FIG. 1

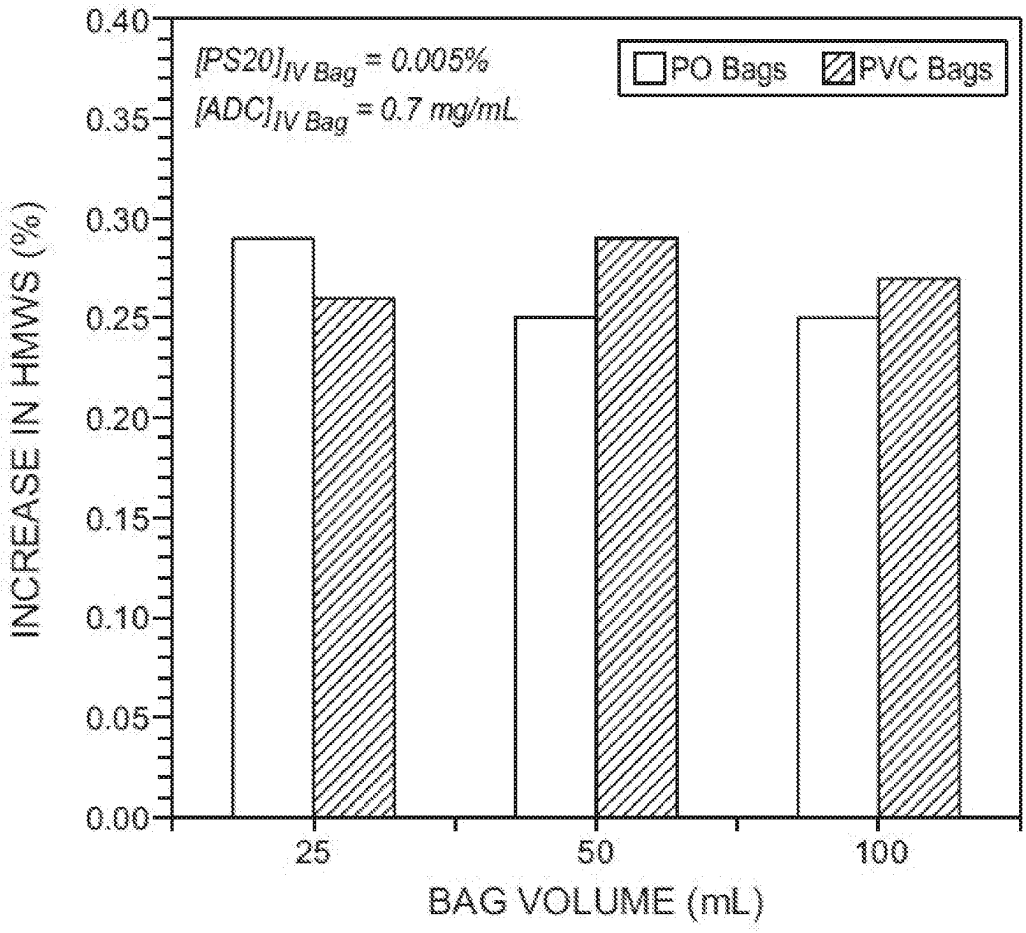

[PS20]IV Bag = 0.005%
[ADC]IV Bag = 0.7 mg/mL
PO Bags
PVC Bags
INCREASE IN HMWS (%)
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
25
50
100
BAG VOLUME (mL)

FIG. 2

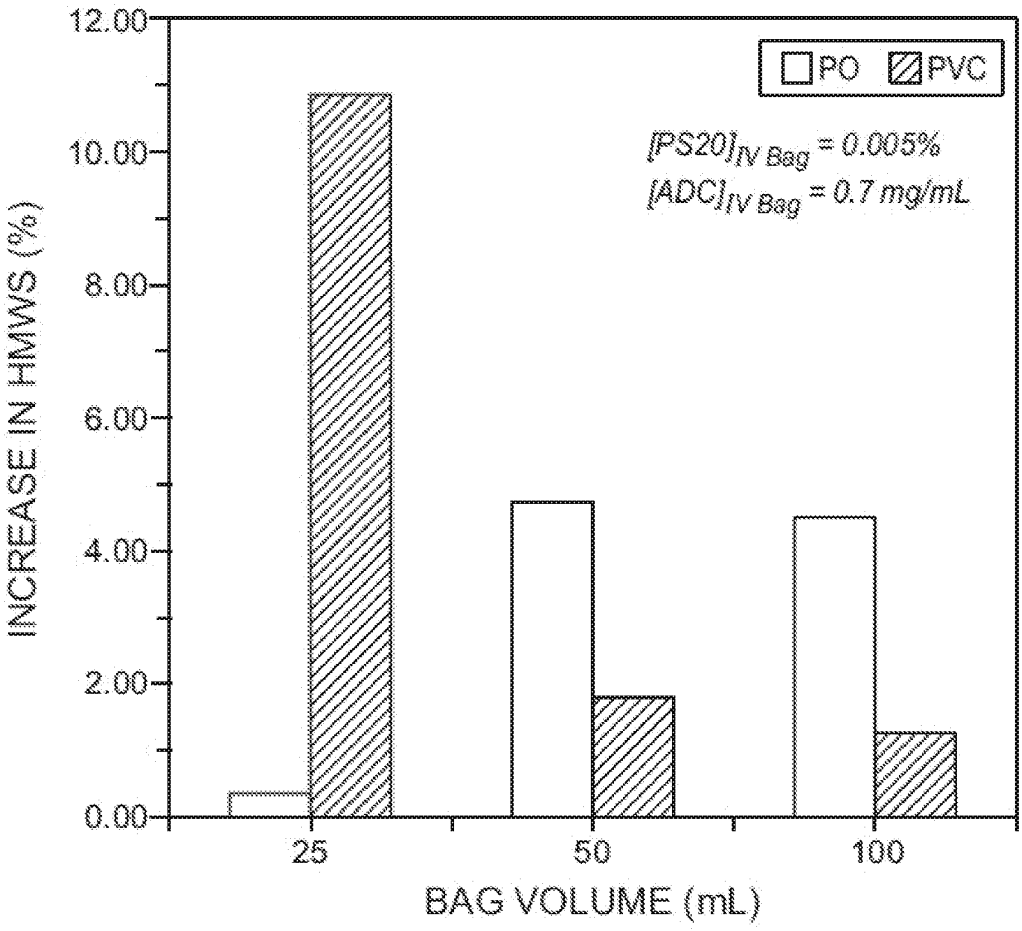

12.00
10.00
8.00
6.00
4.00
2.00
0.00
INCREASE IN HMWS (%)
PO
PVC
[PS20]IV Bag = 0.005%
[ADC]IV Bag = 0.7 mg/mL
25
50
100
BAG VOLUME (mL)

