

References

- Akbuga, J. 1983. Use of chitosonium malateasa matrix in sustained-release tablet. *Int. J. Pharm.* 89: 19-24.
- Baker, R.W. 1987. **Controlled release of biologically active agent.** New York: John Willey & Sons.
- Bamba, M., Puiseux, F., Marty, J.P., and Carstensen, J.T. 1979. Release mechannisms in gelforming sustained release preparations. *Int. J. Pharm.* 2: 307-315.
- Bodmeire, R., and Paeratakul, O. 1989. Spherical agglomerates of water-insoluble drugs. *J. Pharm. Science.* 78: 964-967.
- Bough, W.A., Salter, W.L., Wu A.C.M., and Perkins, B.E. 1978. Influence of manufacturing variables on the characteristics and effectiveness of chitosan products. I. Chemical composition, viscosity, and molecular-weight distribution of chitosan products. *Biotech. Bioeng.* 20: 1931-1943.
- Cardinal, J.R. 1984. Matrix systems. In R.S. Langer, and D.L. Wise (eds.), **Medical Application of Controlled Release**, pp. 41-71. U.S.A.: C.R.C. Press.

- Chien, Y.W. 1983. Potential developments and new approaches in oral controlled-release drug delivery systems. *Drug Dev. Ind. Pharm.* 9: 1291-1330.
- Chomto, P. 1992. **Application of Chitin and Chitosan as disintegrant in Paracetamol tablet.** Master's thesis. Chulalongkorn University.
- Desai, S.J., Simonelli, A.P., and Higuchi, W.I. 1965. Investigation of factors influencing release of solid drug dispersed in inert matrices. *J. Pharm. Sci.* 54: 1459-1464.
- Domard, A., and Rinaudo, M. 1983. Preparation and characterization of fully deacetylated chitosan. *Int. J. Biol. Macromol.* 5: 49-52.
- Flynn, G.L., Yalkowsky, S.H., and Roseman, T.J. 1974. Mass transport phenomena and models: theoretical concepts. *J. Pharm. Sci.* 63: 479-510.
- Hayes, E.R. 1978. Characterization of chitosan. II: The determination of the degree of acetylation of chitosan and chitin. In R.A.A. Muzzarelli, and E.R. Pariser (eds.), *Proc. 1st, Inter. Conf. on Chitin/Chitosan*, pp. 406-420. Boston: MIT SG 78-7.

- Heller, J. 1987. Use of polymer in controlled release of active agents. In J.R. Robinson, and V.H.L. Lee (eds.), **Controlled drug delivery fundamentals and applications**, pp. 374-433. New York: Marcel Dekker.
- Higuchi, T. 1963. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *J. Pharm. Sci.* 52: 1145-1149.
- Hogan, J.E. 1989. Hydroxypropylmethylcellulose sustained release technology. *Drug Dev. Ind. Pharm.* 15: 975-999.
- Hui, H.W., and Robinson J.R. 1987. Design and fabrication of oral controlled release drug delivery system. In J.R. Robinson, and W.H.L. Lee (eds.), **Controlled drug delivery fundamentals and application**, pp. 374-431. New York: Marcel Dekker.
- Imai, T., Shiraishi, S., Saito, H., and Otagiri, M. 1991. Interaction of indomethacin with low molecular weight chitosan, and improvements of some pharmaceutical properties of indomethacin by low Molecular Weight Chitosans. *Int. J. Pharm.* 67: 11-20.
- Jaiyongka, S. 1993. **Effects of deacetylation variables of characterist of chitosan products in relation to tablet-disintegrating properties.** Master's thesis. Chulalongkorn University.

- Karlsen, J. 1991. Excipient properties of chitosan. *Manu. Chem.* 60(6): 18-23.
- Kawashima, Y., Handa, T., Kasai, A., Takenaka, H., and Lin, S.Y. Preparation of a prolonged tablet of aspirin with chitosan. *Chem. Pharm. bull.* 33: 2107-2113.
- _____, Handa, T., Kasai, A., Takenaka, H., and Ando, Y. 1985. Novel method for the preparation of controlled-release theophylline granules coated with a polyelectrolyte complex of sodium polyphosphate-chitosan. *J. Pharm. Sci.* 74: 264-268.
- Leesawat, P. 1991. Controlled release theophylline matrices prepared from co-spray dried theophylline polymer channeling agent. Master's thesis. Chulalongkorn University.
- Lusena, C.V., and Rose, R.C. 1953. Preparation and viscosity of chitosan. *J. Fish. Res. Bd. Can.* 10: 521-522.
- Mima, S., Miya, M., Iyamoto, R., and Yoshikawa, S. 1983. Highly deacetylated chitosan and its properties. *J. Appl. Polym. Sci.* 28: 1909-1917.
- Miyazaki, S., Ishii, K., and Nadai, T. 1981. The use of chitin and chitosan as drug carriers. *Chem. Pharm. Bull.* 29: 3067-3069.

- _____. , Yamaguchi, H., Yokouchi, C., Takada, M., and Hou, W. 1988
Sustained release of indomethacin from chitosan granules in
beagle dogs. *J. Pharm. Pharmacol.* 27: 642-643.
- Nagalaye, A.G., Adusumilli, P., and Bolton, S. 1990. Investigation
of prolonged drug release from matrix formulations of
chitosan. *Drug. Dev. Int. Pharm.* 16: 449-467.
- Peppas, N.A. 1985. Analysis of Fickian and non-Fickian drug
release from polymers. *Pharm. Acta. Helv.* 1985: 110-111.
- Rao, K.V., and Devi, K.P. 1988. Swelling controlled-release systems:
recent developments and applications. *Int. J. Pharm.* 48:
1-13.
- Ritger, P.L., and Peppas, N.A. 1987 a. A simple equation for
description of solute release I. Fickian and non-Fickian
release from non-swellable devices in the form of slabs,
spheres, cylinders or discs. *J. Controlled Release.* 5:
23-36.
- _____. , and Peppas, N.A. 1987 b. A simple equation for
description of solute release II. Fickian and anomalous
release from swellable devices. *J. Controlled Release.* 5:
37-42.

- Sa, M. Bandyopadhyay, A.K., and Gupta B.K. 1990. Development and in-vitro evaluation of etyl cellulose micropelletes as a controlled release dosage form for theophylline. *Drug Dev. Ind. Pharm.* 16: 1153-1169.
- Sawayanagi, Y., Nambu, N., and Nagai, T. 1982. Use of chitosan for sustained-release preparations of water-soluble drugs. *Chem. Pharm. Bull.* 30: 4213-4215
- _____, Nambu, N., and Nagai, T. 1983. Dissolution properties and bioavailability of phenytoin from ground mixtures with chitin or chitosan. *Chem. Pharm. Bull.* 31: 2064-2068.
- Schwartz, J.B., Simonelli, A.P., and Higuchi, W.I. 1968. Drug release from wax matrices I. Analysis of data with first-order kinetics and with the diffusion-controlled model. *J. Pharm. Sci.* 57: 274-277.
- Shiraishi, S., Imai, T. and Otagiri, M. 1993. Controlled release of indomethacin by chitosan-polyelectrolyte complex: optimization and in vivo / in vitro evaluation. *J. Controlled Release.* 25: 217-225.
- Takahashi, T., Takayama, K., Machids, Y., and Nagai, T. 1990. Characteristics of polyion complexes of chitosan with sodium alginate and sodium polyacrylate. *Int. J. Pharm.* 61: 34-41.

Takayama, K., Hirata, M., Machida, Y., Masada, t., Sannan, T., and Nagai, T. 1990. Effect of interpolymer complex formation on bioadhesive property and drug release phenomenon of compressed tablet consisting of chitosan and sodium sodium hyaluronate. *Chem. Pharm. Bull.* 38: 1993-1997.

Thanoo, B.C., Sunny, M.C., and Jayakrishnan, A. 1992. Cross-linked chitosan microspheres: Preparation and evaluation as a matrix for the controlled release of pharmaceuticals. *J. Pharm. Pharmacol.* 44: 283-286.

