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THE KINETICS OF FLUORIDE UPTAKE BY SYNTHETIC HYDROXYAPATITE

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The kinetics of fluoride uptake by synthetic hydroxyapatite from aqueous solution has been studied. Experiments involved exposing 0.1 g of synthetic hydroxyapatite to 5 cm³ of sodium fluoride solution in the concentration range 100-1000 ppm fluoride and determining fluoride concentration at regular time intervals with a fluoride ion-selective electrode. In all cases, uptake was found to follow pseudo-second order kinetics with correlation coefficients of at least 0.998; all systems equilibrated by 24 hours with equilibrium uptake values that varied with the initial fluoride concentration. The kinetic results differ from those previously reported for much lower concentrations of fluoride, but in the present case, the concentrations were of clinical relevance, as they are those used in fluoride-containing dental products. Further work is necessary to determine how well these findings model uptake by natural hydroxyapatite and hence the extent to which they might apply in vivo.

INTRODUCTION

The mineral phase of teeth consists of hydroxyapatite, Hap [4], a substance which may have a variety of minor substitutions within the lattice that have little or no effect on its crystalline structure or form [11]. The various compositions of HAP may be summarised by the formula $\text{Ca}_{(10-x)}(\text{HPO}_4)_x(\text{PO}_4)_{(6-x)}(\text{OH})_{(2-x)}$ where x varies from 0 to 1. The extreme compositions are $x = 0$, which gives stoichiometric hydroxyapatite, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$, with a Ca:P ratio of 1.67, and $x = 1$, which corresponds to $\text{Ca}_9(\text{HPO}_4)(\text{PO}_4)_5(\text{OH})$, which has a Ca:P ratio of 1.50 [11]. Biological apatites are also often carbonate-substituted and slightly calcium-deficient [4].

In vivo, the hydroxyapatite phase is a dynamic substance [6]. In contact with saliva, a saturated solution of calcium and phosphate ions, there is a constant process of deposition and dissolution of HAP known respectively as remineralisation and demineralisation. In a healthy mouth under optimum conditions these processes are in balance and the natural dentition remains sound and healthy. However, in the presence of the oral biofilm known as plaque, there is production of acid, predominantly lactic acid, and this shifts the position of the remineralisation-demineralisation steady state in favour of demineralisation [15]. The result is gradual loss of the mineral phase and onset of the decay process known as caries.

The presence of fluoride has long been known to interfere with this decay [2]. The uptake of fluoride by hydroxyapatite leads to formation of a mineral phase that is more resistant to acid attack than the fluoride-free mineral [8]. In addition, the presence of low concentrations of fluoride in saliva reduces the solubilising effect of saliva, thus making the HAP less able to dissolve in saliva. The net effect of these two changes is that, in the presence of fluoride, dental caries is substantially reduced or even eliminated [4].

Fluoride is therefore used in a variety of dental products, including oral care products such as toothpastes and mouthwashes [4]. Typical concentrations used are 1000 ppm and 200 ppm for toothpastes and mouthwashes respectively. In addition, in many places, low levels of fluoride are added to drinking water or table salt to ensure an adequate supply for good oral health in the populations thus treated [7].

Hydroxyapatite is able to take up fluoride by one of two mechanisms [19]. These are, respectively (for stoichiometric HAP):

- 1) Direct substitution of F^- for OH^- , *ie*

$$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 + 2\text{F}^- \rightarrow \text{Ca}_{10}(\text{PO}_4)_6\text{F}_2 + 2\text{OH}^-$$
- 2) Formation of CaF_2 which occurs as follows:

$$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 + 20\text{F}^- \rightarrow 10\text{CaF}_2 + 6\text{PO}_4^{3-} + 2\text{OH}^-$$

Reaction (i) is associated with a pH change in the surrounding solution towards more alkaline, though this

is readily buffered in vivo. Reaction (ii), fluorapatite formation, appears to occur by a mixture of direct precipitation and recrystallisation of HAp as fluorapatite [16]. In general, new crystalline layers at the HAp surface seem to develop from an amorphous interfacial layer containing the necessary ions (Ca^{2+} , OH^- , PO_4^{3-} and F^-)¹. The precise details of the composition of this interfacial layer determine which crystalline compounds form. These two mechanisms are reasonably well established, and although much is known about them, to date there have been very few studies of their dynamics.

