# Oxidation of 3-(3,4-Dihydroxy Phenyl)-L-Alanine (Levodopa) and 3-(3,4-Dihydroxy Phenyl)-2-Methyl-L-Alanine (Methyl Dopa) by Manganese(III) in Pyrophosphate Media: Kinetic and Mechanistic Study

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ABSTRACT: Manganese(III) (Mn(III)) has been stabilized in weakly acidic solution by means of pyrophosphate and the nature of the complex was elucidated spectrophotometrically. Stoichiometry of Mn(III)-oxidation of levodopa and methyl dopa in pyrophosphate medium was established in the pH range 2.5–4.0 by iodometric and spectrophotometric methods. The reaction shows a distinct variation in kinetic order with respect to [Mn(III)], a first-order dependence in the pH range 1.9–2.6, decreasing to fractional order above pH 3. Other common features include first-order dependence on [dopa], positive fractional order dependence on $[H^+]$, and inverse first-order dependence on [Mn(III)] in the pH range studied. The effects of varying ionic strength and solvent composition were studied. Added ions such as $SO_4^{2-}$ and $ClO_4^-$ alter the reaction rate, probably due to the change in the formal redox potential of Mn(III)–Mn(II) couple because of the changes in coordination environment of the oxidizing species. Evidence for the transient existence of the free radical intermediate is given. Cyclic voltametric sensing of levodopa and methyl dopa has ruled out the formation of dopaquinones as oxidation products in the pH range studied. Activation parameters have been evaluated using the Arrhenius and Erying plots. Mechanisms consistent with the kinetic data have been proposed and discussed. These studies are expected to throw some light on dopa metabolism.
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## INTRODUCTION

Levodopa [1] 3-(3,4-dihydroxyphenyl)-L-alanine is a natural amino acid precursor of dopamine. The dopamine cannot be used as drug because, being poorly lipid soluble, it is not well absorbed in the gut and does not penetrate the central nervous system. Levodopa is particularly effective in the treatment of tremors and hyperkinesia [2]. It can be called an universal antiparkinsonian drug, as it improves all the manifestations of parkinsonism. This drug improves the mood and memory and makes patients more alert and interested in themselves and in their surroundings.

A great deal of attention has been focused on the oxidation of drugs and pharmaceuticals by metal ions. Of these, Mn(III) oxidations are of special significance because of their biological importance. There are a number of reports on the kinetics of oxidations of various substrates by Mn(III) in perchlorate, sulfate, acetate, and pyrophosphate media [4]. Kinetics of oxidation of amino acids by various oxidizing agents in general [5–10] and aquomanganic ions in particular [11–13] have been reported. Quite recently, we have studied the kinetics of Mn(III) oxidation of L-histidine by Mn(III) sulfate in aqueous sulfuric acid [14], L-arginine in pyrophosphate medium [15], L-asparatic acid and L-glutamic acid [16] by Mn(III) in pyrophosphate and acetate media, and lower $\alpha$-amino acids [17–19] by Mn(III) acetate in aqueous acetic acid. There seems to be no report in the literature on the kinetics of oxidation studies that may throw some light on the mechanism of conversion of the compounds in biological systems. Hence, as a part of our work on mechanistic studies on Mn(III) oxidation of organic and inorganic substrates in general and medicinal compounds in particular [14–16,20], we have investigated the stoichiometry and mechanism of oxidation of levodopa and methyl dopa by Mn(III) in pyrophosphate medium.

## EXPERIMENTAL

Manganese(III) pyrophosphate was prepared by the literature method [21] and was standardized by the iodometric method; it was further checked by titrating against standard Fe(II) using diphenyl sulfonate as an internal indicator.

A Shimadzu model UV-Visible spectrophotometer with a 1-cm quartz cell was used for the absorption measurements under the experimental conditions. The $\lambda_{max}$ for the Mn(II) species in a solution of pH 5.0 occurred at 500 nm, which slightly varied as a function of pH.

Pharmaceutically pure levodopa and methyl dopa complying with the pharmacopeial standards (Sun Pharmaceuticals, Baroda) were obtained. Aqueous stock solutions of levodopa and methyl dopa (0.05 mol $dm^{-3}$) were prepared with double-distilled water as required. All other reagents used were of analytical grade.

