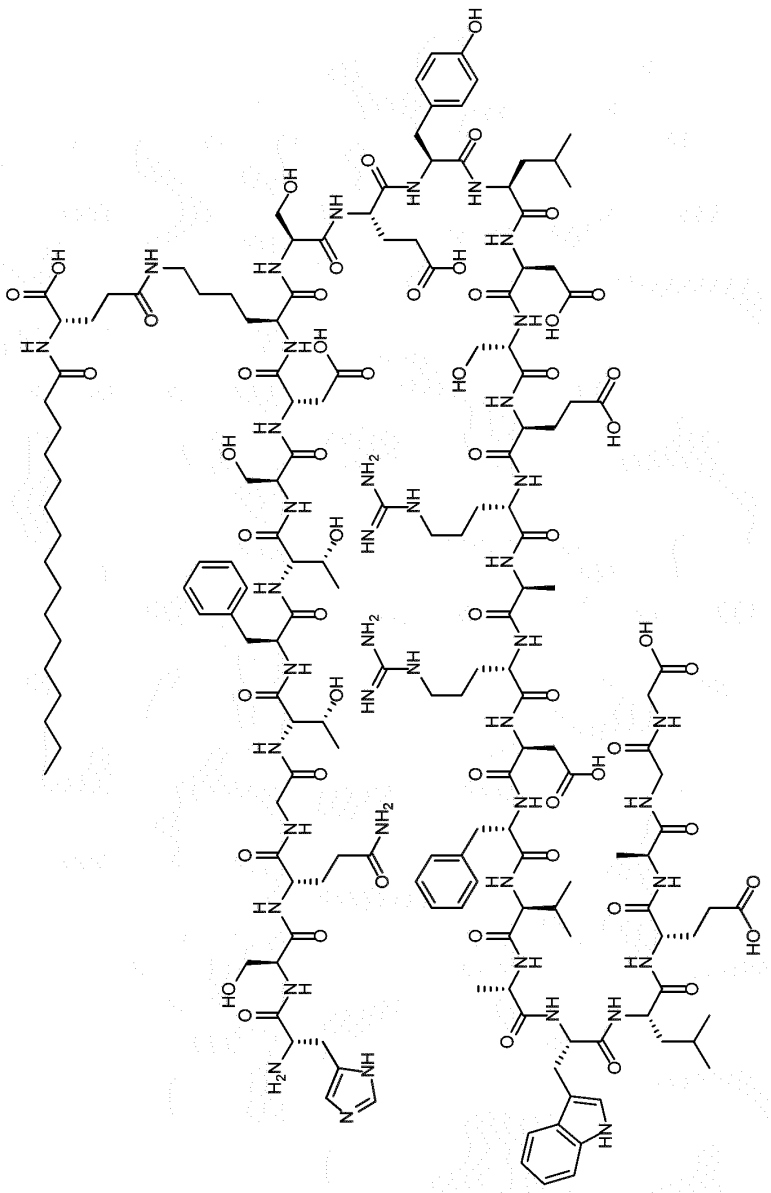


Molecular Formula: $C_{167}H_{252}N_{42}O_{55}$
Molecular Weight: 3728.03618
HisSerGlnGlyThrPheThrSerAspLys[Glu.C(O)C16]SerGluTyrLeuAspSer GluArgAlaArgAspPheValAlaTrpValGluAlaGlyGly (SEQ ID NO:1)

FIG. 1

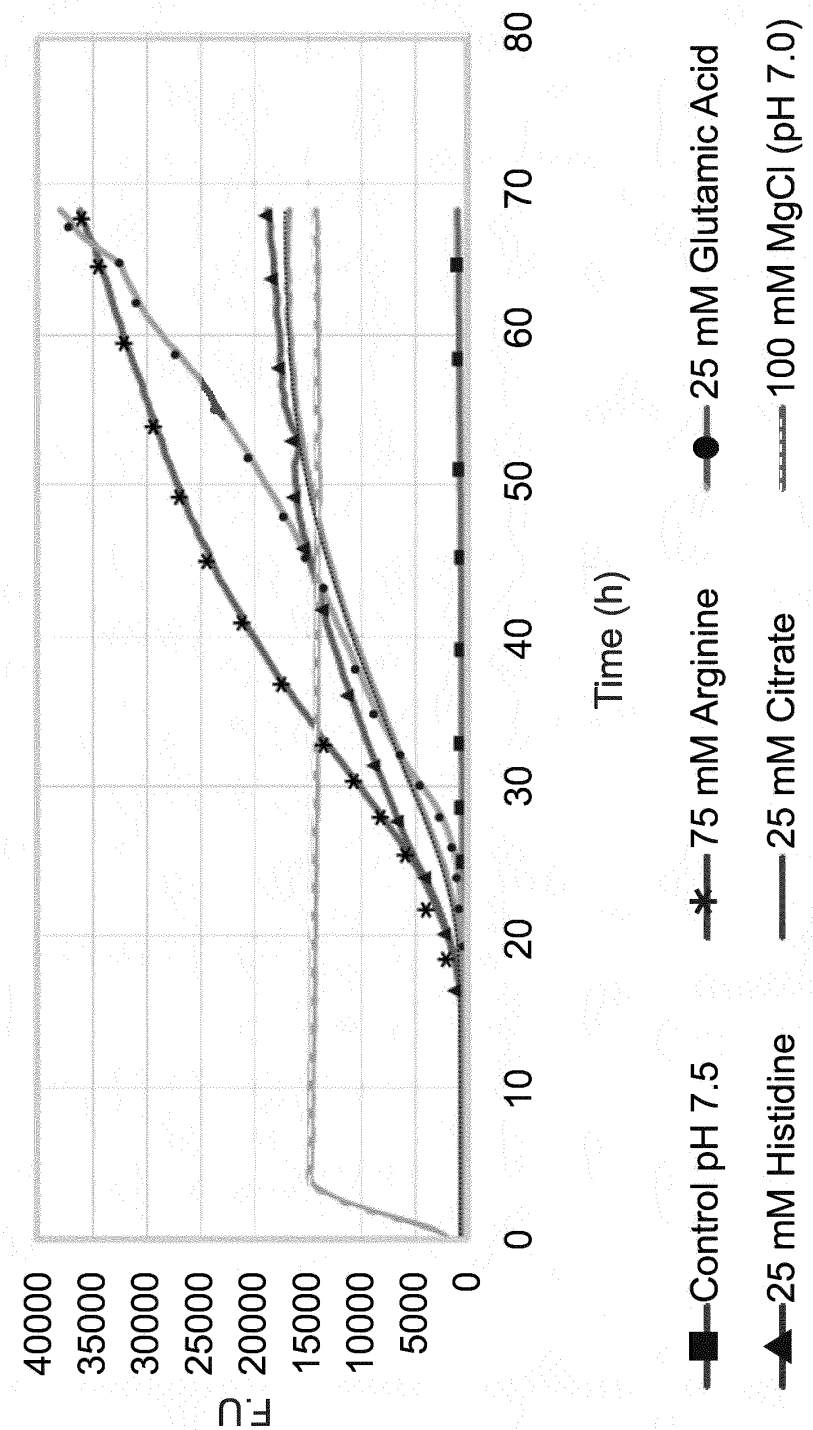

40000
35000
30000
25000
20000
15000
10000
5000
0
F.U
0
10
20
30
40
50
60
70
80
Time (h)
Control pH 7.5
75 mM Arginine
25 mM Glutamic Acid
25 mM Histidine
25 mM Citrate
100 mM MgCl (pH 7.0)

FIG. 2

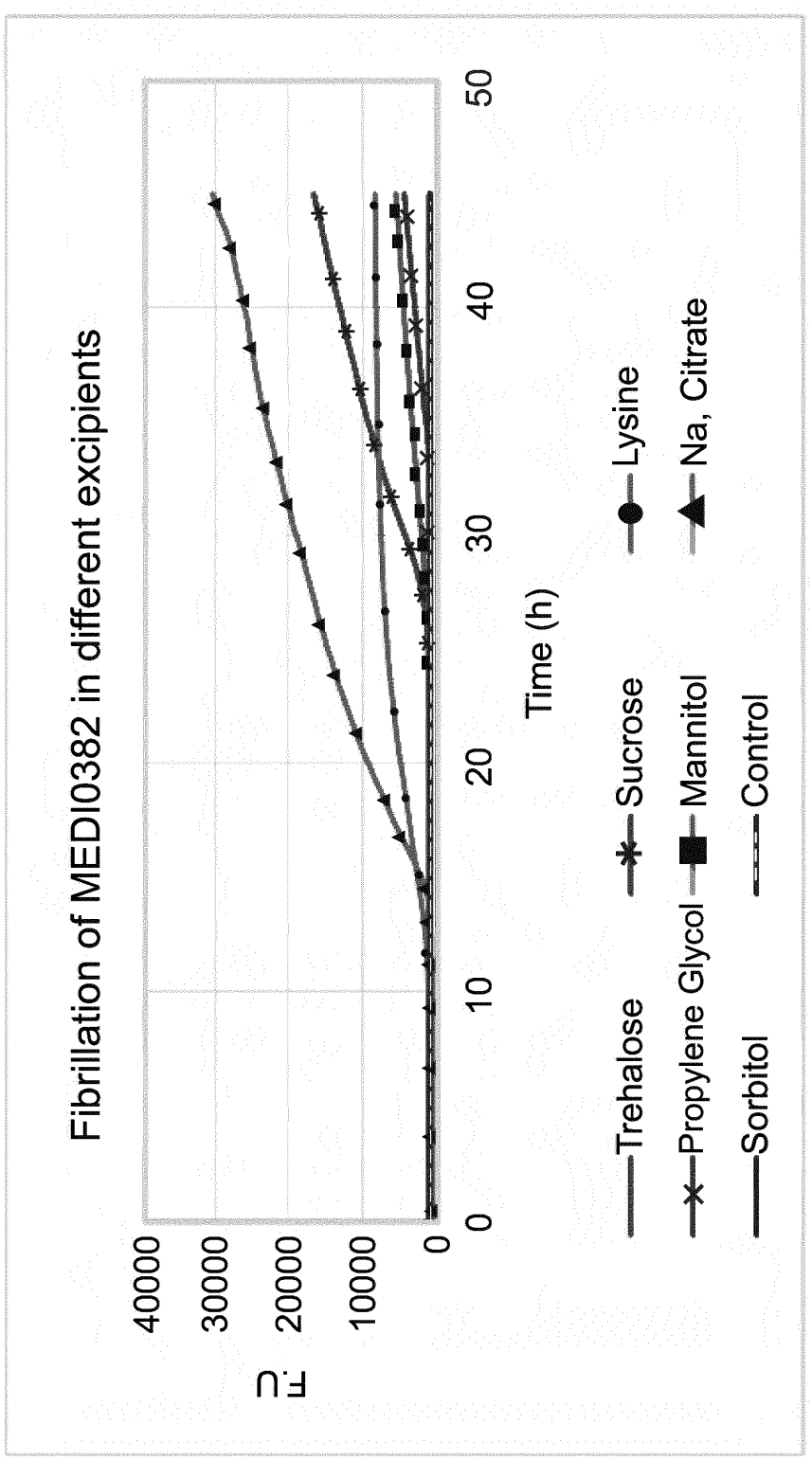

Fibrillation of MEDI0382 in different excipients
F.U
40000
30000
20000
10000
0
0
10
20
30
40
50
Time (h)
Trehalose
Sucrose
Lysine
Propylene Glycol
Mannitol
Na, Citrate
Sorbitol
Control

