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APPENDICES

APPENDIX A

PREPARATION OF REAGENTS

1. 0.1 N Hydrochloric acid

   Dilute 8.5 ml of hydrochloric acid (HCl) with water to 1000 ml.

2. 0.2 M Sodium hydroxide

   Dissolve 8.4 g of sodium hydroxide (NaOH) in water and dilute to 1000 ml.

3. Phosphate buffer solution pH 6.8

   Dissolve 6.8 g of Potassium dihydrogen phosphate (KH_2PO_4) in water 800 ml

   ↓

   Adjust pH to 6.8 with 0.2 M NaOH

   ↓

   Transfer to 1000-ml volumetric flask and adjust to volume with water

4. Zinc sulfate 10 % w/v

   Dissolve 10 g of anhydrous zinc sulfate ($ZnSO_4$) in water and dilute to 1000-ml.

5. Mobile phase

Mobile phase consist of acetonitrile (HPLC grade) and 0.01 M phosphoric acid (HPLC grade) in the ratio of 1:1.

↓

Mix 400 ml of acetonitrile with 400 ml of 0.01 M phosphoric acid

↓

Filter through Nylon pore size 0.45 μ m

↓

Degas using a sonicator for about 30 minutes

APPENDIX B

THE UV SPECTRUM

The UV visible spectrophotometer was used to determined the amount of gliclazide using a 1-cm cell at 226 nm for 0.1 N HCl and at 225 nm for phosphate buffer pH 6.8. The influences of additives in the matrix on absorbance value were measured. Blank matrix shows no peaks in 0.1 N HCl and phosphate buffer pH 6.8 in the region of wavelength used. As shown in Figure 23.

