

## CHAPTER IV

### CONCLUSION

The proposed method (HPLC method) for paracetamol assay required less time than the USP method. The USP method required more than 15 minutes (for reaction absorbance measurement), while the proposed method took less than 10 minutes. The USP method isn't suitable for stability testing of liquid paracetamol preparation although p-aminophenol doesn't interfere. The proposed method can separate degradation impurity especially p-aminophenol. Consequently, the proposed method allows a rapid and specific testing to indicate stability, and quantity of paracetamol in tablet, suspension, syrup, and elixir.

The degradation rate of commercial paracetamol products in this study were between  $7.87 \times 10^{-3}$ - $8.86 \times 10^{-3}$  percent/day for suspensions and  $0.82 \times 10^{-4}$ - $2.28 \times 10^{-4}$  day<sup>-1</sup> for syrups and elixirs at 30°C (average temperature in Thailand was 31°C (25°-37°C)). Activation energy of the studied preparation were 11-17 kcal/mole.

At temperature of 30°C, predicted shelf-lives of liquid paracetamol preparations are between 1.3-3.5 years. It is indicated that shelf-life of available paracetamol preparations are highly varied.

Table 3 Typical Calibration Data for Paracetamol Solution by USP Method.

conc. Paracetamol <sup>a</sup> mcg/ml	Absorbance <sup>b</sup> at 430 nm	% CV
50	0.260 ± 0.001	0.34
75	0.390 ± 0.002	0.56
100	0.520 ± 0.003	0.55
125	0.650 ± 0.003	0.53
150	0.793 ± 0.006	0.70
Slope = 0.005 Intercept = -0.008 Correlation coefficient (R) = 1.0		

<sup>a</sup>From stock solution contained paracetamol 125 mg qs. to 100 ml.

<sup>b</sup>mean value ± S.D. of 5 experiments.



Table 4 Comparative Analysis of Preparation Containing Paracetamol by USP method.

Paracetamol Add, mg/ml	Paracetamol in refrigerated syrup <sup>a</sup>		Paracetamol in incubated syrup <sup>b</sup>	
	Paracetamol found (mg/ml)	% Recovery	Paracetamol found (mg/ml)	% Recovery
24.00	23.81	99.21	24.95	103.94
24.00	23.86	99.42	25.05	104.42
24.00	23.79	99.12	25.00	104.16
24.00	23.81	99.21	25.00	104.16
24.00	23.83	99.29	25.02	104.25
X		99.25		104.19
S.D.		±0.11		±0.17
% CV		0.11		0.17

<sup>a</sup>refrigerated syrup = USP syrup, which was kept in refrigerator for 4 months and cool to room temperature, used for preparing paracetamol preparation.

<sup>b</sup>incubated syrup = USP syrup; which was incubated in 60°C incubator for 4 months and cool to room temperature, used for preparing paracetamol preparation.

Table 5 Percent Amount of Remaining Paracetamol in Paracetamol Suspension #1 by USP Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
52	99.65	18	99.98	22	99.79	15	99.00	8	100.05
108	99.50	37	99.55	53	99.22	25	96.59	14	102.55
172	99.01	60	99.01	79	99.98	46	101.84	28	97.62
256	98.60	102	101.15	110	94.29	52	96.76	49	98.24
310	98.36	159	97.62	140	92.48	90	91.11	56	98.29

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 6 Percent Amount of Remaining Paracetamol in Paracetamol Suspension #2 by USP Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
52	99.50	18	99.34	22	98.94	15	98.56	8	98.08
108	99.16	37	99.90	53	98.00	25	98.56	14	97.00
172	98.80	60	99.38	79	101.24	46	99.94	28	102.17
256	98.00	102	99.09	110	94.17	52	98.59	49	103.63
310	98.00	159	96.79	140	91.79	90	93.17	56	94.40

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 7 Percent Amount of Remaining Paracetamol in Paracetamol Syrup #1 by USP Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
52	99.20	18	100.05	22	98.51	15	99.00	8	98.58
108	98.86	37	99.35	53	100.09	25	97.25	14	96.56
172	98.79	60	99.56	79	101.24	46	99.02	28	101.63
256	98.00	102	99.19	110	96.70	52	100.94	49	101.63
310	97.68	159	96.51	140	94.41	90	95.44	56	101.79

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 8 Percent Amount of Remaining Paracetamol in Paracetamol Syrup #2 by USP Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
52	99.85	18	99.18	22	99.14	15	98.38	8	98.12
108	99.32	37	99.40	53	101.38	25	99.45	14	100.53
172	98.90	60	100.34	79	101.05	46	100.02	28	100.04
256	98.06	102	104.77	110	98.50	52	99.93	49	101.65
310	98.00	159	98.52	140	95.32	90	93.37	56	95.74

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 9 Percent Amount of Remaining Paracetamol in Paracetamol  
Elixir #1 by USP Method

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
52	99.51	18	99.60	22	98.33	15	98.00	8	97.57
108	99.45	37	100.35	53	97.48	25	95.09	14	100.17
172	99.00	60	99.27	79	104.14	46	95.99	28	99.67
256	98.48	102	98.41	110	93.26	52	94.88	49	95.11
310	98.20	159	96.36	140	91.01	90	91.35	56	93.90

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature



Table 10 Percent Amount of Remaining Paracetamol in Paracetamol  
Elixir #2 by USP Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
52	97.75	18	100.00	22	97.12	15	98.20	8	98.65
108	97.00	37	98.92	53	96.56	25	95.06	14	101.80
172	96.05	60	97.90	79	97.85	46	94.21	28	95.45
256	94.86	102	96.01	110	90.00	52	92.21	49	93.00
310	94.10	159	93.42	140	84.72	90	86.81	56	90.05

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 11 Typical Calibration Data for Paracetamol Solution by HPLC Method.

Final concentration mcg/ml	D/IS Ratio <sup>a</sup> (mean±S.D.)	% CV
20	0.519 ± 0.006	1.22
30	0.774 ± 0.006	0.74
40	1.008 ± 0.012	1.14
50	1.276 ± 0.010	0.78
60	1.521 ± 0.013	0.83
<p style="text-align: center;">Slope = 0.025 Intercept = 0.017 Correlation coefficient = 1.0</p>		

<sup>a</sup> Data represent three replicate injections of standard solutions ; D/IS is the ratio of the peak height of paracetamol at some concentration divided by the peak height of sulpyrin at a concentration of 3.4 mg/ml.



Table 12 Percent Amount of Remaining Paracetamol in Paracetamol Suspension #1 by HPLC Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
45	99.75	35	99.30	21	99.01	20	97.78	13	97.78
105	99.60	66	98.92	47	97.67	41	96.01	29	95.85
170	99.00	113	98.01	74	96.02	70	93.33	50	93.33
240	98.69	168	97.10	115	93.21	114	90.11	70	90.11
300	98.50	224	96.21	155	91.01	133	88.10	98	85.60

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 13 Percent Amount<sup>a</sup> of Remaining Paracetamol in Paracetamol  
Suspension #2 by HPLC Method

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
45	99.60	35	99.20	21	98.32	20	98.01	13	97.78
105	99.18	66	98.39	47	96.56	41	96.11	29	95.42
170	98.86	113	97.68	74	95.56	70	93.50	50	92.22
240	98.72	168	96.56	115	93.33	114	90.01	70	89.45
300	98.00	224	95.75	155	91.11	133	88.21	98	86.01

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 14 Percent Amount of Remaining Paracetamol in Paracetamol Syrup #1 by HPLC Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
45	99.30	35	99.30	21	99.00	20	98.87	13	98.50
105	98.87	66	98.65	47	97.87	41	97.78	29	96.56
170	98.50	113	97.86	74	96.87	70	95.86	50	94.67
240	98.00	168	97.00	115	95.56	114	93.11	70	92.85
300	97.75	224	96.21	155	94.00	133	92.21	92	91.01

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 15 Percent Amount of Remaining Paracetamol in Paracetamol Syrup #2 by HPLC Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
45	99.70	35	99.50	21	99.01	20	98.75	13	99.01
105	99.61	66	98.97	47	98.12	41	97.78	29	97.78
170	98.90	113	98.05	74	96.95	70	95.96	50	95.74
240	98.50	168	97.21	115	95.45	114	94.21	70	93.62
300	98.00	224	96.28	155	94.31	133	93.11	98	91.91

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 16 Percent Amount<sup>a</sup> of Remaining Paracetamol in Paracetamol Elixir #1 by HPLC Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
45	99.80	35	99.20	21	98.25	20	98.08	13	97.92
105	99.25	66	98.54	47	96.41	41	95.11	29	94.01
170	98.90	113	97.62	74	94.87	70	92.93	50	91.00
240	98.54	168	96.76	115	92.50	114	88.43	70	87.54
300	98.40	224	95.78	155	90.08	133	86.78	98	83.46

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature

Table 17 Percent Amount of Remaining Paracetamol in Paracetamol  
Elixir #2 by HPLC Method.

Percent amount <sup>a</sup> of paracetamol after incubation									
31°C <sup>b</sup>		40°±0.5°C		55°±0.5°C		60°±0.5°C		70°±0.5°C	
Days	Percent	Days	Percent	Days	Percent	Days	Percent	Days	Percent
0	100.00	0	100.00	0	100.00	0	100.00	0	100.00
45	97.84	35	99.01	21	95.90	20	93.75	13	95.00
105	97.01	66	97.83	47	91.64	41	98.58	29	88.70
170	96.00	113	95.03	74	87.40	70	83.33	50	81.91
240	95.00	168	92.00	115	82.20	114	75.00	70	74.80
300	94.22	224	89.88	155	77.20	133	70.83	98	65.74

<sup>a</sup>mean value of 2 experiments

<sup>b</sup>average room temperature





Table 18 Specific Rate Constant, K, for Paracetamol in  
Paracetamol Suspension #1 at Different Temperature<sup>a</sup>.

Temperature (°C)	K (Percent/day)	R*
70	$1.44 \times 10^{-1} \pm 0.12 \times 10^{-1}$	0.998
60	$0.87 \times 10^{-1} \pm 0.06 \times 10^{-1}$	0.998
55	$0.59 \times 10^{-1} \pm 0.4 \times 10^{-1}$	0.998
40	$0.17 \times 10^{-1} \pm 0.01 \times 10^{-1}$	0.999

<sup>a</sup>Determination by HPLC method.

R\* = Correlation coefficient

Table 19 Specific Rate Constant, K, for Paracetamol in  
Paracetamol Suspension #2 at Different Temperature<sup>a</sup>.

