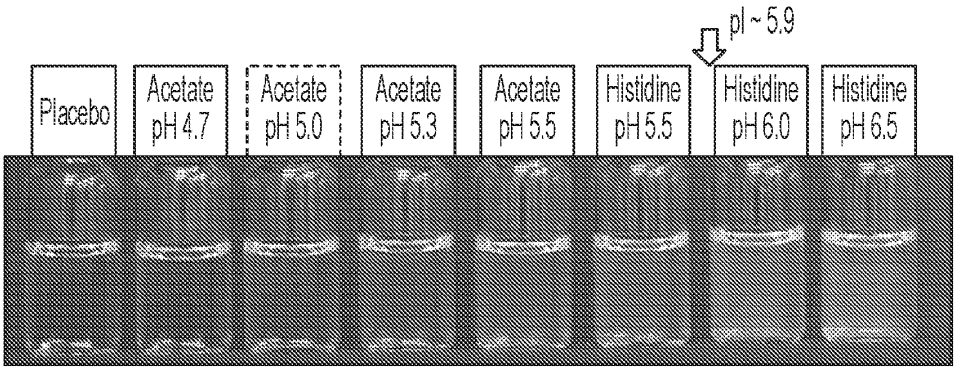

pI ~ 5.9
Placebo
Acetate pH 4.7
Acetate pH 5.0
Acetate pH 5.3
Acetate pH 5.5
Histidine pH 5.5
Histidine pH 6.0
Histidine pH 6.5

FIG. 1

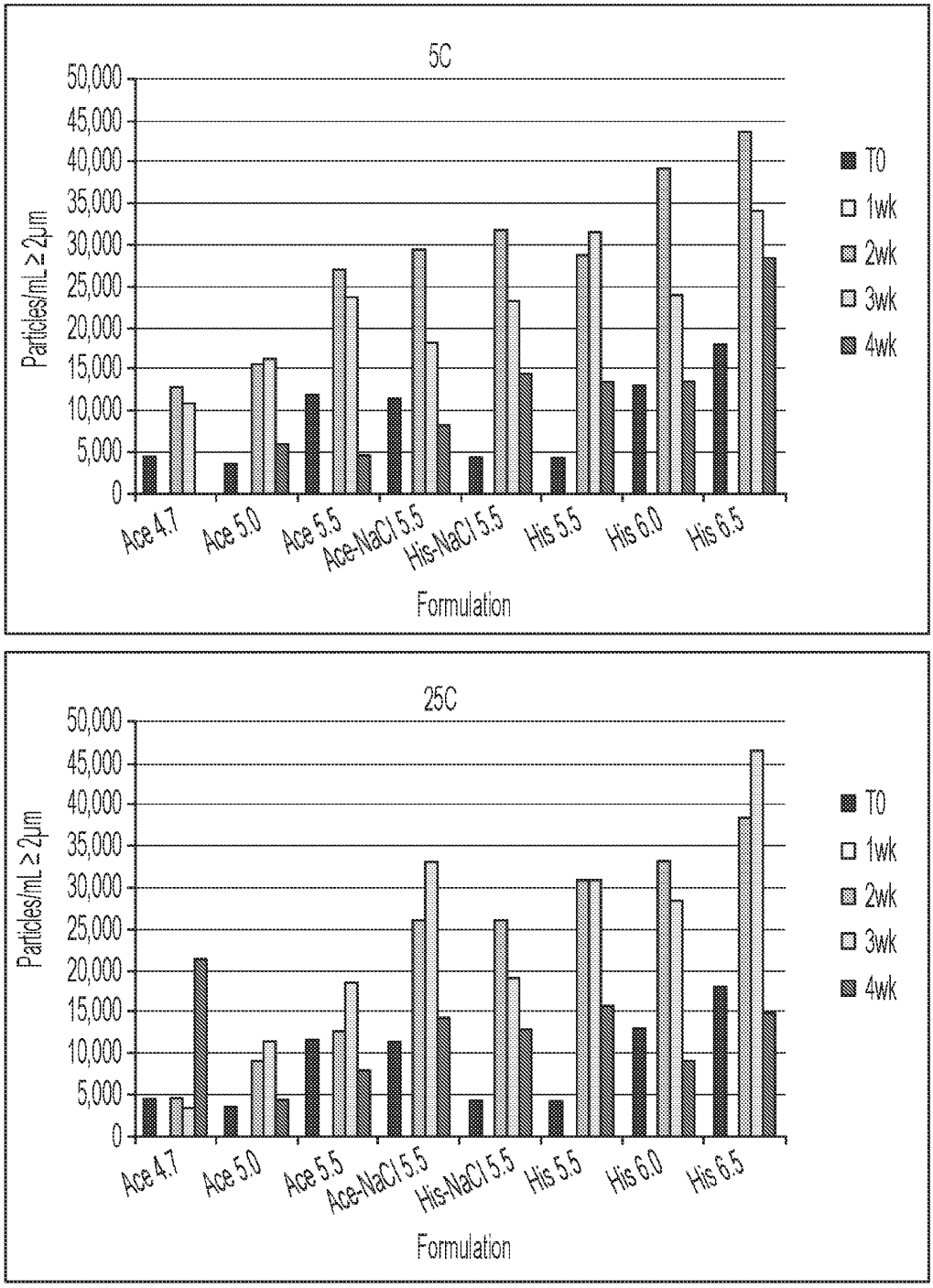

5C
Particles/mL ≥ 2µm
50,000
45,000
40,000
35,000
30,000
25,000
20,000
15,000
10,000
5,000
0
Ace 4.7
Ace 5.0
Ace 5.5
Ace-NaCl 5.5
His-NaCl 5.5
His 5.5
His 6.0
His 6.5
Formulation
T0
1wk
2wk
3wk
4wk
25C
Particles/mL ≥ 2µm
50,000
45,000
40,000
35,000
30,000
25,000
20,000
15,000
10,000
5,000
0
Ace 4.7
Ace 5.0
Ace 5.5
Ace-NaCl 5.5
His-NaCl 5.5
His 5.5
His 6.0
His 6.5
Formulation
T0
1wk
2wk
3wk
4wk