FIG. 3

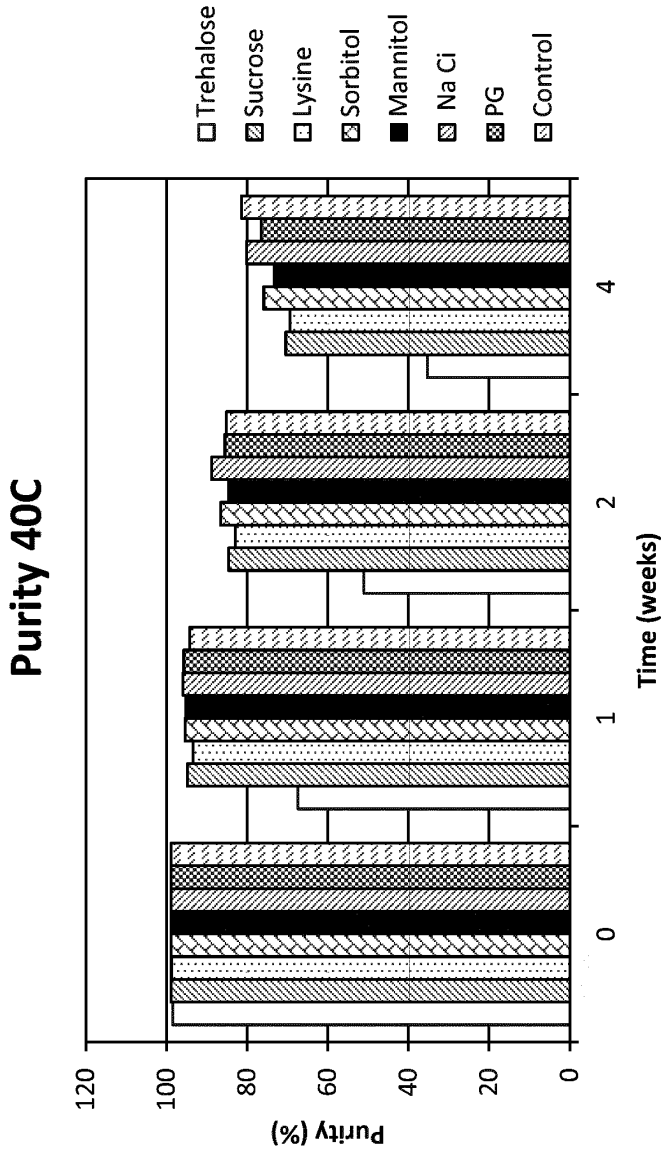

Purity 40C
Trehalose
Sucrose
Lysine
Sorbitol
Mannitol
Na Ci
PG
Control
Purity (%)
120
100
80
60
40
20
0
0
1
2
4
Time (weeks)

FIG. 4

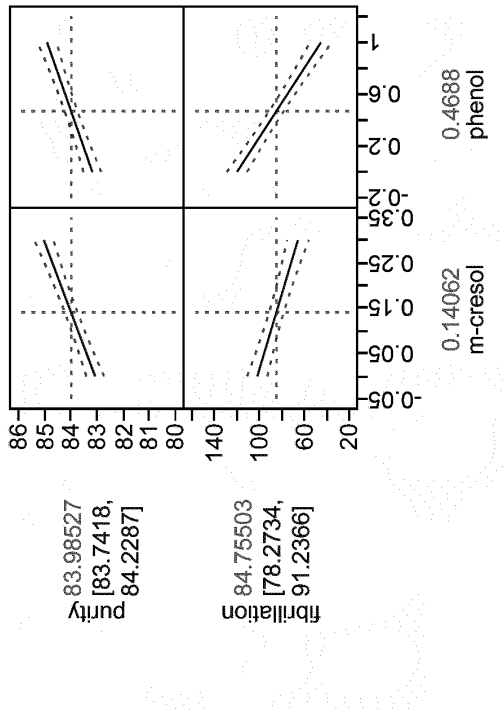

83.98527
[83.7418,
84.2287]
purity
84.75503
[78.2734,
91.2366]
fibrillation
0.14062
m-cresol
0.4688
phenol

FIG. 5

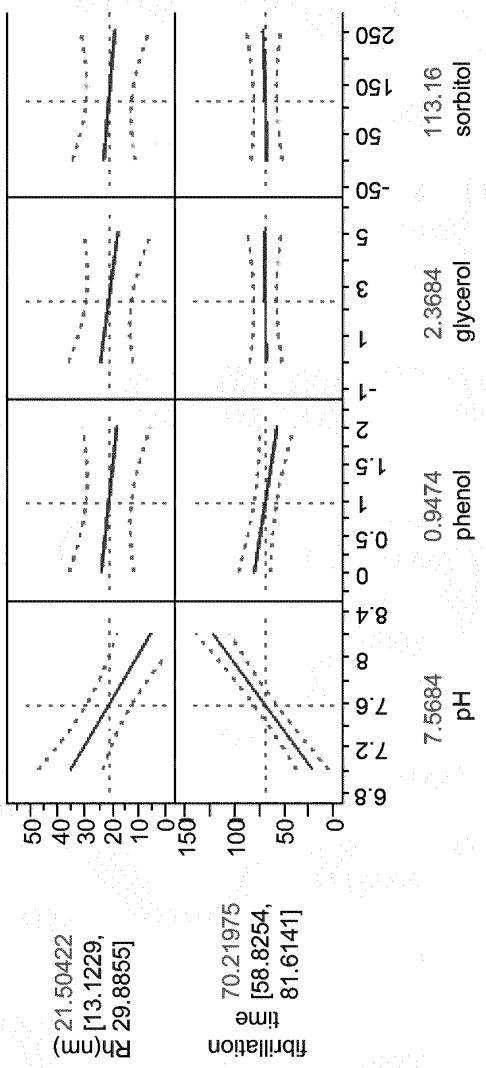

21.50422
[13.1229,
29.8855]
Zh(nm)
70.21975
[58.8254,
81.6141]
fibrillation
time
7.5684
pH
0.9474
phenol
2.3684
glycerol
113.16
sorbitol

FIG. 6

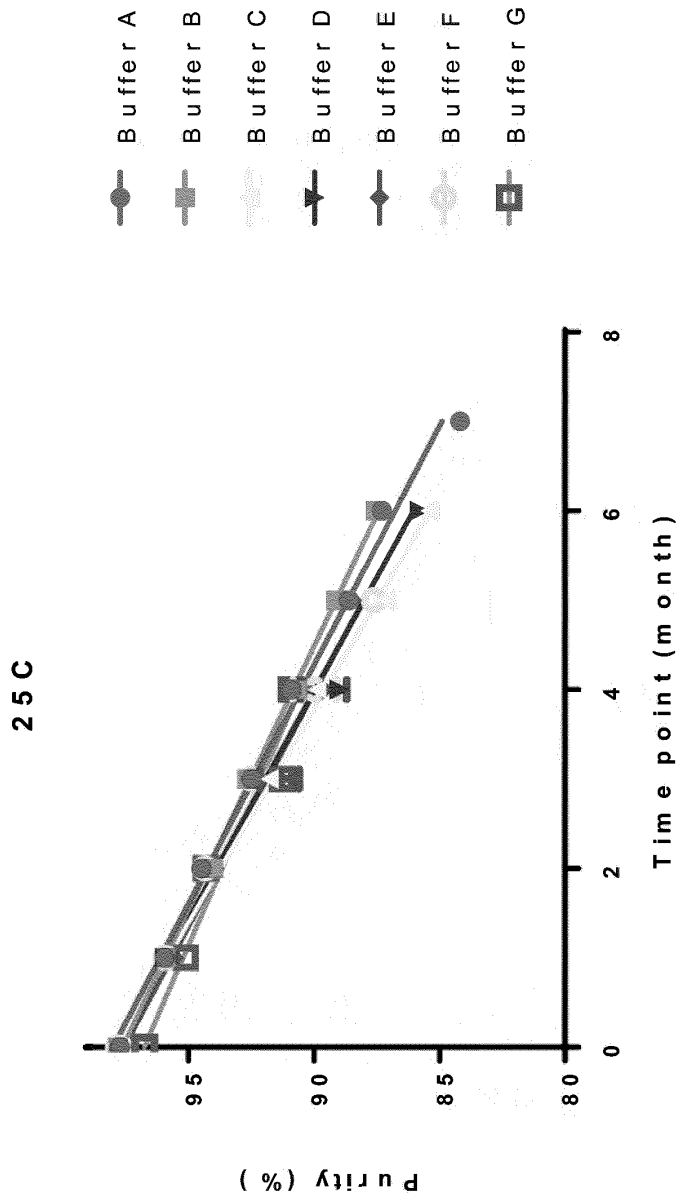

Buffer A
Buffer B
Buffer C
Buffer D
Buffer E
Buffer F
Buffer G
25C
Purity (%)
95
90
85
80
0
2
4
6
8
Time point (month)