Temperature (°C)	K (Percent/day)	R*
70	$1.43 \times 10^{-1} \pm 0.10 \times 10^{-1}$	0.998
60	$0.87 \times 10^{-1} \pm 0.04 \times 10^{-1}$	0.997
55	$0.55 \times 10^{-1} \pm 0.07 \times 10^{-1}$	0.996
40	$0.19 \times 10^{-1} \pm 0.02 \times 10^{-1}$	0.996

<sup>a</sup>Determination by HPLC method.

R\* = Correlation coefficient

Table 20 Specific Rate Constant, K, for Paracetamol in  
Paracetamol Syrup #1 at Different Temperature<sup>a</sup>.

Temperature (°C)	K (day <sup>-1</sup> )	R*
70	$1.01 \times 10^{-3} \pm 0.08$	0.998
60	$0.62 \times 10^{-3} \pm 0.03$	0.999
55	$0.39 \times 10^{-3} \pm 0.03$	0.998
40	$0.17 \times 10^{-3} \pm 0.01$	0.998

<sup>a</sup>Determination by HPLC method.

R\* = Correlation coefficient

Table 21 Specific Rate Constant, K, for Paracetamol in  
Paracetamol Syrup #2 at Different Temperature<sup>a</sup>.

Temperature (°C)	K (day <sup>-1</sup> )	R*
70	$8.9 \times 10^{-4} \pm 0.9 \times 10^{-4}$	0.997
60	$5.2 \times 10^{-4} \pm 0.4 \times 10^{-4}$	0.998
55	$3.8 \times 10^{-4} \pm 0.3 \times 10^{-4}$	0.998
40	$1.7 \times 10^{-4} \pm 0.1 \times 10^{-4}$	0.999

<sup>a</sup>Determination by HPLC method.

R\* = Correlation coefficient

Table 22 Specific Rate Constant, K, for Paracetamol in  
Paracetamol Elixir #1 at Different Temperature<sup>a</sup>.

Temperature (°C)	K (day <sup>-1</sup> )	R*
70	$1.85 \times 10^{-3} \pm 0.14 \times 10^{-3}$	0.998
60	$1.06 \times 10^{-3} \pm 0.08 \times 10^{-3}$	0.998
55	$0.66 \times 10^{-3} \pm 0.04 \times 10^{-3}$	0.999
40	$0.19 \times 10^{-3} \pm 0.01 \times 10^{-3}$	0.998

<sup>a</sup>Determination by HPLC method.

R\* = Correlation coefficient

Table 23 Specific Rate Constant, K, for Paracetamol in  
Paracetamol Elixir #2 at Different Temperature<sup>a</sup>.

Temperature (°C)	K (day <sup>-1</sup> )	R*
70	$4.25 \times 10^{-3} \pm 0.21 \times 10^{-3}$	0.999
60	$2.51 \times 10^{-3} \pm 0.01 \times 10^{-3}$	0.998
55	$1.93 \times 10^{-3} \pm 0.10 \times 10^{-3}$	1.000
40	$0.50 \times 10^{-3} \pm 0.07 \times 10^{-3}$	0.995

<sup>a</sup>Determination by HPLC method

R\* = Correlation coefficient

Table 24 Activation Energy of Paracetamol in Commercial Liquid Paracetamol Preparations.

Product	$E_a \pm t_{1-\frac{\alpha}{2}} S_a$	R*
Paracetamol Suspension #1	15.5 $\pm$ 2.3	0.995
Paracetamol Suspension #2	14.6 $\pm$ 1.7	0.997
Paracetamol Syrup #1	12.8 $\pm$ 1.7	0.996
Paracetamol Syrup #2	11.7 $\pm$ 0.8	0.999
Paracetamol Elixir #1	16.4 $\pm$ 1.9	0.997
Paracetamol Elixir #2	15.4 $\pm$ 1.8	0.997

R\* = Correlation coefficient



Table 25 Arrhenius Relation of Paracetamol in Commercial Liquid  
Paracetamol Preparations.

Product	Predicted rate at 35°C		Predicted rate at 30°C	
	$K_{av}$	$(K \pm t_{1-\frac{\alpha}{2}} \frac{S_y}{2})$	$K_{av}$	$(K \pm t_{1-\frac{\alpha}{2}} \frac{S_y}{2})$
Su1	$1.19 \times 10^{-2}$	$0.70 \times 10^{-2} - 2.03 \times 10^{-2}$	$7.87 \times 10^{-3}$	$4.13 \times 10^{-3} - 1.50 \times 10^{-2}$
Su2	$1.32 \times 10^{-2}$	$0.88 \times 10^{-2} - 1.96 \times 10^{-2}$	$8.86 \times 10^{-3}$	$5.48 \times 10^{-3} - 1.43 \times 10^{-2}$
Sy1	$1.19 \times 10^{-4}$	$0.78 \times 10^{-4} - 1.81 \times 10^{-4}$	$0.87 \times 10^{-4}$	$0.51 \times 10^{-4} - 1.40 \times 10^{-4}$
Sy2	$1.23 \times 10^{-4}$	$1.03 \times 10^{-4} - 1.46 \times 10^{-4}$	$0.89 \times 10^{-4}$	$0.72 \times 10^{-4} - 1.10 \times 10^{-4}$
El1	$1.28 \times 10^{-4}$	$0.83 \times 10^{-4} - 1.97 \times 10^{-4}$	$0.82 \times 10^{-4}$	$0.49 \times 10^{-4} - 1.38 \times 10^{-4}$
El2	$3.47 \times 10^{-4}$	$2.31 \times 10^{-4} - 5.20 \times 10^{-4}$	$2.28 \times 10^{-4}$	$1.40 \times 10^{-4} - 3.74 \times 10^{-4}$

<sup>a</sup>the 95% confidence limit of prediction.



Table 25 Arrhenius Relation of Paracetamol in Commercial Liquid  
Paracetamol Preparation (Continue).

Product	Predicted rate at 25°C		Predicted rate at 20°C	
	$K_{av}$	$(K+t_1-\frac{a}{2}S_y)$	$K_{av}$	$(K+t_1-\frac{a}{2}S_y)$
Su1	$5.11 \times 10^{-3}$	$2.38 \times 10^{-3} - 1.10 \times 10^{-2}$	$3.27 \times 10^{-3}$	$1.34 \times 10^{-3} - 1.99 \times 10^{-3}$
Su2	$5.90 \times 10^{-3}$	$3.33 \times 10^{-3} - 1.04 \times 10^{-2}$	$3.87 \times 10^{-3}$	$1.99 \times 10^{-3} - 7.53 \times 10^{-3}$
Sy1	$0.59 \times 10^{-4}$	$0.32 \times 10^{-4} - 1.08 \times 10^{-4}$	$4.07 \times 10^{-5}$	$2.22 \times 10^{-5} - 8.22 \times 10^{-5}$
Sy2	$6.44 \times 10^{-5}$	$5.02 \times 10^{-5} - 8.25 \times 10^{-5}$	$4.59 \times 10^{-5}$	$3.43 \times 10^{-5} - 6.13 \times 10^{-5}$
El1	$5.19 \times 10^{-5}$	$2.79 \times 10^{-5} - 9.64 \times 10^{-5}$	$3.23 \times 10^{-5}$	$1.56 \times 10^{-5} - 6.66 \times 10^{-5}$
El2	$1.48 \times 10^{-4}$	$0.83 \times 10^{-4} - 2.66 \times 10^{-4}$	$9.52 \times 10^{-5}$	$4.81 \times 10^{-5} - 1.88 \times 10^{-4}$

<sup>a</sup>the 95% confidence limit of prediction.

Su1 = Suspension #1

Su2 = Suspension #2

Sy1 = Syrup #1

Sy2 = Syrup #2

El1 = Elixir #1

El2 = Elixir #2

Table 26 Shelf-lives ( $t_{90}$ ) of Paracetamol in Commercial Liquid Paracetamol Preparations.

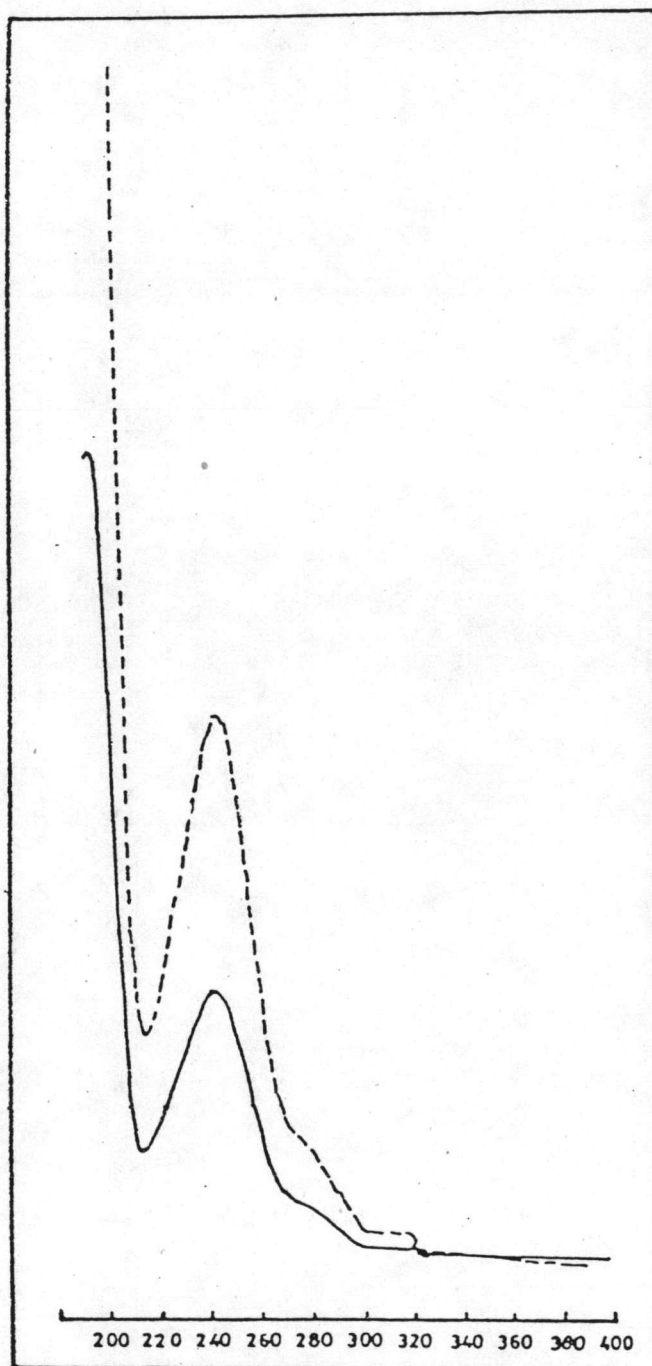
Product	Predicted Shelf-life <sup>a</sup> (years)			
	35°C $t_{90}$ (av) <sup>b</sup>	30°C $t_{90}$ (av) <sup>b</sup>	25°C $t_{90}$ (av) <sup>b</sup>	20°C $t_{90}$ (av) <sup>b</sup>
Suspension #1	2.3	3.5	5.4	8.4
Suspension #2	2.1	3.1	4.6	7.1
Syrup #1	2.4	3.4	4.9	7.1
Syrup #2	2.3	3.2	4.5	6.3
Elixir #1	2.2	3.5	5.6	8.9
Elixir #2	0.8	1.3	2.0	3.0

<sup>a</sup>the 95% confidence limit of predicted shelf-life ( $t_{90} \pm t_{1-\frac{\alpha}{2}} S_p$ )  
calculate from equation in appendix part.

