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Formation and properties of composites comprised of calcium-deficient hydroxyapatites and ethyl alanate polyphosphazenes

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Abstract Composites comprised of calcium-deficient hydroxyapatite (HAp) and biodegradable polyphosphazenes were formed via cement-type reactions at physiologic temperature. The composite precursors were produced by blending particulate hydroxyapatite precursors with 10 wt% polymer using a solvent/non-solvent technique. HAp precursors having calcium-to-phosphate ratios of 1.5 (CDH) and 1.6 (CDS) were used. The polymeric constituents were poly[bis(ethyl alanato)phosphazene] (PNEA) and poly[(ethyl alanato)$_1$ (p-phenylphenoxy)$_1$ phosphazene] ($PNEA_{50}PhPh_{50}$). The effect of incorporating the phenyl phenoxy group was evaluated as a means of increasing the mechanical properties of the composites without retarding the rates of HAp formation. Reaction kinetics and mechanistic paths were characterized by pH determination, X-ray diffraction analyses, scanning electron microscopy, and infrared spectroscopy. The mechanical properties were analyzed by compression testing. These analyses indicated that the presence of the polymers slightly reduced the rate HAp formation. However, surface hydrolysis of polymer ester groups permitted the formation of calcium salt bridges that provide a mechanism for bonding with the HAp. The compressive strengths of the composites containing $PNEA_{50}PhPh_{50}$ were superior to those containing PNEA, and were comparable to those of HAp produced in the absence of polymer. The current composites more closely match the structure of bone, and are thus strongly recommended to be used as bone cements where high loads are not expected.

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1 Introduction

Bone can be considered a porous composite comprised of collagen mineralized by hydroxyapatite [1]. HAp imparts strength and rigidity to the tissue while collagen serves to direct mineral growth in a manner that confers toughness [1]. Hard tissue analogs based on HAp alone lack toughness and, therefore, tend to fail catastrophically. Consequently, development of synthetic composites that emulate the properties of natural tissue, coupled with an ability to resorb by cell-mediated processes, is desirable. Additionally, an ideal bone analog material should be amenable to introduction into a bone defect as a workable, moldable, and fast-setting putty that hardens in vivo without causing damage to the surrounding tissue.

Stoichiometric hydroxyapatite (SHAp, $Ca_{10}(PO_4)_6(OH)_2$) is frequently regarded as a model for bone mineral. The Ca/P ratio of this composition is 1.67. HAp, however, is not a compound of fixed composition and can incorporate many substituents [2]. In natural bone carbonate substitutes for phosphate, and this affects the Ca/P ratio [3]. A general compositional formula for non-substituted HAp is $Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x}$, where x ranges from 0 to

1 [4]. In particular, the ratio of Ca/P in HAp can vary between the compositional limits of about 1.5 and 1.67. When the Ca/P ratio is below 1.67, the HAp is calcium-deficient. The extent of calcium deficiency affects the stability of HAp, increases its bioactivity, and increases its solubility product [5]. Two calcium-deficient compositions were presently studied; these are Ca/P = 1.5 and 1.6 and are referred to as CDH and CDS, respectively.

Polyphosphazenes are characterized by a phosphorus–nitrogen backbone with two functional groups attached to each phosphorus atom [6]. Biodegradable polyphosphazenes are attractive constituents for bone analog composites because their presence confers toughness and they degrade into biologically recognizable byproducts [7, 8]. Further, the degradation rates of polyphosphazenes can be varied by changing the lengths and compositions of the side groups [9].

Our strategy has been to tailor the compositions of polyphosphazenes, the Ca/P ratios of hydroxyapatite and the processing methods and to establish the rates of composite formation, coupled with limited evaluations of mechanical properties. Thus, aspects of the formation and behavior of HAp-polyphosphazene composites intended for use as bone analogs have been studied previously [10–14]. Significantly, HAp formation in the presence of a polyphosphazene bearing acidic groups requires less than 24 h for complete conversion of precursor minerals [12]. In addition, some polymers undergo surface hydrolysis to produce calcium cross-linkages. These salt-bridged regions then provide sites for nucleation of HAp on the polymer surface [13].

