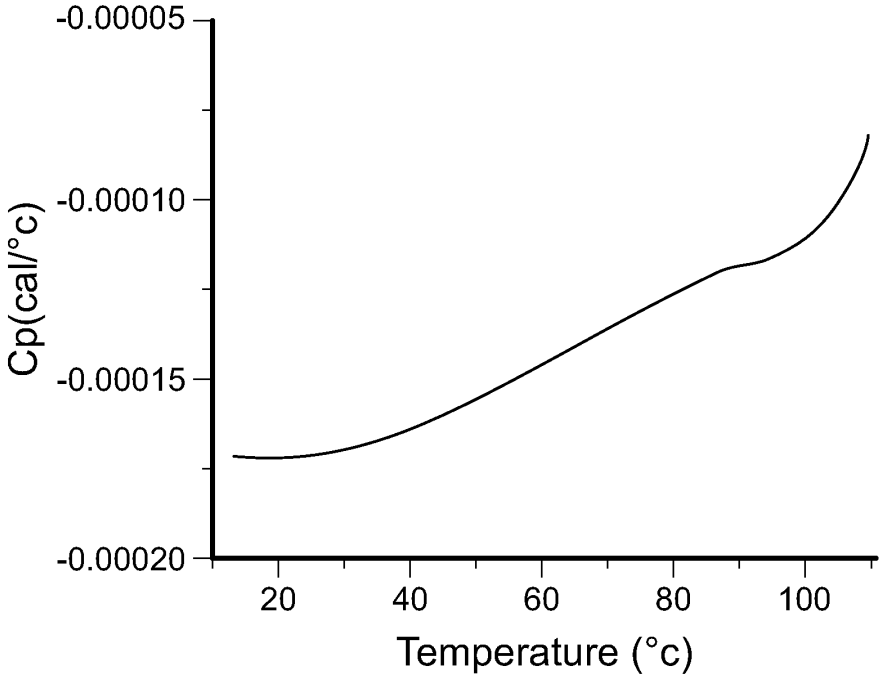

-0.00005
-0.00010
-0.00015
-0.00020
Cp(cal/°c)
20
40
60
80
100
Temperature (°c)

FIG. 1

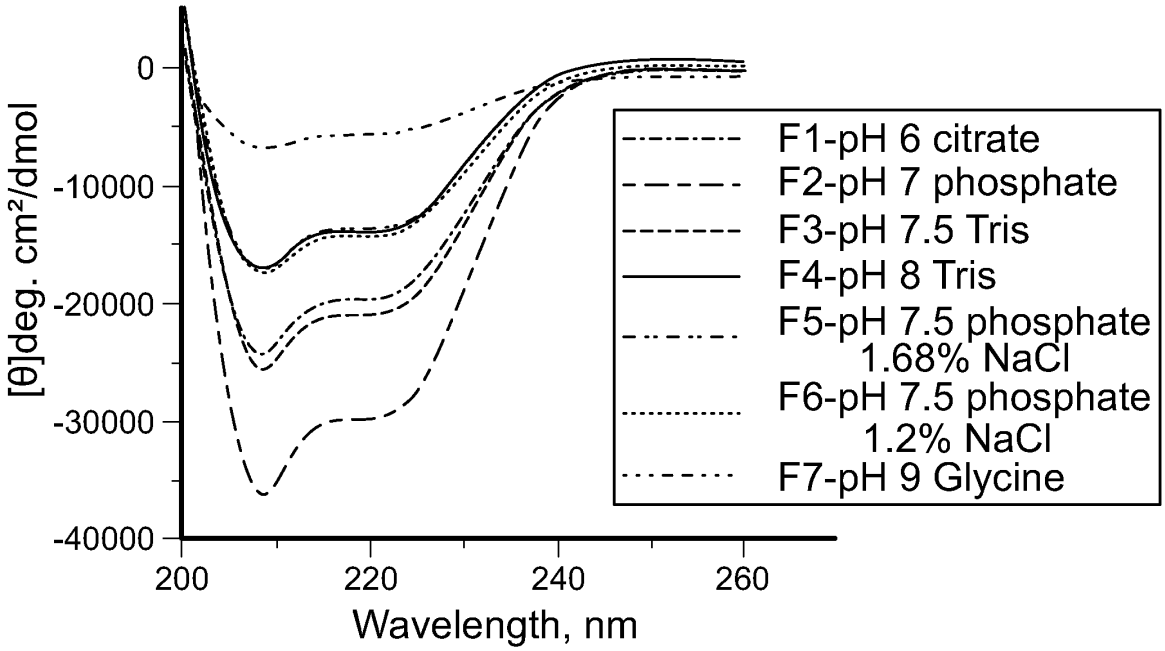

0
-10000
-20000
-30000
-40000
[θ]deg. cm²/dmol
200
220
240
260
Wavelength, nm
F1-pH 6 citrate
F2-pH 7 phosphate
F3-pH 7.5 Tris
F4-pH 8 Tris
F5-pH 7.5 phosphate 1.68% NaCl
F6-pH 7.5 phosphate 1.2% NaCl
F7-pH 9 Glycine

FIG. 2

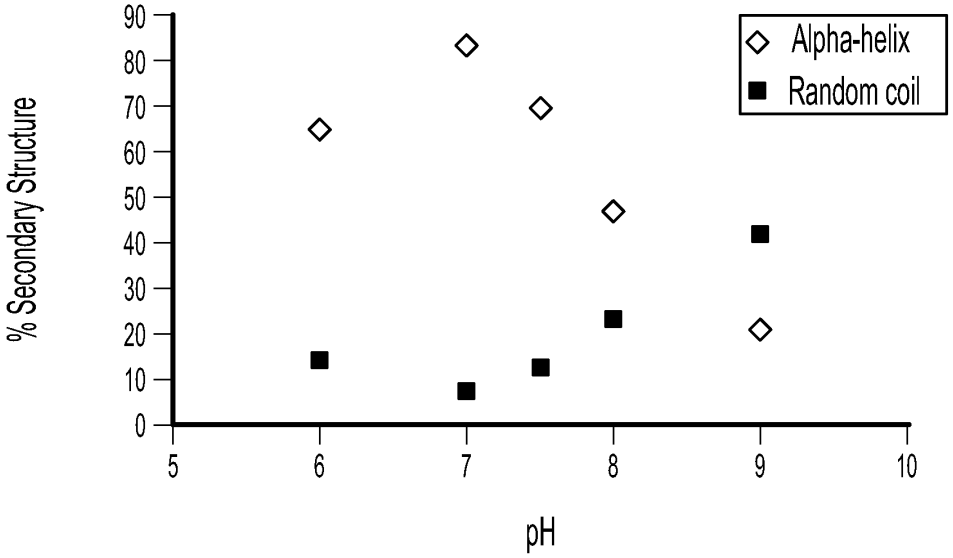

% Secondary Structure
90
80
70
60
50
40
30
20
10
0
5
6
7
8
9
10
pH
Alpha-helix
Random coil

FIG. 3

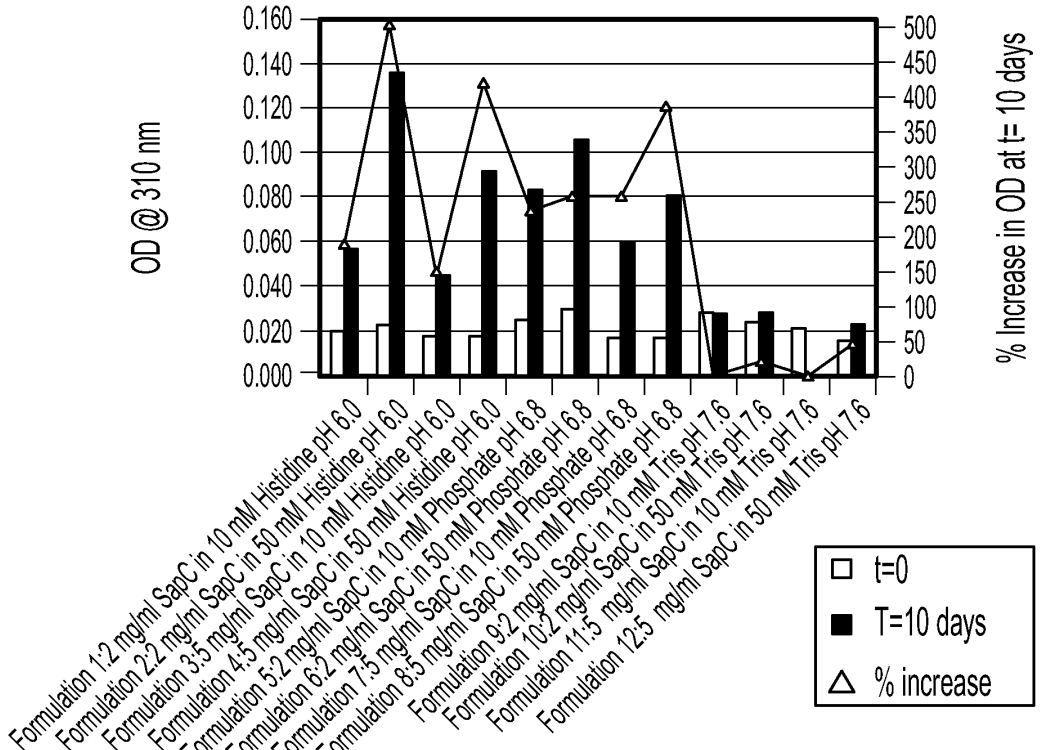

OD @ 310 nm
0.160
0.140
0.120
0.100
0.080
0.060
0.040
0.020
0.000
% Increase in OD at t= 10 days
500
450
400
350
300
250
200
150
100
50
0
Formulation 1:2 mg/ml SapC in 10 mM Histidine pH 6.0
Formulation 2:2 mg/ml SapC in 50 mM Histidine pH 6.0
Formulation 3:5 mg/ml SapC in 10 mM Histidine pH 6.0
Formulation 4:5 mg/ml SapC in 50 mM Histidine pH 6.0
Formulation 5:2 mg/ml SapC in 10 mM Phosphate pH 6.8
Formulation 6:2 mg/ml SapC in 50 mM Phosphate pH 6.8
Formulation 7:5 mg/ml SapC in 10 mM Phosphate pH 6.8
Formulation 8:5 mg/ml SapC in 50 mM Phosphate pH 6.8
Formulation 9:2 mg/ml SapC in 10 mM Tris pH 7.6
Formulation 10:2 mg/ml SapC in 50 mM Tris pH 7.6
Formulation 11:5 mg/ml SapC in 10 mM Tris pH 7.6
Formulation 12:5 mg/ml SapC in 50 mM Tris pH 7.6
t=0
T=10 days
% increase

