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Kinetics Studies of Oxidation of Furosemide by Acidic Potassium Permanganate

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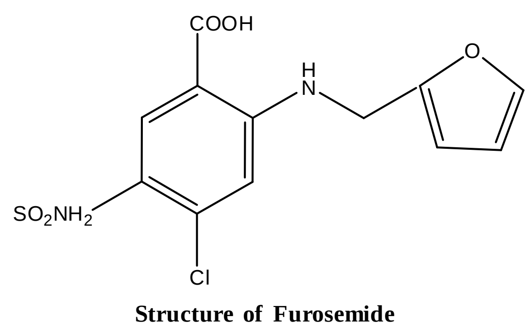
Abstract

The Kinetic of oxidation of Furosemideby potassium permanganate has been studied in the presence of acidic medium. The reaction is first order with respect to $KMnO_4$ as well as Furosemideconcentration. The reaction rate has been determined at different temperature and different thermodynamic parameters have been calculated which shows that the reaction rate increase with increase in temperature. With increase in the concentration of acid the reaction rate increases. A suitable mechanism has been proposed.

Key words: Kinetics, Mechanism, Oxidation, Furosemide, potassium permanganate, thermodynamic parameters, etc.

Introduction

Drug that facilitate diuresis are widely used for the treatment of edematous conditions and in the management of hypertension and other conditions for which the increase in urinary flow can relieve symptoms. 5-Aminosulphnyl-4-chloro-2-furanylmethyl acid (furosemide)[1-2] is a potent and widely used diuretic in the treatment of edematous states associated with cardiac, chronic renal failure, hypertension, congestive heart failure and cirrhosis of the liver[3-5]. Their principal site of action is the thick ascending limp of the loop of Henle. Furosemide with a prompt action is fairly rapidly absorbed after oral administration and shows a strong diuretic effect of short duration[6-7].



Structure of Furosemide

Furosemide, chemically known as 4-chloro-Nfurfuryl-5sulfamoylanthranilic acid, is an anthranillic acid derivative[8-10], which is been used as strong diuretic (Rankin, Williams, & Lemke, 2002). Both adults and children's are treated with furosemide available under brand anme Lasix either orally or by intravenous[11-14]. Although lot of literature is available on the reaction between NAD and other substances, the oxidation kinetics of Furosemide using permanganate is not studied so for. Therefore, we decided to undertake kinetic study of the Furosemide.

Material and Method

Chemical which are used in this experiment are highly purified and AR grade, the solutions were used in this study were prepared by using distilled acetic acid[15] and double distilled water. Solution of Furosemide were prepared by using double distilled water and this solution was used for kinetic studies. The reaction was carried out in glass stoppered Pyrex boiling tube. The Kinetics of reaction was followed in the temperature range 30°C to 50°C.

Kinetic Measurement:

The kinetic of reaction were measured by using double beam spectrophotometer model No AU2100 of Systronic Company which is having inbuilt software. The Kinetic of reaction were measured at 520nm wavelength up to the 85% completion of reaction.

Stoichiometry of reaction:

The Stoichiometry of the reaction were determined by envying out several sets of experimental with varying amount of oxidising agent potassium permanganate over Furosemide in acetic acid using in H_2SO_4. The remaining potassium permanganate was then analysed spectrophotometrically the result indicates that 1 mole of Furosemide react with 1 mole of potassium permanganate[16].

Product Analysis:

In a typical experiment, a mixture of Furosemide (0.1 mole) and Potassium permanganate (0.01 mole) was made up to50ml with acetic acid in presence of HCL (0.8 mole). The mixture was kept in the dark for twelve hours hours until completion of oxidation. It was then treated overnight with an excess (125 ml) of a freshly filtered saturated solution of 2, 4-dinitrophenylhydrazine in 2M HCL. The precipitated 2, 4-dinitrophenylhydrazine (DNP) was collected by filtration, dried, recrystallized from ethanol and weighed. The product of acid before and after sterilization was 1.0g (90%) and 0.82g(78%) respectively. The product was also confirmed by melting point, which matches with original acid[17].

