Hexacyanoferrate(III), ([Fe(CN)₆]³⁻) has been widely used to oxidise numerous organic and inorganic compounds in alkaline media. The authors¹,² have suggested that alkaline hexacyanoferrate(III) ion simply acts as an electron abstracting reagent in redox reactions. However, Speakman and Waters³ have suggested different paths of oxidation of aldehydes, ketones and nitroparaffins. Singh and co-workers⁴,⁵ while discussing the oxidations of formaldehyde, acetone and ethyl methyl ketone have suggested that the oxidation takes place via an electron transfer process resulting in the formation of a free radical intermediate.

4-(2-Hydroxy-3-isopropylaminopropoxy) phenylacetamide, commercially known as atenolol (ATN), a β-adrenoreceptor blocking agent is used as antihypertensive drug⁶. It is also used for anti-angina treatment to relieve symptoms, improve tolerance and as an anti-arrhythmic to help regulate heartbeat and infections. It is also used in management of alcohol withdrawal, in anxiety states, migraine prophylaxis, hyperthyroidism and tremor. The derivative of oxidation product of atenolol finds its importance in biological systems such as plant growth hormones, herbicides, etc. A literature survey reveals that there is no report on the kinetics of oxidation of atenolol by any oxidants, except in two cases⁷,⁸. Thus the study of ATN becomes important because of its biological
significance and selectivity towards the oxidants. In view of the lack of literature on the oxidation of atenolol by $[\text{Fe(CN)}_6]^{3-}$, and in order to explore the mechanistic aspects of $[\text{Fe(CN)}_6]^{3-}$ oxidation in alkaline medium, we have chosen atenolol as a substrate. The present study deals with the title reaction to investigate the redox chemistry of $[\text{Fe(CN)}_6]^{3-}$ in such media, and to arrive at a suitable mechanism for the oxidation of atenolol by alkaline hexacyanoferrate (III) ions on the basis of kinetic results.

**EXPERIMENTAL**

**Materials**

All chemicals used were of analytical reagent grade. Solution of atenolol (S.S. Antibiotics Pvt.Ltd, Aurangabad, India) was prepared by dissolving appropriate amount of recrystallised sample in double distilled water. Its IR and NMR spectra checked the purity of the substance. Stock solution of the oxidant, hexacyanoferrate(III) was prepared by dissolving K$_3$Fe(CN)$_6$ (BDH) in double distilled water and standardized the solution iodometrically$^9$. Hexacyanoferrate(II) solution was prepared by dissolving known amount of K$_4$Fe(CN)$_6$ (BDH) in water. Sodium hydroxide (Merck) and sodium perchlorate (BDH) were used to provide the required alkalinity and to maintain ionic strength, respectively.

**Kinetic procedure**

All kinetic measurements were performed under pseudo first-order conditions where [atenolol] was always in excess over $[\text{Fe(CN)}_6]^{3-}$ at a constant ionic strength of 1.50 mol dm$^{-3}$ in alkaline medium at a constant temperature of 25 ±
0.1 °C. The reaction was initiated by mixing previously thermostated solutions of \([\text{Fe(CN)}_6]^{3-}\) and atenolol, which also contained the required amount of NaOH and NaClO₄. The progress of reaction was followed by measuring the absorbance of \([\text{Fe(CN)}_6]^{3-}\) in the reaction solution in a 1cm quartz cell of thermostatted Varian Cary 50 Bio UV-vis spectrophotometer at its absorption maximum, at 420 nm, as a function of time, where the other constituents of the reaction mixture do not absorb significantly. The application of Beer's law for hexacyanoferrate(III) at 420nm, under the reaction conditions had earlier been verified giving \(\varepsilon = 1060 \pm 20\) dm³ mol⁻¹ cm⁻¹ as shown in Fig.VI(i)(p.158). Pseudo first-order rate constants, were obtained from the plots of log[Fe(CN)₆]³⁻ versus time, the plots were linear up to 75% completion of the reaction in alkaline medium and the \(k_{\text{obs}}\) values were reproducible within ±5% and deviation from linearity, was also observed due to retarding effect of one of the products. An example run is given in Table VI(i) (p.159).

