Analysis of Paracetamol by Oxidation with Potassium Iodate

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ABSTRACT--- ***The present paper describes the reaction of Paracetamol with Potassium iodate at 20^{o}C with λmax at 470nm. The reaction product has been utilized kinetically to analyze the drug in Pharmacentical preparations with accurate and reproducible results in a short time.***

Keywords---Paracetamol Potassium Iodate Oxidation

1.INTRODUCTION

Many methods are available in literature for assay of Paracetamol in diverse types of samples including Paracetamol preparations. These methods are as diverse as a simple titrimetric methods to HPLC and spectrophotometric methods. Owing to wide spread use of Paracetamol in different kind of Pharmacentical preparations, rapid and sensitive methods for the determination of Paracetamol are being investigated many spectrophotometric method of determination of Paracetamol are available to literature[1-9]. These are based on hydrolysis of Paracetamol to p-aminophenol and later is reacted with specific reagents to produce coloured substance which is monitored spectrophotometrically. The method assaying of Paracetamol was to react Paracetamol with different reagents so that a coloured species was farmed, the absorbance of which was measured in visible region at appropriate wavelength[3-6]. Hundreds of methods are available in converting the hydrolyzed product to coloured species to estimate Paracetamol[1-3, 6-8].

The present paper describes the reaction of Paracetamol with Potassium iodate at 20^{o}C with λmax at 470nm. The reaction product has been utilized kinetically to analyze the drug in Pharmacentical preparations with accurate and reproducible results in a short time.

1.1. Apparatus

Bausch and Lomb spectronic 1001 and spectronic 20D^{+} spectrophotometer were used to record the absorbance. A controlled temperature water bath (NSW-133) was used.

1.2. Reagents and Solutions

All chemicals used were of analytical or pharmaceutical grade.

The stock solution of potassium iodate (0.1 mol 1^{-1}) was freshly prepared. Double distilled water was used throughout. Paracetamol 2 mg/ml (Wallace, India), or 0.0101 mol 1^{-1} was dissolved in distilled water. The stock solution of Paracetamol should be kept in a well closed dark container to avoid direct contact with light.

Paracetamol was also prepared from pharmaceutical preparations. Tablets to be analyzed were powdered, dissolved in distilled water and filtered through a Whatman No. 1 filter paper The filtrate was adjusted to the final concentration of 2mg/ml. The recommended procedure was followed.

1.3. Procedure for the Determination of Paracetamol

To aliquots containing 0.3-3.5 ml of the Standard Solution of Paracetamol, 4.5 ml of 0.1 mol 1^{-1} potassium iodate was added. After mixing in water bath at 20°C, the solutions were diluted upto the mark with distilled water in a 10 ml volumetric flasks, The contents were then immediately transferred to the spectrophotometrics cell and after one minute, the absorbance was recorded every 30 sec time-intervals at 470 nm. The blank was prepared in the same way but omitting Paracetamol sample. The calibration graph can be obtained by plotting log V (initial rate of reaction) versus log C (concentration of Paracetamol).

2.RESULTS AND DISCUSSION

The reaction of Paracetamol with potassium iodate (IO_3^-) gives rise to the formation of a yellow color product. The intensity of the yellow color increases with time and changes to orange color, having an absorption maximum at 470 nm (Fig. 4.1). From the absorption spectra, it is observed that pure Paracetamol in distilled water is having a maxima at 280

nm (Fig.4.2) and a shift in maxima is attained after adding potassium iodate (Fig. 4.1). This type of shift is contributed to the oxidation reaction, where the 1, 2-dihydroxy moiety is oxidized to 1, 2-quinone moiety. The proposed reaction mechanism is presented in Fig. 4.3.

The slopes (dA/dt) of the absorbance-time curve obtained from

Fig. 4.4 are used to measure the initial rate of reaction (V), for solution containing different concentrations of Paracetamol. The differential method has been used to calculate the rate constant and true order of the reaction using the following equation:

$$V = K_{t-} C^{n}$$

According to Laidler, V is the initial rate of the reaction, K_t is the rate constant with respect to the concentration of a particular reactant, and n is the true order (true order is defined as the order with respect to concentration). Therefore, the reaction is made pseudo first order by taking one reagent in a small amount than the other.