FIG. 7

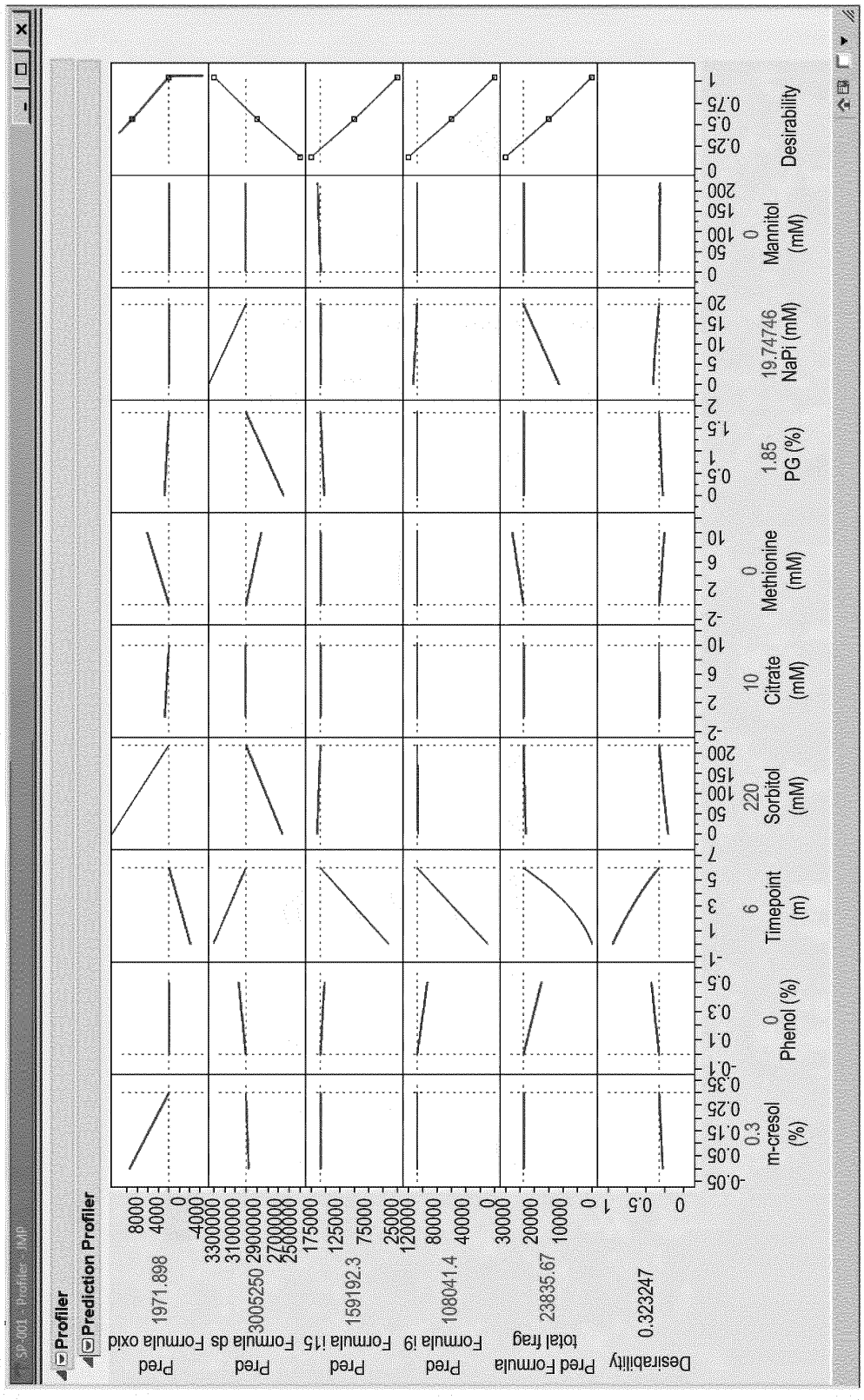

Profiler
Prediction Profiler
Pred Formula oxid
Pred Formula ds
Pred Formula i15
Pred Formula i9
Pred Formula total frag
Desirability
m-cresol (%)
Phenol (%)
Timepoint (m)
Sorbitol (mM)
Citrate (mM)
Methionine (mM)
PG (%)
NaPi (mM)
Mannitol (mM)
Desirability

FIG. 8

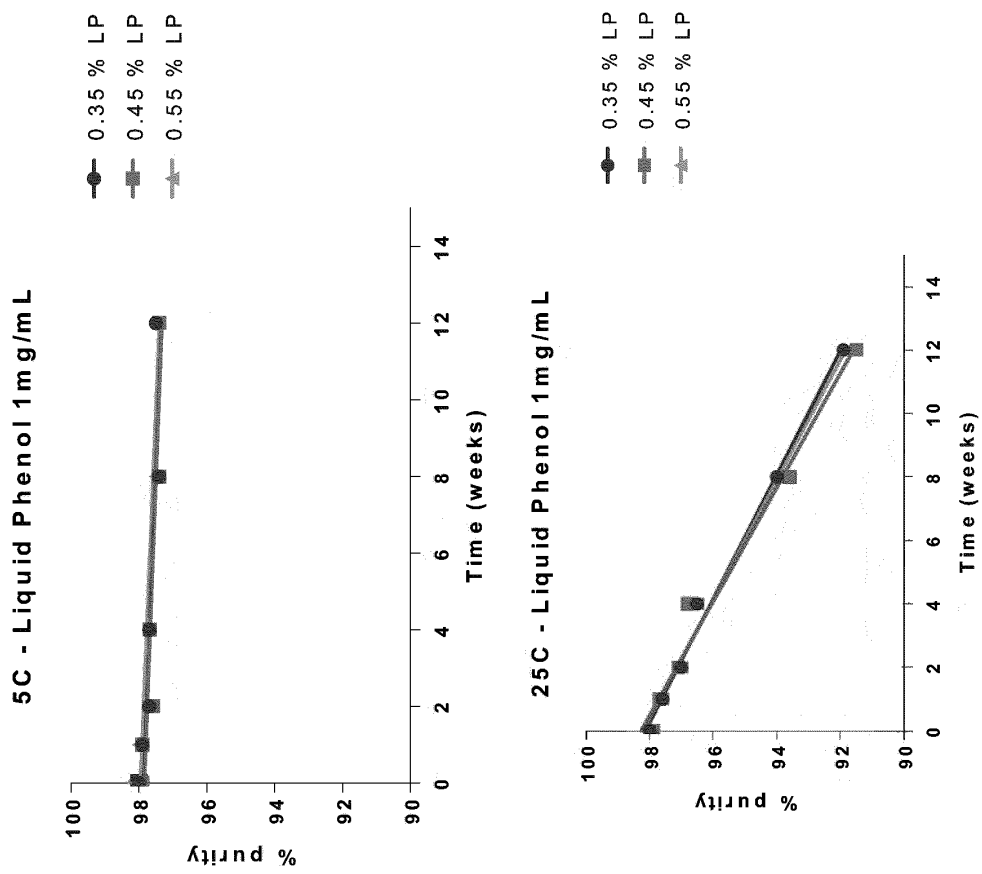
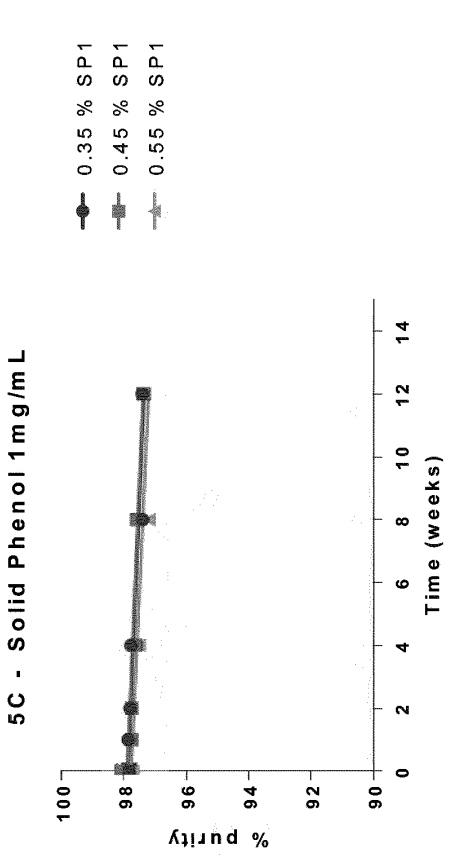

5C - Liquid Phenol 1mg/mL
0.35 % LP
0.45 % LP
0.55 % LP
% purity
Time (weeks)
100
98
96
94
92
90
0
2
4
6
8
10
12
14
25C - Liquid Phenol 1mg/mL
0.35 % LP
0.45 % LP
0.55 % LP
% purity
Time (weeks)

FIG. 9


5C - Solid Phenol 1mg/mL
0.35 % SP1
0.45 % SP1
0.55 % SP1
% purity
Time (weeks)
100
98
96
94
92
90
0
2
4
6
8
10
12
14

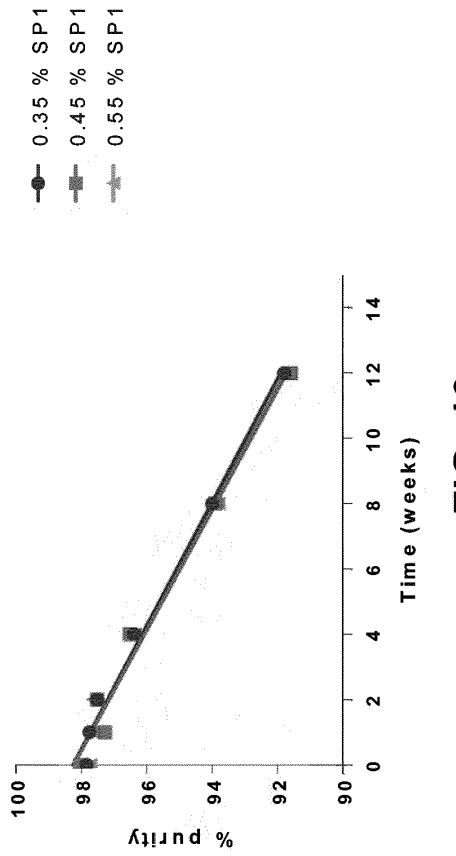

25C - Solid Phenol 1mg/mL
0.35 % SP1
0.45 % SP1
0.55 % SP1
% purity
Time (weeks)
100
98
96
94
92
90
0
2
4
6
8
10
12
14

