FIG. 1

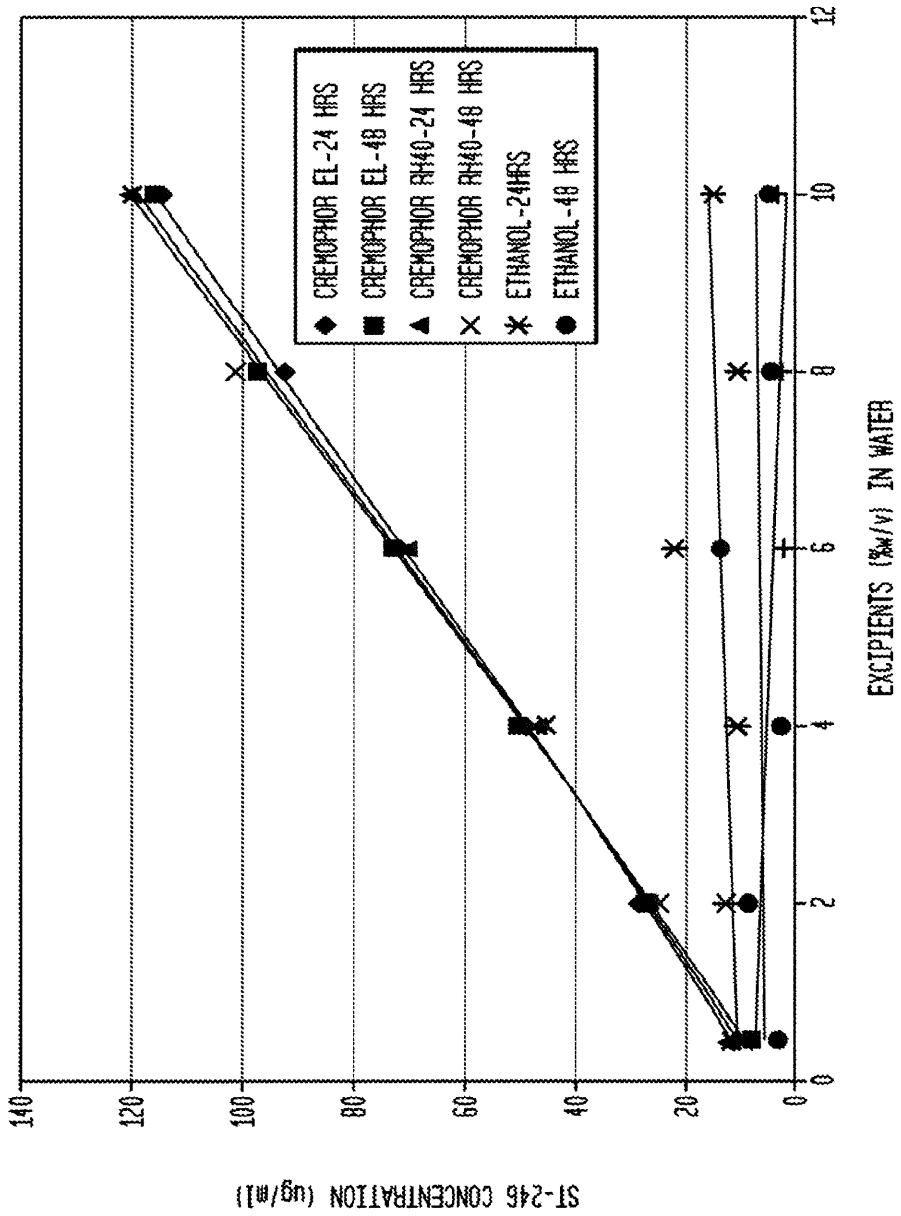

CREMOPHOR EL-24 HRS
CREMOPHOR EL-48 HRS
CREMOPHOR RH40-24 HRS
CREMOPHOR RH40-48 HRS
ETHANOL-24HRS
ETHANOL-48 HRS
ST-246 CONCENTRATION (ug/ml)
EXCIPIENTS (%w/v) IN WATER
0
20
40
60
80
100
120
140
0
2
4
6
8
10
12

FIG. 2

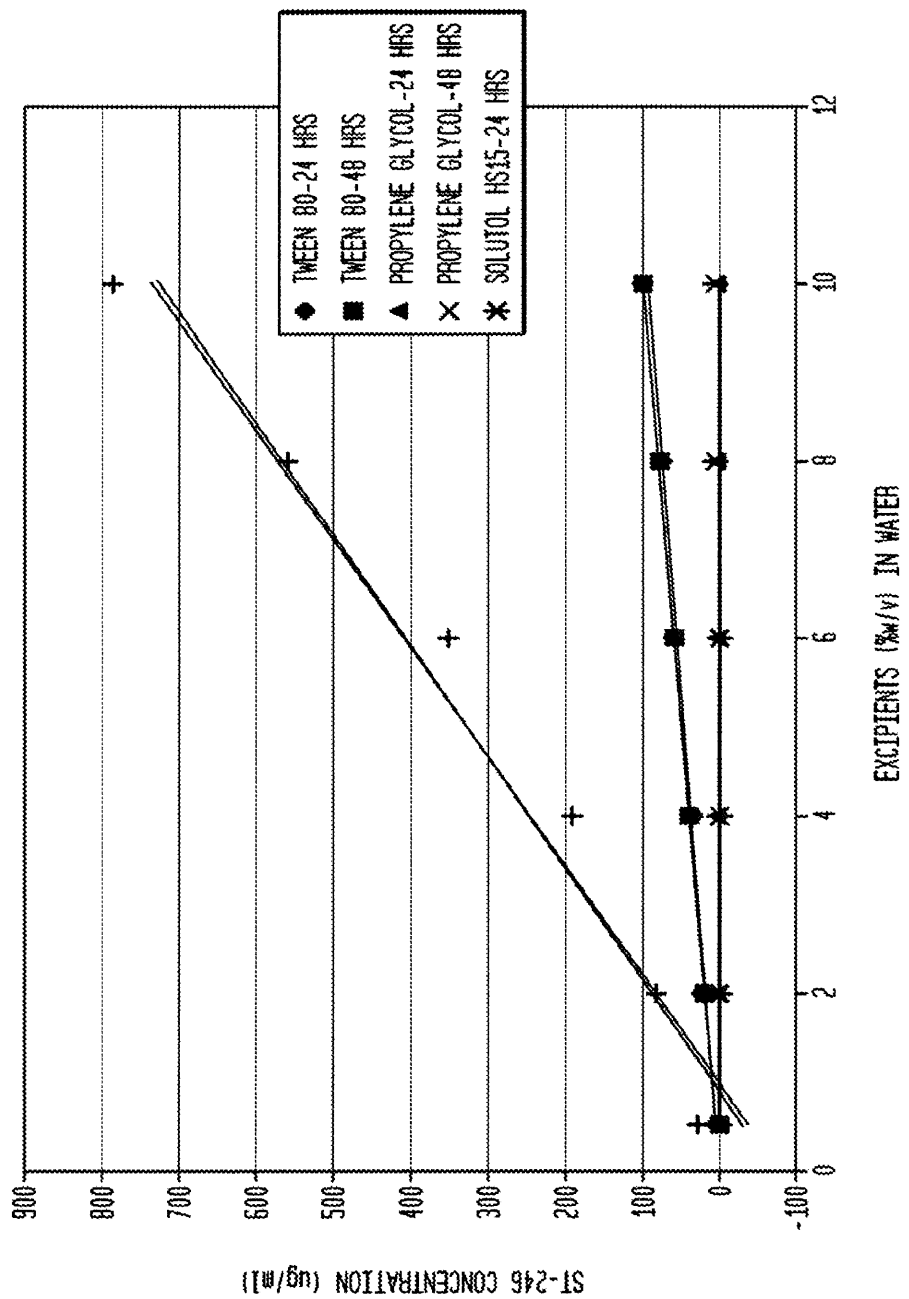

TWEEN 80-24 HRS
TWEEN 80-48 HRS
PROPYLENE GLYCOL-24 HRS
PROPYLENE GLYCOL-48 HRS
SOLUTOL HS15-24 HRS
ST-246 CONCENTRATION (ug/ml)
EXCIPIENTS (%w/v) IN WATER
900
800
700
600
500
400
300
200
100
0
-100
0
2
4
6
8
10
12

