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# Composite formation from hydroxyapatite with sodium and potassium salts of polyphosphazene

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The low temperature synthesis of composites potentially suitable as bone substitutes which form *in vivo*, was investigated. The composites were comprised of stoichiometric hydroxyapatite (SHAp) and water-soluble poly phosphazenes. These constituents were selected because of their biocompatibility, and were mixed as powders with a phosphate buffer solution (PBS) to form the composites. The effects of poly[bis(sodium carboxylatophenoxy)phosphazene] (Na-PCPP) or poly[bis(potassium carboxylatophenoxy) phosphazene] (K-PCPP) on stoichiometric hydroxyapatite (SHAp) formation from tetracalcium phosphate and anhydrous dicalcium phosphate were assessed. The kinetics and reaction chemistries of composite formation were followed by isothermal calorimetry, X-ray diffraction, infrared spectroscopy and scanning electron microscopy. In the presence of 1% by weight of polyphosphazenes, composites comprised of SHAp and calcium cross-linked polymer salts were formed. Thus a mechanism for binding between polymer chains was established. Elevated proportions (5 and 10% by weight) of polyphosphazene, however, resulted in the inhibition of SHAp formation. This is attributed to the formation of viscous polymer solution coatings on the calcium phosphate precursors, retarding their reaction, and consequently inhibiting SHAp formation.


## 1. Introduction

Hard tissues such as bone, dentine and enamel are composites of hydroxyapatite (HAp) and collagen with HAp being the major component [1, 2]. The combinations of hydroxyapatite and collagen in these composites confer unique properties to hard tissues [2]. It is a desirable objective to simulate these characteristics using synthetic composites [3]. Compositions based on hydroxyapatite and suitable polymers, are expected to exhibit structures and properties which emulate natural composites [4]. Hydroxyapatite confers bioactive properties to the composites and the polymeric phase can provide reinforcement to the composite thereby reducing the brittleness of the HAp. Several synthetic polymers hav ebeen investigated as reinforcing phase in composite preparation with HAp [5, 6]. These include bioinert polymers such as polyethylene and polymethylmethacrylate, and biodegradable polymers such as poly(lactide-*co*-glycolide) and poly($\varepsilon$-caprolactone) [7–10]. In addition to these, natural polymers such as gelatin, chitosan as well as collagen have been extensively investigated for composite preparation [11, 12].

Various methods are currently employed for HAp-polymer composite preparation such as extrusion [5], hot pressing [14], and solvent-evaporation [15]. However, formation of composites at physiologic temperature is highly favorable from practical and clinical perspectives for biomedical applications [16]. Recently, several attempts were made to develop HAp-polymer composites where hydroxyapatite can be synthesized at physiologic temperature through a cement-like reaction in the presence of various polymers [17–20]. The present study deals with the preparation of composites of SHAp and a novel class of inorganic polymer, polyphosphazene, at and near a physiologic temperature.

Polyphosphazenes constitute a group of polymers with an alternating backbone of phosphorous and nitrogen atoms, with each phosphorous atom bearing two side groups [21]. Because these side groups determine

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the polymer characteristics, their variation provides polymers with a wide spectrum of properties suitable for biomedical applications [22]. A wide range of applications have been identified for polyphosphazenes, including inert biomaterials for cardiovascular and dental uses as well as biodegradable and water-soluble biomaterials for drug delivery applications [22]. Polyphosphazenes, which slowly biodegrade, are of interest as constituents of synthetic bone analogues and the high biocompatibility of many of these polymers have been reported [23].

The suitability of poly[bis(carboxylato phenoxy) phosphazene] and its esters in composite preparation with HAp has been investigated. Thus, Greish *et al.* investigated the formation of SHAp in the presence of poly[bis(carboxylato phenoxy) phosphazene] (acid-PCPP) [24], its ethyl ester (ethyl-PCPP) and propyl ester (propyl-PCPP) [25]. During composite formation, each of these polymers cross-linked with calcium forming the calcium salt of the polymer, Ca-PCPP. Acid-PCPP underwent an acid-base reaction to form the calcium salt, Ca-PCPP [24]. The alkyl-PCPP polyesters were found to hydrolyze slowly on their surfaces forming thin layer of Ca-PCPP [25]. TenHuisen *et al.* studied the formation of calcium-deficient hydroxyapatite in the presence of poly[bis(sodium carboxylatophenoxy) phosphazenes], Na-PCPP [26]. Calcium ions were found to exchange with sodium ions in the Na-PCPP, forming a cross-linked polymer [26].

Low-temperature formation of HAp can take place either through acid-base [27] or hydrolysis [28] reactions of suitable calcium phosphate precursors. An acid-base reaction between an acidic calcium phosphate, such as $CaHPO_4$ (DCPA) or $CaHPO_4{\cdot}2H_2O$ (DCPD) and tetracalcium phosphate ($Ca_4(PO_4)_2O$, TetCP), can yield stoichiometric [29] or calcium-deficient [30] hydroxyapatite (SHAp, or CD-HAp, respectively, depending on the molar ratios of the starting materials). The CD-HAp can also be formed by the hydrolysis of $\alpha$-tricalcium phosphate, ($\alpha$-$Ca_3(PO_4)_2$, $\alpha$-TCP [28].

