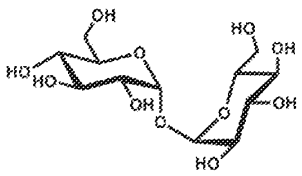
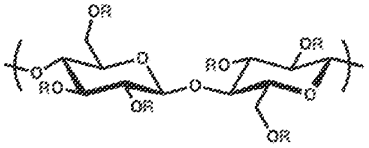
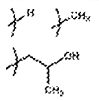
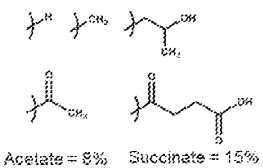
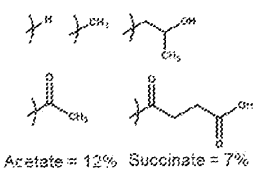
FIG. 1

Trehalose



Generic structure of cellulose



#	Name	R groups	MW[1]	T_g[2]
1	Metolose		100 kD	151° C
2	AS-LF	 Acetate = 8% Succinate = 15%	100 kD	92° C
3	AS-HF	 Acetate = 12% Succinate = 7%	100 kD	103° C
4	Trehalose	None	0.342 kD	110° C

[1]MW was measured using gel permeation chromatography except in case of trehalose
[2]Glass transition temperature was measured using differential scanning calorimetry

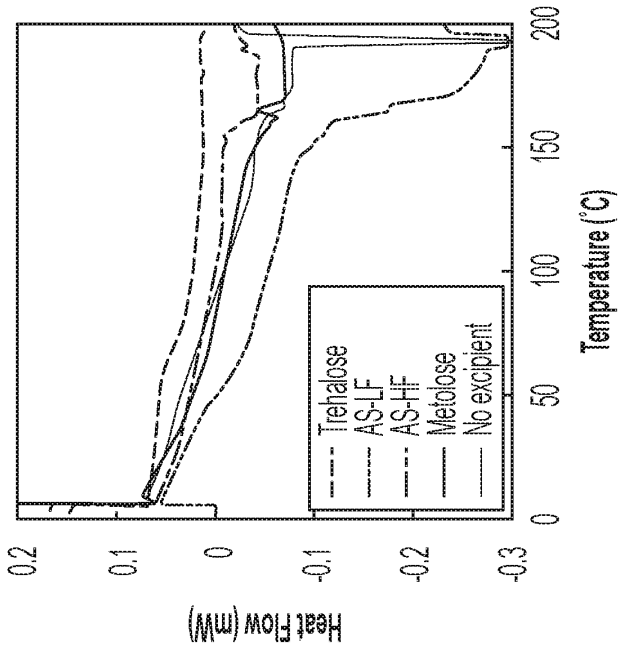

Heat Flow (mW)
0.2
0.1
0
-0.1
-0.2
-0.3
0
50
100
150
200
Temperature (°C)
Trehalose
AS-LF
AS-HF
Metolose
No excipient

FIG. 2

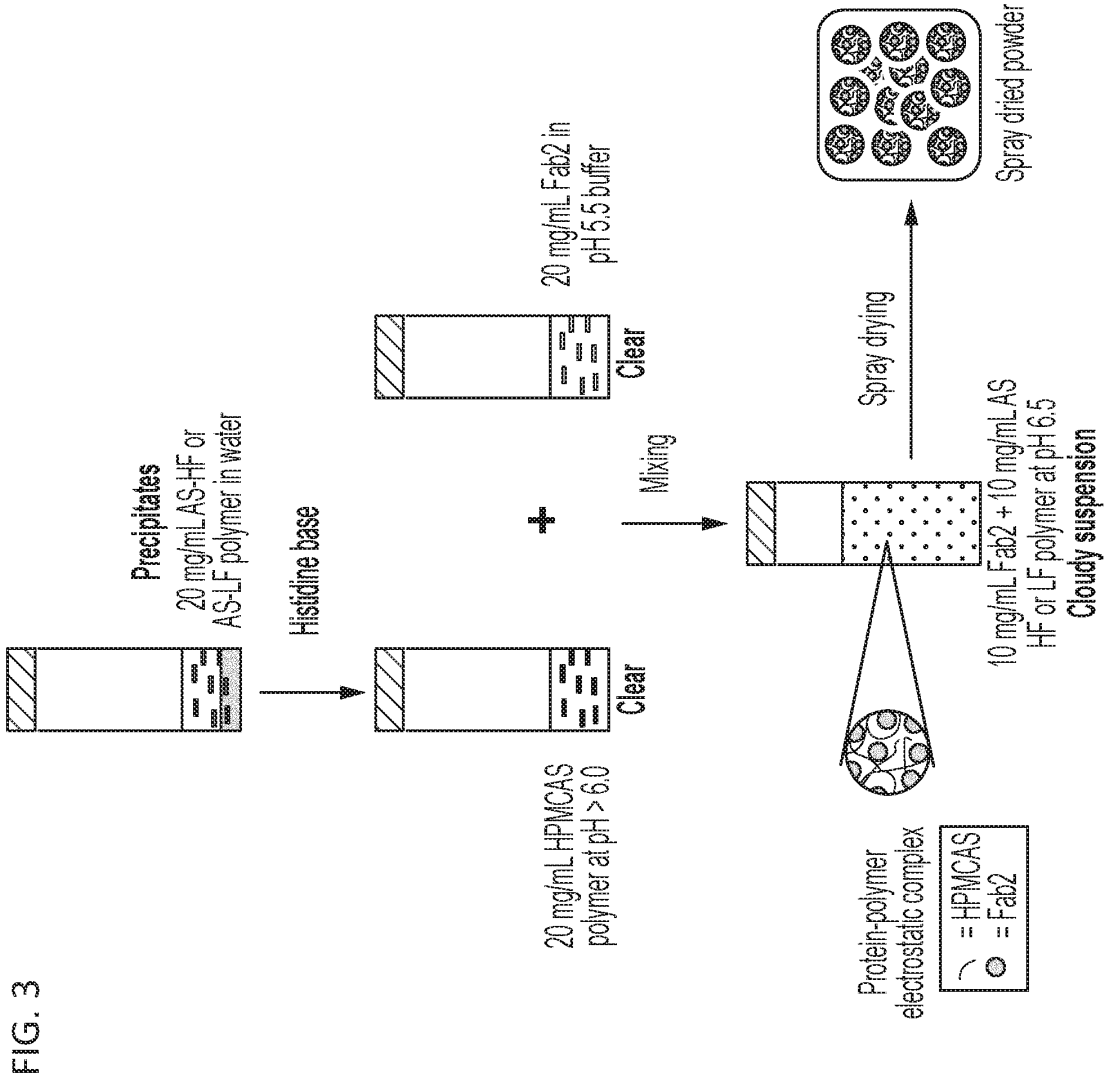

Precipitates
20 mg/mL AS-HF or
AS-LF polymer in water
Histidine base
20 mg/mL HPMCAS
polymer at pH > 6.0
Clear
20 mg/mL Fab2 in
pH 5.5 buffer
Clear
Mixing
10 mg/mL Fab2 + 10 mg/mL AS
HF or LF polymer at pH 6.5
Cloudy suspension
Spray drying
Spray dried powder
Protein-polymer
electrostatic complex
= HPMCAS
= Fab2

