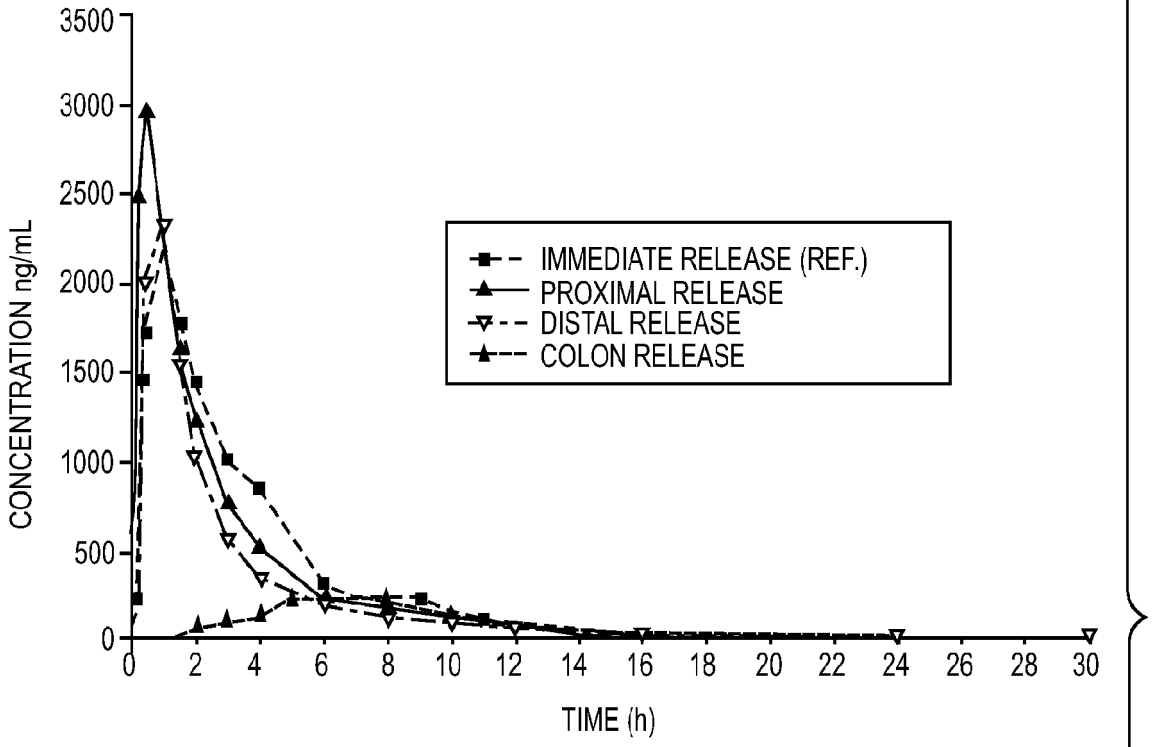
Fig. 1

MEAN PLASMA CONCENTRATIONS OF FEBUXOSTAT (LINEAR TOP AND LOG-LINEAR BOTTOM) FOLLOWING ADMINISTRATION OF A SINGLE ORAL DOSE OF 80 mg FEBUXOSTAT RELEASED IN VARIOUS LOCATIONS THE G1 TRACT IN 12 SUBJECTS



