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APPENDIX

Table 1. Solubility of Cimetidine.

Solvent	Ratio	Solubility
Ethanol	-	soluble
Methanol	-	soluble
Chloroform	-	less soluble
Ethyl acetate	-	less soluble
Hexane	-	less soluble
Chloroform:methanol	50 : 50	soluble
	60 : 40	soluble
	70 : 30	soluble
	80 : 20	soluble
Ethyl acetate: methanol	50 : 50	soluble
	60 : 40	soluble
	70 : 30	soluble
	80 : 20	soluble
Hexane: ethanol	50 : 50	soluble
	60 : 40	soluble
	70 : 30	soluble
	80 : 20	less soluble

Table 2. Thin Layer Chromatography of Cimetidine.

Developing Solvent	Ratio	R_f value[a]	k'
Chloroform:methanol	70 : 30	0.90	0.11
	80 : 20	0.80	0.25
	85 : 15	0.52	0.92
	90 : 10	0.36	1.78
Ethyl acetate: methanol	80 : 20	0.36	1.78
Hexane:ethanol	80 : 20	0.09	10.11
Chloroform:methanol: ammonia solution	70:30:0.5	0.95	0.05
	75:25:0.5	0.82	0.22

Sample size 10 µl of cimetidine 10 mg/ml in methanol

[a] Mean value of three experiments.

Table 3. Selection of Flow Rate and Retention Time.

Flow Rate ml/min	Solvent I		Solvent II	
	Pressure atm.	Retention time min [a]	Pressure atm.	Retention time min [a]
1.5	45	11.35	45	10.20
2.0	55	8.30	55	7.18
2.5	65	6.04	65	5.00
3.0	75	4.28	75	3.10

Solvent I chloroform:methanol, ratio 80:20

Solvent II chloroform:methanol, ratio 70:30

Sample size 5 µl of cimetidine 1 mg/ml in mobile phase

[a] Mean value of three experiments.

Table 4. Values of Peak Height and Peak Area versus Concentration of Cimetidine.

Concn. µg Injected.	Peak Height mm.[a]	% CV.	Peak Area mm^2 [a]	% CV.	Retention time. min [a]
1.5	32.0	0.00	314.7	1.43	3.10
3.0	64.6	0.89	574.0	1.32	3.08
4.5	98.3	0.59	939.7	0.90	3.11
6.0	130.3	0.89	1254.0	0.42	3.09
7.5	165.0	0.00	1505.0	0.20	3.09
9.0	189.7	0.30	1787.0	1.40	3.12

Mobile phase chloroform:methanol, ratio 70:30

UV-detector 240 nm, 0.1 AUFS

[a] Mean value of three experiments.

Table 5. Precision of Peak Height and Peak Area for Cimetidine.

Injection.	Peak Height mm.	Peak Area mm^2.
1	163.5	1506.1
2	162.5	1497.3
3	164.5	1568.9
4	164.0	1550.1
5	162.0	1491.8
6	163.0	1510.5
7	164.0	1546.8
8	163.0	1501.9
9	163.5	1519.8
10	164.0	1544.1
Mean	163.4	1523.7
Std. Dev.	± 0.77	± 26.62
Coeff. of var.	0.47 %	1.75 %

Sample size 5 µl of cimetidine 1.5 mg/ml in mobile phase.
Mobile phase chloroform:methanol, ratio 70:30
UV-detector 240 nm, 0.1 AUFS

Table 6. Percent Labelled Amount of Cimetidine in Cimetidine Tablet Using HPLC Method, Non-aqueous Titration Method and Spectrophotometric Method.

Sample	Percent Labelled Amount of Cimetidine.		
	HPLC Method	Titration Method	Spectrophotometric Method
1	99.63	99.29	98.44
2	99.54	100.04	98.55
3	100.17	99.70	99.08
4	99.53	100.81	98.12
5	99.83	100.05	98.17
6	99.96	101.88	98.82
7	99.55	100.36	99.18
8	99.38	100.39	98.61
9	99.54	99.48	98.78
10	99.88	100.41	99.06
Mean	99.70	100.24	98.68
Std. Dev.	± 0.25	± 0.74	± 0.37
Coeff. of var.	0.25 %	0.74 %	0.37 %

Table 7. Percent Recovery of Cimetidine in Cimetidine Tablet by HPLC Method, Nom-aqueous Titration Method and Spectrophotometric Method.

Sample	HPLC Method			Titration Method			Spectrophotometric Method		
	Amount Added, mg	Amount Found, mg	% Recovery	Amount Added, mg	Amount Found, mg	% Recovery	Amount Added, mg	Amount Found, mg	% Recovery
1	2.01	2.01	99.90	1.99	1.97	99.14	1.84	1.85	100.77
2	1.98	1.96	99.27	1.96	1.94	99.24	1.97	1.95	99.25
3	2.02	2.02	100.18	1.99	1.97	99.19	1.88	1.85	98.36
Mean			99.78			99.19			99.46
Std. Dev.			± 0.47			± 0.05			± 1.22
Coeff. of var.			0.47%			0.05 %			1.23 %

Table 7. (continue) Percent Recovery of Cimetidine in Cimetidine Tablet by HPLC Method, Non-aqueous Titration Method and Spectrophotometric Method.

Sample	HPLC Method			Titration Method			Spectrophotometric Method		
	Amount Added, mg	Amount Found, mg	% Recovery	Amount Added, mg	Amount Found, mg	% Recovery	Amount Added, mg	Amount Found, mg	% Recovery
1	6.03	5.98	99.26	5.97	6.02	100.86	5.72	5.85	102.31
2	6.00	5.97	99.53	5.93	5.99	101.15	5.67	5.71	100.78
3	6.06	6.10	100.75	6.00	6.08	101.35	5.69	5.80	101.86
Mean			99.85			101.12			101.86
Std. Dev.			± 0.73			± 0.25			± 0.79
Coeff. of var.			0.73%			0.25%			0.78%

Table 7. (continue) Percent Recovery of Cimetidine in Cimetidine Tablet by HPLC Method, Non-aqueous Titration Method and Spectrophotometric Method.

Sample	HPLC Method			Titration Method			Spectrophotometric Method		
	Amount Added, mg	Amount Found, mg	% Recovery	Amount Added, mg	Amount Found, mg	% Recovery	Amount Added, mg	Amount Found, mg	% Recovery
1	10.02	10.12	100.99	9.92	9.90	99.85	9.44	9.56	101.33
2	9.97	10.00	100.28	9.86	9.93	100.69	9.51	9.70	101.99
3	9.95	9.93	99.80	9.84	9.84	100.04	9.57	9.68	101.21
Mean			100.36			100.19			101.51
Std.Dev.			± 0.60			± 0.44			± 0.42
Coeff. of var.			0.60%			0.44%			0.41 %

Table 8. Various Commercial Pharmaceutical Dosage Forms of Cimetidine.