2.1. Features of the Calibration Graph

Calibration graph (Fig. 4.5) constructed by plotting log V (initial

rate of reaction) versus log C (concentration of Paracetamol in mol 1^{-1}), shows a linearity in the concentration range of 60-700 µg/ml. Fig. 4.5 is used to calculate the order as well as the rate constant. The order is found to be +1.0 and the rate constant is found to be 2.69×10^{-4} at 470 nm. The data used for constructing the calibration graph are listed in Table 4.1.

A correlation coefficient of 1.0000 is obtained from data presented in Table 4.1. The factors of the regression line equation (y = m x + b) are calculated and utilized to find out the concentration of Paracetamol. Where, y = V (initial rate of reaction); x = unknown concentration; m = slope and b = intercept. Therefore, $y = 3.2 \times 10^{-4} X + 2.85 \times 10^{-4}$.

2.2. Effect of Reaction Variables on the Rate of Reaction

2.2.1. Effect of Iodate

The effect of iodate on the rate of reaction has been studied in the range (5×10^{-3}–5.5×10^{-2} mol 1^{-1}). A plot of log V (initial rate of reaction) versus log [IO_3^-] (Fig. 4.6) shows that the initial rate of reaction increases, reaches a maximum value and then decreases with increase in [IO_3^-]. Therefore, 4.5×10^{-2} mol 1^{-1} of iodate is used throughout the experiment, which gives a convenient results.

2.2.2. Effect of Temperature

The effect of temperature on the rate of reaction has been studied in the range (293-323 K). The absorbance-time curve (Figure 4.7) shows the temperature dependence and increase in absorbance with time. The reaction shows a linear relationship with temperature. A plot of ln K (reaction rate) versus 1/T is linear at 293-323 K (Fig. 4.8). Therefore, the optimum reaction temperature 293 K is used throughout the experiment.

The effect of temperature on the rate of reaction is checked to evaluate $\Delta E^{\#}$ (energy of activation) using Arrhenius equation, $K = Ae^{-\Delta E\#.RT}$. The estimation of the free energy of activation from the relation $K_1 = (KT/h)e^{-\Delta E\#.RT}$ (where K and h are the Boltzmann's and Plank‘s constants, respectively). The values of AH” and AS” are calculated from the Gibb's Helmholtz equation, $\Delta G^{\#} = \Delta H^{\#} - T\Delta S^{\#}$. A plot of $\Delta G^{\#}/T$ versus 1/T (Fig. 4.9) is also drawn. The results are summarized in Table 4.2.

2.3. Standard Addition Technique

The proposed kinetic method is found to be precise and accurate. This was confirmed by applying the standard addition technique. The standard solution of Paracetamol is added to the solution of pharmaceutical (studied sample) containing different concentrations. The results are summarized in Table 4.3.

2.4. Interferences

Some common recipients such as lactose, glucose, sucrose, fructose and starch, which are usually added in the preparation of tablets, show no influence in .the determination and the maximum tolerance amounts were calculated using procentual change in absorbance of Paracetamol measured value. The results are recorded in Table 4.5.

Table 4.1: Data used for constructing calibration graph for Paracetamol: log V (initial rate of reaction vs. log C (Paracetamol concentration), keeping Paracetamol concentration constant (0.0101 mol 1^{-1}) at 20^0C

Concentration of Paracetamol (C) mol 1^{-1}	Initial rate of reaction (V)	log (V)	log (C) mol 1^{-1}
3.04×10^{-3}	0.33×10^{-3}	-3.48	-2.52
5.07×10^{-3}	0.5×10^{-3}	-3.30	-2.30
8.11×10^{-3}	0.666×10^{-3}	-3.178	-2.09
0.01	0.83×10^{-3}	-3.08	-2.00
0.012	1×10^{-3}	-3.00	-1.92
0.015	1.25×10^{-3}	-2.90	-1.82
0.020	1.5×10^{-3}	-2.82	-1.69
0.025	1.916×10^{-3}	-2.717	-1.60
0.030	2.16×10^{-3}	-2.66	-1.52
0.035	2.5×10^{-3}	-2.60	-1.45

Table 4.2: Activation parameters for the reaction of Paracetamol with potassium iodate

$\Delta E^{\#}$ K.Cal/mol	$\Delta G^{\#}$ K. Cal/mole	$\Delta H^{\#}$ K.cal/mole	$-\Delta S^{\#}$ Cal/mole deg^{-1}
9.93	21.2	10.2	67.0