The current study specifically investigates the formation and properties of composites comprised of two calcium-deficient HAp compositions and polyphosphazene-ethyl alanine-based polymers. In particular, composites consisting of two polyphosphazene preparations, a biodegradable poly(phosphazene-ethylalanine) homopolymer and a substituted copolymer with phenyl-phenoxy (PhPh) in place of 50% alanine, were investigated. The polymers are thus referred to as PNEA and $PNEA_{50}PhPh_{50}$. The composites currently described exhibit advantages not realized in previously examined systems. Calcium-deficient HAp compositions exhibit greater bioactivity than does fully stoichiometric HAp [15]. While previous studies have established that incorporation of polymer tends significantly to decrease the strengths of the composites [16], use of blocky side chains was anticipated to increase mechanical properties [17]. This anticipation is based on incorporation of bulky side groups having been shown to increase the tensile strengths of polyphosphazenes [18]. In addition, polyphosphazenes with ethyl-alanine and ethyl or propyl oxybenzoate side groups were observed to allow cells to attach and proliferate [19]. Finally, the polymers used in this study have been shown to biodegrade over time in vivo, and to invoke only a mild to moderate inflammatory response [20].

2 Materials and methods

2.1 HAp precursor synthesis

The CDH and CDS precursor powders were synthesized from mixtures of tetracalcium phosphate (TetCP, $Ca_4(PO_4)_2O$) and monocalcium phosphate monohydrate (MCPM, $Ca(H_2PO_4)_2{\cdot}H_2O$) at Ca/P ratios of 1.5 and 1.6, respectively. TetCP was prepared by ball milling $CaCO_3$ (Osram-Sylvania, PA) and MCPM (FMC Corp., NY) at a 3:1 molar ratio for 16 h in heptane (Alfa Aesar, Ward Hill, MA). After filtering and drying, the particulate TetCP precursors were fired in air at 1,400°C for 1 h and quenched rapidly. X-ray diffraction (XRD) was used to confirm phase purity. The TetCP was ground by hand, passed through a 63 μm sieve, ball milled, and attrition milled to reduce particle size. TetCP and MCPM were then mixed in the desired Ca/P ratio (1.5 and 1.6) and ball milled in heptane. After synthesis, the precursor powders were stored in a desiccator under vacuum. An average of five determinations of the TetCP particle dimensions as observed by SEM indicated a particle size of 2.5 μm.

2.2 Polymer synthesis

2.2.1 Reagents and equipment

Figure 1 shows the structure of PNEA (Polymer **1**) and $PNEA_{50}PhPh_{50}$ (Polymer **2**). Synthesis reactions were carried out under an atmosphere of dry argon using standard Schlenk line techniques. Hexachlorocyclotriphosphazene (Ethyl Corp. and PCS) was obtained from a trimer–tetramer mixture by recrystallization from heptane followed by sublimation (30°C/0.2 mm Hg). Poly(dichlorophosphazene) was prepared by the ring-opening polymerization of hexachlorotriphosphazene in a sealed evacuated Pyrex tube at

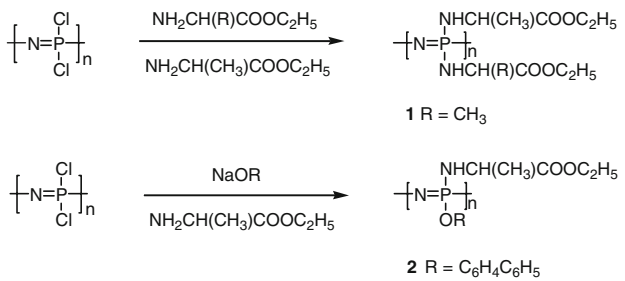

Fig. 1 Basic reaction mechanisms and structures of PNEA (Polymer **1**) and $PNEA_{50}PhPh_{50}$ (Polymer **2**)

250°C. The same batch of poly(dichlorophosphazene) was used in the synthesis of polymers **1** and **2**. Ultra pure, anhydrous tetrahydrofuran (THF), toluene and triethylamine were obtained from a solvent dispensing system designed by JC Meyer. L-Alanine ethyl ester hydrochloride (Chem Impex International Inc), 4-phenylphenol (all from Aldrich), and sodium hydride (60% dispersion in mineral oil, Aldrich) were used as received. Spectra/Por regenerated cellulose dialysis membranes with a molecular weight cut-off of 12,000–14,000 were used for purification of the polymers. ^{31}P NMR (145 MHz) and ^{1}H NMR (360 MHz) data were obtained with use of a Bruker 360 MHz spectrometer. ^{31}P NMR chemical shifts are reported in ppm relative to 85% H_3PO_4 at 0 ppm. Gel permeation chromatography (GPC) was carried out with use of a Hewlett-Packard HP-1090 liquid chromatograph fitted with an HP-1047A refractive index detector and two phenogel 10-μm linear columns (Phenomenex, CA), calibrated with polystyrene standards (Polysciences, PA). The samples were eluted at 40°C with a 0.1 wt% solution of tetra-n-butylammonium nitrate (Aldrich, WI) in THF (EM Science, NJ). Glass transition temperatures were determined from a TA Instruments Q10 differential scanning calorimetry (DSC) apparatus with a heating rate of 10°C/min.

