Potassium permanganate is widely used as an oxidising agent in synthetic as well as in analytical chemistry and also as a disinfectant. The general importance of permanganate is given in Chapter III (p.64). No mechanistic information is available to distinguish between a direct one-electron reduction to Mn(VI) and a mechanism, in which a hypomanganate is formed in a two-electron reduction followed by a rapid oxidation of the hypomanganate ion. 

The study of neuroleptic drugs becomes important because of their biological significance and selectivity towards the oxidant to yield different products. Gabapentin is prescribed usually in combination with other medications for the prevention of seizure in people suffering from seizure disorders. It is sometimes prescribed for the management of neuralgia (nerve pain). Its anticonvulsant mechanism of action is not known. Gabapentin has been prescribed off-label for the treatment of some mood disorders, anxiety, and tardive dyskinesia (a neurological syndrome caused by the long-term use of neuroleptic drugs).

Ruthenium(III) is known to be an efficient catalyst in several redox reactions particularly in alkaline medium. The mechanism of catalysis can be quite complicated due to the formation of different intermediate complexes, free radicals and different oxidation states of ruthenium. The kinetics of fast reactions between
ruthenate(VII), RuO₄⁺, and manganate(VI), i.e. MnO₄²⁻ have been studied⁴ and the reaction is presumed to proceed via an outer-sphere mechanism. The rapid exchange between MnO₄²⁻ and MnO₄⁻ has been studied in detail by a variety of techniques⁵. The uncatalysed reaction between gabapentin and permanganate in alkaline medium has been studied⁶. A micro amount of ruthenium(III) is sufficient to catalyse the reaction in alkaline medium and a variety of mechanisms are possible. Thus, in order to explore the mechanism of oxidation by permanganate ion in aqueous alkaline medium and to check the selectivity of gabapentin towards permanganate in catalysed system, we have selected ruthenium(III) as a catalyst. The present study deals with the title reaction to investigate the redox chemistry of permanganate, ruthenium(III) and gabapentin in such media and to arrive at a plausible mechanism.

EXPERIMENTAL

Materials

Stock solution of gabapentin (sd-fine chemicals) was prepared by dissolving the appropriate amount of sample in double distilled water. The solution of potassium permanganate (BDH) was prepared and standardized against oxalic acid⁷. Potassium manganate solution was prepared as described by Carrington and Symons⁸. The solution was standardized by measuring the absorbance on a Hitachi 150-20 spectrophotometer with a 1 cm quartz cell at 608 nm (ε = 1530 ± 20 dm³ mol⁻¹ cm⁻¹). The ruthenium(III) solution was prepared by dissolving a known weight of RuCl₃ (s.d.fine-chem) in 0.20 mol dm⁻³ HCl. Mercury was added to the
ruthenium(III) solution to reduce any ruthenium(IV) formed during the preparation of ruthenium(III) stock solution and was kept for a day. The ruthenium(III) concentration was assayed by EDTA titration.

All other reagents were of analytical grade and their solutions were prepared by dissolving the requisite amounts of the samples in double distilled water. NaOH and NaClO₄ were used to provide the required alkalinity and to maintain the ionic strength respectively.

**Kinetic Procedure**

All kinetic measurements were performed under pseudo-first order conditions with [Gabapentin] excess over [MnO₄⁻] at a constant ionic strength of 2.0 mol dm⁻³. The reaction was initiated by mixing previously thermostatted solutions of MnO₄⁻, and gabapentin which also contained the necessary quantities of ruthenium(III), NaOH and NaClO₄ to maintain the required alkalinity and ionic strength respectively. The temperature was uniformly maintained at 25 ± 0.1° C. The course of reaction was followed by monitoring the decrease in the absorbance of MnO₄⁻ in a 1cm quartz cell of a Hitachi model 150-20 Spectrophotometer at its absorption maximum of 526 nm as a function of time. The application of Beer's law to permanganate at 526 nm had been verified, giving ε = 2083 ± 50 dm³ mol⁻¹ cm⁻¹ (Literature ε = 2200 dm³ mol⁻¹ cm⁻¹) as studied in Chapter III (p.68). The first order rate constants (k₀) were evaluated by plots of log (Aₜ-A₀) versus time, where Aₜ and A₀ refers to absorbancies at time t and ∞ respectively. The first order plots in almost
all cases were linear to 80% completion of the reaction and $k_\epsilon$ were reproducible within ±5%.