In the current study we have investigated the kinetics and mechanism of composite formation of SHAp with Na-PCPP/K-PCPP using the precursors TetCP and DCPA in the presence of different proportions of the corresponding polymers.

## 2. Materials and methods

### 2.1. Synthesis of SHAp precursors

A powder mixture of TetCP and DCPA was used as the precursor for SHAp preparation. TetCP was prepared as described previously [14] by a solid state sintering of a powder mixture of $CaCO_3$ (Osram Sylvania, PA) and $Ca(H_2PO_4)_2{\cdot}H_2O$ (MCPM) (FMC, NY) at 1310 °C for 2 h. The sintered product was rapidly quenched to room temperature. Formation of a phase-pure TetCP was confirmed by X-ray diffraction. The fired product was ball-milled followed by attrition milling in *n*-heptane for 24 and 8 h, respectively. The average particle size of the TetCP powder was 2.5 $\mu$m as determined by scanning electron microscopy.

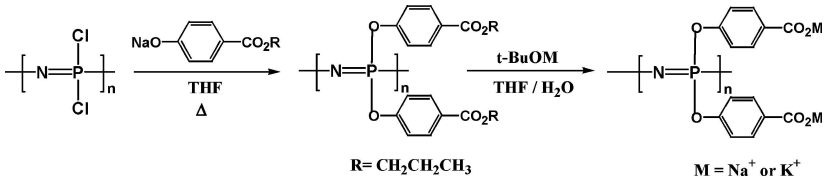
A powder mixture of TetCP and MCPM (with a particle size 1.5 $\mu$m) was comminuted in *n*-heptane using zirconia media. A mechanochemical reaction takes place between the reactants leading to polymineralic products having a Ca/P ratio of 1.67. The resultant slurry was filtered, dried at room temperature then stored under vacuum to avoid hydration.

### 2.2. Synthesis of poly[bis(sodium/potassium carboxylatophenoxy) phosphazene]

Hexachlorocyclotriphosphazene (Nippon Fine Chemical Co., Japan) was purified by recrystallization from heptane and was sublimed at 55 °C (0.05 mmHg). Poly(dichlorophosphazene) was prepared by the ring opening polymerization of hexachlorocyclotriphosphazene at 250 °C as described previously [31]. Potassium *tert*-butoxide (Aldrich, WI), sodium hydride (60% dispersion in mineral oil, Aldrich), propyl 4-hydroxybenzoate (Aldrich), Tetra-*n*-butylammonium bromide (Aldrich), and dialysis tubing (Spectra/Por membrane, MWCO 12-14000, Spectrum Laboratories Inc., CA) were used as received. Hydrochloric acid solutions were made by diluting concentrated hydrochloric acid (EM Science, NJ) to the appropriate molarity using distilled water. Tetrahydrofuran (EM Science, NJ) was dried over sodium benzophenone ketyl and was distilled under an atmosphere of dry argon. All reactions were performed under an atmosphere of dry argon with standard Schlenk techniques. Scheme 1 shows the preparation of Na- and K-PCPP.

### 2.3. Synthesis of poly[bis(propyl oxybenzoate)phosphazene] (Scheme 1; b)

The sodium salt of propyl 4-hydroxybenzoate was prepared by the addition of propyl 4-hydroxybenzoate (118.01 g, 0.655 mol) in tetrahydrofuran (THF) (150 ml) to a stirred suspension of sodium hydride (25.80 g, 0.645 mol) in THF (1.25 L). The reaction mixture was stirred overnight at room temperature. A solution of poly(dichlorophosphazene) (Scheme 1; a) (15.0 g, 0.129 mol) in THF (1 L) was added dropwise to the sodium salt solution at room temperature. After




*Scheme 1*

complete addition of the poly(dichlorophosphazene) solution, the reaction mixture was refluxed for 48 h. The polymer solution was then cooled, and precipitated into aqueous acid (0.02 M HCl), dried, dissolved in a minimal amount of THF and reprecipitated into deionized $H_2O$ (once) and Hexanes (twice). The resultant polymer poly[bis(propyl-oxybenzoate) phosphazene] (Scheme 1; b) was dried under vacuum to give a white fibrous polymer. (**1**); $^1$H NMR ($CD_2Cl_2$): $\delta$ 0.92 (t, 3H), 1.67 (m, 2H), 4.10 (br t, 2H), 6.63 (dd, 2H), 7.44 (dd, 2H); $^{13}$C NMR ($CD_2Cl_2$): $\delta$ 10.75, 22.55, 66.91, 120.60, 127.50, 131.30, 154.59, 165.56; $^{31}$P NMR ($CD_2Cl_2$): $\delta$ $-19.45$; $M_n = 2.42 \times 10^5$, $M_w = 6.79 \times 10^5$, PDI = 2.8.