FIG. 4

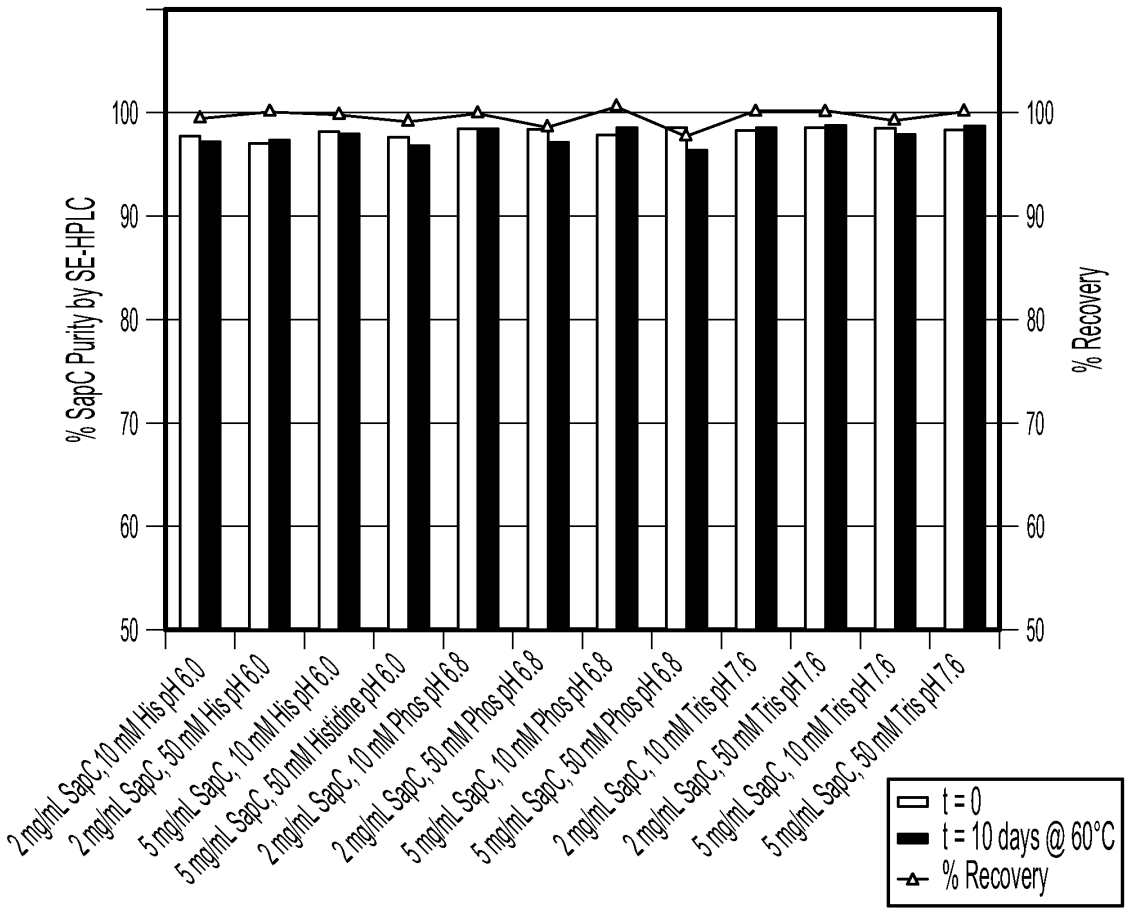

% SapC Purity by SE-HPLC
% Recovery
100
90
80
70
60
50
2 mg/mL SapC, 10 mM His pH 6.0
2 mg/mL SapC, 50 mM His pH 6.0
5 mg/mL SapC, 10 mM His pH 6.0
5 mg/mL SapC, 50 mM Histidine pH 6.0
2 mg/mL SapC, 10 mM Phos pH 6.8
2 mg/mL SapC, 50 mM Phos pH 6.8
5 mg/mL SapC, 10 mM Phos pH 6.8
5 mg/mL SapC, 50 mM Phos pH 6.8
2 mg/mL SapC, 10 mM Tris pH 7.6
2 mg/mL SapC, 50 mM Tris pH 7.6
5 mg/mL SapC, 10 mM Tris pH 7.6
5 mg/mL SapC, 50 mM Tris pH 7.6
t = 0
t = 10 days @ 60°C
% Recovery

FIG. 5

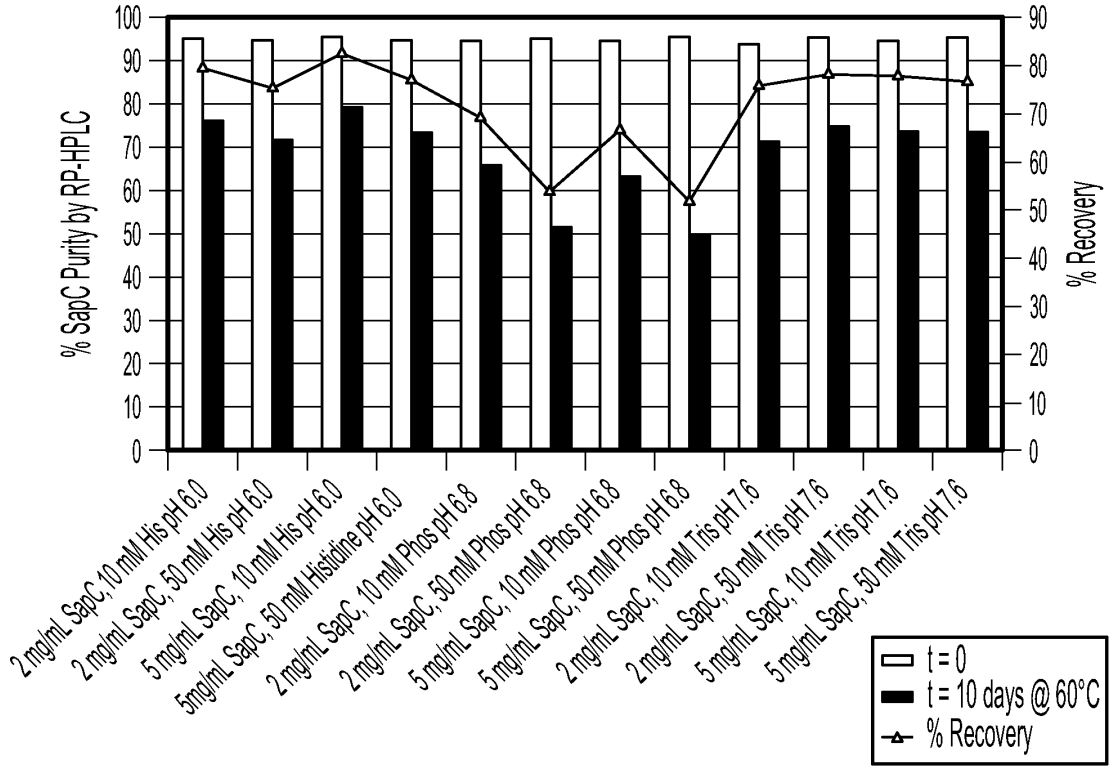

% SapC Purity by RP-HPLC
% Recovery
100
90
80
70
60
50
40
30
20
10
0
2 mg/mL SapC, 10 mM His pH 6.0
2 mg/mL SapC, 50 mM His pH 6.0
5 mg/mL SapC, 10 mM His pH 6.0
5mg/mL SapC, 50 mM Histidine pH 6.0
2 mg/mL SapC, 10 mM Phos pH 6.8
2 mg/mL SapC, 50 mM Phos pH 6.8
5 mg/mL SapC, 10 mM Phos pH 6.8
5 mg/mL SapC, 50 mM Phos pH 6.8
2 mg/mL SapC, 10 mM Tris pH 7.6
2 mg/mL SapC, 50 mM Tris pH 7.6
5 mg/mL SapC, 10 mM Tris pH 7.6
5 mg/mL SapC, 50 mM Tris pH 7.6
t = 0
t = 10 days @ 60°C
% Recovery

FIG. 6

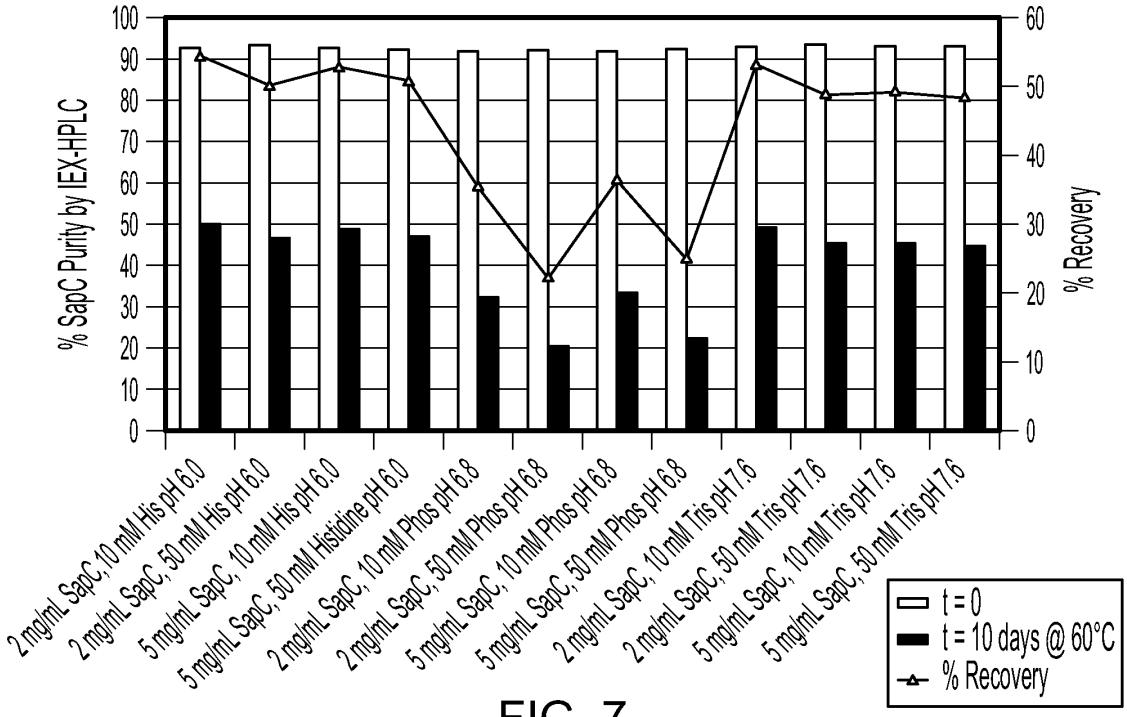

% SapC Purity by IEX-HPLC
% Recovery
100
90
80
70
60
50
40
30
20
10
0
60
50
40
30
20
10
0
2 mg/mL SapC,10 mM His pH 6.0
2 mg/mL SapC, 50 mM His pH 6.0
5 mg/mL SapC, 10 mM His pH 6.0
5 mg/mL SapC, 50 mM Histidine pH 6.0
2 mg/mL SapC, 10 mM Phos pH 6.8
2 mg/mL SapC, 50 mM Phos pH 6.8
5 mg/mL SapC, 10 mM Phos pH 6.8
5 mg/mL SapC, 50 mM Phos pH 6.8
2 mg/mL SapC, 10 mM Tris pH 7.6
2 mg/mL SapC, 50 mM Tris pH 7.6
5 mg/mL SapC, 10 mM Tris pH 7.6
5 mg/mL SapC, 50 mM Tris pH 7.6
t = 0
t = 10 days @ 60°C
% Recovery

FIG. 7

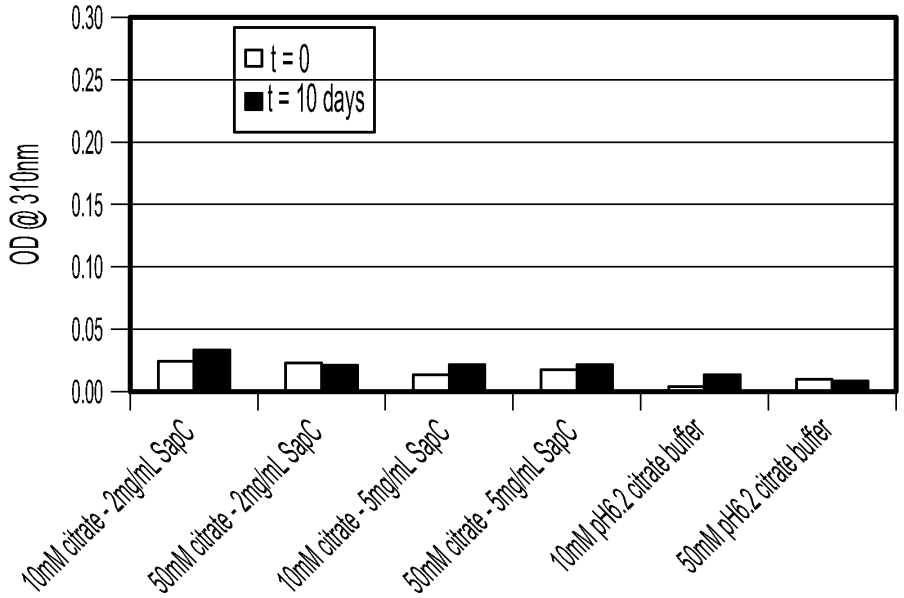

OD @ 310nm
0.30
0.25
0.20
0.15
0.10
0.05
0.00
t = 0
t = 10 days
10mM citrate - 2mg/mL SapC
50mM citrate - 2mg/mL SapC
10mM citrate - 5mg/mL SapC
50mM citrate - 5mg/mL SapC
10mM pH6.2 citrate buffer
50mM pH6.2 citrate buffer