2.2.2 *Synthesis of polymer **1***

L-Alanine ethyl ester was prepared by treatment of alanine ethyl ester hydrochloride (106.04 g, 0.690 mol) in refluxing THF (500 ml) with triethylamine (288 ml, 2.071 mol). After the solution had been stirred for 24 h, the reaction mixture was filtered and the filtrate was added to a stirred solution of poly(dichlorophosphazene) (20.00 g, 0.173 mmol) in THF (2000 ml). The reaction mixture was then stirred at room temperature for 48 h. The insoluble salts were removed by filtration and a white fibrous polymer was obtained by precipitation of the viscous polymer solution into hexanes. Purification of the polymer was accomplished by repeated precipitations from THF into hexanes (3X), followed by dialysis against a THF/methanol (50/50) mixture for 3 days. ^{31}P NMR ($CDCl_3$), ppm: δ −3.5; ^{1}H NMR ($CDCl_3$), ppm: δ 4.1–4.08 (3.6H), 1.4–1.27 (3H), 1.29–1.19 (3H). M_n = 89000, M_w = 196000, PDI = 2.2. Tg = −10°C.

2.2.3 *Synthesis of polymer **2***

Poly(dichlorophosphazene) (20.0 g, 0.173 mol) was dissolved in THF (2,000 ml). In a separate reaction vessel, p-phenylphenol (32.31 g, 0.173 mol) was added to a suspension of sodium hydride (4.36 g, 0.173 mol) in THF (250 ml) and the reaction was allowed to proceed for 24 h. Sodium p-phenylphenoxide solution was then added slowly to the polymer solution via an addition funnel. The reaction was allowed to proceed at room temperature for 24 h. L-Alanine ethyl ester (116.64 g, 0.759 mol) in THF (700 ml) was then added to the reaction mixture that contained the partially substituted polymer. The reaction solution was then heated at reflux for 48 h. The polymer was purified by repeated precipitations from THF into hexanes (3X) and methanol (2X). ^{31}P NMR: ($CDCl_3$), ppm: δ −5.2, −7.3, −17.97; ^{1}H NMR ($CDCl_3$), ppm: δ 7.8–7.2 (9H), 4.8–3.9 (3.8H), 1.3–0.6 (6H). M_n = 1,020,000, M_w = 1,900,000, PDI = 1.86. Tg = 35°C.

2.2.4 *Preparation of composite precursors*

Composite precursors containing polymers **1** or **2** and CDH or CDS precursors were synthesized by an emulsion technique. Briefly, 1.5 g of polymer was dissolved in 30 ml of methanol (for polymer **1**) or dimethylformamide (for polymer **2**). The polymer solution was then added dropwise to a vigorously stirred suspension of 15 g of the HAp precursor in 1 l of heptane (Fisher Scientific, USA) and 50 ml of dimethylformamide at room temperature. The suspension was stirred for 10 min and the excess solvent was evaporated to dryness using a rotary evaporator. The resultant solid was dried under vacuum at 50°C for 72 h, and then stored in a desiccator under vacuum.

2.3 Analytical methods employed

The variations in pH with time were measured using an Orion 920 pH meter. 0.5 g composite precursors were initially mixed with a small amount of water using a mortar and pestle before being placed in a double-walled glass beaker with 35 ml of distilled, de-ionized water. The temperature of the reaction vessel was held constant at 37°C. The mixture was stirred continuously with nitrogen bubbled through. The reaction pH was followed for 24 h. At the end of each experiment, the slurry was filtered and the separated solids were flushed with acetone to stop further reaction. After drying, the solids were examined for their phase compositions by XRD and infrared spectroscopy. XRD analyses used an automated X-ray diffractometer (Scintag, Inc., Sunnyvale, CA), with a step size of 0.02°, a scan rate of 2° per minute, and a scan range from 20 to 40° 2θ. Phases present in the pattern were compared to JCPDS cards 00-009-0432 (HAp), 00-09-0080 (DCPA), and 00-25-1137 (TetCP) [21]. IR analyses used a Nexus 670 FT-IR spectrometer (Thermo Nicolet Corp., MA) on pellets consisting of KBr and 2 wt% sample over a range from 4,000 to 650 cm^{-1}.

