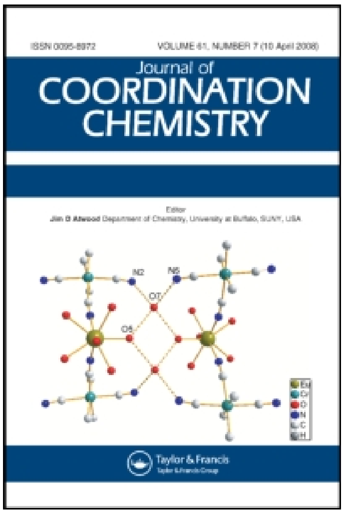

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INTERACTION OF PHOSPHATE WITH IRON(III) IN ACIDIC MEDIUM, EQUILIBRIUM AND KINETIC STUDIES

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Equilibrium reactions of iron(III) with phosphate were studied spectrophotometrically by UV–Vis in the pH range of ~1.0–2.20. The STAR-94 Program was used to determine the number of absorbing species as well as the stoichiometries and formation constants of the complex species. Some literature values were further confirmed and new values of different stoichiometries were obtained. The kinetics and mechanism of Fe(III) with phosphate were studied in acidic medium. The reactive phosphate species were found to be only H_3PO_4 and $H_2PO_4^-$ and for Fe(III) were only Fe^{3+}, $FeOH^{2+}$ and $Fe(OH)_2^+$. The observed rate constants were pH as well as T_{phos} (total concentration of phosphate) dependent, *i.e.* $K_{obs,i} = A_i + B_iT_{phos} + C_iT_{phos}^2$ (at a given pH).

Keywords: Iron (III) phosphate; Formation constants; Reaction mechanism

INTRODUCTION

In a previous study of the reaction kinetics of Fe(III) with pyridoxal-5-phosphate (PLP), a vitamin B_6 compound, it was suggested that the phosphate group was the reactive site [1] and not the phenoxy group as in the study of Fe(III) with the non-phosphorylated compound of vitamin B_6, pyridoxal [2]. Moreover, it was found that Fe(III) can effectively bind phosphate when it was used in oral administration for patients of renal failiure [3]. Quite recently, it has also been reported that iron(III) phosphate can replace Al(III) or Ca(II) phosphates in treating hyperphosphatemia [4] avoiding the accumulation of Al(III) and Ca(II) that lead to encephalopathy and hypercalcemia, respectively. In order to shed light on the stability and lability of the Fe(III)–phosphate species and their application in biological systems, the equilibria and kinetics of the system were studied in this work.

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EXPERIMENTAL

Materials

Sodium dihydrogen phosphate, an analytically pure chemical compound (E-Merck) was used without further purification. The stock solution of $FeCl_3$ was dissolved in an equivalent amount of HCl. It was checked for $FeCl_3$ concentration by complexometric methods [5].

Ionic strength (I) was kept constant at 0.15 M by adding the appropriate amount of 2.0 M NaCl solution to all solutions in this work.

Measurements

The pH measurements were made using a Metrohm pH-meter provided with Metrohm combined glass electrode. The pH-meter was calibrated with three buffers (2.00, 4.00 and 7.00). In addition, the pH meter was calibrated with the titration of NaOH (0.1 M) against HCl (0.1 M) at $I = 0.15$ M NaCl. The calculated and measured pH values were different by ~ 0.016 pH units which may account for the effect of glass junction-potential and the activity coefficient of the H^+ ion.

Kinetic measurements were carried out using the Applied Photophysics stopped-flow kinetics instrument model DX-17MV provided with data processor. The rate data were the average of at least 3 runs. The calculated rate constants were used to compose the observed pseudo-first order rate curves. Matching between calculated rate and experimental curves were within experimental errors. The temperature was adjusted to 25 ± 0.1°C by Caron circulator. The ionic strength was kept constant at 0.15 M NaCl. In running the rate data, the Fe(III) solutions were kept at very low pH (~ 0.9) and $I = 0.15$ M (HCl + NaCl) to avoid iron(III) hydrolysis and precipitation of iron (III) hydroxides. The ligands were adjusted to higher pH values, not less than 11 at $I = 0.15$ M (NaOH + NaCl). The mixed solutions were measured for the final pH after mixing. The final concentration of Fe(III) (T_{Fe}) was kept constant at 5.0×10^{-4} M and the final phosphate concentration T_{phos} varied between $(5.0\text{–}20.0)10^{-3}$ M.

The equilibria of Fe(III)–phosphates were studied by spectrophotometric methods in acidic media such that T_{phos} are greater than T_{Fe}. A Cary 500 spectrophotometer was used to collect the spectral data in the 225–400 nm wavelength range. The solution pH was adjusted with the addition of Na_2CO_3 to minimize local precipitation of iron hydroxides. The solution was flushed with purified nitrogen gas prior to taking the spectra to remove any traces of CO_2, which absorbs in the UV region.

