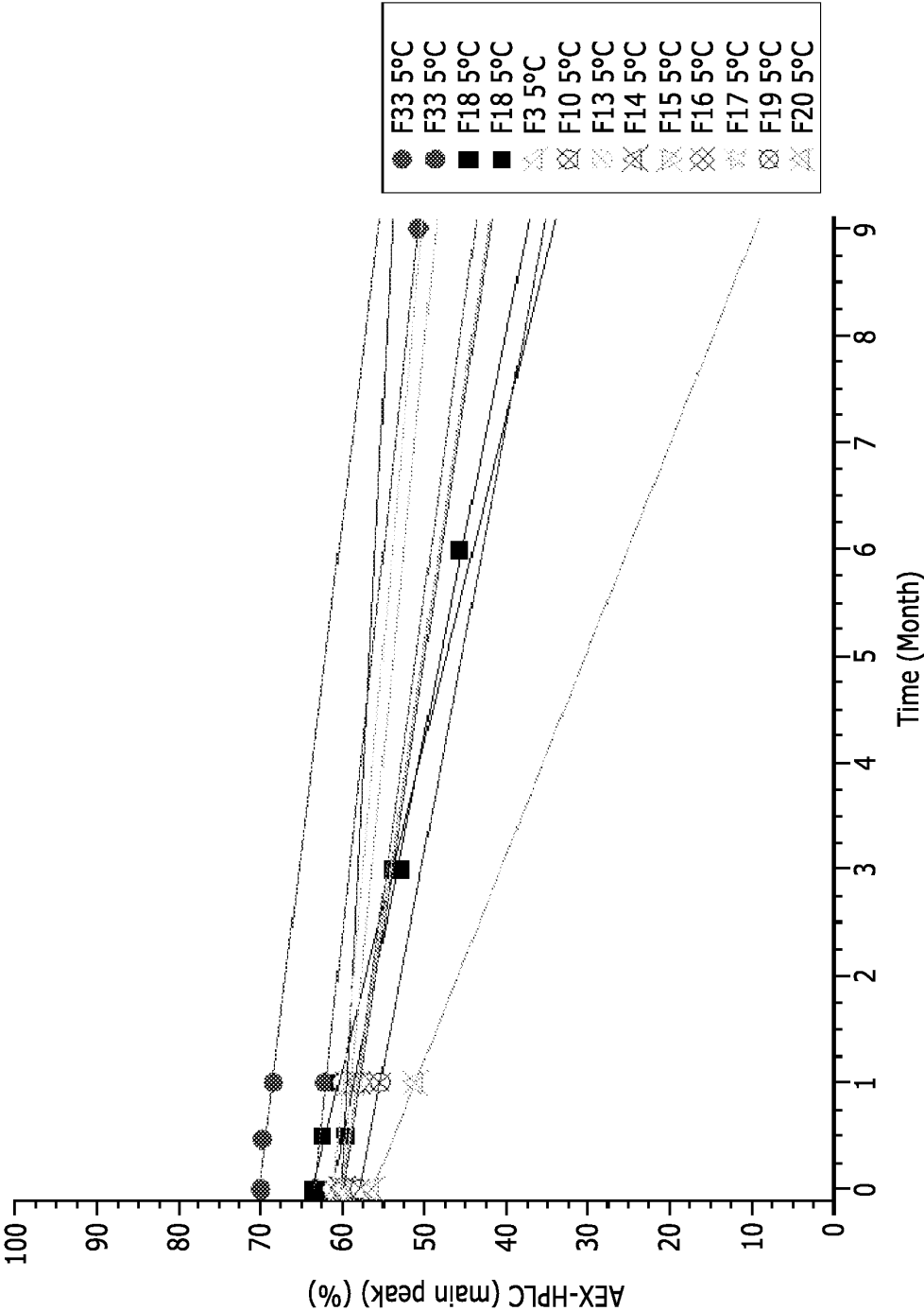


FIG. 9

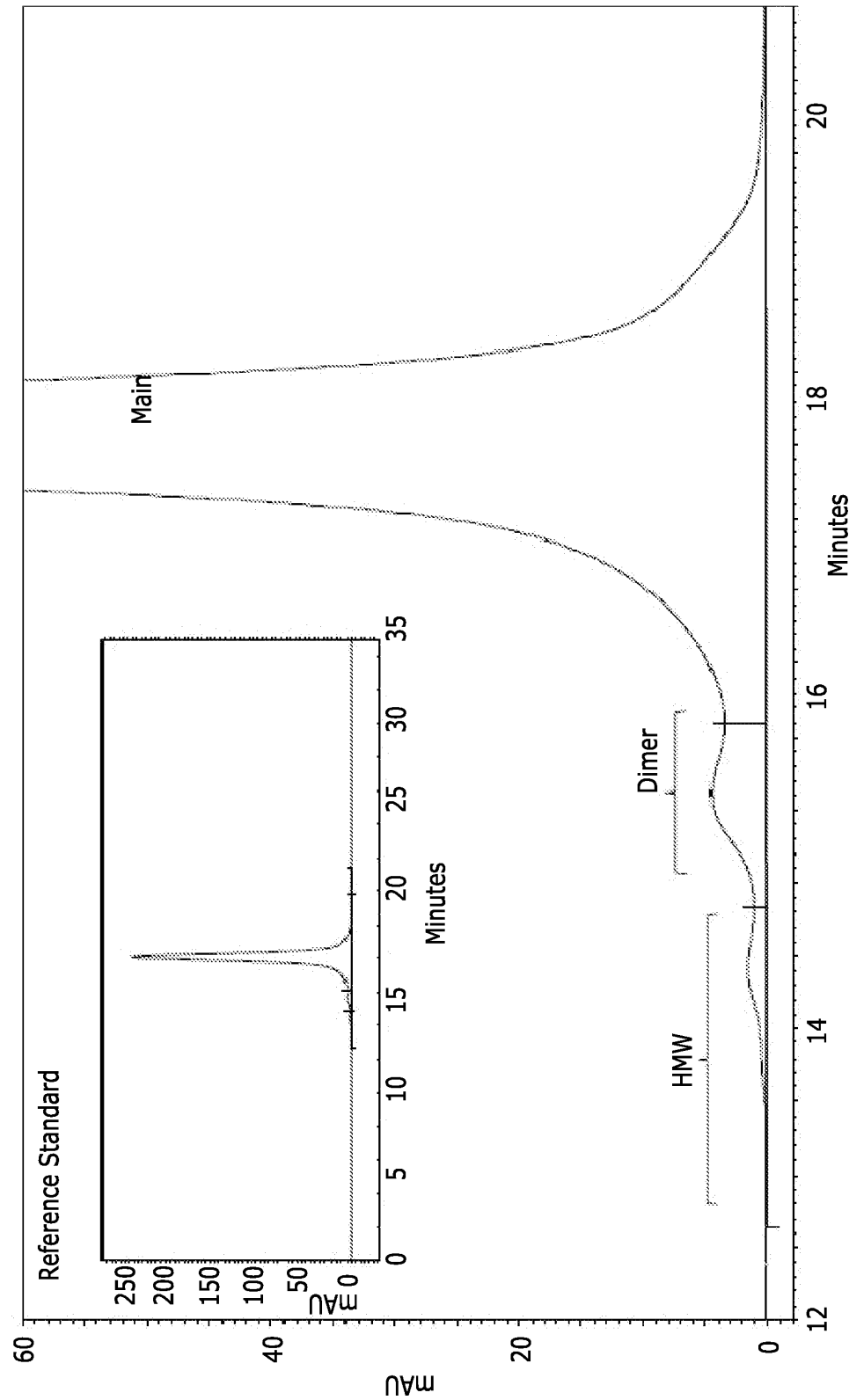


FIG. 10

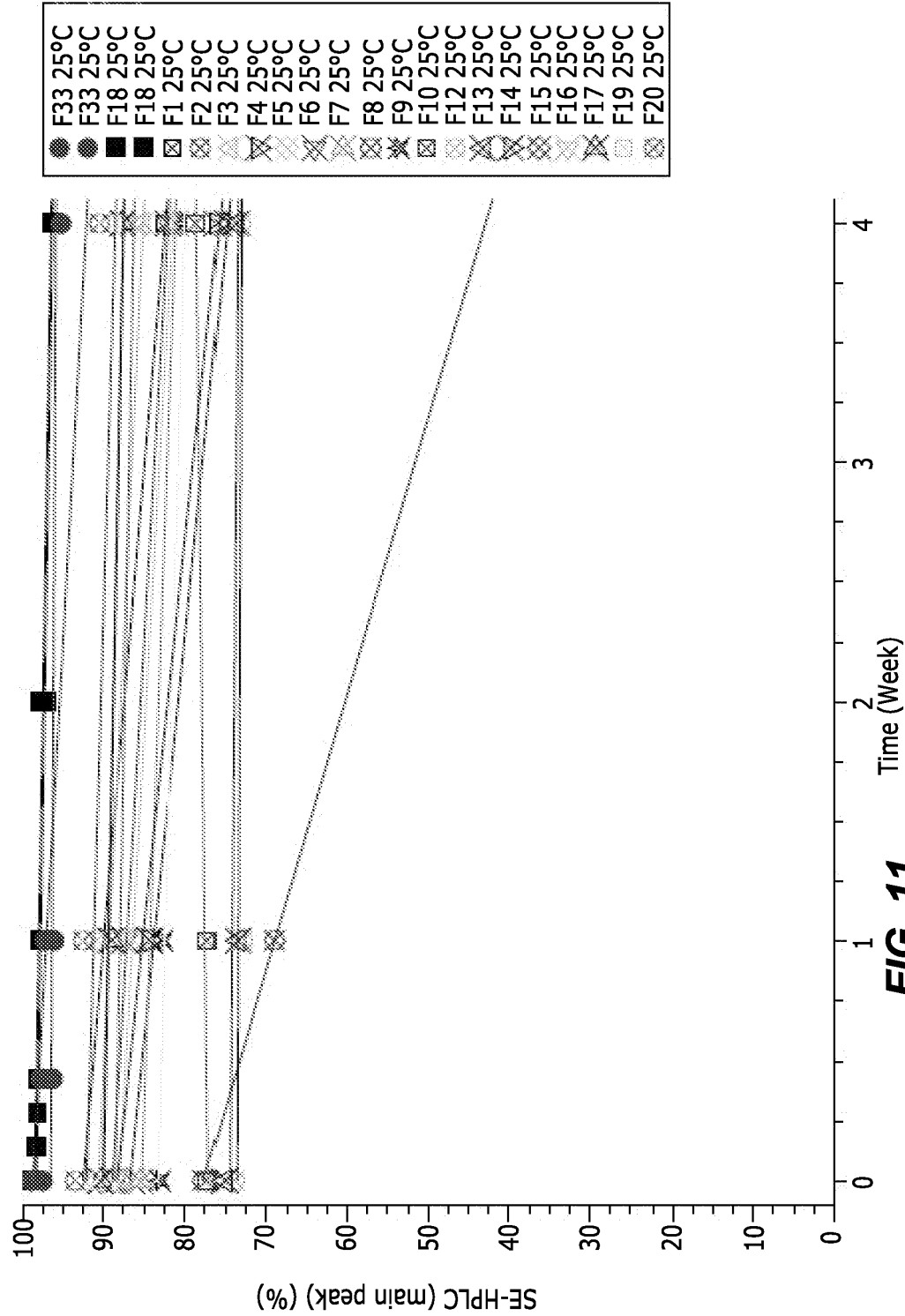


FIG. 11

