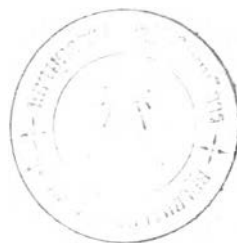


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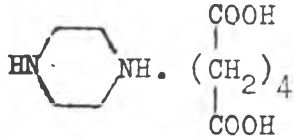
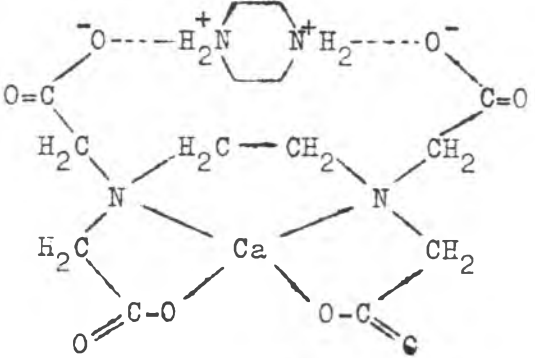
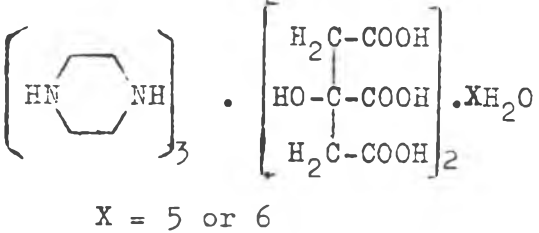
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APPENDIX

Table 1 Chemical Structure of Piperazine Salts

name	chemical structure	formula	molecular weight
Piperazine adipate		$C_4H_{10}N_2 \cdot C_6H_{10}O_4$	232.3
Piperazine calcium edetate		$C_{14}H_{24}CaN_4O_8$	416.45
Piperazine citrate	 <p style="text-align: center;">X = 5 or 6</p>	$(C_4H_{10}N_2)_3 \cdot 2C_6H_8O_7$	642.66 (anhydrous)

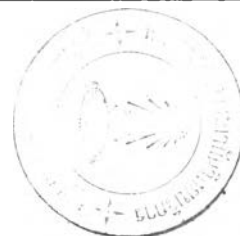


Table 1. (Continued) Chemical Structure of Piperazine Salts.

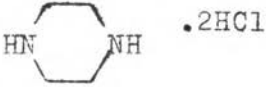
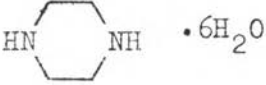
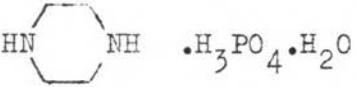
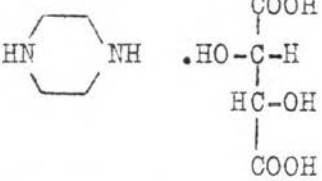
name	chemical structure	formula	molecular weight
Piperazine dihydrochloride		$C_4H_{10}N_2 \cdot 2HCl$	159.06
Piperazine hexahydrate		$C_4H_{10}N_2 \cdot 6H_2O$	194.2
Piperazine phosphate		$C_4H_{10}N_2 \cdot H_3PO_4 \cdot H_2O$	202.1
Piperazine tartrate		$C_4H_{10}N_2 \cdot C_4H_6O_6$	236.23

Table 2. Completeness of Extraction with Various Concentrations of Sodium Hydroxide and Number of Extractions

Normality of Sodium Hydroxide	Extraction			
	No. 5		No. 6	
	Absorbance ^a	S.D.	Absorbance ^a	S.D.
6	1.259	± 0.003	1.236	± 0.004
8	0.432	± 0.004	0.152	± 0.003
9	0.080	± 0.003	0.013	± 0.001
10	0.017	± 0.001	0.004	± 0.002

^aMean value of five determinations

Table 3. Conformity to Beer's Law Between Concentrations of Piperazine as Hexahydrate and Absorbance of Piperazine-Dye Complex

Concentration mcg/ml.	Sulfonphthalein Dye			
	BCG	BTB	BCP	BPB
	Absorbance ^a	Absorbance ^a	Absorbance ^a	Absorbance ^a
77.8	0.073	0.138	0.180	0.172
155.6	0.220	0.291	0.371	0.362
233.4	0.387	0.432	0.562	0.565
311.2	0.523	0.576	0.743	0.686
466.9	0.836	0.859	1.083	0.896
622.6	1.109	1.127	1.398	1.124
778.2	1.370	1.382	1.652	1.316
933.8	1.614	1.615	1.840	1.499
1089.4	1.806	1.803	1.956	1.653
1245.1	1.950	1.947	2.024	1.804
1400.8	2.048	2.044	2.058	1.962

^aMean value of four determination

Table 4. Effect of Dye Concentration on Absorbance of Piperazine-Dye Complex

Dye Concentration, ml x (4.00 x 10 ⁻⁴ M)	Mole Ratio Dye to Drug	Sulfonphthalein Dye							
		BCG		BTB		BCP		BPB	
		Abs. ^a	% CV	Abs. ^a	% CV	Abs. ^a	% CV	Abs. ^a	% CV
1.5	1 : 2	0.136	1.26	0.141	2.41	0.186	4.89	0.047	8.57
1.0	1 : 1	0.295	2.70	0.284	3.24	0.391	0.97	0.188	12.02
1.5	3 : 2	0.390	0.67	0.380	0.37	0.469	0.72	0.343	2.54
2.0	2 : 1	0.449	0.97	0.432	1.91	0.522	0.11	0.397	2.07
3.0	3 : 1	0.527	1.56	0.497	2.64	0.586	1.01	0.475	0.79
4.0	4 : 1	0.555	2.04	0.523	2.45	0.639	1.37	0.533	2.10
5.0	5 : 1	0.556	1.06	0.547	2.49	0.655	1.80	0.564	1.05
6.0	6 : 1	0.575	2.99	0.556	1.19	0.674	2.26	0.594	0.80

^aMean value of four determinations, Abs. = Absorbance.