Table 4.3 Results obtained by standard addition technique

S. No.	Claimed amount taken (mg)	Authentic added (mg)	Amount found (mg)	% Recovery +S.D.*	R.S.D., %
1.	1.5	0.5	1.96	98.0+0.05	2.3
2.	2.3	2.7	4.98	99.6+0.15	3.0
3.	3.1	2.9	6.02	100.3+0.12	1.9

*** Average of three determinations**

Table 4.4 **Statistical treatment of data obtained for the determination of Paracetamol in formulation by proposed kinetic method and reference methods (4).**

	Proposed Method	Reference Method
Mean recovery %	100.3	99.96
S.D.	0.05	0.77
± R.S.C. %	1.6	-
N	5	6

n = number of determination

Table 4.5 Maximum amount tolerance of various excipient in the determination of Paracetamol

Common Excipient	Maximum Tolerance (mg)
Glucose	18.02
Fructose	18.02
Sucrose	34.2
Lactose	68.4
Starch	0.08

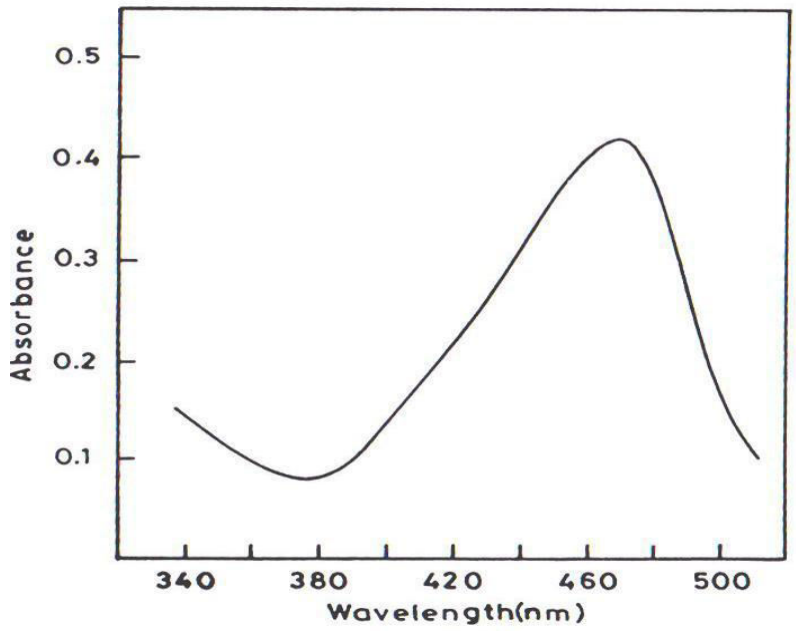

Fig 4.1: Absorption spectrum of Paracetamol with Potassium iodate at 20^0C

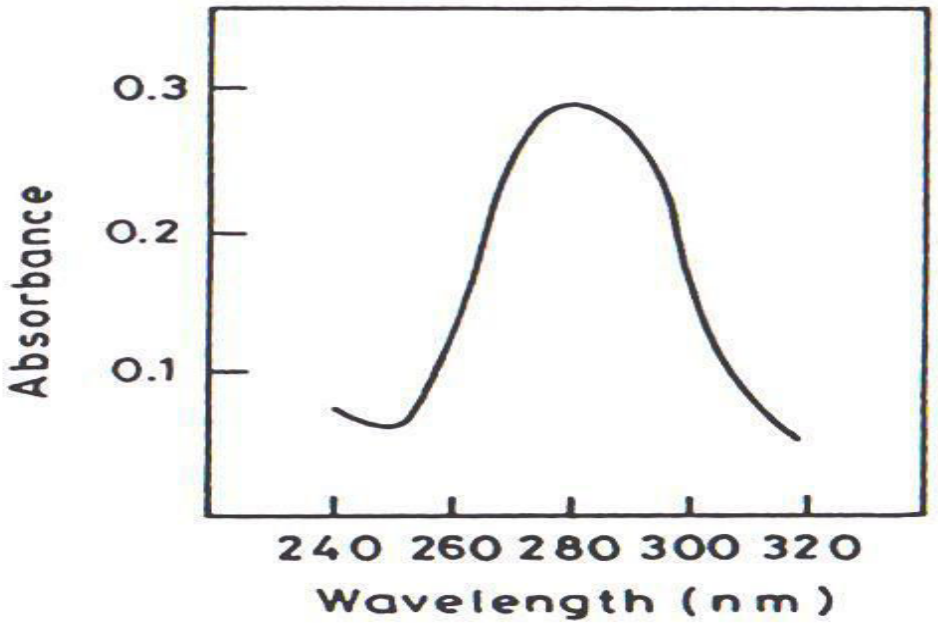

Fig 4.2: Absorption spectrum of Paracetamol in Water

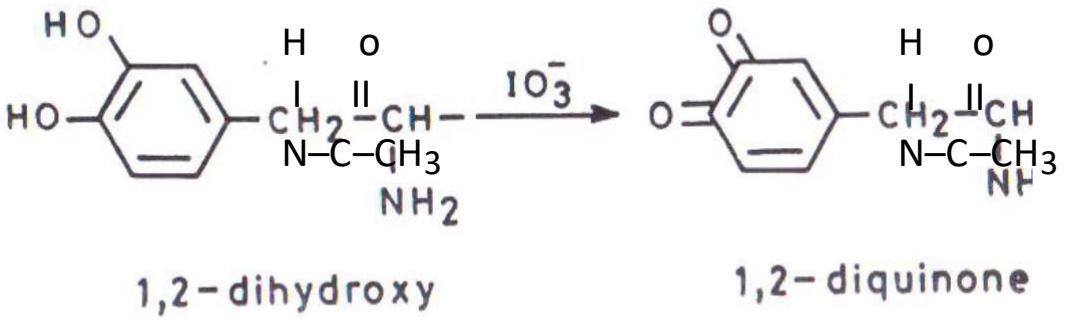

Fig 4.3: Proposed reaction mechanisms for the oxidation of Paracetamol Potassium iodate