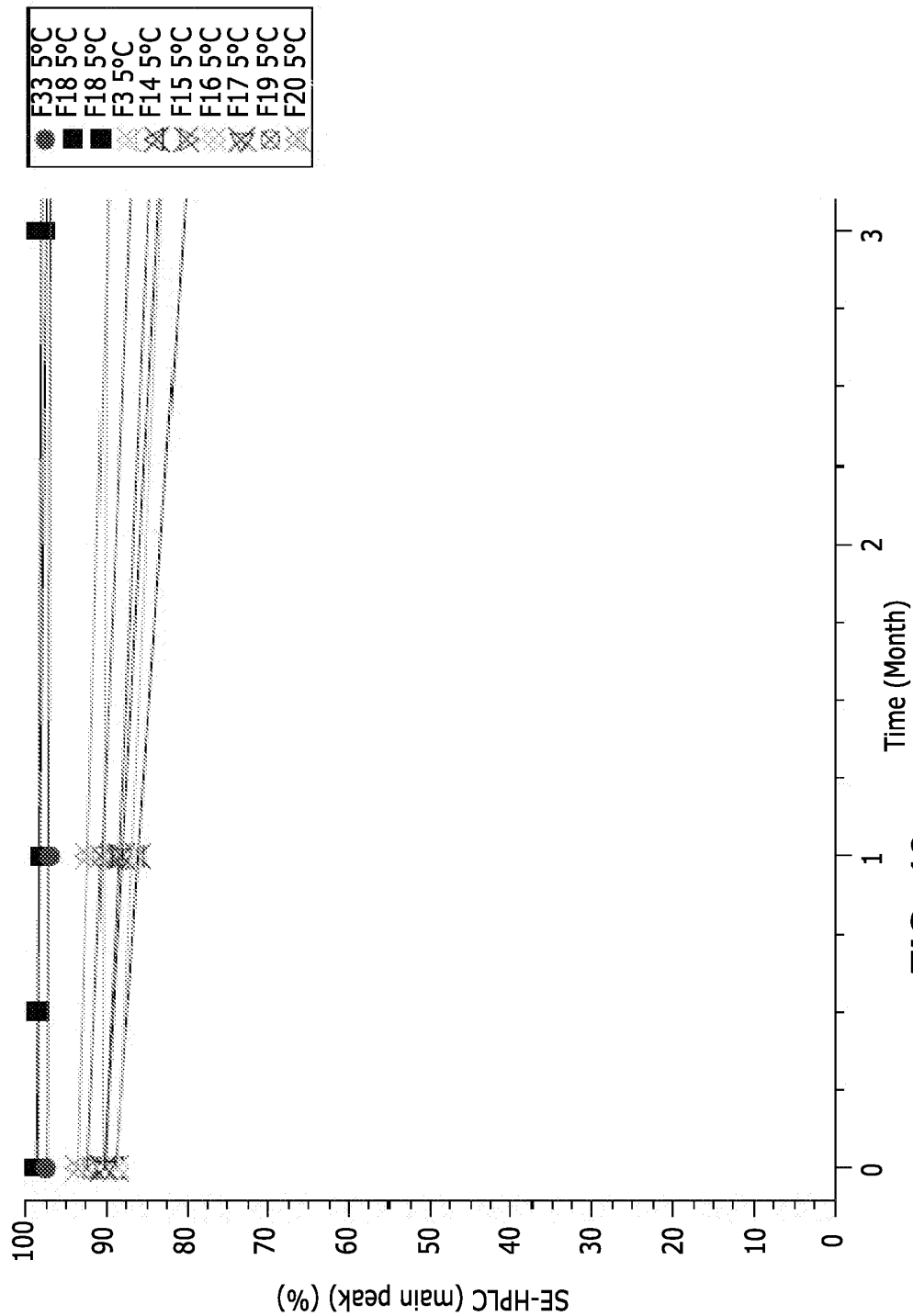


FIG. 12

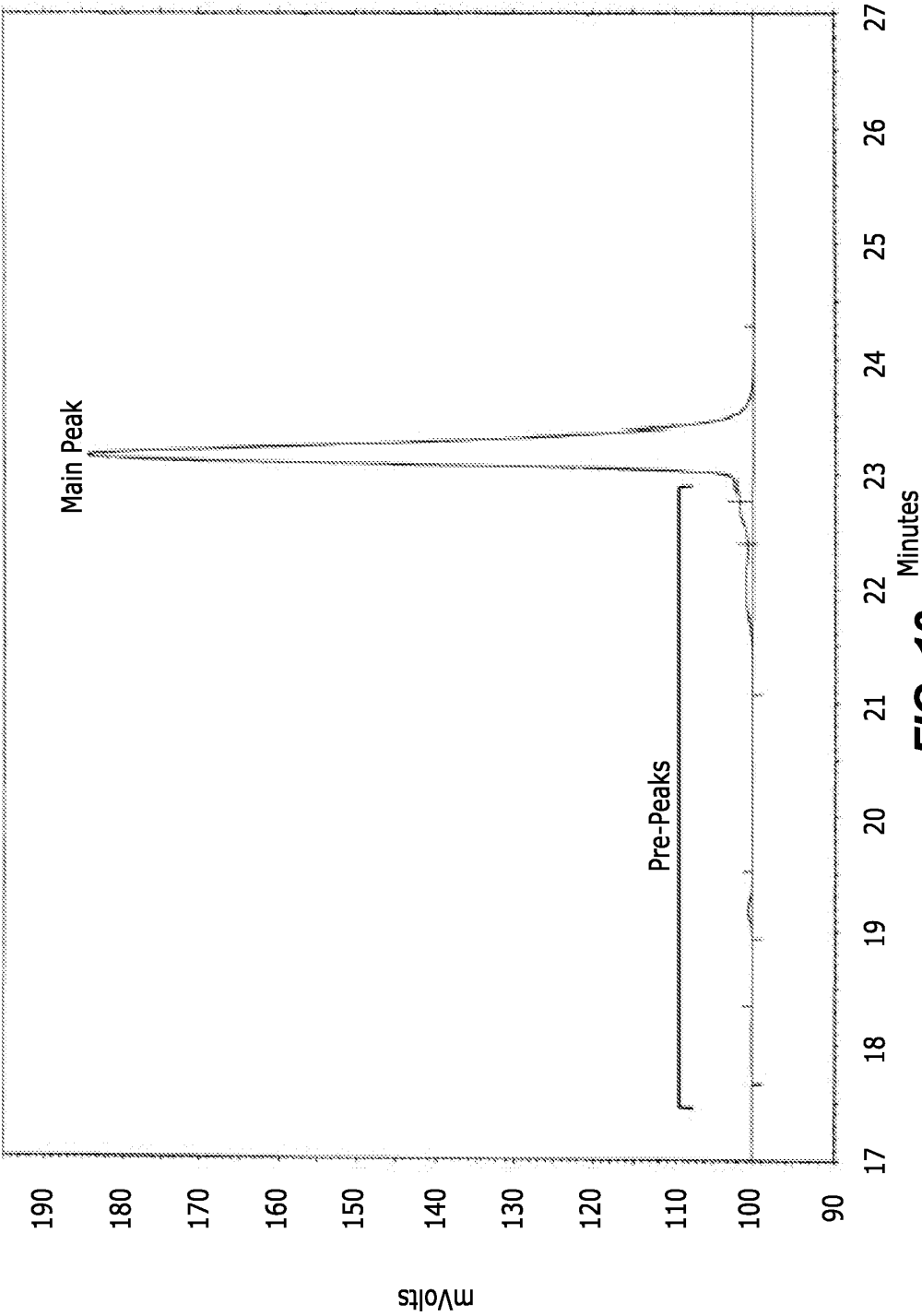


FIG. 13

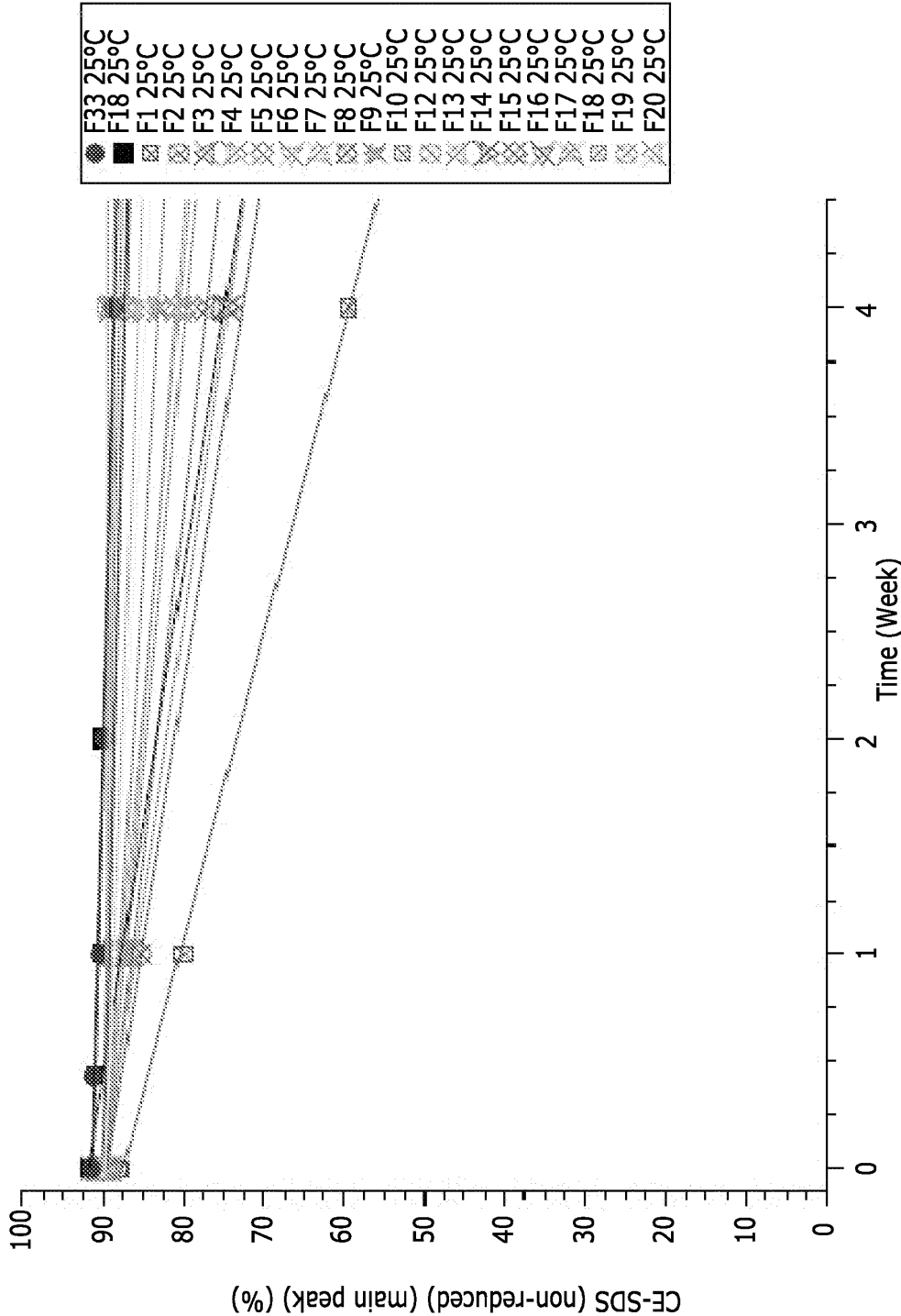
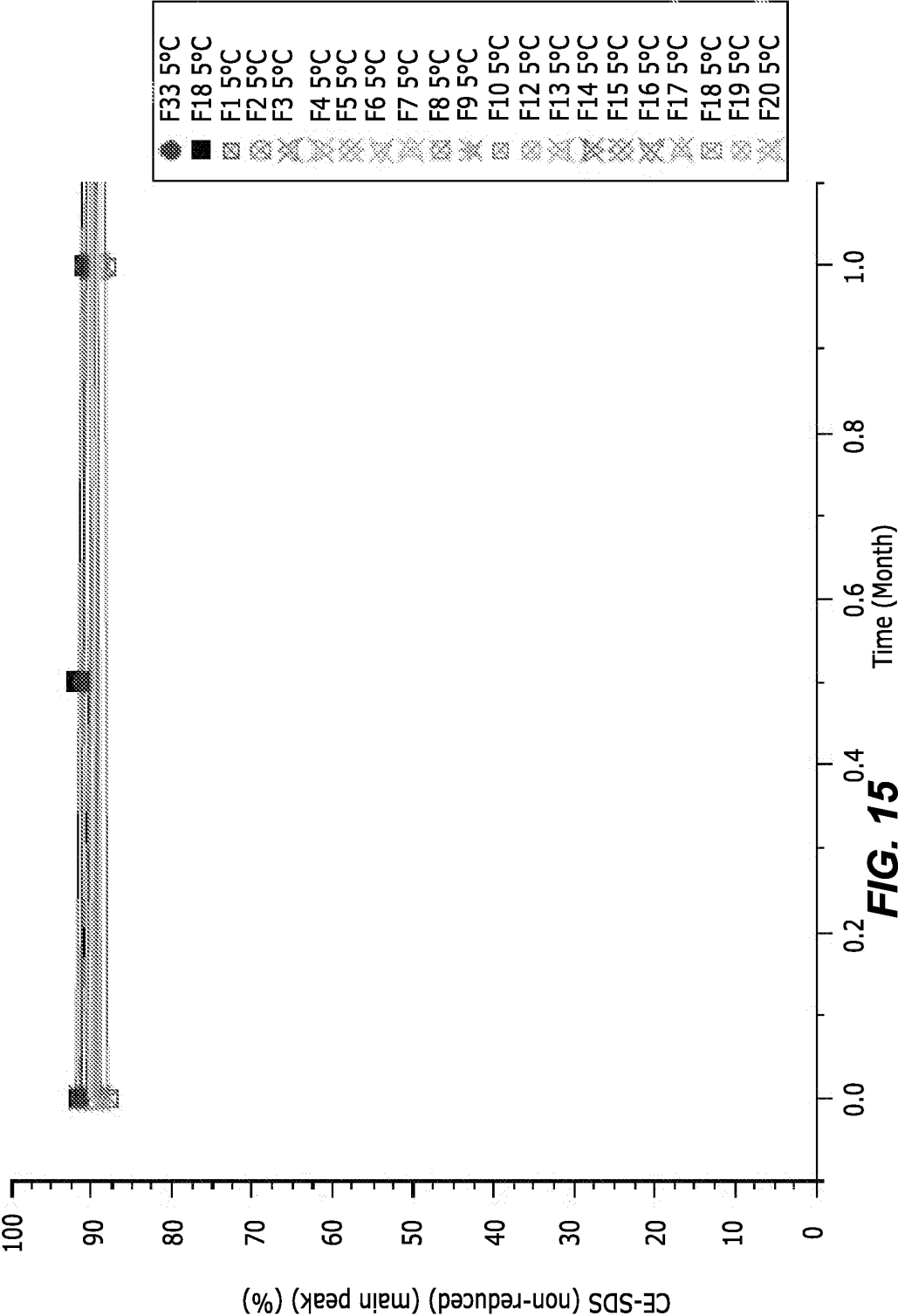


