Fig. 1

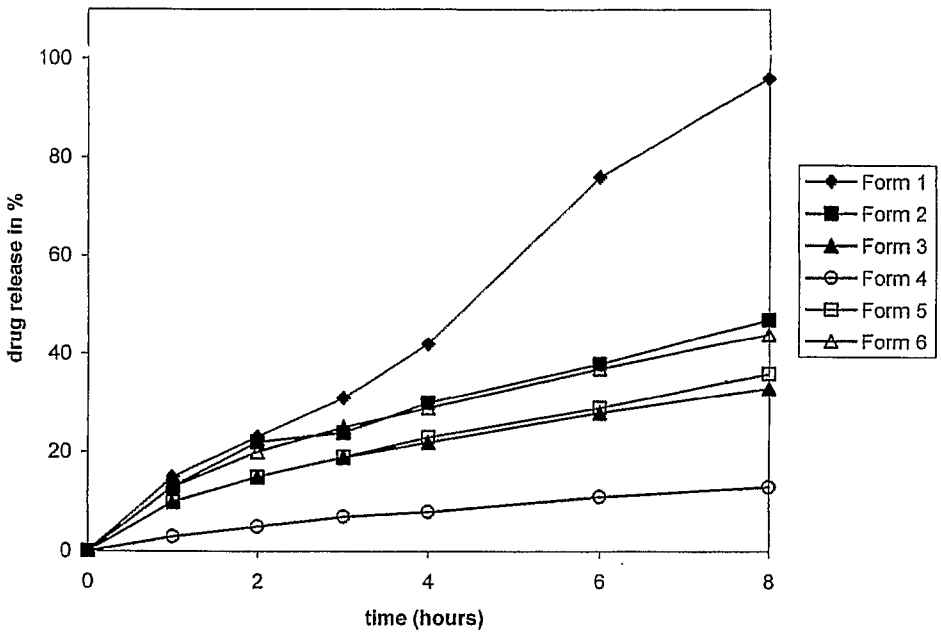

drug release in %
time (hours)
0
20
40
60
80
100
0
2
4
6
8
Form 1
Form 2
Form 3
Form 4
Form 5
Form 6

Fig. 2

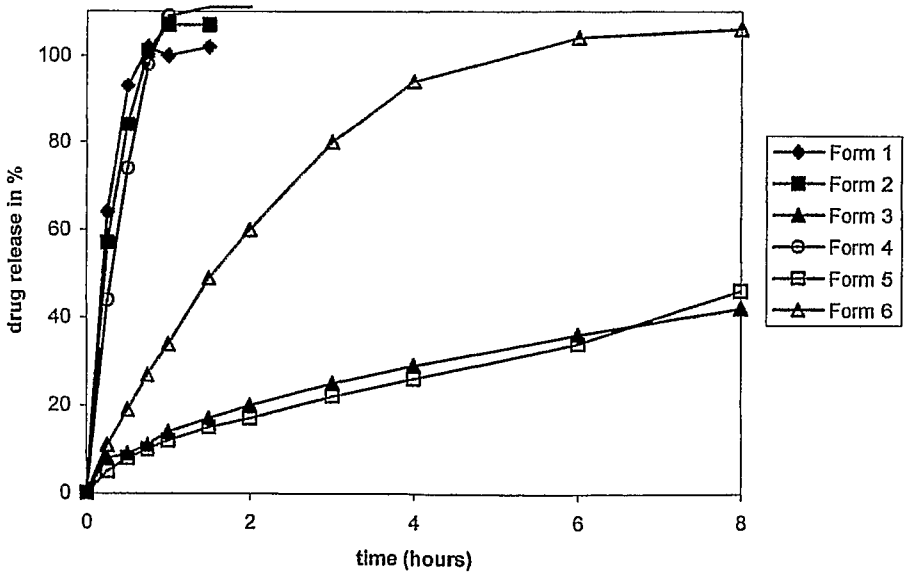

drug release in %
time (hours)
0
20
40
60
80
100
0
2
4
6
8
Form 1
Form 2
Form 3
Form 4
Form 5
Form 6

Fig. 3

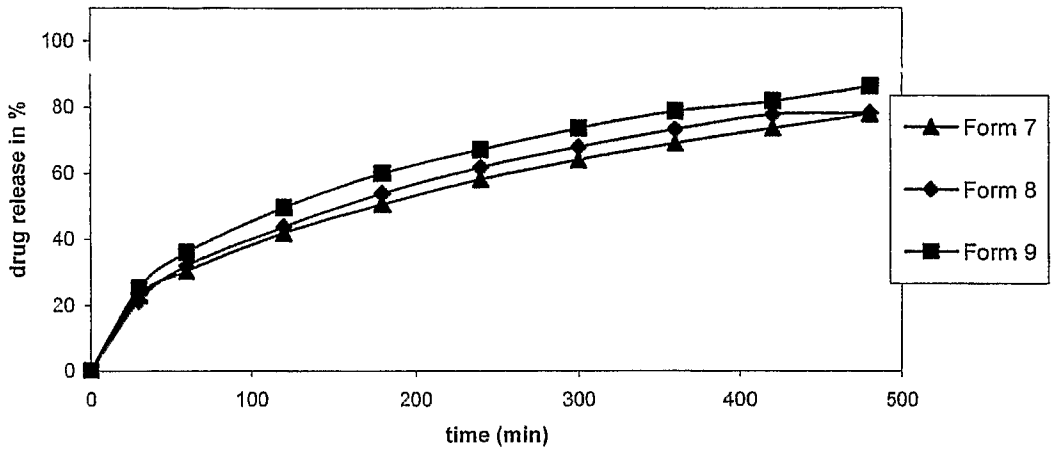
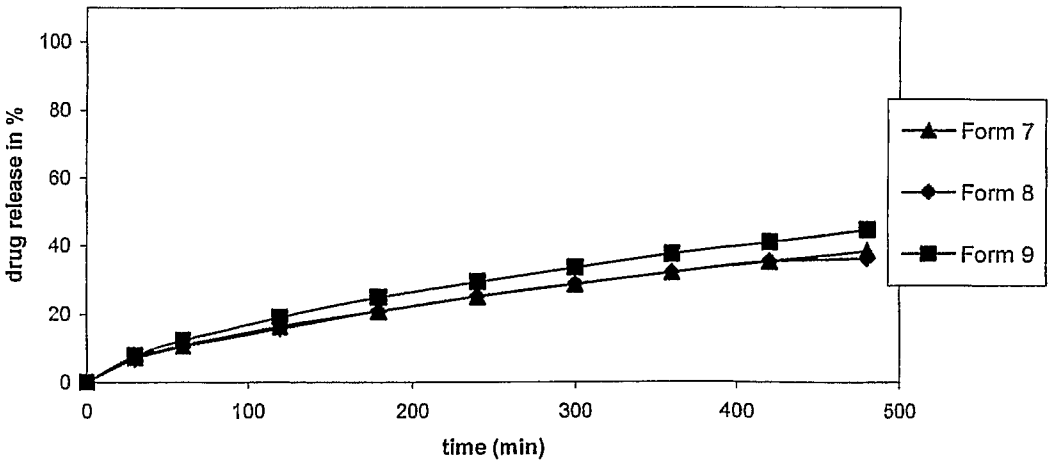

drug release in %
100
80
60
40
20
0
0
100
200
300
400
500
time (min)
Form 7
Form 8
Form 9

Fig. 4


drug release in %
100
80
60
40
20
0
0
100
200
300
400
500
time (min)
Form 7
Form 8
Form 9