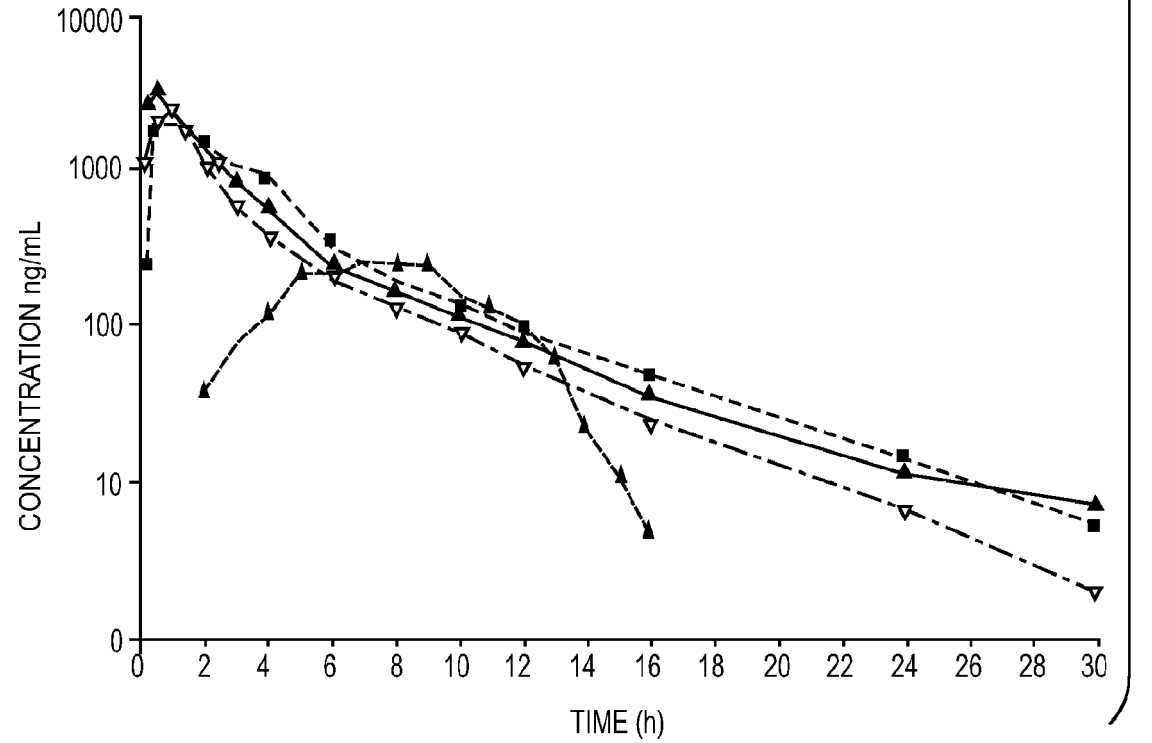


Fig. 2

ESTIMATED PLASMA PROFILE FOR A 3-PULSE 80 mg DOSE OF FEBUXOSTAT, PULSE 1 (D*0.3, t=0) IMMEDIATE RELEASE + PULSE 2 (D*0.3, t=5 h) 5 HOUR DELAYED RELEASE + PULSE 3 (D*0.45*0.4, t=10 h) 10 HOUR DELAYED RELEASE.