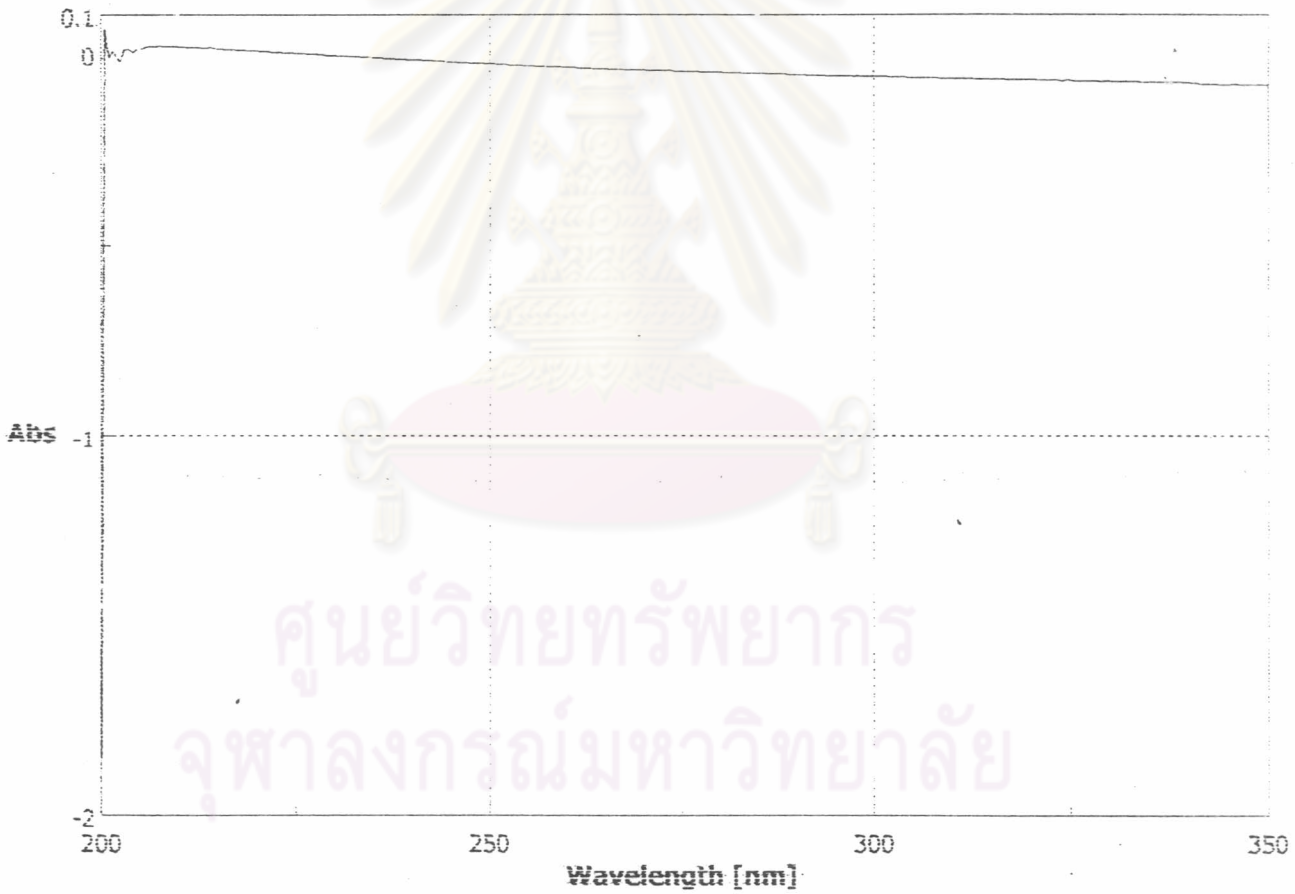

Figure 23 Blank matrix peaks in 0.1 N HCl and phosphate buffer pH 6.8.

APPENDIX C

CALIBRATION CURVE AND VALIDATION

The concentrations versus absorbances of gliclazide plots in various media are shown in Tables 37 and 38. The calibration curves of gliclazide and the correlation of determination are presented also in Figure 24 and 25.

Table 37 Absorbances of gliclazide in 0.1 N HCl at 226 nm.

Concentration (μg/ml)	Absorbance
6.00	0.230
8.40	0.334
12.00	0.460
14.40	0.559
18.00	0.703

Table 38 Absorbances of gliclazide in phosphate buffer pH 6.8 at 225 nm.

Concentration (μg/ml)	Absorbance
6.40	0.244
8.96	0.343
12.80	0.496
15.36	0.603
19.20	0.749

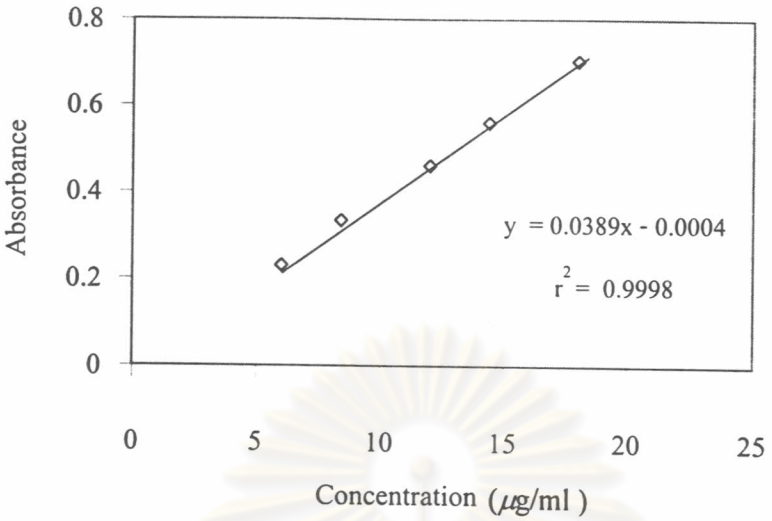

Figure 24 Calibration curves of gliclazide in 0.1 N HCl at 226 nm.

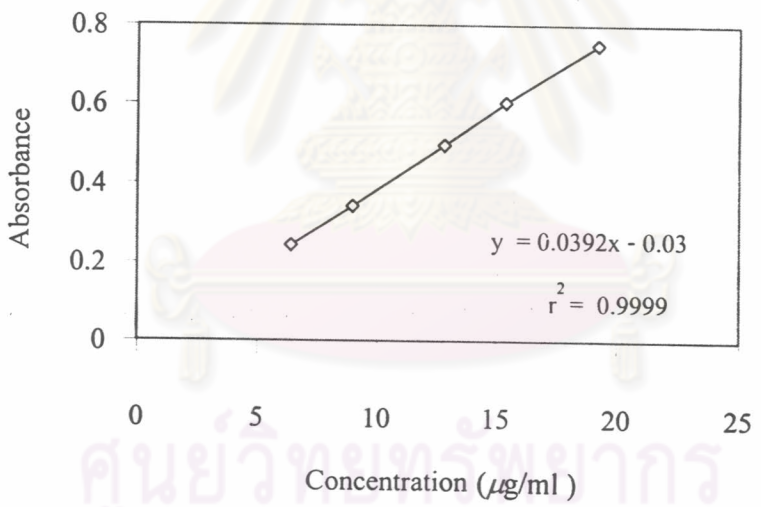

Figure 25 Calibration curves of gliclazide in phosphate buffer pH 6.8 at 225 nm.

