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The behaviour of hydroxyapatite ceramics in an aqueous environment

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Hydroxyapatite ceramic prosthetic materials were exposed for 4 wk to a physiologic solution of known ionic composition as determined by inductively coupled plasma emission spectroscopy. The corrosion medium was kept at 70° C, changed each week for a fresh lot and the 7 d old medium re-analysed to establish the change in ionic content. Scanning electron microscopy was performed on the prosthetic materials to compare their surface ultrastructure before and after the corrosion test. SEM showed that the corrosion exposure seemed to have changed the surface of the ceramics through formation and deposition of spheritical precipitates with diameters up to 1.3 μm. The spectral analysis seemed to lead to the deduction that the corrosion exposure had induced a change in surface composition from Ca : P ratios suggestive of basic calcium phosphates (apatite, beta tricalcium phosphate (β-TCP)) to those perhaps implying equilibrium with monetite and brushite. Ignoring the effect of adsorption of other ions, it is argued that this shift could be attributed to the incorporation of H^+ from the aqueous solution. It is speculated that these surface chemical and morphological changes might be playing a role in the physico-chemical genesis of the bond known to occur between implanted HA and bone tissue.

1. Introduction

Surface reactive implant materials are supposed to possess the property of forming a physico-chemical bond with tissue when they are used for hard tissue replacement [1–3]. This has been said of calcium phosphate-containing implant materials [1, 2, 4, 5] as well as of materials composed of sintered calcium phosphates, notably hydroxyapatite (HA) [3, 6, 7]. The mechanisms leading to this bond formation have not yet been elucidated. The present study was an attempt to investigate whether HA implant materials which have been exposed to a corrosion medium *in vitro* undergo any discernible ultramorphological changes as a result of the exposure. Evidence of morphological changes would imply physico-chemical interaction between the corrosion medium and the surface of the implant material.

Apart from morphological studies, the corrosion medium used was retrieved and subjected to trace element analysis. This was aimed at establishing any causal relationship between ultrastructure and physico-chemical processes, a factor of particular relevance for surface-reactive prosthetic materials.

2. Materials and methods

Sintered macromicroporous HA implant material blocks were used in this study. According to the manufacturer (Heyl Chemisch-pharmazeutische Fabrik, Berlin), the blocks measuring 45 mm × 15 mm × 15 mm had a macroporosity of 30 to 35% (macropore diameter 100 to 1000 μm) and a microporosity of 1% (micropore diameter 0.5 to 1.5 μm). Two blocks were randomly chosen from a batch and cut in half using a diamond disc mounted in a semi-automatic saw. The cutting disc was rotating at a speed of 500 r.p.m. and the blocks were being steadily advanced to the disc at a speed of 3 mm min^{-1}. The four specimens obtained measured 20 mm × 15 mm × 10 mm.

One half of each block was used for the experiment and the other as a control. All four specimens were ultrasonically cleaned in benzol for 6 sec, air dried and weighed several times to constant values using an analysis scale of precision $\pm 10^{-6}$ g.

After the weighing procedure, the two control specimens were coated with 15 to 30 nm gold and viewed in a Leitz AMR 1600T SEM. Each of the two experimental specimens was suspended for a total of 4 wk in 1 litre corrosion medium (Fig. 1) of known trace element content. After every 7 d each specimen was transferred into a fresh medium and the 7 d old medium re-analysed for calcium, phosphorus, zinc, nickel, boron, manganese, aluminium, beryllium, copper and titanium, using inductively coupled plasma (ICP) emission spectral analysis [8].