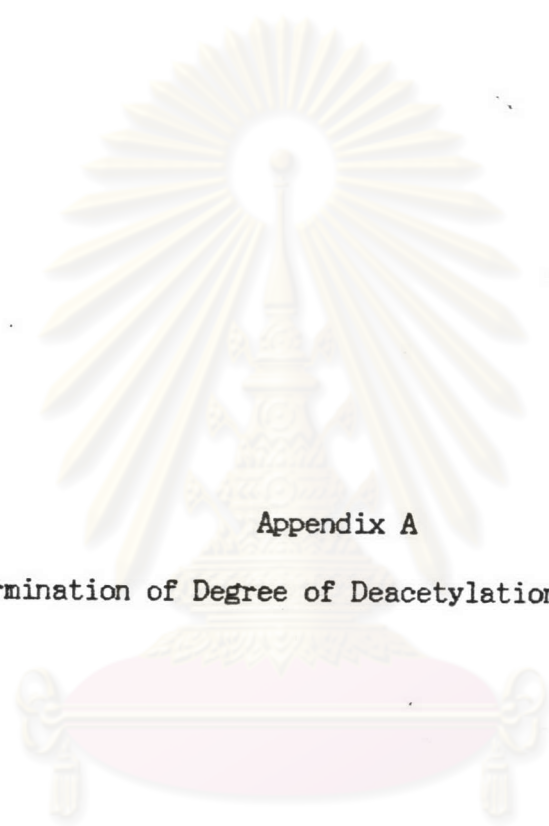


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APPENDICES

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Appendix A

Determination of Degree of Deacetylation of Chitosan

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Determination of Degree of Deacetylation of chitosan

Method of calculation

Sample : CS2(see Table in following page)

Sample solution

Weight of sample (chitosan hydrochloride) 1.008 gm
dissolved in water to 250 ml

Titration

Chitosan hydrochloride solution used 50.0 ml

Volume of standard NaOH(0.0979N) used 6.99 ml

Calculation

Chitosan hydrochloride 1 mol.(197.61672 gm) = NaOH 1 mol

The amount of monomer having NH_2 group in a sample 1.008 gm
= 0.003422 mol

= 0.6762 gm

The amount of monomer having NHCOCH_3 group in sample 1.008 gm

= 1.008-0.6762 gm

= 0.3318 gm

(monomer having $-\text{NHCOCH}_3$ 1 mol=203.19296 gm) = 0.001632 mol

The total amount of monomer in sample 1.008 gm = 0.003422+0.001632 mol

= 0.005064 mol

The degree of deacetylation = $(0.003422/0.005064) \times 100 \%$

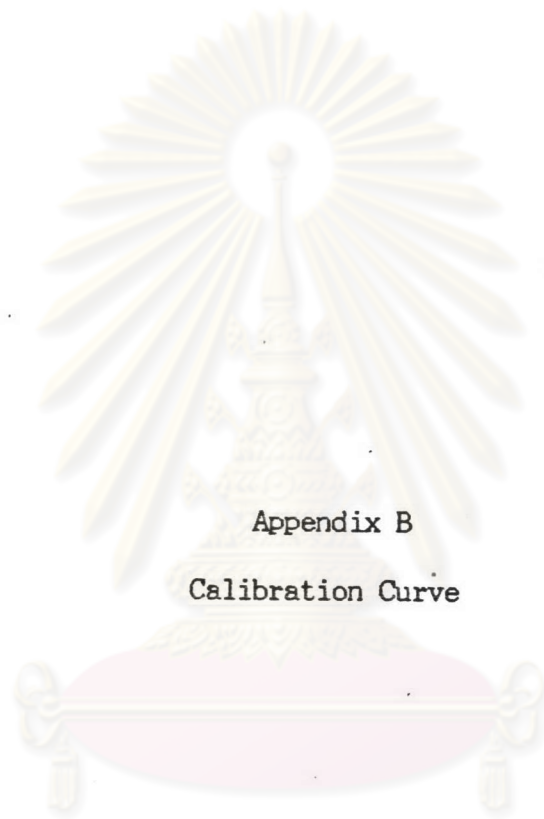
= 67.7 % monomer : 100 monomer

By this method, the degree of deacetylation of various chitosans was calculated and the values are given in the table in the following page

Determination of degree of deacetylation of chitosan

Chitosan	wt. of CS.HCl (gm)	vol. of NaOH used (ml)	Deacetylation (%)	mean (%)
CS 2	1.008	(1) 7.01	67.76	67.69
		(2) 7.07	68.47	
		(3) 6.90	66.84	
CS3.5	1.000	(1) 7.35	71.75	71.75
		(2) 7.34	71.75	
		(3) 7.36	71.35	
CS7	1.000	(1) 7.40	72.35	72.35
		(2) 7.30	71.41	
		(3) 7.50	73.32	
CS10	1.002	(1) 8.05	78.43	78.61
		(2) 8.05	78.43	
		(3) 8.10	79.06	

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Appendix B

Calibration Curve

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Calibration Curve

The concentration versus absorbance of propranolol hydrochloride in buffer pH 1.5 and buffer pH 6.8 at 290 nm were presented in Table 13 and 14 showed a linear relationship with the correlation coefficient =0.999967 and =0.999973, respectively. The standard curve of propranolol HCl was illustrated in Figure 32.

The concentration versus absorbance of propranolol hydrochloride in buffer pH 1.2 and buffer pH 7.5 at 290 nm were presented in Table 15 and 16 showed a linear relationship with the correlation coefficient = 0.99973 and 0.999792, respectively. The standard curve of propranolol HCl was illustrated in Figure 33.

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Table 20 Absorbance of propranolol hydrochloride in buffer pH 1.5
determined at 290 nm

Concentration(mcg/ml)	Absorbance
0	0
10	0.1965
15	0.2940
20	0.3925
25	0.4880
30	0.5875
35	0.6795
40	0.7795
45	0.8760

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Table 21 Absorbance of propranolol hydrochloride in buffer pH 6.8 determined at 290 nm

Concentration (mcg/ml)	Absorbance
0	0
10	0.1915
15	0.2885
20	0.3885
25	0.4840
30	0.5835
35	0.6820
40	0.7775
45	0.8770

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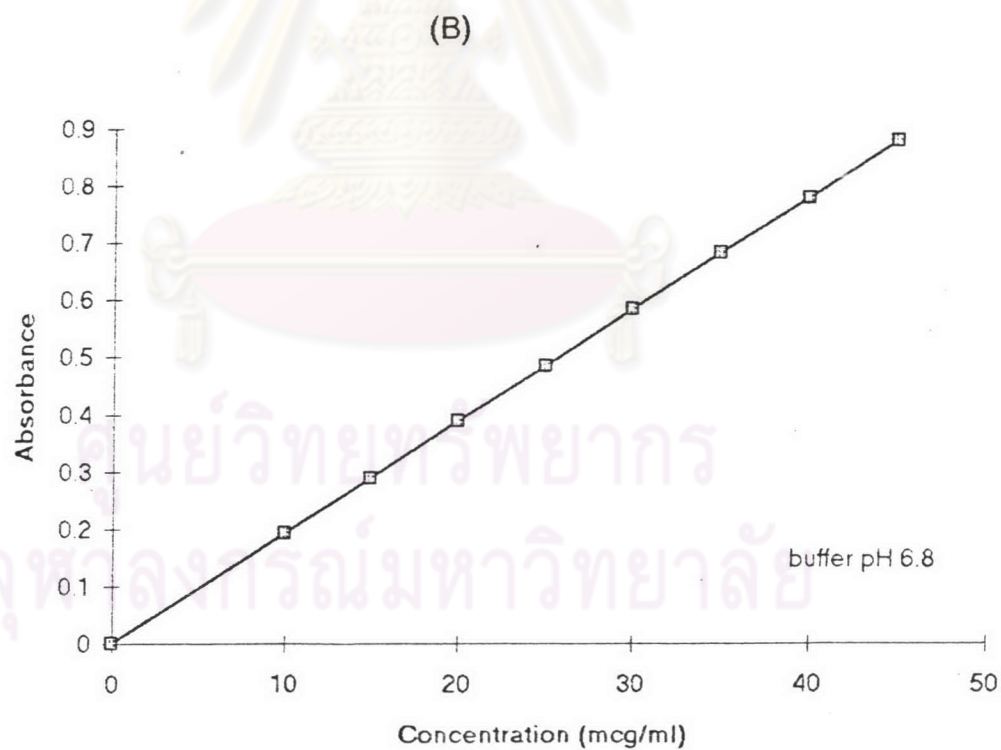
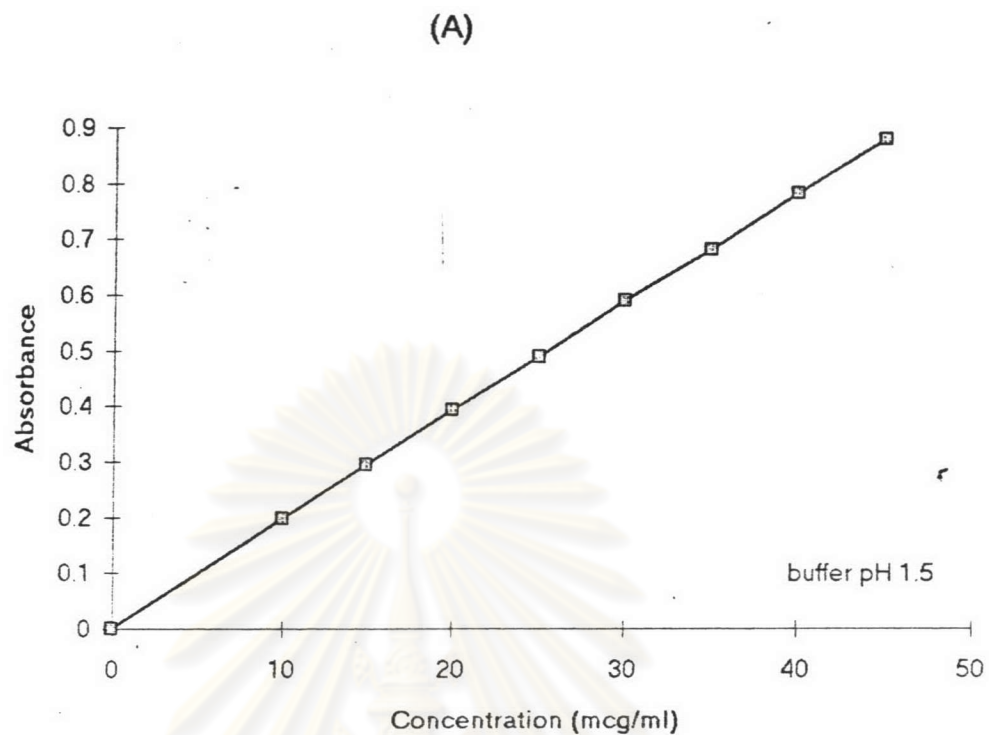