<sup>b</sup> $t_{90}$  average.

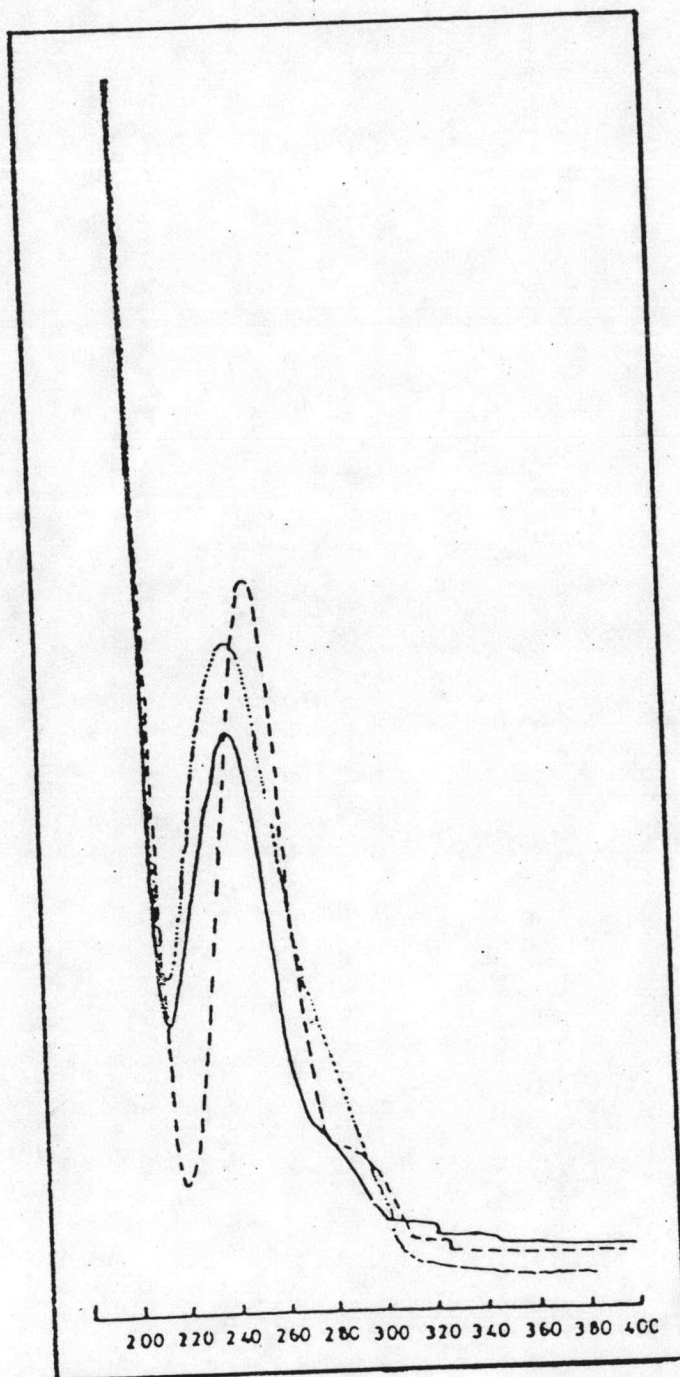
Table 27 Percent Labelled Amount of Paracetamol in Commercial Paracetamol Tablets Using HPLC Method.

Sample	Percent Labelled Amount of Paracetamol	
	Product A	Product B
1	100.65	99.03
2	100.65	98.87
3	100.21	99.09
4	101.09	98.64
5	99.83	99.35
X	100.49	99.00
SD	0.48	0.26
%CV	0.48	0.27



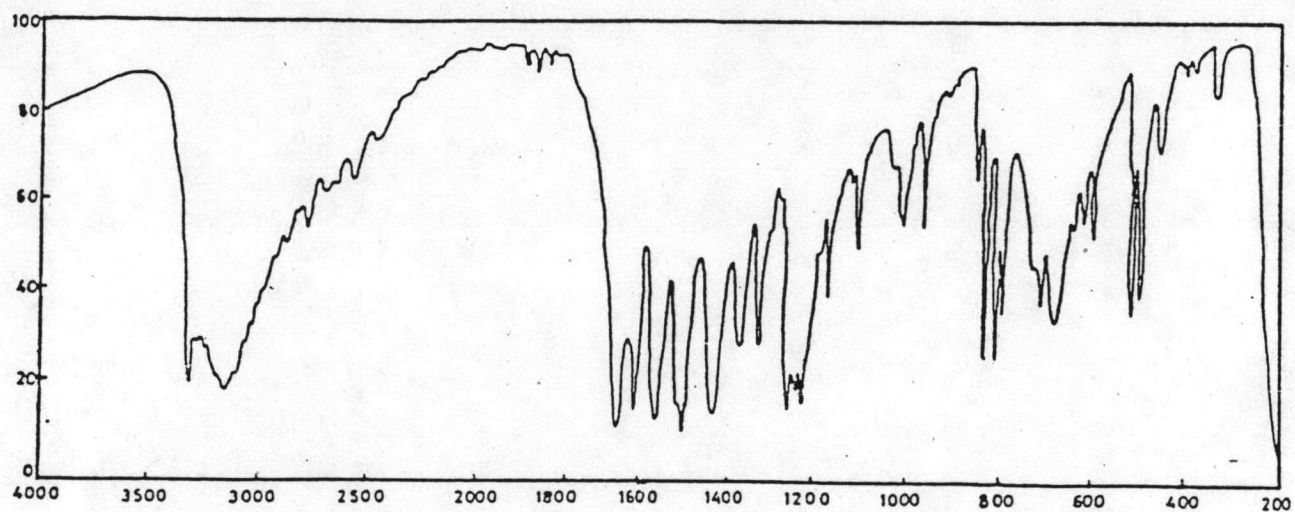
Wavelength (nm)

Figure 1 Ultraviolet Spectrum of Paracetamol in Neutral Water (-)  
and in Water + 5 Drops of 50% HCl (--).



Wavelength (nm)

Figure 2 Ultraviolet Spectrum of Paracetamol in Neutral Methanol (-), in Methanol + 5 Drops of 50% HCl (...), and in Methanol + Sodium Methoxide (---).



Wavelength (nm)

Figure 3 Infrared Spectrum of Paracetamol, KBr Disc.

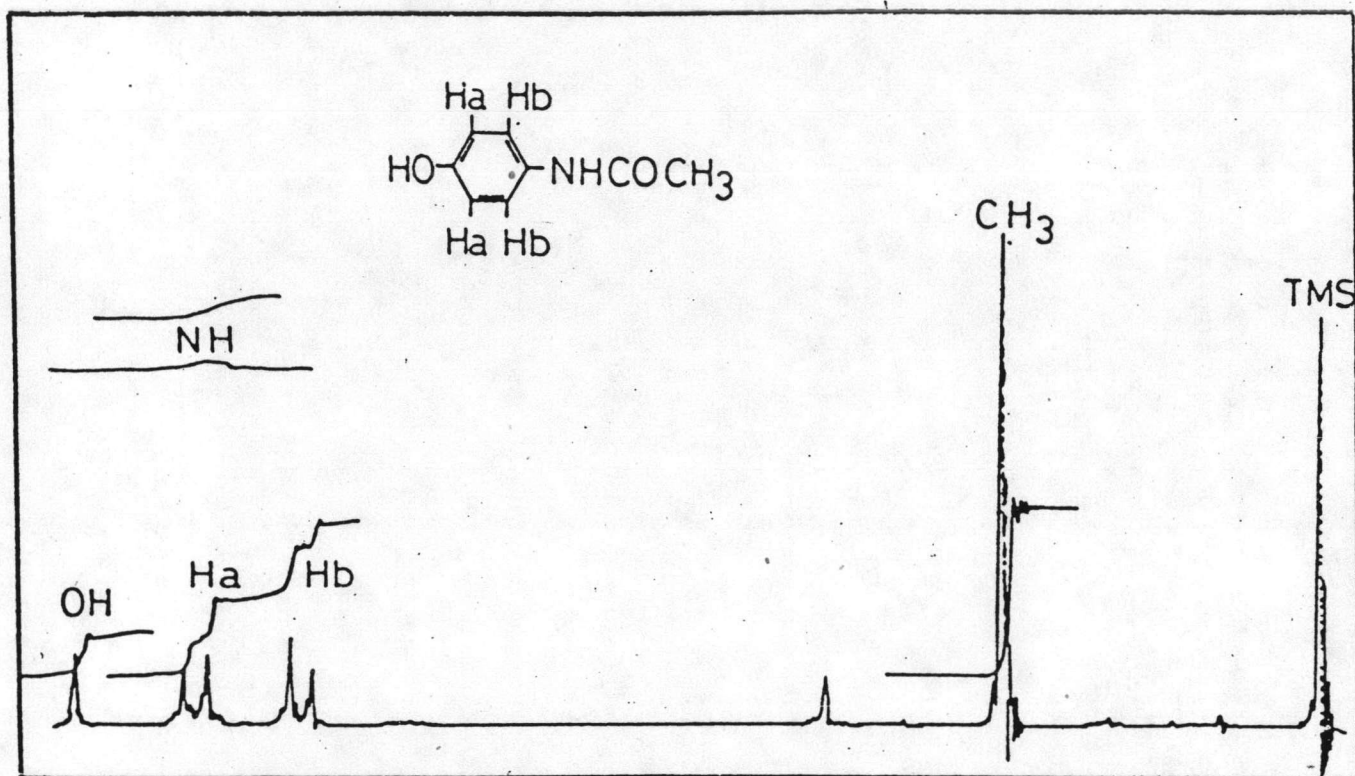


Figure 4  $^1\text{H}$  NMR Spectrum of Paracetamol in Acetone- $d_6$  with TMS as Internal Reference.