### Kinetic Measurements

A known amount of Mn(III) pyrophosphate solution was thermally equilibrated at 318 K. It was added to a mixture of dopa, Mn(II), [$P_2O_7^{4-}$] (for ionic strength), orthophosphoric acid (to maintain pH), and water (to keep total volume constant) taken from another glass-stoppered bottle also maintained at the same temperature. The progress of the reaction was monitored by iodometric estimation of unreacted Mn(III) pyrophosphate present in known aliquots of the mixture withdrawn at regular intervals of time. The course of the reaction was studied to 75% completion. The rate constants calculated were reproducible within $\pm$5%. Identical results were obtained when the reaction was monitored by a spectrophotometric method.

## RESULTS

### Stoichiometry and Product Analysis

The stoichiometry of the reaction between Mn(III) pyrophosphate and levodopa was investigated under excess oxidant conditions. A known amount of levodopa solution ($5.0 \times 10^{-2}$ mol $dm^{-3}$) was allowed to react completely with a 10-fold excess of the Mn(II) at 40°C in the presence of orthophosphoric acid to maintain pH at 4.0. The excess Mn(III) was estimated by iodometric method. The product formed was extracted with ether, the ether was distilled off, and the residue was identified as the aldehyde by its IR spectra, where the —OH stretching frequency was observed in the range 3400–3500 $cm^{-1}$, —CO stretching frequency of aldehyde was observed in the range 1630–1680 $cm^{-1}$, and —CH stretching frequency was observed in the range 2600–3000 $cm^{-1}$.

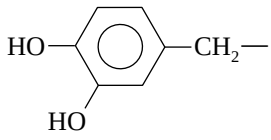
Stoichiometry of the reaction between Mn(III) pyrophosphate and levodopa was found to be 2:1, both at low (<3) and high (>3) pH. Product analysis was carried out under substrate excess conditions as follows.

Reaction mixtures containing levodopa ($5.0 \times 10^{-2}$ mol dm$^{-3}$) and Mn(III) pyrophosphate ($5.0 \times 10^{-3}$ mol dm$^{-3}$) at pH 4.0 and at 40°C were allowed to react completely. One of the products formed was identified as the aldehyde [22] by its 2,4-dinitrophenylhydrazone derivative, which was obtained up to a 90% yield.

The observed stoichiometry can be represented by the equation

$$2\mathrm{Mn(III)} + \mathrm{R{-}CH(NH_2){-}COOH} + \mathrm{H_2O} \longrightarrow 3\mathrm{Mn(II)} + \mathrm{RCHO} + \mathrm{NH_3} + \mathrm{CO_2} + 2\mathrm{H^+} \quad (1)$$

where R is




## [Mn(III)] and [Levodopa] Dependence

The first-order and half-order dependence on Mn(III) at low and high pH ranges, respectively, were indicated by the linearity by log[Mn(III)] versus time plots and $[\mathrm{Mn(III)}]^{1/2}$ versus time plots. The values of pseudo-first-order and pseudo-half-order rate constants were insensitive to changes in initial concentration of Mn(III) (Tables I and II).

At constant $[\mathrm{Mn(III)}]_0$, pH, $[P_2O_7^{4-}]$, and [Mn(II)], the rate constants increased with increase in $[\mathrm{dopa}]_0$ and a plot of log($k$) versus $\log[\mathrm{dopa}]_0$ showed that the order in [dopa] was unity at both the pH ranges.

## Dependence of Rate on pH

The pH of the reaction was varied between 1.9 and 4.0 by varying the orthophosphoric acid concentration at constant [Mn(II)], $[P_2O_7^{4-}]$, and $[\mathrm{Mn(III)}]_0$. The rates decreased with an increase in pH. The order with respect to $[H^+]$ was found to be 0.5 both at low and high pH ranges (Tables III and IV).

## Dependence of Rate on Ionic Strength and [Mn(II)]

The rate increased with decreasing ionic strength obtained by varying the sodium pyrophosphate concentration. Mn(II) was the reduced product of the oxidant, and as the initial concentration of added Mn(II) was increased, the rate progressively decreased and the order with respect to Mn(II) was found to be 1.