FIG. 3

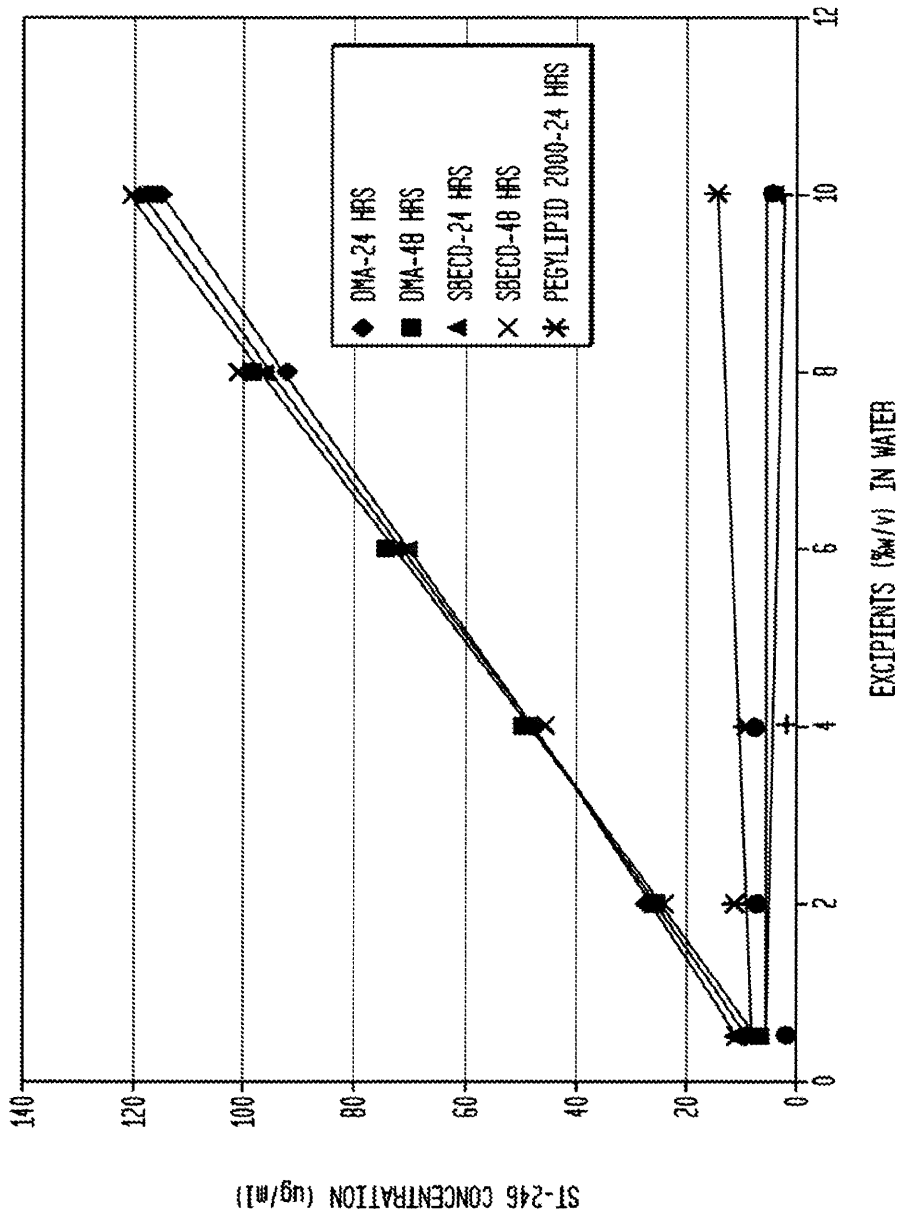

DMA-24 HRS
DMA-48 HRS
SBECD-24 HRS
SBECD-48 HRS
PEGYLIPID 2000-24 HRS
ST-246 CONCENTRATION (ug/ml)
EXCIPIENTS (%w/v) IN WATER
0
20
40
60
80
100
120
140
0
2
4
6
8
10
12

FIG. 4

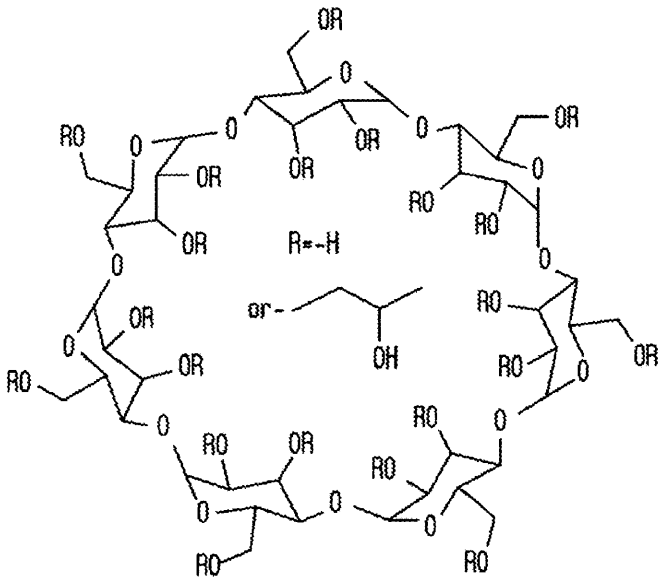


FIG. 5

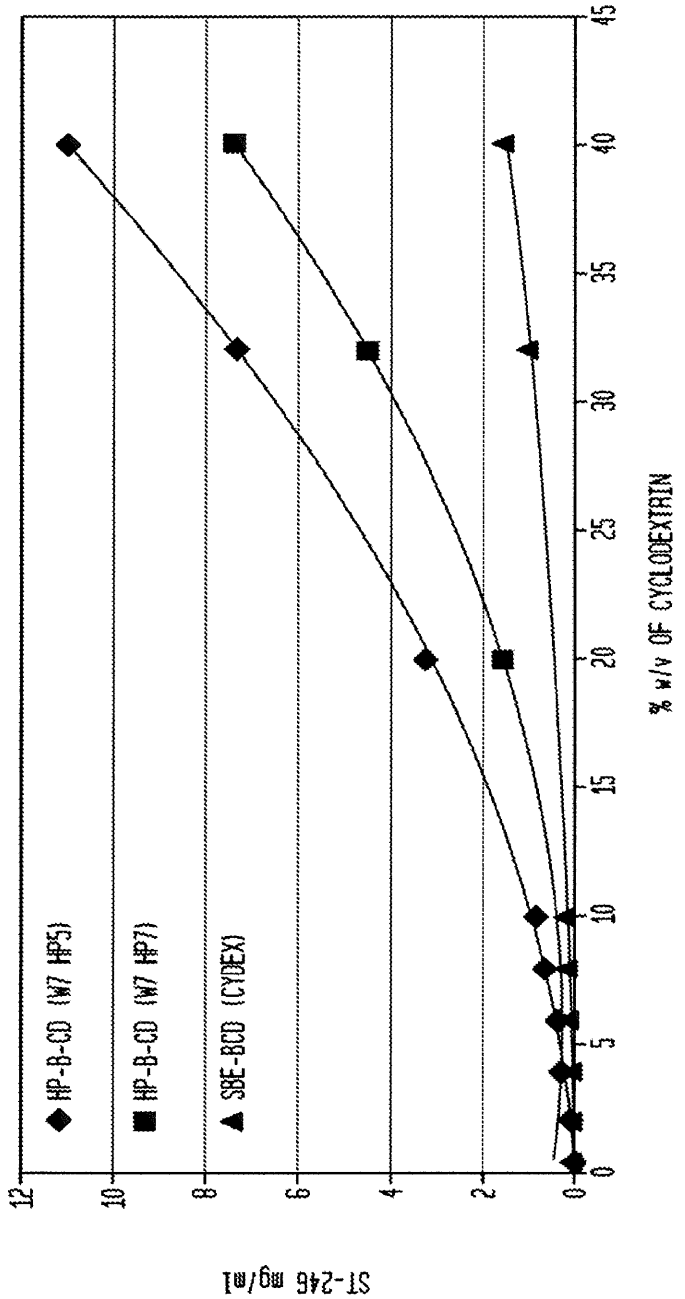

HP-B-CD (W7 HP5)
HP-B-CD (W7 HP7)
SBE-BCD (CYDEX)
ST-246 mg/ml
% w/v OF CYCLODEXTRIN
0
2
4
6
8
10
12
0
5
10
15
20
25
30
35
40
45