Manufacturer	Product	Dosage Form	Composition
Atlantic Laboratories Corp., Ltd.	Citidine	Tablet	each tablet contains 200 mg cimetidine
Smith Kline & French Laboratories. (Australia)Ltd.	Tagamet	Tablet	each tablet contains 200 mg cimetidine
Bruschettini s.r.l. (Italy)	Brumeti-dina	Tablet	each tablet contains 200 mg cimetidine
Berlin Pharmaceutical Industry Ltd. Part.	Cimidine	Tablet	each tablet contains 200 mg cimetidine
Siamerican Pharmaceuticals Co., Ltd.	Ulcidine	Capsule	each capsule contains 200 mg cimetidine
Hero Import Export Ltd., Part.	Gastidine	Capsule	each capsule contains 200 mg cimetidine

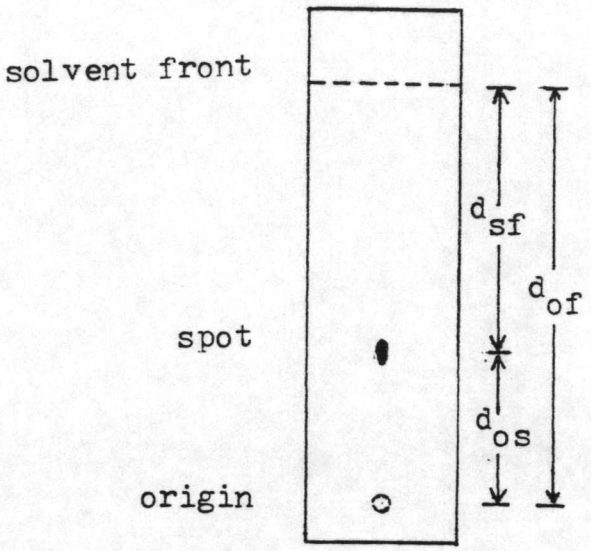
Table 8. (continue) Various Commercial Pharmaceutical Dosage Forms of Cimetidine.

Manufacturer	Product	Dosage Form	Composition
Bruschettini s.r.l. (Italy)	Brumetidina	Injection	each ampoule contains 229 mg of cimetidine hydrochloride equal to 200 mg of basic cimetidine
Smith Kline & French Laboratories (Australia)Ltd.	Tagamet	Injection	each 2 ml contains 200 mg cimetidine protonated with hydrochloric acid in water for injection.

Table 9. Comparative Analysis of Pharmaceutical Preparations Containing Cimetidine.

Formulation	Label Content, mg	HPLC Method [a]			Titration Method [a]			Spectrophotometric Method [a]		
		Amount Found, mg	% Labeled Content	% CV	Amount Found, mg	% Labeled Content	% CV	Amount Found, mg	% Labeled Content	% CV
Tablet A	200/tab	199.44	99.57	0.05	199.44	99.72	0.32	197.32	98.66	0.14
Tablet B	200/tab	198.88	99.44	0.43	201.62	100.81	0.29	196.02	98.01	0.34
Tablet C	200/tab	200.60	100.30	0.35	202.74	101.37	0.30	201.14	100.57	0.27
Tablet D	200/tab	208.94	104.47	0.37	211.84	105.92	0.04	206.20	103.10	0.11
Capsule E	200/cap	196.40	98.20	0.22	196.58	98.29	0.38	196.70	98.35	0.40
Capsule F	200/cap	192.62	96.31	0.65	196.26	98.13	0.36	194.72	97.36	0.56
Injection G	200/2 ml	205.22	102.61	0.22	-	-	-	204.78	102.39	0.38
Injection H	200/2 ml	201.00	100.50	0.52	-	-	-	198.78	99.39	0.26

[a] Mean value of three experiments



$$R_f = \frac{d_{os}}{d_{of}}$$

$$= 1/(k' + 1)$$

$$k' = (1 - R_f)/R_f$$

$$= \frac{d_{sf}}{d_{os}}$$

$$k'_R = \frac{t_R - t_0}{t_0}$$

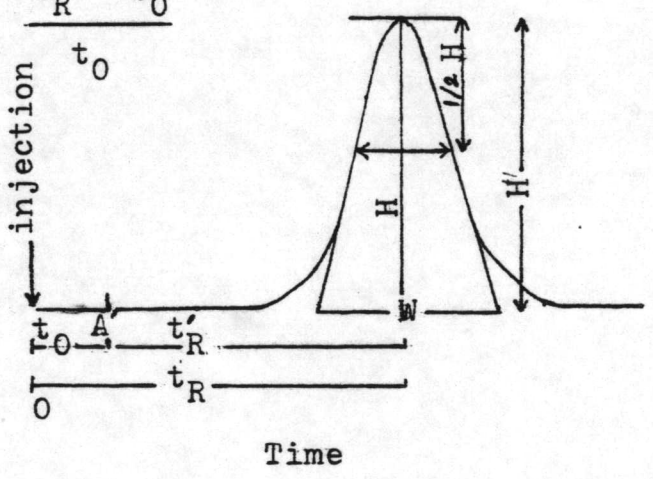
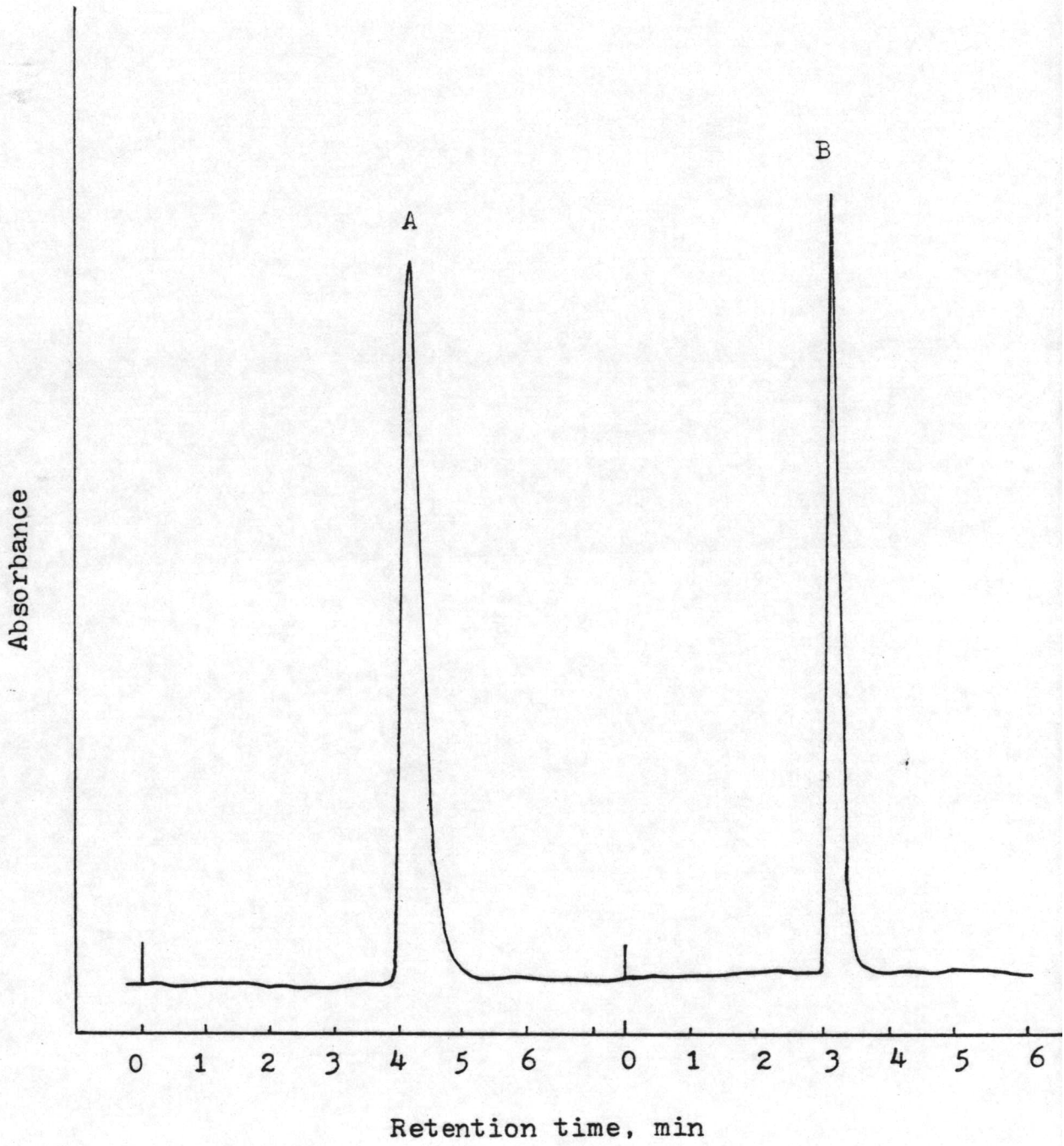