## Dependence of Rate on Added Salts

The effect of added anions like $ClO_4^-$ and $SO_4^{2-}$ on the reaction rate was investigated (Tables V and VI). A slight enhancement in reaction rate with increasing $[ClO_4^-]$ may be due to the establishment of a new Mn(III)/Mn(II) redox couple and also due to ionic strength considerations. The observed retardation with increasing $[SO_4^{2-}]$ could be due to reduction in $[H^+]$ via formation of $HSO_4^-$ as,

$$SO_4^{2-} + H^+ \longrightarrow HSO_4^-$$

**Table I** Pseudo-First-Order Rate Constants ($k_{obs}$) for the Oxidation of Levodopa and Methyl Dopa by Mn(III) Pyrophosphate at 313 K, pH = 2.2, and $[P_2O_7^{4-}] = 1.4 \times 10^{-2}$ mol dm$^{-3}$

| | | | $k_{obs}$ (s$^{-1}$) | |
|---|---|---|---|---|
| Mn(III) $10^3$ (mol dm$^{-3}$) | [Levodopa] $10^2$ (mol dm$^{-3}$) | Mn(II) $10^3$ (mol dm$^{-3}$) | Levodopa | Methyl Dopa |
| 2.5 | 5.0 | 3.0 | 3.74 | 3.22 |
| 5.0 | 5.0 | 3.0 | 3.64 | 3.15 |
| 7.5 | 5.0 | 3.0 | 3.76 | 3.19 |
| 10.0 | 5.0 | 3.0 | 3.76 | 3.21 |
| 5.0 | 2.5 | 3.0 | 2.4 | 1.96 |
| 5.0 | 5.0 | 3.0 | 3.64 | 3.15 |
| 5.0 | 7.5 | 3.0 | 5.69 | 5.12 |
| 5.0 | 10.0 | 3.0 | 6.90 | 5.12 |
| 5.0 | 5.0 | 1.0 | 7.2 | 6.72 |
| 5.0 | 5.0 | 2.0 | 5.2 | 4.76 |
| 5.0 | 5.0 | 3.0 | 3.64 | 3.15 |
| 5.0 | 5.0 | 4.0 | 2.53 | 2.12 |

**Table II** Pseudo-Half-Order Rate Constants ($k_{obs}$) for the Oxidation of Levodopa and Methyl Dopa by Mn(III) Pyrophosphate at 313 K and pH = 4.0

| | | | $10^4\ k_{obs}$ ($mol^{1/2}\ dm^{3/2}\ s^{-1}$) | |
|---|---|---|---|---|
| Mn(III) $10^3$ (mol $dm^{-3}$) | [Sub] (mol $dm^{-3}$) | Mn(III) $10^3$ (mol $dm^{-3}$) | Levodopa | Methyl Dopa |
| 2.5 | 5.0 | 3.0 | 6.88 | 6.42 |
| 5.0 | 5.0 | 3.0 | 7.05 | 6.51 |
| 7.5 | 5.0 | 3.0 | 7.05 | 6.53 |
| 10.0 | 5.0 | 3.0 | 7.05 | 6.56 |
| 5.0 | 2.5 | 3.0 | 3.50 | 3.05 |
| 5.0 | 5.0 | 3.0 | 7.05 | 6.51 |
| 5.0 | 8.0 | 3.0 | 14.9 | 14.53 |
| 5.0 | 12.0 | 3.0 | 21.1 | 19.67 |
| 5.0 | 5.0 | 1.0 | 13.9 | 13.53 |
| 5.0 | 5.0 | 2.0 | 9.9 | 9.52 |
| 5.0 | 5.0 | 3.0 | 7.05 | 6.51 |
| 5.0 | 5.0 | 4.0 | 4.68 | 4.21 |

