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Appendices

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Appendix A

Preparation of Reagents

1. pH 1.2 buffer solution

Dissolve 2.0 g of sodium chloride in water



Add 7.0 ml of hydrochloric acid



Dilute with water to 1 liter, and mix

2. pH 6.8 buffer solution

Dissolve 21.27g of anhydrous dibasic sodium phosphate



And dissolve 4.94 g of citric acid monohydrate in water



Dilute with water to 1 liter, and mix

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Appendix B

The main composition of coated pellets are polymer and core pellets that may be absorbed UV. light at the same wavelength of propranolol hydrochloride (289.0 nm), the same method of drug content determination must be proved. The absorbance value was shown in Table 18 and one outstanding characteristic was shown in Figure 180-183.

Table 18 The absorbance value of the main compositions of coated pellets at 289.0 nm.

main compositions	sample 1	sample 2	sample 3
core lactose	0.008	0.001	0.002
coated core lactose with EURL 100	0.000	0.020	0.000
coated core lactose with EURS 100	0.000	0.000	0.000
coated core lactose with EC 100	0.000	0.000	0.000

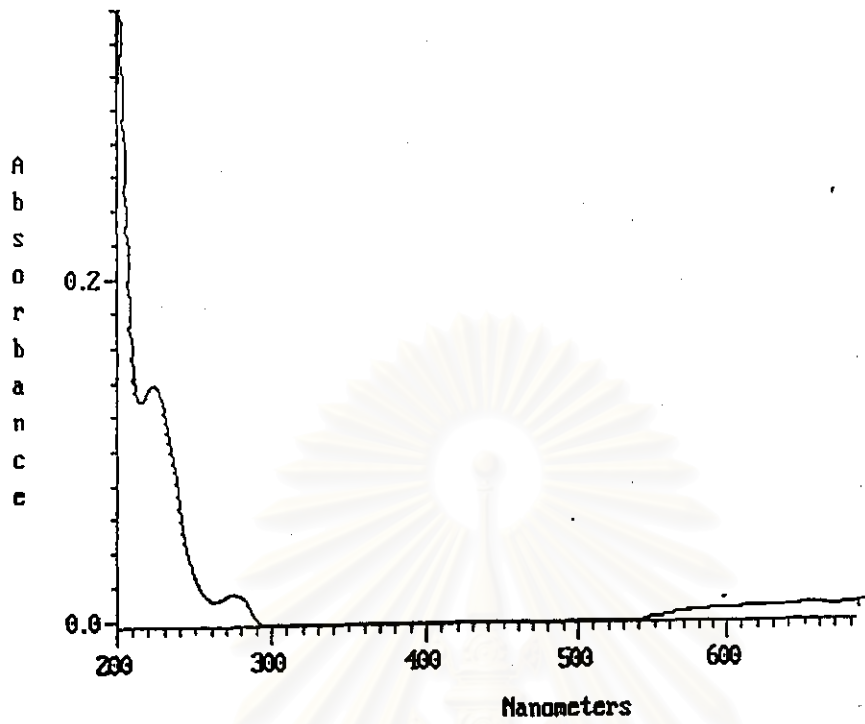


Figure 180 The sample scan of core lactose.

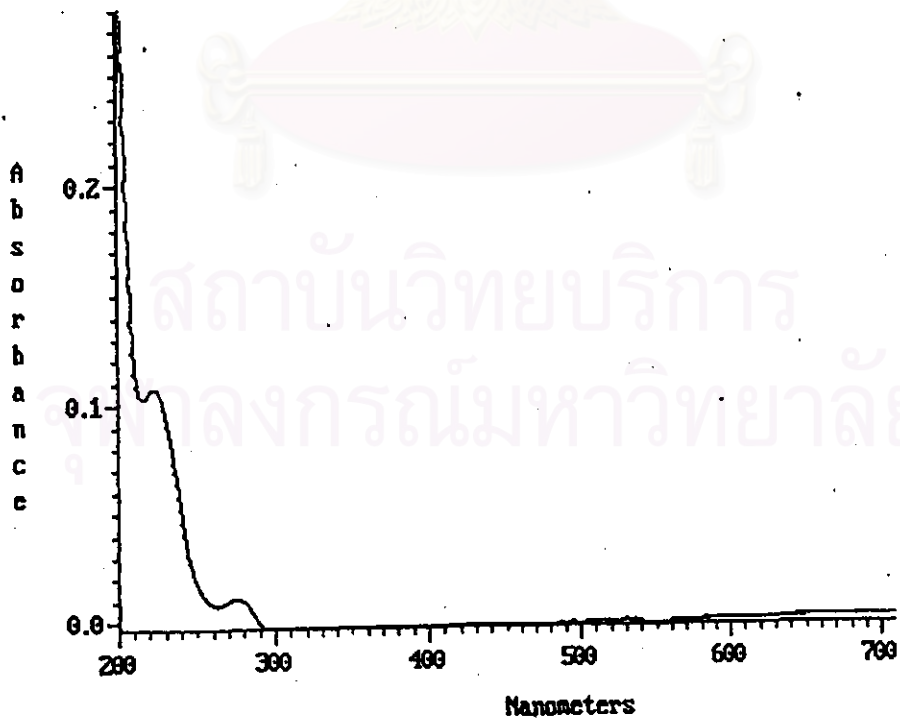


Figure 181 The sample scan of core lactose coated with EURL 100.