During the course of measurements, the solution changed from violet to blue and then to green. The spectrum of the green solution was identical to that of $\text{MnO}_4^2-$. It is probable that the blue colour originated from the violet of permanganate and the green from the manganate, excluding the accumulation of hypomanganate. It is also evident that the absorbance of permanganate decreases at 526 nm whereas the absorbance of manganate increases at 608 nm (as in p.71).

The effect of dissolved oxygen on the rate of reaction was checked by preparing the reaction mixture and following the reaction in an atmosphere of nitrogen. No significant difference between the results obtained under the nitrogen and in the presence of air was observed. In view of the ubiquitous contamination of basic solutions by carbonate, the effect of carbonate on the reaction was also studied. Added carbonate had no effect on the reaction rate. However, fresh solutions were used when conducting the experiments.

A regression analysis of experimental data in order to obtain the regression coefficient, $r$ and standard deviation, $s$ of plots from the regression line was performed with a Pentium - IV personal computer.

RESULTS

Stoichiometry and product analysis

The reaction mixtures containing an excess permanganate concentration over gabapentin, and constant [Ru(III)], 1.0 mol dm$^{-3}$ NaOH and adjusted ionic strength
of 2.0 mol dm$^{-3}$ was allowed to react for 2 hrs in an inert atmosphere at 25 ± 0.1° C. After completion of the reaction, the remaining MnO$_4^-$ was then determined by spectrophotometrically. The results indicated that two moles of MnO$_4^-$ consumed by one mole of gabapentin as given by equation (1).

$$H_2NH_2C\;CH_2COOH \rightarrow HOOH_2C\;CH_2COO^- + 2MnO_4^- + 3OH^- \rightarrow H_2NH_2C\;CH_2COO^- + 2MnO_4^{2-} + NH_2OH + OH^- \; (1)$$

The products were eluted with solvent ether and organic product was submitted to spot tests. The main reaction product was identified as the 1-(Hydroxymethyl) cyclohexane acetic acid by spot test$^{10}$ for free carboxyl group and –OH. The product was also confirmed IR spectra. In gabapentin, the IR spectra$^{11}$ shows that it exists as Zwitter ion indicating the absence of –NH$_2$ and –COOH groups; there is no absorption in the usual -NH stretching i.e.3500-3300 cm$^{-1}$ but instead the bands are observed in the region of 2800-3100 cm$^{-1}$, the band due to NH$_3^+$ stretching and also there is one characteristic band at 1541 cm$^{-1}$ as assignable to NH$_3^+$ deformation vibration. In addition to this there is one more band at 1607 cm$^{-1}$ which is assignable to ionic carboxyl absorption. At 1485 cm$^{-1}$ a band is appeared which is assignable to NH$_3^+$ deformation vibration (second band). Whereas in the product, 1-(Hydroxymethyl) cyclohexane acetic acid, the presence of absorption band at 1681 cm$^{-1}$ indicates the free –COO$^-$ group which was absent in Gabapentin (due to Zwitter ion) and there is a broad valley in the region 3098-3500 cm$^{-1}$ indicating the presence of –OH group as well as carboxylic –OH group. There
is C-O stretching frequency of alcoholic –OH group (Hydroxy methyl group) at 1066 cm⁻¹ indicating the formation of –CH₂-OH group which was absent in Gabapentin and two –OH deformation bands occur at 1329-1320 cm⁻¹.

The product was also confirmed by ¹H NMR spectra. From the spectra of Gabapentin, it is observed that the two –CH₂ peaks appeared at 2.24 and 2.82 δ ppm respectively. The cyclohexyl proton appeared in the region of 1.18-1.31 δ ppm and as earlier suggested that –NH₂ and –COOH peaks are not observed because of Zwitter ion form. In 1-(Hydroxymethyl) cyclohexane acetic acid, the cyclohexyl protons appeared in the region of 1.27-1.65 δ ppm, and two –CH₂ bands appeared at down field to cyclohexyl protons i.e.2.19 - 3.16 δ ppm respectively. Another peak appeared at 4.60 δ ppm due to hydroxy methyl group. It was further observed that the 1-(Hydroxymethyl) cyclohexane acetic acid does not undergo further oxidation under prevailing kinetic conditions.

