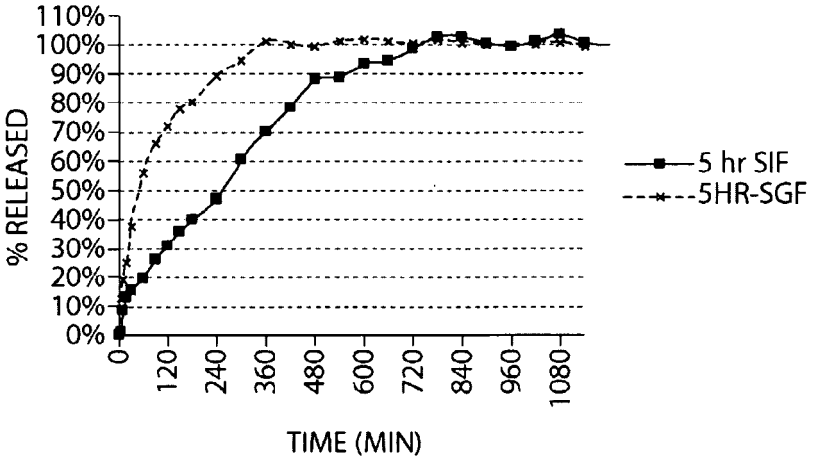

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100%
90%
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0%
% RELEASED
0
120
240
360
480
600
720
840
960
1080
TIME (MIN)
5 hr SIF
5HR-SGF

Fig. 1A

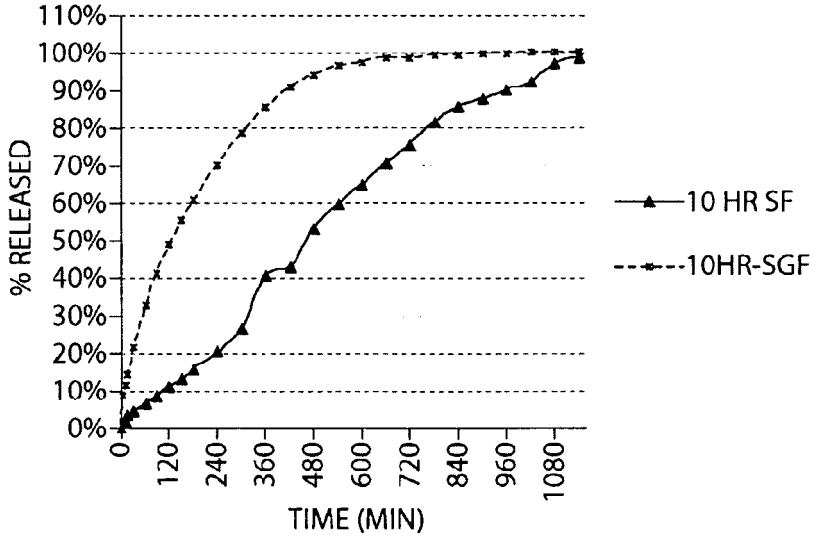

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240
360
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840
960
1080
TIME (MIN)
10 HR SF
10HR-SGF