FIG. 3

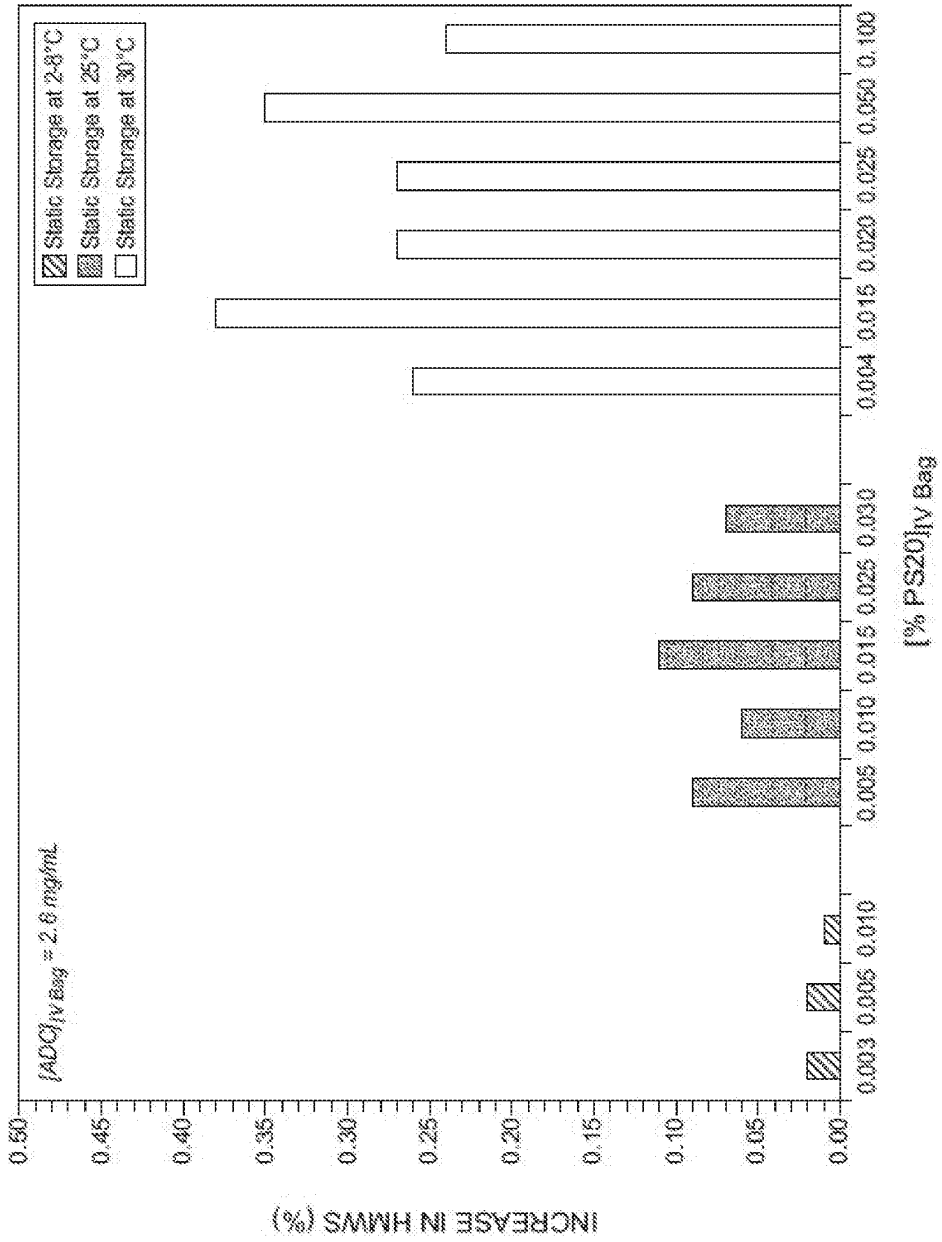

Static Storage at 2-8°C
Static Storage at 25°C
Static Storage at 30°C
[ADC]IV Bag = 2.6 mg/mL
INCREASE IN HMWS (%)
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.003
0.005
0.010
0.005
0.010
0.015
0.025
0.030
0.004
0.015
0.020
0.025
0.050
0.100
[% PS20]IV Bag

FIG. 4

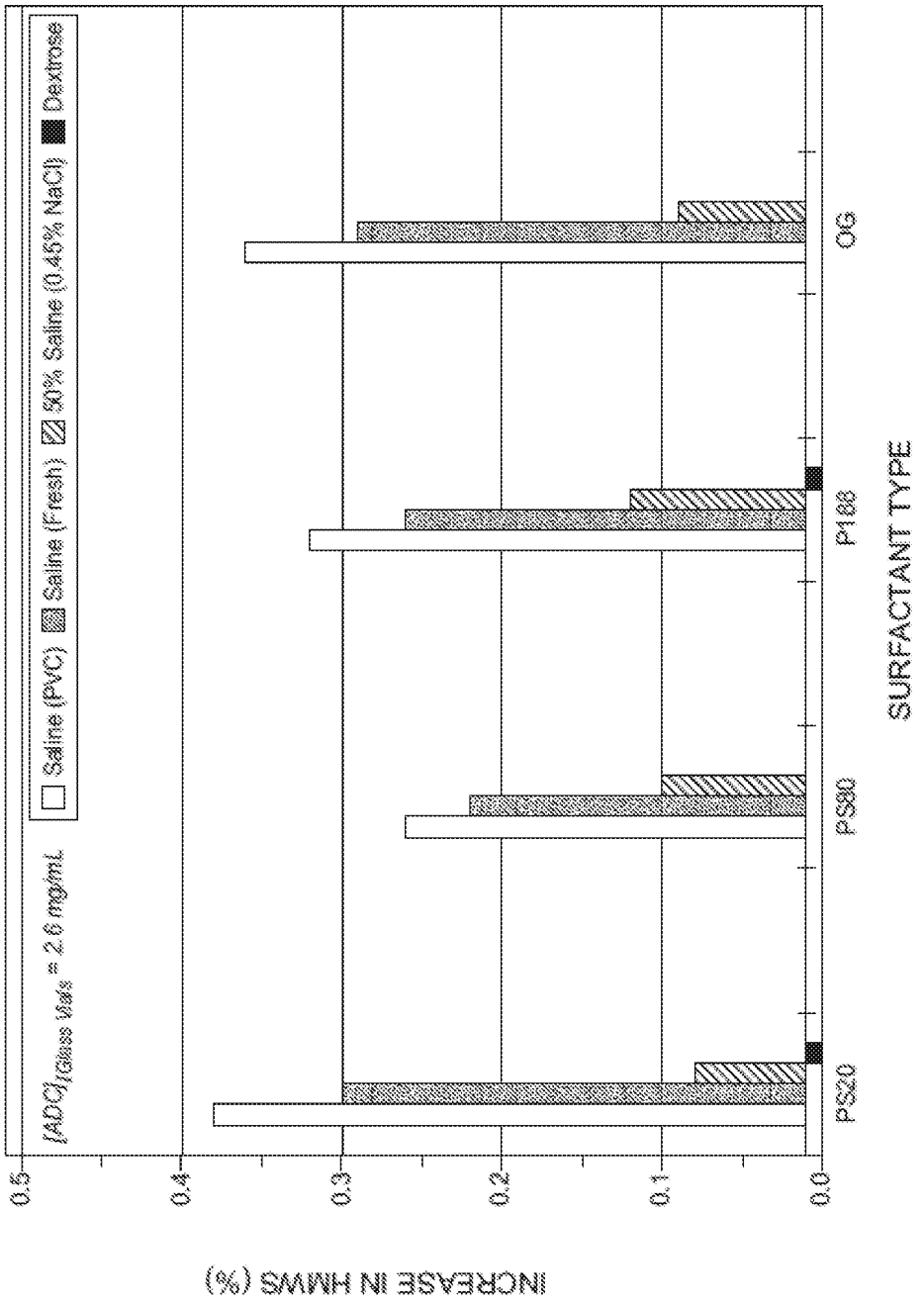

(ADC)IGlass Vials = 2.6 mg/mL
Saline (PVC)
Saline (Fresh)
50% Saline (0.45% NaCl)
Dextrose
INCREASE IN HMWS (%)
0.0
0.1
0.2
0.3
0.4
0.5
PS20
PS80
P188
OG
SURFACTANT TYPE