FIG. 3

FIG. 4A

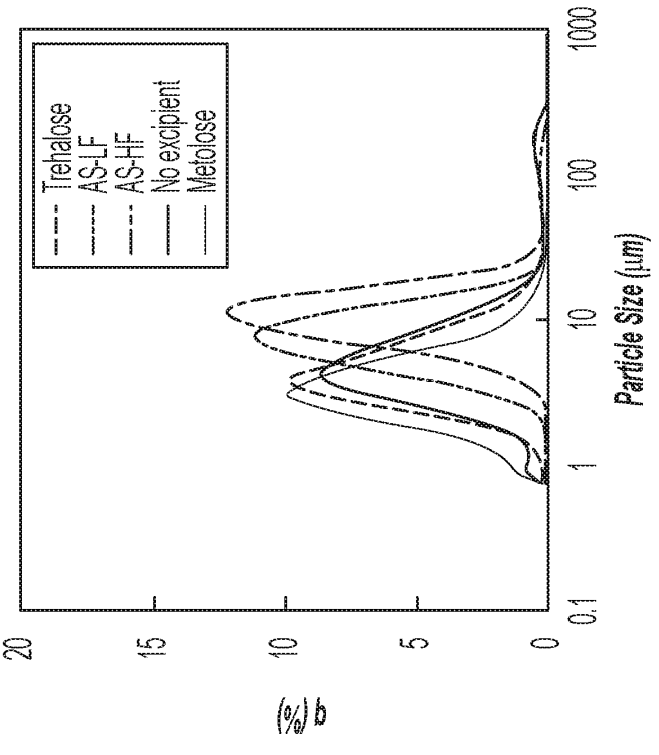
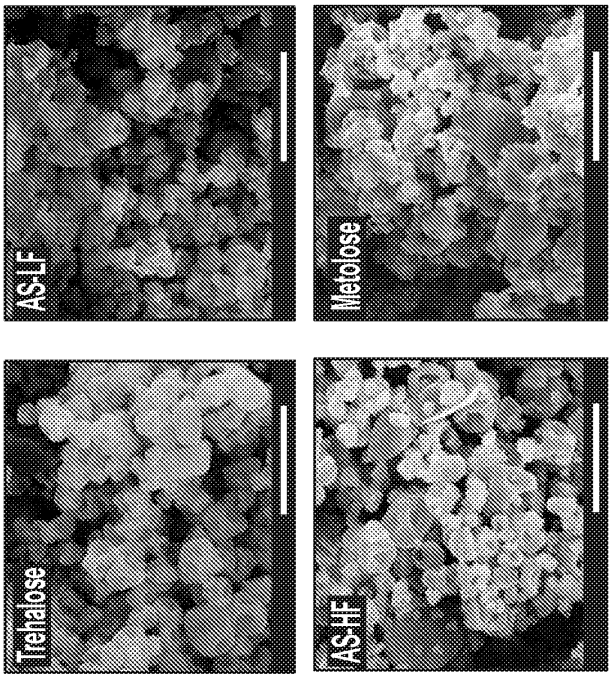

Trehalose
AS-LF
AS-HF
No excipient
Metolose
q (%)
20
15
10
5
0
0.1
1
10
100
1000
Particle Size (μm)

FIG. 4B


Trehalose
AS-LF
AS-HF
Metolose

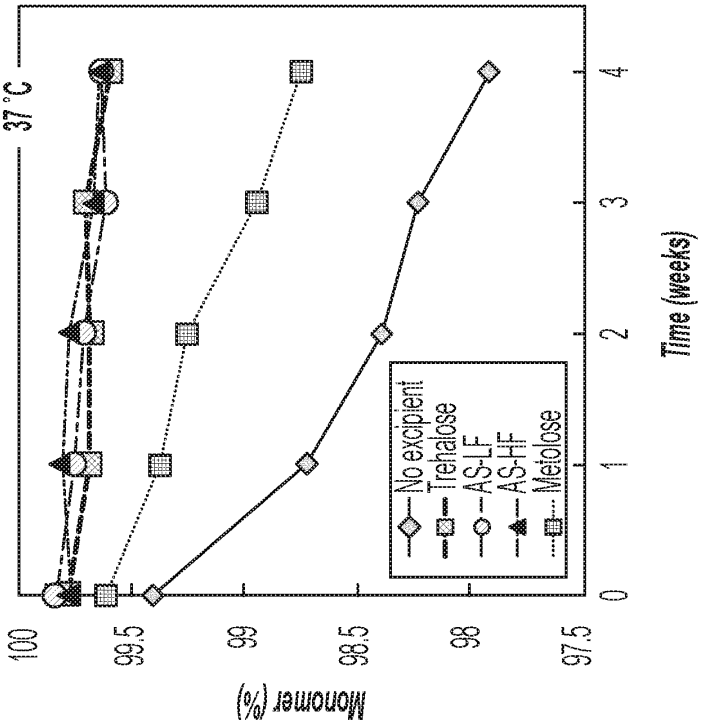

37 °C
Monomer (%)
100
99.5
99
98.5
98
97.5
0
1
2
3
4
Time (weeks)
No excipient
Trehalose
AS-LF
AS-HF
Metolose

FIG. 5B

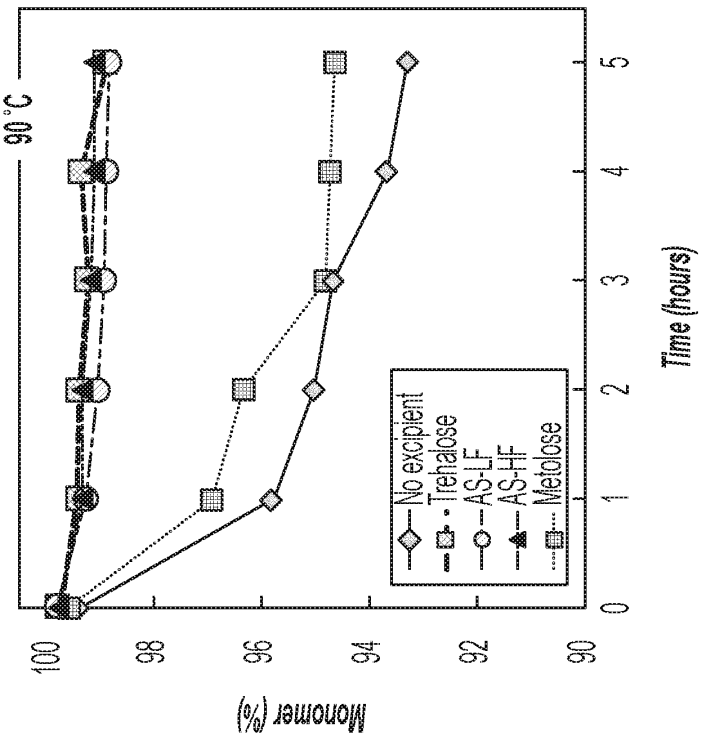

90 °C
Monomer (%)
100
98
96
94
92
90
0
1
2
3
4
5
Time (hours)
No excipient
Trehalose
AS-LF
AS-HF
Metolose

FIG. 5A

FIG. 6A

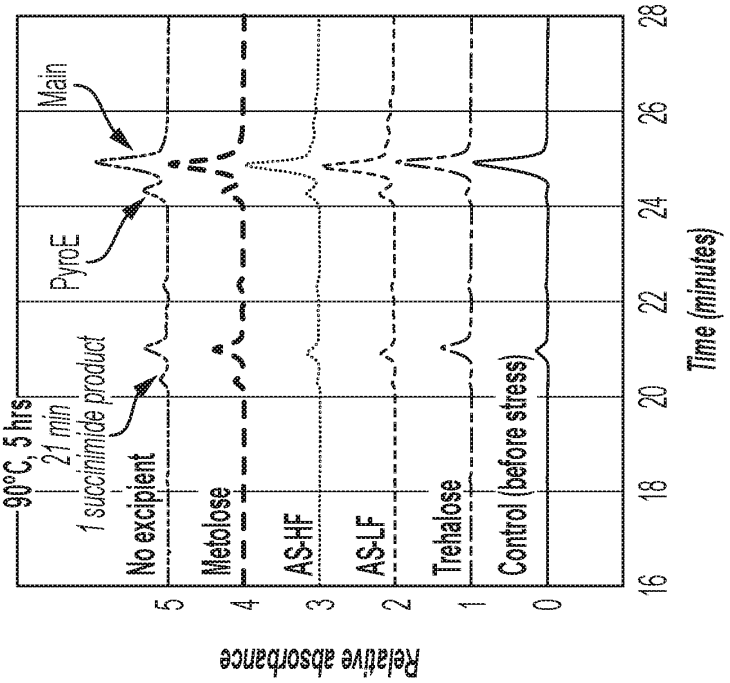

90°C, 5 hrs
21 min
1 succinimide product
No excipient
Metolose
AS-HF
AS-LF
Trehalose
Control (before stress)
PyroE
Main
Relative absorbance
Time (minutes)