In view of the modest concentrations of alkali used in the reaction medium, attention was also given to the effect of the surface of the reaction vessels on the kinetics. Use of polythene / acrylic ware and quartz or polyacrylate cells gave the same results as glass vessels and cells indicating that the surfaces play no important role in the reaction rate.

The effect of dissolved oxygen on the rate of the 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 nitrogen
Figure VI (i)

Verification of Beer's law for $[\text{Fe(CN)}_6]^{3-}$ at 420 nm in 1.0 mol dm$^{-3}$ NaOH.
Table VI (i)

Example run for the oxidation of atenolol by hexacyanoferrate(III) in aqueous alkaline medium at 25 °C

\[
[\text{Fe(CN)}_6^{3-}] = 4.0 \times 10^{-4}; \quad \text{[ATN]} = 8.0 \times 10^{-3};
\]

\[
[\text{OH}^-] = 1.0; \quad I = 1.50 \text{ mol dm}^{-3}.
\]

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Optical density A</th>
<th>( \log A )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>0.421</td>
<td>-0.375</td>
</tr>
<tr>
<td>1.0</td>
<td>0.367</td>
<td>-0.435</td>
</tr>
<tr>
<td>2.0</td>
<td>0.325</td>
<td>-0.488</td>
</tr>
<tr>
<td>3.0</td>
<td>0.281</td>
<td>-0.551</td>
</tr>
<tr>
<td>4.0</td>
<td>0.255</td>
<td>-0.593</td>
</tr>
<tr>
<td>5.0</td>
<td>0.233</td>
<td>-0.632</td>
</tr>
<tr>
<td>6.0</td>
<td>0.207</td>
<td>-0.684</td>
</tr>
<tr>
<td>7.0</td>
<td>0.192</td>
<td>-0.716</td>
</tr>
<tr>
<td>8.0</td>
<td>0.176</td>
<td>-0.754</td>
</tr>
<tr>
<td>9.0</td>
<td>0.158</td>
<td>-0.801</td>
</tr>
<tr>
<td>10.0</td>
<td>0.143</td>
<td>-0.844</td>
</tr>
</tbody>
</table>
and in presence of air was observed. In view of the ubiquitous contamination of carbonate in the basic solutions. Added carbonate up to $1.0 \times 10^{-3} \text{ mol dm}^{-3}$ showed no effect on the reaction rate. However, fresh solutions were used while performing the experiments.

In alkaline medium during the progress of the reaction, the color of the solution changed from yellow to almost colorless, which is verified by titration for $[\text{Fe(CN)}_6]^{3-}$. 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

Five different sets of reaction mixtures containing different concentrations of atenolol and $[\text{Fe(CN)}_6]^{3-}$ with a constant amount of ionic strength ($0.80 \text{ mol dm}^{-3}$) and alkali ($0.20 \text{ mol dm}^{-3}$) were kept for ca.2h at $25 \pm 0.1^\circ \text{C}$ in a $\text{N}_2$ atmosphere. When $[\text{Fe(CN)}_6]^{3-}$ was higher than atenolol, the unreacted $[\text{Fe(CN)}_6]^{3-}$ was found by measuring the absorbance at 420 nm. The results indicated that two moles of $[\text{Fe(CN)}_6]^{3-}$ consumed one mole of atenolol as shown in equation (1)(Table VI(ii) (p.163)).

$$\text{O-CH}_2\text{-CH-CH}_2\text{-NH-CHMe}_2 + 2 \text{Fe(CN)}_3^{3-} + 2 \text{OH}^- \rightarrow \text{O-CH}_2\text{-CO}_2\text{H} + 2\text{Fe(CN)}_6^{4+} + \text{NH}_4^+$$

