
Novel polymer-synthesized ceramic composite-based system for bone repair: An *in vitro* evaluation

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Abstract: The emergence of synthetic bone repair scaffolds has been necessitated by the limitations of both autografts and allografts. Several candidate materials are available including degradable polymers and ceramics. However, these materials possess their own limitations that at least in part may be overcome by combining the two materials into a composite. Toward that end, a novel approach to forming a polymer/ceramic composite has been developed that combines degradable poly(lactide-co-glycolide) microspheres and a poorly crystalline calcium phosphate that is synthesized within the microspheres, which are then fused together to form a porous three-dimensional scaffold for bone repair. The design, fabrication, and characterization of the composite microspheres, the calcium phosphate formed within these microspheres, and the formation of scaffolds were studied. The calcium phosphate formed was analyzed

by x-ray diffraction, Fourier transform infrared spectroscopy, and energy dispersive spectroscopy, and was shown to be similar to native bone in both composition and crystallinity by controlling certain processing parameters such as mixing time, solution pH, and mixing temperature. Scaffolds with porous interconnected structures and mechanical properties in the range of trabecular bone were fabricated via precise control of polymer/ceramic ratios within the microspheres and scaffold heating times. This composite scaffold represents a new and important vehicle for bone-tissue engineering. © 2004 Wiley Periodicals, Inc. *J Biomed Mater Res* 69A: 728–737, 2004

Key words: polymer; calcium phosphate; bone; tissue engineering; microsphere; poly(lactide-co-glycolide); composite; three-dimensional; scaffold

INTRODUCTION

The use of bone grafts and bone-graft substitutes is on the rise, with as many as 500,000–600,000 procedures performed in 1999 alone¹ of which approximately 10% included the use of synthetic bone-graft substitutes.² This rise in bone-graft substitutes is partially fueled by the limitations of conventional bone grafts, namely autografts and allografts. Autografts, the current gold standard of bone grafts, provide excellent healing and an 80–90% success rate,³ but limitations such as donor-site morbidity and supply issues suggest a need for an alternative. Allografts present such an alternative, but are plagued by their

own limitations such as disease-transmission risks and reduced healing due to postharvest treatments.⁴ In this light, many researchers have explored bone-graft substitutes using a variety of materials including degradable polymers and ceramics such as calcium phosphate. The use of calcium phosphate is well reasoned as it is calcium phosphate in the form of hydroxyapatite that makes up the inorganic portion of bone. Several materials are currently available that are formed from crystalline calcium phosphates and show good osteoconduction and osteointegration, but tend to fail catastrophically under load because of their brittle nature, and are therefore unsuitable for load-bearing applications.⁵ Furthermore, many of the calcium phosphate-based bone-graft substitutes are formed from highly crystalline materials that are either nondegradable or degradable over long periods of time.⁶ This slow rate of degradation does not always coincide with normal healing rates of bone, and thus may hinder or slow complete healing.⁷ Studies have also shown enhanced cell attachment and proliferation on poorly crystalline hydroxyapatite.^{8,9} Fi-

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nally, to form calcium phosphate-based bone-graft substitutes into desired shapes, it is necessary to heat the material to high temperatures, preventing these materials from being used as composites with other materials that are sensitive to these extreme temperatures. A noncrystalline calcium phosphate that degrades both more readily and in a shorter time frame than crystalline calcium phosphates would not only more closely approximate the rate of bone healing, but would also be a closer match to the structure of actual bone, which is known to be poorly crystalline.^{10,11} As this calcium phosphate was resorbed or dissolved, it would provide local delivery of necessary ions to form a bioactive layer throughout the scaffold and thus promote further surface mineralization.¹² The addition of a degradable polymer to this amorphous calcium phosphate would allow for better manipulation and control over both macro- and microstructure of the scaffold material, and may reduce the brittleness of the ceramic. Several groups have formed composite structures by either mixing polymer with ceramic powders including hydroxyapatite,^{13–17} and tricalcium phosphate,^{18,19} or precipitating an apatite-like layer on the polymer surface.^{20–22} This work represents an innovative approach to composite formation that may provide new advantages over pre-existing approaches.

In this study, a porous, three-dimensional composite scaffold designed for bone-tissue engineering was developed from polymer/ceramic composite microspheres. The composite microspheres were formed by the *in situ* precipitation of calcium phosphate within the forming polymeric microspheres, allowing for a well-distributed ceramic throughout the scaffold. Synthesis parameters of both the microspheres and the scaffold were controlled to allow for a scaffold possessing a poorly crystalline calcium phosphate similar to bone apatite with mechanical properties similar to trabecular bone. Calcium phosphate formed was characterized using X-ray diffraction (XRD), Fourier transform infrared (FTIR) spectroscopy, and energy dispersive spectroscopy (EDS), whereas scaffolds were examined using both scanning electron microscopy (SEM) and mechanical evaluation.

MATERIALS AND METHODS

Poly(lactide-*co*-glycolide) (85:15) with a molecular weight of 110,000 was purchased from Alkermes (Canton, MA). Calcium nitrate tetrahydrate, ammonium hydrogenphosphate, and ammonium hydroxide were purchased from Sigma Chemical Company (St. Louis, MO). Methylene chloride and polyvinyl alcohol were purchased from Fisher Scientific (Pittsburgh, PA).

