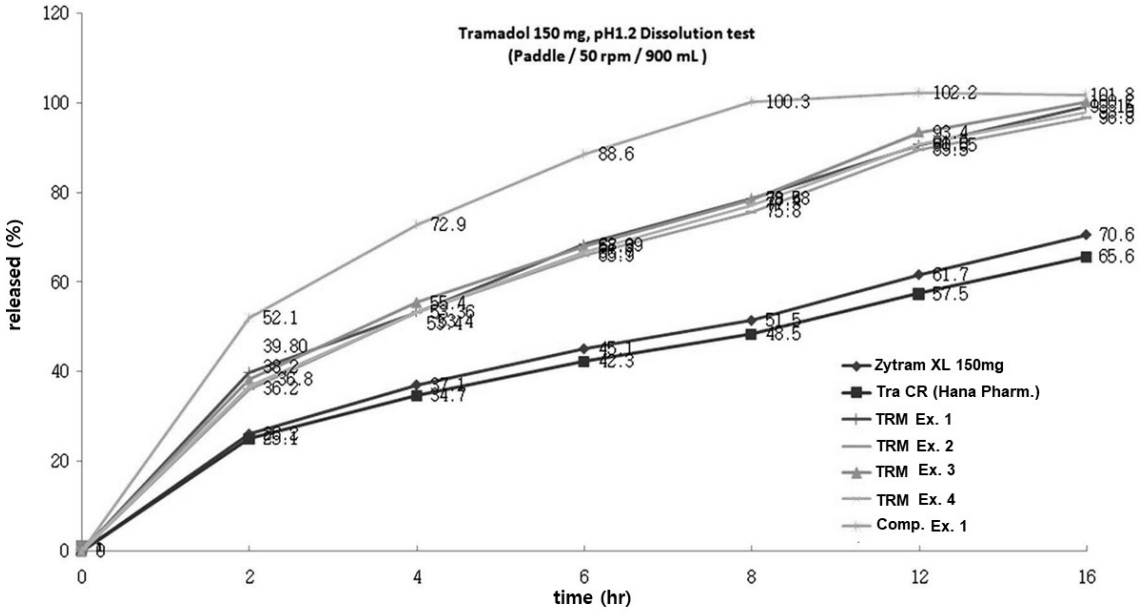
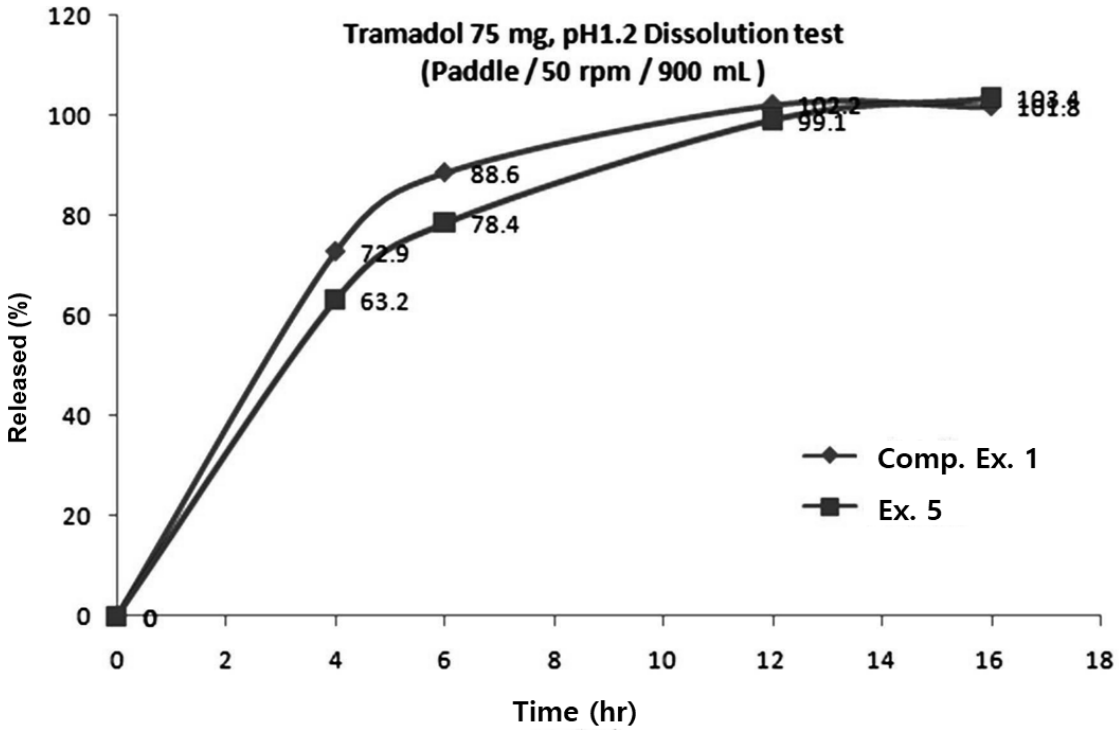
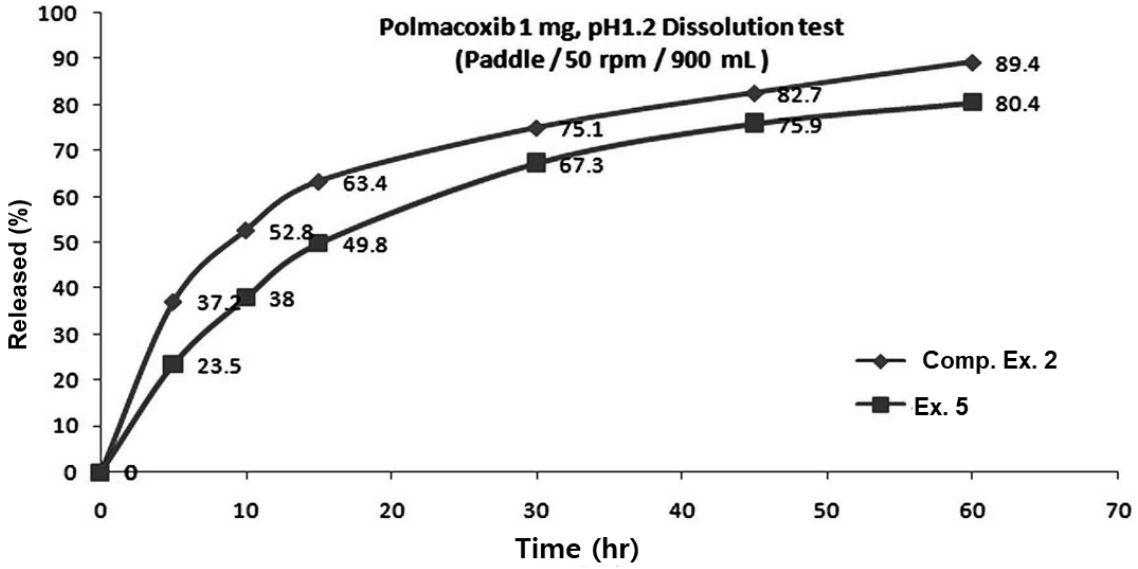
[Fig. 1]