RESULTS AND DISCUSSION

Equilibrium Study

Fe(III) reacted with phosphate in acidic solution to produce a very faint yellow colored solution. The spectra are shown in Fig. 1 at various pH values. Precipitation of an almost white precipitate was encountered at pH values greater than 2.3 limiting pH range. The free iron(III) spectra are characterized by a broad band at ~ 340 nm which usually fades out by increasing the pH. The addition of phosphate to the

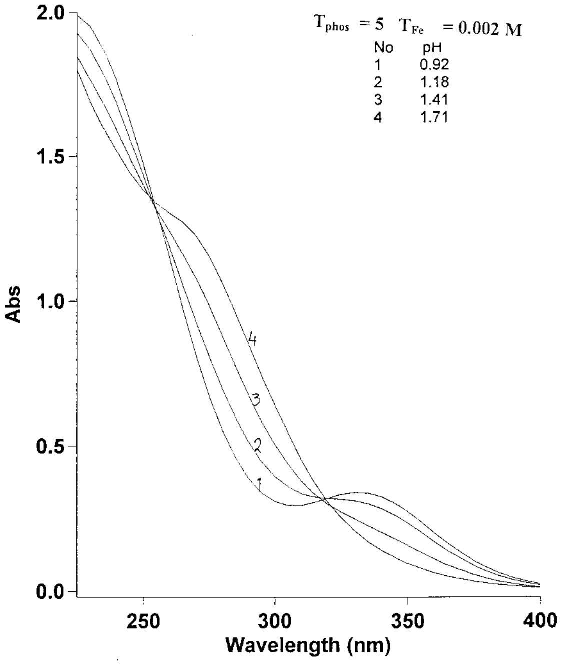


FIGURE 1 Representative spectra of the Fe(III)–phosphate system at different pH values.

TABLE I Summary of formation constants of $Fe_p(PO_4)_l\,H_q$ complexes

System	*Stoichiometric coefficient*			*log β(± σ) [This work]*	*Reported values [Ref]*
	l	*p*	*q*		
$PO_4^{3-} - H^+$	1	0	1		11.30 [12]
	1	0	2		18.00 [12]
	1	0	3		19.95 [12]
$PO_4^{3-} - Fe^{3+}$*	1	1	2	20.71(0.04)	21.49 [11]
	1	1	1	19.89(0.02)	19.53 [11]
	2	1	0	35.66(0.08)	
	2	1	− 2	32.16(0.03)	
	3	1	− 2	49.35(0.07)	
	3	2	− 2	53.12(0.06)	
$Fe^{3+} - OH^-$	0	1	− 1		− 3.05 [8]
	0	1	2		− 6.31 [8]
	0	2	− 2		− 2.79 [8]

*STAR-94 statistical parameters: $\chi_i^2 = 61.0$; *R*-factor = 2.0; Skewness = 0.11; Kurtosis = 4.6; Residual mean in absorbance = 0.0033.

Fe(III) solution also fades out this band with the development of a band shoulder at ~ 265 nm in acidic media. At least two isosbestic points developed in the pH range of ~ 1.0–2.2 which indicated the formation of more than one complex species.

Several equilibrium models were simulated to account for the spectral data using the STAR-94 program [6]. The lowest statistical parameters provided by the program gave the data in Table I for stoichiometries of the complex species and their formation constants. The formation constants of the hydrolyzed species of Fe(III) and the protonation constants of the ligand were kept constant during the simulation process by the STAR-94 program. In addition, the spectral contributions from the hydrolyzed species of Fe(III) were ignored with respect to that of the free Fe(III) as a result of the use of excess concentration of phosphate with respect to the metal ion. The presence of hydrolyzed complex species was found to predominate at pH values > 1.5, indicating that phosphate alone cannot ligate Fe(III). The polymerization of the complex was illustrated by the formation of 3 : 2 : −2 ($PO_4 : Fe^{3+} : H^+$), in which $2OH^-$ ligands may act as bridges between the two Fe(III) moieties. Including other polymeric species in the equilibrium models was not successful. The other monomeric hydrolyzed species exist as an indication of the predominance of the hydrolysis of Fe(III) even in the presence of ligating compounds. However, this also showed that phosphate cannot act as a bidentate ligand since, usually, bidentate or multidentate chelation of iron(III) prevents the formation of hydrolyzed complex in acidic media. The inclusion of other complex species containing more than 3 phosphate moieties in the chemical models were not successful in spite of using excess T_{phos} (the initial concentration of phosphate) with respect to T_{Fe} (the initial concentration of iron(III)).