FIG. 6B

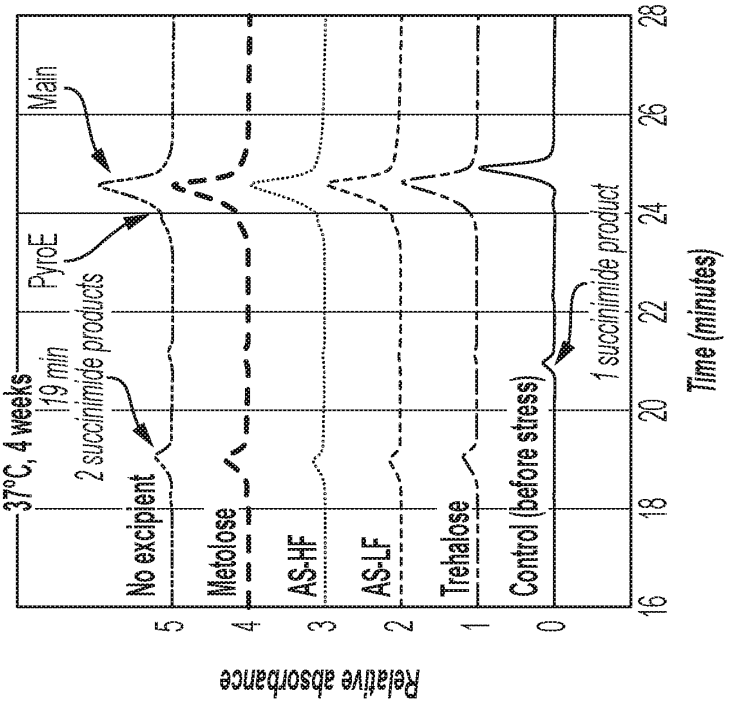

37°C, 4 weeks
19 min
2 succinimide products
No excipient
Metolose
AS-HF
AS-LF
Trehalose
Control (before stress)
1 succinimide product
PyroE
Main
Relative absorbance
Time (minutes)

FIG. 6C

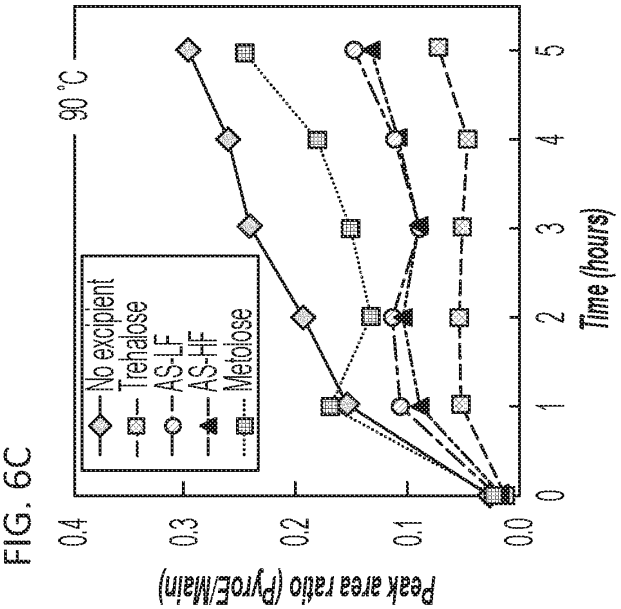
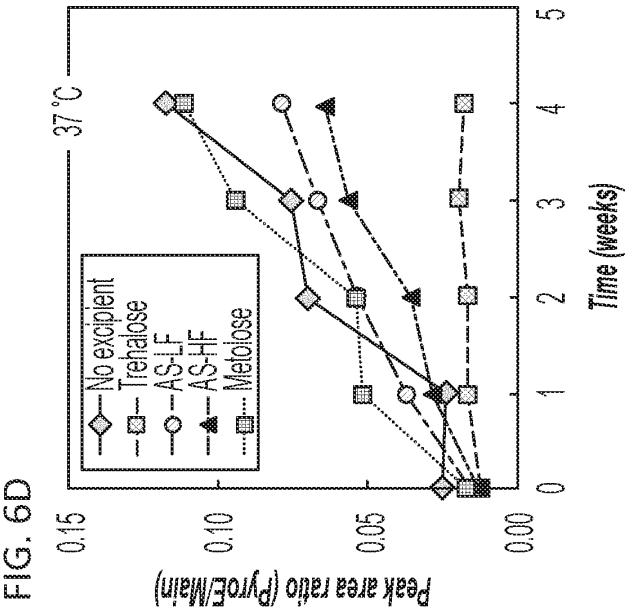

90 °C
No excipient
Trehalose
AS-LF
AS-HF
Metolose
Peak area ratio (PyroE/Main)
0.0
0.1
0.2
0.3
0.4
0
1
2
3
4
5
Time (hours)

FIG. 6D


37 °C
No excipient
Trehalose
AS-LF
AS-HF
Metolose
Peak area ratio (PyroE/Main)
0.00
0.05
0.10
0.15
0
1
2
3
4
5
Time (weeks)

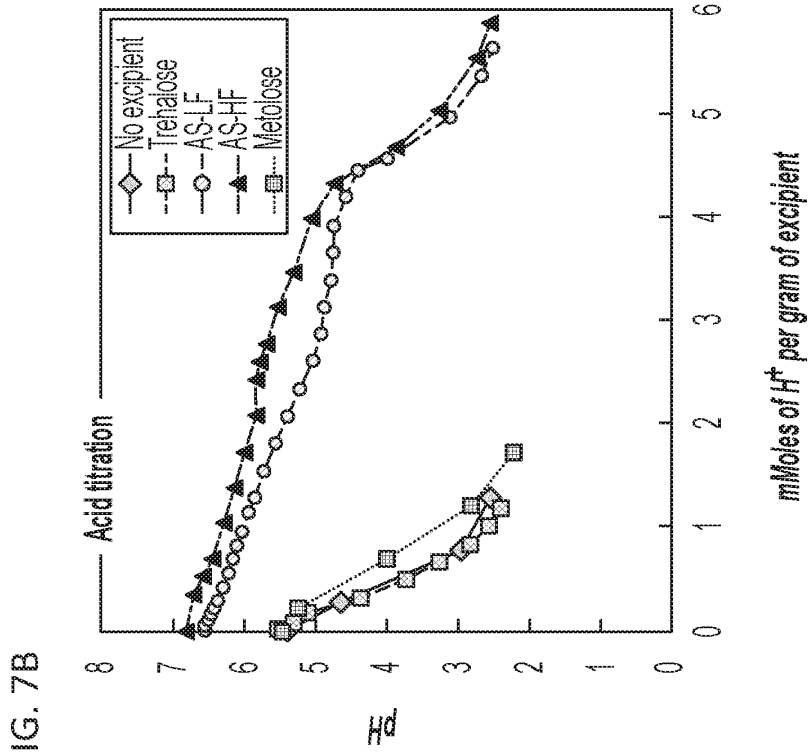

Acid titration
No excipient
Trehalose
AS-LF
AS-HF
Metolose
pH
mMoles of H+ per gram of excipient