FIG. 5A

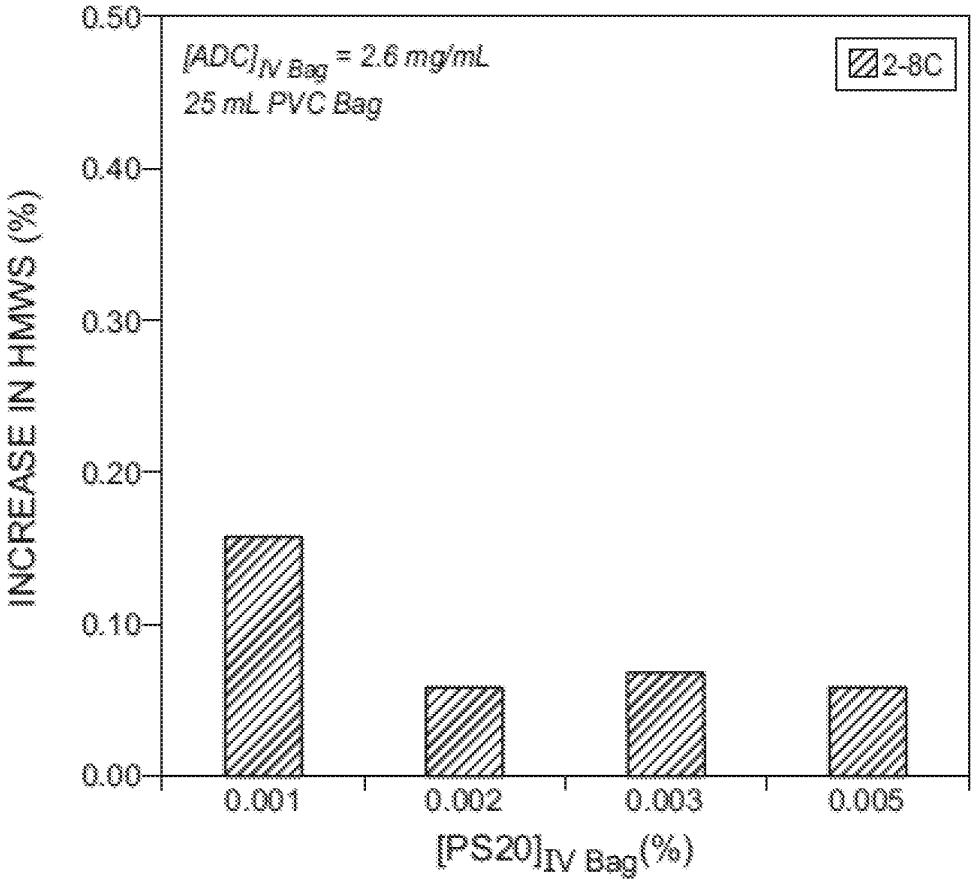

0.50
0.40
0.30
0.20
0.10
0.00
INCREASE IN HMWS (%)
[ADC]IV Bag = 2.6 mg/mL
25 mL PVC Bag
2-8C
0.001
0.002
0.003
0.005
[PS20]IV Bag(%)

FIG. 5B

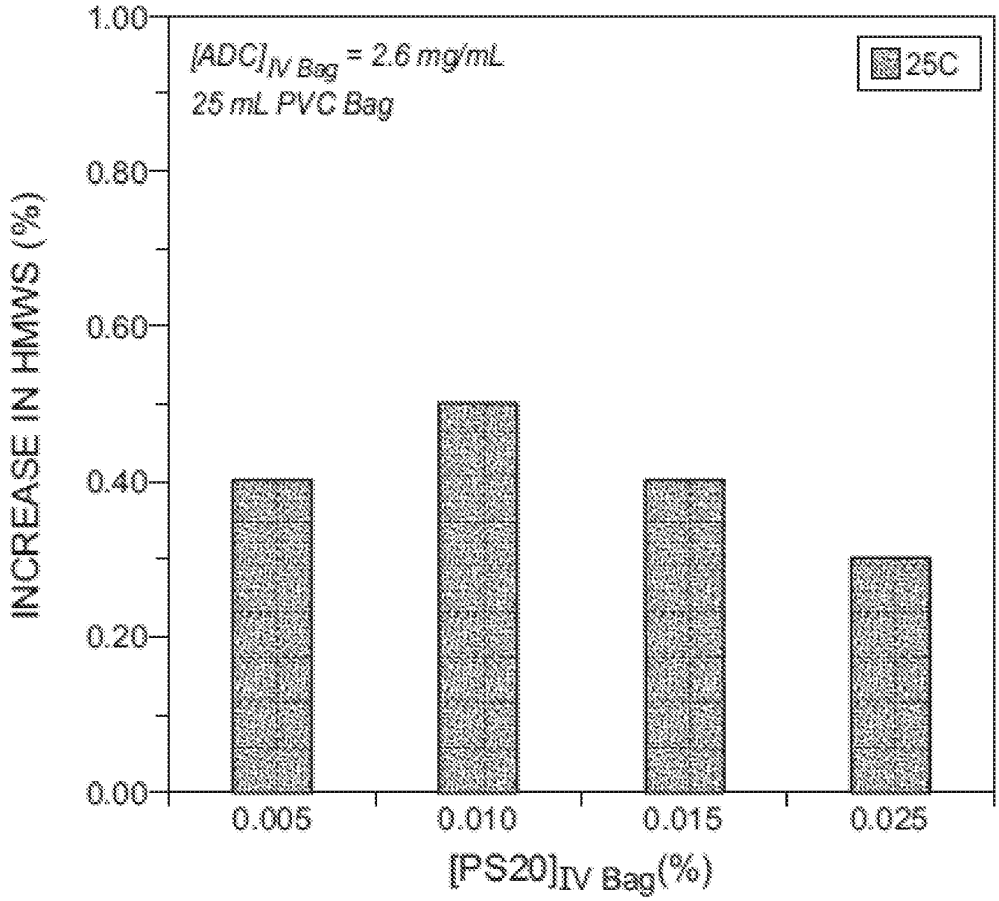

1.00
0.80
0.60
0.40
0.20
0.00
INCREASE IN HMWS (%)
[ADC]IV Bag = 2.6 mg/mL
25 mL PVC Bag
25C
0.005
0.010
0.015
0.025
[PS20]IV Bag(%)

FIG. 5C

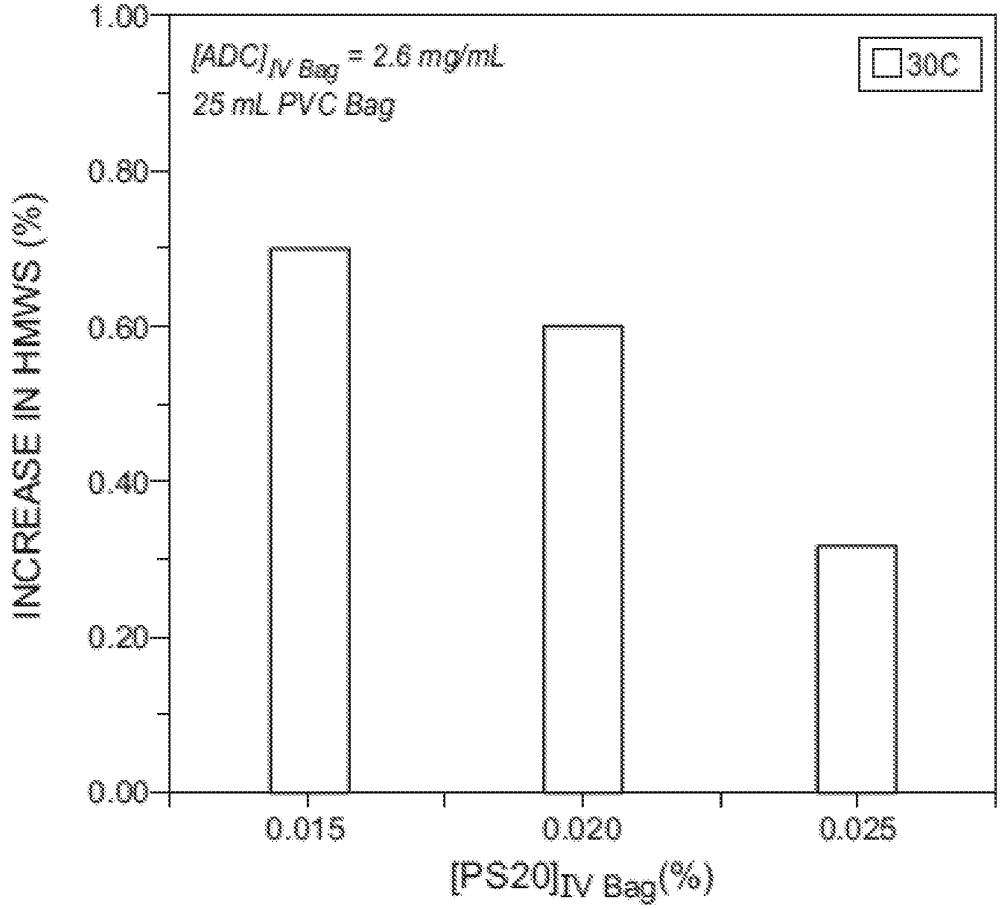

1.00
0.80
0.60
0.40
0.20
0.00
INCREASE IN HMWS (%)
[ADC]IV Bag = 2.6 mg/mL
25 mL PVC Bag
30C
0.015
0.020
0.025
[PS20]IV Bag(%)