FIG. 10

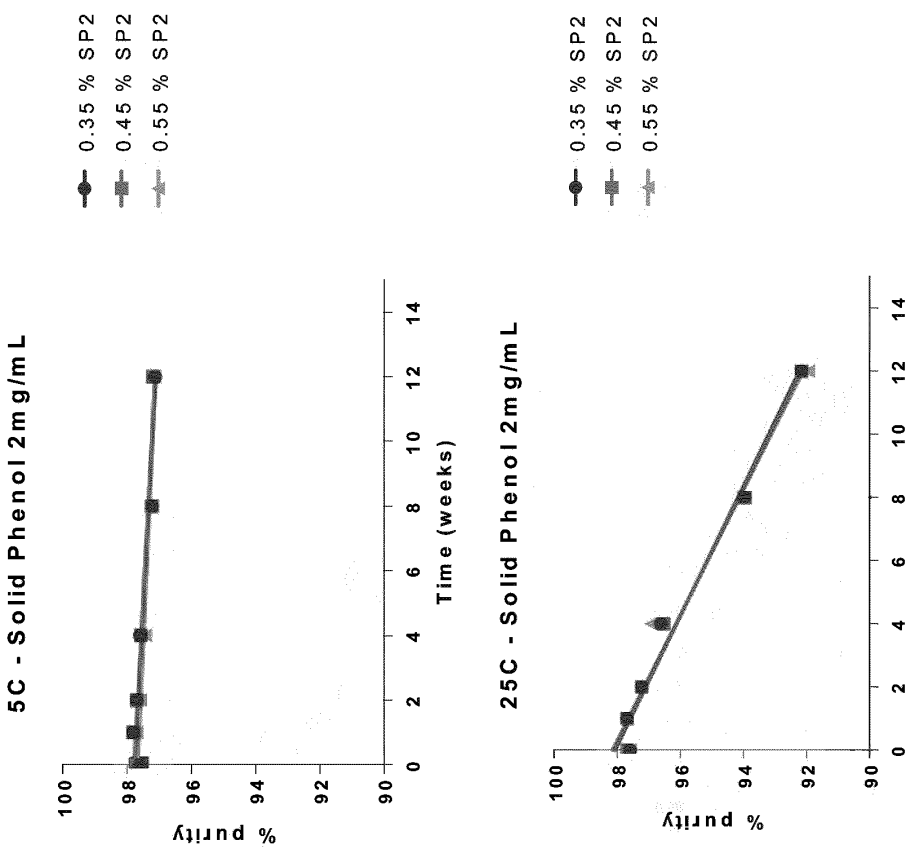

5C - Solid Phenol 2mg/mL
0.35 % SP2
0.45 % SP2
0.55 % SP2
% purity
Time (weeks)
100
98
96
94
92
90
0
2
4
6
8
10
12
14
25C - Solid Phenol 2mg/mL
0.35 % SP2
0.45 % SP2
0.55 % SP2
% purity
Time (weeks)

FIG. 11

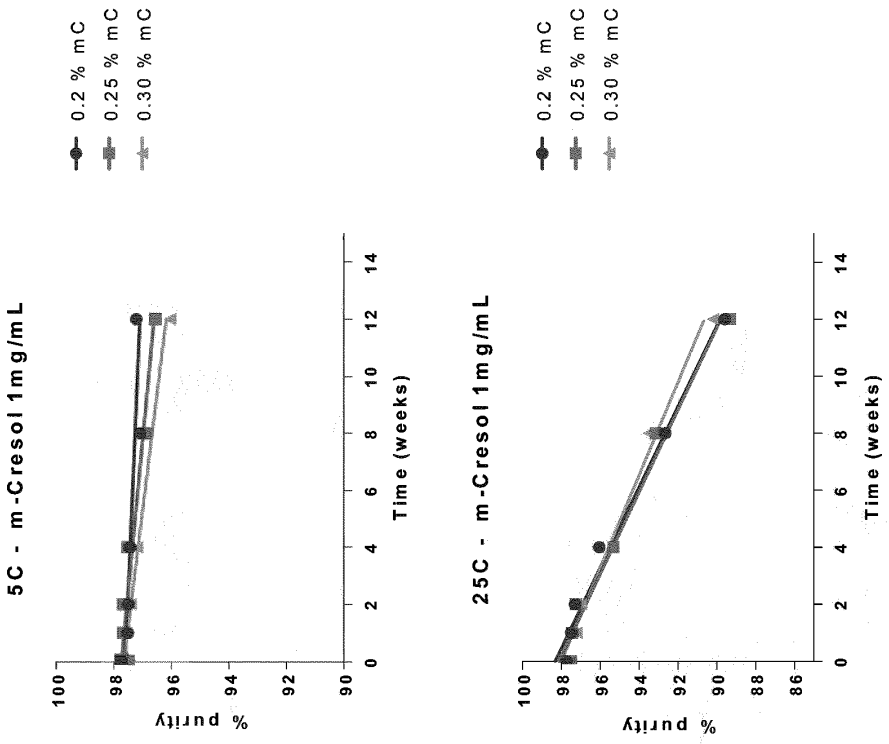
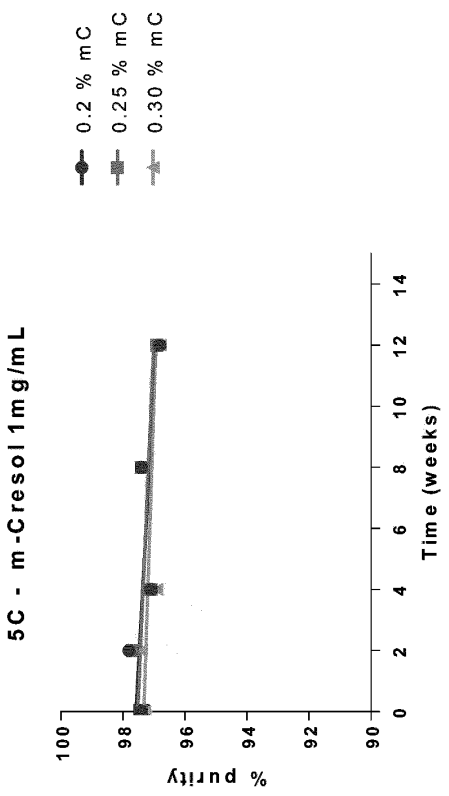

5C - m-Cresol 1mg/mL
0.2 % mC
0.25 % mC
0.30 % mC
% purity
Time (weeks)
25C - m-Cresol 1mg/mL
0.2 % mC
0.25 % mC
0.30 % mC
% purity
Time (weeks)

FIG. 12


5C - m-Cresol 1mg/mL
0.2 % mC
0.25 % mC
0.30 % mC
% purity
Time (weeks)
100
98
96
94
92
90
0
2
4
6
8
10
12
14

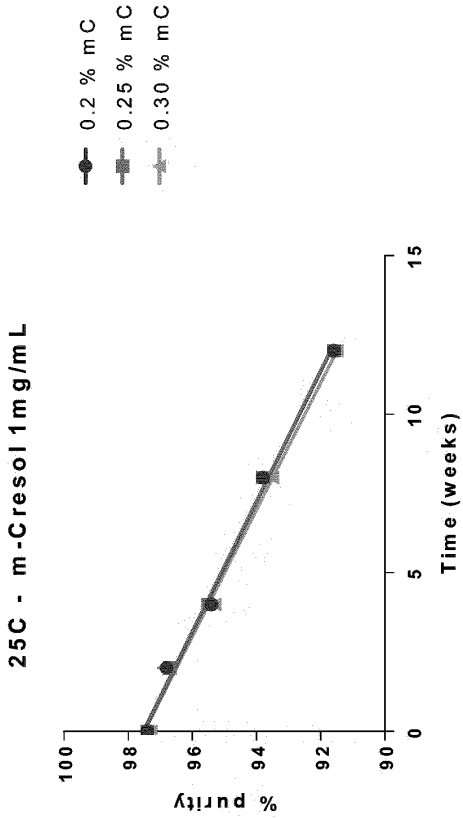
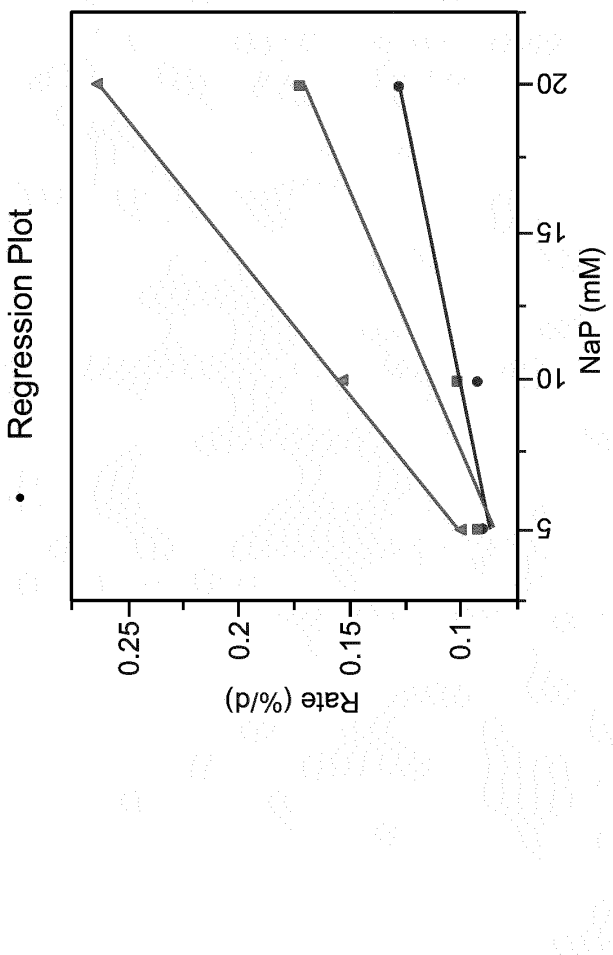

25C - m-Cresol 1mg/mL
0.2 % mC
0.25 % mC
0.30 % mC
% purity
Time (weeks)
100
98
96
94
92
90
0
5
10
15