Figure 32 Calibration curve of propranolol HCl in

A) buffer pH 1.5

B) buffer pH 6.8

Table 22 Absorbance of propranolol hydrochloride in buffer pH 1.2
determined at 290 nm

Concentration (mcg/ml)	Absorbance
0	0
10	0.1950
15	0.2935
20	0.3955
25	0.4915
30	0.5925
35	0.6935
40	0.7915
45	0.8895

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Table 23 Absorbance of propranolol hydrochloride in buffer pH 7.5
determined at 290 nm

Concentration (mcg/ml)	Absorbance
0	0
10	0.1950
15	0.2925
20	0.3920
25	0.4920
30	0.5795
35	0.6780
40	0.7735
45	0.8825

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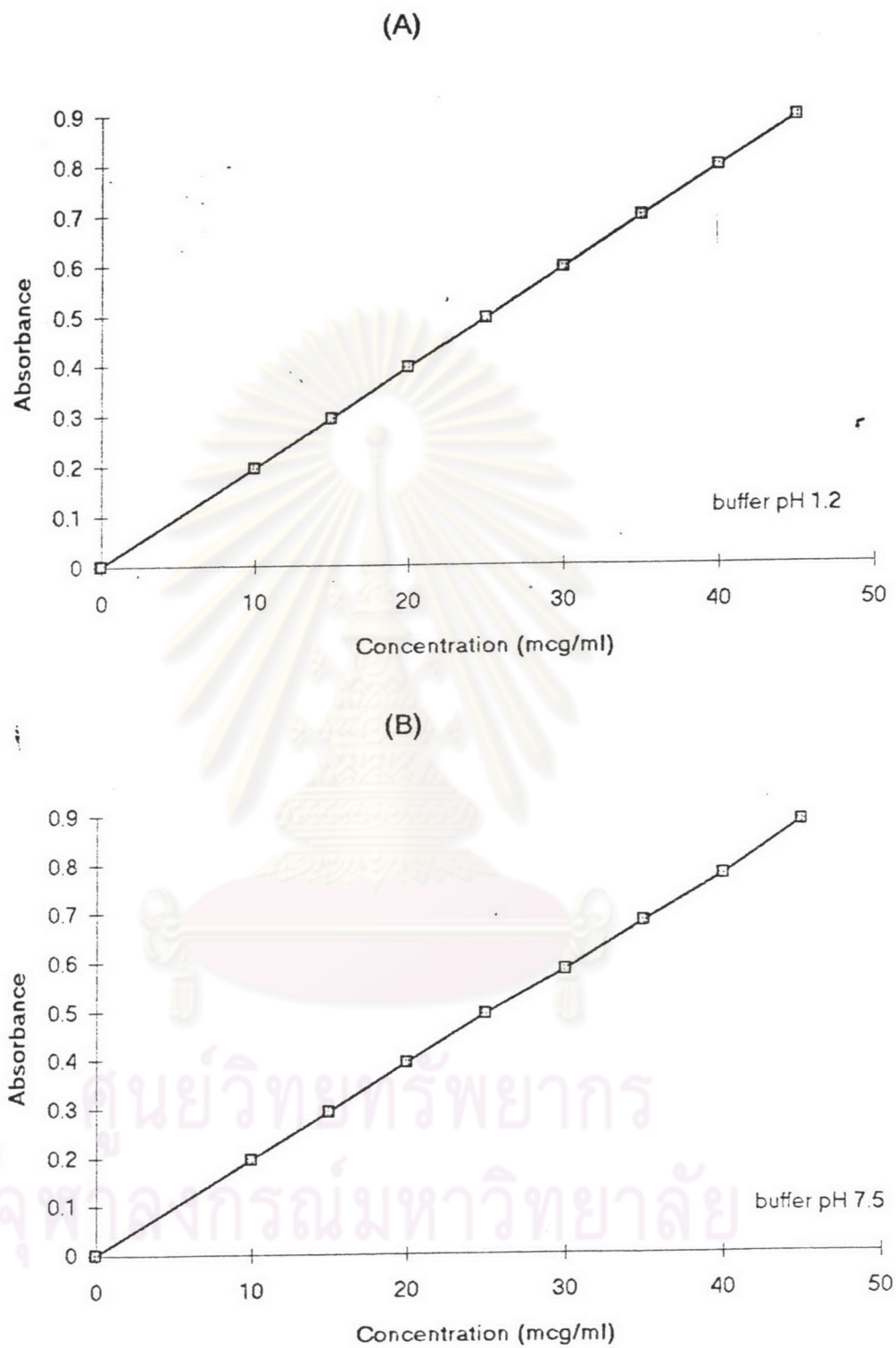
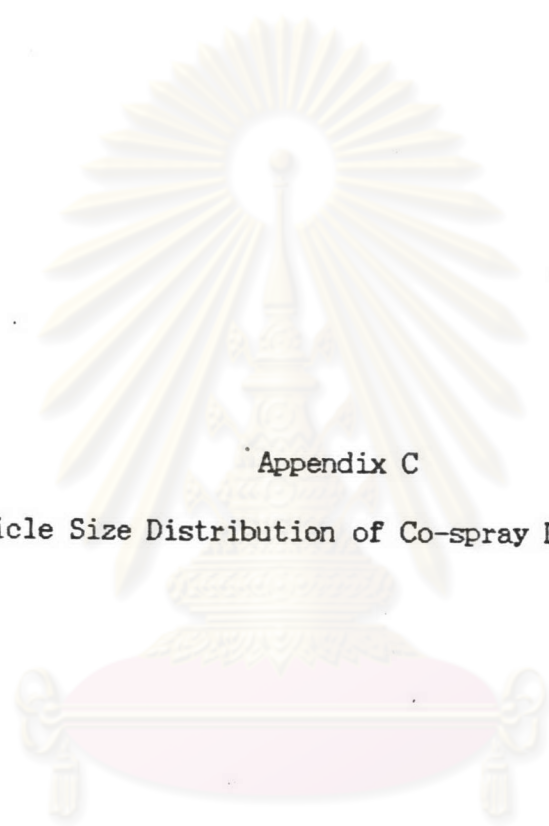


Figure 33 Calibration curve of propranolol HCl in

A) buffer pH 1.2

B) buffer pH 7.5



Appendix C

Particle Size Distribution of Co-spray Dried Powder

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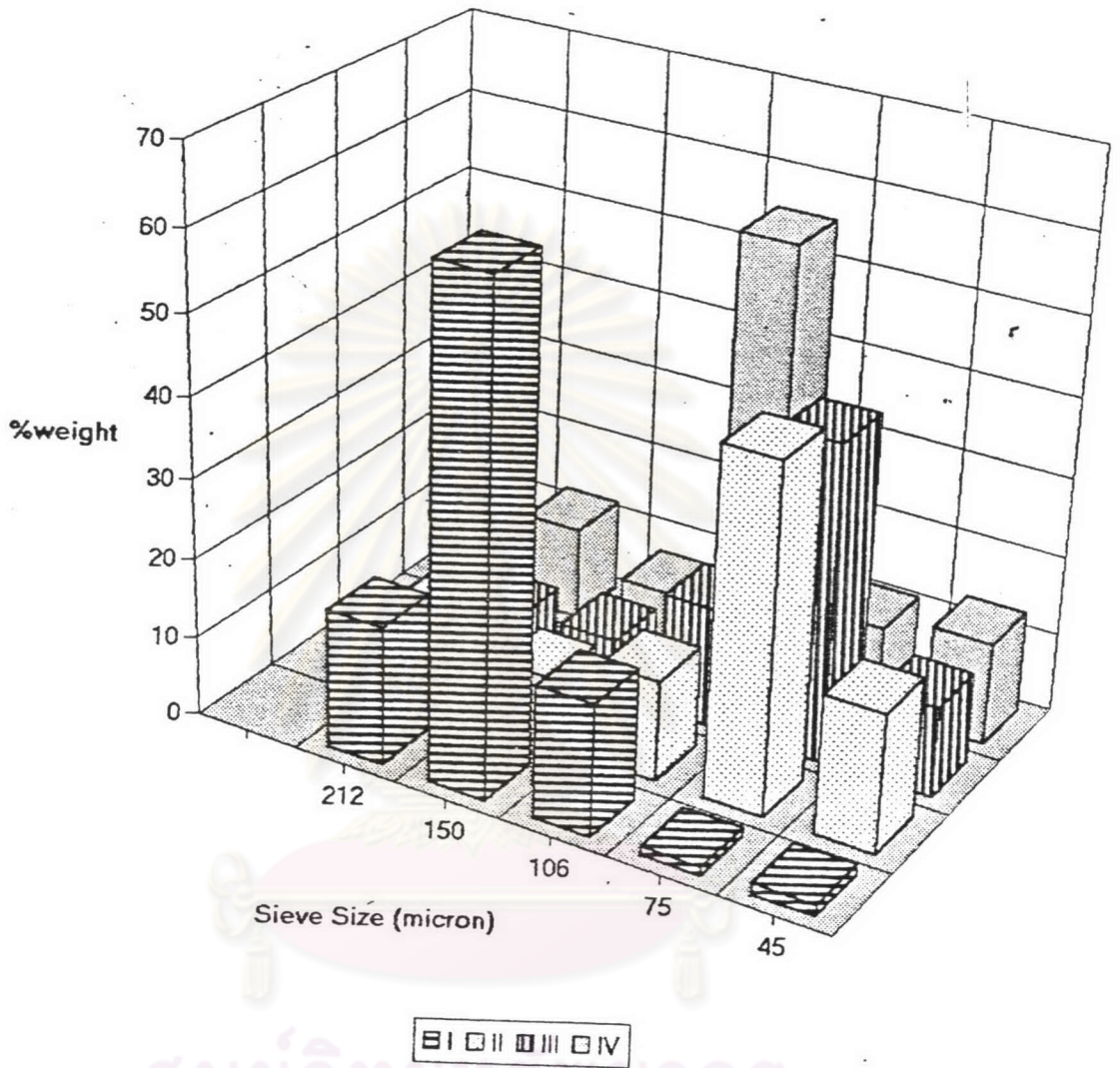