Result and Discussion

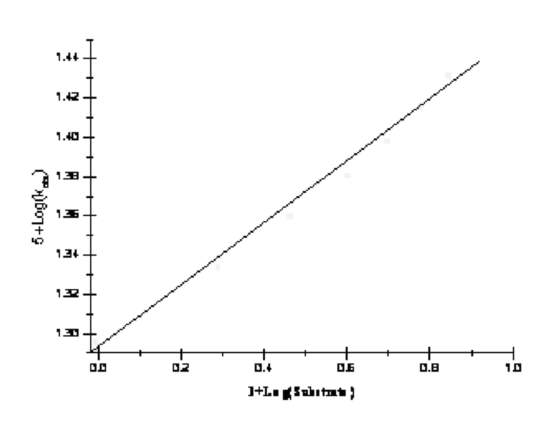
The results of various parameters is given in tabular form and presented with graphs.

1) Effect of variation of concentration of Furosemide:

The oxidation of Furosemide with potassium permanganate in acetic acid in presence of sulphuric acid. By keeping constant concentration of potassium permanganate and H_2SO_4 and by changing the concentration of Furosemide increases the rate of reaction (Table-1) the plot of log of k_{obs} versus log concentration of Furosemide for different initial concentration of metal complex is linear with unit slop, which shows that the first order dependence of rate of reaction on Furosemide[18-20].

Table 1. Effect of variation of concentration of Furosemide

Concentration	Rate K_{obs}
0.001	0.0002
0.002	0.00021
0.003	0.00022
0.004	0.00024
0.005	0.00025
0.006	0.00026
0.007	0.00027



2) Effect of varying oxidising agent potassium permanganate:

In this parameter studying the effect of variation of oxidising agent potassium permanganate on oxidation reaction of Furosemide by keeping constant concentration of Furosemide and concentration of H_2SO_4. The Concentration of oxidising agent increases, increase the rate of reaction Table 2 the plot of 1/log K_{obs} verses log [$KMnO_4$] for different initial concentration of [$KMnO_4$] is linear with unit slop presents the first order dependence of rate on [$KMnO_4$].

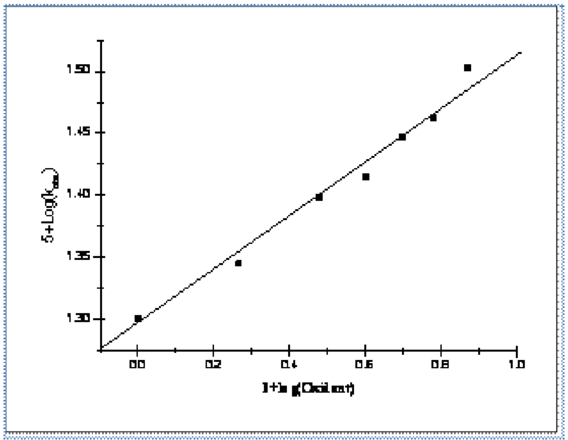


Table 2. Effect of variation of concentration of potassium permanganate.

Concentration	Rate K_{obs}
0.001	0.0002
0.002	0.0002
0.003	0.00025
0.004	0.00026
0.005	0.00028
0.006	0.00029
0.007	0.00032

3) Effect of variation of concentration of sulphuric acid:

In this factor there is study of variation of concentration of sulphuric acid on oxidation of Furosemide. By keeping constant concentration of oxidising agent and substrate changing the $[H_2SO_4]$ we find that the rate increases with increase in $[H_2SO_4]$ Table – 3 and plot of log k Vs log $[H^+]$ was linear with a unit slop indicating first order reaction on $[H^+]$. Fig – 3.

