

FIG. 1A

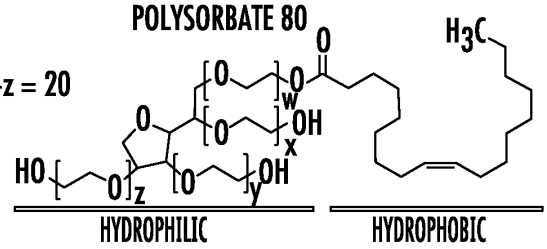

FIG. 1B

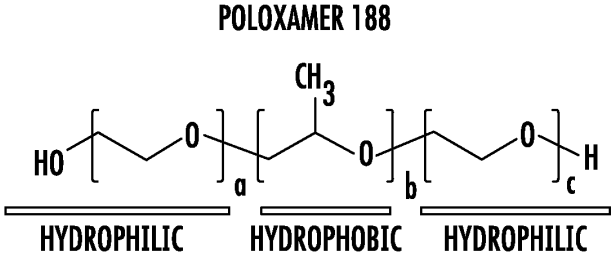

FIG. 1C

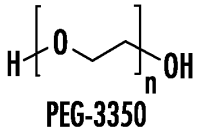

FIG. 1D

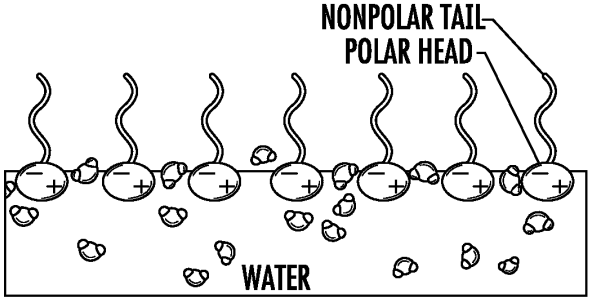

FIG. 1E

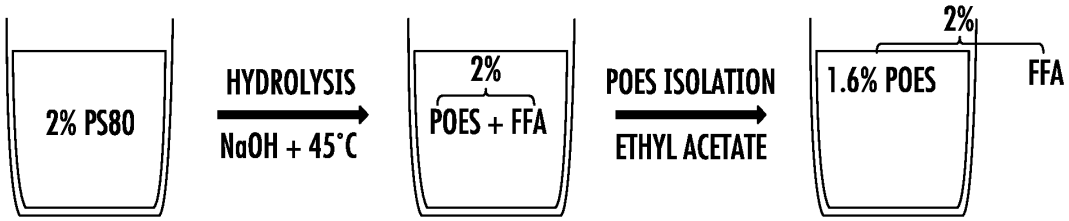
2% PS80
HYDROLYSIS
NaOH + 45°C
2%
POES + FFA
POES ISOLATION
ETHYL ACETATE
2%
1.6% POES
FFA

FIG. 2

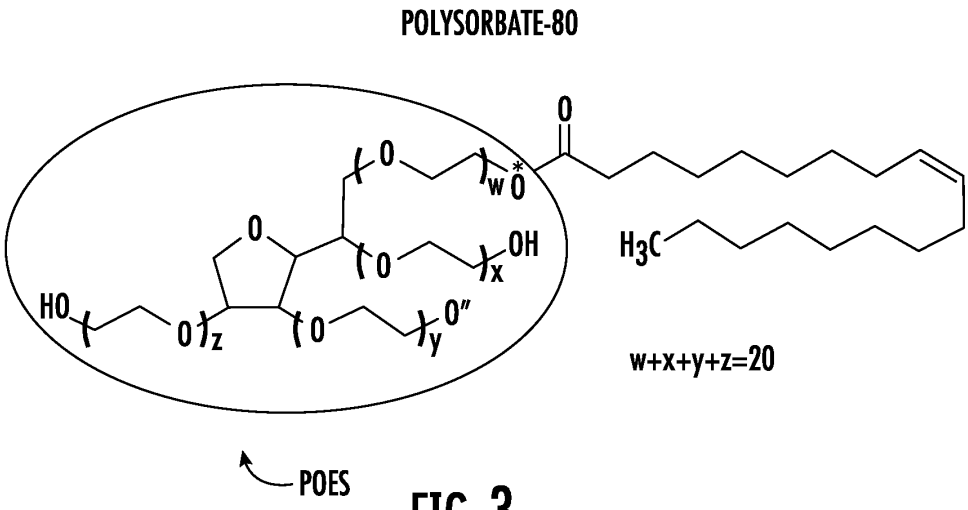
POLYSORBATE-80
HO
OH
H3C
w+x+y+z=20
POES

FIG. 3

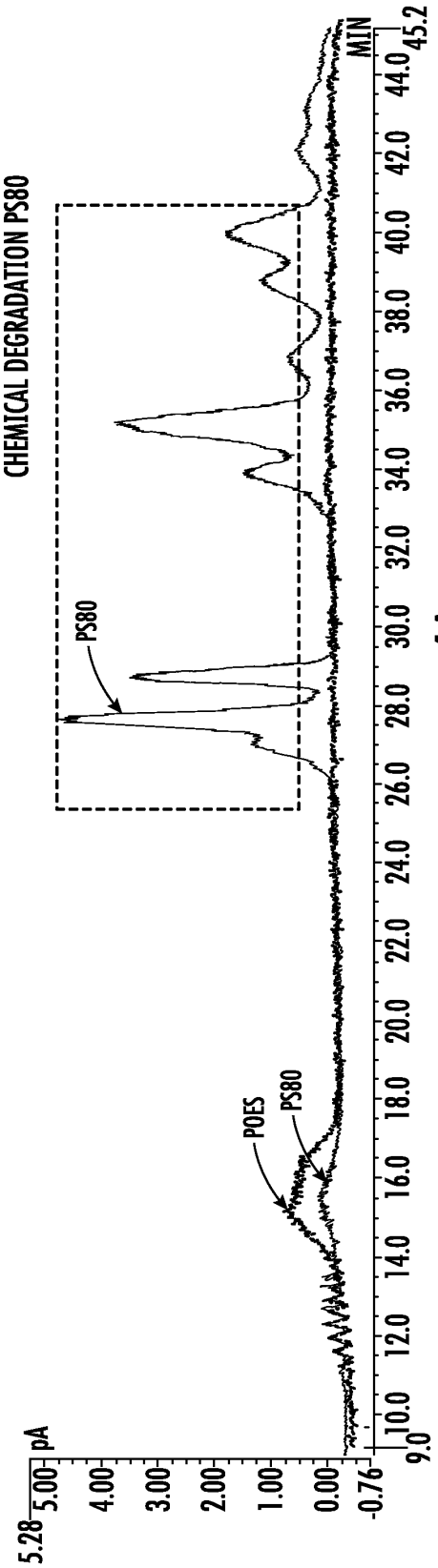
CHEMICAL DEGRADATION PS80
PS80
POES
PS80
pA
5.28
5.00
4.00
3.00
2.00
1.00
0.00
-0.76
9.0
10.0
12.0
14.0
16.0
18.0
20.0
22.0
24.0
26.0
28.0
30.0
32.0
34.0
36.0
38.0
40.0
42.0
44.0
45.2
MIN

FIG. 4A

CHEMICAL DEGRADATION PS20
PS20
PS20
POES
pA
4.32
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
-0.50
-1.02
10.4
12.0
14.0
16.0
18.0
20.0
22.0
24.0
26.0
28.0
30.0
32.0
34.0
36.0
38.0
40.0
42.0
44.2
MIN

FIG. 4B

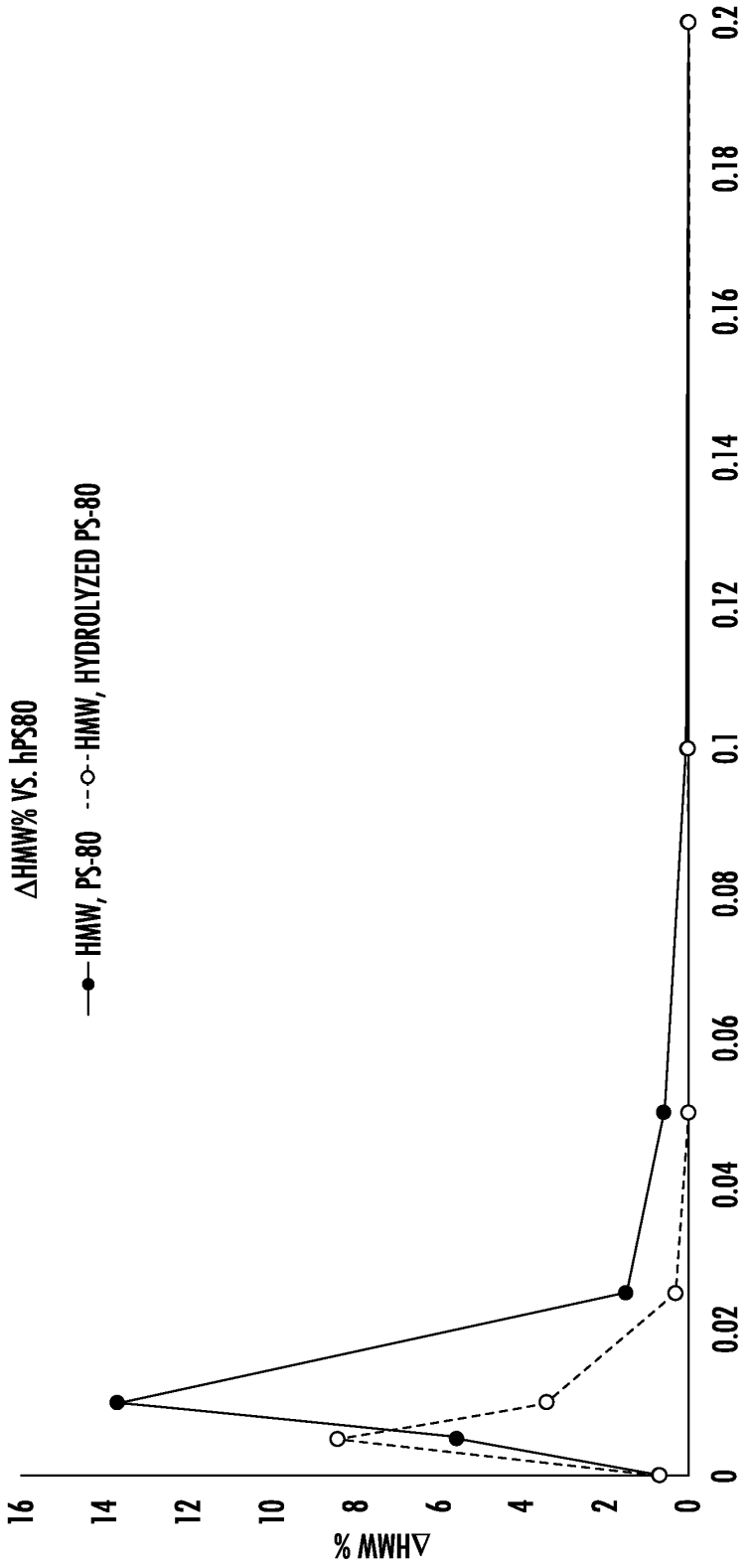
ΔHMW% VS. hPS80
HMW, PS-80
HMW, HYDROLYZED PS-80
ΔHMW %
0
2
4
6
8
10
12
14
16
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
0.18
0.2
EXCIPIENT, %