Fig. 1B

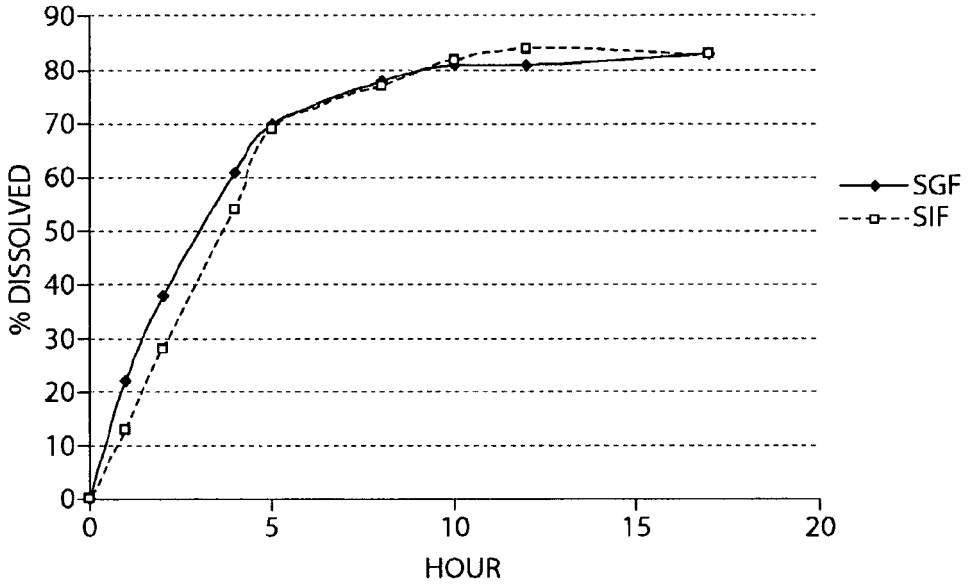

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80
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60
50
40
30
20
10
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% DISSOLVED
0
5
10
15
20
HOUR
SGF
SIF

Fig. 2

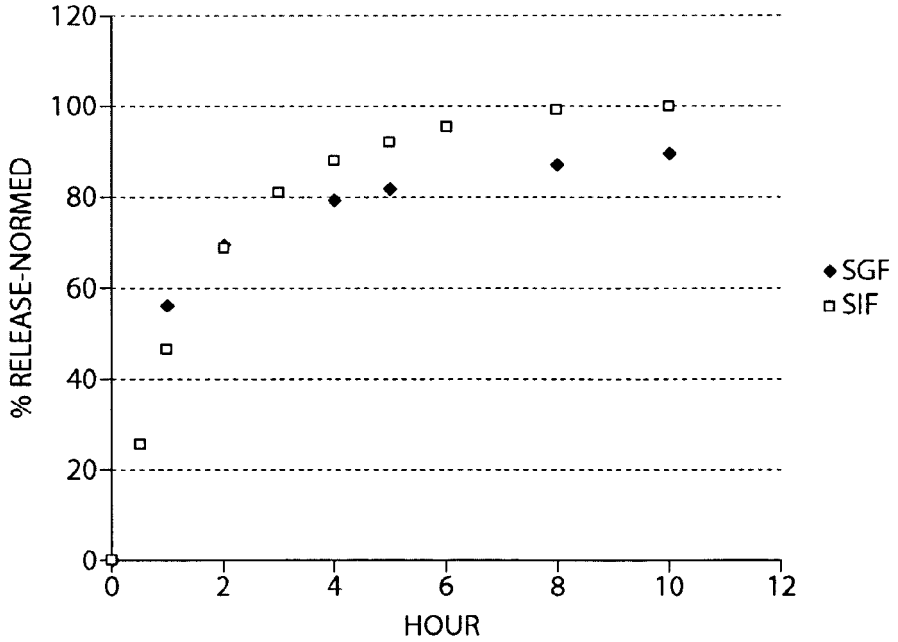

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100
80
60
40
20
0
% RELEASE-NORMED
0
2
4
6
8
10
12
HOUR
SGF
SIF