FIG. 6

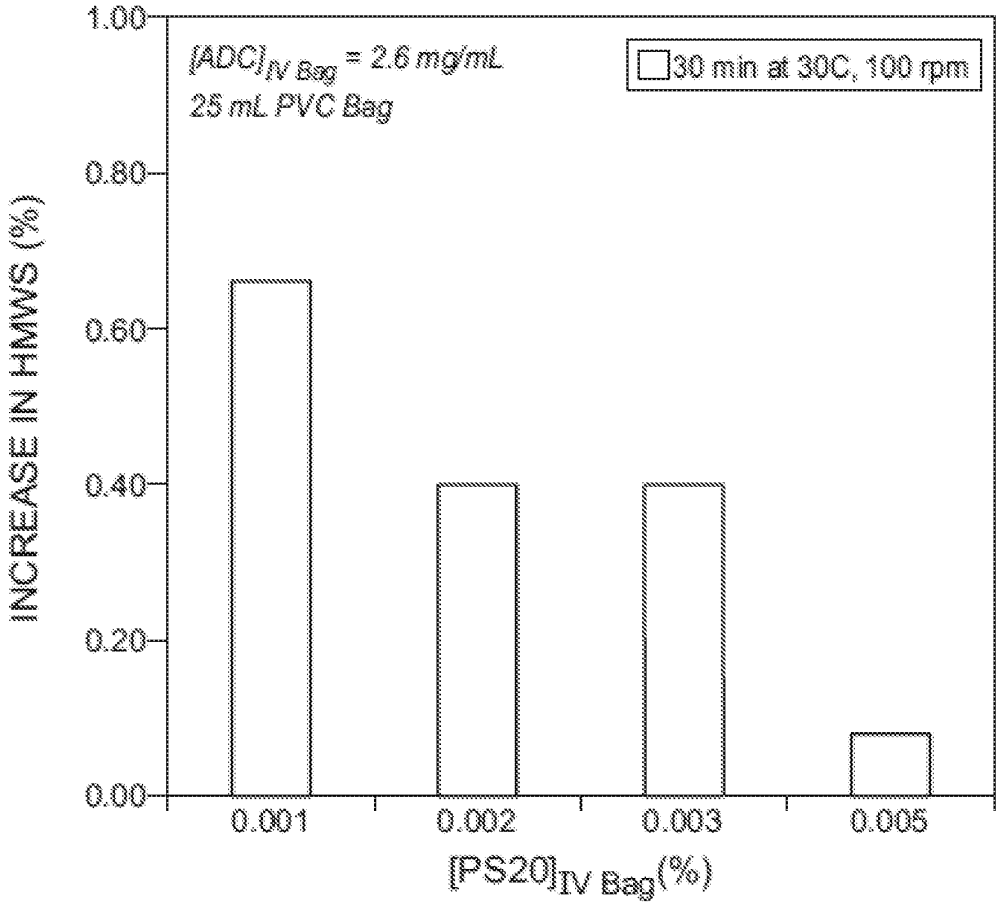

1.00
0.80
0.60
0.40
0.20
0.00
INCREASE IN HMWS (%)
[ADC]IV Bag = 2.6 mg/mL
25 mL PVC Bag
30 min at 30C, 100 rpm
0.001
0.002
0.003
0.005
[PS20]IV Bag(%)

FIG. 7

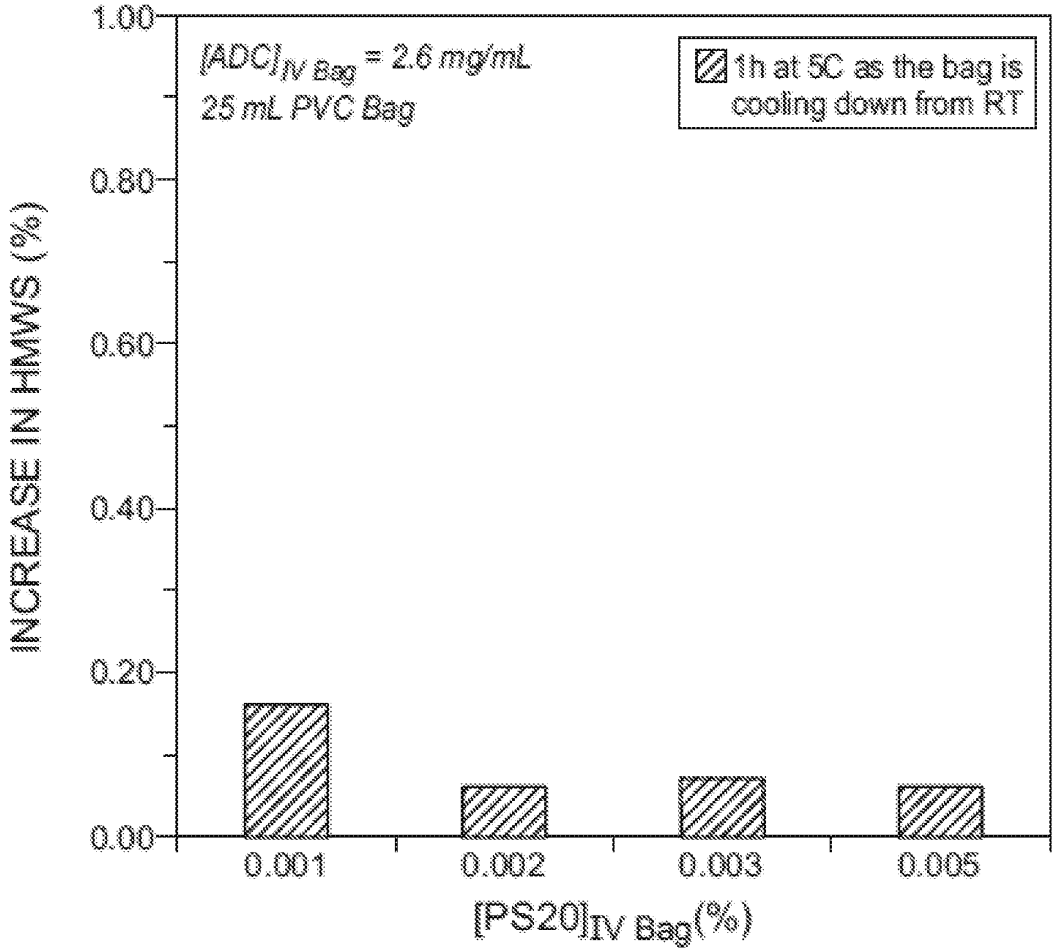

1.00
0.80
0.60
0.40
0.20
0.00
INCREASE IN HMWS (%)
[ADC]IV Bag = 2.6 mg/mL
25 mL PVC Bag
1h at 5C as the bag is cooling down from RT
0.001
0.002
0.003
0.005
[PS20]IV Bag(%)