Kinetic Study

The kinetic study of the Fe(III)-phosphate system was performed at wavelength 260 nm, where the mixture has appreciable absorbance at various pH values. *Pseudo* first order rate conditions were applied in which $T_{\mathrm{phos}} \gg T_{\mathrm{Fe}}$. One step was observed in the millisecond time range. Fig. 2 shows the observed rate constants (k_{obs}) as a function of pH at various phosphate concentrations while Fig. 3 shows k_{obs} as function of T_{Phos} at interpolated pH values. The curves are best represented by the following equation:

$$k_{\mathrm{obs},\,i} = A_i + B_i T_{\mathrm{phos}} + C_i T_{\mathrm{phos}}^2 \quad (\text{at a given pH}_i) \tag{1}$$

The plot of $[(k_{\mathrm{obs}} - A_{\mathrm{i}})/T_{\mathrm{phos}}]$ *vs.* T_{phos} produced a set of straight lines at various pH values, Fig. 4. The values of parameter A in Eq. (1) were estimated from Fig. 4, and the parameters B and C were calculated from Fig. 5. The values of B and C are listed in Table II. The parameters are all reciprocally dependent on hydrogen ion concentrations. The major species of Fe(III) and phosphate in the pH range used are the aquated Fe^{3+}, $Fe(OH)^{2+}$, and $Fe(OH)_2^+$ and H_3PO_4 and $H_2PO_4^-$ in the case of the phosphate. In order to account for the mechanism of the interaction of the solvated Fe(III) species with phosphate species at least 16 pathways should be considered. The set of reactions in Scheme 1 were selected on the following bases :

1. Deprotonation reactions are very rapid with respect to the complex formation reactions and beyond the speed of the stopped-flow techniques.
2. The formation of the second complex from the first is also a fast process and beyond the speed of the stopped-flow techniques.
3. The reactions of the phosphate moieties with iron(III) dimer were ignored due to the experimental conditions used in this work.
4. The formation constants of the chloro complexes of Fe(III) are much lower than that of the aquated and hydroxo complexes of Fe(III).

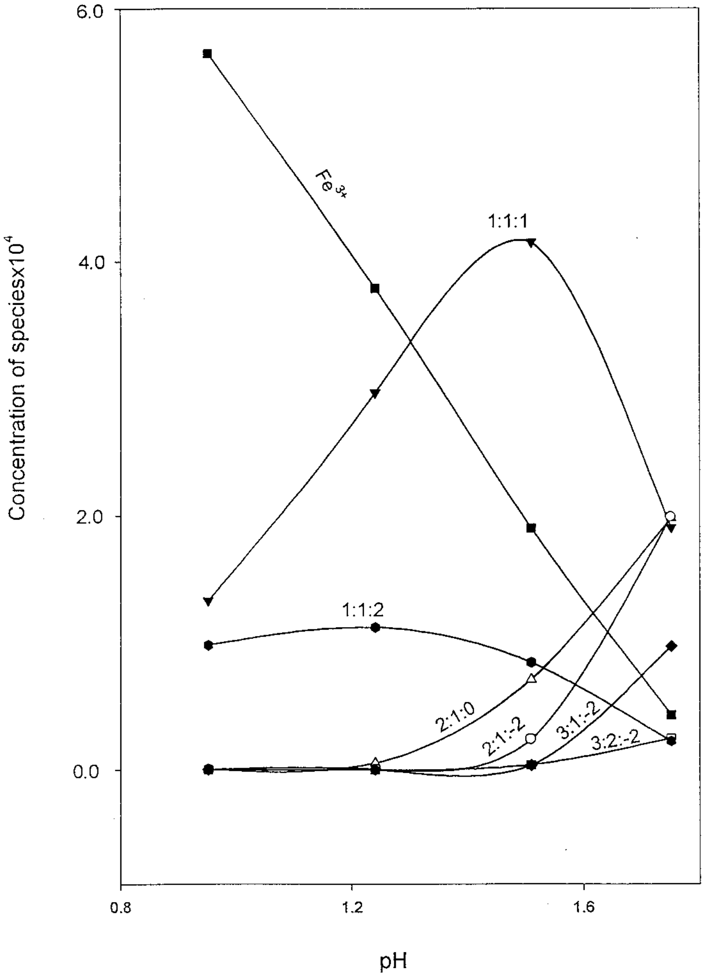


FIGURE 2 Species distribution of the Fe(III)–phosphate system at different pH values.

Slow Processes (Scheme I)

(a) $Fe^{3+} + H_3PO_4 \rightleftharpoons FeH_2PO_4^{2+} + H^+ \quad k_1, k_{-1}$

(b) $FeOH^{2+} + H_3PO_4 \rightleftharpoons FeH_2PO_4^{2+} + H_2O \quad k_2, k_{-2}$

(c) $Fe(OH)_2^+ + H_3PO_4 \rightleftharpoons FeH_2PO_4^{2+} + OH^- + H_2O \quad k_3, k_{-3}$

(Fast process) $\downarrow\uparrow + H_2PO_4$

(d) $Fe^{3+} + 2H_3PO_4 \rightleftharpoons Fe(H_2PO_4)_2^+ + 2H^+ \quad k_4, k_{-4}$

(e) $FeOH^{2+} + 2H_3PO_4 \rightleftharpoons Fe(H_2PO_4)_2^+ + H_2O + H^+ \quad k_5, k_{-5}$