Fig. 3

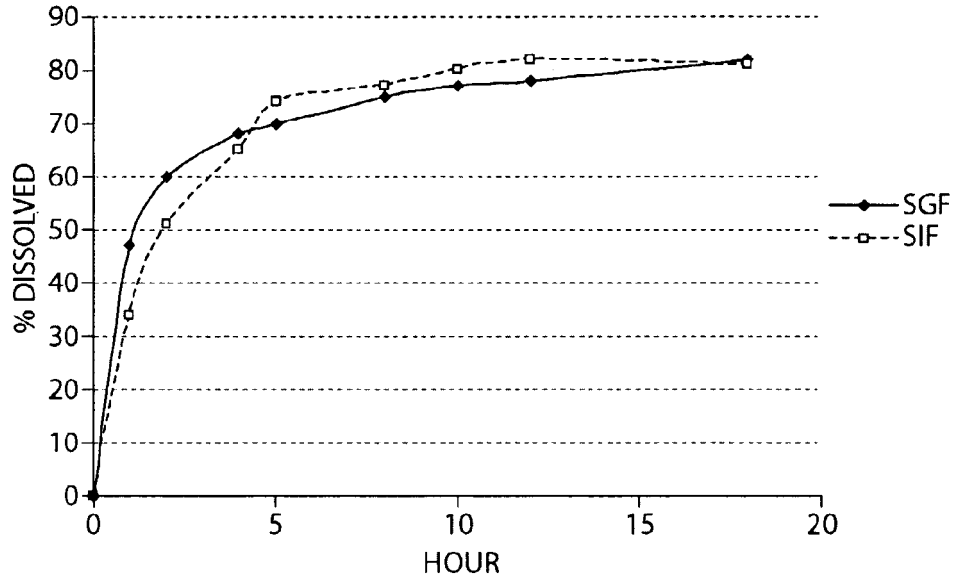

90
80
70
60
50
40
30
20
10
0
% DISSOLVED
0
5
10
15
20
HOUR
SGF
SIF

Fig. 4

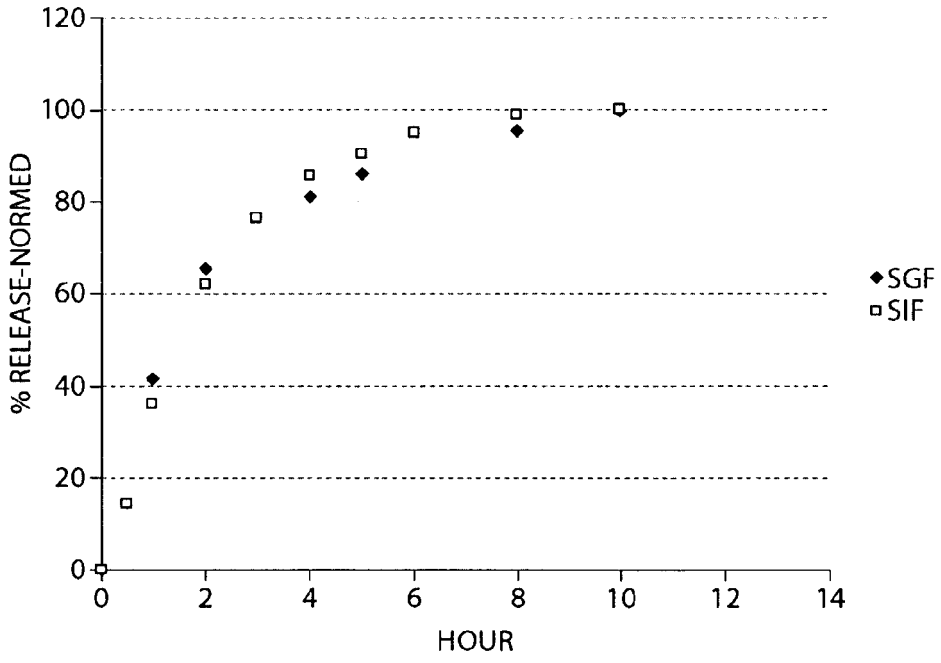

120
100
80
60
40
20
0
% RELEASE-NORMED
0
2
4
6
8
10
12
14