TABLE I
Synthesis Parameters for Composite Microsphere Fabrication

Temperature of Synthesis (°C)	pH of Solution	Mixing Time (h)	Polymer/Ceramic Ratio
20 (room temperature)	7	3	Low
20	7	6	Low
20	7	12	Low
20	7	24	Low
20	10	3	Low
20	10	6	Low
20	10	12	Low
20	10	24	Low, middle, high
4	10	24	Low, middle, high

Microspheres were synthesized at either room temperature or 4°C, at a solution pH of either 7 or 10, for 3, 6, 12, or 24 h. Polymer/ceramic ratios varied between low (0.33), middle (0.67), and high (1.33).

Composite microsphere preparation

Polymer/ceramic microsphere synthesis was a modification of methods described previously.²³ Briefly, calcium nitrate tetrahydrate and ammonium hydrogenphosphate were dissolved separately in distilled, deionized water (DDH₂O) and added to a solution of Poly(lactide-*co*-glycolide) in methylene chloride. Initial molar ratios of calcium nitrate tetrahydrate and ammonium hydrogenphosphate were 1.67 for all groups. The mixture was vortexed for 20 s and added dropwise to a 1% solution of polyvinyl alcohol (MW ~70,000). During mixing, pH was maintained at desired levels using a Titrino pHSTAT (Metrohm, Herisau, Switzerland). After the proper mixing time (see Table I), microspheres were rinsed with DDH₂O, isolated via vacuum filtration, and dried at room temperature for 24 h. Microspheres were then vacuum-dried for an additional 48 h.

Several synthesis parameters were varied as follows. The pH of mixing was maintained at one of two levels, pH 7 and pH 10, to determine effects of solution pH as previously reported.³⁴ Samples were mixed for either 3, 6, 12, or 24 h at both pH levels. Several additional parameters were examined at pH 10 only based on XRD patterns. The effect of reaction temperature was examined by synthesizing composite microspheres at both 4° and 20°C (room temperature), and mixing time of 24 h to examine effects of slowing the solvent evaporation process. The ratio of polymer/ceramic used to synthesize the microspheres was also varied by taking the mass of polymer used in the microsphere formulation and varying it with the combined mass of undissolved calcium nitrate tetrahydrate and ammonium hydrogenphosphate to be dissolved and added to the polymer solution. These ratios were noted as low (0.33), middle (0.67), and high (1.33). Microspheres with these ratios were synthesized both at room temperature and at 4°C.

Calcium phosphate analysis

After the microspheres were vacuum-dried for 48 h, the formed calcium phosphate was extracted from the polymer

TABLE II
Synthesis Conditions of Matrices Analyzed for Mechanical Evaluation

Polymer/Ceramic Ratio	Synthesis Temperature	Heating Time (min)
Low	4°C	30
Middle		60
High	Room temperature	90

Scaffolds tested were formed from microspheres using low, middle, and high polymer/ceramic ratios and either 4°C or room-temperature mixing. Scaffolds formed from these different microspheres were heated for either 30, 60, or 90 min.

by three successive washes in a large excess of methylene chloride (approximately 25:1 v/w ratio), with the polymer solution decanted between washings. This process left behind only the precipitated calcium phosphate, which was analyzed using XRD equipped with a Cu K- α tube to generate X-rays. The XRD provided both a qualitative assessment of crystallinity as well as calcium phosphate phase identification. Furthermore, the calcium phosphate was analyzed for Ca/P ratio using EDS via a scanning electron microscope (Amray 1830-D4). Finally, FTIR spectroscopy (Nicolet, Madison, WI) was conducted to further characterize the precipitated calcium phosphate.

Sintered microsphere scaffold synthesis and evaluation

Matrices were synthesized from microspheres using a previously described method.²⁵ Briefly, composite microspheres were sieved to a specific size range (355–600 μm diameter) using stainless steel sieves and placed in a stainless steel mold that produced cylindrical scaffolds measuring 10 mm in length and 5 mm in diameter (2:1 aspect ratio). Microspheres were heated to 90°C for 30, 60, or 90 min, depending on the composition of the microspheres. After heating, microspheres were allowed to equilibrate to room temperature for 60 min at which time they were removed from the molds and stored protected from moisture.

Mechanical testing

Matrices measuring 5 mm in diameter by 10 mm in length were tested in compression to failure using a uni-axial compression testing machine (Instron, Canton, MA) at a cross-head speed of 15 mm/min. Matrices were formulated from microspheres that were synthesized with low, medium, or high polymer ceramic ratios as described above at both room temperature and 4°C, and were heated for either 30, 60, or 90 min (see Table II). Young's modulus was computed by determining the slope of the stress-versus-strain curve along the elastic portion of the deformation curve. For each condition, six samples were tested.

SEM

Qualitative analysis of microspheres and matrices was done using SEM (Amray 1830-D4) equipped with a tungsten electron gun, at a working distance of 25 mm and an acceleration voltage of 20 KeV. High-magnification images were taken and analyzed for qualitative analysis of surface and pore structures.

Statistics

A one-tailed Student *t* test was used to compare compressive modulus between groups in which $p = 0.05$ and the sample size was $n = 6$.