FIG. 7B

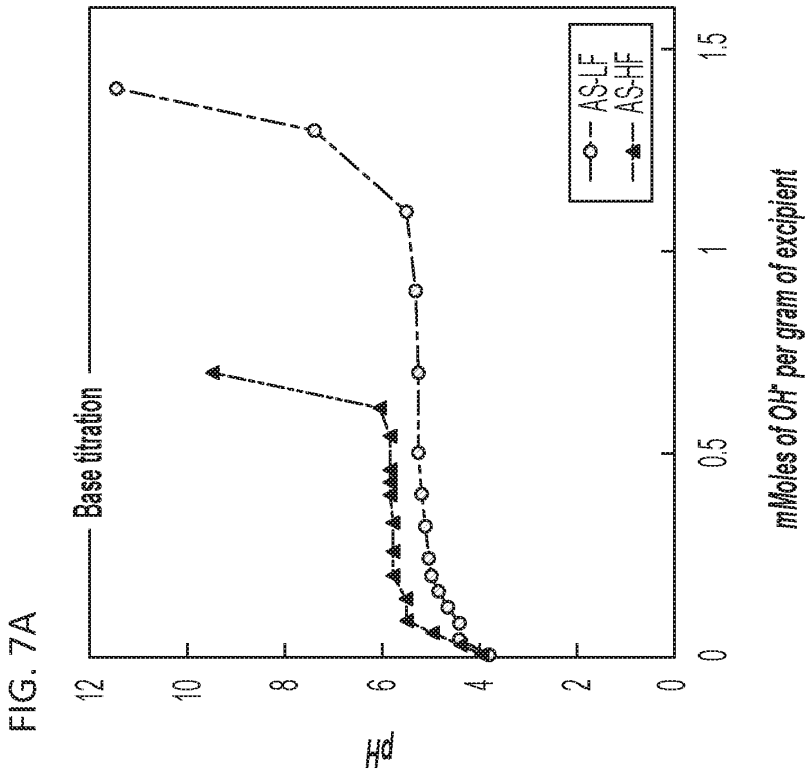

Base titration
AS-LF
AS-HF
pH
mMoles of OH- per gram of excipient

FIG. 7A

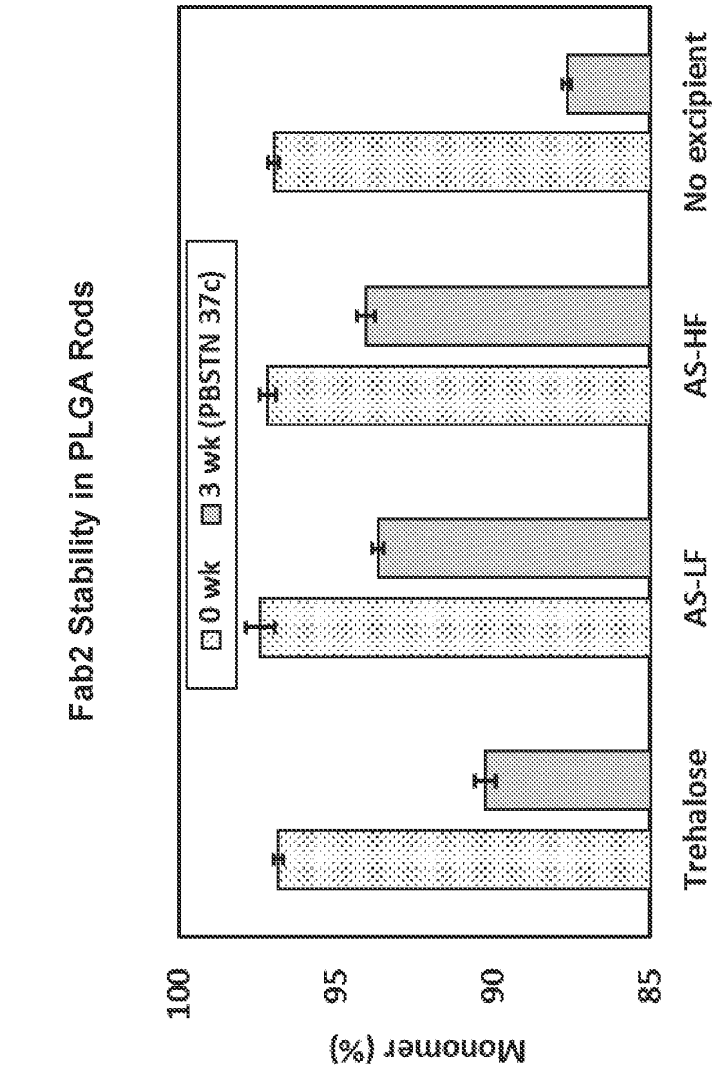

Fab2 Stability in PLGA Rods
0 wk
3 wk (PBSTN 37c)
Monomer (%)
100
95
90
85
Trehalose
AS-LF
AS-HF
No excipient

FIG. 8

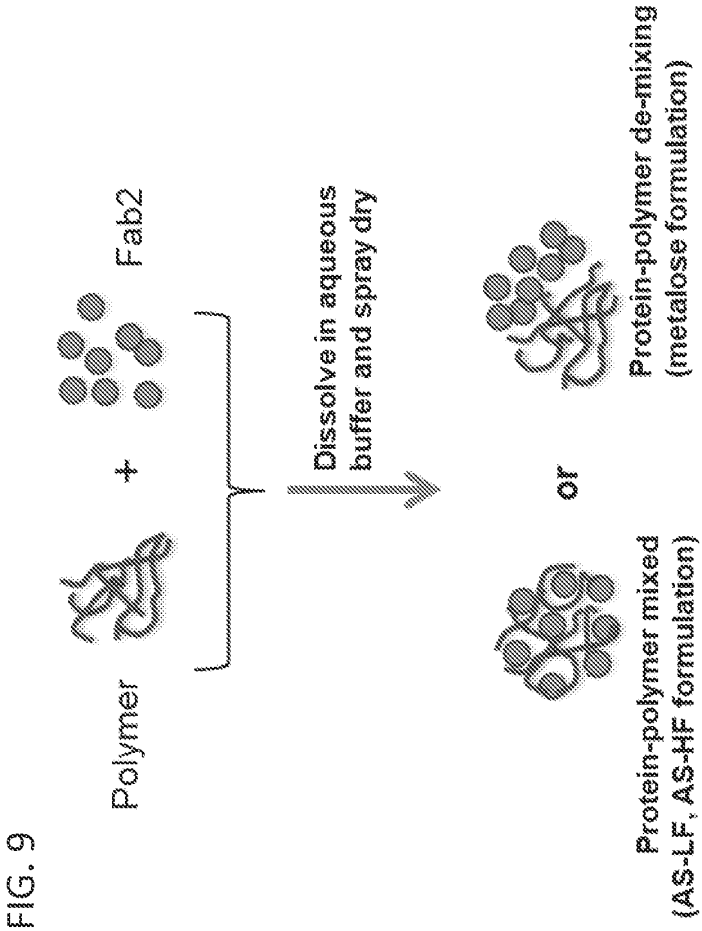

Polymer
+
Fab2
Dissolve in aqueous buffer and spray dry
or
Protein-polymer mixed (AS-LF, AS-HF formulation)
Protein-polymer de-mixing (metalose formulation)

FIG. 9

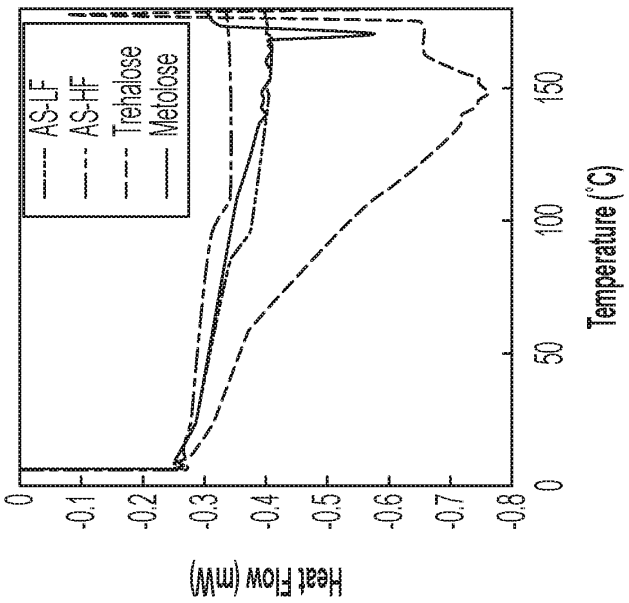

AS-LF
AS-HF
Trehalose
Metobose
Heat Flow (mW)
0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
-0.8
0
50
100
150
Temperature (°C)