Tramadol 150 mg, pH1.2 Dissolution test
(Paddle / 50 rpm / 900 mL)
released (%)
time (hr)
Zytram XL 150mg
Tra CR (Hana Pharm.)
TRM Ex. 1
TRM Ex. 2
TRM Ex. 3
TRM Ex. 4
Comp. Ex. 1
100.3
102.2
88.6
72.9
70.6
65.6
61.7
57.5
52.1
39.80

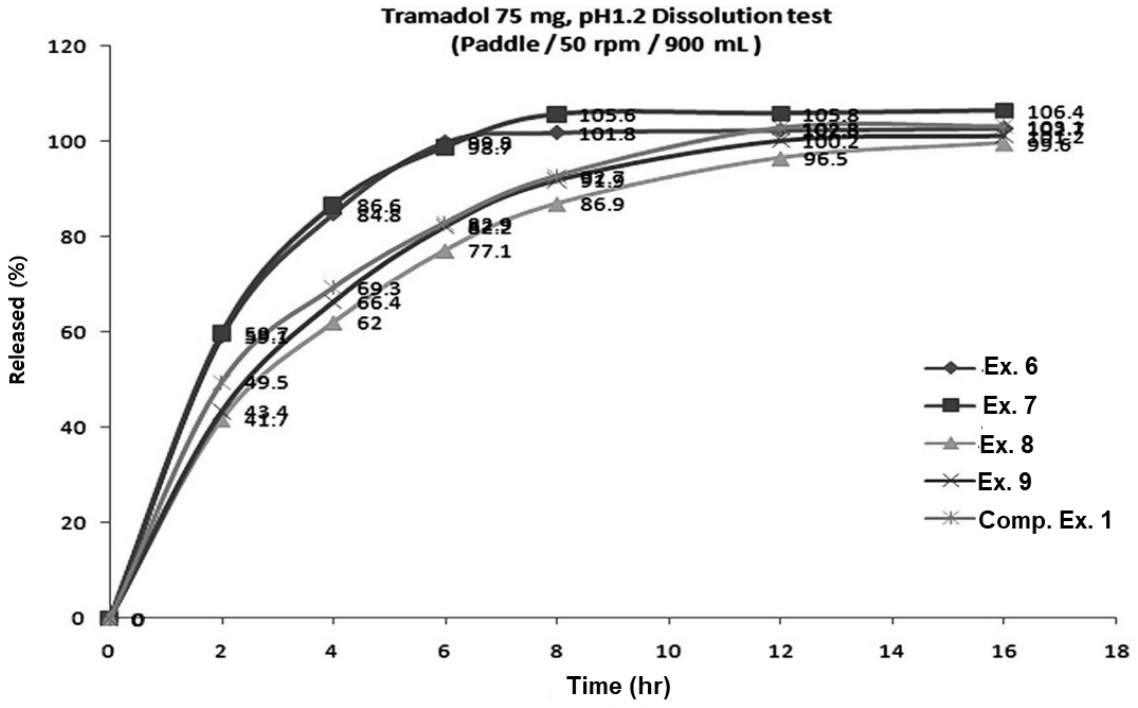
[Fig. 2]


Tramadol 75 mg, pH1.2 Dissolution test
(Paddle / 50 rpm / 900 mL)
Released (%)
Time (hr)
Comp. Ex. 1
Ex. 5
88.6
78.4
72.9
63.2
99.1
0