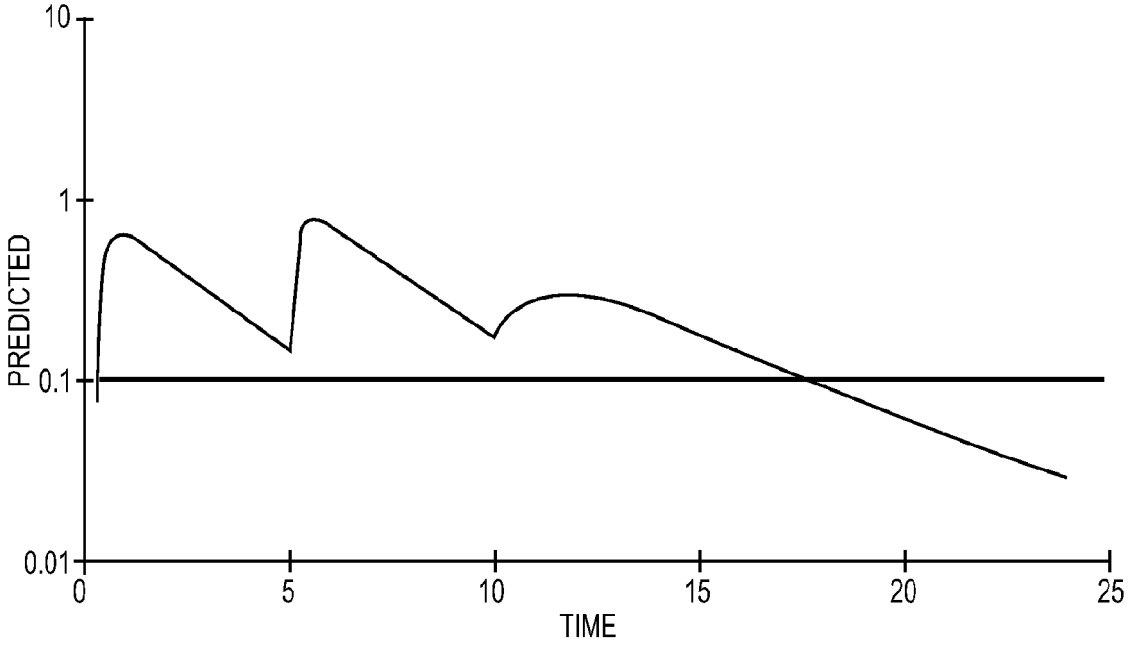


Fig. 3

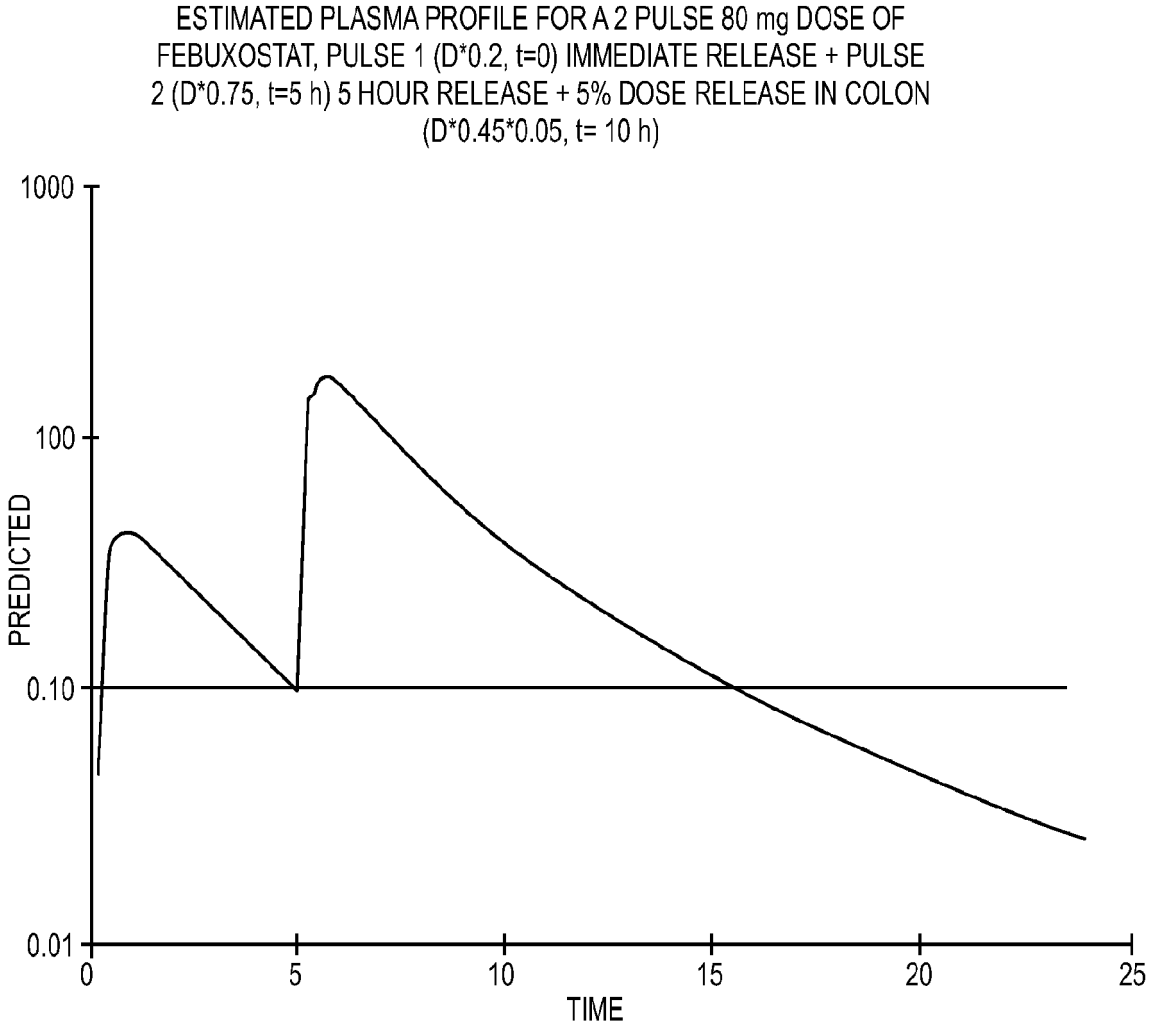

ESTIMATED PLASMA PROFILE FOR A 2 PULSE 80 mg DOSE OF FEBUXOSTAT, PULSE 1 (D*0.2, t=0) IMMEDIATE RELEASE + PULSE 2 (D*0.75, t=5 h) 5 HOUR RELEASE + 5% DOSE RELEASE IN COLON (D*0.45*0.05, t= 10 h)
1000
100
0.10
0.01
PREDICTED
0
5
10
15
20
25
TIME

Fig. 4

ESTIMATED PLASMA PROFILE FOR AN 80 mg EXTENDED RELEASE (ER) FORMULATION OF FEBUXOSTAT, WHEREIN 90% OF ABSORPTION COMPLETED IN 6 HOURS WITH Ka=0.462 h^{-1}, AND 10% OF DOSE WAS ABSORBED FROM THE COLON WITH FREL=0.45.