Reaction Order

As the permanganate oxidation of Gabapentin in alkaline medium proceeds with a measurable rate in absence of ruthenium(III), the catalysed reaction is understood to occur in parallel paths with contributions from both the catalysed and uncatalysed paths. Thus, the total rate constants (kₜ) is equal to the sum of the rate constants of the catalysed (kₖ) and uncatalysed (kₓ) reactions, so kₖ = kₜ – kₓ. Hence the reaction orders have been determined from the slopes of log kₖ versus log concentration plots by varying the concentrations of reductant, Ru(III) and alkali concentration while keeping the others constant.
Effect of [permanganate]

The potassium permanganate concentration was varied in the range of $5.0 \times 10^{-5}$ to $5.0 \times 10^{-4}$ mol dm$^{-3}$ and the linearity of plots of $\log [A_r-A_o]$ versus time ($r>0.9985$, $s<0.027$) indicated (Fig.III(iii)(p.75)) a reaction order of unity in $[\text{MnO}_4^-]$. This was also confirmed by variation of $[\text{MnO}_4^-]$, which did not result any change in the pseudo-first order rate constants, $k_C$ (Table VII(i)(p.192)).

Effect of [gabapentin]

The substrate, gabapentin concentration was varied in the range of $5.0 \times 10^{-4}$ to $5.0 \times 10^{-3}$ mol dm$^{-3}$ at 25° C while keeping other reactants and conditions constant (Table VII(i)(p.192). The reaction order with respect to [Gabapentin] was found to be less than unity as shown in Fig.VII(i)(p.193).

Effect of [alkali]

The effect of alkali on the reaction has been studied at constant concentrations of gabapentin and potassium permanganate and a constant ionic strength of 1.0 mol dm$^{-3}$. The rate constants increased with increasing [OH$^-$] ($r>0.9964$, $s<0.017$) (Table VII(ii)(p.194). The reaction order in [OH$^-$] was found be less than unity as shown in Fig.VII(i)(p.193)).

Effect of [ruthenium(III)]

The Ru(III) concentration was varied in the range of $5.0 \times 10^{-7}$ to $5.0 \times 10^{-6}$ at constant concentration of potassium permanganate, gabapentin and a constant ionic strength of 1.0 mol dm$^{-3}$. The order in [Ru(III)] was found to be unity (Fig.VII (ii)(p.195)).
Effect of ionic strength and relative permittivity

The effect of ionic strength was studied by varying the sodium perchlorate concentration from 0.5 to 2.5 mol dm$^{-3}$ at constant concentrations of permanganate, gabapentin, ruthenium(III) and alkali. It was found that the rate constant increases with increase in concentration of NaClO$_4$ and the plot of log $k_C$ versus $I^{1/2}$ was linear with positive slope which is given ($r>0.9938$, $s<0.015$) (Table VII (iii) (p.196))(Fig VII (iii)(p.197)).

The effect of relative permittivity ($\varepsilon_T$) was studied by varying the t-butanol-water content in the reaction mixture with all other conditions being maintained constant. Attempts to measure the relative permittivities were not successful. However, they were computed from the values of pure liquids$^{12}$. The solvent did not react with the oxidant under the experimental conditions. The rate constants, $k_C$ increased with decrease in the relative permittivities of the medium. The plot of log $k_C$ versus $1/\varepsilon_T$ was linear with positive slope as shown in Fig.VII(iii) (p.197).

Effect of initially added products

The externally added products such as manganate, hydroxyl amine and 1-(Hydroxymethyl) cyclohexane acetic acid did not show any significant effect on the rate of the reaction.
Table VII(i)

Effect of variation of $[\text{MnO}_4^-]$ and $[\text{GP}]$ on Ru(III) catalysed oxidation of Gabapentin by permanganate in aqueous alkaline medium at $25^\circ\text{C}$.