Figure 34 Particle size distribution of Formulations I-IV
co-spray dried powder

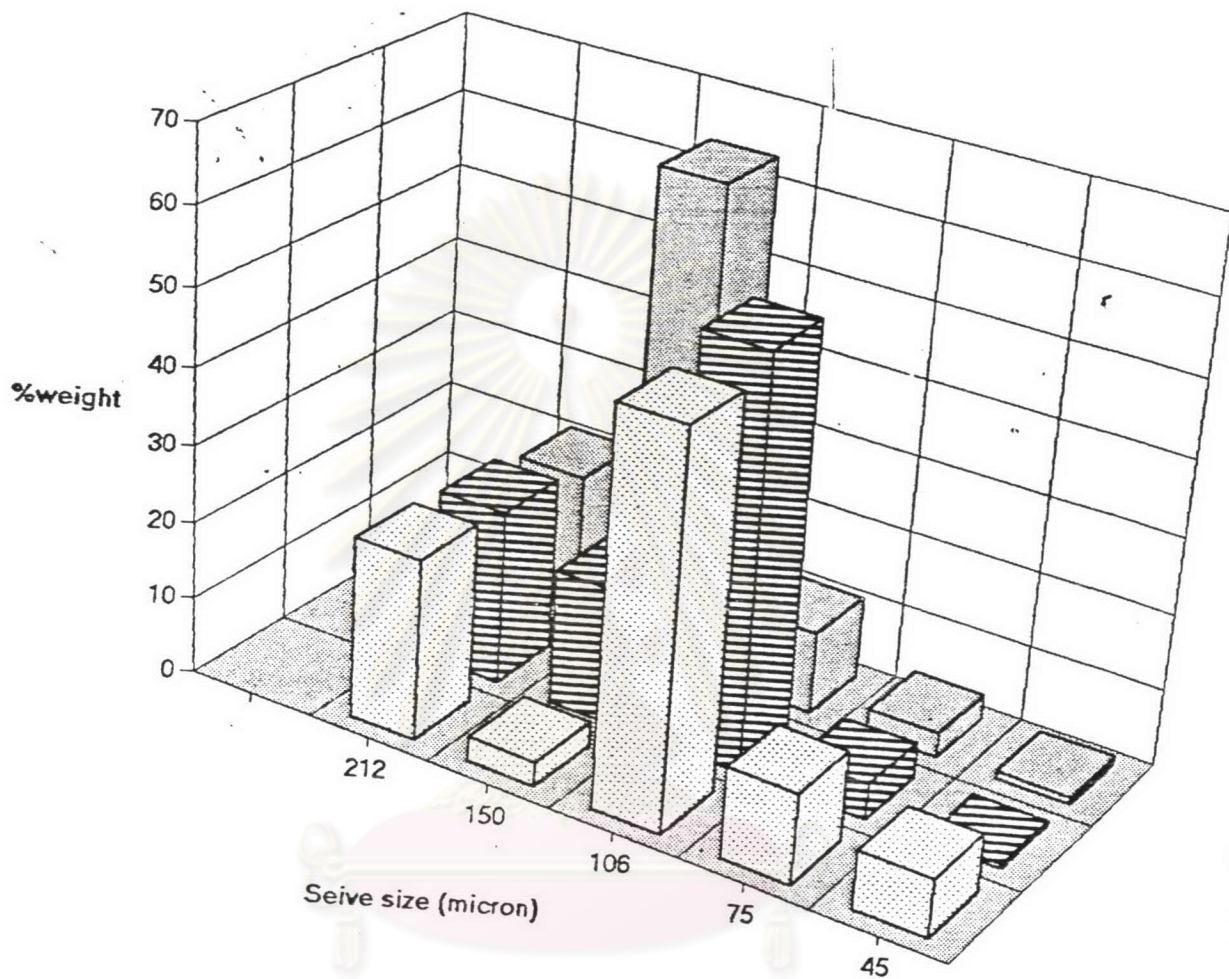
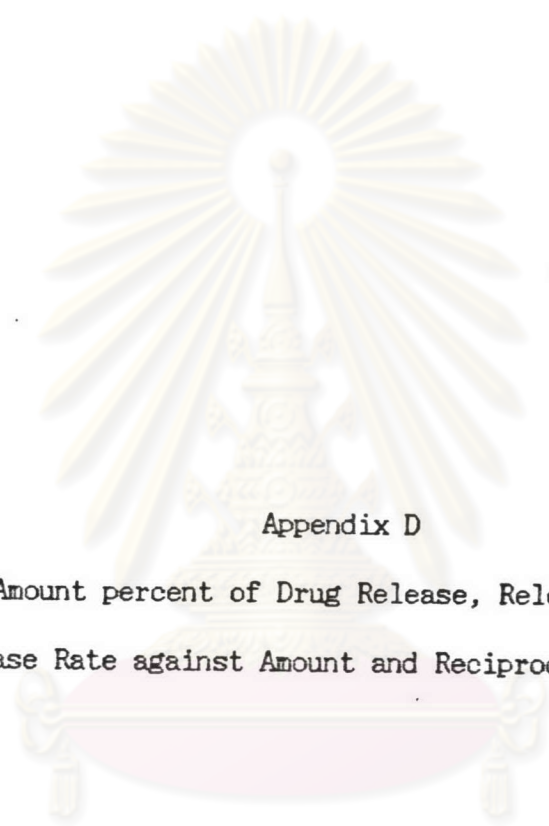


Figure 35 Particle size distribution of Formulations V-VII
co-spray dried powder



Appendix D

Amount percent of Drug Release, Release Rate

Release Rate against Amount and Reciprocal of Amount

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Table 24 Amount of Propranolol Hydrochloride Releasing from Formulation I - III
in buffer pH 1.5 and buffer pH 6.8

