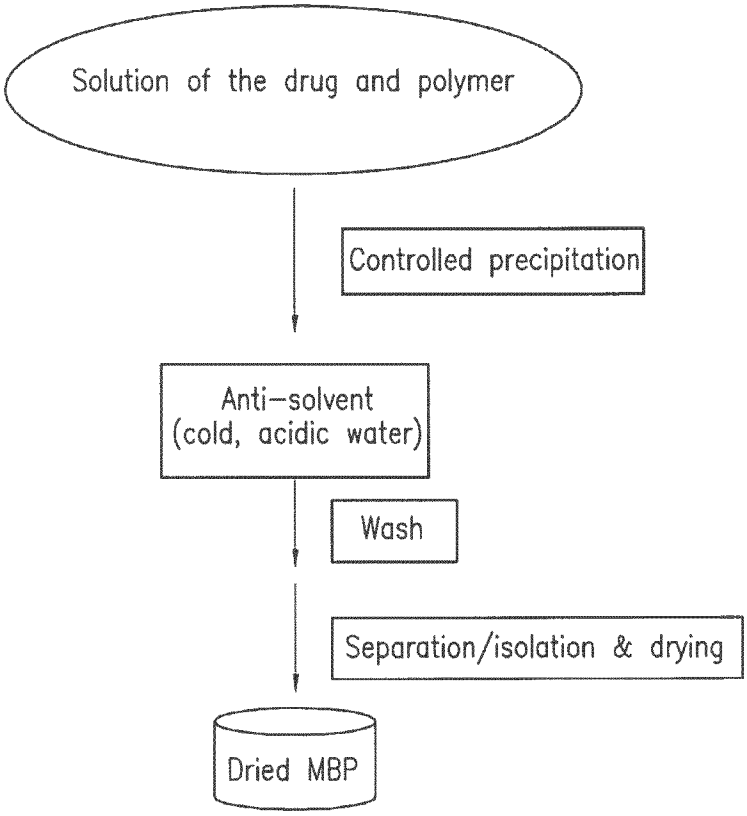

Solution of the drug and polymer
Controlled precipitation
Anti–solvent
(cold, acidic water)
Wash
Separation/isolation & drying
Dried MBP

FIG. 1

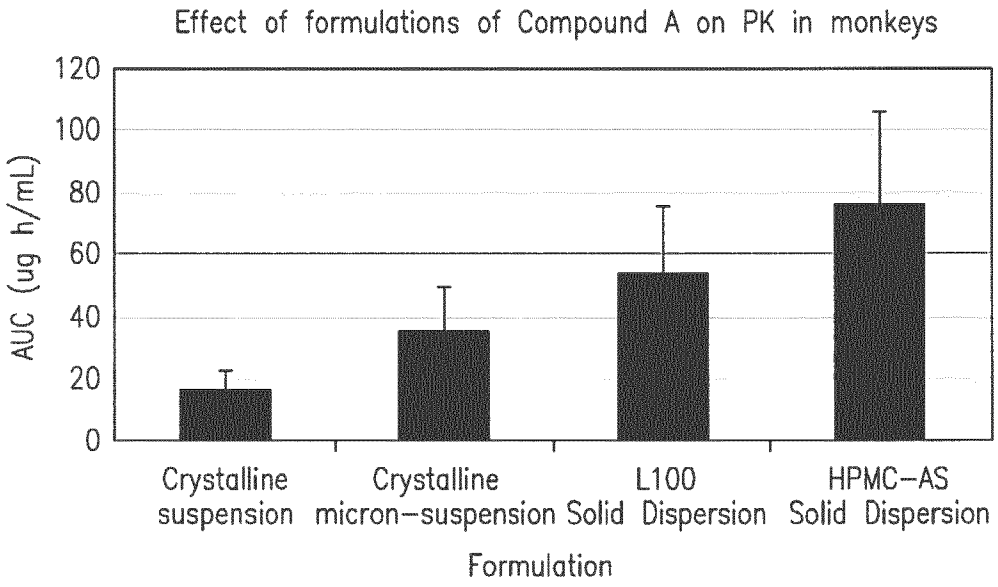

Effect of formulations of Compound A on PK in monkeys
AUC (ug h/mL)
120
100
80
60
40
20
0
Crystalline suspension
Crystalline micron-suspension
L100 Solid Dispersion
HPMC-AS Solid Dispersion
Formulation