FIG. 8

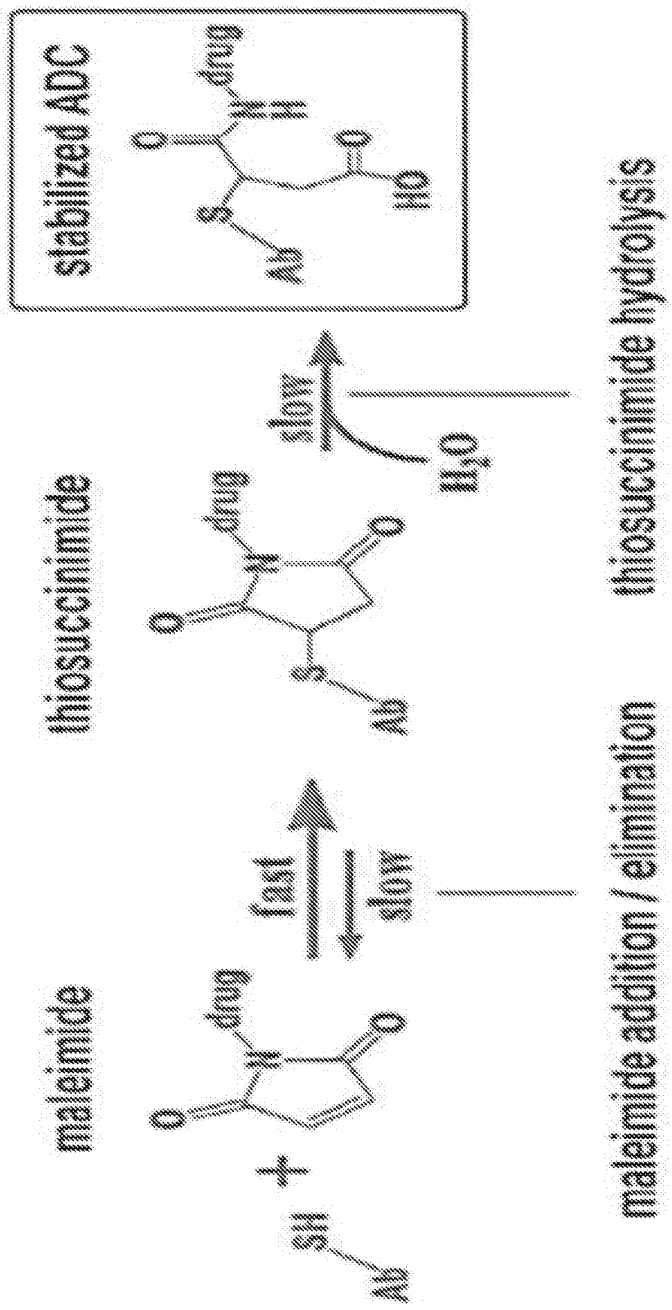

maleimide
thiosuccinimide
stabilized ADC
maleimide addition / elimination
thiosuccinimide hydrolysis
fast
slow
slow
drug
Ab
SH
H2O
HO

FIG. 9

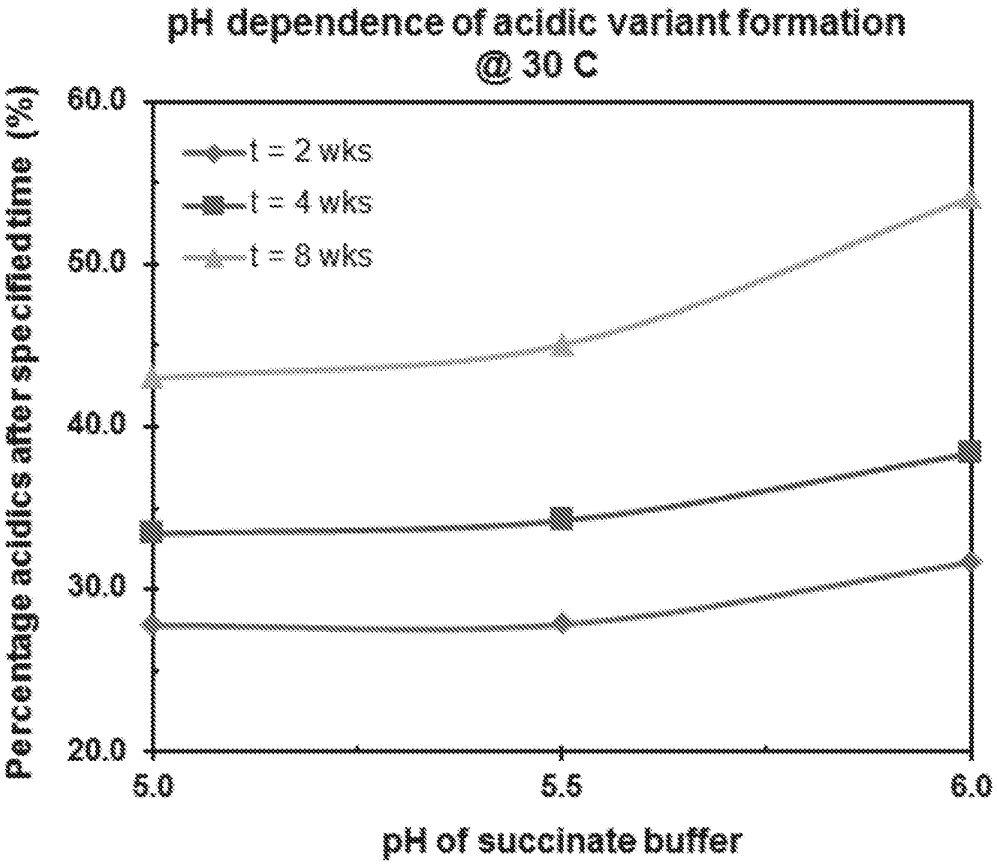

pH dependence of acidic variant formation
@ 30 C
Percentage acidics after specified time (%)
60.0
50.0
40.0
30.0
20.0
t = 2 wks
t = 4 wks
t = 8 wks
5.0
5.5
6.0
pH of succinate buffer

FIG. 10

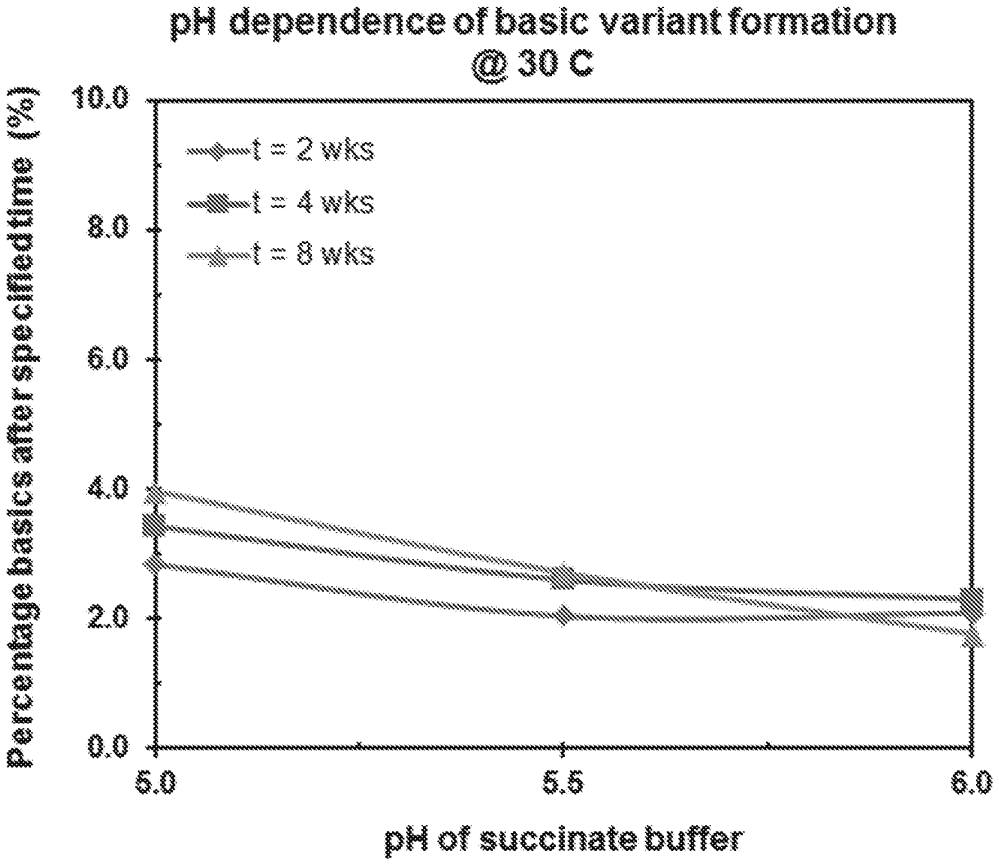

pH dependence of basic variant formation
@ 30 C
Percentage basics after specified time (%)
10.0
8.0
6.0
4.0
2.0
0.0
t = 2 wks
t = 4 wks
t = 8 wks
5.0
5.5
6.0
pH of succinate buffer