FIG. 10

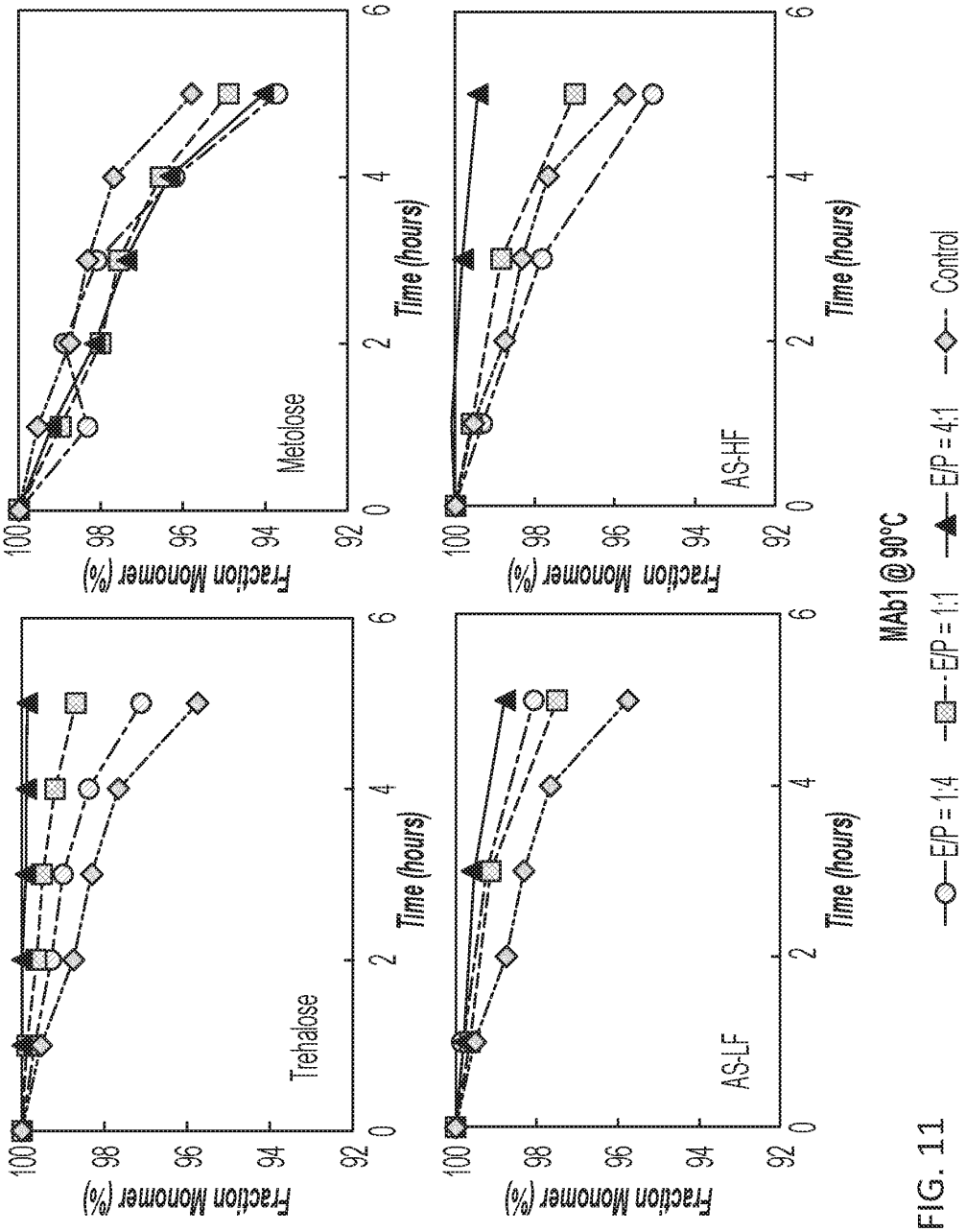

Metolose
AS-HF
Trehalose
AS-LF
Fraction Monomer (%)
Time (hours)
100
98
96
94
92
0
2
4
6
MAb1 @ 90°C
E/P = 1:4
E/P = 1:1
E/P = 4:1
Control

FIG. 11

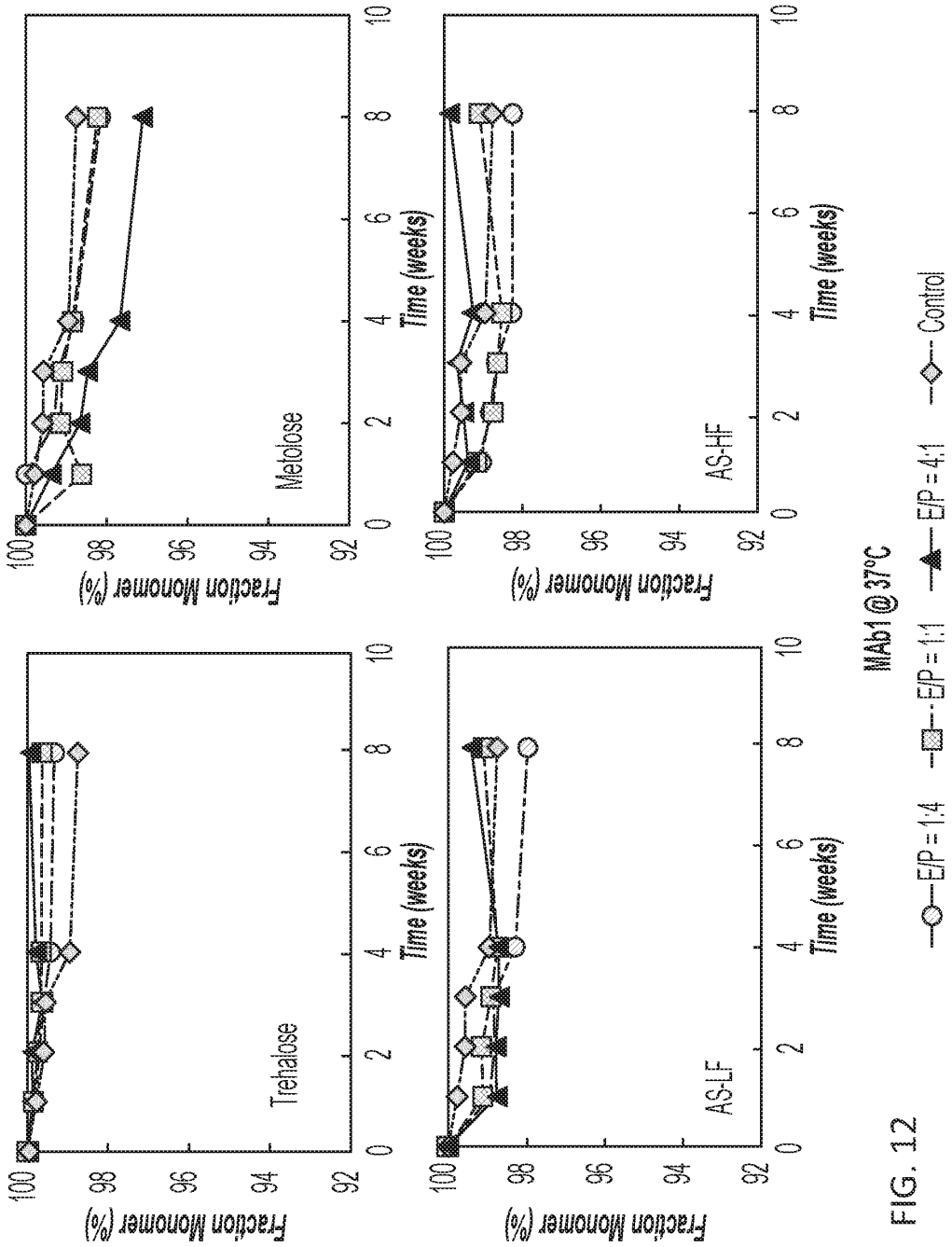

Fraction Monomer (%)
Time (weeks)
Trehalose
Metolose
AS-LF
AS-HF
MAb1 @ 37°C
E/P = 1:4
E/P = 1:1
E/P = 4:1
Control

FIG. 12

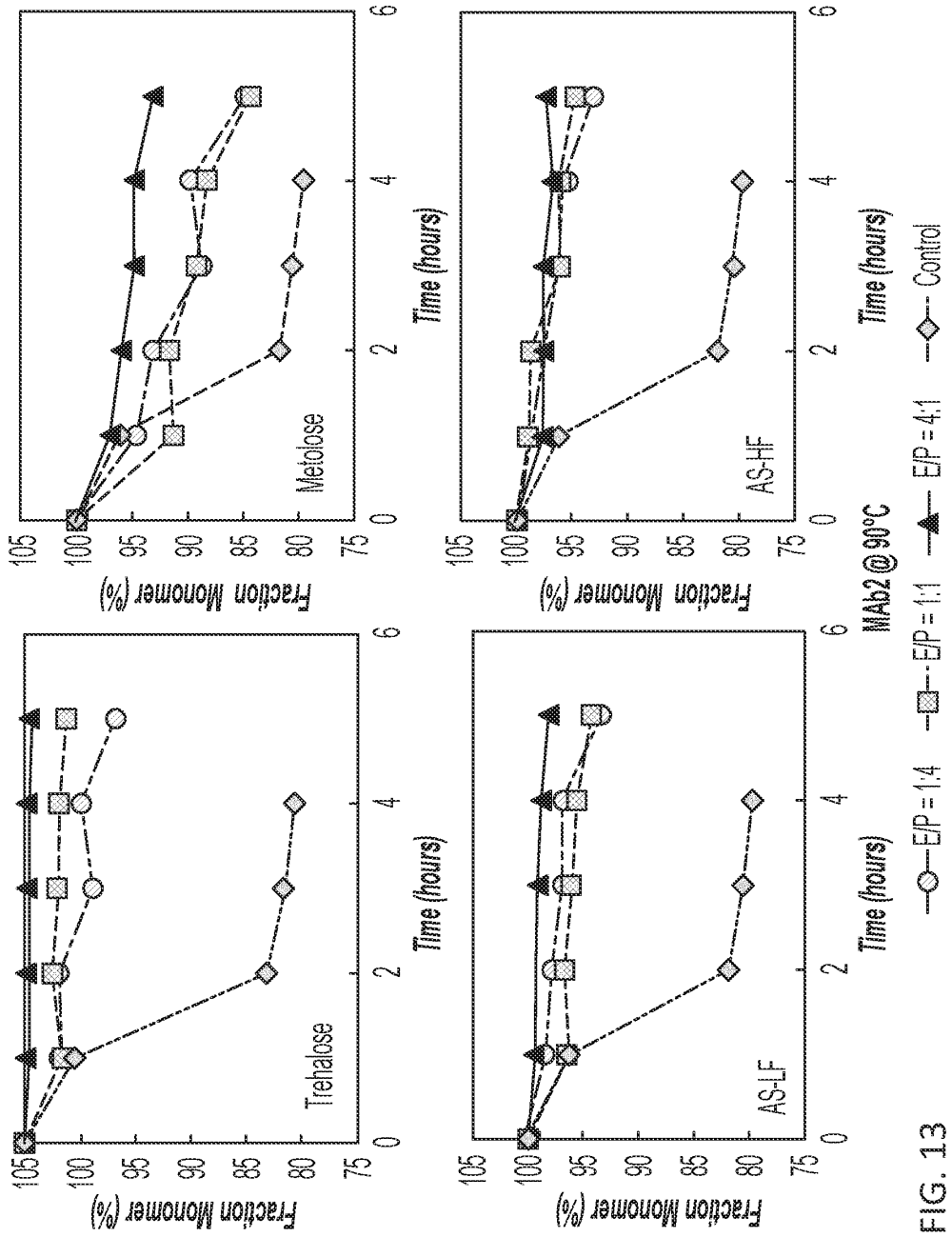

Fraction Monomer (%)
Time (hours)
Trehalose
Metolose
AS-LF
AS-HF
MAb2 @ 90°C
E/P = 1:4
E/P = 1:1
E/P = 4:1
Control