FIG. 14



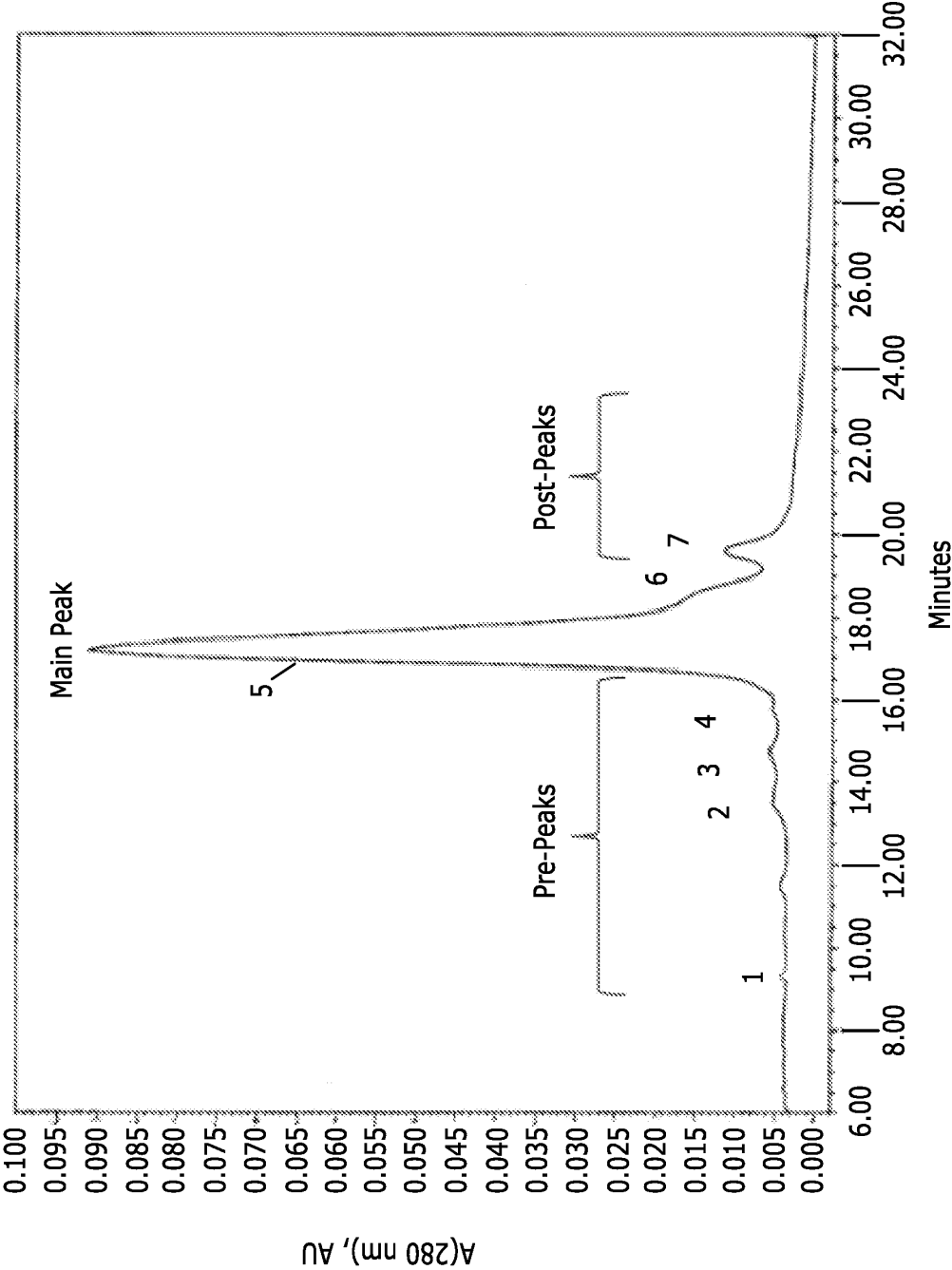


FIG. 16

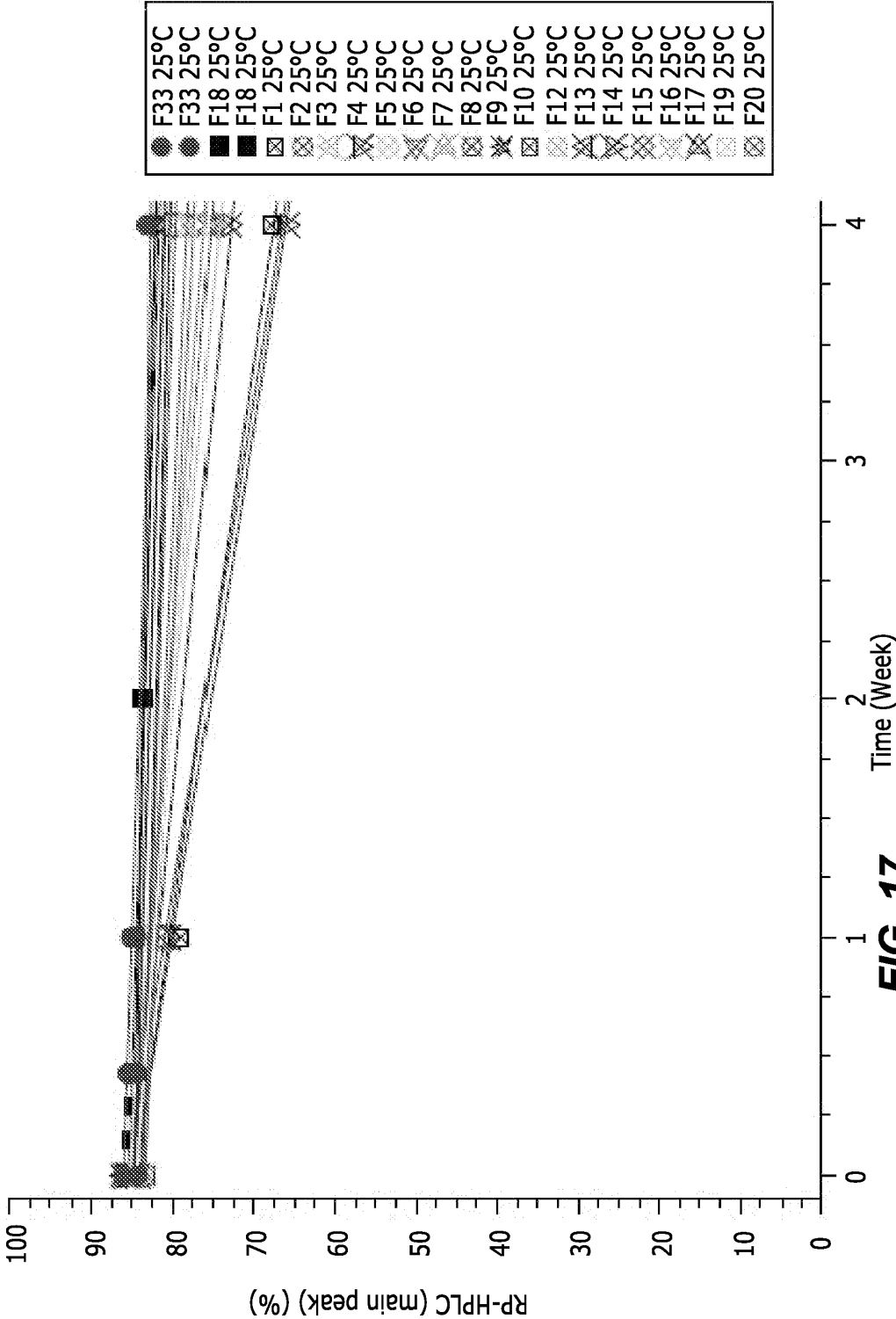
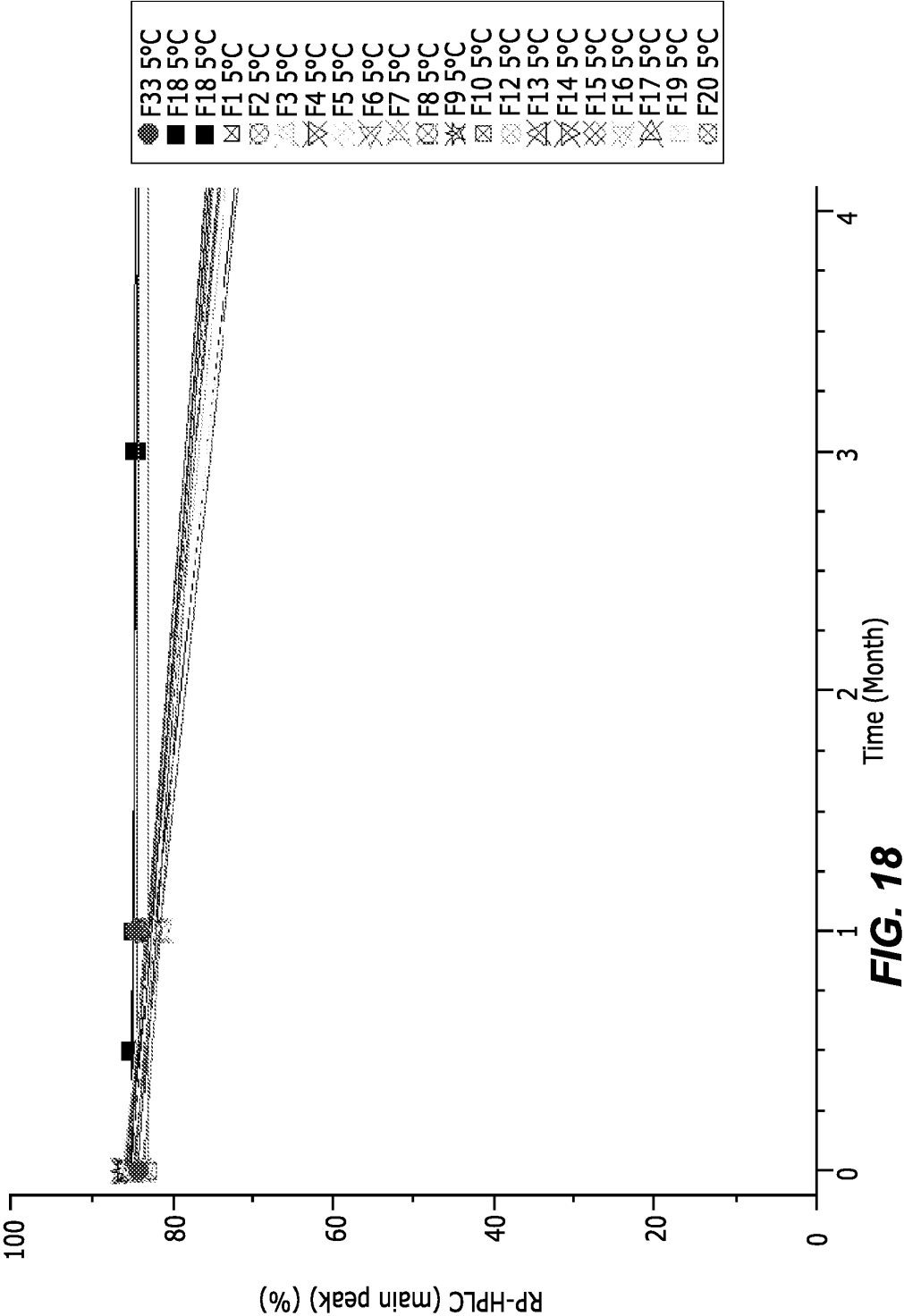


FIG. 17



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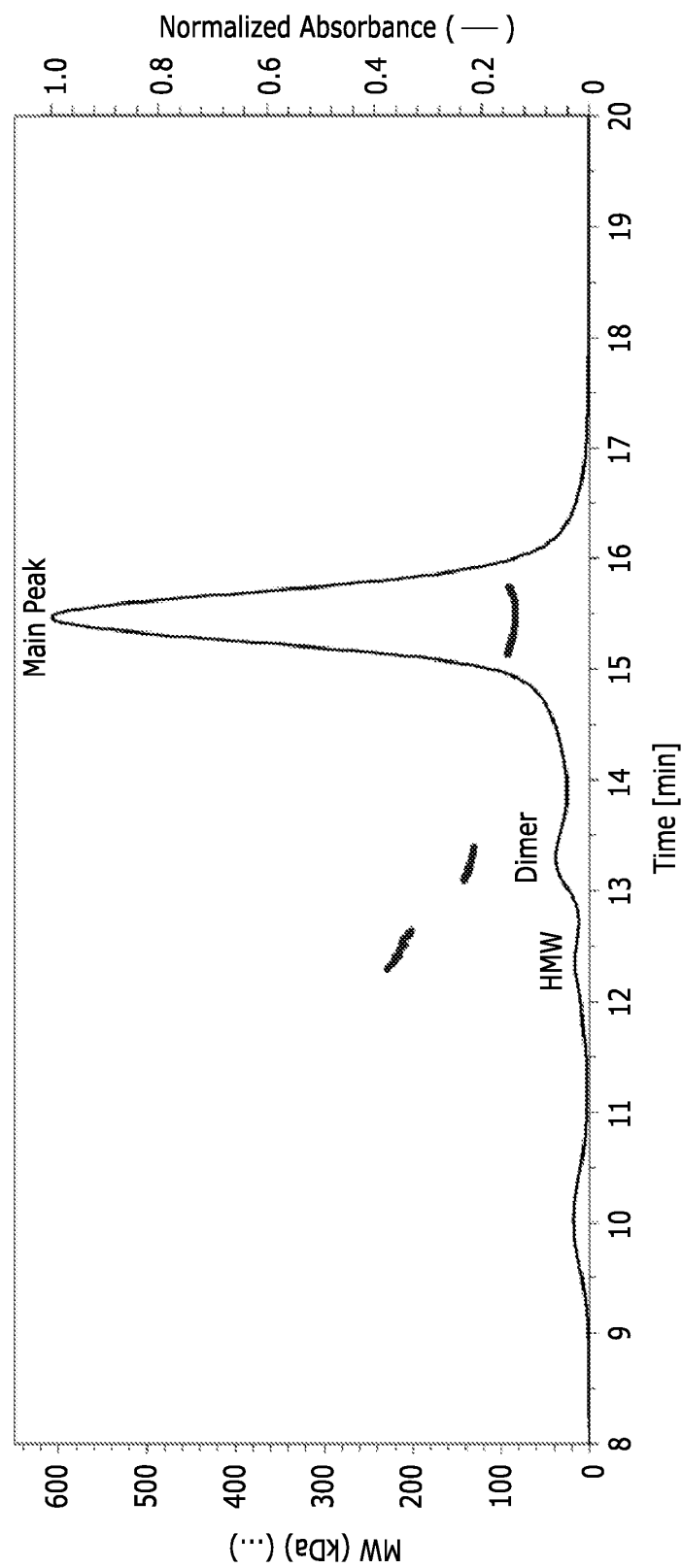