HOUR
SGF
SIF

Fig. 5

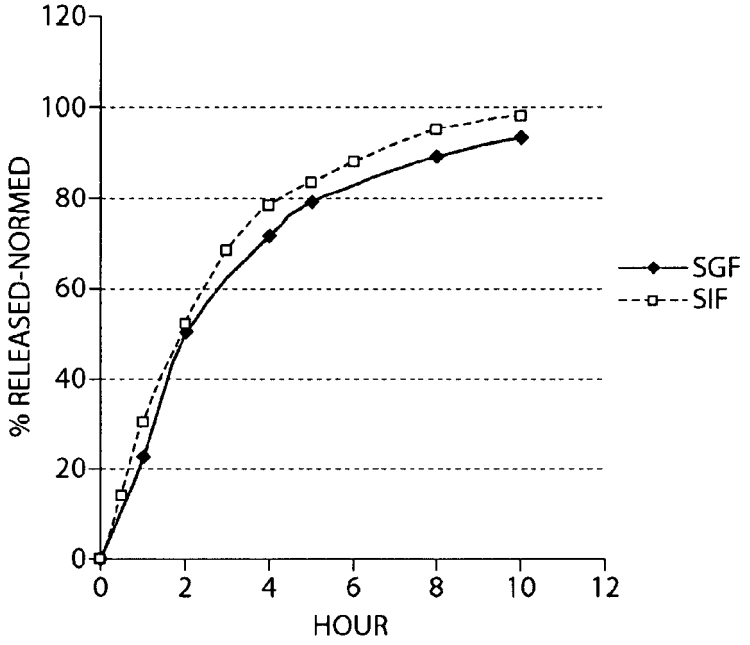

120
100
80
60
40
20
0
% RELEASED-NORMED
0
2
4
6
8
10
12
HOUR
SGF
SIF

Fig. 6

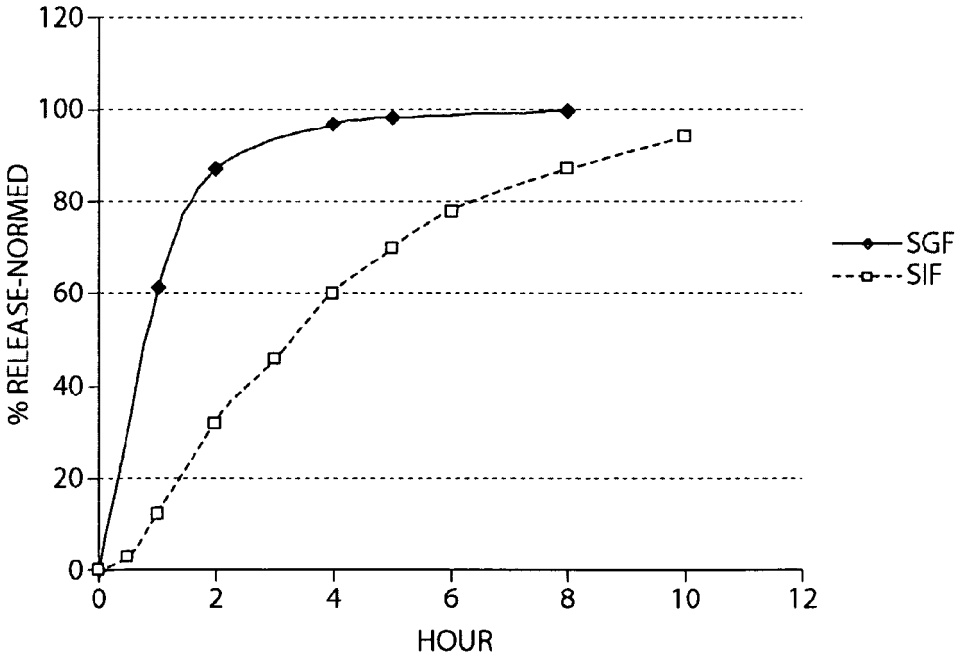
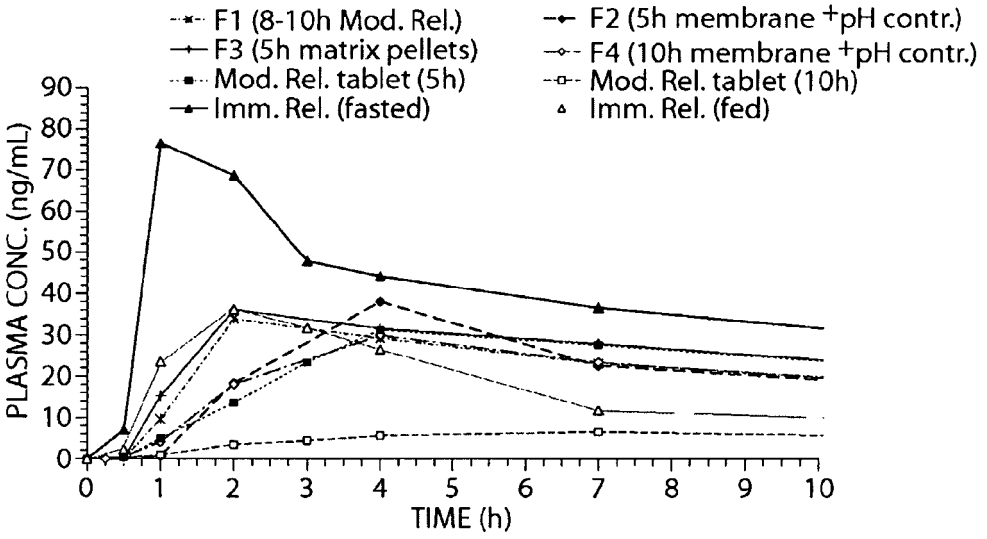