5

Fig. 5

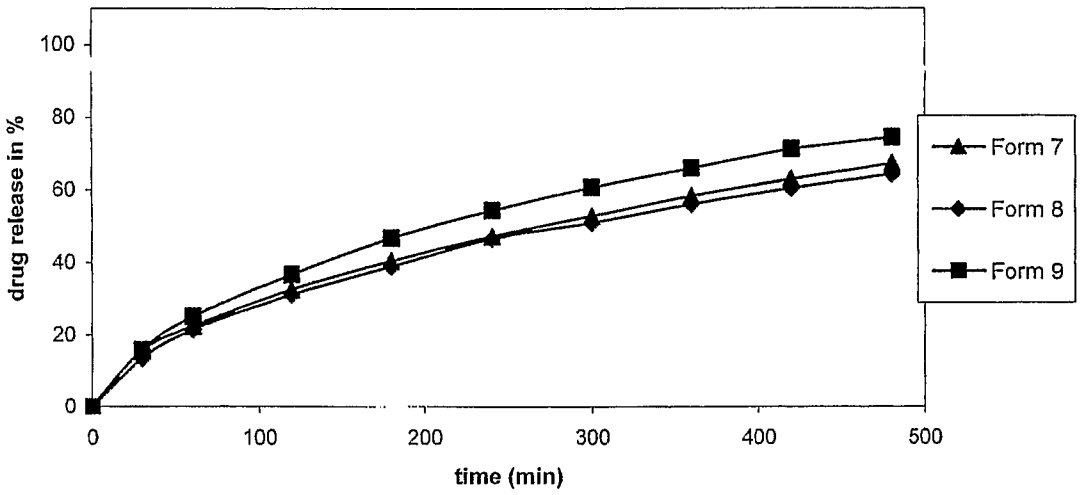


Fig. 6

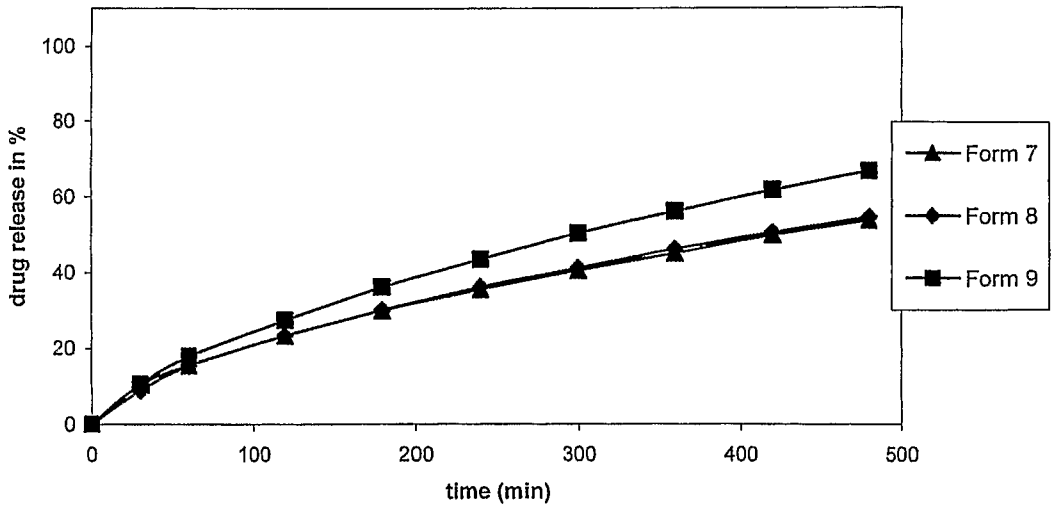


Fig. 7

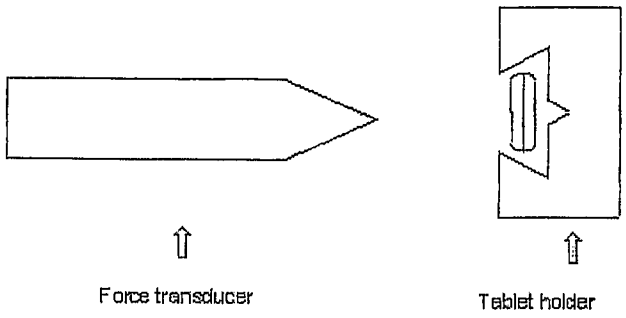
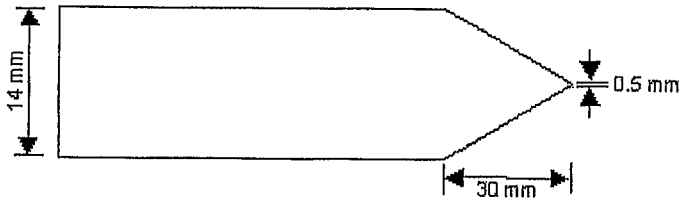
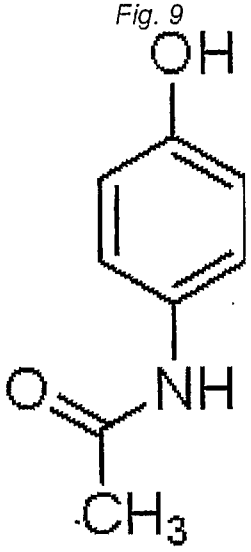


Fig. 8



5

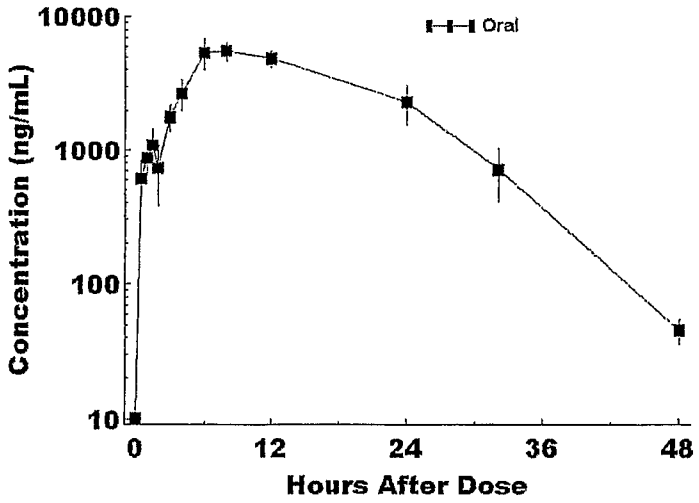
Fig. 9



(9 A)

	Acetaminophen (Form 30)			
Minipigs #	t 1/2 (hr)	Cmax (ng/mL)	Tmax (hr)	AUC (ng·hr/mL)
1	6.8	7074.0	8.0	98100
2	3.6	5368.0	24.0	110000
3	5.0	6295.0	12.0	111000
4	4.7	10577.0	6.0	102000
5	4.8	7889.0	8.0	119000
6	6.2	4945.0	12.0	97000
Mean	5.0°	7024.7	11.7	106000
SEM		2048.0	6.5	8760

(9.B)


10000
1000
100
10
Concentration (ng/mL)
Oral
0
12
24
36
48
Hours After Dose

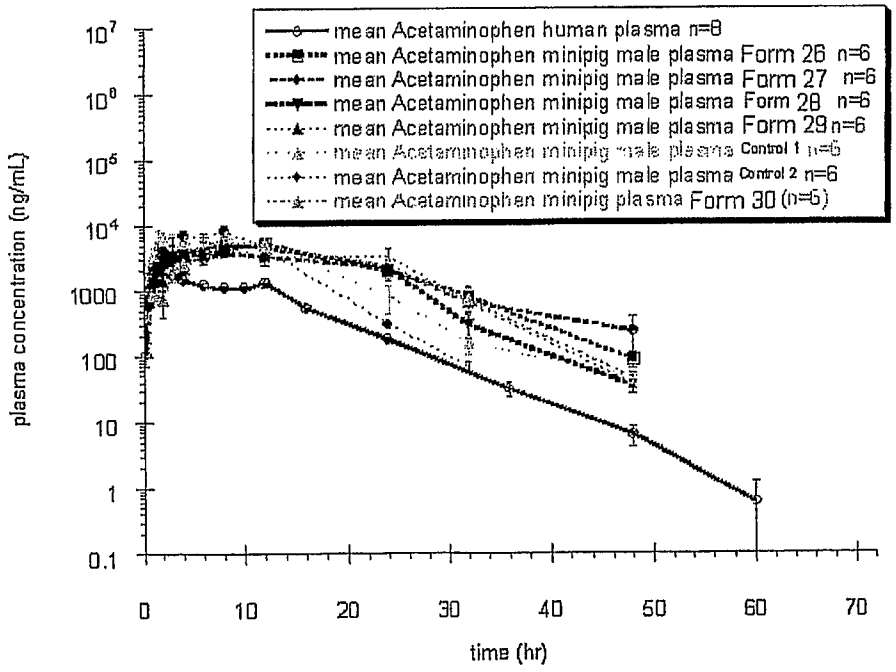
(9 C)

Fig. 10.