Table 5. Effect of Time on Stability of Piperazine-Dye Complex

Time Minutes	Sulfonphthalein Dye							
	BCG		BTE		BCP		BPB	
	Abs. ^a	% CV	Abs. ^a	% CV	Abs. ^a	% CV	Abs. ^a	% CV
10	0.424	1.82	0.414	3.62	0.494	1.92	0.476	6.30
20	0.425	2.85	0.416	3.22	0.501	2.38	0.474	6.54
30	0.428	3.20	0.418	3.01	0.503	3.28	0.479	8.56
40	0.428	3.22	0.418	3.37	0.499	3.89	0.472	8.26
50	0.429	2.35	0.418	3.68	0.505	4.65	0.483	10.97
60	0.429	2.12	0.422	4.22	0.503	3.02	0.496	15.73
120	0.430	3.12	0.421	1.59	0.505	2.65	0.467	7.49
180	0.429	3.31	0.423	1.75	0.498	1.64	0.470	8.00
240	0.424	3.30	0.422	1.85	0.491	1.20	0.468	7.01
300	0.422	3.13	0.423	2.65	0.497	1.3	0.472	8.58
360	0.424	2.64	0.423	2.27	0.501	1.96	0.472	8.58
\bar{X}	0.427		0.420		0.500		0.475	
% CV	0.65		0.93		0.90		1.74	

^aMean value of four determinations, Abs. = Absorbance

Table 6. Effect of Temperature on Stability of Piperazine-Dye
Complex.

Temperature, °C	Sulfonphthalein Dye							
	BCG		BTB		BCP		BPB	
	Abs. ^a	% CV	Abs. ^a	% CV	Abs. ^a	% CV	Abs. ^a	% CV
25	0.412	1.46	0.422	1.71	0.503	0.76	0.478	1.95
40	0.409	2.59	0.422	2.13	0.502	0.34	0.458	3.84
50	0.410	1.64	0.418	1.84	0.503	0.30	0.469	1.53
60	0.407	1.52	0.406	1.53	0.499	0.36	0.440	5.25
70	0.403	0.97	0.385	0.39	0.480	2.96	0.367	4.01
\bar{X}	0.408		0.411		0.497		0.442	
% CV	0.84		3.83		1.98		10.05	

^aMean value of four determinations

Abs. = Absorbance.

Table 7. Comparative of Experimental Parameters on Four Sulfonphthalein

Dyes : BCG, BTB, BCP and BPB

Experimental Parameters	Sulfonphthalein Dye			
	BCG	BTB	BCP	BPB
1). Color of the Complex	yellow	yellow	yellow	yellow
2). Wavelength for maximum absorption (nm.)	420	420	410	412
3). Calibration curve				
-Linear concentration range (mcg/ml)	77.8-466.9	0-466.9	0-466.9	77.8-233.4
-Slope	0.874	0.926	1.164	0.778
-Reproducibility	poor	very good	poor	good

Table 7. (Continued) Comparative of Experimental Parameters of Four
Sulfonphthalein Dyes : BCG, BTB, BCP and BPB

Experimental Parameters	Sulfonphthalein Dyes			
	BCG	BTB	BCP	BPB
4). Dye concentration used with fixed concentration of piperazine. $6\text{H}_2\text{O}$ ml x $(4.00 \times 10^{-4} \text{M})$	3	3	4	4
5). Mole ratio (Dye to Drug)	2 : 1	2 : 1	2 : 1	2 : 1
6). Effect of time	None	Negligible	Negligible	Increase in period of 1 to 2 hours, then decrease
7). Effect of temperature	Stable to 50°C , then decrease	Stable to 40°C , then decrease	Stable to 50°C , then decrease	Decrease when increase temperature

Table 8. Per Cent Labelled Amount of Piperazine as Hexahydrate in
Piperazine Citrate Syrup USP XX.

Sample	Per Cent Labelled Amount of Piperazine as Hexahydrate	
	BTB Method	Official Method ^a .
1	106.01	106.66
2	105.81	106.97
3	106.11	106.30
4	105.69	106.89
5	106.30	106.99
\bar{x}	105.98	106.76
% CV	0.23	0.27

^a USP XX

Table 9. Percentage Recovery of Piperazine Citrate in
Piperazine Citrate Syrup USP XX

Sample No.	BTB Method			Official Method ^a		
	Piperazine Citrate B.P.			Piperazine Citrate B.P.		
	Added,mg	Found,mg	% Recovery	Added,mg	Found,mg	% Recovery
	- 100 mg. -					
1	100.5	102.0	101.49	101.0	101.9	100.89
2	102.2	104.1	101.86	103.0	104.1	101.07
3	101.1	103.7	102.57	100.1	102.2	102.10
4	101.3	103.2	101.88	101.3	102.6	101.28
5	101.2	103.3	102.08	100.6	102.2	101.59
\bar{X}			101.98			101.39
% CV			0.39			0.47

Table 9. (Continued) Percentage Recovery of Piperazine Citrate in
Piperazine Citrate Syrup USP XX

Sample No.	BTB Method			Official Method ^a		
	Piperazine Citrate B.P.			Piperazine Citrate B.P.		
	Added,mg.	Found, mg.	% Recovery	Added,mg.	Found,mg.	% Recovery
	- 125 mg. -					
1	128.4	126.5	98.52	127.5	127.7	100.16
2	125.6	124.8	99.36	126.7	128.0	101.03
3	126.6	125.8	99.37	127.7	128.9	100.94
4	126.1	124.9	99.05	127.9	128.4	100.39
5	126.8	125.1	98.66	126.7	127.9	100.95
\bar{X}			98.99			100.69
% CV			0.40			0.39