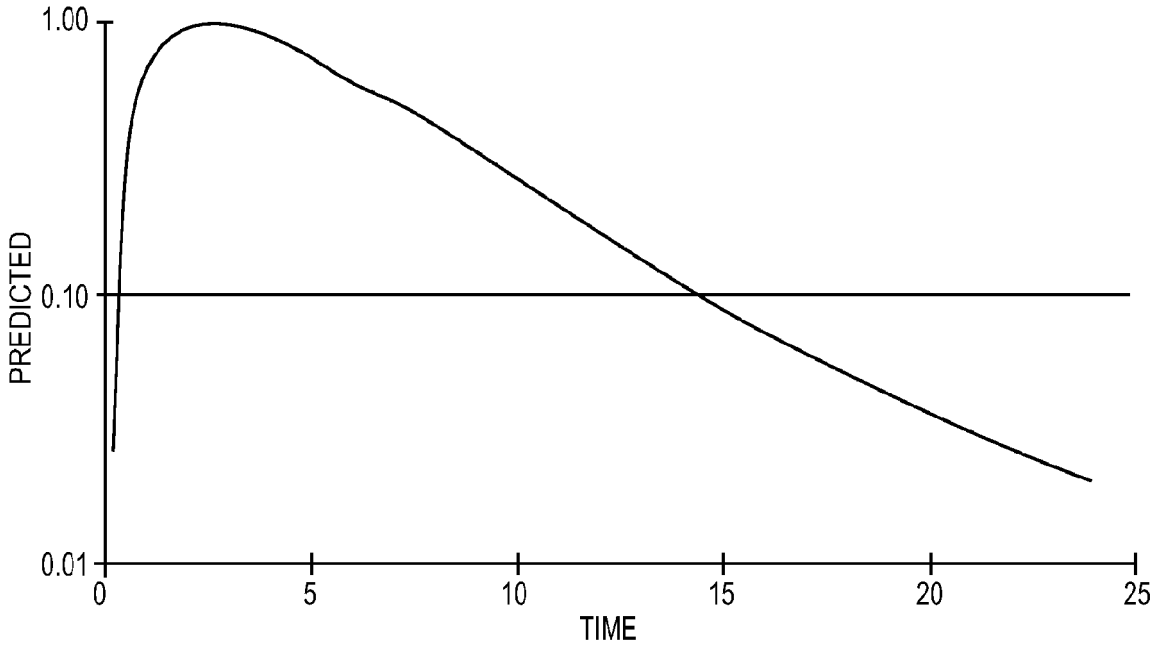


Fig. 5

FEBUXOSTAT MODIFIED RELEASE MATRIX TABLET FORMULATIONS

FORMULATION	A1	B1	C1	D1	E1	F1	G1	H1
FEBUXOSTAT %	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7
HYPROMELLOSE K100LV %	30.0	30.0	15.0	15.0	30.0	15.0	15.0	30.0
AVICEL PH 101 %	34.7	11.6	50.5	15.3	13.1	16.8	46.0	39.2
EUDRAGIT EPO %	6.0	6.0	0	6.0	0.0	0.0	6.0	0.0
LACTOSE %	11.6	34.7	16.8	46.0	39.2	50.5	15.3	13.1
MG STEARATE	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0