FIG. 2A

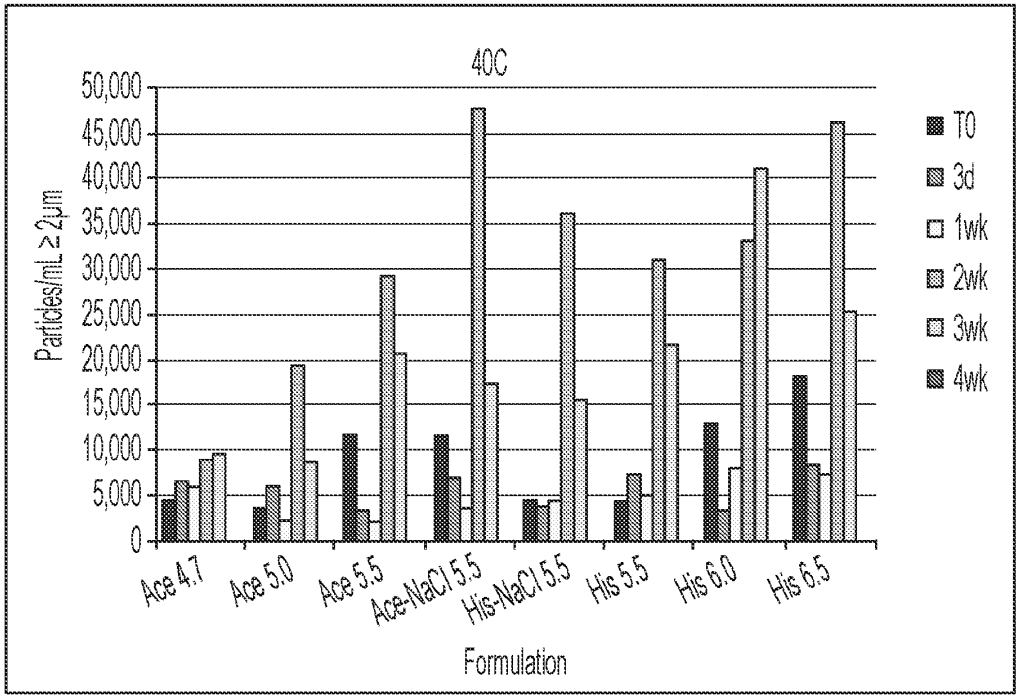


FIG. 2A
CONTINUED

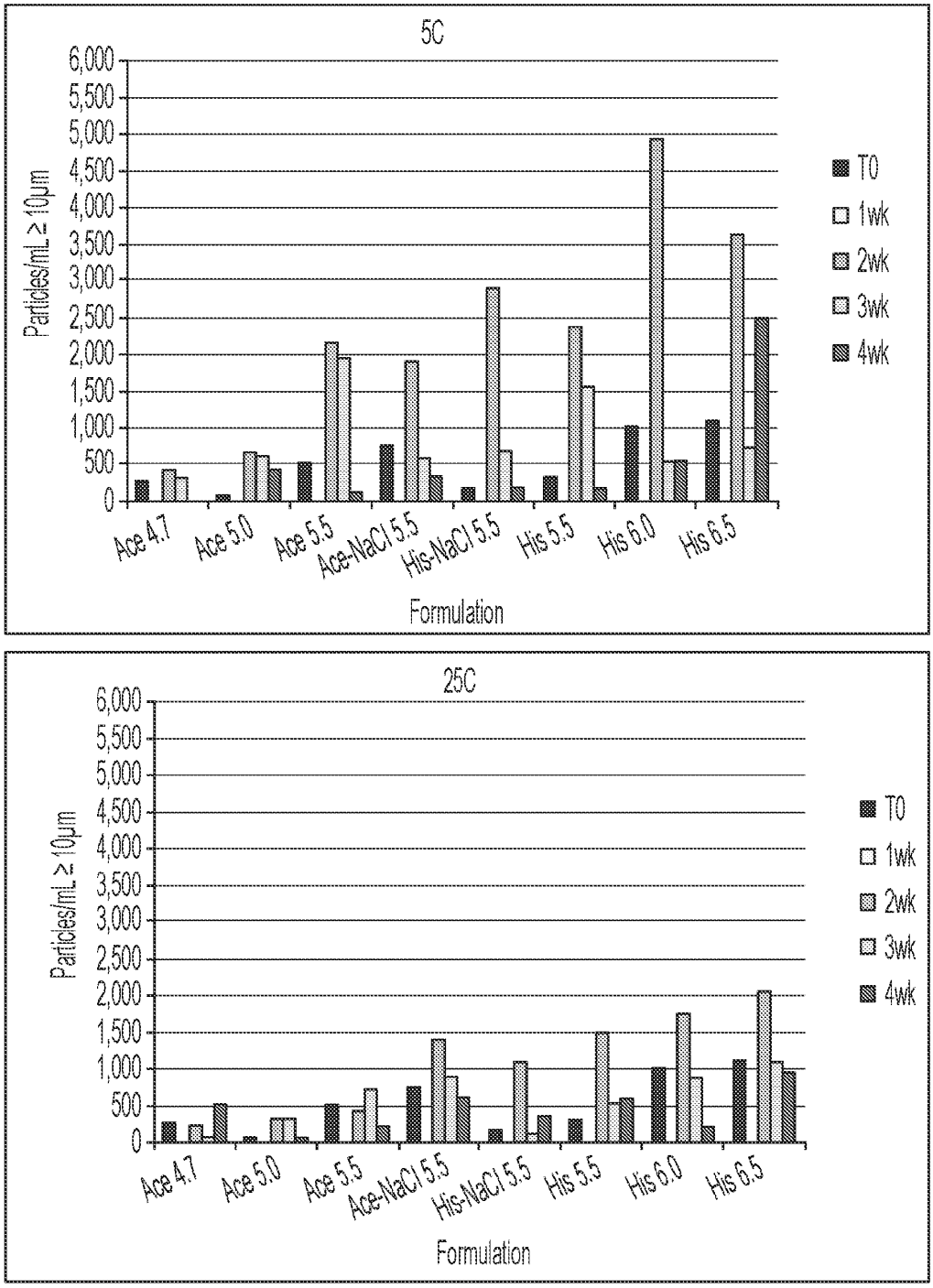

5C
Particles/mL ≥ 10µm
6,000
5,500
5,000
4,500
4,000
3,500
3,000
2,500
2,000
1,500
1,000
500
0
Ace 4.7
Ace 5.0
Ace 5.5
Ace-NaCl 5.5
His-NaCl 5.5
His 5.5
His 6.0
His 6.5
Formulation
T0
1wk
2wk
3wk
4wk
25C
Particles/mL ≥ 10µm
6,000
5,500
5,000
4,500
4,000
3,500
3,000
2,500
2,000
1,500
1,000
500
0
Ace 4.7
Ace 5.0
Ace 5.5
Ace-NaCl 5.5
His-NaCl 5.5
His 5.5
His 6.0
His 6.5
Formulation
T0
1wk
2wk
3wk
4wk

FIG. 2B

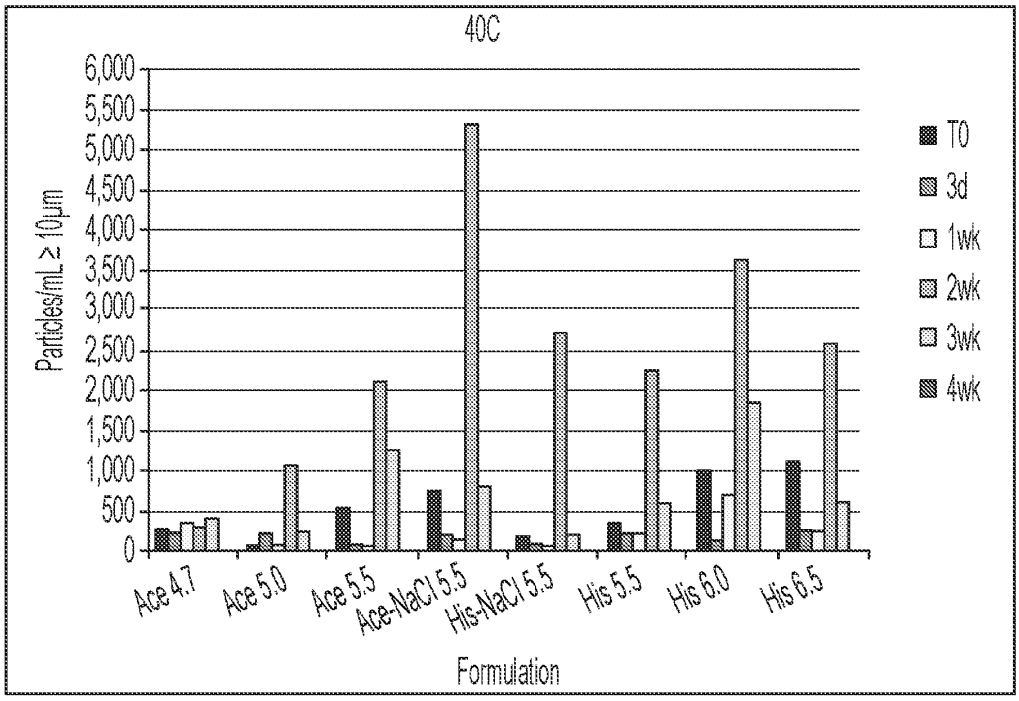


FIG. 2B
CONTINUED

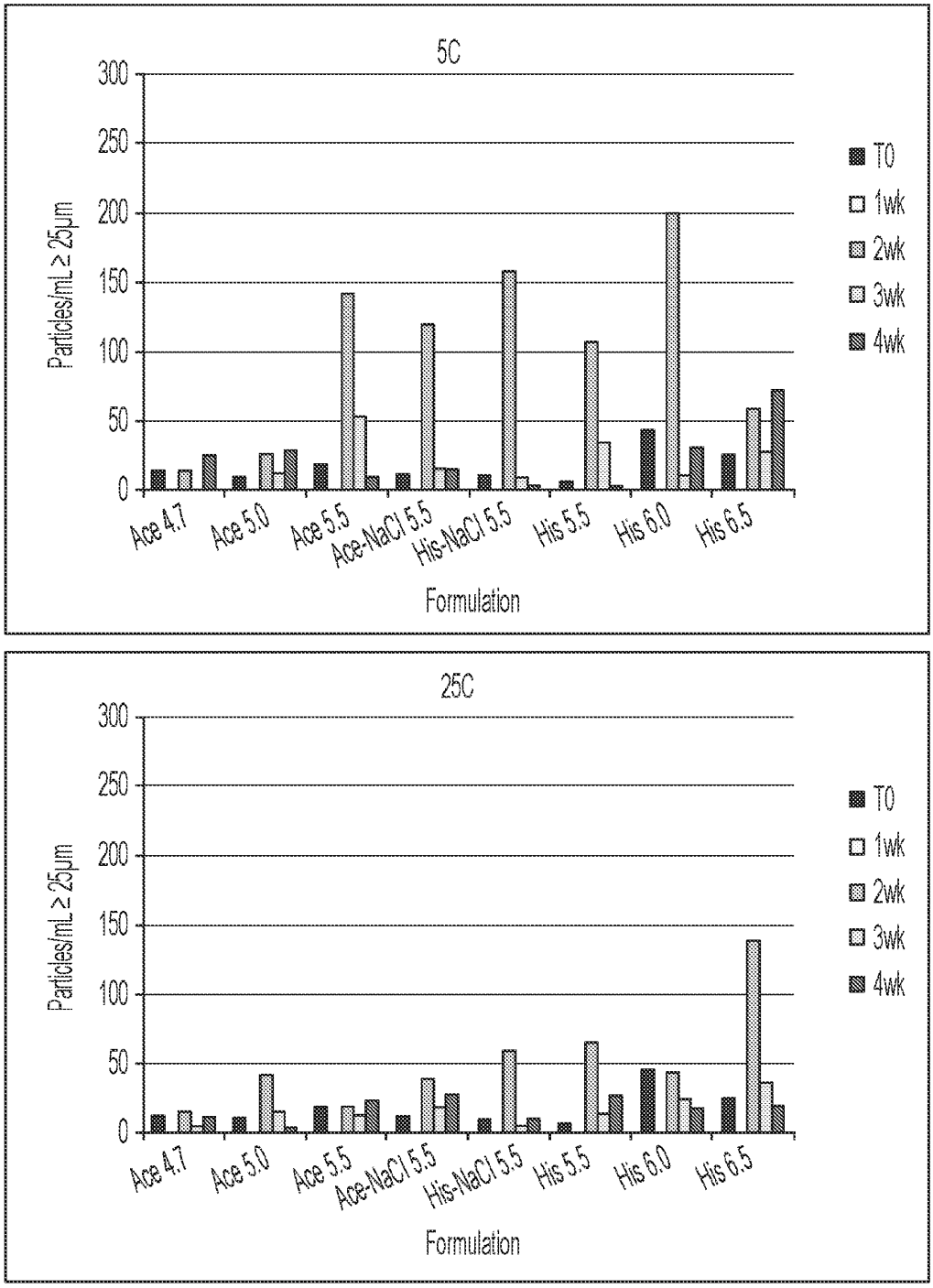

5C
300
250
200
150
100
50
0
Particles/mL ≥ 25µm
T0
1wk
2wk
3wk
4wk
Ace 4.7
Ace 5.0
Ace 5.5
Ace-NaCl 5.5
His-NaCl 5.5
His 5.5
His 6.0
His 6.5
Formulation
25C
300
250
200
150
100
50
0
Particles/mL ≥ 25µm
T0
1wk
2wk
3wk
4wk
Ace 4.7
Ace 5.0
Ace 5.5
Ace-NaCl 5.5
His-NaCl 5.5
His 5.5
His 6.0
His 6.5
Formulation