Figure 1. Relationship between R_f Value and k' (capacity factor)


A
B
Absorbance
0 1 2 3 4 5 6 0 1 2 3 4 5 6
Retention time, min

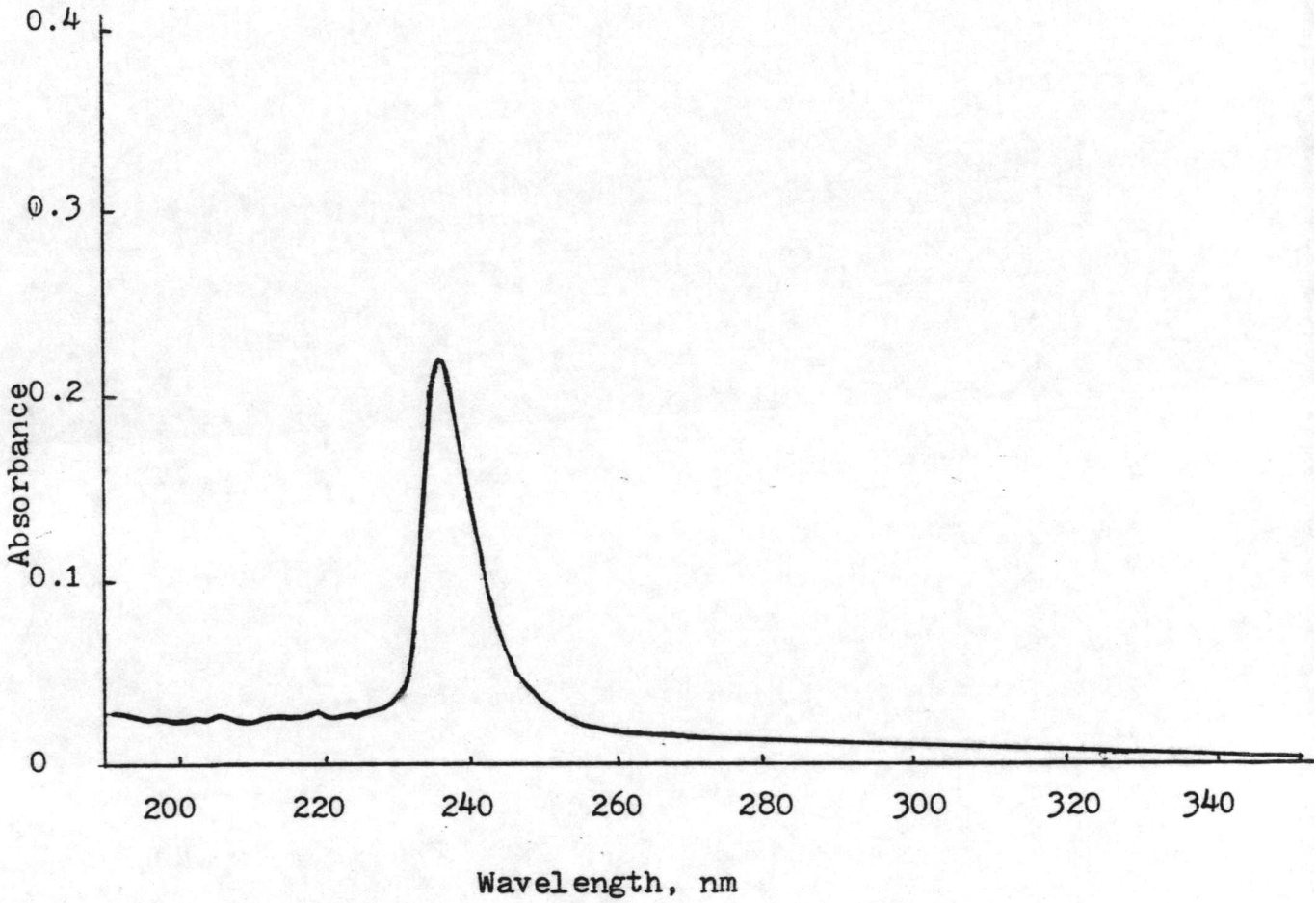


Figure 3 . Absorption Spectrum of Cimetidine by Spectrophotometric method.