$[\text{Ru(III)}]=2.0\times10^{-7};$  \hspace{1cm} $[\text{OH}^-]=0.20;$  

$I = 1.0/\text{mol dm}^{-3}.$

<table>
<thead>
<tr>
<th>$[\text{MnO}_4^-] \times 10^4$ (mol dm$^{-3}$)</th>
<th>$[\text{Gabapentin}] \times 10^3$ (mol dm$^{-3}$)</th>
<th>$k_T \times 10^3$ (s$^{-1}$)</th>
<th>$k_a \times 10^3$ (s$^{-1}$)</th>
<th>Found</th>
<th>Calc.</th>
</tr>
</thead>
<tbody>
<tr>
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<td>1.62</td>
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<td>1.63</td>
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<td>3.03</td>
</tr>
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<td>2.0</td>
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<td>1.61</td>
<td>3.04</td>
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<td>1.63</td>
<td>3.02</td>
<td>3.03</td>
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<td>1.61</td>
<td>3.02</td>
<td>3.03</td>
</tr>
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<td>0.95</td>
</tr>
<tr>
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<td>2.57</td>
<td>0.92</td>
<td>1.65</td>
<td>1.74</td>
</tr>
<tr>
<td>2.0</td>
<td>2.0</td>
<td>4.65</td>
<td>1.61</td>
<td>3.04</td>
<td>3.04</td>
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<td>2.24</td>
<td>4.67</td>
<td>4.81</td>
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<td>5.0</td>
<td>8.57</td>
<td>2.54</td>
<td>6.03</td>
<td>5.43</td>
</tr>
</tbody>
</table>
Figure VII (i)
Order plots with respect to [Gabapentin] and [OH'] on the ruthenium(III) catalysed catalysed oxidation of gabapentin by alkaline permanganate at 25° C and I=1.0 mol dm⁻³. (Conditions as in Table (VII)(i)(p. 192)).
**Table VII(ii)**

Effect of variation of $[\text{OH}^-]$ and Ru(III) catalysed oxidation of gabapentin by permanganate in aqueous alkaline medium at 25° C.

$[\text{Ru(III)}]=2.0 \times 10^{-7}$; $[\text{OH}^-]=0.20$; $I = 1.0$ /mol dm$^{-3}$.

<table>
<thead>
<tr>
<th>$[\text{OH}^-]$ (mol dm$^{-3}$)</th>
<th>$[\text{Ru(III)}] \times 10^7$ (mol dm$^{-3}$)</th>
<th>$k_T \times 10^3$ (s$^{-1}$)</th>
<th>$k_u \times 10^4$ (s$^{-1}$)</th>
<th>$k_C \times 10^3$ (s$^{-1}$)</th>
<th>Found</th>
<th>Calc</th>
</tr>
</thead>
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<td>3.04</td>
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<td>4.41</td>
<td>4.50</td>
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<tr>
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<td>7.79</td>
<td>2.81</td>
<td>4.98</td>
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<td>0.71</td>
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<td>3.02</td>
<td>1.61</td>
<td>1.41</td>
<td>1.51</td>
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<td>2.0</td>
<td>4.65</td>
<td>1.61</td>
<td>3.04</td>
<td>3.03</td>
<td></td>
</tr>
<tr>
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<td>7.74</td>
<td>1.61</td>
<td>6.13</td>
<td>6.06</td>
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</tr>
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<td>5.0</td>
<td>10.0</td>
<td>1.61</td>
<td>8.41</td>
<td>7.58</td>
<td></td>
</tr>
</tbody>
</table>
Figure VII (ii)

Order plot with respect to [Ru(III)] on the Ru(III) catalysed oxidation of gabapentin by alkaline permanganate at 25 °C.
Table VII (iii)

Effect of variation of ionic strength (I) and solvent polarity (γT) on the Ru(III) catalysed oxidation of Gabapentin by permanganate in aqueous alkaline medium at 25° C.

\[
\begin{align*}
[MnO_4^-] &= 2.0 \times 10^{-4}; \\
[Gabapentin] &= 2.0 \times 10^{-3}; \\
[Ru(III)] &= 2.0 \times 10^{-7}; \\
[OH^+] &= 0.20 /\text{mol dm}^{-3}. \\
\end{align*}
\]