Species	Formulation	t1/2 (hr)	Cmax (ng/mL)	Tmax (hr)	AUC (ng.hr/mL)
Minipigs (n=6)	26	5.8 *(0.9)*	5314 *(805)*	9 *(3.3)*	101433 *(13053)*
Minipigs (n=6)	27	5.7 *(0.8)*	4181 *(473)*	9 *(1.4)*	87567 *(4504)*
Minipigs (n=6)	28	4.9 *(1.2)*	6310 *(1384)*	13 *(3.8)*	98100 *(9759)*
Minipigs (n=6)	29	3.5 *(0.2)*	6567 *(3587)*	9.7 *(7.2)*	97500 *(8254)*
Minipigs (n=6)	30	5.2 *(0.4)*	7025 *(2048)*	11.7 *(6.5)*	106000 *(8760)*
Minipigs (n=6)	Control 2	3.3 *(0.1)*	10319 *(3003)*	5.3 *(2.3)*	102000 *(20500)*
Minipigs (n=6)	Control 1	3.5 *(0.2)*	8508 *(2324)*	4.2 *(3)*	110000 *(21100)*
Human (n=8)	Control 1	4.7 *(0.2)*	2262 *(487)*	2.4 *(3.9)*	23700 *(5010)*

(10 A)

5



(10 B)

Fig. 11

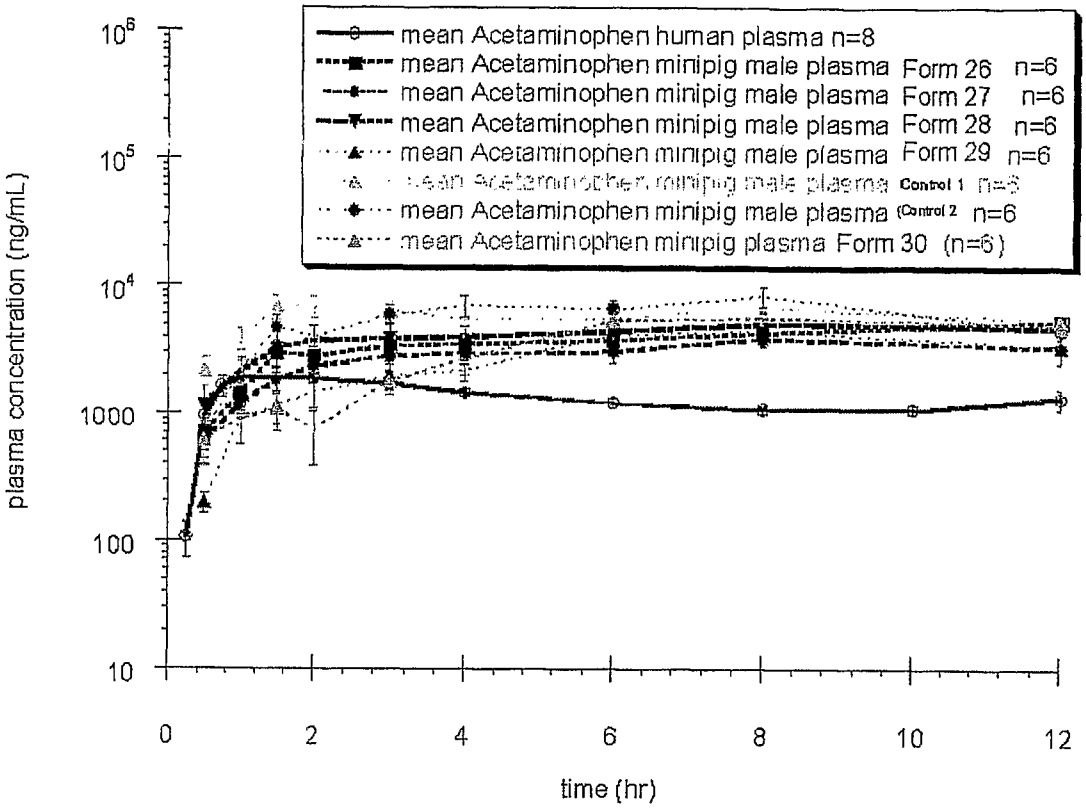

mean Acetaminophen human plasma n=8
mean Acetaminophen minipig male plasma Form 26 n=6
mean Acetaminophen minipig male plasma Form 27 n=6
mean Acetaminophen minipig male plasma Form 28 n=6
mean Acetaminophen minipig male plasma Form 29 n=6
mean Acetaminophen minipig male plasma Control 1 n=6
mean Acetaminophen minipig male plasma Control 2 n=6
mean Acetaminophen minipig plasma Form 30 (n=6)
plasma concentration (ng/mL)
10^6
10^5
10^4
1000
100
10
0
2
4
6
8
10
12
time (hr)

Fig. 12

Species	Formulation	t1/2 (hr)	Cmax (ng/mL)	Tmax (hr)	AUC (ng.hr/mL)
Minipigs (n=6)	26	5.8 *(0.9)*	5314 *(805)*	9 *(3.3)*	101433 *(13053)*
Minipigs (n=6)	27	5.7 *(0.8)*	4181 *(473)*	9 *(1.4)*	87567 *(4504)*
Minipigs (n=6)	28	4.9 *(1.2)*	6310 *(1384)*	13 *(3.8)*	98100 *(9759)*
Minipigs (n=2)	29	3.5 *(0.2)*	8413 *(5977)*	7 *(1.4)*	120000 *(4450)*
Minipigs (n=1)	Control 2	3.5	13142	4	105000
Minipigs (n=2)	Control 1	3.6 *(0.2)*	9255 *(3962)*	4.8 *(4.6)*	111000 *(38400)*
Human (n=8)	Control 1	4.7 *(0.2)*	2262 *(487)*	2.4 *(3.9)*	23700 *(5010)*

(12 A)

(12 B)

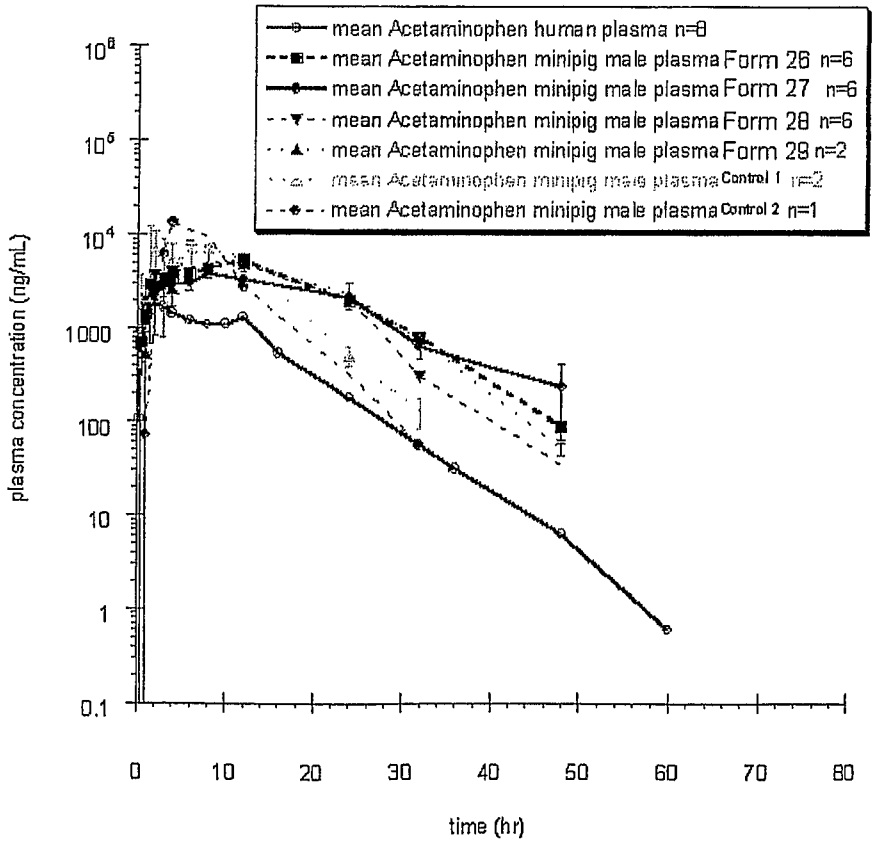
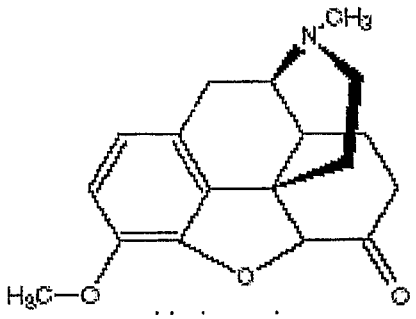