Uptake kinetics for solutes onto inorganic solids have been modelled in three ways, namely first order or second order processes, or by the Elovich equation [9]. Because these equations are based on concentrations of adsorbing species in solution, rather than on adsorption capacities of the solid, they have been termed pseudo-first order and pseudo-second order respectively. For pseudo-first order, the form of the equation used is

$$\ln(q_e - q_t) = \ln(q_e) - k_1 t,$$

where q_e is the uptake at equilibrium in concentration units (e.g. ppm) and q_t the uptake at time t , also in concentration units. For pseudo-second order, the equation is

$$t/q_t = 1/(k_2(q_e^2)) + t/(q_e)$$

The Elovich equation was first developed in the 1930s as an empirical description of the adsorption of gases onto solids [9]. It is expressed as:

$$dq/dt = a \exp(-aq),$$

where a is the initial adsorption rate and a is the desorption constant. Although it has been used for systems other than gas adsorption, for example to model uptake of metallic pollutants onto solids from aqueous solution, it does have important limitations. It only describes a limiting property ultimately reached by the sorption curve, and it is entirely empirical, so cannot be used to obtain any insight into the mechanism of adsorption [9]. Moreover, many of the systems for which it has been claimed to apply have been shown to fit the pseudo-second order equation at least as well, if not better [10]. Indeed, of all the models, pseudo-second order seems to apply most widely [9,10], though pseudo-first order is also reasonably common, especially for low concentrations of adsorbing species.

In the case of fluoride and hydroxyapatite, there appears to have been only one study of the kinetics of uptake. It involved very dilute solutions of fluoride, *ie* of the order of 3×10^{-5} mg/L (30 ppb), adsorbing onto solid hydroxyapatite under both static and stirred conditions [5]. At these concentrations fluoride uptake was shown to be pseudo-first order under static conditions but pseudo-second order with stirring. Concentrations of fluoride were much lower than those used in oral health care and, since the concentration is known to influence

uptake kinetics [9,10], the present study was undertaken to determine uptake kinetics at higher concentrations fluoride ion. It has used potassium fluoride solutions at concentrations equivalent to 100, 250, 500, 750 and 1000 ppm in fluoride, and determined uptake kinetics using synthetic hydroxyapatite as the sorbent. In all cases, data were plotted as both pseudo-first order and pseudo-second order graphs to determine which better described the uptake processes.

EXPERIMENTAL

Potassium fluoride (99.99% pure, ex Sigma-Aldrich, UK) was employed in this study. A stock solution of 1000 ppm in fluoride was prepared by dissolving 0.7632 g KF in 250 cm³ water. Solutions corresponding to 750, 500, 250 and 100 ppm were prepared by appropriate dilutions of this stock solution.

Fluoride uptake experiments in static mode were conducted using synthetic hydroxyapatite (99.99% pure, ex Sigma-Aldrich), with between 0.1002 and 0.1006 g weighed out and exposed to 5 cm³ KF solutions of appropriate concentration in polypropylene centrifuge tubes. A blank experiment demonstrated that there was no fluoride uptake in the absence of hydroxyapatite. Fluoride concentrations were measured with a calibrated fluoride ion selective electrode (Orion 4 Star pH/ISE, ex Thermo Scientific, UK) with determinations at regular time intervals. All experiments were carried out in duplicate.

Data were tested for conformity to either pseudo-first order or pseudo-second order kinetics. The test plots employed were, respectively, $\ln(q_t)$ against t and $t/(q_t)$ against t . Lines of best fit were determined using least squares regression. Correlation coefficients were determined and used to establish which kinetic model best described the data obtained.