RESULTS

Calcium phosphate analysis

Figures 1 and 2 show the effects of pH on the calcium phosphate synthesized at room temperature with a solution pH of 7 and 10, respectively, over varying mixing times. The XRD spectra of calcium phosphate synthesized at pH 7 suggest that the calcium phosphate initially contained what appears to be a heterogeneous mix of brushite and hydroxyapatite (3-h mix) but over time it appears as if a poorly crystalline or nanocrystalline hydroxyapatite appears with brushite still present (24-h mix). In contrast to this, Figure 2 shows calcium phosphate synthesis at pH 10 appearing as nanocrystalline hydroxyapatite after only 3 h of mixing and continuing after 24 h of mixing. EDS of the calcium phosphates indicates that the ratio of calcium to phosphorus ranged from 1.60 to 1.83 as the mixing time increased (Fig. 3). This is similar to the ratio of 1.67 seen in stoichiometric hydroxyapatite. XRD of calcium phosphate from composite microspheres synthesized at both room temperature and 4°C at low, middle, and high polymer ceramic ratios are shown in Figures 4 and 5, and indicate that decreasing the temperature of synthesis had little to no effect on the calcium phosphate synthesized in the low and middle polymer ceramic ratio microspheres, in which both calcium phosphates displayed XRD spectra similar to nanocrystalline hydroxyapatite. However, both temperature and polymer ceramic ratio had an influence on synthesized calcium phosphate at the high ratio, as the XRD spectra once again showed a heterogeneous calcium phosphate at both room temperature and 4°C.

FTIR analysis of calcium phosphate extracted from microspheres synthesized at room temperature with a low polymer ceramic ratio showed peaks at 1030 and 550 cm^{-1} suggesting the presence of phosphate, whereas the peak at 870 cm^{-1} suggests the presence of

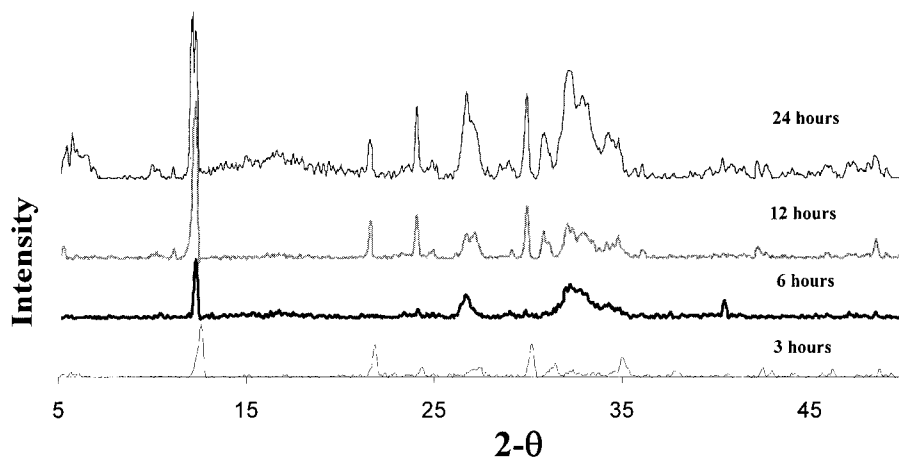


Figure 1. XRD patterns of calcium phosphate extracted from composite microspheres synthesized at pH 7, room temperature, over different mixing times. The shortest mixing times produced a calcium phosphate that was a mixture of more than one phase. It is only after 24 h of mixing that a clear overlap between brushite and nanocrystalline hydroxyapatite emerges.

HPO_4 (see Fig. 6). When synthesis was performed at 4°C , a similar calcium phosphate was seen but with the possible presence of residual calcium nitrate. Analysis of calcium phosphate extracted from microspheres synthesized at room temperature and 4°C with a middle polymer ceramic ratio also showed peaks at 1030 and 550 cm^{-1} suggesting the presence of phosphate, but also had an exaggerated peak at 1380 cm^{-1} suggesting an increased presence of residual calcium nitrate (see Fig. 7).

Sintered microsphere scaffold evaluation

Compression testing revealed a relationship between both microsphere and scaffold preparation and com-

pressive modulus (see Fig. 8). The compressive modulus of the matrices increased from a low of 691 KPa with microspheres synthesized at room temperature, a middle polymer ceramic ratio, and a scaffold heating time of 30 min , to a high of 64.7 MPa with microspheres heated at 4°C , a high polymer ceramic ratio, and a scaffold heating time of 90 min . The effect of each parameter on heating time can be seen as well. Increasing the initial heating time from 30 to 60 min resulted in an increase in compressive modulus from 691 KPa to 4.7 MPa . Scanning electron micrographs of a 30-min heat time and a 120-min heat time show the increased fusion between neighboring microspheres that occurs with an increase in heating time (see Fig. 9).