Fig. 6

DISSOLUTION PROFILES OF FEBUXOSTAT MODIFIED RELEASE MATRIX TABLETS (50 mg) IN pH 6.8, 0.5M PHOSPHATE BUFFER

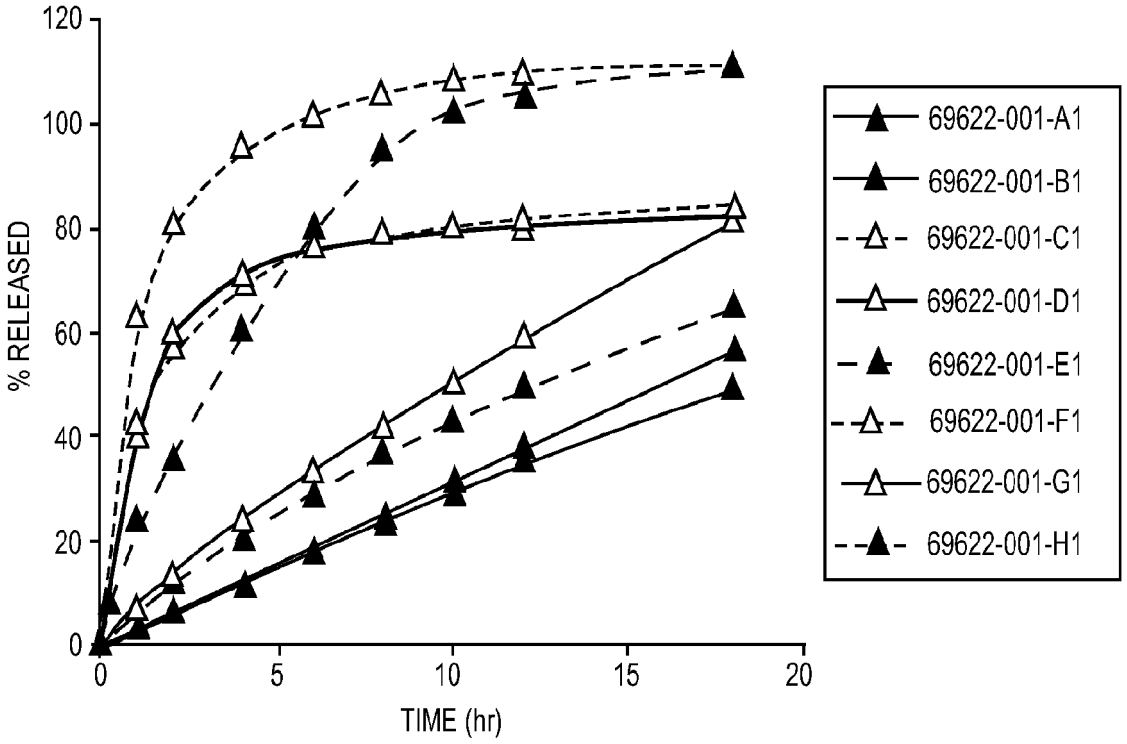


Fig. 7

PLASMA CONCENTRATION VERSUS TIME PROFILES IN DOGS FOR THE FEBUXOSTAT FORMULATIONS DESCRIBED IN EXAMPLE 10

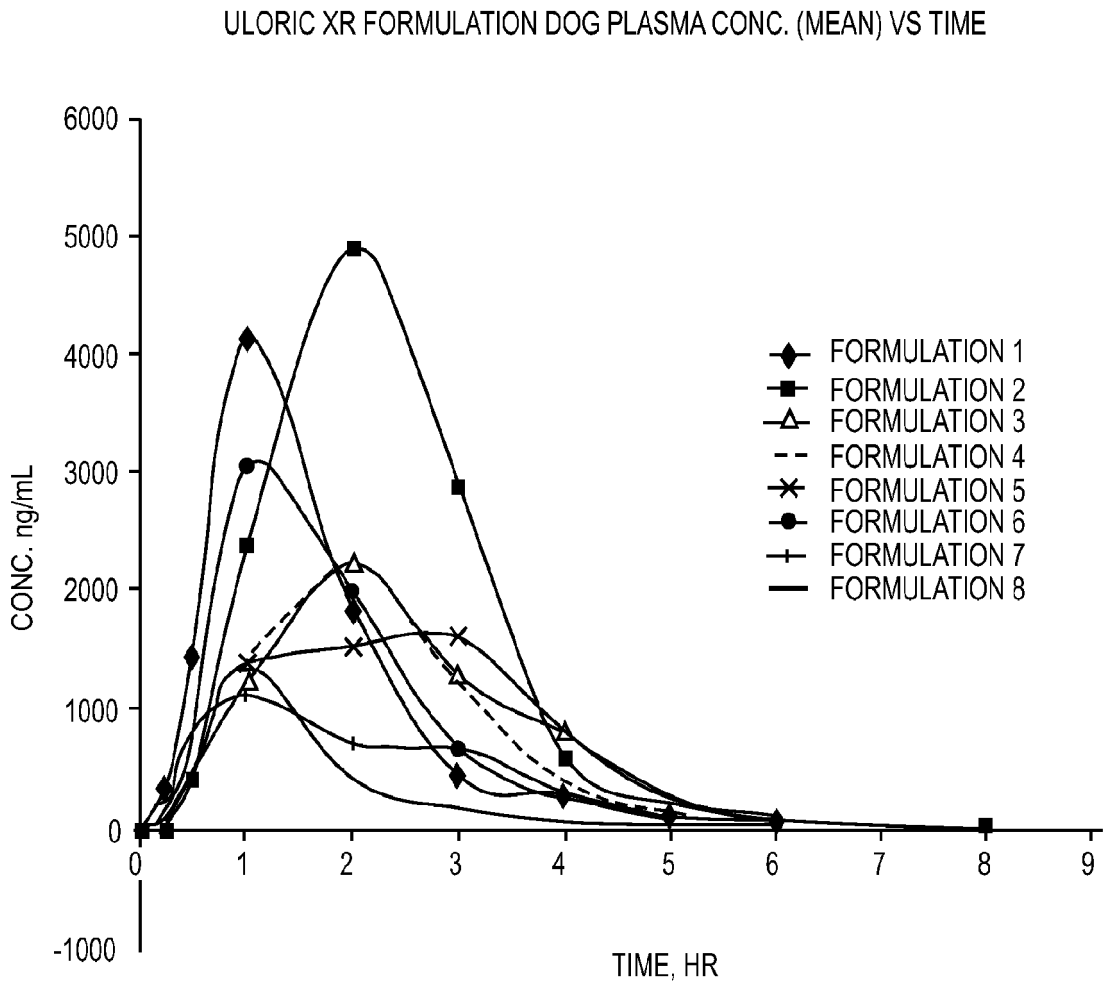


Fig. 8A

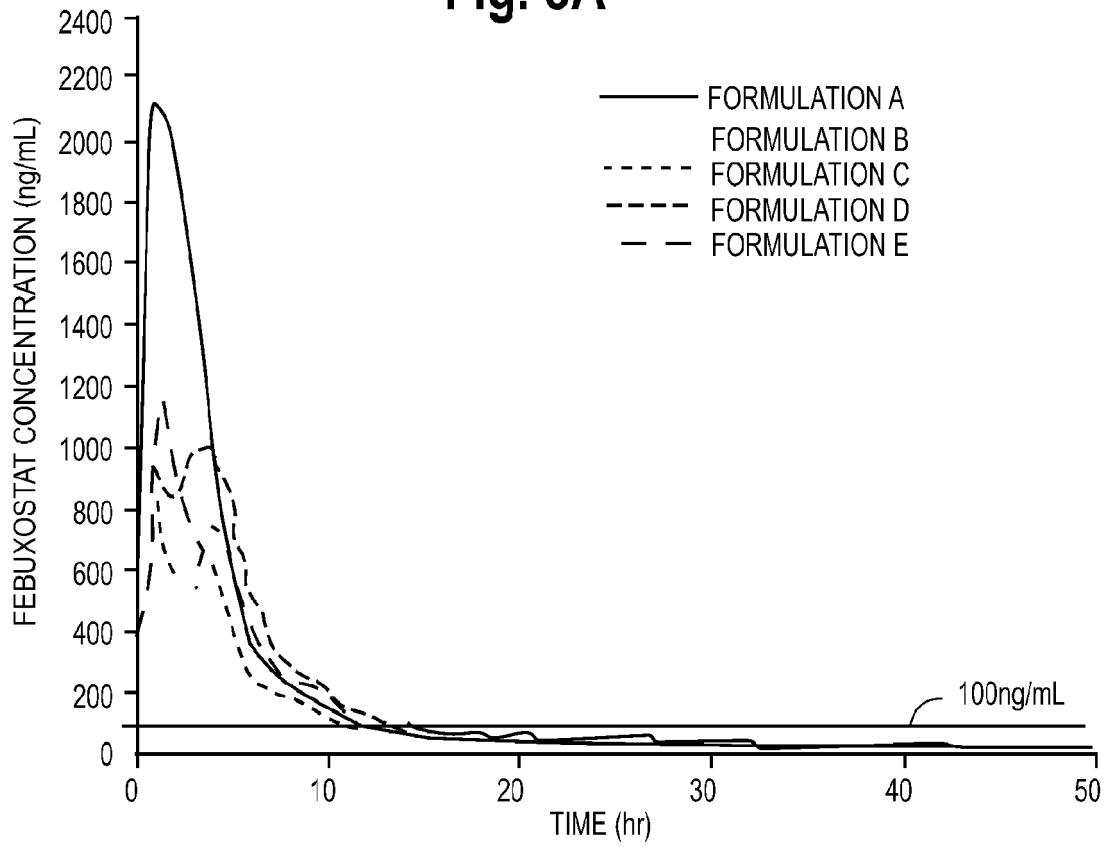

FORMULATION A