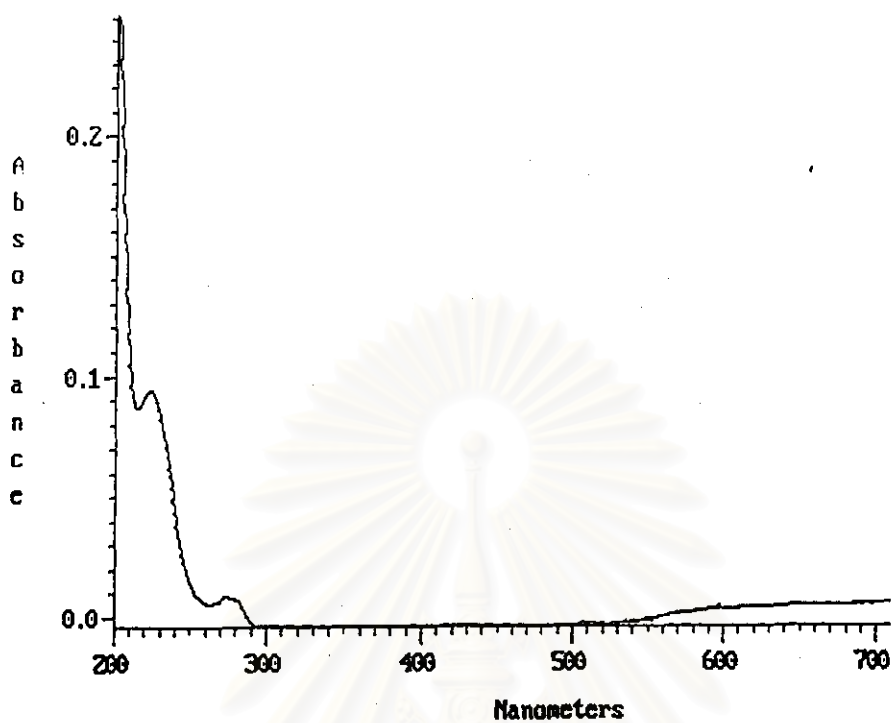


Figure 182 The sample scan of core lactose coated with EURS 100.

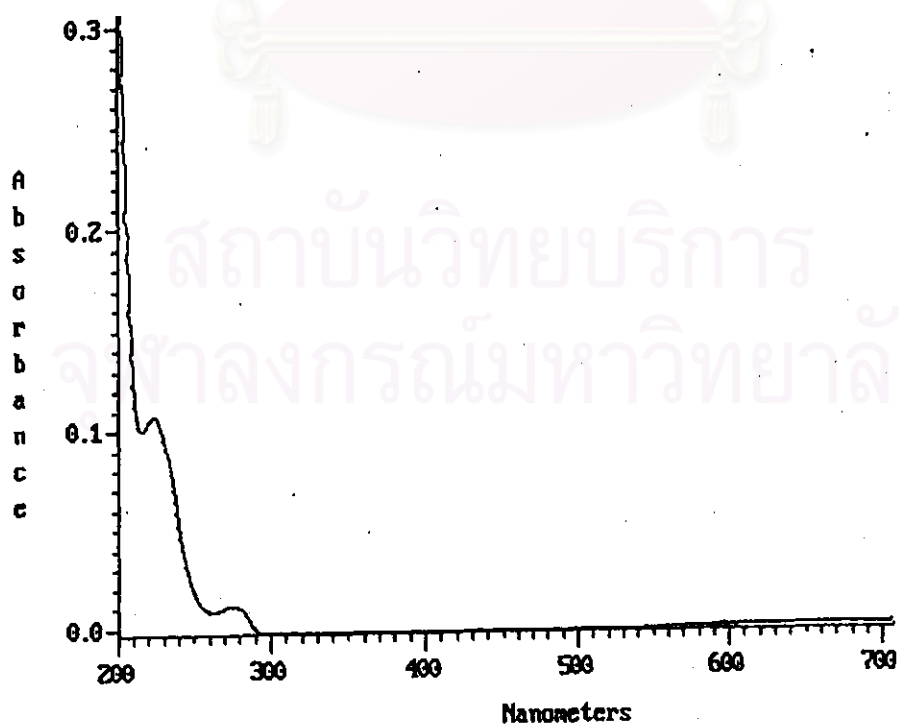


Figure 183 The sample scan of core lactose coated with EC 100.

Appendix C

Calibration curve

The UV absorbance at specific wavelength for each of standard concentrations of propranolol hydrochloride in acid buffer pH 1.2., phosphate buffer pH 6.8 and methanol are presented in Table 19, 20, and 21, respectively. The typical calibration curve obtained by regression analysis of these data are illustrated in Figure 184, 185, and 186, respectively.

Table 19 Absorbance of propranolol hydrochloride in acid buffer pH 1.2 at 289.0 nm.

Concentration (mcg/ml)	Absorbance
0	0
20	0.374
24	0.459
28	0.526
32	0.612
36	0.667
40	0.758

Coefficient of determination = 0.9992 ; $y = 0 + 0.0188 x$

(y = absorbance ; x = concentration)

Table 20 Absorbance of propranolol hydrochloride in phosphate buffer pH 6.8 at 289.0 nm.

Concentration (mcg/ml)	Absorbance
0	0
20	0.361
24	0.440
28	0.532
32	0.599
36	0.673
40	0.740

Coefficient of determination = 0.9991 ; $y = 0.0029 + 0.0181 x$

(y = absorbance ; x = concentration)

Table 21 Absorbance of propranolol hydrochloride in methanol at 289.0 nm.

Concentration (mcg/ml)	Absorbance
0	0
12	0.241
16	0.323
20	0.404
24	0.488
28	0.568
32	0.651

Coefficient of determination = 0.9999 ; $y = 0.00173 + 0.2036x$

(y = absorbance ; x = concentration)

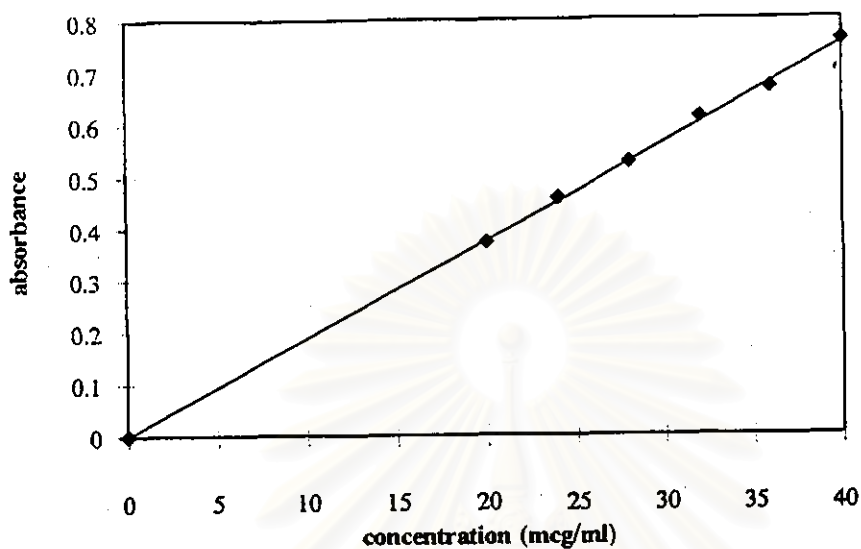


Figure 184 Typical calibration curve of propranolol hydrochloride in acid buffer pH 1.2.