FIG. 5

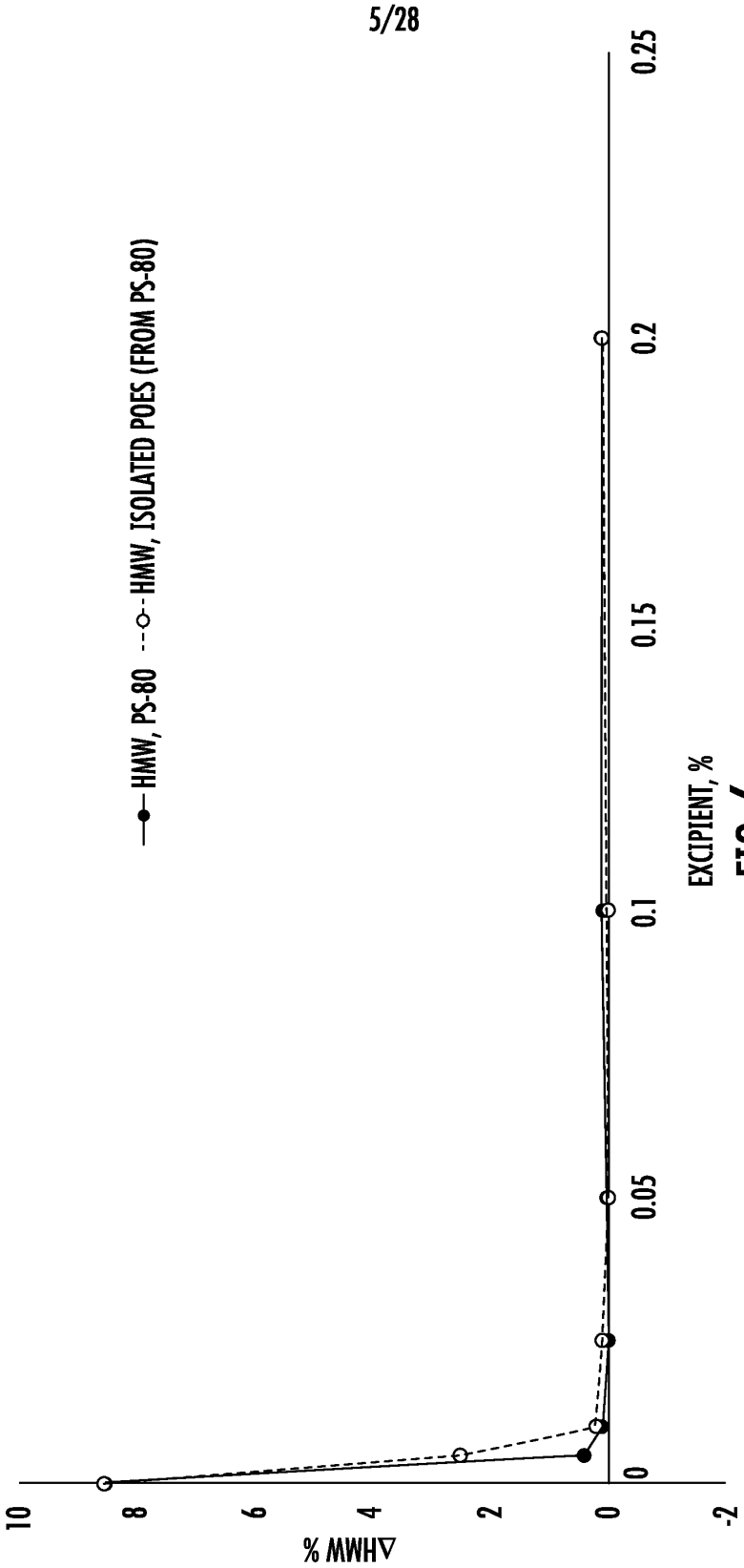
HMW, PS-80
HMW, ISOLATED POES (FROM PS-80)
ΔHMW %
10
8
6
4
2
0
-2
0
0.05
0.1
0.15
0.2
0.25
EXCIPIENT, %

FIG. 6

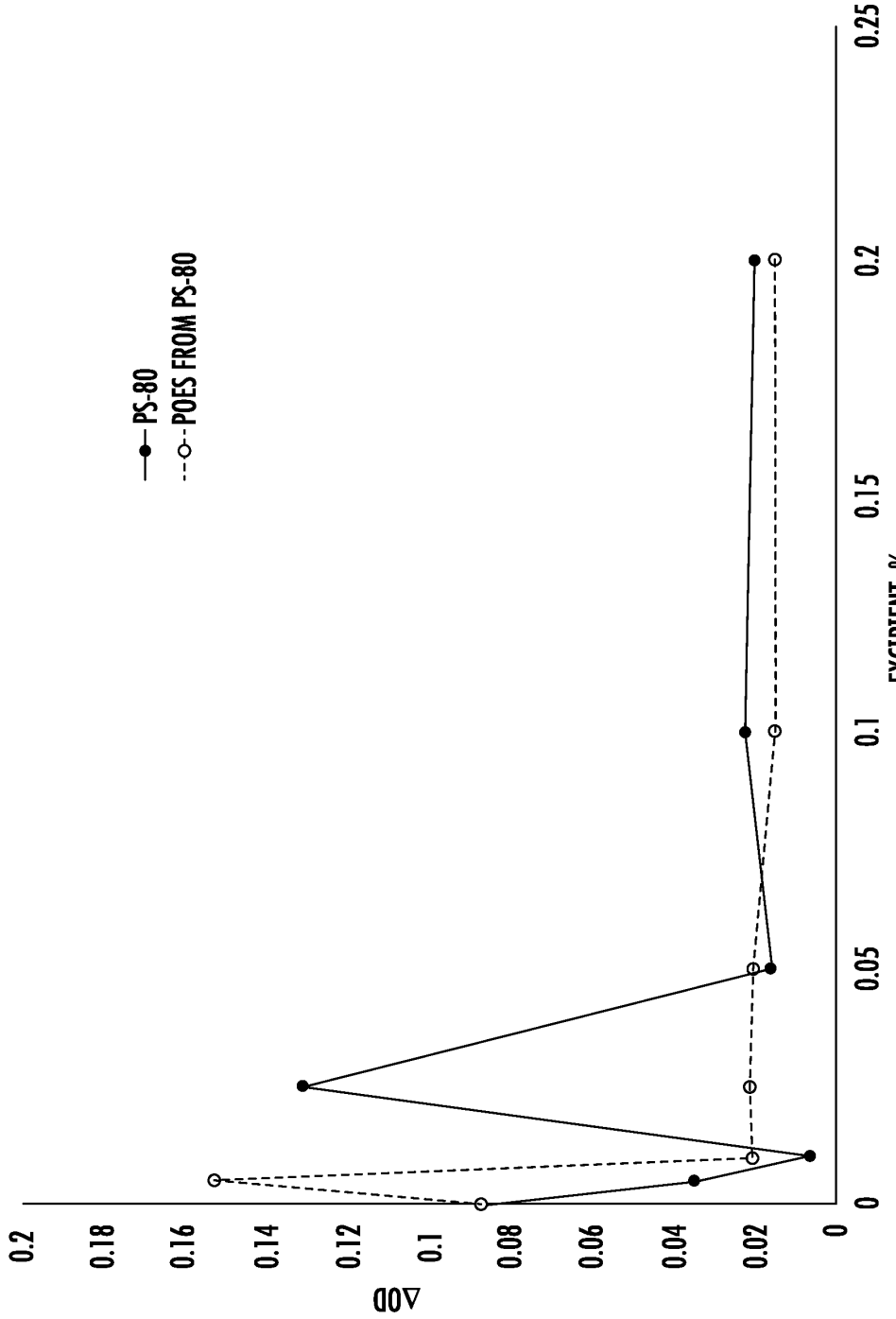
PS-80
POES FROM PS-80
ΔOD
0.2
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.05
0.1
0.15
0.2
0.25
EXCIPIENT, %

FIG. 7

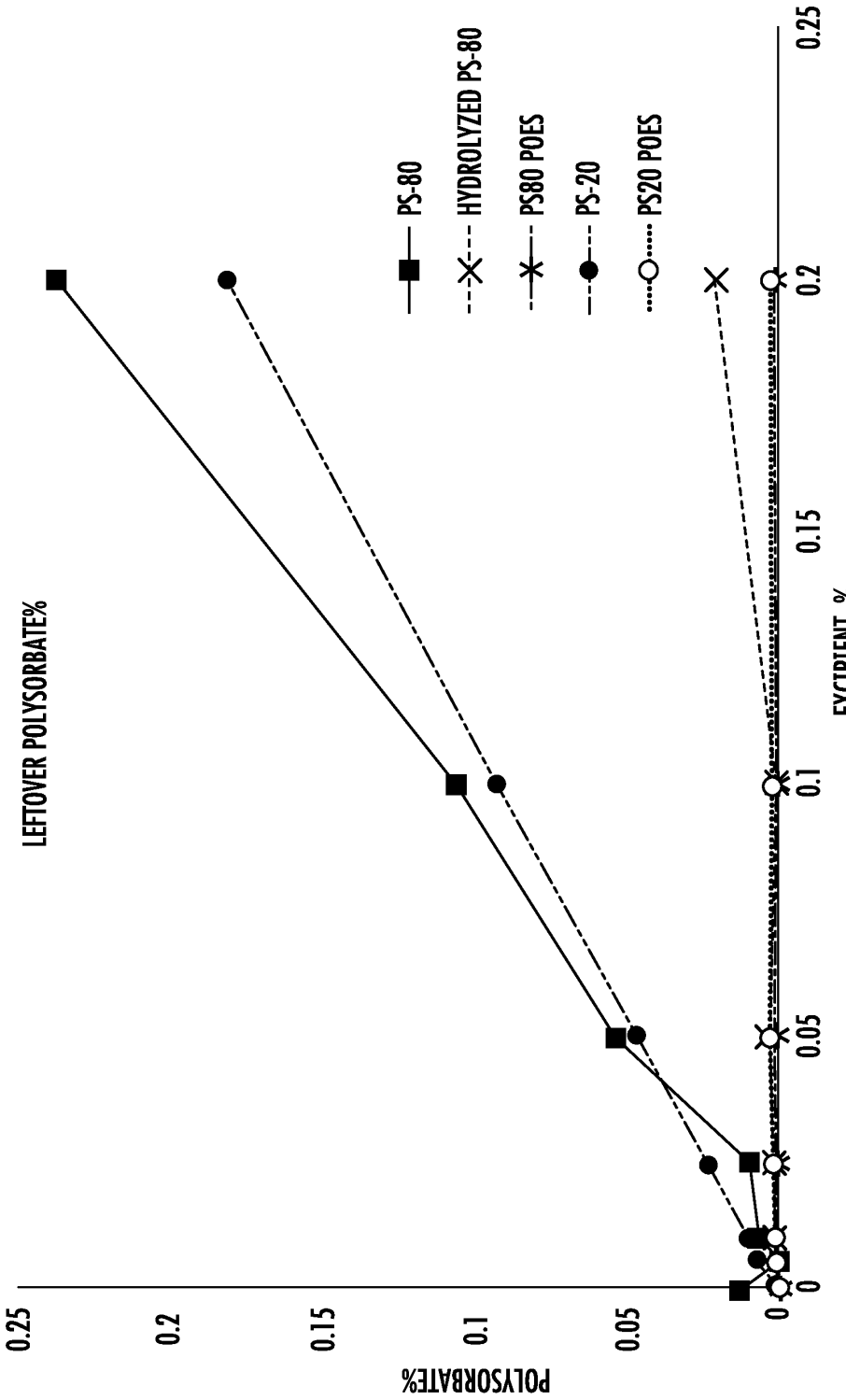
LEFTOVER POLYSORBATE%
POLYSORBATE%
EXCIPIENT, %
PS-80
HYDROLYZED PS-80
PS80 POES
PS-20
PS20 POES
0
0.05
0.1
0.15
0.2
0.25

FIG. 8

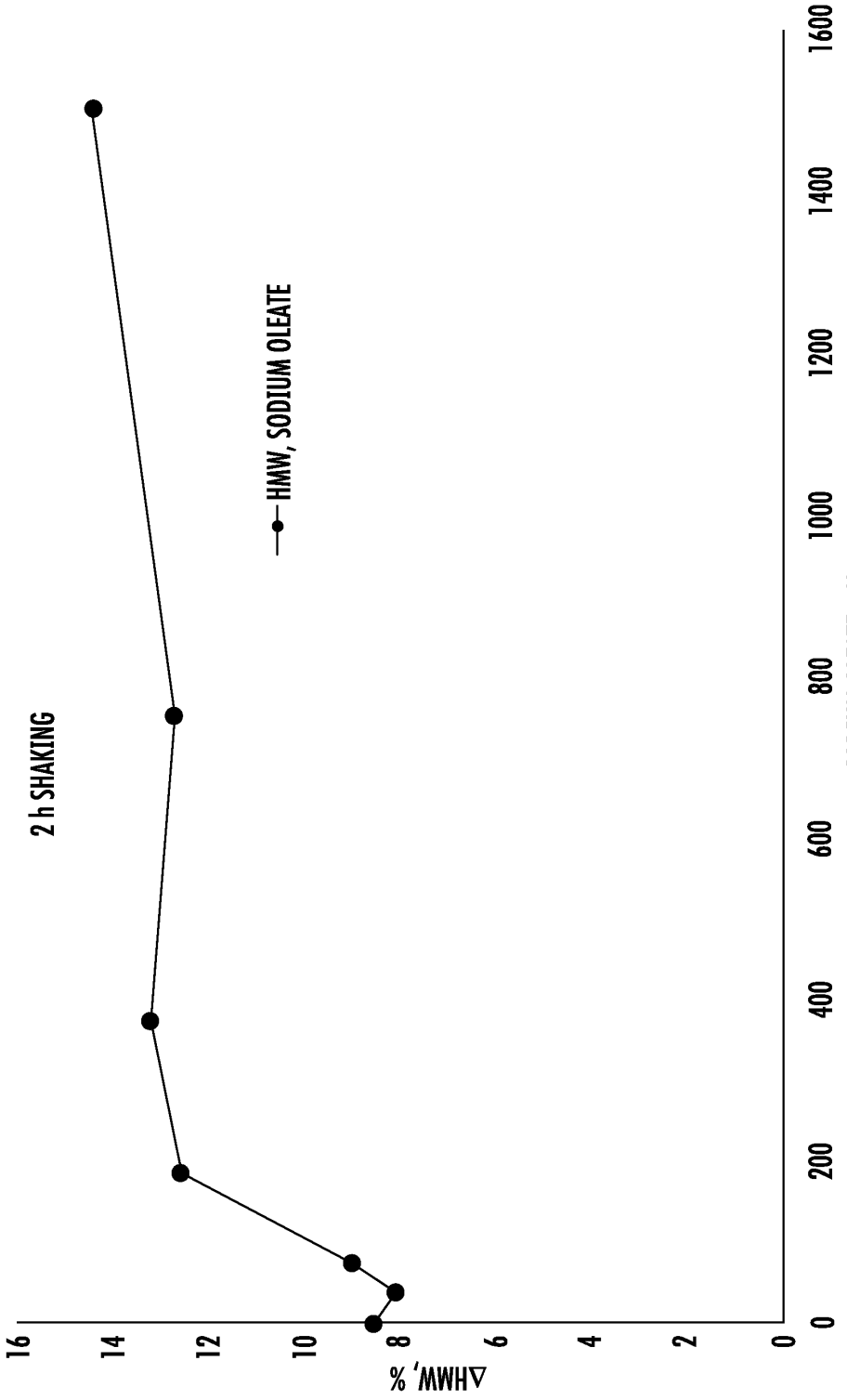
2 h SHAKING
HMW, SODIUM OLEATE
ΔHMW, %
SODIUM OLEATE, uM
0
2
4
6
8
10
12
14
16
0
200
400
600
800
1000
1200
1400
1600