120
100
80
60
40
20
0
% RELEASE-NORMED
0
2
4
6
8
10
12
HOUR
SGF
SIF

Fig. 7

PK OF RO4917323 IN CYNOMOLGUS MONKEYS (PRELIMINARY DATA) FOLLOWING DIFFERENT IMMEDIATE AND MODIFIED RELEASE FORMULATIONS DOSE: 0.3 mg/kg



PARAMETER	UNIT	F1	F2	F3	F4
ACTUAL DOSE	[mg/kg]	0.25	0.26	0.29	0.25
Cmax ± SD	[ng/mL]	34.6 ± 7.4	38 ± 11.1	38.5 ± 14.1	33.2 ± 9.6
tmax ± SD	[h]	3.2 ± 2.5	4.0 ± 0.0	3.5 ± 2.6	5.5 ± 1.7
t1/2 ± SD	[h]	8.4 ± 2.1	7.9 ± 5.5	9.3 ± 2.9	8.4 ± 5.3
AUC(0-inf) ± SD	[(ng·h)/mL]	481 ± 158	442 ± 45.3	569 ± 172	481 ± 228
AUC(0-48h) ± SD	[(ng·h)/mL]	477 ± 152	434 ± 40.3	551 ± 143	409 ± 178
AUC(0-inf)/DOSE ± SD	[(ng·h)/mL] (mg/kg)	1924 ± 632	1700 ± 174	1962 ± 593	1924 ± 912
AUC(0-48h)/DOSE ± SD	[(ng·h)/mL] (mg/kg)	1908 ± 608	1669 ± 155	1900 ± 493	1636 ± 712