FIG. 8

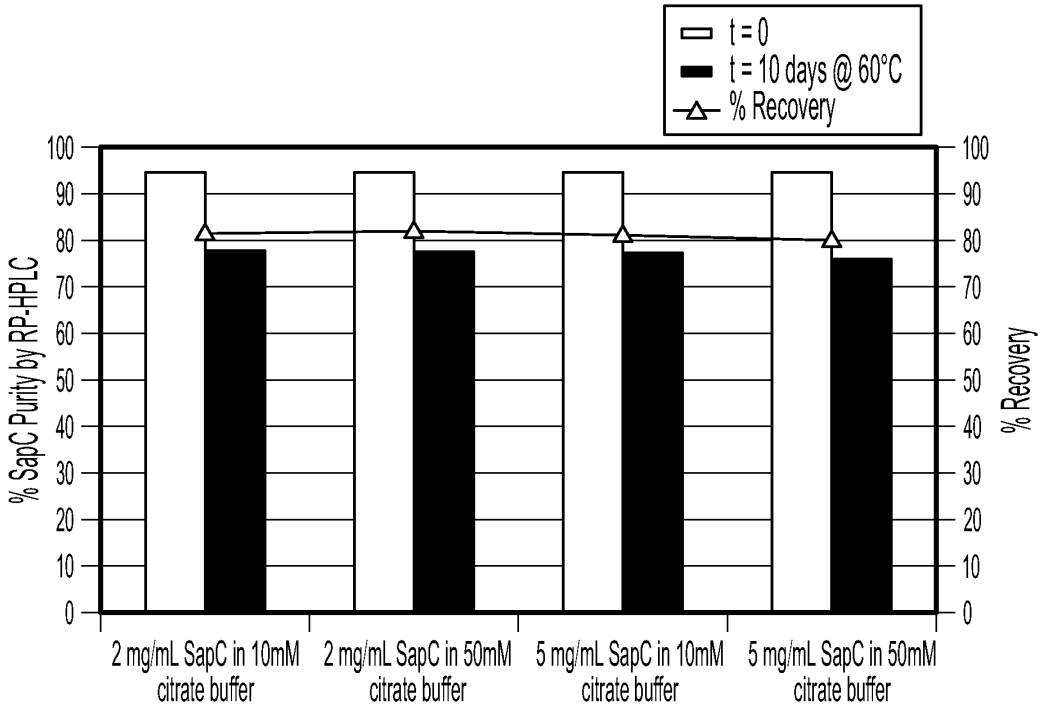

t = 0
t = 10 days @ 60°C
% Recovery
% SapC Purity by RP-HPLC
% Recovery
100
90
80
70
60
50
40
30
20
10
0
2 mg/mL SapC in 10mM citrate buffer
2 mg/mL SapC in 50mM citrate buffer
5 mg/mL SapC in 10mM citrate buffer
5 mg/mL SapC in 50mM citrate buffer

FIG. 9

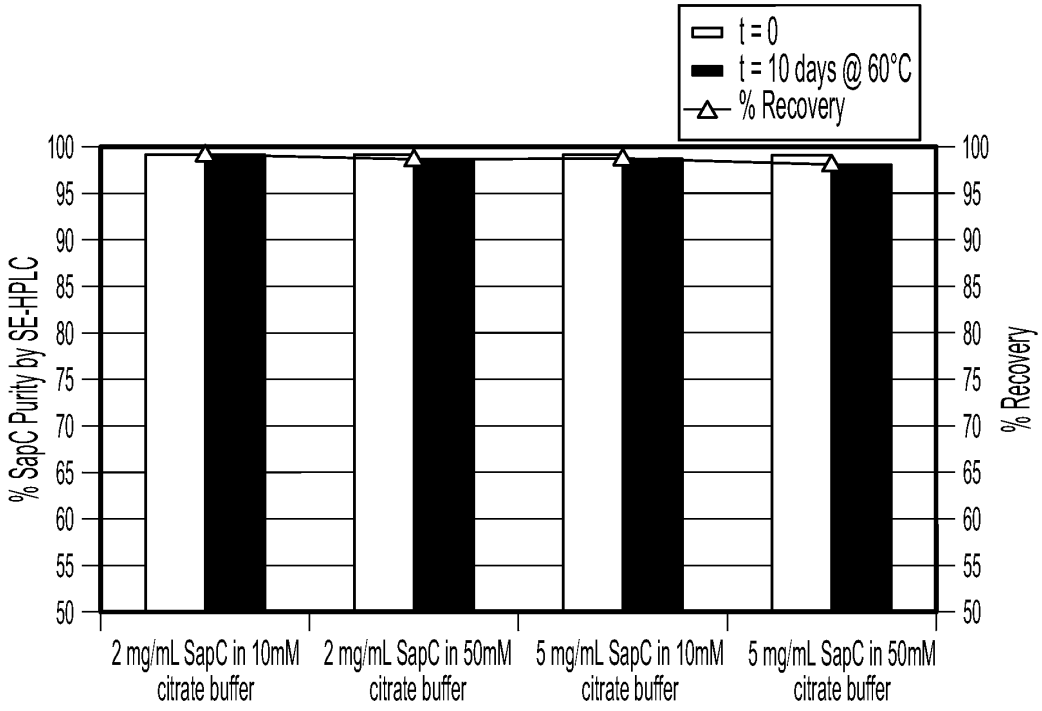

t = 0
t = 10 days @ 60°C
% Recovery
% SapC Purity by SE-HPLC
% Recovery
100
95
90
85
80
75
70
65
60
55
50
2 mg/mL SapC in 10mM citrate buffer
2 mg/mL SapC in 50mM citrate buffer
5 mg/mL SapC in 10mM citrate buffer
5 mg/mL SapC in 50mM citrate buffer

FIG. 10

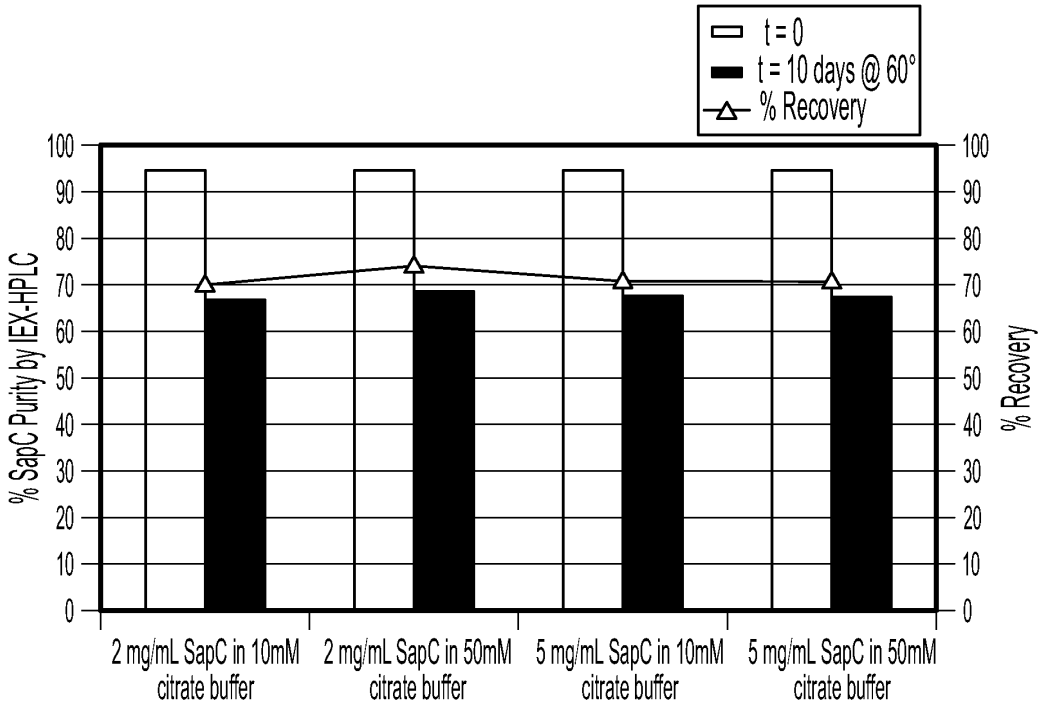

t = 0
t = 10 days @ 60°
% Recovery
% SapC Purity by IEX-HPLC
% Recovery
100
90
80
70
60
50
40
30
20
10
0
2 mg/mL SapC in 10mM citrate buffer
2 mg/mL SapC in 50mM citrate buffer
5 mg/mL SapC in 10mM citrate buffer
5 mg/mL SapC in 50mM citrate buffer

FIG. 11

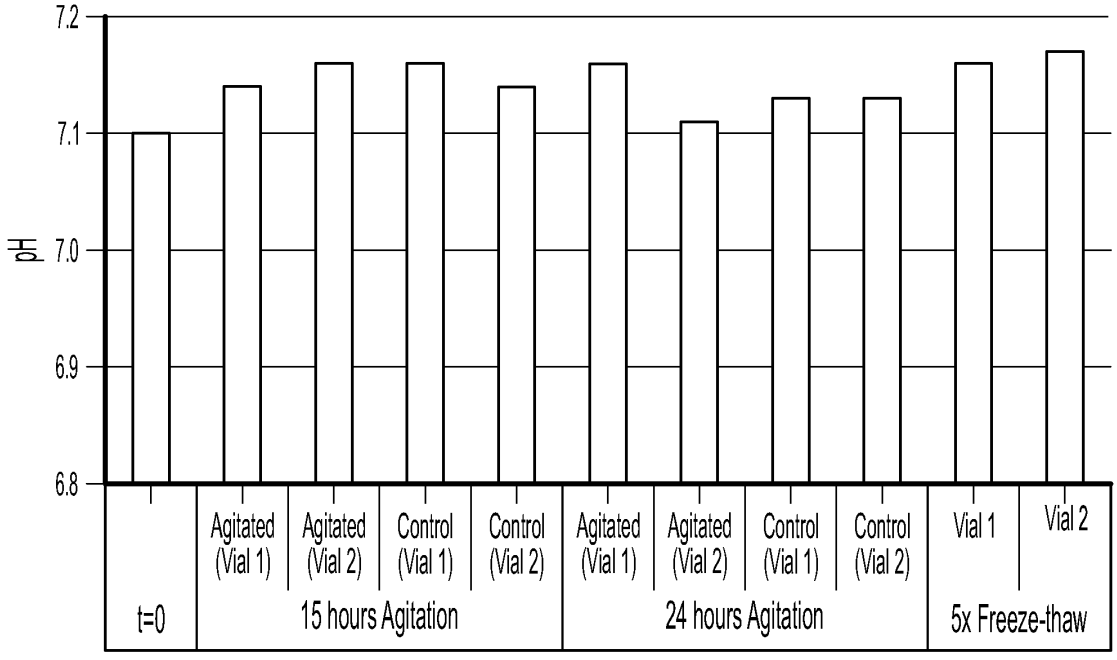

pH
7.2
7.1
7.0
6.9
6.8
t=0
Agitated (Vial 1)
Agitated (Vial 2)
Control (Vial 1)
Control (Vial 2)
15 hours Agitation
Agitated (Vial 1)
Agitated (Vial 2)
Control (Vial 1)
Control (Vial 2)
24 hours Agitation
Vial 1
Vial 2
5x Freeze-thaw