FIG. 6

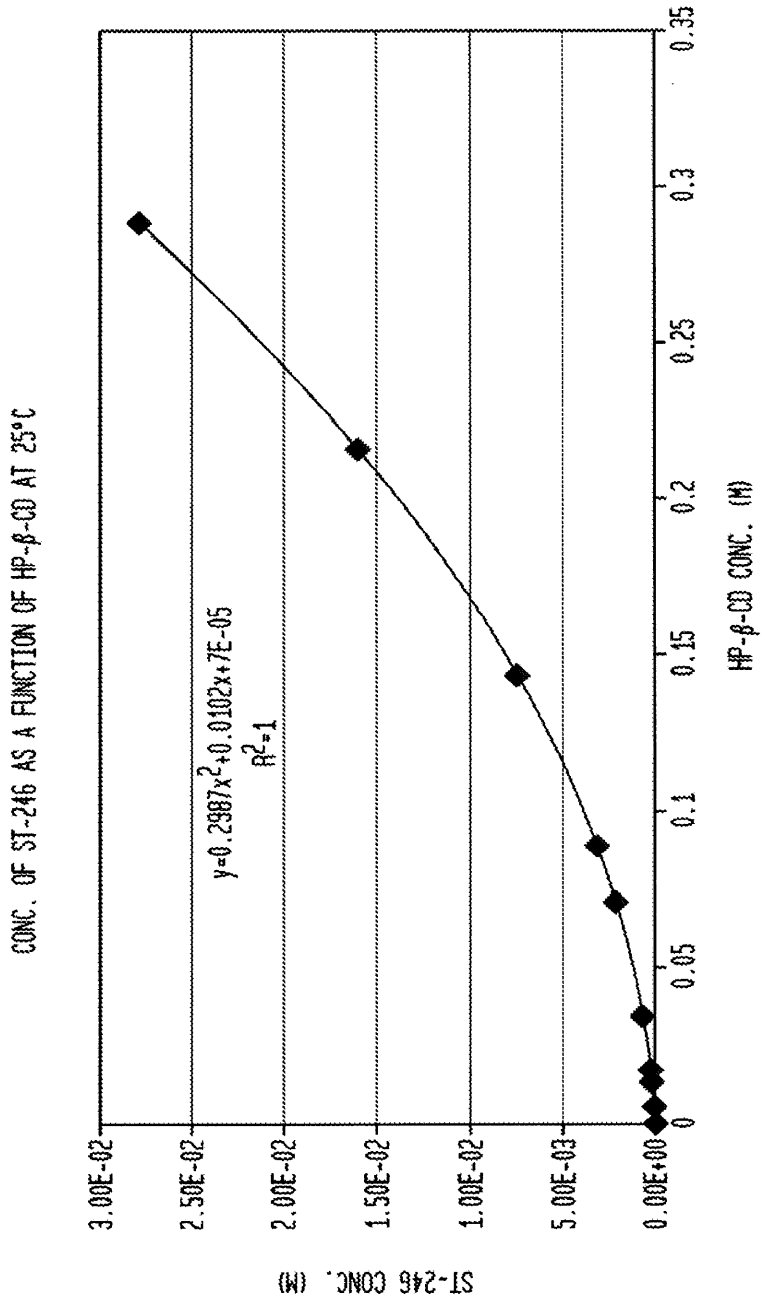
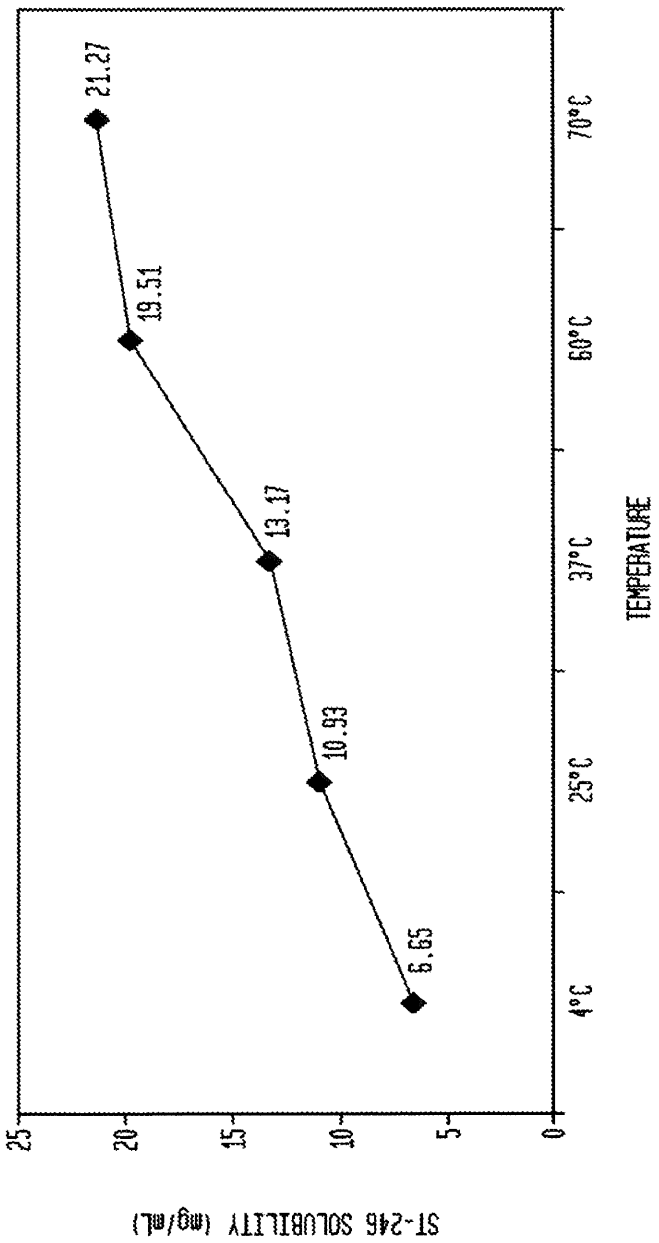

CONC. OF ST-246 AS A FUNCTION OF HP-β-CD AT 25°C
y=0.2987x²+0.0102x+7E-05
R²=1
ST-246 CONC. (M)
HP-β-CD CONC. (M)
3.00E-02
2.50E-02
2.00E-02
1.50E-02
1.00E-02
5.00E-03
0.00E+00
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35

FIG. 7


ST-246 SOLUBILITY (mg/mL)
25
20
15
10
5
0
21.27
19.51
13.17
10.93
6.65
4°C
25°C
37°C
60°C
70°C
TEMPERATURE

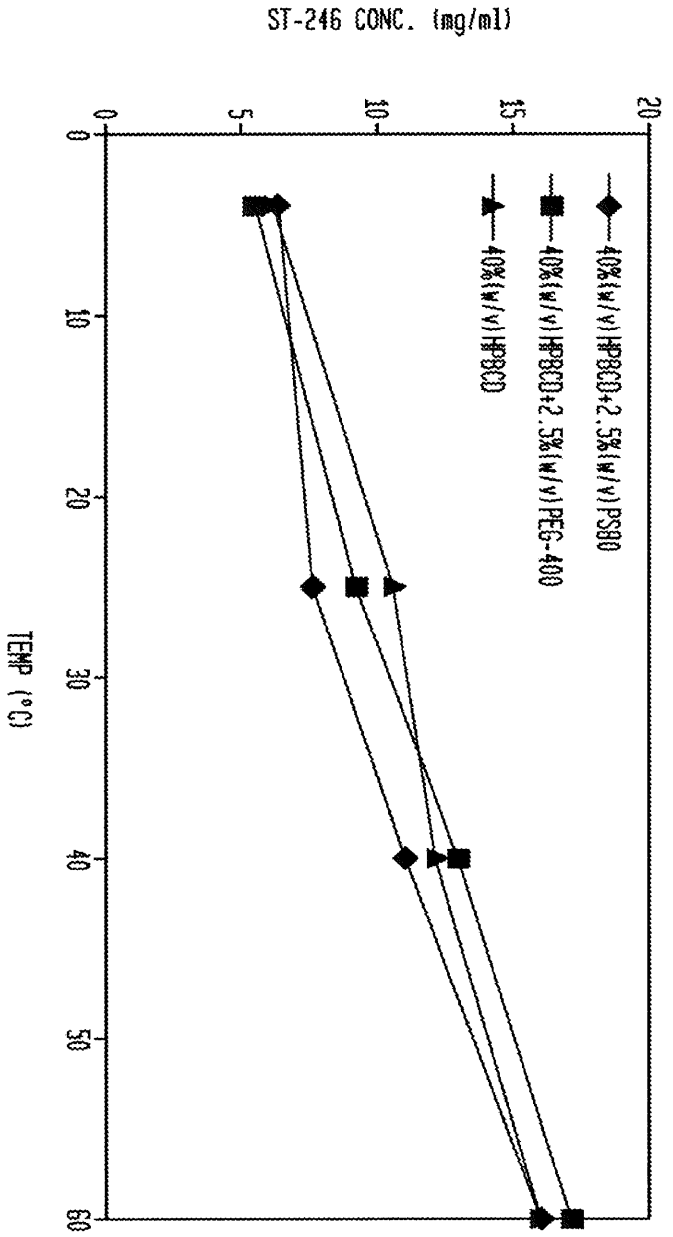

ST-246 CONC. (mg/ml)
0
5
10
15
20
0
10
20
30
40
50
60
TEMP (°C)
40%(w/v)HPBCD+2.5%(w/v)PS80
40%(w/v)HPBCD+2.5%(w/v)PEG-400
40%(w/v)HPBCD

FIG. 8

FIG. 9

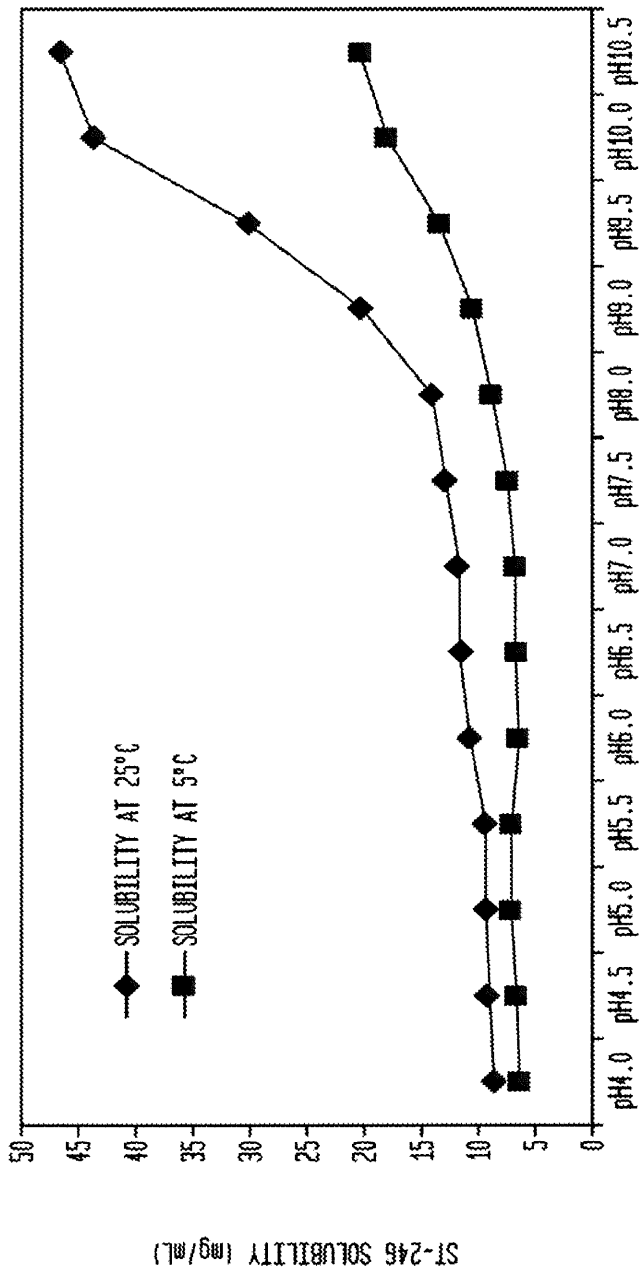

ST-246 SOLUBILITY (mg/mL)
0
5
10
15
20
25
30
35
40
45
50
SOLUBILITY AT 25°C
SOLUBILITY AT 5°C
pH4.0
pH4.5
pH5.0
pH5.5
pH6.0
pH6.5
pH7.0
pH7.5
pH8.0
pH9.0
pH9.5
pH10.0
pH10.5