FIG. 19

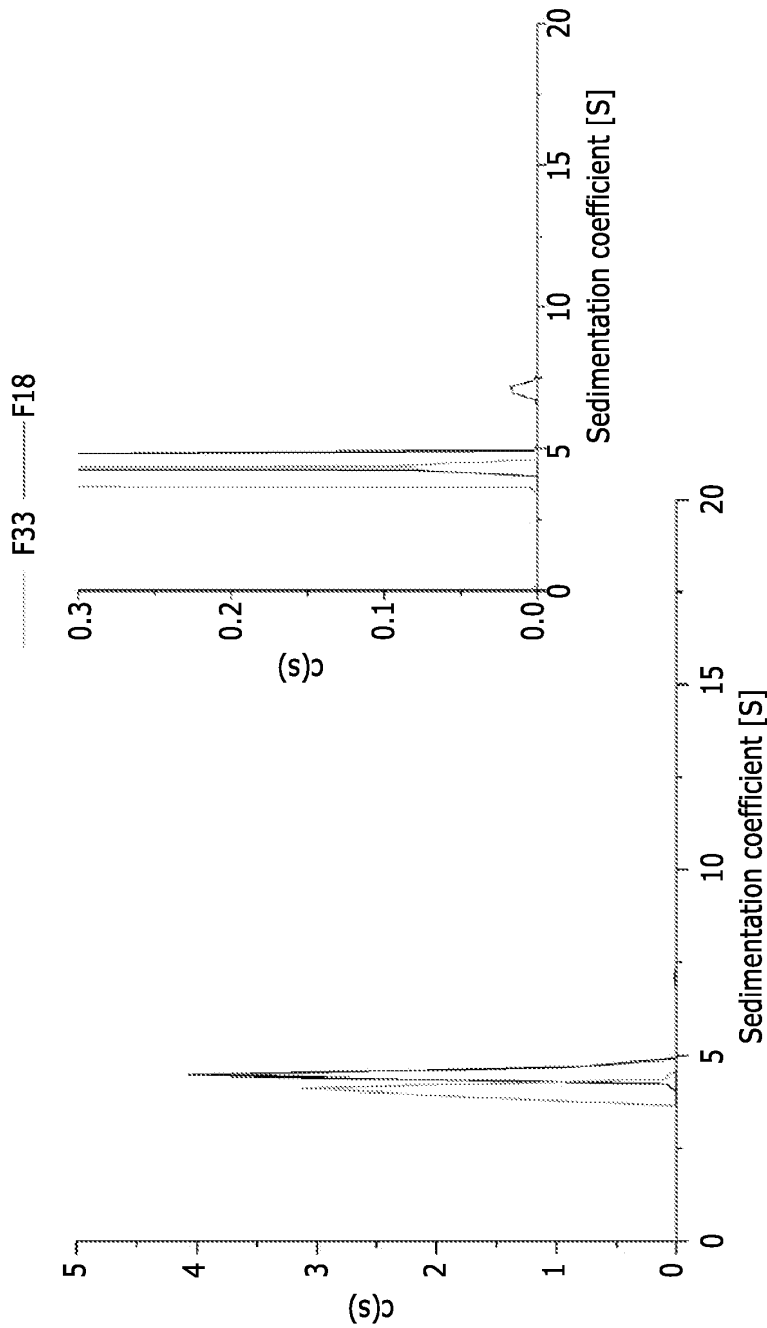


FIG. 20

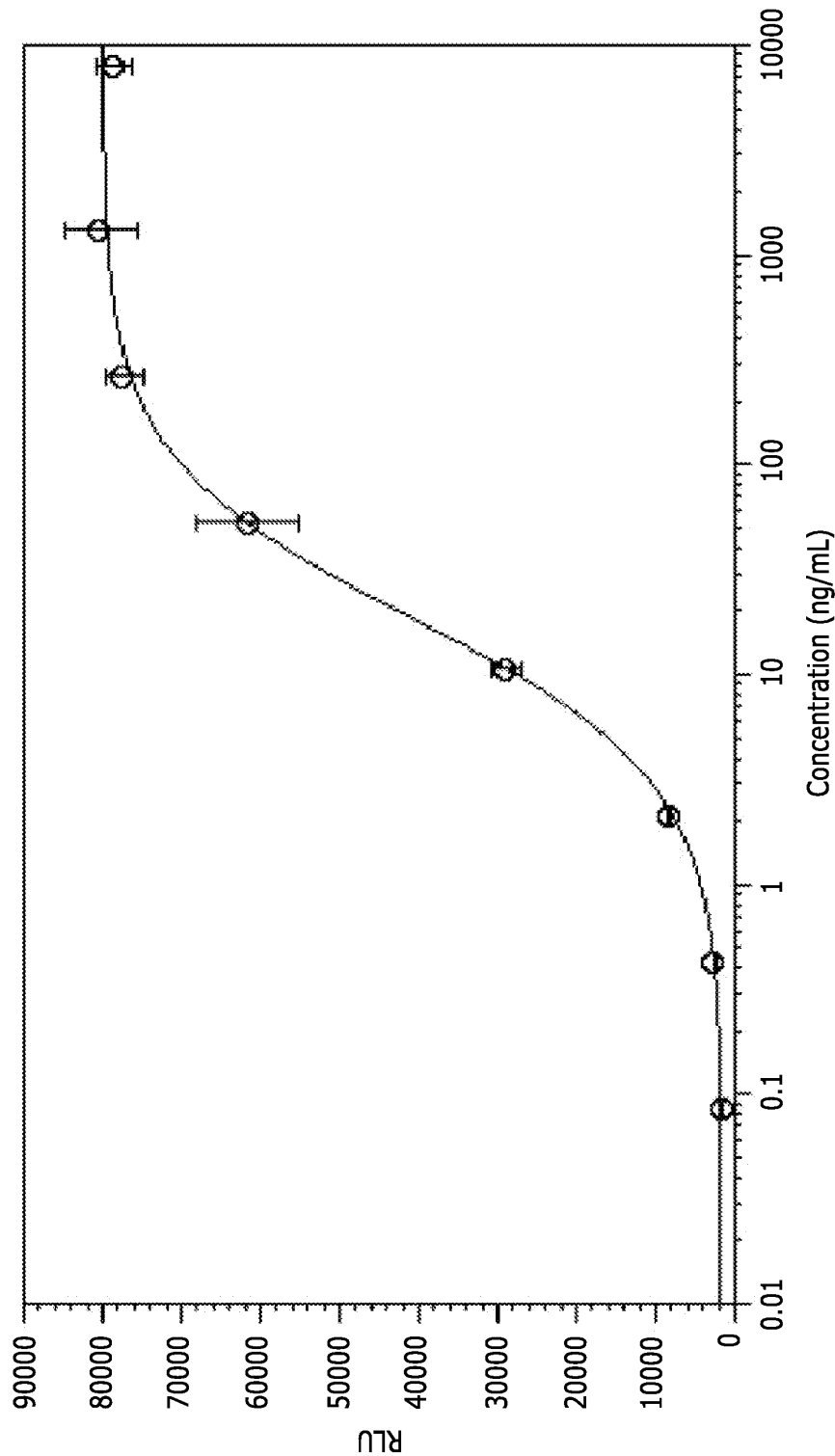


FIG. 21

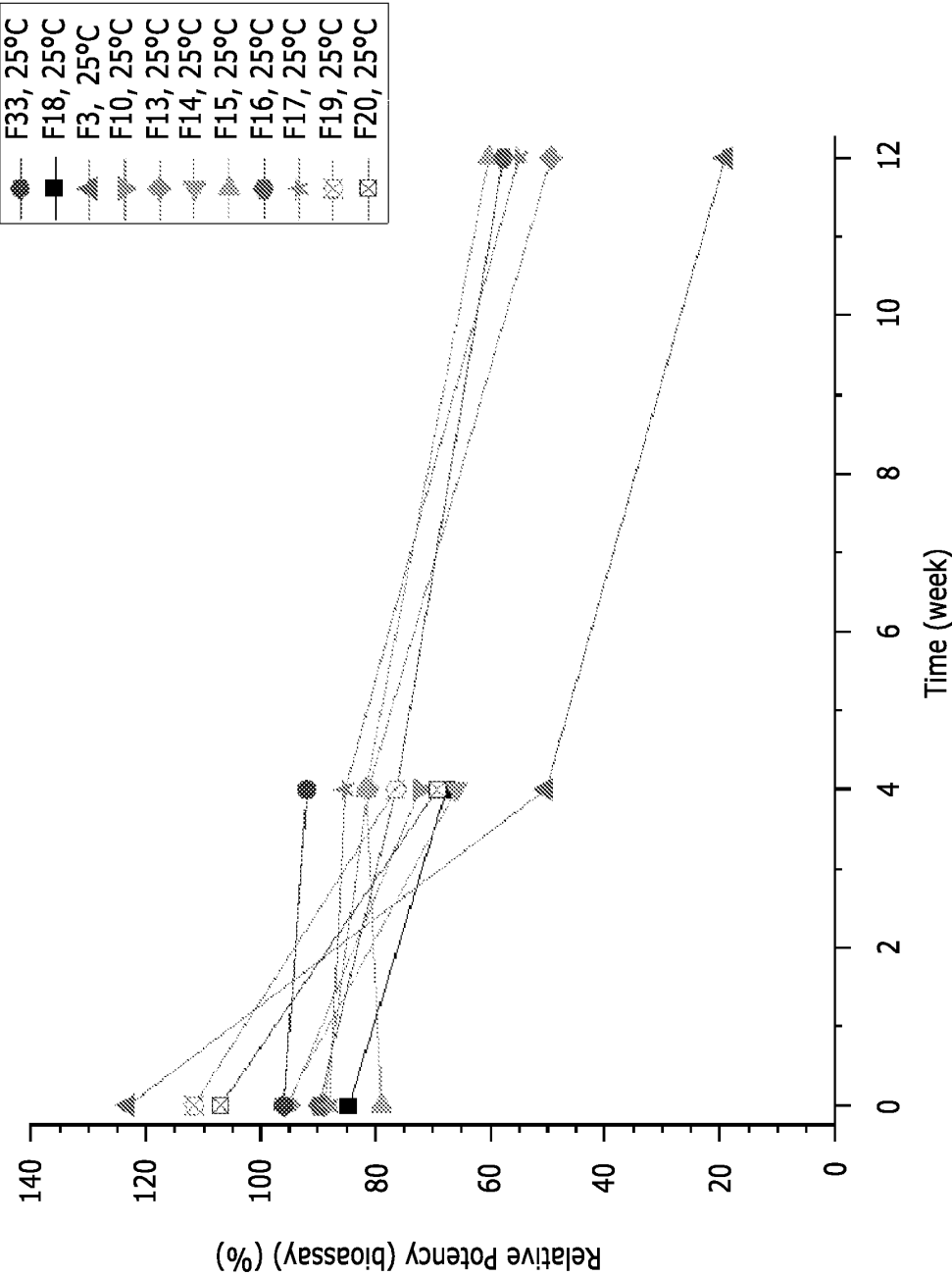
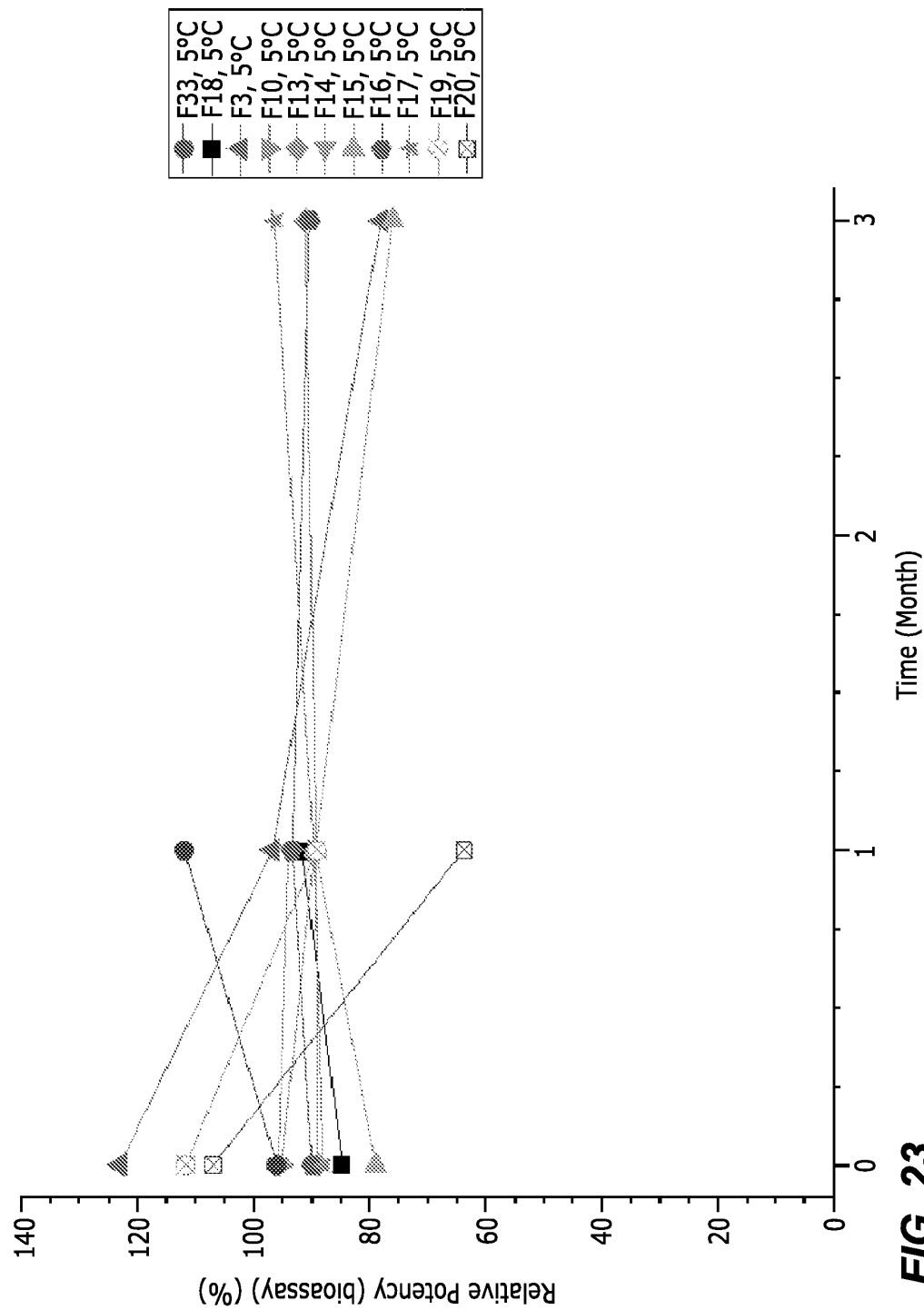