$$+ \text{CH}_3\text{-NH-CHMe}_2 + \text{H}_2\text{O}$$
The reaction product, 4-carboxy-methoxy-phenyl acetic acid, was extracted with ether and recrystallised from aqueous alcohol and the purity was checked by HPLC. It was identified as 4-carboxy methoxy phenyl acetic acid by its I.R. spectrum, which showed a band at (v) 1690 cm\(^{-1}\) due to >C=O stretching and a broad band at 2845 cm\(^{-1}\) due to O-H stretching. 4-carboxy methoxy phenyl acetic acid was further characterized by \(^1\)H NMR spectrum (DMSO), showed chemical shifts (\(\delta\)) at 10 ppm(s, due to carboxylic OH, 2H), 7.7 ppm (s, at due to aromatic,2H(a)).6.9ppm (s, at due to aromatic, 2H(b)), 4.6ppm(s, due to methylene, 2H(c)),3.5ppm (s, due to methylene, 2H(d)) respectively and Mass spectra ESI technique (solvents: Acetonitrile + water + ammonium acetate) (M\(^+\) +17) (ammoniated) 228 and (M\(^+\) ) m/z 211. Ammonia was identified by using Nessler’s reagent. N- isopropyl methylamine, which is soluble in water, was identified by spot test. It was observed that the 4-carboxy methoxy phenyl acetic acid and N-isopropyl methyl amine do not undergo further oxidation under the present kinetic conditions.

The spectral changes during the reaction are shown in Fig.VI(ii)(p.162).It is evident that [Fe(CN)\(_6\)]\(^{3-}\) decreases at 420 nm.

**Reaction Order**

The reaction orders were determined from the slopes of log \(k_{obs}\) versus log (concentration) plots by varying the concentration of reductant and alkali in turn, while keeping others constant.
Figure VI (ii)

Spectral changes occurring in the oxidation of atenolol by hexacyanoferrate(III) in aqueous alkaline medium at 25 °C

$[\text{Fe(CN)}_6]^{3-} = 4.0 \times 10^{-4}$, $[\text{ATN}] = 8.0 \times 10^{-3}$, $[\text{OH}^-] = 1.0$ and $I = 1.50/\text{mol dm}^{-3}$ with scanning time interval=1 min.)
Table VI (ii)
Stoichiometry of oxidation of atenolol by hexacyanoferrate (III) in aqueous alkaline medium at 25 °C

\[ [\text{OH}^-] = 1.0; \quad I = 1.50 / \text{mol dm}^{-3}. \]

<table>
<thead>
<tr>
<th>Taken</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\text{Fe(CN)}_6^3-] \times 10^4) (mol dm(^{-3}))</td>
<td>([\text{ATN}] \times 10^4) (mol dm(^{-3}))</td>
</tr>
<tr>
<td>4.0</td>
<td>2.0</td>
</tr>
<tr>
<td>5.0</td>
<td>2.0</td>
</tr>
<tr>
<td>6.0</td>
<td>1.0</td>
</tr>
<tr>
<td>8.0</td>
<td>2.0</td>
</tr>
<tr>
<td>8.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>
Effect of [Hexacyanoferrate(III)]

The hexacyanoferrate(III) concentration was varied in the $1.0 \times 10^{-4}$ to $1.0 \times 10^{-3}$ mol dm$^{-3}$ range and linearity of plots of log [Abs] versus time ($r>0.9913$, $s<0.029$) up to 75% of the completion of the reaction (Fig.VI(iii)(p.166)) indicate the order in $[\text{Fe(CN)}_6]^{3-}$ as unity. This result was also confirmed by varying the $[\text{Fe(CN)}_6]^{3-}$ which did not show any change in pseudo first -order rate constants as given in Table VI(iii)(p.165) ($r>0.9834$, $s<0.013$).

Effect of [Atenolol]

The substrate, atenolol was varied in the range of $1.0 \times 10^{-3}$ to $1.0 \times 10^{-2}$ mol dm$^{-3}$ at $25 \degree C$ keeping all other reactants concentrations and conditions constant as given in Table VI(iv)(p.167). The $k_{obs}$ values were increased with increase in concentration of atenolol indicating an apparent less than unit order dependence on [atenolol] (Fig.VI(iv)(p.168))($r \geq 0.989$, $s \leq 0.0046$).

