Calcium-containing inorganic polymers as potential bioactive materials

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Abstract In vitro studies are reported of the behaviour of potassium aluminosilicate inorganic polymers containing 10 wt% $Ca(OH)_2$, nanostructured calcium silicate and $Ca_3(PO_4)_2$ exposed to simulated body fluid (SBF). Heating to 600 °C lowers the alkalinity of $Ca_3(PO_4)_2$-containing samples, but their X-ray powder diffraction characteristics, ^{27}Al, ^{29}Si and ^{43}Ca MAS NMR spectra are unchanged by heating. Exposure of the heated compounds to SBF usually results in the formation of the crystalline biomineral phases hydroxylapatite and hydroxycarbonate apatite in the samples containing $Ca(OH)_2$ and $Ca_3(PO_4)_2$, but scanning electron microscopy/energy dispersive spectroscopy suggests that all the samples in the present study form calcium phosphates on exposure to SBF. This conclusion is also consistent with the removal of P from the SBF by all the samples. The concentrations of Al leached from the samples containing nanostructured calcium silicate and $Ca_3(PO_4)_2$ (0.05 and 0.47 ppm, respectively) are acceptable for biomaterials use, but apart from the $Ca_3(PO_4)_2$-containing sample, which takes up Ca from the SBF, the levels of Ca released into the SBF by the other samples are well in excess of the published optimum amount for stimulation of new bone growth by gene transcription in osteoblasts. Only the calcium silicate-containing samples release Si into the SBF, but in a concentration that falls short of the optimum amount. The strength of all the present compounds after heating is probably adequate for applications as biomaterials, but the $Ca_3(PO_4)_2$-containing compound shows slightly greater strength. Thus, on balance, the $Ca_3(PO_4)_2$-containing compound appears to be the most promising as a bioactive material.

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Introduction

Conventional inorganic polymers, sometimes known as geopolymers, are aluminosilicate materials based on a clay mineral such as kaolinite in which the structure has been perturbed by thermal removal of structural water at up to 800 °C, or by high-energy grinding [1]. When the solid aluminosilicate is reacted at near-ambient temperature with an alkali silicate solution at high pH, it forms a strong, durable material [2]. In addition to applications such as low-energy substitutes for Portland cement, fireproof panels and encapsulation of hazardous waste [3], inorganic polymers have been proposed [4–6] as bioactive materials capable of forming bone-like minerals by interaction with blood plasma. Several potential problems arise when an aluminosilicate geopolymer is brought into contact with living cells; the highly alkaline nature of the material can induce cell death, and there is a possibility of leaching of aluminium from the implant. The effect of aluminium in living organisms is controversial; Yap et al. [7], Geyer

et al. [8] and Hanston et al. [9] report that aluminium concentrations <2 ppm lead to brain disease, although lower concentrations of aluminium may be beneficial and stimulate the proliferation of osteoblasts and new bone formation [7]. Studies of gene-expression stimulation by the ionic products of a commercial bioactive glass (Bioglass® 45S5) indicate that the mechanism of new bone formation involves the stimulation of gene transcription in osteoblasts by Ca and Si ions leached from the glass [10]; the critical concentrations of these ionic species lie in the range 15–20 ppm of Si and 6–8 ppm of Ca.

In one approach to the development of bioactive inorganic polymers, a standard potassium geopolymer composition was heat treated at 250–625 °C to immobilise the leachable alkali and render the material sufficiently porous to allow the permeation of bone-forming fluids [5]. Heat treatment at 500 °C proved to be successful in fixing both the leachable alkali and aluminium in the geopolymer structure, giving a material that was stable both in vitro and in vivo [5]; however, there was no evidence that these compounds formed hydroxycarbonate apatite (HCA) or any other bioactive phase, suggesting they lacked inherent bioactivity.

In an attempt to introduce bioactive functionality into geopolymers, the known bioactive compounds hydroxyapatite (HA), tricalcium phosphate (TCP) and mixtures of both were added to potassium geopolymers which were then heat treated at 500 °C to introduce porosity [4]. In vivo studies in rabbits showed these materials were non-toxic up to 1 month and bonding to the bone was inferred from observations of bone penetration into the implants. Longer term in vivo experiments [6] using the same material showed that samples of about 64% porosity and compressive strengths of about 5 MPa represented the best compromise and that the implants were stable up to 6 months, with negligible leaching of Al into the blood up to 750 h. The decrease in pH from 10 to 7 upon heating was inferred from ^{1}H MAS NMR to be due to a reduction in the number of protons in the structure, although bound water is always present even up to 500 °C, either trapped in closed pores and/or associated with $(SiO)_3$–Al–OH groups [6].