### 2.4. Synthesis of poly[bis(sodium/potassium carboxylatophenoxy) phosphazene] (Scheme 1; c)

Poly[bis(propyl-oxybenzoate) phosphazene] (Scheme 1; b) (15.0 g, 0.0372 mol) was dissolved in THF (1 L) and was added dropwise to a stirred solution of potassium *tert*-butoxide (58.42 g, 0.521 mol) in water (5 ml)/THF (750 ml) mixture. The reaction mixture was stirred at room temperature for 20 h, after which time the white precipitate was removed via filtration, dissolved in deionized water, and was purified by dialysis against deionized water (4 days). The polymer solution was removed from the dialysis membrane and concentrated to a viscous solution under reduced pressure which was precipitated into THF to yield poly[bis(potassium carboxylato phenoxy) phosphazene] (Scheme 1; c) as a brittle white solid; $^1$H NMR ($D_2O$): $\delta$ 6.95 (br, 2H), 7.69 (br, 2H); $^{31}$P NMR ($D_2O$): $\delta$ $-18.2$.

## 3. Reaction kinetics

Kinetics of formation of SHAp and SHAp-Na-PCPP and SHAp-K-PCPP composites were studied by isothermal calorimetry (Thermometrics Corp., CA) using a method that has been described by Prosen *et al.* [32]. Calorimetric analyses of SHAp formation was carried out in the presence and absence of Na- and K-PCPP. The SHAp precursor powder was mixed with Na-PCPP and K-PCPP at 1, 5 or 10% by weight. Reaction kinetics were studied at 37.4 and 50 °C. In a typical experiment, SHAp precursors and Na- and K-PCPP powders were interground using a mortar and pestle and ball milled to achieve homogeneity. These mixtures (1.5 g) were placed in a copper cup that is internally coated with gold. The liquid medium, Dulbecco's phosphate buffer solution (PBS) (Invitrogen Corporation, Carlsbad, CA), was placed in a syringe above the powder mixture and both were equilibrated to the reaction temperature under investigation. When thermal equilibrium was reached, the phosphate buffer was injected onto the powder (the liquid-to-solid (TetCP+DCPA +[Na/(K)-PCPP]) ratio was 2-to-1, by weight). The rate of heat evolution during the reaction was determined as the voltage output as a function of time from thermopiles surrounding the calorimeter cup. Data points were collected every 3 s, and were converted to heats of reaction using a thermoelectric coefficient determined by calibration. Heat evolution was determined for 10 h. Total heat evolution (in kJ/mole of SHAp) was established by integrating the rate data using the trapezoid rule.

### 3.1. Reaction chemistry

The variations in the solution chemistry with time were investigated by determining the changes in pH. The hydroxyapatite precursor-polymer mixture (3 g) was placed in a plastic cup containing PBS solution. A liquid-to-solid (TetCP+DCPA +[Na/(K)-PCPP]) weight ratio of 25-to-1, was used. The pH measurements were carried out for composites containing 1% by weight of Na/(K)-PCPP. The plastic cup was placed in a 400 cc double-walled beaker, pre-equilibrated at 37.4 °C and maintained at that temperature by a water bath connected to the beaker. The suspension was maintained under $N_2$ gas with stirring to avoid accumulation of carbonates and formation of carbonate apatite. The pH of the solution was measured every 5 s for a period of 24 h using a calibrated pH electrode interfaced to an Orion 920 pH meter.

### 3.2. Instrumentation

X-ray diffraction (XRD) analyses were performed using an automated diffractometer (Scintag, Inc., Sunnyvale, CA), with a step size of 0.02°, scan rate of 2° per min, and a scan range from 20° to 40° $2\theta$. Phase evolution during the formation of SHAp in the presence and absence of Na- and K-PCPP was followed by comparing the XRD patterns with JCPDS cards 9-432, 25-1137, and 9-80 for HAp, TetCP and DCPA, respectively. Infrared spectrometry was performed on the polymer and composite samples (2.0 wt% in KBr) using a Mattson Instruments GL 4020 infrared spectrometer equipped with a P/N 4500 series diffuse reflectance infrared Fourier transform (Graseby/Specac).

Solution-state nuclear magnetic resonance (NMR) spectra were obtained at 298 K using a Bruker WM-360 NMR spectrometer resonating at 360.23 MHz for $^1$H, 145.81 MHz for $^{31}$P, and 90.56 MHz for $^{13}$C. All $^1$H and $^{13}$C NMR samples were prepared with deuterated chloroform (Isotec, 99.9%, OH), deuterated THF (Isotec, 99.5%, OH), deuterated dimethyl sulfoxide (Isotec, 99%, OH), or deuterium oxide (Isotec, 99.9%, OH) and referenced to tetramethylsilane (TMS). $^{31}$P NMR shifts are relative to 85% phosphoric acid as an external reference, with positive shift values downfield from the reference. Molecular weights were estimated using a Hewlett-Packard HP 1090 gel permeation chromatograph equipped with and HP-1047A refractive index detector, two Phenogel 10$\mu$ linear columns (Phenomenex, CA), and calibrated versus polystyrene standards (Polysciences, PA).

The samples were eluted at 40 °C with a 0.1 wt% solution of tetra-*n*-butylammonium nitrate (Aldrich) in THF (Omnisolv). Polymer glass transition temperatures were determined by differential scanning calorimetry (DSC) using a Perkin-Elmer-7 thermal analysis system. Approximately 30 mg samples were hermetically sealed in aluminum pans and heated at 10, 20, and 40 °C/min from –100 to 100 °C under dry $N_2$.