FIG. 13

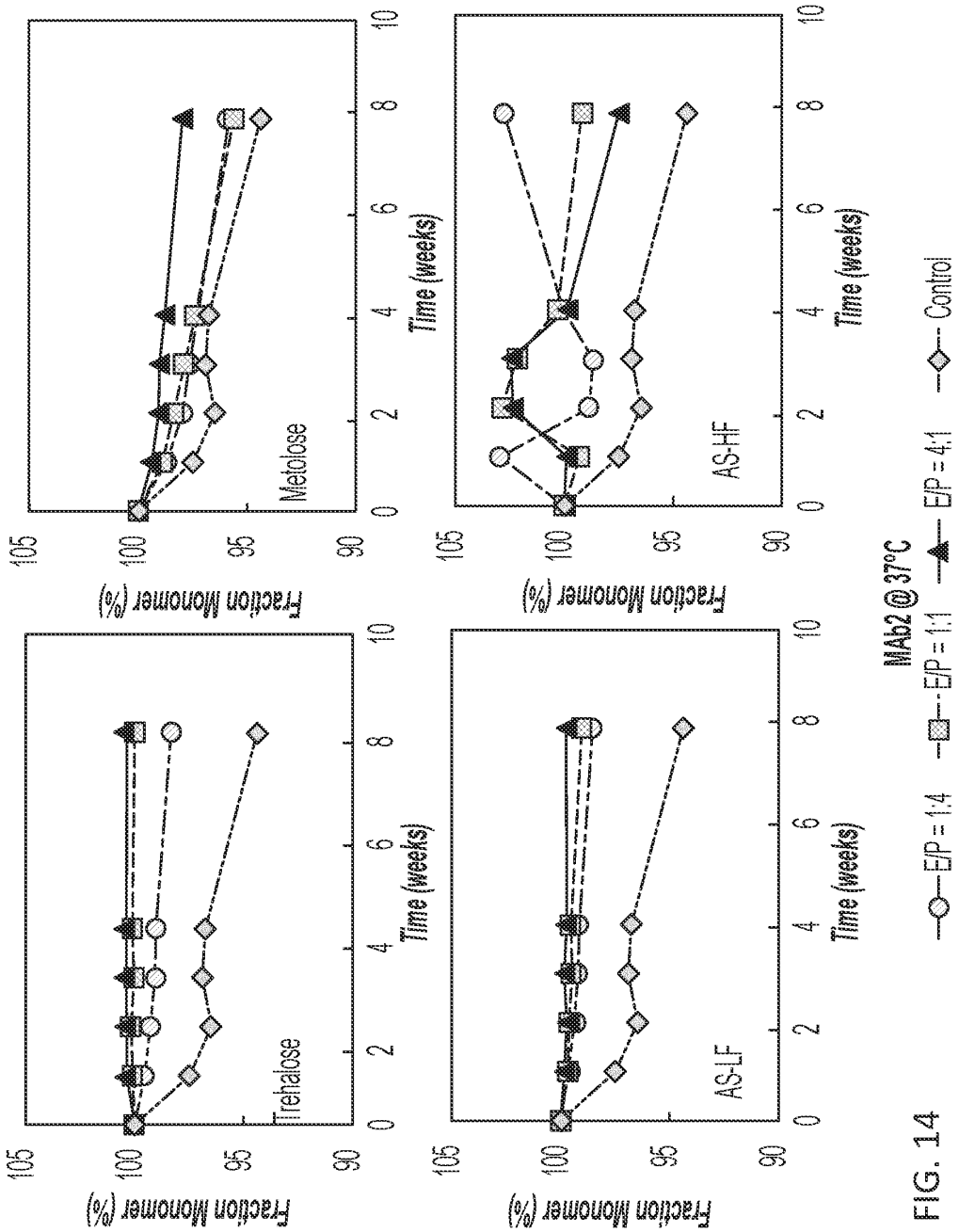

Fraction Monomer (%)
Time (weeks)
Trehalose
Metolose
AS-LF
AS-HF
MAb2 @ 37°C
E/P = 1:4
E/P = 1:1
E/P = 4:1
Control

FIG. 14

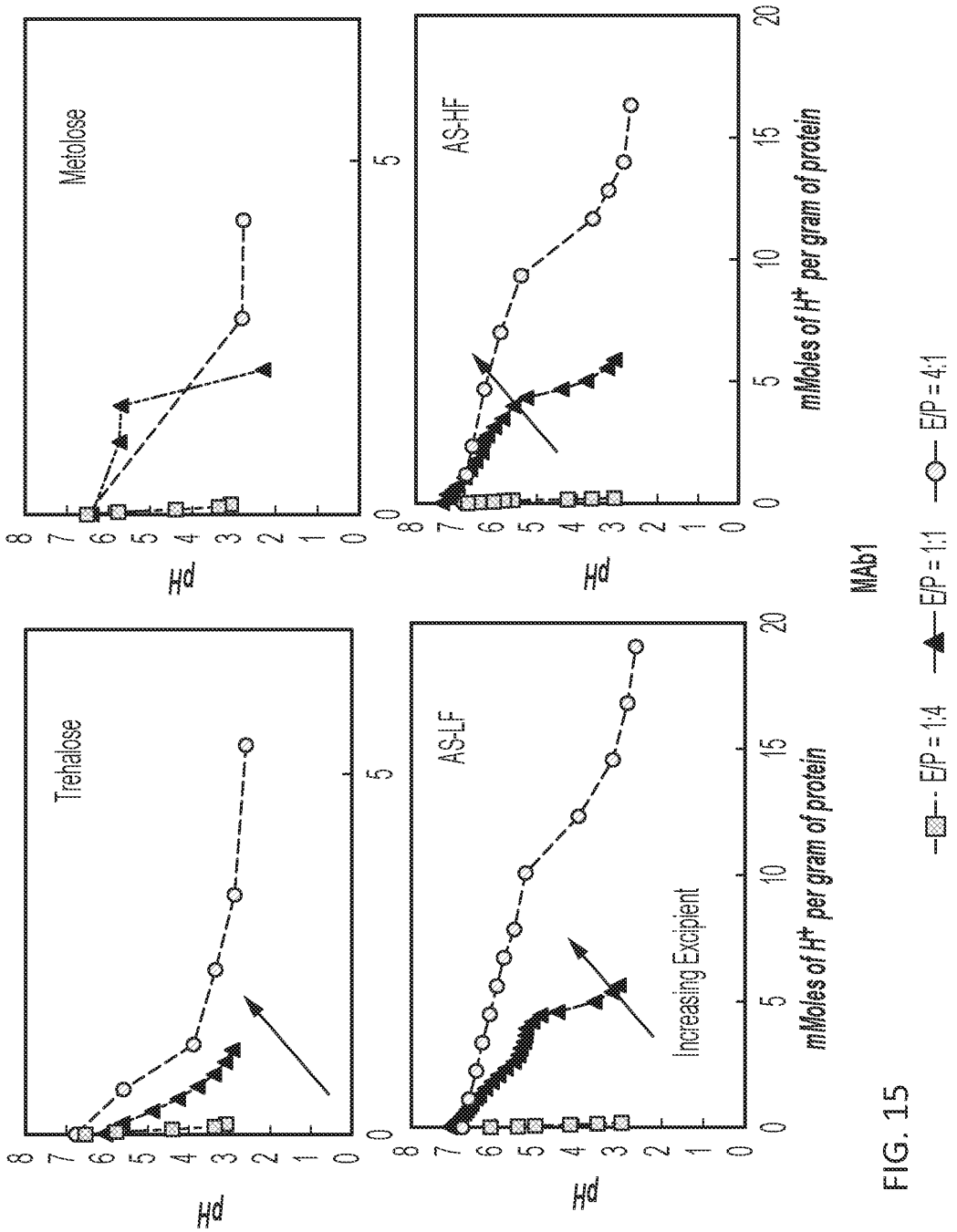

Metolose
AS-HF
Trehalose
AS-LF
pH
mMoles of H+ per gram of protein
Increasing Excipient
MAb1
E/P = 1:4
E/P = 1:1
E/P = 4:1