The aim of the present work was to synthesise inorganic polymers with inherent bioactivity based on the previous successful synthesis of potassium compounds containing a range of calcium compounds including $Ca(OH)_2$, amorphous nanostructured calcium silicate and $Ca_3(PO_4)_2$ [11]. The effect of heating on the transfer of alkalinity from these materials into simulated body fluid (SBF) was investigated in vitro, and the mechanical strength and leaching of ionic species in SBF were determined. The effect of exposure to SBF on the structure of the inorganic polymers was determined by ^{27}Al, ^{29}Si and natural abundance ^{43}Ca MAS NMR, and the formation of new crystalline bone-forming phases was determined by X-ray powder diffraction (XRD).

Experimental

The potassium aluminosilicate inorganic polymers were prepared from New Zealand halloysite clay (Imerys Premium grade) dehydroxylated at 600 °C for 12 h. This was thoroughly mixed with potassium silicate solution (K66, Ineos Silicas, UK) and KOH (BDH reagent grade) dissolved in distilled water such that the molar composition was $SiO_2/Al_2O_3 = 3.24$, $K_2O/SiO_2 = 0.19$ and $H_2O/K_2O = 24.4$. This base composition was used to prepare samples containing 10 wt% $Ca(OH)_2$ (BDH reagent grade), amorphous nanostructured calcium silicate of composition $CaSi_{1.67}O_{3.75}·3H_2O$ (kindly supplied by Prof. J.H. Johnston and Dr. T. Borrmann), or $Ca_3(PO_4)_2$ (BDH reagent grade). XRD showed the $Ca(OH)_2$ to be highly crystalline, conforming to portlandite, PDF no. 44-1841, and the nanostructured calcium silicate to be an amorphous phase with additional major peaks of poorly crystalline calcium silicate hydrate (PDF no. 33-0306) and calcite, $CaCO_3$ (PDF no. 47-1743). The calcium phosphate was highly crystalline, but consisted of a mixture of calcium phosphate (PDF no. 17-0499) and basic calcium hydrogen phosphate (PDF no. 46-0905). After thorough mixing, the samples were placed in lubricated cylindrical polycarbonate moulds 30-mm diameter and 25-mm high, any trapped air was removed and the samples were compacted using a vibrating table, sealed in plastic bags and cured at 40 °C overnight. After demoulding and drying at 40 °C, the samples were stored in sealed plastic bags for further testing.

Prior to in vitro testing by exposure to SBF, the samples were heated to 600 °C at a heating rate of 3.5°/min before cooling at the natural furnace rate. These slow heating and cooling rates were used to minimise the risk of cracking the samples.

The SBF was of the improved Kokubo type, prepared according to the method of Oyane et al. [12] and stored in polythene bottles in a refrigerator until required. The inorganic polymer samples were immersed in 50 ml of SBF in closed plastic jars and placed in a water bath at 37.5 ± 0.5 °C for varying periods up to 7 weeks. To counteract depletion of the ionic species in the SBF due to the formation of biominerals by the inorganic polymer samples, the SBF was replaced every 2 weeks.

The unheated, heated and SBF-treated samples were investigated by a number of techniques, as follows.

Both powder and monolithic surfaces were examined by XRD (Philips PW 1700 with computer-controlled goniometer and graphite monochromator, using CoKα radiation). ^{29}Si, ^{27}Al and natural abundance ^{43}Ca solid-state MAS NMR was carried out under the following conditions.

The ^{29}Si spectra were acquired at 11.7 T (99.926 MHz) using a Bruker Avance spectrometer and a 5-mm Doty MAS probe spun at 5–6 kHz with a 6 μs ($\pi/10$) pulse

and a 30-s delay, the spectra being referenced to tetramethylsilane.

The 11.7 T ^{27}Al spectra were acquired at 130.224 MHz using a 4-mm Doty MAS probe spun at 10–12 kHz, with 1 s (π/10 pulse for solution), the spectra referenced to $Al(H_2O)_6^{3+}$.

The 14.1 T natural abundance ^{43}Ca MAS NMR spectra were acquired at 40.388 MHz using a Chemagnetics spectrometer and a 9.5-mm Varian probe spun at 3.5 kHz. A 3.5–4 μs (π/9 pulse for solution) RAPT enhanced single-pulse sequence was used [13, 14], with a delay of 0.5 s found to give the best signal-to-noise ratio. Between 59,227 and 117,824, scans were acquired per spectrum and the spectra were referenced to 1 M $CaCl_2$ solution [15].

Solid samples for electron microscopy were coated with 16 nm of carbon (for backscattered electron imaging and energy dispersive spectroscopy (EDS) analysis) or with 18 nm of gold/platinum for high-resolution imaging. The scanning electron microscope was a JEOL JSM-6500F, operated at 15 kV for the EDS analyses.

In order to determine whether the mechanical strength of these inorganic polymers is compromised by heating to reduce the alkalinity, the tensile strengths of the samples were determined by the Brazil method, in which cylindrical samples are broken by applying stress across their diameter [16]. The tensile strength σ is then given by,

$$\sigma = 2P/\pi Dt, \tag{1}$$

where P is the applied load and D and t are the diameter and thickness of the specimen, respectively. The tensile strength tests were carried out on 6–10 replicates using an Instron Universal testing machine with a 250-kN load cell and a crosshead speed of 1 mm/min.