FIG. 22



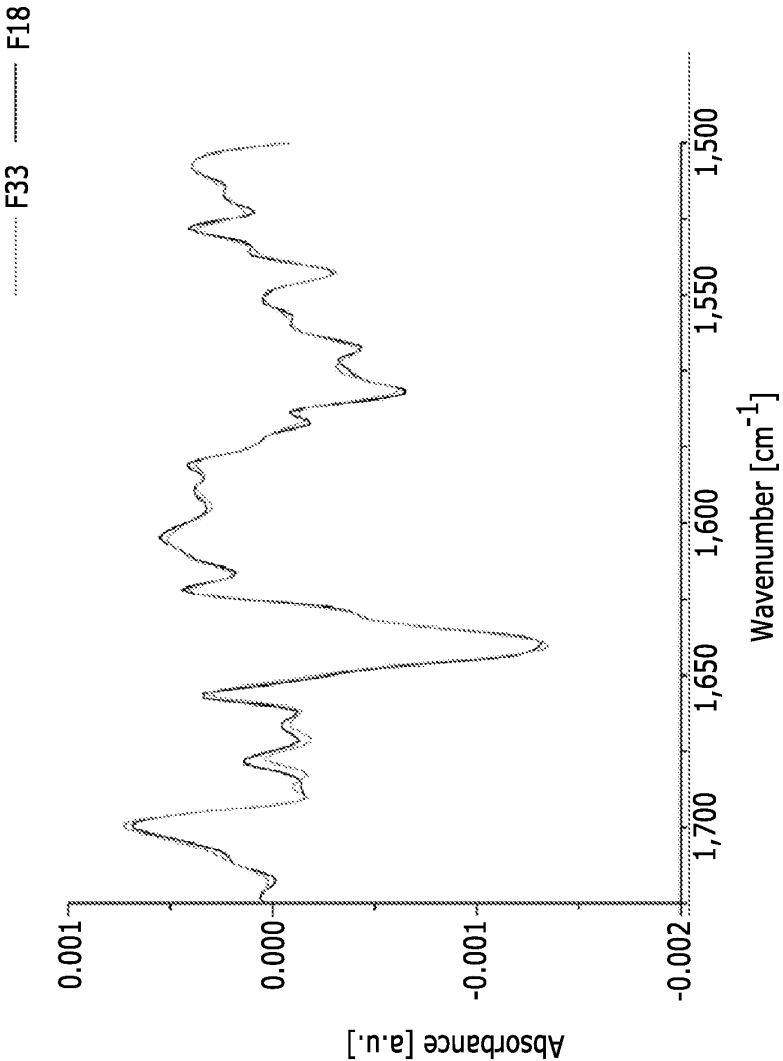


FIG. 24

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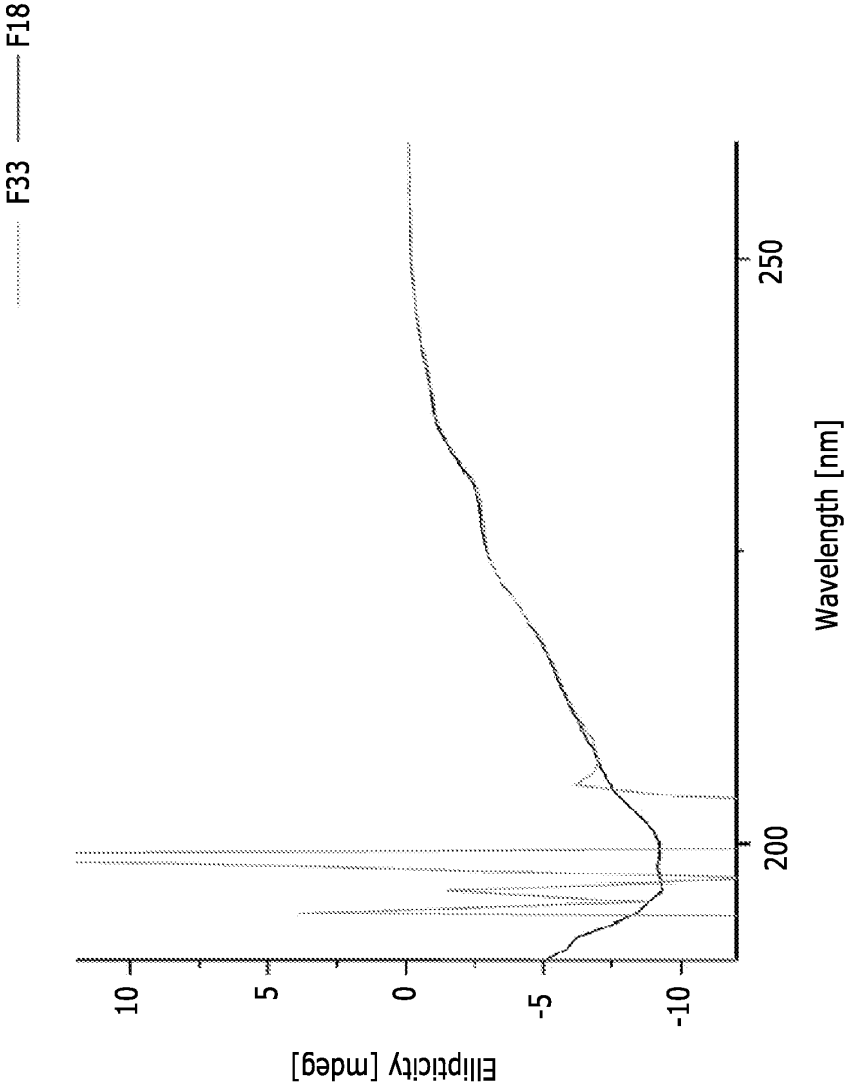


FIG. 25

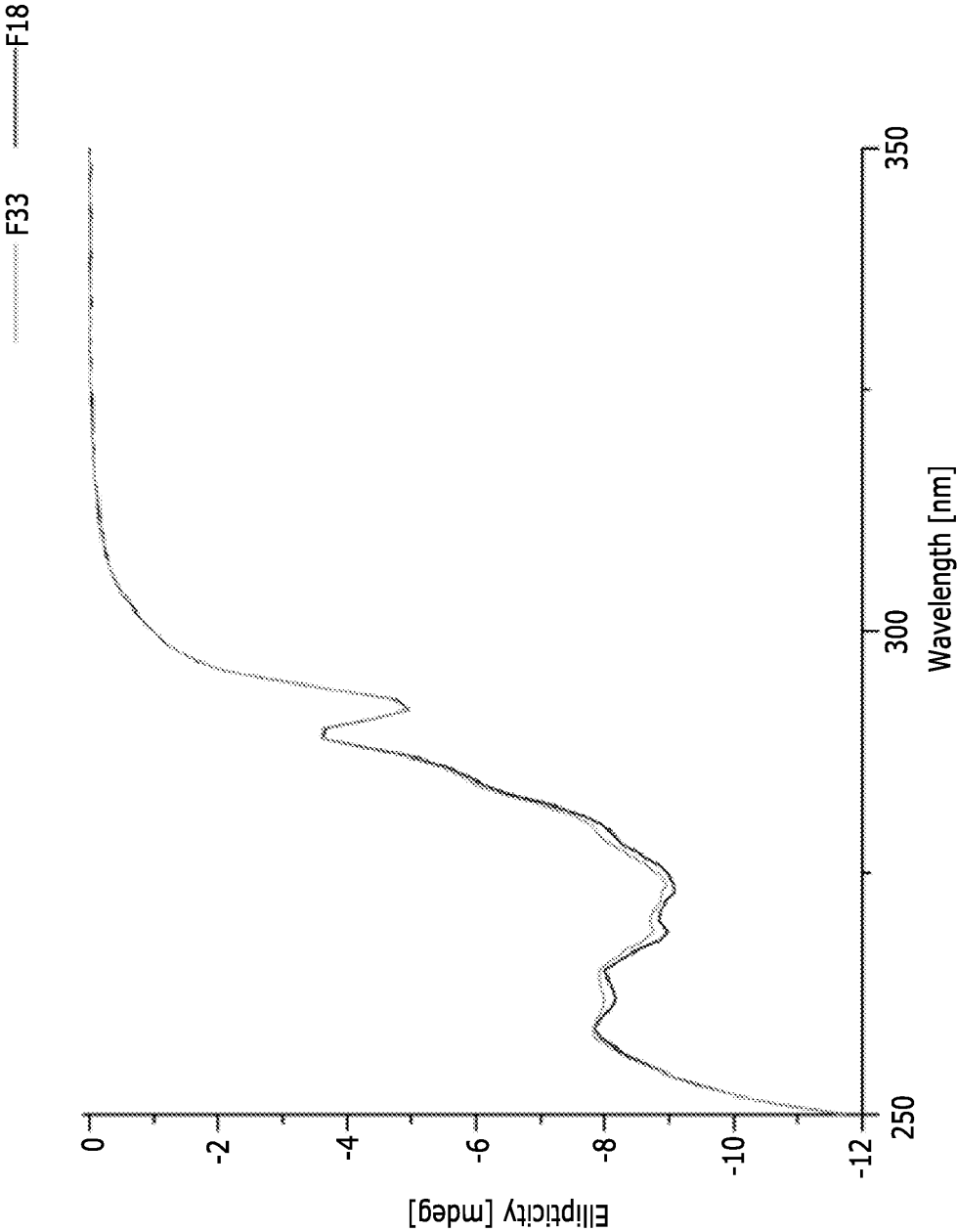


FIG. 26

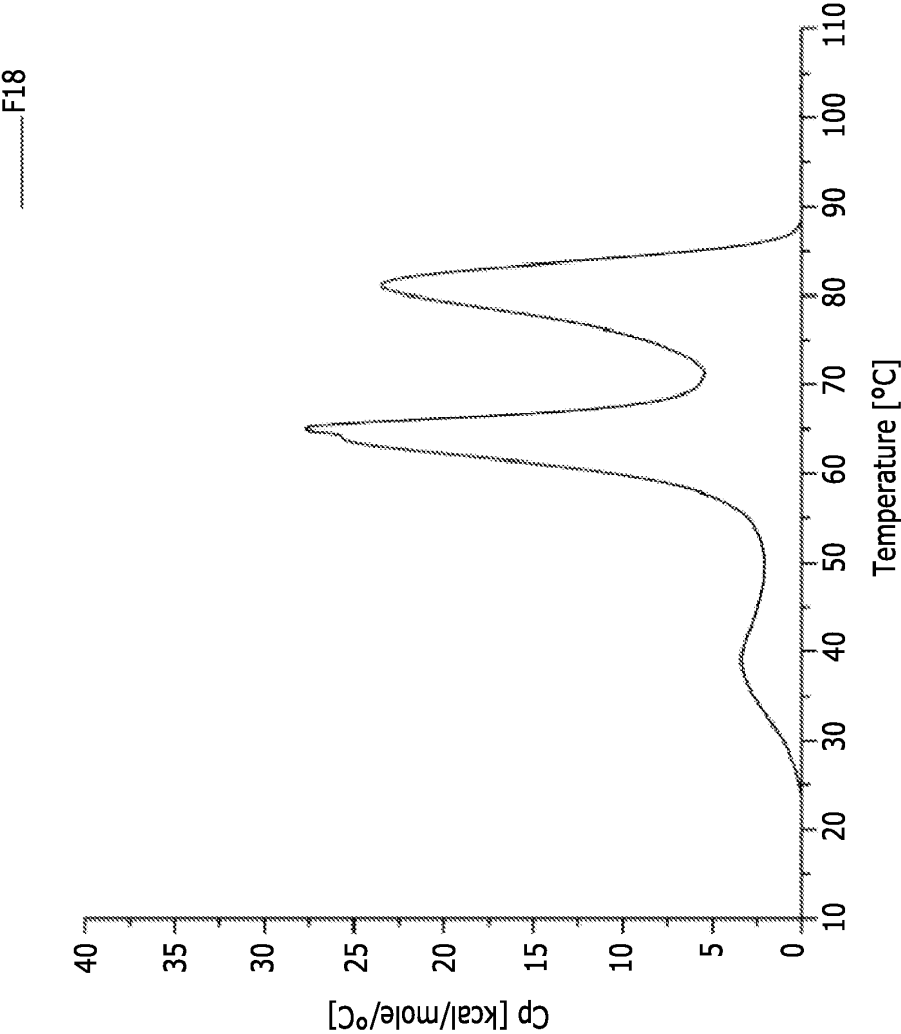


FIG. 27A

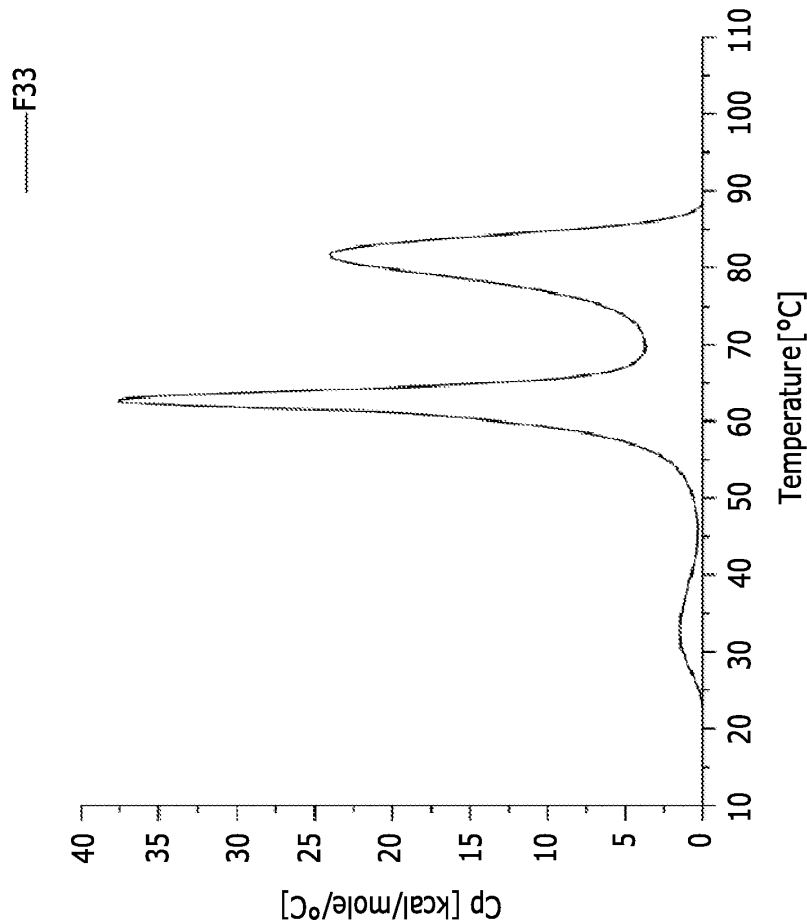


FIG. 27B

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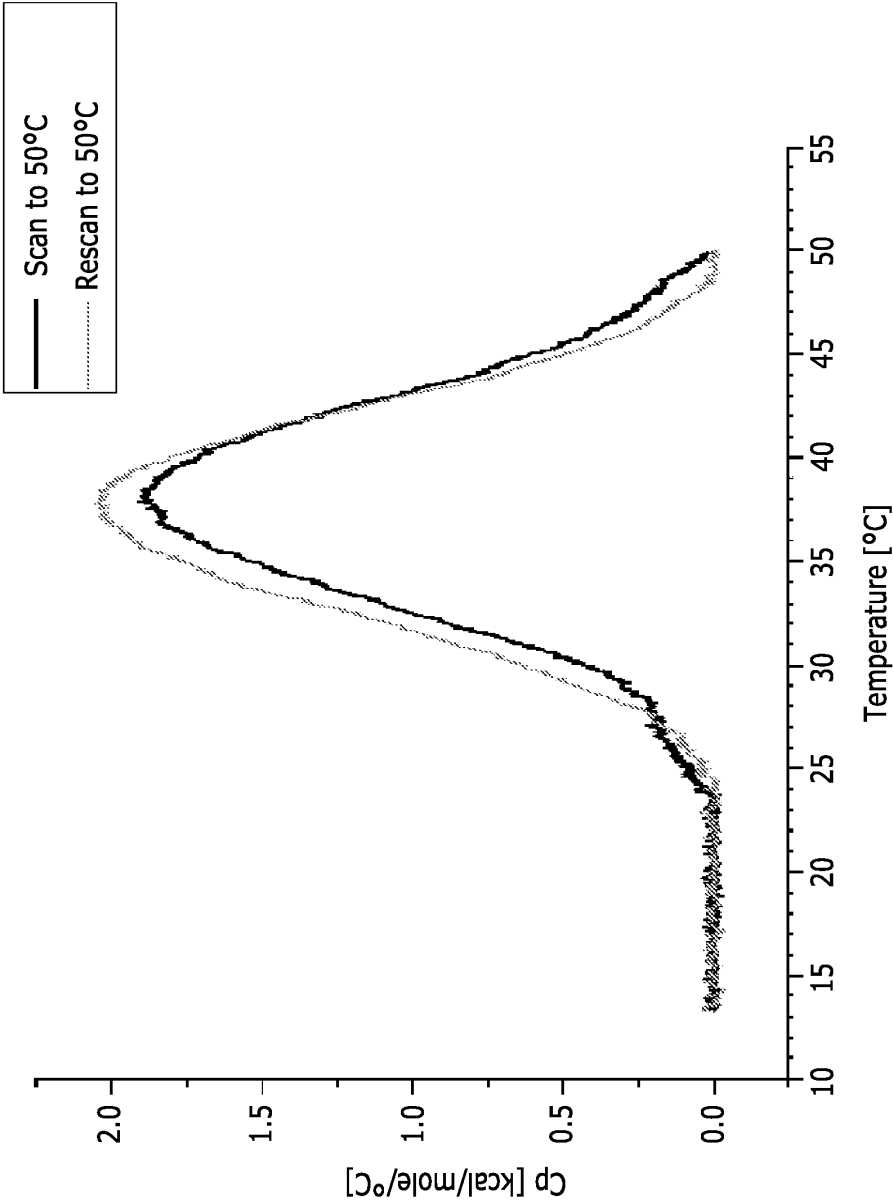