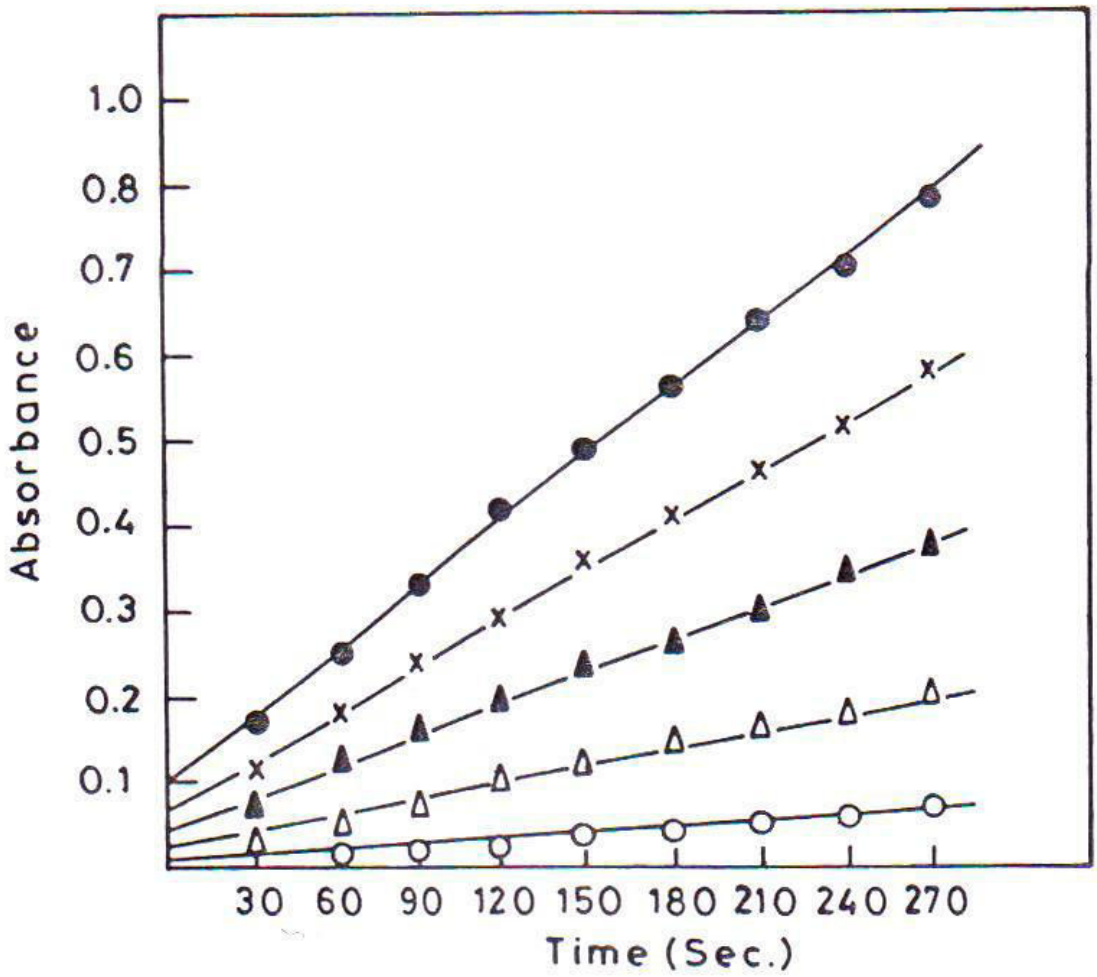

Fig 4.4: Kinetic graph for the reaction of Paracetamol with potassium iodate (4.5×10^{-2} mol l^{-1}) at 20^0C; λ_{max} = 470 nm (o) 3.04×10^{-4} mol l^{-1}; (Δ) 8.11×10^{-4} mol l^{-1} (Δ) 1.52×10^{-3} mol l^{-1}; (x) 2.53×10^{-3} mol