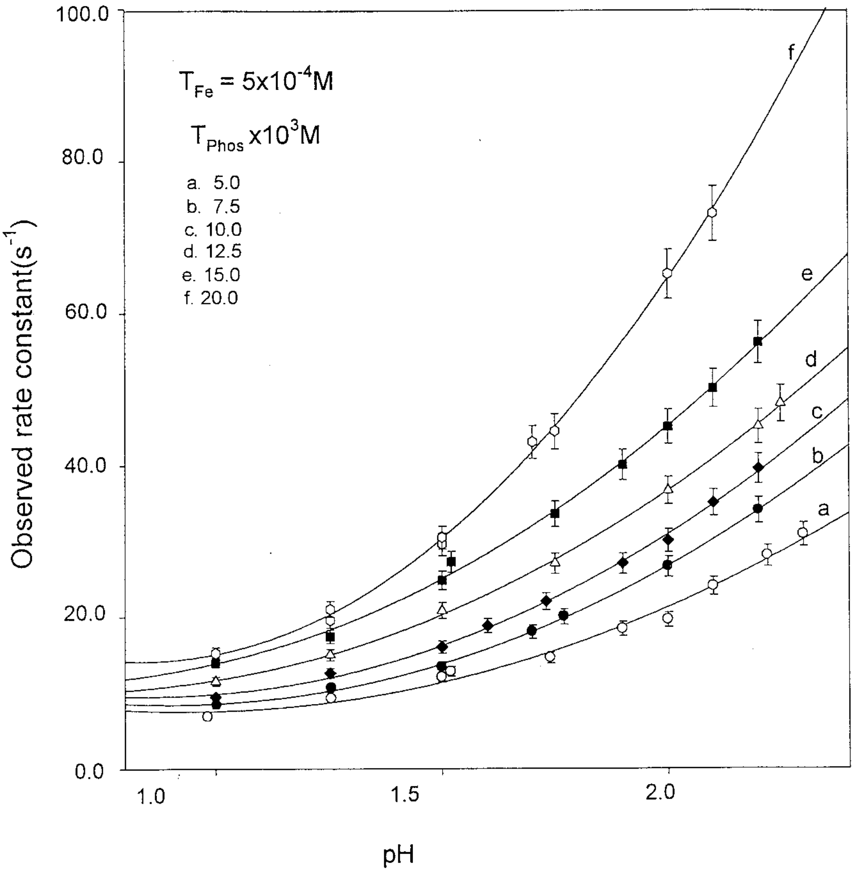


FIGURE 3 The observed rate constants as function of the pH values at different concentration of phosphate.

(f) $Fe(OH)_2^+ + 2H_3PO_4 \rightleftharpoons Fe(H_2PO_4)_2^+ + 2H_2O \quad k_6, k_{-6}$

(g) $Fe^{3+} + H_2PO_4^- \rightleftharpoons FeH_2PO_4^{2+} + \quad k_7, k_{-7}$

(h) $FeOH^{2+} + H_2PO_4^- \rightleftharpoons FeH_2PO_4^{2+} + OH^- \quad k_8, k_{-8}$

(i) $Fe(OH)_2^+ + H_2PO_4^- \rightleftharpoons FeH_2PO_4^{2+} + 2OH^- \quad k_9, k_{-9}$

(j) $Fe^{3+} + 2H_2PO_4^- \rightleftharpoons Fe(H_2PO_4)_2^+ \quad k_{10}, k_{-10}$

(k) $FeOH^{2+} + 2H_2PO_4^- \rightleftharpoons Fe(H_2PO_4)_2^+ + OH^- \quad k_{11}, k_{-11}$

(l) $Fe(OH)_2^+ + 2H_2PO_4^- \rightleftharpoons Fe(H_2PO_4)_2^+ + 2OH^- \quad k_{12}, k_{-12}$

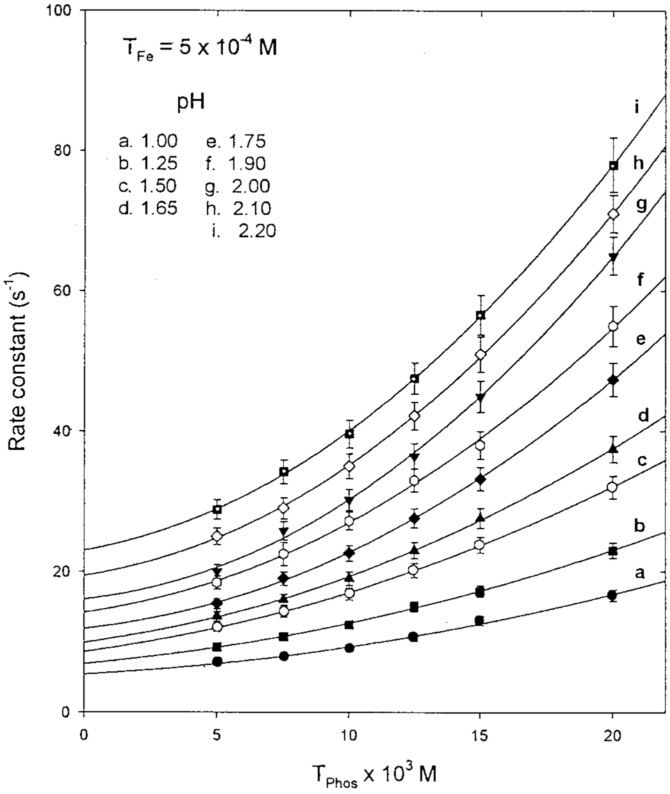


FIGURE 4 The observed rate constants as function of different concentration of phosphate at interpolated pH values.