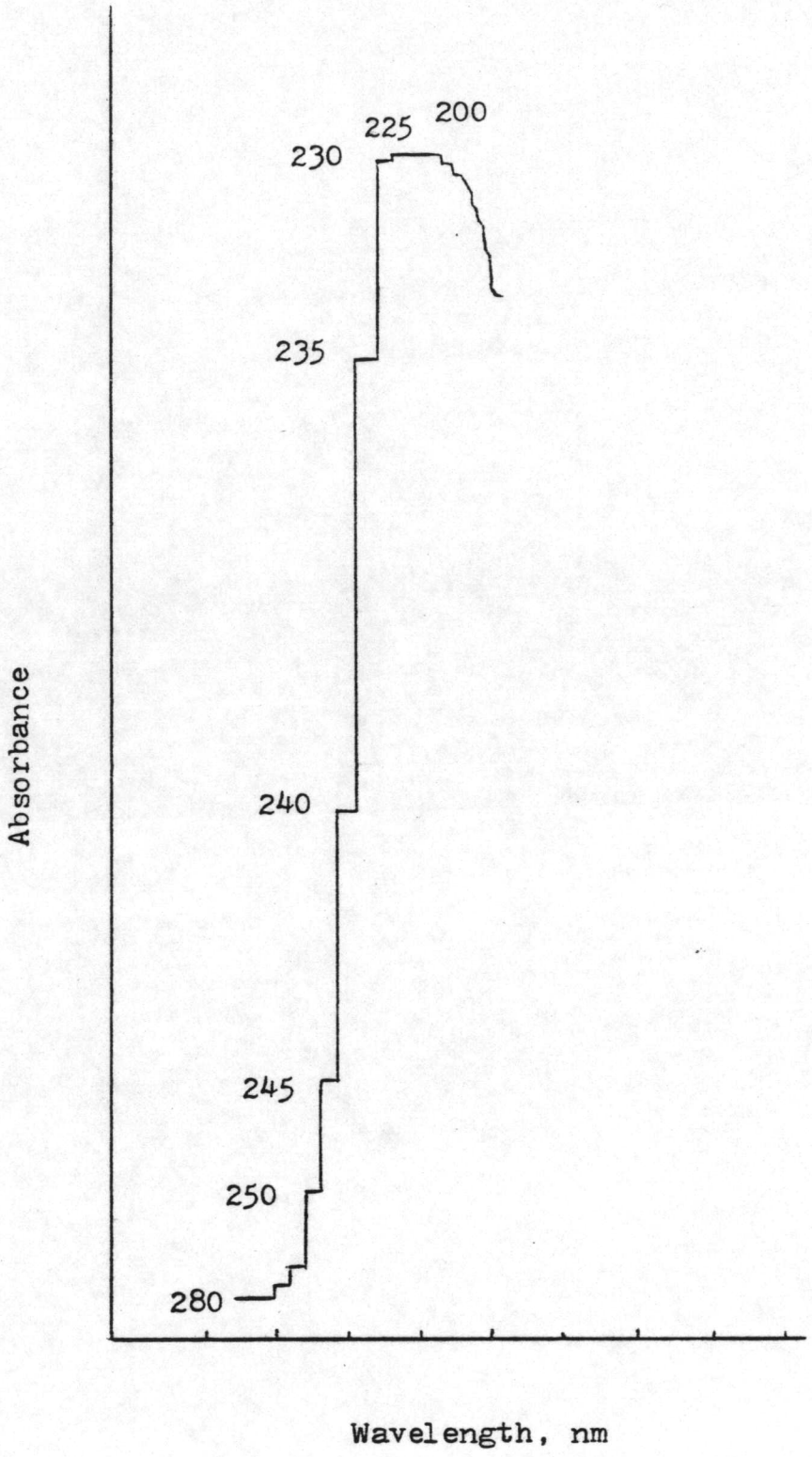


Figure 4. Absorption Spectrum of Cimetidine by HPLC Method.