FIG. 2

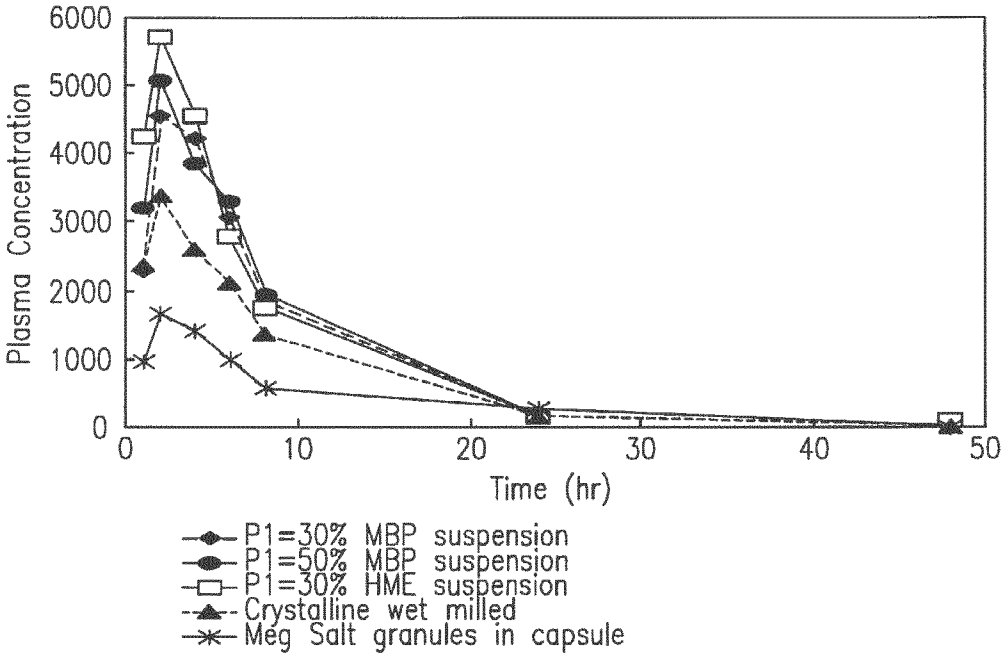

Plasma Concentration
6000
5000
4000
3000
2000
1000
0
0
10
20
30
40
50
Time (hr)
P1=30% MBP suspension
P1=50% MBP suspension
P1=30% HME suspension
Crystalline wet milled
Meg Salt granules in capsule