Effect of [alkali]

The effect of alkali on the reaction has been studied at constant concentrations of atenolol and $[\text{Fe(CN)}_6]^{3-}$ and a constant ionic strength of $1.50$ mol dm$^{-3}$. The rate constants increased with increasing $[\text{OH}^-]$ ($r>0.9568$, $s<0.016$) (Table VI(iv)(p.167), Fig.VI(iv)(p.168).

Effect of ionic strength and relative permittivity

The effect of ionic strength was studied by varying the [NaClO$_4$] in the reaction mixture. The ionic strength of the reaction medium was varied from 1.0 to 2.0 mol dm$^{-3}$ at constant $[[\text{Fe(CN)}_6]^{3-}$, [atenolol] and [alkali] as given in Table VI.
Table VI(iii)

Effect of variation of $[\text{Fe(CN)}_6]^{3-}$ on the oxidation of atenolol at 25° C.

$[\text{ATN}] = 4.0 \times 10^{-3}; \quad [\text{OH}^-] = 1.0;$

$I = 1.50 \text{ mole dm}^{-3}.$

<table>
<thead>
<tr>
<th>$[\text{Fe(CN)}_6]^{3-} \times 10^4$ (mole dm$^{-3}$)</th>
<th>$k_{\text{obs}} \times 10^3$, (s$^{-1}$)</th>
<th>Found</th>
<th>calc</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>1.72</td>
<td>1.64</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>1.74</td>
<td>1.64</td>
<td></td>
</tr>
<tr>
<td>4.0</td>
<td>1.70</td>
<td>1.64</td>
<td></td>
</tr>
<tr>
<td>6.0</td>
<td>1.73</td>
<td>1.64</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1.74</td>
<td>1.64</td>
<td></td>
</tr>
</tbody>
</table>
Figure VI (iii)

First order plots of aqueous alkaline hexacyanoferrate(III) oxidation of atenolol at 25 °C

$[\text{Fe(CN)}_6^{3-}] \times 10^4$: (1) 1.0, (2) 2.0, (3) 4.0, (4) 6.0, (5) 10 /mol dm$^3$

(Conditions as in Table VI (iii) (p. 165)
Effect of variation of [atenolol] and [OH\(^-\)] on the oxidation of atenolol by alkaline hexacyanoferrate(III) at 25º C.

\([\text{Fe(CN)}_{6}]^{3-} = 8.0 \times 10^{-4}; \quad \text{I} = 1.50 \text{ /mol dm}^{-3}\]

<table>
<thead>
<tr>
<th>[ATN] (\times 10^3) (mol dm(^{-3}))</th>
<th>[OH(^-)] (mol dm(^{-3}))</th>
<th>(k_{\text{obs}} \times 10^3) (s(^{-1}))</th>
<th>Found</th>
<th>Calc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>1.0</td>
<td>0.49</td>
<td>0.45</td>
<td></td>
</tr>
<tr>
<td>3.0</td>
<td>1.0</td>
<td>1.05</td>
<td>1.01</td>
<td></td>
</tr>
<tr>
<td>6.0</td>
<td>1.0</td>
<td>1.50</td>
<td>1.46</td>
<td></td>
</tr>
<tr>
<td>8.0</td>
<td>1.0</td>
<td>1.70</td>
<td>1.64</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1.0</td>
<td>1.90</td>
<td>1.78</td>
<td></td>
</tr>
<tr>
<td>8.0</td>
<td>0.1</td>
<td>0.39</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td>8.0</td>
<td>0.3</td>
<td>0.92</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>8.0</td>
<td>0.6</td>
<td>1.25</td>
<td>1.33</td>
<td></td>
</tr>
<tr>
<td>8.0</td>
<td>0.8</td>
<td>1.52</td>
<td>1.51</td>
<td></td>
</tr>
<tr>
<td>8.0</td>
<td>1.0</td>
<td>1.70</td>
<td>1.64</td>
<td></td>
</tr>
</tbody>
</table>
Order plots with respect to [atenolol] and [OH\textsuperscript{-}] on the oxidation of atenolol by alkaline hexacyanoferrate(III) at 25\textdegree C and I=1.50 mol dm\textsuperscript{-3}.

