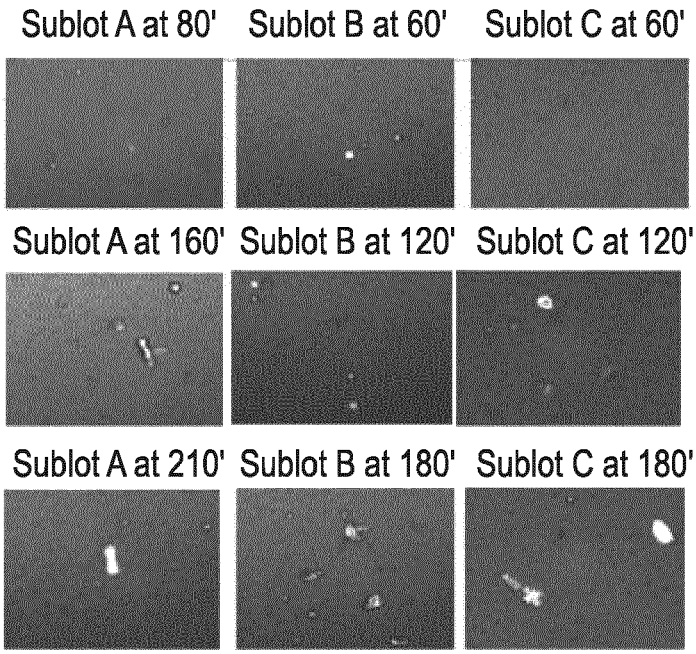
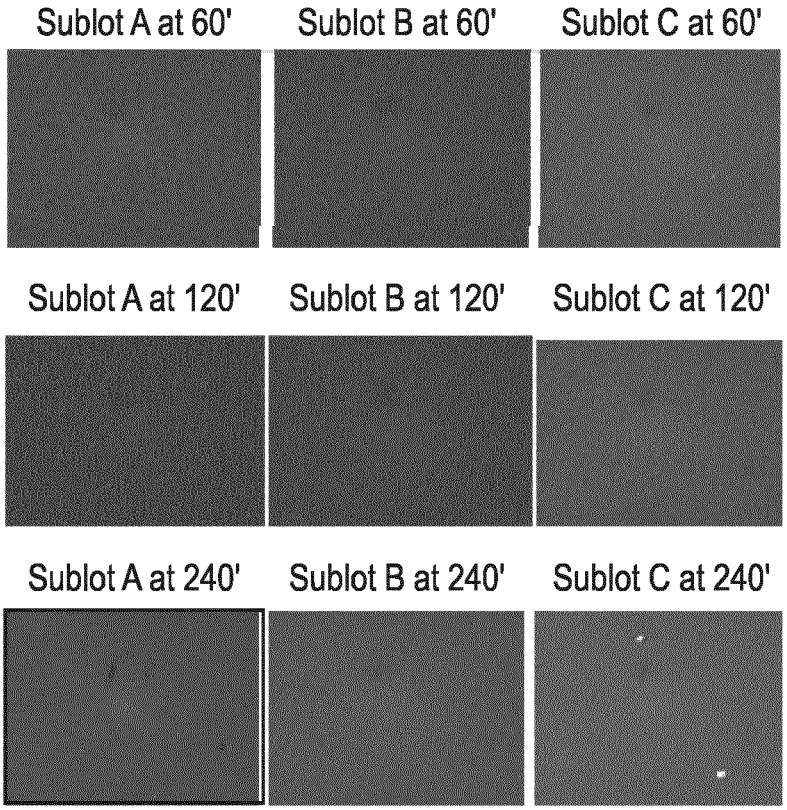