**Table III** Effect of Variation of $[P_2O_7^{4-}]$ and Methyl Dopa by Mn(III) Pyrophosphate at $[Mn(III)] = 5.0 \times 10^{-3}$ mol $dm^{-3}$, $[Mn(II)] = 3.0 \times 10^{-3}$ mol $dm^{-3}$, and $[Dopa] = 5.0 \times 10^{-2}$ mol $dm^{-3}$

| $[P_2O_7^{4-}]$ | | Temperature | $10^2\ k_{obs}$ ($s^{-1}$) | |
|---|---|---|---|---|
| $10^2$ (mol $dm^{-3}$) | pH | (K) | Levodopa | Methyl Dopa |
| 0.76 | 2.2 | 313 | 5.98 | 5.46 |
| 0.92 | 2.2 | 313 | 5.29 | 4.83 |
| 1.40 | 2.2 | 313 | 3.64 | 3.15 |
| 2.00 | 2.2 | 313 | 2.83 | 2.37 |
| 1.40 | 1.9 | 313 | 6.60 | 6.17 |
| 1.40 | 2.0 | 313 | 5.29 | 4.76 |
| 1.40 | 2.6 | 313 | 1.69 | 1.28 |
| 1.40 | 2.2 | 303 | 1.70 | 1.61 |
| 1.40 | 2.2 | 308 | 2.69 | 2.22 |
| 1.40 | 2.2 | 323 | 7.43 | 6.92 |

**Table IV** Effect of Variation of $[SO_4^{2-}]$ and Solvent Effects on the Rate of Oxidation of Levodopa and Methyl Dopa by Mn(III) Pyrophosphate at 313 K, pH = 4.0, $[Mn(III)] = 5.0 \times 10^{-3}$ mol $dm^{-3}$, $[Mn(II)] = 3.0 \times 10^{-3}$ mol $dm^{-3}$, $[P_2O_7^{4-}] = 1.4 \times 10^{-2}$ mol $dm^{-3}$, $[Sub] = 5.0 \times 10^{-3}$ mol $dm^{-3}$

| | $k_{obs}$ ($mol^{1/2}\ dm^{-3/2}\ s^{-1}$) | | | $k_{obs}$ ($mol^{1/2}\ dm^{-3/2}\ s^{-1}$) | | | | $k_{obs}$ ($mol^{1/2}\ dm^{-3/2}\ s^{-1}$) | |
|---|---|---|---|---|---|---|---|---|---|
| $SO_4^{2-}$ (mol $dm^{-3}$) | Levodopa | Methyl Dopa | $ClO_4 \times 10^2$ (mol $dm^{-3}$) | Levodopa | Methyl Dopa | Percentage of Absolute Alcohols | Dielectric Constant | Levodopa | Methyl Dopa |
| 5.0 | 6.5 | 6.01 | 5.0 | 7.5 | 7.15 | 3.0 | 76.7 | 6.9 | 6.51 |
| 10.0 | 6.1 | 5.63 | 10.0 | 7.8 | 7.38 | 5.0 | 75.2 | 6.4 | 6.01 |
| 17.4 | 5.8 | 5.41 | 16.7 | 8.2 | 7.76 | 10.0 | 72.9 | 6.1 | 5.9 |

**Table V** Effect of Variation of $[SO_4^{2-}]$ and Solvent on the Oxidation of Dopa by Mn(III) Pyrophosphate at 313 K, pH = 2.2, $[Mn(III)] = 1.4 \times 10^{-2}$ mol dm$^{-3}$, $[Dopa] = 5.0 \times 10^{-2}$ mol dm$^{-3}$

| | $k_{obs}$ (mol$^{1/2}$ dm$^{-3/2}$ s$^{-1}$) | | | $k_{obs}$ (mol$^{1/2}$ dm$^{-3/2}$ s$^{-1}$) | | Percentage of Absolute Alcohols | Dielectric Constant | $k_{obs}$ (mol$^{1/2}$ dm$^{-3/2}$ s$^{-1}$) | |
|---|---|---|---|---|---|---|---|---|---|
| $SO_4^{2-}$ (mol dm$^{-3}$) | Levodopa | Methyl Dopa | $ClO_4 \times 10^2$ (mol dm$^{-3}$) | Levodopa | Methyl Dopa | | | Levodopa | Methyl Dopa |
| 5.0 | 3.2 | 2.78 | 5.0 | 3.9 | 3.51 | 3.0 | 76.7 | 6.9 | 6.51 |
| 10.0 | 2.5 | 2.16 | 10.0 | 4.2 | 3.77 | 5.0 | 75.2 | 6.4 | 6.01 |
| 17.4 | 2.3 | 1.97 | 16.7 | 4.6 | 4.26 | 10.0 | 72.9 | 6.1 | 5.9 |

## Dependence of Rate on Temperature

The reaction was carried out at 303, 308, 313, and 323 K at constant ionic strength, pH, and Mn(III), both at low (2.2) and high (4.0) pH. Arrhenius and Erying plots of log $k$ versus $1/T$ gave good straight lines. From the slopes and intercepts, the values of the activation parameters for both levodopa and methyl dopa were calculated (Table VII).