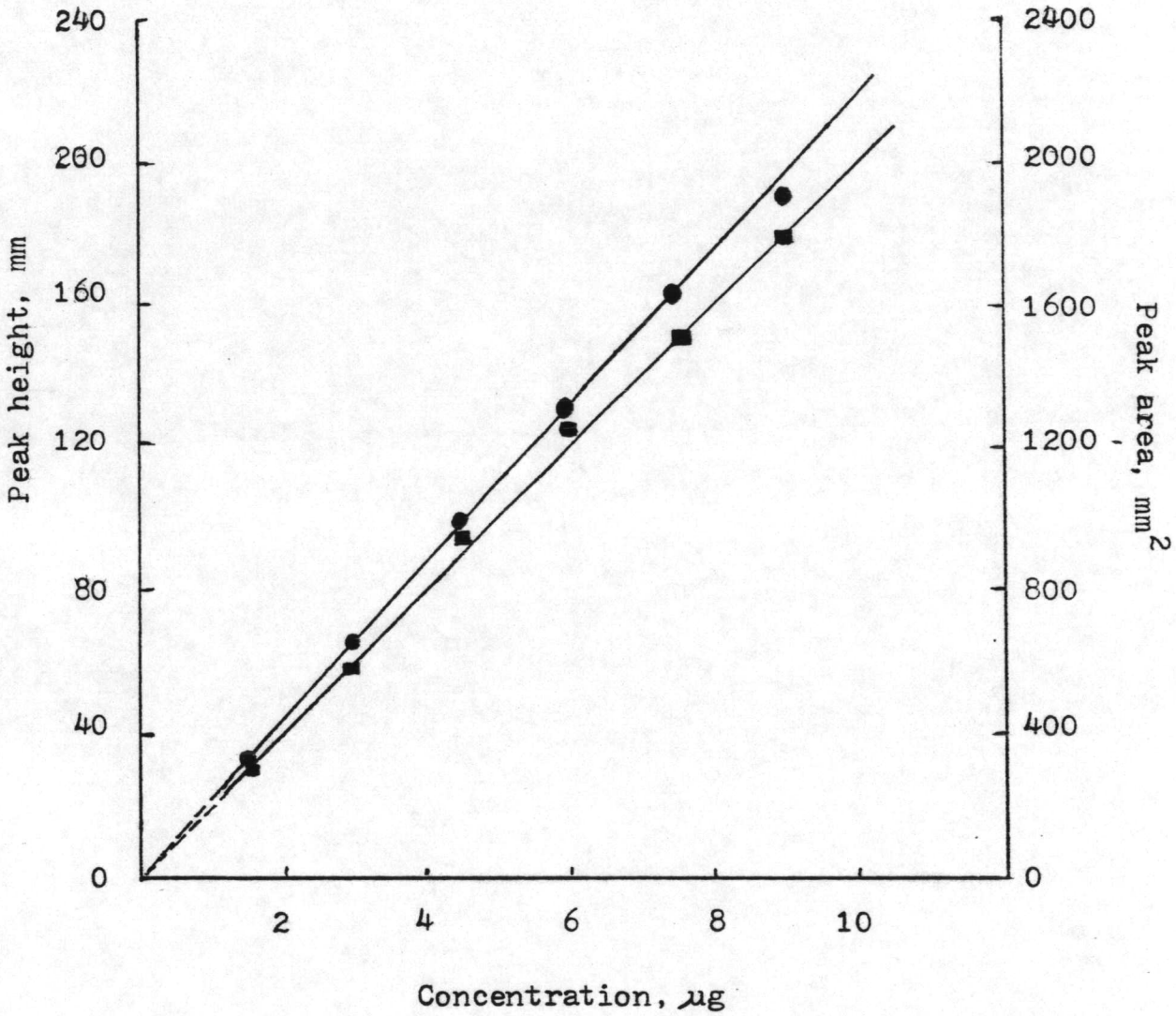
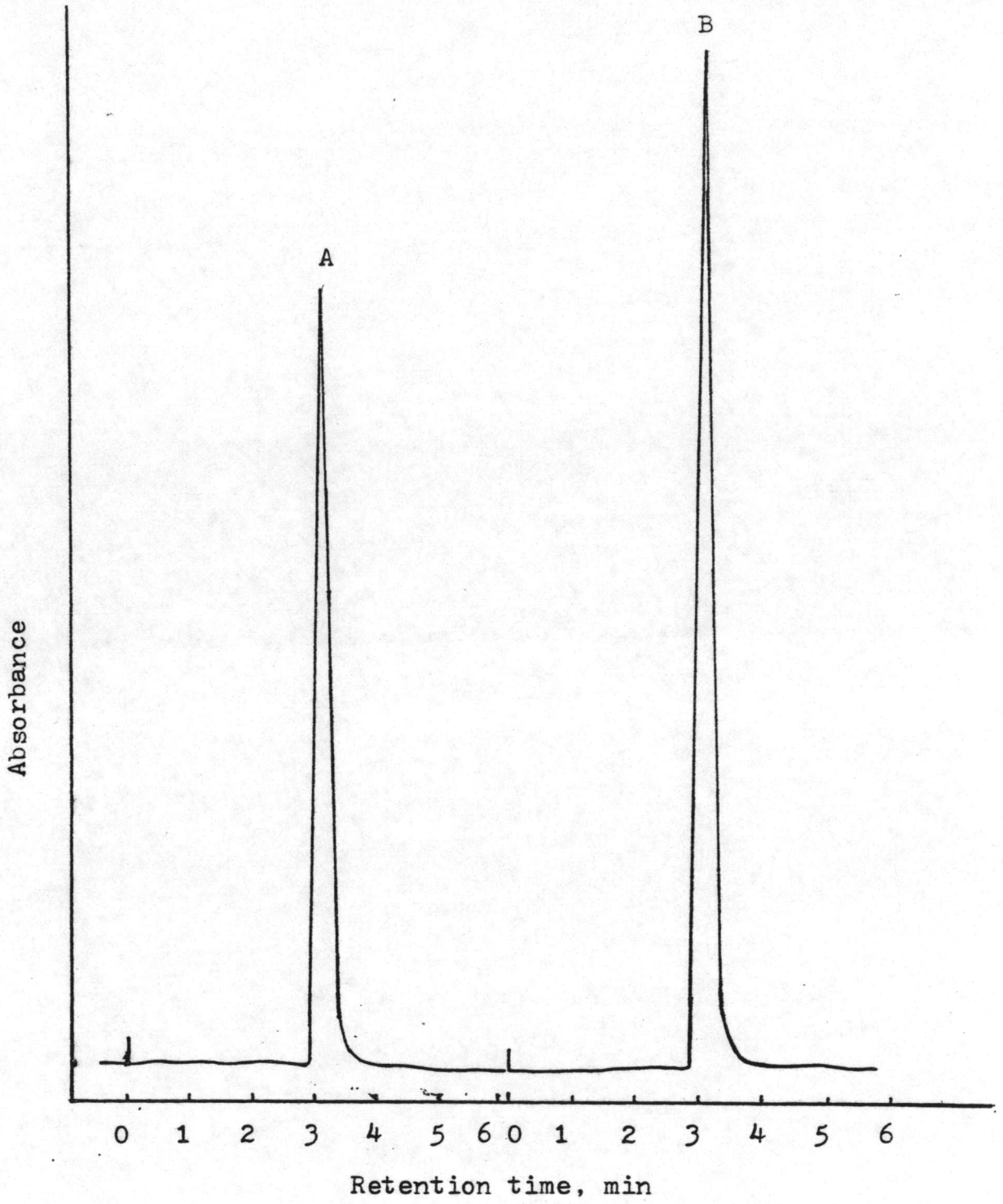
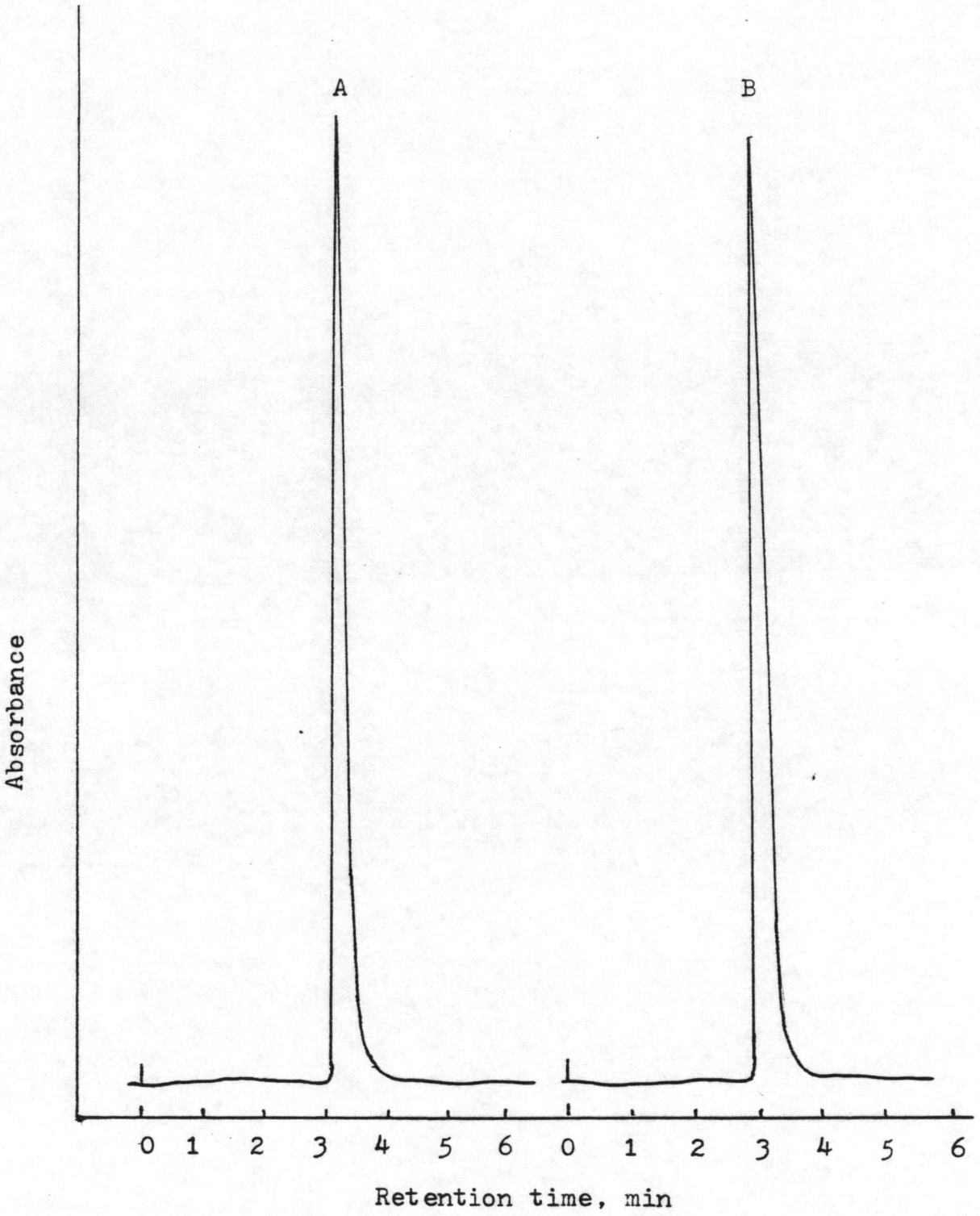