Fig. 13

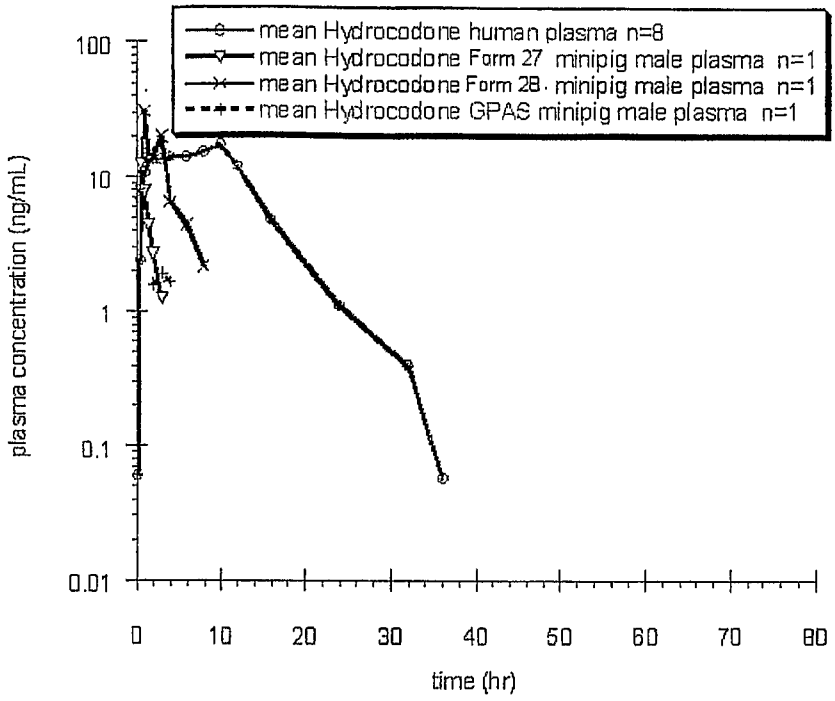


(13 A)

5

Species	Formulation	t1/2 (hr)	Cmax (ng/mL)	Tmax (hr)	AUC (ng.hr/mL)
Minipigs	Form 26	n.c	n.c	n.c	n.c
Minipigs (n=1)	Form 27	0.8	12.4	0.5	16.4
Minipigs (n=1)	Form 28	2.5	30.6	1	85.9
Minipigs	Form 29	n.c	n.c	n.c	n.c
Minipigs (n=1)	Control 2	n.c	1.9	3	5.2
Minipigs	Control 1	n.c	n.c	n.c	n.c
Human (n=8)	Control 1	6.5 *(0.3)*	18.5 *(1.3)*	8.6 *(1.5)*	331 *(23.2)*

(13 B)


mean Hydrocodone human plasma n=8
mean Hydrocodone Form 27 minipig male plasma n=1
mean Hydrocodone Form 28 minipig male plasma n=1
mean Hydrocodone GPAS minipig male plasma n=1
plasma concentration (ng/mL)
100
10
1
0.1
0.01
0
10
20
30
40
50
60
70
80
time (hr)

(13 C)

5

Fig.14

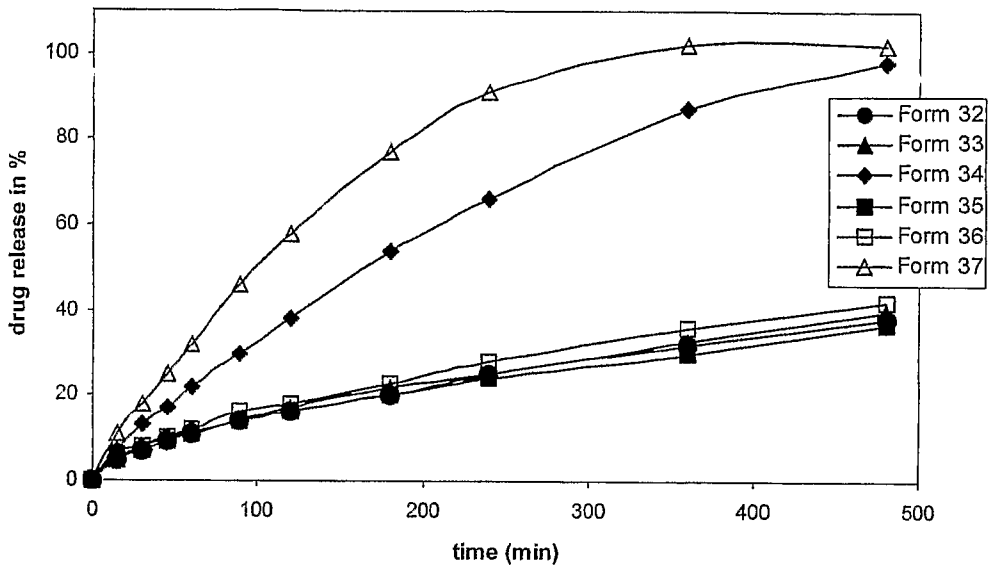

drug release in %
time (min)
Form 32
Form 33
Form 34
Form 35
Form 36
Form 37
0
20
40
60
80
100
0
100
200
300
400
500

Fig.15

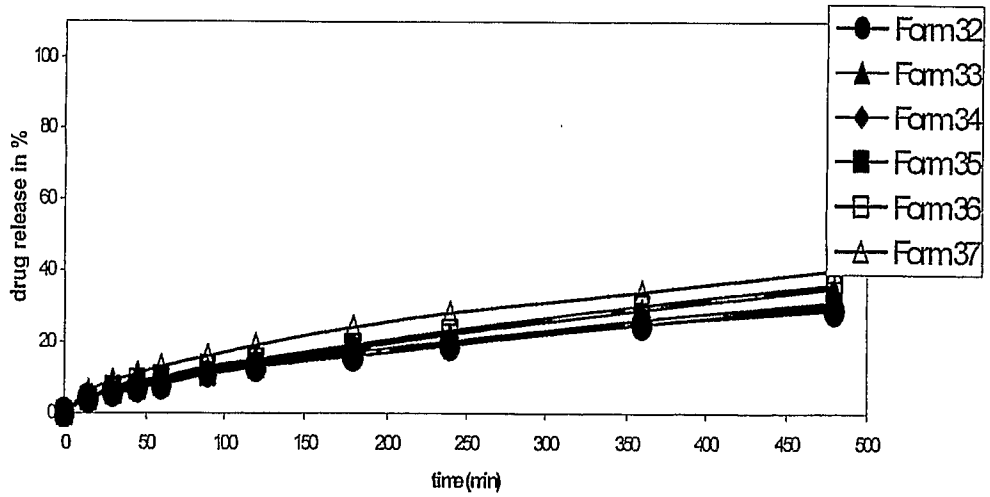

drug release in %
time(min)
Form32
Form33
Form34
Form35
Form36
Form37
0
20
40
60
80
100
0
50
100
150
200
250
300
350
400
450
500