The tensile strengths of samples after immersion in SBF were not determined because the small number of samples available would have given statistically unsatisfactory results. After immersion of the inorganic polymer samples in SBF, the Al, Si, P, K and Ca concentrations of the SBF were determined by inductively coupled plasma-atomic emission spectrometry (ICP-AES), and changes in its pH were monitored as a function of immersion time using an RS V5969 portable pH meter.

Results and discussion

Reduction of alkalinity by heating

Changes in the pH of the SBF are shown in Fig. 1 as a function of soaking time for the calcium inorganic polymers and the reference compound without calcium. All the samples produce a brief initial decrease in the pH of the SBF, but after equilibration the pH gradually increases with
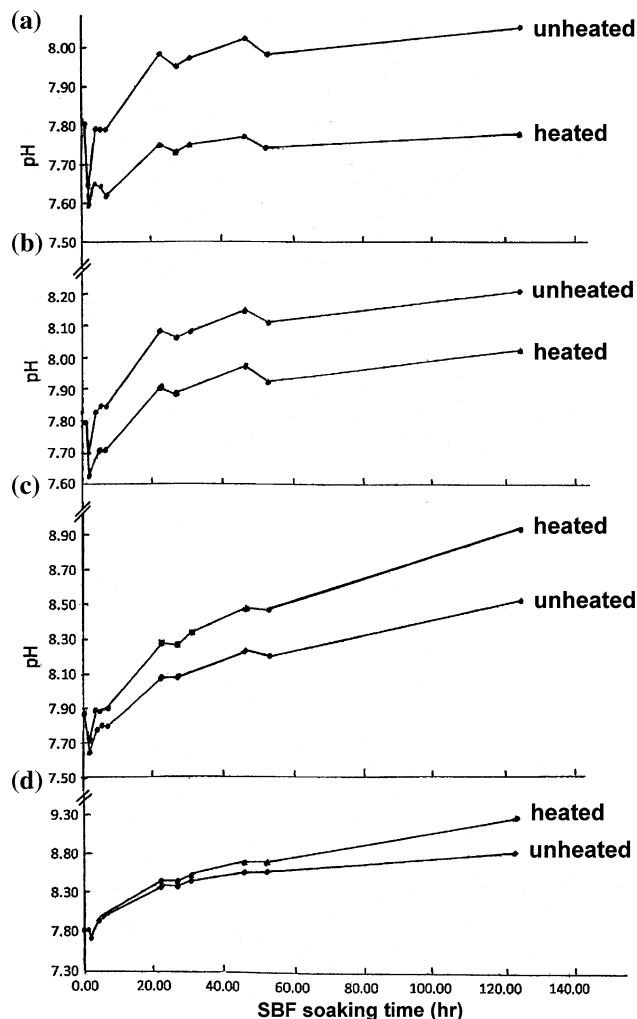

Fig. 1 Effect of heating at 600 °C on the pH of SBF after exposure to various Ca-containing inorganic polymers, as a function of soaking time. **a** Control sample, **b** sample containing $Ca_3(PO_4)_2$, **c** sample containing $Ca(OH)_2$, **d** sample containing nanostructured calcium silicate

time. This increase in the pH of the SBF produced by both the reference material (Fig. 1a) and the compound containing $Ca_3(PO_4)_2$ (Fig. 1b) is significantly lower in samples heated to 600 °C, whereas the reverse is the case with the compounds containing $Ca(OH)_2$ (Fig. 1c) and nanostructured calcium silicate (Fig. 1d). These pH values recorded as the samples approaching equilibrium are higher than those reported by Oudadesse et al. [5, 6], but their experiments were conducted in distilled water and are, therefore, not directly comparable, as some of the present bulk samples showed evidence of reaction with the SBF (formation of microcracks with gas evolution). The results for the phosphate-containing compounds may be understood in terms of the solubility of calcium phosphate in aqueous alkaline conditions, under which the stable phase at pH >4.2 is hydroxylapatite (HA) [17].

Unhydrated high-temperature calcium phosphate phases, such as TCP, interact with water or body fluids at 37 °C to form hydroxyl apatite. Thus, the solubility of TCP at the surface of the sample approaches the solubility of HA and decreases the solution pH [17]. On the other hand, the higher overall alkalinity of the samples containing nano-structured calcium silicate may reflect the higher content of KOH required to synthesise these samples. In terms of pH and material stability in SBF, the heated reference inorganic polymer and the heated calcium phosphate compound are the most promising.