FIG. 3

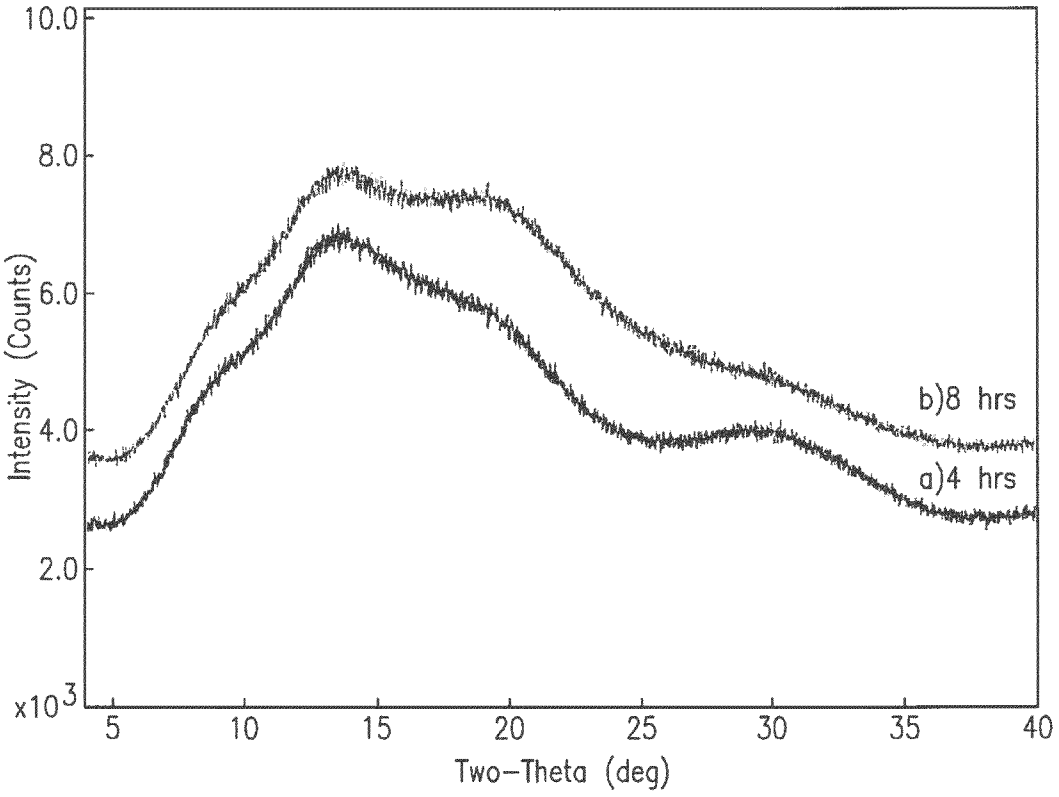

10.0
8.0
6.0
4.0
2.0
x10^3
Intensity (Counts)
5
10
15
20
25
30
35
40
Two-Theta (deg)
b)8 hrs
a)4 hrs

FIG. 4

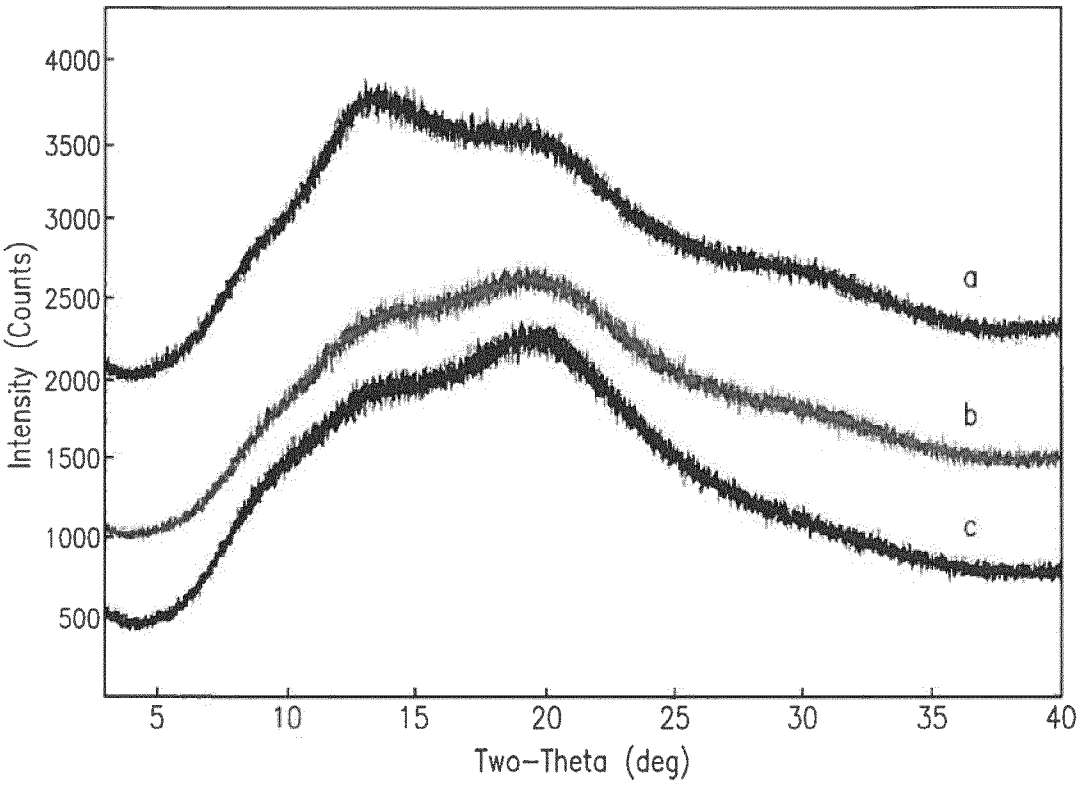

4000
3500
3000
2500
2000
1500
1000
500
Intensity (Counts)
5
10
15
20
25
30
35
40
Two-Theta (deg)
a
b
c