Fig. 16

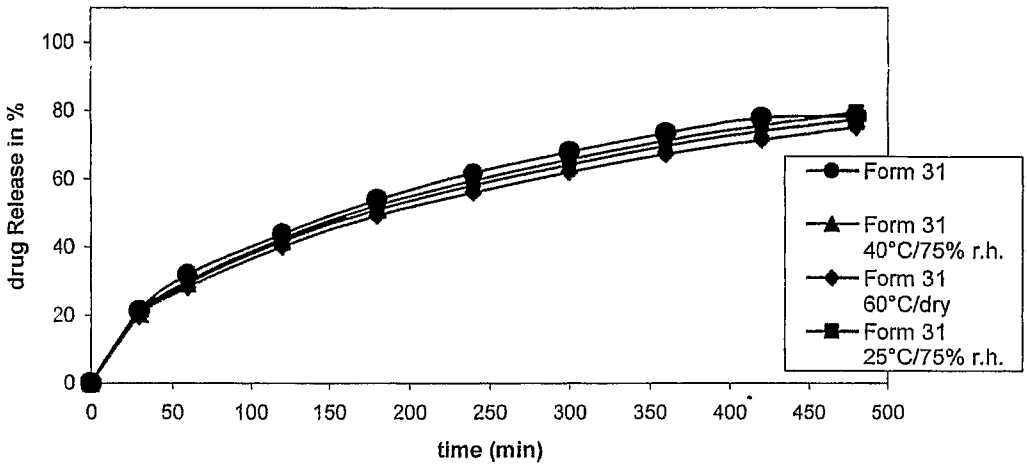

drug Release in %
100
80
60
40
20
0
0
50
100
150
200
250
300
350
400
450
500
time (min)
Form 31
Form 31 40°C/75% r.h.
Form 31 60°C/dry
Form 31 25°C/75% r.h.

Fig. 17

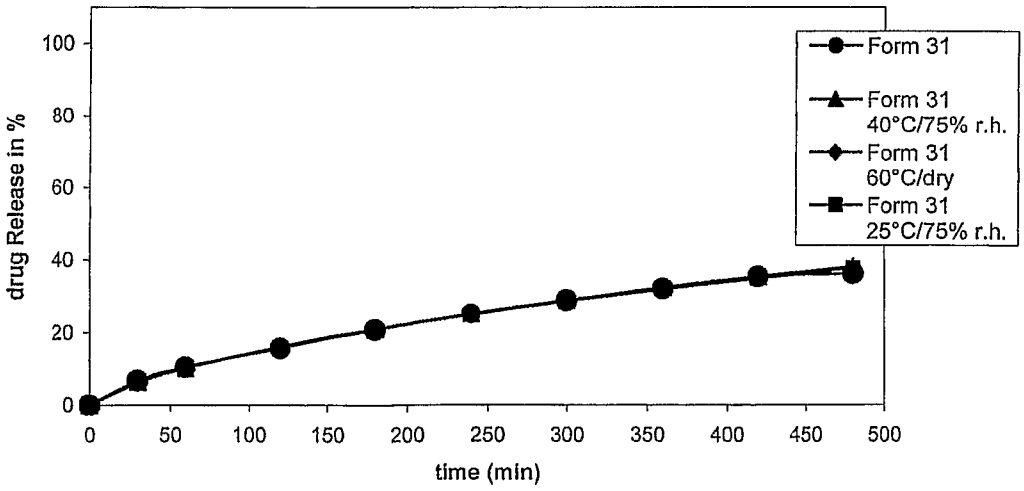

drug Release in %
100
80
60
40
20
0
0
50
100
150
200
250
300
350
400
450
500
time (min)
Form 31
Form 31 40°C/75% r.h.
Form 31 60°C/dry
Form 31 25°C/75% r.h.

Fig. 18

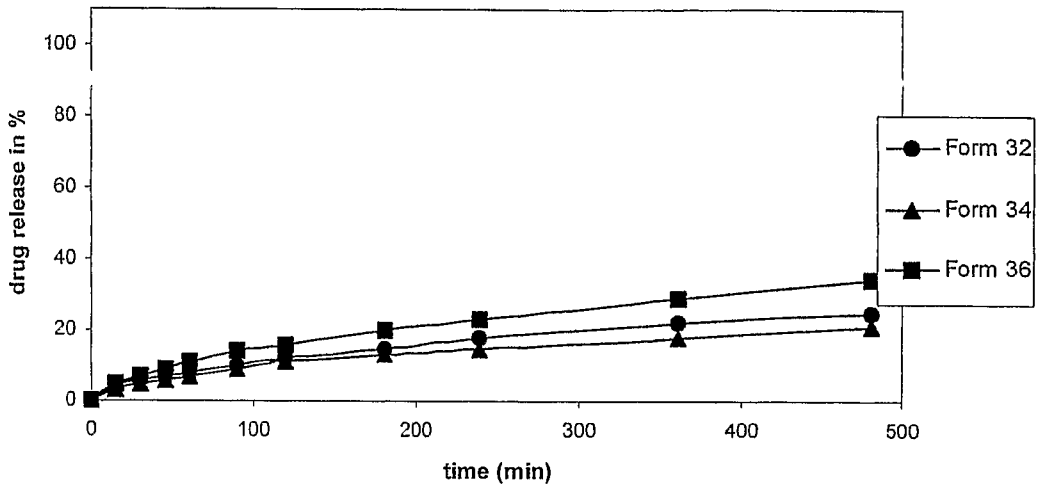

drug release in %
100
80
60
40
20
0
0
100
200
300
400
500
time (min)
Form 32
Form 34
Form 36

Fig. 19

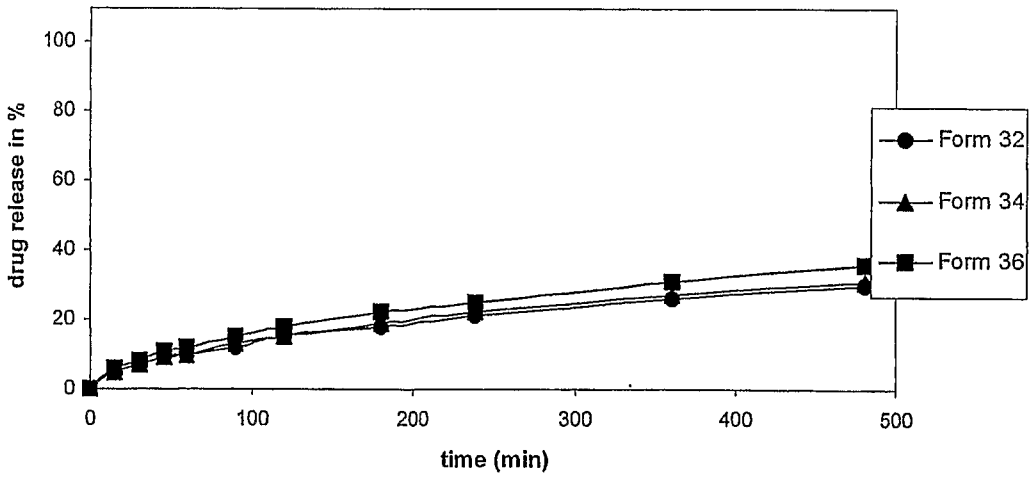

drug release in %
100
80
60
40
20
0
0
100
200
300
400
500
time (min)
Form 32
Form 34
Form 36