Cremophor formulation

FIG. 1



Capmul formulation

FIG. 2

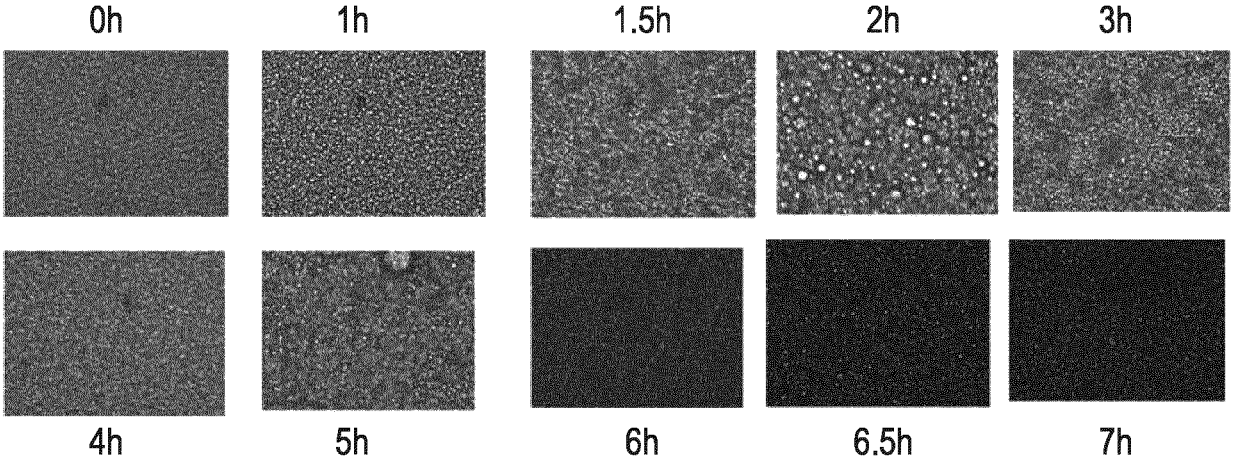


FIG. 3

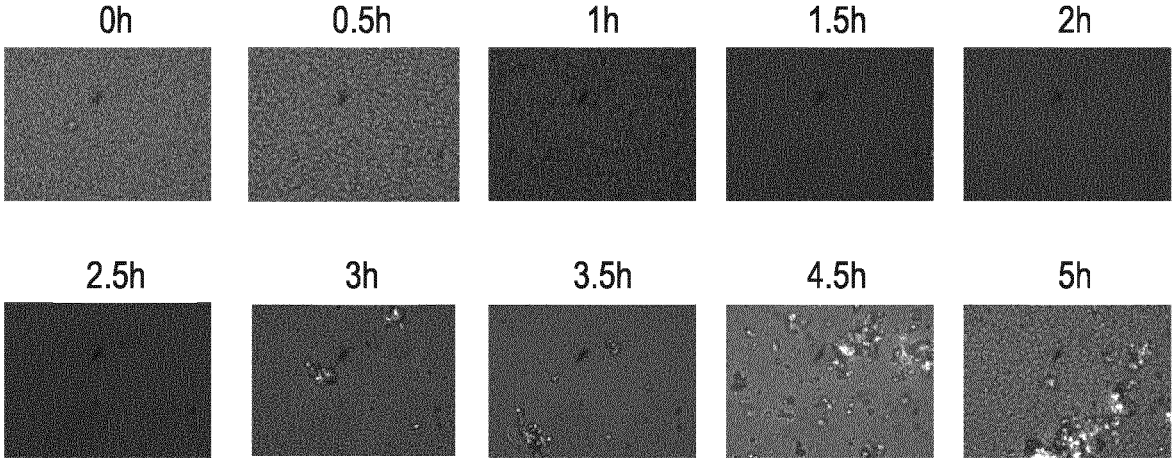


FIG. 4

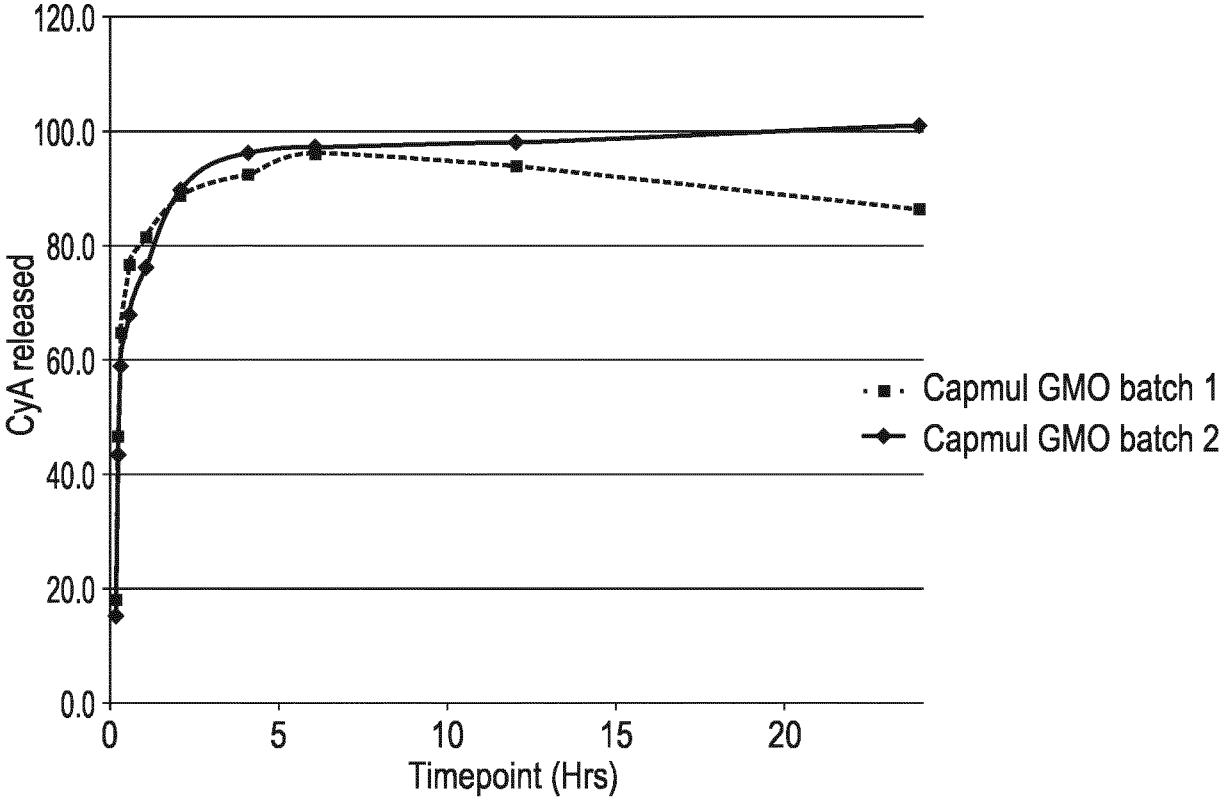

120.0
100.0
80.0
60.0
40.0
20.0
0.0
CyA released
0
5
10
15
20
Timepoint (Hrs)
Capmul GMO batch 1
Capmul GMO batch 2

FIG. 5

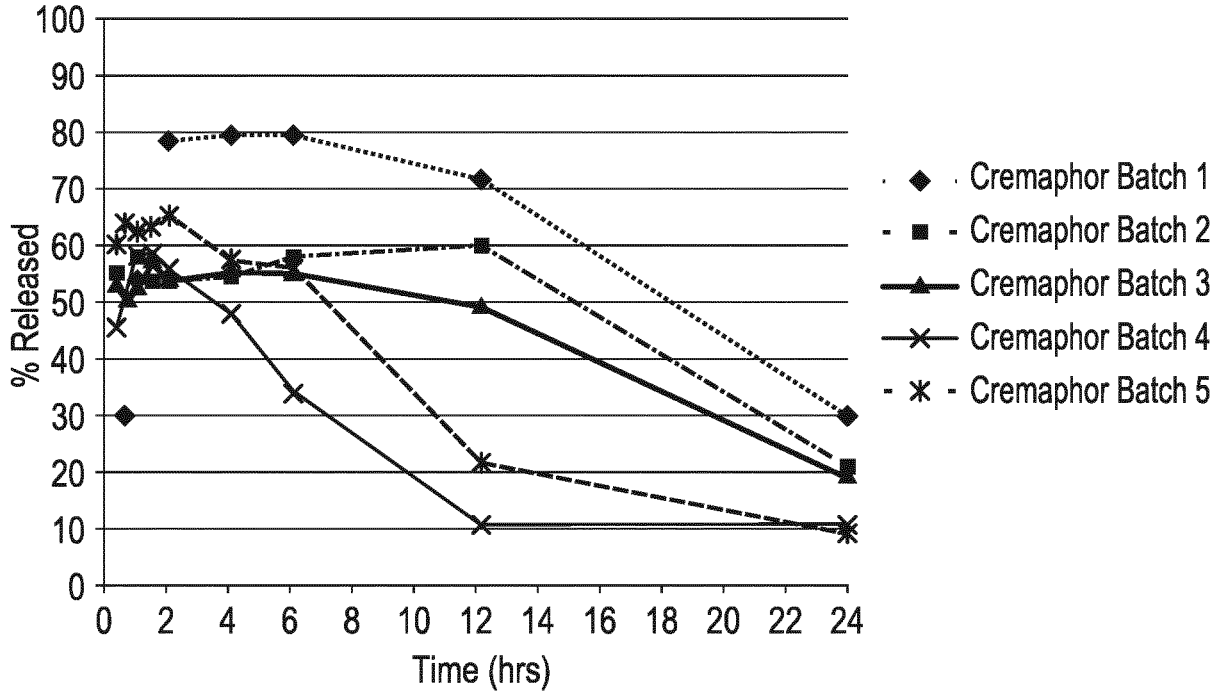

100
90
80
70
60
50
40
30
20
10
0
% Released
0
2
4
6
8
10
12
14
16
18
20
22
24
Time (hrs)
Cremaphor Batch 1
Cremaphor Batch 2
Cremaphor Batch 3
Cremaphor Batch 4
Cremaphor Batch 5

FIG. 6

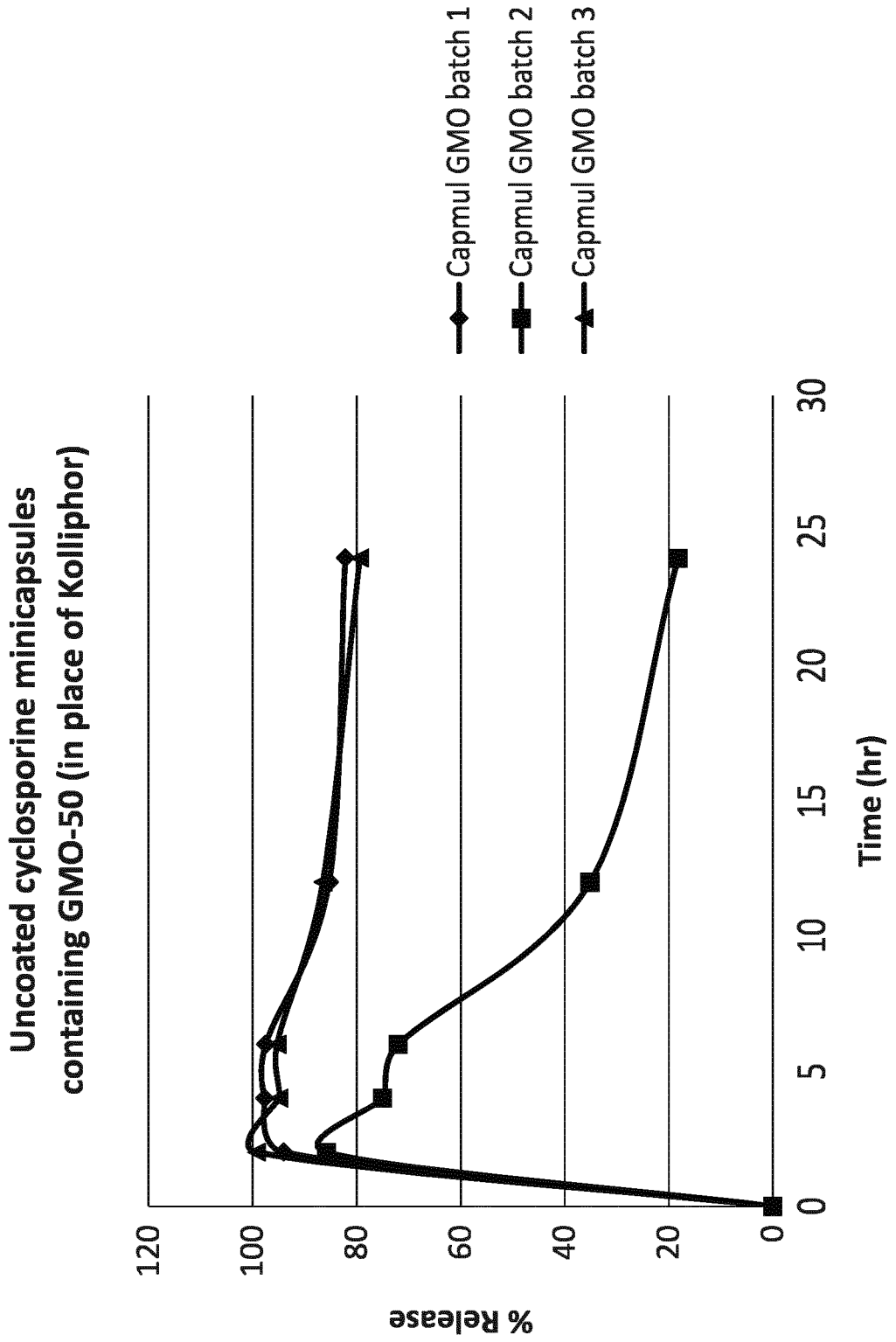

Uncoated cyclosporine minicapsules containing GMO-50 (in place of Kolliphor)
Capmul GMO batch 1
Capmul GMO batch 2
Capmul GMO batch 3
% Release
120
100
80
60
40
20
0
0
5
10
15
20
25
30
Time (hr)