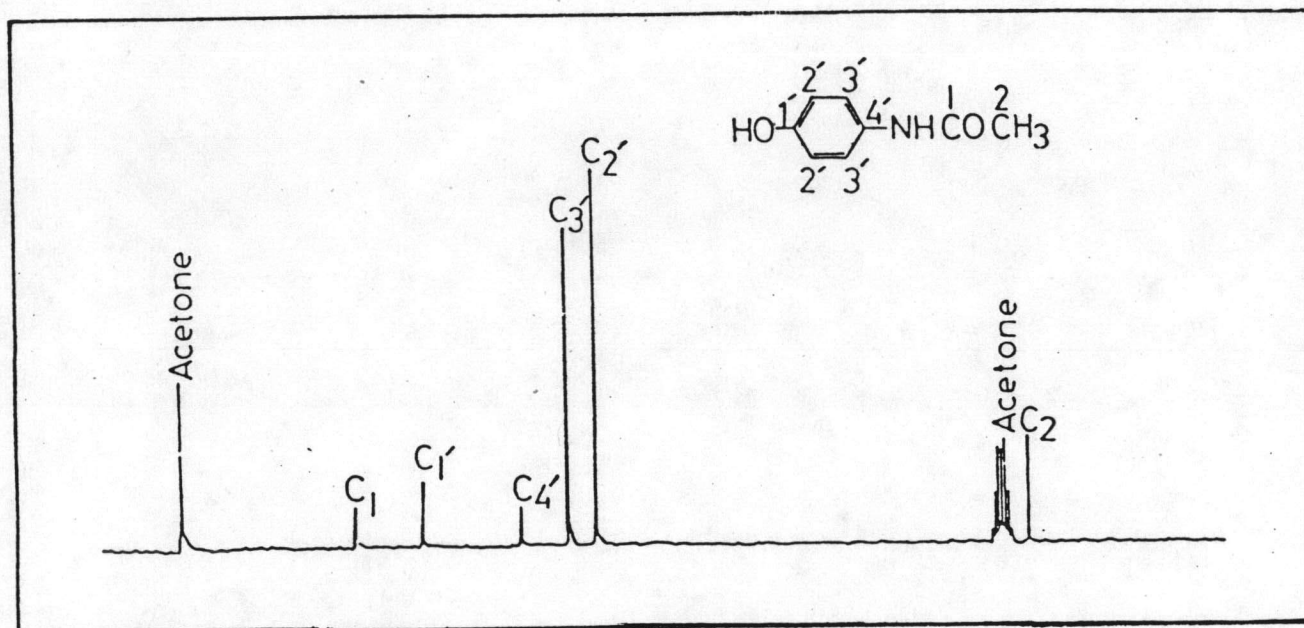


Figure 5 Noise-decoupled  $^{13}\text{C}$  NMR Spectrum of Paracetamol  
in Acetone- $d_6$  with TMS as Internal Reference.



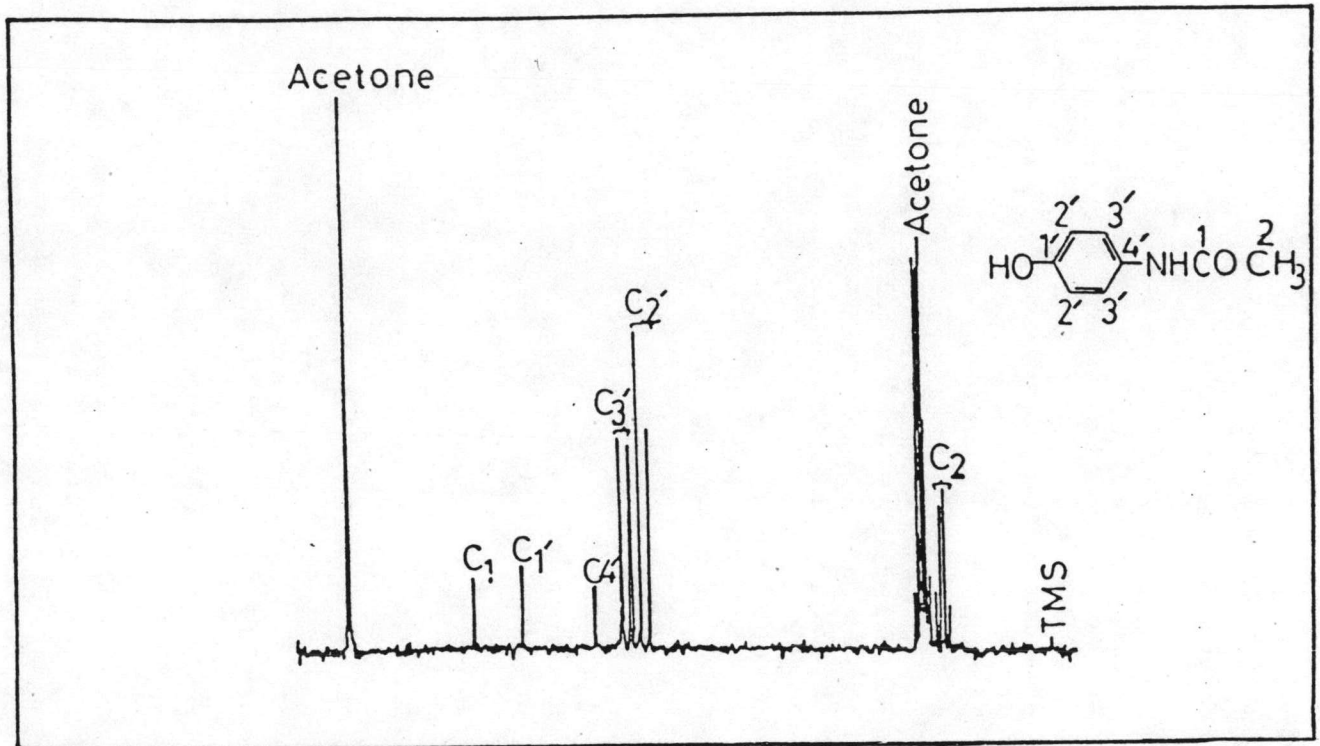


Figure 6 Off-Resonance  $^{13}\text{C}$  NMR Spectrum of Paracetamol in Acetone- $D_6$  with TMS as Internal Reference.

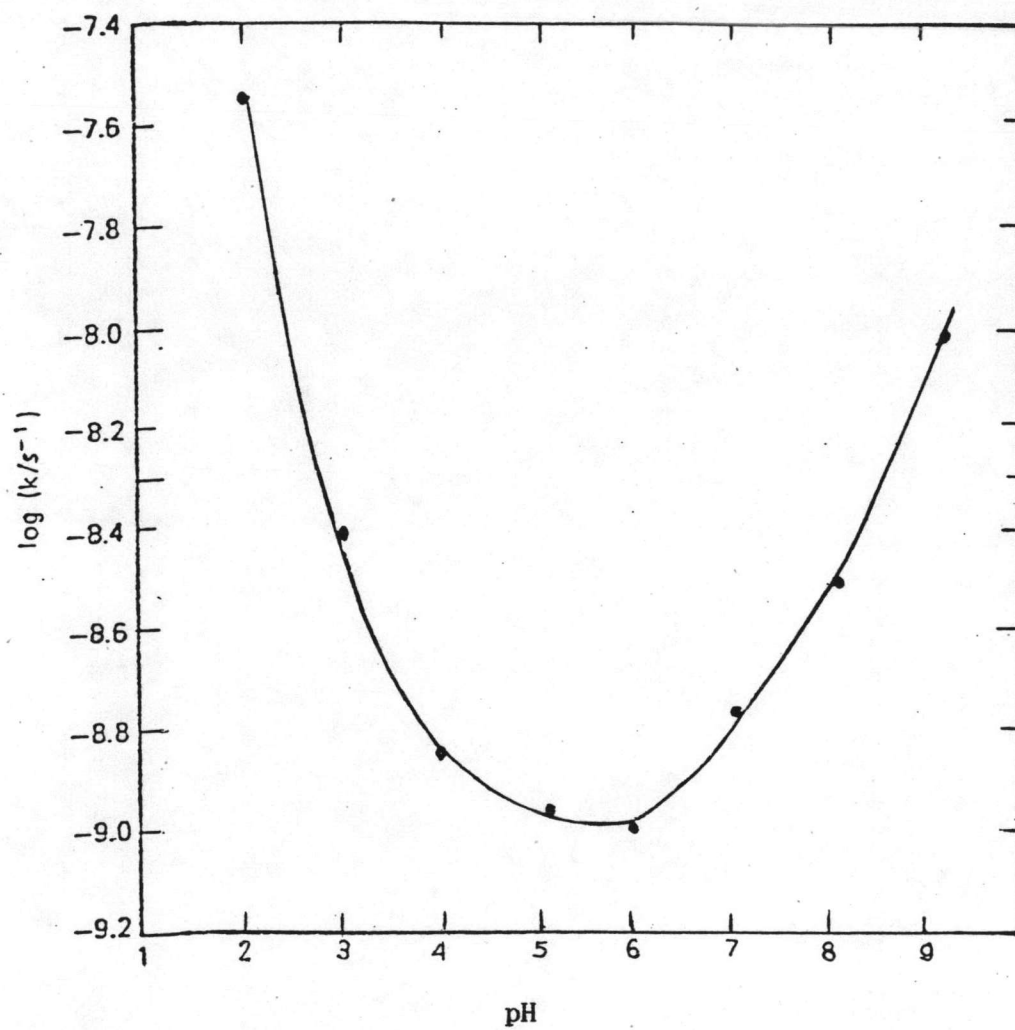


Figure 7 pH-Rate Profile for Hydrolysis of Paracetamol at 25°C (Rate Constant in s<sup>-1</sup>).