Fig. 20

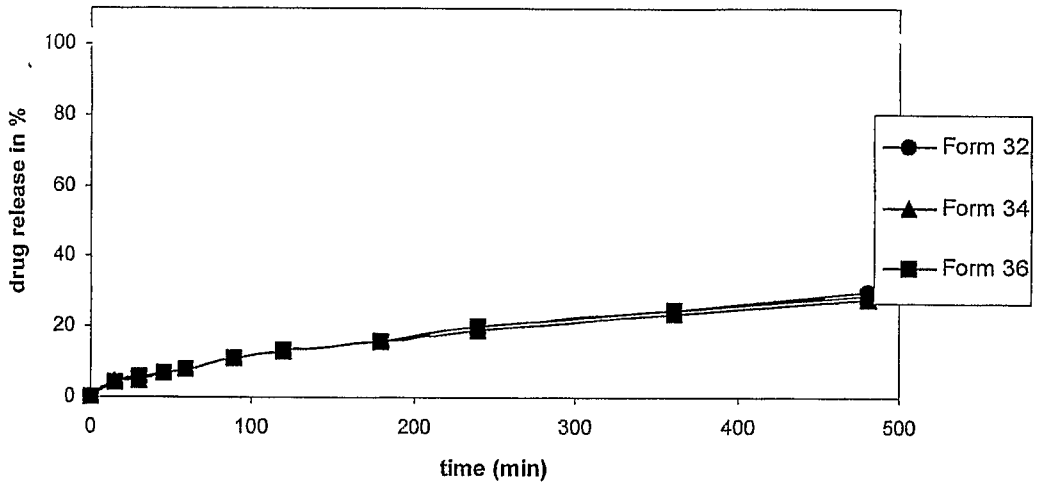

drug release in %
100
80
60
40
20
0
0
100
200
300
400
500
time (min)
Form 32
Form 34
Form 36

Fig. 21

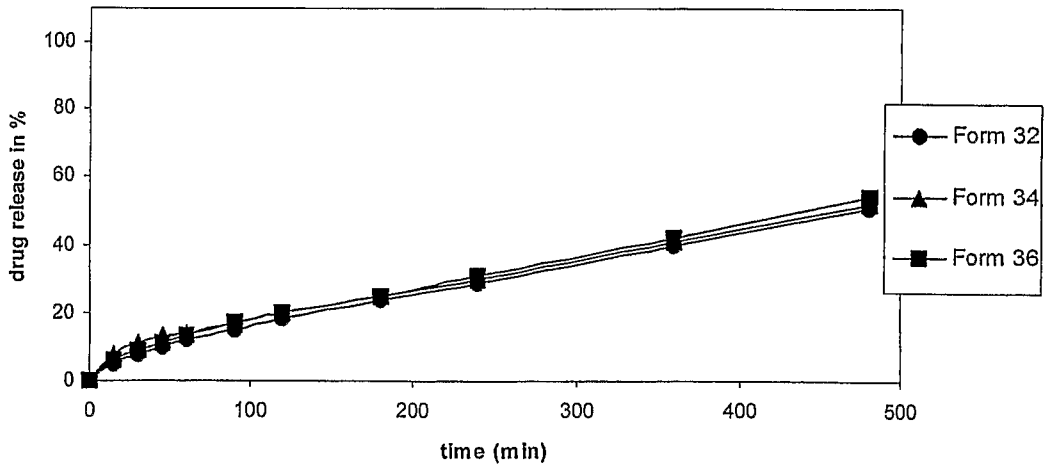

drug release in %
100
80
60
40
20
0
0
100
200
300
400
500
time (min)
Form 32
Form 34
Form 36

Fig. 22

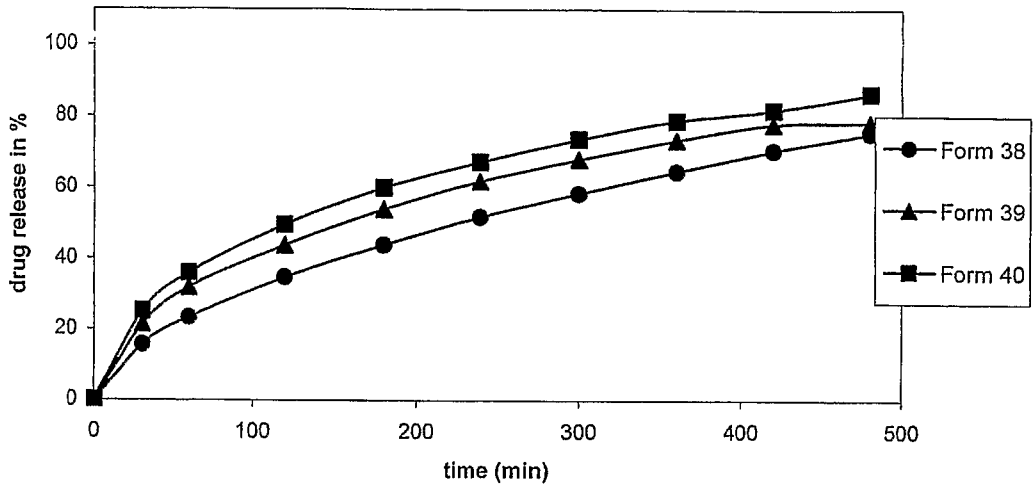
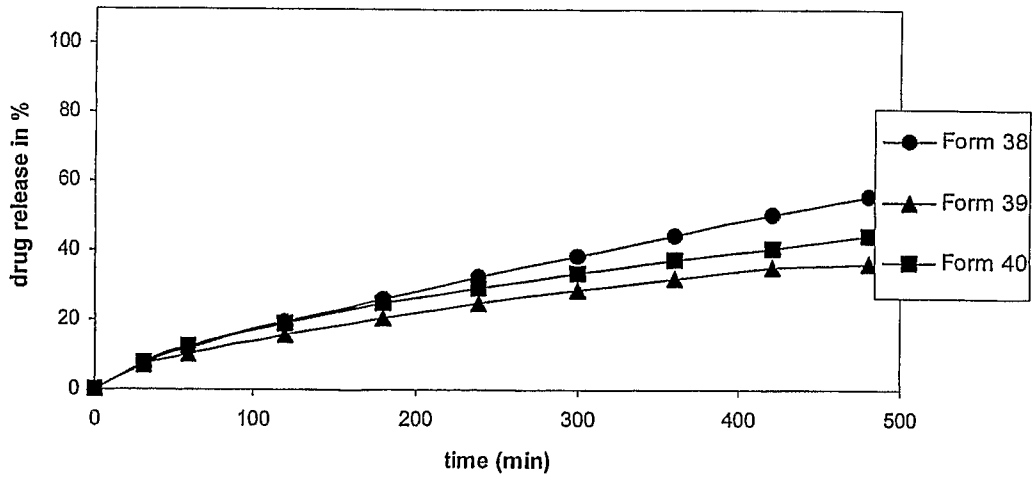