(Conditions as in Table (VI)(iv)(p.167)).
It was found that ionic strength had no effect on reaction rate. The relative permittivity ($\varepsilon_T$) effect on the reaction was studied by varying the solvent polarity using different quantities of t-butyl alcohol–water content in solvent (water) from 5 to 25% in the reaction mixture with all other conditions being constant at a constant concentration for other reactants. Attempts to measure the relative permittivity ($\varepsilon_T$) were unsuccessful. However, they were computed from the values of pure liquids. There was no reaction of the solvent with the oxidant under the experimental conditions used. The increase in the t-butanol content in the reaction medium leads to the increase in the rate of reaction. The plot of log $k_{obs}$ versus $1/\varepsilon_T$ was linear with negative slope, which is given in Fig. VI(v) (p. 171). ($r \geq 0.976$, $s \leq 0.0054$).

Effect of initially added products

Initially added product, i.e., K$_4$Fe(CN)$_6$ [Fe(CN)$_6$$^{4-}$] in the range, 1.0 x10$^{-4}$ mol dm$^{-3}$ to 1.5 x10$^{-3}$ mol dm$^{-3}$ keeping other conditions constant, has been studied. As the initial concentration of [Fe(CN)$_6$$^{4-}$] increased, the rate progressively decreased. This illustrates the retarding nature of the product. Another product, 4-carboxy-methoxy-phenyl acetic acid did not show any significant effect on the rate of reaction.

Polymerization study

The reaction mixture containing acrylonitrile was kept for 24 h in an inert atmosphere. On diluting the reaction mixture with methanol, we obtained white
Table VI (v)

Effect of variation of ionic strength (I) and solvent polarity ($\epsilon_T$) on the oxidation of atenolol by aqueous alkaline hexacyanoferrate(III) at 25 °C.

$[\text{Fe(CN)}_6^{3-}] = 4.0 \times 10^{-4}$; $[\text{ATN}] = 8.0 \times 10^{-3}$; $[\text{OH}^-] = 1.0$;

\[ I = 1.50 /\text{mol dm}^{-3}; \]

<table>
<thead>
<tr>
<th>$I$ (mol dm$^{-3}$)</th>
<th>$k_{\text{obs}} \times 10^3$ (s$^{-1}$)</th>
<th>$%$ of t-butanol-water</th>
<th>$\epsilon_T$</th>
<th>$k_{\text{obs}} \times 10^3$ (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>1.76</td>
<td>5</td>
<td>75.12</td>
<td>1.90</td>
</tr>
<tr>
<td>1.2</td>
<td>1.76</td>
<td>10</td>
<td>71.74</td>
<td>1.80</td>
</tr>
<tr>
<td>1.5</td>
<td>1.75</td>
<td>15</td>
<td>67.99</td>
<td>1.71</td>
</tr>
<tr>
<td>1.6</td>
<td>1.74</td>
<td>20</td>
<td>64.99</td>
<td>1.60</td>
</tr>
<tr>
<td>2.0</td>
<td>1.73</td>
<td>25</td>
<td>60.36</td>
<td>1.50</td>
</tr>
</tbody>
</table>
Figure VI (v)

Effect of dielectric constant ($\varepsilon_T$) on oxidation of atenolol by aqueous alkaline hexacyanoferrate(III) at 25 °C

(Conditions as in Table VI (v)(p. 170)
precipitate indicating the presence of free radical intervention in the reaction. The blank experiments of either [Fe(CN)₆]³⁻, or atenolol 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.¹⁴

Effect of Temperature

The rate of the reaction was measured at four different temperatures, with keeping other conditions constant. The rate was found to increase with increase in temperature. The values of $k_{obs} \times 10^{-3}$ s⁻¹ were 1.75, 2.31, 2.93, 3.86 at 25, 30, 35, 40 °C respectively. The energy of activation corresponding to these constants was evaluated from the Arrhenius plot of log $k_{obs}$ versus $1/T$ (Fig. VI (vi)(p.174) $(r \geq 0.9780, s \leq 0.0095)$, and other activation parameters were obtained and tabulated in Table VI(vi) (p.173).