<table>
<thead>
<tr>
<th>I (mol dm(^{-3}))</th>
<th>(k_C \times 10^3) (s(^{-1}))</th>
<th>% of (\varepsilon_T)</th>
<th>(k_C \times 10^3) (s(^{-1}))</th>
</tr>
</thead>
<tbody>
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<td>0.5</td>
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<td>5</td>
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<tr>
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<td>10</td>
<td>71.85</td>
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<tr>
<td>1.5</td>
<td>3.74</td>
<td>15</td>
<td>68.36</td>
</tr>
<tr>
<td>2.0</td>
<td>4.79</td>
<td>20</td>
<td>64.87</td>
</tr>
<tr>
<td>2.5</td>
<td>6.23</td>
<td>25</td>
<td>61.60</td>
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</table>

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Figure VII (iii)

Effect of variation of ionic strength (I) and solvent polarity ($\varepsilon_T$) on the Ru(III) catalysed oxidation of gabapentin by permanganate in aqueous alkaline medium at 25° C. (Conditions as in Table VII(iii) (p.196)
Polymerisation study

The reaction mixture was mixed with acrylonitrile monomer and kept for 2 hrs in an inert atmosphere. On diluting with methanol a white precipitate was formed, indicating the intervention of free radicals in the reaction. The blank experiments of either MnO₄⁻ or gabapentin alone with acrylonitrile did not induce polymerization under the same conditions as those induced with reaction mixtures. Initially added acrylonitrile decreases the rate indicating the free radical intervention, which is the case in earlier work.¹³

Effect of temperature

The rate of the reaction was measured at four different temperatures with varying [OH⁻], keeping other conditions constant. The rate was found to increase with increase in temperature. The rate constants, k of the slow step of Scheme 1 were obtained from the intercept of the plots of [Ru(III)]/kc versus 1/[GP] (r ≥ 0.976 & s ≤ 0.0064) for different temperatures. The values of kc at different temperatures are tabulated in Table VII(iv)(a)(p.199). The energy of activation corresponding to these constants were evaluated from the Arrhenius plot of log k(Y* ca) versus 1/T (Fig.VII(iv)(p.201) (r ≥ 0.948 & s ≤ 0.00592) and other activation parameters with respective slow step were calculated (as shown in chapter II(p.47)) and are tabulated in Table VII(iv) (p.199). These values are comparable with the uncatalysed reaction.
Table III (iv)

(a) Effect of temperature on the Ru(III) catalysed permanganate oxidation of Gabapentin in an aqueous alkaline medium at 25 °C.

\[ [\text{L-proline}] = 2.0 \times 10^{-3}; \quad [\text{OH}^-] = 0.20; \]

\[ [\text{MnO}_4^-] = 2.0 \times 10^{-4}; \quad [\text{Ru(III)}] = 2.0 \times 10^{-7}; \]

\[ I = 1.0 /\text{mol dm}^{-3}. \]

<table>
<thead>
<tr>
<th>Temp (K)</th>
<th>(k \times 10^{-4})</th>
<th>(\log k)</th>
<th>(1/T \times 10^3)</th>
<th>(Y^*_{\text{calc}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>298</td>
<td>5.75</td>
<td>4.759</td>
<td>3.35</td>
<td>4.772</td>
</tr>
<tr>
<td>303</td>
<td>6.05</td>
<td>4.782</td>
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<td>4.802</td>
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<tr>
<td>308</td>
<td>6.69</td>
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<tr>
<td>313</td>
<td>7.36</td>
<td>4.867</td>
<td>3.19</td>
<td>4.866</td>
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</table>

(b) Thermodynamic activation parameters with respect to slow step of Scheme 1.

<table>
<thead>
<tr>
<th>Activation parameters</th>
<th>Values</th>
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</thead>
<tbody>
<tr>
<td>(E_a) (kJ mol(^{-1}))</td>
<td>13.0 ± 0.5</td>
</tr>
<tr>
<td>(\Delta H^#) (kJ mol(^{-1}))</td>
<td>11.0 ± 0.5</td>
</tr>
<tr>
<td>(\Delta S^#) (J K(^{-1})mol(^{-1}))</td>
<td>-299 ± 10</td>
</tr>
<tr>
<td>(\Delta G^#) (kJ mol(^{-1}))</td>
<td>102 ± 60</td>
</tr>
</tbody>
</table>
Fig. VII (iv)

Effect of temperature on the Ru(III) catalysed oxidation of permanganate by Gabapentin in aqueous alkaline medium at 25 °C.