Figure 5. Calibration Curve of Cimetidine.

Key : ● = peak height

■ = peak area


B
A
Absorbance
0 1 2 3 4 5 6 0 1 2 3 4 5 6
Retention time, min


A
B
Absorbance
0 1 2 3 4 5 6 0 1 2 3 4 5 6
Retention time, min

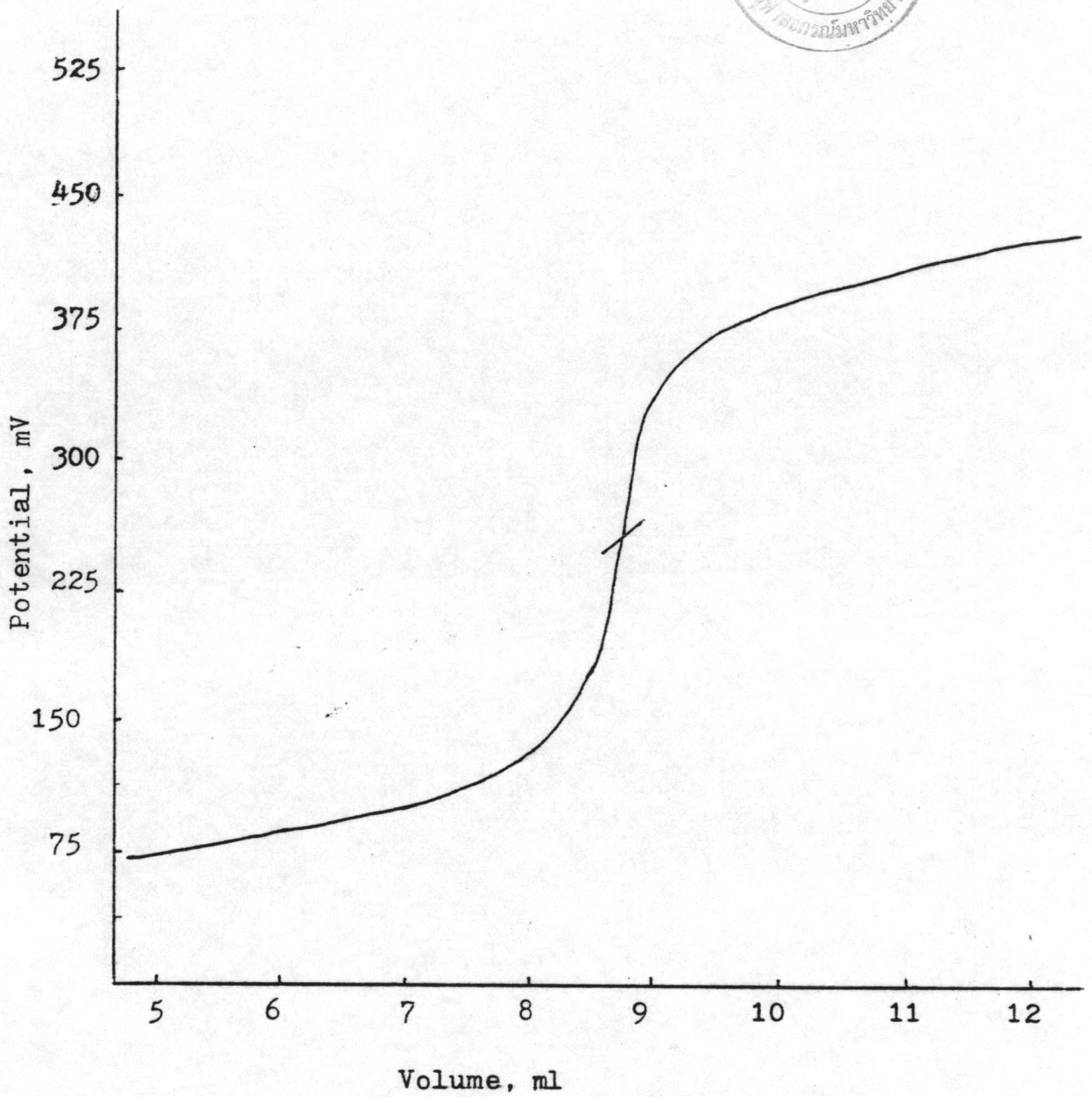
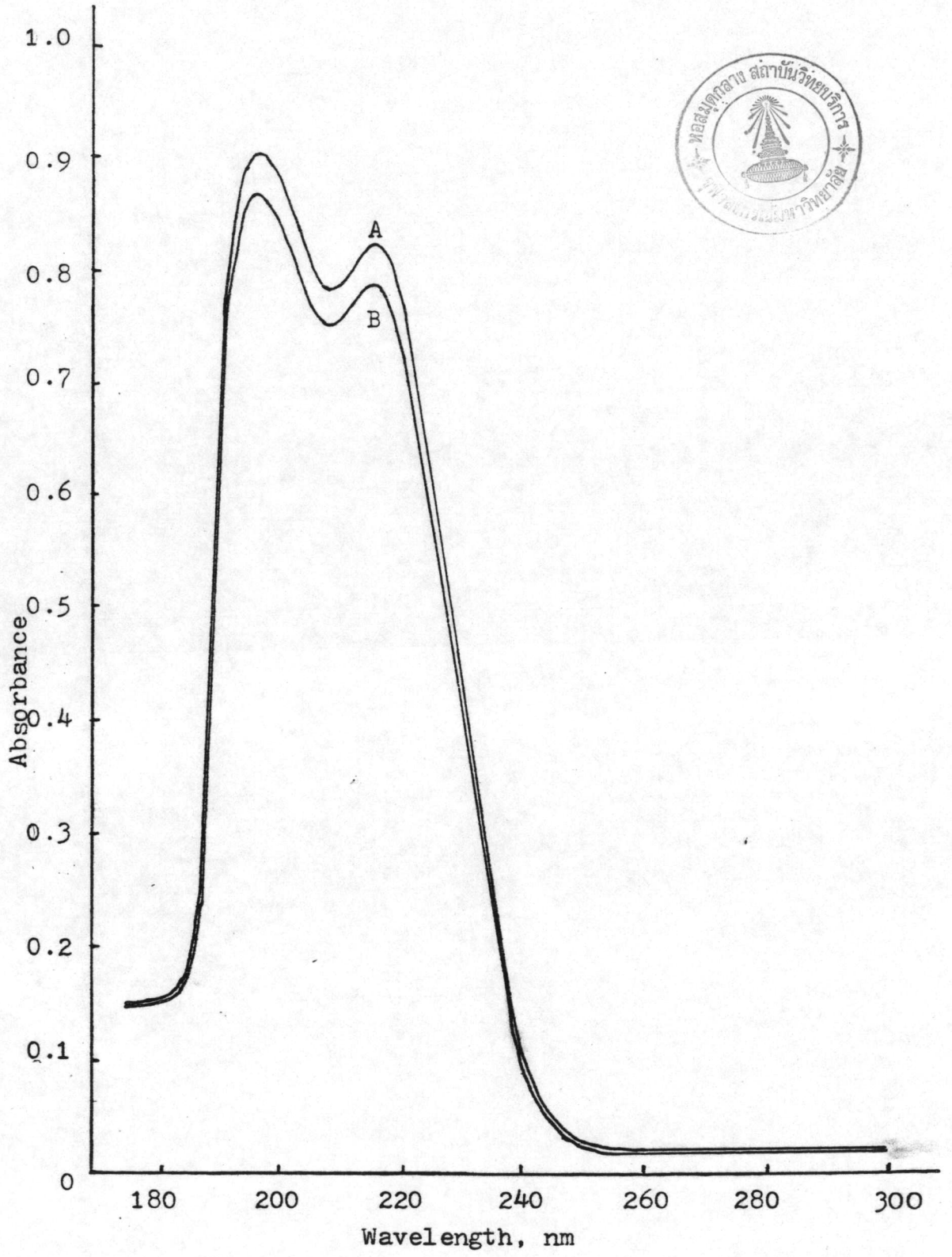