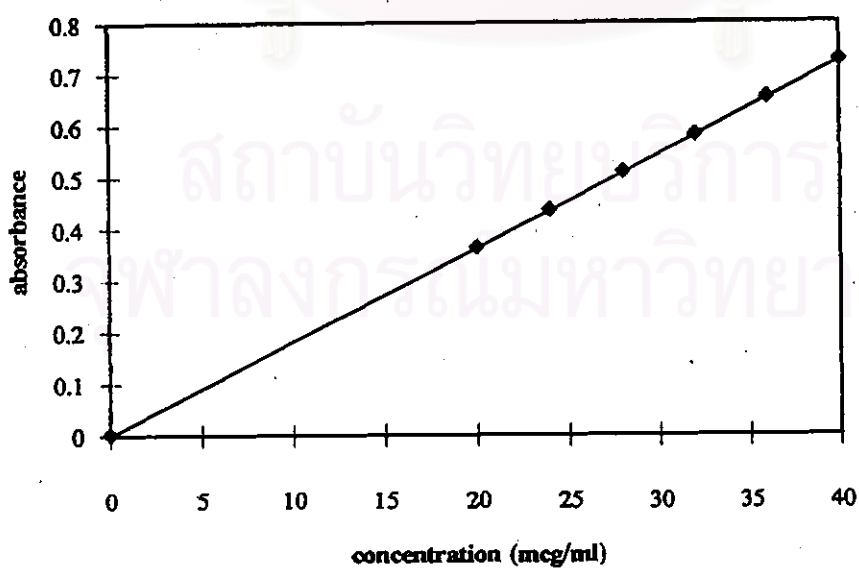


Figure 185 Typical calibration curve of propranolol hydrochloride in phosphate buffer pH 6.8.

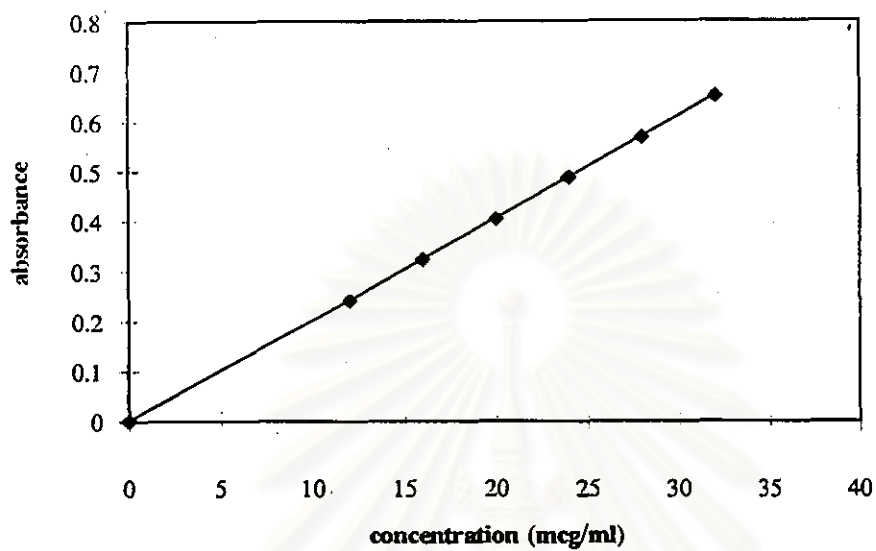


Figure 186 Typical calibration curve of propranolol hydrochloride in methanol.

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Appendix D

Dissolution Data

The cumulative percentage of drug dissolved from uncoated pellets, propranolol hydrochloride sustained-release pellets formulation 1-39, Inderal[®]LA160, and three combinations formulation which duplicated dissolution in 2 mediums as acid buffer pH 1.2 and phosphate buffer pH 6.8 were presented in Table 22-38. And by pH change method, cumulative percentage of drug dissolved from Inderal[®]LA160 and three combinations formulation were presented in Table 39.



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Table 22 Percent release of propranolol hydrochloride from uncoated pellets and coated pellets formulation 1-3 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Time	Dissolution medium	
		Acid buffer pH 1.2 Mean (SD)	Phosphate buffer pH 6.8 Mean (SD)
uncoated pellets	0	0 (0)	0 (0)
	0.5	96.89 (1.02)	100.46 (0.97)
	1	98.37 (1.22)	102.49 (0.29)
	2	100.69 (0.51)	103.20 (2.14)
	3	102.24 (0.26)	104.47 (1.78)
	4	103.74 (0.63)	104.84 (1.36)
	5	105.94 (0.20)	106.71 (0.68)
	6	107.41 (0.12)	107.83 (1.34)
1	0	0 (0)	0 (0)
	0.5	100.83 (2.63)	101.16 (0.45)
	1	102.85 (1.53)	105.09 (1.13)
	2	103.38 (1.28)	104.74 (0.38)
	3	103.40 (1.12)	104.68 (0.99)
	4	103.40 (1.18)	105.90 (0.98)
	5	102.00 (0.93)	106.98 (0.66)
	6	103.45 (2.30)	107.30 (0.46)
2	0	0 (0)	0 (0)
	0.5	102.63 (0.00)	56.71 (3.72)
	1	106.16 (0.83)	104.20 (1.74)
	2	108.23 (1.03)	107.81 (2.15)
	3	109.63 (3.95)	108.14 (1.85)
	4	108.30 (0.87)	108.75 (1.39)
	5	108.45 (0.52)	109.11 (1.36)
	6	108.00 (0.17)	109.61 (1.29)
3	0	0 (0)	0 (0)
	0.5	54.03 (1.73)	17.96 (3.24)
	1	100.20 (2.83)	85.21 (4.38)
	2	101.45 (0.69)	104.16 (0.80)
	3	101.35 (0.95)	106.15 (0.90)
	4	101.12 (3.91)	-