FIG. 2C

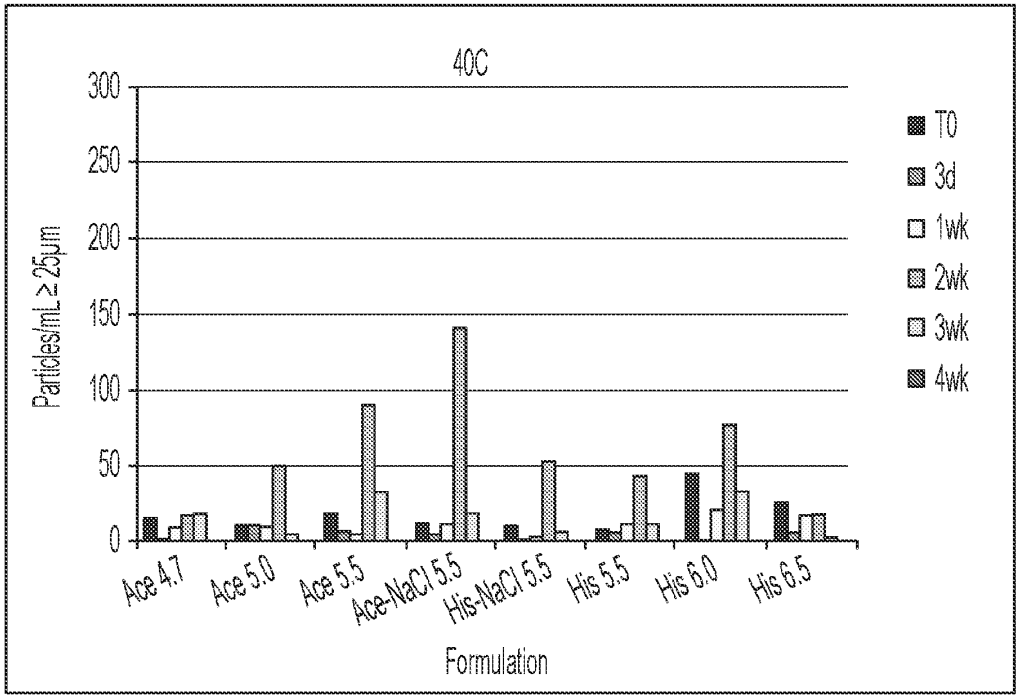


FIG. 2C
CONTINUED

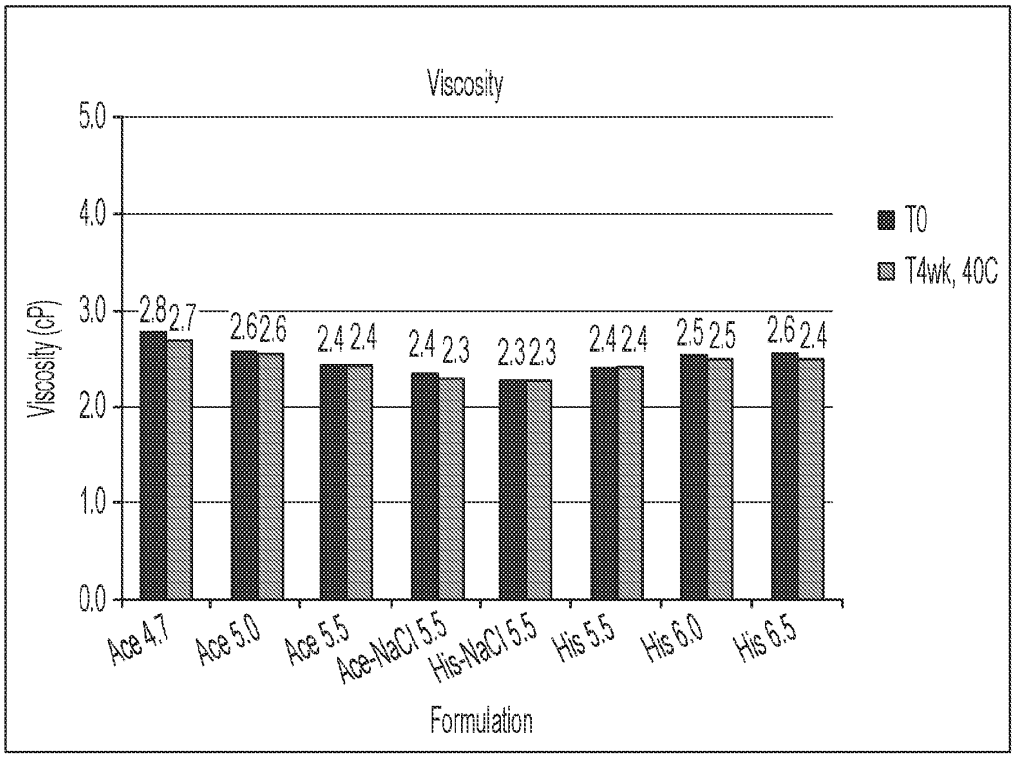

Viscosity
5.0
4.0
3.0
2.0
1.0
0.0
Viscosity (cP)
2.8 2.7
2.6 2.6
2.4 2.4
2.4 2.3
2.3 2.3
2.4 2.4
2.5 2.5
2.6 2.4
Ace 4.7
Ace 5.0
Ace 5.5
Ace-NaCl 5.5
His-NaCl 5.5
His 5.5
His 6.0
His 6.5
Formulation
T0
T4wk, 40C

FIG. 3

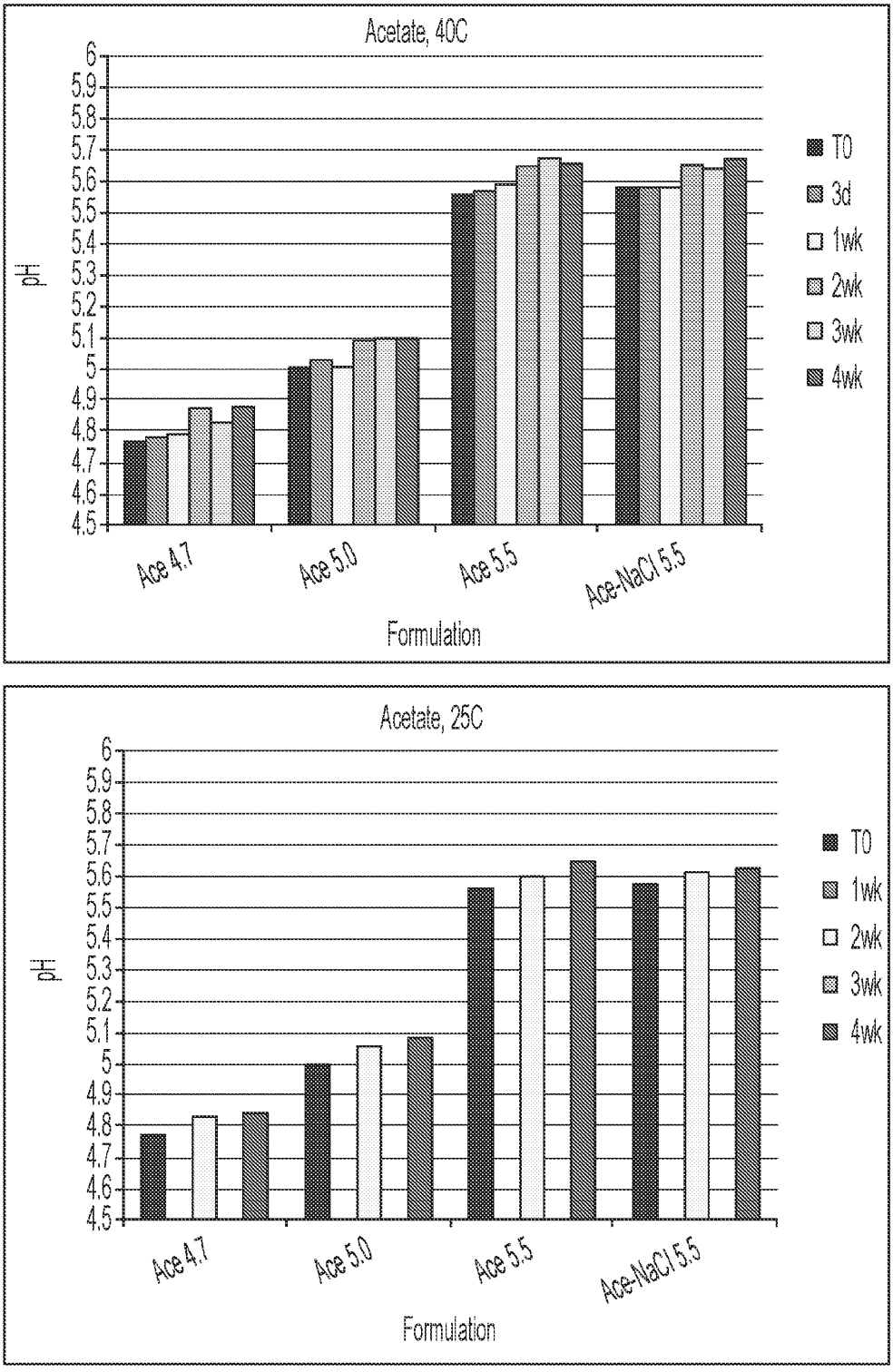

Acetate, 40C
pH
6
5.9
5.8
5.7
5.6
5.5
5.4
5.3
5.2
5.1
5
4.9
4.8
4.7
4.6
4.5
T0
3d
1wk
2wk
3wk
4wk
Ace 4.7
Ace 5.0
Ace 5.5
Ace-NaCl 5.5
Formulation
Acetate, 25C
pH
6
5.9
5.8
5.7
5.6
5.5
5.4
5.3
5.2
5.1
5
4.9
4.8
4.7
4.6
4.5
T0
1wk
2wk
3wk
4wk
Ace 4.7
Ace 5.0
Ace 5.5
Ace-NaCl 5.5
Formulation