FIG. 10

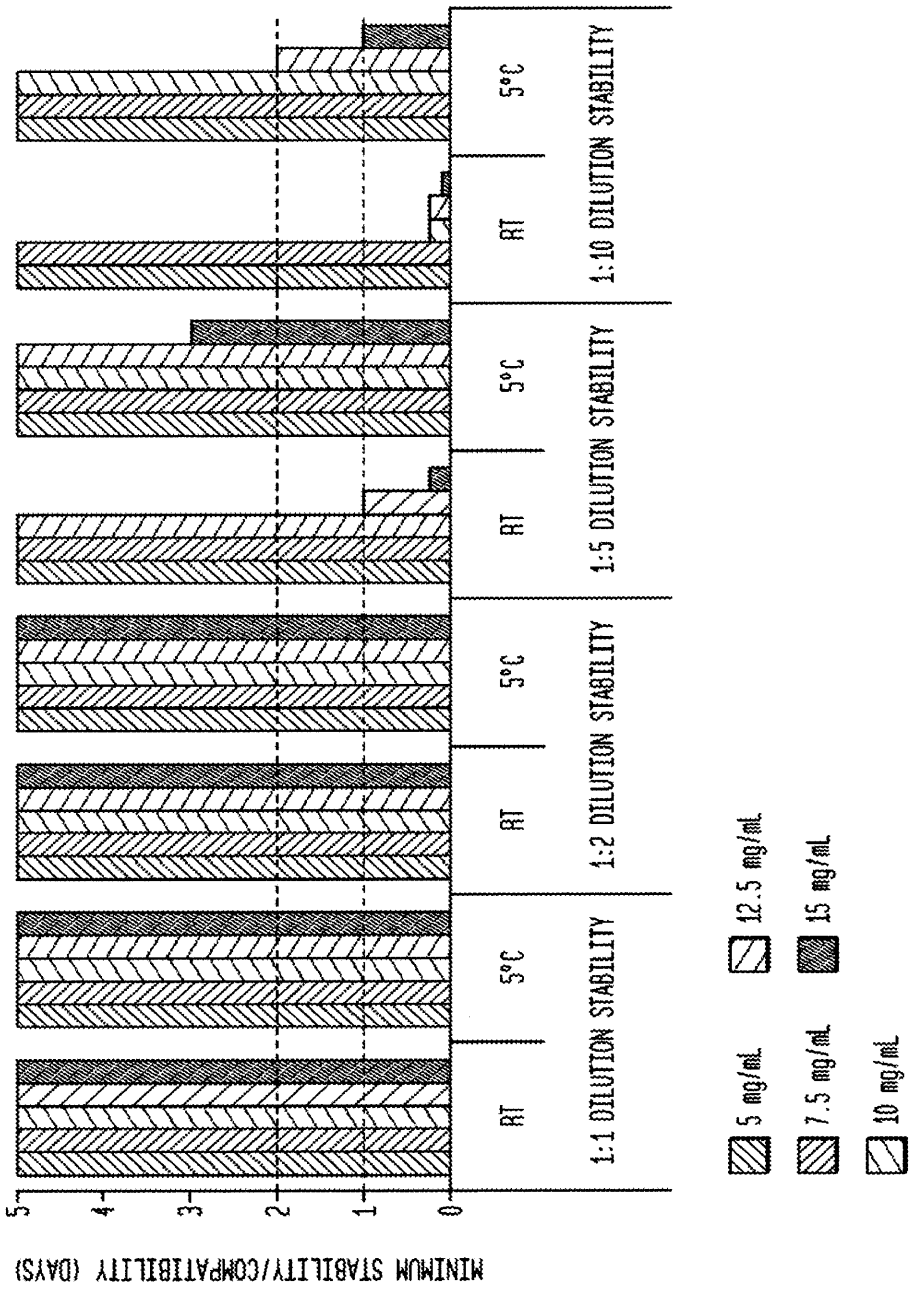

MINIMUM STABILITY/COMPATIBILITY (DAYS)
0
1
2
3
4
5
RT
5°C
1:1 DILUTION STABILITY
RT
5°C
1:2 DILUTION STABILITY
RT
5°C
1:5 DILUTION STABILITY
RT
5°C
1:10 DILUTION STABILITY
5 mg/mL
7.5 mg/mL
10 mg/mL
12.5 mg/mL
15 mg/mL