(Conditions as in Table VII(iv) (p.199)
DISCUSSION

Permanganate ion, MnO₄⁻, is a powerful oxidant in an aqueous alkaline medium. As it exhibits many oxidation states, the stoichiometric results and pH of the reaction media play an important role. Under the prevailing experimental conditions at pH >12, the reduction product of Mn(VII) is stable and further reduction of Mn(VI) might be stopped¹⁴. The Diode Array Rapid Scan Spectrophotometric (DARSS) studies have shown that at pH > 12, the product of Mn(VII) is Mn(VI) and no further reduction was observed as reported¹⁵ by Simandi et al. However, on prolonged standing, the green Mn(VI) is reduced to Mn(IV) under our experimental conditions.

The permanganate in alkaline medium exhibits various oxidation states, such as Mn(VII), Mn(V) and Mn(VI). The colour of the solution changed from violet to blue and further to green excluding the accumulation of hypomanganate. The violet colour originates from pink of permanganate and blue from hypomanganate is observed during the course of the reaction. The colour change of KMnO₄ solution from violet Mn(VII) ion to dark green Mn(VI) ion through blue Mn(V) ion has been observed. It is interesting to identify the probable species of ruthenium(III) chloride in alkaline medium. Electronic spectral studies¹⁶ have confirmed that ruthenium(III)chloride exists in hydrated form as [Ru(H₂O)₆]³⁺. In the present study it is quite probable that the species [Ru(H₂O)₅OH]²⁺ might assume the general form [Ru(III)(OH)x]³⁻. The value of x would always be less than six because there are no definite reports of any hexahydroxy species of ruthenium. The remainder of the coordination sphere will be filled by
water molecule. Hence under the experimental conditions $[\text{OH}^-] > [\text{Ru}^{\text{III}}]$, $\text{Ru}^{\text{III}}$ is mostly present as the hydroxylated species $[\text{Ru}(\text{H}_2\text{O})_2\text{OH}]^{2+}$.

The reaction between permanganate and Gabapentin in alkaline medium has a stoichiometry of 2:1 with a first order dependence on the $[\text{MnO}_4^-]$ and $[\text{Ru(III)}]$ and less than unit order dependence on both the [alkali] and [Gabapentin]. No effect of added products such as 1-(Hydroxymethyl) cyclohexane acetic acid and ammonium hydroxide was observed. It is known that Gabapentin exists in the form of Zwitter ion in aqueous medium. In acidic medium, it exists in the protonated form, whereas in basic medium, it is fully in the deprotonated form according to the following equilibria.

Gabapentin in the deprotonated form reacts with ruthenium(III) species to form a complex (C). This complex (C) reacts with permanganate species in a slow step to form a free radical derived from Gabapentin which further reacts with another permanganate species in a fast step to yield the products. The experimental results can be accommodated in Scheme 1 as given below.
The probable structure of the complex (C) is