Fast Processes

$$
\begin{aligned}
&FeH_2PO_4^{2+} \rightleftharpoons FeHPO_4^{+} + H^{+}\\
&\quad \uparrow\downarrow\ +H_2PO_4^{-}\\
&Fe(H_2PO_4)_2^{+} \rightleftharpoons Fe(PO_4)_2^{3-} + 4H^{+}
\end{aligned}
$$

where k_i and k_{-i} are the forward and backward rate constants.

The rate of the mechanism described in Scheme 1 can be described by the following differential equation:

$$Q_2(dC_2/dt) = T_{\mathrm{Fe}}(Q_4/Q_3) - C_2\{(Q_2 \cdot Q_4/Q_3) + Q_5\} \qquad (2)$$

and the integrated form is

$$\ln\,(C_{2\infty}/(Cl_{2\infty} - C_{2t})) = \ln(\mathrm{As}_{2\infty}/(\mathrm{As}_{2\infty} - \mathrm{As}_{2t})) = kt \qquad (3)$$

($\mathrm{As}_{2\infty}$ and As_{2t} are the absorbances of C_2 at infinite time t_∞ and time t)

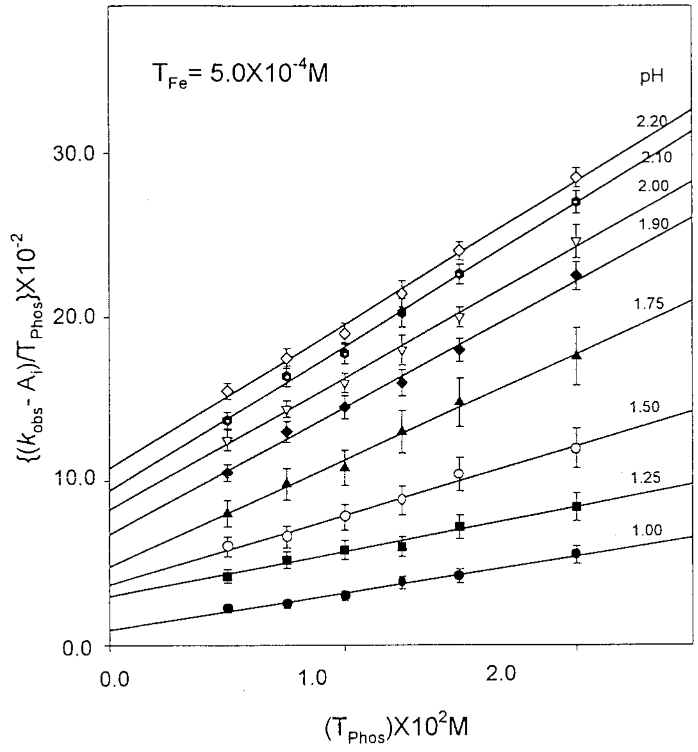


FIGURE 5 The plot of $[(k_{obs} - A_i)/T_{phos}]$ *vs.* T_{phos}.

TABLE II Summary of the parameters A, B and C and other pertinent data as function of (H^+)

pH	$H \times 10^2 M$	$(H)^{-1}$	α_0	A_i	$B_i \times 10^{-2}$	$C_i \times 10^{-4}$	$(B_i/\alpha_o) \times 10^{-2}$	$(C_{i-}/\alpha_0^2) \times 10^{-4}$
1.00	10.0	10.00	1.00	6.0	1.0	2.30	1.110	2.30
1.25	5.60	17.90	0.83	7.0	2.5	2.80	3.010	4.38
1.50	3.16	31.60	0.74	9.0	3.8	4.20	5.140	7.67
1.75	1.78	56.20	0.61	11.7	4.85	6.60	7.950	17.84
1.90	1.26	79.40	0.53	13.2	6.7	7.90	12.64	28.20
2.00	1.00	100.00	0.47	15.0	8.0	8.40	17.02	38.20
2.10	0.79	125.90	0.41	17.2	8.8	9.30	21.46	54.70
2.20	0.63	158.70	0.36	21.0	10.0	9.50	27.78	73.10

and

$$k = (Q_4/Q_3) + (Q_5/Q_2) \tag{4}$$

where

$C_1 = (FeH_2PO_4)$,
$C_2 = (Fe(H_2PO_4)_2)$,
$Q_2 = 1 + K_c/(H_2PO_4)$ (where $K_c = (FeH_2PO_4)(H_2PO_4)/(Fe(H_2PO_4)_2)$)