FIG. 11

PHARMACOKINETIC PROFILE OF ST-246 IV FORMULATION IN MONKEYS

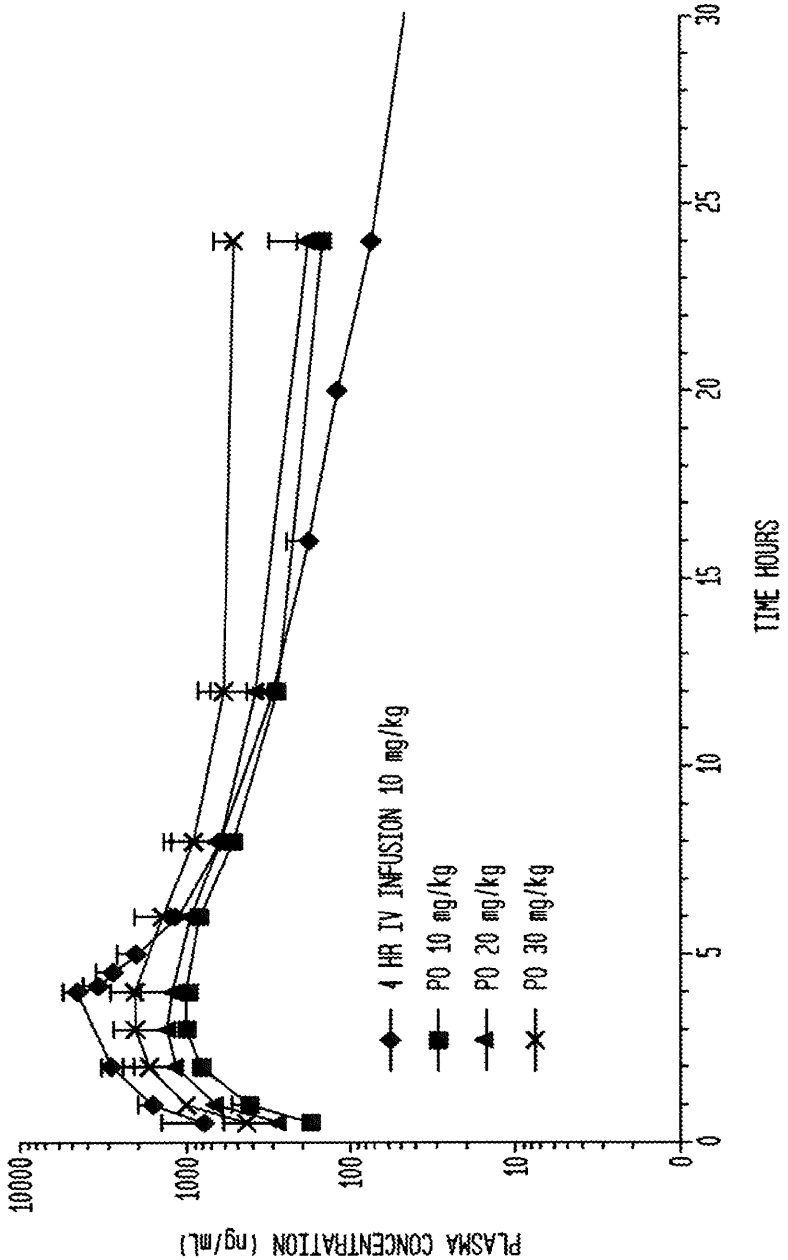


FIG. 12

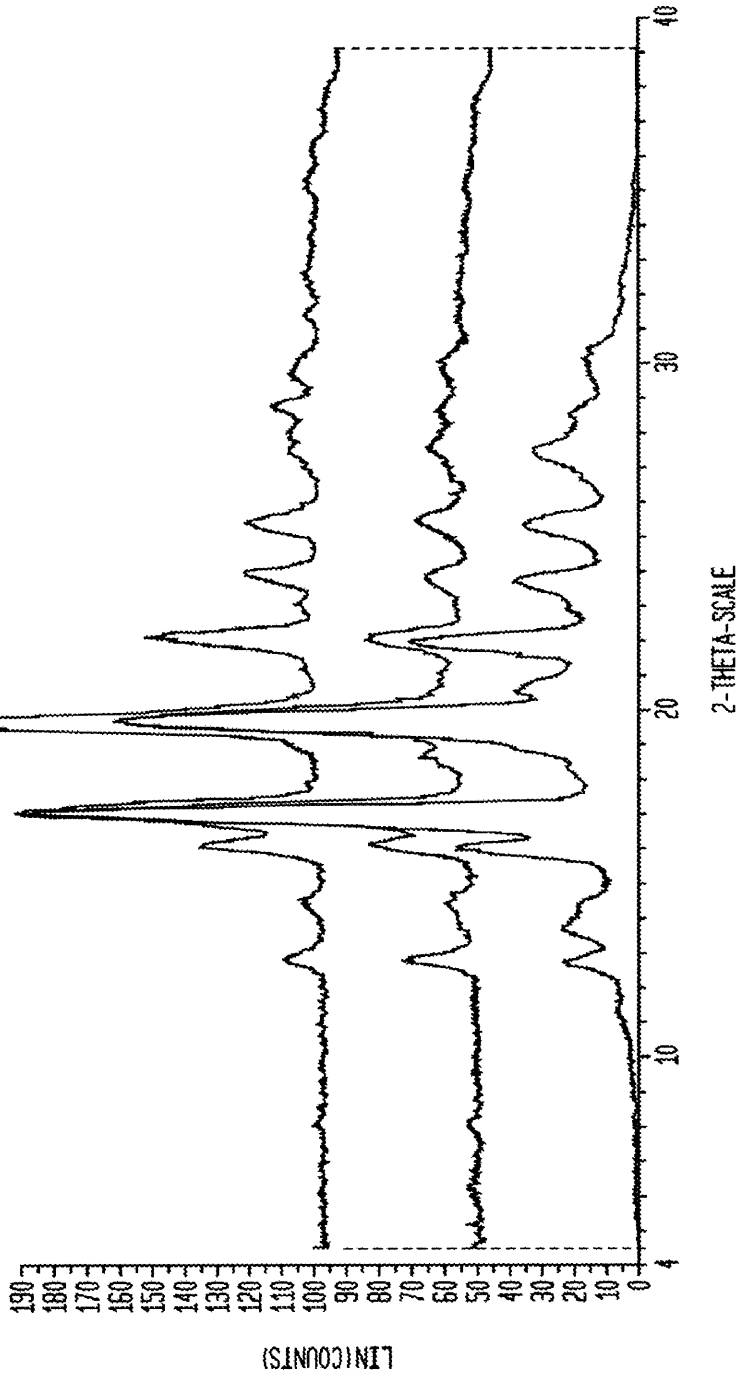

LIN(COUNTS)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
4
10
20
30
40
2-THETA-SCALE

FIG. 13

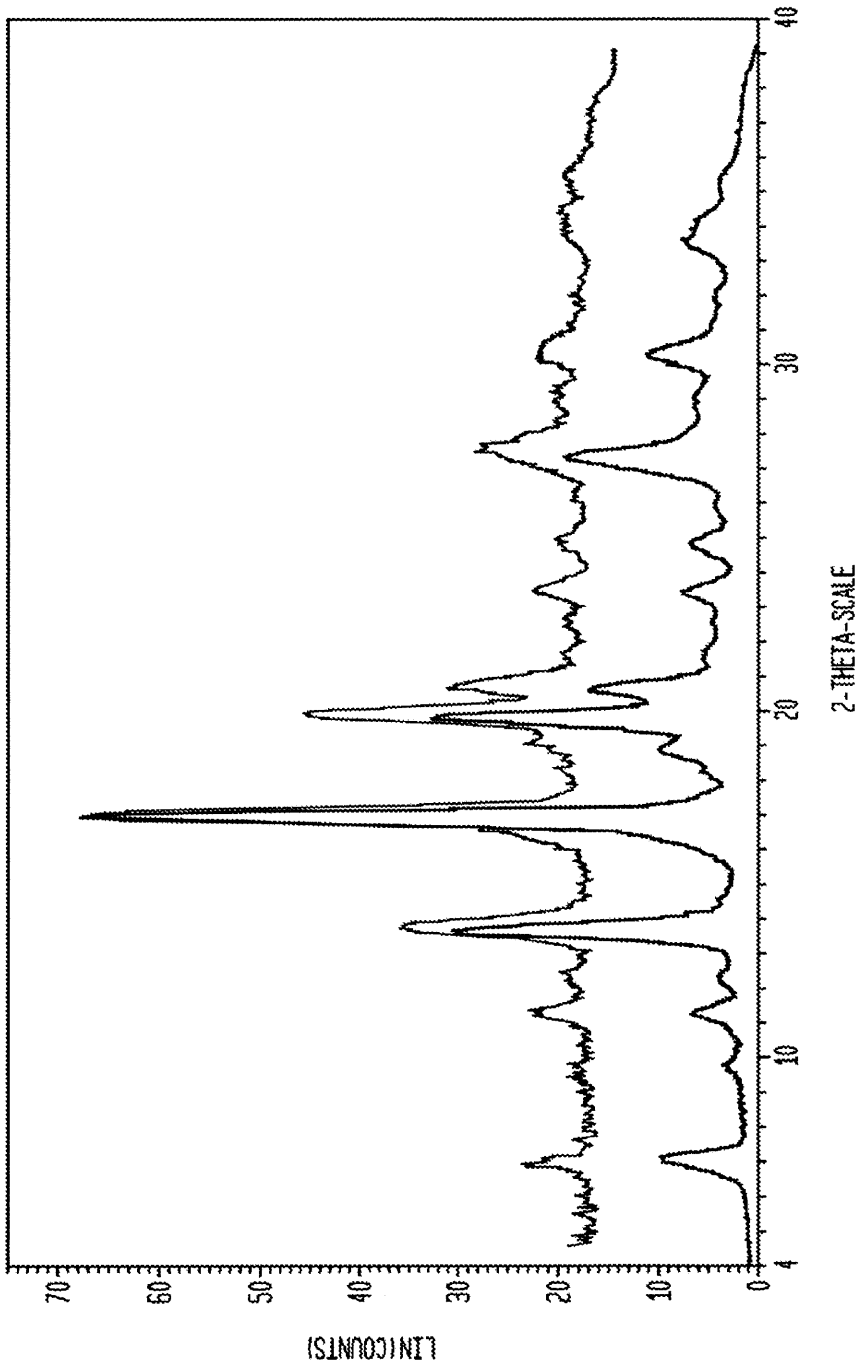


FIG. 14

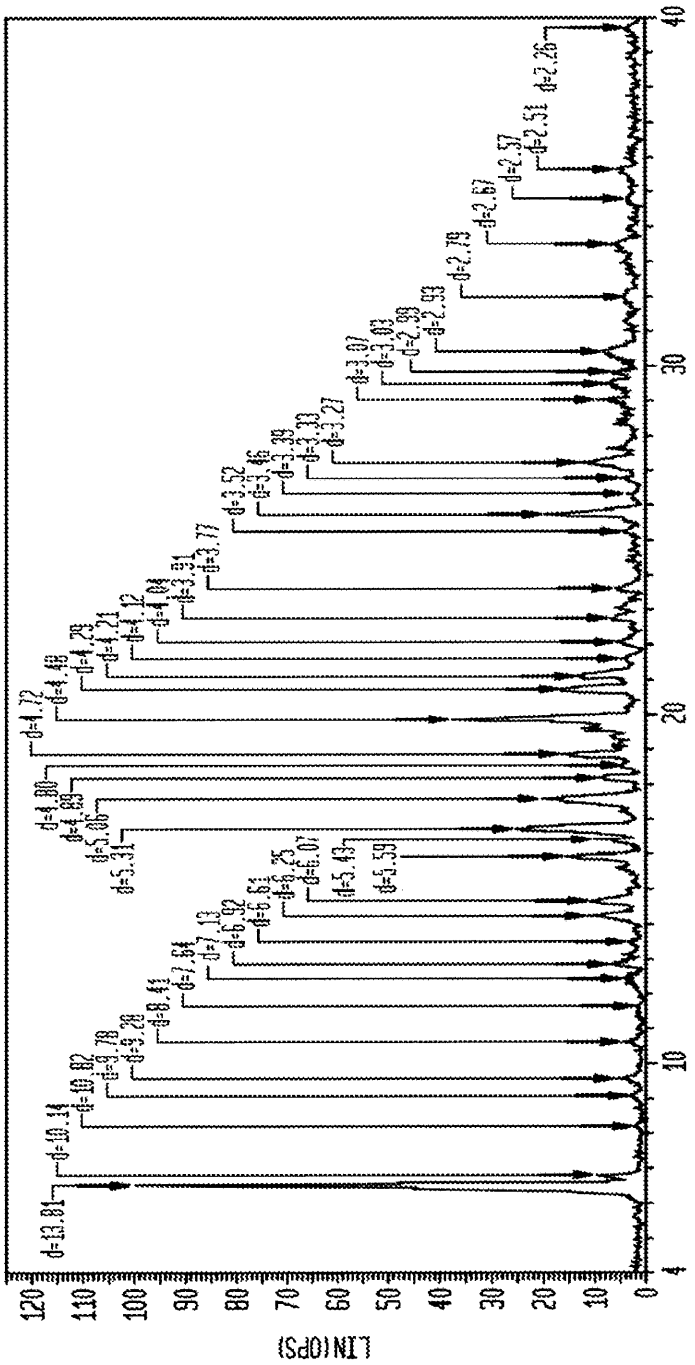

d=13.81
d=10.14
d=10.82
d=9.78
d=9.28
d=8.41
d=7.84
d=7.13
d=6.92
d=6.61
d=6.25
d=6.07
d=5.43
d=5.59
d=5.31
d=5.05
d=4.83
d=4.80
d=4.72
d=4.48
d=4.29
d=4.21
d=4.12
d=4.04
d=3.91
d=3.77
d=3.52
d=3.46
d=3.39
d=3.33
d=3.27
d=3.07
d=3.03
d=2.98
d=2.93
d=2.79
d=2.67
d=2.57
d=2.51
d=2.26
LIN(CPS)
2-THETA-SCALE