FIG. 4A

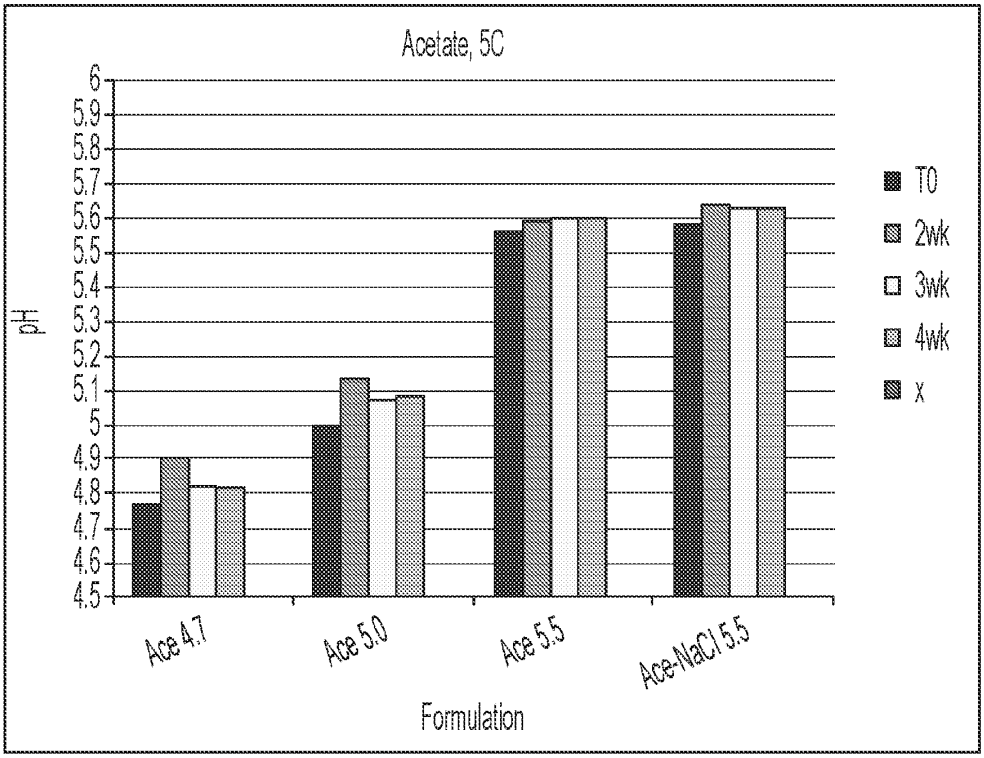


FIG. 4A
CONTINUED

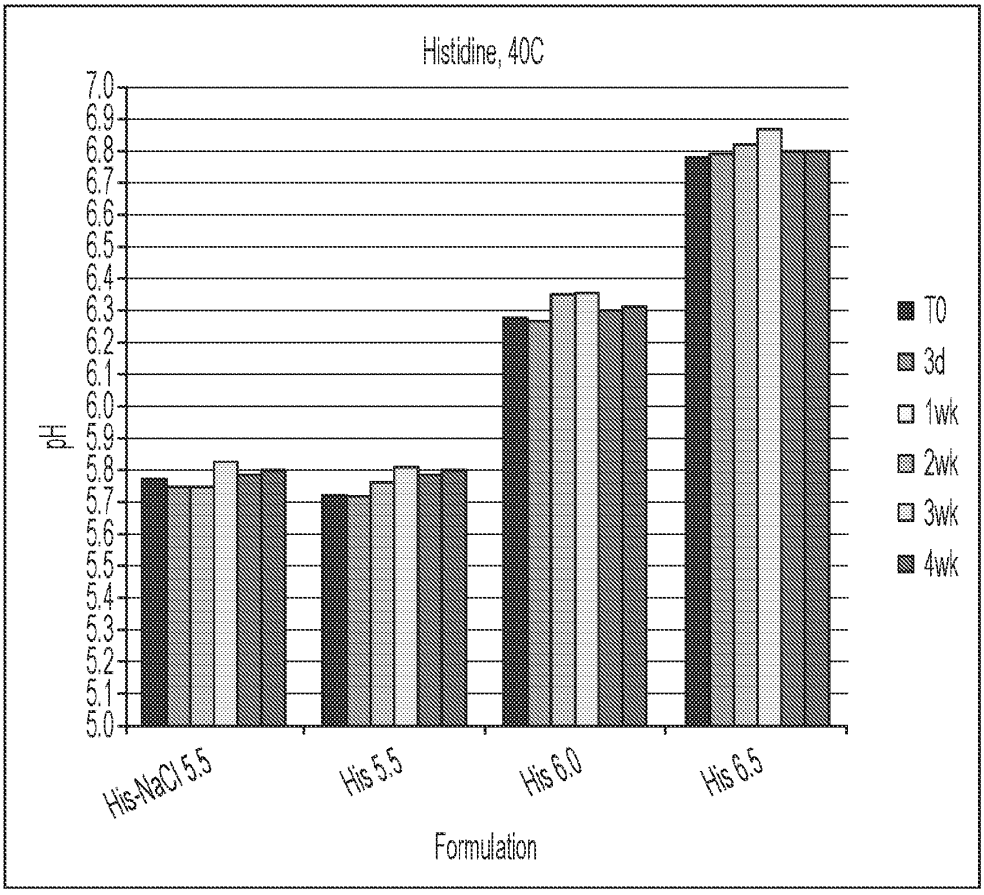

Histidine, 40C
pH
7.0
6.9
6.8
6.7
6.6
6.5
6.4
6.3
6.2
6.1
6.0
5.9
5.8
5.7
5.6
5.5
5.4
5.3
5.2
5.1
5.0
T0
3d
1wk
2wk
3wk
4wk
His-NaCl 5.5
His 5.5
His 6.0
His 6.5
Formulation

FIG. 4B

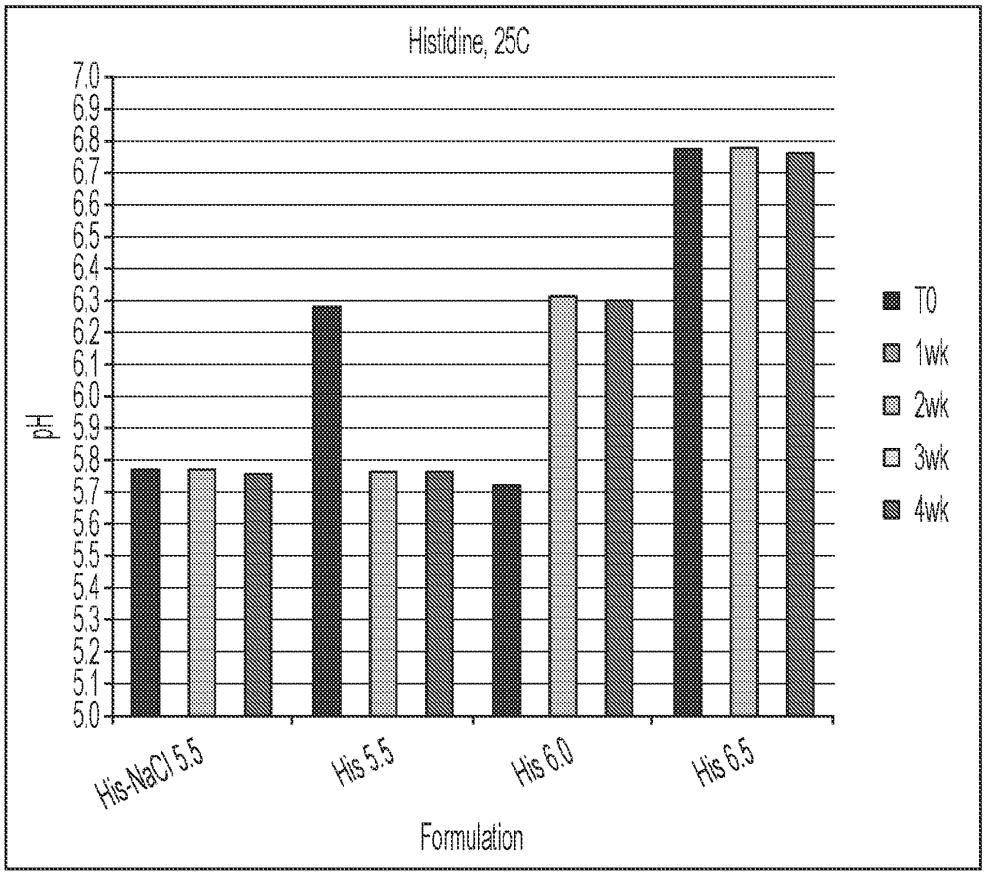


FIG. 4B
CONTINUED

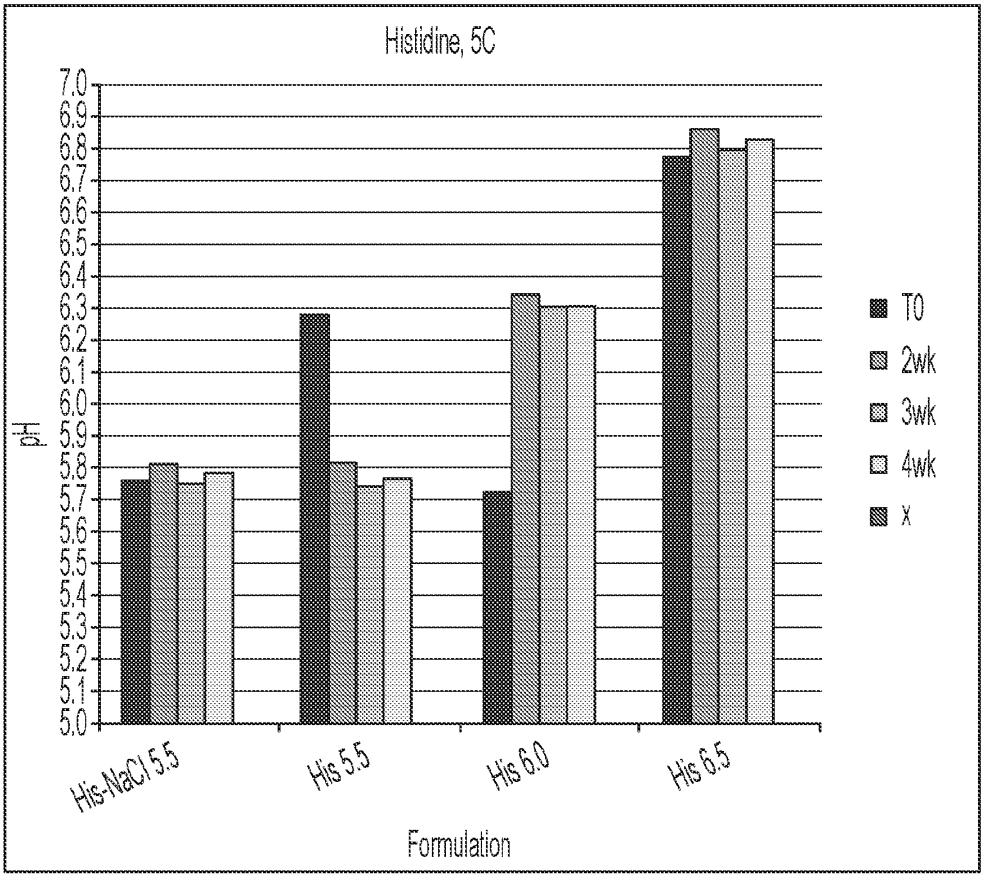


FIG. 4B
CONTINUED

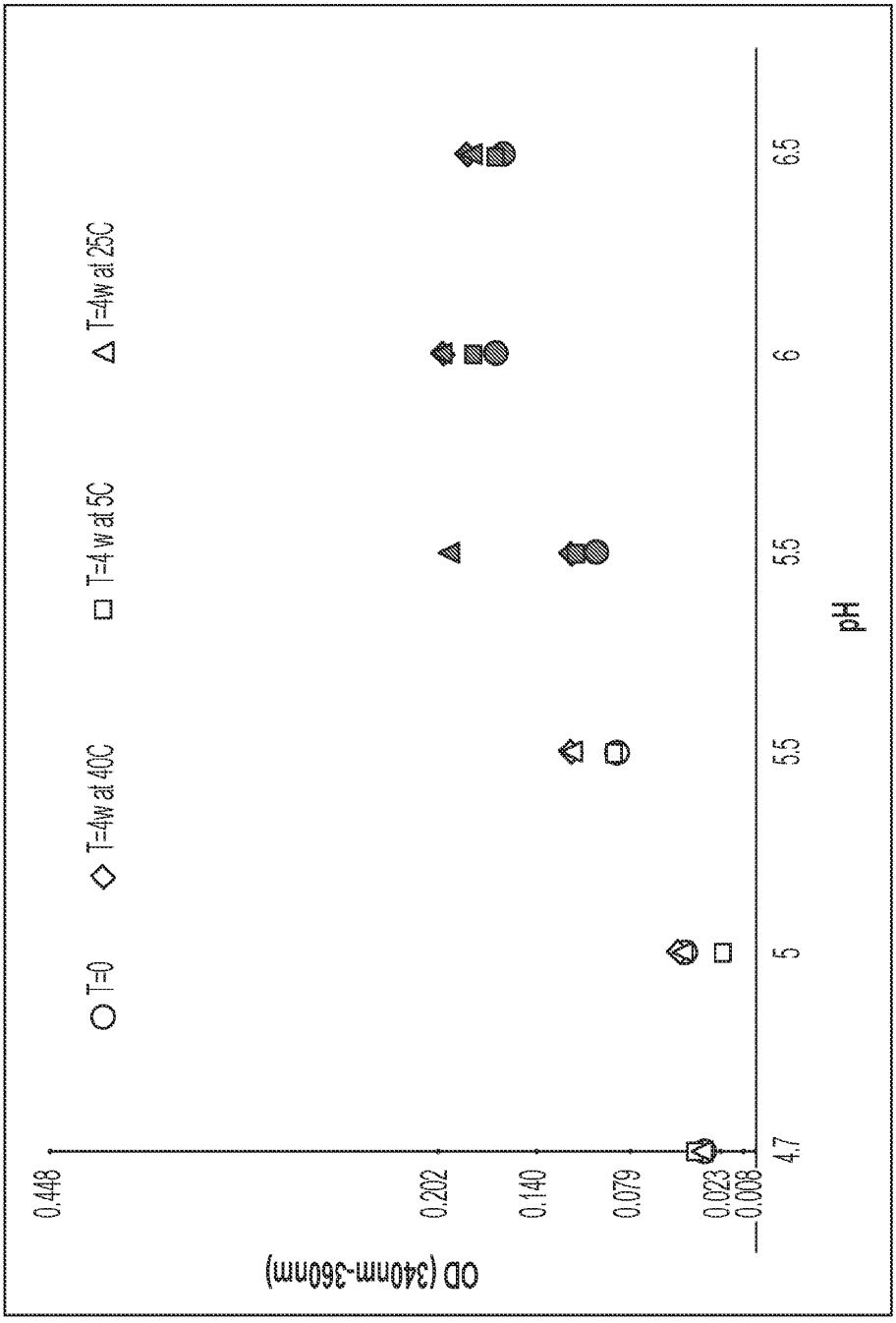

OD (340nm-360nm)
0.448
0.202
0.140
0.079
0.023
0.008
pH
4.7
5
5.5
5.5
6
6.5
T=0
T=4w at 40C
T=4 w at 5C
T=4w at 25C

