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The Kinetics of Adsorption of Calcium and Magnesium Ions on to an Insoluble Sodium Polyphosphate

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ABSTRACT

The adsorption kinetics of calcium and magnesium on to an insoluble sodium polyphosphate were determined at 25°, 37°, and 49°C. The adsorption process has two distinct phases, an initial rapid phase lasting 10–20 min and a slow phase which occurs over several hours. The data were fitted to a two-site adsorption model by nonlinear least squares regression and the rate constants of the rapid and slow adsorption phases were estimated. Experimental adsorption rates for magnesium are lower than for calcium and this may be because the greater energy of dehydration of magnesium ions hinders adsorption. The high experimental adsorption densities for both ions suggest that the effective surface area is substantially larger than the estimate obtained by helium adsorption. It is suggested that the large apparent surface area may be due to the deposition of a gel layer of insoluble calcium or magnesium polyphosphates on the surface.

INTRODUCTION

The simplest oxyacid of phosphorous is the tetrahedral molecule orthophosphoric acid, which in aqueous solution has one strongly dissociating and two weakly dissociating protons. If the tetrahedra link by sharing single oxygen atoms, the resulting polymers are called condensed phosphates. There are many condensed phosphates, most of which are polyanionic species although some neutral molecules (e.g., P_4O_{10}) do exist. Condensed phosphates exist as linear or cyclic molecules and also as branched molecules isomeric with the linear and cyclic structures.

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Maddrell's phosphate type II (MPI) is a member of a group of linear-chain structures, which are described by the general formula, $M_{(n+2)}P_nO_{(3n+1)}$, where M is an alkali metal such as sodium (1). The simplest member of the group is sodium pyrophosphate, where $n = 2$. The lower members ($n < 10$) and the high polymers ($n > 100$) form well-characterized crystalline solids, whereas the intermediate polymers are amorphous glassy mixtures often referred to as oligophosphates. The metaphosphates are cyclic structures described by the formula $(MPO_3)_n$. When n is very large, $n \approx (n + 1) \approx (n + 2)$, and hence the high polymeric polyphosphates approximate metaphosphate composition (2). The very high polymers, commonly with values of n of the order 10^2–10^4, are usually terminated by OH groups rather than 0-metal groups and should be written as $M_n(H_2P_nO_{(3n+1)})$ (2).

MPI is a very high molecular weight polymer, prepared by subjecting $NaH_2PO_4 \cdot H_2O$ to a variety of heating and cooling cycles (3). This results in low- and high-temperature forms which may be distinguished by x-ray diffraction (ASTM index) and infrared spectroscopy (4). Type II, the high-temperature form is regarded as being practically insoluble in water (1) and was selected for study as an adsorbent for cationic drugs. Furthermore, the insolubility of MPI is simply related to the very high molecular weight (1).

The first phase of such a project was to elucidate the mechanism and kinetics of adsorption of such cations. However, this is complicated by the potential micellization of the drugs, the lack of an accurate definition of the size of the hydrated cation, and the initial rapidity of the process which makes mathematical modeling difficult due to a paucity of data. The choice of the inorganic divalent cations calcium and magnesium offered some simplifying advantages. These two ions: (a) do not micellize, (b) display a slower rate of adsorption, (c) belong to the same periodic group—and so the effect of ionic size and hydration may become apparent, and (d) have been widely studied in other systems (5–18).

The kinetics, equilibrium, and/or thermodynamics of adsorption of calcium and magnesium have been studied on a wide variety of surfaces, including oxides and silica (5–10), hydroxyapatite (11), phosphate salts of tetravalent metals (12–15), and mixed phosphate or silicate salts (16–18). In those cases where a distinction between the adsorption behavior of the two ions could be made, calcium adsorbed more rapidly or had a greater affinity for the surface (5,9–14,16,17). However, magnesium had a greater affinity than calcium for silica (6) and hematite (α-Fe_2O_3) (7).