FIG. 12

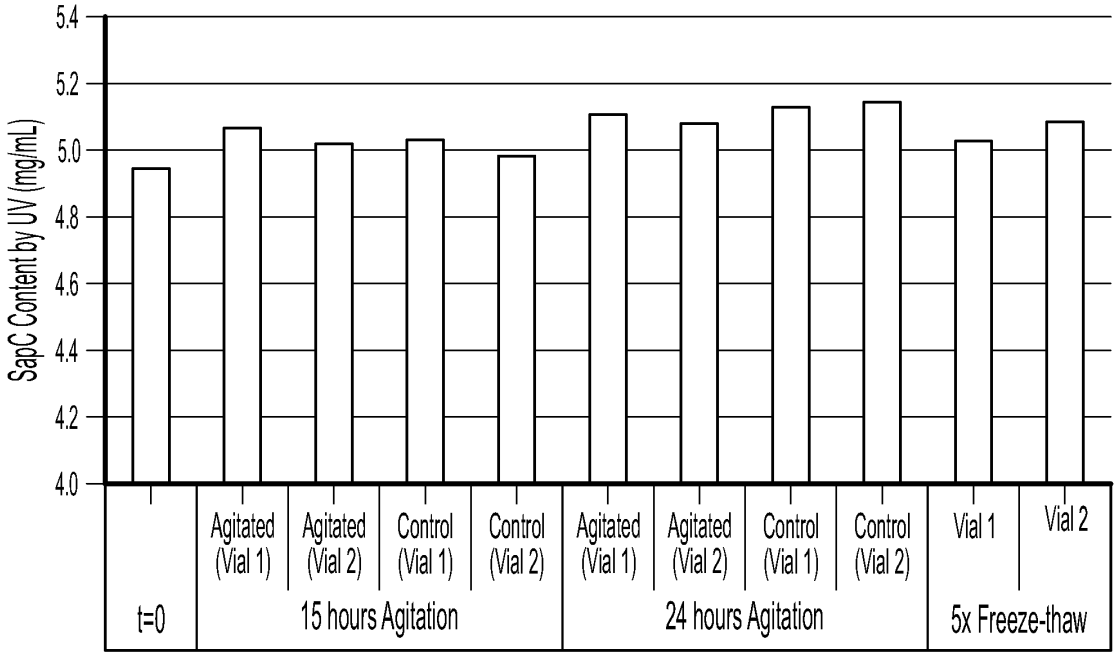

SapC Content by UV (mg/mL)
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
Agitated (Vial 1)
Agitated (Vial 2)
Control (Vial 1)
Control (Vial 2)
Agitated (Vial 1)
Agitated (Vial 2)
Control (Vial 1)
Control (Vial 2)
Vial 1
Vial 2
t=0
15 hours Agitation
24 hours Agitation
5x Freeze-thaw

FIG. 13

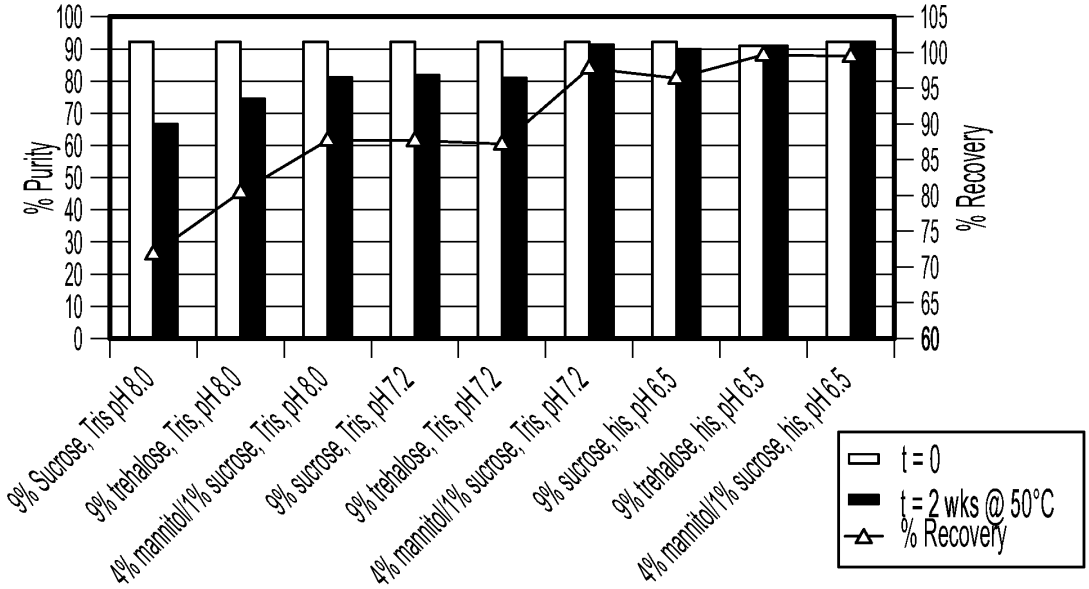

% Purity
% Recovery
9% Sucrose, Tris pH 8.0
9% trehalose, Tris, pH 8.0
4% mannitol/1% sucrose, Tris, pH 8.0
9% sucrose, Tris, pH 7.2
9% trehalose, Tris, pH 7.2
4% mannitol/1% sucrose, Tris, pH 7.2
9% sucrose, his, pH 6.5
9% trehalose, his, pH 6.5
4% mannitol/1% sucrose, his, pH 6.5
t = 0
t = 2 wks @ 50°C
% Recovery

FIG. 14

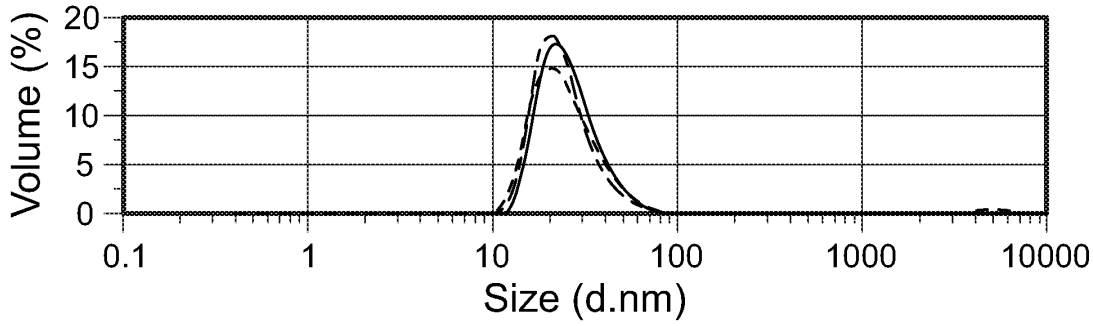


FIG. 15A

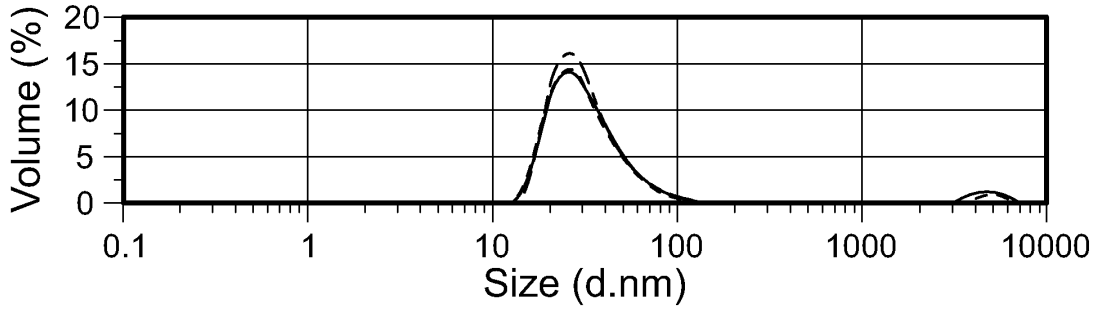


FIG. 15B

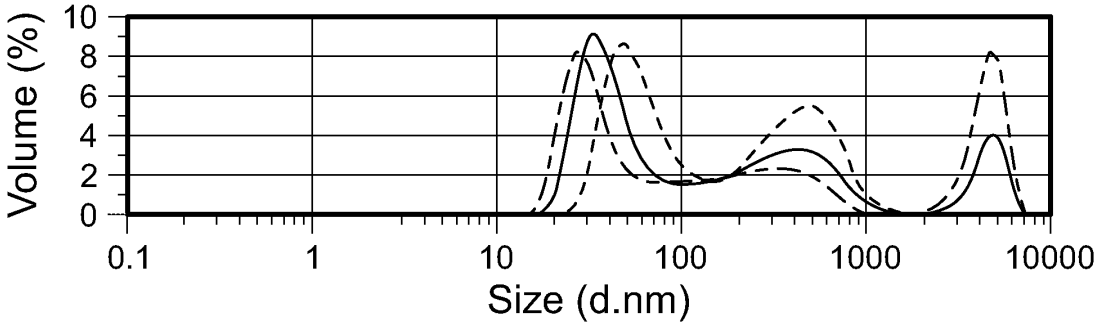


FIG. 16A

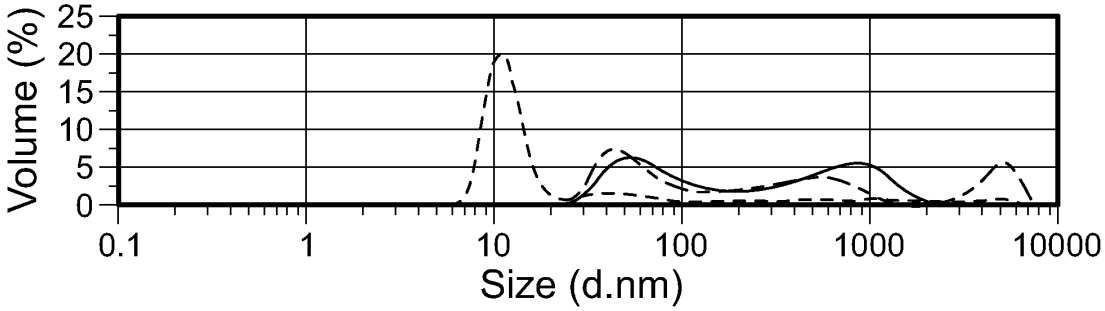


FIG. 16B

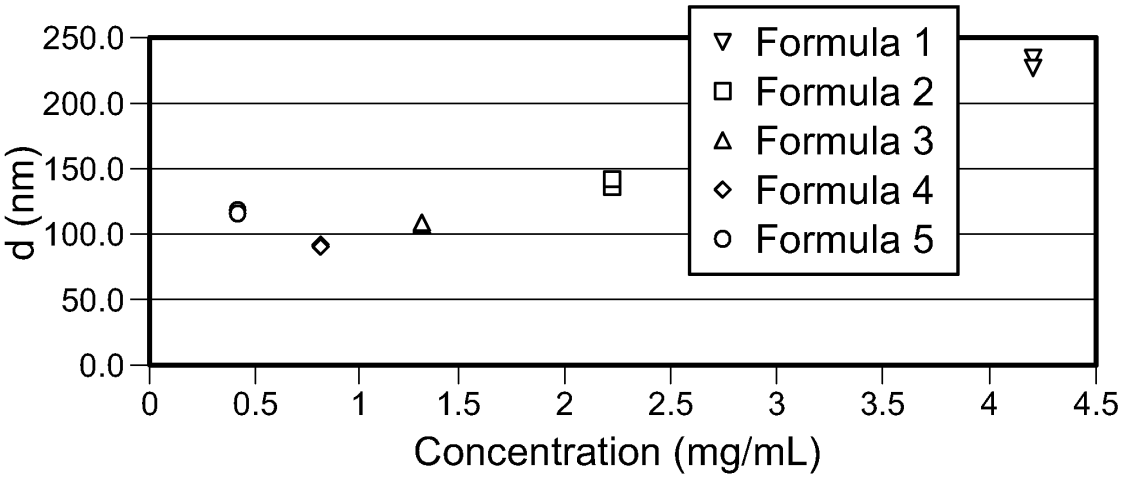

Formula 1
Formula 2
Formula 3
Formula 4
Formula 5
d (nm)
250.0
200.0
150.0
100.0
50.0
0.0
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
Concentration (mg/mL)