FIG. 5

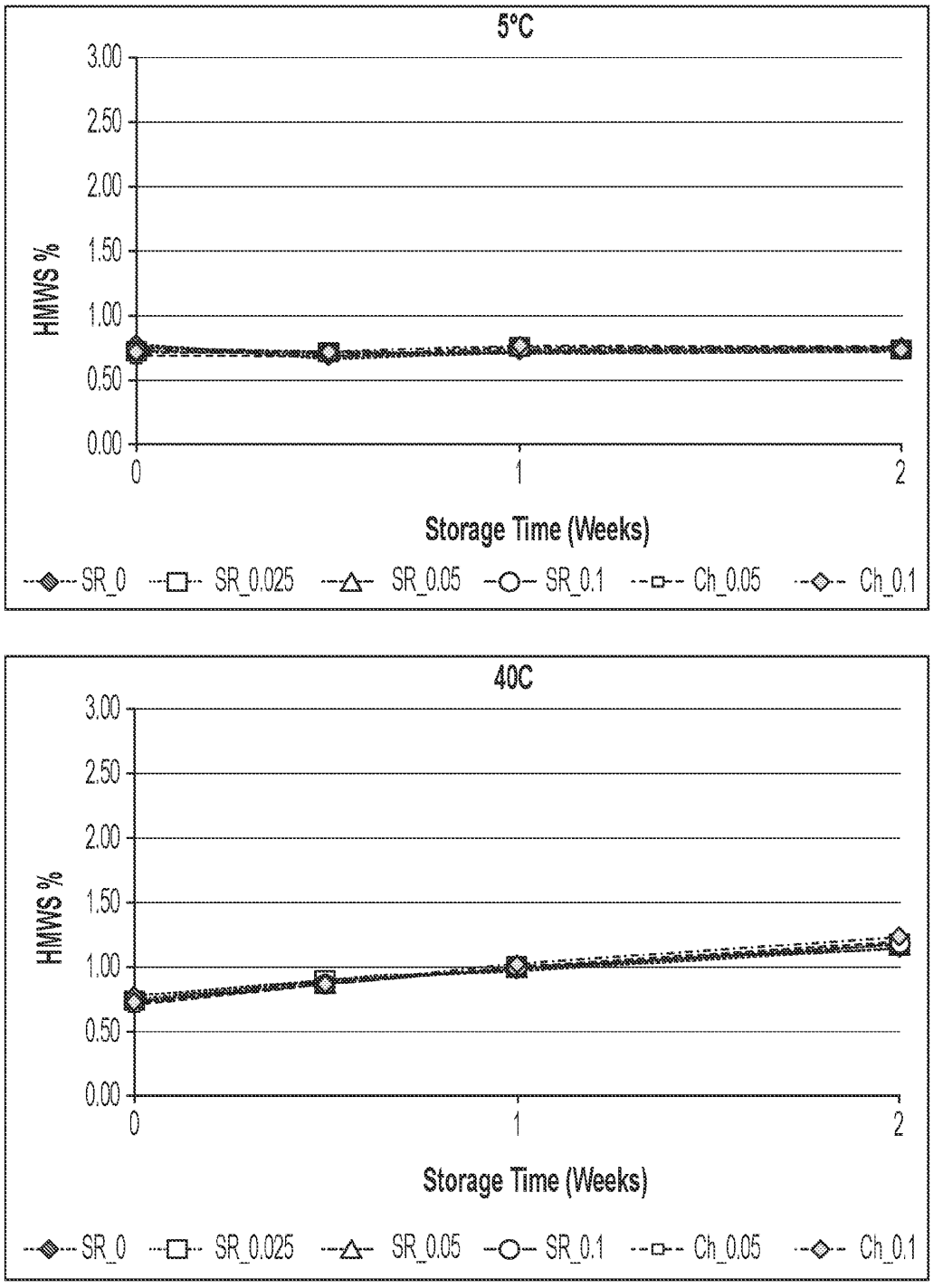
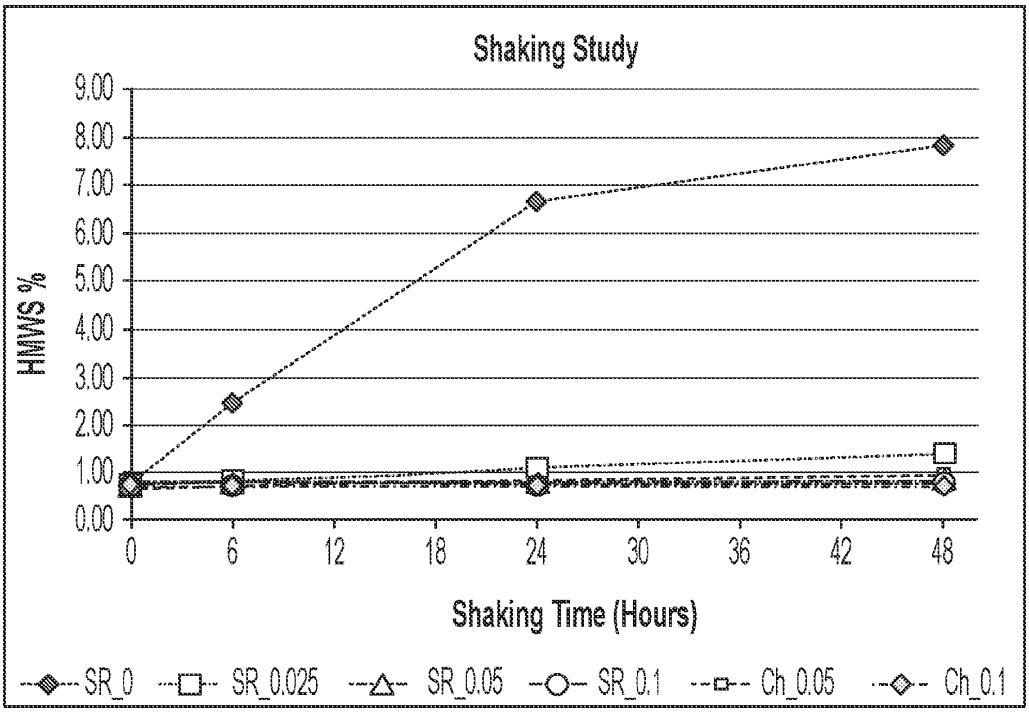

5°C
3.00
2.50
2.00
1.50
1.00
0.50
0.00
HMWS %
0
1
2
Storage Time (Weeks)
SR_0
SR_0.025
SR_0.05
SR_0.1
Ch_0.05
Ch_0.1
40C
3.00
2.50
2.00
1.50
1.00
0.50
0.00
HMWS %
0
1
2
Storage Time (Weeks)
SR_0
SR_0.025
SR_0.05
SR_0.1
Ch_0.05
Ch_0.1

