Fabrication and mechanical properties of PLA/HA composites: A study of in vitro degradation

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Abstract

The adverse effects of stress shielding from the use of high-modulus metallic alloy bio-implant materials has led to increased research into developing polymer–ceramic composite materials that match the elastic modulus of human bone. Of particular interest are poly-L-lactic acid–hydroxyapatite (PLA/HA)-based composites which are fully resorbable in vivo. However, their bioresorbability has a deleterious effect on the mechanical properties of the implant. The purpose of this study is to investigate, from a micromechanistic perspective, the in vitro degradation behavior of such composites manufactured using a simple hot-pressing route for two different hydroxyapatite particles: a fine-grained (average particle size ∼5 μm) commercial powder or coarser whiskers (∼25–30 μm long, ∼5 μm in diameter). We observed that composites with ceramic contents ranging between 70 and 85 wt.% have mechanical properties that match reasonably those of human cortical bone. However, the properties deteriorate with immersion in Hanks' Balanced Salt Solution due to the degradation of the polymer phase. The degradation is more pronounced in samples with larger ceramic content due to the dissolution of the smaller amount of polymer between the ceramic particles.
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1. Introduction

The tremendous health and economical repercussion of biomaterials for orthopedic applications has been highlighted in many reports, with more than $50 billion being spent annually on reconstructive devices [1–4]. For example, according to the U.S. National Center for Health Statistics (NCHS), 152,000 total hip replacements and 299,000 knee replacements were performed in 2000 and 59,000 revisions of hip and knee replacements were performed the same year [5]. This number is likely to increase as younger people receive such implants and the population lives longer.

Despite the success of existing materials and technologies, implant materials still have serious shortcomings related to their physical and biochemical compatibility with the surrounding bone that hamper implant fixation and can cause damage to the surrounding bone, limiting implant life in many cases. The search for strong implant materials has led to the use of materials initially developed for other, more traditional engineering applications such as stainless steel, cobalt–chromium or titanium alloys and novel ceramics such as alumina or zirconia that are not only stronger but also stiffer than the bone they replace. However, living bone is responsive to its environment and implants that are stiffer than bone bear a greater proportion of the load, shielding the surrounding tissue from its normal stress levels [6] and promoting osteoporosis [7]. The result is that the surrounding tissue is resorbed and the implant becomes loose over time, often requiring expensive revisionary surgery to remove the implant and the surrounding necrotic bone tissue. Furthermore, though these materials are biocompatible, unlike natural bone, they cannot self-repair or adapt to changing physiological conditions [8] and cannot be resorbed over time. On the other end of the spectrum, lactic and glycolic acid polymers are now in widespread use in biodegradable supports for orthopedic applications, but their mechanical properties limit their use predominantly to a limited number of non-load-bearing applications [9,10].

Bone itself is an organic–inorganic composite and it is logical that the search for a new generation of implant materials should focus on hybrid materials that combine the strength and stiffness of an inorganic compound with the flexibility, toughness and resorbability of an organic phase. The objective of this work is to use hydroxyapatite (HA), a calcium

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phosphate that is closely related to the mineral component of bone, to reinforce poly-L-lactic acid (PLA), a polymer currently used in many orthopedic applications [9,10]. Degradation of pure PLA implants in the body is known to produce intermediate acidic products that often lead to adverse inflammatory responses [11]; addition of HA could also help to buffer such products [12]. The goal of our work is to develop a simple processing route that will allow us to fabricate materials with controlled microstructure such that the factors that control the final properties (proportion of the components, particle size and shape of the inorganic phase etc.) can be explored systematically, particularly in the context of in vitro degradation in a simulated body fluid.

2. Experimental procedures

2.1. Materials

In order to prepare the poly-L-lactic acid–hydroxyapatite composites, 1–5 g of PLA (Purasorb PL, Purac America, Lincolnshire, IL; Inherent viscosity=2.39 dl/g) were dissolved in 20 ml of methylene chloride at room temperature, while continuously mixing using a magnetic stirrer. Complete dissolution of the PLA in the solvent took approximately 50 min. Commercially available, HA powders (Alfa Aesar, Ward Hill, MA) where calcined at 1100 °C for 1 h and sieved to a particle size <35 μm. Hydroxyapatite whiskers were prepared by the molten salt method described by Tas [13]. Both forms of HA were then added to the solution, and the slurry was mixed in a shaker with alumina balls for about 15 min to create a homogeneous slurry that was subsequently cast into a cylindrical teflon mold (25 mm in diameter and 19 mm in length) and dried for 48 h at room temperature to remove all traces of the solvent used. The dried pellets were then hot pressed in air using a uniaxial press (Carver Inc., Wabash, IN) with a stainless steel die (25 mm in diameter). The applied pressure was 45 MPa and pressing temperature–time combinations of 180 °C for 15 min and 220 °C for 5 min were used for the calcined HA, while 220 °C for 5 min was employed for the
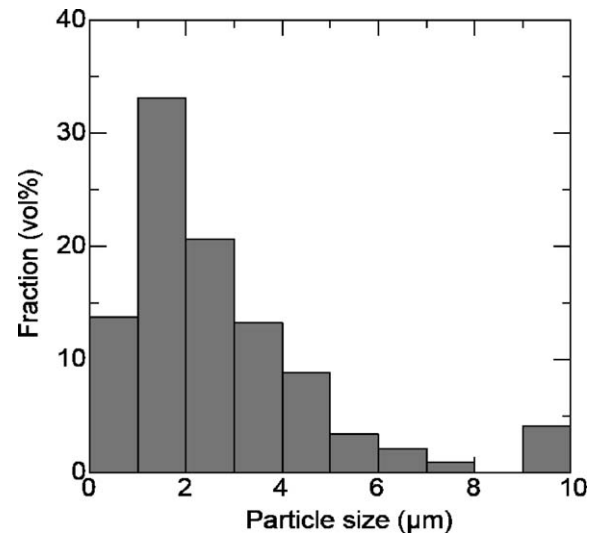