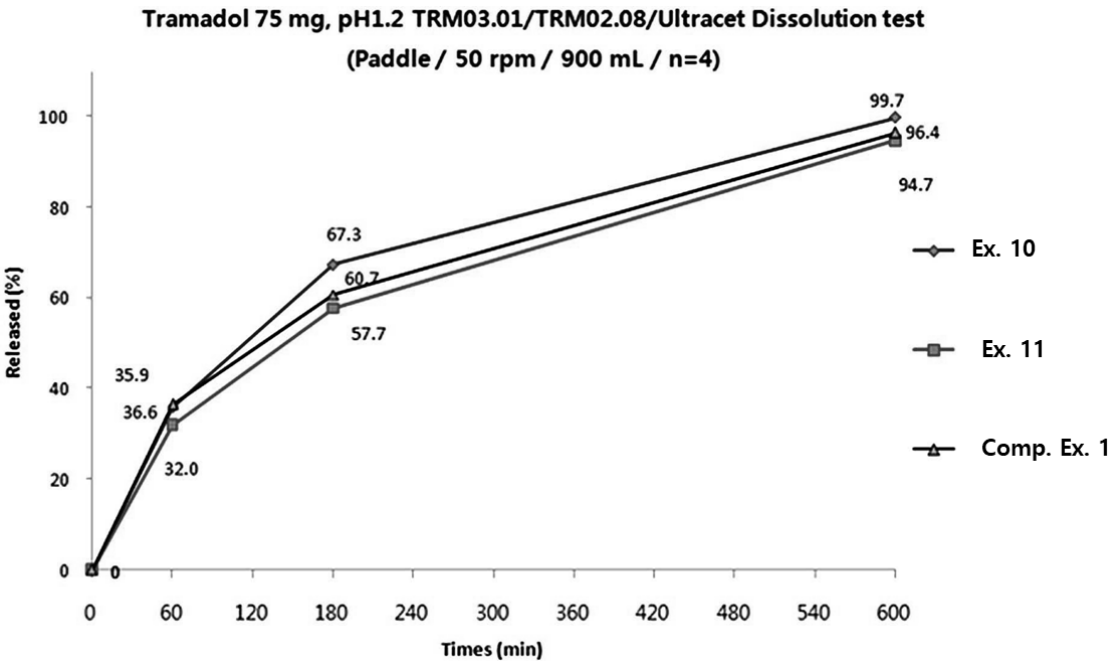
[Fig. 3]


Polmacoxib 1 mg, pH1.2 Dissolution test
(Paddle / 50 rpm / 900 mL)
Released (%)
Time (hr)
Comp. Ex. 2
Ex. 5
89.4
82.7
75.1
63.4
52.8
37.2
0
80.4
75.9
67.3
49.8
38
23.5

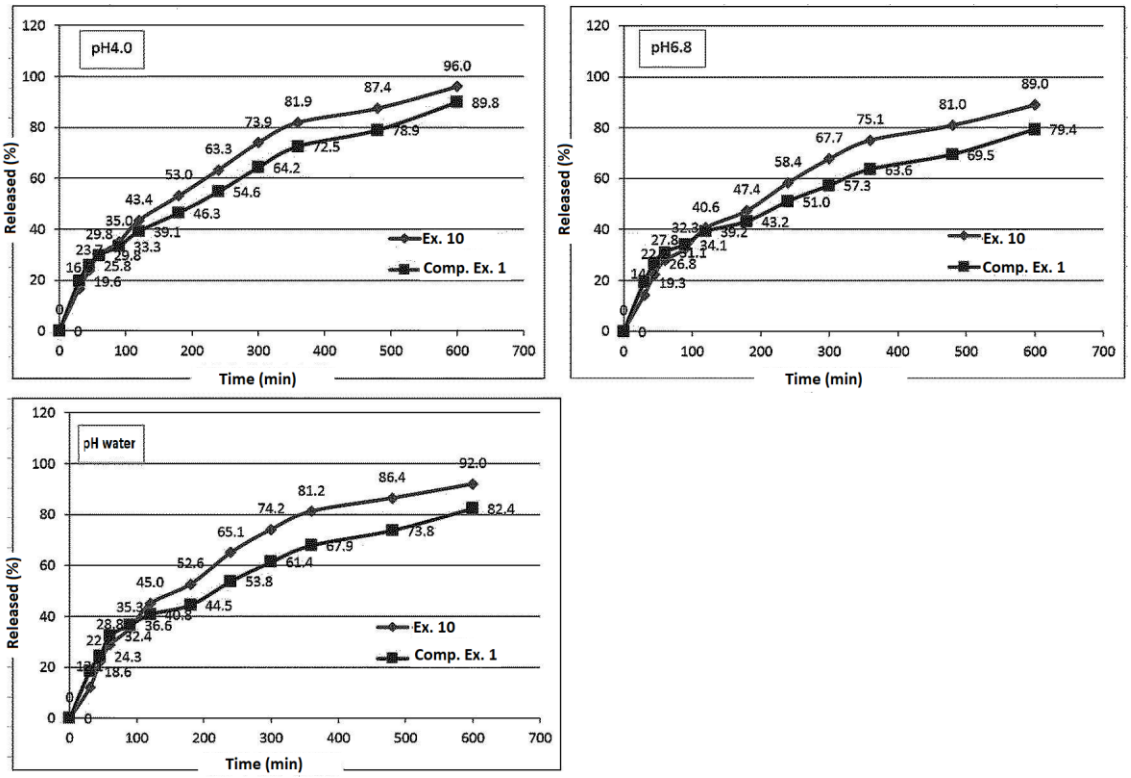
[Fig. 4]