X-ray powder diffraction

Representative XRD traces of the potassium inorganic polymers containing 10 wt% of the calcium compounds are shown in Fig. 2. The as-prepared sample containing $Ca(OH)_2$ (Fig. 2a) is a typical inorganic polymer showing an amorphous baseline feature centred at about $32°2\theta$ with superimposed sharp reflections of quartz and cristobalite
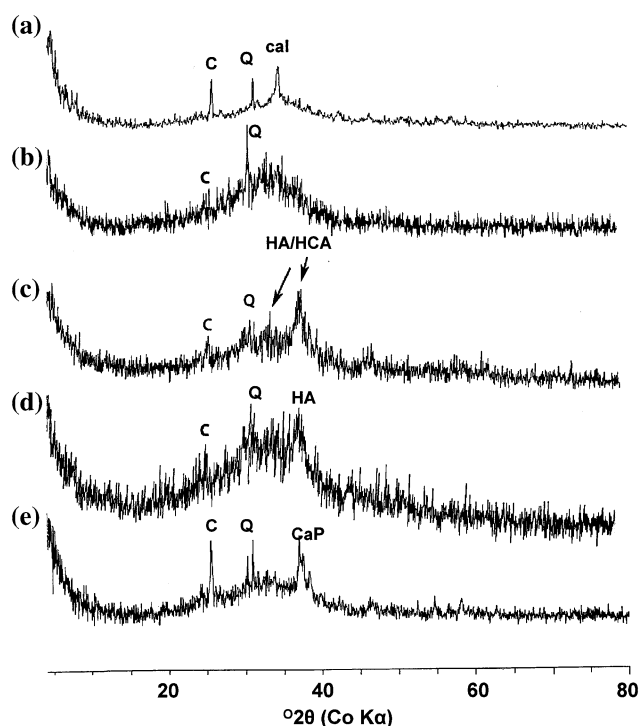

Fig. 2 Typical X-ray powder diffractograms of various Ca-containing aluminosilicate inorganic polymers. **a** As-synthesised sample containing $Ca(OH)_2$, **b** sample containing $Ca(OH)_2$, 600 °C, (also sample containing nanostructured calcium silicate, unheated and heated at 600 °C), **c** sample containing $Ca(OH)_2$, 600 °C, soaked in SBF, **d** sample containing nanostructured calcium silicate, 600 °C, soaked in SBF, **e** sample containing $Ca_3(PO_4)_2$, unheated, heated at 600 °C and soaked in SBF. *C* cristobalite (PDF no. 39-1425), *Q* quartz (PDF no. 33-1161), *cal* calcite (PDF no. 5-586), *HA* hydroxylapatite (PDF no. 9-432), *HCA* hydroxycarbonate apatite (PDF no. 19-272), *CaP* calcium hydrogen phosphate hydroxide (PDF no. 46-0905)

impurities from the halloysite reactant. This sample also contains the major reflection of calcite ($CaCO_3$) resulting from atmospheric carbonation of some of the $Ca(OH)_2$ (although crystalline $Ca(OH)_2$ is undetectable by XRD in these samples, its presence in an X-ray amorphous form is indicated by the scanning electron microscopy (SEM)/EDS results (below)). Apart from the loss of the calcite reflection, the XRD trace is unchanged after heating to 550–600 °C to reduce the alkalinity (Fig. 2b). After 4 weeks immersion in SBF, these samples previously heated at 600 °C show XRD evidence of the formation of both the bone-forming minerals HA (PDF no. 09-432) and hydroxylcarbonate apatite (PDF no. 19-272) (Fig. 2c). Samples pre-heated at 500 °C also show the presence of these new phases after SBF soaking, but in a less crystalline form. From the point of view of HA and HCA formation, these samples containing $Ca(OH)_2$ appear to be good candidates as bioactive materials.

The as-prepared samples containing 10 wt% nano-structured calcium silicate show a typical inorganic polymer XRD pattern with no additional reflections (Fig. 2b); this XRD trace is unchanged by heating at 600 °C, but on soaking for 4 weeks in SBF, broad new reflections of poorly crystalline HA and HCA appear (Fig. 2d).

The XRD pattern of as-prepared inorganic polymer containing 10 wt% $Ca_3(PO_4)_2$ (Fig. 2e) is that of a typical inorganic polymer with superimposed sharp reflections of calcium hydrogen phosphate hydroxide (PDF no. 46-0905), which are unchanged either by heating to 600 °C or by soaking in SBF. As the reflections of the calcium phosphate phase in the as-prepared inorganic polymer coincide with those of the products of biomineralization, these results cannot unambiguously prove the occurrence of such in vitro reactions, although SEM observations (below) show a change in morphology after soaking in SBF, which may be associated with the formation of new X-ray amorphous phases.

There is no XRD evidence of bioactivity in the control polymers not containing calcium compounds.