For compressive testing, the precursor powders were combined with water at a powder-to-liquid weight ratio of 2.5-to-1 and mixed on a glass plate using a metal spatula.

The paste was pressed by hand into cylindrical-shaped molds (12.7 mm in height and 6.35 mm in diameter). Three pellets were made for each composite. The samples were cured in a humidified atmosphere at 37°C for 24 h. Compressive testing was performed using an Instron 4202 testing instrument (Instron, MA) using a cross-head speed of 0.3 mm/min. The fractured surfaces were coated with gold, and examined for their microstructure using SEM (Hitachi S-3500N, Japan) at an accelerating voltage of 5 kV.

3 Results and discussion

The kinetics and variations in solution chemistry during CDHAp (Ca/P = 1.5) formation [4] and during SHAp (Ca/P = 1.67) formation [22] have been previously investigated; those of intermediate Ca/P ratios and those of composites containing the present polymers have not been determined. Thus to establish the kinetics of reaction and to determine whether there should be concern for pH excursions to a cytotoxic range, pH variations during the conversion of precursors to HAp were assessed.

The variations in the pH during the conversion reactions of the calcium phosphates in the absence of polymer are shown in Fig. 2. The variations in pH are attributable to the dissolution behavior of both TetCP and DCPA, which in turn depend on the relative proportions of these constituents in the initial powder mixture [23]. The pH of the "CDS" solution showed a rapid initial increase to 7.5 within the first 30 min, while that of the "CDH" solution reached a value of 8.5 within the same time frame. These were followed by slower increases in pH to about 9.2 after 8 h for the "CDS" solution and a maximum of 10.2 after about 12 h. This behavior is the result of the initial preferential dissolution of the basic phase, TetCP. TetCP when

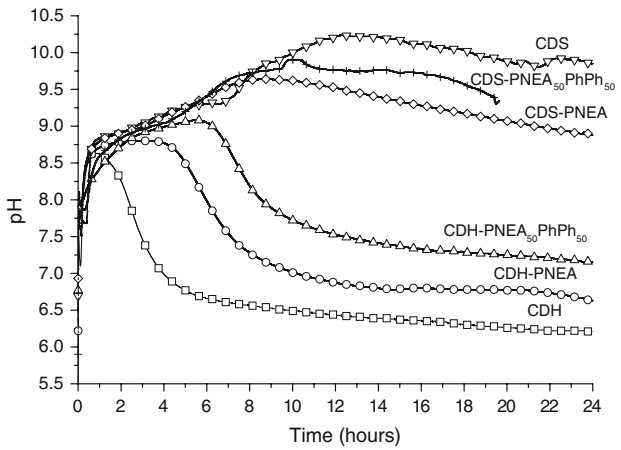

Fig. 2 The variations in pH with time for the HAp compositions and composite compositions studied

hydrolyzed in the absence of DCPA will eventually produce a pH of about 12.3. Both the extent of pH increase and the duration of the period of pH rise are the consequence of a greater proportion of TetCP in the CDS precursor mixture. Similar behavior was previously observed during the conversion of precursors to SHAp [22]. An analysis of the dissolution behavior of TetCP and DCPA under quasi-equilibrium conditions [5] indicated that a solution with a pH of about 7.4 should be obtained. For values above this, the dissolution of TetCP controls the pH; for values below it DCPA dissolution is controlling. The present data for CDS conversion indicate that TetCP dissolution controls the pH even though the HAp eventually formed is calcium deficient. The period over which TetCP dissolution controls the solution chemistry is greatly reduced for CDH conversion. After reaching a maximum value of about 8.6 after an hour and a half of reaction, pH of the CDH solution began to decrease. This decrease is the result of preferential DCPA dissolution. After about 6 h of reaction the pH attained a value slightly below 7 and subsequent pH changes are small. The presently observed behavior and that previously reported for the formation of stoichiometric HAp [22] indicate the mechanistic path to HAp formation involves more than one rate limiting step. These data also indicate that the conversion to more highly calcium deficient compositions occurs more rapidly and presents conditions anticipated to be less aggressive to local cells.

Figure 2 also compares the effects of the presence of the polymers on pH curves obtained during the conversion of CDS and CDH precursors. While the variations were similar to those in the absence of polymer, the results indicate that the presence of polymer modulated the extent of the pH increase in the "CDS" solution while appearing to slightly retard the rate of CDH conversion. Composite comprised of CDS and PNEA produced a value of 9.5 after 8 h and then decreased, while composites comprised of CDS and $PNEA_{50}PhPh_{50}$ produced a pH value of 9.7 before decreasing. These differences are the result of the formation of carboxylic acid groups in the highly basic media by the hydrolysis of the ethyl ester groups attached to the alanine moieties. The effects on pH are more pronounced in the presence of PNEA because it contains twice the proportion of alanine ester substitutions compared to $PNEA_{50}PhPh_{50}$ and can thus form more acidic groups when hydrolyzed. The formation of the carboxylic acid groups leads to the formation of calcium salts of these polymers via an acid–base reaction [12]. As will be subsequently described, this phenomenon also affects mechanical properties.