FIG. 5

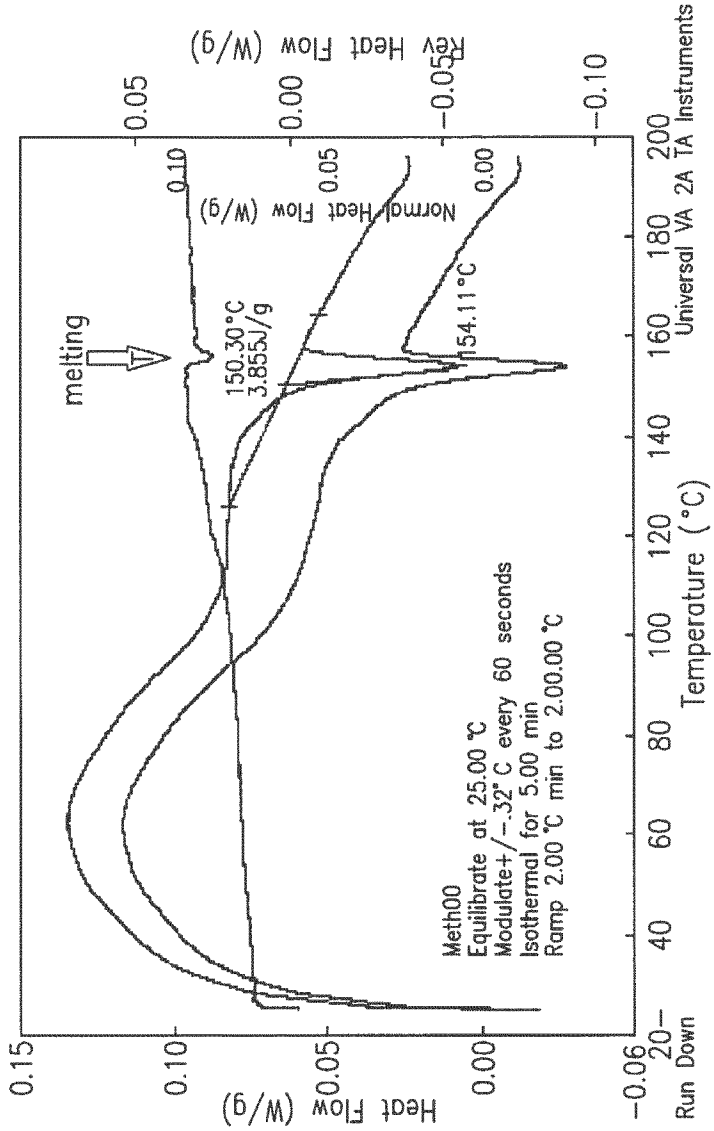

Rev Heat Flow (W/g)
0.05
0.00
−0.05
−0.10
Normal Heat Flow (W/g)
0.10
0.05
0.00
melting
150.30°C
3.855J/g
154.11°C
Meth00
Equilibrate at 25.00 °C
Modulate+/−.32° C every 60 seconds
Isothermal for 5.00 min
Ramp 2.00 °C min to 2.00.00 °C
Heat Flow (W/g)
0.15
0.10
0.05
0.00
−0.06
Run Down
20
40
60
80
100
120
140
160
180
200
Temperature (°C)
Universal VA 2A TA Instruments