Table 23 Percent release of propranolol hydrochloride from coated pellets formulation 4-7 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Time	Dissolution medium	
		Acid buffer pH 1.2 Mean (SD)	Phosphate buffer pH 6.8 Mean (SD)
4	0	0 (0)	0 (0)
	0.5	85.57 (4.07)	17.99 (2.54)
	1	104.77 (0.52)	65.89 (4.82)
	2	107.42 (0.98)	99.96 (1.79)
	3	107.50 (1.69)	100.96 (2.11)
	4	107.35 (0.73)	101.00 (2.54)
	5	0 (0)	0 (0)
5	0	0 (0)	0 (0)
	0.5	99.78 (3.16)	96.04 (1.09)
	1	101.49 (0.82)	99.82 (0.65)
	2	102.40 (0.25)	99.46 (1.06)
	3	102.50 (3.16)	100.44 (1.36)
	4	102.72 (1.21)	99.87 (1.23)
	5	102.41 (2.76)	100.93 (1.43)
6	0	0 (0)	0 (0)
	0.5	101.13 (1.76)	53.63 (1.99)
	1	102.85 (3.08)	94.53 (1.41)
	2	103.76 (2.47)	101.64 (1.04)
	3	103.70 (1.84)	100.75 (1.79)
	4	102.70 (1.18)	102.04 (0.65)
	5	102.70 (1.67)	102.23 (0.40)
	6	103.70 (1.68)	102.76 (1.42)
7	0	0(0)	0(0)
	0.5	92.60 (4.98)	17.59 (3.05)
	1	101.41 (0.15)	73.15 (3.36)
	2	101.50 (3.58)	98.81 (1.15)
	3	101.30 (1.71)	99.71 (0.42)
	4	101.40 (1.31)	100.38(1.30)
	5	101.00 (1.75)	100.27 (1.28)
	6	102.21 (1.84)	100.68 (2.68)
	7	102.50 (1.69)	-
8	101.40 (1.87)	-	

Table 24 Percent release of propranolol hydrochloride from coated pellets formulation 8-10 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Time	Dissolution medium	
		Acid buffer pH 1.2 Mean (SD)	Phosphate buffer pH 6.8 Mean (SD)
8	0	0 (0)	0 (0)
	0.5	89.31 (1.35)	6.55 (2.26)
	1	102.57 (4.54)	43.57 (5.43)
	2	102.71 (4.68)	94.85 (1.04)
	3	102.50 (1.70)	101.66 (0.69)
	4	102.31 (4.01)	101.97 (0.93)
9	0	0 (0)	0 (0)
	0.5	98.74 (3.90)	88.52 (2.28)
	1	99.15 (3.68)	95.67 (0.41)
	2	100.14 (2.87)	97.03 (1.08)
	3	101.05 (3.98)	97.58 (0.51)
	4	101.00 (4.18)	97.27 (1.54)
	5	100.96 (0.84)	98.46 (0.80)
	6	-	98.24 (0.50)
10	0	0 (0)	0 (0)
	0.5	95.24 (4.57)	53.13 (2.56)
	1	97.70 (2.87)	88.56 (2.40)
	2	97.51 (1.83)	94.30 (2.22)
	3	98.00 (3.69)	95.23 (3.24)
	4	97.50 (2.09)	94.71 (3.06)
	5	-	94.67 (3.85)
	6	-	96.27 (4.11)

Table 25 Percent release of propranolol hydrochloride from coated pellets formulation 11-13 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Time	Dissolution medium	
		Acid buffer pH 1.2	Phosphate buffer pH 6.8
		Mean (SD)	Mean (SD)
11	0	0 (0)	0 (0)
	0.5	97.54 (1.84)	12.11 (4.14)
	1	99.07 (1.83)	60.33 (3.52)
	2	99.68 (2.27)	96.29 (1.15)
	3	99.50 (3.65)	100.07 (0.70)
	4	99.60 (91.47)	101.35 (0.56)
	5	99.51 (2.14)	101.90 (0.67)
	6	99.20 (1.54)	101.83 (1.89)
12	0	0 (0)	0 (0)
	0.5	95.75 (1.22)	6.45 (0.88)
	1	101.15 (1.80)	42.52 (2.45)
	2	101.79 (1.24)	94.03 (2.01)
	3	101.10 (2.27)	99.93 (1.59)
	4	101.20 (1.45)	101.62 (1.13)
	5	101.57 (2.87)	103.43 (1.79)
	6	101.37 (4.89)	102.43 (1.84)
13	0	0 (0)	0 (0)
	0.5	98.74 (1.25)	61.55 (0.57)
	1	103.73 (1.35)	97.83 (0.52)
	2	103.92 (2.57)	105.77 (2.62)
	3	103.10 (3.790)	104.67 (0.91)
	4	103.18 (1.84)	105.19 (0.41)
	5	103.30 (1.13)	105.27 (0.66)
	6	103.37 (4.75)	105.58 (0.52)
	7	-	105.78 (0.24)
	8	-	106.07 (0.63)
	9	-	106.30 (1.18)
	10	-	105.67 (0.77)
11	-	106.28 (0.21)	
12	-	107.33 (0.22)	

Table 26 Percent release of propranolol hydrochloride from coated pellets formulation 14-16 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Time	Dissolution medium	
		Acid buffer pH 1.2	Phosphate buffer pH 6.8
		Mean (SD)	Mean (SD)
14	0	0 (0)	0 (0)
	0.5	83.63 (3.56)	5.88 (0.33)
	1	99.67 (0.57)	44.92 (2.68)
	2	99.24 (3.65)	92.70 (0.86)
	3	99.50 (3.90)	100.39 (0.66)
	4	100.00 (3.33)	102.39 (1.37)
	5	101.30 (4.92)	102.19 (0.40)
	6	102.50 (2.95)	102.99 (0.39)
	7	101.90 (1.48)	102.82 (0.62)
	8	-	103.75 (0.27)
	9	-	103.82 (0.30)
	10	-	105.59 (2.41)
	11	-	103.50 (0.98)
12	-	104.53 (0.99)	
15	0	0 (0)	0 (0)
	0.5	91.56 (2.78)	2.94 (0.21)
	1	104.24 (4.55)	20.23 (0.27)
	2	104.37 (2.94)	83.87 (1.93)
	3	104.00 (4.74)	100.94 (2.26)
	4	104.20 (3.40)	105.16 (1.61)
	5	104.20 (1.84)	104.95 (2.03)
6	104.31 (1.68)	105.22 (2.90)	
16	0	0 (0)	0 (0)
	0.5	64.33 (1.52)	2.10 (0.52)
	1	102.44 (2.77)	6.07 (0.96)
	2	104.06 (1.78)	47.81 (2.86)
	3	104.07 (0.14)	82.73 (3.28)
	4	104.40 (2.51)	93.77 (2.03)
	5	104.00 (1.58)	99.76 (1.68)
	6	104.06 (3.96)	101.84 (2.52)
7	-	103.32 (2.55)	