Figure 3 shows the XRD patterns of the solids produced from the CDS and CDH precursors after 24 h of reaction. The patterns were compared with the standard patterns of HAp, TetCP and DCPA from the JCPDS file [21]. The

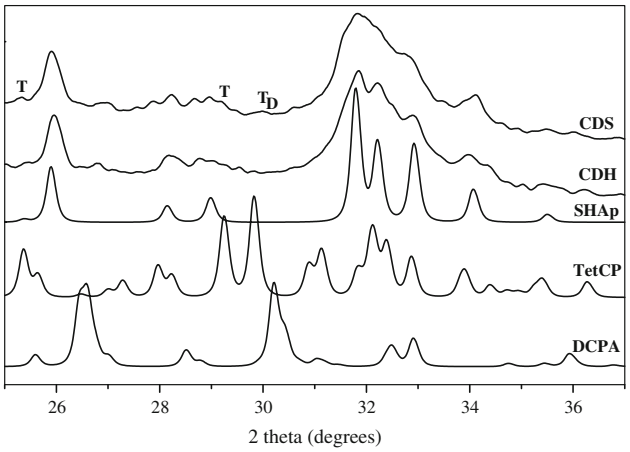

Fig. 3 X-ray diffraction patterns of CDH and CDS powders after 24 h of reaction compared to those of stoichiometric HAp and precursor phases TetCP and DCP

major phase observed was HAp. HAp having slightly better crystallinity was observed in the CDH pattern as evidenced by the resolution of the Ap HAp peaks at 31.79°, 32.21° and 32.93°. Moreover, traces of residual TetCP and DCPA were observed in the pattern for CDS solids, namely identifiable peaks at 29.9°, 29.4° and 25.4° for TetCP and 30.1° for DCPA. Residual TetCP and DCPA peaks were barely above the limit of detection in the solids produced from CDH. This accords with the slow conversion kinetics of the CDS precursors compared to the CDH precursors.

Figure 4a compares the XRD patterns of the solids obtained after 24 h reaction of CDS precursors in the presence and absence of the polymers. The major phase observed was HAp. However, the presence of unreacted TetCP and DCPA were more extensive than in the polymer-free samples, indicating that the presence of polymer hindered the conversion to HAp. This is more pronounced in composites containing $PNEA_{50}PhPh_{50}$. Previous studies showed the proclivity of the ester groups pendant on polyphosphazenes to adsorb onto calcium phosphate precursors thereby inhibiting precursor hydrolysis [14]. The incomplete reaction in the current composites confirms this occurrence.

Similar inhibition was observed for the reactions of composites of CDH precursors with PNEA and $PNEA_{50}PhPh_{50}$, as evidenced in Fig. 4b. These observations indicate that these polymers adsorb on the surfaces of both the CDS and CDH precursors. Adsorption then interferes with the dissolution of the rate limiting precursor constituent. For CDH, an elevated pH is retained for a longer period in the presence of the polymers and the pH eventually reached in the absence of polymer is lower, as was shown in Fig. 2.

Moreover, although $PNEA_{50}PhPh_{50}$ contains fewer hydrolyzable groups, the slow kinetics may also be attributed