Table 39 Peak area ratio of gliclazide to methyl 4-hydroxybenzoate in rabbit plasma (n=3).

Concentration (μg/ml)	Peak area ratio	Inversely estimated concentration (μg/ml)	% Recovery
1	0.076	1.15	115.00
2	0.202	1.86	93.00
4	0.509	3.92	98.00
6	0.927	6.04	100.67
8	1.245	7.89	98.63
16	2.610	16.19	101.19
		Mean	101.08
		SD	7.41
		% C.V.	7.33

$r^2 = 0.9997$, $y = 0.1692 x - 0.1163$

Table 40 Accuracy of analytical method for determination of gliclazide in rabbit plasma (n=3).

Concentration (μg/ml)	Peak area ratio	Inversely estimated concentration (μg/ml)	% Recovery
1.5	0.127	1.44	96.00
5	0.784	5.32	106.40
10	1.628	10.31	103.10
		Mean	101.83
		SD	5.31
		% C.V.	5.22

Table 41 Within run precision of analytical method for determination of gliclazide in rabbit plasma (n=3).

Concentration (μg/ml)	Inversely estimated concentration (μg/ml)			Mean (SD)	% C.V.
	1	2	3		
1.5	1.61	1.69	1.43	1.58(0.13)	8.45
5	5.23	5.85	5.42	5.50 (0.32)	5.78
10	10.73	11.07	9.94	10.58 (0.58)	5.48

Table 42 Between run precision of analytical method for determination of gliclazide in rabbit plasma (n=3).

Concentration (μg/ml)	Inversely estimated concentration (μg/ml)			Mean (SD)	% C.V.
	1	2	3		
1.5	1.64	1.45	1.39	1.49 (0.13)	8.74
5	5.43	4.78	5.32	5.18 (0.35)	6.72
10	10.75	9.44	11.13	10.44 (0.89)	8.49

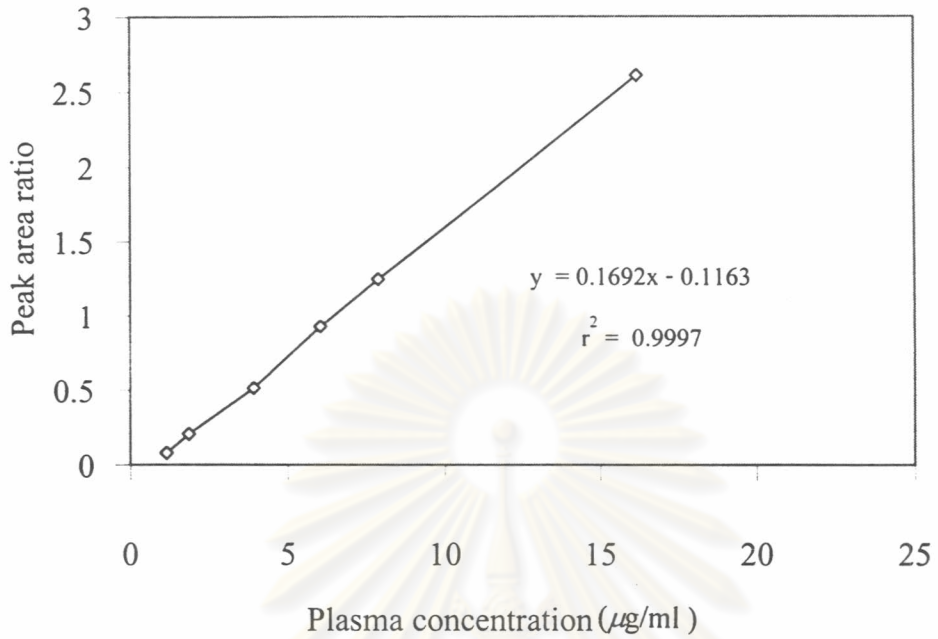

Figure 26 Calibration curves of gliclazide in rabbit plasma.