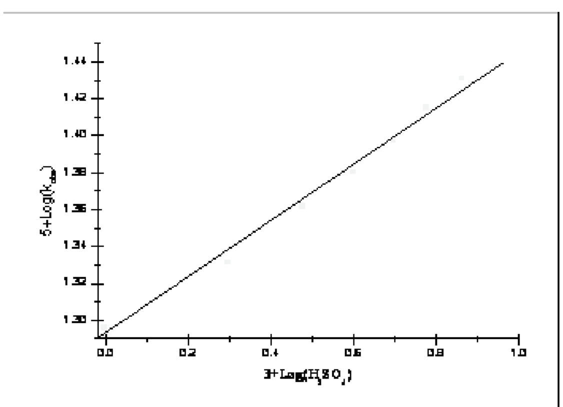


Table 3. Effect of variation of concentration of sulphuric acid

Concentration	Rate K_{obs}
0.001	0.0002
0.002	0.00021
0.003	0.00023
0.004	0.00024
0.005	0.00025
0.006	0.00026
0.007	0.00027

4) Effect of salts on reaction rate:

The effect of salts on the reaction rate was studied by adding various concentration by salt. By keeping constant concentration by oxidising agent substrate and acid. It was observed that the rate of oxidation was not altered by the addition of salts.

Table 4. Effect of salts on reaction rate

Concentration	Rate K_{obs}
1	0.00024
2	0.00023
3	0.00024
4	0.00024
5	0.00027
6	0.00025
7	0.00026

5) Effect of Temperature:

The study of effect of temperature on rate of oxidation of Furosemide by potassium permanganate has been studied at different temperature by keeping all other factors constant concentration with changing temperature from 303K to 323K. The rate constants are given in Table-5 as the temperature increases the values by rate constant also increases that shows rate of reaction depends of temperature the Arhenious plot 10gk Vs. 1/T were found to be linear fig – 4. The activation energy (Ea) were calculated from the clop of the plots from this values the thermodynamic parameters $\Delta H^{\#}$, $\Delta S^{\#}$ $\Delta G^{\#}$ was calculated Table – 6.

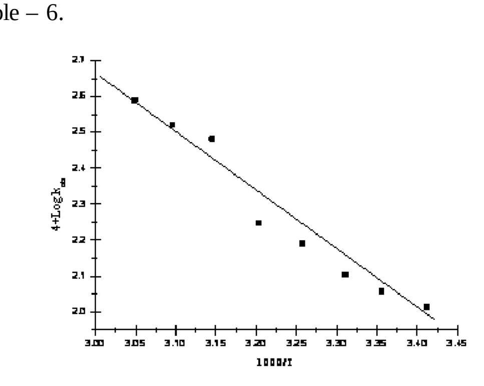


Table 5. Effect of Temperature

Sr. No.	Rate K	T^0C	T^0K	1/T	logK	2+logK	1000/T	$4+_{LOG}\ K_{OBS}$
1	0.0103	293	293	0.0034	-1.9871	0.0128	3.412969	2.012837
2	0.0114	298	298	0.0033	-1.9431	0.0569	3.355705	2.056905
3	0.0127	303	303	0.0033	-1.8962	0.1038	3.30033	2.103804
4	0.0155	308	308	0.0032	-1.8096	0.1903	3.246753	2.190332
5	0.0177	313	313	0.0031	-1.752	0.2479	3.194888	2.247973
6	0.0304	318	318	0.0031	-1.5171	0.4828	3.144654	2.482874
7	0.0333	323	323	0.0031	-1.4775	0.5224	3.095975	2.522444
8	0.039	328	328	0.003	-1.4089	0.591	3.04878	2.591065

Table 6. Thermodynamic parameters

Ea	53137
$\Delta H^{\#}$	50452
$\Delta S^{\#}$	-123
$\Delta G^{\#}$	90179

Conclusion

The oxidation of Furosemide increases in acetic acid in acid medium shows that the oxidation of Furosemide of potassium permanganate is in presence of acidic medium with effect of oxidising agent, substrate an acid and temperature the reaction is first order dependence. The addition of salt does not alter the rate of oxidation reaction. The mechanism of the reaction were given with the activation parameters the negative value of $\Delta S^{\#}$ provides support to the formation ofrigid transition state[21-22]. The overall mechanistic sequence described here is constituent with product and mechanistic study.