The variation in reaction rate with the dielectric constant of the reaction mixture was investigated by adding ethanol to the solvent. The observed decrease in rate with the decrease in dielectric constant is in conformity with Amis [23] and other theories [24,25] (i.e., it indicates the importance of specific solvent–solute interactions) (Tables IV and V).

**Table VI** Effect of Variation of $[P_2O_7^{4-}]$, pH and Temperature on the Rate of Oxidation of Levodopa and Methyl Dopa by Mn(III) Pyrophosphate at $[Mn(III)] = 5.0 \times 10^{-4}$ mol dm$^{-3}$, $[Sub] = 5.0 \times 10^{-2}$ mol dm$^{-3}$, and $[Mn(II)] = 3.0 \times 10^{-3}$ mol dm$^{-3}$

| $[P_2O_7^{4-}]$ $10^2$ (mol dm$^{-3}$) | pH | Temperature (K) | $k_{obs}$ (mol$^{1/2}$ dm$^{-3/2}$ s$^{-1}$) | |
|---|---|---|---|---|
| | | | Levodopa | Methyl Dopa |
| 0.76 | 4.0 | 313 | 11.5 | 10.97 |
| 0.92 | 4.0 | 313 | 10.71 | 10.23 |
| 1.40 | 4.0 | 313 | 7.05 | 6.51 |
| 2.00 | 4.0 | 313 | 6.10 | 5.63 |
| 1.40 | 3.0 | 313 | 20.14 | 19.92 |
| 1.40 | 3.5 | 313 | 10.70 | 10.24 |
| 1.40 | 3.8 | 313 | 8.51 | 7.91 |
| 1.40 | 4.0 | 313 | 7.50 | 6.51 |
| 1.40 | 4.0 | 303 | 2.40 | 1.98 |
| 1.40 | 4.0 | 308 | 5.10 | 4.67 |
| 1.40 | 4.0 | 313 | 7.50 | 6.51 |
| 1.40 | 4.0 | 323 | 14.10 | 13.52 |

**Table VII** Activation Parameters of Levodopa and Methyl Dopa at High and Low pH

| | Levodopa | | Methyl Dopa | |
|---|---|---|---|---|
| | pH = 4.0 | pH = 2.2 | pH = 4.0 | pH = 2.2 |
| $E_a$ (kJ mol$^{-1}$) | 53.99 | 57.44 | 47.78 | 42.50 |
| log $A$ | 5.85 | 8.15 | 4.74 | 5.59 |
| $\Delta H^{\#}$ (kJ mol$^{-1}$) | 55.52 | 58.01 | 47.86 | 43.27 |
| $\Delta S$ (JK$^{-1}$ mol$^{-1}$) | 128.09 | −87.65 | −153.40 | −135.71 |
| $\Delta G^{\#}$ (kJ mol$^{-1}$) | 40.036 | 27.376 | 74.96 | 42.43 |

## DISCUSSION

### Electrochemical Studies

The electrochemical oxidation of levodopa with platinum electrode in pyrophosphate buffer (pH = 1.25) shows a well-defined anodic peak at $E_{pa}$ = 0.571 V (Fig. 1) and a complementary cathodic peak appearing at $E_{pc}$ = 0.381 V. The electrooxidation product of levodopa has been identified to be the dopaquinone, the oxidation of catechol moiety. The peak current increases with sweep rate and also with concentration of dopa. The anodic peak potential shifts on lowering pH, probably due to the involvement of protons in the electrochemical oxidation of levodopa. $E_{pa}$ increases from 0.54 to 1.0 V as the pH changes from 1.01 to 9.8 (Fig. 2). This suggests that as the pH is increased oxidation of catechol moiety of dopa to dopaquinone becomes more difficult. Similar dependence of half-wave potential on pH was reported by investigation of levodopa with a polycarbazole electrode [26]. Therefore, it is inferred that Mn(III) oxidation of dopa takes place directly through decarboxylation and deamination of amino acid and catechol moiety does not get oxidized to quinone in the pH range studied. Further, separate experiments were performed, in which Mn(III) pyrophosphate was made to react with catechol by maintaining the experimental condition, and oxidation of the catechol was found to be negligible.