In order to interpret the adsorption of metal ions on to oxide surfaces, it has been noted (10) that there are three important factors: (a) the Coulombic attraction between species of opposite charge, (b) the formation of specific ion-surface complexes (i.e., specific adsorption), and (c) the related effects of ionic radius and hydration. As well as these factors, the effect of hydration of the surface must also be considered.

It is apparent that two similar divalent cations will experience similar Coulombic forces of attraction. Therefore, differences between calcium and magnesium may be due to specific surface complexation reactions or to differences in their size and/or the energetics of their hydration and dehydration. That calcium is not always preferred over magnesium suggests that surface factors (such as hydration) or specific complexation processes may be important. Several authors have discussed the importance of the energetics of ion hydration (19,20) and surface hydration (21) with regard to cation adsorption selectivity. A review on the bioinorganic chemistry of calcium has briefly contrasted the hydration and complexation of calcium and magnesium (22).

MATERIALS AND METHODS

Materials

The insoluble sodium polyphosphate glass (Maddrell's phosphate type II) and the buffered indicator tablets were purchased from the Sigma Chemical Company and E. Merck, respectively. All other reagents were of analytical reagent quality and were used as received.

Spectroscopic Analysis and Fundamental Properties

The MPI powder was dried over silica gel at 0.1 torr for 96 hr. It was examined by x-ray diffraction spectroscopy (Phillips PW1050 Goniometer and PW1051 Counter) using CuK_α radiation, infrared spectroscopy (Perkin-Elmer 599) of a 2% dispersion in KBr and solid-state ^{31}P nuclear magnetic resonance spectroscopy (Bruker CXP/300) indirectly referenced to 85% phosphoric acid, by performing dipolar-decouple/magic-angle spinning and ^{31}P-^{1}H cross-polarization analyses. The particles were examined by scanning electron microscopy (Phillips 505) and were subjected to particle size analysis by

Fraunhoffer laser diffraction methods employing a Malvern 2600D.

Surface Area and Density Determination

The specific surface area was determined with a Perkin-Elmer Sorptiometer 212D. The outgassing for this continuous flow technique was completed in 4 hr at 25°C, by flushing the sample with helium gas. The density of the powder was determined with water at 25°C in a specific gravity bottle and was employed in the calculation of the specific surface area.

Kinetic Procedures

The adsorption reactions occurred in a water-jacketed glass vessel, in which 100 ml of 0.05 M solutions of calcium or magnesium chloride were stirred magnetically with a Teflon-coated bar. The temperature within the reaction vessel was maintained within 0.1°C of the nominal temperature. Five grams of MPI were quickly added to commence an experiment. Although the powder is readily wetted by the aqueous solution and is rapidly suspended by the stirrer, as adsorption occurs the MPI becomes more coarsely aggregated. Twenty to 30 sec before the required sampling time, the stirrer was turned off to allow the aggregated suspension time to settle and reveal sufficient supernatant for sampling. The sample was taken within ±3 sec of the nominated time. The procedure was repeated until sufficient samples had been collected or the suspensions became impossibly aggregated. The volume of the sample was not replaced, but the total sample volume never exceeded more than 8% of the initial volume. The residual amounts of adsorbate were determined by the analytical procedures described below, and the calculation of the amount adsorbed allowed for that quantity of adsorbate removed in the sample aliquots. All experiments were performed in quadruplicate. Control experiments confirmed that the cations did not adsorb on to the experimental apparatus.

Analytical Methods

For the chelometric titration of calcium and magnesium, a buffered indicator tablet and 2 ml of an ammonia buffer (5.4% ammonium chloride and 35% ammonia liquid in water) were added prior to titration with 0.005 M EDTA. As advised by the manufacturer of the indicator, the EDTA was neutral and was stored in a polyethylene reservoir. The titrant was standardized with a solution of calcium chloride prepared from calcium carbonate which was dried to constant weight at 105°C, dissolved in a few drops of concentrated hydrochloric acid, and made up to volume with distilled water.