Tramadol 75 mg, pH1.2 Dissolution test
(Paddle / 50 rpm / 900 mL)
Released (%)
Time (hr)
Ex. 6
Ex. 7
Ex. 8
Ex. 9
Comp. Ex. 1
106.4
105.6
101.8
96.5
86.9
77.1
69.3
66.4
62
49.5
41.7
0

[Fig. 5]

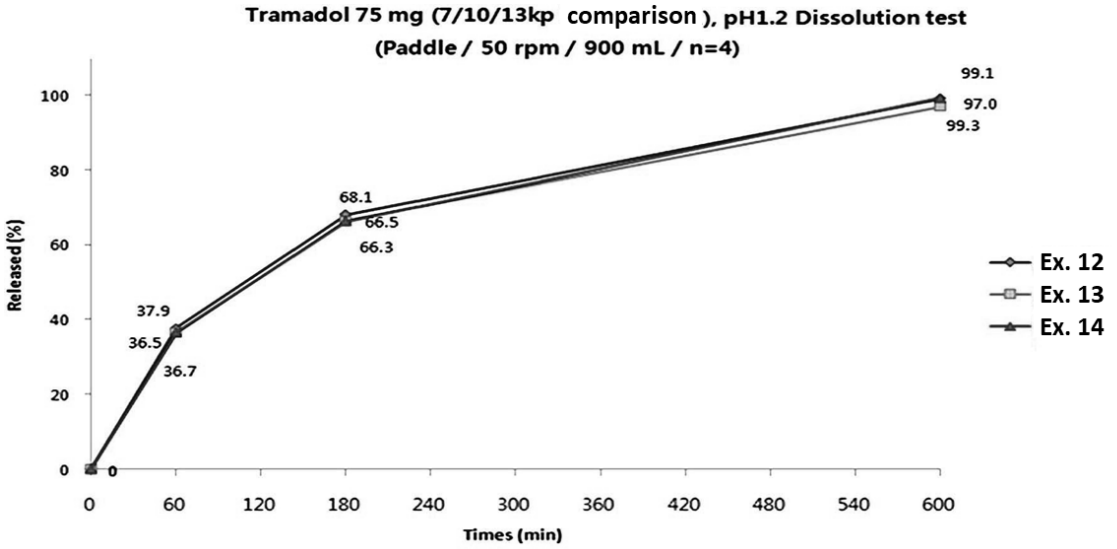

Tramadol 75 mg, pH1.2 TRM03.01/TRM02.08/Ultracet Dissolution test
(Paddle / 50 rpm / 900 mL / n=4)
Released (%)
Times (min)
Ex. 10
Ex. 11
Comp. Ex. 1
99.7
96.4
94.7
67.3
60.7
57.7
35.9
36.6
32.0

[Fig. 6]