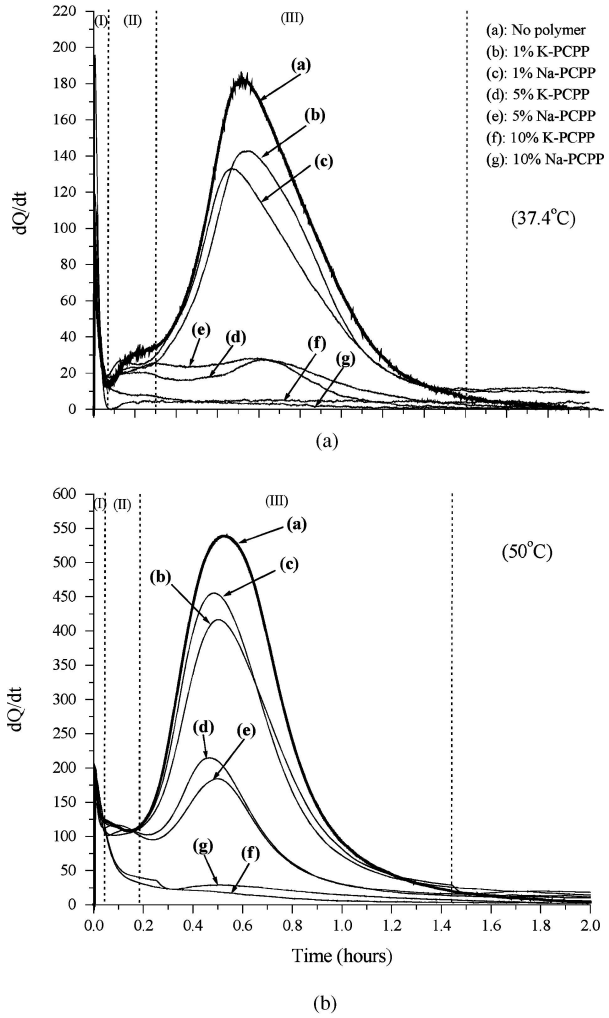



*Figure 1* Rates of heat evolution curves for the formation of HAp at A: 37.4 and B: 50 °C in presence of 0, 1, 5 and 10 wt% of Na- and K-PCPP. Areas marked I, II and III limits the mixing, nucleation and growth periods of reaction.

The final $T_g$ was determined through extrapolation to 0 °C/min heating rate. The $T_g$ was taken as the inflection point of the endotherm transition.

## 4. Results and discussion

Formation of HAp by cement-like reactions is exothermic and takes place through dissolution-precipitation process [33]. The rates of heat evolution during formation of SHAp in the presence of 1, 5, and 10% (by weight) of Na and K salts of PCPP at 37.4 °C are shown in Fig. 1(A). The heat evolved during SHAp formation in the absence of polymer is the control. It has been found that heat evolution begins immediately after mixing of the starting reactants with liquid, giving rise to three peaks that represent three stages of the reaction. A sharp peak occurs within the first few minutes of reaction, and is attributed to wetting and initial dissolution of the reactants; it is thus named "mixing peak" [34]. All samples showed mixing peak of the same intensity, irrespective of the type and concentration of polymer. Reactions at 50 °C (Fig. 1(B)) showed mixing peaks of greater intensity than those at 37.4 °C. As reported earlier the formation of HAp via cement-type reactions takes place through dissolution-precipitation processes [34]. Initial dissolution of the reactants elevated the concentrations of calcium and phosphate ions in the system thereby, promoting the precipitation of SHAp nuclei [34]. The process is exothermic and results in a second peak (nucleation peak) that begins after about 30 and 5 min, respectively at 37.4 and 50 °C. "Nucleation" peaks were observed in samples that contained 1 and 5% (by weight) of both Na- and K-PCPP at 37.4, as shown in Fig. 1(A). Mixtures containing 1% Na- and K-PCPP did not show distinct nucleation peaks at 50 °C, which indicated faster kinetics of SHAp formation at the higher temperature. The effect of increasing temperature on the kinetics of formation of HAp-polyphosphazene composites has been studied previously [25, 26, 35]. Nucleation peaks were observed in samples that contained 5% of Na- and K-PCPP after about 5 min of reaction at 50 °C. Thus, increasing the polymer (Na- and K-PCPP) concentration in the composite lead to a decrease in the rate of SHAp formation. However, when the proportions of Na- and K-PCPP were increased to 10% by weight of the precursors, no nucleation peaks were detected at either temperature. Following the nucleation peaks, during which SHAp nuclei form, is the appearance of growth peaks. These are associated with the bulk conversion of precursors to SHAp [34]. Growth peaks are shown in Fig. 1(A) and (B). Growth peaks initiate after 60 and 12 min, reach maximum intensities after 120 and 30 min, and end after 5 and 1.5 h at 37.4 and 50 °C, respectively. The intensities of growth peaks at 50 °C were three