Decreasing the microsphere synthesis temperature resulted in an increase in modulus from 4.71 to 22.9

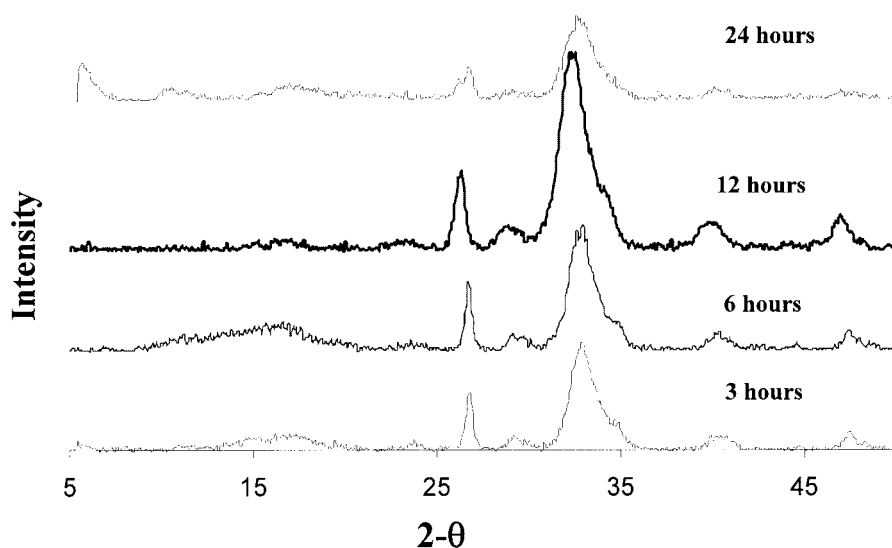


Figure 2. XRD patterns of calcium phosphate extracted from composite microspheres synthesized at pH 10, room temperature, over different mixing times. Nanocrystalline hydroxyapatite appears as early as 3 h and remains after 24 h of mixing.

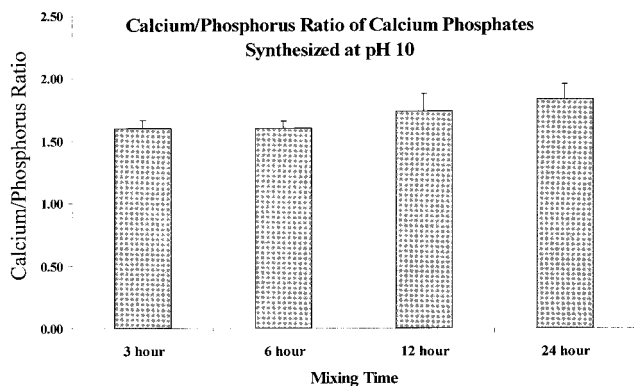


Figure 3. Calcium/phosphorus ratios of calcium phosphates extracted from composite microspheres synthesized at room temperature as determined by EDS. Ratios ranged from 1.6 to 1.83 as the mixing time increased from 3 h to 24 h.

MPa. Cross-sections of two microspheres, one synthesized at room temperature and the other at 4°C show the difference in wall thickness of the resulting microspheres (see Fig. 10). Finally, an increase in the polymer ceramic ratio used to synthesize the microspheres that were formed at 4°C also served to increase the compressive modulus from 31.3 to 64.2 MPa despite the decrease in heating time, a modulus increase of >100%. This modulus is within the range of trabecular bone.²⁶ SEM images of the microspheres with different polymer ceramic ratios revealed that as the polymer ceramic ratio increased, the amount of ceramic seen on the surface of the microspheres decreased (see Fig. 11).

DISCUSSION

Microsphere evaluation

The need for alternatives to currently available bone-graft substitutes has generated numerous candi-

dates, many of which are composites of polymer and calcium phosphate. This combination is well founded as calcium phosphate is the inorganic material of bone and has been shown to be bioactive, osteoconductive,⁵ and, in some instances, osteoinductive.²⁷ The combination of calcium phosphate, which on its own is brittle and limited in its applications,⁵ and polymer is also well founded as the addition of the polymer can impart beneficial properties such as mechanical toughness, resistance to brittle failure, and formability to the calcium phosphate, as well as expand potential applications of such a composite material to include drug and growth factor delivery capabilities.²⁸ However, many of the matrices studied use crystalline forms of calcium phosphate in combination with a complementary material. This calcium phosphate is either slowly resorbable or not resorbable at all, which may provide for high compressive and tensile strengths but may not be the most appropriate solution for bone healing.

The composite microspheres were examined under several different processing parameters. The effects of these parameters on calcium phosphate formed and overall mechanical properties of the composite microsphere scaffold were determined. The calcium phosphate that was formed within the polymeric microspheres showed a dependency on pH, but not on mixing time or mixing temperature. Indeed, when mixing time was varied but mixed at a pH of 10, XRD patterns suggested a nanocrystalline hydroxyapatite was formed after only 3 of mixing and maintained that phase up to 24 h of mixing. The calcium phosphate extracted from microspheres formed at pH 7 was more dependent on mixing duration, with shorter mixing times forming phases more similar to brushite and longer mixing times yielding a biphasic calcium phosphate with what appeared to be a mix of brushite and hydroxyapatite. Interestingly, the calcium phosphate