Table 9. (Continued) Percentage Recovery of Piperazine Citrate in Piperazine Citrate Syrup USP XX

Sample No.	BTB Method			Official Method ^a		
	Piperazine Citrate B.P.			Piperazine Citrate B.P.		
	Added,mg.	Found,mg.	% Recovery	Added,mg.	Found,mg.	% Recovery
	- 150 mg. -					
1	148.7	150.6	101.28	151.8	151.7	99.93
2	150.3	151.5	100.80	151.3	152.4	100.73
3	149.0	150.1	100.74	150.9	149.3	98.94
4	149.1	151.5	101.61	150.8	152.2	100.93
5	150.7	151.3	100.40	152.5	152.6	100.07
\bar{X}			100.97			100.12
% CV			0.47			0.78

^aUSP XX

Table 10. Various Commercial Pharmaceutical Dosage Forms of
Piperazine and Its Salts

Manufacturer	Product	Dosage form	Dose
1). L.P. Standard Laboratories	Piperin	Syrup	each 5 ml. contains 500 mg. of piperazine as hexahydrate
2). Milano Lab Ltd Part	Mila-worm	Syrup	each 5 ml. contains 750 mg. of piperazine as hexahydrate
3). K.L.C. Laboratories	K.L.C. worm syrup	Syrup	each 4 ml. contains 600 mg. of piperazine as hexahydrate
4). Bayer	Upixon	Syrup	each 4 ml. contains 600 mg. piperazine hydrate, neutralized with citric acid
5). ACDHON Co Ltd	Piperazine citrate elixir BPC 1973	Elixir	each 5 ml. contains 750 mg. of piperazine as hexahydrate
6). Rasm Panich Pharmacy	Lolo-brand elixir	Elixir	each 5 ml. contains 937 mg. of piperazine citrate

Table 10 (Continued) Various Commercial Pharmaceutical Dosage Forms of
Piperazine and Its Salts

Manufacturer	Product	Dosage form	Dose
7). T.C. Pharmaceutical, Ltd part	Piperazine citrate elixir	Elixir	each 100 ml. contains 18 gm. of piperazine citrate
8). Pharnasant Laboratories, Co, Ltd.	Piperazine citrate	Tablet	each tablet contains 500 mg. of piperazine as hexahy- drate
9). A.T. Pharmaceutical	Piperazine citrate tablet	Coated tablet	each tablet contains 335 mg. of piperazine citrate, anhydrous
10). R.P. Scherer PTY Ltd MELB	Pipercaps capsule	Capsule	each capsule contains 300 mg. of piperazine adipate

Table 11. Analysis of Piperazine and Its Salts in Commercial
Pharmaceutical Dosage Forms

Product	Dosage Form	Piperazine Salt	Labelled Content,mg.	Per cent Labelled Claimed ^a			
				BTB Method		Official Methods	
				%	% CV	%	%CV
A	Syrup	Piperazine as hexahydrate	500 mg. per 5 ml.	99.72	0.48	101.54	0.79 ^b
B	Syrup	Piperazine as hexahydrate	750 mg. per 5 ml.	108.07	0.69	106.94	0.07 ^c
C	Syrup	Piperazine as hexahydrate	600 mg. per 4 ml.	96.15	0.37	97.18	0.08 ^c
D	Syrup	Piperazine hydrate	600 mg. per 4 ml.	97.31	0.22	97.29	0.06 ^c
E	Elixir	Piperazine as hexahydrate	750 mg. per 5 ml.	92.55	0.88	92.98	0.08 ^c
F	Elixir	Piperazine citrate	937 mg. per 5 ml.	97.75	0.25	97.92	0.04 ^c
G	Elixir	Piperazine citrate	18 gm per 100 ml.	96.89	0.26	98.19	0.08 ^c

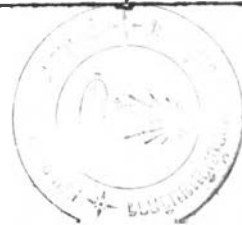


Table 11. (Continued) Analysis of Piperazine and Its Salts in Commercial
Pharmaceutical Dosage Forms

Product	Dosage Form	Piperazine Salt	Labelled Content, mg.	Per Cent Labelled Claimed ^a			
				BTB Method		Official Methods	
				%	% CV	%	% CV
H	Tablet	Piperazine citrate	500 mg. as piperazine · 6 H ₂ O per tablet	93.41	0.70	92.04	0.51 ^b
I	Coated tablet	Piperazine citrate, anhydrous	335 mg. per tablet	87.96	0.76	86.65	0.99 ^b
J	Capsule	Piperazine adipate	300 mg. per capsule	95.68	0.41	96.48	0.13 ^d

^aMean value of five determinations

^bUSP XX

^cBPC 1973

^dB.P.1980

Table 12. Linear Concentration Range of Piperazine as Hexahydrate
with Four Sulfonphthalein Dyes : BCG, ETB, BCP and BPB.

Sulfonphthalein Dye	Linear Concentration Range of Piperazine as Hexahydrate mcg/ml.	Slope of the Straight Line Portion
BCG	77.8 - 466.9	0.874
ETB	0 - 466.9	0.926
BCP	0 - 466.9	1.164
BPB	77.8 - 233.4	0.778

Table 13. Effect of Bromphenol Blue Concentration on Color of
Piperazine - Bromphenol Blue Comple.