DISCUSSION

Variation of the concentrations of the oxidant ([Fe(CN)₆]³⁻), substrate (atenolol) and alkali, while keeping others constant showed that the reaction is first order in oxidant and less than unit order in alkali and substrate concentrations. Table VI(iv)(p.167). The reaction between atenolol and [Fe(CN)₆]³⁻ in NaOH has a stoichiometry of 1:2. It has been observed that the presence of ferrocyanide [Fe(CN)₆]⁴⁻ retards the rate of reduction of ferricyanide by atenolol. However, the retardation is small, increasing the initial concentration of the ferrocyanide produced only a 4% reduction in rate and this has been attributed to a secondary salt effect.¹⁵ Based on the experimental results, a mechanism can be proposed for which all the
Table VI (vi)

(a) Effect of temperature on the hexacyanoferrate(III) oxidation of atenolol in an aqueous alkaline medium at 25 °C.

<table>
<thead>
<tr>
<th>Temp (K)</th>
<th>$k_{obs} \times 10^{-1}$ (s$^{-1}$)</th>
<th>log $k_{obs}$</th>
<th>1/T x $10^{3}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>298</td>
<td>1.75</td>
<td>-2.755</td>
<td>3.35</td>
</tr>
<tr>
<td>303</td>
<td>2.31</td>
<td>-2.636</td>
<td>3.30</td>
</tr>
<tr>
<td>308</td>
<td>2.93</td>
<td>-2.533</td>
<td>3.27</td>
</tr>
<tr>
<td>313</td>
<td>3.86</td>
<td>-2.413</td>
<td>3.19</td>
</tr>
</tbody>
</table>

(b) Thermodynamic activation parameters for the oxidation of atenolol by alkaline hexacyanoferrate(III) with respect to slow step of Scheme 1.

<table>
<thead>
<tr>
<th>Activation parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_a$ (kJ mol$^{-1}$)</td>
<td>40 ± 2</td>
</tr>
<tr>
<td>log A</td>
<td>4 ± 1</td>
</tr>
<tr>
<td>$\Delta H^#$ (kJ mol$^{-1}$)</td>
<td>38 ± 2</td>
</tr>
<tr>
<td>$\Delta S^#$ (J K$^{-1}$mol$^{-1}$)</td>
<td>-173 ± 10</td>
</tr>
<tr>
<td>$\Delta G^#$ (kJ mol$^{-1}$)</td>
<td>90 ± 4</td>
</tr>
</tbody>
</table>
Figure VI (vi)
Effect of temperature on the oxidation of atenolol by hexacyanoferrate(III) in aqueous alkaline medium at 25 °C (with respective to slow step of Scheme 1 p.177).
(Conditions as in Table VI (vi) (p.173))
observed orders in each constituent such as [oxidant], [reductant] and [OH⁻] may be well accommodated. Oxidation of atenolol by hexacyanoferrate (III) in NaOH media is a non-complementary reaction with oxidant undergoing two equivalent changes.

The results indicate that the alkali combines first with atenolol to give a hydrolysed form of atenolol i.e., anionic form of atenolol in a prior equilibrium step, which is also supported by the observed fractional order in [OH⁻] and [ATN]. This anionic form of atenolol reacts with ferrocyanide species to give a complex (C), which decomposes in a slow step to give an anionic free radical derived from atenolol and [Fe(CN)₆]³⁻ product. The existence of such a type of anionic free radical was also mentioned in the literature. K₂ is the equilibrium constant comprising the equilibrium to bind atenolol to [Fe(CN)₆]³⁻. This free radical in turn reacts with one more mole of [Fe(CN)₆]³⁻ species in a fast step to yield the products as given in Scheme 1.