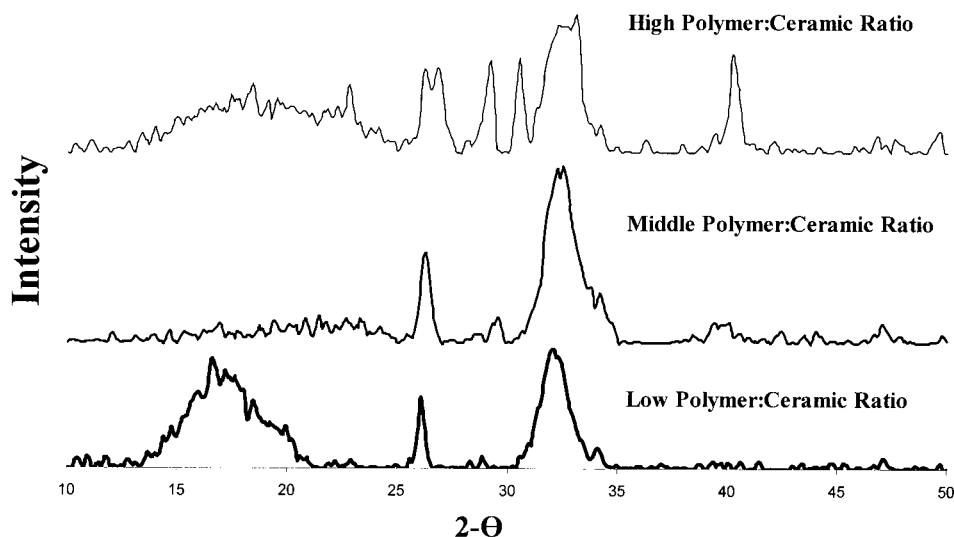


Figure 4. Room-temperature synthesis of CaP with polymer/ceramic ratios of 1.5:4.5 (low), 3.0:4.5 (middle), and 3.0:2.25 (high).

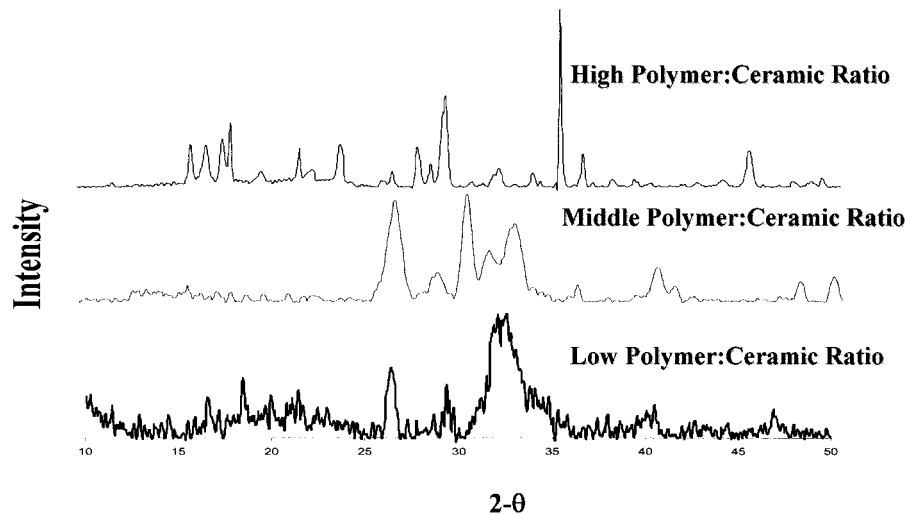


Figure 5. Cold-temperature synthesis of CaP with polymer/ceramic ratios of 1.5:4.5 (low), 3.0:4.5 (middle), and 3.0:2.25 (high).

that was synthesized at pH 10 has a crystallographic profile that is very similar to that of natural bone,^{10,29,30} and this dependence on pH agrees with that found in the literature.^{24,31} However, these are the first studies to show this relationship with calcium phosphate synthesized within a polymeric microsphere.

EDS analysis of the calcium phosphate extracted from low polymer ceramic ratio microspheres synthesized at room temperature showed a gradual increase in Ca/P ratio as mixing time increased. This suggests the possibility that, at the earliest time points, a hydroxyapatite precursor may have been present such as

brushite, which has a Ca/P ratio of 1.0, and slowly converted to hydroxyapatite which has a Ca/P ratio of 1.67. Liu et al.²⁴ have described the precipitation of calcium phosphate in an aqueous environment and have shown that octacalcium phosphate is a precursor to hydroxyapatite. This belief has been put forth as the likely path for hydroxyapatite synthesis *in vivo*, with the resulting calcium phosphate being amorphous but becoming more crystalline as the animals age.³² Further studies are warranted that examine the effects of an aqueous environment on the calcium phosphate formed and its ability to dissolve into solution. If the calcium phosphate is able to dissolve

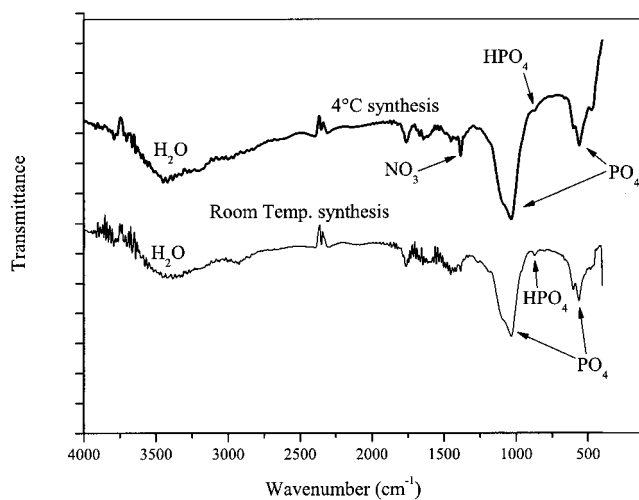


Figure 6. FTIR spectra of calcium phosphate extracted from low polymer/ceramic ratio microspheres synthesized at room temperature and 4°C. Calcium phosphate appears similar to poorly crystalline hydroxyapatite with an indication of residual calcium nitrate in the calcium phosphate synthesized at 4°C.