FIG. 17

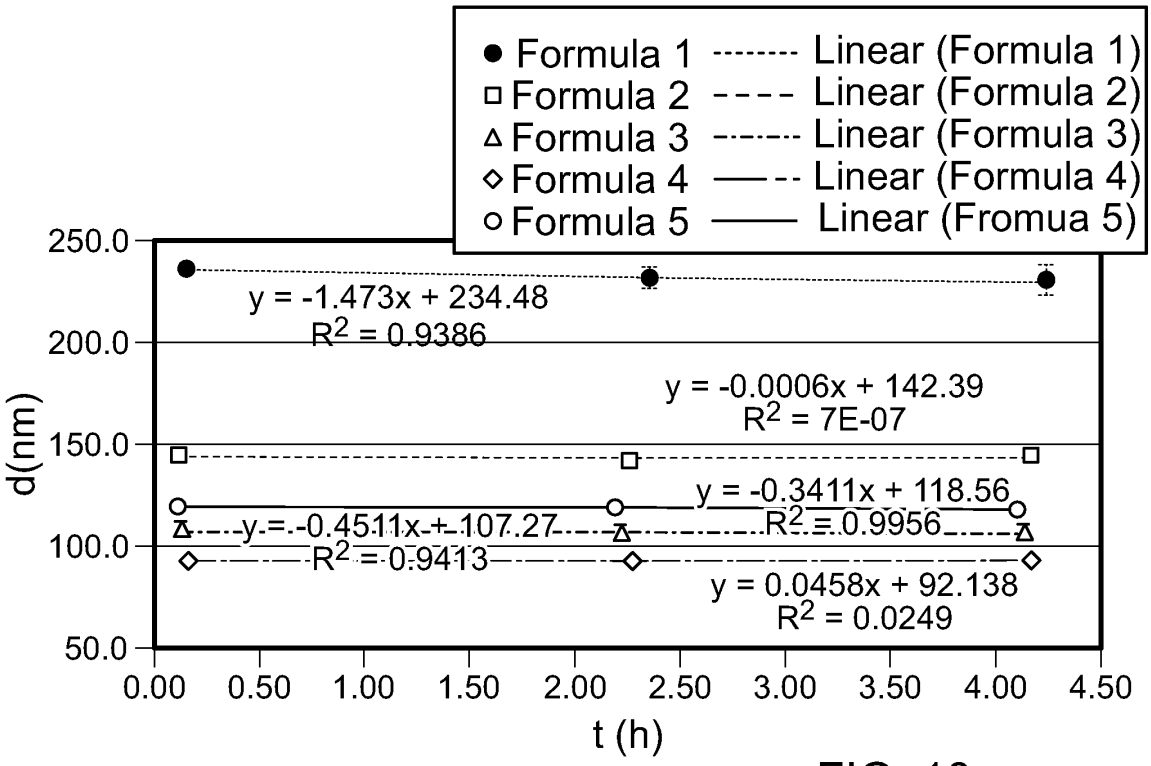

Formula 1
Formula 2
Formula 3
Formula 4
Formula 5
Linear (Formula 1)
Linear (Formula 2)
Linear (Formula 3)
Linear (Formula 4)
Linear (Fromua 5)
y = -1.473x + 234.48
R2 = 0.9386
y = -0.0006x + 142.39
R2 = 7E-07
y = -0.3411x + 118.56
R2 = 0.9956
y = -0.4511x + 107.27
R2 = 0.9413
y = 0.0458x + 92.138
R2 = 0.0249
d(nm)
250.0
200.0
150.0
100.0
50.0
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
t (h)

FIG. 18

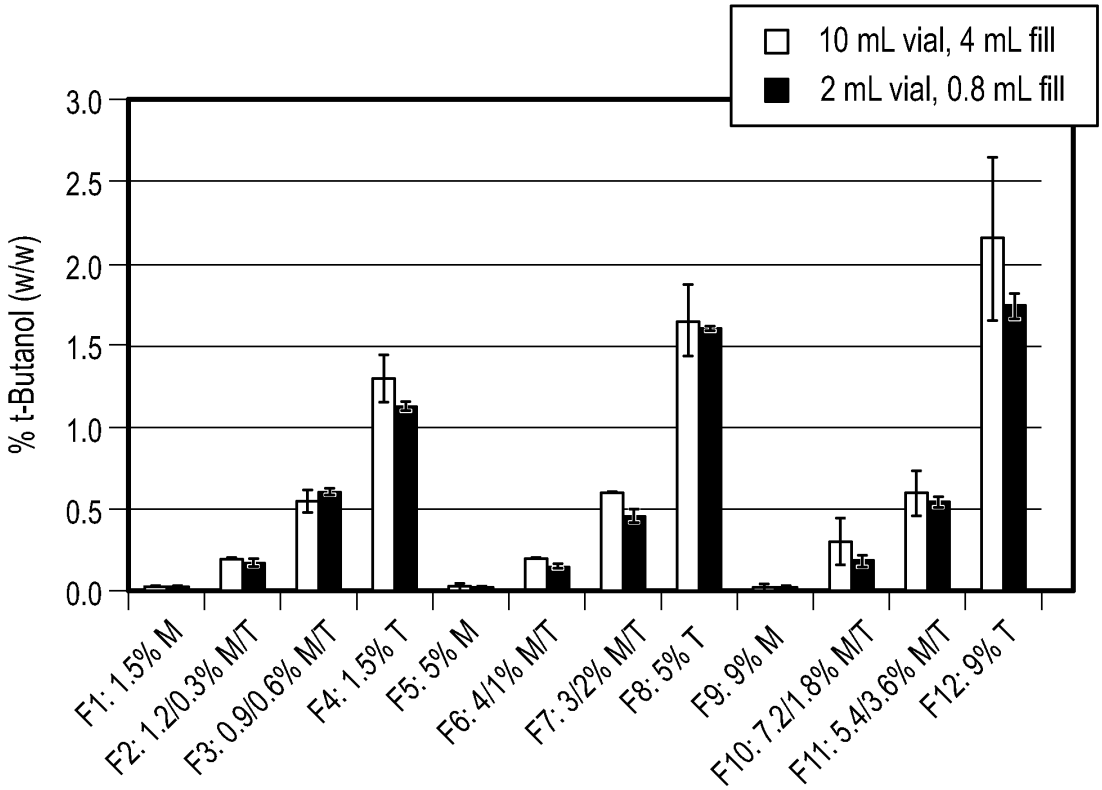

10 mL vial, 4 mL fill
2 mL vial, 0.8 mL fill
% t-Butanol (w/w)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
F1: 1.5% M
F2: 1.2/0.3% M/T
F3: 0.9/0.6% M/T
F4: 1.5% T
F5: 5% M
F6: 4/1% M/T
F7: 3/2% M/T
F8: 5% T
F9: 9% M
F10: 7.2/1.8% M/T
F11: 5.4/3.6% M/T
F12: 9% T

FIG. 19

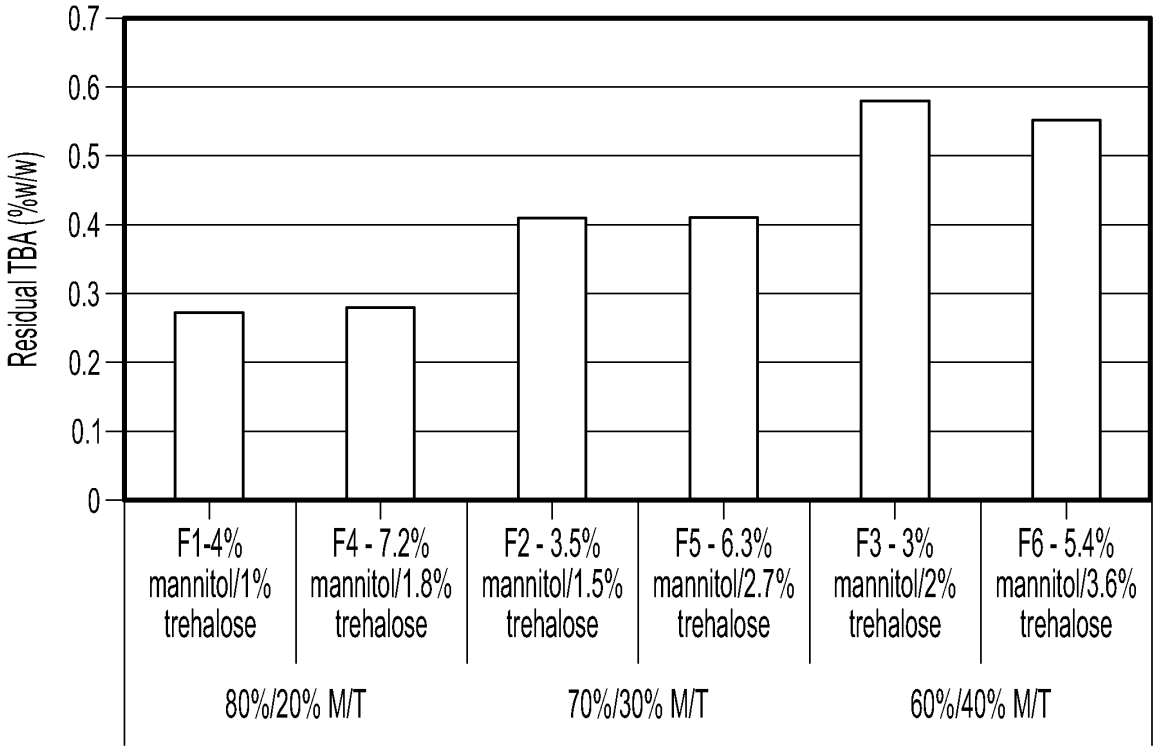

Residual TBA (%w/w)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
F1-4% mannitol/1% trehalose
F4 - 7.2% mannitol/1.8% trehalose
F2 - 3.5% mannitol/1.5% trehalose
F5 - 6.3% mannitol/2.7% trehalose
F3 - 3% mannitol/2% trehalose
F6 - 5.4% mannitol/3.6% trehalose
80%/20% M/T
70%/30% M/T
60%/40% M/T