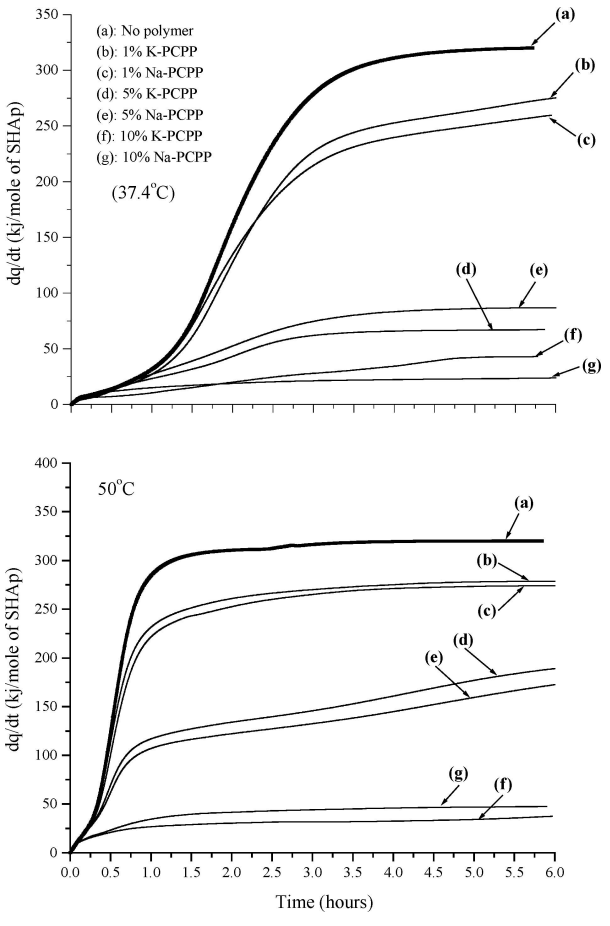



*Figure 2* Total heat evolution during the formation of HAp at A: 37.4 °C and B: 50 °C in the presence of 0, 1, 5 and 10 wt% of Na- and K-PCPP.

times those at 37.4 °C. Growth peaks were reduced in the presence of 1% of Na- and K-PCPP as compared to SHAp formation in the absence of polymers at both temperatures. Composites that contained 5% Na- and K-PCPP showed growth peaks of reduced intensity at both temperatures. In the presence of 10% by weight of Na- and K-PCPP, growth peaks were absent. Thus increases in the concentration of the polymer from 5 to 10% completely inhibits the formation of SHAp. This accounts for the absence of a nucleation peak in the case of composites that have 10% by weight of polymer. The curves shown in Fig. 2 illustrate the extents of heat evolution during the first 6 h of reaction. Table I lists total heats evolved during this period.

Fig. 3 compares pH variations at 37.4 °C during SHAp formation in composites that contained 1% by weight of Na- and K-PCPP and polymer-free samples. The increase in pH is primarily controlled by the rate of dissolution of the basic precursor, TetCP, and has been described [36]. The variations of pH in the presence of 1% K-PCPP were virtually identical to those in the absence of the polymer. The presence of 1% Na-PCPP brought about a slow increase in pH over a period of 5 h. Thus the presence of 1% Na-PCPP in the composites showed faster kinetics of reaction compared to 1% K-PCPP at 37.4 °C. The origin of these effects will be discussed subsequently.

Fig. 4 shows XRD patterns of the composites that contain 1, 5, and 10% (by weight) of Na-PCPP at 37.4 and 50 °C after reaction for 6 h. Phase evolution was followed by evaluating changes in the intensities of TetCP peaks at $2\theta$ values of 25.4, 29.4 and 29.9°, DCPA peaks with $2\theta$ values of 26.5 and 30.1°, and SHAp peaks with $2\theta$ values of 25.9 and 31.8°. HAp was the only crystalline phase ultimately present in the polymer-free samples. In samples that contained 1% Na-PCPP, the presence of residual TetCP was detected in samples reacted at 37.4 °C after 24 h. TetCP peaks were not detected in samples that contained 1% Na-PCPP at 50 °C, where SHAp was the only crystalline solid observed. DCPA was not detected at either temperature. Increasing the proportion of Na-PCPP to 5% resulted in the presence of unreacted TetCP and DCPA regardless of reaction temperature. When 10% of Na-PCPP was present, unreacted TetCP and DCPA were the only crystalline phases detected after reaction at 37.4 °C for 24 h. A small amount of HAp was observed when the reaction was carried out at 50 °C. Similar results were obtained for composites containing 1, 5 and 10% by weight of K-PCPP.

Figs. 5(a) and (b) show the phase composition of composites that contained 1 and 10% K-PCPP after curing at 37.4 °C for 1, 3, 6, 12, and 24 h. The XRD patterns in Fig. 5(a) show that SHAp was formed after

TABLE I Heat of reaction values of composites containing 0, 1, 5 and 10% by weight of Na- and K-PCPP at 37.4 and 50 °C

| % M-PCPP (M: Na, K) | $\Delta H_r$ (kj/mole of SHAp) | |
|---|---|---|
| | 37.4 °C | 50 °C |
| 0 (No M-PCPP) | 319.7 ± 0.25 | 320 ± 0.35 |
| 1 | | |
| Na | 258.3 ± 1.21 | 278.57 ± 0.4 |
| K | 272.87 ± 1.96 | 273.87 ± 1.25 |
| 5 | | |
| Na | 86.53 ± 0.55 | 171.87 ± 0.32 |
| K | 67.27 ± 0.25 | 188.47 ± 0.5 |
| 10 | | |
| Na | 42.97 ± 0.15 | 47.57 ± 0.4 |
| K | 23.7 ± 0.3 | 37 ± 0.2 |