FIG. 9

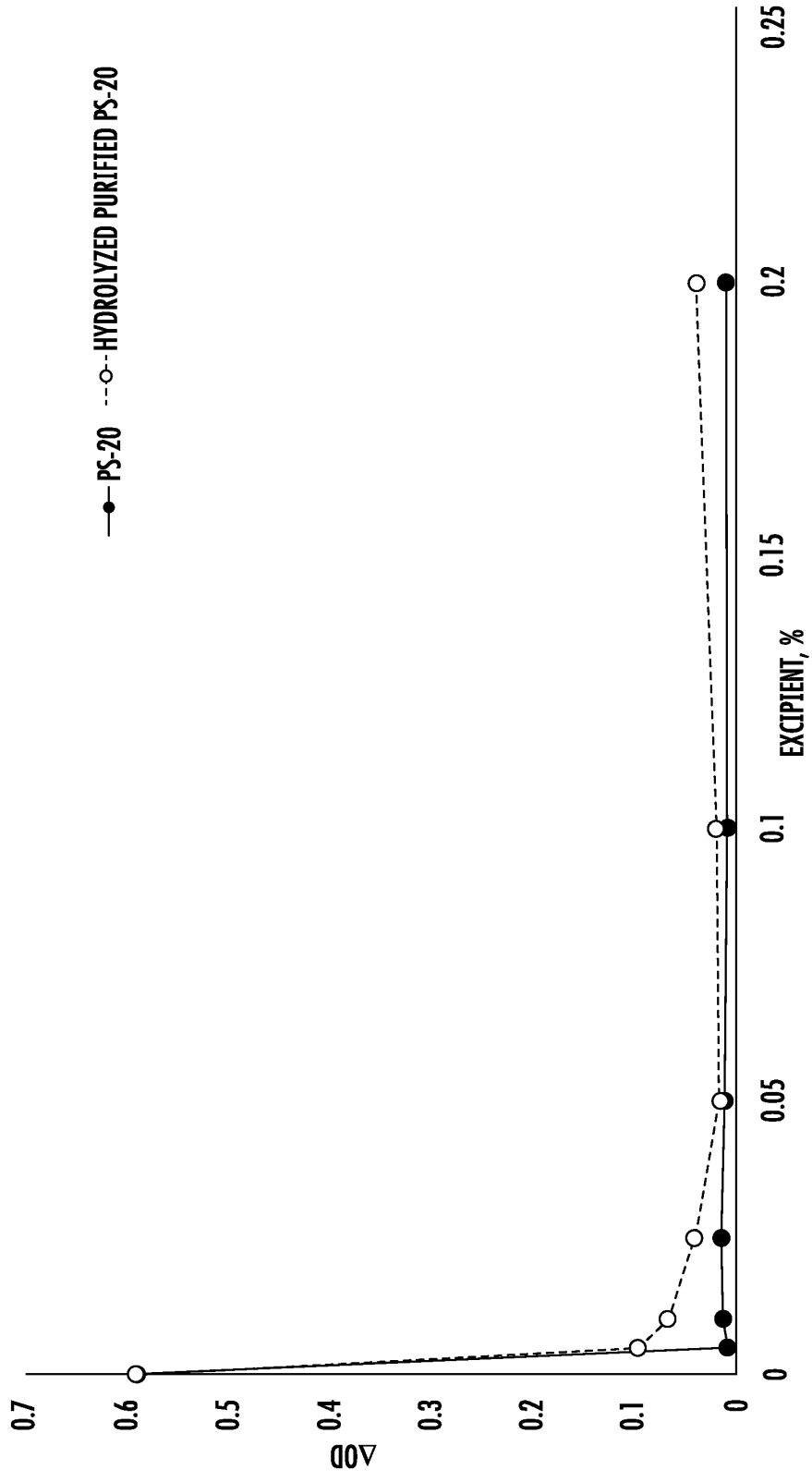
PS-20
HYDROLYZED PURIFIED PS-20
ΔOD
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.05
0.1
0.15
0.2
0.25
EXCIPIENT, %

FIG. 10

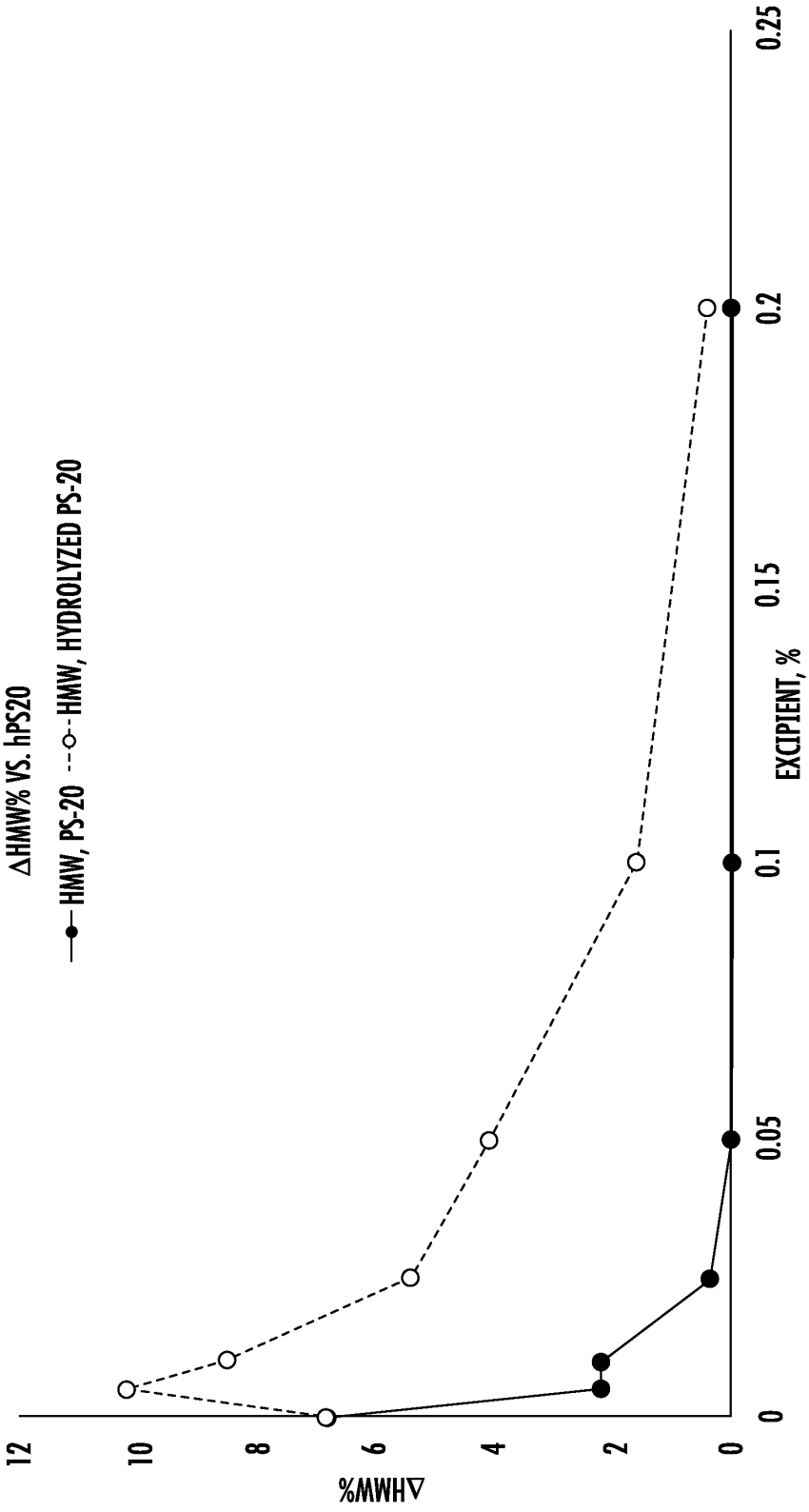
ΔHMW% VS. hPS20
HMW, PS-20
HMW, HYDROLYZED PS-20
ΔHMW%
EXCIPIENT, %
0
2
4
6
8
10
12
0
0.05
0.1
0.15
0.2
0.25

FIG. 11

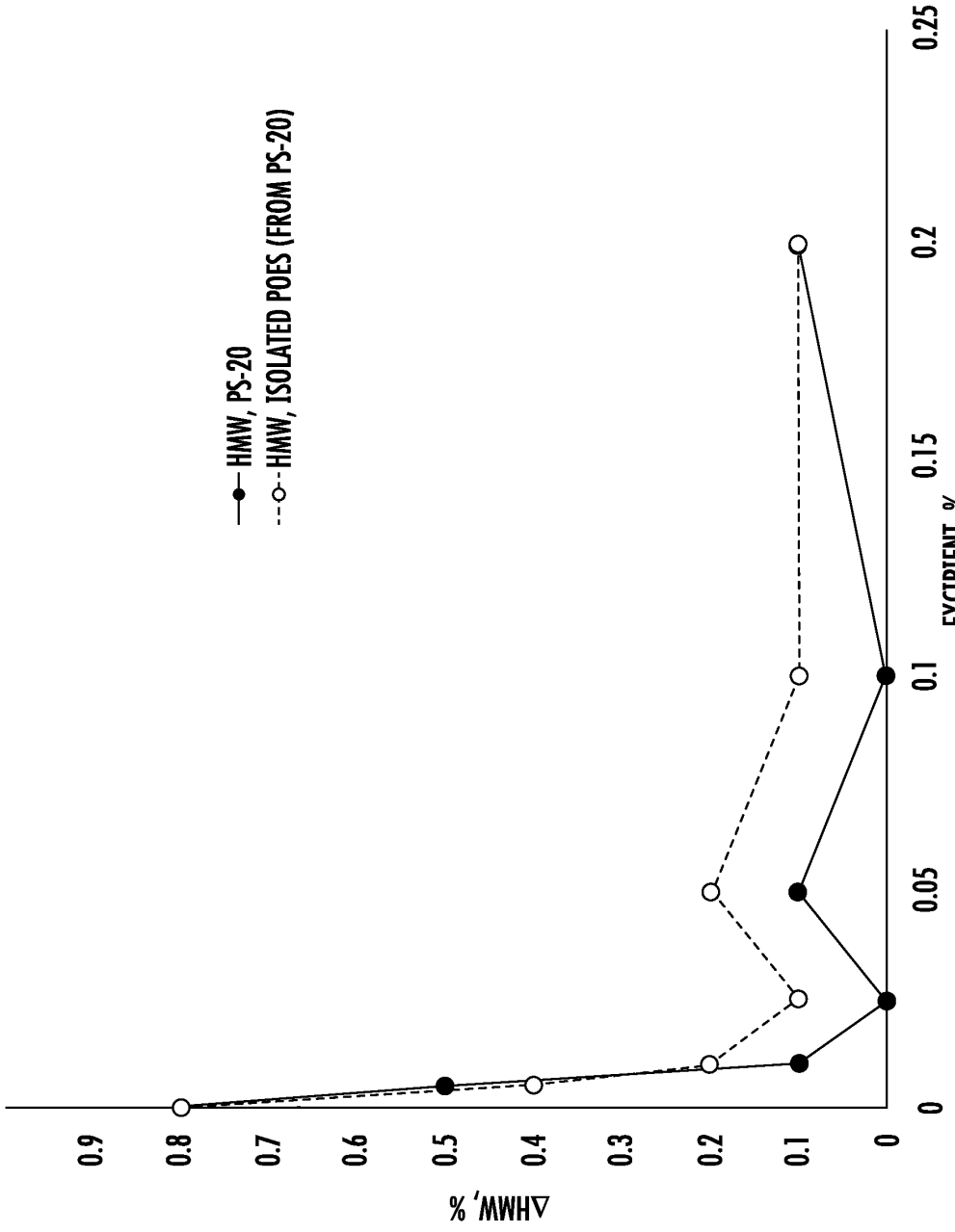
HMW, PS-20
HMW, ISOLATED POES (FROM PS-20)
ΔHMW, %
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
0
0.05
0.1
0.15
0.2
0.25
EXCIPIENT, %