FIG. 7

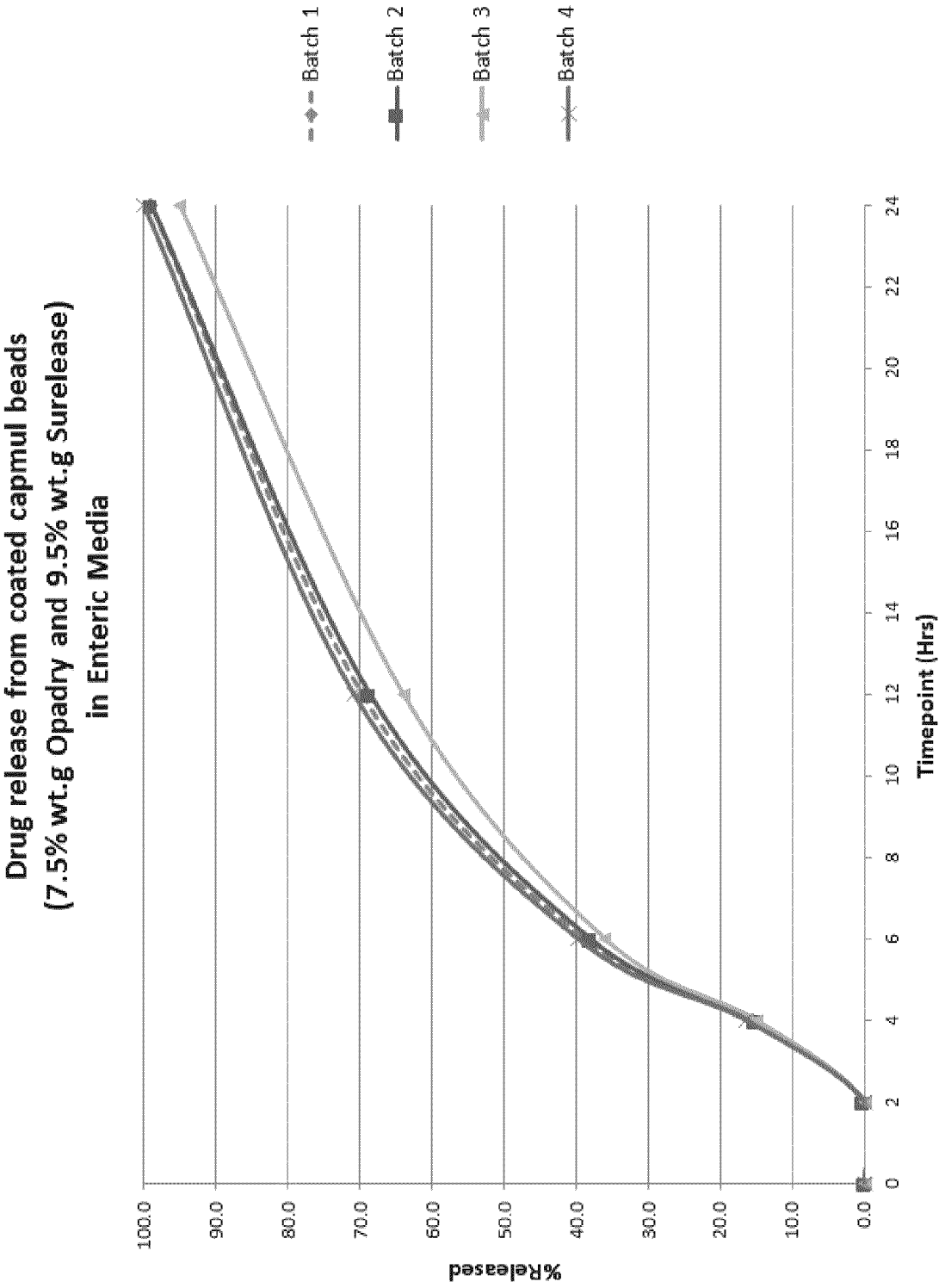

Drug release from coated capmul beads
(7.5% wt.g Opadry and 9.5% wt.g Surelease)
in Enteric Media
Batch 1
Batch 2
Batch 3
Batch 4
%Released
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
0
2
4
6
8
10
12
14
16
18
20
22
24
Timepoint (Hrs)

FIG. 8

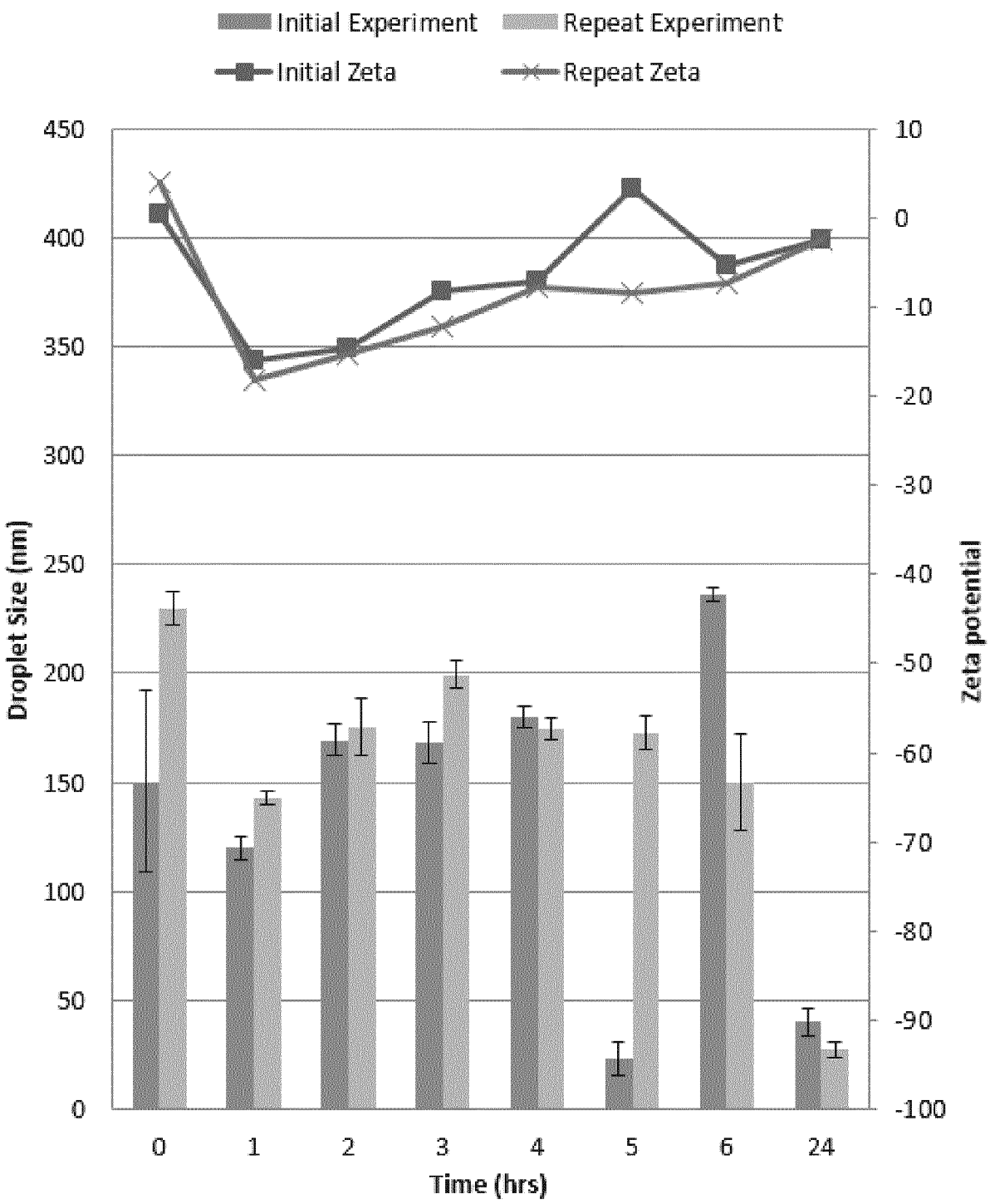

Initial Experiment
Repeat Experiment
Initial Zeta
Repeat Zeta
Droplet Size (nm)
Zeta potential
Time (hrs)
450
400
350
300
250
200
150
100
50
0
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
0
1
2
3
4
5
6
24