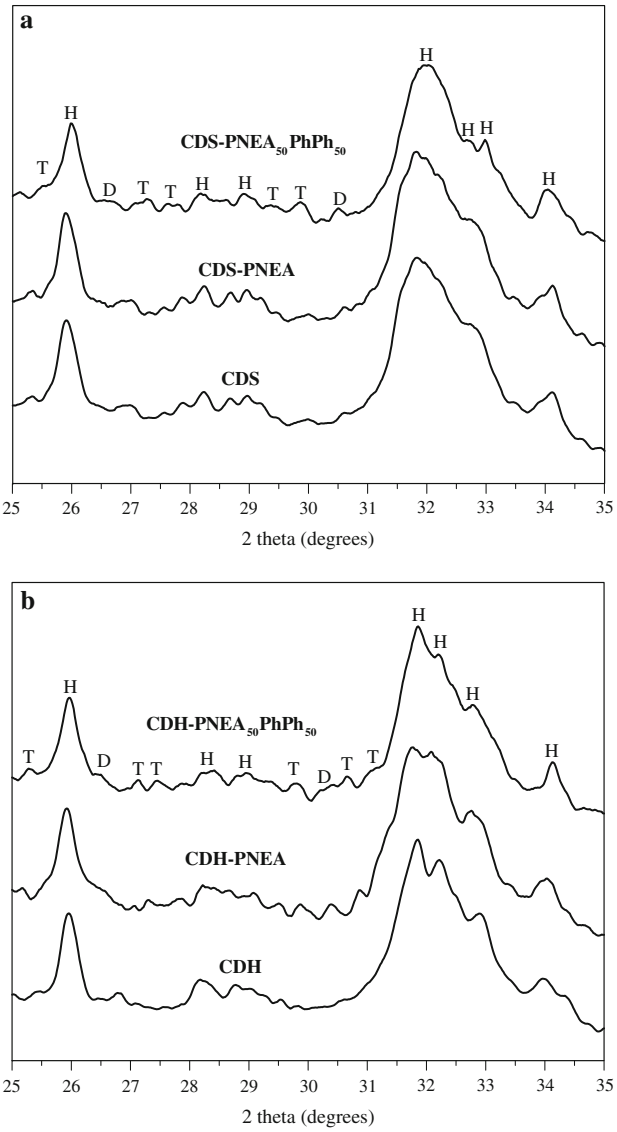

Fig. 4 XRD patterns of CDS composites (**a**) and CDH composites (**b**) compared to the respective polymer free compositions

to the presence of the bulky, hydrophobic phenyl phenoxy group. The decreased formation rate was confirmed by XRD analyses of the CDH composites, as seen in Fig. 4b. Unreacted TetCP and DCPA were observed in composites containing CDH and $PNEA_{50}PhPh_{50}$ and are present to a greater extent than in the composite containing PNEA.

Figure 5 shows the SEM micrographs of the fracture surfaces of samples from CDS precursors (a) and composites of CDS with PNEA (b) and $PNEA_{50}PhPh_{50}$ (c). All micrographs show the HAp needle-like crystallites, approximately 1 μm in length, in assemblages as pseudomorphs of the reactant precursors. The HAp crystallites closely resemble bone apatite in shape and size. The presence of unreacted precursors, termed R for reactant in the micrographs, can also be observed, with an increased

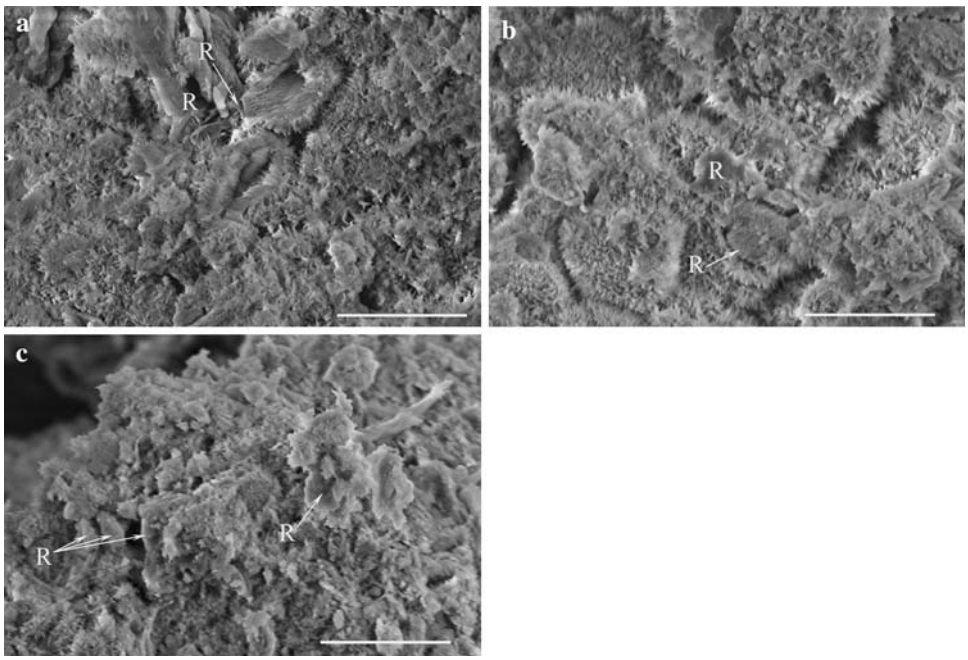

Fig. 5 SEM images of fracture surfaces of CDS without polymer (**a**), CDS with PNEA (**b**), and CDS with $PNEA_{50}PhPh_{50}$. R denotes calcium phosphate reactant remaining after 24 h of reaction in these samples. Bar represents 5 μm

extent in Fig. 5c. Figure 5b also shows the presence of flake-like assemblages of apatite crystallites. The presence of this flake-like morphology was not as noticeable in the composites containing $PNEA_{50}PhPh_{50}$. These morphological differences may be the result of differences in the proportion of the adsorbing ester group in these polymers.