FIG. 28

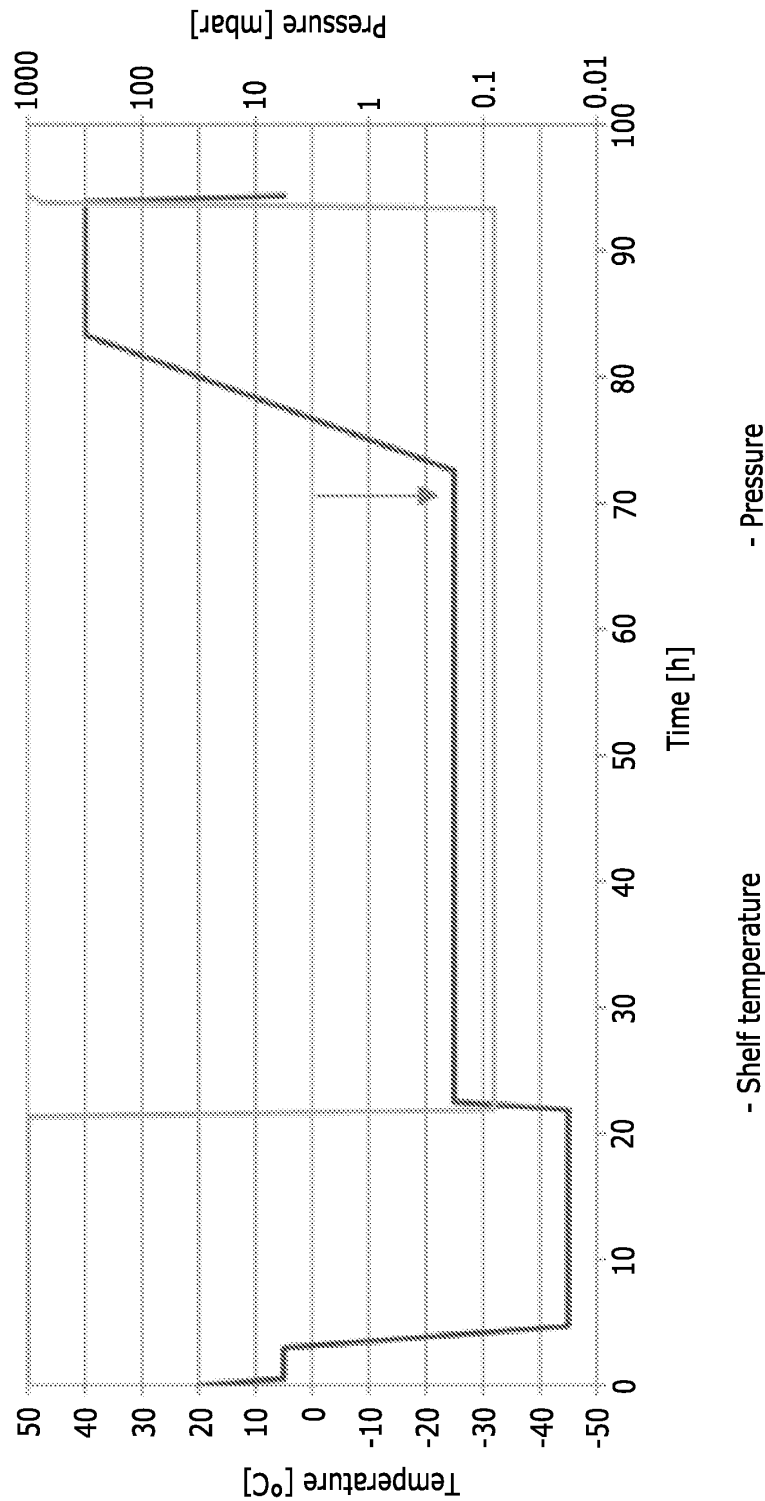


FIG. 29

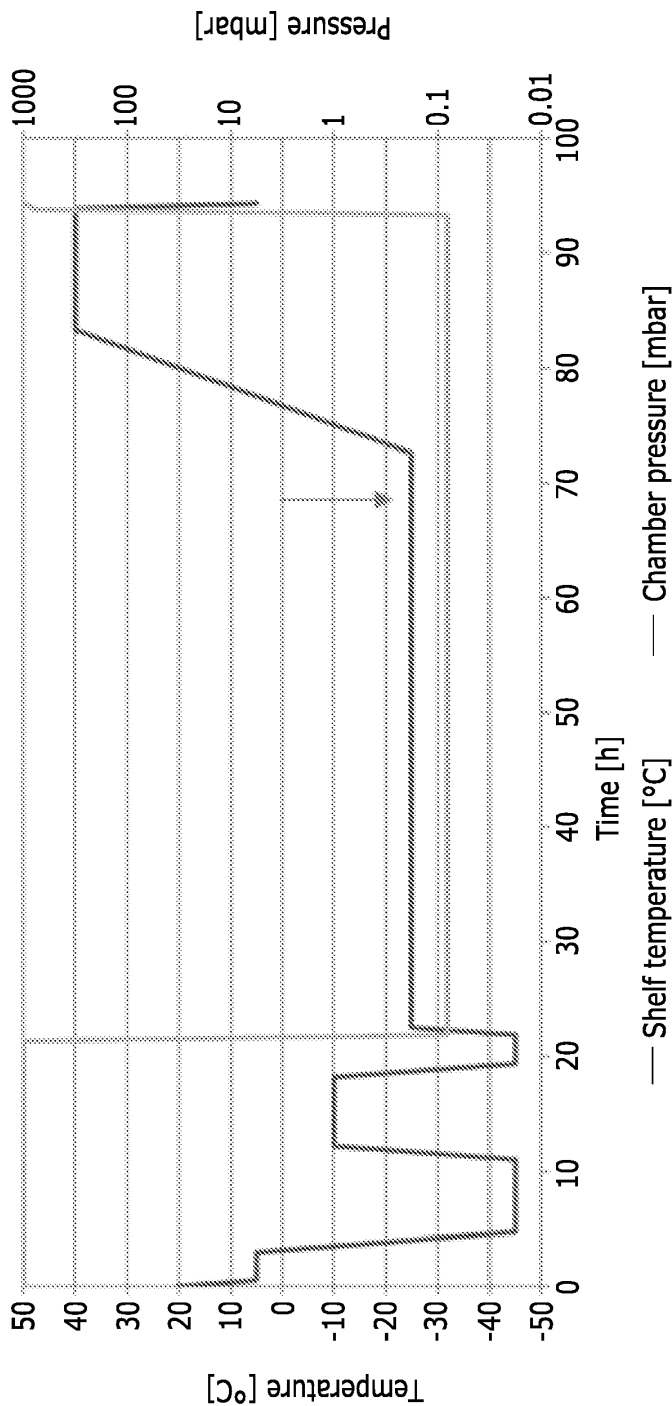


FIG. 30A

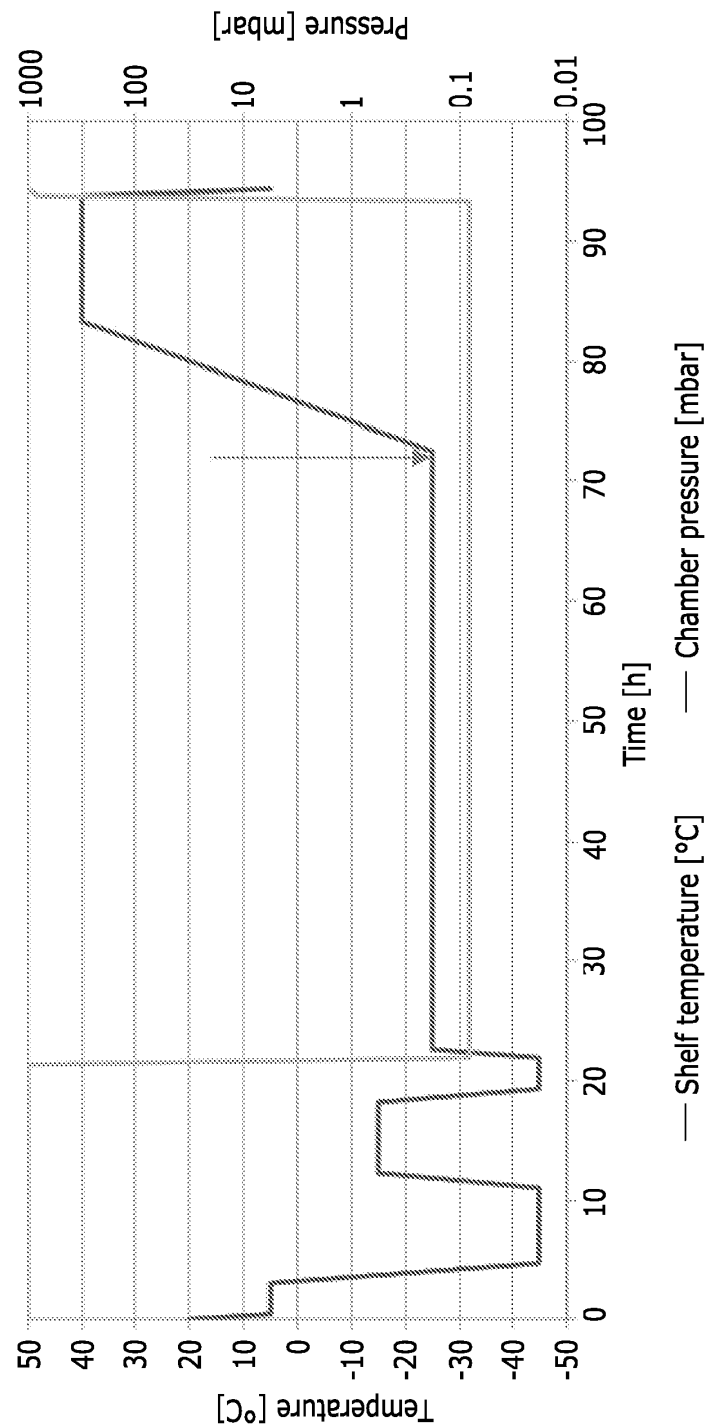


FIG. 30B

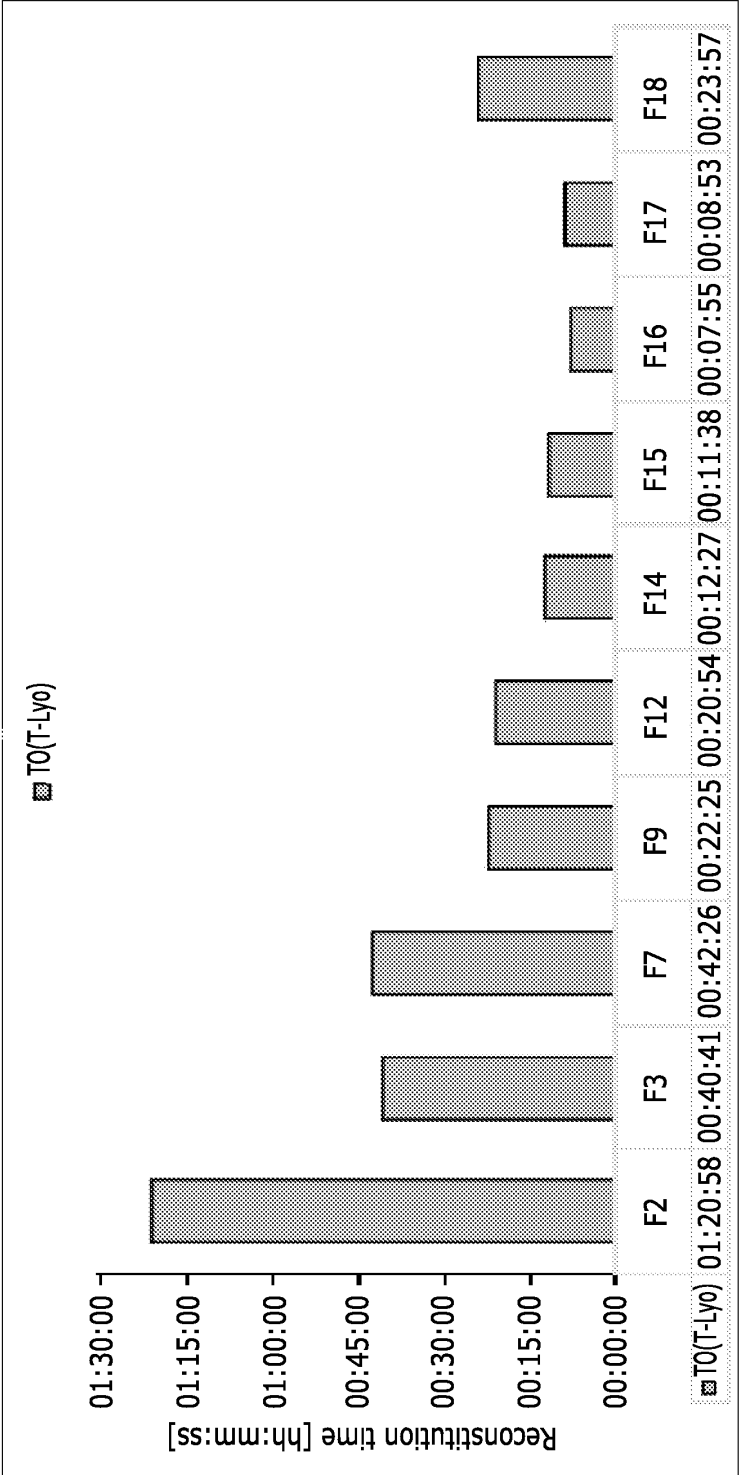


FIG. 31

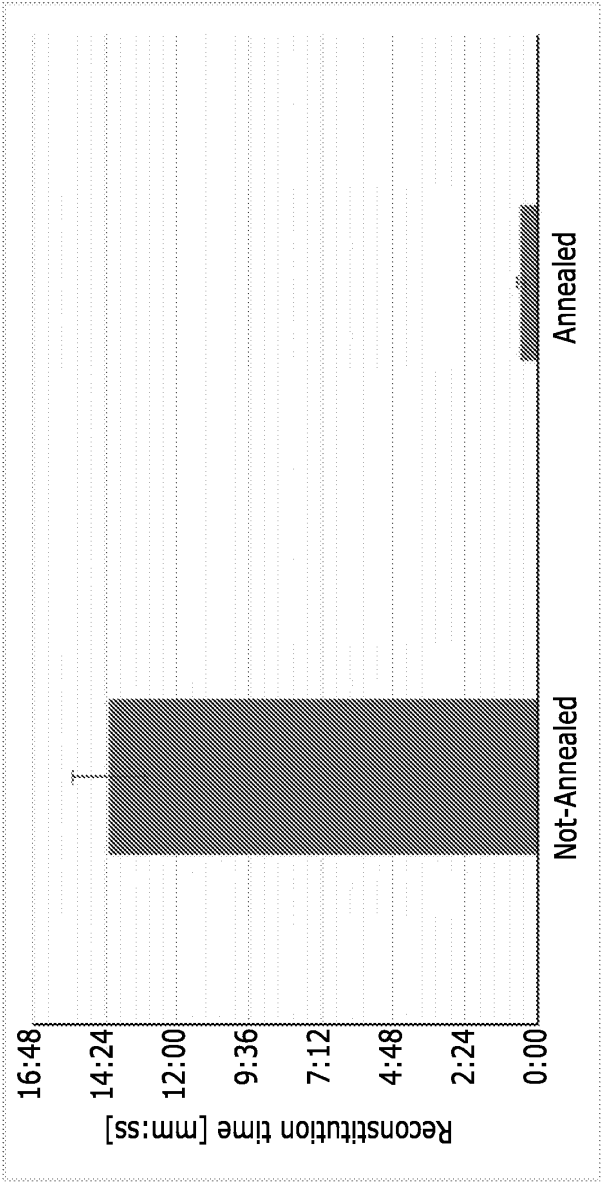


FIG. 32