Fig. 8

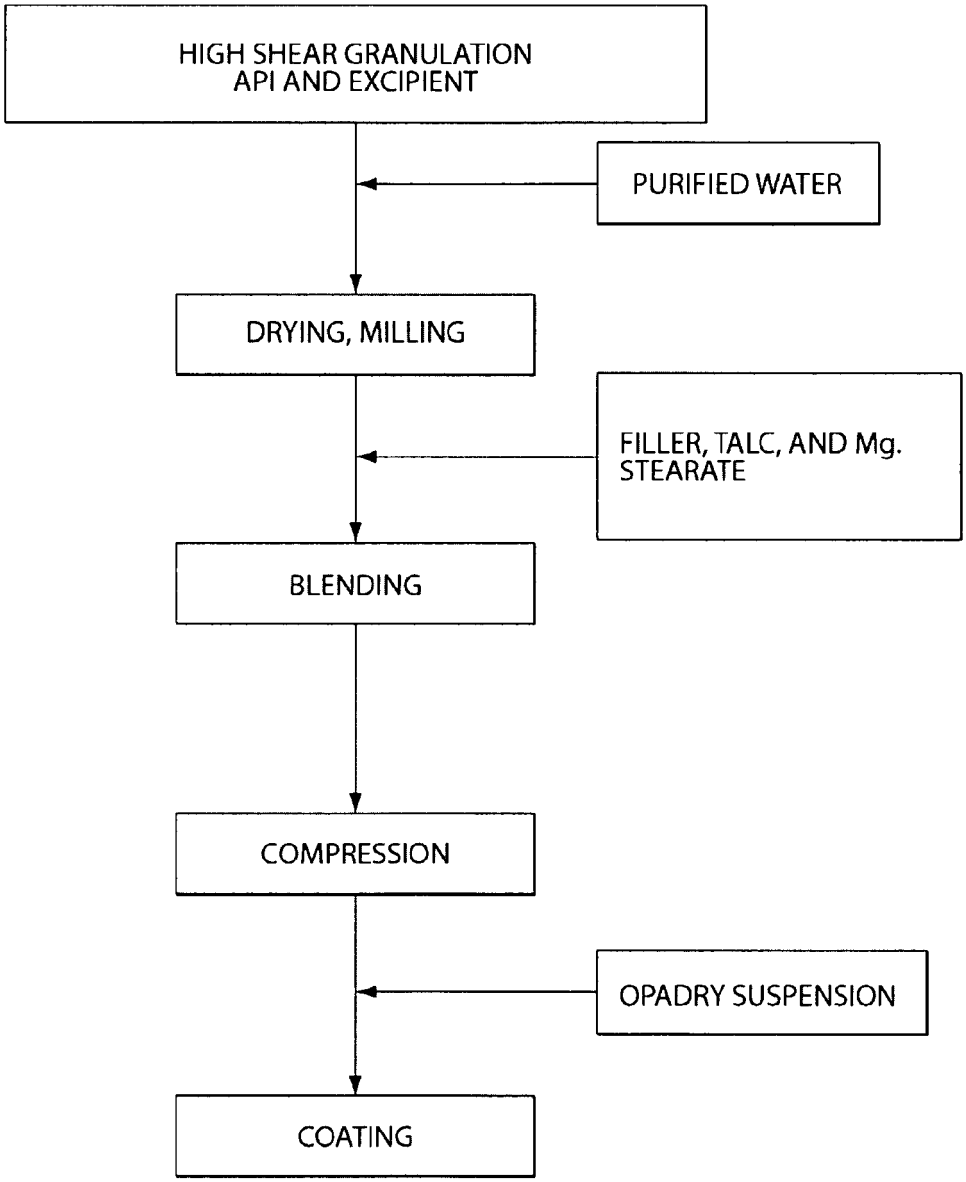

HIGH SHEAR GRANULATION
API AND EXCIPIENT
PURIFIED WATER
DRYING, MILLING
FILLER, TALC, AND Mg.
STEARATE
BLENDING
COMPRESSION
OPADRY SUSPENSION
COATING

Fig. 9

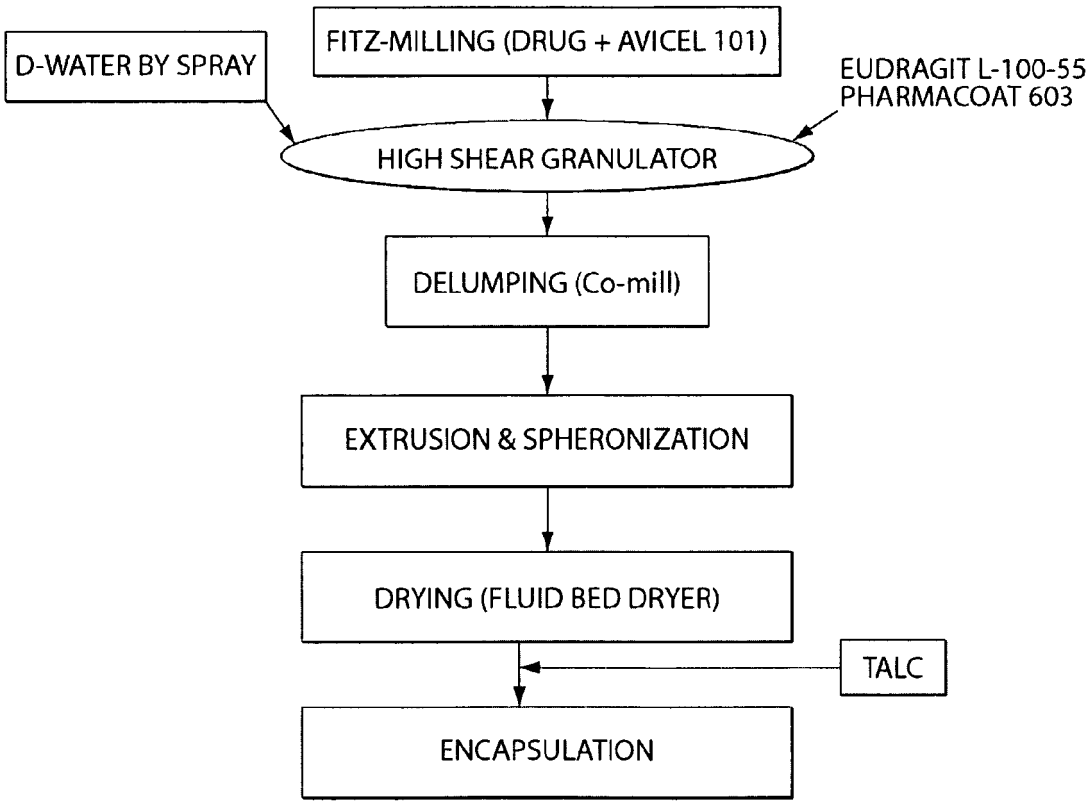

D-WATER BY SPRAY
FITZ-MILLING (DRUG + AVICEL 101)
EUDRAGIT L-100-55
PHARMACOAT 603
HIGH SHEAR GRANULATOR
DELUMPING (Co-mill)
EXTRUSION & SPHERONIZATION
DRYING (FLUID BED DRYER)
TALC
ENCAPSULATION