FIG. 13

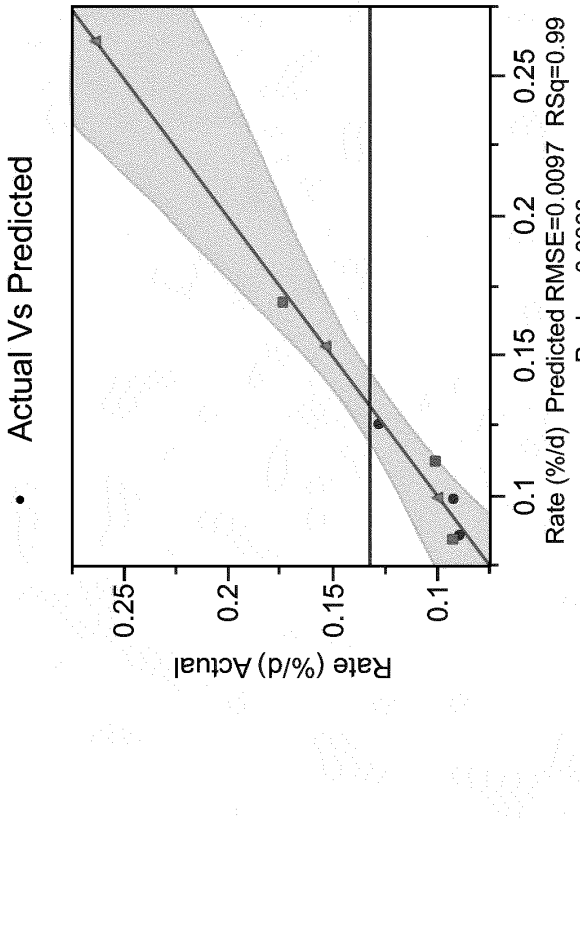


Effect Tests

Source	Nparm	DF	Sum of Squares	F Ratio	Prob > F
NaP (mM)	1	1	0.01438190	151.4337	0.0012*
NaP Type	2	2	0.00756245	39.8143	0.0069*
NaP (mM)*NaP Type	2	2	0.00402225	21.1761	0.0170*

All terms significant

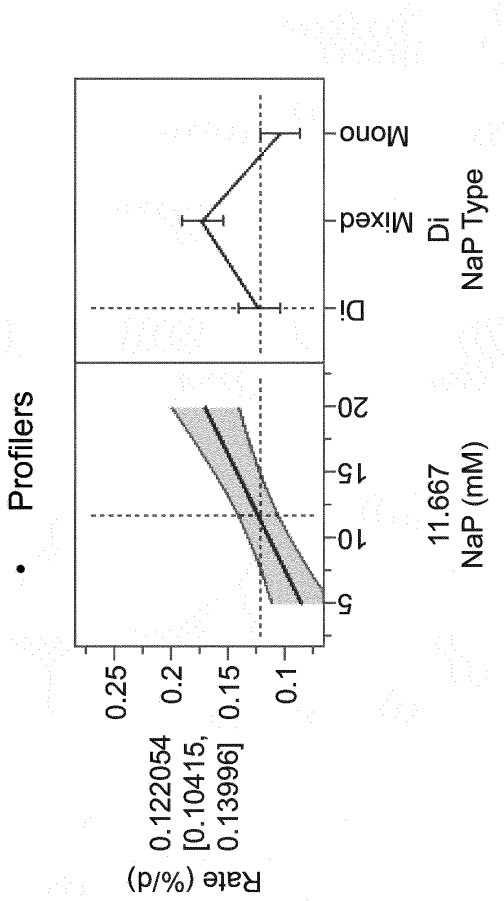
FIG. 14A



Least Squares Means Table

Level	Last Sq Mean	Std Error	Lower 95%	Upper 95%	Mean
Di	0.12205208	0.00562647	0.10414614	0.13995803	0.122052
Mixed	0.17212473	0.00562647	0.15421878	0.19003067	0.172125
Mono	0.10349053	0.00562647	0.08558458	0.12139648	0.103491

FIG. 14B


Profilers
Rate (%/d)
0.122054
[0.10415,
0.13996]
0.25
0.2
0.15
0.1
5
10
15
20
11.667
NaP (mM)
DI
Mixed
Mono
Di
NaP Type

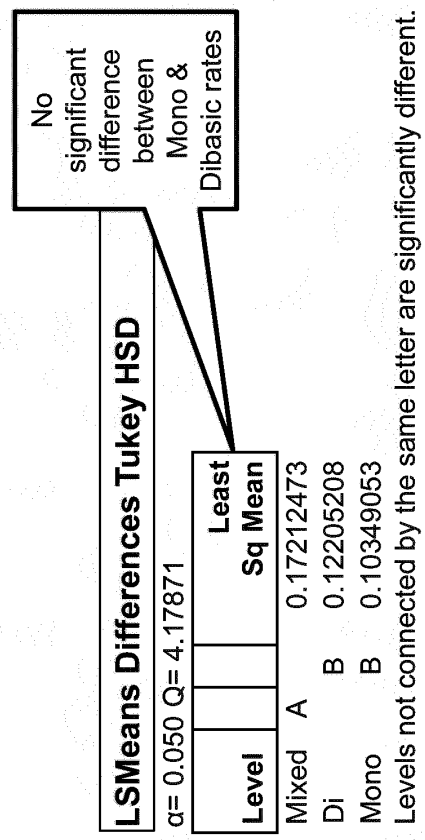

No significant difference between Mono & Dibasic rates
LSMeans Differences Tukey HSD
α= 0.050 Q= 4.17871
Level
Least Sq Mean
Mixed A 0.17212473
Di B 0.12205208
Mono B 0.10349053
Levels not connected by the same letter are significantly different.

FIG. 14C

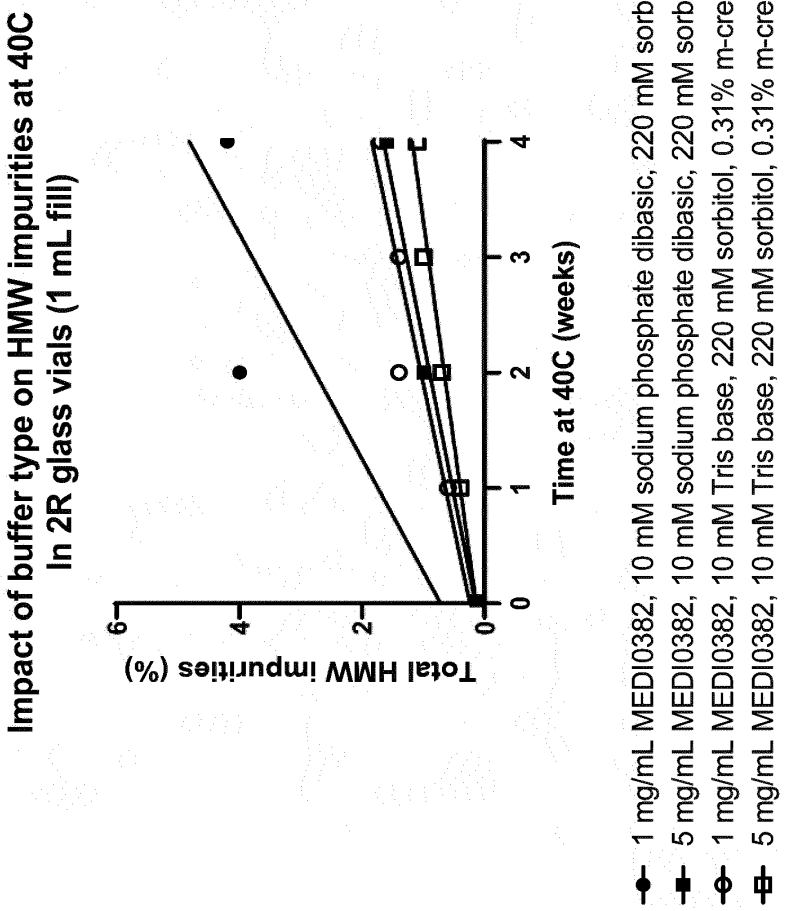

Impact of buffer type on HMW impurities at 40C
In 2R glass vials (1 mL fill)
Total HMW impurities (%)
0
2
4
6
0
1
2
3
4
Time at 40C (weeks)
1 mg/mL MEDI0382, 10 mM sodium phosphate dibasic, 220 mM sorbitol, 0.31% m-cresol, pH 8.1
5 mg/mL MEDI0382, 10 mM sodium phosphate dibasic, 220 mM sorbitol, 0.31% m-cresol, pH 8.1
1 mg/mL MEDI0382, 10 mM Tris base, 220 mM sorbitol, 0.31% m-cresol, pH 8.1
5 mg/mL MEDI0382, 10 mM Tris base, 220 mM sorbitol, 0.31% m-cresol, pH 8.1

FIG. 15

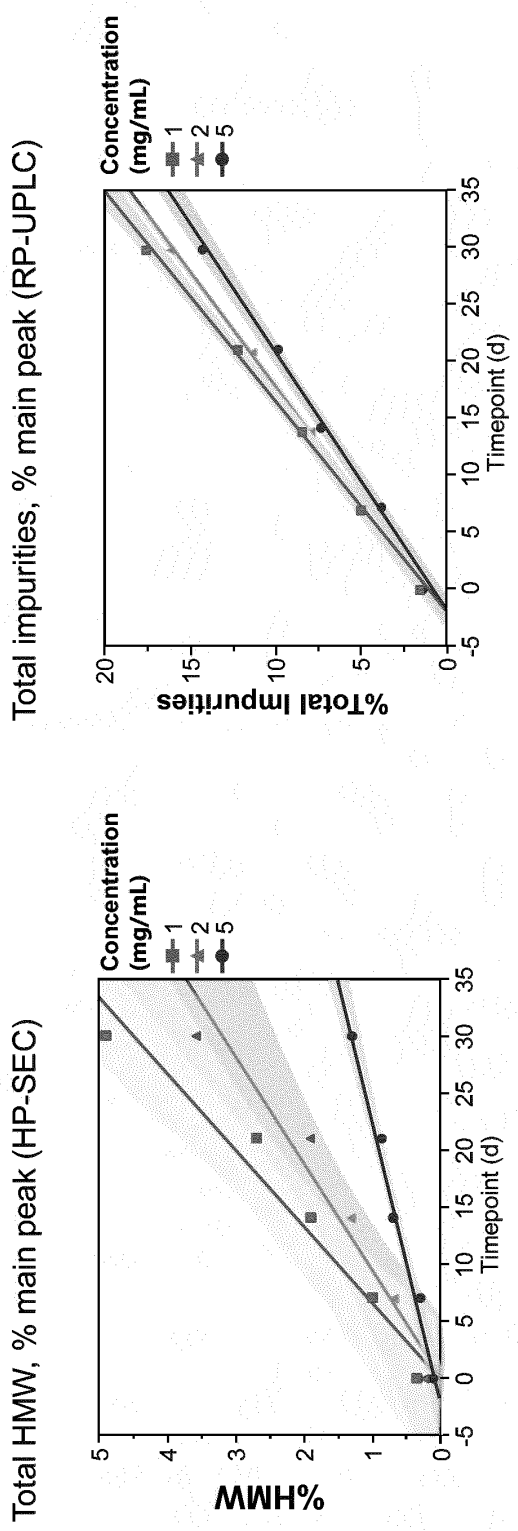

Total HMW, % main peak (HP-SEC)
%HMW
Timepoint (d)
Concentration (mg/mL)
1
2
5
Total impurities, % main peak (RP-UPLC)
%Total Impurities
Timepoint (d)
Concentration (mg/mL)
1
2
5