$Q_3 = 1 + \beta_{1\mathrm{OH}}(\mathrm{H}^+)^{-1} + \beta_{2\mathrm{OH}}(\mathrm{H}^+)^{-2} \sim 1$; (where $\beta_{1\mathrm{OH}}$ and $\beta_{2\mathrm{OH}}$ are the first and second overall hydrolysis constants of Fe (III)),

$$\begin{aligned} Q_4/Q_3 \sim Q_4 = {} & \{k_1 + (k_2\beta_{1\mathrm{OH}} + k_7 k_{1\mathrm{h}})(\mathrm{H}^+)^{-1} + (k_3\beta_{2\mathrm{OH}} + k_8 K_{1\mathrm{h}}\beta_{1\mathrm{OH}})(\mathrm{H}^+)^{-2} \\ & + (k_9\beta_{2\mathrm{OH}}K_{1\mathrm{h}})(\mathrm{H}^+)^{-3}\}\alpha_0 T_{\mathrm{phos}} + \{k_4 + (k_5\beta_{1\mathrm{OH}})(\mathrm{H}^+)^{-1} \\ & + (k_6\beta_{2\mathrm{OH}} + K_{1\mathrm{h}}^2 k_{10})(\mathrm{H}^+)^{-2} + (k_{11}K_{1\mathrm{h}}^2\beta_{1\mathrm{OH}})(\mathrm{H}^+)^{-3} \\ & + (k_{12}K_{1\mathrm{h}}^2\beta_{2\mathrm{OH}})(\mathrm{H}^+)^{-4}\}\alpha_0^2 T_{\mathrm{phos}}^2 \end{aligned} \tag{5}$$

where α_0 is $= (\mathrm{H}^+)^3\ \{(\mathrm{H}^+)^3 + (\mathrm{H}^+)^2 K_{1\mathrm{h}} + (\mathrm{H}^+)\ K_{1\mathrm{h}}K_{2\mathrm{h}} + K_{1\mathrm{h}}K_{2\mathrm{h}}K_{3\mathrm{h}}\}^{-1}$ and $K_{1\mathrm{h}}$, $K_{2\mathrm{h}}$ and $K_{3\mathrm{h}}$ are the deprotonation stepwise constants of phosphoric acid; and

$$\begin{aligned} (Q_5/Q_2) \approx Q_5 = {} & \{k_{-1}(\mathrm{H}^+) + k_{-2} + k_{-3}(\mathrm{OH}^-) + k_{-7} + k_{-8}(\mathrm{OH}) \\ & + k_{-9}(\mathrm{OH}^-)^2\}(K_c/\alpha_1 T_{\mathrm{phos}}) \\ & + \{k_{-4}(\mathrm{H}^+)^2 + k_{-5}(\mathrm{H}^+) + k_{-6} + k_{-10} + k_{-11}(\mathrm{OH}^-) + \mathrm{k}_{-12}(\mathrm{OH}^-)^2\} \end{aligned} \tag{6}$$

The coefficients of Eq. (1) could be correlated with the coefficients of Eqs. (4) and (5) such that

$$\mathrm{A} = \{k_{-6} + k_{-10} + k_{-11}(\mathrm{OH}^-) + k_{-12}(\mathrm{OH}^-)^2\}; \tag{7}$$

(since 'A' is not function of the reciprocal of T_{Phos} and is independent of hydrogen ion concentration, the terms containing such variables were ignored from Eq. (5)).

$$\begin{aligned} \mathrm{B} = {} & \{k_1 + (k_2\beta_{1\mathrm{OH}} + k_7 K_{1\mathrm{h}})(\mathrm{H}^+)^{-1} + (k_3\beta_{2\mathrm{OH}} + k_8 K_{1\mathrm{h}}\beta_{1\mathrm{OH}})(\mathrm{H}^+)^{-2} \\ & + (k_9\beta_{2\mathrm{OH}}K_{1\mathrm{h}})(\mathrm{H}^+)^{-3}\}\alpha_0, \end{aligned} \tag{8}$$

and

$$\begin{aligned} C = {} & \{k_4 + (k_5\beta_{1\mathrm{OH}})(\mathrm{H}^+)^{-1} + (k_6\beta_{2\mathrm{OH}} + K_{1\mathrm{h}}^2 k_{10})(\mathrm{H}^+)^{-2} + (k_{11}K_{1\mathrm{h}}^2\beta_{1\mathrm{OH}}) \\ & (\mathrm{H}^+)^{-3} + (k_{1\mathrm{h}}^2 k_{1h}^2\beta_{2\mathrm{OH}})(\mathrm{H}^+)^{-4}\}\alpha_0^2 \end{aligned} \tag{9}$$