Data Analyses

At any sampling time, the concentration of the cation remaining in solution was expressed as a fraction of the initial solution concentration. The fractional amount remaining was regressed against time by nonlinear least squares regression using NONLIN (23). Three different polyexponential equations were fitted to each data set and the statistical criteria of Boxenbaum and coworkers (24) were used to select the most suitable equation.

RESULTS AND DISCUSSION

Spectroscopic Analyses and Fundamental Properties

The data obtained from x-ray diffraction and infrared spectroscopic analysis of the MPI were compared to the standard literature and it was concluded that the powder was Maddrell's phosphate type II. The broad infrared (IR) peak at about 3500 cm^{-1}, which resisted drying, and the ^{31}P nuclear magnetic resonance spectra suggested the presence of P-OH groups.

The mean particle size, geometric standard deviation, and density of the commercial sample were 11.3 μm, and 2.61 and 2.69 g/cm^3, respectively. The scanning electron micrographs showed that the particles were aspherical and no larger than about 15 μm. The surfaces of the particles were very rough, but it was not clear whether the surface "outcrops" were smaller adhering particles. Some of the particles appear to have striations.

The Kinetics of Adsorption of Calcium and Magnesium

The residual concentrations of cation in solution at the various sampling times were normalized by expressing each concentration as a fraction of the original concentration, i.e., Q_T/Q_{ZERO}. When $\log_{10}(Q_T/Q_{ZERO})$ was plotted against time, a straight line could be drawn by eye through the points at long times but the points at short times deviated positively from the extrapolated line. A typical set of solution data are plotted in Fig. 1. The data sets were individually subjected to nonlinear

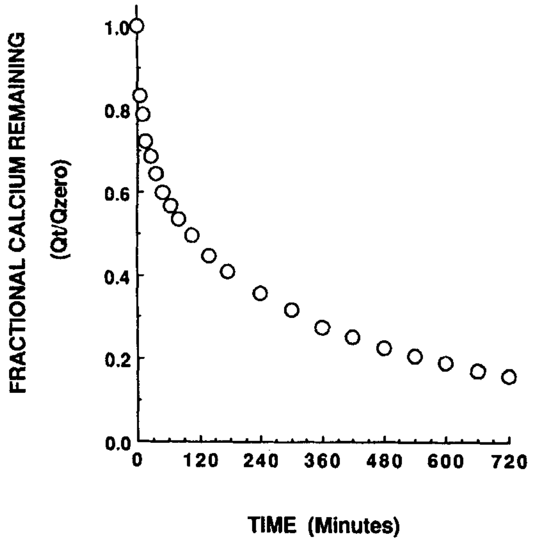


Figure 1. The change in fractional quantity of calcium in solution during adsorption onto MPI at 25°C. The fractional quantity is expressed as Q_T/Q_{ZERO}, where Q_T and Q_{ZERO} are the quantities present at any time during the experiment and initially, respectively.

least squares regression by NONLIN; the initial parameter estimates were obtained graphically.

Three different bi- or triexponential equations were fitted to each set of data.

$$Q_T/Q_{ZERO} = A\exp(-\alpha t) + B\exp(-\beta t) \tag{1}$$

$$Q_T/Q_{ZERO} = k + A\exp(-\alpha t) + B\exp(-\beta t) \tag{2}$$

$$Q_T/Q_{ZERO} = C\exp(-\gamma t) + A\exp(-\alpha t) + B\exp(-\beta t) \tag{3}$$

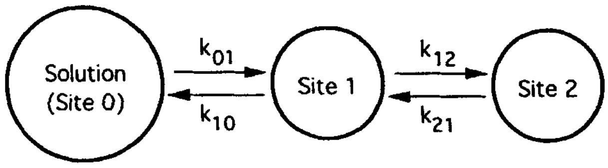
where A, B, C, α, β, γ, and k represent the fitted model-independent parameters. Using an F test (24), it was shown that Eq. (2) provided a significantly ($p = 0.05$) improved fit compared to Eq. (1), while Eq. (3) did not provide a significant improvement over Eq. (2). All of the presented results pertain to the parameter estimates obtained with Eq. (2). At infinite time, Eq. (2) reduces to $Q_T/Q_{ZERO} = k$. Clearly, k represents that fraction of the original quantity of ion which is present in solution at equilibrium, and therefore Eq. (2) provides a conceptually pleasing representation of the adsorption process, compared to Eqs. (1) and (3), which, at infinite time, predict that $Q_T/Q_{ZERO} = 0$.