Multinuclear solid-state MAS NMR

Typical ^{27}Al and ^{29}Si MAS NMR spectra are shown in Fig. 3. The ^{27}Al spectra (Fig. 3a–c) are all very similar, showing the typical dominant tetrahedral resonance of an inorganic polymer containing these calcium compounds [11]. The asymmetry in the resonance from the AlO_4 site with a tail to negative shift is consistent with some degree of structural disorder producing a spread of quadrupole interaction parameters [18]. Apart from a slight broadening, the spectra of the as-prepared samples are essentially unchanged by heating or soaking in SBF, suggesting that the polymer structural unit is unaffected by these
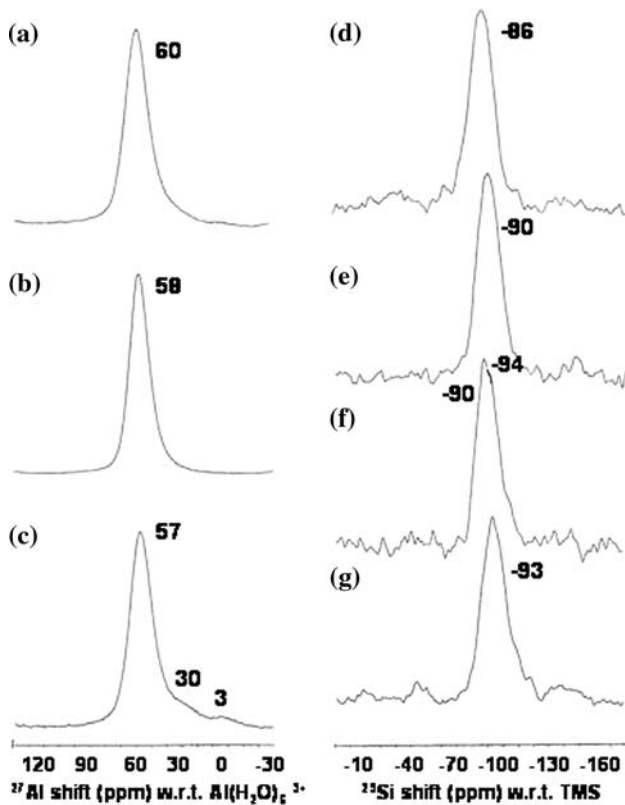
Fig. 3 **a–c** Typical 11.7 T ^{27}Al MAS NMR spectra, **d–g** typical 11.7 T ^{29}Si MAS NMR spectra. **a** and **d** Sample containing $Ca(OH)_2$, unheated, heated at 600 °C and soaked in SBF, **b** sample containing nanostructured calcium silicate, unheated, heated at 600 °C and soaked in SBF, **c** and **g** sample containing $Ca_3(PO_4)_2$, unheated, heated at 600 °C and soaked in SBF, **e** sample containing nanostructured calcium silicate, unheated, heated at 600 °C, **f** sample containing nanostructured calcium silicate soaked in SBF

Fig. 4 Typical 14.1 T natural abundance ^{43}Ca MAS NMR spectra of inorganic polymers containing 10 wt% $Ca_3(PO_4)_2$. **a** Pure $Ca_3(PO_4)_2$ (from ref. 11), **b** sample containing $Ca_3(PO_4)_2$, unheated, **c** sample containing $Ca_3(PO_4)_2$, heated 600 °C, **d** sample containing $Ca_3(PO_4)_2$, heated 550 °C, soaked in SBF, **e** pure synthetic hydroxyl apatite. Chemical shift values are the centre-of-gravity peak positions. Uncertainties are shown in *parenthesis*

treatments. The ^{29}Si spectra (Fig. 3d–g) are likewise typical of samples containing these calcium compounds [11], and are essentially unchanged by heating or soaking in SBF.

A selection of ^{43}Ca MAS NMR spectra of the samples containing 10 wt% $Ca_3(PO_4)_2$ is shown in Fig. 4. The spectra of the $Ca_3(PO_4)_2$ reagent (Fig. 4a) and the as-prepared phosphate-containing polymer (Fig. 4b) are as previously published [11] (but with a difference in reported chemical shifts resulting from the adoption of a recently recommended calibration procedure [15]). Heating of this sample and its subsequent soaking in SBF produces little difference in the centre-of-gravity (COG) position of the ^{43}Ca NMR resonance, which broadens on heating and narrows again on soaking, attaining a final COG and width similar to that of synthetic hydroxyapatite (Fig. 4d) [19, 20]. Thus, the environment of the calcium is essentially unchanged from its original state in the starting phosphate reagent by its incorporation in the inorganic polymer or by its subsequent heating and exposure to SBF.
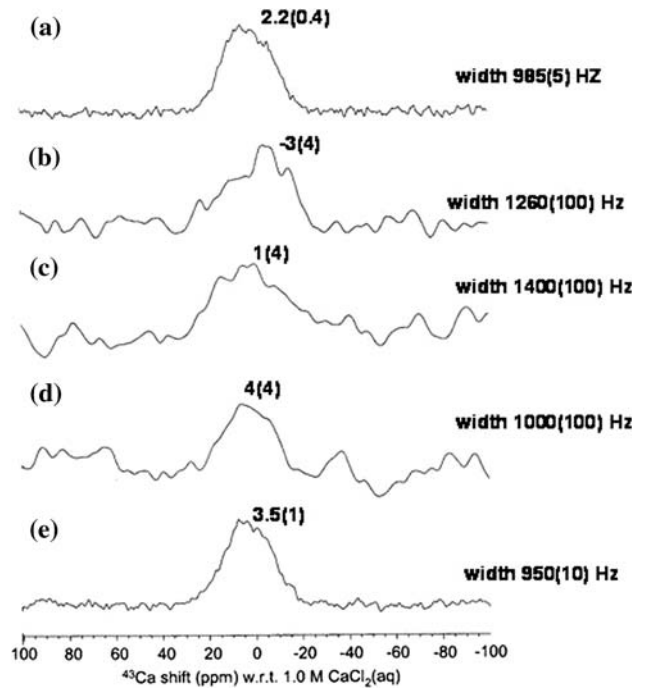
Changes in the ionic composition of the SBF during the in vitro experiments