The parameter 'A' (Table II) was found to be linearly dependent on $(\mathrm{H}^+)^{-1}$ with an intercept equal to 5.5 ± 0.3, standing for $(k_{-6} + k_{-10})$, and slope equal to $(9.6 \pm 0.3) \times 10^{-2}$ and stands for $k_{-11}K_{\mathrm{W}}$ (K_{W} is the ionic product of water $= 10^{-13.76}$ [9] at the ionic strength of 0.15 M); i.e. $k_{-11} = 6 \times 10^{12}\ \mathrm{M}^{-1}\,\mathrm{s}^{-1}$. On the other hand, the parameter 'B' divided by α_0 was found to be quadratically dependent on $(\mathrm{H}^+)^{-1}$ with the first coefficient ~ 0; i.e. $k_1 \sim 0$, the second coefficient is equal to 15 ± 2 and stands for $(k_2\beta_{1\mathrm{OH}} + k_7 K_{1\mathrm{h}})$, and the third coefficient is equal to $(2 \pm 1)10^{-2}$ and stands for $(k_3\beta_{2\mathrm{OH}} + k_8 K_{1\mathrm{h}}\beta_{1\mathrm{OH}})$. If the assumption is made that one term may be ignored with respect to the other one can conclude that $k_2 = 2 \times 10^4\,\mathrm{M}^{-1}\,\mathrm{s}^{-1}$, $k_3 = 2 \times 10^4\ \mathrm{M}^{-1}\,\mathrm{s}^{-1}$, $k_7 = 1 \times 10^3\,\mathrm{M}^{-1}\,\mathrm{s}^{-1}$ and $k_8 = 2 \times 10^3\,\mathrm{m}^{-1}\,\mathrm{s}^{-1}$. In addition, the parameter 'C' divided by α_0^2 was also found to be reciprocally dependent on the hydrogen ion concentration with the first coefficient equal to ~ 0; i.e. $k_4 = 0$, the second coefficient is equal to 3.0×10^3 which stands for $(k_5 \beta_{1OH})$; i.e. $k_5 = 3 \times 10^5\,M^{-1}\,s^{-1}$ and the third coefficient is equal to 1.3×10^{-3} and stands for $(k_6\beta_{2OH} + K_{1h}^2 k_{10})$. If we apply the same assumption by ignoring one term with respect to the other in the third coefficient one can arrive to $k_6 = 3 \times 10^3\ M^{-2}\,s^{-1}$ and $k_{10} = 10\,M\,s^{-1}$.

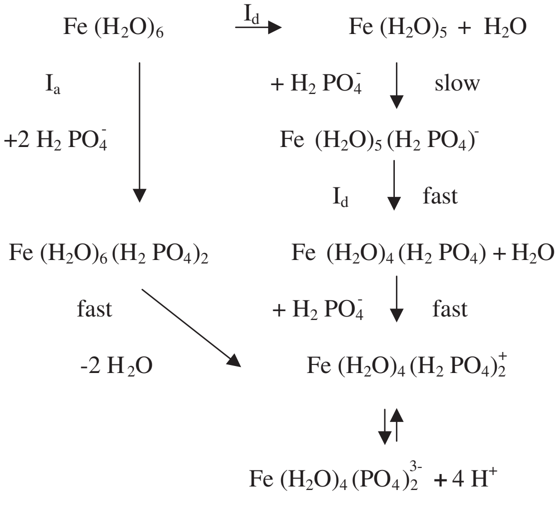
DISCUSSION

Iron transport in living organisms follows the same trend as bioassimilation of substances and their subsequent distribution among the body components. This trend depends primarily upon the ease with which they traverse biological membranes. Two types of transport are considered, active and passive transport. Active transport has many features, among them the transport against concentration gradient and if the substance is charged, against a potential gradient. On the other hand, passive transport is diffusion-controlled and only permits the transit of lipophillic molecules. However, there are some exceptions to the above classification in cases where pores exist in the membrane, facilitated diffusion through saturation mechanism or extrusion of vesicles for larger particles [13]. Most of the iron(III) phosphate complexes obtained in this work are charged and hydrophilic species which are unable to penetrate the membrane due to the high energy required to establish transit from an aqueous into a lipid phase. So it should be expected that active transport is the main type of transport used by iron(III) phosphate complexes.

Due to the steric hinderance exhibited by a six coordinating monodentate ligands such as phosphate groups, iron(III) may attain octahedral structure by forming mixed hydroxo complexes. This is evidenced by the presence of $(PO_4^{3-} : Fe^{3+} : H^+)$ $2 : 1 : -2$ and $3 : 1 : -2$ at pH values > 1.4. There is also the possibility of polymerization illustrated by the presence of $3 : 2 : -2$ species at pH values > 1.6, Fig. 2, where the Fe^{3+} dimerization is probably through two bridged hydroxide species. Although the concentrations of the polymeric species at lower pH values are not appreciable, they will be of greater magnitude at a biological value of 7.4, if it is assumed that there are no extra equilibrium species. Polymerization is not popular if phosphate complexes of Fe^{3+} are employed for clinical uses. They are difficult to clear *via* the kidney.