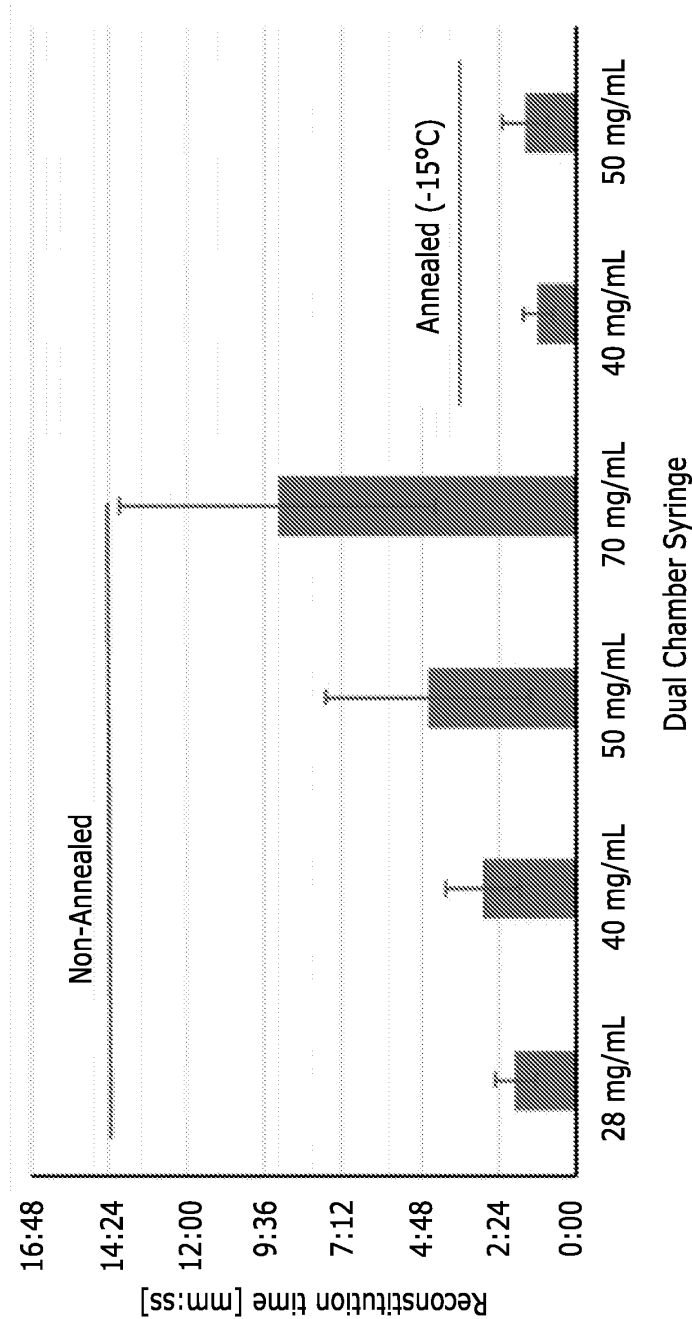


FIG. 33A

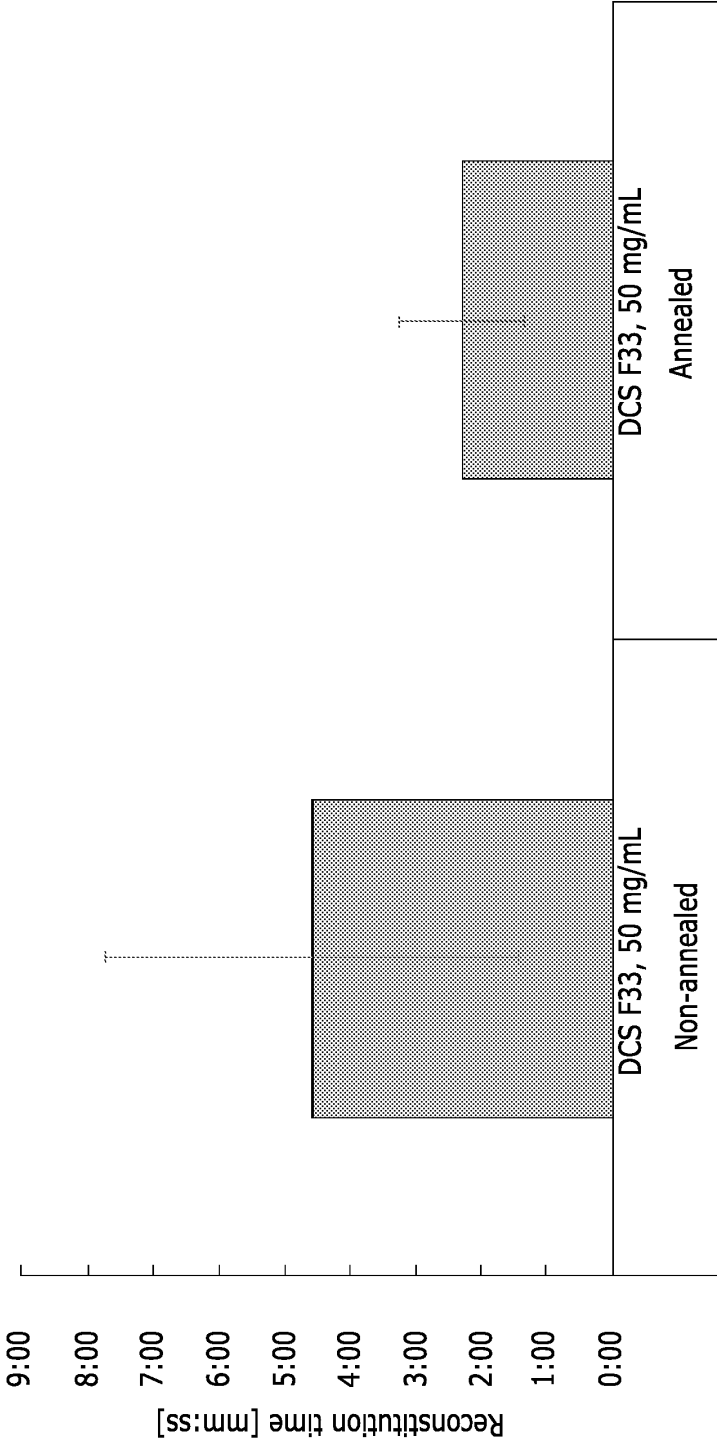


FIG. 33B

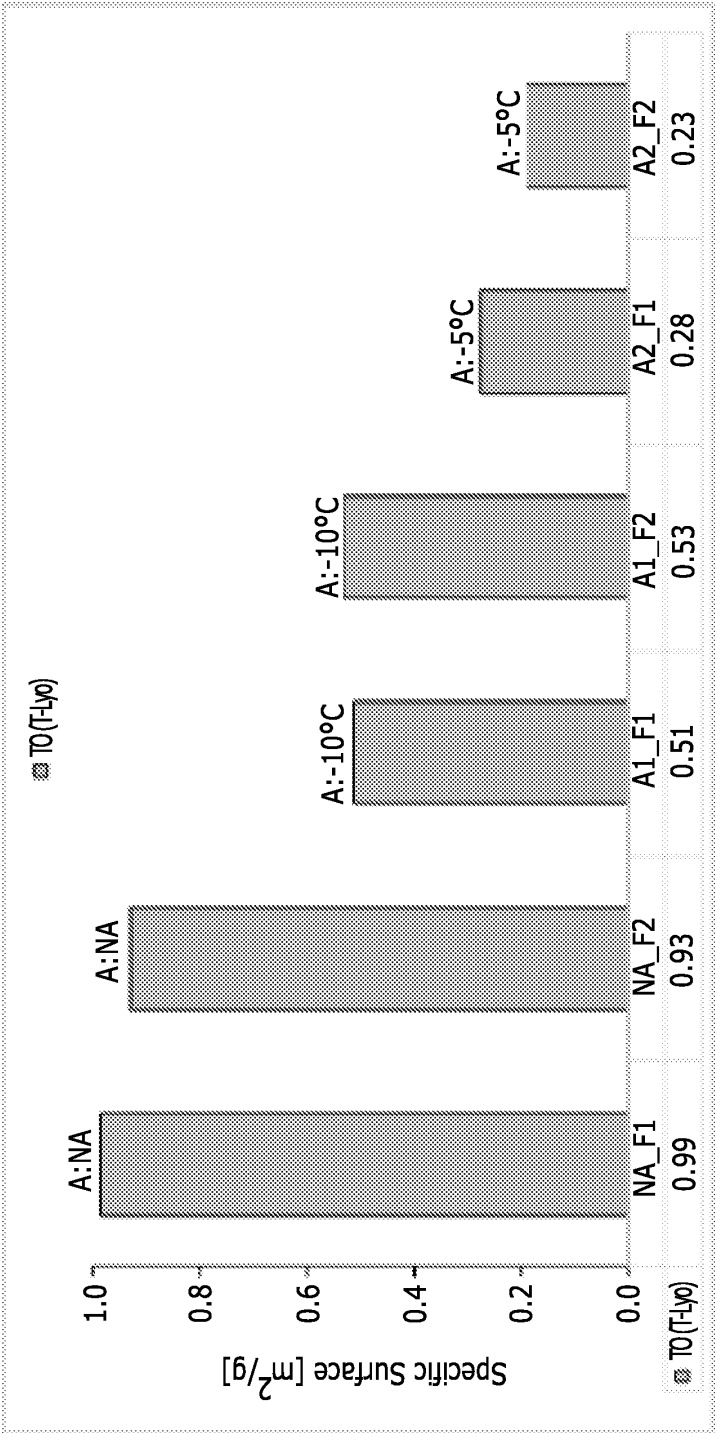


FIG. 34

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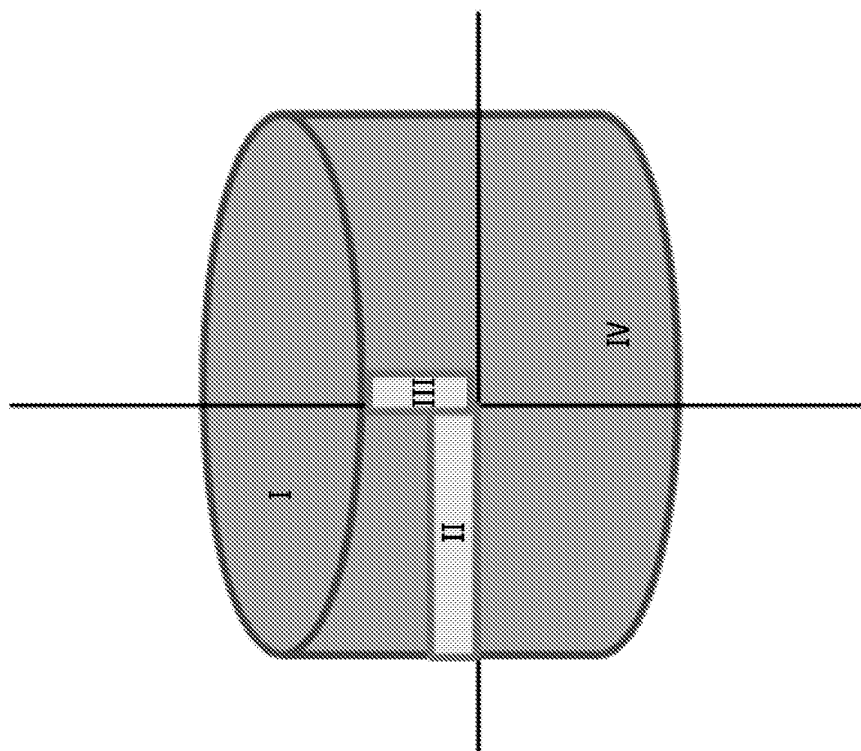
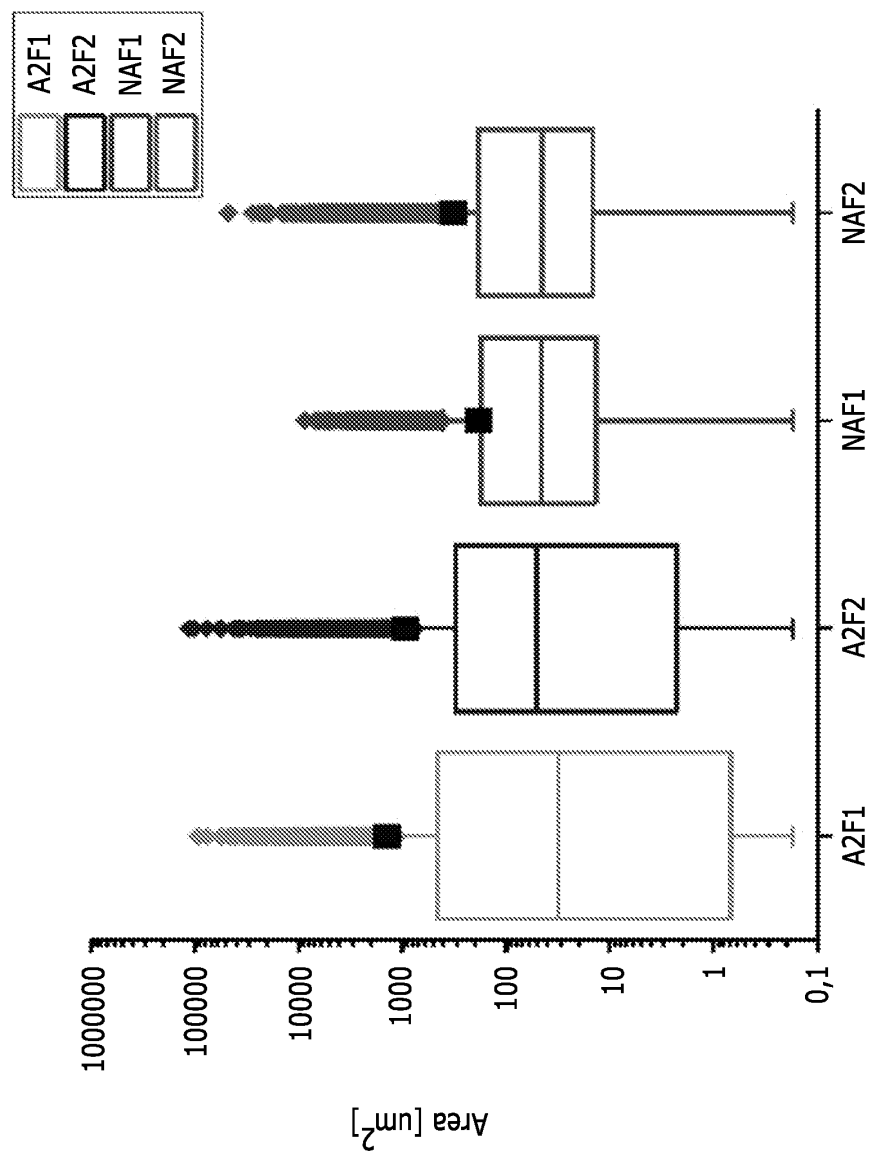