FIG. 11

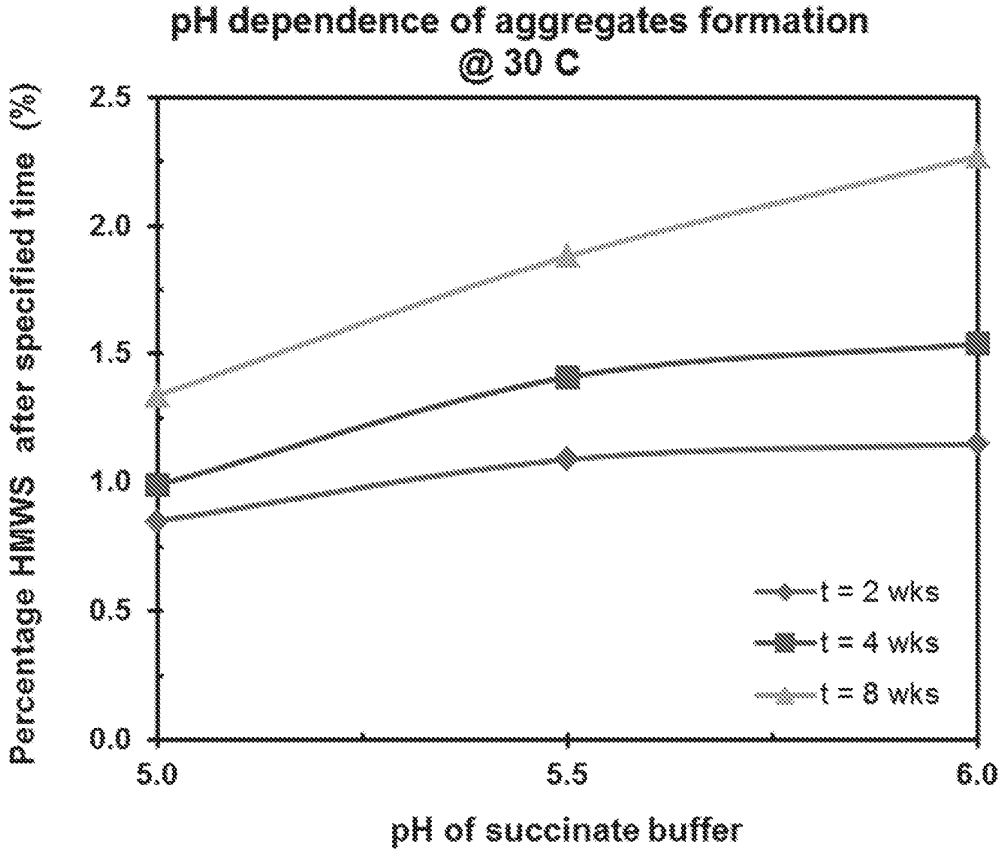

pH dependence of aggregates formation
@ 30 C
Percentage HMWS after specified time (%)
2.5
2.0
1.5
1.0
0.5
0.0
5.0
5.5
6.0
pH of succinate buffer
t = 2 wks
t = 4 wks
t = 8 wks

FIG. 12

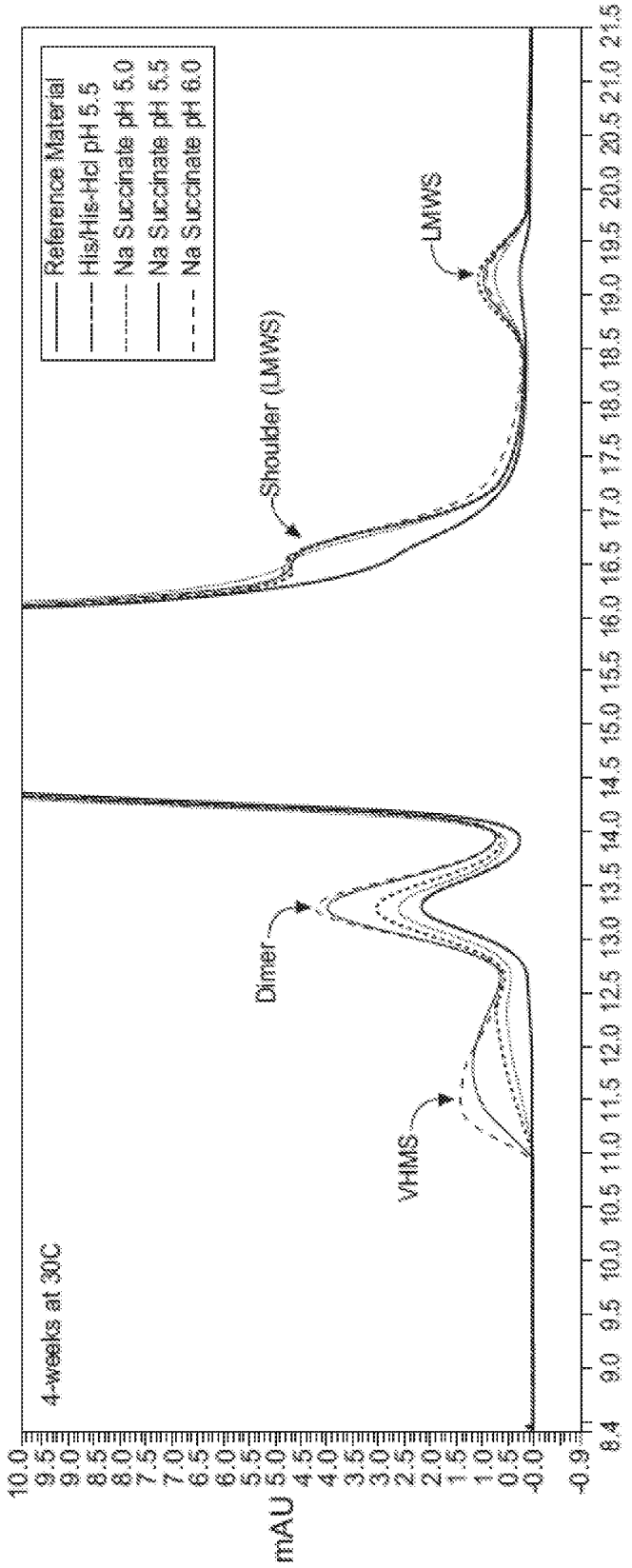

Reference Material
His/His-Hcl pH 5.5
Na Succinate pH 5.0
Na Succinate pH 5.5
Na Succinate pH 6.0
4-weeks at 30C
Shoulder (LMWS)
LMWS
Dimer
VHMS
mAU
Minutes