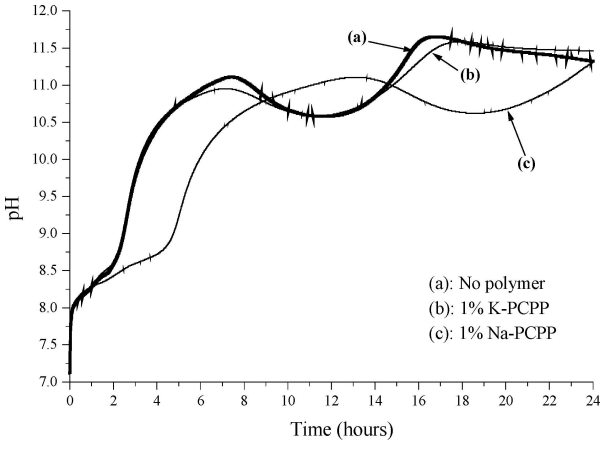



*Figure 3* Variations in solution pH as a function of time during HAp formation at 37.4 °C in presence of 0 and 1 wt% of Na- and K-PCPP.

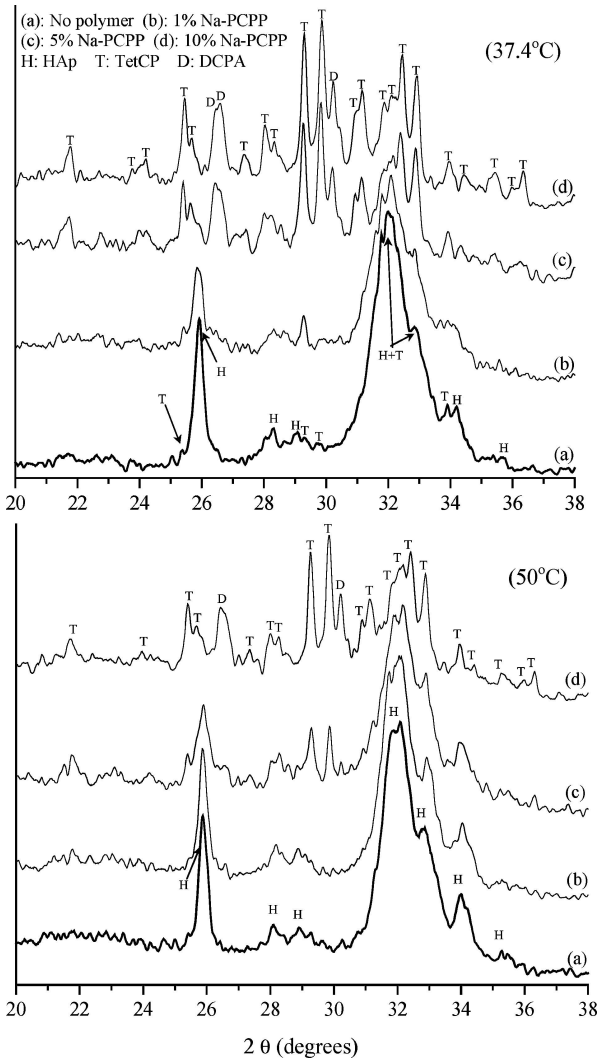



*Figure 4* X-ray diffraction patterns indicating the formation of HAp at A: 37.4 and B: 50 °C in the presence of 0, 1, 5 and 10 wt% of Na-PCPP.