Spectral evidence for such a catalyst-substrate complex was obtained from the UV-vis, spectra of both ruthenium (III) and ruthenium(III) - gabapentin mixtures, in which a bathochromic shift of ruthenium(III) from 219 to 225 nm and hyperchromicity was observed at 225 nm. This is also evident from the plot of $1/k_c$ versus $1/[GP]$ (Michaelis-Menten plot) ($r \geq 0.968$ & $s \leq 0.00582$) which shows a
straight line with non zero intercept (Fig. VII (v)(p.207)). Such type of substrate-
catalyst complex formation has also been observed in other studies\textsuperscript{18}. The observed
modest enthalpy of activation, relatively low value of the entropy of activation and
higher rate constant for the slow step of the mechanism, indicate that oxidation
presumably occurs by an inner-sphere mechanism. This conclusion is supported by
earlier work\textsuperscript{19}. Since Scheme 1 is in accordance with generally well accepted
principle of non-complementary oxidations taking place in a sequence of one-
electron steps, the reaction would involve a radical intermediate. Since
permanganate is a one electron oxidant in alkaline medium, the reaction between
substrate and oxidant would give rise to a radical intermediate. Free radical
scavenging experiment revealed such a possibility. This type of radical intervention
in the oxidation of amino acids has also been observed earlier\textsuperscript{20}. According to
Scheme 1,
\begin{align*}
\text{rate}_{\text{cat}} &= \text{rate}_{\text{total}} - \text{rate}_{\text{uncat}} \\
\text{Rate}_{\text{cat}} &= k [C][\text{MnO}_4^-] \\
&= k K_1 K_2 [\text{GP}]_t [\text{MnO}_4^-]_f [\text{OH}']_f [\text{Ru(III)}]_f
\end{align*}
(2)
Total concentration of gabapentin, \([\text{GP}]_t\), is given by (Subscripts \(t\) and \(f\) stand for
total and free respectively)
\begin{align*}
[\text{GP}]_t &= [\text{GP}]_t + [\text{GP}']_t + [C] \\
&= [\text{GP}]_t + K_2 [\text{Ru(III)}][\text{GP}] + K_1 [\text{OH}'][\text{GP}] + K_1 \\
&= [\text{GP}]_t + K_1 [\text{OH}'][\text{GP}] + K_1 K_2 [\text{Ru(III)}][\text{OH}'][\text{GP}] \\
&= [\text{GP}]_t \{1 + K_1 [\text{OH}'] + K_1 K_2 [\text{OH}'][\text{Ru(III)}]\}
\end{align*}
Therefore, \[ [\text{GP}]_f = \frac{[\text{GP}]_t}{1 + K_1 [\text{OH}^-] + K_1 K_2 [\text{OH}^-][\text{Ru(III)}]} \] (3)

Similarly, \[ [\text{OH}^-]_f = \frac{[\text{OH}^-]_t}{1 + K_1 [\text{GP}] + K_1 K_2 [\text{Ru(III)}][\text{GP}]} \] (4)
\[ [\text{Ru(III)}]_f = \frac{[\text{Ru(III)}]_t}{1 + K_1 K_2 [\text{OH}^-][\text{GP}]} \] (5)

Substituting equation (3), (4) and (5) in (2), we get
\[
\text{Rate}_{\text{cat}} = \frac{k K_1 K_2 [\text{GP}] [\text{MnO}_4^-] [\text{Ru(III)}] [\text{OH}^-]}{(1+K_1 [\text{OH}^-] + K_1 K_2 [\text{OH}^-][\text{Ru(III)}])(1+K_1 [\text{GP}] + K_1 K_2 [\text{Ru(III)}][\text{GP}])(1+K_1 K_2 [\text{OH}^-][\text{GP}] )}
\] (6)

The terms \((K_1 K_2 [\text{OH}^-][\text{Ru(III)}])\) and \((1+K_1 [\text{GP}] + K_1 K_2 [\text{Ru(III)}][\text{GP}] )\) in the denominator of equation (6) approximate to unity in view of low concentration of gabapentin(GP) and ruthenium (III) used. (omitting the subscripts t and f), in terms of rate constants,
\[
k_C = k_T - k_u = \frac{k K_1 K_2 [\text{GP}][\text{Ru (III)}][\text{OH}^-]}{(1+K_1 [\text{OH}^-])(1+K_1 K_2 [\text{GP}][\text{OH}^-])}
\]
\[
k_C = \frac{k K_1 K_2 [\text{GP}][\text{Ru(III)}][\text{OH}^-]}{1 + K_1 K_2 [\text{GP}][\text{OH}^-] + K_1 [\text{OH}^-] + K_1^2 K_2 [\text{OH}^-]^2 [\text{GP}]}
\]

Neglecting square term in view of low value compared to unity, we get
\[
k_C = \frac{k K_1 K_2 [\text{GP}][\text{Ru(III)}][\text{OH}^-]}{1 + K_1 K_2 [\text{GP}][\text{OH}^-] + K_1 [\text{OH}^-]}
\] (7)
The above equation (7) can be rearranged to the following form which is used for the verification of the rate law.

\[
\frac{[\text{Ru(III)}]}{k_c} = \frac{1}{k K_1 K_2 [\text{GP}][\text{OH}']} + \frac{1}{k K_2 [\text{GP}]} + \frac{1}{k} \quad (8)
\]