The kinetics of oxidation of L-phenylalanine at pH range 0.91–1.45 was carried out recently [18] in pyrophosphate medium. It was shown that the rate of oxidation decreases with an increase in pH. At pH > 2, the reaction becomes extremely slow; therefore, kinetics of oxidation of phenylalanine at higher pH could not be carried out as a comparative study. Also, now it can be inferred that the two —OH groups present in levodopa activate the oxidation of amino acid moiety.

Kinetics of another methylated derivative of levodopa, methyl dopa, was studied under identical experimental conditions. The rate of oxidation of methyl dopa was found to be slower than that of levodopa, probably due to the steric effect of the $-CH_3$ group present in the amino acid chain.

The observed results of first- and half-order dependence on Mn(III), first-order dependence on [dopa], and fractional-order dependence on [Mn(II)] can be accounted for by the mechanism given.

### Oxidation at Low pH Range (1.9–2.6)

In acidic medium, Mn(III) pyrophosphate can be considered to be a metal chelate (a coordinated compound with a ring structure) anion having the composition $Mn(H_2P_2O_7)_3^{3-}$. The observed results of first-order dependence each on [dopa] $Mn(H_2P_2O_7)_3^{3-}$ and inverse fraction-order dependence each on Mn(II) $[(H_2P_2O_7)_3^{3-}]$ and $[H_2P_2O_7^{2-}]$ can be explained with the proposed mechanism.

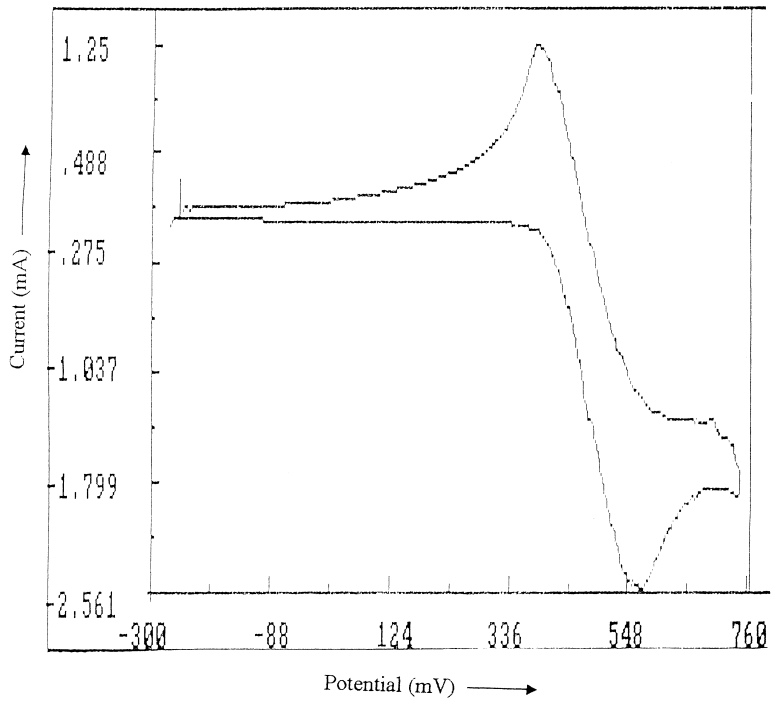



**Figure 1** Cyclic voltametric curve of levodopa in pyrophosphate buffer at platinum electrode. Sweep rate = 50 mV $s^{-1}$, pH = 1.25, temp. = 298 K, concentration of levodopa = 2 mM, and electrolyte = 20 mM pyrophosphate.