FIG. 16A

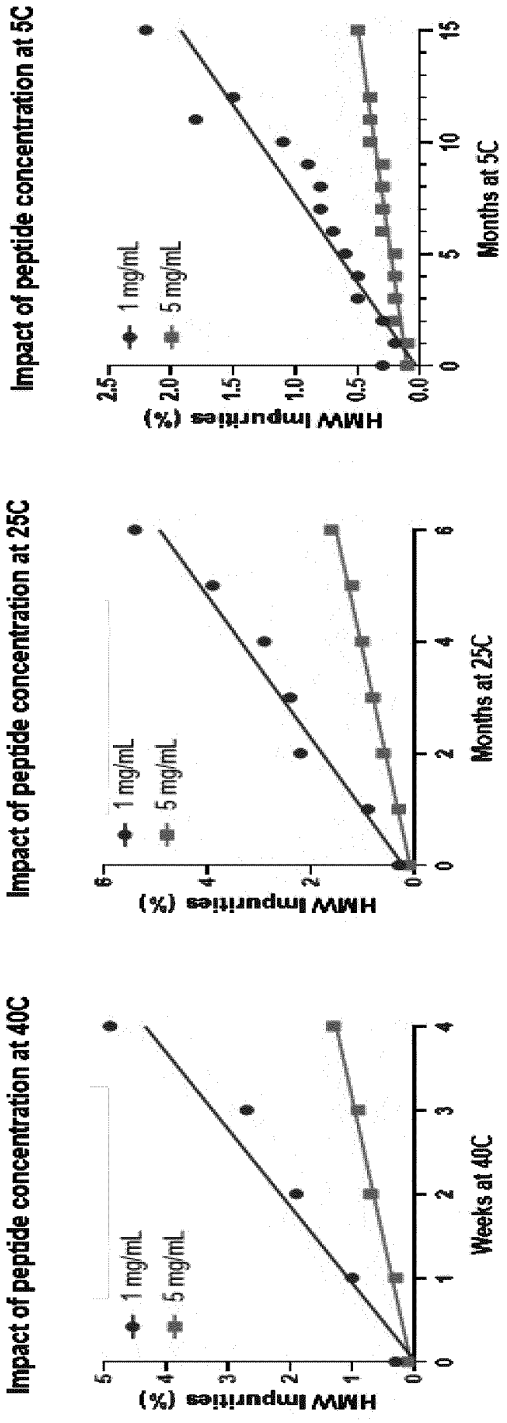

Impact of peptide concentration at 40C
HMW Impurities (%)
1 mg/mL
5 mg/mL
Weeks at 40C
Impact of peptide concentration at 25C
HMW Impurities (%)
1 mg/mL
5 mg/mL
Months at 25C
Impact of peptide concentration at 5C
HMW Impurities (%)
1 mg/mL
5 mg/mL
Months at 5C

FIG. 16B

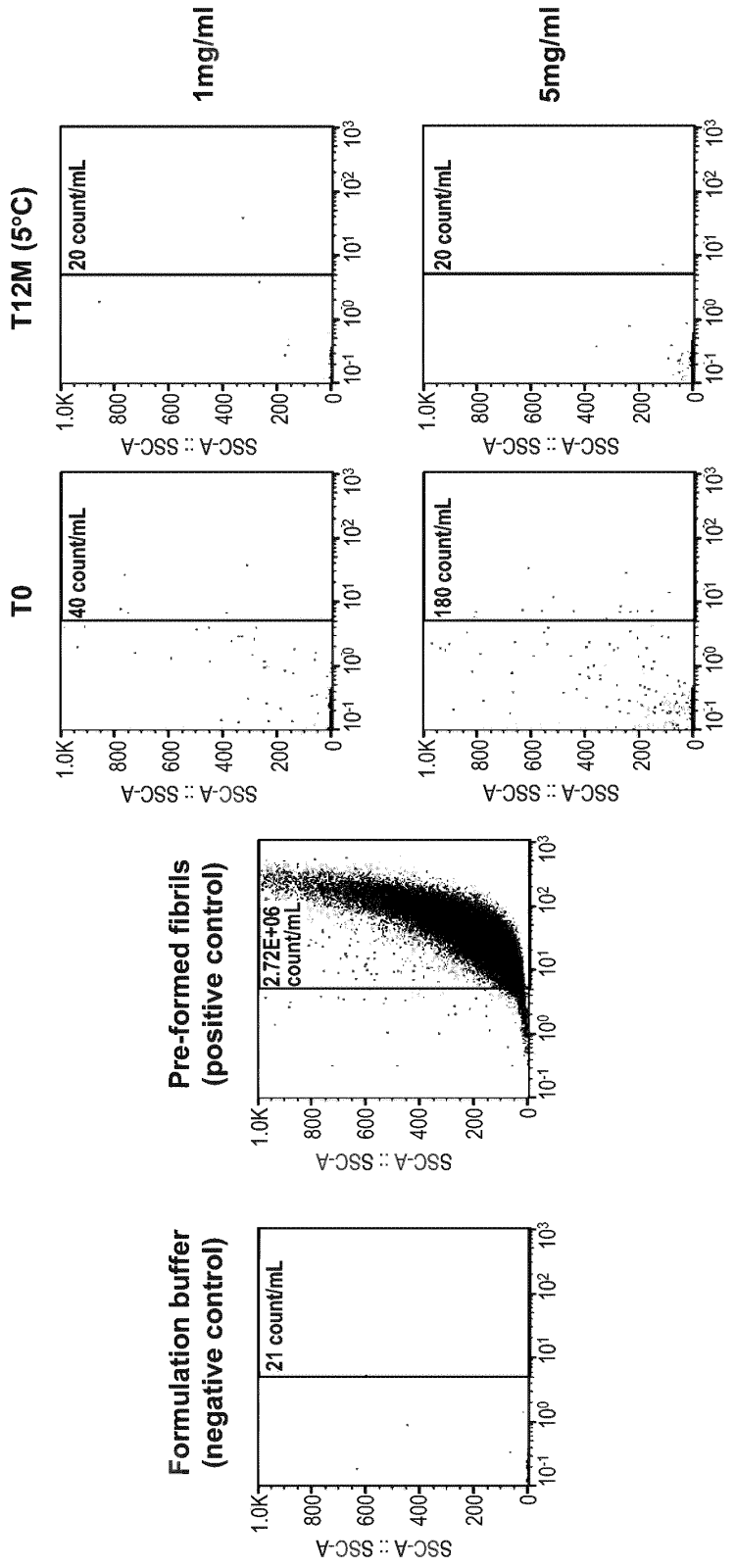

1mg/ml
5mg/ml
T12M (5°C)
T0
20 count/mL
20 count/mL
40 count/mL
180 count/mL
2.72E+06 count/mL
21 count/mL
Pre-formed fibrils (positive control)
Formulation buffer (negative control)
SSC-A :: SSC-A
1.0K
800
600
400
200
0
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}

FIG. 17

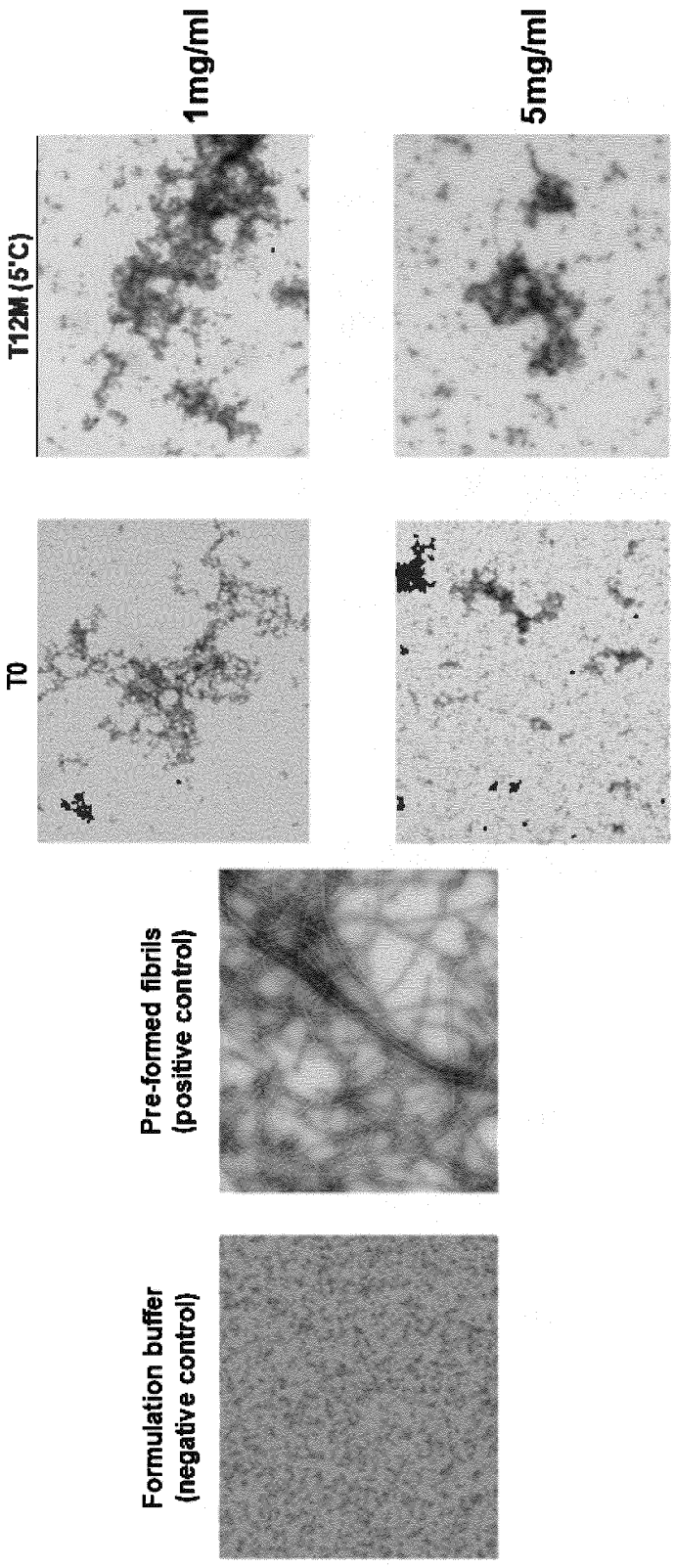

1mg/ml
5mg/ml
T12M (5°C)
T0
Pre-formed fibrils (positive control)
Formulation buffer (negative control)