FIG. 20

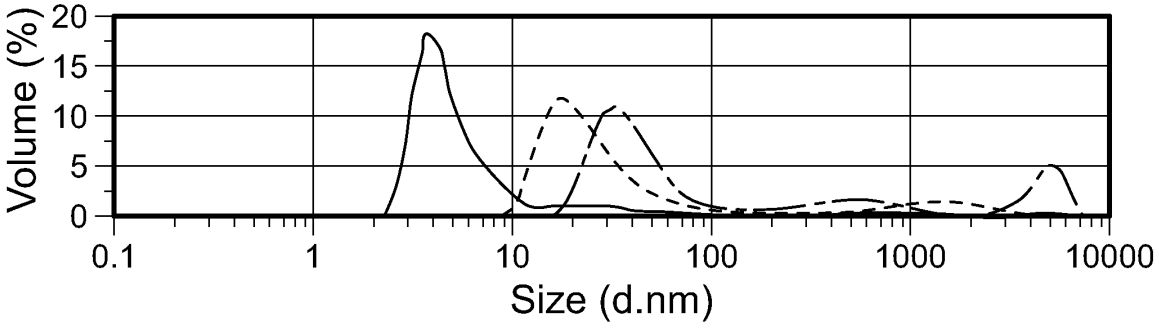


FIG. 21A

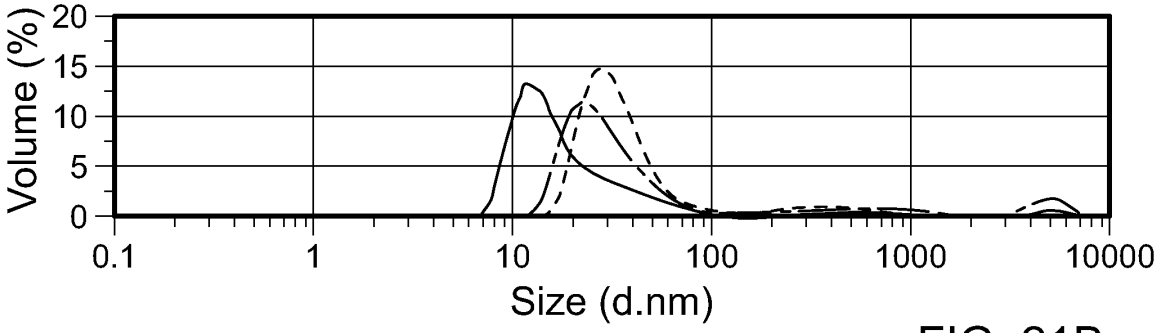


FIG. 21B

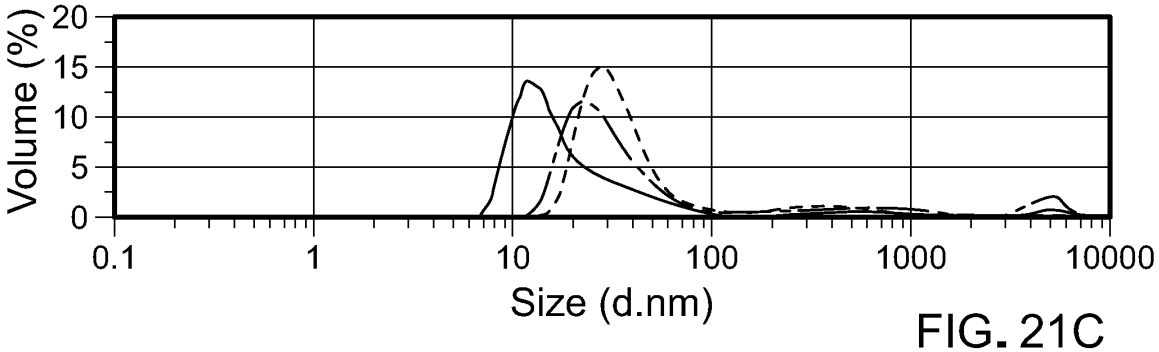


FIG. 21C

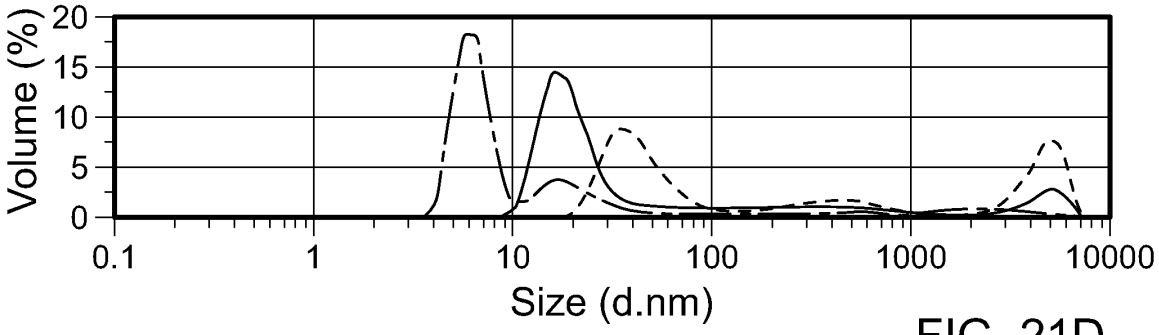


FIG. 21D

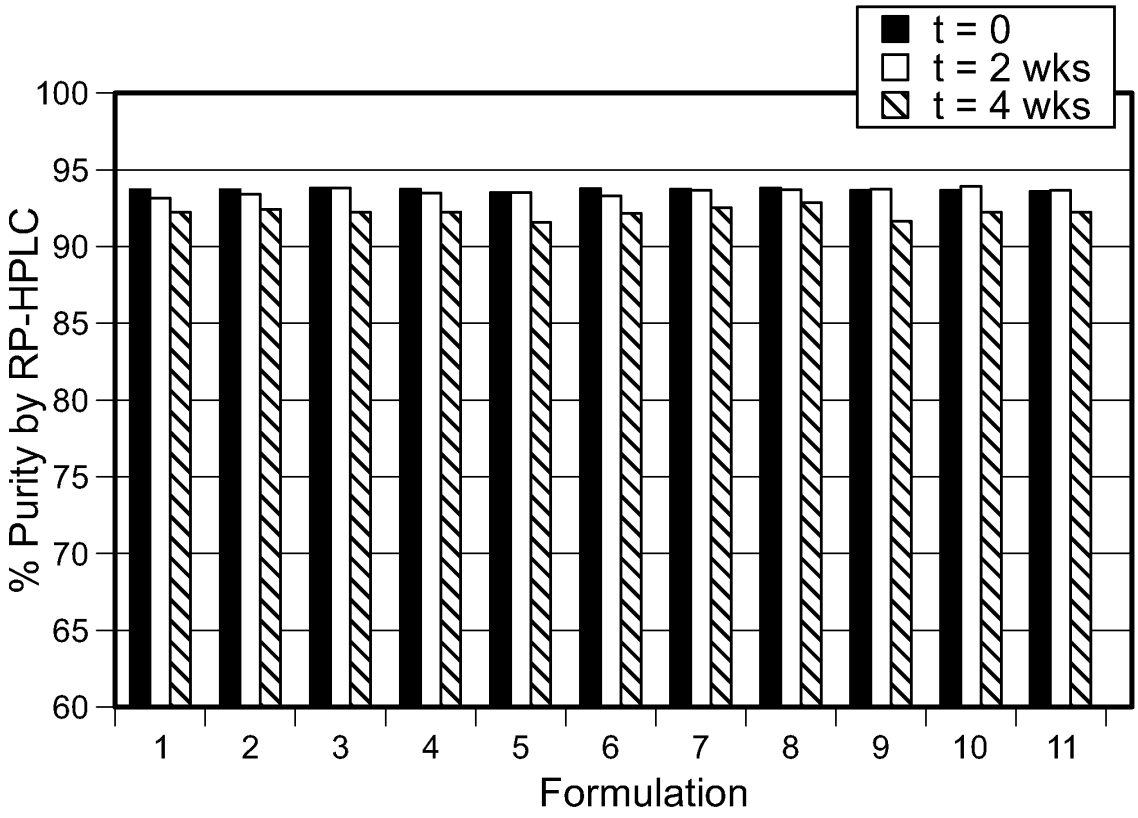

t = 0
t = 2 wks
t = 4 wks
100
95
90
85
80
75
70
65
60
% Purity by RP-HPLC
1
2
3
4
5
6
7
8
9
10
11
Formulation

FIG. 22

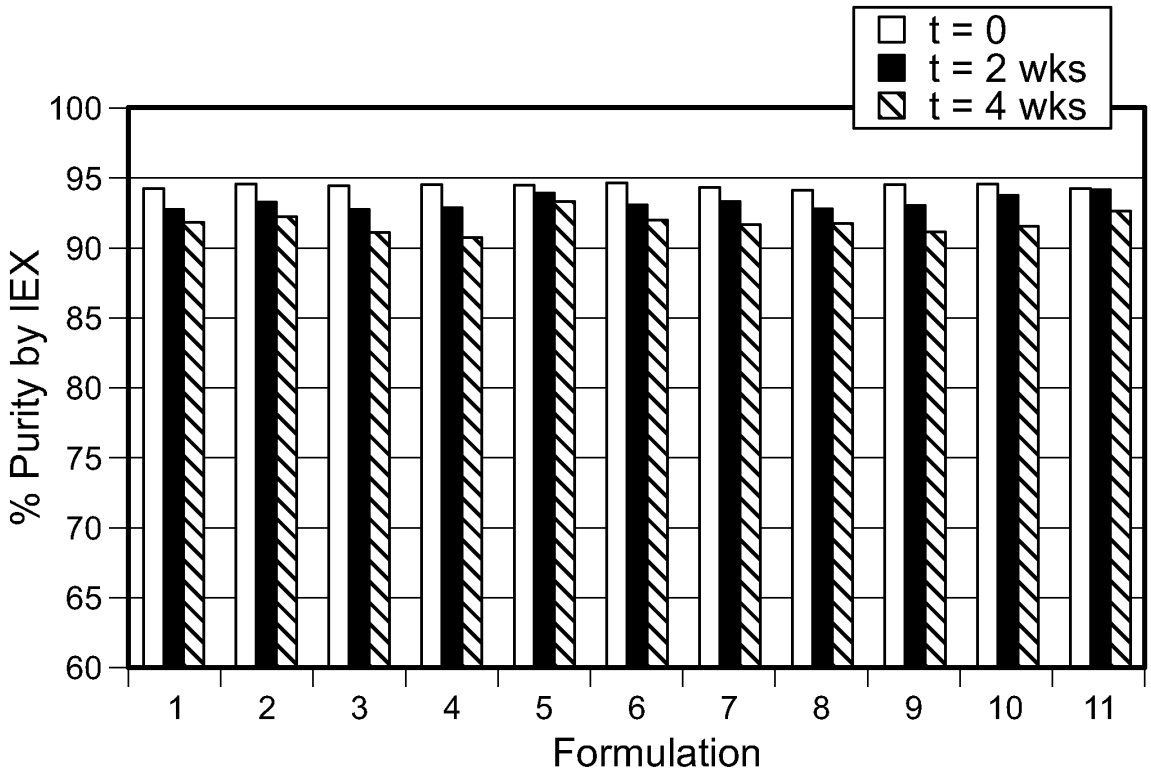

t = 0
t = 2 wks
t = 4 wks
100
95
90
85
80
75
70
65
60
% Purity by IEX
1
2
3
4
5
6
7
8
9
10
11
Formulation

FIG. 23

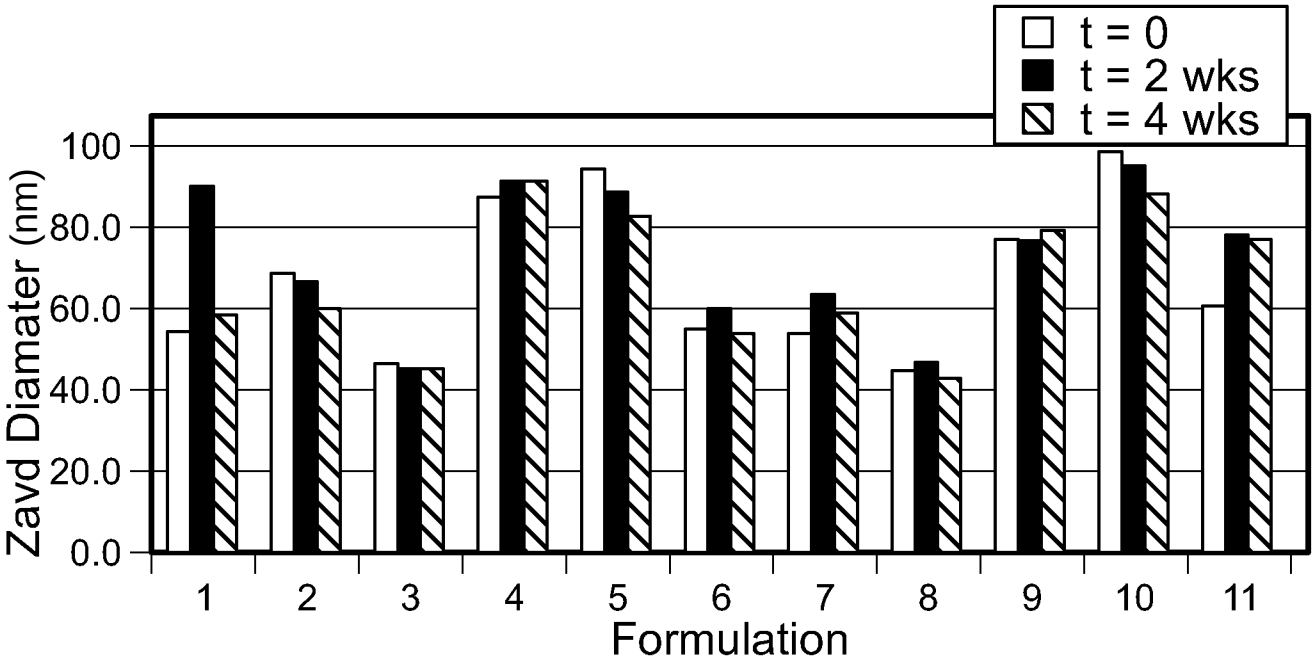

t = 0
t = 2 wks
t = 4 wks
Zavd Diamater (nm)
100
80.0
60.0
40.0
20.0
0.0
1
2
3
4
5
6
7
8
9
10
11
Formulation