FIG. 9

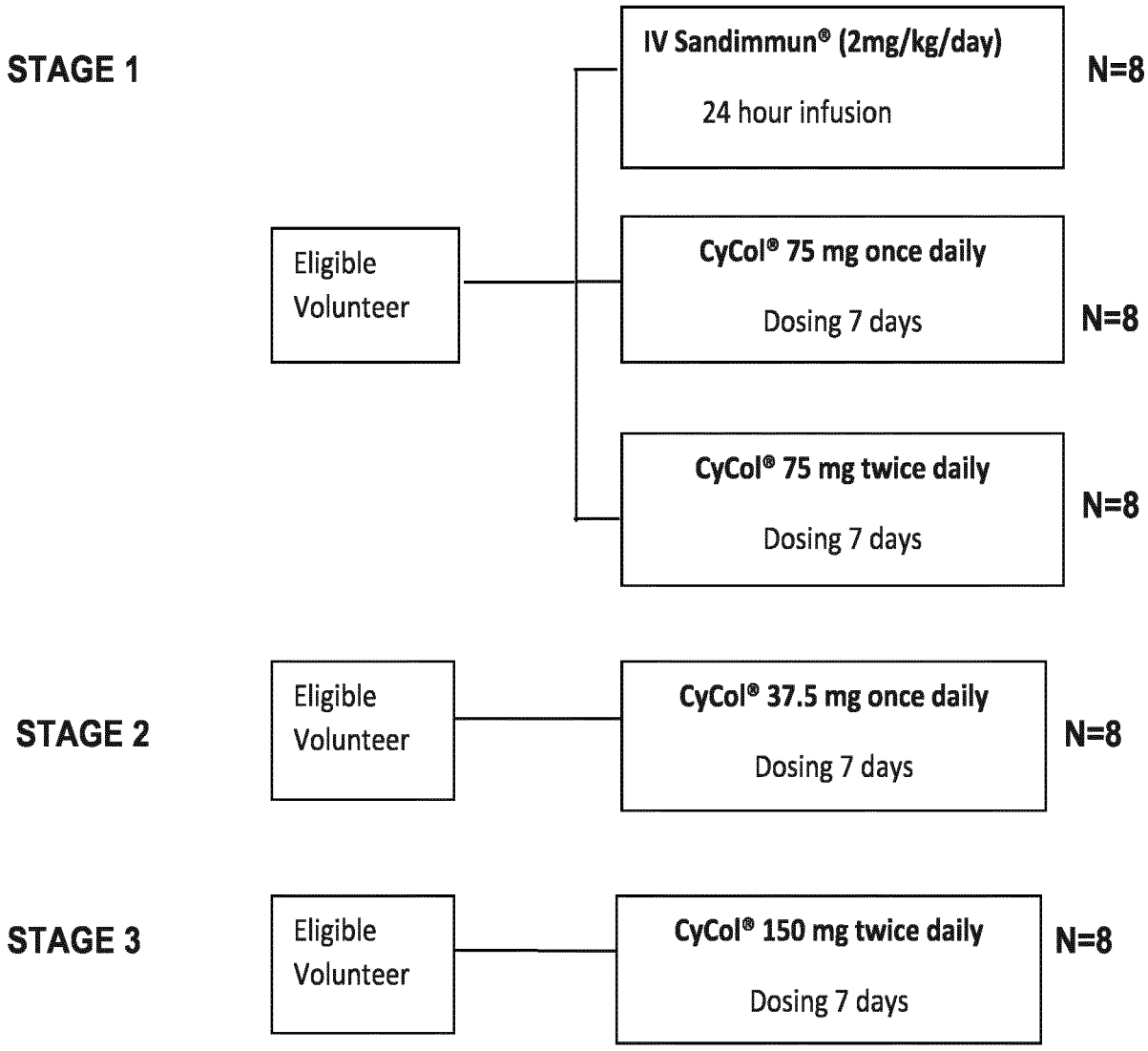

STAGE 1
IV Sandimmun® (2mg/kg/day)
24 hour infusion
N=8
Eligible Volunteer
CyCol® 75 mg once daily
Dosing 7 days
N=8
CyCol® 75 mg twice daily
Dosing 7 days
N=8
STAGE 2
Eligible Volunteer
CyCol® 37.5 mg once daily
Dosing 7 days
N=8
STAGE 3
Eligible Volunteer
CyCol® 150 mg twice daily
Dosing 7 days
N=8

FIG. 10

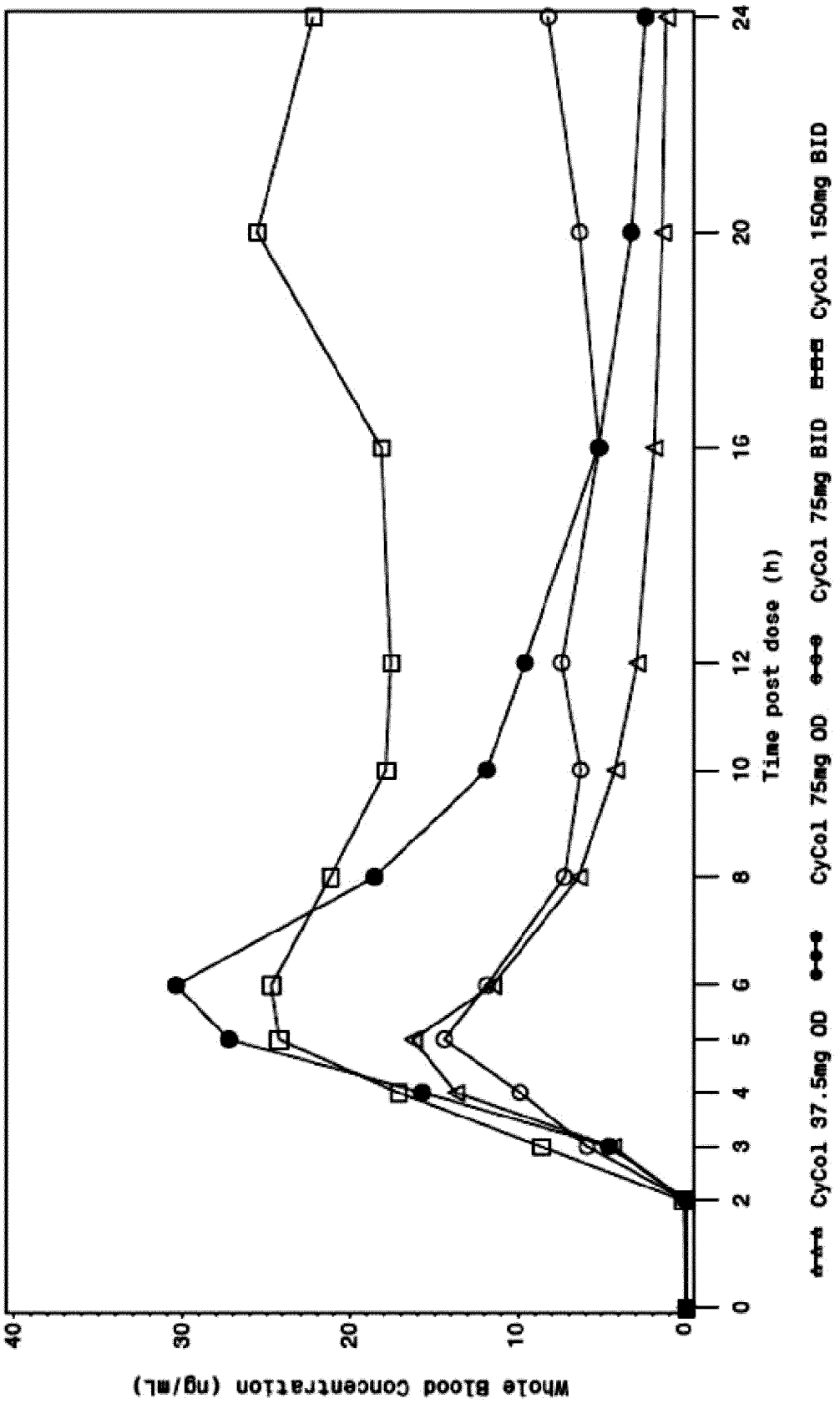

Whole Blood Concentration (ng/mL)
0
10
20
30
40
0
2
3
4
5
6
8
10
12
16
20
24
Time post dose (h)
CyCol 37.5mg OD
CyCol 75mg OD
CyCol 75mg BID
CyCol 150mg BID