Concentration of BPB, ml. x 4.00×10^{-4} M	Color of the Complex	Precipitate Formed
0.5	Purple	Present
1	Greenish blue	Present
1.5	Emerald green	Present
2	Yellowish green	None
3	Yellow	None
4	Yellow	None
5	Yellow	None
6	Greenish yellow	None

Table 14 Chemical Structure of Four Sulfonphthalein Dyes

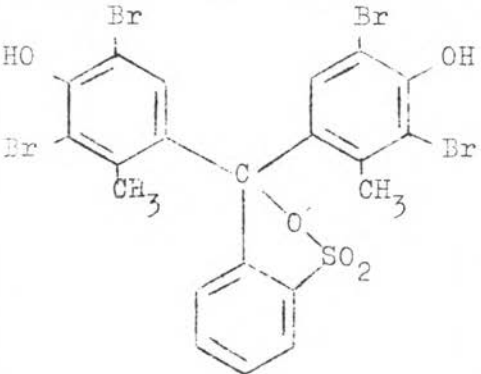
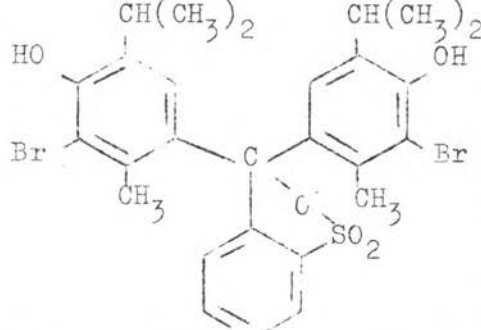
Name	Chemical Structure	Formula	Molecular Weight	Transition Range
Bromocresol green (BCG)		$C_{21}H_{14}Br_4O_5S$	698.05	3.8 - 5.4 yellow - blue green
Bromthymol blue (BTB)		$C_{27}H_{28}Br_2O_5S$	624.39	6.0 - 7.6 yellow - blue

Table 14. (Continued) Chemical Structure of Four Sulfonphthalein Dyes

Name	Chemical Structure	Formula	Molecular Weight	Transition Range
Bromocresol purple (BCP)		$C_{21} H_{16} Br_2 O_5 S$	540.24	5.2 - 6.8 yellow - purple
Bromphenol blue (BPB)		$C_{19} H_{10} Br_4 O_5 S$	670.02	3.0 - 4.6 yellow - purple

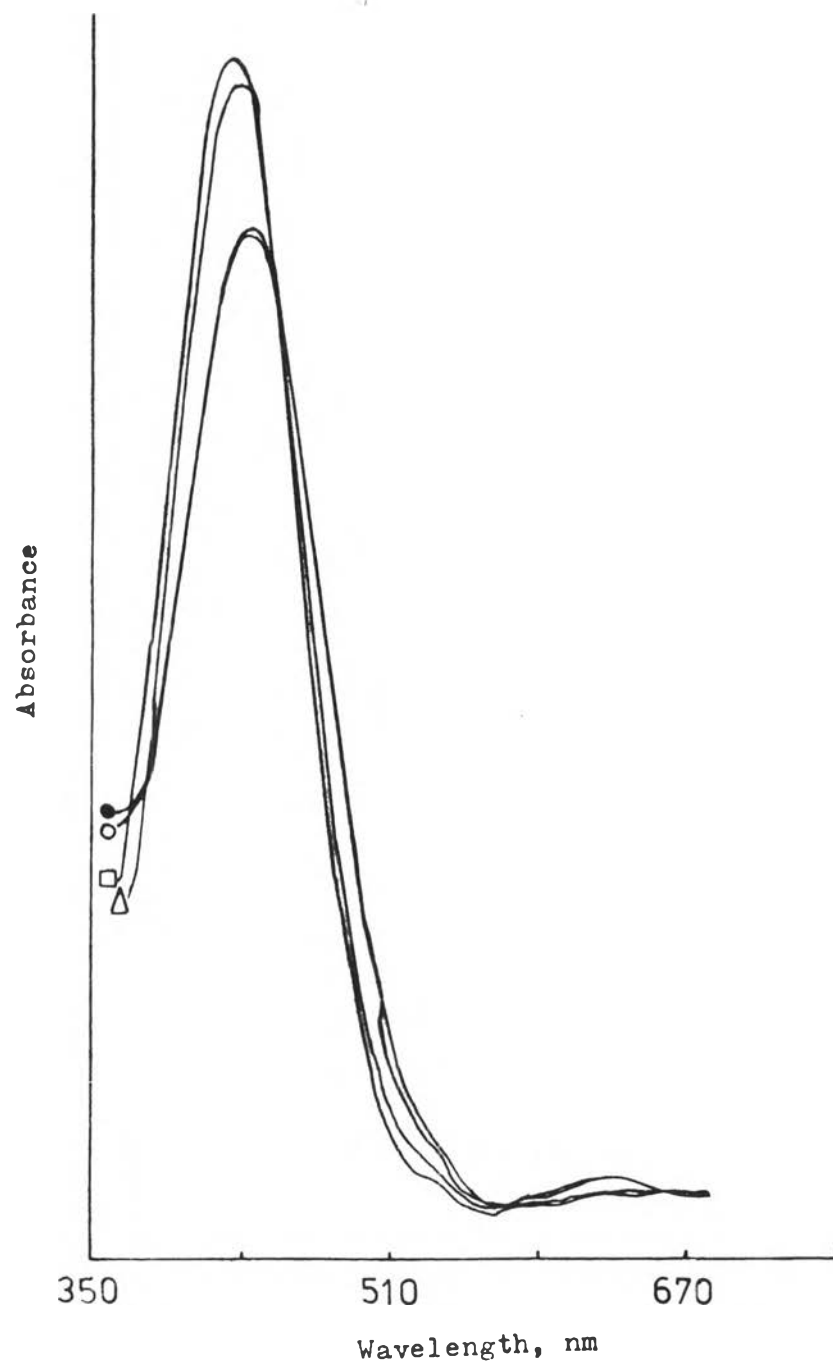


Figure 1. Absorption spectra of piperazine-dye complex.

Key : ○, BCG; ●, BTB; □, BCP; △, BPB.