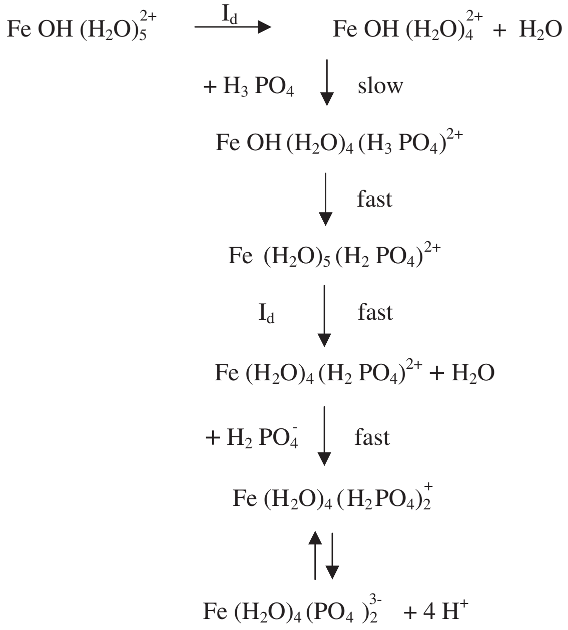
Kinetic results showed that the rate constants for reactions (b), (c), (f), (g), and (h) (except reaction (e)) are in the range of 10^2–10^4 for the octahedral substitution reactions of Fe(III) [7]. Although the reactivity of $(FeOH)^{2+}$ is well documented, that of $(Fe(OH)_2)^+$ is not. Very few reports indicate activity for the latter species [8]. It is common practice to assume that the formation of the second complex is slower than formation of the first complex. The higher rate constant of reaction (e) suggests that the reactivity of the first ligating phosphate species exceeds that of the hydroxy species. A similar result was previously found when Fe(III)–pyridoxol reacted with glycinehydroxamate [9], where pyridoxol (a vitamin B_6 compound) acted as a monodentate ligand ligating Fe(III) through the phenoxy group. Anations of $(FeOH)^{2+}$ by $(HSO_4)^{-1}$ and $(SO_4)^{-2}$ to form $(Fe(H_2O)_4OHSO_4)$ have also been reported with rate constants of 1.4×10^5 and 3×10^5, respectively [10]. The hydroxo species was not lost in the suggested mechanism. In this work the backward rate constants are reciprocally dependent on hydrogen ion concentration which suggest loss of the hydroxy species from the inner sphere of the formed complex. One should expect that the extra bonding between the vacant *d*-orbitals of S- or P-containing ligands and the filled *d*-orbitals of iron(III) species may play a significant role in enhancing the rate of complex formation. In addition it seems that the formation of protonated complex species are preferable over unprotonated species in the mechanism in Scheme 1, although this is not compatible with the results obtained from the equilibrium study, Table I. This incompatibility may be overcome by assuming that there is a subsequent fast deprotonation not detected by the stopped-flow techniques. Moreover, the role of chloro complexes of the Fe(III) species was not accounted for in the mechanism described in Scheme 1 due to their very low stabilities compared with the aquated and hydrolyzed species of the Fe(III) ions. The formation of two overlapped rate reactions may indicate that the phosphate cannot act as a bidentate ligand since it is rarely a bidentate ligand behaving in a similar manner in reacting with Fe(III) ion species.

The mechanism shown in Scheme 1 does not actually represent the true situation for indirect substitution reactions preferred by octahedral complexes. Scheme 2 (a and b) describes a detailed mechanism where some of the reactions can be envisaged to occur undetected by the stopped-flow techniques. The low reactivity of the aquated free Fe(III) toward the phosphate with respect to the other hydroxy species, except reactions (g) and (i) in Scheme 1, suggested an I_a mechanism rather than I_d mechanism. However, the latter can be assumed to occur if the entering group is negatively charged as in case of reaction (g) or when the first ligand labilizes the *trans* water allowing its replacement with another ligand as in reaction (i) in Scheme 1. The formation of $Fe(H_2O)_4(H_2PO_4)_2^+$, as in reaction (i), through an I_a mechanism involves a three body collision making it less probable as evidenced by the low value of its rate constant k_{10}.



SCHEME 2a.

An I_d mechanism was suggested for reactions involving the hydroxo species of iron (III) [14] as a result of the *trans* labilizing effect of the OH^- moiety on Fe(III). In such cases the reactive species is H_3PO_4 at pH values < 1.4 as shown by the value of k_2, and by $H_2PO_4^-$ at pH values > 1.4 as shown by the value of k_8. An I_d mechanism



SCHEME 2b.

may also be visualized in the formation of 2 : 1 complex as a result of the *trans* labilizing effect of the first coordinated H_2PO_4, Scheme 2b.

The reactivity of $Fe(OH)_2^+$ may be explained similarly to that of $FeOH^{2+}$ by an I_d mechanism except that H_3PO_4 is the only reactive phosphate species.

The kinetic results showed that the backward rate constants are not of appreciable magnitude with respect to the forward rate constants except reaction (k) (Scheme 1) where $k_{-11} = 6 \times 10^{12}\ M^{-1}\ s^{-1}$ indicating that these reactions are of low kinetic lability in acidic media and probably of high kinetic lability in basic media. In other words, the dissociation of these complexes in biological systems is low in acidic and neutral media and probably is high in basic media.

The rate of the interaction of phosphate with Fe(III) is at least ten times greater than that of PLP with Fe(III). Although both systems showed formation of two complex species 1 : 1 and 1 : 2 (Fe(III): phosphate or PLP), yet in the iron(III)–PLP system the rates of formation of both species were in different time ranges with the second step slower than the first step while for Fe(III)–phosphate the two steps were overlapped, with the second step faster than the first step. It may be concluded that the faster (first step) rate in the Fe(III)–PLP is due to the interaction of the phosphate moiety of PLP with Fe(III) and the second slow step was due to the interaction of phenolic moiety with Fe(III).

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