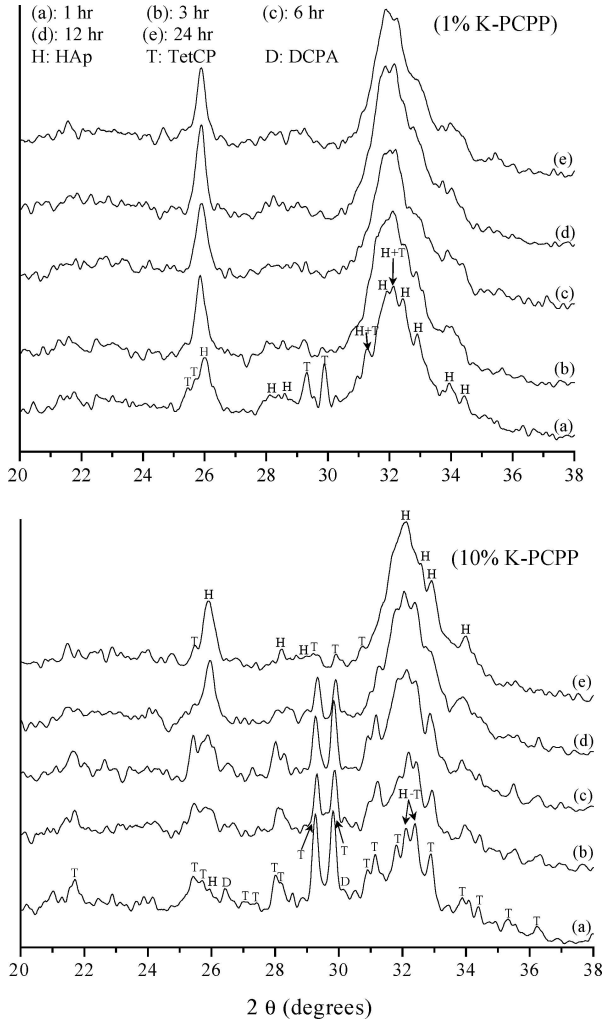



*Figure 5* X-ray diffraction patterns showing the phase evolution of solids during formation of HAp with time at 37.4 °C in the presence of A: 1% and B: 10% K-PCPP after 1, 3, 6, 12 and 24 h of reaction.

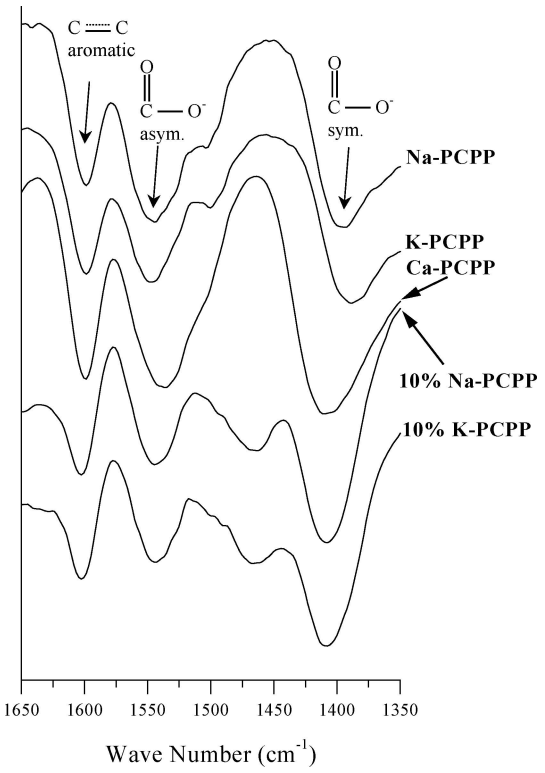



*Figure 6* Infrared spectra of composites containing 10% Na- and K-PCPP prepared at 37.4 °C, in comparison with standard Na-, K- and Ca-PCPP samples.

3 h at 37.4 °C in samples containing 1% K-PCPP. The formation of HAp in samples contained 10% K-PCPP was a very slow process as shown in Fig. 5(b). This was similar to the results obtained from the composites that contained Na-PCPP, as discussed before. Powder mixtures of the SHAp precursors and Na- or K-PCPP were prepared before mixing with PBS solutions, because solutions that contained 5 and 10% of Na- and K-PCPP were highly viscous. In presence of high concentrations of the polymers, the highly viscous polymer solutions adsorb on the reactants surfaces. This adsorption results in the formation of calcium cross-linked salt layers at the interface between the polymer layer and the underlying calcium phosphate reactants. Formation of these layers results in a slower rate of formation of HAp, as observed in Figs. 1 and 2.

Fig. 6 shows infrared spectra of composites containing 10% Na- and K-PCPP compared to standard Na-, K- and Ca-PCPP samples. A sample that contained calcium cross-linked polymer salt was prepared as reported previously [24], by precipitation of acid-PCPP into a dilute calcium chloride solution. A band at 1600 $cm^{-1}$ in the standard samples is characteristic to C═C bond in the aromatic group of PCPP [37]. This band remained unchanged for Na- and K-PCPP in the composites. The symmetric absorption mode of the carboxylate anion in Na- and K- and Ca-PCPP standard samples appeared at 1544, 1544 and 1538 $cm^{-1}$, respectively [37]. In the composites, this band was shifted to 1542 $cm^{-1}$ in the presence of Na- and K-PCPP. On the other hand, the asymmetric mode of absorption of the carboxylate anion in Na-, K- and Ca-PCPP appears at 1397, 1392 and 1407 $cm^{-1}$, respectively [37]. This band appeared at 1407 $cm^{-1}$ in the composites that contained 10% Na- and K-PCPP. These results indicate the formation of calcium cross-linked polymer salt in the composites. Formation of the salt takes place via an ion exchange reaction [26], as shown in Fig. 7. Calcium ions released in the solution replace sodium or potassium ions in their corresponding polymers. The solubility of the polymers and the resultant coating of the precursors facilitate the exchange reaction at the interface between them. The present results indicate the concurrent formation of HAp and the polymer salt.