The relevant portions of the spectra obtained by FTIR analyses of CDS and CDH, as well as their composites with PNEA and $PNEA_{50}PhPh_{50}$, are shown in Fig. 6. Orthophosphates are characterized by their strong and broad band within the range 980–1,100 cm^{-1} [24]. This band appears in all spectra. However the inferior features of this band, i.e. the broadness and poor resolution, in the spectra

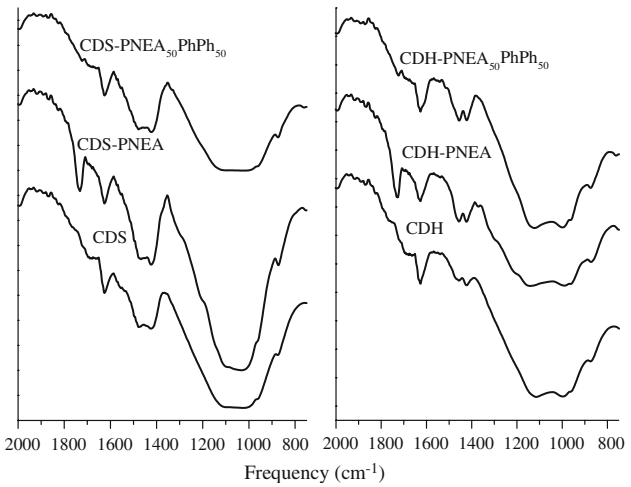

Fig. 6 Infrared spectra of the composites compared to their respective polymer-free compositions

of the composites compared to the polymer-free samples confirms the presence of unreacted TetCP [25]. Two bands appear in all samples within the range 1,400–1,500 cm^{-1}. These bands are relatively weaker in both CDS and CDH spectra than in those from the composites. Both the carbonyl group (C=O) of CO_2 and the carboxylate (COO^-) group are known to absorb within this range [24]. These bands in polymer-free samples suggest minor carbonate incorporation in both CDS and CDH, and is more pronounced in CDS than CDH. This is anticipated because of the opportunity to extract CO_2 from air. The second band that appears at 1,463 cm^{-1} and 1,474 cm^{-1} in the spectra of CDH and CDS, respectively, was shifted in the spectra of the composites to 1,454 cm^{-1} (CDH/PNEA), 1,456 cm^{-1} (CDH/$PNEA_{50}PhPh_{50}$), 1,469 cm^{-1} (CDS/PNEA) and CDS/$PNEA_{50}PhPh_{50}$ retained its absorption wave number at 1,474 cm^{-1}. The clear difference in the strength of these bands, as well as the shift in the second band, indicates the presence of carboxylate anions (COO^-) in the composites with variable degrees. The higher shift in the CDH composites compared to the CDS composites indicates the presence of more carboxylate anions in the former composites. Moreover, a small band was observed at 1,372 cm^{-1} in the spectrum of the CDH composite with PNEA and was absent in the spectra of the other composites. This band, which is also characteristic of the carboxylate anion functional group [24], indicates that composites containing CDH and PNEA possessed the highest concentration of the hydrolyzed ester group, the carboxylate anion. Hydrates associated with orthophosphates absorb within the range 1,600–1,750 cm^{-1} [24]. This explains the bands appearing at 1,647 and 1,626 cm^{-1} in the spectra of

polymer-free CDH and CDS samples, respectively. However, a stronger band appeared in the spectra of the composites within the same range; namely at 1,636 cm^{-1} (CDH/PNEA), 1,624 cm^{-1} (CDH/$PNEA_{50}PhPh_{50}$), 1,628 cm^{-1} (CDS/PNEA) and 1,626 cm^{-1} (CDS/$PNEA_{50}PhPh_{50}$). The higher intensity of these bands, together with the different values at which they appear, corresponds to the asymmetric stretching mode of the carboxylate anion (COO^-) which normally appears around 1,610 cm^{-1} [24]. A final band was only observed in the spectra of the composites of both CDH and CDS with PNEA, at 1,730 and 1,732 cm^{-1}, respectively. A very weak shoulder was observed in the composites of CDH and CDS with $PNEA_{50}PhPh_{50}$ around the same values. This is characteristic of the absorption of the unhydrolyzed ester (R–COOR) group, which normally appears at 1,730–1,735 cm^{-1} [24]. Taken together these results indicate that almost complete hydrolysis of the ester group in the alanate branch of the polymer in the composites of $PNEA_{50}PhPh_{50}$ regardless of whether the inorganic component was CDH or CDS and that less than 100% of the ester groups initially present in PNEA were hydrolyzed. These IR results are consistent with the variations in pH and the extent of conversion as established by XRD.