APPENDIX D

DISSOLUTION DATA

Table 43 Percentage amounts of gliclazide dissolved from matrices containing various amounts of HPMC.

HPMC 20% (F1)

Percentage amount of drug release											
Time (hr)	0.1 N HCl					Time (hr)	Phosphate Buffer pH 6.8				
	1	2	3	Mean	SD		1	2	3	Mean	SD
0	0	0	0	0	0	0	0	0	0	0	0
1	24.60	23.15	20.25	22.67	2.21	1	18.49	15.94	19.26	17.90	1.74
2	43.51	42.29	41.60	42.47	0.97	2	29.58	29.41	29.72	29.57	0.15
3	70.86	65.45	62.03	66.11	4.45	4	51.08	52.09	50.93	51.37	0.63
4	92.80	92.29	84.91	90.00	4.41	8	81.48	85.65	86.40	84.51	2.65
6	99.85	99.64	94.60	98.03	2.97	12	95.29	98.45	99.31	97.68	2.12

HPMC 40% (F2)

Percentage amount of drug release											
Time (hr)	0.1 N HCl					Time (hr)	Phosphate Buffer pH 6.8				
	1	2	3	Mean	SD		1	2	3	Mean	SD
0	0	0	0	0	0	0	0	0	0	0	0
1	8.21	8.67	9.55	8.81	0.68	1	8.70	7.70	12.44	9.61	2.50
2	16.95	16.84	17.05	16.95	0.10	2	17.37	19.49	20.29	19.05	1.51
3	27.08	27.42	27.68	27.40	0.30	4	34.14	38.03	37.59	36.59	2.13
4	40.71	37.77	38.87	39.11	1.49	8	58.40	58.92	62.69	60.00	2.34
6	58.86	56.80	57.43	57.70	1.05	12	86.56	78.69	82.38	82.55	3.94

Table 43 (Continued) Percentage amounts of gliclazide dissolved from matrices containing various amounts of HPMC.

HPMC 60% (F3)

Percentage amount of drug release											
Time	0.1 N HCl					Time	Phosphate Buffer pH 6.8				
(hr)	1	2	3	Mean	SD	(hr)	1	2	3	Mean	SD
0	0	0	0	0	0	0	0	0	0	0	0
1	4.55	4.39	5.92	4.96	0.84	1	5.74	6.82	8.80	7.12	1.55
2	8.80	7.97	10.27	9.01	1.16	2	16.37	9.86	9.55	11.92	3.85
3	15.23	14.78	16.51	15.51	0.90	4	23.17	17.55	19.60	20.11	2.84
4	21.17	20.71	21.78	21.22	0.54	8	48.41	33.79	34.08	38.76	8.36
6	32.58	33.15	37.02	34.25	2.42	12	72.55	48.20	48.79	56.51	13.89

Table 44 Percentage amounts of gliclazide from matrices containing various amounts of xanthan gum.

5% Xanthan gum (F4)

Percentage amount of drug release											
Time	0.1 N HCl					Time	Phosphate Buffer pH 6.8				
(hr)	1	2	3	Mean	SD	(hr)	1	2	3	Mean	SD
0	0	0	0	0	0	0	0	0	0	0	0
1	42.97	43.18	53.72	46.62	6.14	1	7.17	8.80	8.07	8.01	0.82
2	74.42	77.38	84.04	78.62	4.93	2	19.12	27.39	21.59	22.70	4.25
3	101.45	96.14	95.25	97.61	3.35	4	65.70	65.07	51.01	60.59	8.30
4	103.56	99.23	102.13	101.64	2.21	8	94.02	99.67	96.68	96.79	2.83
6	102.83	94.96	102.91	100.24	4.57	12	104.38	104.28	103.15	103.94	0.68

7% Xanthan gum (F5)

Percentage amount of drug release											
Time	0.1 N HCl					Time	Phosphate Buffer pH 6.8				
(hr)	1	2	3	Mean	SD	(hr)	1	2	3	Mean	SD
0	0	0	0	0	0	0	0	0	0	0	0
1	20.88	16.20	13.27	16.78	3.84	1	7.50	6.29	6.80	6.86	0.61
2	49.50	46.74	33.17	43.13	8.74	2	19.63	16.92	19.37	18.64	1.50
3	84.83	65.00	54.84	68.22	15.25	4	54.88	58.00	61.68	58.18	3.40
4	105.93	87.07	73.64	88.88	16.22	8	99.57	94.61	98.05	97.41	2.54
6	100.44	94.05	82.90	92.47	8.87	12	102.18	104.13	104.15	103.49	1.13

Table 44 (Continued) Percentage amounts of gliclazide from matrices containing various amounts of xanthan gum.