l^{-1} (o) 3.54×10^{-3} mol l^{-1}

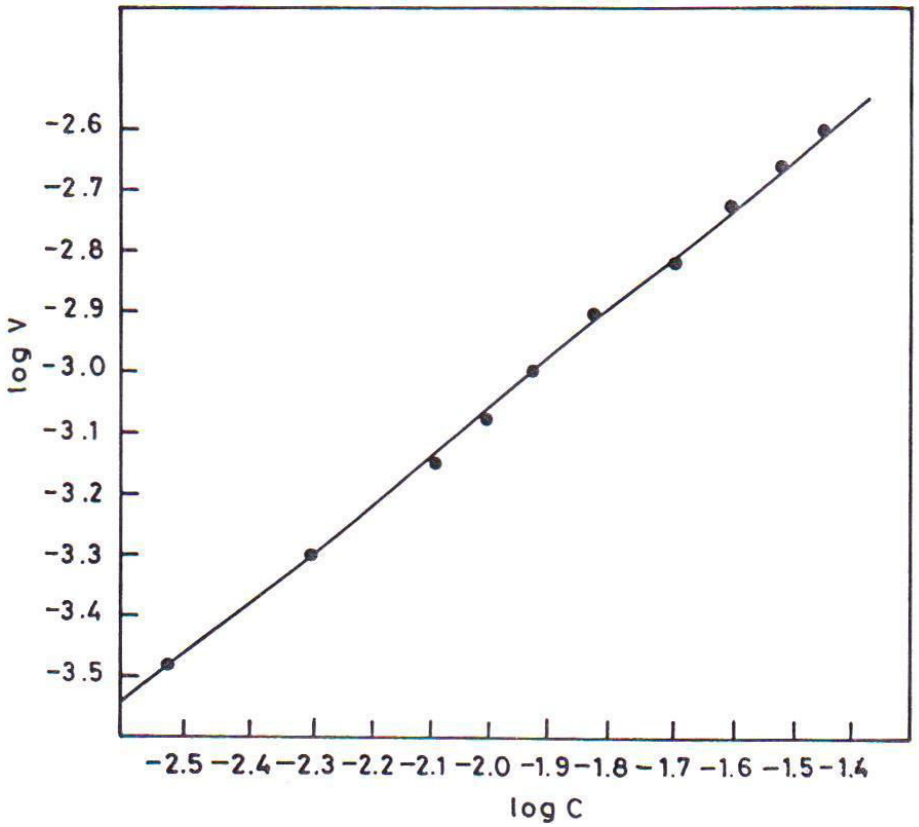

Fig 4.5: Calibration graph for Paracetamol log V (initial rate of reaction) Vs. Log C (Concentration mol 1^{-1}) using 4.5 x 10 -2 mol 1-1 potassium iodate at 20^0C; λ_{max} = 470 nm