The corrosion medium was a so-called complete electrolyte solution as used for intravenous infusions, with its pH stabilized at 7.2 by a tris-buffer. The temperature of the medium was kept constant at 70° C using a water bath and a thermostat (Fig. 1). Each specimen was suspended on a nylon string such that it lay below the meniscus of the medium. The vessel containing specimen and medium was hermatically

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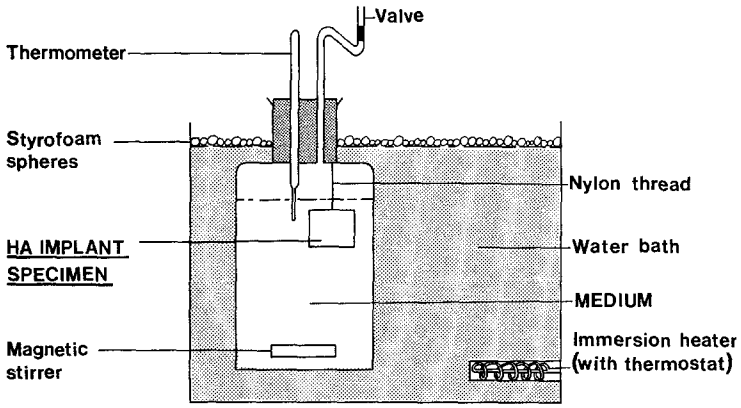

Figure 1 Diagrammatic representation of the apparatus and equipment used for the corrosion assay.

closed and equipped with a safety valve in case of excessive pressure. The vessel was supplied with a magnetic stirrer to ensure uniform distribution of heat and a thermometer to check the constancy of the temperature. Heat loss was minimized by covering the surface of the water bath with commercially available styrofoam spheres.

At the end of 4 wk the specimens were removed from the medium, dried for several days at 60° C and kept for 96 h under vacuum conditions ($\sim 10^{-3}$ torr) before being reweighed. Subsequently they were coated with 15 to 30 nm gold and studied by SEM.

3. Results

3.1. Weight

Within the limits and accuracy of the scale used, the weight values of the specimens before and after the corrosion test were practically unchanged, so the actual values are not reproduced here.

3.2. Scanning electron microscopy

Figs 2 and 3 represent the SEM results. Apart from the roughness due to sawing, the surfaces of the control specimens appeared smooth (Fig. 2). In contrast, the surfaces of the experimental specimens had developed, and were covered with spherical structures with diameters up to 0.3 μm (Fig. 3). This change in the surface morphology of the ceramics is thought to have been caused by corrosion.

3.3. Trace element analysis

The data for calcium and inorganic phosphate (P_i) – represented by phosphorus – are given in Figs 4, 5 and Table I. The values of all the other elements as determined in the medium before and after the corrosion test were not significant enough to warrant treatment here.

The two specimens (designated A and B) dissolved differently. With specimen A the concentration of calcium and phosphate going into solution increased each week, reaching a maximum at the end of the assay (Fig. 4, Table I). Specimen B, on the other hand, experienced its strongest dissolution stress during the first week, the stress decreasing up to the third week, to slightly increase towards the end of the assay (Fig. 5, Table I). In respect to the quantity of ions going into solution, specimen B lost more calcium and phosphate to the medium than specimen A. Over the duration of the corrosion test, specimen B lost 1.6 times as many ions as did specimen A (Table I).

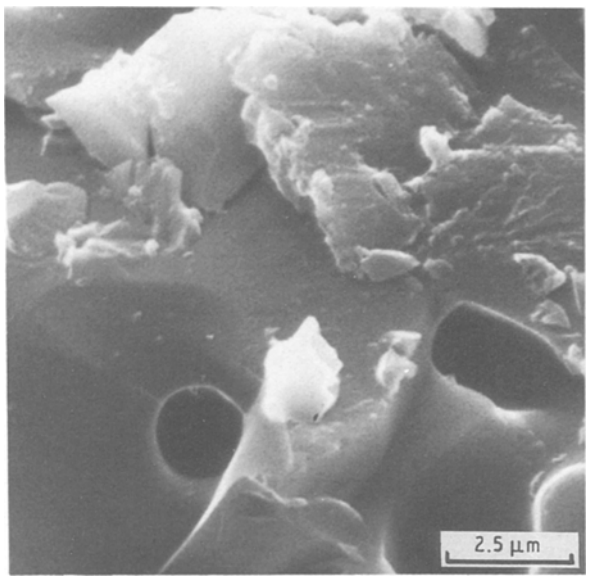

Figure 2 Surface appearance of HA before exposure to the corrosion medium. Apart from sawing debris, the ceramic surface appears smooth.