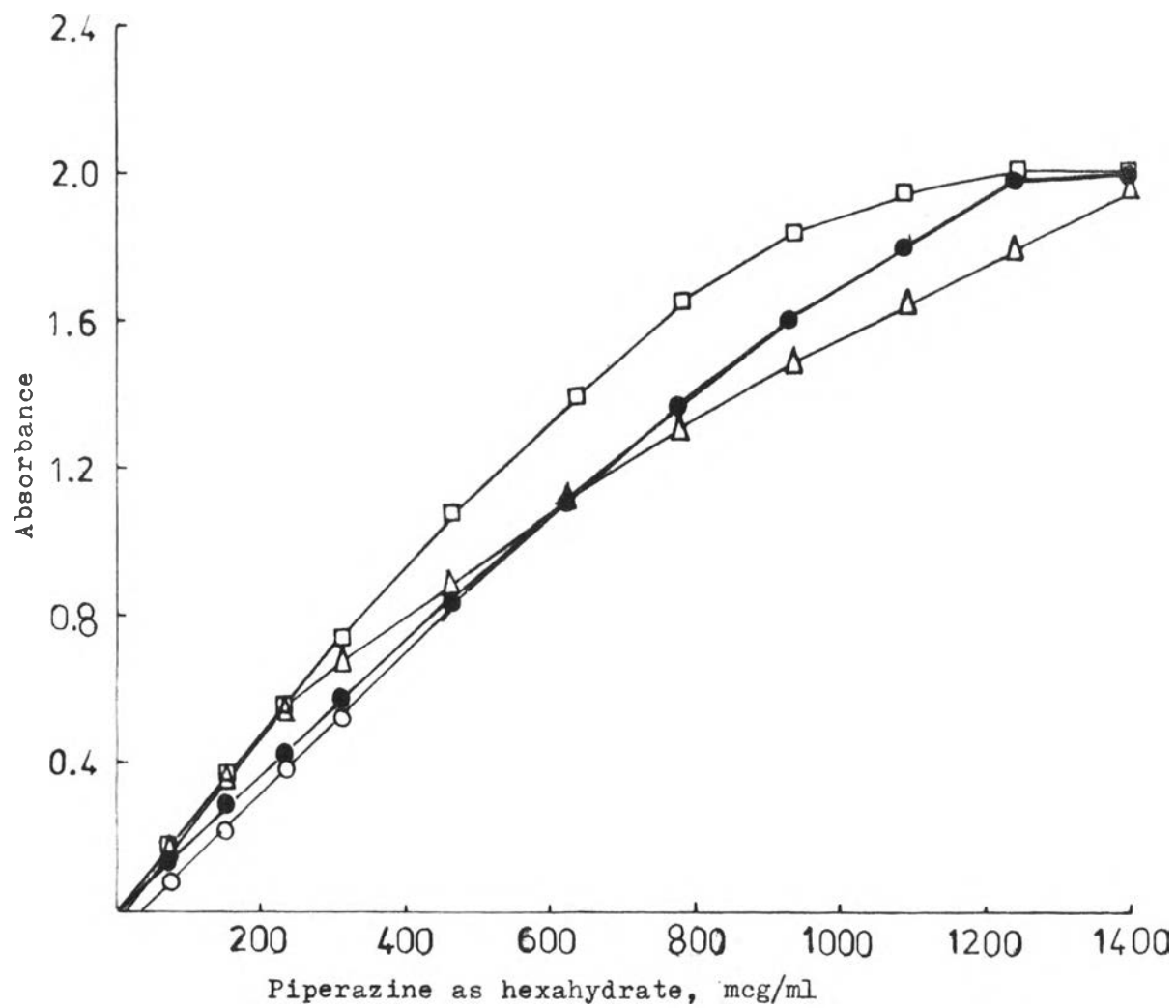


Figure 2. Calibration curve of standard piperazine as hexahydrate. Key : ○, BCG; ●, BTB; □ BCP, △, BPB.