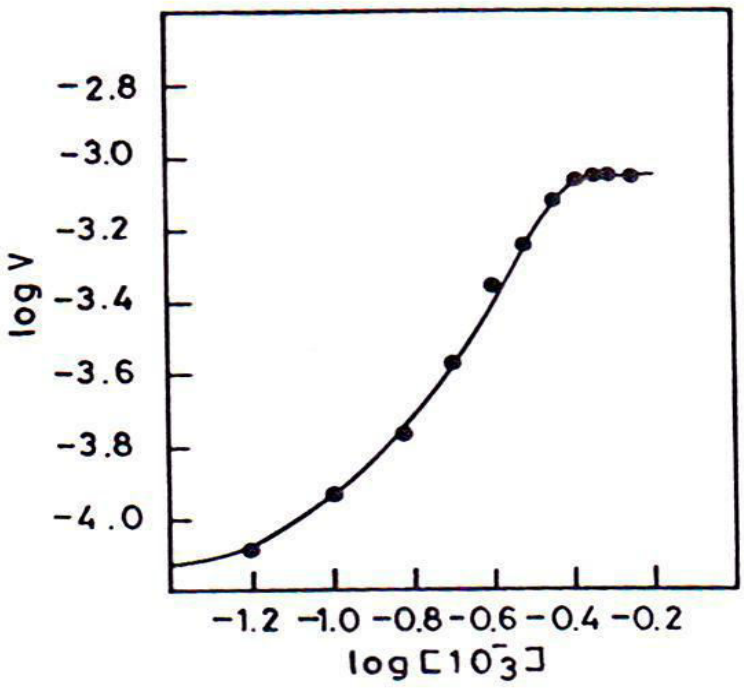

Fig 4.6: Effect of potassium iodate on the reaction rate log V (initial rate of reaction) Vs. log [IO^-_3] using 0.2 mg/ml paracetamol at 20^0C; λ_{max} = 470 nm

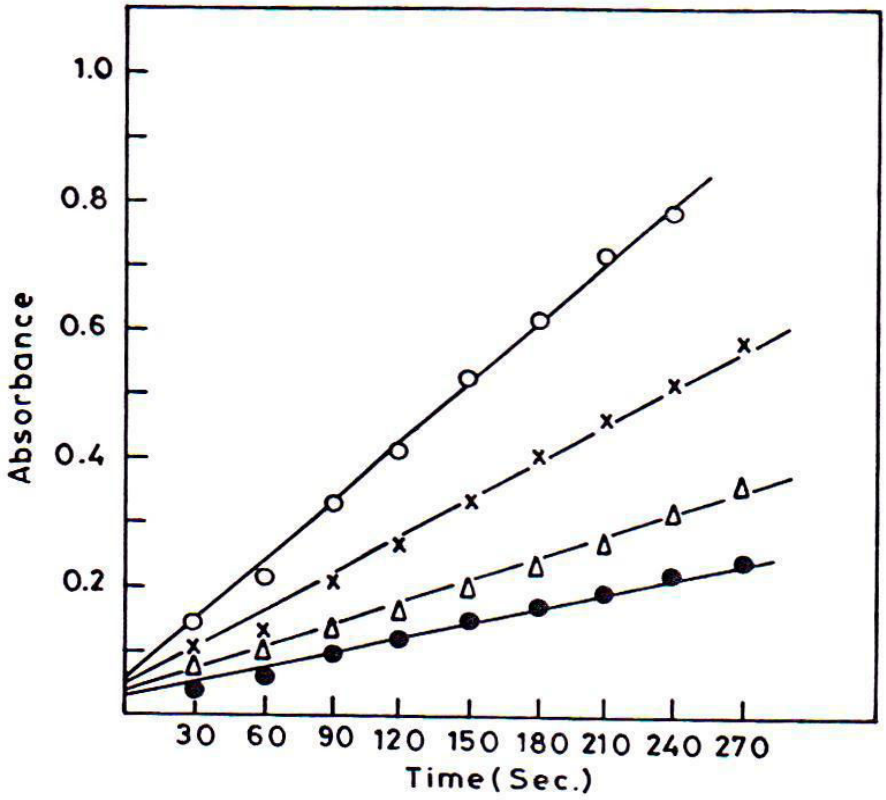

Fig 4.7: Temperature dependence of the kinetic plots for the reaction of Paracetamol with potassium iodate. Absorbance Vs. time (o) 20^0C (Δ) 30^0C (x) 40^0C (o) 50^0C