9% Xanthan gum (F6)

Percentage amount of drug release											
Time	0.1 N HCl					Time	Phosphate Buffer pH 6.8				
(hr)	1	2	3	Mean	SD	(hr)	1	2	3	Mean	SD
0	0	0	0	0	0	0	0	0	0	0	0
1	4.67	2.59	3.67	3.64	1.04	1	7.40	6.22	2.87	5.50	2.35
2	8.12	5.12	6.48	6.57	1.50	2	19.07	10.97	6.16	12.07	6.53
3	12.83	7.50	11.96	10.76	2.86	4	45.10	34.48	26.85	35.48	9.17
4	17.01	10.10	16.56	14.56	3.87	8	95.00	80.66	67.98	81.21	13.52
6	27.63	21.57	22.04	23.75	3.37	12	104.20	103.45	90.41	99.35	7.76

Table 45 Percentage amounts of gliclazide from matrices containing commercial product.

Percentage amount of drug release											
Time (hr)	0.1 N HCl					Time (hr)	Phosphate Buffer pH 6.8				
	1	2	3	Mean	SD		1	2	3	Mean	SD
0	0	0	0	0	0	0	0	0	0	0	0
1	21.33	22.42	20.61	21.45	0.91	1	17.08	19.60	21.50	19.39	2.22
2	45.16	45.21	44.53	44.97	0.38	2	34.34	34.79	35.10	34.74	0.39
3	78.64	78.53	81.54	79.57	1.71	4	61.37	61.50	64.45	62.44	1.74
4	87.61	90.31	91.43	89.78	1.96	8	88.96	94.88	91.95	91.93	2.96
6	94.44	95.59	96.65	95.56	1.11	12	99.52	99.54	95.57	98.21	2.29

Table 46 Percentage amounts of gliclazide from matrices containing HPMC and xanthan gum in pH change method.

Percentage amount of drug release											
Time	HPMC					Time	xanthan gum				
(hr)	1	2	3	Mean	SD	(hr)	1	2	3	Mean	SD
0	0	0	0	0	0	0	0	0	0	0	0
1	26.50	27.27	26.73	26.83	0.32	1	15.54	14.33	15.53	15.13	0.70
2	46.94	49.22	48.01	48.06	0.93	2	44.85	37.62	41.62	41.36	3.62
3	54.11	57.63	58.01	56.59	1.76	3	64.04	57.52	62.80	61.46	3.46
4	69.00	71.40	72.76	71.05	1.56	4	81.81	80.00	78.52	80.11	1.65
8	99.16	98.96	100.24	99.45	0.56	8	92.81	90.33	91.10	91.41	1.27
12	99.37	98.22	100.42	99.34	0.90	12	91.43	96.97	92.43	93.61	2.95

Table 47 Percentage amounts of gliclazide from matrices containing commercial product in pH change method.

Time	Percentage amount of drug release				
(hr)	1	2	3	Mean	SD
0	0	0	0	0	0
1	24.00	22.67	17.01	21.23	3.03
2	50.46	49.46	39.91	46.61	4.76
3	66.79	66.06	61.79	64.88	2.21
4	95.20	93.80	85.55	91.52	4.26
8	96.73	95.85	95.70	96.09	0.45
12	97.62	97.64	97.26	97.51	0.17

Table 48 Similarity factor (f_2) and difference factor (f_1) of HPMC and xanthan gum gliclazide matrix tablets in pH change method when compared with commercial product.

Statistical Factor	Formulation	
	HPMC 20% (F1)	Xanthan gum 7% (F5)
f_2	51.11	59.53
f_1	9.81	8.32

VITA

Mr. Pipat Tantiwattanasirikul was born on March 12, 1976 in Bangkok, Thailand. He received Bachelor Degree of Science in Pharmacy from Faculty of Pharmacy, Chulalongkorn University, Bangkok, Thailand in 1999. After graduation, he worked at manufacturing company from 1999 to 2001 before entering the Master's degree program in Industrial Pharmacy at Chulalongkorn University.