FIG. 24

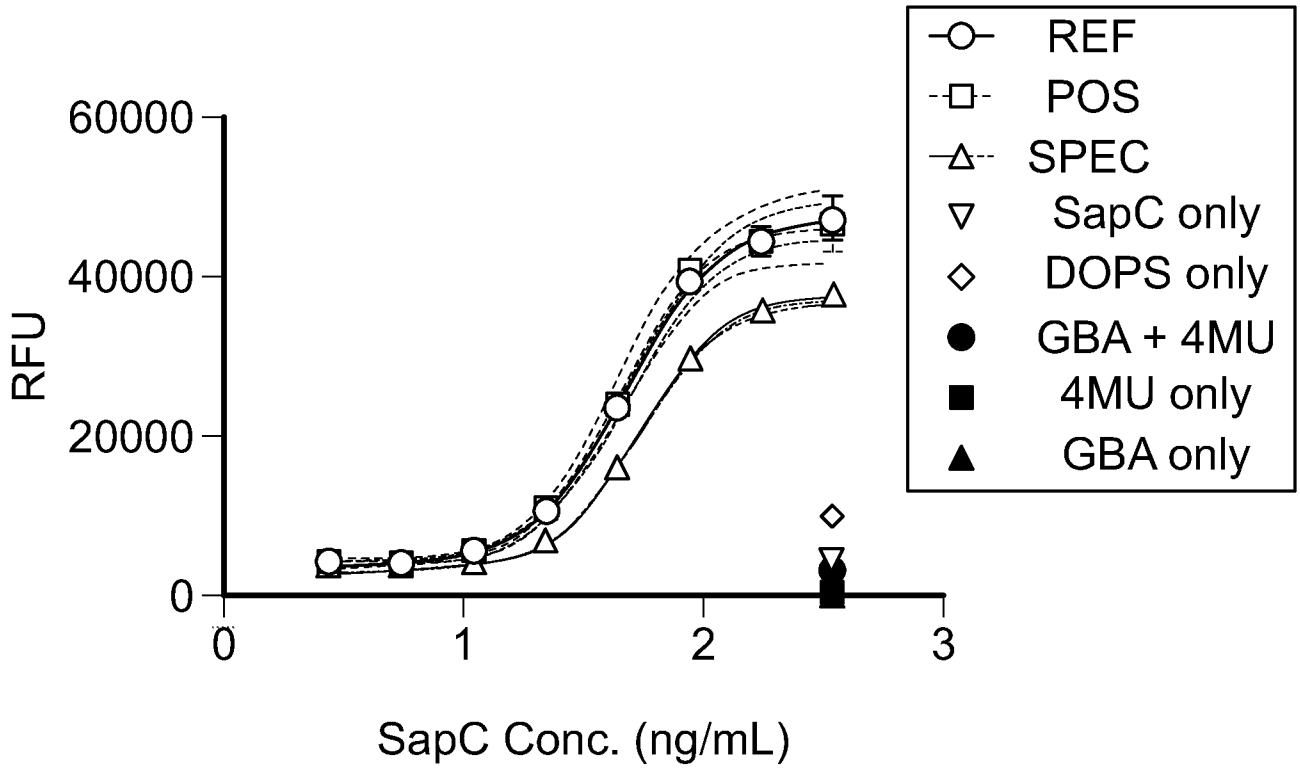

REF
POS
SPEC
SapC only
DOPS only
GBA + 4MU
4MU only
GBA only
RFU
60000
40000
20000
0
0
1
2
3
SapC Conc. (ng/mL)

FIG. 25

DOSE (mg/kg)	0.7	1.1	1.4	1.8	2.4
N	1	3	3	3	8
Mean Age	64	53	58	49	54
F:M	0:1	0:3	2:1	1:2	2:2
Solid Tumor	0	2	1	1	5
Improved RANO (n/*N* DY113) Partial Response	1/1	1/1	1/2	-	-
HGG	1	1	2	2	3
Improved RECIST (n/*N* DY113)	1/1				2/2
Non-related Discontinuation		3	3	2	7
Adverse Events (*n Cases, n Events*)	1,15	3,54	3,37	3,32	8,80
Moderate Severity, Related		3,6	1,1	1,2	2,2
Fatigue		2,2		1,2	1,1
Neutropenia		1,1			
EKG		1,2			
Balance		1,1			
Nervous		1,1			
Dysarthria		1,1			
Urinary			1,1		
BP					1,1
Serious, Non-related	1,1	1,4	1,3	1,3	3,5
GI		1,1	1,1		1,3
Hyponatremia		1,1			
Weakness			1,1		

HGG: High Grade Glioma, RECIST :Response Evaluation Criteria in Solid Tumors, RANO: Response Assessment in Neuro-onocology Criteria

FIG. 26

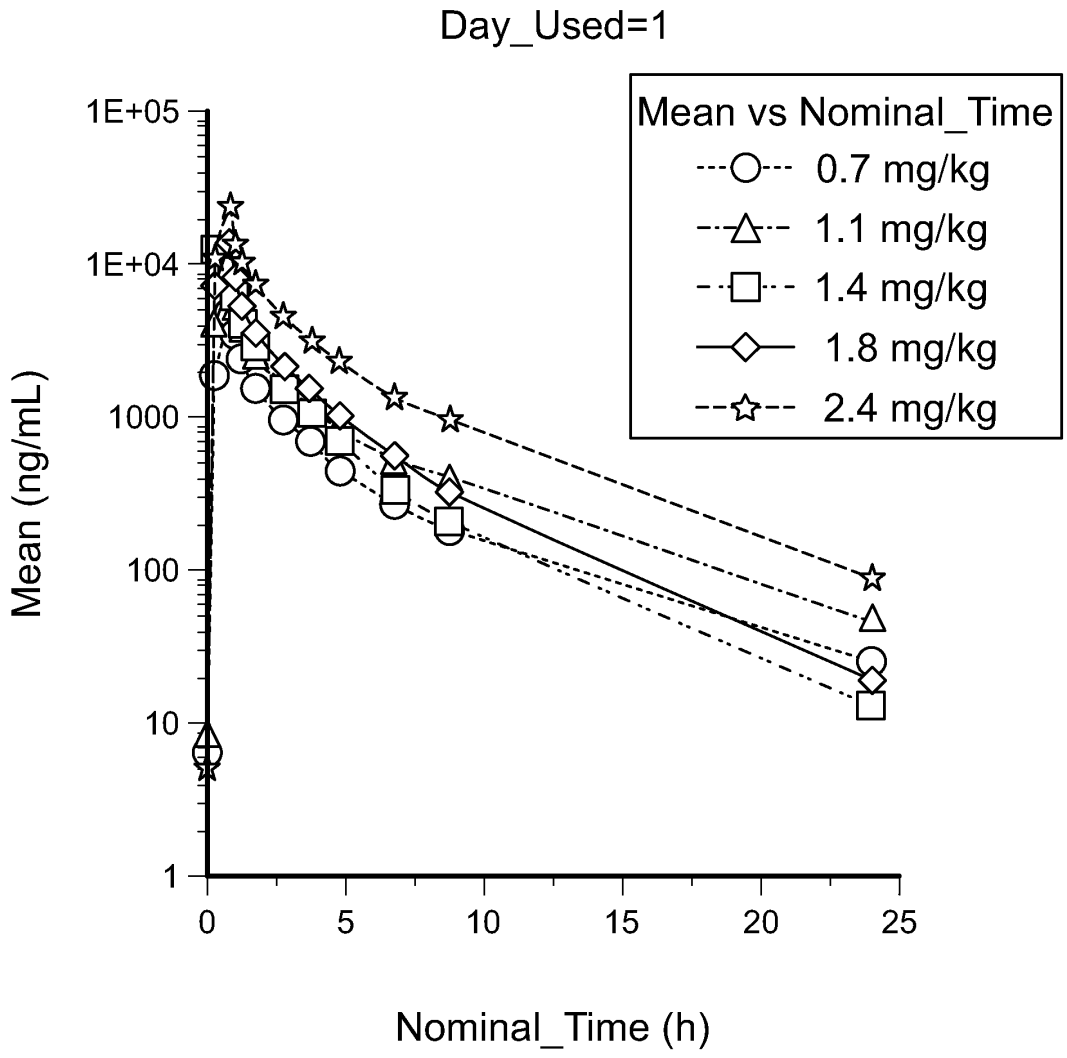

Day_Used=1
Mean vs Nominal_Time
0.7 mg/kg
1.1 mg/kg
1.4 mg/kg
1.8 mg/kg
2.4 mg/kg
1E+05
1E+04
1000
100
10
1
Mean (ng/mL)
0
5
10
15
20
25
Nominal_Time (h)

FIG. 27A

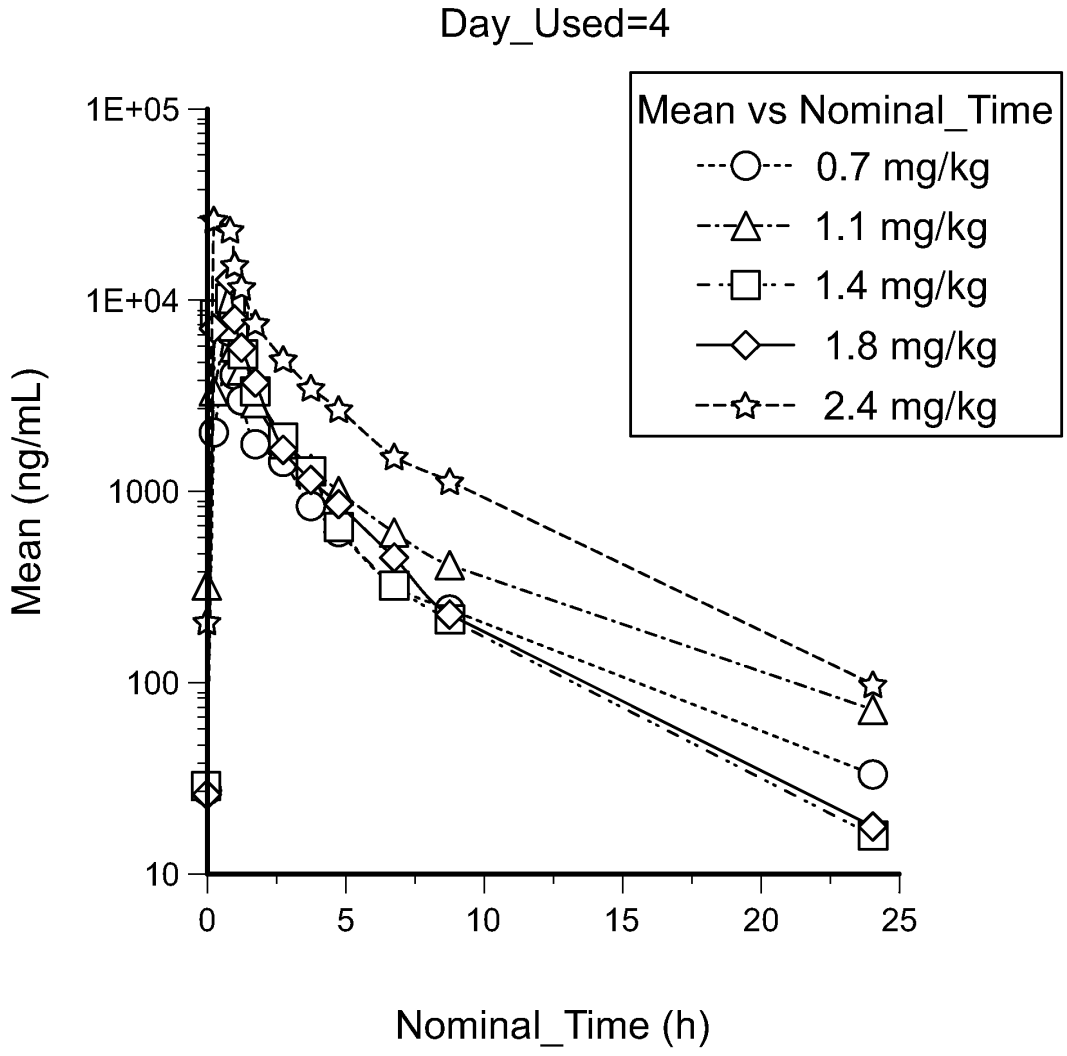

Day_Used=4
Mean vs Nominal_Time
0.7 mg/kg
1.1 mg/kg
1.4 mg/kg
1.8 mg/kg
2.4 mg/kg
1E+05
1E+04
1000
100
10
Mean (ng/mL)
0
5
10
15
20
25
Nominal_Time (h)