FIG. 6



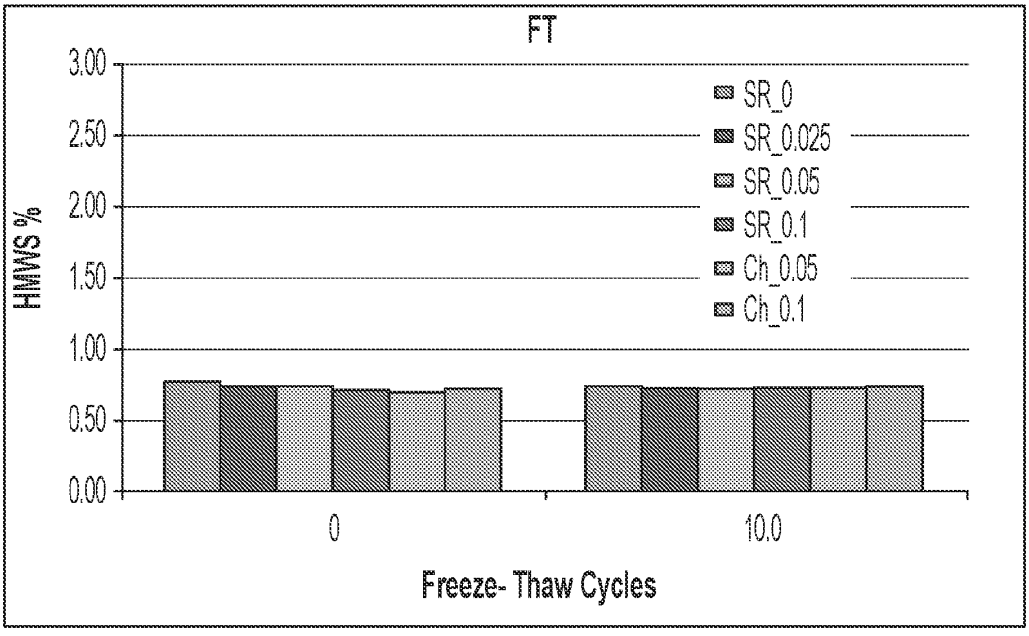


FIG. 6
CONTINUED

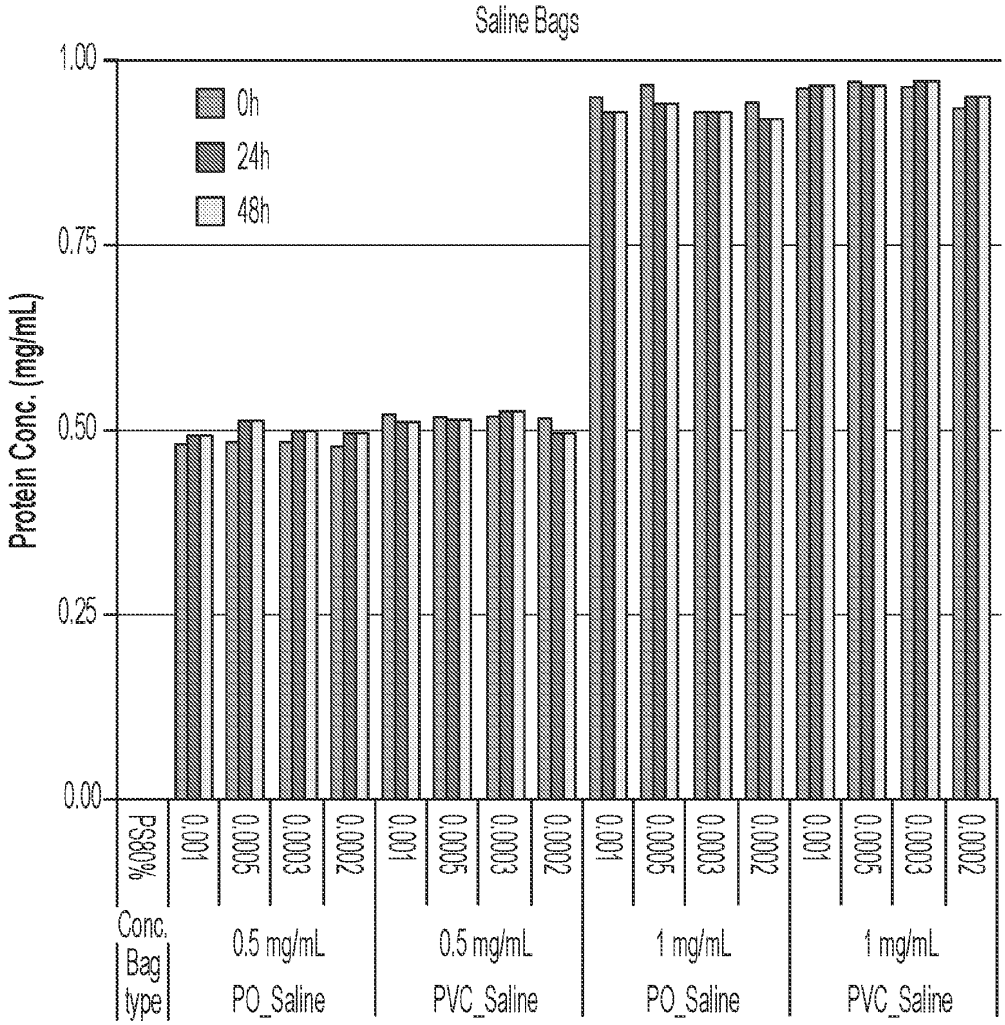

Saline Bags
1.00
0.75
0.50
0.25
0.00
Protein Conc. (mg/mL)
0h
24h
48h
PS80%
0.001
0.0005
0.0003
0.0002
0.001
0.0005
0.0003
0.0002
0.001
0.0005
0.0003
0.0002
0.001
0.0005
0.0003
0.0002
Conc.
Bag type
0.5 mg/mL
PO_Saline
0.5 mg/mL
PVC_Saline
1 mg/mL
PO_Saline
1 mg/mL
PVC_Saline

FIG. 7A

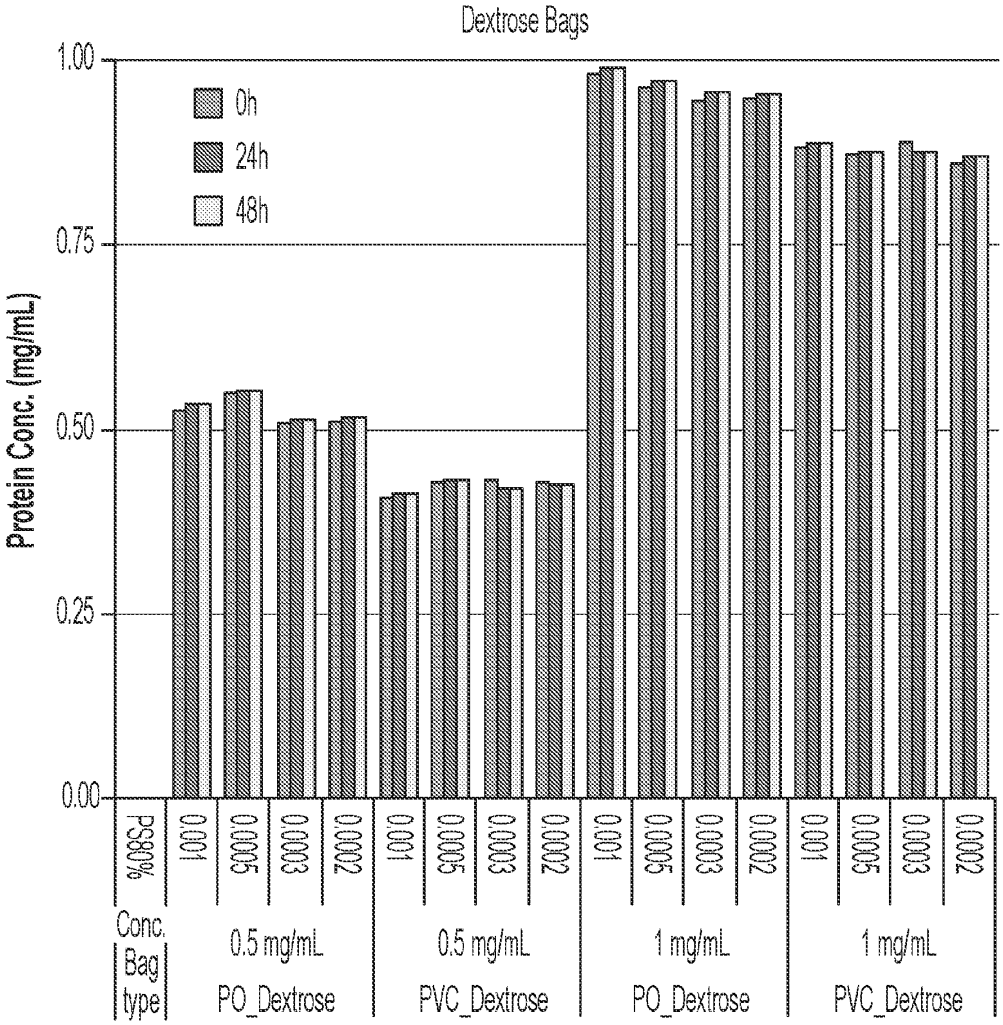


FIG. 7A
CONTINUED

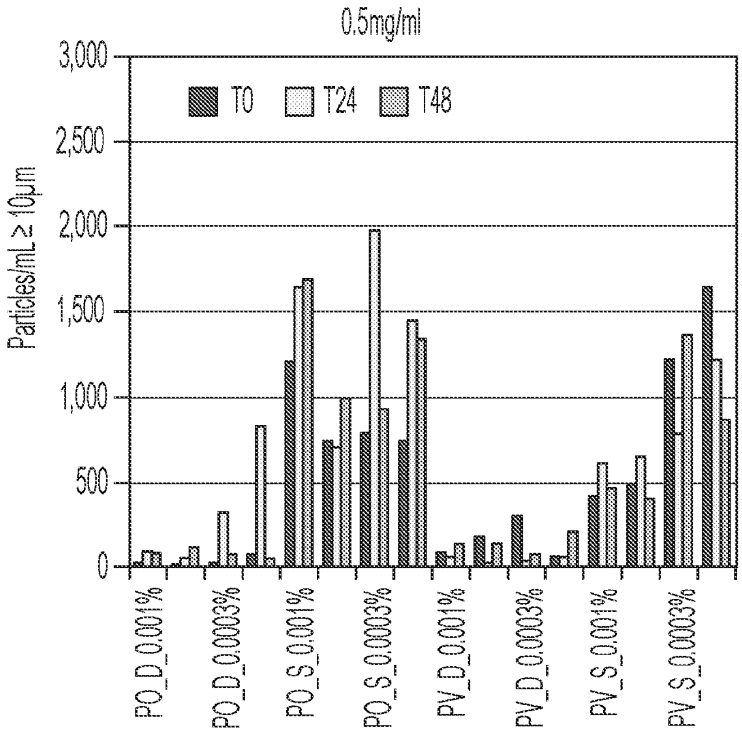

0.5mg/ml
3,000
2,500
2,000
1,500
1,000
500
0
Particles/mL ≥ 10µm
T0
T24
T48
PO_D_0.001%
PO_D_0.0003%
PO_S_0.001%
PO_S_0.0003%
PV_D_0.001%
PV_D_0.0003%
PV_S_0.001%
PV_S_0.0003%