FORMULATION B
FORMULATION C
FORMULATION D
FORMULATION E
100ng/mL
FEBUXOSTAT CONCENTRATION (ng/mL)
TIME (hr)
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50

Fig. 8B

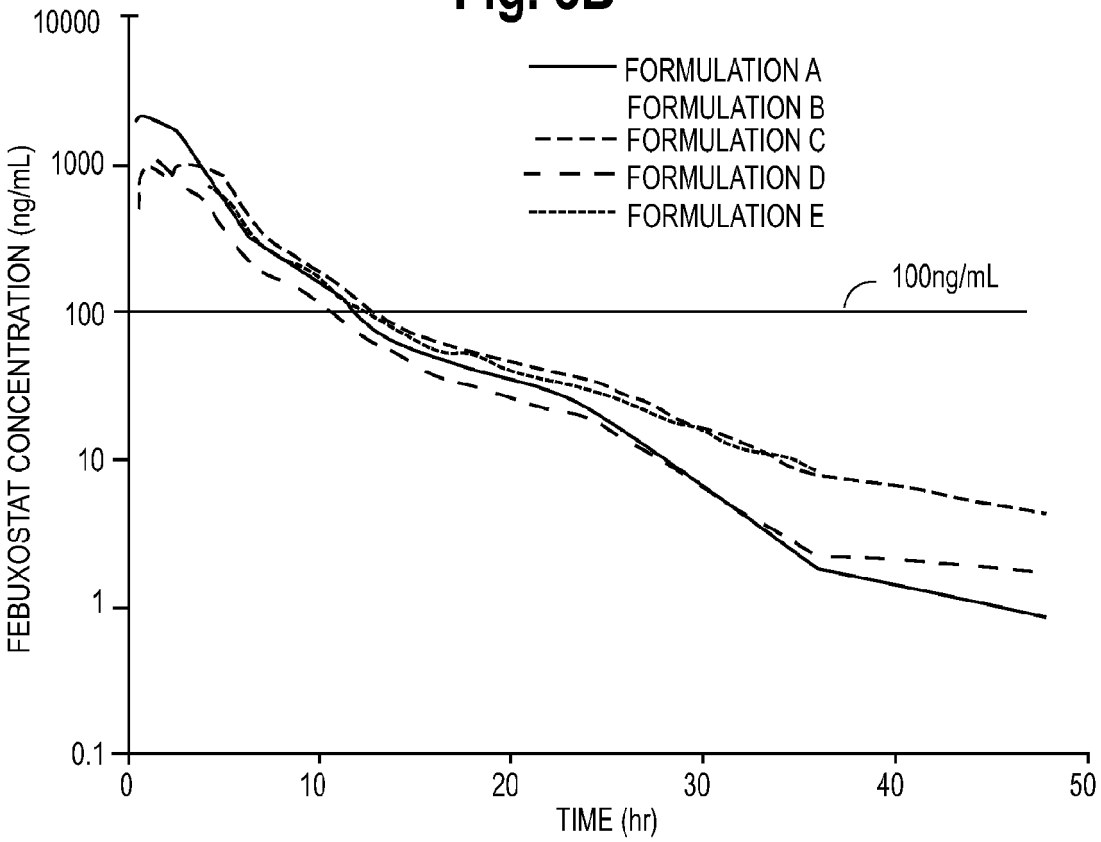

FORMULATION A
FORMULATION B
FORMULATION C
FORMULATION D
FORMULATION E
100ng/mL
FEBUXOSTAT CONCENTRATION (ng/mL)
TIME (hr)
10000
1000
100
10
1
0.1
0
10
20
30
40
50