RESULTS

No uptake of fluoride was found to occur in the centrifuge tubes containing no HAp. This demonstrated that HAp was the only species showing adsorption of fluoride, and that fluoride ions did not become adsorbed onto the polypropylene walls of the storage vessels.

Experimental data for fluoride concentration with time for the first hour of adsorption for all five fluoride concentrations are shown in Table 1. The systems had equilibrated by 24 hours and did not change over the following week in all five cases. Equilibrium uptake varied with initial fluoride concentration, and was greatest for the 1000 ppm solution.

The loss of fluoride from solution has been recalculated as "equivalent fluoride uptake", the results for which appear in Table 2. With the exception of the 1000 ppm solution, uptake followed clear patterns with immediate effect, *ie* from the initial fluoride determination

at 5 minutes. For 1000 ppm, uptake appeared to fluctuate somewhat at this time, and steady uptake began from the 10 minute determination.

Test plots for pseudo-first order ($\ln(q_t)$ vs t) and pseudo-second order ($t/(q_t)$ vs t) are shown as Figures 1 and 2 respectively. Correlation coefficients showing conformity of these plots to the best fit straight lines are shown in Table 3.

DISCUSSION

The results show that the pseudo-second order equation best describes fluoride uptake by synthetic hydroxyapatite at all concentrations studied, *ie* from 100 to 1000 ppm. The pseudo-second order equation was derived as a general case assuming that there were two possible sites for sorption of the species of interest on the solid component [9,10]. However, it is not straightforward to relate kinetics of adsorption to the mechanism and there is no reason why two adsorption processes should necessarily give second order kinetics.

It should be noted that many systems have been found to follow pseudo-second order kinetics and this model seems to be more widely applicable than the pseudo-first order one [9]. In all cases, a chemical reaction at the surface seems to be significant in the rate-determining step.

The chemistry of hydroxyapatite and its interaction with fluoride has been widely studied [11], and shown to involve two possible reactions, as described in the Introduction [12,19]. These reactions are favoured under different conditions. At low fluoride concentrations, reaction 1, formation of fluorapatite, is favoured. It appears to occur at the surface through initial adsorption of F^- ions at calcium sites, followed by exchange with OH^- ions. At higher fluoride concentration, CaF_2 forms (reaction 2) by a surface precipitation process. The reason that this is favoured by higher concentrations is that calcium fluoride has a finite though very small solubility, namely $1.6 \times 10^{-5} \text{ g/cm}^3$ at 20°C [14], and at low concentrations of fluoride, little or no CaF_2 precipitates out of solution. Under such conditions, the F^-/OH^- exchange mechanism is favoured.

Table 1. Fluoride concentrations (ppm) at various time intervals for different initial concentrations.

Time (min)	1000 ppm	700 ppm	500 ppm	250 ppm	100 ppm
0	1000	750	500	250	100
5	959	660	419	189	67.5
10	870	622	400	184	66.3
15	825	600	388	180	65.1
20	796	586	378	178	64.5
25	775	572	371	176	63.7
30	759	562	367	175	63.3
35	748	556	362	173	62.9
40	737	551	359	172	62.5
45	730	544	356	172	62.1
50	721	539	353	171	61.1
60	709	531	349	170	60.2
Equilibrium (24 h)	670	524	345	170	55.2

Table 2. Equivalent uptake of fluoride (ppm) at various time intervals for different initial concentrations.

Time (min)	1000 ppm	700 ppm	500 ppm	250 ppm	100 ppm
0	0	0	0	0	0
5	41	90	80	61	32.5
10	130	128	100	66	33.7
15	175	150	112	70	34.9
20	204	164	122	72	36.5
25	225	178	129	74	36.3
30	241	188	133	75	36.7
35	252	194	138	77	37.1
40	263	199	141	78	37.5
45	270	206	144	78	37.9
50	279	211	147	79	38.9
60	291	219	151	80	39.8
Equilibrium (24 h)	330	226	155	80	44.8