Formulation	Time(hr)	Time 1/2	Dissolution medium					
			Buffer pH1.5			Buffer pH6.8		
			Mean(%)	S.D.	LOG % drug remained	Mean(%)	S.D.	LOG % drug remained
I	0	0.00	0.00	0.00	2.00	0.00	0.00	2.00
	0.5	0.71	16.88	1.07	1.92	20.93	2.87	1.90
	1	1.00	27.70	1.21	1.86	35.59	4.61	1.81
	1.5	1.22	35.69	1.45	1.81	47.83	5.12	1.72
	2	1.41	41.55	1.19	1.77	56.86	5.17	1.63
	3	1.73	51.16	1.28	1.69	70.56	4.84	1.47
	4	2.00	58.67	1.30	1.62	80.03	3.98	1.36
	5	2.24	64.94	0.98	1.54	86.52	3.27	1.13
	6	2.45	70.44	0.76	1.47	90.61	2.73	0.97
	7	2.65	75.49	0.55	1.39	93.23	2.26	0.83
	8	2.83	79.89	0.67	1.30	94.90	1.93	0.71
	9	3.00	83.78	0.80	1.21	96.36	1.67	0.60
10	3.16	87.33	0.98	1.10	97.17	1.41	0.45	
11	3.32	90.77	2.03	0.96	98.18	1.40	0.26	
12	3.46	94.68	3.11	0.72	98.92	1.23	0.03	
II	0	0.00	0.00	0.00	2.00	0.00	0.00	2.00
	0.5	0.71	25.95	0.50	1.87	28.75	3.36	1.85
	1	1.00	37.64	0.47	1.79	45.81	4.54	1.73
	1.5	1.22	50.14	2.68	1.70	57.34	5.07	1.63
	2	1.41	60.21	1.54	1.60	65.99	5.13	1.53
	3	1.73	74.56	1.81	1.40	80.52	2.95	1.29
	4	2.00	83.82	2.11	1.21	89.51	1.91	1.02
	5	2.24	89.72	1.89	1.01	94.93	1.26	0.70
	6	2.45	94.24	1.65	0.76	97.92	0.85	0.32
	7	2.65	97.94	1.85	0.31	99.65	0.68	-0.46
	8	2.83	100.26	1.55	-	-	0.53	-
	9	3.00	-	1.54	-	-	0.49	-
10	3.16	-	-	-	-	0.49	-	
11	3.32	-	-	-	-	-	-	
12	3.46	-	-	-	-	-	-	
III	0	0.00	0.00	0.00	2.00	0.00	0.00	2.00
	0.5	0.71	26.76	0.44	1.86	27.60	3.48	1.86
	1	1.00	38.68	1.01	1.79	41.66	5.39	1.76
	1.5	1.22	52.10	3.09	1.68	52.96	5.69	1.67
	2	1.41	62.29	2.22	1.58	62.30	6.39	1.58
	3	1.73	78.50	2.38	1.33	76.02	6.45	1.38
	4	2.00	86.94	0.92	1.12	86.51	4.33	1.13
	5	2.24	94.01	2.75	0.78	93.20	2.15	0.83
	6	2.45	97.36	1.75	0.42	96.77	1.44	0.51
	7	2.65	100.14	1.40	-	99.08	0.93	-0.04
	8	2.83	-	0.93	-	-	-	-
	9	3.00	-	0.77	-	-	-	-
10	3.16	-	0.59	-	-	-	-	
11	3.32	-	-	-	-	-	-	
12	3.46	-	-	-	-	-	-	

Table 25 Amount of Propranolol Hydrochloride Releasing from Formulation IV
in buffer pH 1.5 and in buffer pH 6.8

Formulation	Time(hr)	Dissolution medium						
		Buffer pH1.5			Buffer pH6.8			
		Time1/2	Mean(%)	S.D.	LOG % drug remained	Mean(%)	S.D.	LOG % drug remained
IV	0	0.00	0.00	0.00	2.00	0.00	0.00	2.00
	0.5	0.71	30.58	1.02	1.84	26.10	3.76	1.87
	1	1.00	45.16	1.22	1.74	38.44	5.34	1.79
	1.5	1.22	59.05	4.52	1.61	49.16	3.48	1.71
	2	1.41	71.78	3.68	1.45	56.77	2.90	1.64
	3	1.73	87.64	2.25	1.09	67.83	2.77	1.51
	4	2.00	95.39	0.83	0.66	76.37	2.82	1.37
	5	2.24	98.64	1.37	0.13	82.48	2.74	1.24
	6	2.45	100.02	1.93	-	86.51	2.64	1.13
	7	2.65	-	2.04	-	89.51	2.62	1.02
	8	2.83	-	-	-	91.24	2.45	0.94
	9	3.00	-	-	-	92.85	2.43	0.85
	10	3.16	-	-	-	93.85	2.31	0.79
11	3.32	-	-	-	-	-	-	
12	3.46	-	-	-	-	-	-	

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Table 26 Amount of Propranolol Hydrochloride Releasing from Formulation V-VII in buffer pH 1.5 and in buffer pH 6.8

Formulation	Time(hr)	Dissolution medium						
		Buffer pH1.5				Buffer pH6.8		
		Time1/2	Mean(%)	S.D.	LOG % drug remained	Mean(%)	S.D.	LOG % drug remained
V	0	0.00	0.00	0.00	2.00	0	0.00	2.00
	0.5	0.71	16.43	0.73	1.92	21.16	2.18	1.90
	1	1.00	26.86	1.13	1.86	36.01	3.57	1.81
	1.5	1.22	34.31	1.53	1.82	47.17	5.07	1.72
	2	1.41	40.60	1.98	1.77	56.28	4.85	1.64
	3	1.73	50.88	2.62	1.69	70.05	5.16	1.48
	4	2.00	59.25	2.98	1.61	79.68	4.58	1.31
	5	2.24	66.67	3.15	1.52	86.23	2.99	1.14
	6	2.45	77.46	5.44	1.35	90.13	2.14	0.99
	7	2.65	89.62	3.63	1.02	92.62	1.64	0.87
	8	2.83	97.93	1.58	0.32	94.35	1.27	0.75
	9	3.00	99.49	1.05	-0.29	95.29	1.02	0.67
10	3.16	100.05	1.34	-	96.15	0.86	0.58	
11	3.32	-	-	-	97.13	0.85	0.46	
12	3.46	-	-	-	98.96	0.92	0.02	
VI	0	0.00	0.00	0.00	2.00	0.00	0.00	2.00
	0.5	0.71	14.51	0.64	1.93	20.06	1.50	1.90
	1	1.00	23.86	0.87	1.88	34.48	1.55	1.82
	1.5	1.22	31.18	0.94	1.84	41.24	4.48	1.77
	2	1.41	36.75	1.02	1.8	53.06	3.59	1.67
	3	1.73	46.55	1.06	1.73	67.36	2.66	1.51
	4	2.00	54.44	1.14	1.66	77.38	2.51	1.35
	5	2.24	61.27	1.33	1.59	84.61	2.21	1.19
	6	2.45	67.73	1.70	1.51	89.49	1.93	1.02
	7	2.65	73.68	2.22	1.42	93.02	1.82	0.84
	8	2.83	79.06	2.34	1.32	95.44	1.66	0.66
	9	3.00	86.02	6.08	1.14	97.58	1.57	0.38
10	3.16	94.68	7.44	0.72	98.88	1.44	0.05	
11	3.32	-	3.10	-	99.77	1.44	-	
12	3.46	-	2.08	-	-	1.37	-	
VII	0	0.00	0	0.00	2.00	0.00	0	2.00
	0.5	0.71	13.52	0.53	1.94	23.41	2.91	1.88
	1	1.00	22.36	0.70	1.89	37.09	4.7	1.80
	1.5	1.22	29.21	0.87	1.85	47.02	5.7	1.72
	2	1.41	34.8	1.00	1.81	55.17	6.44	1.65
	3	1.73	43.89	0.93	1.75	68.45	5.87	1.50
	4	2.00	51.51	0.85	1.68	77.92	3.44	1.34
	5	2.24	58.07	0.75	1.62	83.80	2.36	1.21
	6	2.45	63.4	0.68	1.56	87.76	1.82	1.09
	7	2.65	68.8	0.78	1.49	90.43	1.49	0.98
	8	2.83	73.54	0.80	1.42	92.10	1.34	0.90
	9	3.00	83.78	7.07	1.21	93.58	1.26	0.81
10	3.16	94.03	6.13	0.78	94.35	1.17	0.75	
11	3.32	99.22	2.24	-0.11	95.18	1.17	0.68	
12	3.46	101.02	1.09	-	95.92	1.15	0.61	

Table 27 Amount of Propranolol Hydrochloride Releasing from Formulation V-VII in pH Change Method

Formulation	Time(hr)	Time1/2	Mean(% S.D.	LOG % drug
V	0	0.00	0.00	2.00
	0.5	0.71	17.15	0.68
	1	1.00	27.45	1.15
	1.5	1.22	35.09	1.55
	2	1.41	46.28	0.25
	3	1.73	60.22	3.49
	4	2.00	80.40	2.58
	5	2.24	90.20	1.82
	6	2.45	95.62	1.52
	7	2.65	98.73	1.35
	8	2.83	100.00	1.35
	9	3.00	-	-
	10	3.16	-	-
VI	0	0.00	0.00	2.00
	0.5	0.71	13.91	0.24
	1	1.00	23.05	0.34
	1.5	1.22	29.53	0.47
	2	1.41	40.51	0.28
	3	1.73	51.58	0.28
	4	2.00	68.41	4.08
	5	2.24	82.24	0.81
	6	2.45	90.08	0.50
	7	2.65	96.08	1.61
	8	2.83	99.54	0.89
	9	3.00	-	-
	10	3.16	-	-
VII	0	0.00	0.00	2.00
	0.5	0.71	13.21	0.67
	1	1.00	22.01	0.76
	1.5	1.22	28.72	0.90
	2	1.41	39.47	0.46
	3	1.73	51.00	0.41
	4	2.00	66.10	4.84
	5	2.24	82.02	0.72
	6	2.45	89.39	0.66
	7	2.65	94.12	0.92
	8	2.83	97.35	0.99
	9	3.00	98.96	1.11
	10	3.16	99.88	1.04
11	3.32	100.35	0.91	
12	3.46	-	1.20	

Table 28 Amount of Propranolol Hydrochloride Releasing from Formulation VII in pH Change Method