FIG. 11

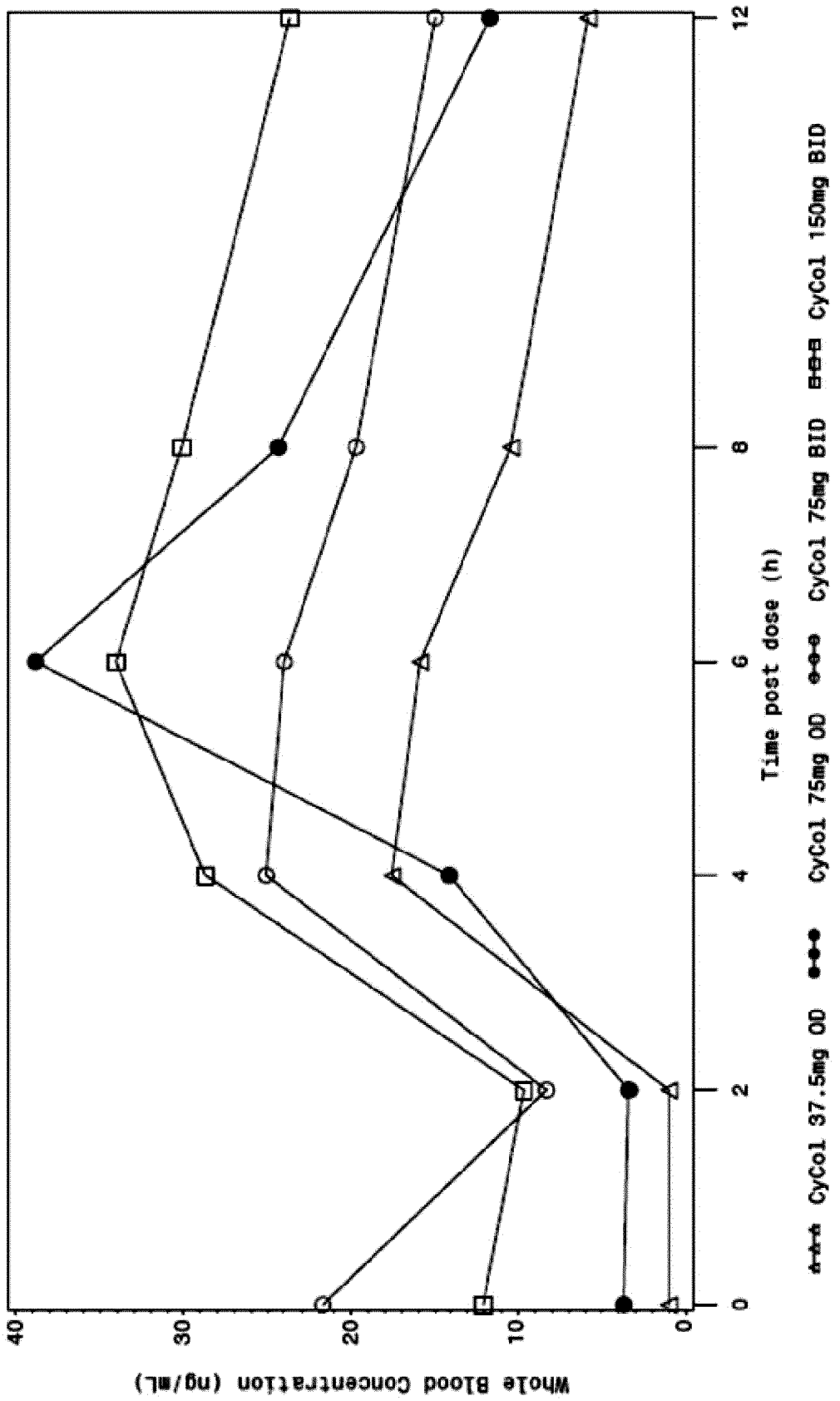

Whole Blood Concentration (ng/mL)
0
10
20
30
40
0
2
4
6
8
12
Time post dose (h)
CyCol 37.5mg OD
CyCol 75mg OD
CyCol 75mg BID
CyCol 150mg BID

FIG. 12

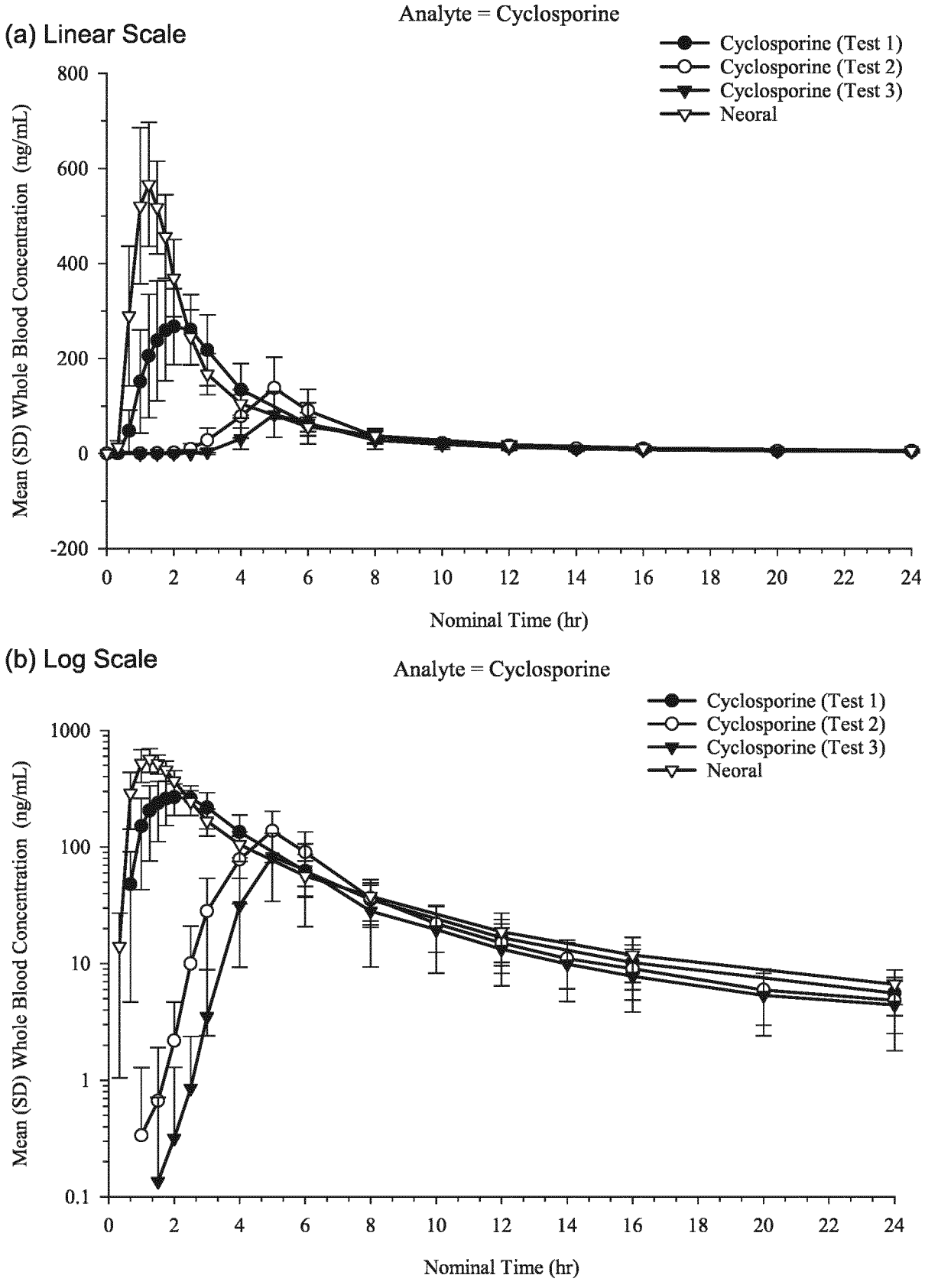

(a) Linear Scale
Analyte = Cyclosporine
Cyclosporine (Test 1)
Cyclosporine (Test 2)
Cyclosporine (Test 3)
Neoral
Mean (SD) Whole Blood Concentration (ng/mL)
800
600
400
200
0
-200
0 2 4 6 8 10 12 14 16 18 20 22 24
Nominal Time (hr)
(b) Log Scale
Analyte = Cyclosporine
Cyclosporine (Test 1)
Cyclosporine (Test 2)
Cyclosporine (Test 3)
Neoral
Mean (SD) Whole Blood Concentration (ng/mL)
1000
100
10
1
0.1
0 2 4 6 8 10 12 14 16 18 20 22 24
Nominal Time (hr)

FIG. 13

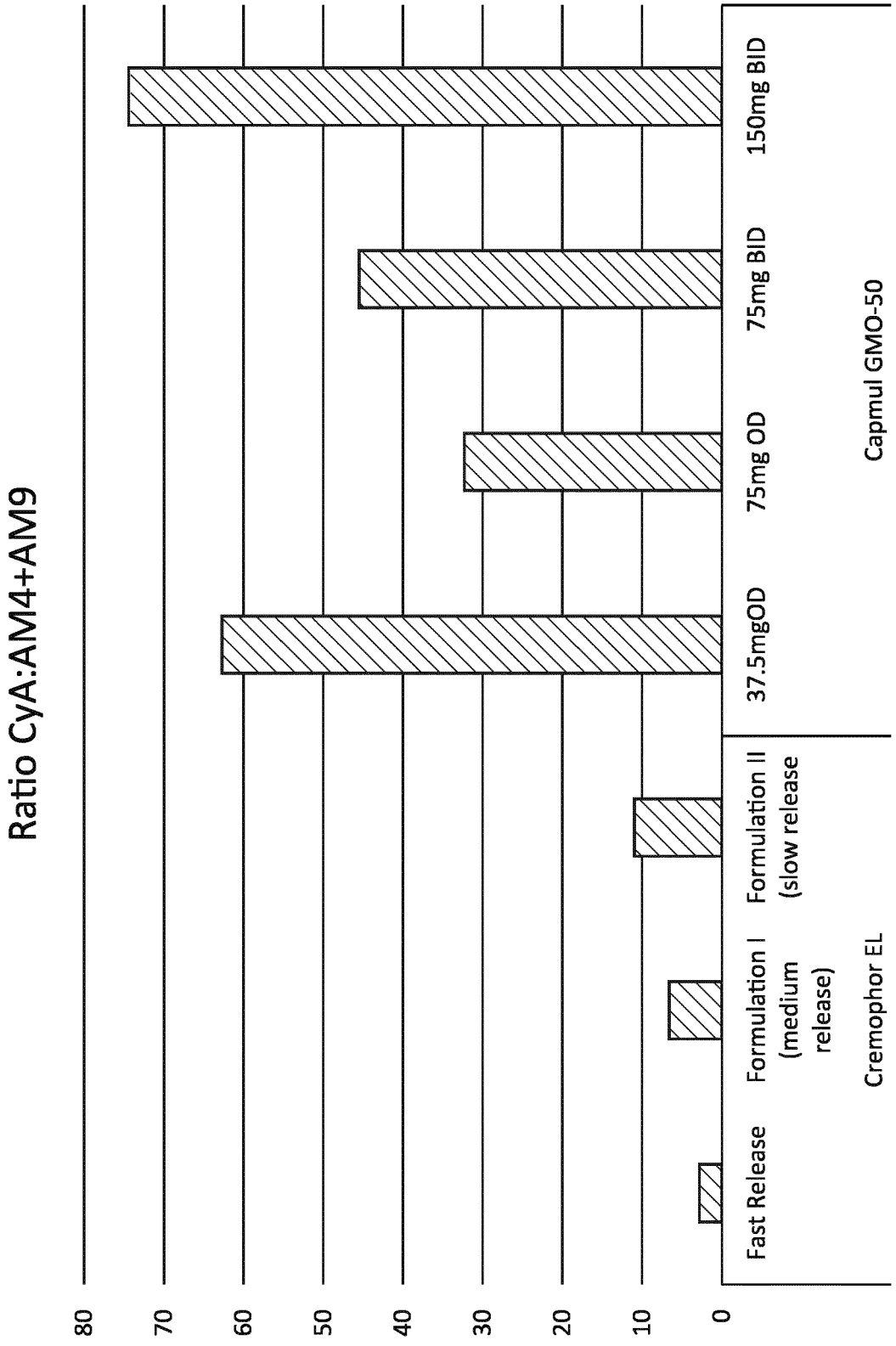

Ratio CyA:AM4+AM9
80
70
60
50
40
30
20
10
0
Fast Release
Formulation I (medium release)
Formulation II (slow release
Cremophor EL
37.5mgOD
75mg OD
75mg BID
150mg BID
Capmul GMO-50