FIG. 13

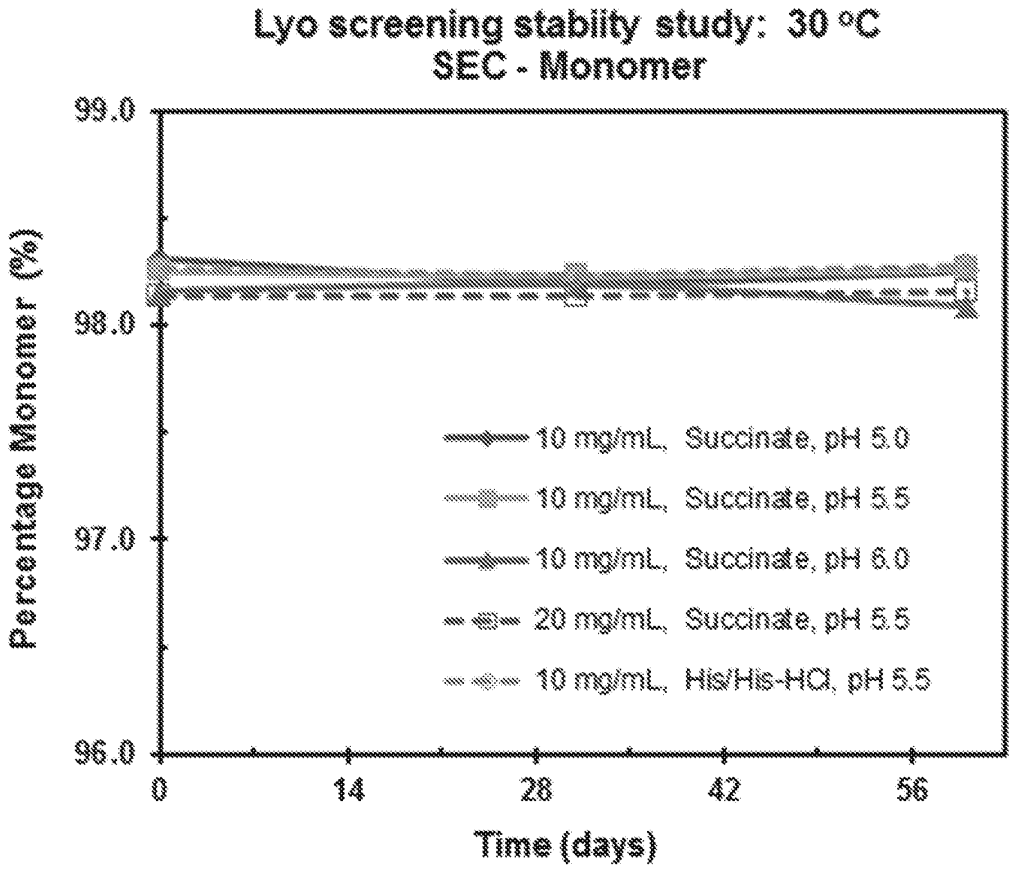

Lyo screening stability study: 30 °C
SEC - Monomer
Percentage Monomer (%)
99.0
98.0
97.0
96.0
0
14
28
42
56
Time (days)
10 mg/mL, Succinate, pH 5.0
10 mg/mL, Succinate, pH 5.5
10 mg/mL, Succinate, pH 6.0
20 mg/mL, Succinate, pH 5.5
10 mg/mL, His/His-HCl, pH 5.5

FIG. 14

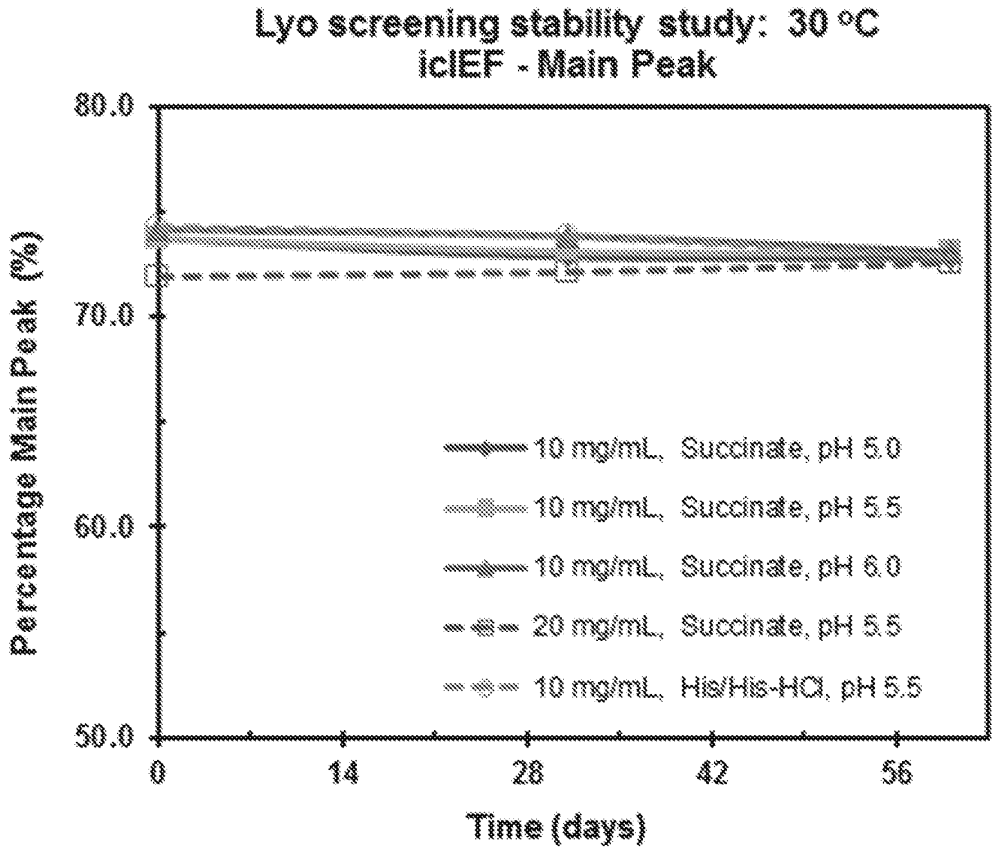
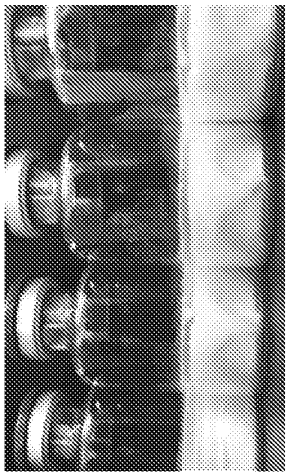
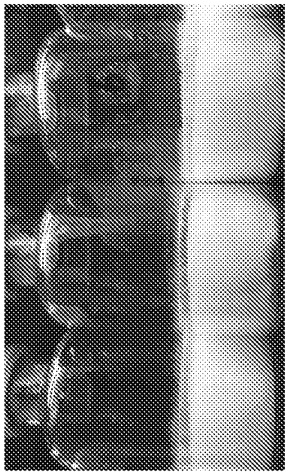

Lyo screening stability study: 30 °C
icIEF - Main Peak
Percentage Main Peak (%)
80.0
70.0
60.0
50.0
0
14
28
42
56
Time (days)
10 mg/mL, Succinate, pH 5.0
10 mg/mL, Succinate, pH 5.5
10 mg/mL, Succinate, pH 6.0
20 mg/mL, Succinate, pH 5.5
10 mg/mL, His/His-HCl, pH 5.5