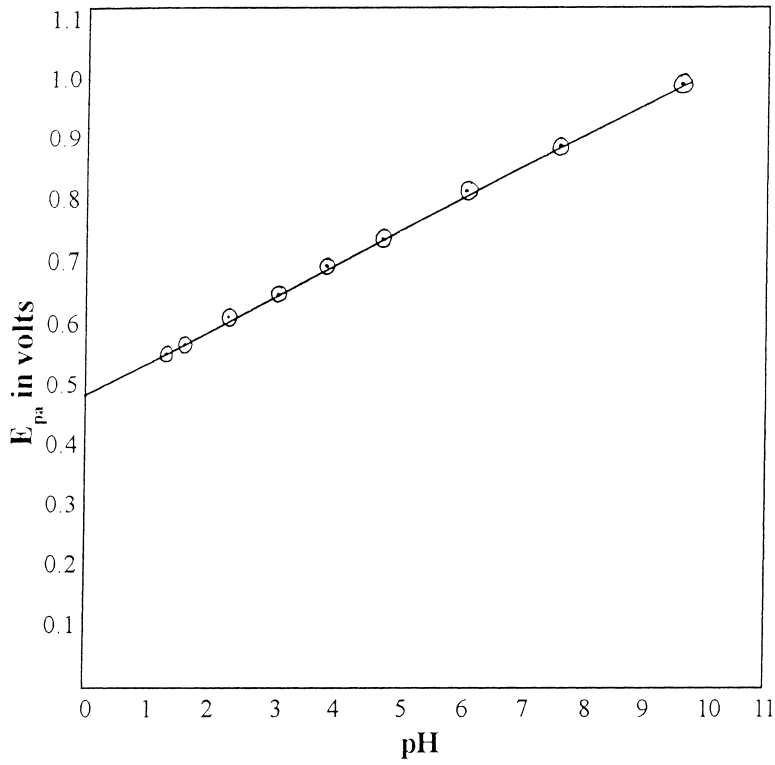
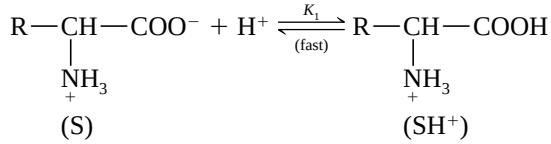
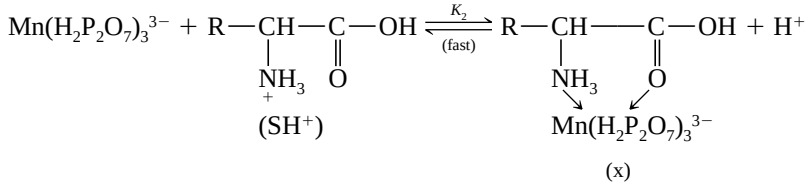



**Figure 2** Effect of pH on anodic peak potential of levodopa in pyrophosphate buffer at platinum electrode. Sweep rate = 50 mV $s^{-1}$, pH = 1.25, temp. = 298 K, concentration of levodopa = 2 mM, and electrolyte = 20 mM pyrophosphate.




(2)

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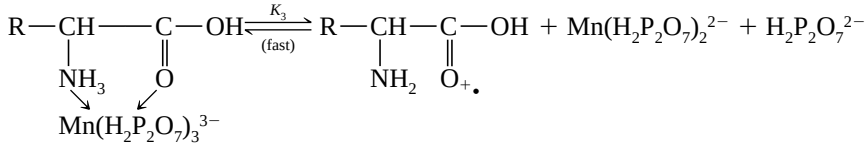


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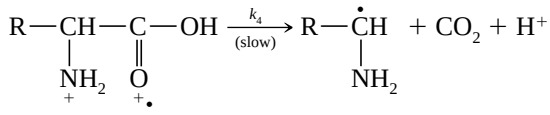


(5)

$$Mn(H_2P_2O_7)_3^{3-} + R-\underset{\displaystyle NH_2}{\overset{\displaystyle \cdot}{C}}H + H_2O \xrightarrow{\text{fast}} R-CHO + Mn(H_2P_2O_7)_2^{2-} + NH_4^+ + H_2P_2O_7^{2-}$$

(z) (6)

$SH^+$ represent the mono cationic forms of the substrate, levodopa, *X* is Mn(III)–substrate complex anion, *Y* is the free radical cation, and *Z* is the free radical.

The existence of a transient free radical intermediate was indicated by the positive test involving polymerization of olefinic monomers. The evidence for the *in situ* formation of transition metal–substrate complex species is available in the literature [27].