FIG. 12

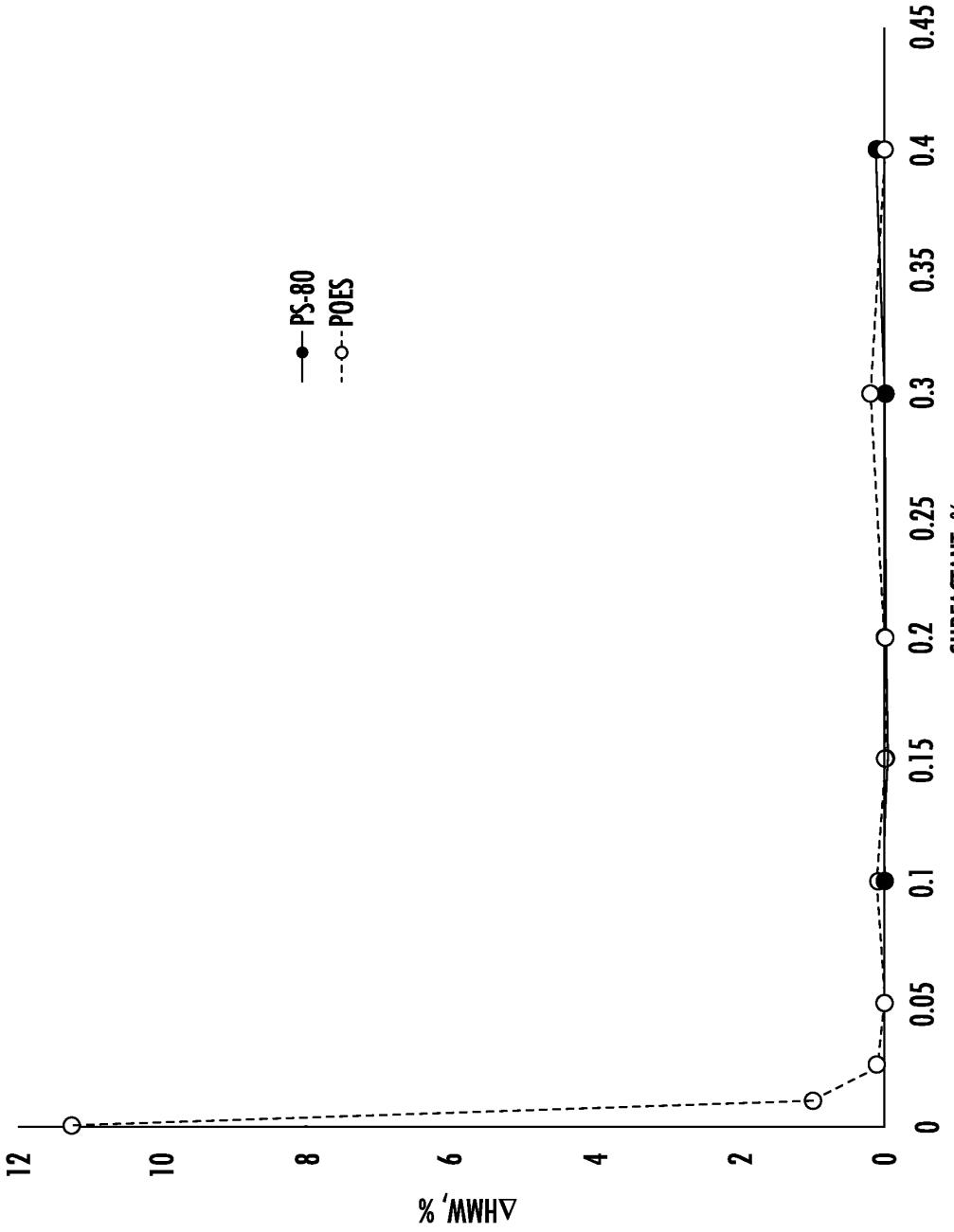
PS-80
POES
ΔHMW, %
12
10
8
6
4
2
0
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
SURFACTANT, %

FIG. 13

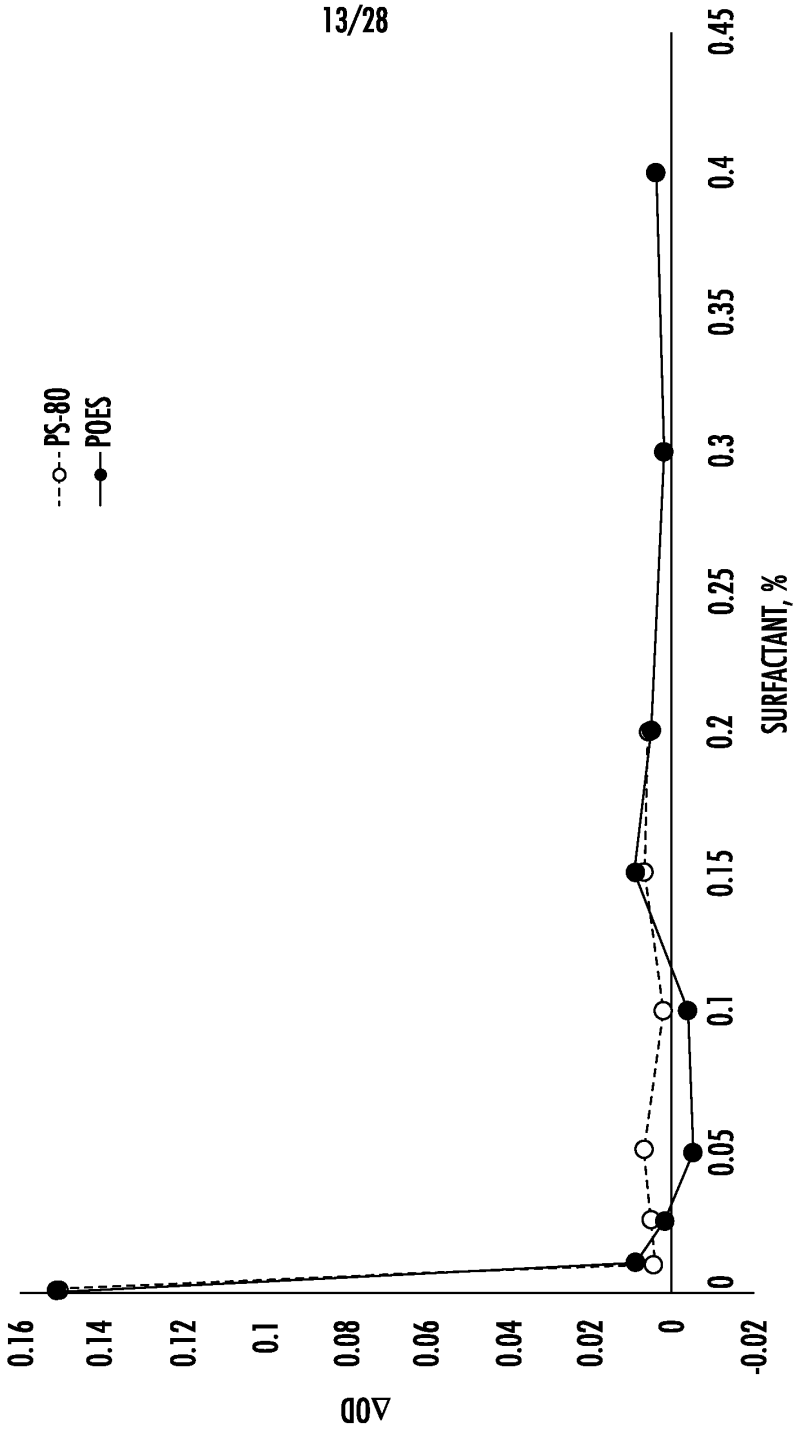
PS-80
POES
ΔOD
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
-0.02
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
SURFACTANT, %

FIG. 14

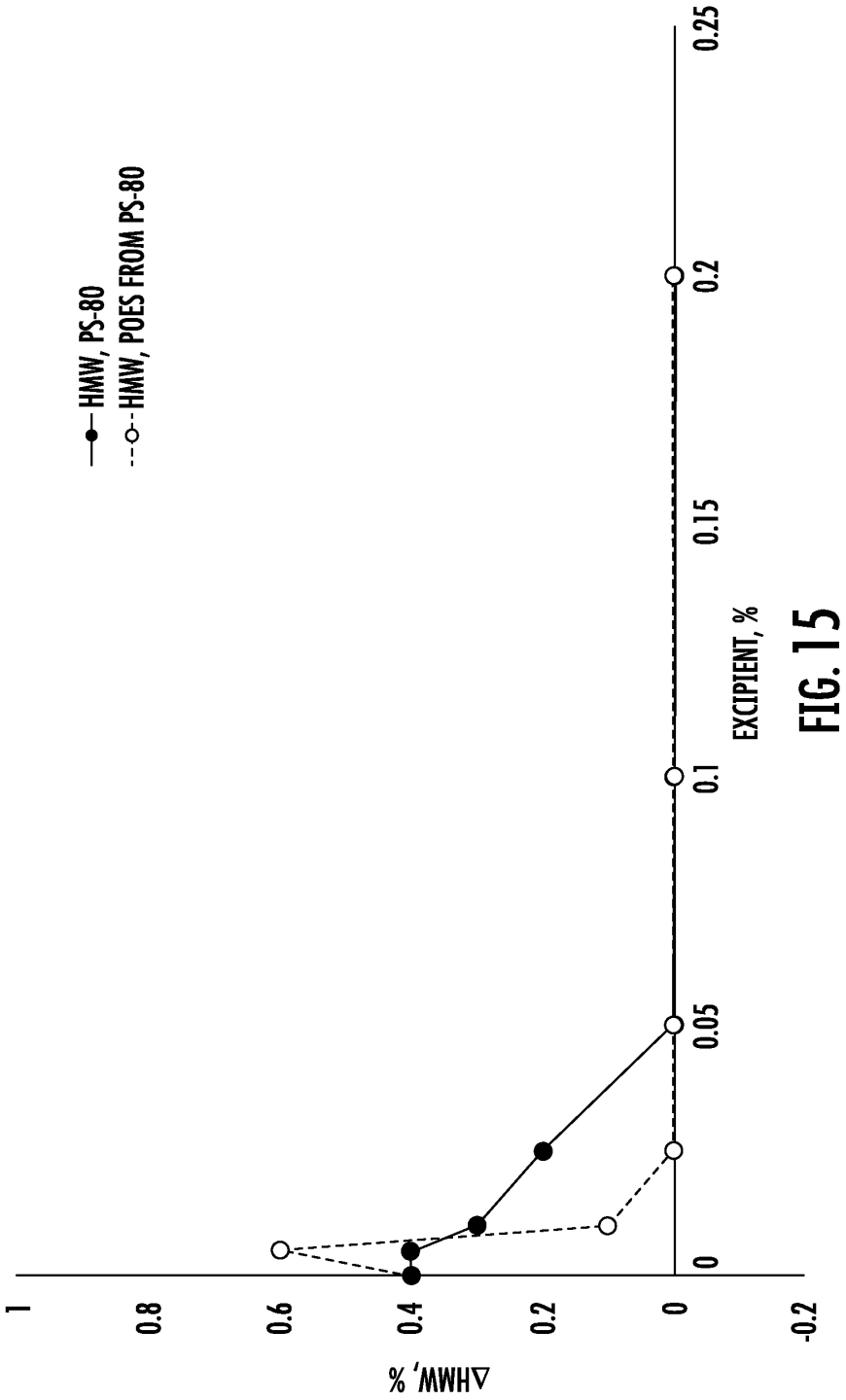
HMW, PS-80
HMW, POES FROM PS-80
ΔHMW, %
1
0.8
0.6
0.4
0.2
0
-0.2
0
0.05
0.1
0.15
0.2
0.25
EXCIPIENT, %