Table 1 presents the ICP analyses for P, Al, Ca and Si of the SBF in which the reference sample and the samples containing the Ca compounds had been soaked for the first 2-week period before replenishment of the SBF. All the inorganic polymers, including the reference sample, absorbed phosphorus from the SBF, its concentration dropping during the first 2 weeks from 57 to ∼0 ppm in all but the inorganic polymer containing $Ca_3(PO_4)_2$; in that case about 6 ppm of phosphorus remained. These results are consistent with the formation of new phosphate phases by reaction with the inorganic polymers, even though XRD did not confirm the formation of such new compounds in the reference polymer or the phosphate-containing material.

Although aluminium was not present at a detectable level in the SBF, all the inorganic polymers released some aluminium into the SBF, more particularly during the first 2-week period, but dropping after the change of the SBF at the end of the second week. During the first 2-week period, the greatest aluminium release (about 2.7 ppm) was from the sample containing $Ca(OH)_2$, and the lowest

Table 1 ICP analysis of the SBF elemental content after soaking the various samples up to the time of the first SBF replenishment. Estimated errors in the P, Al and Si analyses are ±10 and ±6% for Ca

Element	Soaking time (weeks)	Reference (ppm)	$Ca(OH)_2$ (ppm)	Ca silicate (ppm)	$Ca_3(PO_4)_2$ (ppm)
P	0	57	57	57	57
	1	1.5	0	0	8
	2	1.0	0	0	6
Al	0	0	0	0	0
	1	0.1	2.7	0.05	0.45
	2	0.15	2.5	0.05	0.47
Ca	0	85	85	85	85
	1	30	180	20	15
	2	30	210	5	5
Si	0	4.4	4.4	4.4	4.4
	1	2.2	0.4	6.3	1.2
	2	1.8	0.7	8.9	1.0

release (0.05 ppm) was from the sample containing nanostructured calcium silicate. The reference sample and that containing $Ca_3(PO_4)_2$ released 0.15 and 0.47 ppm of aluminium, respectively, during the first 2 weeks, but in common with all the other samples, this release dropped off significantly after the first change of SBF (0.05 and 0.1 ppm from the reference and $Ca_3(PO_4)_2$-containing samples, respectively).

Although these aluminium concentrations are reasonably low, as noted above, the literature is contradictory with regard to safe (and possibly beneficial) levels. On this basis, the safest material is probably that containing nanostructured calcium silicate, but the $Ca_3(PO_4)_2$-containing samples may be equally safe.

The leaching behaviour of calcium and silicon in the SBF is of particular interest, as these elements have been shown to be implicated in new bone formation by the stimulation of gene transcription in osteoblasts [10]. The inorganic polymers containing $Ca(OH)_2$ were found to release Ca to the SBF, the concentration of this element rising to 210 ppm after 2 weeks, and increasing to 500–600 ppm after replenishment of the SBF. By contrast, the reference inorganic polymers and those containing calcium phosphate take up calcium from the SBF, the concentrations decreasing to 30 and 5 ppm, respectively, during the first 2 weeks of soaking. Upon replenishment of the SBF, a similar decrease in calcium concentration was found for these two materials, suggesting the removal of Ca by formation of an insoluble compound or X-ray amorphous gel on the sample surface.

The behaviour of the samples containing nanostructured calcium silicate is intermediate between these two extremes. During the first 2 weeks of soaking, these inorganic polymers remove almost all the calcium from the SBF, but after replenishment of the solution, the samples re-release the absorbed calcium back to the solution,

resulting in an increase in Ca concentration to 200 ppm. The replenishment of the SBF increases the concentration of Ca^{2+} in solution, disturbing the equilibrium and causing some of the previously formed Ca compound on the surface to re-dissolve. Apart from the $Ca_3(PO_4)_2$-containing samples, which take up Ca from the SBF, the Ca levels released from the other materials are well in excess of the optimum level of 6–8 ppm, even allowing for the fact that the initial Ca concentration in the SBF is 85 ppm.

Although the SBF formulation does not include silicon, the initial Si level is 4.4 ppm, which is introduced either as an impurity from the reagents or from the glassware. All the samples, other than those containing nanostructured calcium silicate, absorb this Si from the SBF. The amount of Si taken up from the SBF varies with the different samples, the greatest amount being taken up by the $Ca(OH)_2$-containing samples, which absorb almost all of the Si. The samples containing nanostructured calcium silicate release 8.9-ppm Si into the SBF after 2 weeks, but on replenishment of the solution, the Si is reabsorbed and its concentration falls to 2.6 ppm after a further 2 weeks. Thus, only the calcium silicate-containing samples have the potential to release the Si necessary for gene transcription; however, the amount released falls somewhat short of the optimum 15–20 ppm.