FIG. 6a

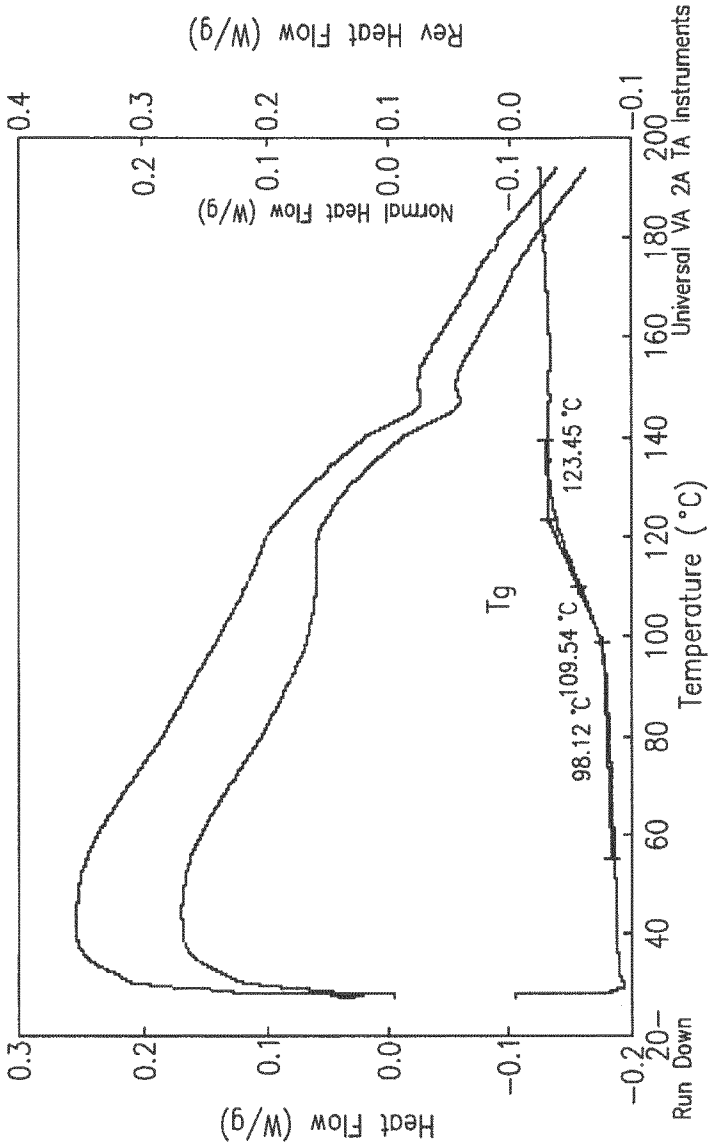

Rev Heat Flow (W/g)
Normal Heat Flow (W/g)
Heat Flow (W/g)
Temperature (°C)
Universal VA 2A TA Instruments
Run Down
Tg
98.12 °C
109.54 °C
123.45 °C