FIG. 7B

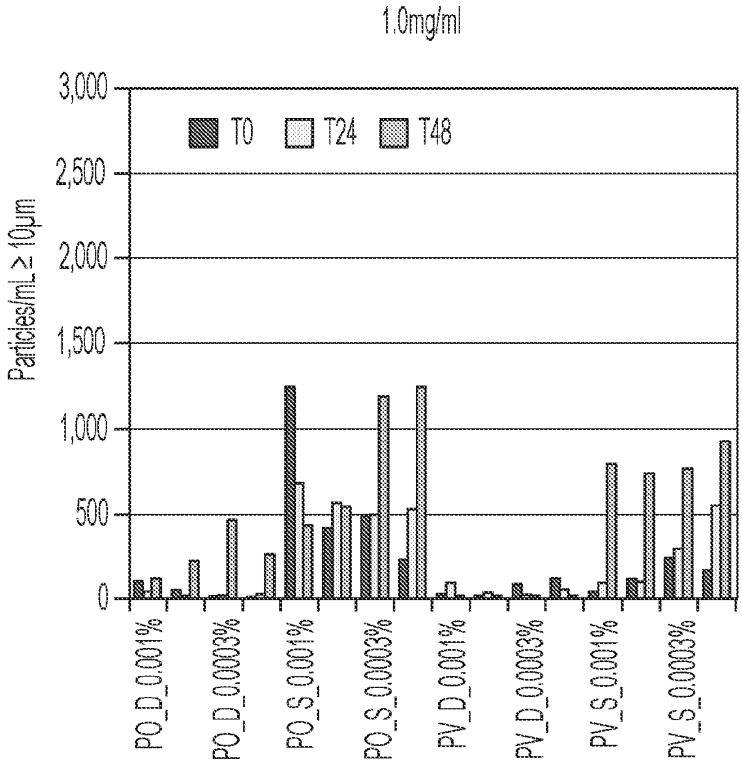


FIG. 7B
CONTINUED

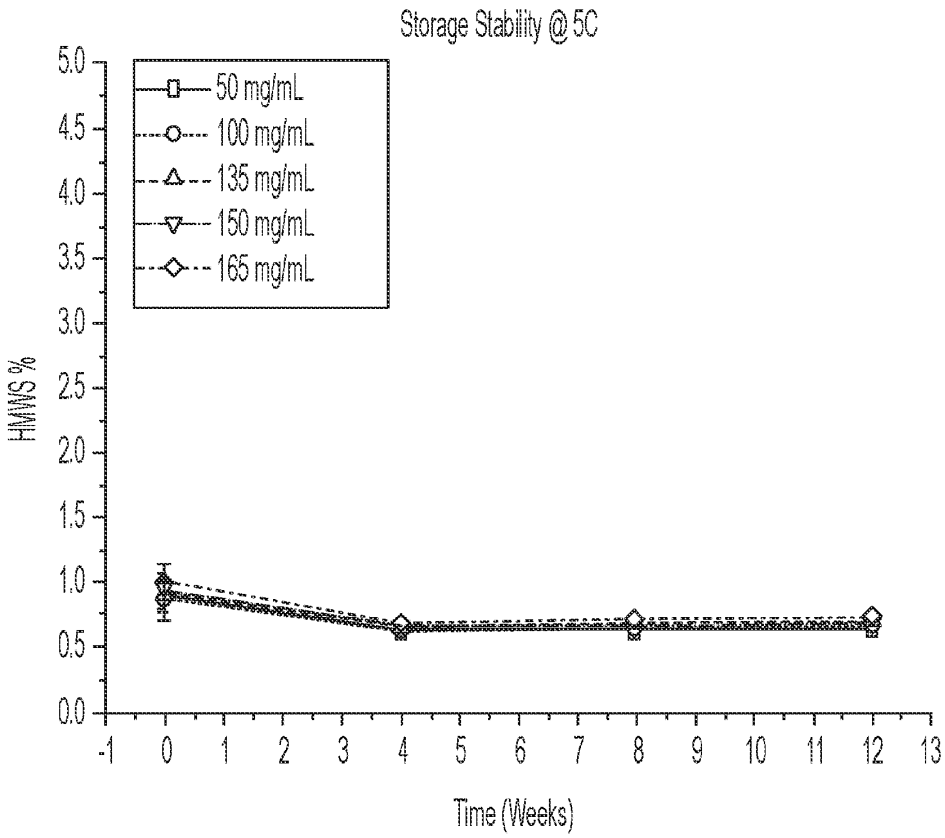

Storage Stability @ 5C
50 mg/mL
100 mg/mL
135 mg/mL
150 mg/mL
165 mg/mL
HMWS %
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
Time (Weeks)

FIG. 8A

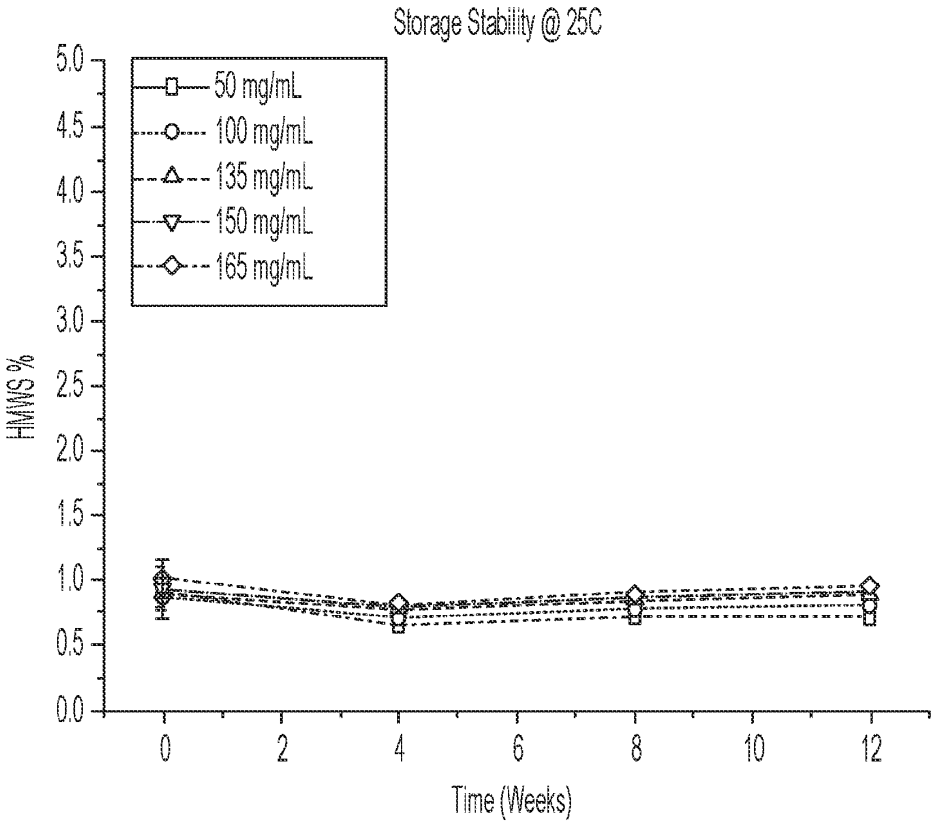


FIG. 8A
CONTINUED

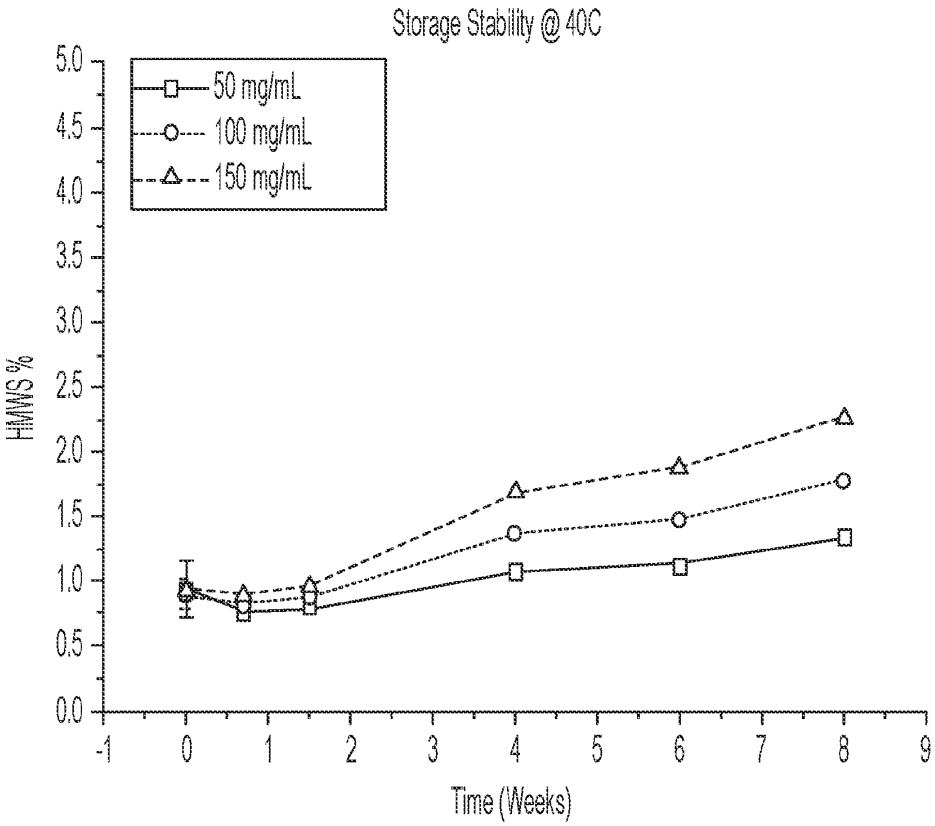


FIG. 8A
CONTINUED

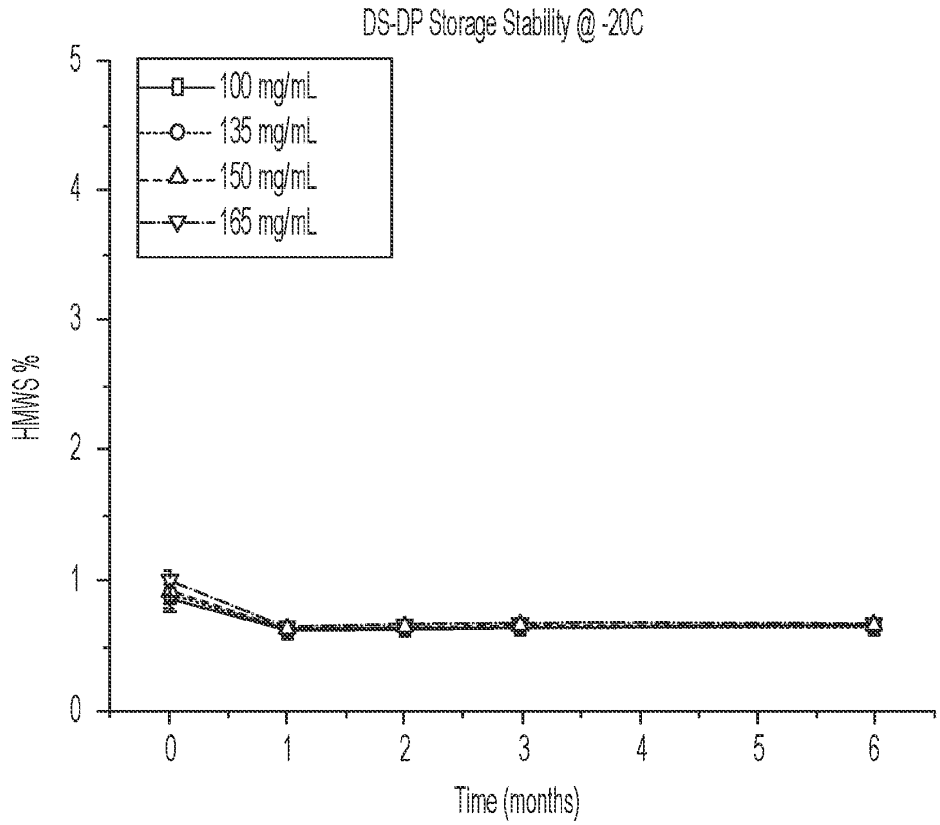

DS-DP Storage Stability @ -20C
100 mg/mL
135 mg/mL
150 mg/mL
165 mg/mL
HMWS %
0
1
2
3
4
5
0
1
2
3
4
5
6
Time (months)