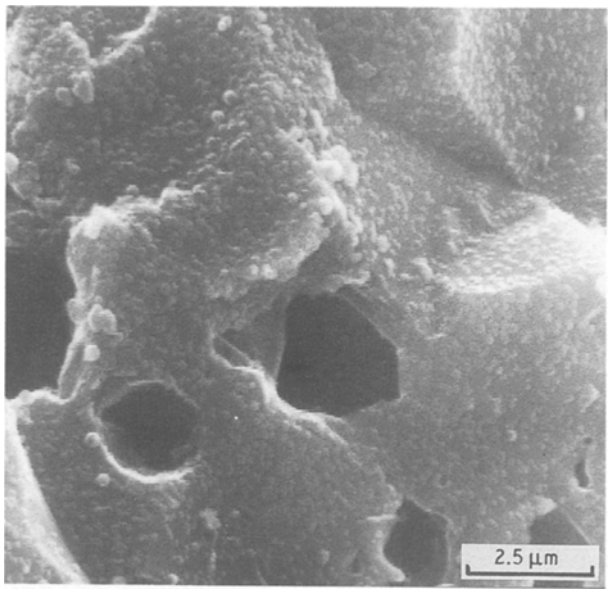

Figure 3 Structure of the HA surface after 4 wk exposure to corrosion medium. The surface is diffusively covered with fine nodular protuberances apparently resulting from interaction of the medium with the HA surface.

TABLE I Dissolution data of specimens A and B over the period of 4 wk at 70° C. The concentration of calcium and phosphate as determined each week are given with their corresponding Ca : P molar ratios

	Specimen A					Specimen B				
	Time (wk)				Total	Time (wk)				Total
	1	2	3	4		1	2	3	4	
$[Ca^{2+}]$ (p.p.m.)	3.285	3.269	3.972	5.536	16.062	9.030	7.033	4.955	5.475	26.493
$[P_i]$ (p.p.m.)	1.659	1.918	2.495	3.497	9.569	5.044	4.151	3.103	3.314	15.612
$[Ca^{2+}]$ (10^8 mol)	8.196	8.156	9.910	13.812	40.075	22.530	17.547	12.363	13.660	66.100
$[P_i]$ (10^8 mol)	5.356	6.192	8.055	11.290	30.894	16.285	13.402	10.018	10.699	50.404
$[Ca^{2+}]/[P_i]$ (mol)	1.53	1.32	1.23	1.22		1.38	1.31	1.23	1.28	

It was interesting to note that with increasing test duration the Ca : P molar ratio became progressively less in both specimens despite their different course of dissolution. The retrieved first-week medium of specimen A showed a Ca : P (molar) ratio of 1.53; in the fourth-week medium the ratio had dropped to 1.22. The first-week medium of specimen B showed a ratio of 1.38 that had dropped to 1.23 in the third-week medium, to increase slightly to 1.28 in the fourth-week medium.

The medium in this study was changed every week, to simulate the *in vivo* open system. The trace element analysis results suggest that when an HA ceramic is exposed to an open aqueous system whose pH is around the physiological value, the Ca : P ratio at its surface could drop to equilibrate finally at some minimum value (here ~ 1.2).

4. Discussion

If a sparingly soluble ionic compound in solid state $AB_{(s)}$ is introduced into a solvent, much of it will dissociate into the dissolved state $A^+_{(l)}$ and $B^-_{(l)}$ until equilibrium is reached at the saturation point, so that

$$AB_{(s)} \rightleftharpoons A^+_{(l)} + B^-_{(l)} \quad (1)$$

During the process the rate of dissolution and the actual amount of solute dissolved are a function of factors such as temperature, effective area of solute, as well as the compound's solubility coefficient relative to the solvent in question. Because the dissolution process is a reversible change, the dissolved solute is not an absolute, but a net shift, governed by the saturation point.