Table 27 Percent release of propranolol hydrochloride from coated pellets formulation 17-18 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Time	Dissolution medium	
		Acid buffer pH 1.2	Phosphate buffer pH 6.8
		Mean (SD)	Mean (SD)
17	0	0 (0)	0 (0)
	0.5	6.86 (0.25)	6.21 (0.27)
	1	36.25 (1.45)	21.47 (0.89)
	2	83.16 (0.76)	53.44 (1.59)
	3	97.79 (2.18)	72.17 (0.93)
	4	97.72 (1.67)	82.19 (1.25)
	5	99.87 (2.04)	87.60 (0.93)
	6	102.24 (1.22)	90.70 (0.78)
	7	103.37 (2.58)	95.22 (0.83)
	8	-	97.64 (0.31)
	9	-	98.51 (1.10)
	10	-	100.29 (0.52)
	11	-	101.77 (0.20)
12	-	101.70 (0.97)	
18	0	0 (0)	0 (0)
	0.5	1.64 (0.46)	1.97 (0.33)
	1	7.10 (0.78)	3.57 (0.57)
	2	28.66 (5.51)	10.37 (0.64)
	3	65.09 (1.02)	23.78 (0.32)
	4	86.41 (0.51)	39.37 (1.43)
	5	97.52 (0.77)	54.30 (0.65)
	6	103.23 (0.38)	63.92 (1.17)
	7	105.49 (1.10)	72.68 (0.52)
	8	-	83.14 (4.38)
	9	-	83.73 (1.11)
	10	-	88.30 (1.26)
	11	-	89.71 (1.37)
12	-	93.25 (1.62)	

Table 28 Percent release of propranolol hydrochloride from coated pellets formulation 19-20 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Dissolution medium				
	Time	$\sqrt{\text{Time}}$	Acid buffer pH 1.2 Mean (SD)	Phosphate buffer pH 6.8 Mean (SD)	Log % drug remained
19	0	0	0 (0)	0 (0)	2
	0.5	0.71	1.44 (0.44)	1.66 (0.02)	1.99
	1	1	2.44 (0.32)	2.09 (0.36)	1.99
	2	1.41	9.23 (1.52)	2.40 (0.19)	1.99
	3	1.73	44.88 (2.27)	4.13 (0.49)	1.98
	4	2	75.93 (3.01)	8.83 (0.66)	1.96
	5	2.24	97.02 (1.75)	16.92 (0.73)	1.92
	6	2.45	100.23 (1.79)	27.35 (0.60)	1.86
	7	2.65	-	38.83 (0.76)	1.79
	8	2.83	-	49.73 (0.93)	1.70
	9	3	-	58.75 (1.22)	1.62
	10	3.16	-	68.71 (2.22)	1.50
	11	3.32	-	73.31 (0.49)	1.43
12	3.46	-	78.25 (0.35)	1.34	
20	0	0	0 (0)	0 (0)	2
	0.5	0.71	0.67 (0.10)	1.24 (0.17)	1.99
	1	1	1.34 (0.40)	1.34 (0.13)	1.99
	2	1.41	3.65 (0.30)	1.64 (0.10)	1.99
	3	1.73	20.69 (1.39)	2.26 (0.41)	1.98
	4	2	47.37 (2.80)	4.27 (0.62)	1.96
	5	2.24	84.39 (4.93)	7.96 (0.35)	1.93
	6	2.45	91.55 (1.79)	13.94 (0.23)	1.89
	7	2.65	99.13 (1.20)	21.83 (0.54)	1.84
	8	2.83	102.40 (1.80)	30.66 (1.19)	1.79
	9	3	105.04 (1.22)	38.22 (0.40)	1.68
	10	3.16	105.40 (0.27)	52.12 (2.72)	1.63
	11	3.32	-	56.74 (0.24)	1.57
12	3.46	-	62.57 (0.64)	-	

Table 29 Percent release of propranolol hydrochloride from coated pellets formulation 21-22 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Time	Dissolution medium	
		Acid buffer pH 1.2 Mean (SD)	Phosphate buffer pH 6.8 Mean (SD)
21	0	0 (0)	0 (0)
	0.5	5.02 (0.47)	4.73 (0.91)
	1	11.40 (0.34)	12.20 (1.49)
	2	24.49 (0.31)	27.49 (2.33)
	3	35.59 (0.31)	38.82 (2.08)
	4	42.33 (0.73)	47.73 (1.55)
	5	45.79 (0.16)	55.31 (2.00)
	6	46.77 (0.98)	62.06 (2.00)
	7	54.70 (0.82)	66.21 (1.35)
	8	74.09 (0.94)	69.73 (1.95)
	9	78.92 (1.25)	72.87 (1.25)
	10	83.14 (0.94)	75.44 (1.52)
	11	86.61 (0.89)	77.78 (1.03)
12	89.26 (1.32)	79.48 (1.72)	
22	0	0 (0)	0 (0)
	0.5	0.73 (0.14)	1.05 (0.29)
	1	1.30 (0.08)	1.41 (0.10)
	2	2.90 (0.10)	3.05 (0.09)
	3	5.60 (0.28)	5.76 (0.05)
	4	5.72 (0.08)	6.04 (0.09)
	5	7.25 (0.25)	7.34 (0.18)
	6	8.64 (0.27)	8.70 (0.07)
	7	10.764 (0.28)	10.34 (0.31)
	8	12.12 (0.22)	12.18 (0.13)
	9	13.80 (0.41)	15.05 (0.23)
	10	15.70 (0.32)	16.27 (0.08)
	11	17.85 (0.29)	17.28 (0.12)
12	19.35 (0.22)	21.01 (0.09)	