FIG. 15

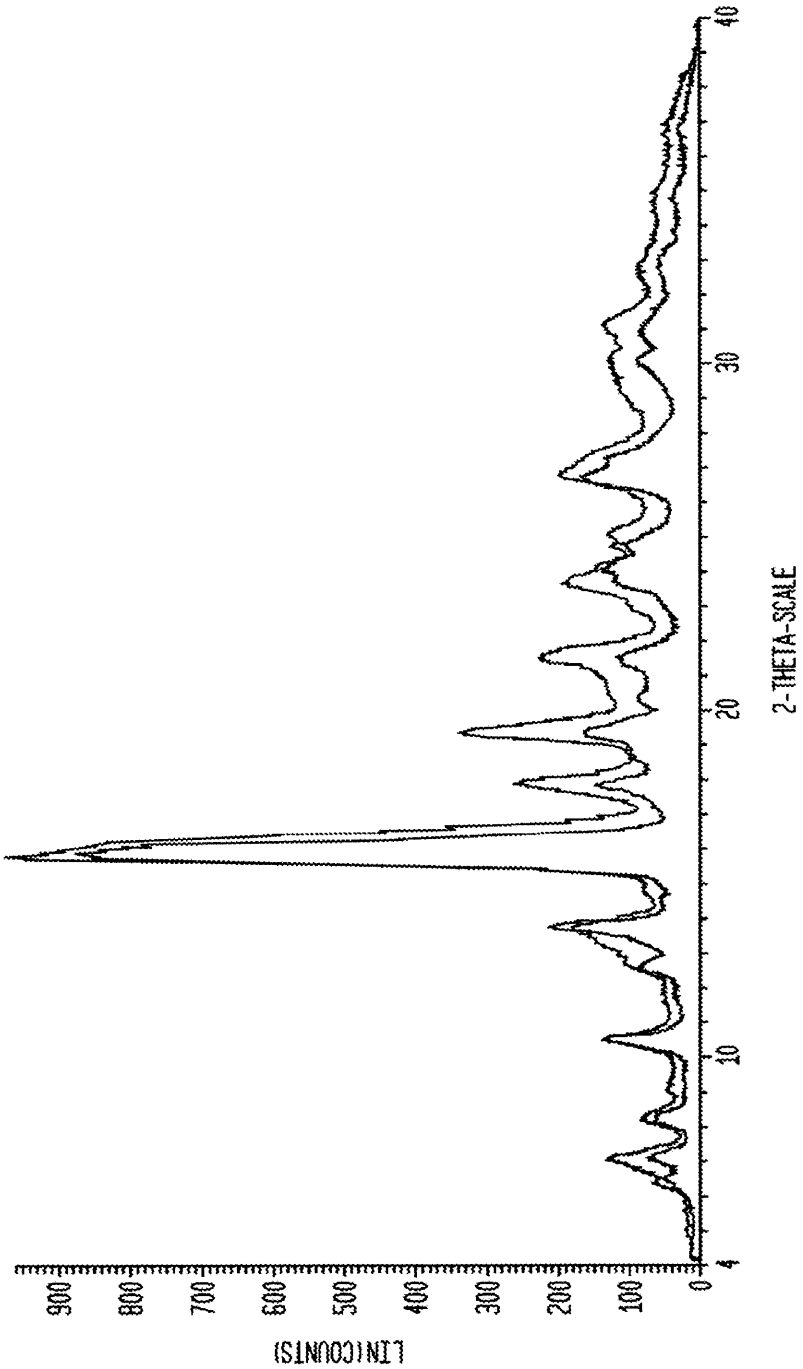

LIN(COUNTS)
900
800
700
600
500
400
300
200
100
0
4
10
20
30
40
2-THETA-SCALE

FIG. 16

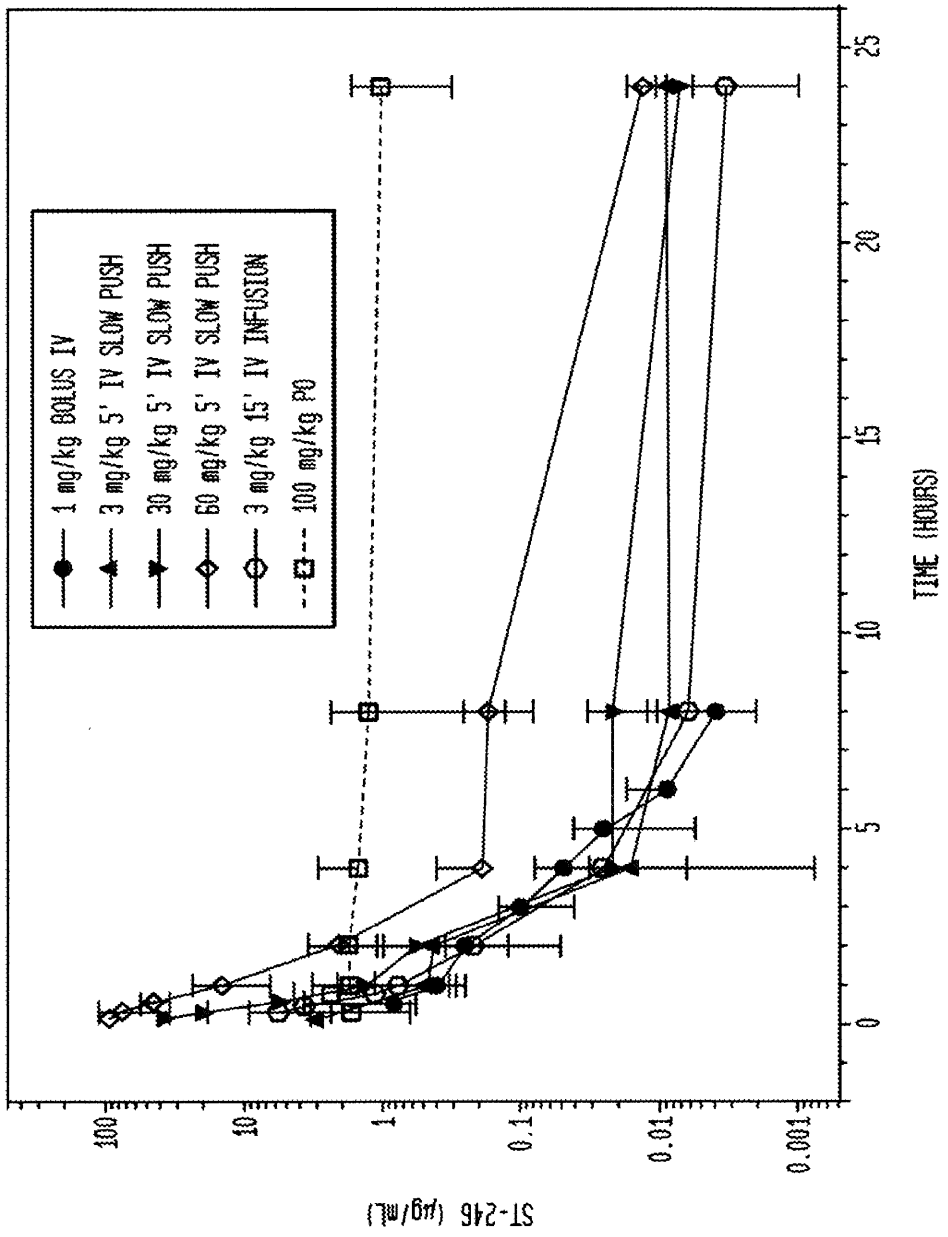

1 mg/kg BOLUS IV
3 mg/kg 5' IV SLOW PUSH
30 mg/kg 5' IV SLOW PUSH
60 mg/kg 5' IV SLOW PUSH
3 mg/kg 15' IV INFUSION
100 mg/kg PO
ST-246 (µg/mL)
100
10
1
0.1
0.01
0.001
0
5
10
15
20
25
TIME (HOURS)