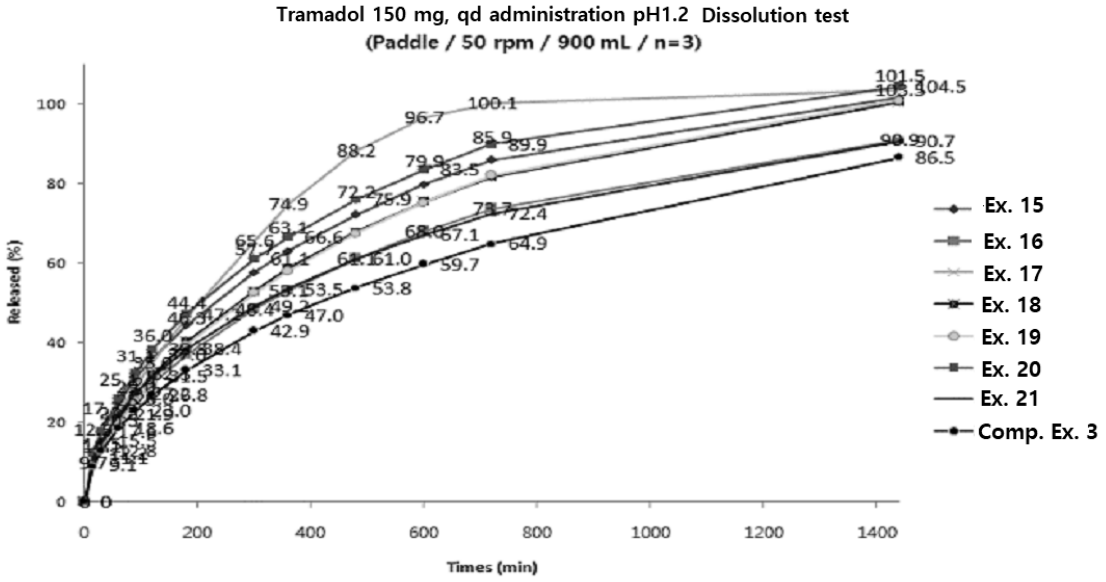

pH4.0
pH6.8
pH water
Released (%)
Time (min)
Ex. 10
Comp. Ex. 1

5

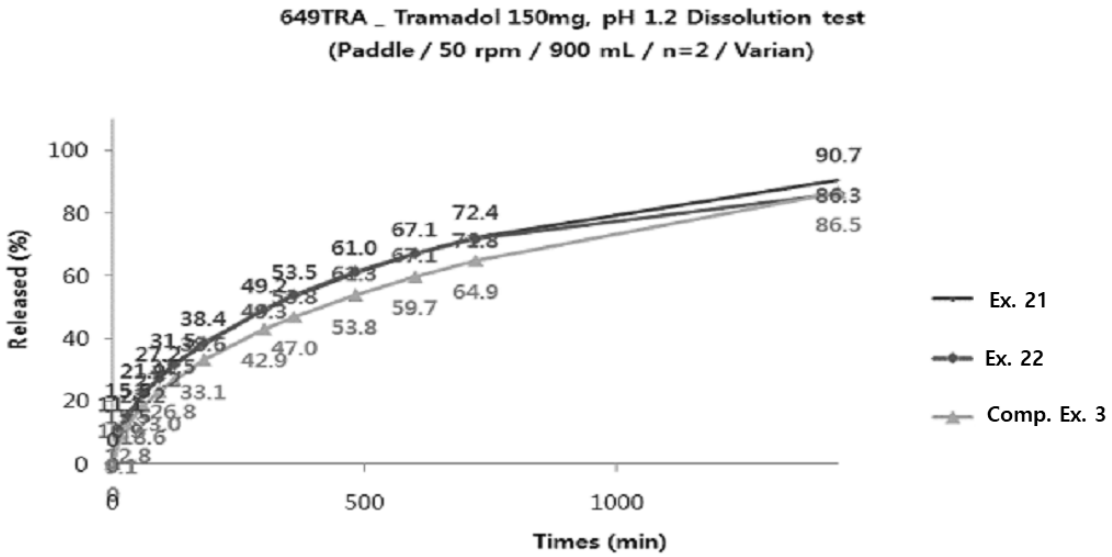
[Fig. 7]


Tramadol 75 mg (7/10/13kp comparison), pH1.2 Dissolution test
(Paddle / 50 rpm / 900 mL / n=4)
Released (%)
Times (min)
Ex. 12
Ex. 13
Ex. 14
99.1
97.0
99.3
68.1
66.5
66.3
37.9
36.5
36.7
0

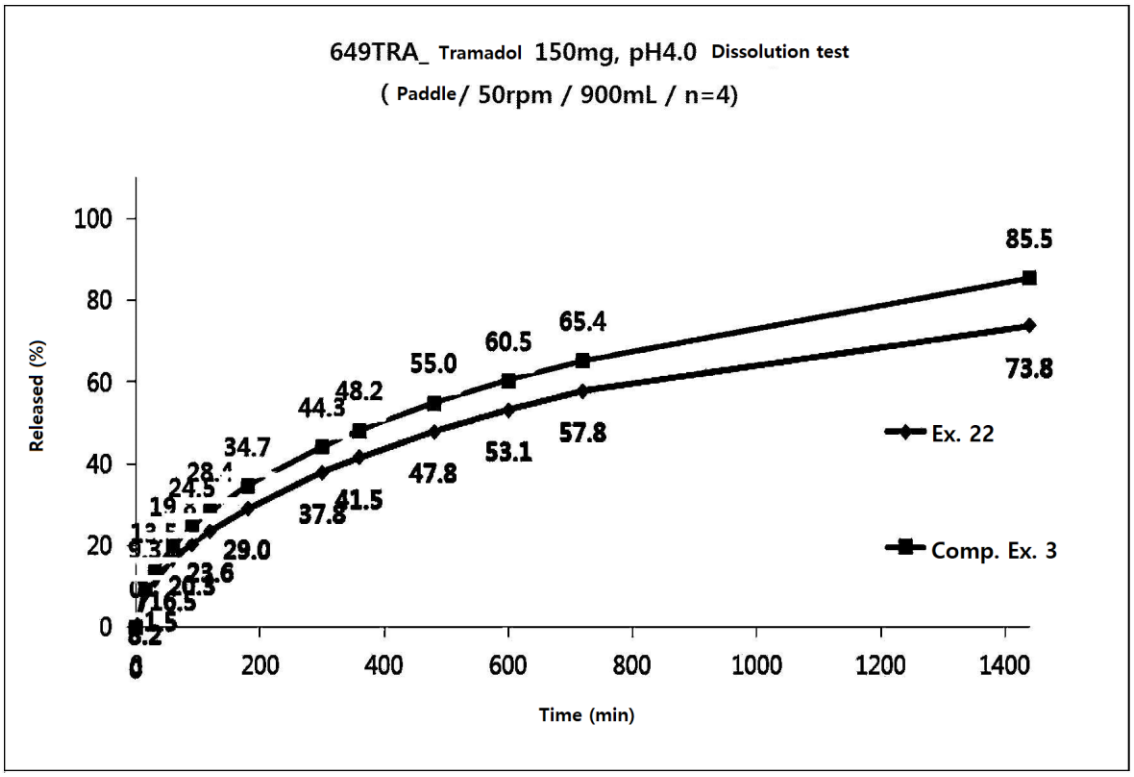
[Fig. 8]