The methods used to prepare composite precursors for this study are not optimal with respect to maximizing mechanical properties. A physical mixture of particulate polymer in a matrix of HAp would not be expected to exhibit properties superior to that of the HAp alone. However, strength testing would reveal potential mechanical property benefits associated with the formation of an interfacial bond between HAp and polymer. Compressive strength data for the CDH and CDS/PNEA and $PNEA_{50}PhPh_{50}$ composites are shown in Fig. 7. Composites containing $PNEA_{50}PhPh_{50}$ show an improved compressive strength over those containing PNEA.

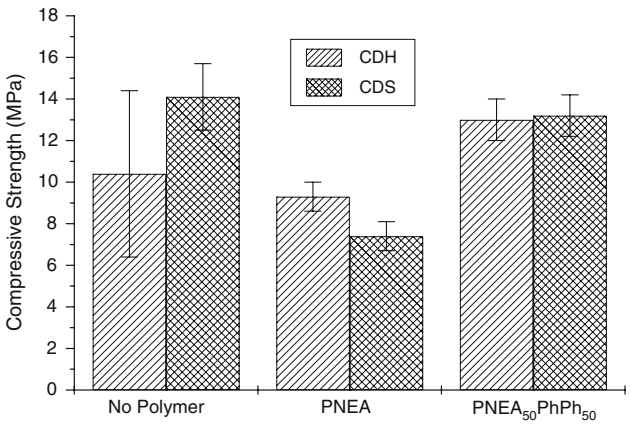

Fig. 7 Average compressive strengths of CDS and CDH HAp compositions and of composites containing PNEA and $PNEA_{50}PhPh_{50}$. Error bars represent the standard deviation for each group of samples

As mentioned above, composites containing PNEA possessed more carboxylate groups, which were expected to form bonding sites with Ca, and hence produce composites with better mechanical properties. However, the complete hydrolysis of the ester groups of $PNEA_{50}PhPh_{50}$ combined with the presence of bulky phenyl phenoxy groups in $PNEA_{50}PhPh_{50}$ appear to act in synergy to improve the mechanical properties of the composites. The complete hydrolysis of the ester groups in $PNEA_{50}PhPh_{50}$ appears to permit the polymer to form a stronger interface with the HAp via the formation of the cross-linked calcium polycarboxylate. Moreover, bulky functional groups are known to improve the overall strengths of the polymers themselves [17]. Consequently, composites comprised of $PNEA_{50}PhPh_{50}$ exhibited no reduction in compressive strength compared to the polymer-free HAp, thus indicating that tailoring the polymer side-groups can influence mechanical properties.

4 Summary

Composites of hydroxyapatite and polyphosphazene were formed at physiologic temperature. Composites were formed using two calcium-deficient hydroxyapatite compositions (CDH, Ca/P = 1.5 and CDS Ca/P = 1.6) and two biodegradable polyphosphazene polymers. The precursor mixtures were reacted in water for 24 h. Variations in pH values during HAp formation in composites produced using CDS were lower than those during HAp formation from CDS with no polymer present. This is due to hydrolysis of the ethyl ester group on the alanine side chain to form carboxyl groups. CDH converts to HAp more rapidly than CDS. CDH conversion in the presence of polymer was retarded and the solution pH remained higher because DCPA dissolution was slowed due to polymer adsorption. IR analyses revealed that polymer adsorption promotes the formation of Ca salt bridges and improves the bond between the composite constituents. Potential cross-linking, where COO^- groups are observed, was established by FTIR. The mechanical properties of the composites show significant differences depending on the polymers. Despite incomplete reaction over 24 h of the calcium phosphate precursors, composites containing $PNEA_{50}PhPh_{50}$ exhibited higher compressive strength. Thus, tailoring of polyphosphazene side groups affected the mechanical properties of the composites. Based on the results of the current study, the composites prepared are suggested to be used as bone cements where high loads are not expected.

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