Formulation	Time(hr)	Time 1/2	Mean(% S.D.)	LOG % d remained	
VII pH (1.2, 7.5)	0	0.00	0.00	0.00	2.00
	0.5	0.71	12.90	0.18	1.94
	1	1.00	19.06	0.18	1.91
	1.5	1.22	28.20	0.56	1.86
	2	1.41	34.69	0.24	1.81
	3	1.73	44.56	0.58	1.74
	4	2.00	58.15	3.94	1.62
	5	2.24	72.84	2.61	1.43
	6	2.45	81.78	1.33	1.26
	7	2.65	88.32	1.22	1.07
	8	2.83	90.97	1.81	0.96
	9	3.00	93.95	1.11	0.78
	10	3.16	94.89	1.04	0.71
11	3.32	95.67	0.91	0.64	
12	3.46	95.98	1.20	0.60	

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Table 29 Release rate of propranolol hydrochloride from Formulation I - VII
in buffer pH 1.5

Release Rate (%/hour)							
Mean Time	I	II	III	IV	V	VI	VII
0.25	33.76	51.90	53.52	61.61	32.86	29.02	27.52
0.75	21.64	23.38	23.84	29.16	20.86	18.70	17.68
1.25	15.98	25.00	26.84	27.78	14.90	14.64	13.70
1.75	11.72	20.14	20.38	25.46	12.58	11.14	11.18
2.5	9.61	14.35	16.21	15.86	10.28	9.80	9.09
3.5	7.51	9.26	8.94	7.75	8.37	7.89	7.62
4.5	6.27	5.90	7.07	3.25	7.42	6.83	6.56
5.5	5.50	4.52	3.35	1.38	10.79	6.46	5.33
6.5	5.05	3.70	2.78		12.16	5.95	5.40
7.5	4.40	2.32			8.31	5.38	4.74
8.5	3.89					6.96	10.24
9.5	3.55					8.66	10.25
10.5	3.44						5.19
11.5	3.91						2.20

Table 30 Release rate of propranolol hydrochloride from Formulation I -VII
in buffer pH 6.8

Release Rate (%/hour)							
Mean Time	I	II	III	IV	V	VI	VII
0.25	41.86	57.50	55.20	52.20	42.32	40.12	46.82
0.75	29.32	34.12	28.12	24.68	29.70	28.84	27.36
1.25	24.48	23.06	22.60	21.44	22.32	13.52	19.86
1.75	18.06	17.30	18.68	15.22	18.22	23.64	16.30
2.5	13.88	14.53	13.72	11.06	13.77	14.30	13.28
3.5	9.47	8.99	10.49	8.54	9.63	10.02	9.47
4.5	6.49	5.42	6.69	6.11	6.55	7.23	5.88
5.5	4.09	2.99	3.57	4.03	3.90	4.88	3.96
6.5	2.62	1.73	2.31	3.00	2.49	3.53	2.67
7.5	1.67	1.16	1.38	1.73	1.73	2.42	1.67
8.5	1.46			1.61	0.94	2.14	1.48
9.5	0.81			1.04	0.86	1.30	0.77
10.5	1.01				0.98	0.89	0.83
11.5	0.74				1.83		0.74

Table 31 Release rate of propranolol hydrochloride from Formulation V- VII in pH change method

Mean Time	Release Rate (%/hour)			
	V	VI	VII	VII (pH1.2,7.5)
0.25	34.30	27.82	26.42	25.80
0.75	20.60	18.28	17.60	12.32
1.25	15.28	12.96	13.42	18.28
1.75	22.38	21.96	21.50	12.98
2.5	13.94	11.07	11.53	9.87
3.5	20.18	16.83	15.10	13.59
4.5	9.80	13.83	15.92	14.69
5.5	5.42	7.84	7.37	8.94
6.5	3.10	6.00	4.73	6.54
7.5	1.27	3.46	3.23	2.65
8.5			1.61	2.98
9.5			0.92	0.94
10.5				0.78
11.5				0.31

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Table 32 Percentage of labeled amount of propranolol hydrochloride dissolved at the various time

Time (hours)	Amount dissolved
1	not more than 20%
3	between 20% and 45%
6	between 45% and 80%
12	not less than 80%



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Table 33 Value for rate, amount released, and the corresponding reciprocal for the release of Formulations I-IV

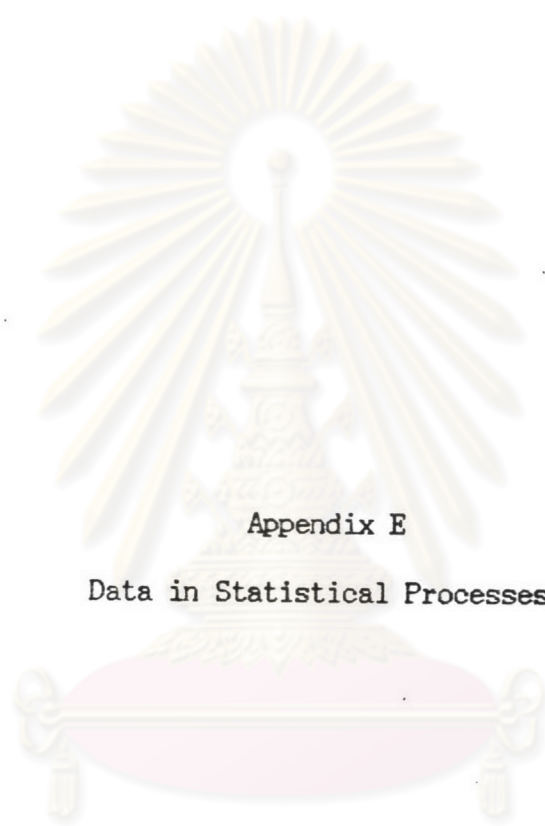
Formulation	Dissolution medium					
	buffer pH1.5			buffer pH6.8		
	dQ/dt	Q	1/Q	dQ/dt	Q	1/Q
I	33.76	16.88	0.059	41.86	20.93	0.048
	21.64	27.70	0.036	29.32	35.59	0.028
	15.98	35.69	0.028	24.48	47.83	0.02
	11.72	41.55	0.024	18.06	56.86	0.018
	9.61	51.16	0.02	13.70	70.56	0.014
	7.51	58.67	0.017	9.47	80.03	0.012
	6.27	64.94	0.015	6.49	86.52	0.012
	5.50	70.44	0.014	4.09	90.61	0.011
	5.05	75.49	0.013	2.62	93.23	0.011
	4.40	79.89	0.012	1.67	94.90	0.01
	3.89	83.78	0.012	1.46	96.36	0.01
	3.55	87.33	0.011	0.81	97.17	0.01
	3.44	92.77	0.011	1.01	98.18	0.01
	3.91	94.68	0.01	0.74	98.92	0.01
II	51.90	25.95	0.038	57.50	28.75	0.035
	23.38	37.64	0.026	34.12	45.81	0.022
	25.00	50.14	0.02	23.06	57.34	0.017
	20.14	60.21	0.017	17.30	65.99	0.015
	14.35	74.56	0.013	14.53	80.52	0.012
	9.26	83.82	0.012	8.99	89.51	0.011
	5.90	89.72	0.011	5.42	94.93	0.01
	4.52	94.24	0.011	2.99	97.92	0.01
	3.70	97.94	0.01	1.73	99.65	0.01
	2.32	100.26	0.01			
III	53.52	26.76	0.037	56.20	27.60	0.036
	23.84	38.68	0.026	28.12	41.66	0.024
	26.84	52.10	0.019	22.60	52.96	0.019
	20.83	62.29	0.016	18.68	62.30	0.016
	16.21	78.50	0.013	13.72	76.02	0.013
	8.44	86.94	0.012	10.49	86.51	0.012
	7.07	94.01	0.011	6.69	93.20	0.011
	3.35	97.36	0.01	3.57	96.77	0.01
	2.78	100.14	0.01	2.31	99.08	0.01
IV	61.16	30.58	0.033	52.20	26.10	0.038
	29.16	45.16	0.022	24.68	38.44	0.026
	27.78	59.05	0.017	21.44	49.16	0.02
	25.46	71.78	0.014	15.22	56.77	0.018
	15.86	87.64	0.011	11.06	67.83	0.015
	7.75	95.39	0.01	8.54	76.37	0.013
	3.25	98.64	0.01	6.11	82.48	0.012
	1.38	100.02	0.01	4.03	86.51	0.012
				3.00	89.51	0.011
				1.73	91.24	0.011
			1.61	92.85	0.011	

Table 34 Value for rate, amount released, and the corresponding reciprocal for the release of Formulations V-VII