Tramadol 150 mg, qd administration pH1.2 Dissolution test
(Paddle / 50 rpm / 900 mL / n=3)
Released (%)
Times (min)
Ex. 15
Ex. 16
Ex. 17
Ex. 18
Ex. 19
Ex. 20
Ex. 21
Comp. Ex. 3
101.5
104.5
100.1
96.7
88.2
89.9
86.5
74.9
72.4
64.9
59.7
53.8
47.0
42.9
33.1
0

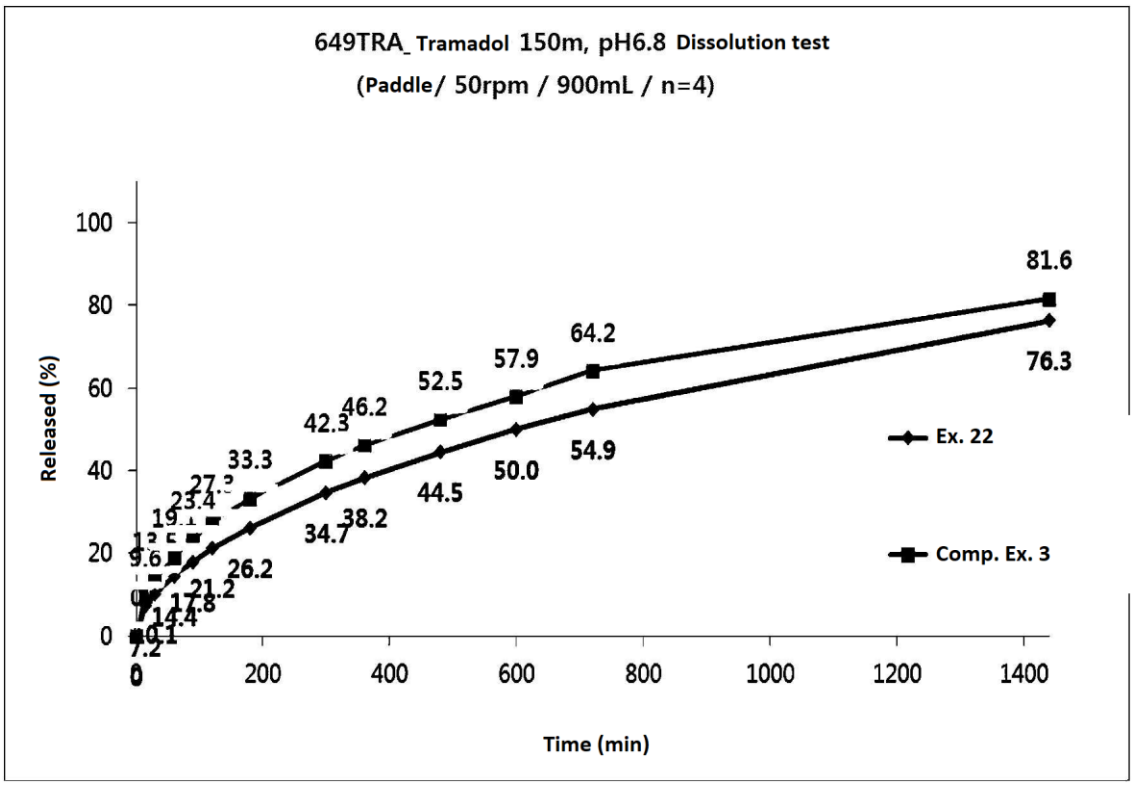
[Fig. 9]


649TRA _ Tramadol 150mg, pH 1.2 Dissolution test
(Paddle / 50 rpm / 900 mL / n=2 / Varian)
Released (%)
Times (min)
Ex. 21
Ex. 22
Comp. Ex. 3
90.7
86.3
86.5
72.4
67.1
61.0
53.5
49.2
38.4
64.9
59.7
53.8
47.0
42.9
33.1
26.8
18.6
12.8
0
500
1000

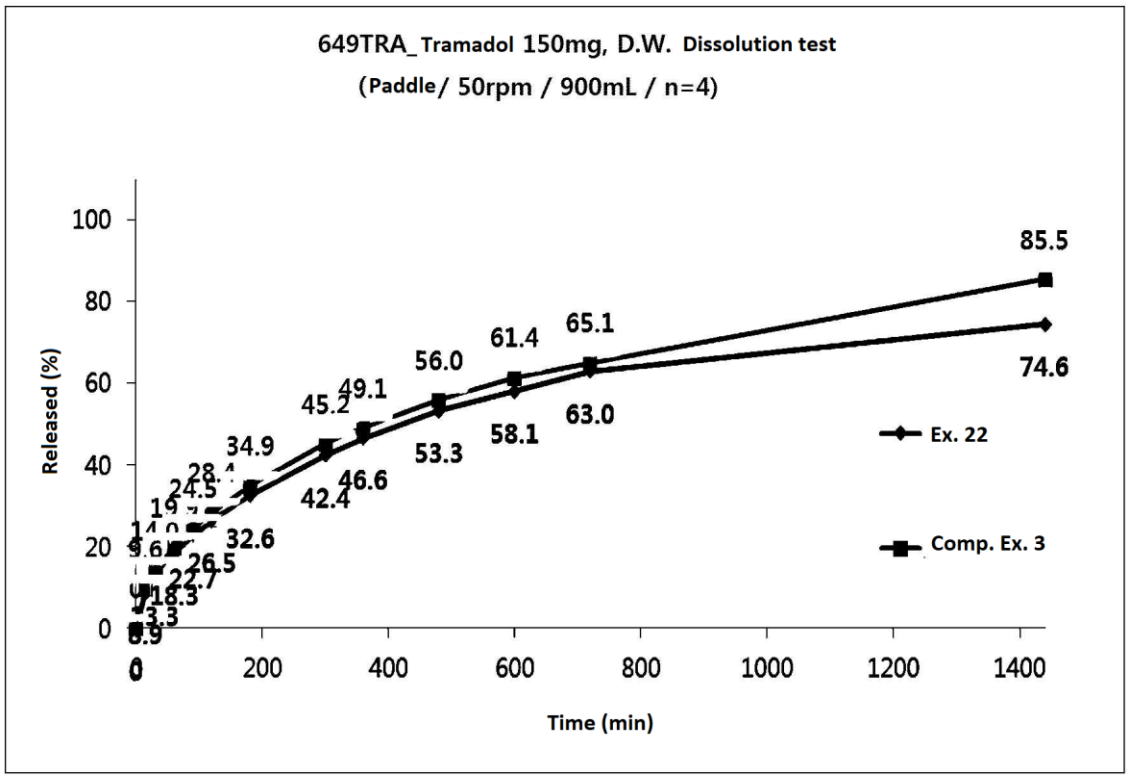
[Fig. 10]