Fig. 10

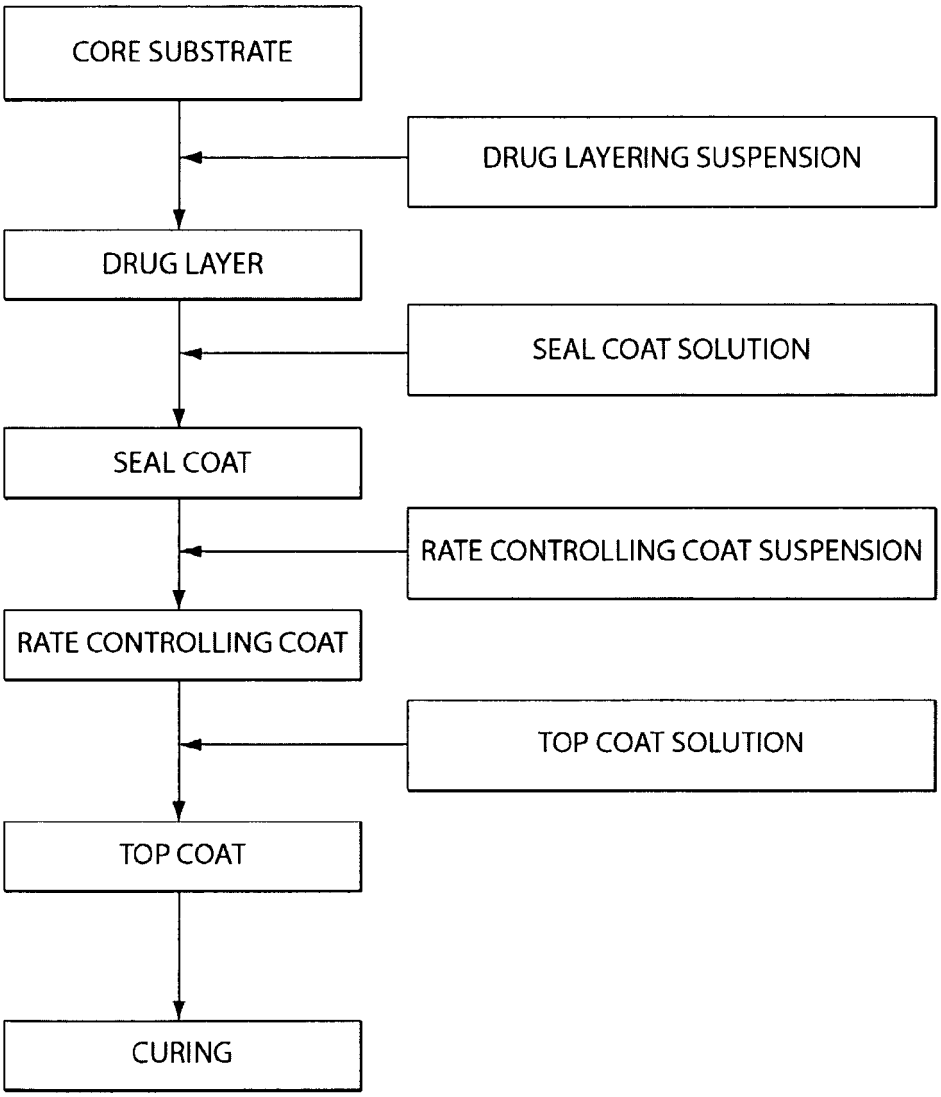

CORE SUBSTRATE
DRUG LAYERING SUSPENSION
DRUG LAYER
SEAL COAT SOLUTION
SEAL COAT
RATE CONTROLLING COAT SUSPENSION
RATE CONTROLLING COAT
TOP COAT SOLUTION
TOP COAT
CURING

Fig. 11