Scanning electron microscopy

Figure 5 shows a selection of scanning electron micrographs of the heated and SBF-soaked inorganic polymers. The sample containing $Ca(OH)_2$ heated to 600 °C shows a homogeneously distributed mixture of lath-shaped and agglomerate morphologies (Fig. 5a). EDS shows the lath-shaped crystals to contain exclusively Ca, whereas the agglomerates are the aluminosilicate polymer, indicating a lack of reaction between the calcium compound and the

Fig. 5 SEM images of Ca-containing inorganic polymers. **a** Sample containing Ca(OH)$_2$ heated 600 °C, **b** sample containing nanostructured calcium silicate heated at 600 °C, **c** sample containing nanostructured calcium silicate heated at 600 °C soaked in SBF, **d** sample containing Ca$_3$(PO$_4$)$_2$, heated 600 °C, soaked in SBF
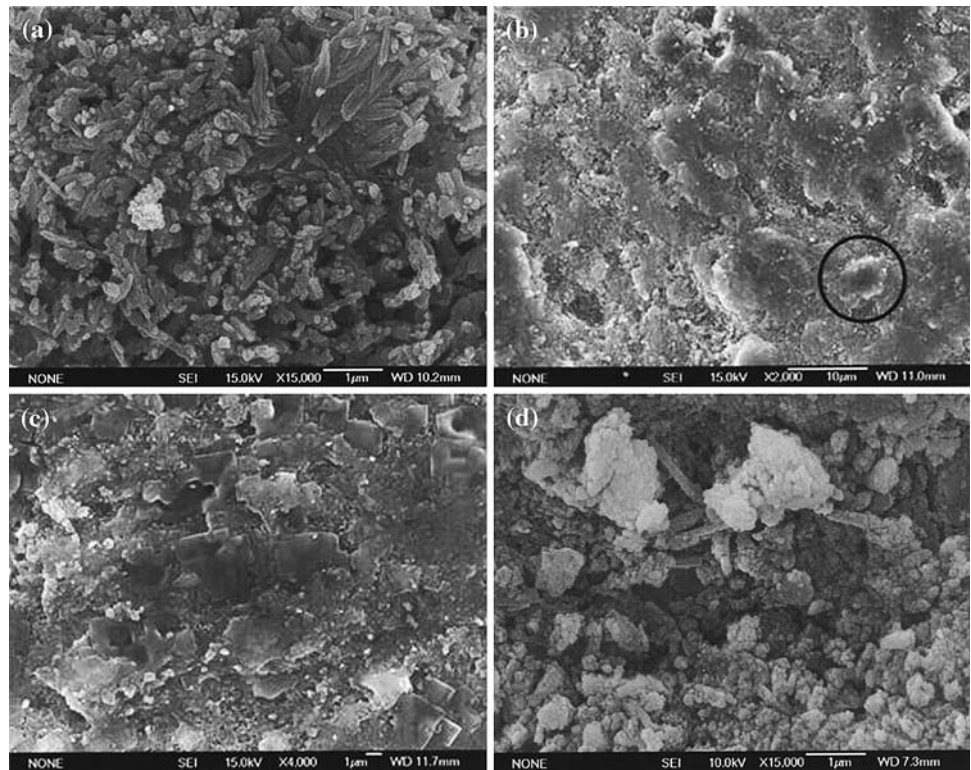
aluminosilicate. After exposure to SBF for 7 weeks, EDS shows that the Ca-rich regions have become associated with phosphorus from the SBF, confirming the formation of calcium phosphate phases, whereas the composition of the aluminosilicate-rich agglomerates remains unchanged.

The morphology of the heated polymer containing calcium silicate (Fig. 5b) contains agglomerates of large particles and other areas of very fine nanoporous texture. EDS shows that the distribution of Ca is not homogeneous, containing Ca-rich features (one of which is circled in Fig. 5b) that are not associated with Si. This suggests that the Si from the original calcium silicate has entered the geopolymer structure, leaving the Ca in isolated microregions of oxide or carbonate. On exposure of this sample to SBF, cubic crystals are formed (Fig. 5c), shown by EDS to contain Na and Cl. This sodium chloride has crystallised from the SBF by nucleating and growing on the underlying crystal aggregates. EDS also shows that the Ca-rich regions of Fig. 5b become associated with P from the SBF, forming the HA identified by XRD.