649TRA_ Tramadol 150mg, pH4.0 Dissolution test
(Paddle/ 50rpm / 900mL / n=4)
Released (%)
Time (min)
Ex. 22
Comp. Ex. 3
85.5
73.8
65.4
60.5
55.0
48.2
44.3
34.7
29.0
57.8
53.1
47.8
41.5
37.8
0
200
400
600
800
1000
1200
1400

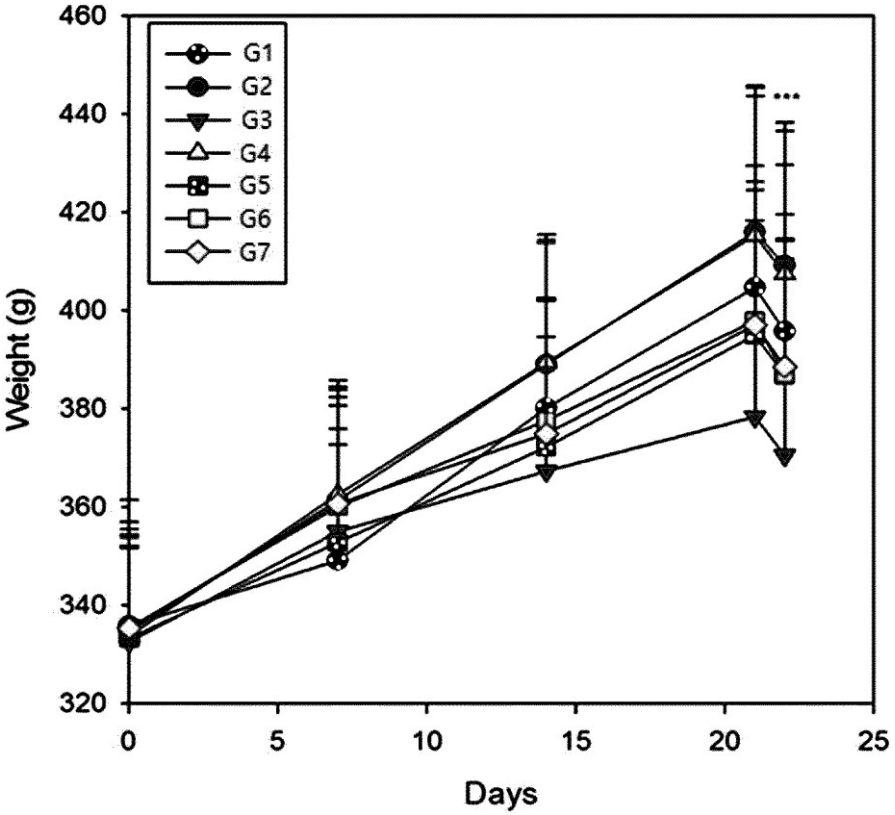
[Fig. 11]


649TRA_ Tramadol 150m, pH6.8 Dissolution test
(Paddle/ 50rpm / 900mL / n=4)
Released (%)
Time (min)
Ex. 22
Comp. Ex. 3
81.6
76.3
64.2
57.9
52.5
46.2
42.3
33.3
26.2
54.9
50.0
44.5
38.2
34.7
0
200
400
600
800
1000
1200
1400
0
20
40
60
80
100

[Fig. 12]