FIG. 15

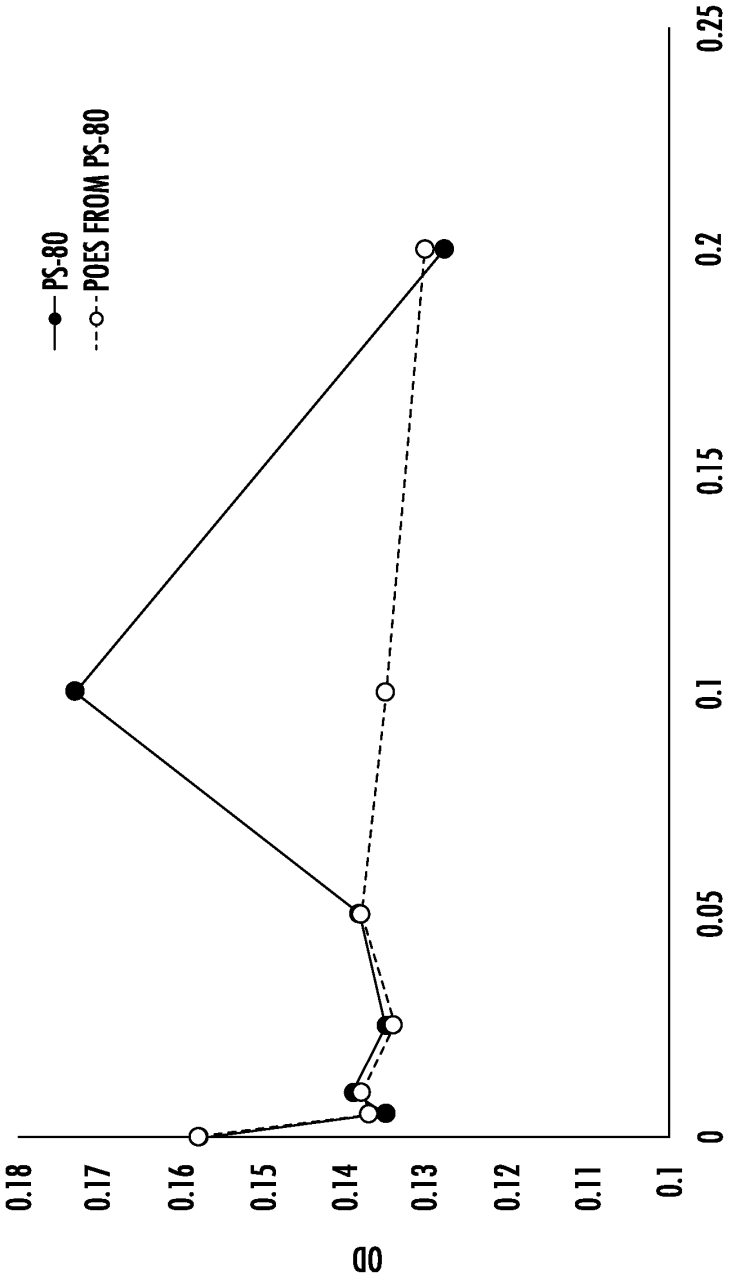
PS-80
POES FROM PS-80
OD
0.18
0.17
0.16
0.15
0.14
0.13
0.12
0.11
0.1
0
0.05
0.1
0.15
0.2
0.25
EXCIPIENT, %

FIG. 16

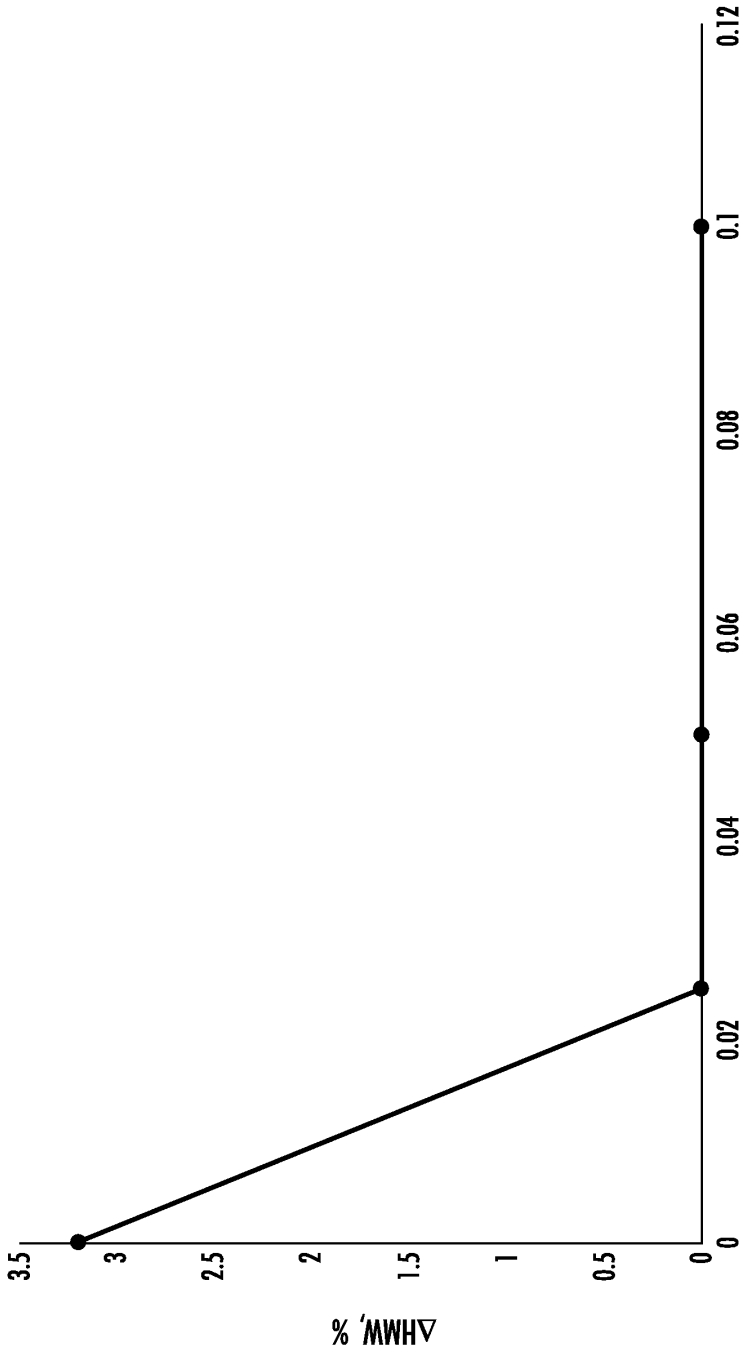

FIG. 17

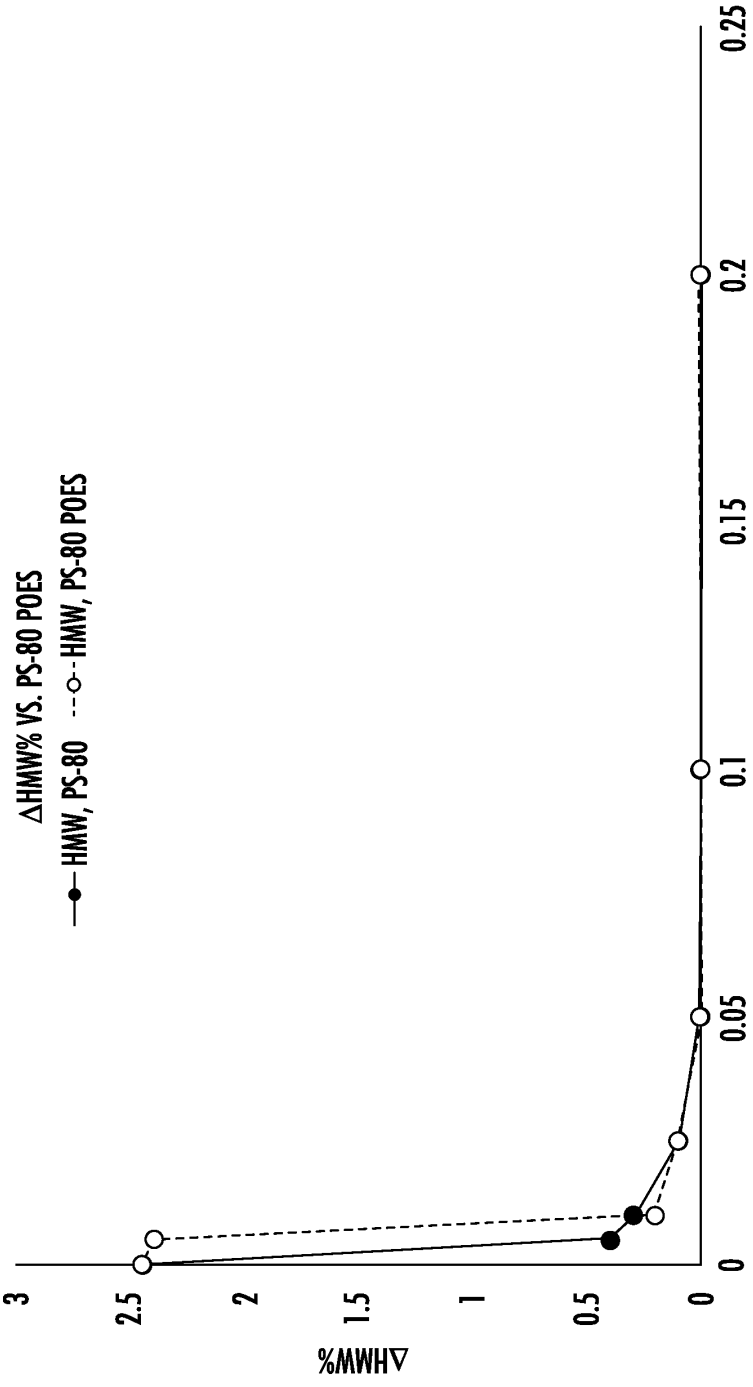
ΔHMW% VS. PS-80 POES
HMW, PS-80
HMW, PS-80 POES
ΔHMW%
3
2.5
2
1.5
1
0.5
0
0
0.05
0.1
0.15
0.2
0.25
EXCIPIENT, %

FIG. 18

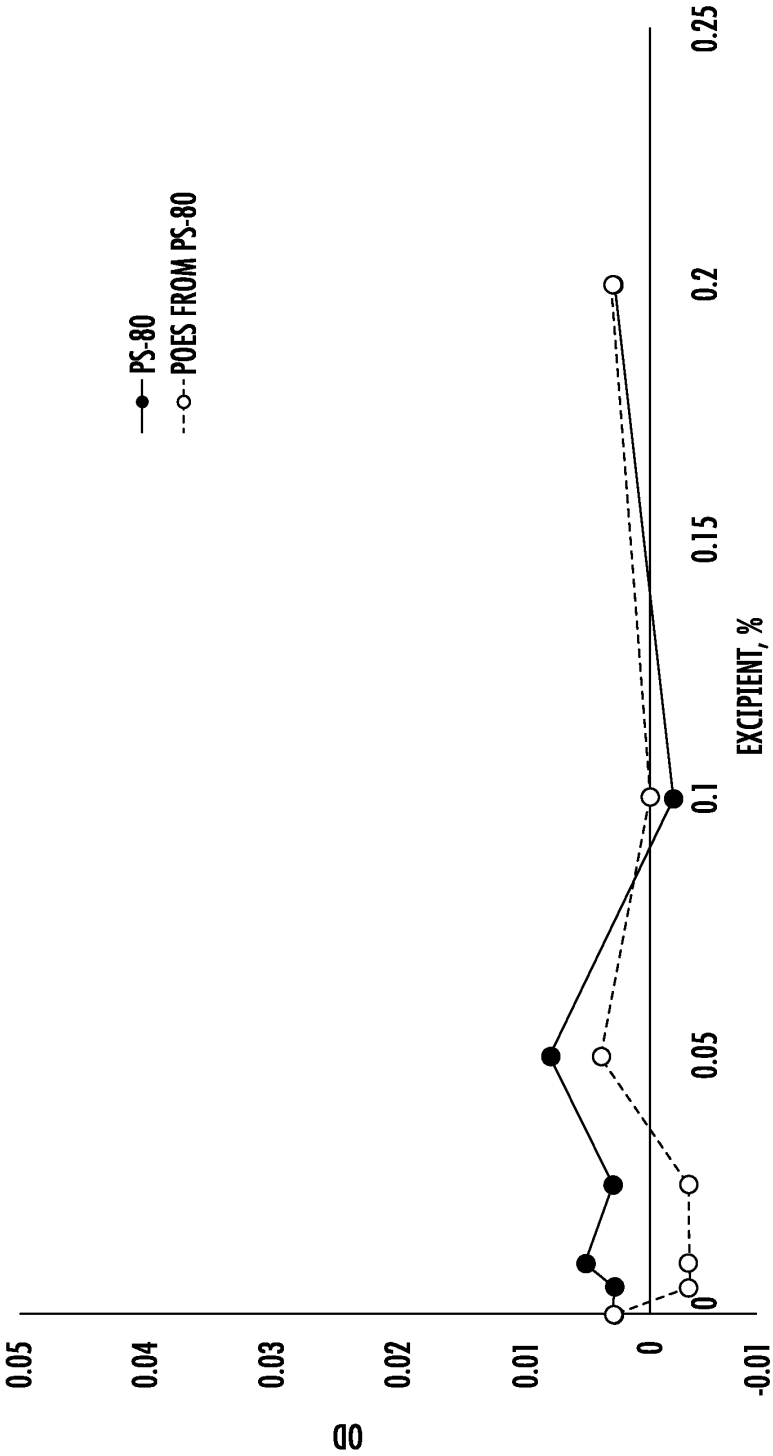
PS-80
POES FROM PS-80
OD
0.05
0.04
0.03
0.02
0.01
0
-0.01
0
0.05
0.1
0.15
0.2
0.25
EXCIPIENT, %