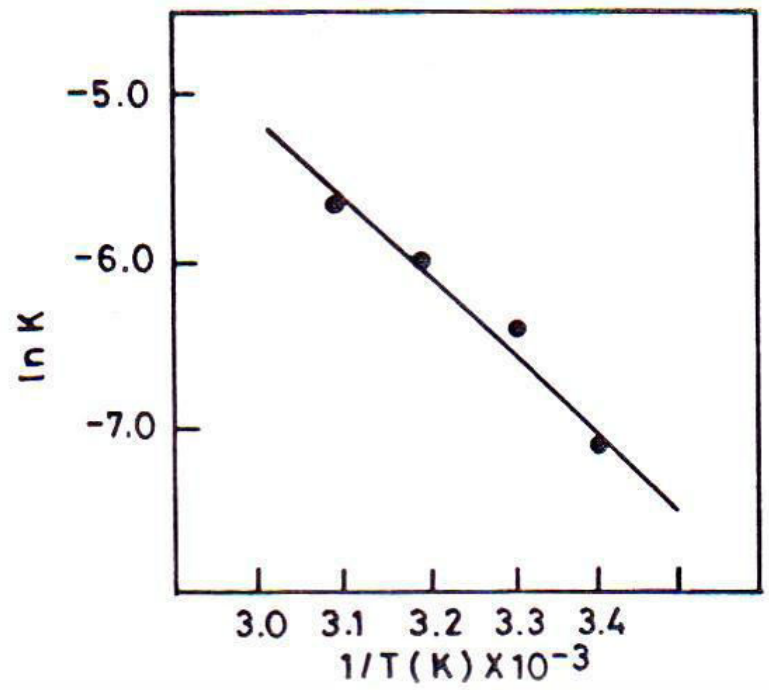

Fig 4.8: Dependence of reaction rate on temperature plot of In K Vs. 1/T

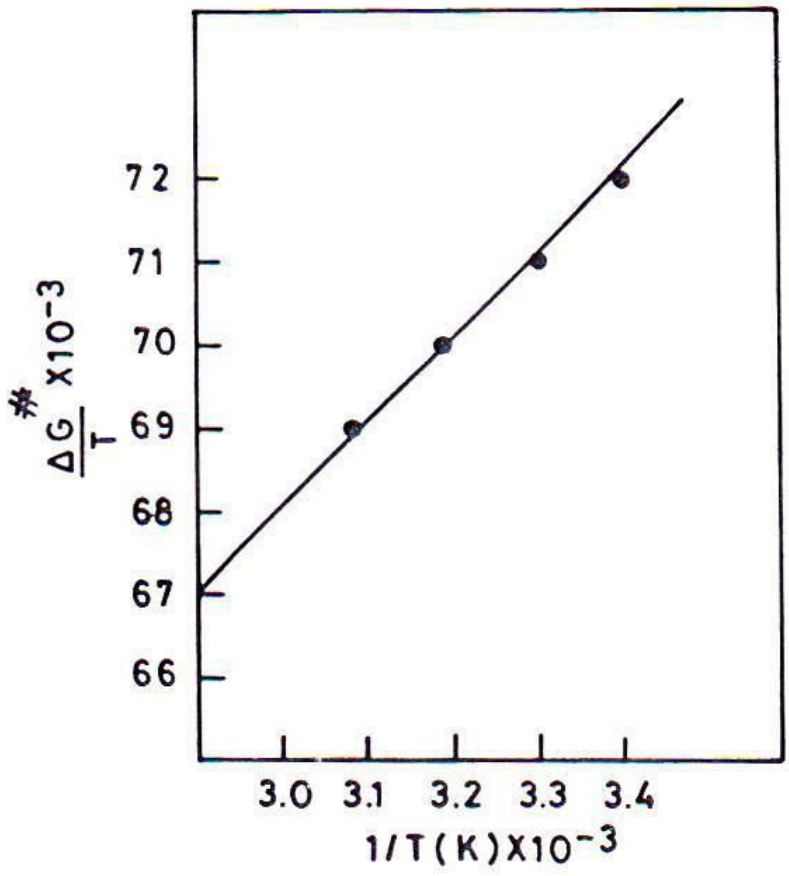

Fig 4.9: Dependence of Gibb's free energy on temperature. Plot of $\Delta G^{\#}/T$ Vs 1/T

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