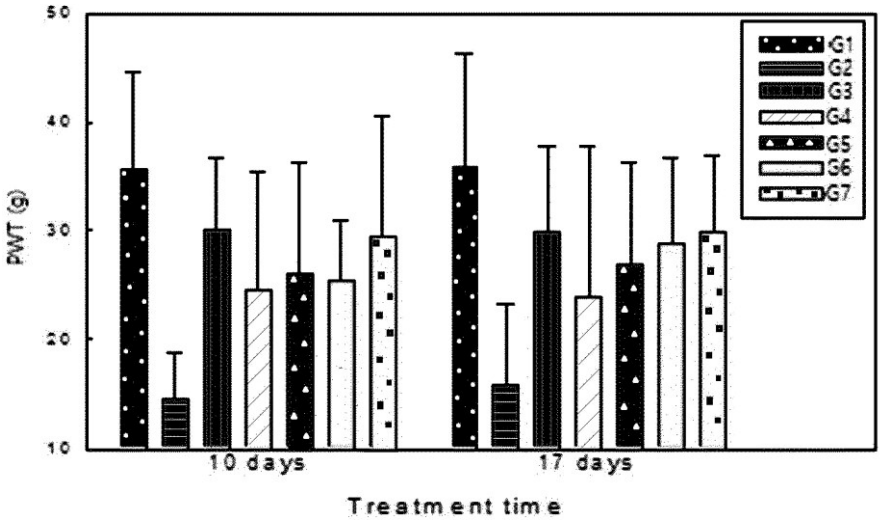

649TRA_Tramadol 150mg, D.W. Dissolution test
(Paddle/ 50rpm / 900mL / n=4)
Released (%)
Time (min)
Ex. 22
Comp. Ex. 3
85.5
74.6
65.1
63.0
61.4
58.1
56.0
53.3
49.1
46.6
45.2
42.4
34.9
32.6
26.5
24.5
22.7
18.3
0
200
400
600
800
1000
1200
1400
100
80
60
40
20
0

[Fig. 13]

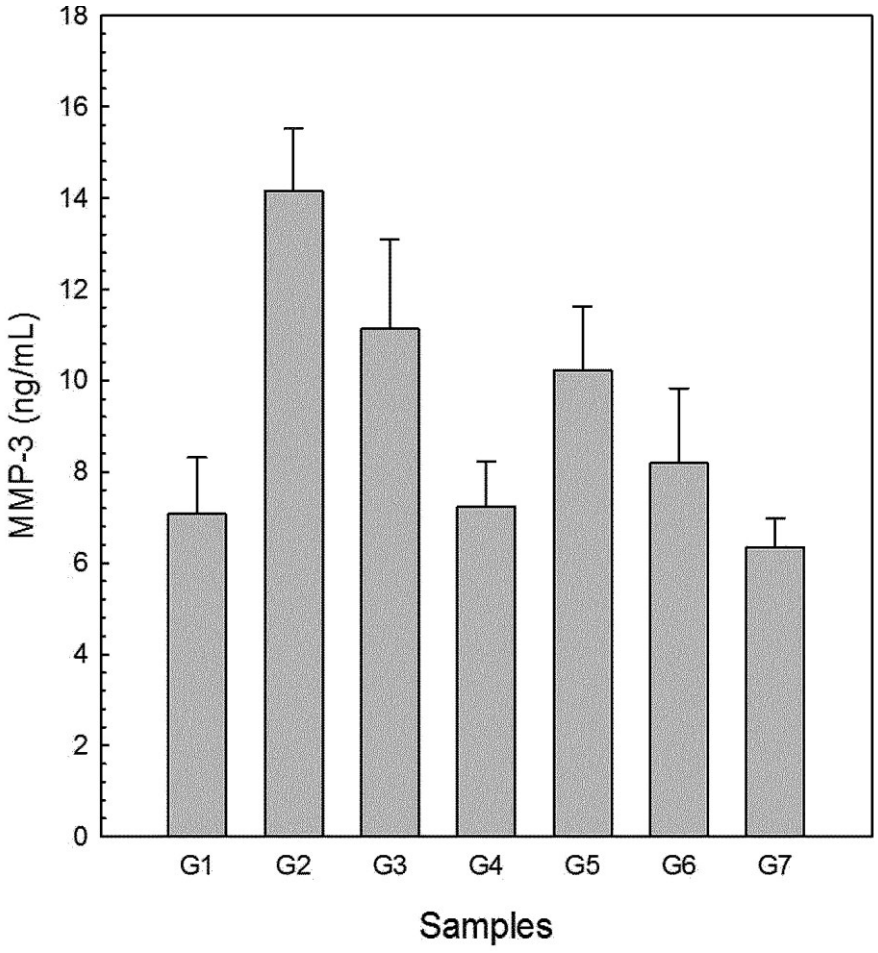


***Fasted in the 22nd day

[Fig. 14]



[Fig. 15]



[Fig. 16]

Group	A. No	Organ	Necropsy findings	No. of animals affected
G1	10	Stomach, Liver	NRF*	0
G3	10	Stomach, Liver	Gastric wall thickening	5
			Gastric mucosal petechial hemorrhages	4
			Gastric mucosal hyperemia	3
			Stomach ulcer	1
G4	10	Stomach, Liver	NRF	0
G5	10	Stomach, Liver	Liver nodules	1
			Gastric wall thickening	3
			Gastric mucosal petechial hemorrhages	3
G7	10	Stomach, Liver	Gastric mucosal petechial hemorrhages	2

[Fig. 17]

Group	Desquamation, Cardiac/fundic gland (0, 1+~4+)	Erosion, Cardiac/fundic gland (0, 1+~4+)
G1	None	None
G3	1+ 4/10 (cardiac, No. 24, 25, 27, 28)	None
G4	1+ 4/10 (cardiac, No. 31, 35, 38, 40)	None
G5	1+ (fundic, No. 41) 1+ (cardiac No. 48)	1+ (cardiac, No. 43) 2+ (fundic, No. 46, 49) 3+ (fundic, No. 48)
G7	None	None