Formulation	Dissolution medium					
	buffer pH1.5			buffer pH6.8		
	dQ/dt	Q	1/Q	dQ/dt	Q	1/Q
V	32.86	16.43	0.061	42.32	21.16	0.047
	20.86	26.86	0.037	29.70	36.01	0.028
	14.90	34.31	0.029	22.32	47.17	0.021
	12.58	40.60	0.025	18.22	56.28	0.018
	10.28	50.88	0.02	13.77	70.05	0.014
	8.37	59.25	0.017	9.63	79.68	0.012
	7.42	66.67	0.015	6.55	86.23	0.012
	10.79	77.46	0.013	3.90	90.13	0.011
	12.16	89.62	0.011	2.49	92.62	0.011
	8.31	97.93	0.01	1.73	94.35	0.01
	1.56	99.49	0.01	0.94	95.29	0.01
	0.56	100.05	0.01	0.86	96.15	0.01
				0.98	97.13	0.01
				1.83	98.96	0.01
VI	29.02	14.51	0.069	27.82	13.91	0.072
	18.70	23.86	0.042	18.28	23.05	0.043
	14.64	31.18	0.032	12.96	29.53	0.034
	11.14	36.75	0.027	21.96	40.51	0.025
	9.80	46.55	0.021	11.07	51.58	0.019
	7.89	54.44	0.018	16.83	68.41	0.015
	6.83	61.27	0.016	13.83	82.24	0.012
	6.46	67.73	0.015	7.84	90.08	0.011
	5.95	73.68	0.014	6.00	96.08	0.01
	5.38	79.06	0.013	3.46	99.54	0.01
	6.96	86.02	0.012	1.73	101.27	0.01
8.66	94.68	0.01				
VII	27.04	13.52	0.074	46.82	23.41	0.043
	17.68	22.36	0.045	27.36	37.09	0.027
	13.70	29.21	0.034	19.86	47.02	0.021
	11.18	34.80	0.029	16.30	55.17	0.018
	9.09	43.89	0.023	13.28	68.45	0.015
	7.62	51.51	0.019	9.47	77.92	0.013
	6.56	58.07	0.017	5.88	83.80	0.012
	5.33	63.40	0.016	3.96	87.76	0.011
	5.40	68.80	0.014	2.67	90.43	0.011
	4.74	73.54	0.014	1.67	92.10	0.011
	10.24	83.78	0.012	1.48	93.58	0.011
	10.25	94.03	0.011	0.77	94.35	0.01
	5.19	99.22	0.01	0.83	95.18	0.01
2.20	101.42	0.01	0.74	95.92	0.01	

Table 35 Values for rate, amount release, and the corresponding reciprocal for the release of Formulation V-VII from pH change

Formulation	dQ/dt	Q	1/Q
V	34.30	17.15	0.058
	20.60	27.45	0.036
	15.28	35.09	0.028
	22.38	46.28	0.022
	13.94	60.22	0.017
	20.18	80.40	0.012
	9.80	90.20	0.011
	5.42	95.62	0.01
	3.11	98.73	0.01
	1.27	100.00	0.01
VI	27.82	13.91	0.072
	18.28	23.05	0.043
	12.96	29.53	0.034
	21.96	40.51	0.025
	11.07	51.58	0.019
	16.83	68.41	0.015
	13.83	82.24	0.012
	7.84	90.08	0.011
	6.00	96.08	0.01
	3.46	99.54	0.01
1.73	101.27	0.01	
VII	26.42	13.21	0.076
	17.60	22.01	0.045
	13.42	28.72	0.035
	21.50	39.47	0.025
	11.53	51.00	0.02
	15.10	66.10	0.015
	15.92	82.02	0.012
	7.37	89.39	0.011
	4.73	94.12	0.011
	3.23	97.35	0.01
1.61	98.96	0.01	
0.92	99.88	0.01	
0.47	100.35	0.01	
VII(1.2.7.5)	25.80	12.90	0.078
	12.32	19.06	0.052
	18.28	28.20	0.035
	12.98	34.69	0.029
	9.87	44.56	0.022
	13.59	58.15	0.017
	14.69	72.84	0.014
	8.94	81.78	0.012
	6.54	88.32	0.011
	2.65	90.97	0.011
2.98	93.95	0.011	
0.94	94.89	0.01	
0.78	95.67	0.01	
0.31	95.98	0.01	



Appendix E

Data in Statistical Processes

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Table 36 Comparison of linearity between plots of rate of release against reciprocal amount and amount of propranolol hydrochloride releasing from the matrices in buffer pH 6.8

Formulation	Matrices	Correlation coefficient of rate	
		versus Q	versus 1/Q
I	1	0.9871	0.7523
	2	0.9839	0.8387
	3	0.9454	0.8113
	4	0.9927	0.8202
	5	0.9154	0.9366
	6	0.9918	0.8672
V	1	0.9195	0.8744
	2	0.993	0.8162
	3	0.9589	0.8896
	4	0.9724	0.7374
	5	0.9637	0.9568
VI	1	0.9439	0.8032
	2	0.9892	0.9846
	3	0.9915	0.9704
	4	0.9892	0.9831
	5	0.9905	0.9828
	6	0.9588	0.8651
VII	1	0.9684	0.9545
	2	0.9399	0.9802
	3	0.8842	0.9408
	4	0.9429	0.9759
	5	0.9054	0.9201
	6	0.9767	0.9384

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T-test(unpaired)

$$t = \frac{(\bar{X}_1 - \bar{X}_2) - (\mu_1 - \mu_2)}{\sqrt{\frac{S_p^2}{n_1} + \frac{S_p^2}{n_2}}}$$

$$S_p^2 = \frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2}$$

$$S = \sqrt{\frac{\sum(X_i - \bar{X})^2}{(n-1)}}$$

S_p^2 - pooled variance

degree of freedom - $n_1 + n_2 - 2$

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Hypothesis $H_0 : \mu_1 - \mu_2 = 0$

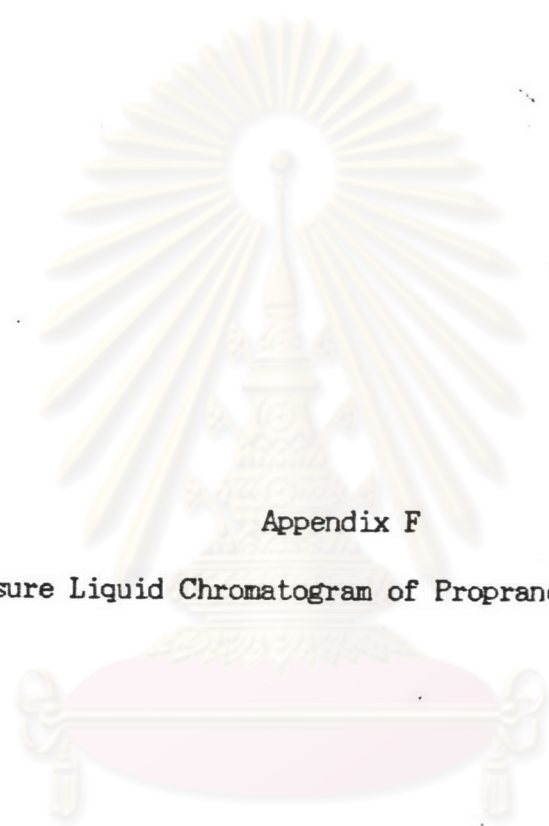
$H_a : \mu_1 - \mu_2 \neq 0$

Table 37 t-test of linearity between rate of release against reciprocal amount and amount (data from Table 36)

products	t-value	Significance test
Formulation I	4.651	S
Formulation V	2.741	S
Formulation VI	1.381	NS
Formulation VII	-0.884	NS



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Appendix F

High Pressure Liquid Chromatogram of Propranolol Hydrochloride

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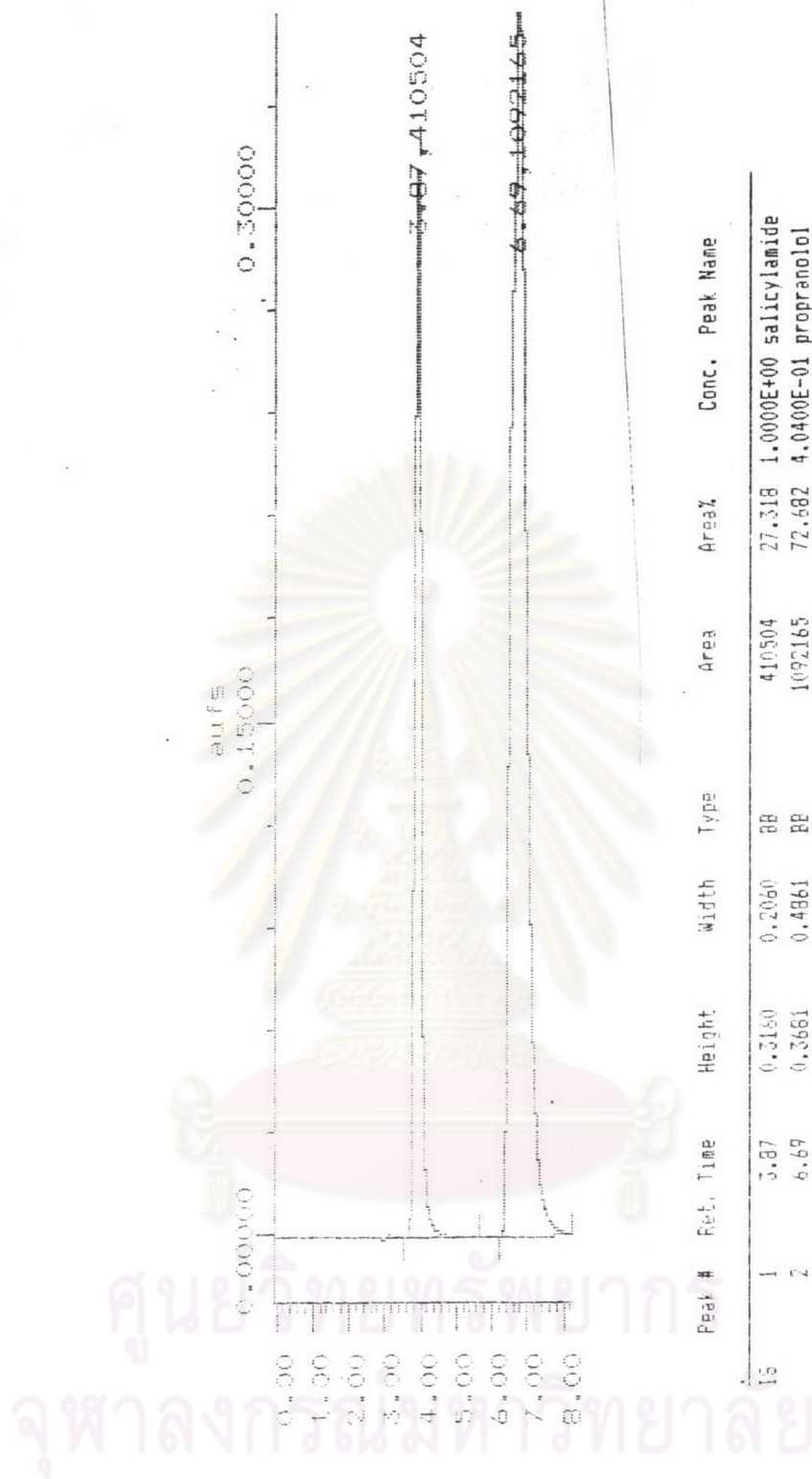