FIG. 14

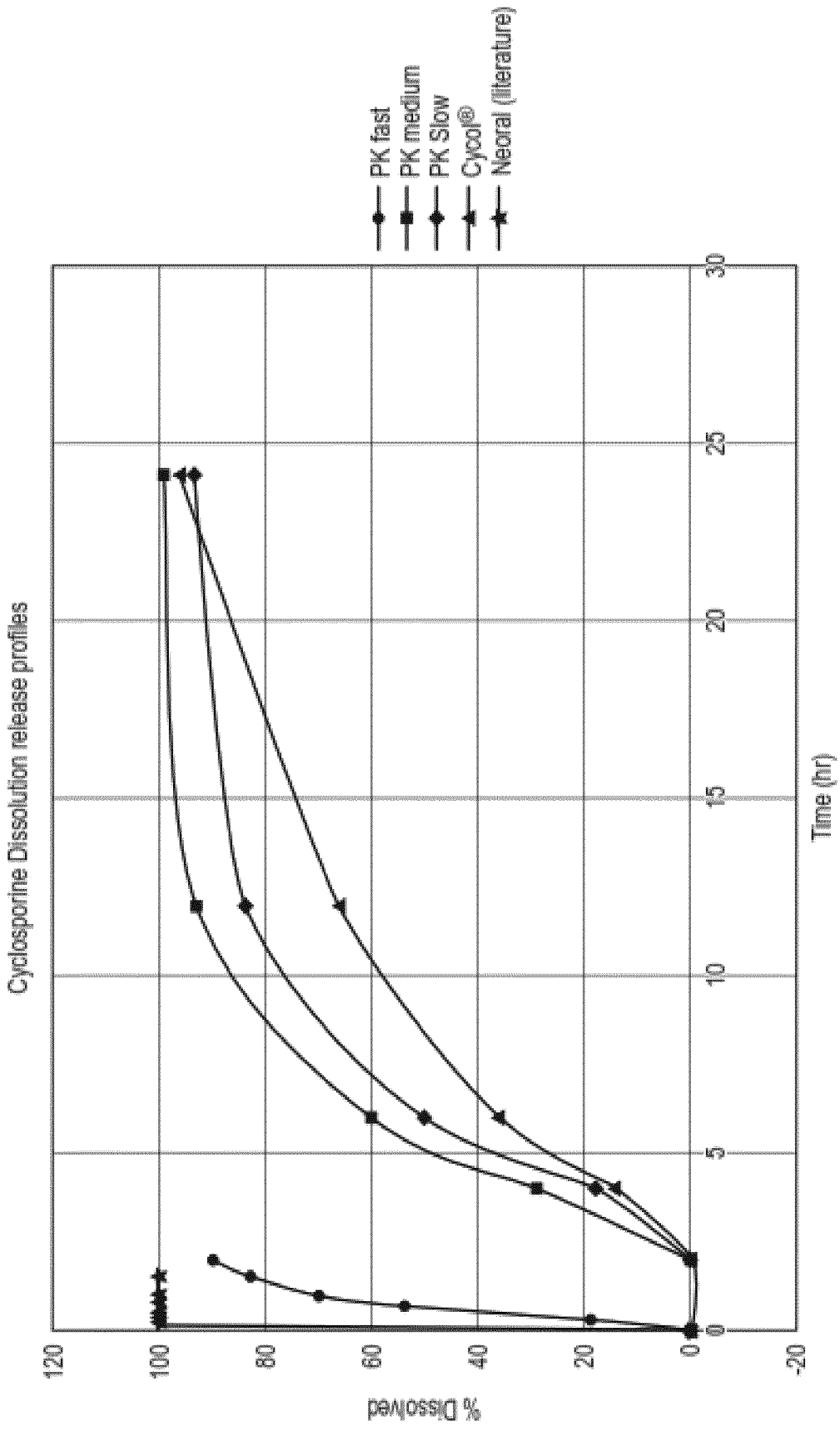
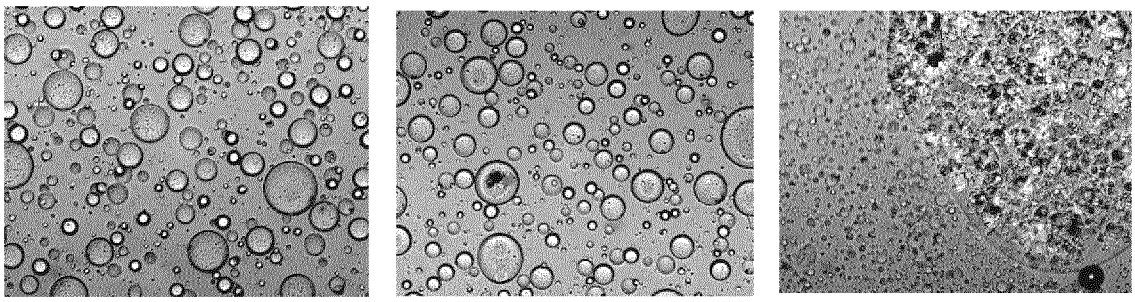
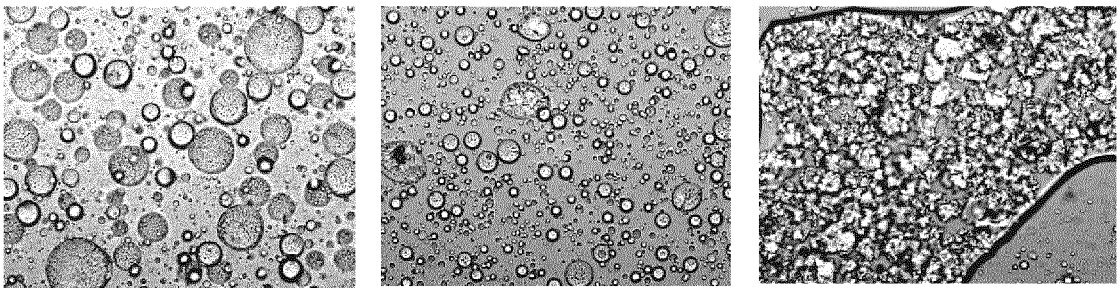

Cyclosporine Dissolution release profiles
PK fast
PK medium
PK Slow
Cycol®
Neoral (literature)
% Dissolved
120
100
80
60
40
20
0
-20
0
5
10
15
20
25
30
Time (hr)

FIG. 15



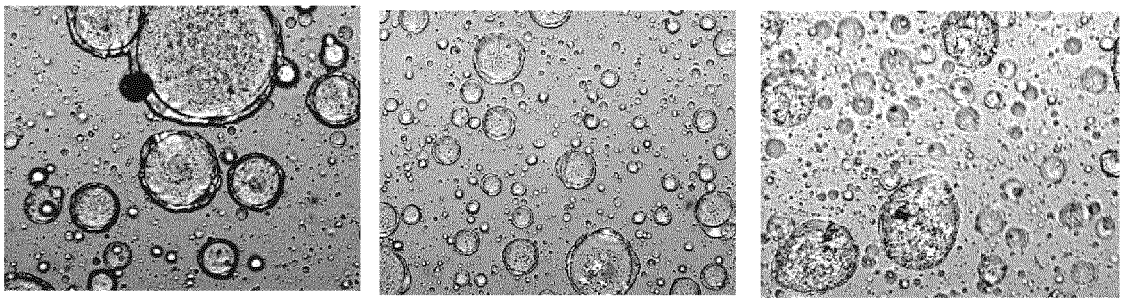
(t0) (t = 2 hours) (t = 2 hours 30 mins)

FIG. 16A



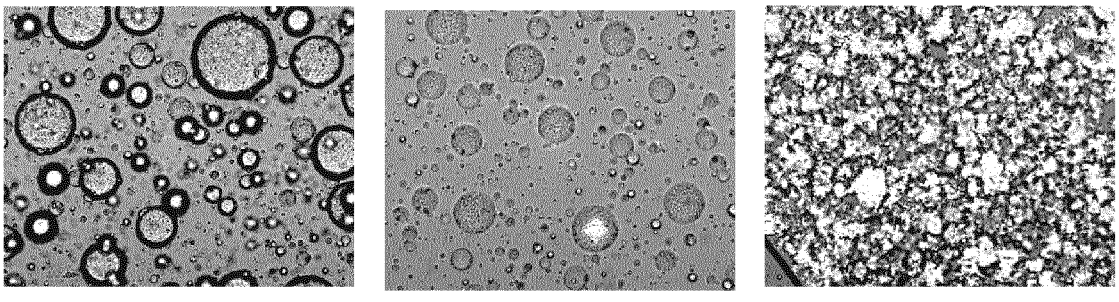
(t0) (t = 2 hours) (t = 2 hours 30 mins)