FIG. 17

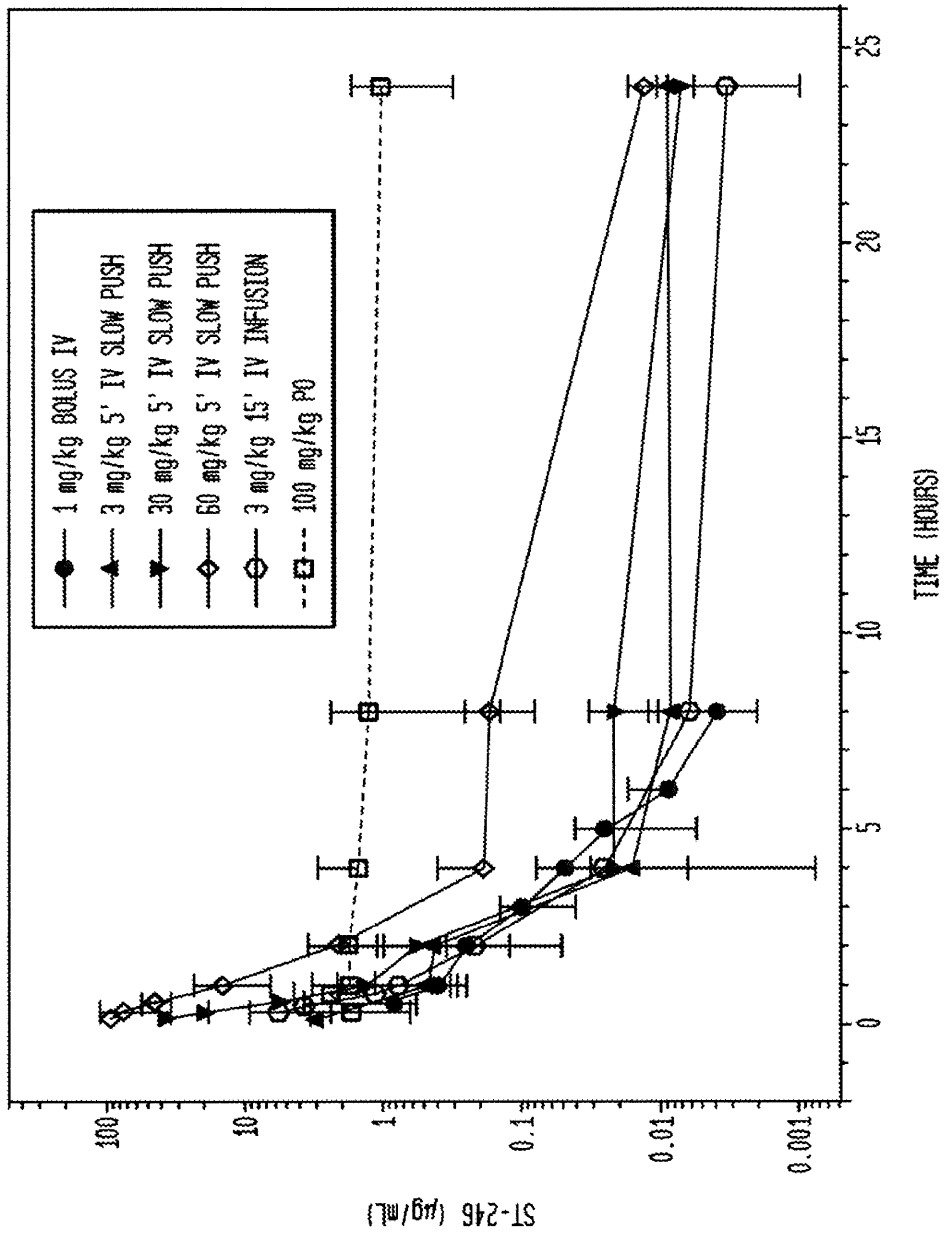

1 mg/kg BOLUS IV
3 mg/kg 5' IV SLOW PUSH
30 mg/kg 5' IV SLOW PUSH
60 mg/kg 5' IV SLOW PUSH
3 mg/kg 15' IV INFUSION
100 mg/kg PO
ST-246 (µg/mL)
100
10
1
0.1
0.01
0.001
0
5
10
15
20
25
TIME (HOURS)

FIG. 18

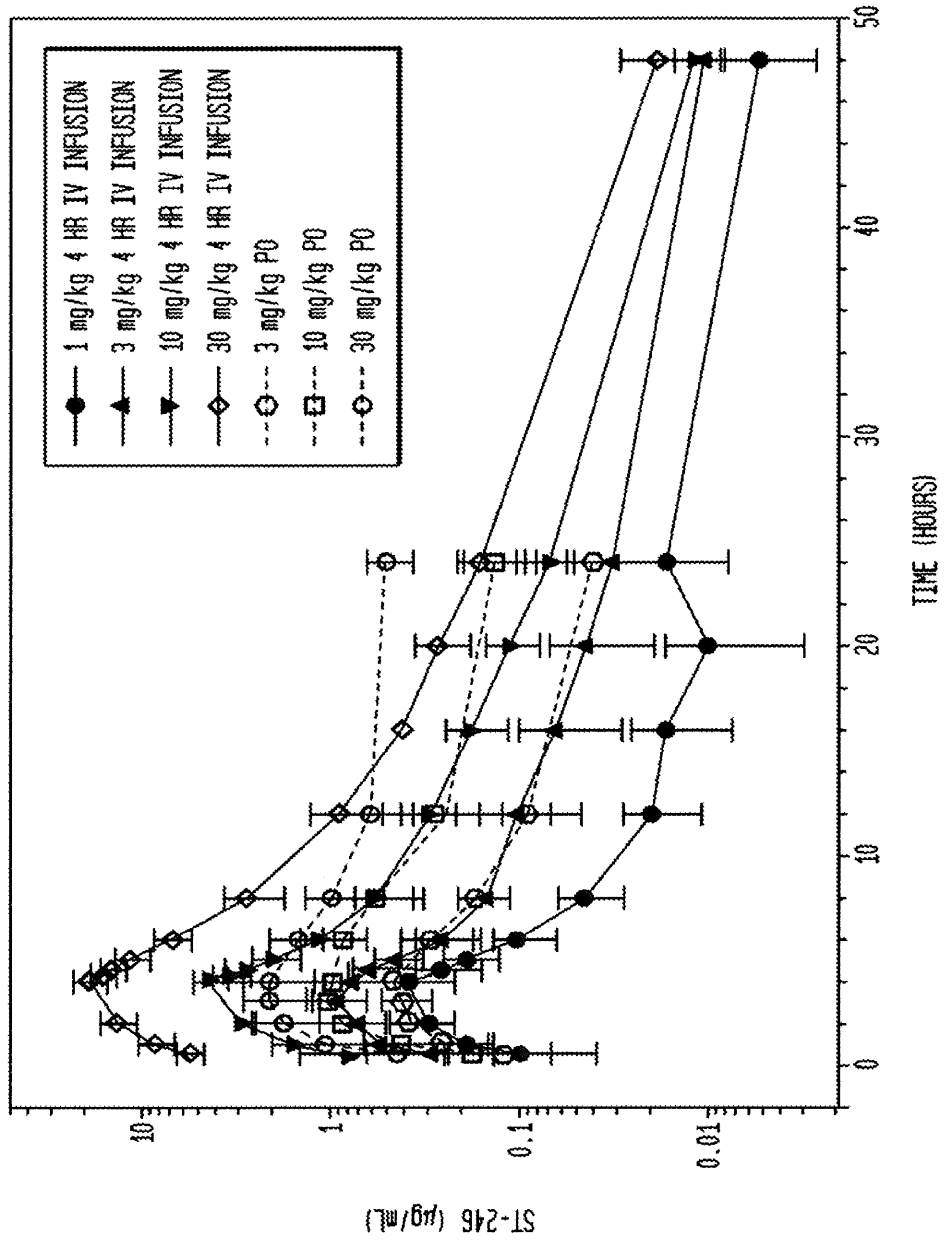

1 mg/kg 4 HR IV INFUSION
3 mg/kg 4 HR IV INFUSION
10 mg/kg 4 HR IV INFUSION
30 mg/kg 4 HR IV INFUSION
3 mg/kg PO
10 mg/kg PO
30 mg/kg PO
ST-246 (μg/mL)
10
1
0.1
0.01
0
10
20
30
40
50
TIME (HOURS)

FIG. 19

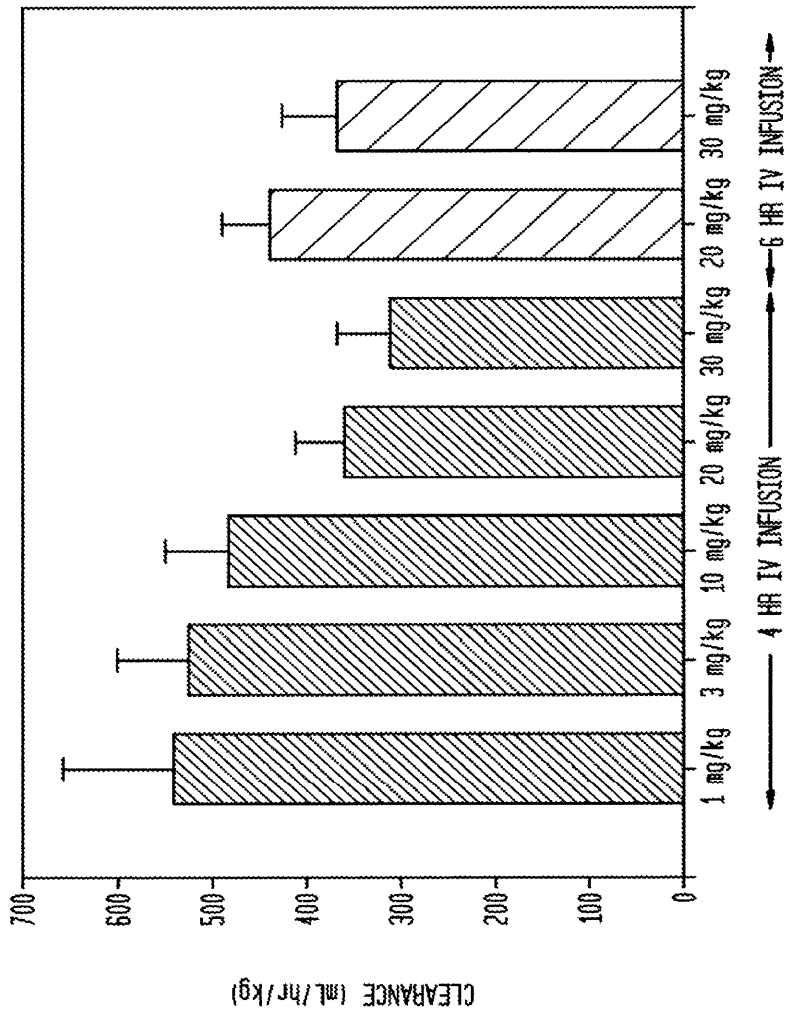

CLEARANCE (mL/hr/kg)
700
600
500
400
300
200
100
0
1 mg/kg
3 mg/kg
10 mg/kg
20 mg/kg
30 mg/kg
20 mg/kg
30 mg/kg
4 HR IV INFUSION
6 HR IV INFUSION