The analogies between this treatment of the adsorption data and traditional compartmental pharmacokinetic analysis are apparent. Equations (1)-(3) have often been employed to describe drug plasma concentrations according to a simple two- or three-compartamental model. However, it must be remembered that, although attractively realistic anatomical interpretations of the compartments may be reached, they are essentially hypothetical and are invoked to allow the mathematical description of the data.

Likewise, it is possible to impose realistic physical interpretations on the compartments or adsorption sites in this experimental system. Figure 2 shows both two-adsorption site interpretations of Eq. (2). The systems consist of a solution phase (i.e., site 0), from which the samples are taken for assay, and two adsorption sites. Adsorption site 1 is labile; i.e., adsorption and desorption occur very rapidly. Site 2 is a slow site at which the adsorption density slowly increases. After a sufficient period of time, site 2 becomes the dominant contributor to the overall adsorption density. The two systems are described as: (a) the sequential model in which adsorption onto site 1 occurs and then the adsorbate is relocated on to site 2, and (b) the parallel site model in which adsorption onto the two sites occurs simultaneously. It should be noted that transfer between all adsorption sites is by reversible equilibria.

Equation (1) describes a system similar to the sequential model, except that the transfer from site 1 to 2 is irreversible. Equation (3) describes a system similar to the parallel-site model, except that there are three adsorption sites and the transfer from the solution compartment to one of the sites is irreversible. The introduction

(a) Seqential adsorption site model



(b) Parallel adsorption site model

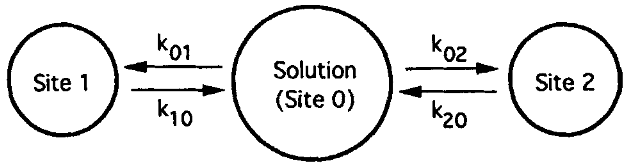


Figure 2. The two-compartmental interpretations of Eq. (2) which were employed in the nonlinear regression of the adsorption data.

of an irreversible transfer to any adsorption site, assuming that site is not saturated, allows the concentration of the ion remaining in solution to decrease to zero at infinite time. This is not consistent with the usual observations in this and other experimental adsorption systems.

However, the measured data are solution concentrations and the adsorption densities are calculated as $Q_{ZERO} - Q_T$. It is impossible to experimentally distinguish between sites 1 and 2, and the calculated adsorption densities are the total of the densities at the two sites. Therefore, it is not possible to unambiguously propose a particular model. With this in mind, the discussion is limited to the model-independent parameters estimated by NONLIN (e.g., k, A, α . . .) rather than the model-dependent microconstants (e.g., k_{10}, k_{12}, etc.) shown in Fig. 2.

The mean adsorption densities for calcium and magnesium are shown in Figs. 3 and 4, respectively. It is apparent that an increased temperature causes a marked reduction in the equilibration time, and that the adsorption density of calcium always exceeds that of magnesium. The kinetic data, summarized in Table 1, show that the adsorption rates of magnesium are considerably slower than those for calcium. The beta phases are some 20 times slower than the alpha phases and an increase in the temperature accelerates both the alpha and beta phases.