FIG. 6b

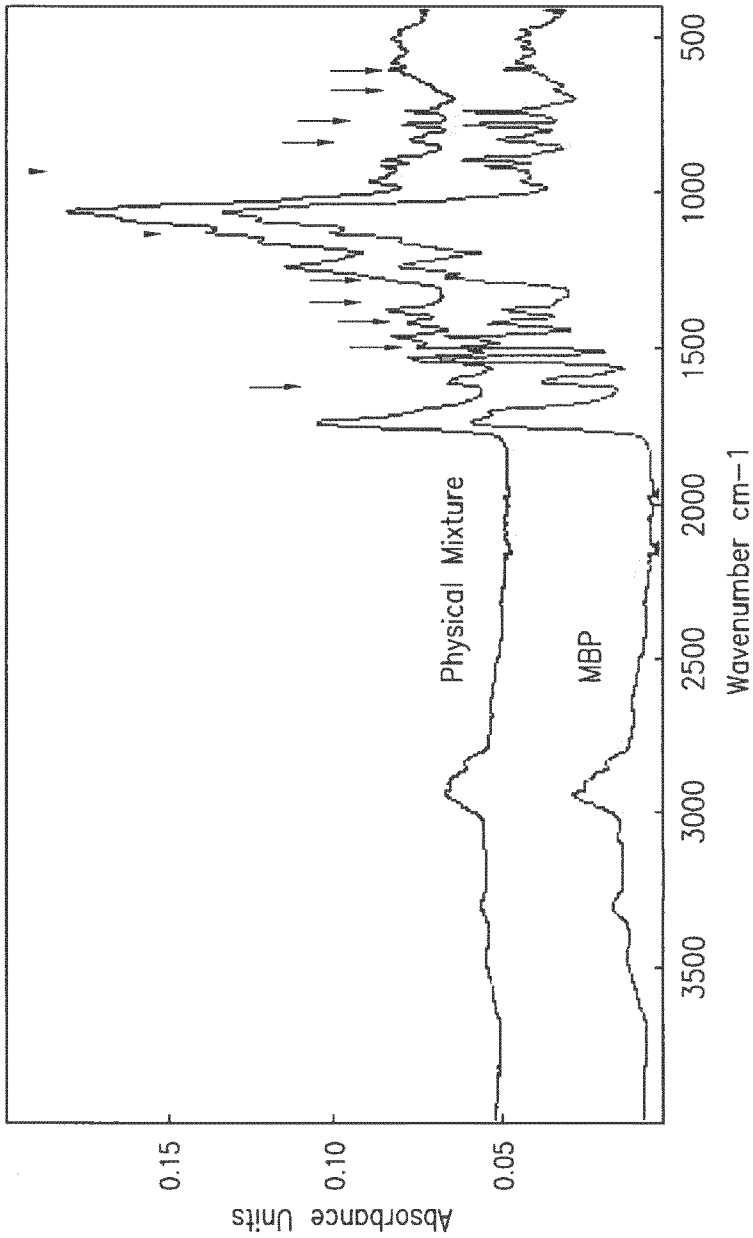

Absorbance Units
0.15
0.10
0.05
Physical Mixture
MBP
3500
3000
2500
2000
1500
1000
500
Wavenumber cm−1

FIG. 7

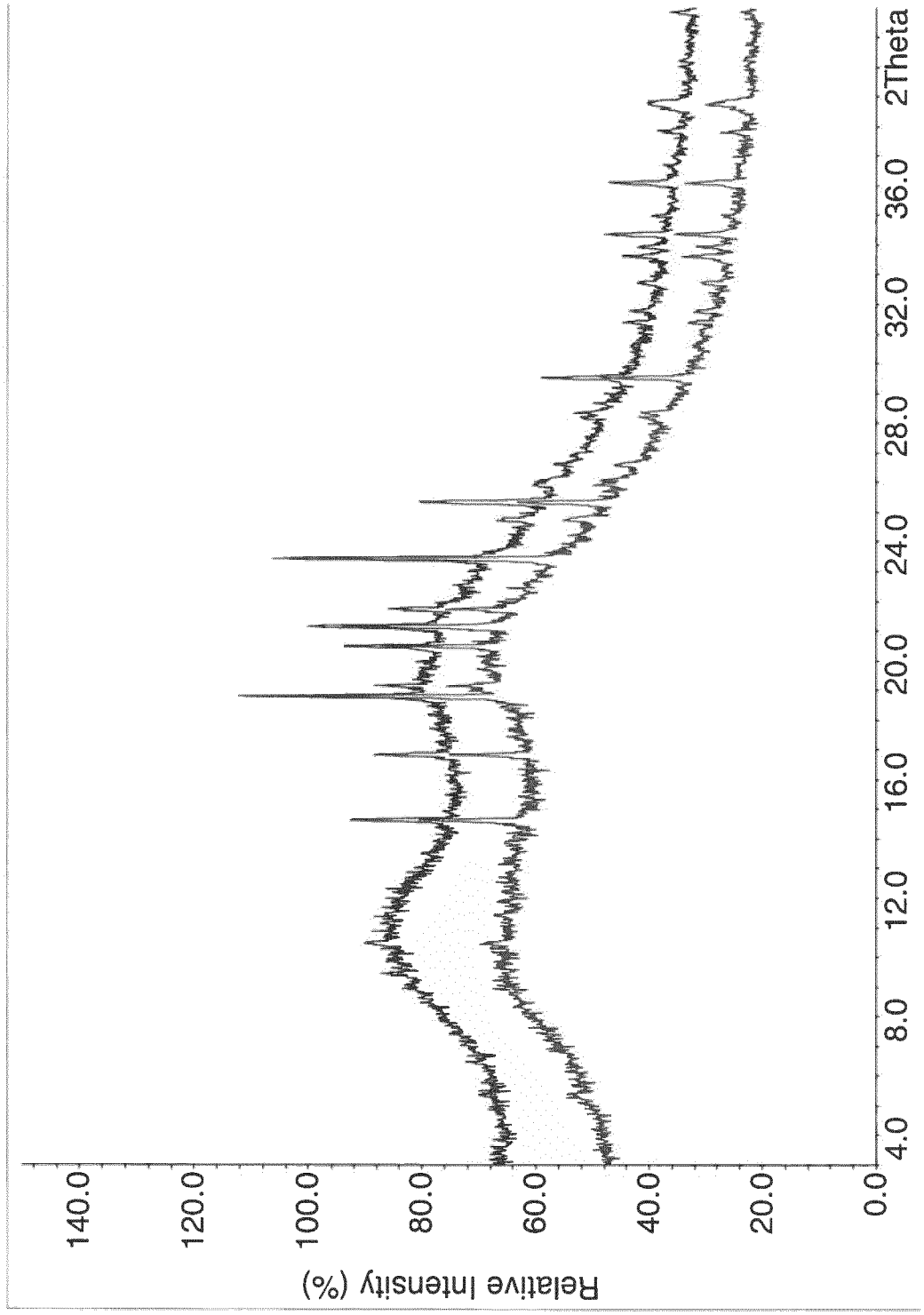

Relative Intensity (%)
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
4.0
8.0
12.0
16.0
20.0
24.0
28.0
32.0
36.0
2Theta