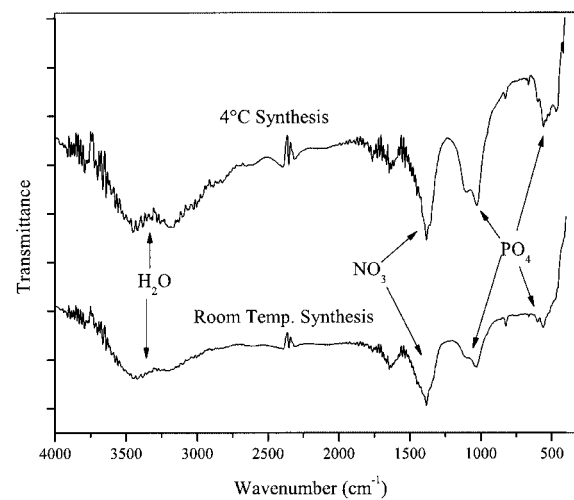


Figure 7. FTIR spectra of calcium phosphate extracted from middle polymer/ceramic ratio microspheres synthesized at room temperature and 4°C. Although peaks suggesting poorly crystalline hydroxyapatite are present, a more robust indication of calcium nitrate is also apparent.

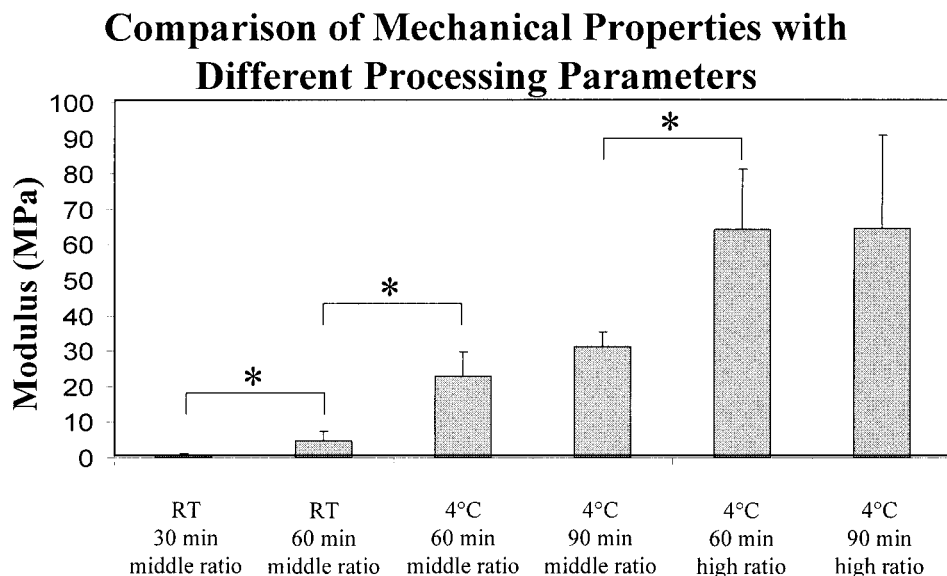


Figure 8. Comparison of compressive modulus across changes in microsphere synthesis temperature between room temperature (RT = 20°C) and 4°C, changes in polymer/ceramic ratio of the microspheres between middle and high, and changes in scaffold heating time between 30, 60, and 90 min, shows a dependence of mechanical properties on these parameters. *Statistically significant changes ($p < 0.05$).

into the ambient solution, ions will be locally available for calcium phosphate reprecipitation that may enhance bone bonding and mineralized tissue formation *in vivo*.¹²

FTIR examination of the calcium phosphate synthesized at pH 10 showed a poorly crystalline apatite-like calcium phosphate when the microspheres were formed at either room temperature or 4°C and with a low polymer ceramic ratio. As the polymer ceramic ratio was increased, there appeared to be some residual calcium nitrate in the calcium phosphate. This was also present in the 4°C calcium phosphate with the low polymer ceramic ratio but was insignificant. How-

ever, it appeared more prevalent as the polymer content increased which suggests that some of the unreacted calcium nitrate was becoming encapsulated within the polymeric microspheres. This is an important fact because scaffold mechanical properties were shown to be partially dependent on polymer ceramic ratio. This residual calcium nitrate is not of any concern regarding overall biocompatibility of the composite material as toxicity studies examining the effects of calcium nitrate in amounts far exceeding those present within the microspheres showed no adverse effects on normal osteoblast proliferation (unpublished data). Thus far, the calcium phosphate synthesized within