Fig. 23



5

Fig. 24

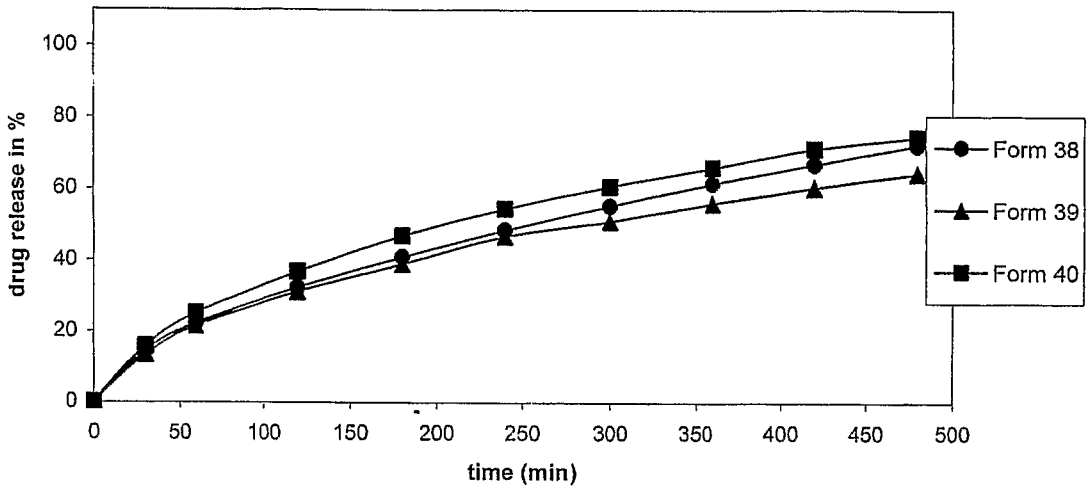
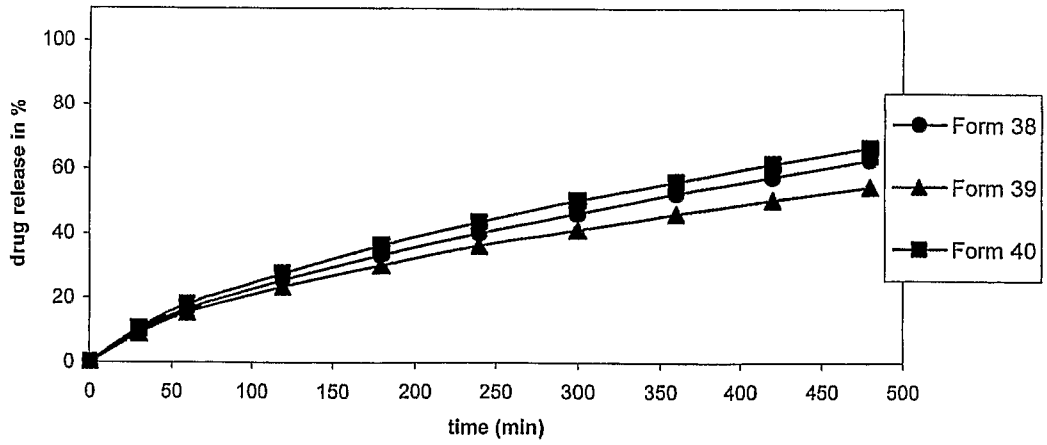


Fig.25



5

Fig. 26

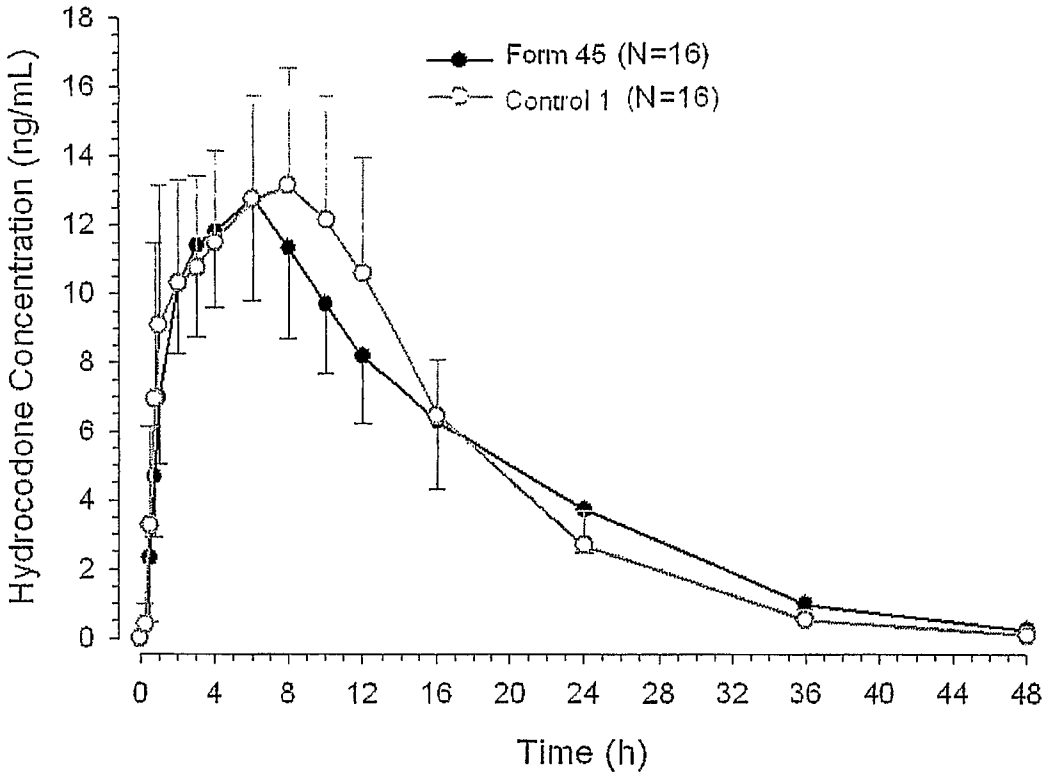

Hydrocodone Concentration (ng/mL)
18
16
14
12
10
8
6
4
2
0
Form 45 (N=16)
Control 1 (N=16)
0
4
8
12
16
20
24
28
32
36
40
44
48
Time (h)

Fig. 27

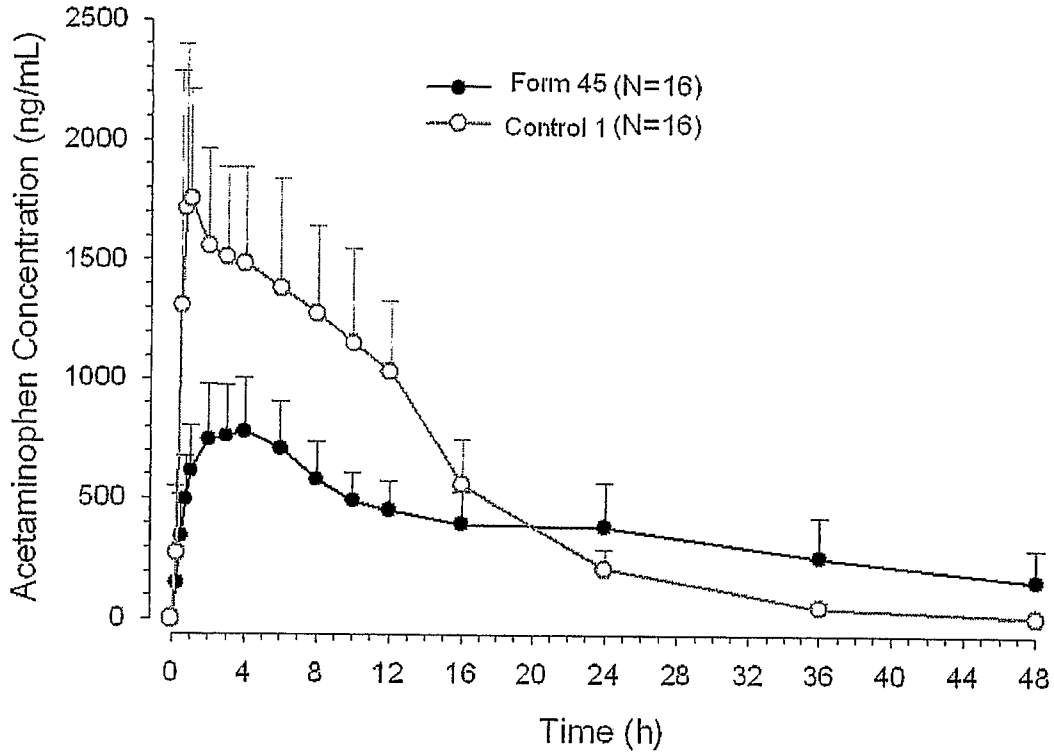
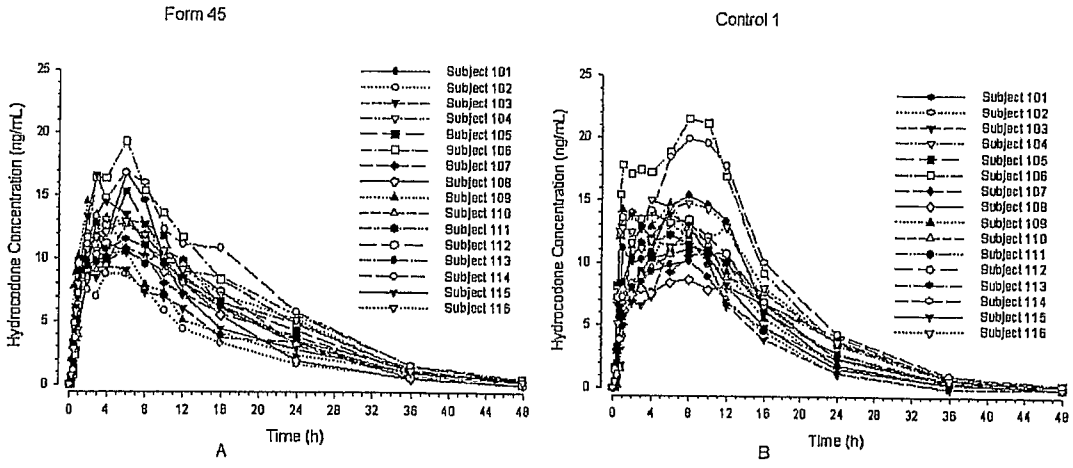