FIG. 18

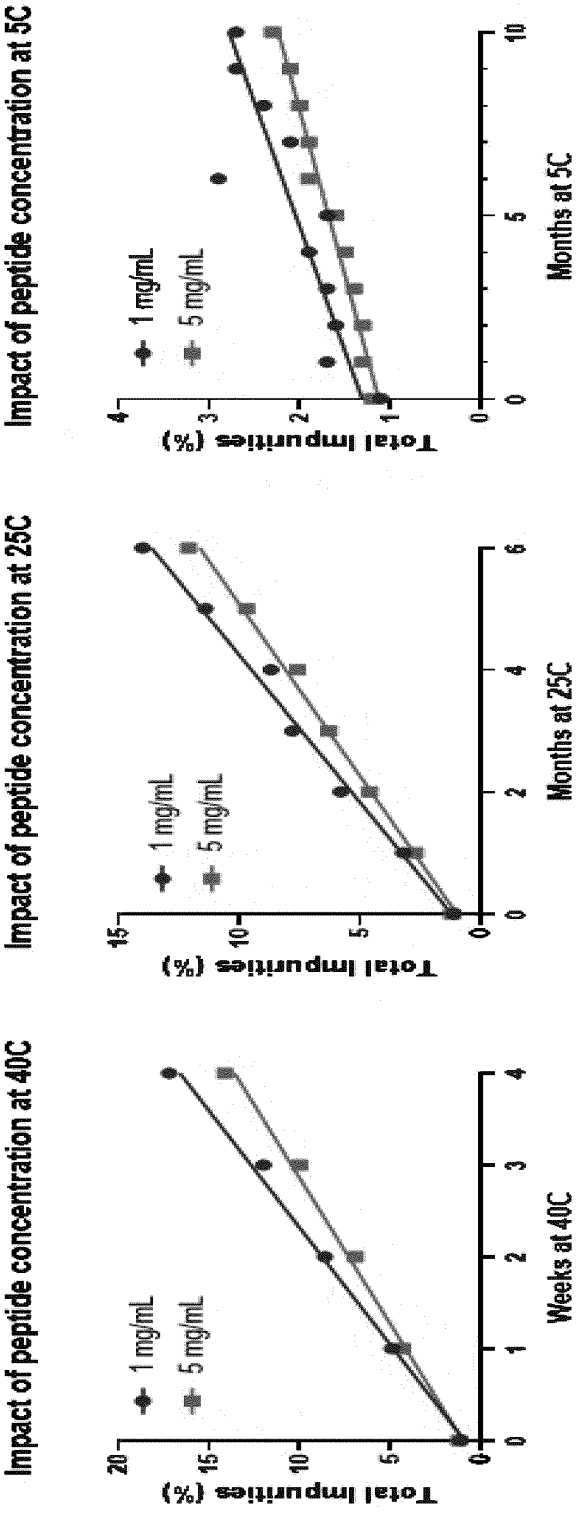

Impact of peptide concentration at 40C
Total Impurities (%)
1 mg/mL
5 mg/mL
Weeks at 40C
Impact of peptide concentration at 25C
Total Impurities (%)
1 mg/mL
5 mg/mL
Months at 25C
Impact of peptide concentration at 5C
Total Impurities (%)
1 mg/mL
5 mg/mL
Months at 5C

FIG. 19

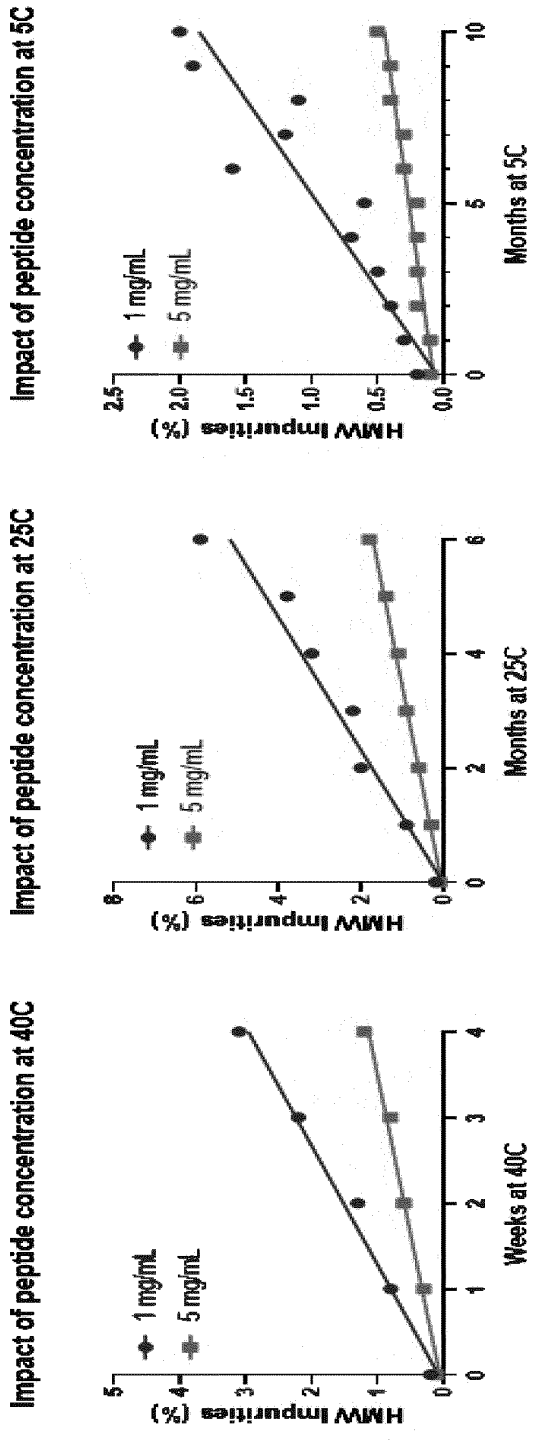

Impact of peptide concentration at 40C
HMW Impurities (%)
1 mg/mL
5 mg/mL
Weeks at 40C
Impact of peptide concentration at 25C
HMW Impurities (%)
1 mg/mL
5 mg/mL
Months at 25C
Impact of peptide concentration at 5C
HMW Impurities (%)
1 mg/mL
5 mg/mL
Months at 5C

FIG. 20

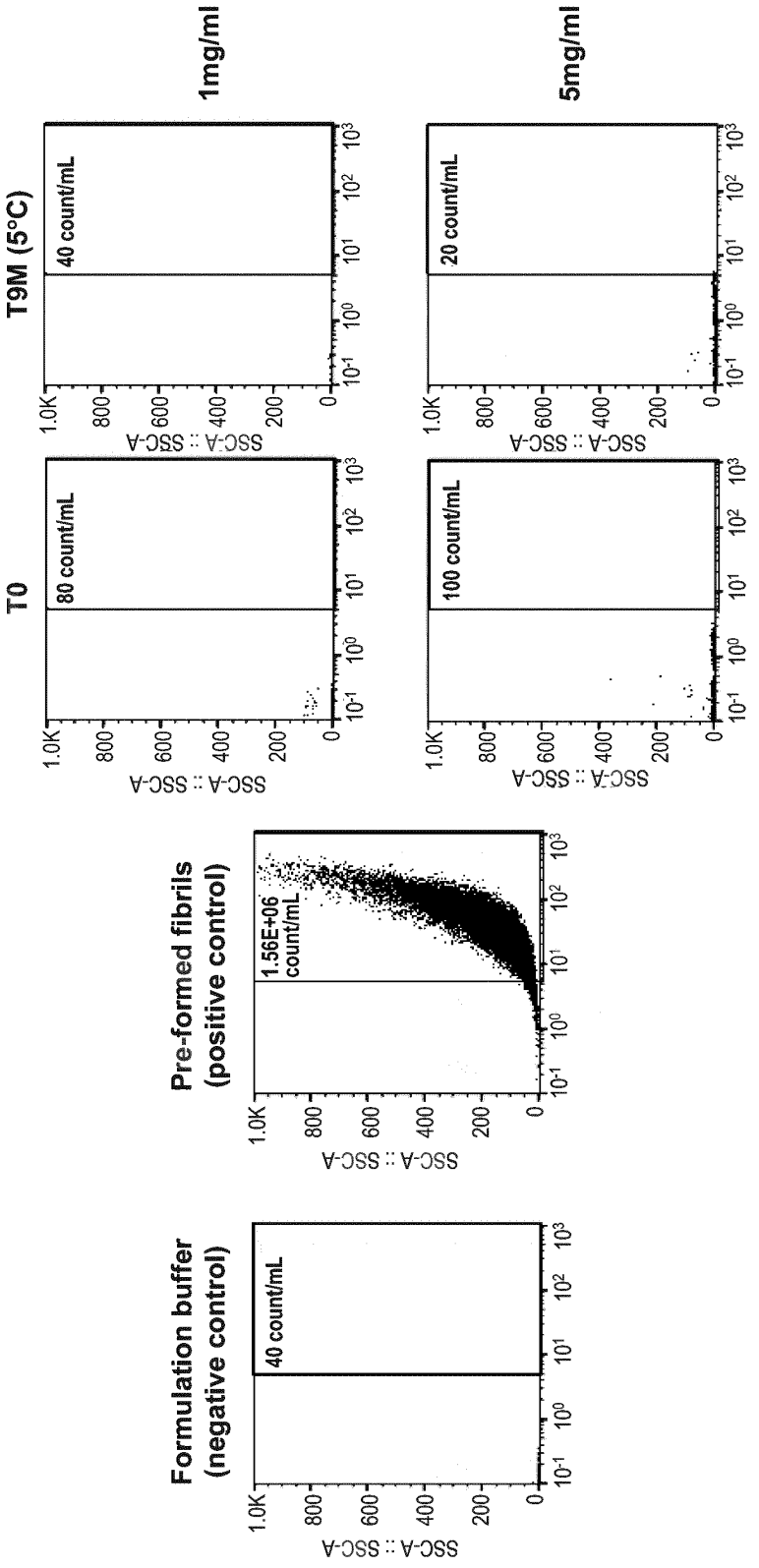

1mg/ml
5mg/ml
T9M (5°C)
T0
40 count/mL
80 count/mL
20 count/mL
100 count/mL
Pre-formed fibrils (positive control)
1.56E+06 count/mL
Formulation buffer (negative control)
40 count/mL
SSC-A :: SSC-A