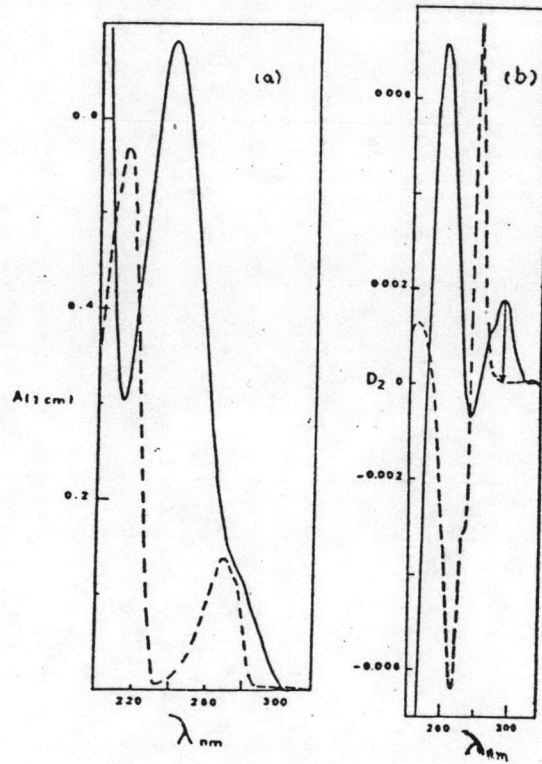


Figure 8 Zero Order Absorption Spectra (a) and Second Derivative Spectra (b) of 1 mg% w/v Paracetamol (-) and Its Degradation Product (---) in 0.1 N HCl.

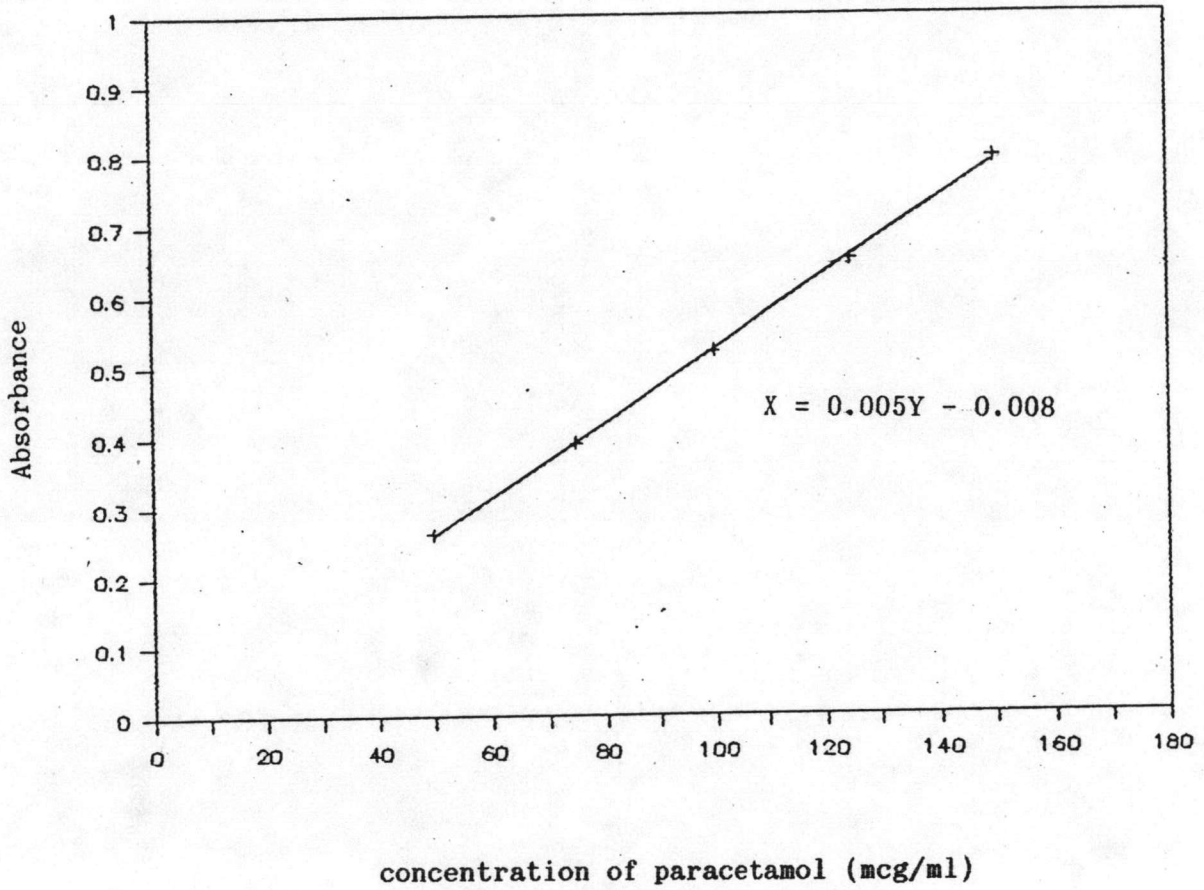


Figure 9 Typical Calibration Curve of Paracetamol with USP Method.

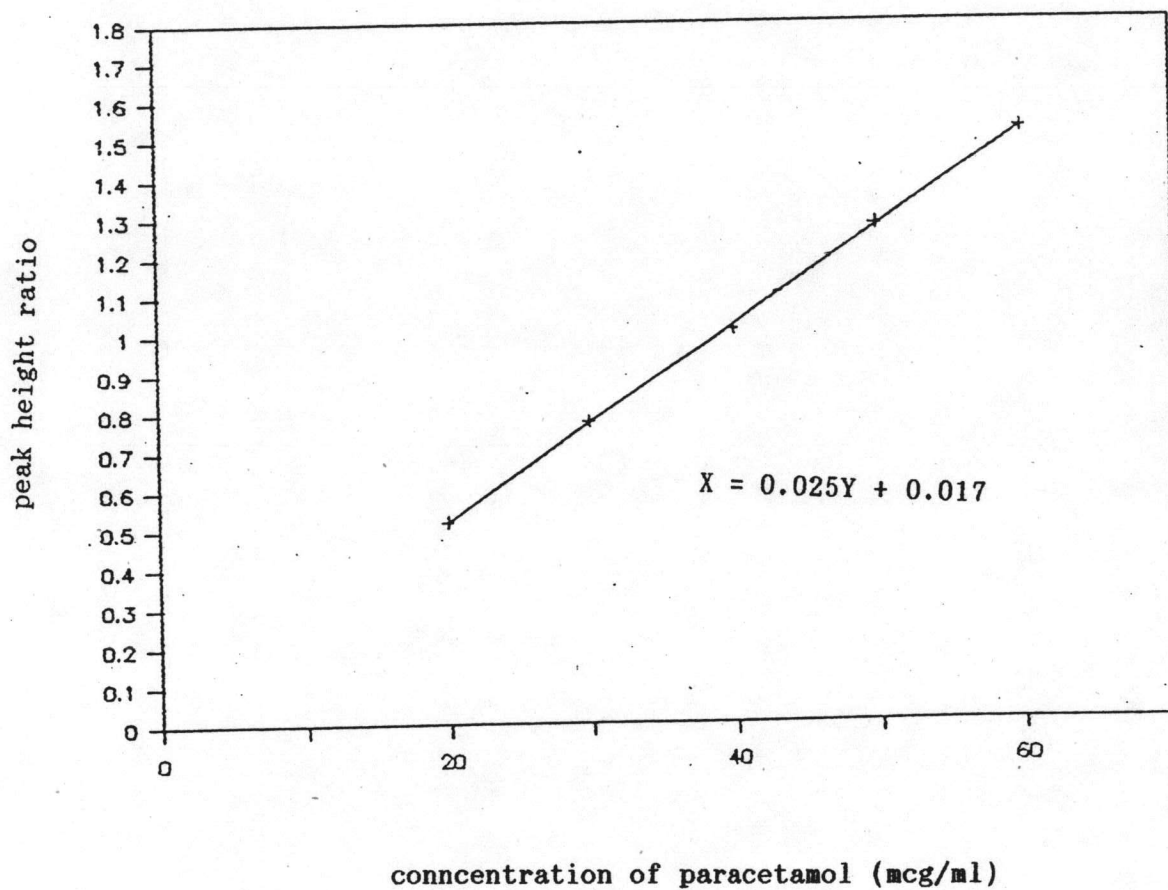


Figure 10 Typical Curve of the Ratio of the Peak Height Paracetamol Divided the Peak Height of Internal Standard (Sulpyrin) versus Concentration of Paracetamol (by HPLC Method).

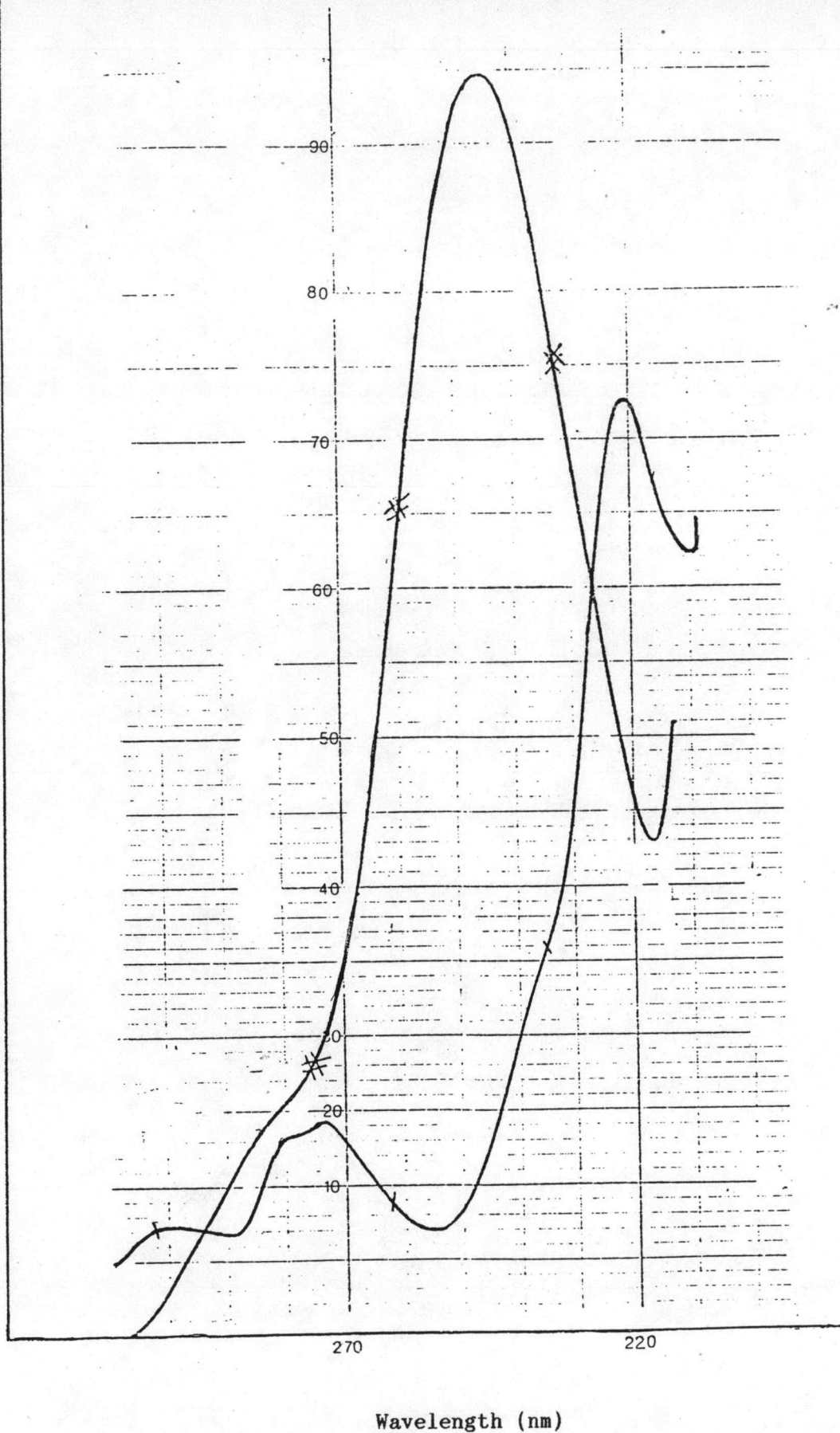


Figure 11 Ultraviolet Spectrum of 2.5 mg% Paracetamol (#) and 2.5 mg% P-aminophenol (-) in Phosphate Buffer pH4 : Methanol (85/15 v/v).