Fig. 9

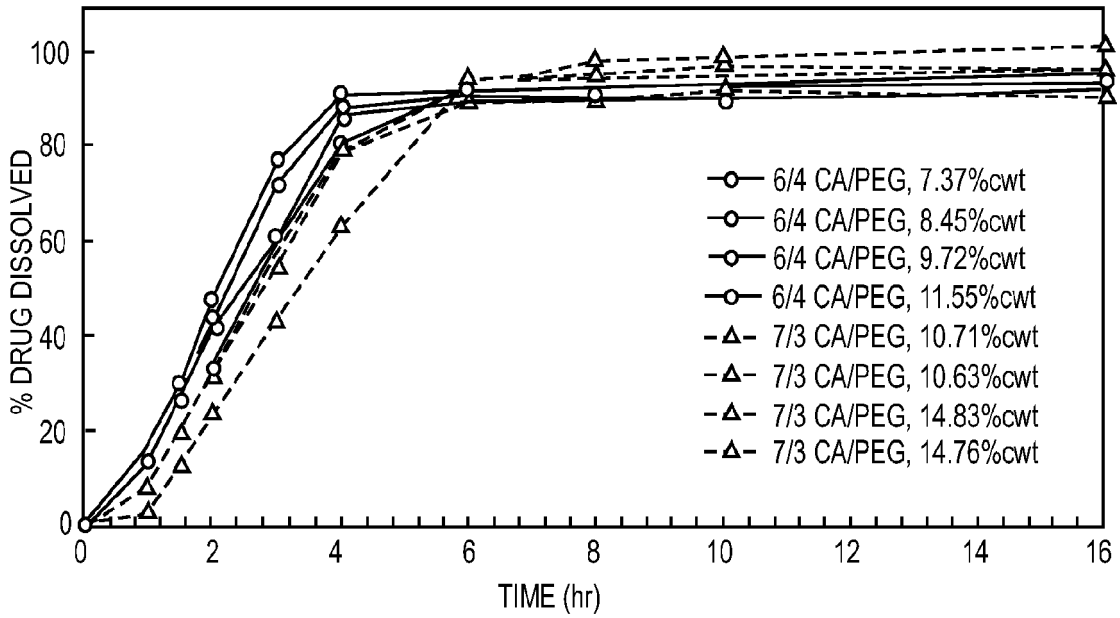

100
80
60
40
20
0
% DRUG DISSOLVED
0
2
4
6
8
10
12
14
16
TIME (hr)
6/4 CA/PEG, 7.37%cwt
6/4 CA/PEG, 8.45%cwt
6/4 CA/PEG, 9.72%cwt
6/4 CA/PEG, 11.55%cwt
7/3 CA/PEG, 10.71%cwt
7/3 CA/PEG, 10.63%cwt
7/3 CA/PEG, 14.83%cwt
7/3 CA/PEG, 14.76%cwt