Fig. 8a

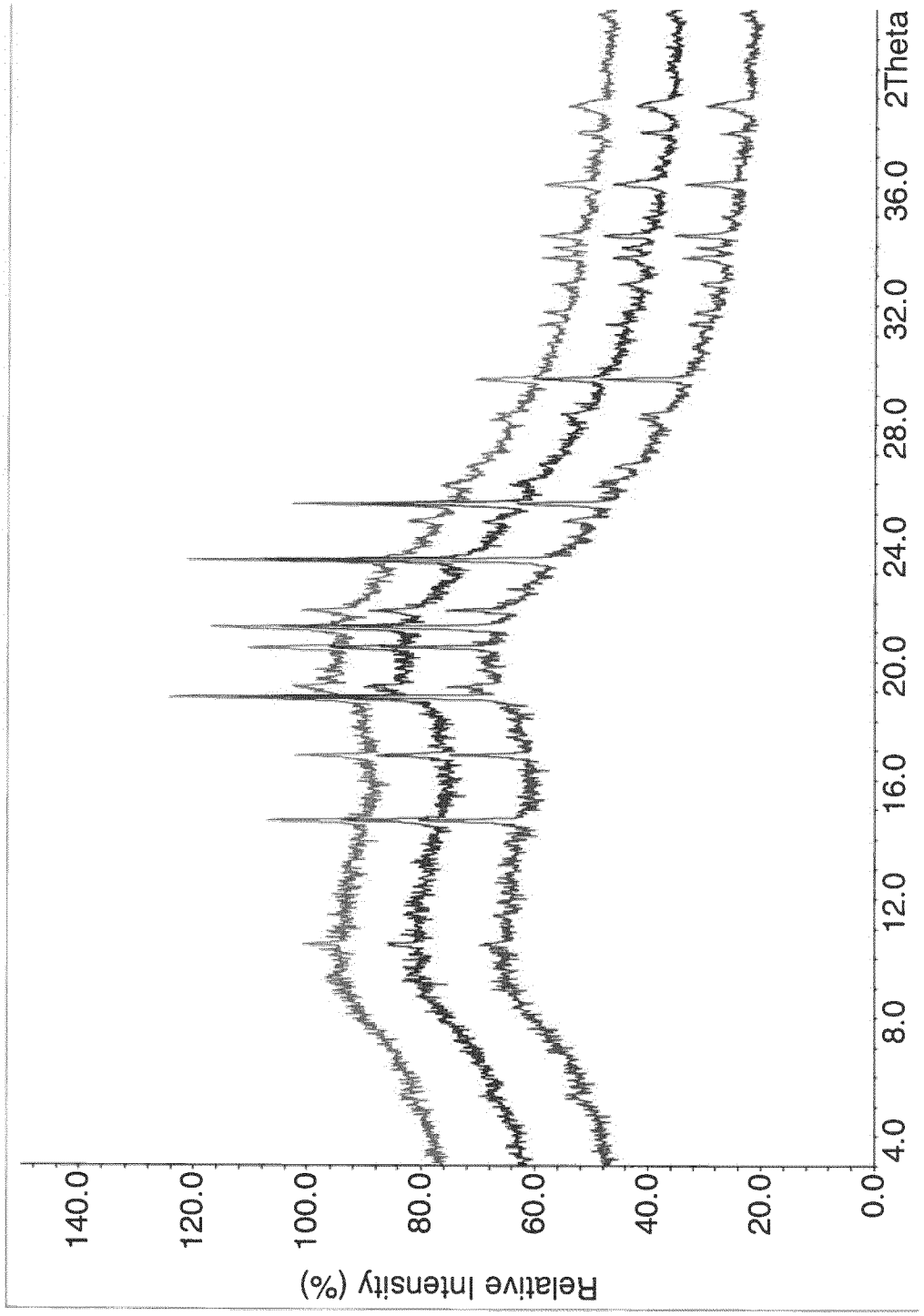

Relative Intensity (%)
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
4.0
8.0
12.0
16.0
20.0
24.0
28.0
32.0
36.0
2Theta