On the assumption that the surface-reactive implant materials [1, 4–7] behave like sparingly soluble compounds when introduced into aqueous solution, this study was designed to enquire into the *in vitro* ionic activity between an HA implant material and such a medium, with a view to possible extrapolation to their *in vivo* behaviour subsequent to implantation.

SEM showed that the corrosion process induced a colloidal transformation of the ceramic crystal surfaces. During the process the implant crystals (diameter 5 to 8 μm) developed spherical structures (diameter up to 0.3 μm) that can be interpreted as reprecipitated spherocrystallites and crystallite clusters.

The results of the trace element analysis are not meant to be equated with the dissolution behaviour of HA ceramics *per se*; the number of specimens tested (two), the runs of ICP emission spectral analysis carried out (eight), as well as the period of observation (4 wk) are too limited to allow such an assumption. However, the analysis does confirm the SEM results, that the HA implant materials interacted physicochemically with the physiological corrosion medium.

The quantitative difference in dissolution behaviour of the specimens could be a reflection of structural and chemical deviations in the material composition of the two specimens. X-ray diffractometry on a random-choice densely sintered specimen from the same batch had shown a β-TCP (whitlockite) inclusion phase

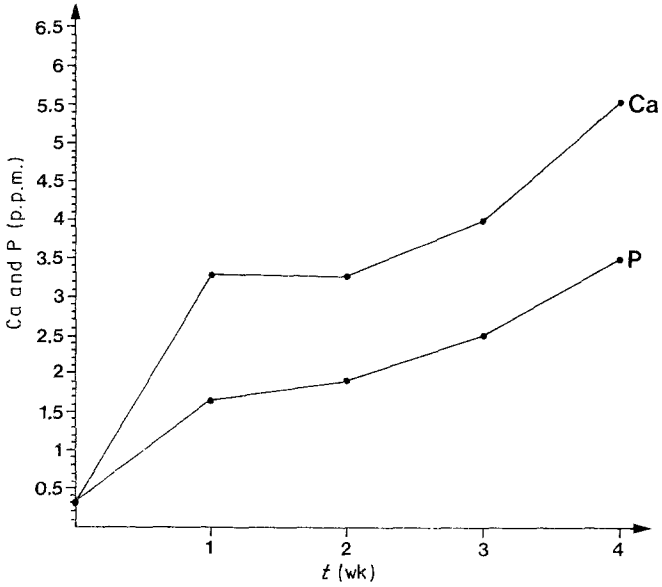

Figure 4 Schematic representation of the dissolution behaviour of specimen A showing the concentration of calcium (Ca) and inorganic phosphate (P) ions plotted against time.

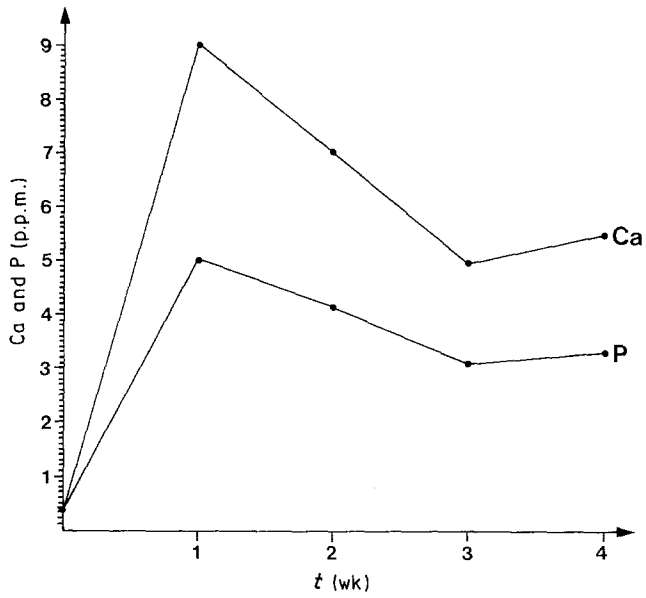

Figure 5 Schematic representation of the dissolution of specimen B showing the concentration of calcium (Ca) and inorganic phosphate (P) ions going into solution plotted against time.

making up 20% of the total ceramic composition [9]. Jarcho [10] has stated that densely sintered β-TCP is, depending on solution pH, 12 to 22 times more soluble than pure densely sintered HA. The difference in the solution behaviour observed in the present study could thus be an indication of differing inclusion phase content, notably β-TCP.