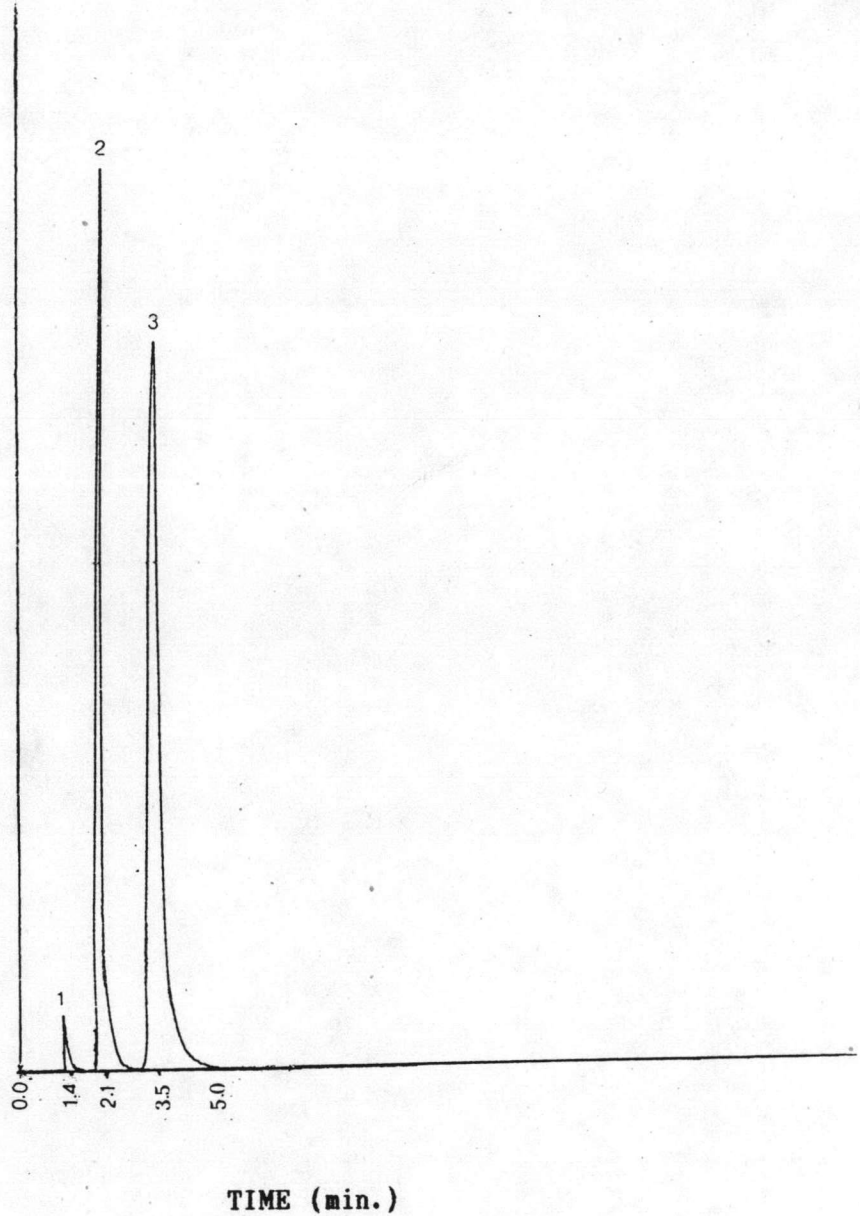


Figure 12 HPLC Separation of P-aminophenol, Paracetamol and Sulpyrin on a 15-cm x 4.6 mm Zobax Cs Column, Methanol/ 0.01%  $\text{KH}_2\text{PO}_4$  in Water pH<sub>4</sub> (15:85 v/v), 2.0 ml/min; Detection, 254 nm., Attenuation 256; Ambient Temperature; Recorder 2 min/cm.; Injection Volume, 20  $\mu\text{l}$ ; Peak Identity, (1) P-aminophenol, (2) Paracetamol, and (3) Sulpyrin (Internal Standard).

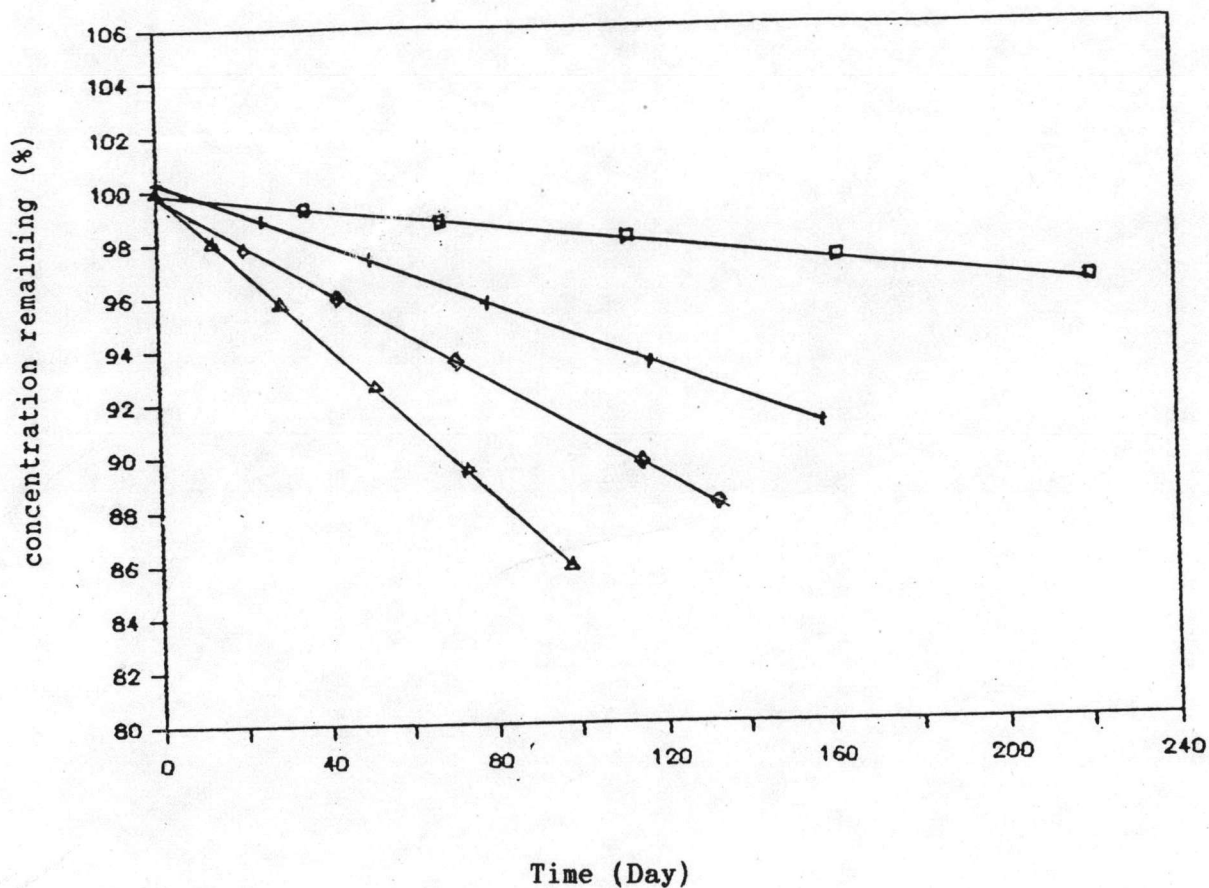


Figure 13 Concentration Remaining (From Linear Regression Equation) Versus Time of Paracetamol in Paracetamol Suspension #1; 40°C (□); 55°C (+); 60°C (◇); 70°C (△).