Fig. 28



5

Fig. 29

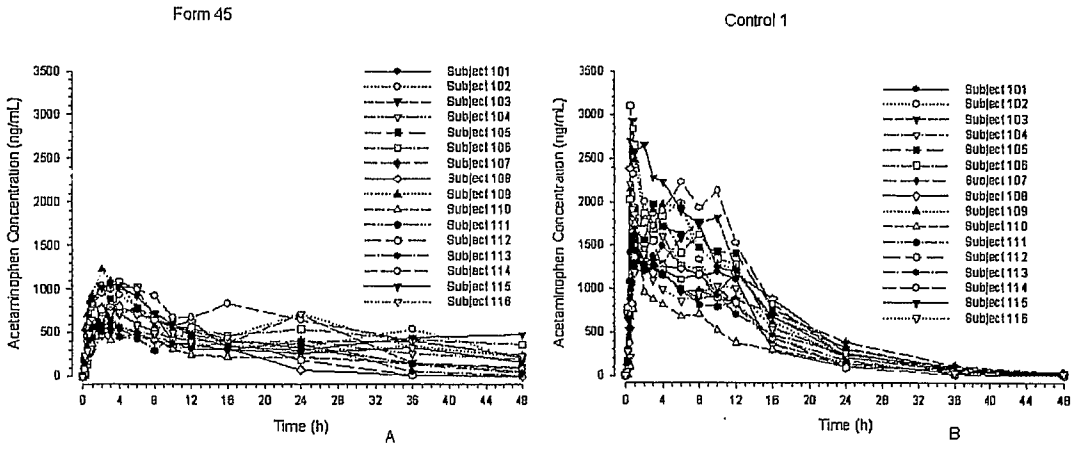

Form 45
Control 1
Acetaminophen Concentration (ng/mL)
Time (h)
Subject 101
Subject 102
Subject 103
Subject 104
Subject 105
Subject 106
Subject 107
Subject 108
Subject 109
Subject 110
Subject 111
Subject 112
Subject 113
Subject 114
Subject 115
Subject 116
A
B

Fig. 30

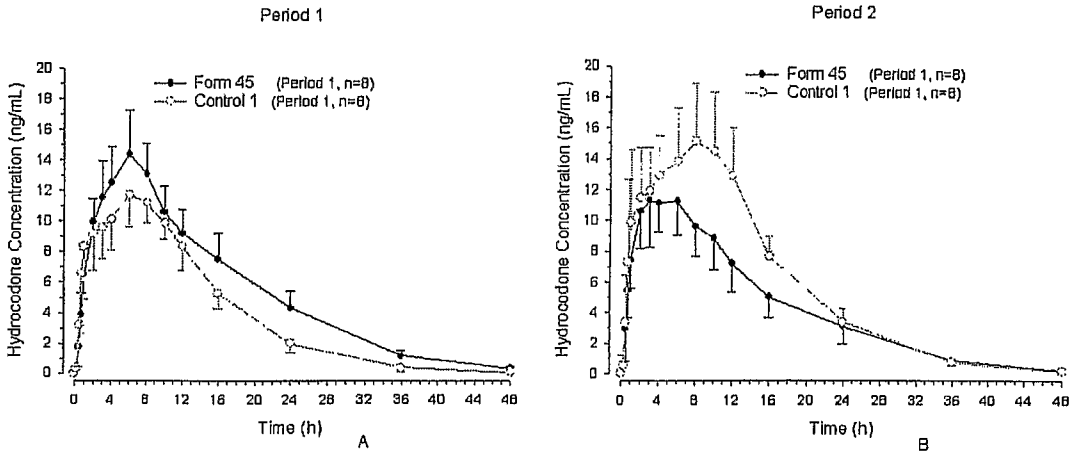

Period 1
Period 2
Hydrocodone Concentration (ng/mL)
Time (h)
Form 45 (Period 1, n=8)
Control 1 (Period 1, n=8)
A
B

Fig. 31

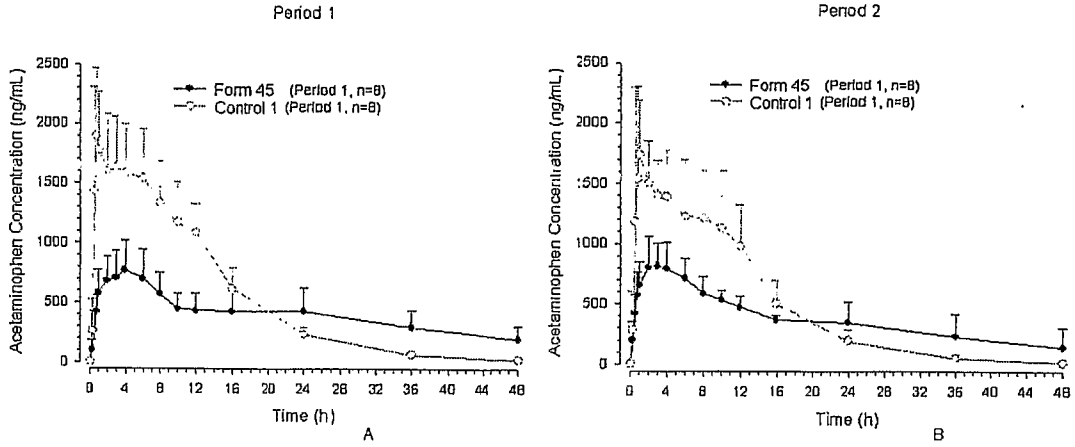
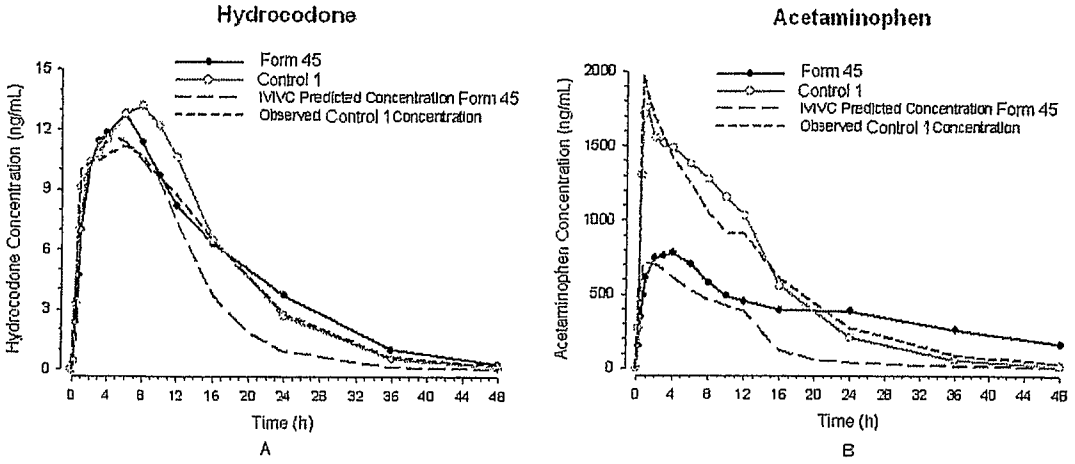


Fig. 32



5

Fig. 33