FIG. 15A



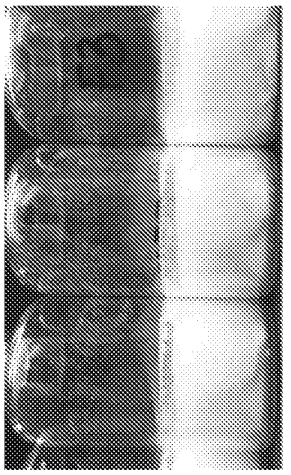
10 mg/mL
260mM sucrose
Moisture ~2.4%

FIG. 15B



10 mg/mL
180 mM sucrose
Moisture ~1.9%

FIG. 15C



10 mg/mL
120mM sucrose
Moisture ~1.5%

FIG. 16A



FIG. 16B

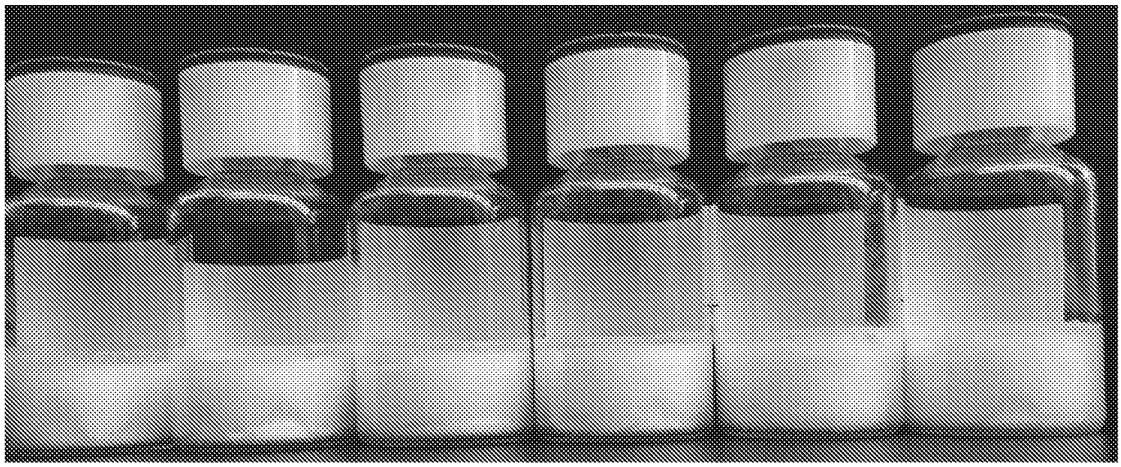


FIG. 17

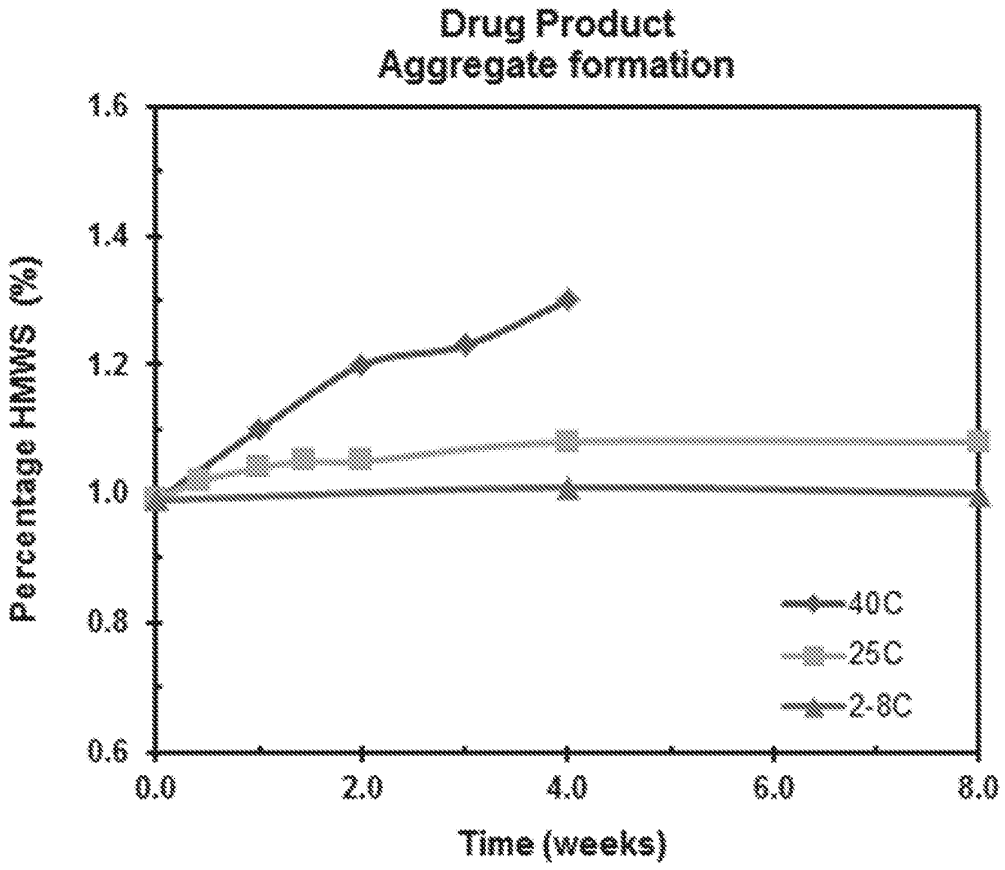
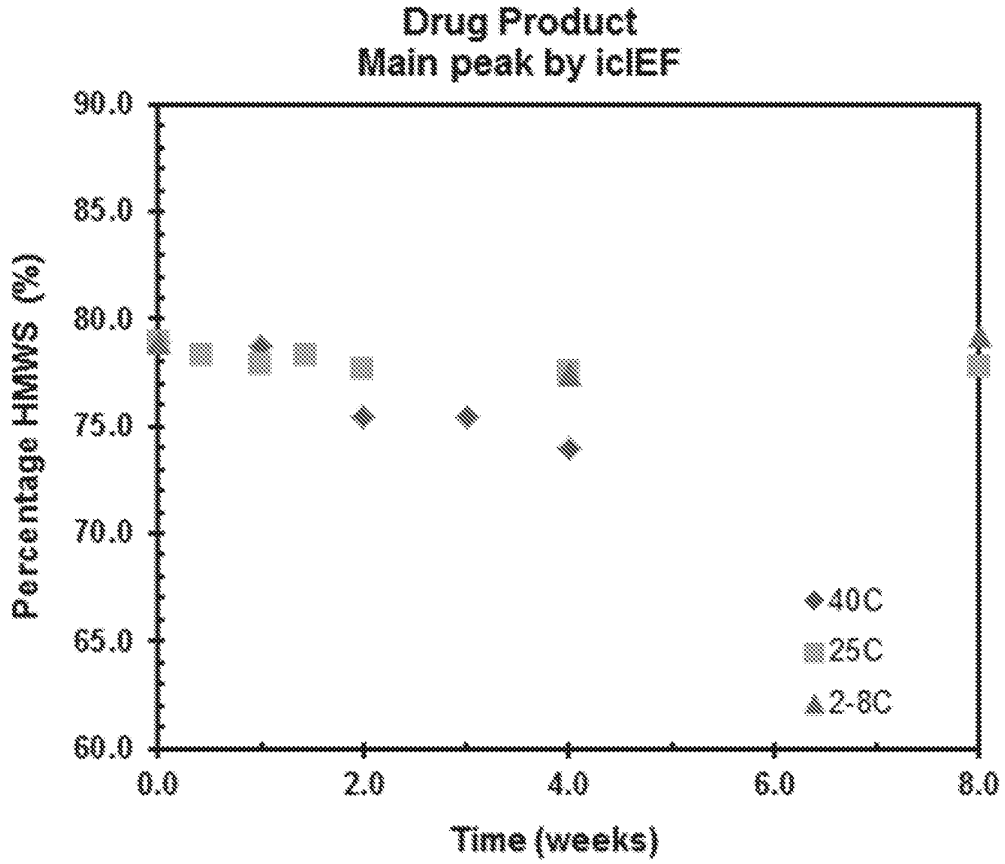

Drug Product
Aggregate formation
Percentage HMWS (%)
1.6
1.4
1.2
1.0
0.8
0.6
0.0
2.0
4.0
6.0
8.0
Time (weeks)
40C
25C
2-8C

FIG. 18


Drug Product
Main peak by iclEF
Percentage HMWS (%)
90.0
85.0
80.0
75.0
70.0
65.0
60.0
0.0
2.0
4.0
6.0
8.0
Time (weeks)
40C
25C
2-8C