The shifting of the Ca : P ratio with increasing exposure time appears to be a property of calcium phosphates in aqueous solution. It seems that when HA materials are introduced into an aqueous environment their surfaces initially release ions into solution in accordance with their stoichiometry, but then, depending on pH, incorporate H^+ into their surface layers, thus eventually equilibrating with the surrounding solution at progressively lower Ca : P ratios. Below an attempt is made to guess at the dynamics that could be involved.

If HA materials contain β-TCP inclusions, these ought initially to be hydrolysed to hydroxyapatite [11]. Further, the "hydroxyapatites" made by calcination correspond more to "hydroxyoxyapatites" due to the oxyapatite ($Ca_{10}(PO_4)_6O^{2-}$) inclusions [12, 13]. In aqueous solution, oxyapatite is unstable and reacts with water according to

$$Ca_{10}(PO_4)_6O^{2-}_{(s)} + H_2O_{(l)} \rightleftharpoons 10Ca^{2+}_{(l)} + 6PO^{3-}_{4(l)} + 2OH^-_{(l)} \quad (2)$$

When HA in solid state is brought into contact with water, it initially goes congruently into solution

$$Ca_{10}(PO_4)_6(OH)_{2(s)} \rightleftharpoons 10Ca^{2+}_{(l)} + 6PO^{3-}_{4(l)} + 2OH^-_{(l)} \quad (3)$$

The foregoing must imply that at least up to this stage the intermediate products of β-TCP, oxyapatite and HA in solution all correspond to the dissolution products of HA. However, the Ca^{2+}, PO_4^{3-} and OH^- in solution can react with each other and with the hydronium ions (H_3O^-) of the medium. PO_4^{3-} are unstable and in neutral and acidic conditions accept H^+ to be reduced to monohydrogenphosphate ions

$$6PO^{3-}_{4(l)} + H^+_{(l)} \rightleftharpoons 6HPO^{2-}_{4(l)} \quad (4)$$

The PO_4^{2-} can then react with part of the Ca^{2+} released in Equations 2 and 3 to be reprecipitated as less-soluble monetite and brushite [14]

$$6PO^{2-}_{4(l)} + 6Ca^{2+}_{(l)} \rightleftharpoons 6CaHPO_{4(s)} \xrightleftharpoons{H_2O_{(l)}} 6HPO_4 \cdot H_2O_{(s)} \quad (5)$$

Further, OH^- can react with the remaining Ca^{2+} to be precipitated as less-soluble $Ca(OH)_2$ [14]

$$4Ca^{2+}_{(l)} + 8OH^-_{(l)} \rightleftharpoons 4Ca(OH)_{2(s)} \quad (6)$$

If complexes of the products of Equations 5 and 6 are precipitated on to the HA material surface, the composition of the material is bound to change. The overall effect of the equations depicted here is the incorporation of HPO_4^{2-} into the implant material surface. This would be expected to lead to a progressive drop in the Ca : P ratio, which is in agreement with Table I. This means that after considerable exposure to aqueous solutions, the surface composition of the HA materials no longer corresponds to the equilibrium state reached at manufacture but instead tends to the acidic (calcium-deficient) direction.

5. Conclusions

It is suggested that similar dissolution–reprecipitation phenomena could be operative at the implant/tissue interface *in vivo* following implantation of the so-called surface-reactive materials, and could partly constitute the "bioactive properties" of these materials. The formation of calcium-deficient compounds at the implant surfaces is made even more probable by the low pH induced into the implant bed following the inevitable implantation trauma. After surgery the pH value drops from the physiological value of 7.4 down to 5.19 and does not normalize until several days after the operation [15].

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