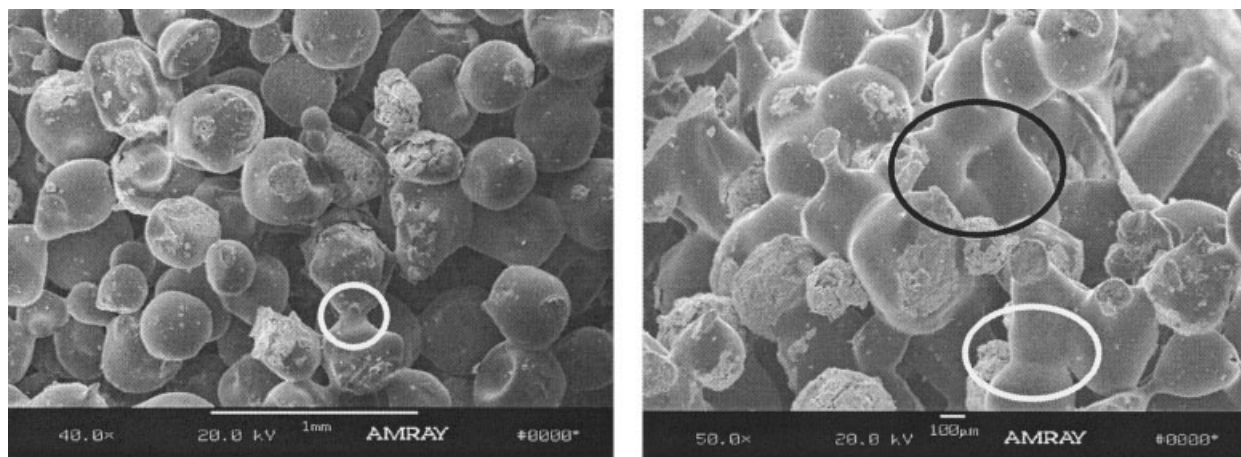


Figure 9. The effect of heating time is seen on scanning electron micrographs of the scaffold heated for 30 min (left) and 120 min (right). Fusion can be seen between microspheres after only 30 min of heating (white circle on left image) but after added heating time, the degree of fusion has increased (white circle on right image). However, extended heating times can lead to pore closure as seen on the scaffold heated for 120 min (black circle). Original magnification, 40× (left) and 50× (right).

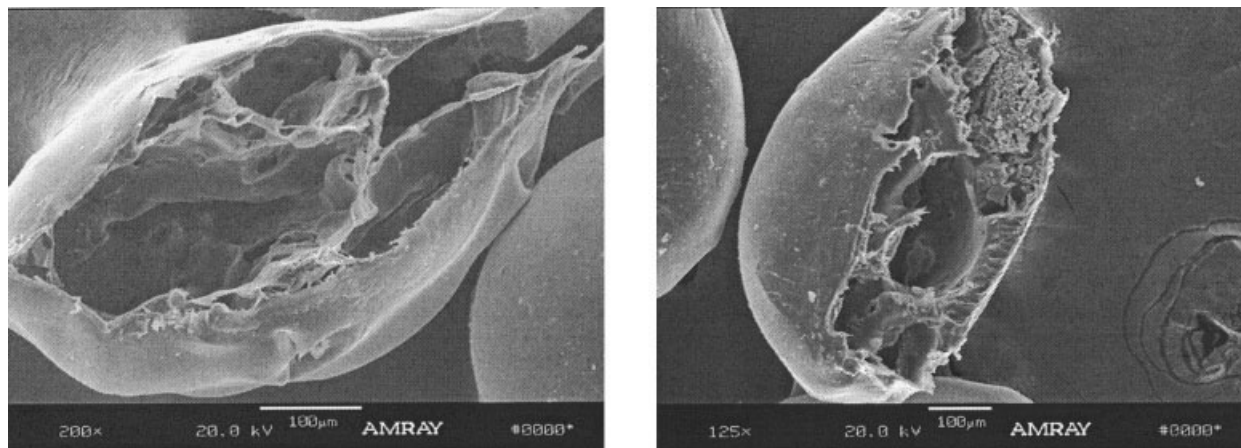


Figure 10. SEM images of split microspheres synthesized at room temperature (left) and 4°C (right). Wall thickness is noted to be greater in the microsphere synthesized at 4°C which may be responsible for the increase in mechanical properties seen from matrices fabricated from those microspheres. Original magnification, 200× (left) 125× (right).

the polymeric microspheres appears similar to bone in its crystallographic structure, Ca/P ratio, and content.

Scaffold evaluation

The mechanical properties were shown to be dependent on several parameters including microsphere synthesis temperature, polymer ceramic ratio within the microspheres, and heating time of the scaffold. By reducing the synthesis temperature of the microspheres, it can be seen that the wall thickness of the microsphere was increased (see Fig. 10). This may be due to the interaction between the calcium and phosphorus within each microsphere. Durucan and Brown³³ have reported that the synthesis of calcium phosphate causes an increase in heat of reaction over

time. Therefore, the formation of calcium phosphate within a microsphere may give off enough heat to evaporate the solvent that is locally available during microsphere formation. If this process is cooled to a 4°C environment, one may surmise that the heat produced by the calcium phosphate formation would be less, and therefore the expansion of the microsphere itself might be less, resulting in a less porous or thicker-walled microsphere. With thicker and therefore stronger microsphere walls, physical bonds between microspheres could be surmised to be stronger with a stronger scaffold as a net effect. This was confirmed by the compression testing data as the microsphere synthesis temperature was reduced (see Fig. 8). Figure 9 shows scanning electron micrographs of matrices after two different heating times, 30 and 120 min. The white circle on the SEM image of the scaffold heated for 30