FIG. 27B

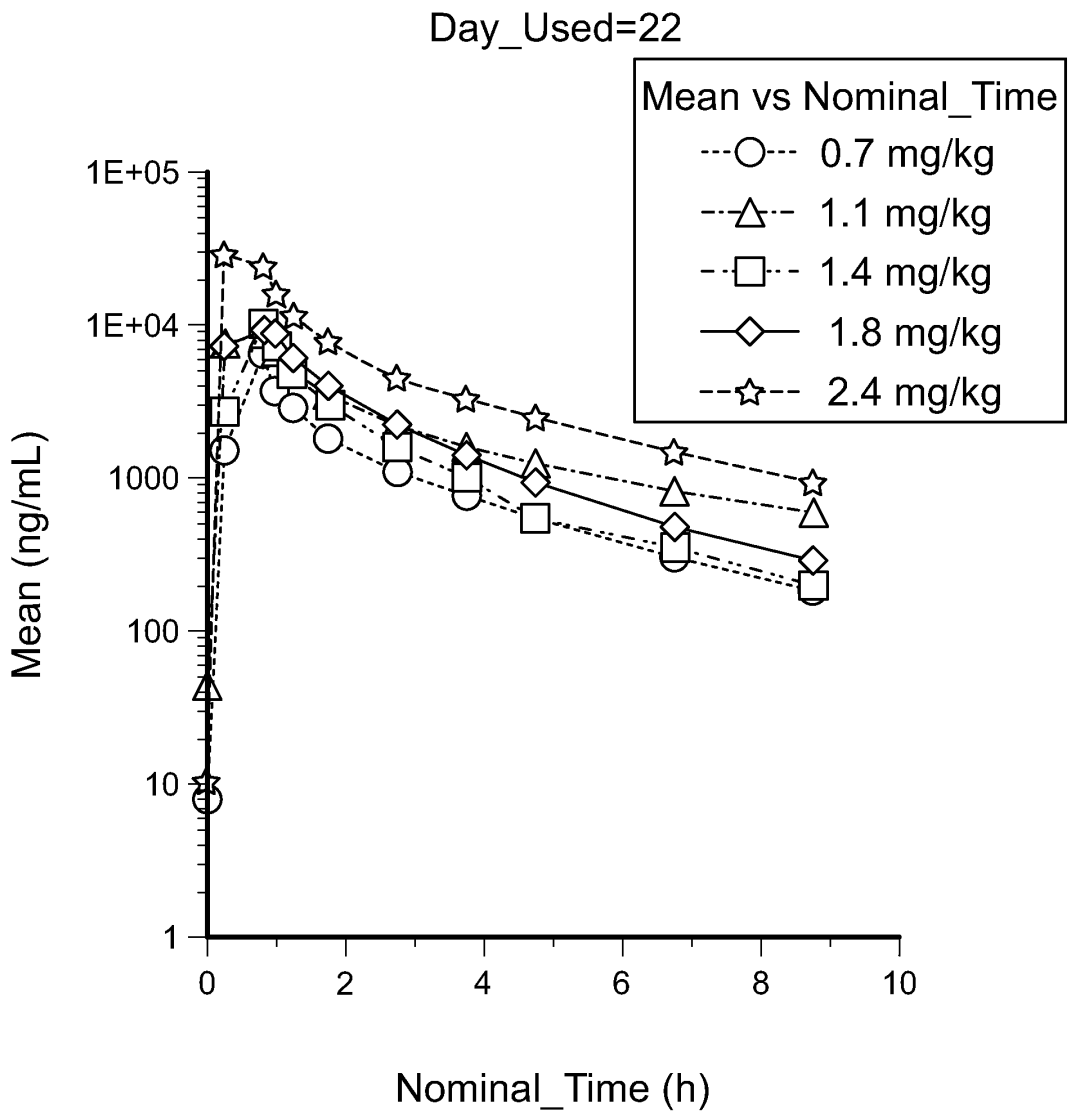

Day_Used=22
Mean vs Nominal_Time
0.7 mg/kg
1.1 mg/kg
1.4 mg/kg
1.8 mg/kg
2.4 mg/kg
1E+05
1E+04
1000
100
10
1
Mean (ng/mL)
0
2
4
6
8
10
Nominal_Time (h)

FIG. 27C

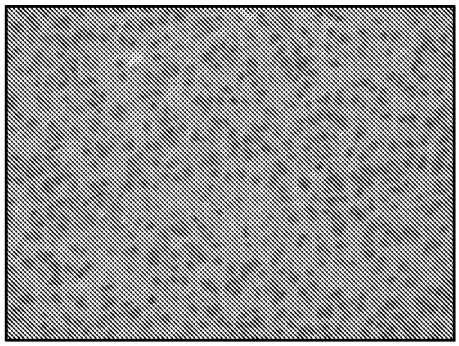


FIG. 28A

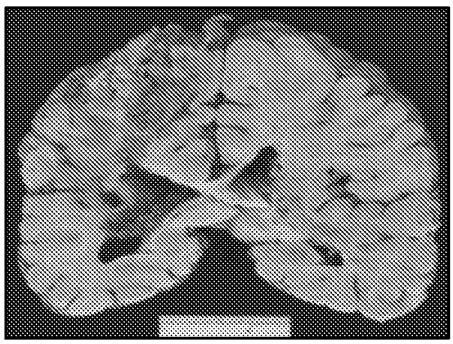


FIG. 28B

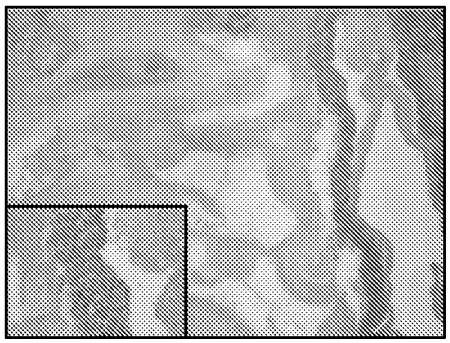


FIG. 28C

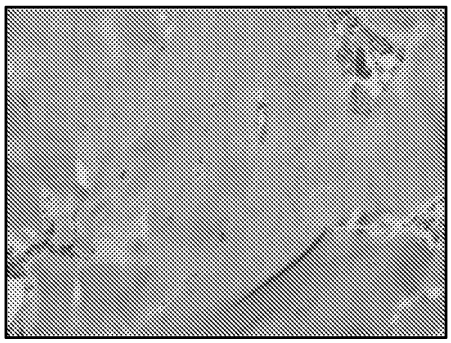


FIG. 28D

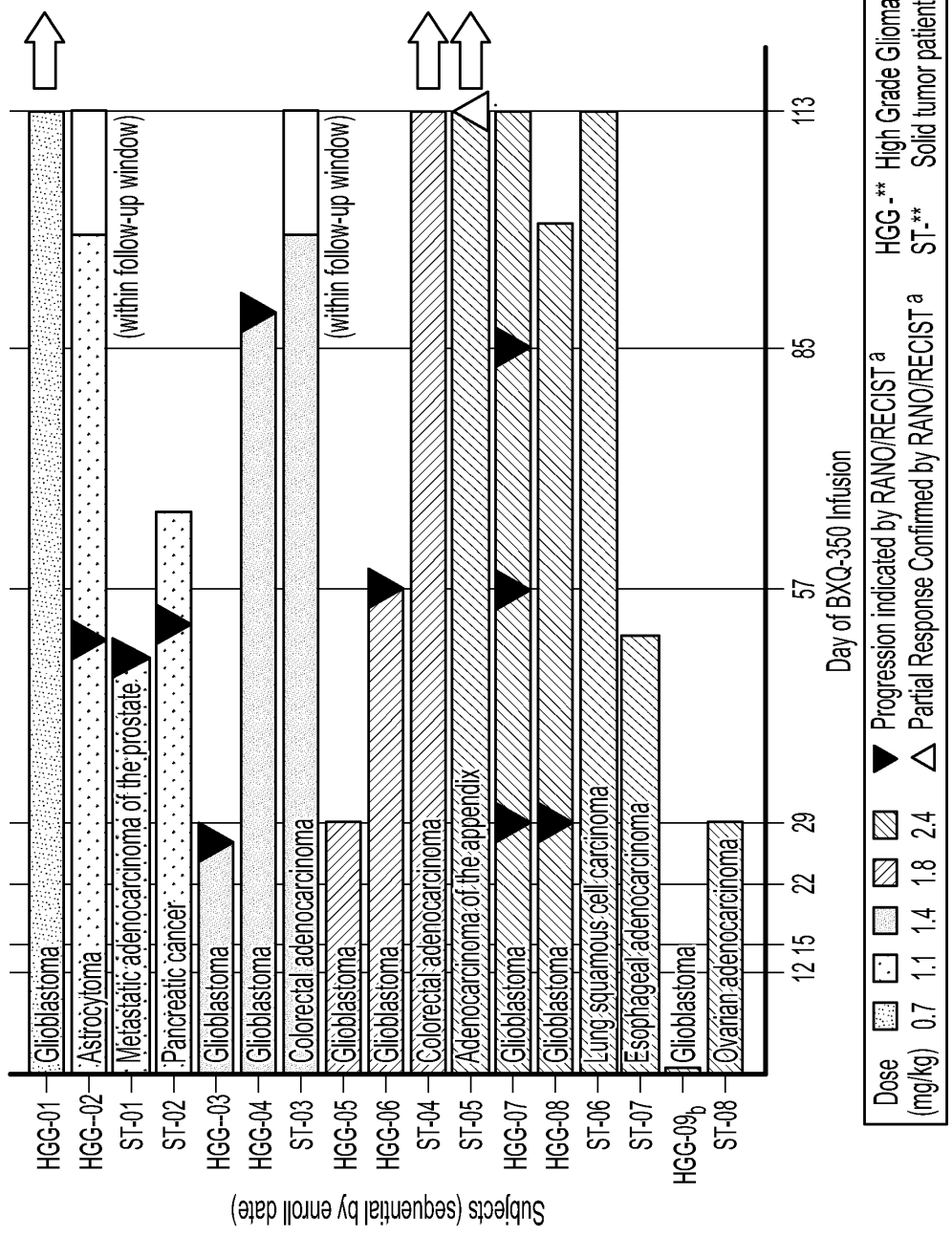


FIG. 29

a Stable disease per RANO/RECIST performed in the study was maintained unless marked with red/green arrows, other clinical deterioration or signs/symptoms of progression not confirmed by study imaging are not shown

b Subject HGG-09 was withdrawn for reasons not related to study intervention following the first dose

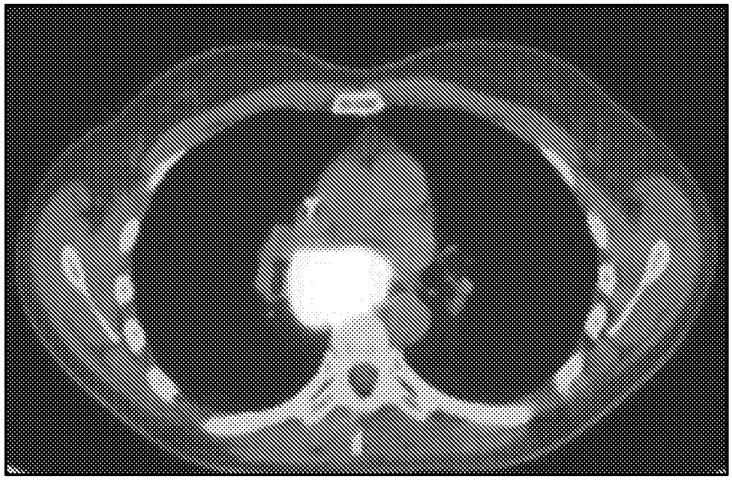


FIG. 30A

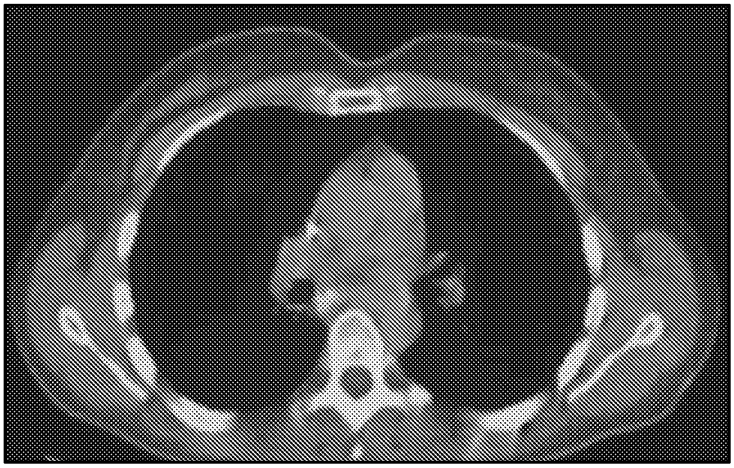


FIG. 30B