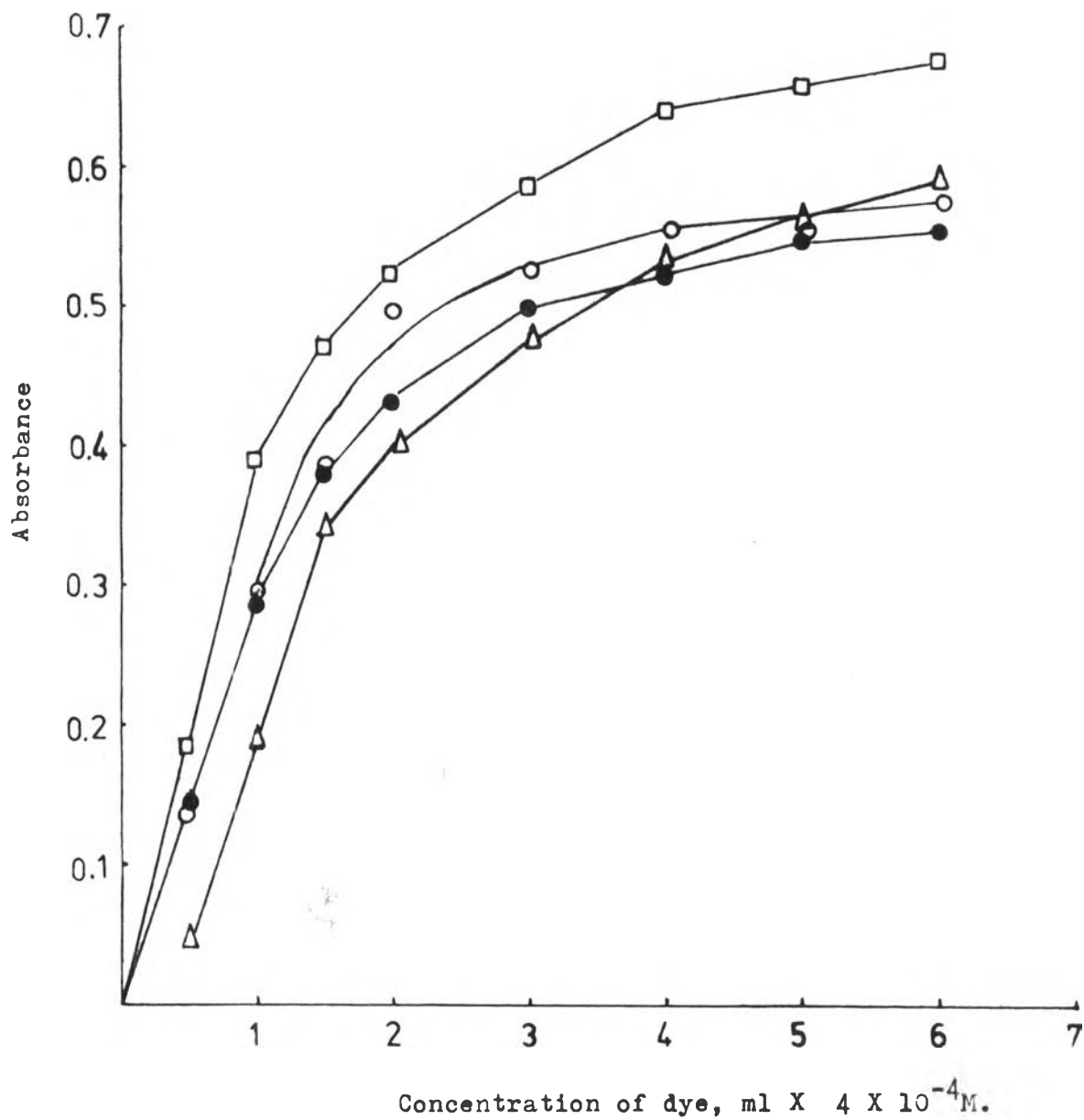


Figure 3. Effect of dye concentration on absorbance of piperazine-dye complex. Key : ○, BCG; ●, BTB; □, BCP; △, BPB.

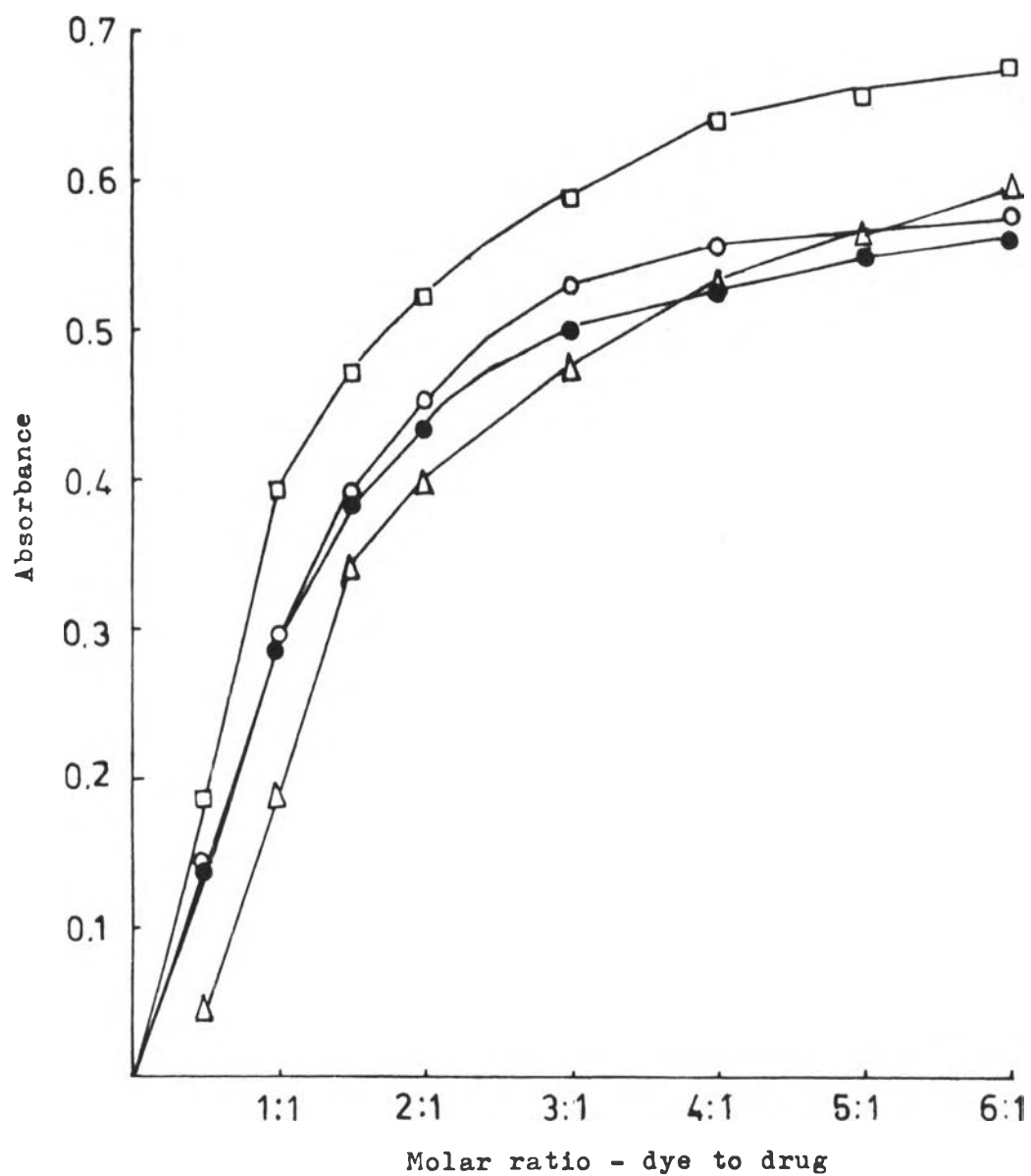


Figure 4. Mole ratio curve (vary molarity of dye but fix molarity of drug). Key : ○, BCG; ●, BTB, □, BCP; △, BPB.