Table 30 Percent release of propranolol hydrochloride from coated pellets formulation 23-24 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Dissolution medium		
		Acid buffer pH 1.2	Phosphate buffer pH 6.8
	Time	Mean (SD)	Mean (SD)
23	0	0 (0)	0 (0)
	0.5	0.72 (0.09)	0.85 (0.08)
	1	1.03 (0.23)	1.16 (0.02)
	2	1.62 (0.48)	2.07 (0.05)
	3	2.21 (0.91)	2.90 (0.08)
	4	2.83 (1.08)	3.55 (0.05)
	5	3.23 (1.23)	4.57 (0.10)
	6	3.96 (1.17)	5.18 (0.11)
	7	4.38 (1.37)	5.57 (0.13)
	8	5.42 (1.71)	6.60 (0.16)
	9	6.04 (1.69)	7.21 (0.08)
	10	7.17 (1.78)	8.97 (0.16)
	11	8.36 (1.43)	9.39 (0.03)
12	9.31 (1.84)	11.12 (0.12)	
24	0	0 (0)	0 (0)
	0.5	0.63 (0.09)	1.11 (0.16)
	1	0.75 (0.06)	1.25 (0.24)
	2	0.81 (0.14)	1.20 (0.43)
	3	1.08 (0.29)	1.08 (0.15)
	4	1.18 (0.36)	1.27 (0.19)
	5	1.24 (0.37)	1.22 (0.11)
	6	1.38 (0.35)	1.40 (0.11)
	7	1.45 (0.34)	1.73 (0.08)
	8	1.73 (0.33)	1.90 (0.30)
	9	2.20 (0.33)	2.17 (0.12)
	10	2.42 (0.32)	2.40 (0.17)
	11	2.68 (0.44)	2.75 (0.25)
12	3.22 (0.45)	2.94 (0.22)	

Table 31 Percent release of propranolol hydrochloride from coated pellets formulation 25-26 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Dissolution medium					
	Acid buffer pH 1.2			Phosphate buffer pH 6.8		
	Time	$\sqrt{\text{Time}}$	Mean (SD)	Log % drug remained	Mean (SD)	Log % drug remained
25	0		0 (0)		0 (0)	
	0.5		12.43 (2.44)		3.36 (0.50)	
	1		39.23 (4.12)		19.34 (1.49)	
	2		54.43 (4.89)		50.22 (2.87)	
	3		76.87 (4.32)		64.06 (3.20)	
	4		92.92 (2.75)		79.20 (4.18)	
	5		100.51 (0.85)		91.15 (2.93)	
	6		102.99 (0.62)		99.05 (1.56)	
	7		103.99 (1.08)		102.82 (0.64)	
	8		105.09 (1.09)		103.67 (1.01)	
26	0	0	0 (0)	2	0 (0)	2
	0.5	0.71	1.57 (0.36)	1.99	1.25 (0.13)	1.99
	1	1	3.82 (0.32)	1.98	2.54 (0.22)	1.99
	2	1.41	6.99 (1.15)	1.97	5.94 (0.46)	1.97
	3	1.73	12.25 (1.51)	1.86	8.61 (0.54)	1.96
	4	2	27.26 (0.29)	1.69	13.30 (0.86)	1.94
	5	2.24	50.71 (1.47)	1.43	21.63 (1.24)	1.89
	6	2.45	72.84 (2.06)	1.04	32.35 (8.13)	1.83
	7	2.65	88.94 (1.34)	0.43	53.86 (0.77)	1.66
	8	2.83	97.29 (0.06)	-	71.50 (0.56)	1.45
	9	3	101.18 (0.29)	-	85.91 (1.39)	1.15
	10	3.16	104.01 (0.08)	-	95.37 (0.18)	0.67
	11	3.32	105.70 (0.83)	-	101.50 (0.75)	-
12	3.46	106.31 (0.55)	-	105.14 (0.72)	-	

Table 32 Percent release of propranolol hydrochloride from coated pellets formulation 27-28 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Dissolution medium					
	Acid buffer pH 1.2			Phosphate buffer pH 6.8		
	Time	$\sqrt{\text{Time}}$	Mean (SD)	Log % drug remained	Mean (SD)	Log % drug remained
27	0	0	0 (0)	2	0 (0)	2
	0.5	0.71	0.58 (0.06)	1.99	1.23 (0.52)	1.99
	1	1	0.93 (0.10)	1.99	1.31 (0.23)	1.99
	2	1.41	1.76 (0.44)	1.99	1.62 (0.42)	1.99
	3	1.73	4.09 (0.38)	1.98	2.66 (0.64)	1.99
	4	2	4.97 (0.69)	1.98	3.31 (0.71)	1.99
	5	2.24	9.09 (0.29)	1.96	4.93 (1.25)	1.98
	6	2.45	17.86 (1.38)	1.91	6.84 (1.89)	1.97
	7	2.65	37.28 (3.11)	1.80	10.78 (2.49)	1.95
	8	2.83	54.86 (4.12)	1.65	17.82 (3.43)	1.92
	9	3	71.60 (2.95)	1.45	27.07 (1.64)	1.86
	10	3.16	85.99 (0.95)	1.15	47.83 (3.26)	1.72
	11	3.32	95.16 (1.12)	0.68	62.75 (4.11)	1.57
12	3.46	99.62 (0.54)	-	75.23 (4.17)	1.39	
28	0		0 (0)		0 (0)	
	0.5		6.37 (0.49)		4.51 (0.66)	
	1		30.89 (1.22)		20.62 (1.13)	
	2		54.27 (2.49)		47.89 (3.66)	
	3		89.28 (1.47)		85.62 (1.47)	
	4		102.38 (0.74)		89.92 (1.77)	
	5		104.14 (0.54)		99.87 (1.15)	
	6		104.32 (0.51)		102.96 (2.11)	
7		-		103.71 (1.68)		