According to equation (8), the plots of \([\text{Ru(III)}]/k_c\) versus \(1/[\text{GP}]\) \((r > 0.9978, s \leq 0.048)\) and \([\text{Ru(III)}]/k_c\) versus \(1/[\text{OH}']\) \((r > 0.9823, s \leq 0.049)\) should be linear with non-zero intercept, which is verified in Fig. VII(v)(p.207). The slopes and intercepts of such plots lead to the values of \(k, K_1\) and \(K_2\) at 25°C of \(5.75 \pm 0.2 \times 10^4\) dm\(^3\) mol\(^{-1}\) s\(^{-1}\), \(3.43 \pm 0.1\) dm\(^3\) mol\(^{-1}\) and \(4.40 \pm 0.06 \times 10^2\) dm\(^3\) mol\(^{-1}\) respectively. Using these values, the rate constants under different experimental conditions were calculated by equation (7) and compared with experimental data. There is a good agreement between them, which supports the Scheme 1. The value of \(K_1\) is in good agreement with earlier work\(^6\).

The effect of ionic strength on the rate can be understood essentially on the basis of ionic species as in Scheme 1. The effect of solvent on the reaction kinetics has been described detail in the literature. In the present study the rate determining step involves the reaction between two ions and so equation (9) is applicable:

\[
\ln k = \ln k_{\infty} - Z_A Z_B e^2/k_B T r_{AB} \in_T \quad (9)
\]

where \(k_{\infty}\) is the rate constant in a medium of infinite dielectric constant, \(r_{AB}\) is the sum of the ionic radii and \(Z_A\) and \(Z_B\) are the charges on the two ions and \(\in_T\) is the dielectric constant of the medium. The observed linear plot of log \(k_{\text{obs}}\) vs. \(1/\in_T\) with
Figure VII (v)

Verification of rate law (7) in the form of (8)

(Condition as in Table VII (i)(ii)(p.192);(ii)(p.194))
positive slope (Fig. VII(iii)(p. 197)) is in accordance with equation (9) as $Z_A$ and $Z_B$ have opposite charges (Scheme 1)(p.203). The values of $\Delta H^\circ$ and $\Delta S^\circ$ were both favourable for electron transfer process. The less negative value of $\Delta S^\circ$, suggests the complex is less ordered than the reactants.

The thermodynamic quantities for the first equilibrium step in Scheme 1 and activation parameters for the limiting step in Scheme 1 can be evaluated as follows: The hydroxyl ion concentration as in Table VII(ii)(p.194) was varied at four different temperatures and the $K_1$ value was determined at each temperature. The values of $K_1$ (dm$^3$ mol$^{-1}$) were obtained as 3.43, 3.81, 4.34 and 4.95 at 25, 30, 35 and 40$^\circ$ C respectively. A Vant Hoffs plot was made for the variation of $K_1$ with temperature (i.e., log $K_1$ versus $1/T$) ($r > 0.9835$, $S<0.041$) and the values of the enthalpy of the reaction, $\Delta H$, entropy of the reaction, $\Delta S$, and free energy reaction, $\Delta G$, were calculated as $19.08$ k J mol$^{-1}$, $17.7$ JK$^{-1}$ mol$^{-1}$ and $-13.8$ k J mol$^{-1}$, respectively. A comparison of these values with those obtained for the slow step of the reaction shows that these values mainly refer to the rate limiting step, supporting the fact that the reaction before the rate determining step is slow and involves more activation energy.$^{21}$

**Catalytic Effect**

The activation parameters are compared with the uncatalysed reaction.$^6$ The difference in the activation parameters for the catalysed and uncatalysed reactions, explains the catalytic effect on reaction. The catalyst, ruthenium(III) forms a complex with gabapentin which shows more
reducing property than gabapentin itself and hence the catalyst, Ru(III) lowers the energy of activation.

**Importance of the chapter VII**

It is interesting that the oxidant species \([\text{MnO}_4^-]\) requires a pH > 12, below which the system becomes disturbed and the reaction will proceed further to give a reduced product of the oxidant as Mn(IV), which slowly develops yellow turbidity. Hence, it becomes apparent that in carrying out this reaction the role of pH in a reaction medium is crucial. It is also noteworthy that under the conditions studied the reaction occurs in two successive one-electron reductions (Scheme 1) rather than two-electron in a single step. A micro amount of Ru(III) is sufficient to catalyse the title reaction. The description of the mechanism is consistent with all the experimental evidence including both kinetic and product studies.
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