Figure 36 High pressure liquid chromatogram of propranolol hydrochloride standard

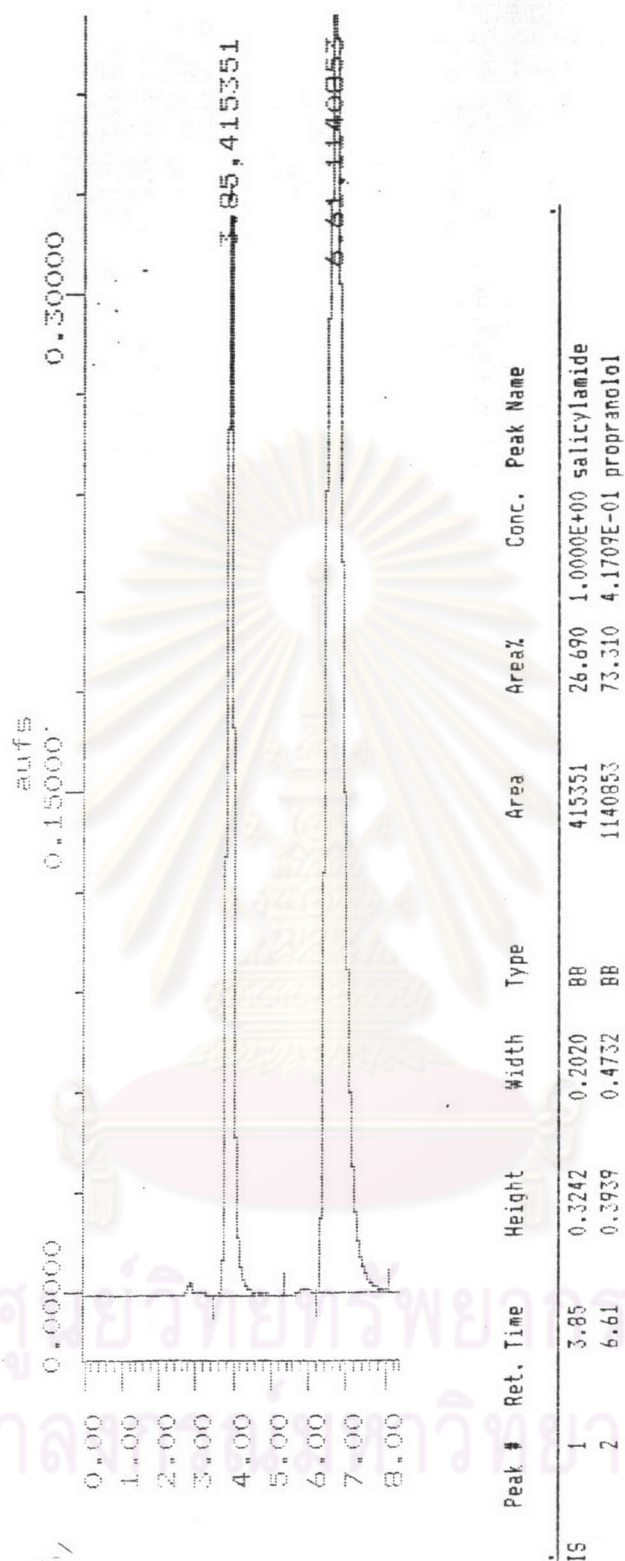


Figure 37 High pressure liquid chromatogram of propranolol hydrochloride from co-spray dried powder of Formulation I

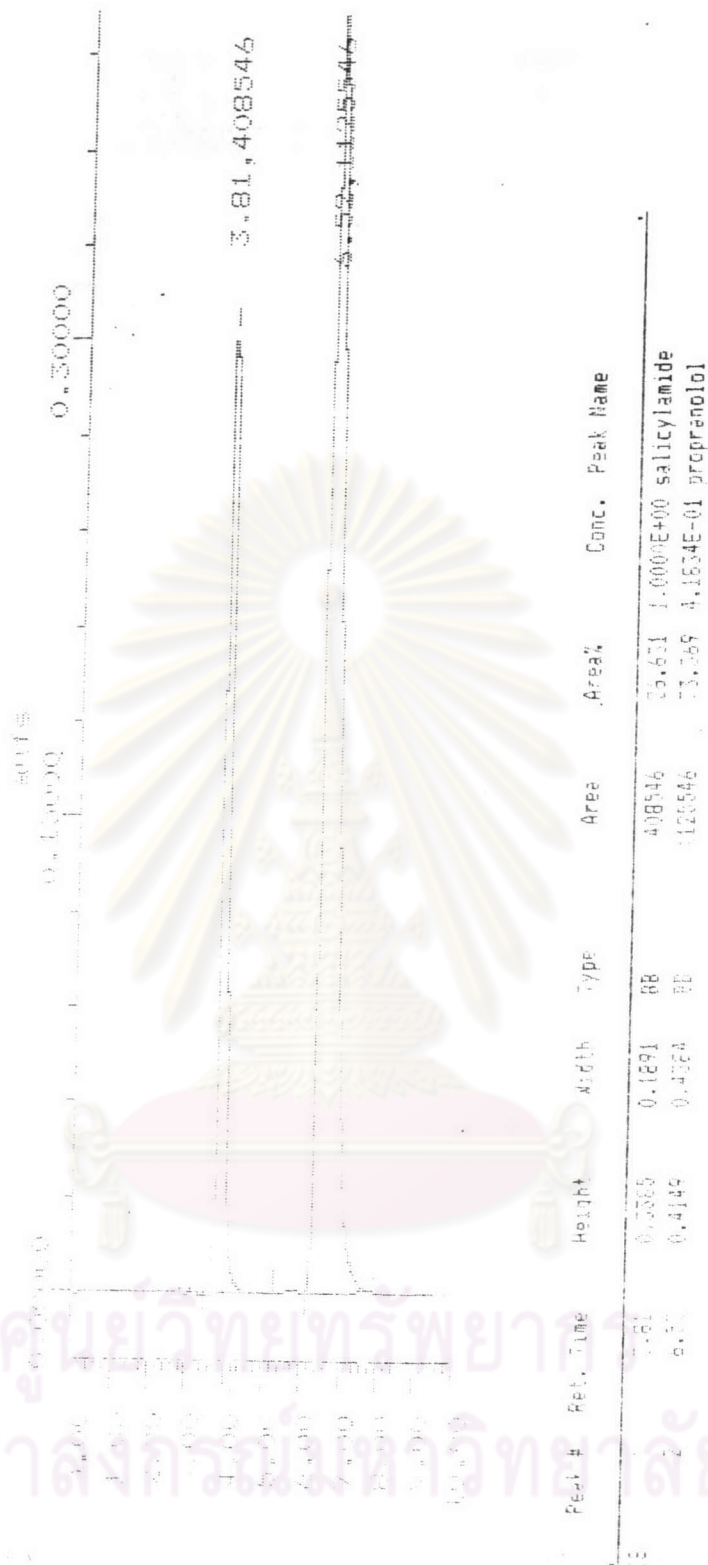


Figure 38 High pressure liquid chromatogram of propranolol hydrochloride from co-spray dried powder of Formulation II

Biography

Miss sasitorn prugnahachaikul was born on February 16, 1962. She got her degree in bachelor of Science in Pharmacy in 1985 from Faculty of Pharmacy, Chulalongkorn University, bangkok, Thailand.



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