Table 33 Percent release of propranolol hydrochloride from coated pellets formulation 29-30 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Dissolution medium					
	Acid buffer pH 1.2			Phosphate buffer pH 6.8		
	Time	$\sqrt{\text{Time}}$	Mean (SD)	Log % drug remained	Mean (SD)	Log % drug remained
29	0		0 (0)		0 (0)	
	0.5		3.18 (0.18)		2.82 (0.11)	
	1		15.90 (0.84)		8.81 (0.68)	
	2		27.41 (2.05)		25.54 (0.79)	
	3		51.61 (3.43)		51.57 (3.09)	
	4		78.43 (2.26)		54.36 (0.06)	
	5		94.50 (1.65)		73.85 (1.13)	
	6		100.41 (1.45)		77.72 (0.98)	
	7		101.79 (1.40)		89.08 (0.98)	
	8		102.88 (1.41)		96.00 (0.77)	
	9		104.31 (1.17)		102.05 (0.44)	
	10		105.40 (1.11)		102.24 (0.64)	
30	0	0	0 (0)	2	0 (0)	2
	0.5	0.71	1.04 (0.12)	1.99	0.97 (0.11)	1.99
	1	1	2.12 (0.53)	1.99	1.24 (0.23)	1.99
	2	1.41	3.83 (0.17)	1.98	2.23 (0.90)	1.99
	3	1.73	8.62 (0.44)	1.96	3.43 (1.07)	1.99
	4	2	23.47 (0.62)	1.88	5.87 (1.06)	1.97
	5	2.24	50.07 (1.16)	1.70	12.08 (0.70)	1.94
	6	2.45	75.84 (1.42)	1.38	25.30 (1.16)	1.87
	7	2.65	93.77 (0.790)	0.79	44.52 (0.69)	1.74
	8	2.83	99.83 (1.72)	-	62.35 (1.00)	1.58
	9	3	103.55 (0.74)	-	76.51 (1.64)	1.37
	10	3.16	103.66 (0.63)	-	86.37 (1.68)	1.13
11	3.32	104.76 (0.66)	-	94.32 (2.54)	0.75	
12	3.56	105.85 (0.67)	-	101.06 (1.61)	-	

Table 34 Percent release of propranolol hydrochloride from coated pellets formulation 31-32 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Dissolution medium					
	Acid buffer pH 1.2			Phosphate buffer pH 6.8		
	Time	$\sqrt{\text{Time}}$	Mean (SD)	Log % drug remained	Mean (SD)	Log % drug remained
31	0		0 (0)		0 (0)	
	0.5		15.39 (3.94)		4.61 (0.88)	
	1		39.85 (5.68)		20.90 (2.93)	
	2		85.04 (3.35)		55.21 (4.82)	
	3		98.34 (0.47)		80.24 (3.78)	
	4		99.97 (0.49)		92.56 (2.55)	
	5		100.25 (0.31)		95.22 (2.24)	
	6		-		97.05 (2.70)	
	7		-		98.43 (2.42)	
8		-		99.72 (1.01)		
32	0	0	0 (0)	2	0 (0)	2
	0.5	0.71	1.97 (0.29)	1.99	1.52 (0.03)	1.99
	1	1	5.42 (0.59)	1.96	4.07 (0.19)	1.98
	2	1.41	21.68 (1.21)	1.89	9.53 (0.48)	1.96
	3	1.73	59.16 (0.48)	1.61	26.37 (3.63)	1.87
	4	2	87.64 (1.23)	1.09	48.22 (5.57)	1.71
	5	2.24	95.09 (0.61)	0.69	66.20 (5.38)	1.53
	6	2.45	98.52 (0.65)	0.17	83.52 (3.70)	1.22
	7	2.65	99.38 (0.22)	-	91.80 (1.86)	0.91
	8	2.83	99.74 (0.20)	-	95.24 (1.14)	0.68
	9	3	100.25 (0.79)	-	97.52 (0.86)	0.39
	10	3.16	101.29 (0.80)	-	98.70 (0.27)	0.11
	11	3.32	102.34 (0.81)	-	-	-
12	3.46	103.38 (0.81)	-	-	-	

Table 35 Percent release of propranolol hydrochloride from coated pellets formulation 33-35 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Dissolution medium					
	Time	√Time	Acid buffer pH 1.2		Phosphate buffer pH 6.8	
			Mean (SD)	Log % drug remained	Mean (SD)	Log % drug remained
33	0	0	0 (0)	2	0 (0)	2
	0.5	0.71	0.97 (0.18)	1.99	0.82 (0.12)	1.99
	1	1	1.31 (0.26)	1.99	1.28 (0.40)	1.99
	2	1.41	4.81 (1.81)	1.98	1.97 (0.47)	1.99
	3	1.73	16.75 (3.40)	1.92	4.20 (1.00)	1.98
	4	2	49.83 (0.90)	1.70	10.37 (0.50)	1.95
	5	2.24	76.51 (1.14)	1.37	25.71 (1.45)	1.87
	6	2.45	93.21 (0.85)	0.83	46.49 (3.89)	1.73
	7	2.65	97.17 (1.08)	0.45	61.87 (2.64)	1.58
	8	2.83	99.52 (1.42)	-	76.49 (1.41)	1.37
	9	3	99.73 (0.75)	-	85.29 (0.58)	1.17
	10	3.16	100.79 (0.76)	-	89.32 (0.41)	1.03
	11	3.32	101.60 (1.32)	-	92.38 (0.23)	0.88
12	3.46	102.65 (1.34)	-	95.27 (1.27)	0.67	
34	0		0 (0)		0 (0)	
	0.5		5.01 (2.69)		3.84 (0.26)	
	1		35.80 (5.15)		12.97 (0.92)	
	2		95.45 (1.79)		62.10 (2.56)	
	3		101.29 (0.29)		64.49 (4.59)	
	4		101.90 (0.54)		92.01 (0.96)	
	5		102.35 (0.70)		99.73 (1.11)	
6		-		101.92 (0.59)		
35	0		0 (0)		0 (0)	
	0.5		4.32 (0.32)		4.86 (1.84)	
	1		17.70 (1.82)		10.07 (0.92)	
	2		62.03 (3.09)		29.32 (2.54)	
	3		92.83 (0.74)		55.82 (1.39)	
	4		99.44 (1.14)		84.41 (6.21)	
	5		100.72 (1.46)		90.53 (0.40)	
	6		100.69 (1.73)		95.17 (0.69)	
	7		-		98.20 (0.74)	
	8		-		98.96 (1.02)	
9		-		100.03 (1.00)		