Fig. 8 shows scanning electron micrographs of a composite that contained 5% by weight of Na-PCPP after 3 and 24 h of reaction. Figs. 8(a) and (b) show the coating of the precursor powder at low magnification. Fig. 8(c) shows a scanning electron micrograph of a composite containing 5% Na-PCPP after 24 h. The micrograph together with EDX analysis suggests the formation of SHAp on the crosslinked salt coating. These results further indicate that an exchange reaction takes place between the Na-PCPP and calcium ions in the medium, to form a cross-linked polymer network, as was shown previously by TenHuisen *et al.* [26]. Formation of the network takes place over time at the interface between the coating and the underlying calcium

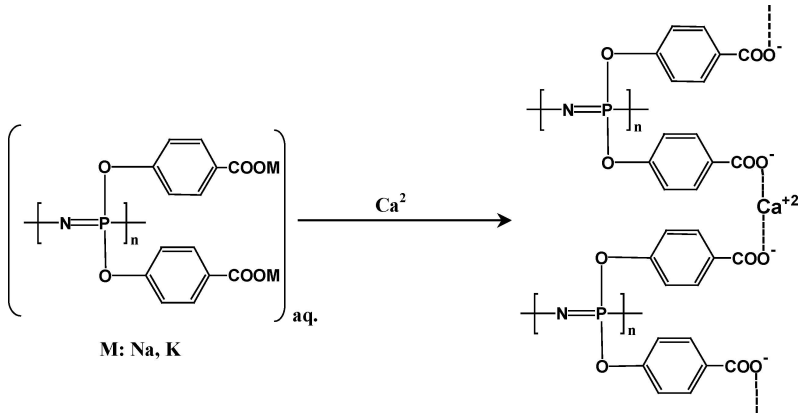



*Figure 7* Schematic representation of the mechanism of formation of calcium cross-linked polymer salt.

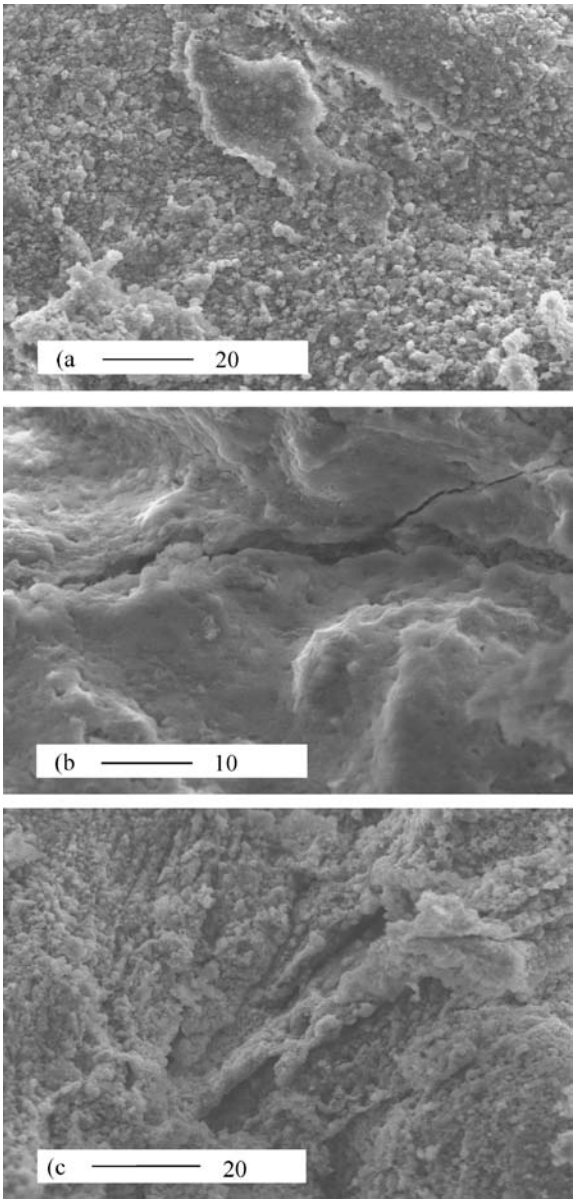



*Figure 8* Scanning electron micrographs of a composite containing 5 wt% of Na-PCPP at different magnifications prepared at 37.4 °C for 3 h (a, b), and (c) 24 h.

phosphate precursors. The presence of HAp may be attributed to its nucleation on the polymer salt network. Reactions that take place at the interface between the inorganic and polymer precursors also allow the inorganic precursors to react with each other to form HAp. Because this occurs at a slow rate, minor amounts of TetCP were observed in the composites. However, despite the development of a coating, these results show that, despite the coating that retarded the slow kinetics (Figs. 1(a) and 2(a)), SHAp was detected as the major phase after 24 h (Fig. 5(b)).

## 5. Summary

The formation of SHAp via an acid-base reaction between TetCP and DCPA in the presence of poly[bis(sodium carboxylatophenoxy) phosphazene (Na-PCPP) and poly[bis(potassium carboxylatophenoxy) phosphazene (K-PCPP) at 37.4 and 50 °C inhibited SHAp formation depending on the proportion of polymer used. At low proportions of polymer, calcium ions entering solution during SHAp formation exchanged with sodium and potassium ions in the polymers, forming a cross-linked polymer salt, and SHAp was the major calcium phosphate present after 24 h. In the presence of high proportions of the polymers, however, highly viscous polymer solutions coated the calcium phosphate reactants and inhibited HAp formation. In this instance, apatite deposits formed slowly on the coated precursors, suggesting that the coatings have limited permeability. The inhibition effect was reduced at a higher reaction temperature. Moreover, to minimize the inhibition of formation of HAp, lower molecular weight polymers are suggested to be used.

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