Fig. 8b

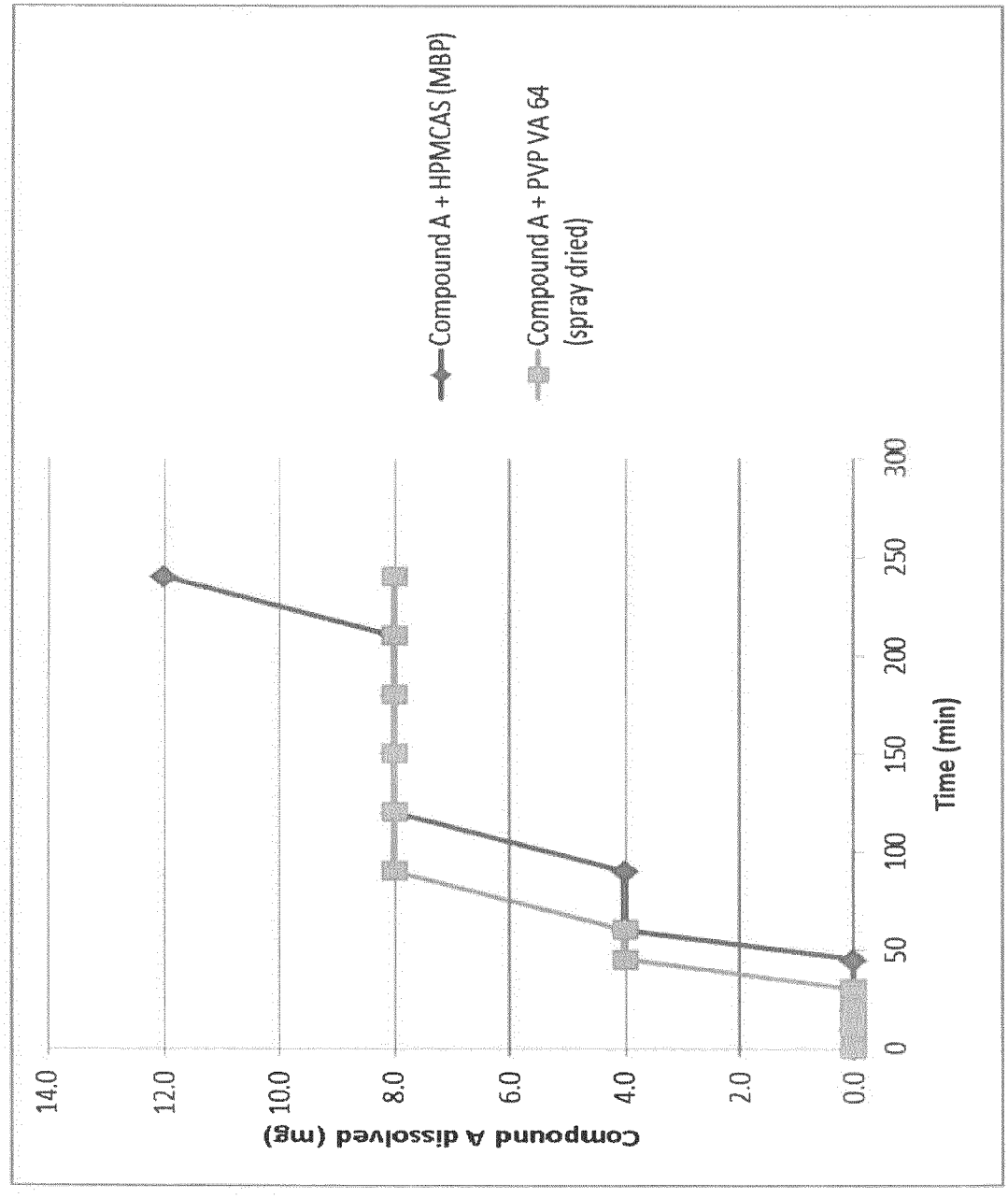

Compound A + HPMCAS (MBP)
Compound A + PVP VA 64 (spray dried)
Compound A dissolved (mg)
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
0
50
100
150
200
250
300
Time (min)

Fig. 9