Spectral evidence for such an oxidant- substrate complex was obtained from the uv-vis spectra of atenolol, and ([Fe(CN)₆]³⁻). A bathochromic shift, λ_{max}, of ca. 13 nm from 261 to 174 nm is observed together with hyperchromicity at 274 nm. Such complex between a substrate and a catalyst has been observed in other studies. These results indicate a mechanism of the type as in Scheme 1.
Scheme 1

Probable structure of the complex is given by
Since Scheme 1 is in accordance with the generally well-accepted principle of non-complementary oxidations taking place in sequence of one-electron steps, the reaction between the substrate and oxidant would afford radical intermediate. A free radical scavenging experiment revealed such a possibility. The rate law can be derived as follows

\[
\frac{d [\text{Fe(CN)}_6]^{3-}}{dt} = kK_1K_2 [\text{ATN}]_f [\text{OH}^-]_f [\text{Fe(CN)}_6]^{3+}_f \tag{2}
\]

\[
[\text{ATN}]_f = [\text{ATN}]_f + [\text{ATN}^+] + C
\]

The total concentration of atenolol is given by (where t and f stands for total free respectively)

\[
[\text{ATN}]_t = [\text{ATN}]_f + K_1 [\text{ATN}][\text{OH}^-] + K_2 [\text{ATN}][\text{Fe(CN)}_6]^{3+} \tag{3}
\]

Similarly

\[
[\text{ATN}]_t = [\text{ATN}]_f + [\text{ATN}^+] + C \tag{3}
\]

\[
[\text{OH}^-]_t = [\text{OH}^-]_f + [\text{ATN}^+] + C \tag{4}
\]

\[
[\text{Fe(CN)}_6]^{3-}_t = [\text{Fe(CN)}_6]^{3-}_f + C
\]
\[
\begin{align*}
&= [\text{Fe(CN)}_6]^{3^-} + K_1 K_2 [\text{ATN}] [\text{OH}^-] [\text{Fe(CN)}_6]^{3^-} \\
&= [\text{Fe(CN)}_6]^{3^-} [1 + K_1 K_2 [\text{ATN}] [\text{OH}^-]] \\
[\text{Fe(CN)}_6]^{3^-} &= \frac{[\text{Fe(CN)}_6]^{3^-}}{[1 + K_1 K_2 [\text{ATN}] [\text{OH}^-]]} \quad (5)
\end{align*}
\]

Substituting equation (3), (4) and (5) in equation (2) we get,

\[
\text{Rate} = \frac{k K_1 K_2 [\text{ATN}] [\text{OH}^-] [\text{Fe(CN)}_6]^{3^-}}{(1 + K_1 [\text{OH}^-] + K_1 K_2 [\text{ATN}] [\text{OH}^-])(1 + K_1 K_2 [\text{ATN}] [\text{OH}^-])}
\]

Since \([\text{Fe(CN)}_6]^{3^-}\) used is very low as compared to unity, therefore above equation can be written as,

\[
\text{Rate} = \frac{k K_1 K_2 [\text{ATN}] [\text{OH}^-] [\text{Fe(CN)}_6]^{3^-}}{(1 + K_1 [\text{OH}^-])(1 + K_1 [\text{ATN}] + 1 + K_1 K_2 [\text{ATN}] [\text{OH}^-])}
\]

\[
= \frac{k K_1 K_2 [\text{ATN}] [\text{OH}^-] [\text{Fe(CN)}_6]^{3^-}}{1 + K_1 K_2 [\text{ATN}] [\text{OH}^-] + K_1 K_2 [\text{ATN}] [\text{OH}^-]^2}
\]

Neglecting square terms in view of low value as compared to unity,

\[
\text{Rate} = \frac{k K_1 K_2 [\text{ATN}] [\text{OH}^-] [\text{Fe(CN)}_6]^{3^-}}{1 + K_1 K_2 [\text{ATN}] [\text{OH}^-] + K_1 [\text{OH}^-]}
\]

Equation (6) can be rearranged to equation (7) which is suitable for verification

\[
\frac{1}{k_{\text{obs}}} = \frac{1}{K_1 K_2 [\text{ATN}] [\text{OH}^-]} + \frac{1}{k K_2 [\text{ATN}]} + \frac{1}{k} \quad (7)
\]
According to equation (7), other conditions being constant, the plots of \(1/k_{\text{obs}}\) versus \(1/\text{[ATN]}\) \((r>0.9814, s<0.0143)\), \(1/k_{\text{obs}}\) versus \(1/\text{[OH]}\) \((r>0.895, s<0.0221)\) should be linear as shown in Fig. VI(vii)(p.180). From the slopes and intercepts, the values of \(K_1\), \(K_2\) and \(k\) could be derived as \(0.044 \pm 0.001\text{dm}^3\text{mol}^{-1}\), \(5 \pm 0.2 \times 10^3\text{ dm}^3\text{mol}^{-1}\) and \(2.60 \pm 0.10 \times 10^3\text{ s}^{-1}\) respectively. Using these values, the rate constants under different experimental conditions and there is a reasonable agreement between the calculated and experimental values (Table VI(vi) (p.167)