FIG. 8B

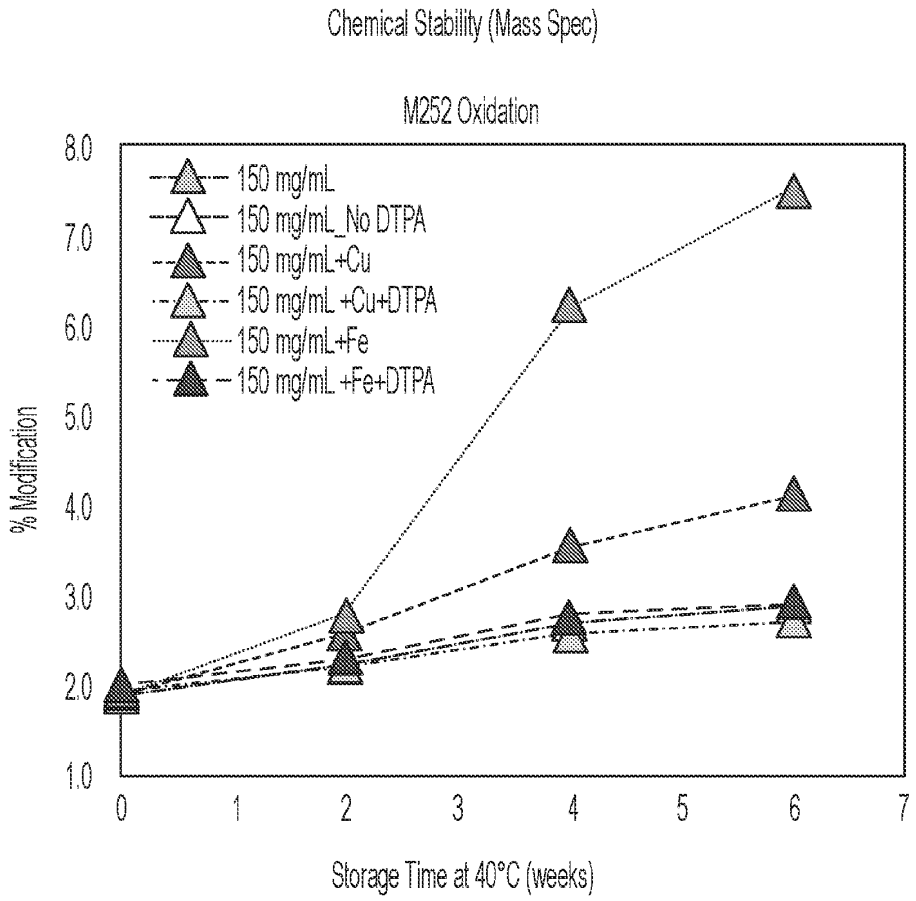

Chemical Stability (Mass Spec)
M252 Oxidation
% Modification
Storage Time at 40°C (weeks)
150 mg/mL
150 mg/mL_No DTPA
150 mg/mL+Cu
150 mg/mL +Cu+DTPA
150 mg/mL+Fe
150 mg/mL +Fe+DTPA
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
1
2
3
4
5
6
7

FIG. 9

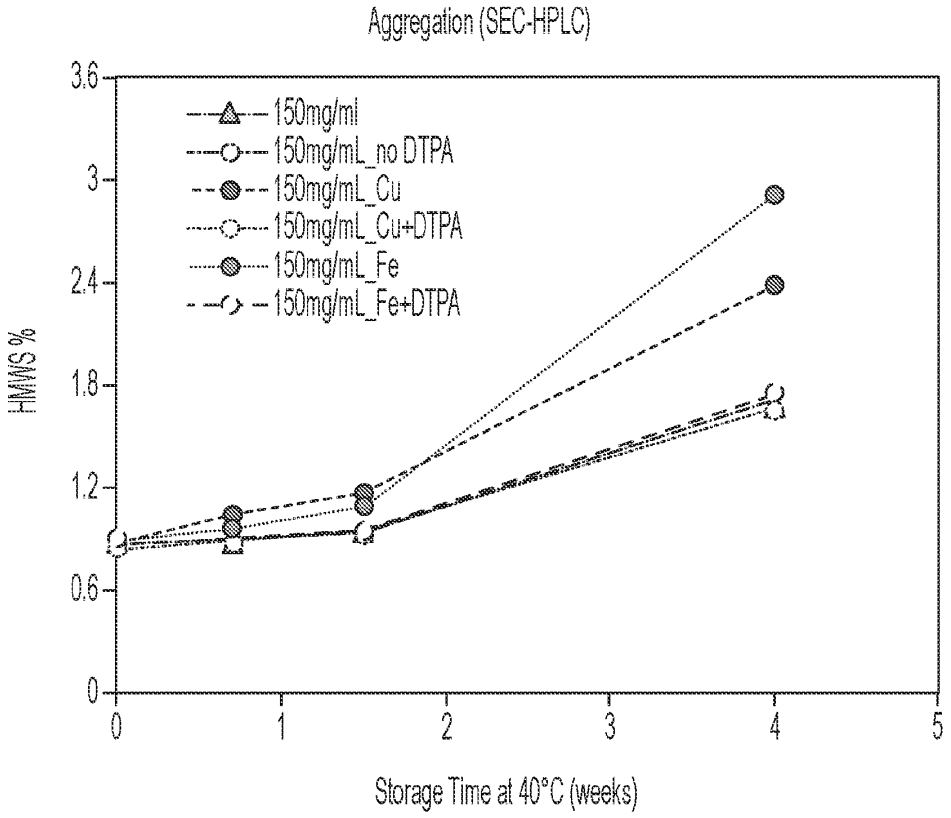


FIG. 9
CONTINUED

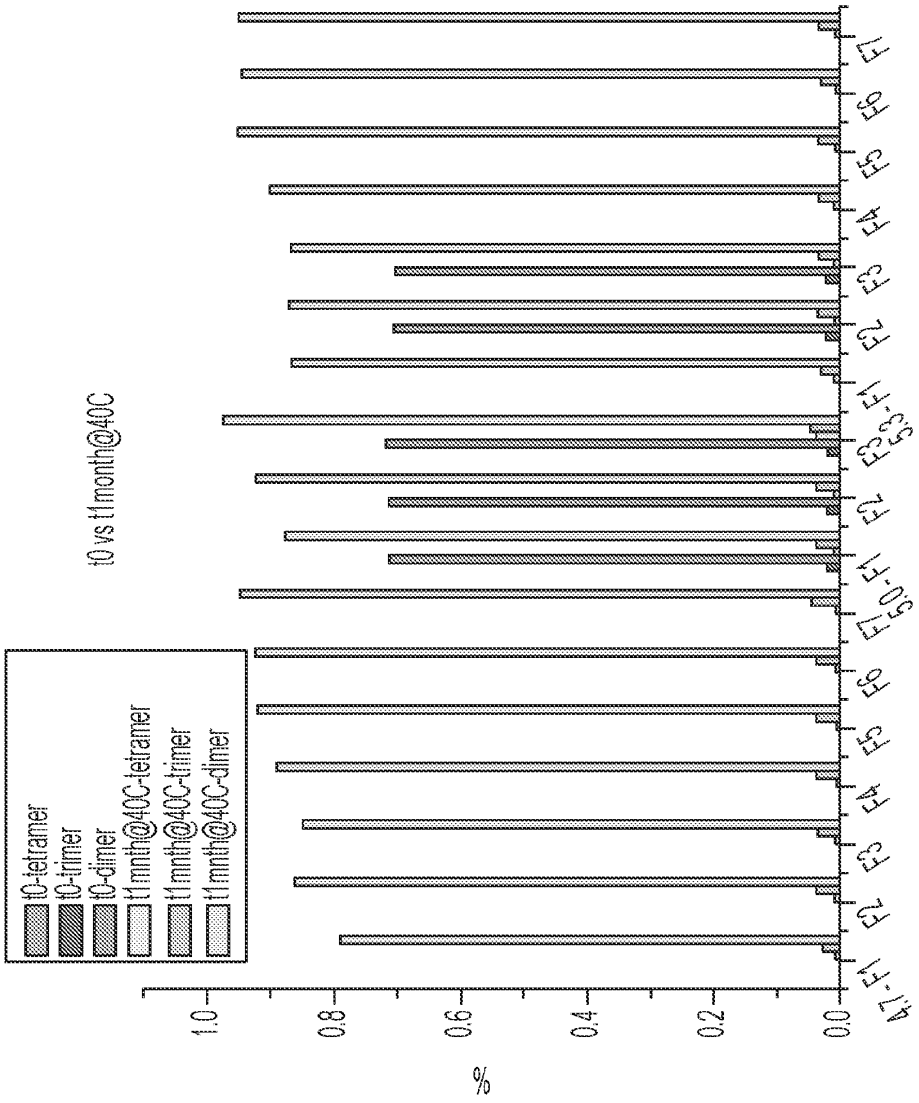

t0 vs t1month@40C
t0-tetramer
t0-trimer
t0-dimer
t1mnth@40C-tetramer
t1mnth@40C-trimer
t1mnth@40C-dimer
1.0
0.8
0.6
0.4
0.2
0.0
%
F1-F4
F5
F6
F7-F9
F10-F13
F14
F15
F16
F17
F18
F19
F20
F21

FIG. 10

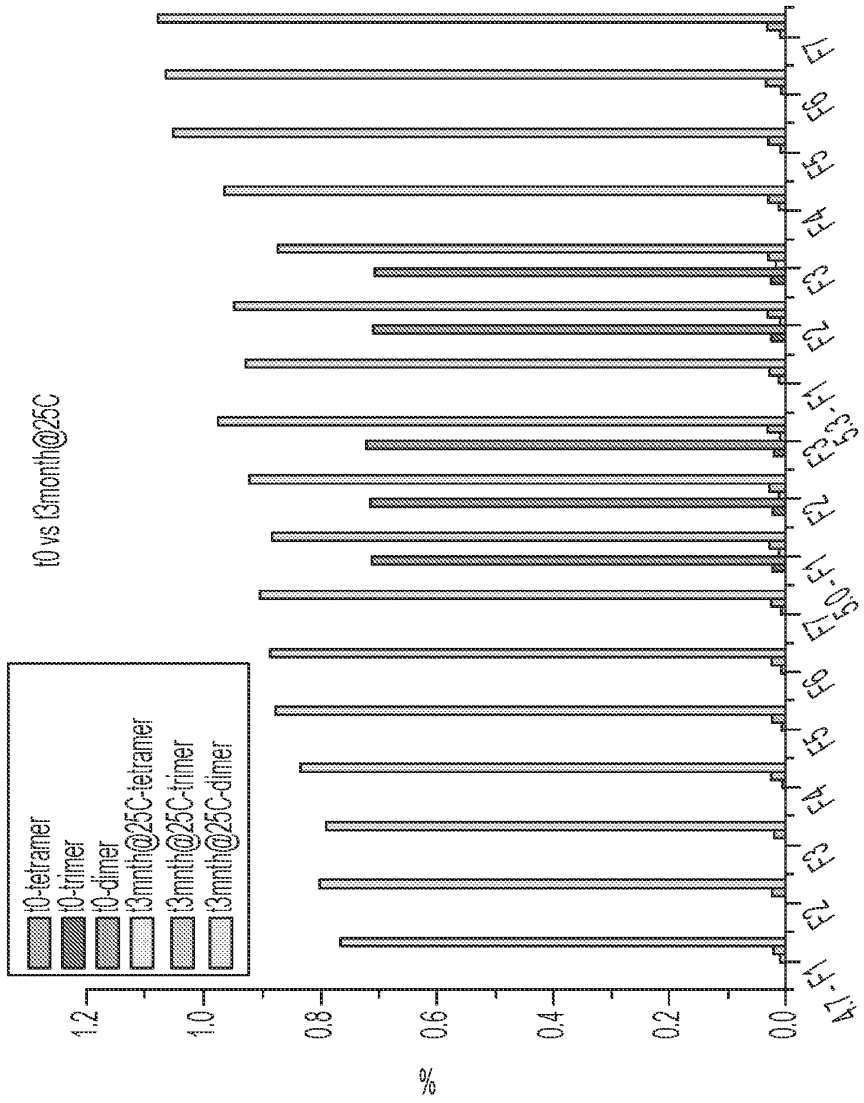


FIG. 10
CONTINUED