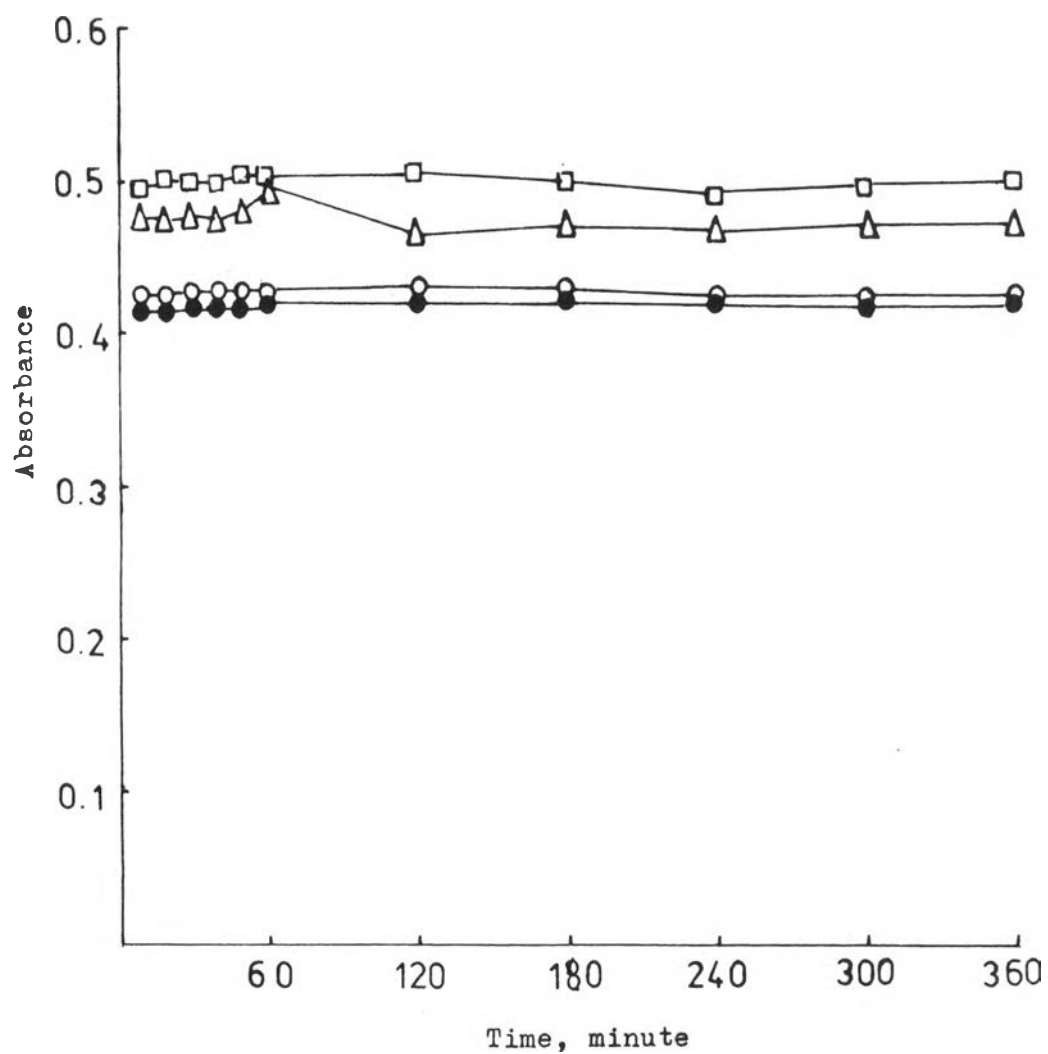


Figure 5. Effect of time on stability of piperazine-dye complex. Key : ○, BCG; ●, BTB; □, BCP; △, BPB.