The rate of dopa oxidation is given by

$$\text{Rate} = -d[Mn(H_2P_2O_7)_3^{3-}]/dt = k_4[Y] \quad (7)$$

Applying the steady-state approximation to the intermediate species, *X* and *Y*, solving for *Y* and substituting in eq. (7),

$$k_{obs} = K_1k_2K_3k_4[S][H^+]/\{k_2[Mn(H_2P_2O_7)_2^{2-}][H^+][H_2P_2O_7^{2-}] + K_3k_4 \quad (8)$$

The plots of $k_{obs}$ versus [S] are linear passing though the origin, supporting the rate law.

Further,

$$\frac{1}{k_{obs}} = \frac{1}{K_1K_3k_4}\frac{[Mn(H_2P_2O_7)_2^{2-}][H_2P_2O_7^{2-}]}{[S]} + \frac{1}{K_1k_2[S][H^+]} \quad (9)$$

proof of $1/k_{obs}$ versus $1/[H^+]$ was linear with the intercepts on the ordinate axis. These observations support the derived rate low and hence the mechanism.

## Oxidation at High pH Range (3.0–4.5)

An explanation for half-order kinetics involves a fast reversible dissociation step preceding the rate-determining step. One possibility is that all the Mn(III) is essentially in the form of polymeric species $Mn_2(H_2P_2O_7)_6^{6-}$, with a small amount of kinetically active monomeric species $Mn(H_2P_2O_7)_3^{3-}$. This is supported by the strong tendency of Mn(III) pyrophosphate in pyrophosphate medium to form polymers/oligomers.

The following scheme accounts for the observed kinetics:

$$Mn_2(H_2P_2O_7)_6^{6-} \overset{K_1}{\rightleftharpoons} Mn(H_2P_2O_7)_3^{3-}$$

$$S + H^+ \overset{K_2}{\rightleftharpoons} SH^+$$

$$Mn(H_2P_2O_7)_3^{3-} + SH^+ \overset{K_3}{\rightleftharpoons} X^1 + H^+$$

$$X^1 \overset{k_4}{\rightleftharpoons} Y^1 + (H_2P_2O_7)_2^{2-} + H_2P_2O_7^{2-} \quad (13)$$

$$Y^1 \underset{\text{slow}}{\overset{k_5}{\rightleftharpoons}} Z^1 + H^+ \quad (14)$$

$$Z^1 + Mn(H_2P_2O_7)_3^{3-} \overset{\text{(fast)}}{\rightleftharpoons} \text{products} \quad (15)$$

$X^1$ and $Y^1$ are the transient intermediate and $Z^1$ is the free radical.

By solving for $X^1$ and $Y^1$ with the application of steady-state approximation, one gets

$$k_5[Y^1] = \frac{K_1K_2^{1/2}\,k_3k_4k_5[Mn_2(H_2P_2O_7)_6^{6-}]^{1/2}[S][H^+]}{k_{-4}[Mn(H_2P_2O_7)_2^{2-}][H_2P_2O_7^{2-}] + \{k_{-3}[H^+] + k_4\} - k_{-4}[Mn(H_2P_2O_7)_2^{2-}][H_2P_2O_7^{2-}] - k_{-5}\{k_{-3}[H^+] + k_4\}} \quad (16)$$

The negative value of entropy of activation both at low and high pH might be due to the associative process involved. The transition state might involve an associated species formed by solvation, consequently lowering entropy of activation.

## CONCLUSION

Kinetics of Mn(III) oxidations of $\alpha$-amino acids have been investigated in sulfuric, perchlorate, acetic acid, and pyrophosphate media by our group [14–17,20] and by others [11–13,18,19]. The order in [amino acid] obtained was generally one in all cases, while inverse dependencies on [$H^+$] and [Mn(II)] are the other common features. Kinetic order in [Mn(III)] is found to be ½, 1, and 2 in different situations. In the present study, the half- and first-order kinetics observed might be due to kinetically active oxidizing species, $Mn_2(H_2P_2O_7)_6^{6-}$ and $Mn(H_2P_2O_7)_3^{3-}$, respectively. Comparison of cyclic voltametric behavior of levodopa in pyrophosphate media [28] and this study has shown that the oxidative pathways of electrochemical and chemical processes are diametrically different.

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