FIG. 15

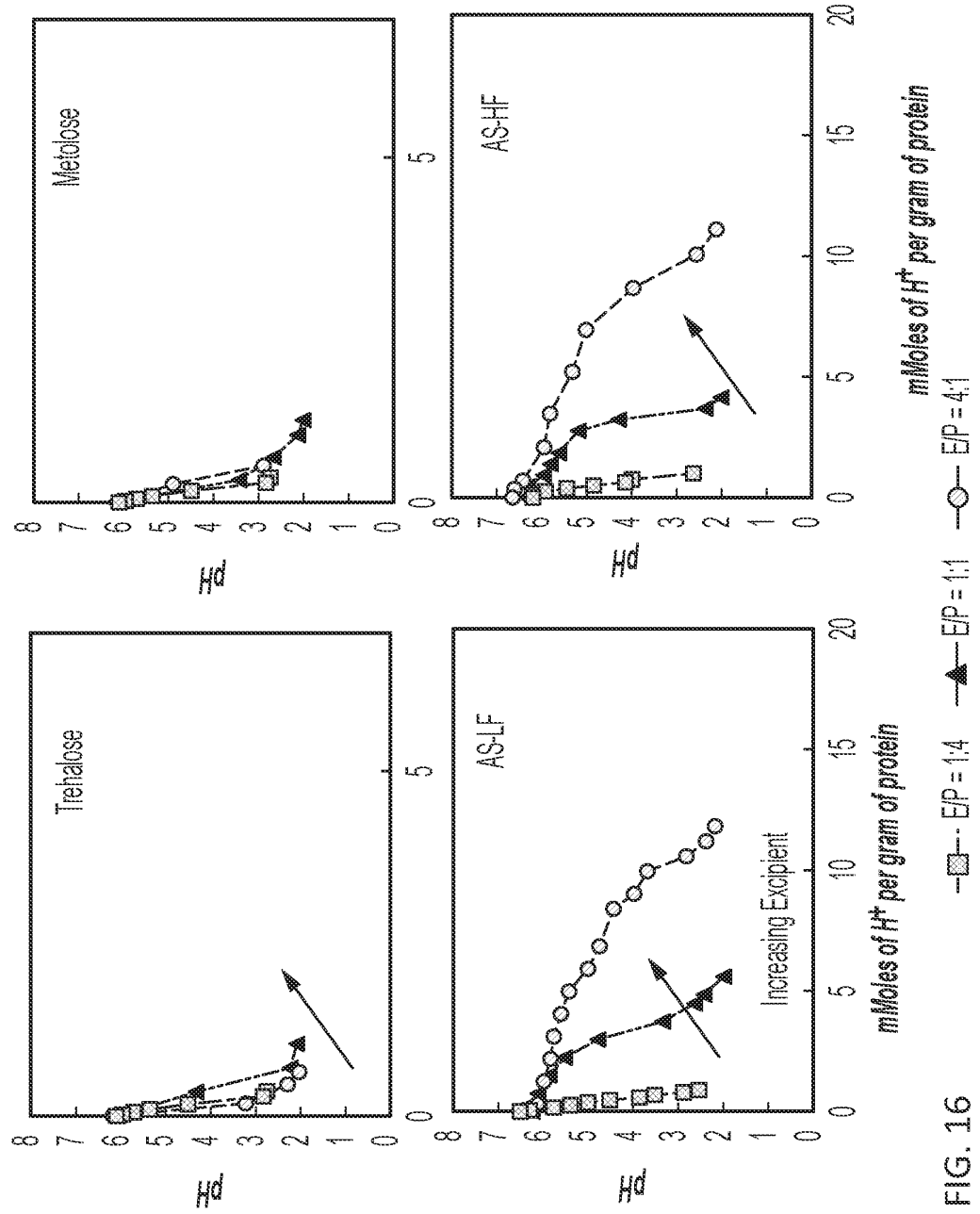

Metolose
AS-HF
Trehalose
AS-LF
Increasing Excipient
pH
mMoles of H+ per gram of protein
E/P = 1:4
E/P = 1:1
E/P = 4:1

FIG. 16

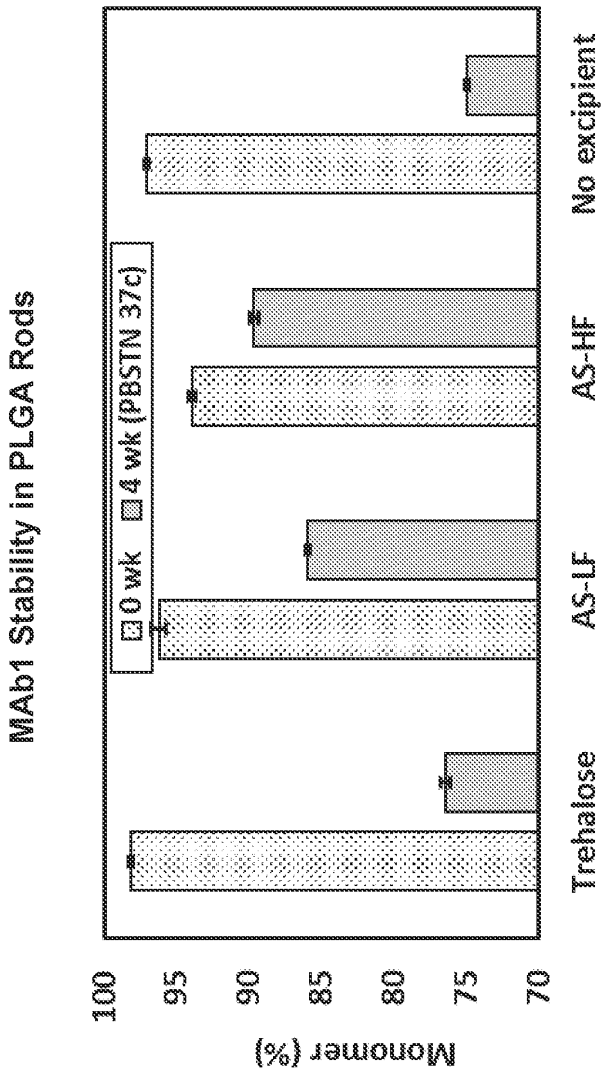

MAb1 Stability in PLGA Rods
0 wk
4 wk (PBSTN 37c)
Monomer (%)
100
95
90
85
80
75
70
Trehalose
AS-LF
AS-HF
No excipient

FIG. 17

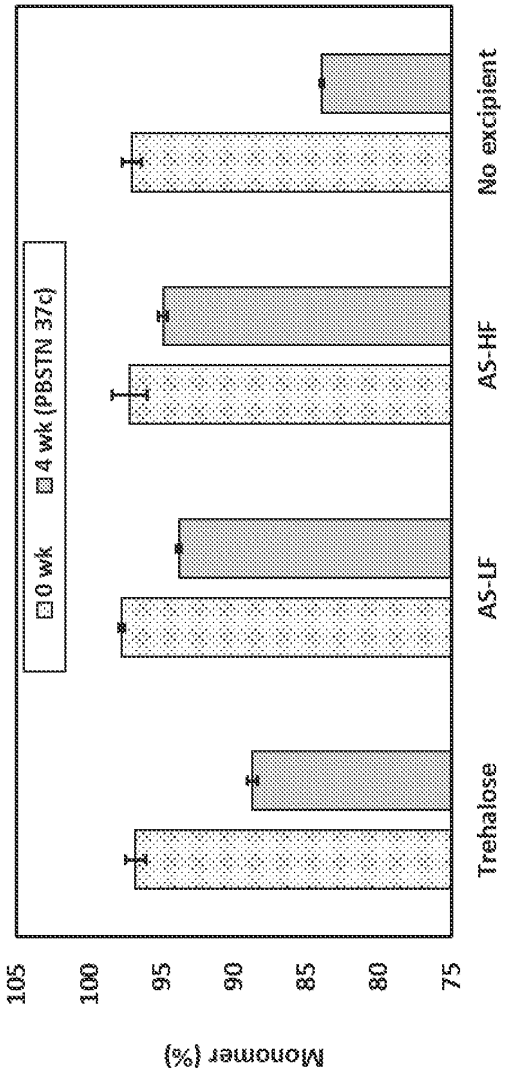

Monomer (%)
105
100
95
90
85
80
75
0 wk
4 wk (PBSTN 37c)
Trehalose
AS-LF
AS-HF
No excipient