As the adsorption density of the ions increases, they will form a uniform monolayer if the distribution of anionic sites permits. If the atomic radius of the cation is known, the theoretical monolayer capacity may be estimated, by assuming: (a) the ions behave as nondeformable spheres arranged in hexagonal close packing, and (b) that based upon their projected area they can never occupy more than 84.2% of a planar surface. It has been suggested (25,26) that a useful estimate of the effective radius of an ion in solution is given by the sum of the crystal radius and the diameter of a water molecule. Using crystal radii for calcium and magnesium of 0.99×10^{-10} m and 0.65×10^{-10} m, respectively (9), and 2.76×10^{-10} m as the diameter of water (26), the calculated areas of the hydrated ions at the MPI/solution interface are 44.2×10^{-20} m^2 for calcium and 36.5×10^{-20} m^2 for magnesium.

Since the maximum experimental adsorption densities, at 49°C, are 902 and 725 μmol/g for calcium and magnesium, respectively, a monolayer with maximum packing density requires an available surface area of about 286 m^2/g. If the ions are completely dehydrated prior to adsorption, the effective area at the interface will be smaller (e.g., 3.1×10^{-20} m^2 for calcium) and the area required to satisfy the adsorption density would be about 20 m^2/g.

The measured specific surface area of MPI is about 2 m^2/g. Although this value is low in comparison to other inorganic phosphates such as hydroxyapatite, it is similar to the value of 1.6 m^2/g reported for dicalcium phosphate dihydrate (27). If we assume that the mean particle diameter determined by laser diffraction approximates the volume surface diameter, then it is possible

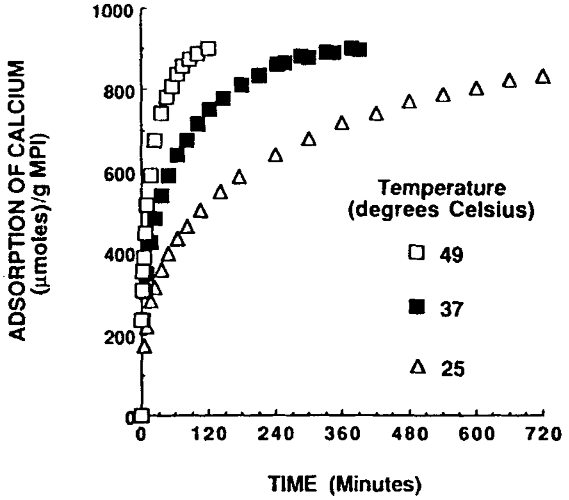


Figure 3. The kinetic profiles of adsorption of calcium on to an insoluble sodium polyphosphate at various temperatures.

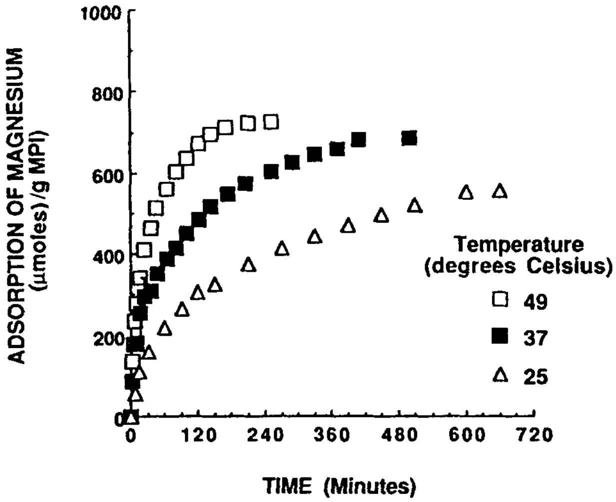


Figure 4. The kinetic profiles of adsorption of magnesium on to an insoluble sodium polyphosphate at various temperatures.