FIG. 20A

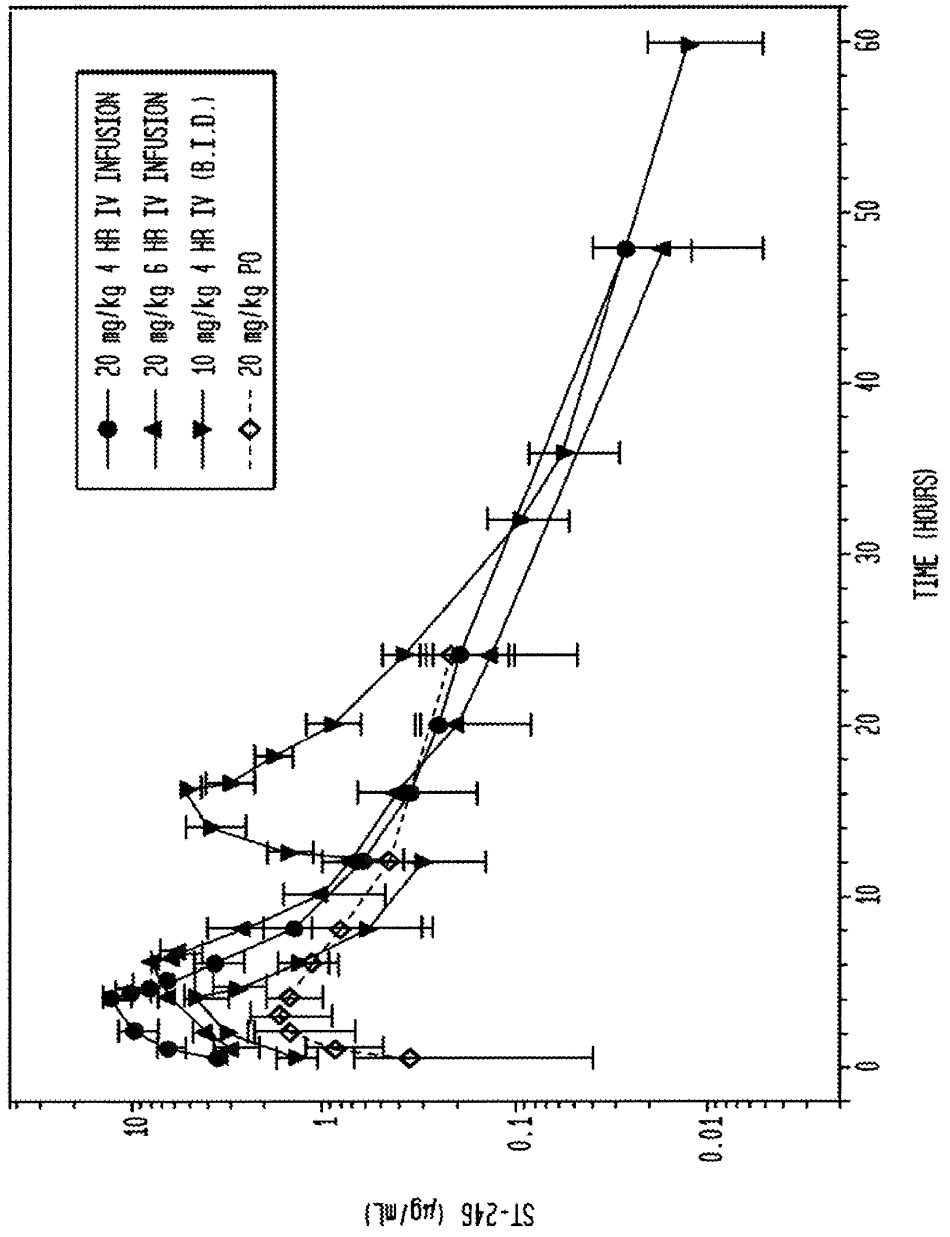
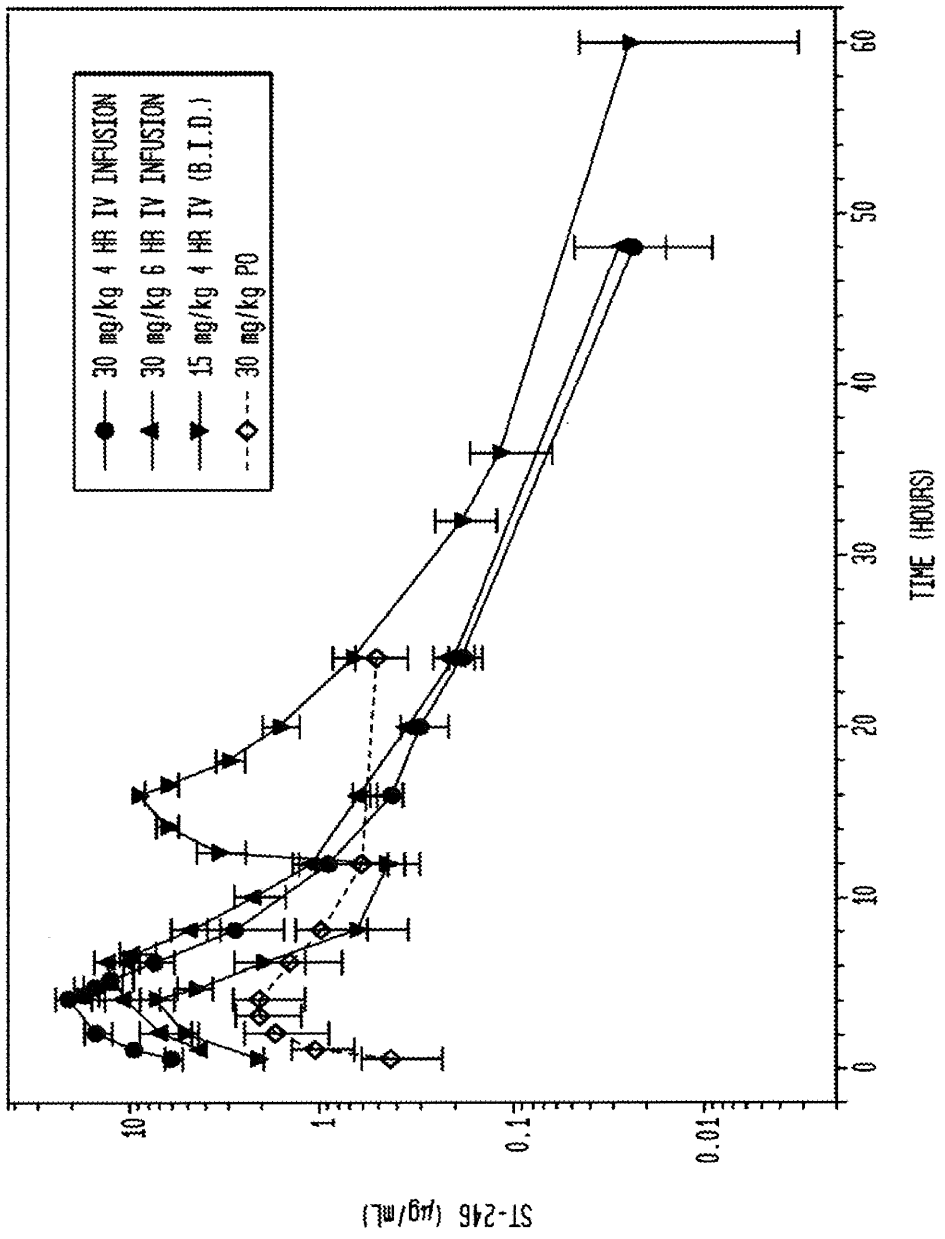

20 mg/kg 4 HR IV INFUSION
20 mg/kg 6 HR IV INFUSION
10 mg/kg 4 HR IV (B.I.D.)
20 mg/kg PO
ST-246 (μg/mL)
10
1
0.1
0.01
0
10
20
30
40
50
60
TIME (HOURS)

FIG. 20B


30 mg/kg 4 HR IV INFUSION
30 mg/kg 6 HR IV INFUSION
15 mg/kg 4 HR IV (B.I.D.)
30 mg/kg PO
ST-246 (μg/mL)
10
1
0.1
0.01
0
10
20
30
40
50
60
TIME (HOURS)