FIG. 19

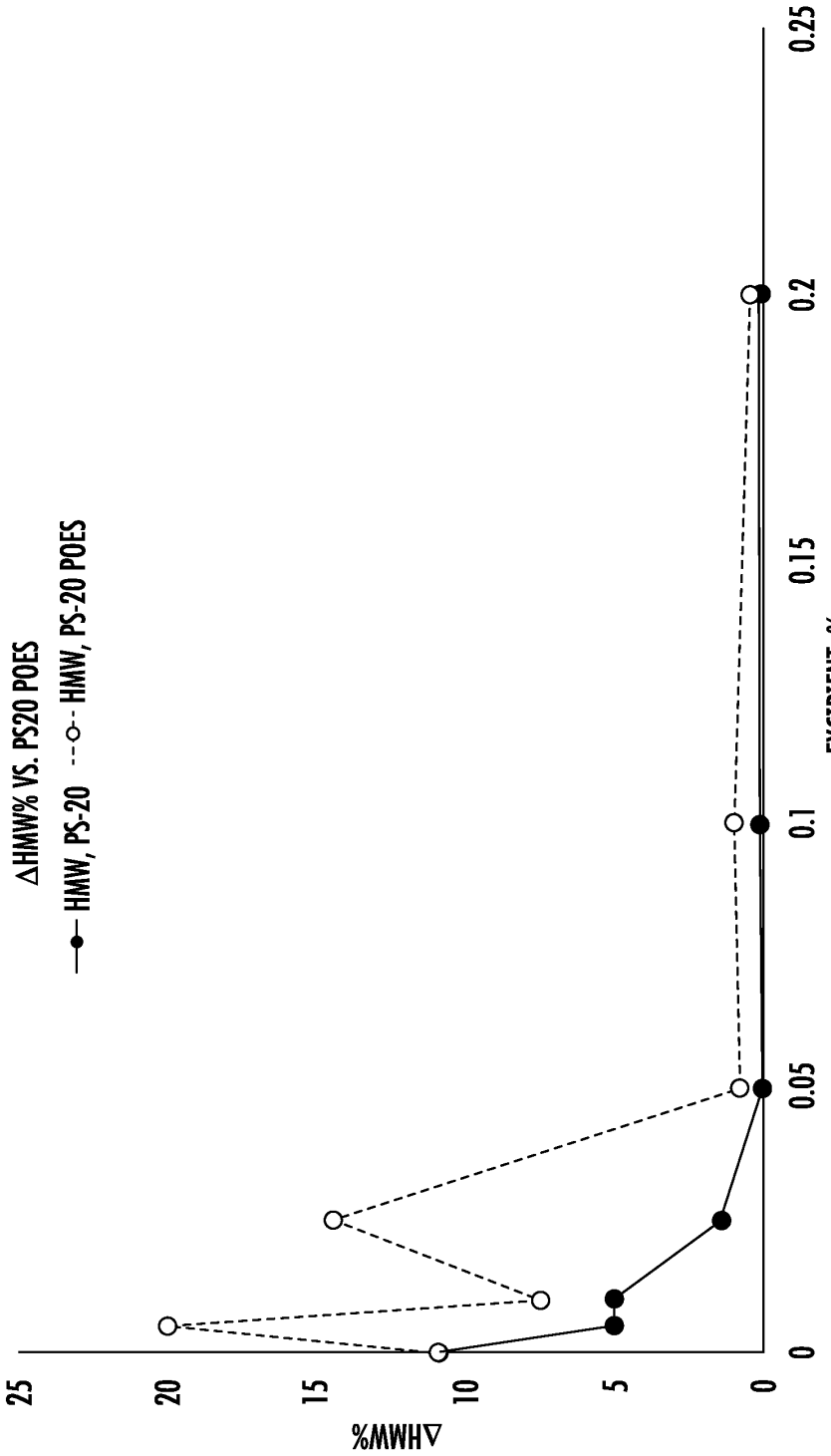
ΔHMW% VS. PS20 POES
HMW, PS-20
HMW, PS-20 POES
ΔHMW%
25
20
15
10
5
0
0
0.05
0.1
0.15
0.2
0.25
EXCIPIENT, %

FIG. 20

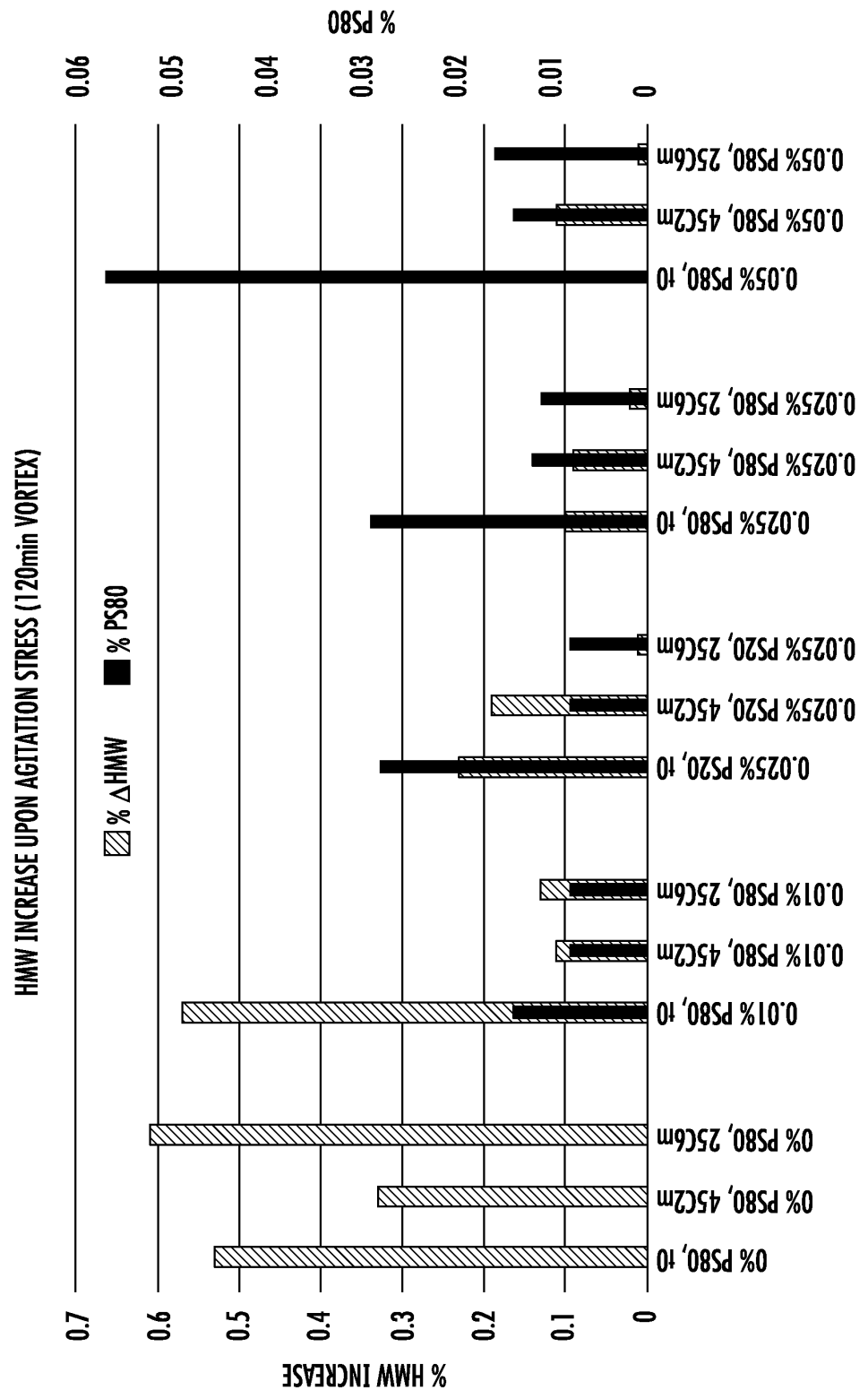
HMW INCREASE UPON AGITATION STRESS (120min VORTEX)
% ΔHMW
% PS80
% HMW INCREASE
% PS80
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.06
0.05
0.04
0.03
0.02
0.01
0
0% PS80, t0
0% PS80, 45C2m
0% PS80, 25C6m
0.01% PS80, t0
0.01% PS80, 45C2m
0.01% PS80, 25C6m
0.025% PS20, t0
0.025% PS20, 45C2m
0.025% PS20, 25C6m
0.025% PS80, t0
0.025% PS80, 45C2m
0.025% PS80, 25C6m
0.05% PS80, t0
0.05% PS80, 45C2m
0.05% PS80, 25C6m