FIG. 16B



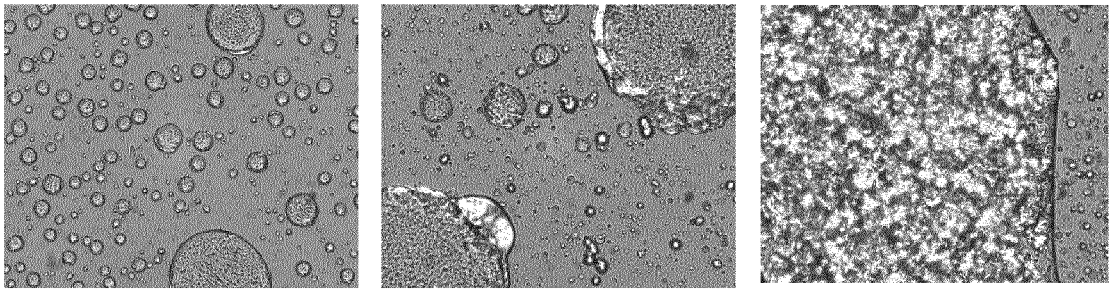
(t=0) (t = 1 hour) (t = 1 hour 30 mins)

FIG. 16C



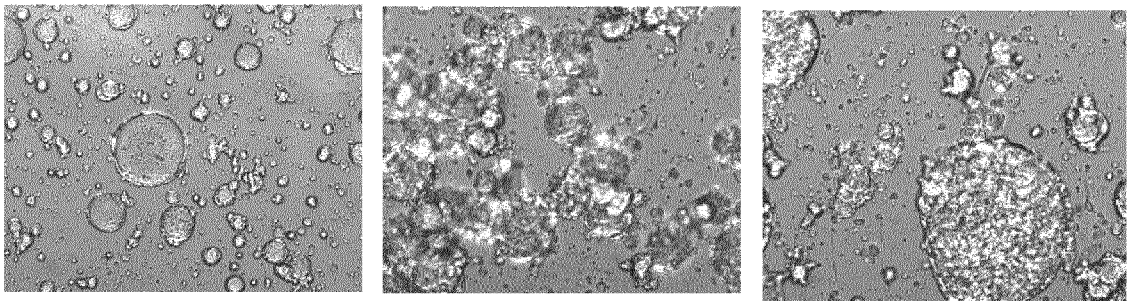
(t=0) (t = 3 hours 30 mins) (t = 4 hours 30 mins)

FIG. 17A



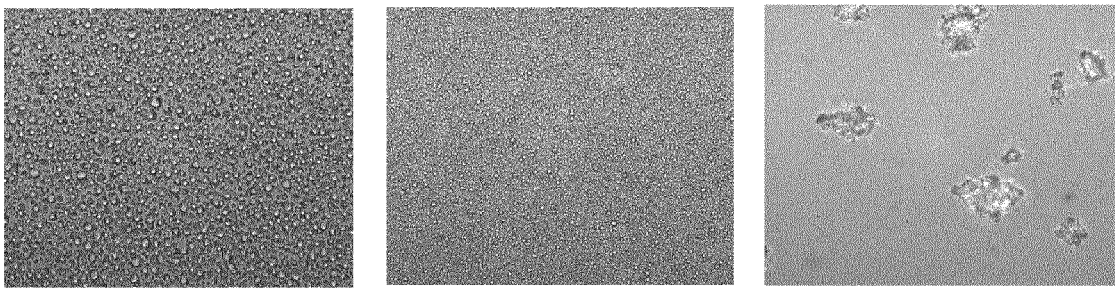
(t0) (t = 1 hour 30 mins) (t = 3 hours 30 mins)

FIG. 17B



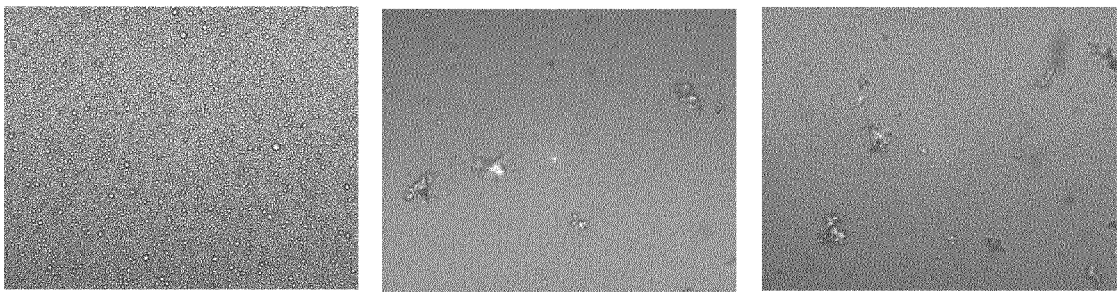
(t=0) (t = 30 mins) (t = 1 hour)

FIG. 17C



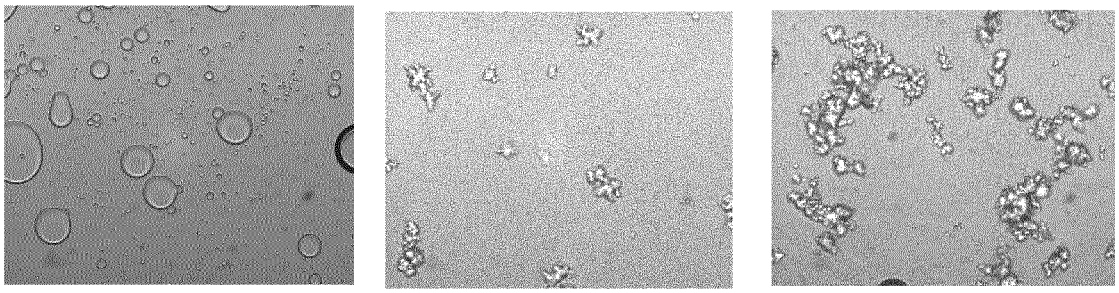
(t=0) (t = 2 hours 30 mins) (t = 4 hours)

FIG. 18A



(t=0) (t = 4 hours) (t = 4 hours 30 mins)

FIG. 18B



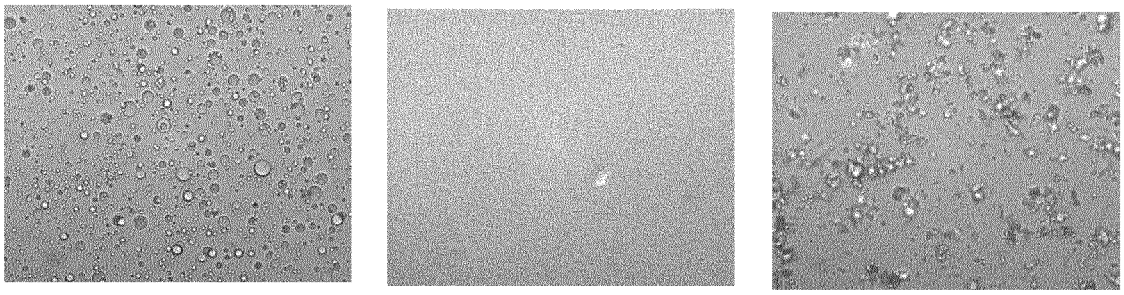
(t=0) (t = 2 hours) (t = 3 hours 30 mins)

FIG. 18C



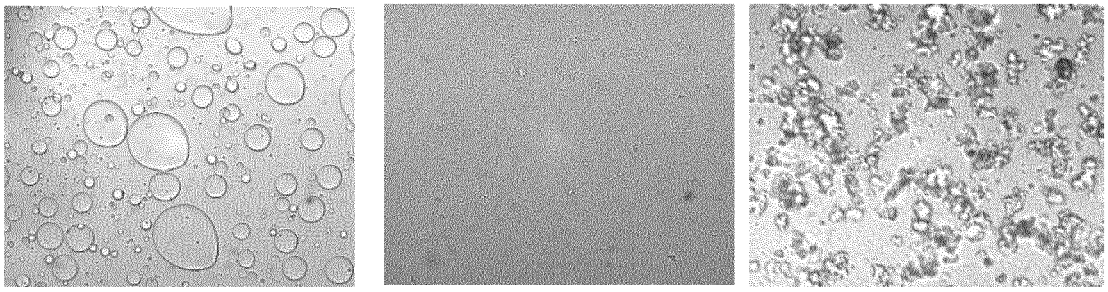
(t=0) (t = 3 hours) (t = 5 hours 30 mins)