- Mechanism of oxidation of Furosemide by potassium permanganate.

$$H^+ + Mno_4^- \longrightarrow HMnO_4$$

This point has been also confirmed by previous researchers. Hence Mn (VII) could be considered as the reactive specie and this probably exists to a certain extent as $HMnO_4$.

As the concentration is increased the formation of $HMnO_4$ is favoured and hence increases the oxidation may be assumed to be taking place by Mn (VII) in the form of either MnO_4 or $HMnO_4$ or both depending on the acid concentration. The linear plot of log k Vs log (H_2SO_4) and log k Vs. Ho indicates that the reactions are acid catalysed, but none of the above plots gives an ideal slope for unity[23-24].

Derivation of Rate Law :

$$Mno_4 + H^+ \overset{K_1}{\rightleftharpoons} HMnO_4$$

$$\text{Furosemide} + HMnO_4 \overset{K_2}{\rightleftharpoons} C$$

$$C \longrightarrow \text{Product}$$

$$[MnO_4] = [MnO_4^-] + [HMnO_4]$$

$$= [MnO_4^-] + k_1 [MnO_4^-] [H^+]$$

$$= [MnO_4^-] + [1+k_1[H^+]]$$

$$\text{Rate} = \frac{k\ k_2[MnO_4^-]\ [\text{Furosemide}]}{1+k_1[H^+]}$$

$$[MnO_4][\text{Furosemide}] \frac{\text{Rate} \quad K\ K_2}{1+k_1[H]} = \overline{\qquad}$$

$$K_{obs} = \frac{k\ k_2}{1+k_1[H+]}$$

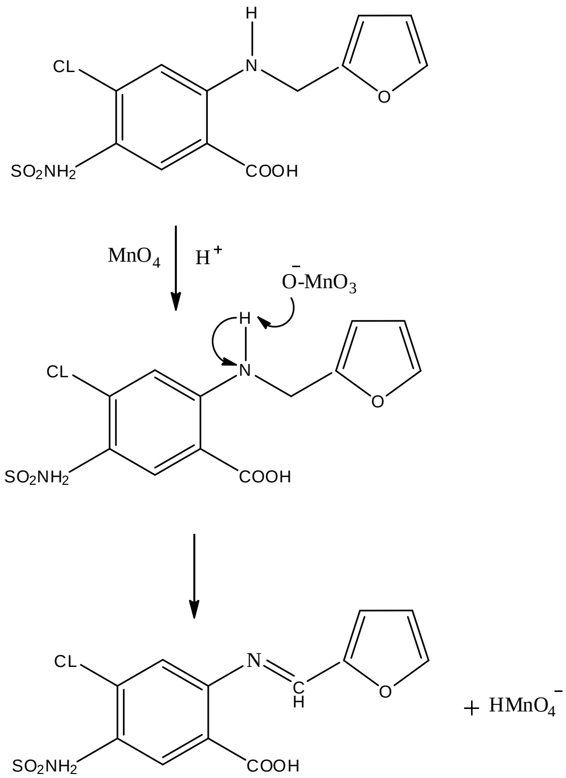
$$K_{obs} \frac{1}{k\ K_2 K\ K_2} = \frac{1}{\ } + \frac{k_1[H^+]}{\ }$$

Mechanism of oxidation of metal complexes :

$$Mno_4^- + H^+ \overset{K_1}{\rightleftharpoons} HMnO_4$$

$$H_2SO_4 \rightleftharpoons H^+ + HSO_4$$

$$H^+ + MnO_4 \longrightarrow HMnO_4$$



Acid

Compound (III) being highly unstable disproportionate to give acid and the corresponding oxide. The rate law can be expressed by equation (1).

$$\frac{-d[Mn(VII)]}{dt} = k\,[\text{Furosemide}]\,[MnO_4]_{Total}$$

The effect of temperature on reaction rate was studied which shows the increase in reaction rate with increase in temperature[25] (Table 5 and 6).

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