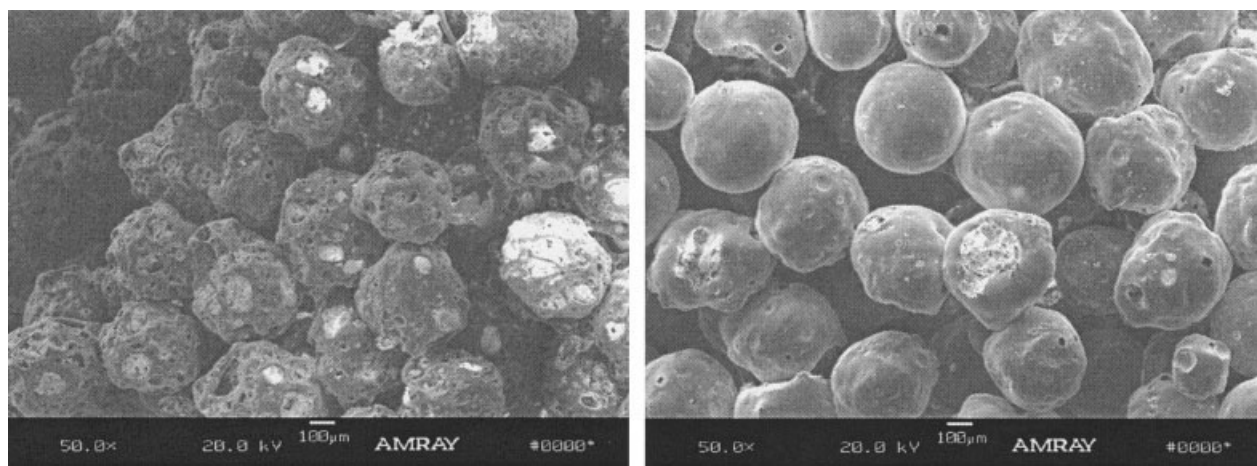


Figure 11. Scanning electron micrographs of composite microspheres with low (left) and high (right) polymer/ceramic ratios. It can be seen that with lower polymer content, there is more calcium phosphate on the surface of the microspheres, whereas as the polymer content increases, these appearances become fewer in number. It is suggested that the greater polymer coverage of the microspheres leads to better bonding, and thus a stronger scaffold (original magnification, 50×).

min shows the bond between two neighboring microspheres. This bond is responsible for the strength of the scaffold. The SEM image of the scaffold heated for 120 min also shows a bond between microspheres (white circle) that is more robust and more extensive than that in the scaffold heated for 30 min. As this bond increased with longer heating times, the strength of the scaffold increased as well. However, as the heating time increased, the risk that microspheres could fuse together increased as well (dark circle). As the bond between neighboring microspheres increased, it is more likely that pores that formed between adjacent microspheres had closed, thus compromising the interconnected pore structure of the scaffold. Therefore, it is beneficial to increase heating to increase strength, but only to the extent that the porous structure is maintained. Figure 8 shows a maximum heating time of 90 min because the mechanical properties were enhanced with this heating time but not to the point of closing pores. Thus, an optimal heating time has been established that maximizes mechanical properties while minimizing structural compromise.

Equally important to mechanical strength is the surface available for microsphere–microsphere bonding. To bond the microspheres together, the composite scaffold is heated above the glass-transition temperature of the polymer, approximately 57°C. By heating above the glass-transition temperature, the polymeric chains are energized and begin to interwine with those of the neighboring microspheres. As more time passes, the extent of intertwining increases and the bond is enhanced. However, this can only take place if the two surfaces in contact with each other are polymeric. In the instance in which calcium phosphate is available on the surface and is in contact with either polymer or calcium phosphate on the neighboring microsphere, bonding will not take place. Indeed, to sinter calcium phosphate, the scaffold would need to be heated to temperatures that would remove the polymer completely through decomposition. As the polymeric content of the microsphere decreases, and thus the potential for calcium phosphate to be on the surface of the microsphere increases, the bonds between microspheres will decrease and the scaffold will lose mechanical strength. Therefore, it can be surmised that as the polymer ceramic content decreases, the mechanical properties of the scaffold will also decrease. This is supported by the data noted in Figure 8. As the polymer content of the microsphere increases, and thus surfaces available for bonding increases, the mechanical properties will also increase. From this, it could be surmised that a purely polymeric microsphere would have optimal mechanical properties. Borden et al.²⁵ showed that a purely polymeric microsphere scaffold had a compressive modulus greater than that seen here. However, the addition of the calcium phosphate

is theorized to have benefits to cell culture and *in vivo* healing and therefore cannot be adequately shown here. Therefore, it is important to realize that the existence of calcium phosphate is necessary, but must be optimized to create a scaffold with suitable mechanical properties but enough calcium phosphate to facilitate mineral formation and healing *in vitro* and *in vivo*. It is with this in mind that a poorly crystalline calcium phosphate was synthesized within the microspheres. Future studies will examine the ability of the calcium phosphate to dissolve in solution and deliver ions locally for new mineral formation. These findings in conjunction with those here will assist in the development of an optimized composite scaffold for bone-tissue engineering.

CONCLUSIONS

Polymer/ceramic composite scaffolds based on microsphere technology have been formed by a unique approach that involves synthesizing calcium phosphate within the forming microspheres. These are the first studies in the referred literature to extensively examine calcium phosphates synthesized within polymeric microspheres for bone-tissue engineering. Careful manipulation of processing parameters resulted in scaffolds containing a poorly crystalline calcium phosphate that resembles that seen in bone as confirmed by XRD, FTIR, and EDS analysis of the calcium phosphate. Variations in polymer/ceramic ratio of the microspheres and heating time of the composite scaffold have resulted in a three-dimensional porous scaffold with mechanical properties within the range of trabecular bone, supporting the application of this scaffold for bone repair.

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