Fig. 10

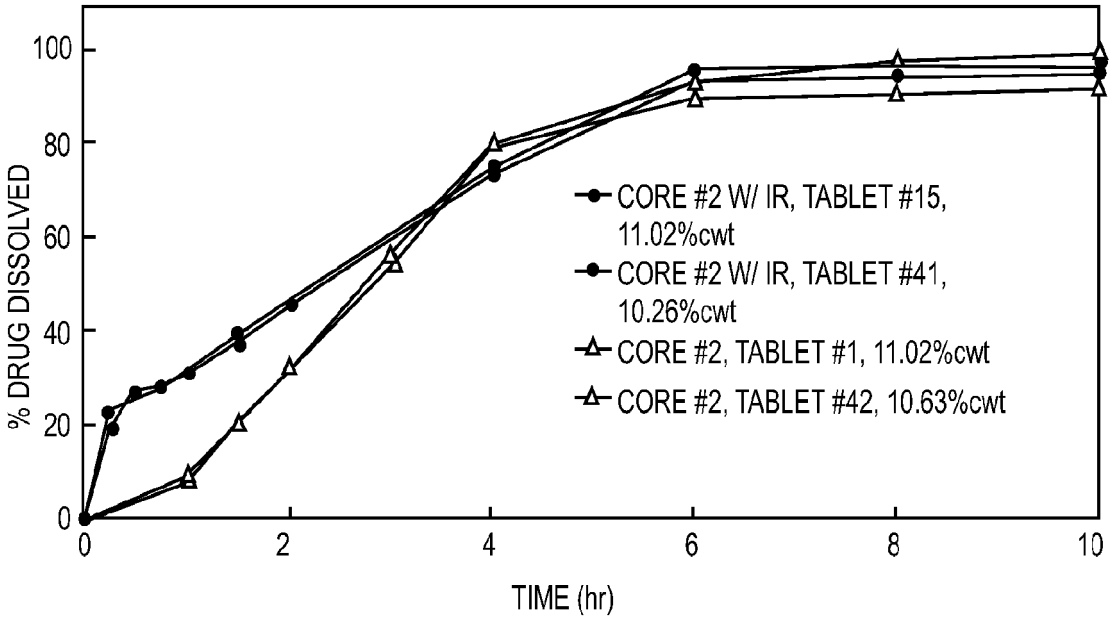
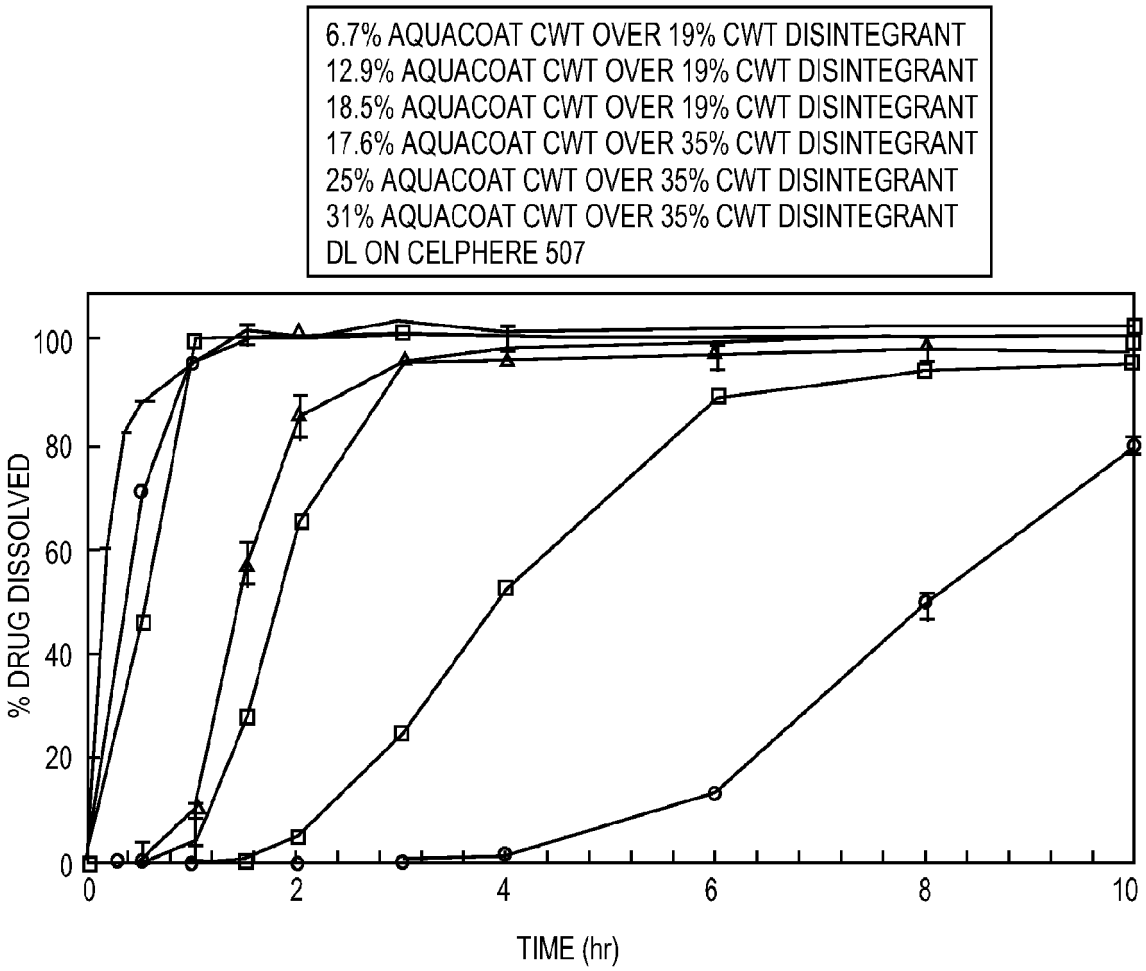

100
80
60
40
20
0
% DRUG DISSOLVED
0
2
4
6
8
10
TIME (hr)
CORE #2 W/ IR, TABLET #15, 11.02%cwt
CORE #2 W/ IR, TABLET #41, 10.26%cwt
CORE #2, TABLET #1, 11.02%cwt
CORE #2, TABLET #42, 10.63%cwt

Fig. 11


6.7% AQUACOAT CWT OVER 19% CWT DISINTEGRANT
12.9% AQUACOAT CWT OVER 19% CWT DISINTEGRANT
18.5% AQUACOAT CWT OVER 19% CWT DISINTEGRANT
17.6% AQUACOAT CWT OVER 35% CWT DISINTEGRANT
25% AQUACOAT CWT OVER 35% CWT DISINTEGRANT
31% AQUACOAT CWT OVER 35% CWT DISINTEGRANT
DL ON CELPHERE 507
% DRUG DISSOLVED
0
20
40
60
80
100
0
2
4
6
8
10
TIME (hr)