FIG. 18

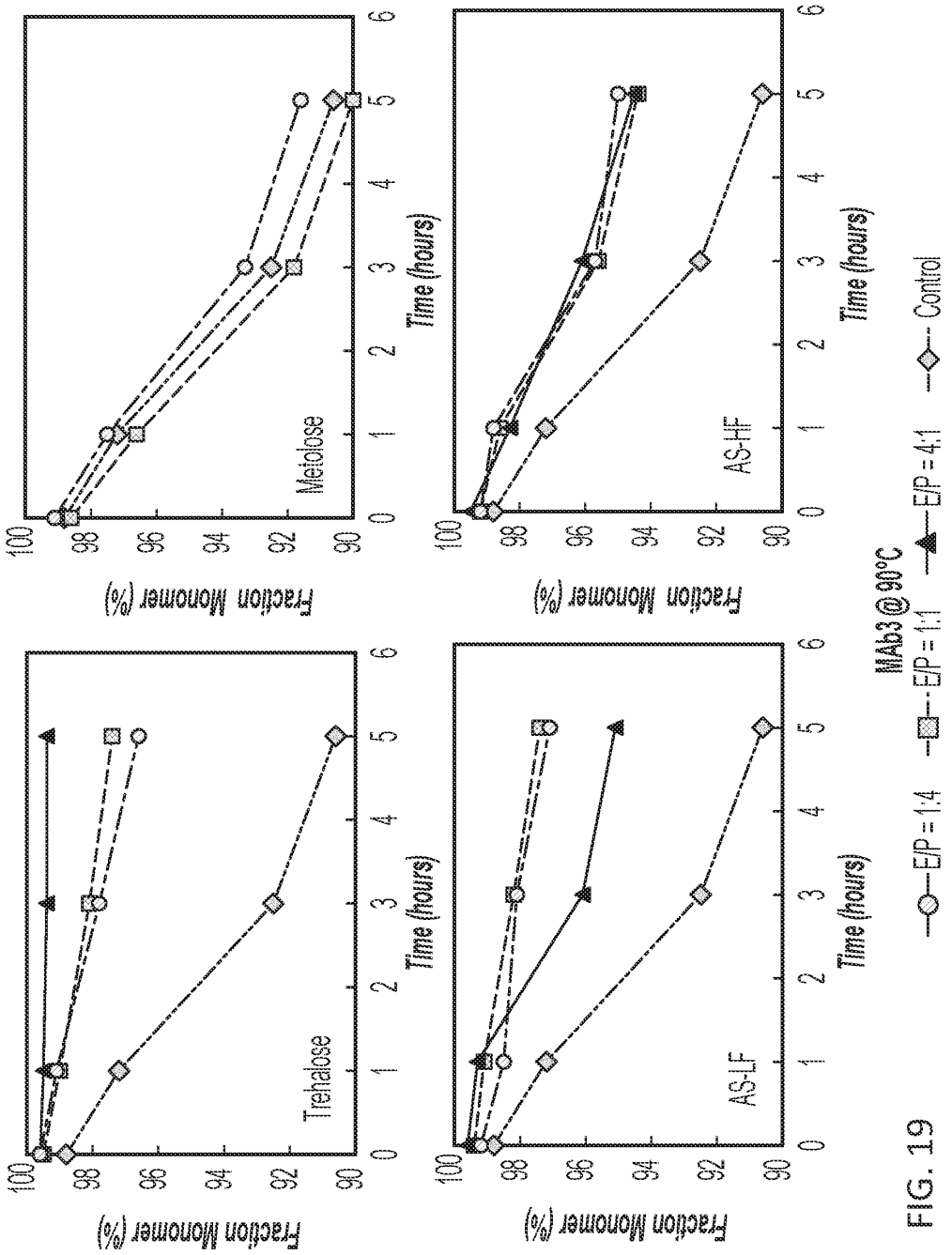

Trehalose
Meiolose
AS-LF
AS-HF
Fraction Monomer (%)
Time (hours)
MAb3 @ 90°C
E/P = 1:4
E/P = 1:1
E/P = 4:1
Control

FIG. 19

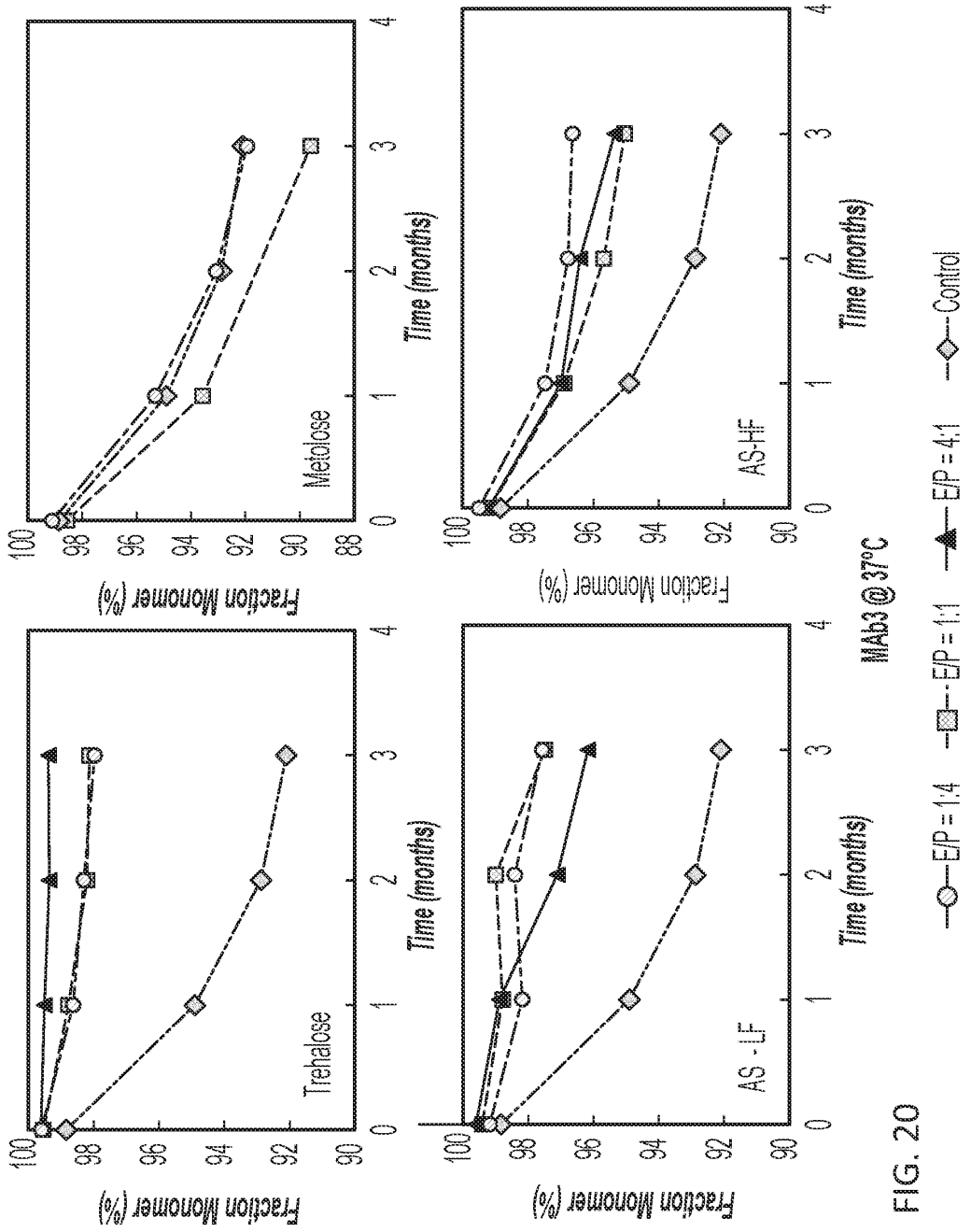

Metolose
AS-HF
Trehalose
AS - LF
Fraction Monomer (%)
Time (months)
MAb3 @ 37°C
E/P = 1:4
E/P = 1:1
E/P = 4:1
Control

FIG. 20