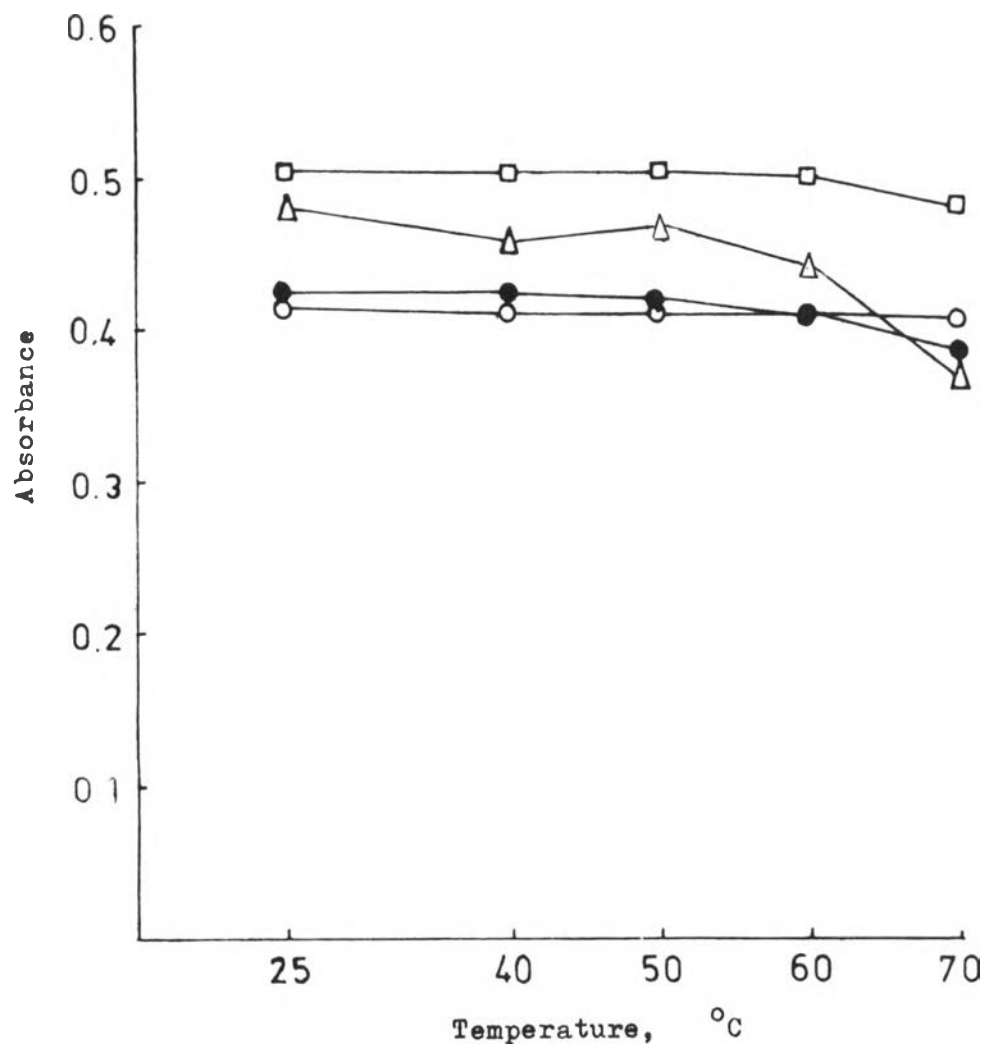


Figure 6. Effect of temperature on stability of piperazine-dye complex. Key : ○, ECG; ●, BTB; □, BCP; △, BPB.

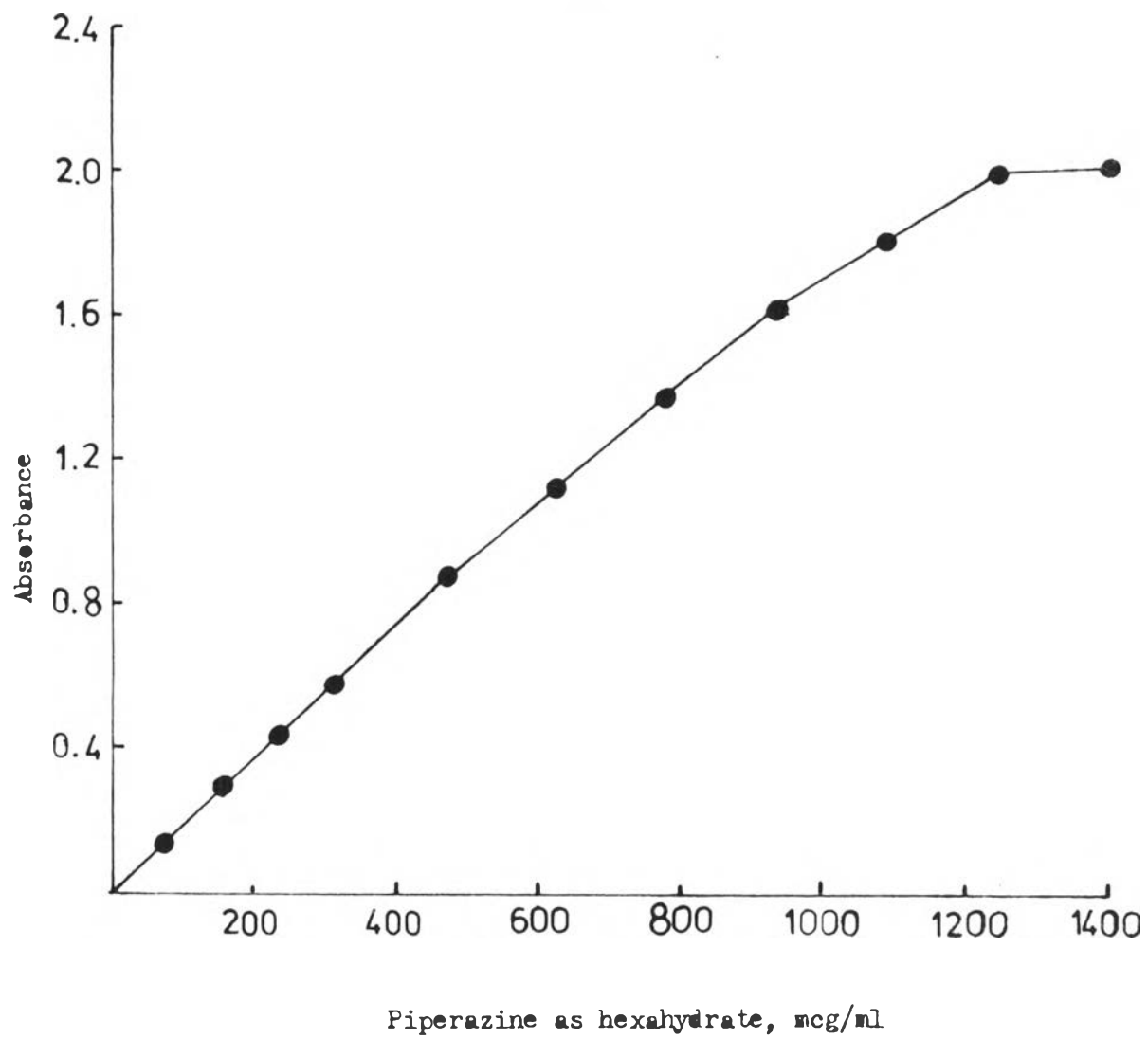


Figure 7. Calibration curve of standard piperazine as hexahydrate with bromthymol blue.

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