The negligible effect of ionic strength on the rate qualitatively explains the involvement of a neutral molecule in Scheme 1 of the proposed mechanism. The effect of solvent on the reaction rate is described\(^{19}\). The plot of \(\log k_{\text{obs}}\) versus \(1/\varepsilon_T\) is expected to be linear with negative slope for a reaction between a negative ion and a neutral molecule, whereas a positive slope results for a positive ion and a neutral molecule. In our present study a plot of \(\log k_{\text{obs}}\) versus \(1/\varepsilon_T\) is linear with negative slope as shown in Fig. VI(v)(p.171)\((r>0.9987, s<0.0396)\), which supports the involvement of negative ion as given in Scheme 1.

The negative value of \(\Delta S^\#\) indicates the formation of complex in the reaction as shown in Scheme 1. A more negative \(\Delta S^\#\) value suggests that the complex is more ordered than the reactants. 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, indicates that oxidation presumably occurs by an inner-sphere mechanism. This conclusion is supported by earlier work\(^{20}\).

(Conditions as in Table VI(iv)(p.167)
Importance of the chapter VI

The reduction of hexacyanoferrate(III) by atenolol in alkaline medium involves the retardation by one of the products, $K_4Fe(CN)_6$ and the overall mechanistic sequence described is consistent with product, mechanistic and kinetic studies.
REFERENCES

1. E.P. Kelson and P. P. Phengy, 
2. A.I.Vovk, I.V.Muraveva,V.P.Kukhar and V.F.Baklan, Russ.J.Gen.chem., 
   70,1108 (2000).
3. P.T.Speakman and W.A.waters, 
4. V.N. Singh, M.C.Gangwar, B.B.L Saxena and M.P. Singh, 
5. V.N.Singh, M.P.Singh and B.B.L Saxena, 
6. M. White, A.Fourney, E. Mikes and F.H.H.Leenen, 
   Am. J. Hypertens, 1999, 12, 151.
7. G.C. Hiremath, R.M. Mulla and S.T. Nandibewoor, 
8. M. B. Bellakki, R T Mahesh and S. T. Nandibewoor, 
9. G.H. Jeffery, J. Bassett, J. Mendham and R.C. Denney, 
   "Vogel's Text Book of Quantitative Chemical Analysis". ELBS. 5th edn. 
10. S. A. Farokhi, 
    "Kinetic and Mechanistic Study of Oxidation of Some Organic- Compounds" 
12. F. Fiegl, 
13. D.R. Lide. (Ed), 
14. I.M. Kolthoff, E.J. Meehan and E.M. Carr,  
   *J. Am. chem. Soc.*, 75, 1439 (1953);  
   S.Bhattacharya and P. Banerjee,  
15. J. H. Swinehart,  
16. V. Uma, B. Sethuram and T.N. Rao,  
   *React Kinet Catal Lett*, 18, 283 (1981);  
   D.L.Kamble, R. B. Chougale and S.T.Nandibewoor,  
17. P.S Kalsi,  
   "*Organic Reactions and their Mechanisms*", New Delhi; New Age  
18. S.A. Farokhi and S.T. Nandibewoor,  
19. E. S. Amis  
   "*Solvent Effects on Reaction Rates and Mechanisms*", Academic Press New  
   K.J. Laidler,  
   "*Chemical Kinetics*", Tata McGraw-Hill  publication company  
   Ltd, New Delhi, 1976, p 230.  
20. I.M. Martinez, M. A. Pitarque and R. V.Eldik,  
   S.A Farokhi and S. T. Nandibewoor,  