FIG. 21

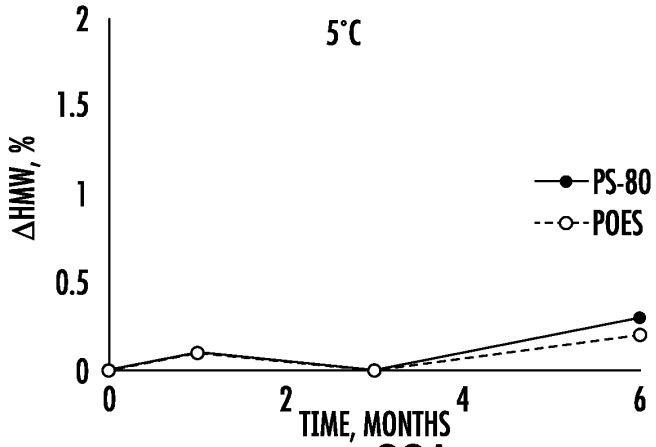

FIG. 22A

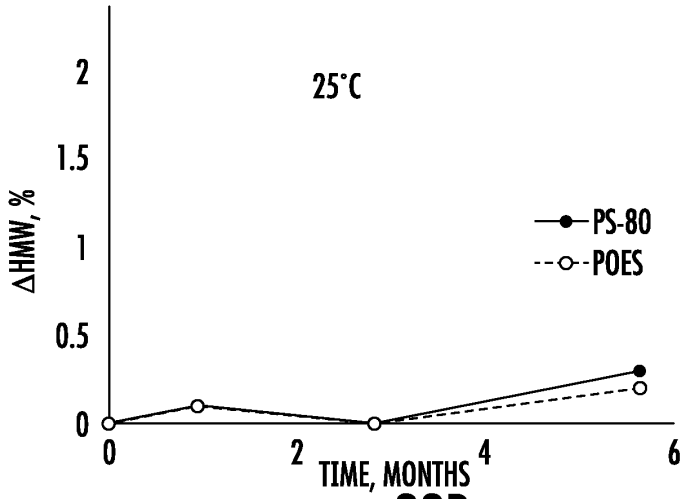

FIG. 22B

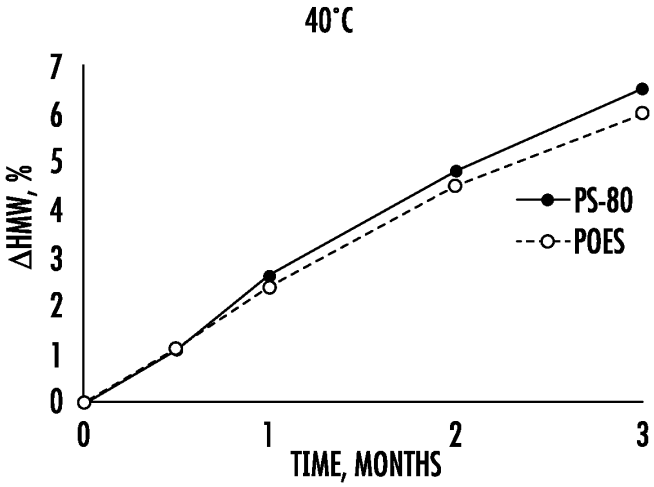

FIG. 22C

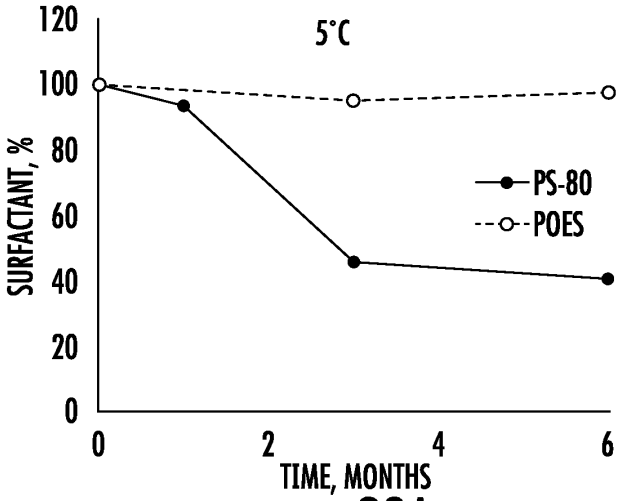

FIG. 23A

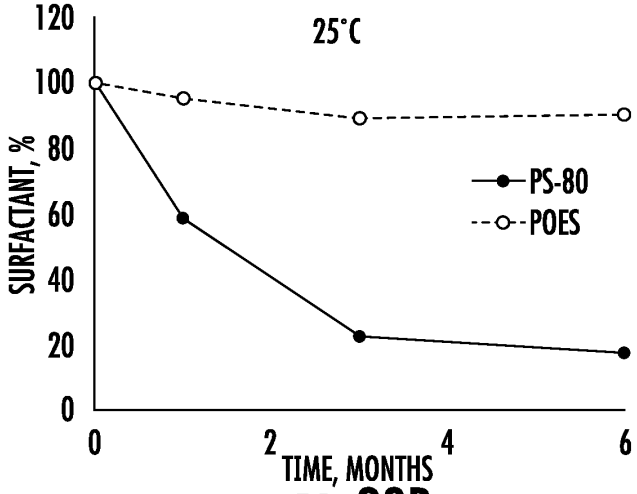

FIG. 23B

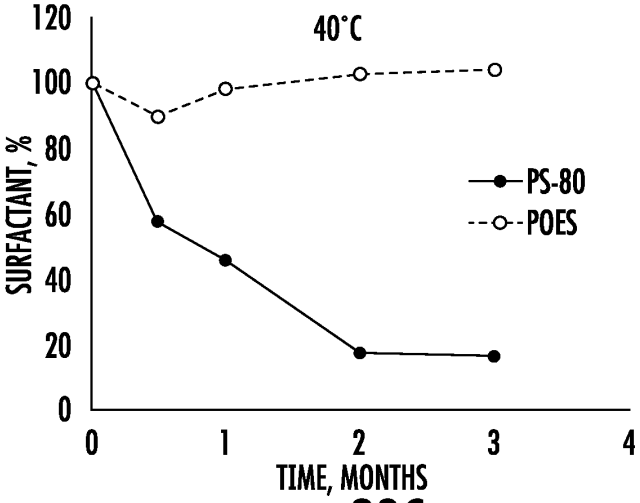

FIG. 23C

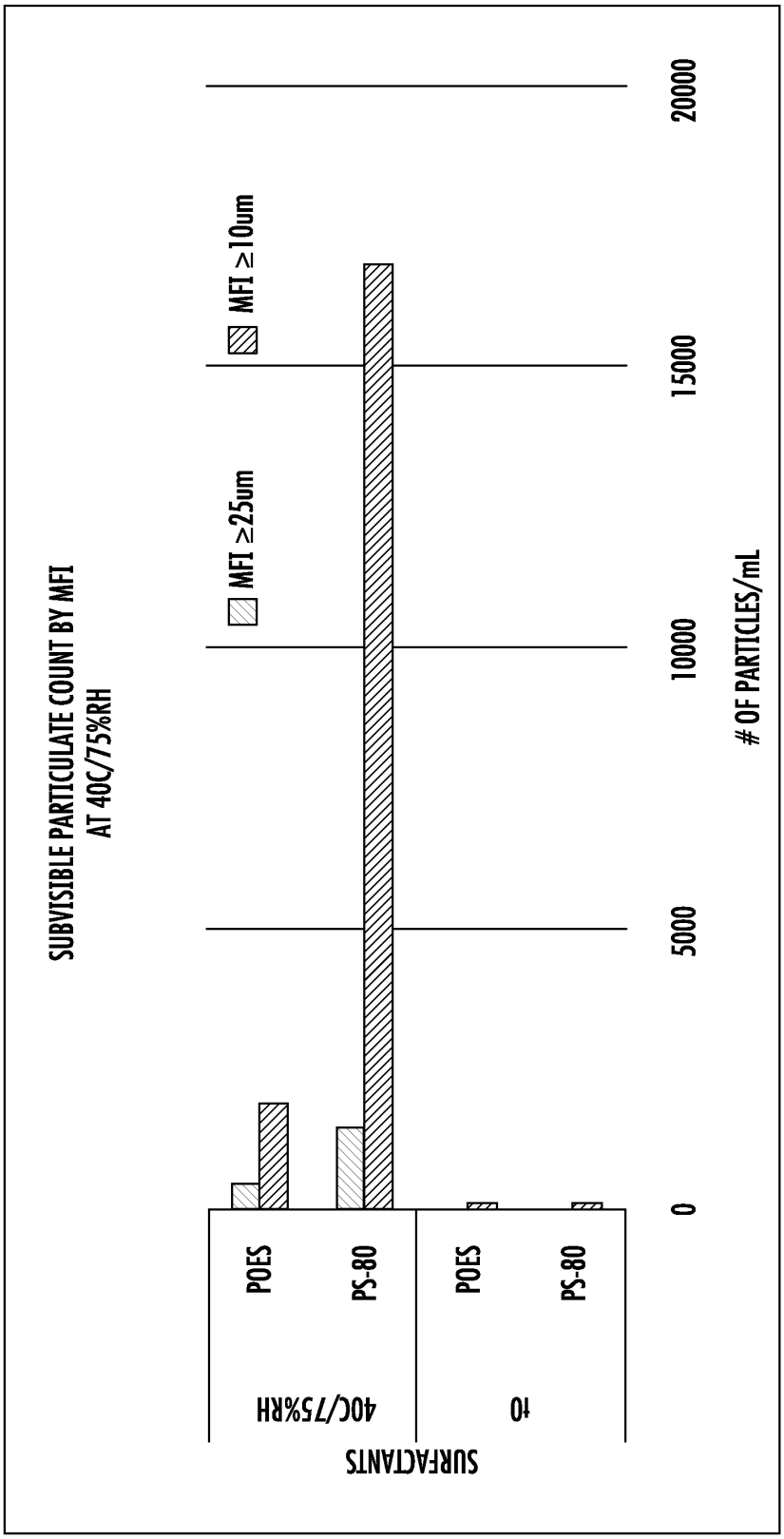
SUBVISIBLE PARTICULATE COUNT BY MFI
AT 40C/75%RH
MFI ≥10um
MFI ≥25um
OF PARTICLES/mL
0
5000
10000
15000
20000
POES
PS-80
POES
PS-80
40C/75%RH
t0
SURFACTANTS