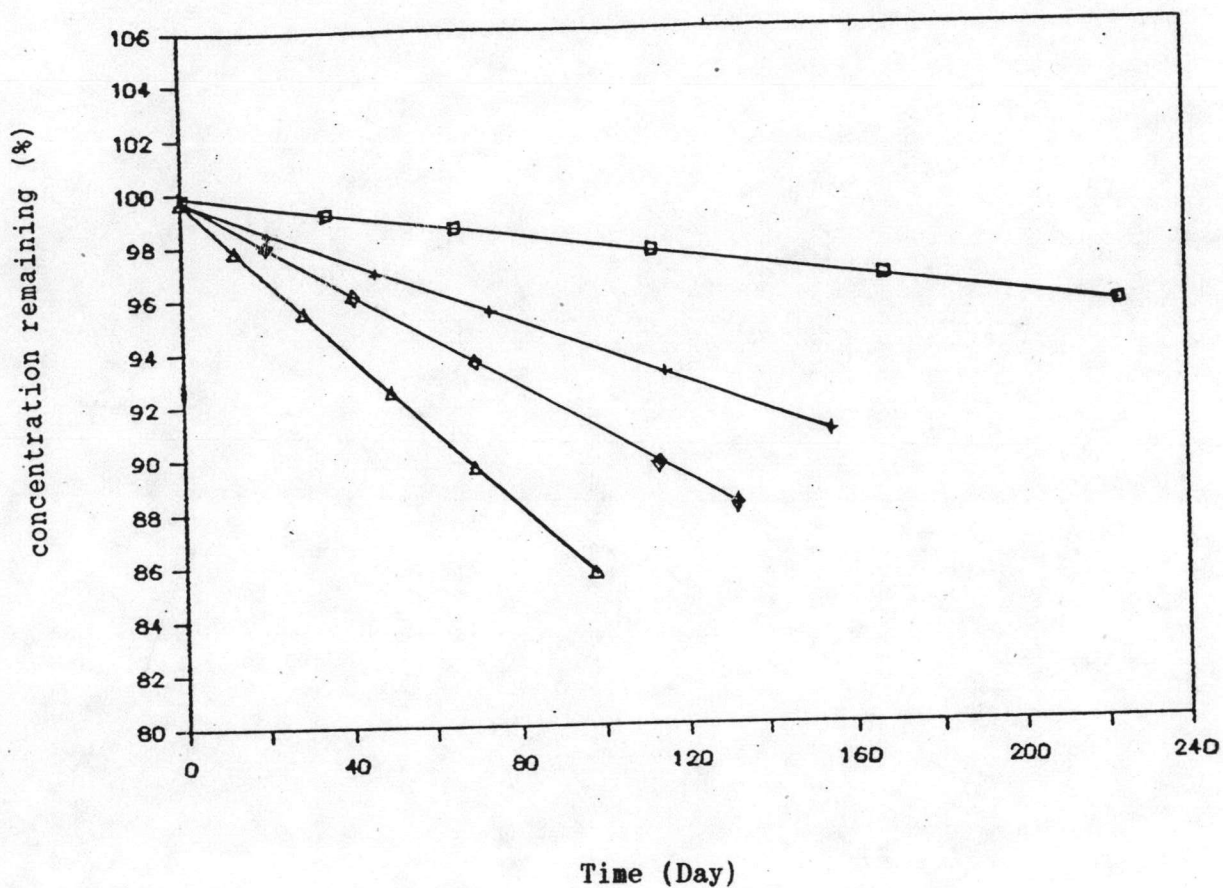


Figure 14 Concentration Remaining (From Linear Regression Equation) Versus Time of Paracetamol in Paracetamol Suspension #2; 40°C (□); 55°C (+); 60°C (◇); 70°C (△).

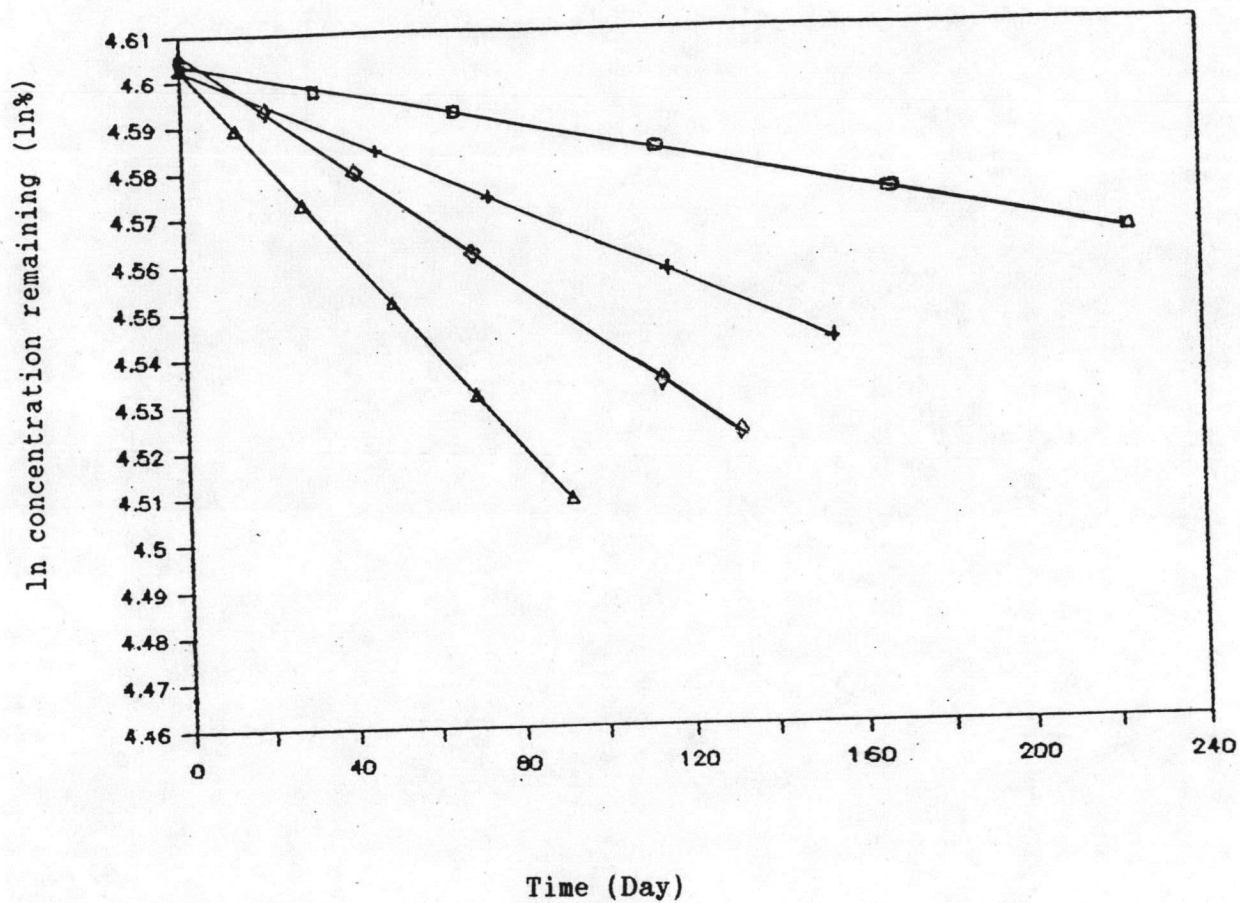


Figure 15 ln Concentration Remaining (From Linear Regression Equation) Versus Time of Paracetamol in Paracetamol Syrup #1; 40°C (□); 55°C (+); 60°C (◇); 70°C (△).

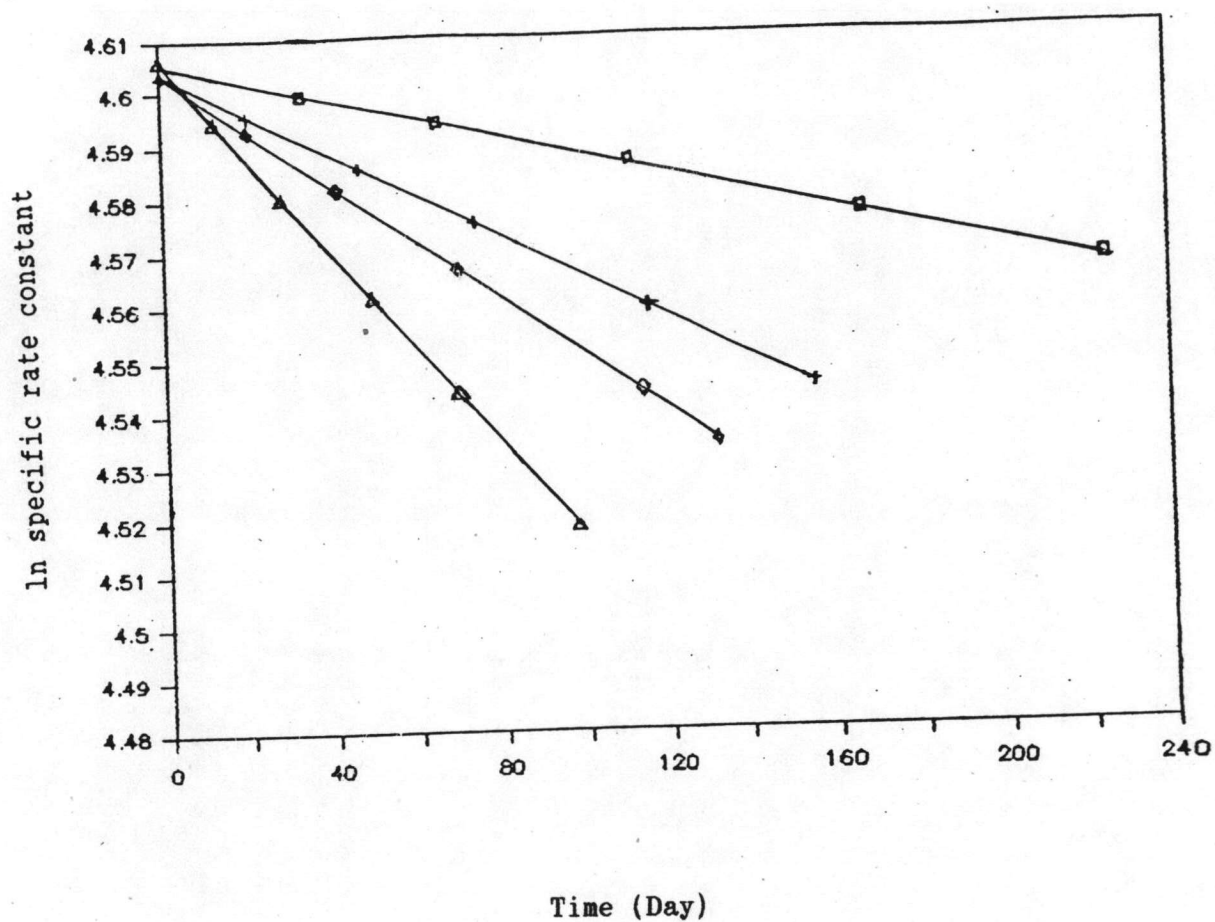


Figure 16 ln Concentration Remaining (from Linear Regression Equation) Versus Time of Paracetamol in Paracetamol syrup #2; 40°C (□); 55°C (+); 60°C (◇); 70°C (△).