FIG. 35



F1 and F2 = formulation F33 at 50mg/mL and 28 mg/mL protein concentration respectively
A2 = freeze dried with an annealing step (A2)
NA = freeze dried without an annealing step (NA)

FIG. 36

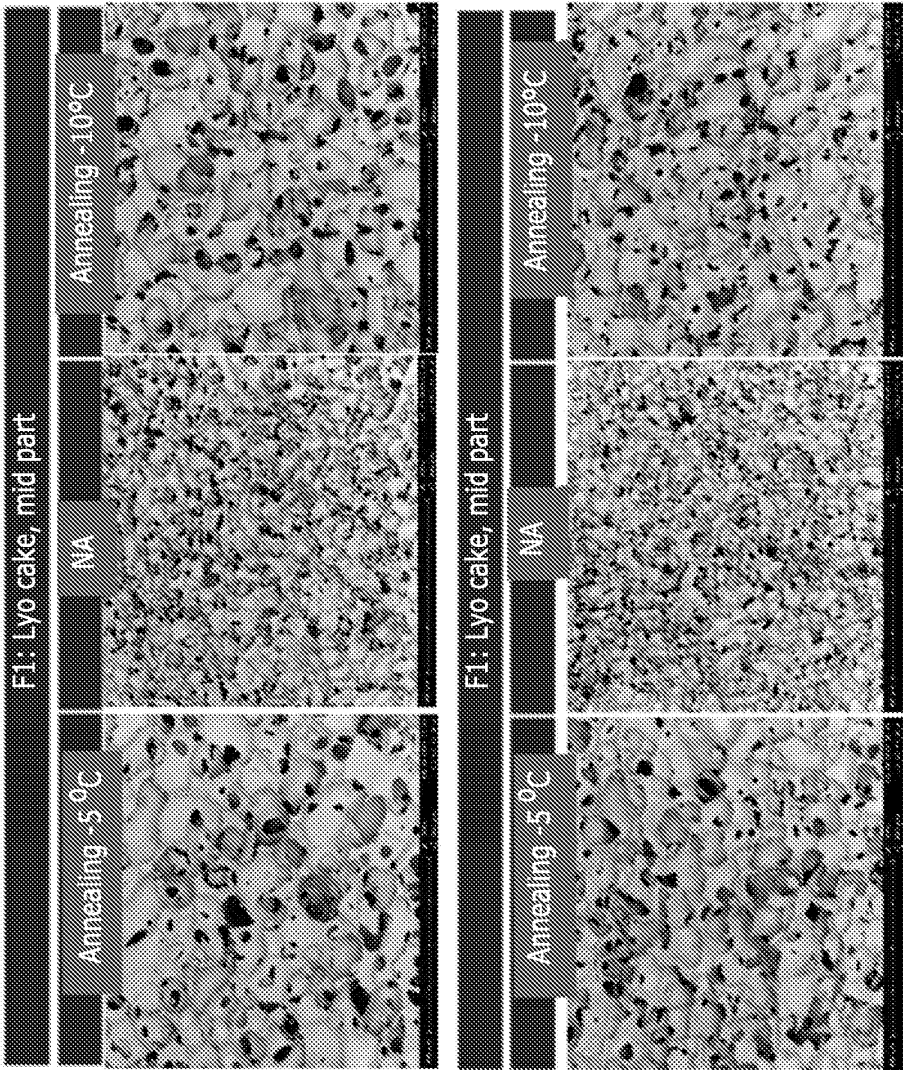


FIG. 37

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Test ²	F15						
	T0 (lyo)	T3M	T6M	T9M	T12M	T0 (lyo)	T3M
Protein Concentration (mg/mL)	98.9	102.3	100.9	n.a.	99.8	101.2	103.8
pH	7.4	7.5	7.4	n.a.	7.4	7.4	7.5
AEX-HPLC (main peak) (%)	59.4	56.7	57.5	54.1	57.9	59.4	57.3
AEX-HPLC (pre-peaks) (%)	7.3	9.2	7.8	12.6	8.0	7.1	8.9
AEX-HPLC (post-peaks) (%)	33.2	34.1	34.7	33.4	34.1	33.5	33.8
SE-HPLC (main peak) (%)	90.0	89.5	89.5	88.5	90.2	88.5	88.1
SE-HPLC (HMW) (%)	3.4	3.2	3.2	3.7	2.9	4.7	4.3
SE-HPLC (dimer) (%)	6.5	7.1	7.2	7.8	6.7	6.7	7.4
SE-HPLC (LMW) (%)	0.1	0.2	0.2	0.1	0.3	0.1	0.1
RP-HPLC (main peak) (%)	82.0	81.7	81.5	80.9	81.6	81.6	81.7
RP-HPLC (pre-peak) (%)	7.2	7.5	7.8	8.1	6.9	7.1	7.0
RP-HPLC (post-peak) (%)	10.8	10.7	10.7	11.1	11.6	11.3	11.3
CE-SDS (main peak) (reduced) (%)	91.1	91.4	91.7	n.a.	89.9	91.4	91.4
CE-SDS (pre-peaks) (reduced) (%)	7.1	6.6	6.2	n.a.	5.9	7.0	6.7
CE-SDS (post-peaks) (reduced) (%)	1.8	2.0	2.1	n.a.	4.2	1.6	1.9
CE-SDS (main peak) (non-reduced) (%)	89.7	88.3	87.9	87.0	88.8	89.8	88.0
CE-SDS (pre-peaks) (non-reduced) (%)	9.3	10.0	10.6	7.9	7.6	9.3	10.1
CE-SDS (post-peaks) (non-reduced) (%)	1.0	1.7	1.5	5.1	3.6	0.9	1.9
Relative Potency (Cell-based bioassay) (%)	105%	110%	85%	89%	88%	75%	116%
Subvisible particulates (MFI) ¹	2,255	13,027	6,036		9,464	18,398	24,576
Particles ≥ 2µm	177	1,548	975	n.a.	997	1,498	3,188
Particles ≥ 10µm	7	311	247		198	389	424
Particles ≥ 25µm							
RMC (%)	0.1	0.1	0.1	n.a.	0.2	0.1	0.1
Reconstitution time [min:sec]	11:38	14:28	14:13	25:02	33:37	07:55	08:25

AEX-HPLC = anion-exchange-high performance liquid chromatography; CE-SDS = capillary electrophoresis sodium dodecyl sulfate; HMW = high molecular weight; LMW = low molecular weight; NT = not tested; NA = not applicable; RP-HPLC = reversed phase-high performance liquid chromatography; SE-HPLC = size exclusion -high performance liquid chromatography; RMC = residual moisture content;

¹MFI measurements: F15-17 diluted to 30mg/ml and data corrected for dilution factor; F33 undiluted

²The following additional analytical methods were performed without substantial changes over the course of the stability study of F15-F17 (data not shown):

FIG. 38

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F16			F17					F33			
T6M	T9M	T12M	T0 (Iyo)	T3M	T6M	T9M	T12M	T0 (Iyo)	T3M	T6M	T14M
104.1	n.a.	101.4	102.8	105.3	102.2	n.a.	101.3	69.4	67.5	72.4	n.a.
7.5	n.a.	7.4	7.7	7.8	7.7	n.a.	7.8	7.3	7.3	7.2	n.a.
57.6	55.6	58.1	59.9	58.2	57.9	56.1	59.1	61.9	63.5	63.4	62.5
7.5	10.6	7.2	6.9	8.3	7.1	10.3	7.1	8.4	7.7	8.4	7.8
34.9	33.8	34.7	33.3	33.5	35.0	33.5	33.8	29.8	28.8	28.3	29.8
88.6	87.3	89.1	89.7	89.7	89.9	88.8	90.6	93.2	93.1	94.0	92.7
4.1	4.8	3.9	4.0	3.5	3.3	4.0	3.1	2.7	2.7	2.3	2.5
7.2	7.9	6.7	6.2	6.7	6.6	7.1	6.1	3.9	4.2	3.5	4.8
0.2	0.1	0.3	0.1	0.1	0.2	0.1	0.2	0.2	0.1	0.3	0.1
81.7	81.5	81.4	83.0	82.8	82.4	82.6	82.9	84.1	84.9	83.9	83.8
7.4	7.6	6.7	7.2	7.2	7.8	7.4	6.8	8.4	7.5	8.2	8.1
10.8	11.0	11.8	9.9	10.1	9.8	9.9	10.3	7.4	7.6	7.9	8.1
92.2		90.5	91.6	92.0	92.0		90.5	n.a.			
6.0	n.a.	6.1	7.0	6.2	6.4	n.a.	6.2				
1.9		3.4	1.5	1.8	1.7		3.3				
88.1	87.6	89.5	89.9	88.8	88.3	89.1	89.5	89.3	n.a.		90.8
10.5	8.1	7.8	9.0	9.7	10.4	7.2	9.2	10.7			9.2
1.4	4.2	2.7	1.1	1.5	1.3	3.7	1.3	0.0			0.0
74%	85%	82%	111%	97%	68%	85%	88%	86%	97%	90%	91%
8,757	n.a.	4,693	1,541	24,470	16,971	n.a.	8,171	9,905	984	327	1,172
1,039		459	155	3,089	2,382		884	1,106	73	15	64
233		85	28	643	481		240	176	15	0	9
0.1	n.a.	0.2	0.0	0.1	0.1	n.a.	0.1	0.1	0.1	0.1	0.4
14:11	19:08	07:10	08:53	08:24	12:51	21:29	14:15	14:18 ± 01:12	11:07 ± 05:56	10:22 ± 02:19	04:43 ± 00:31

Visual appearance, OD₃₅₀, OD₅₅₀, T_{agg, onset}, T_{m, onset}, T_m, T_g and XRD. For F33, no major changes were determined with the following analytical methods: Visual appearance, turbidity and color.

FIG. 38 (Continued)

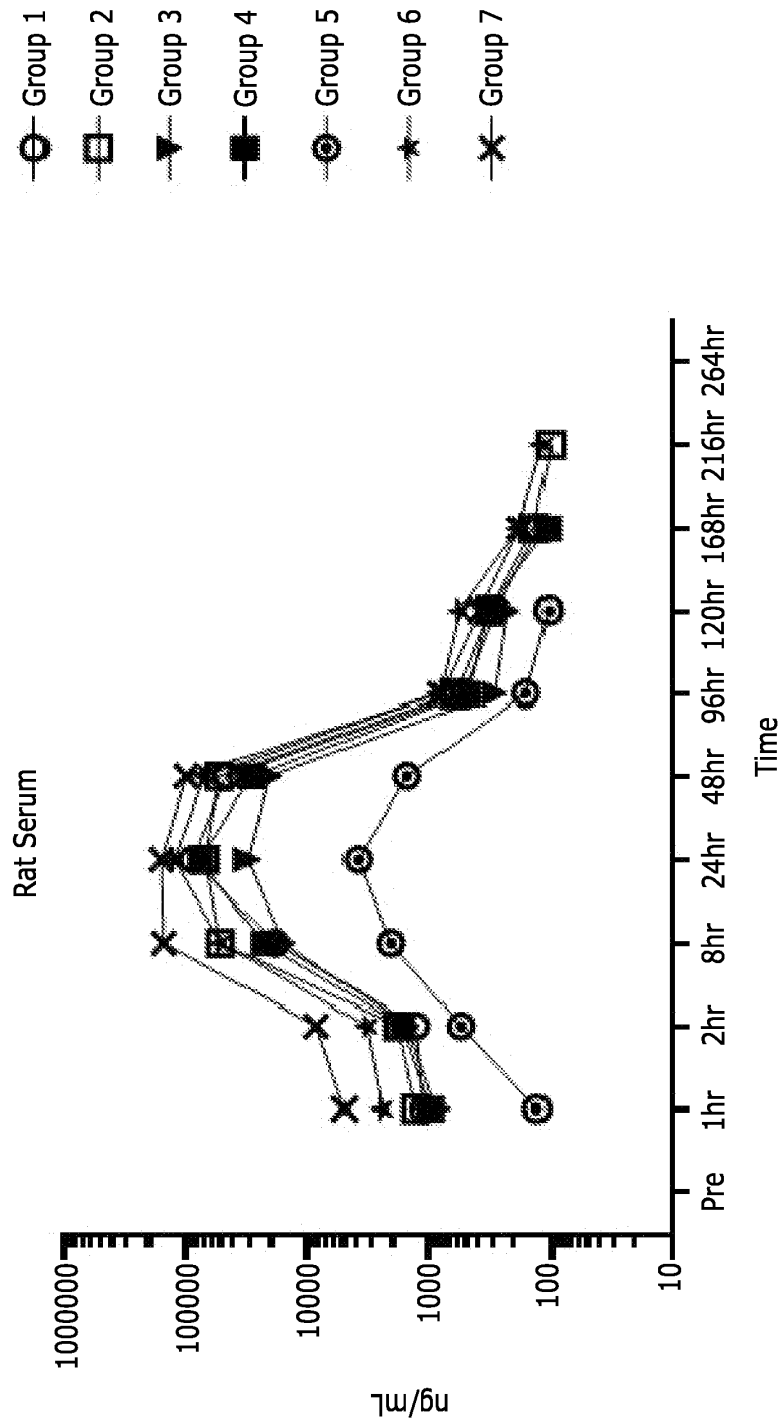


FIG. 39

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Group	Tmax (h)	Cmax (ng/mL)	Cmax_D (kg*ng/mL/mg)	AUClast (h*ng/mL)	AUClast_D (h*kg*ng/mL/mg)	Tlast (h)	AUCINF_obs (h*ng/mL)
1	48	88100	881	3320000	33200	192	3320000
2	48	91100	911	3550000	35500	192	3560000
3	48	31400	314	1320000	13200	144	1320000
4	48	75800	758	2380000	23800	192	2380000
5	48	3890	38.9	142000	1420	144	143000
6	48	126000	1260	4900000	49000	240	4900000
7	48	161000	1610	7100000	71000	192	7100000

FIG. 40