FIG. 24

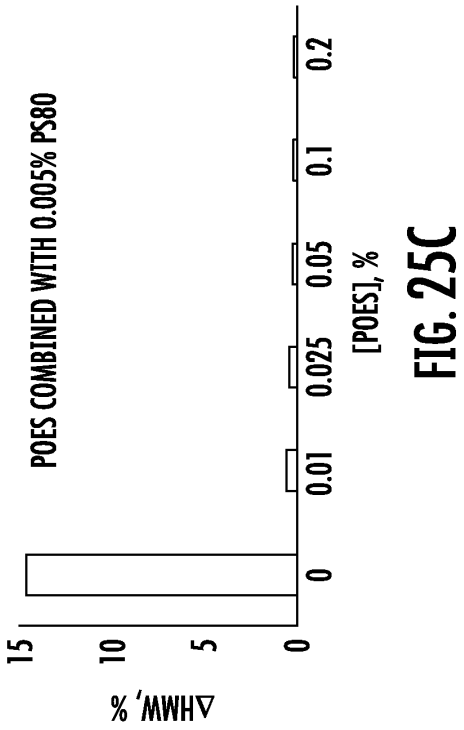

FIG. 25C

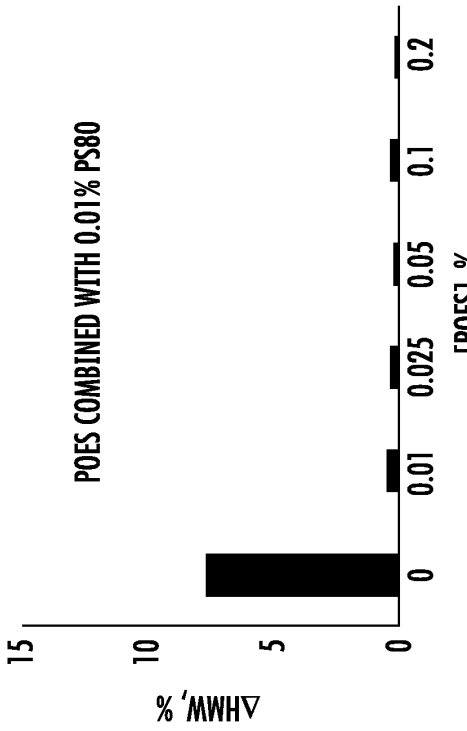

FIG. 25D

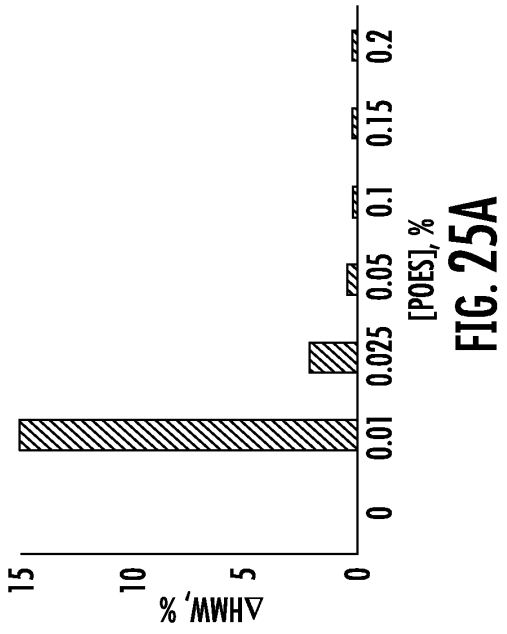

FIG. 25A

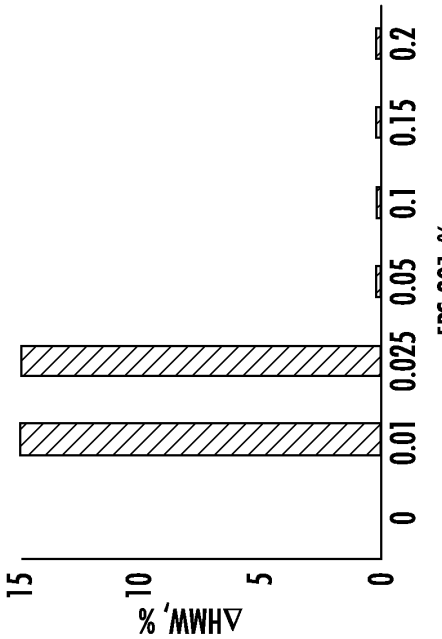

FIG. 25B

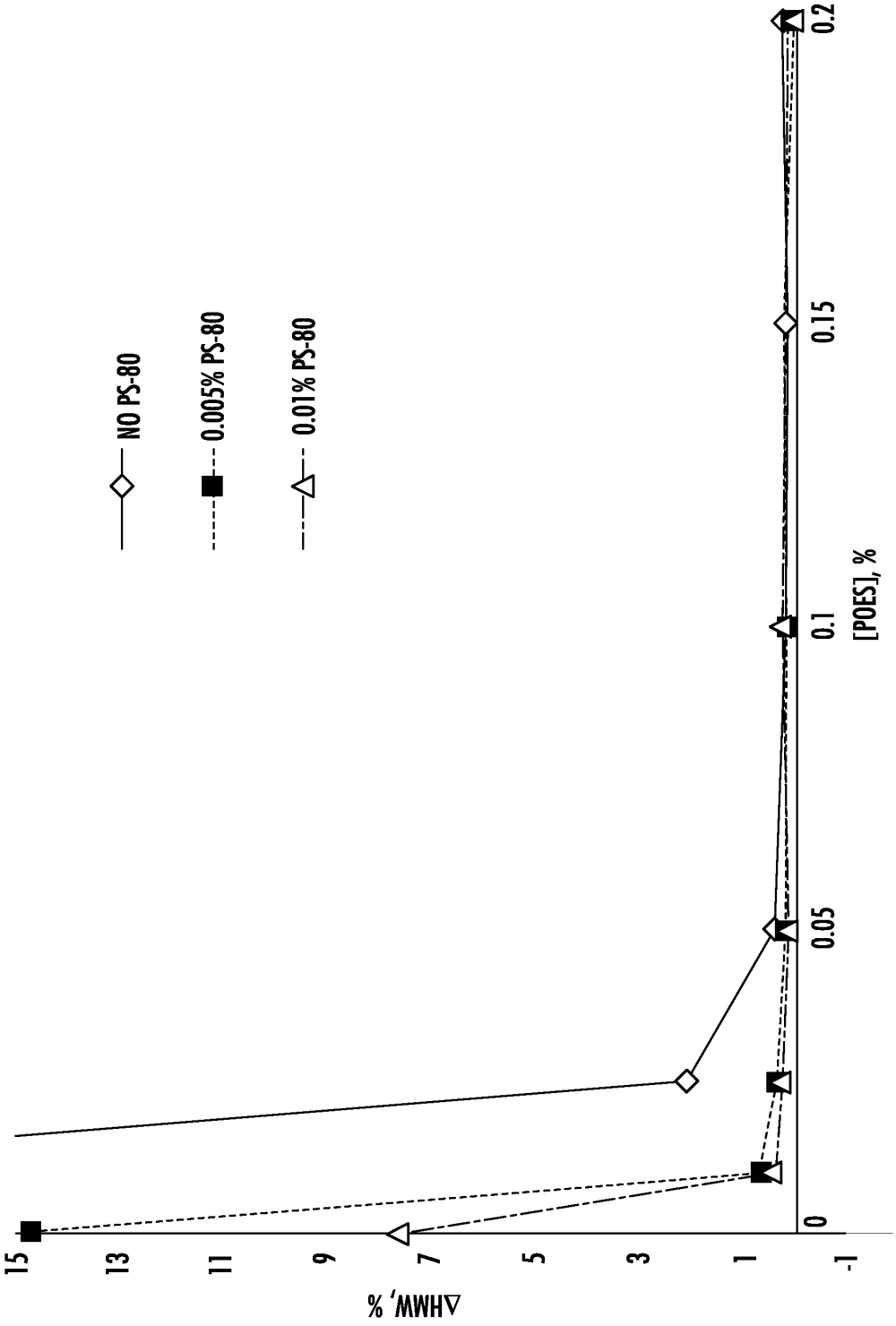
NO PS-80
0.005% PS-80
0.01% PS-80
ΔHMW, %
15
13
11
9
7
5
3
1
-1
0
0.05
0.1
0.15
0.2
[POES], %

FIG. 26

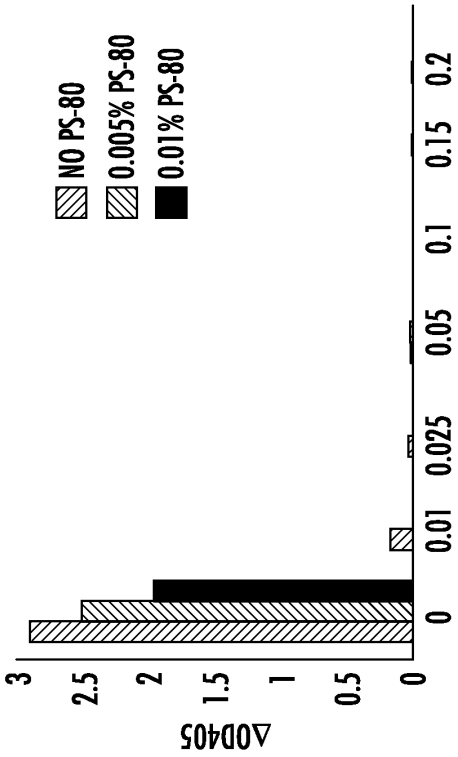

FIG. 27B

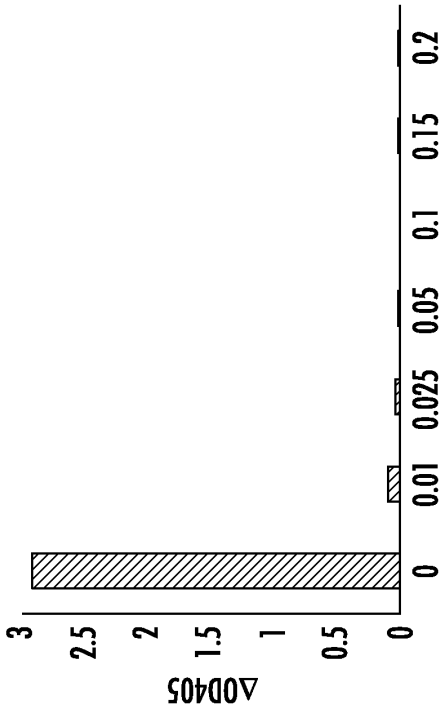

FIG. 27A

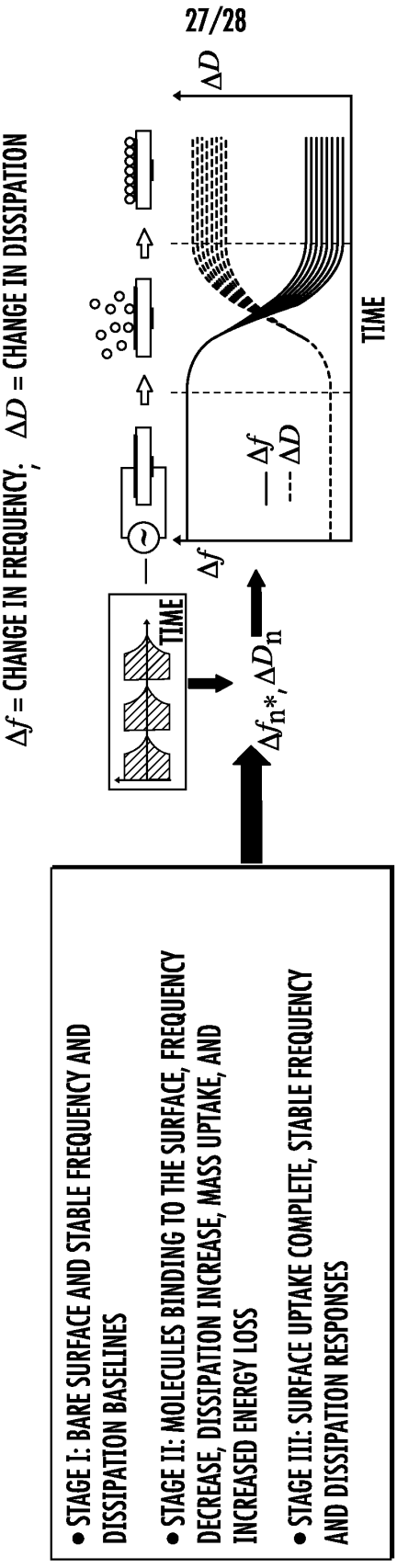
Δf = CHANGE IN FREQUENCY, ΔD = CHANGE IN DISSIPATION
• STAGE I: BARE SURFACE AND STABLE FREQUENCY AND DISSIPATION BASELINES
• STAGE II: MOLECULES BINDING TO THE SURFACE, FREQUENCY DECREASE, DISSIPATION INCREASE, MASS UPTAKE, AND INCREASED ENERGY LOSS
• STAGE III: SURFACE UPTAKE COMPLETE, STABLE FREQUENCY AND DISSIPATION RESPONSES
TIME
Δf
ΔD
TIME
Δf
ΔD
Δf_n*, ΔD_n

FIG. 28

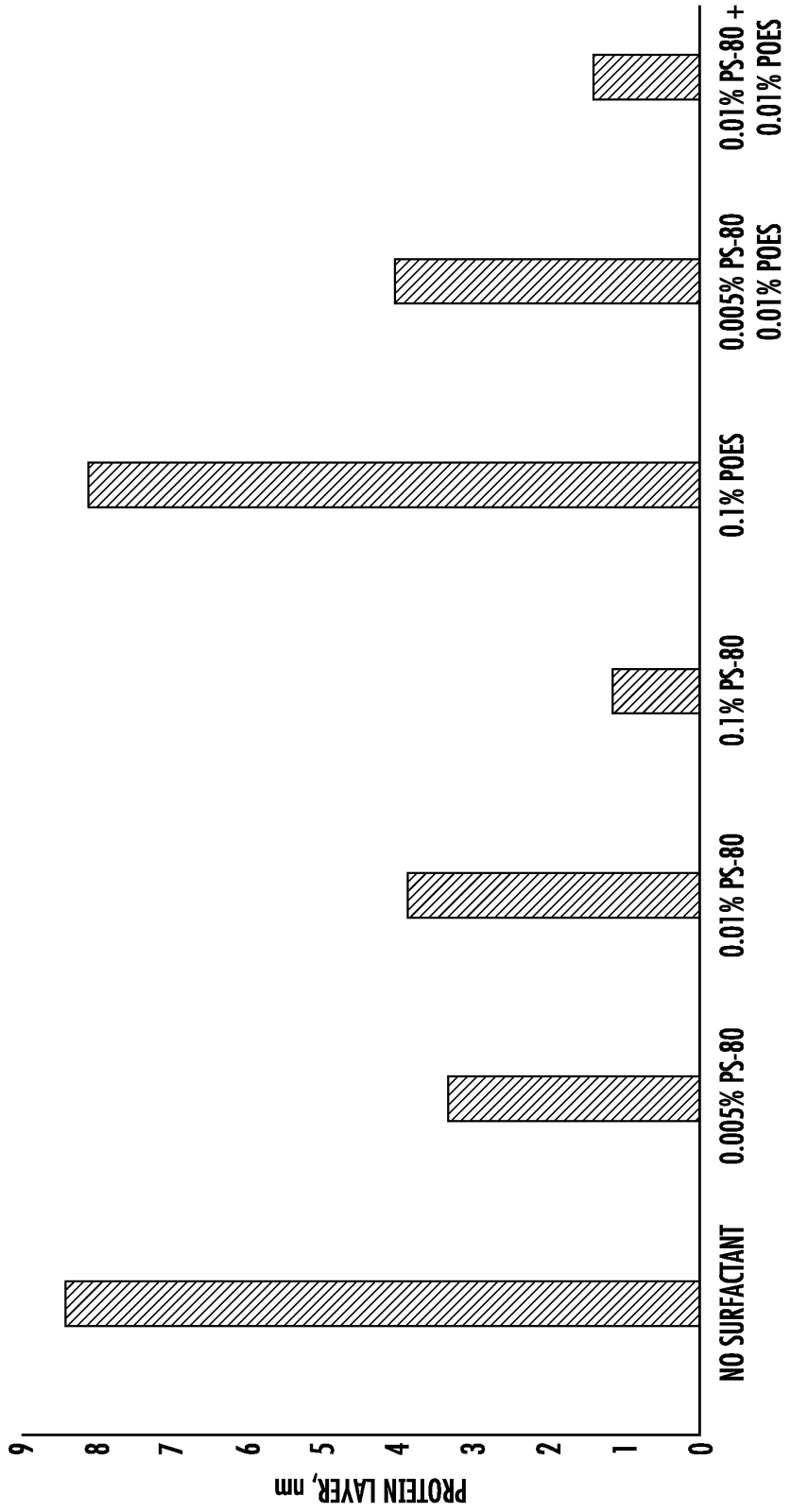
PROTEIN LAYER, nm
0
1
2
3
4
5
6
7
8
9
NO SURFACTANT
0.005% PS-80
0.01% PS-80
0.1% PS-80
0.1% POES
0.005% PS-80 0.01% POES
0.01% PS-80 + 0.01% POES

FIG. 29