FIG. 19A



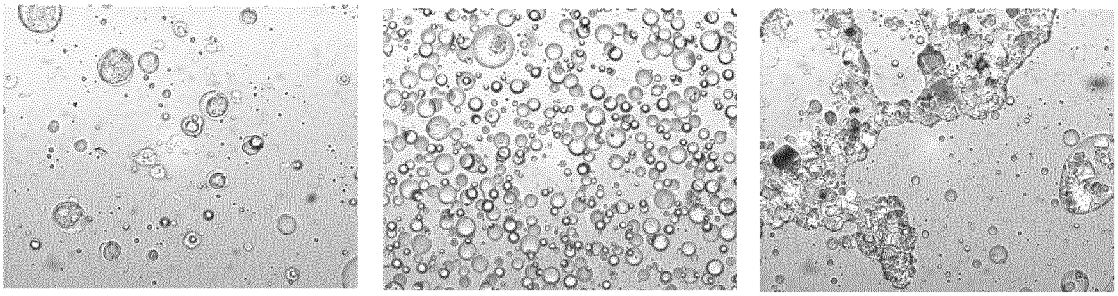
(t=0) (t = 2 hours) (t = 4 hours 30 mins)

FIG. 19B



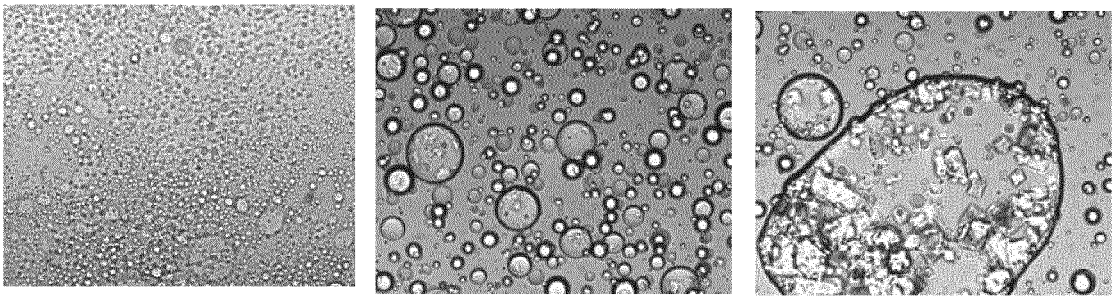
(t=0) (t = 2 hours) (t = 5 hours)

FIG. 19C



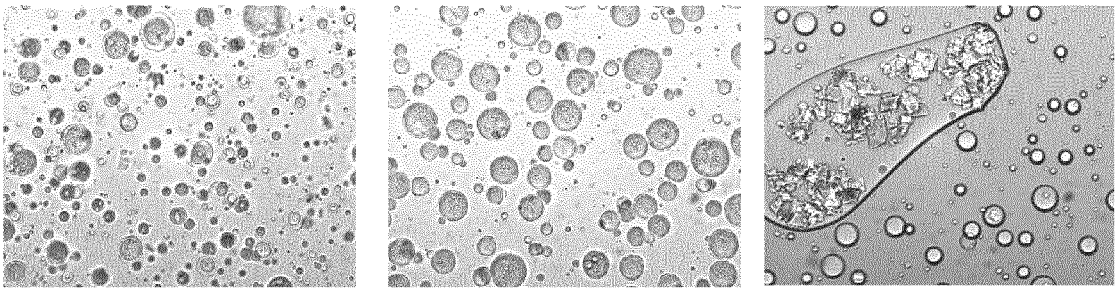
(t=0) (t = 1 hour 30 mins) (t = 3 hours)

FIG. 20A



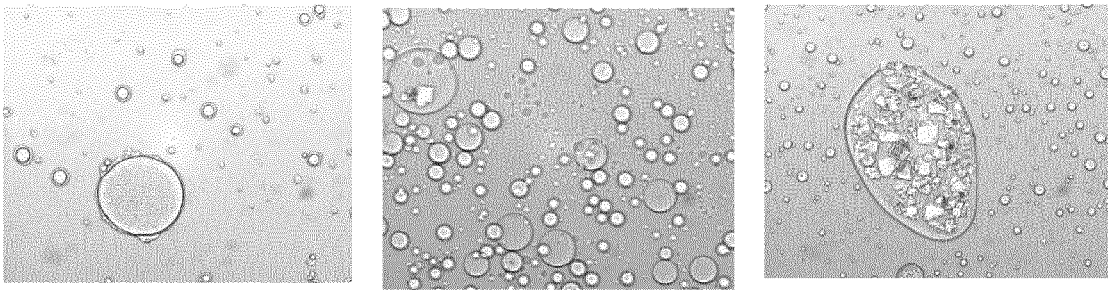
(t=0) (t = 2 hours 30 mins) (t = 4 hours 30 mins)

FIG. 20B



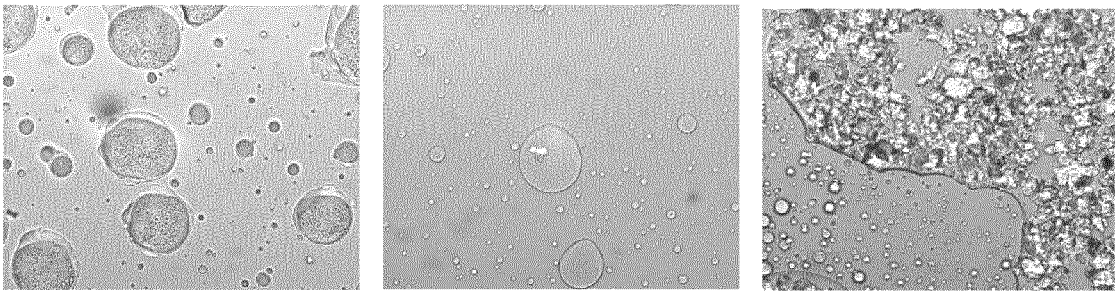
(t=0) (t = 1 hour 30 mins) (t = 3 hours 30 mins)

FIG. 20C



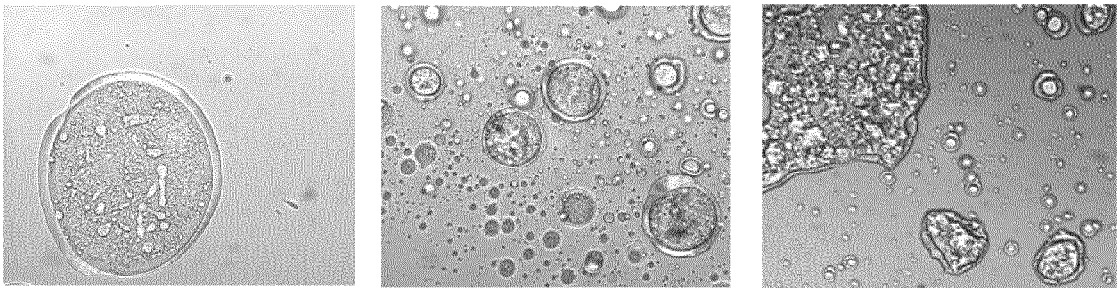
(t0) (t = 1 hour 30 mins) (t = 3 hours)

FIG. 21A



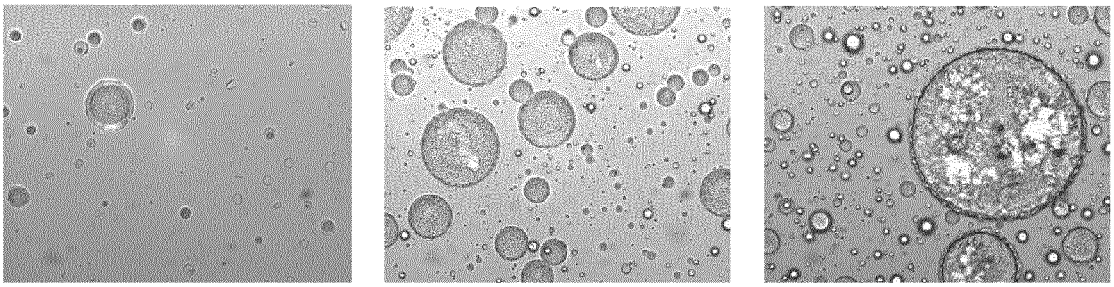
(t=0) (t = 1 hour) (t = 2 hours)

FIG. 21B



(t0) (t = 1 hour) (t = 2 hours)

FIG. 21C



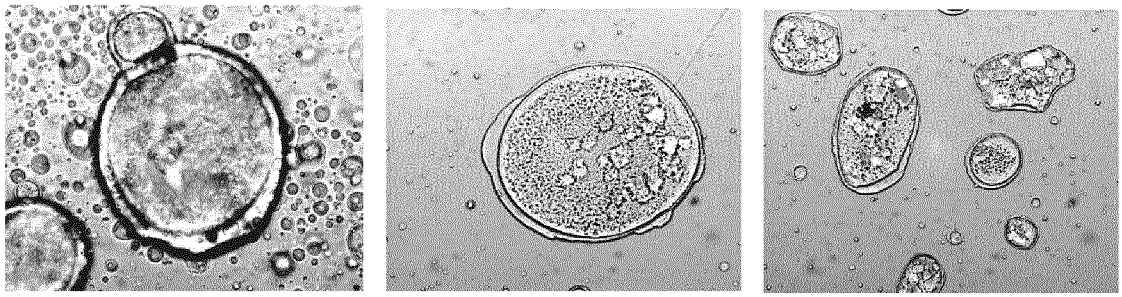
(t0) (t = 1 hour) (t = 1 hour 30 mins)

FIG. 22A



(t0) (t = 1 hour) (t = 2 hours 30 mins)

FIG. 22B



(t0) (t = 1 hour) (t = 1 hour 30 mins)

FIG. 21C