Figure 8. Titration Curve of Cimetidine.



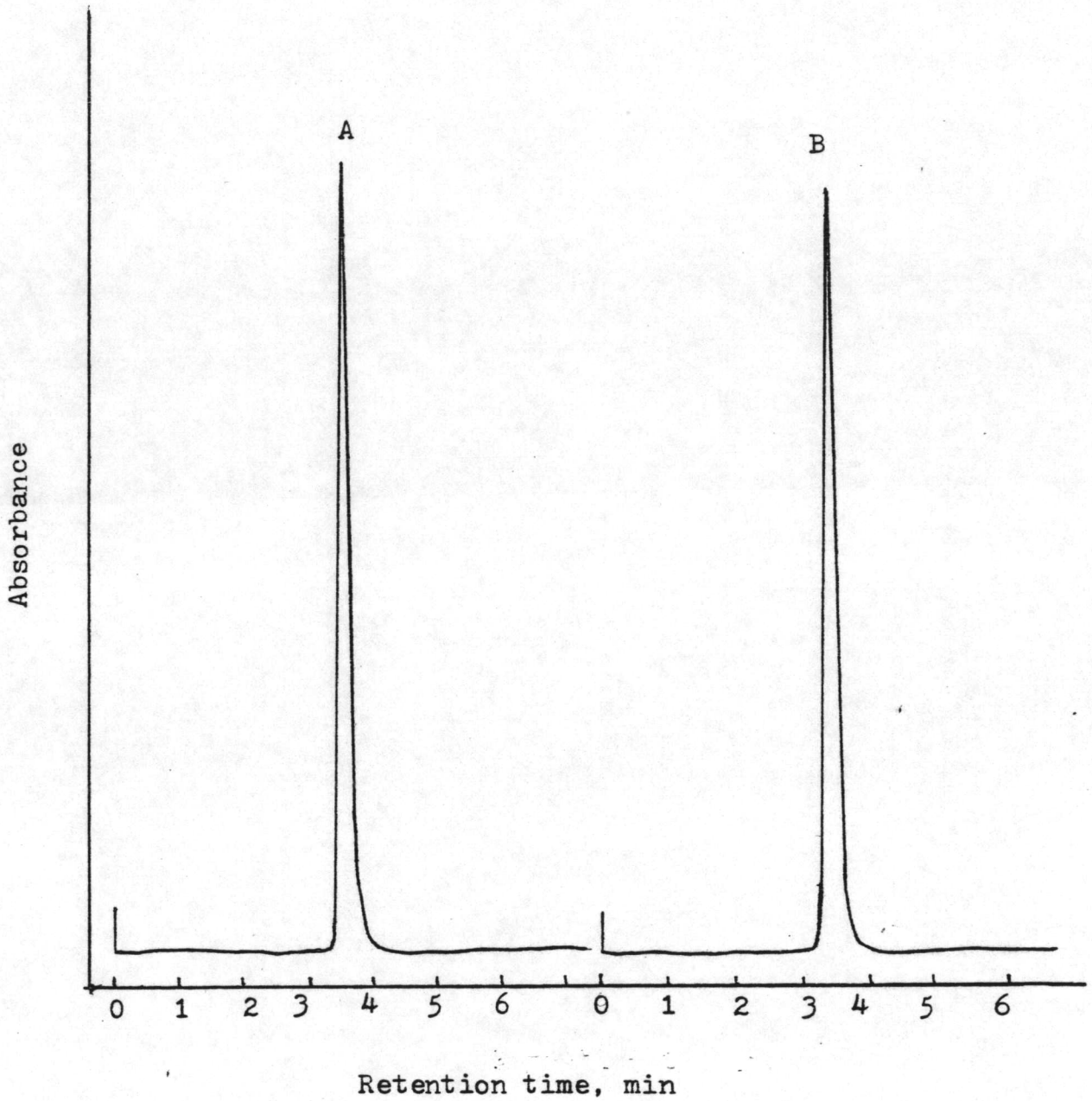
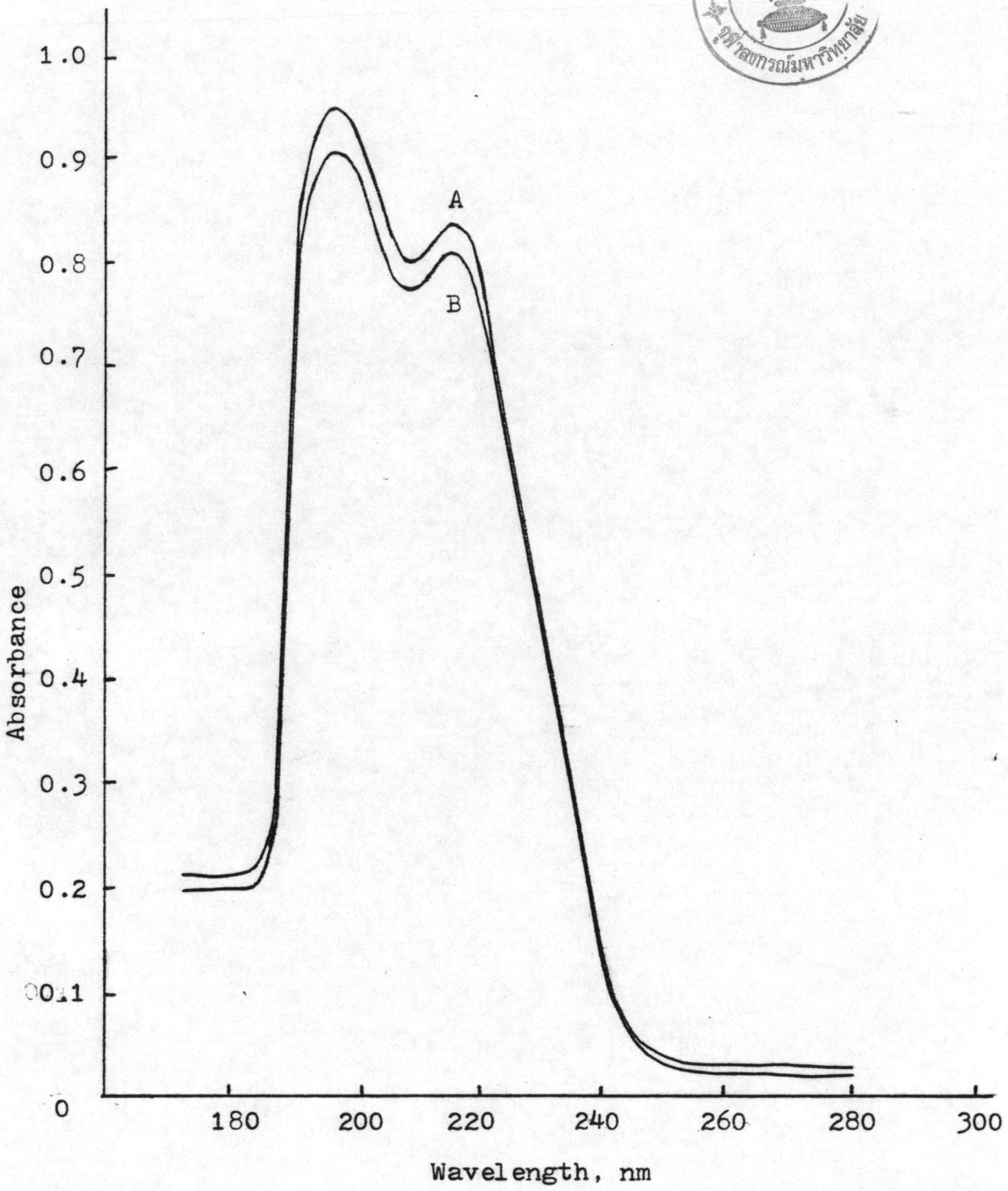
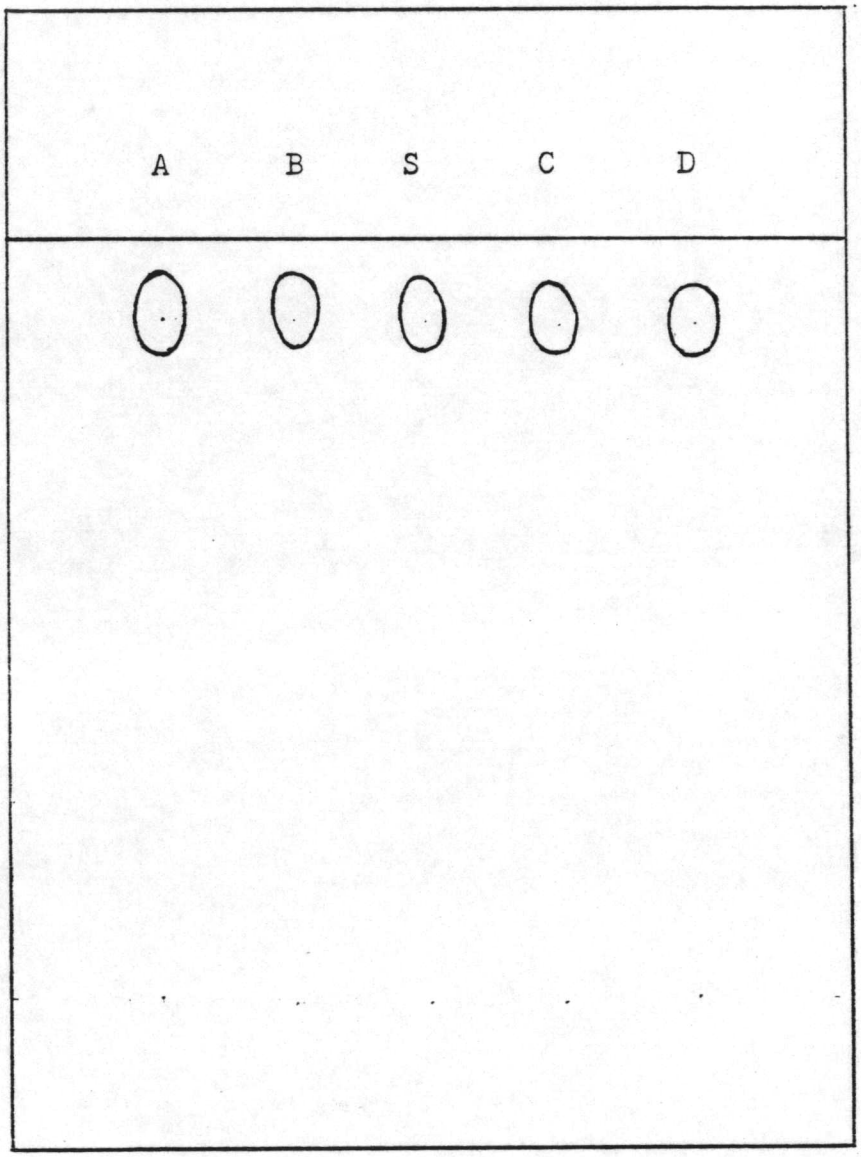


Figure 11 . Absorption Spectra of Cimetidine in Injection Dosage Form Analysis.

A = cimetidine standard

B = cimetidine sample


1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Absorbance
A
B
180
200
220
240
260
280
300
Wavelength, nm


A
B
S
C
D

BIOGRAPHY

Miss Nidapan Ruangrittinon was born on the 6th February, 1953, graduated with a B.Sc. in Pharmacy (Honour) from Chulalongkorn University in 1975, and is now working in Drug Analysis Division, Department of Medical Sciences, Ministry of Public Health.