Table 36 Percent release of propranolol hydrochloride from coated pellets formulation 36-37 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Time	Dissolution medium	
		Acid buffer pH 1.2 Mean (SD)	Phosphate buffer pH 6.8 Mean (SD)
36	0	0 (0)	0 (0)
	0.5	0.79 (0.15)	1.08 (0.03)
	1	2.44 (0.39)	1.69 (0.51)
	2	14.50 (1.59)	4.97 (0.96)
	3	56.85 (3.06)	17.77 (0.87)
	4	88.49 (2.45)	69.66 (0.33)
	5	98.46 (3.34)	69.66 (0.33)
	6	99.66 (2.99)	83.01 (0.86)
	7	100.03 (1.91)	90.59 (0.77)
	8	-	93.88 (1.22)
	9	-	96.08 (1.23)
	10	-	96.75 (0.90)
	11	-	98.11 (1.26)
12	-	99.38 (1.02)	
37	0	0 (0)	0 (0)
	0.5	1.16 (0.25)	1.09 (0.14)
	1	2.42 (0.36)	1.85 (0.42)
	2	5.39 (1.30)	4.43 (0.85)
	3	7.93 (1.50)	6.30 (1.17)
	4	9.44 (1.67)	8.23 (1.39)
	5	11.28 (1.93)	10.06 (1.40)
	6	12.97 (1.96)	11.70 (1.53)
	7	14.69 (2.07)	13.45 (1.68)
	8	16.62 (1.90)	14.81 (1.84)
	9	18.75 (2.11)	16.37 (1.79)
	10	20.69 (2.11)	18.27 (1.96)
	11	22.86 (2.13)	19.66 (1.83)
12	25.11 (2.20)	21.33 (1.60)	

Table 37 Percent release of propranolol hydrochloride from coated pellets formulation 38-39 in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Dissolution medium		
	Time	Acid buffer pH 1.2 Mean (SD)	Phosphate buffer pH 6.8 Mean (SD)
38	0	0 (0)	0 (0)
	0.5	0.61 (0.14)	0.96 (0.36)
	1	0.81 (0.06)	1.07 (0.12)
	2	1.38 (0.14)	1.54 (0.28)
	3	2.08 (0.12)	2.07 (0.42)
	4	2.65 (0.23)	2.64 (0.42)
	5	3.13 (0.30)	3.24 (0.46)
	6	3.67 (0.20)	3.47 (0.42)
	7	4.23 (0.19)	4.01 (0.38)
	8	4.55 (0.48)	4.33 (0.43)
	9	5.17 (0.67)	4.97 (0.43)
	10	5.80 (0.47)	5.58 (0.37)
	11	6.47 (0.21)	5.91 (0.41)
12	7.63 (0.72)	6.57 (0.46)	
39	0	0 (0)	0 (0)
	0.5	0.67 (0.12)	0.93 (0.13)
	1	0.76 (0.11)	0.99 (0.05)
	2	0.86 (0.26)	1.23 (0.26)
	3	0.97 (0.21)	1.30 (0.12)
	4	1.17 (0.21)	1.52 (0.30)
	5	1.43 (0.68)	1.52 (0.31)
	6	1.52 (0.08)	1.60 (0.43)
	7	1.38 (0.17)	2.34 (0.12)
	8	1.82 (0.56)	2.31 (0.27)
	9	1.97 (0.36)	2.54 (0.47)
	10	2.05 (0.36)	2.62 (0.55)
	11	2.36 (0.32)	2.55 (0.55)
12	2.54 (0.26)	2.94 (0.73)	

Table 38 Percent release of propranolol hydrochloride from Inderal[®]LA160 and sustained release propranolol hydrochloride capsules in acid buffer pH 1.2 and phosphate buffer pH 6.8.

Formulation	Time	Dissolution medium	
		Acid buffer pH 1.2 Mean (SD)	Phosphate buffer pH 6.8 Mean (SD)
Inderal [®] LA160 mg	0	0 (0)	0 (0)
	0.5	5.44 (0.22)	4.07 (0.32)
	1	11.08 (0.88)	10.29 (0.39)
	2	21.13 (1.55)	22.75 (0.44)
	3	29.97 (2.32)	32.92 (0.56)
	4	37.38 (2.94)	41.77 (0.89)
	5	43.57 (3.03)	48.87 (0.89)
	6	50.29 (1.91)	56.14 (0.69)
	7	54.77 (2.01)	60.65 (1.48)
	8	59.60 (3.84)	63.85 (0.85)
	9	63.17 (2.68)	69.40 (1.27)
	10	67.37 (2.69)	72.88 (0.98)
	11	71.13 (2.74)	75.50 (1.57)
	12	72.40 (2.75)	77.03 (1.48)
sustained release propranolol hydrochloride capsules	0	0 (0)	0 (0)
	0.5	3.66 (0.41)	3.88 (0.52)
	1	9.06 (1.10)	13.43 (2.31)
	1.5	17.14 (0.91)	19.22 (1.40)
	2	21.88 (0.88)	21.15 (3.36)
	4	40.26 (1.52)	48.54 (2.06)
	6	54.46 (0.81)	58.75 (0.42)
	8	70.27 (2.44)	78.89 (0.97)
	10	81.61 (1.96)	91.48 (1.83)
	12	92.21 (1.54)	103.15 (2.00)
	14	100.43 (3.89)	107.06 (1.98)
	18	107.44 (1.870)	109.00 (0.69)
	24	110.11 (1.58)	110.85 (0.08)

Table 39 Percent release of propranolol hydrochloride from Inderal[®]LA160 and sustained release propranolol hydrochloride capsules by pH change method.

Formulation	Time	Mean (SD)
Inderal [®] LA160 mg	0	0 (0)
	0.5	5.197 (0.11)
	1	11.66 (1.34)
	1.5	17.10 (1.22)
	2	21.22 (2.30)
	4	36.66 (1.79)
	6	58.87 (1.56)
	8	67.54 (1.79)
	10	74.68 (3.35)
	12	78.54 (2.69)
	14	82.63 (2.76)
	18	89.36 (1.12)
	24	98.79 (1.04)
	sustained release propranolol hydrochloride capsules	0
0.5		4.03 (0.84)
1		13.29 (1.21)
1.5		17.45 (2.31)
2		21.16 (2.83)
4		43.01 (0.88)
6		59.44 (1.52)
8		70.12 (0.10)
10		80.68 (0.97)
12		84.22 (1.41)
14		93.61 (1.32)
18		104.20 (0.92)
24		107.13 (0.74)

Vitae

Miss Intira Coowanitwong was born on March 14, 1974 in Chulalongkorn Hospital, Bangkok. She got her degree in Bachelor of Science in Pharmacy in 1995 from Faculty of Pharmacy, Rangsit University, Bangkok, Thailand. At the present moment, she is going to study her Ph.D. in the United States of America. Her current and future degrees will be honored to Rangsit University, Chulalongkorn University, and her parents.



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