FIG. 21

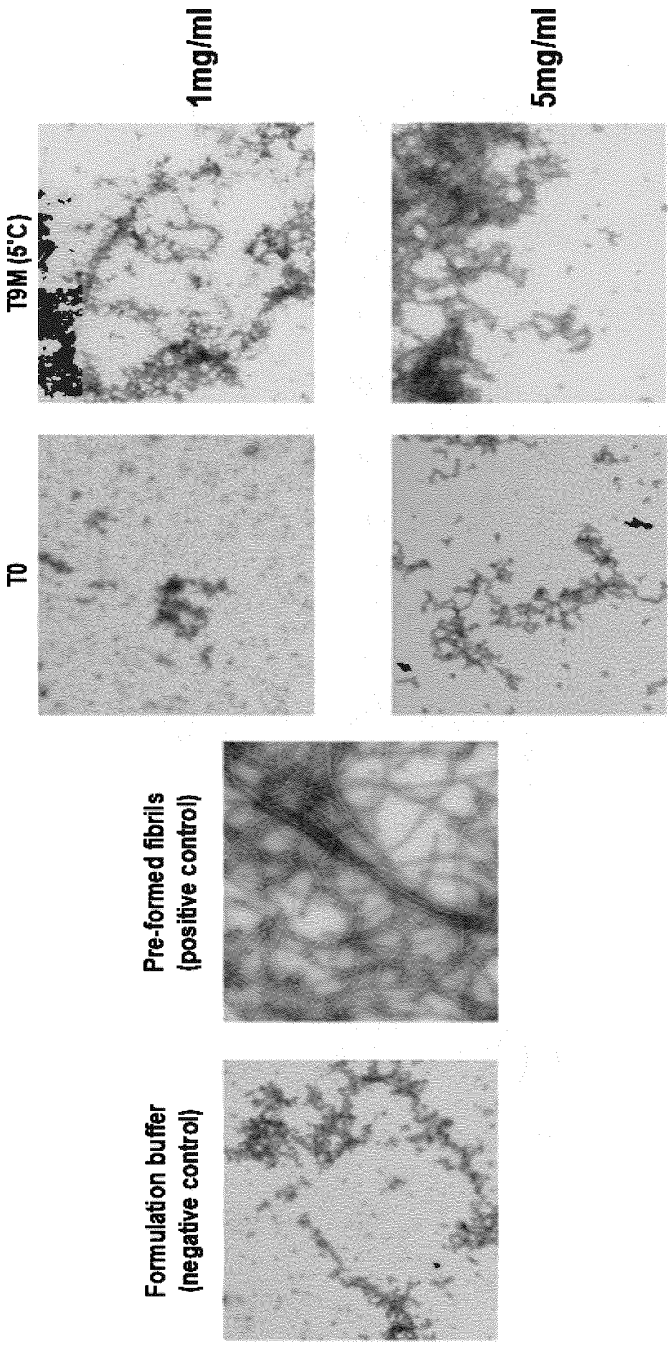

1mg/ml
5mg/ml
T9M (5°C)
T0
Pre-formed fibrils (positive control)
Formulation buffer (negative control)

FIG. 22

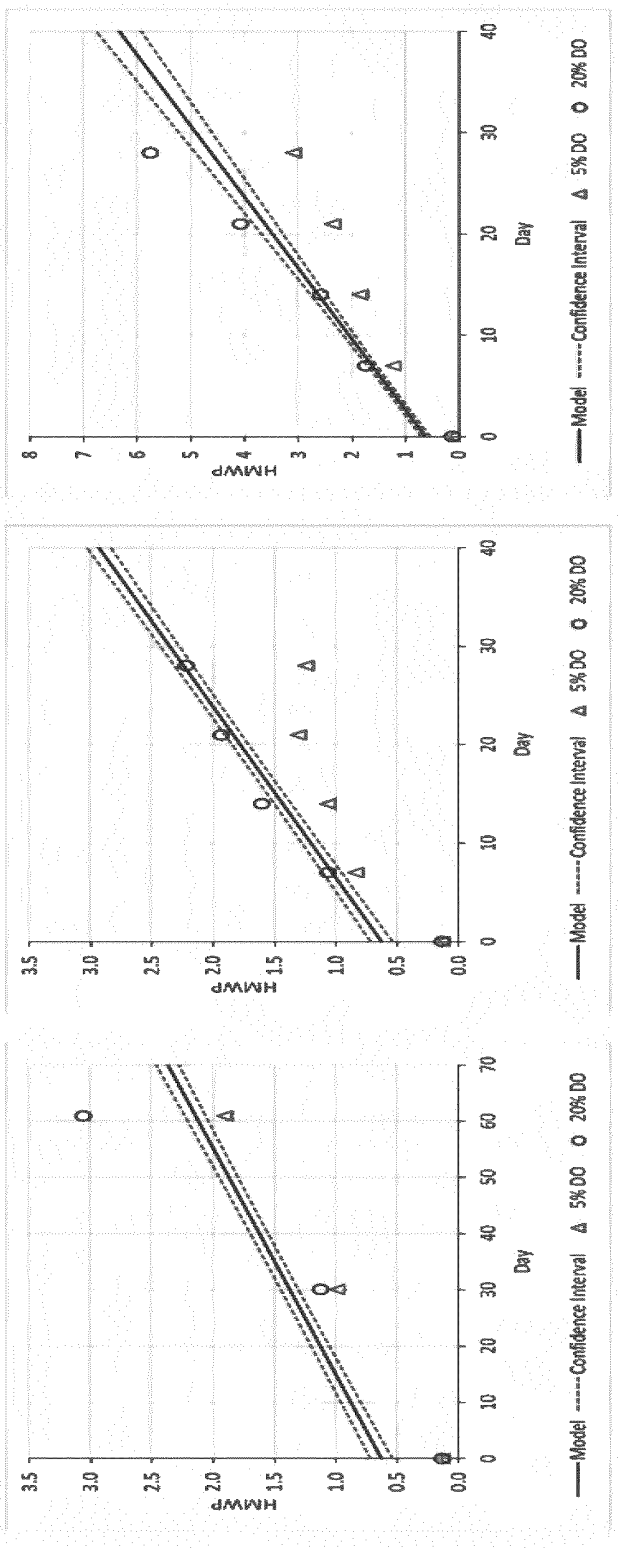


FIG. 23

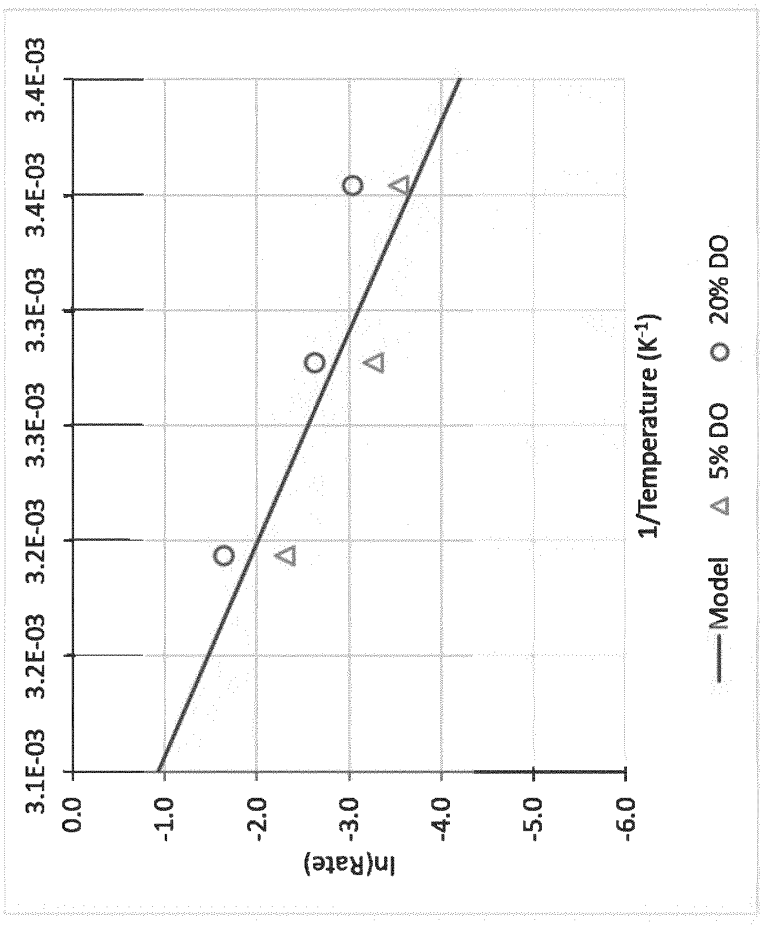

3.1E-03
3.2E-03
3.2E-03
3.3E-03
3.3E-03
3.4E-03
3.4E-03
0.0
-1.0
-2.0
-3.0
-4.0
-5.0
-6.0
ln(Rate)
1/Temperature (K-1)
Model
5% DO
20% DO

FIG. 24