The microstructure of the heated inorganic polymer containing Ca$_3$(PO$_4$)$_2$ contains very fine 30–140 nm particles forming 200–500 nm agglomerates. EDS shows that the Ca and P are associated with each other, but occur in regions not homogeneously distributed throughout the sample; the Ca$_3$(PO$_4$)$_2$ is, therefore, behaving as a filler in the polymer matrix. After exposure to SBF, the

morphology changes slightly, with the appearance of 500 nm to 1.4 μm acicular crystals, together with pores ranging in size from <30 to 200 nm (Fig. 5d). EDS indicates that SBF treatment causes all the elements to be distributed more homogeneously throughout the sample, possibly due to the exchange of Ca, Si and P from the SBF to the polymer and the exchange of Al from the sample to the SBF, as indicated by the ICP analyses of the SBF. Any new phases formed in these exchange reactions must be X-ray amorphous, as XRD does not indicate the formation of new crystalline phases.

Strength measurements

The average tensile strengths of the inorganic polymers both before and after heating at 600 °C are shown in Table 2, and a selection of literature values for tensile strengths of bone and bioactive materials in Table 3. Direct comparison of the present strengths with literature values for other bioactive materials is problematic, as the values depend on the test method, of which there are a number and in most cases have not been not specified. For example, the two tensile strength values for Bioglass® shown in Table 2 are very different, the lower value having been determined by a method similar to that used in this work, and therefore, more directly comparable with the present values. It is known that diametral tensile strengths are much lower than

Table 2 Tensile strengths, determined by the Brazil method, of Ca-containing potassium inorganic polymers, unheated and heated at 600 °C

Sample	Tensile strength (unheated) (MPa)	Tensile strength (heated) (MPa)
Control	2.5 (0.2)	1.2 (0.7)
Ca(OH)$_2$	4.0 (1)	1.5 (0.7)
Ca silicate	1.0 (0.4)	1.4 (0.3)
Ca$_3$(PO$_4$)$_2$	2.9 (0.4)	1.7 (0.8)

Standard deviations in parenthesis

Table 3 Literature values reported for tensile strengths of various bioceramics and bone, determined by an unknown test method unless indicated

Material	Tensile strength (MPa)	Reference
Bone	60–160	[20]
Cancellous bone	3	[21]
Hydroxyl apatite	80	[21]
Bioglass®	42	[21]
Bioglass®	5.54 (0.529)[a]	[22]
Bioglass®/polyethylene	10.15	[21]
Bioglass®/polysulfone	1.5	[21]
Apatite-wollastonite glass–ceramic/polyethylene	14.87	[21]

Reported standard deviation in parenthesis

[a] Determined by the diametral compression test method

compressive strengths; reported measurements of the compressive strength σ_c and tensile strength σ_t for a porcelain ceramic [23] indicate that for this material, the two strengths are related by:

$$\sigma_t = 0.091\sigma_c - 4.4. \qquad (2)$$

This suggests that compressive strengths could be up to 11 times greater than tensile strengths; if this reasoning holds for the present materials, then their strengths could be comparable with the bone and Bioglass®/polymer composites. This may be particularly true of the Ca$_3$(PO$_4$)$_2$ inorganic polymer which is the strongest of the materials heated to 600 °C, although slightly weaker than Bioglass® tested by the same method.

Conclusions

Potassium aluminosilicate inorganic polymers containing 10 wt% Ca(OH)$_2$, nanostructured calcium silicate and Ca$_3$(PO$_4$)$_2$ have been investigated in vitro as possible bioactive ceramics. The as-synthesised samples were typical X-ray amorphous aluminosilicate inorganic polymers

displaying normal ^{27}Al and ^{29}Si MAS NMR spectra. Heating the samples to 600 °C lowered the amount of alkali leached from the control samples and those containing Ca$_3$(PO$_4$)$_2$ into the SBF, whereas samples containing Ca(OH)$_2$ and calcium silicate leached more alkali after heating, possibly reflecting the higher alkali content used in their synthesis. The XRD inorganic polymer characteristics and MAS NMR spectra are unchanged by heating, but after soaking in SBF, XRD indicates that the samples containing Ca(OH)$_2$ and Ca$_3$(PO$_4$)$_2$ contain crystalline biomineral phases (HA and hydroxylcarbonate apatite). The formation of HA in the Ca$_3$(PO$_4$)$_2$-containing materials was confirmed by ^{43}Ca MAS NMR. However, SEM/EDS suggests the formation of calcium phosphate compounds in all the samples exposed to SBF, including those containing nanostructured calcium silicate; the phosphate formed in these materials is, therefore, X-ray amorphous. The formation of phosphate phases in all the inorganic polymers is consistent with their uptake of P from the SBF. All the samples release small amounts of Al into the SBF, the lowest concentrations being from the samples containing calcium silicate, followed by Ca$_3$(PO$_4$)$_2$. All the polymers take up Si from the SBF, except the calcium silicate samples which release Si into the SBF. The strength of all the present materials is probably adequate for biomedical purposes, but the Ca$_3$(PO$_4$)$_2$-containing materials are the strongest after heating. All these measurements suggest that any of the present compounds may be suitable candidates as a bioactive material, but the combined properties of the Ca$_3$(PO$_4$)$_2$-containing compounds make them the most attractive of the present materials.

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