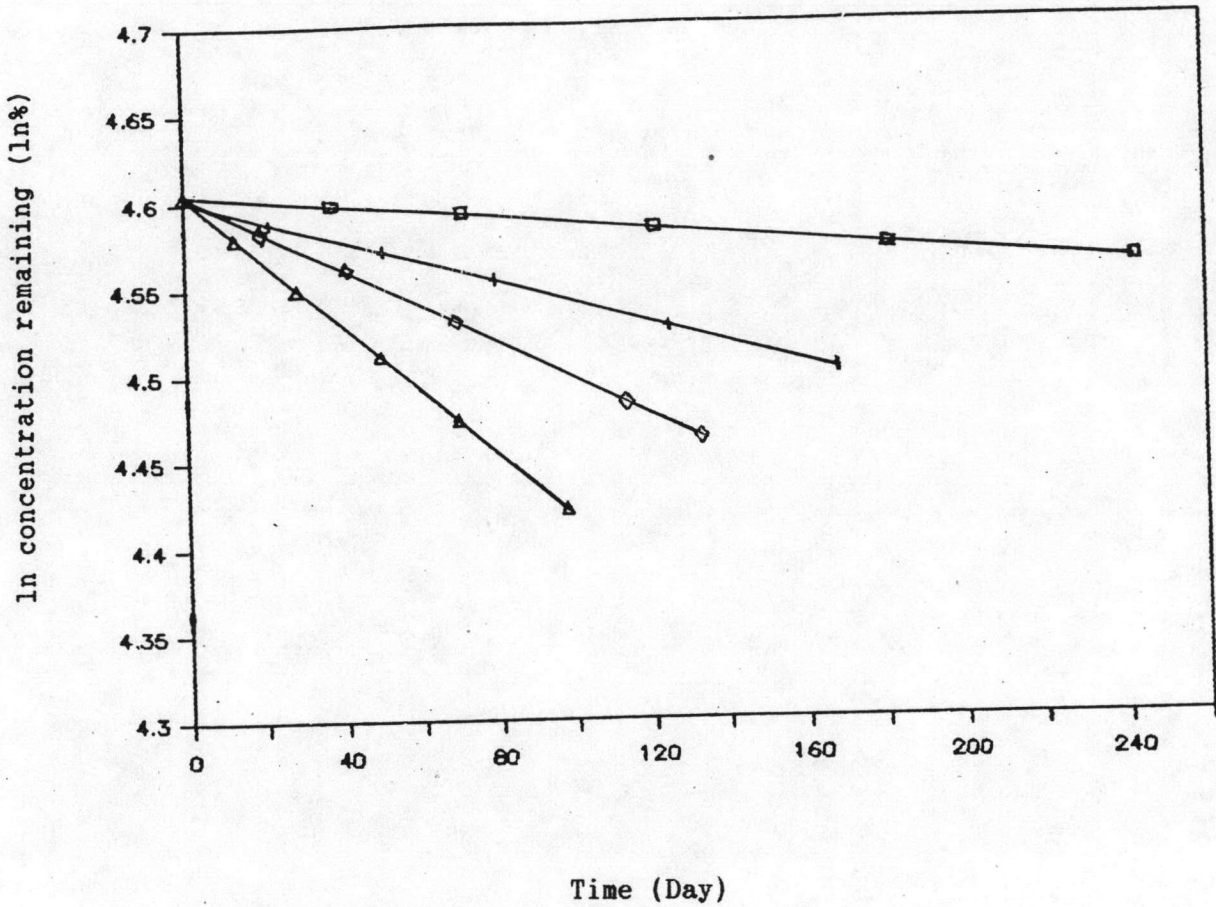


Figure 17 ln Concentration Remaining (from Linear Regression Equation) Versus Time of Paracetamol in Paracetamol Elixir #1; 40°C (□); 55°C (+); 60°C (◇); 70°C (△).

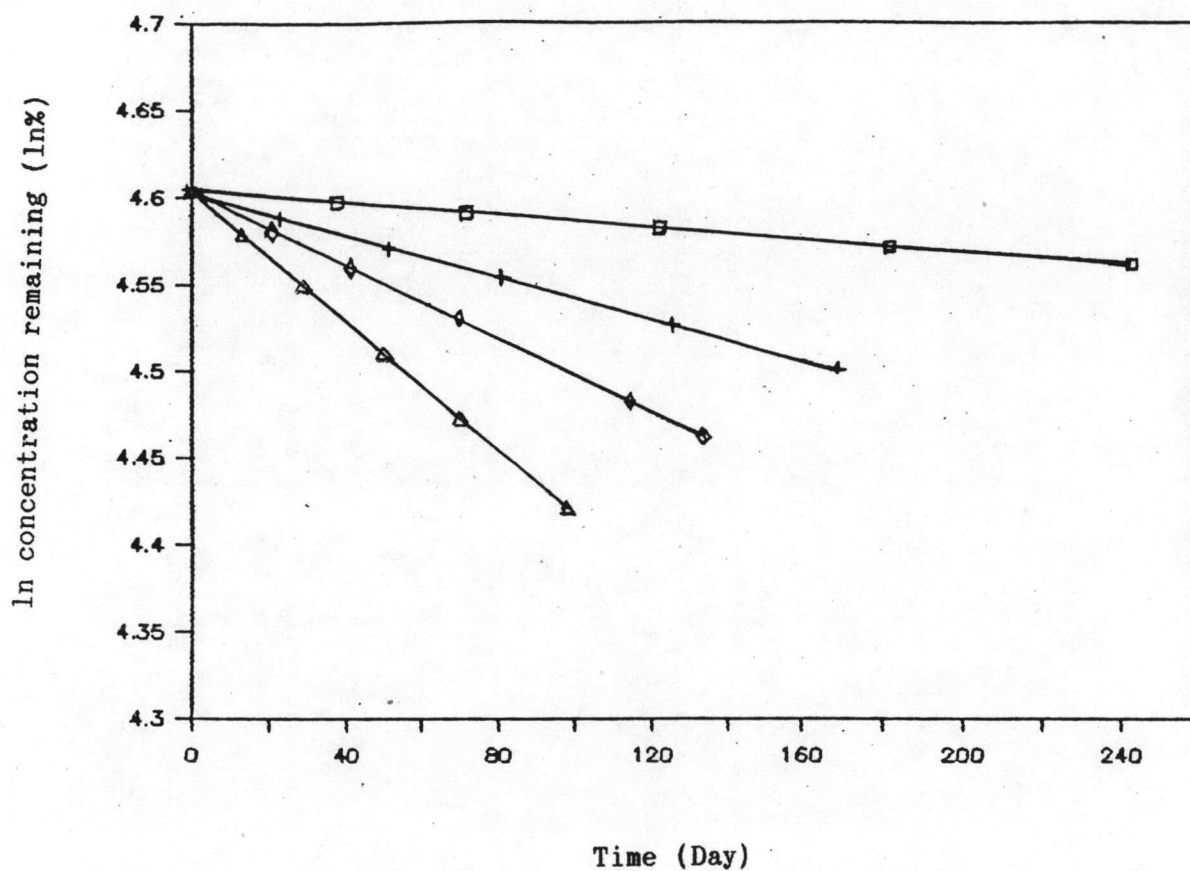


Figure 18 In Concentration Remaining (from Linear Regression Equation) Versus Time of Paracetamol in Paracetamol Elixir #2; 40°C (□); 55°C (+); 60°C (◇); 70°C (△).

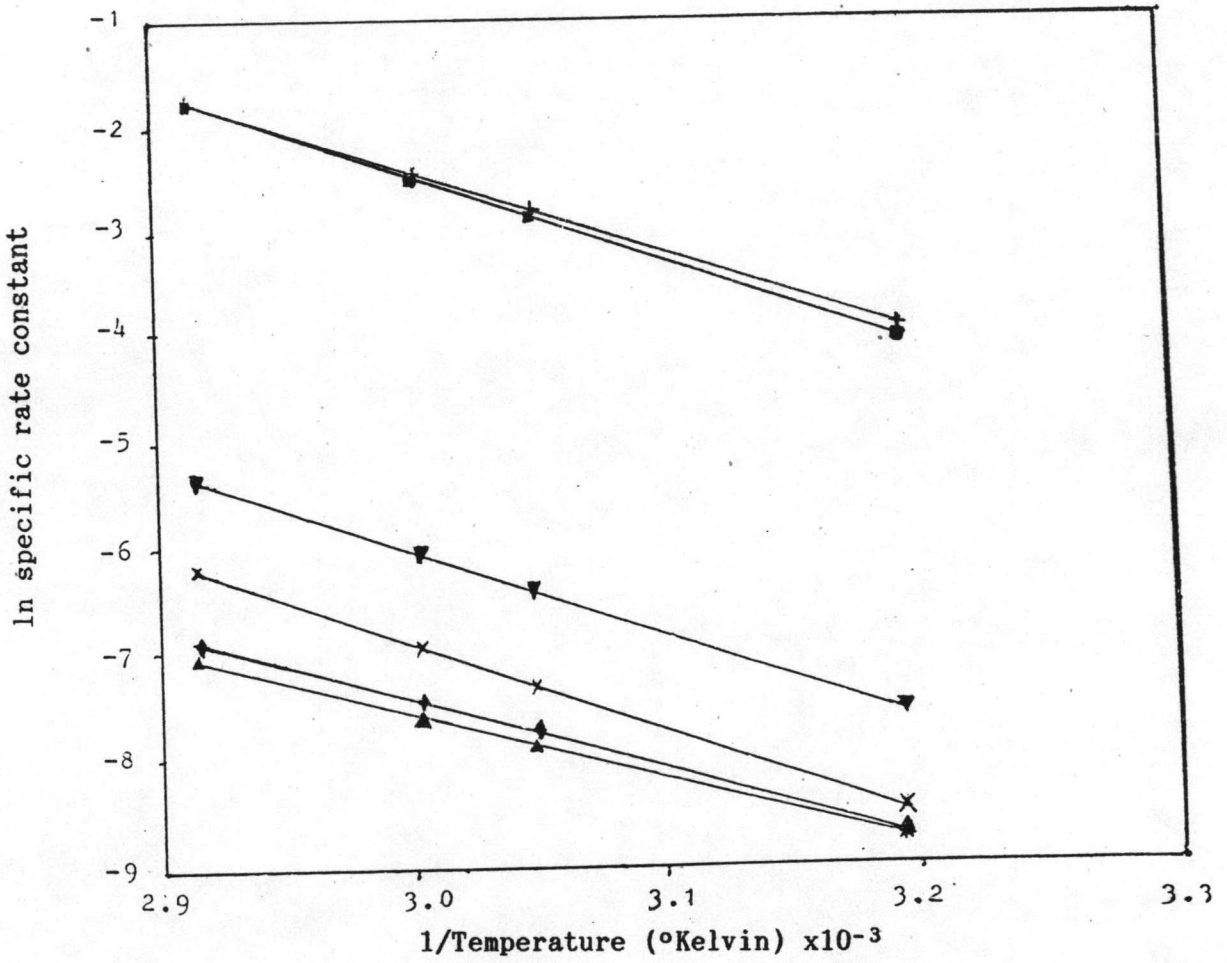


Figure 19 Arrhenius Plot of ln Specific Rate Constant (from Linear Regression Equation) of Paracetamol; Suspension #1 (■); Suspension #2 (+); Syrup #1 (◆); Syrup #2 (▲) Elixir #1 (X); Elixir #2 (▼).