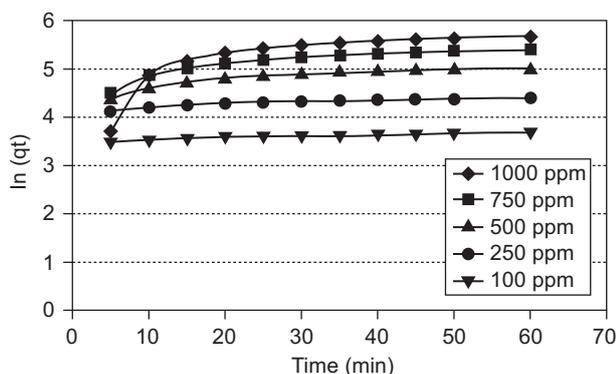


Figure 1. Pseudo-first order plots for fluoride uptake by HAp.

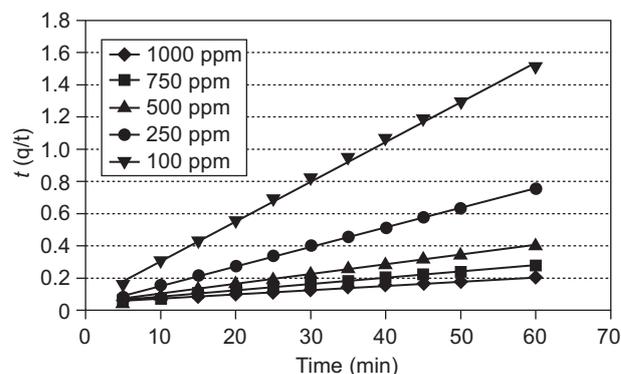


Figure 2. Pseudo-second order plots for fluoride uptake by HAp.

Table 3. Correlation coefficients of kinetic plots for different initial fluoride concentrations.

Plot	1000 ppm	700 ppm	500 ppm	250 ppm	100 ppm
Pseudo-1 st order	0.705	0.741	0.827	0.895	0.919
Pseudo-2 nd order	0.999	0.999	0.998	0.999	0.999

from 10 minutes onwards

Although there is no direct link between second order uptake kinetics and two possible adsorption processes, the change in the balance between the possible reactions does seem to be associated with a change from first order to second order kinetics [5]. The results obtained in the present study, using more clinically realistic fluoride concentrations, show pseudo-second order kinetics in all cases, a finding that is consistent with the occurrence of both possible uptake reactions.

Uptake of fluoride occurs to only a limited extent, and depends on the particle size of the hydroxyapatite [11,13]. At 37.4°C, the highest level of fluoridation recorded was 72% [11], and values of 3-4% appear more common for coarser grained Hap [13]. This is consistent with studies that have shown that only a thin film of fluorapatite forms, approximately three atomic layers in depth, on hydroxyapatite in the presence of fluoride [3]. The bulk remains unchanged because the fluoride ion is unable to diffuse into the solid HAp.

It is known that synthetic and natural hydroxyapatite differ. Natural HAp is capable of existing with a variety of uncontrolled substitutions, including of hydroxyl by carbonate, and also of occurring with slight non-stoichiometry [17]. It is also known to have a greater capacity for fluoride uptake than synthetic Hap [18]. Whether these differences in chemistry affect the kinetics of fluoride uptake in the range of the present study is not clear and requires further investigation. More work is needed to understand more fully the kinetics of fluoride uptake under clinical conditions using fluoride concentrations typical of those found in mouthwashes and toothpastes.

CONCLUSIONS

Fluoride uptake by synthetic hydroxyapatite from aqueous solutions of potassium fluoride in static conditions has been shown to follow pseudo-second order kinetics in the concentration range 100-1000 ppm. This contrasts with a previous study of fluoride sorption, which showed pseudo-first order uptake in static conditions

at concentrations around 30 ppb. Pseudo-second order uptake occurs where two sorption mechanisms can operate freely, as have previously been identified and reported. Because there are known differences between synthetic and natural hydroxyapatite, further work is necessary to determine the significance of the present findings for fluoride uptake by tooth mineral phase under clinical conditions.

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