Table 1

The Half-lives (in minutes, and their standard deviations) for the Alpha and Beta Adsorption Phases of Calcium and Magnesium on to MPI at 25°, 37°, and 49°C

Ion	Phase	Half-lives (min) at Three Temperatures (°C) 25	37	49
Ca^{2+}	Alpha	5.46 (0.23)	2.65 (0.08)	0.95 (0.08)
	Beta	165.43 (7.87)	61.89 (0.16)	20.13 (0.21)
Mg^{2+}	Alpha	14.85 (1.79)	5.50 (0.16)	2.41 (0.21)
	Beta	254.00 (9.31)	103.63 (1.53)	39.56 (0.79)

to calculate an estimate of the specific surface area according to Eq. (4), where ρ is the particle density and d_{vs} is the volume surface diameter (28). Due to the approximate nature of this calculation, no Hatch-Choate corrections were made.

$$\text{Specific surface area} = 6/(\rho d_{vs}) \qquad (4)$$

This yields a value of about 0.2 m^2/g, which indicates that the measured value is credible, since the calculated value will not account for surface irregularities which will increase the true area.

Clearly, the measured adsorption densities greatly exceed the densities which would be expected from the adsorption of a monolayer. The simplest interpretation is that the adsorption data suggest the apparent presence of a large available surface area, and this shows that under identical conditions magnesium has a lower affinity for MPI.

Various models for ion adsorption assume that the ions and the surface are (at least) partially dehydrated upon adsorption (25). The simplified Born model for ion hydration predicts that magnesium, with its smaller crystal radius, would have the larger free energy of hydration and would be less readily dehydrated. This is supported by data cited in Ref. 22 which show that the rate of exchange of water molecules between the bulk solution and the inner hydration sphere is about 10^3 times faster for calcium than magnesium.

The progressive conversion theory of ion exchange (29) proposes that progressively deeper layers or shells of a reactive ion exchanger are converted by the exchanging ion as it penetrates into the exchanger particles. Such penetration would demand that the MPI particles have a porous surface region. Such porosity may be preexisting or may develop in situ due to the adsorption process itself. The latter is akin to the proposal that a gel layer of hydrolysates forms on the surface of oxides and that chemisorption occurs within that layer (30). If the ions are completely dehydrated upon penetration into a surface gel layer, the thickness of that layer would only be about 150 × 10^{-10} m for calcium, even if the ions occupied only 10% of the theoretically available volume.

CONCLUSIONS

The Suggested Mechanism

Ionic adsorption due to Coulombic attraction must be preceded by diffusion from the bulk solution to the surface. It is probable that only partial dehydration of the cation would be necessary for adsorption to occur. The large hydrated magnesium ions would have a lower mobility than the calcium ions, while at the surface, magnesium would be less readily dehydrated than calcium. Therefore calcium will have the higher initial adsorption rate. We propose that the ionic diffusion and (partial) dehydration, and the initial ion exchange between the cations and surface sodium ions, constitute the rapid alpha phase.

It is known that MPI dissolves slightly in water (1) and that calcium and magnesium may catalyze the hydrolysis of long-chain polyphosphates (31). It has also been observed in this laboratory that the complexes formed between soluble sodium polyphosphates and these cations are viscous and adhesive when hydrated. Therefore, the cations would react with dissolved MPI at the surface to form adhesive complexes which may be deposited on the MPI surface as a complex layer. This may promote the aggregation of the particles of MPI in suspension. Aggregation may also be induced nonspecifically by the presence of the divalent cations in solution through compression of an electrical double layer around the MPI particles. Further interaction between the cations and fresh MPI surface can only occur after the cations have diffused between the aggregated particles penetrated into and diffused through the complex layer. We suggest that this constitutes the slow beta phase.

While the diffusion of both ions would be reduced by the surface complex layer and aggregated particles, calcium with its larger crystal radius would be expected to be more adversely affected. However, the calcium beta rate is faster than that for magnesium. It should be noted that the net rate of adsorption is due to an equilibrium between uptake and desorption at the surface. Since the crystal radii of calcium and sodium are very similar, while the radius of magnesium is smaller than sodium, the calcium ion may be more compatible with the crystal lattice of MPI. This could lead to a greater desorption rate of magnesium and may account for the faster net adsorption and the higher overall adsorption density obtained with calcium.

In future papers we will relate these findings to the study of the adsorption of organic cations on to MPI and provide further evidence that Maddrell's phosphate type II may be a useful excipient in the formulation of sustained-release tablets.

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