Fig. 2. Particle size distribution of the calcined HA powders.

HA whiskers. The final hydroxyapatite content ranged between 50% and 90% by weight of the composite for the calcined HA, while compositions of 70% and 80% by weight were investigated for the HA whiskers.

2.2. Microstructural characterization

The microstructure and phase distribution/chemical composition of the powders and the pressed compacts (as received and after in vitro degradation—see Section 2.3) were analyzed by X-ray diffraction (XRD), optical microscopy and scanning electron microscopy (SEM) with associated energy-dispersive spectroscopy (SEM-EDS). The diffraction was performed using a Siemens D500 diffractometer (Siemens AG, Munich, Germany), the optical microscopy using an Axiotech microscope (Carl Zeiss AG, Oberkochen, Germany), and the SEM work using an environmental scanning electron microscope S-4300SE/N (Hitachi, USA). The theoretical density of the compacts was determined using the law of mixtures and compared to measurements performed by the Archimedes' method.
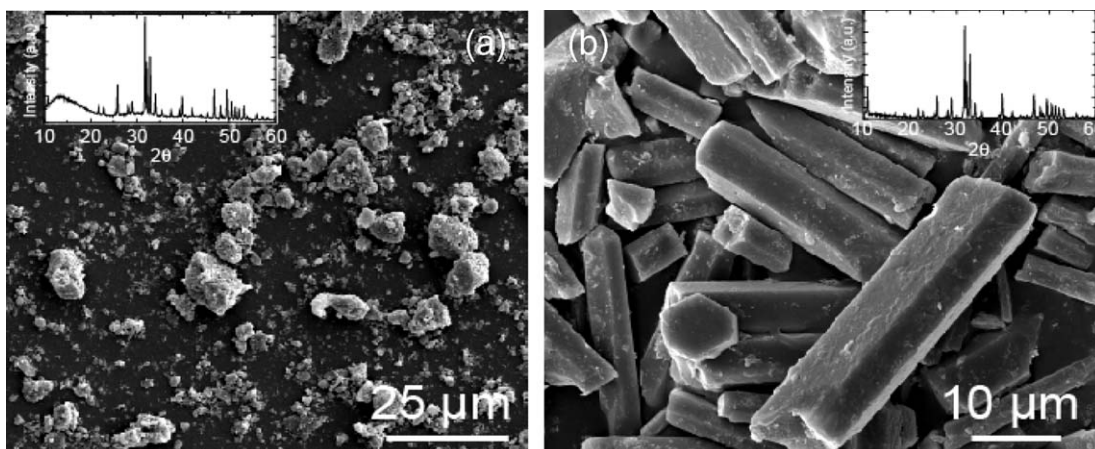

Fig. 1. Scanning electron micrographs and associated XRD patterns of: (a) calcined HA powder and (b) HA whiskers prepared using the molten salt method. In both cases, the diffraction patterns correspond to pure hydroxyapatite.

2.3. Mechanical characterization

The mechanical properties of the composites were evaluated both in the as-received condition and following degradation in vitro. Three mechanical parameters—Young's modulus, bending strength and fracture toughness—were measured, the latter two being evaluated for composites considered promising based on the modulus values obtained. The Young's modulus was measured using an instrumented, depth-sensing (dynamic) microindentation technique. Specifically, a Vickers indentor was attached to the actuator of an ELF® 3200 series voice-coil mechanical testing machine (EnduraTEC Inc., Minnetonka, MN). For elastic modulus determination, the loading curve involved engaging the indenter with the surface of the polished (up to 1200 grit) specimens, loading at a constant displacement rate of 0.01 mm/s and then unloading at the same rate. The unloading load-displacement data thus

obtained were used to determine the elastic modulus based on classical indentation theory introduced by Boussing (reviewed in Ref. [14]), simplified by Sneddon [15], and generalized by Pharr et al. [16], the so-called Oliver–Pharr method. Three such measurements were made on each composite in four conditions—as received, after storage in a simulated environment, and Hanks' Balanced Salt Solution (HBSS) for 1, 10 and 20 days.

To evaluate the strength of the composites produced, three-point bending strength tests were conducted in the four conditions mentioned above. Specifically, unnotched, nominally flaw-free, beams $\sim 1 \times 2.5 \times 12$ mm were sectioned. The tests involved loading the beams to failure at a rate of ~ 0.01 mm/s under three-point bending (center-to-end loading span=5.15 mm) using the ELF® 3200 series voice-coil mechanical testing machine. The load-displacement data thus obtained were analyzed to assess the (ultimate) bending strength.
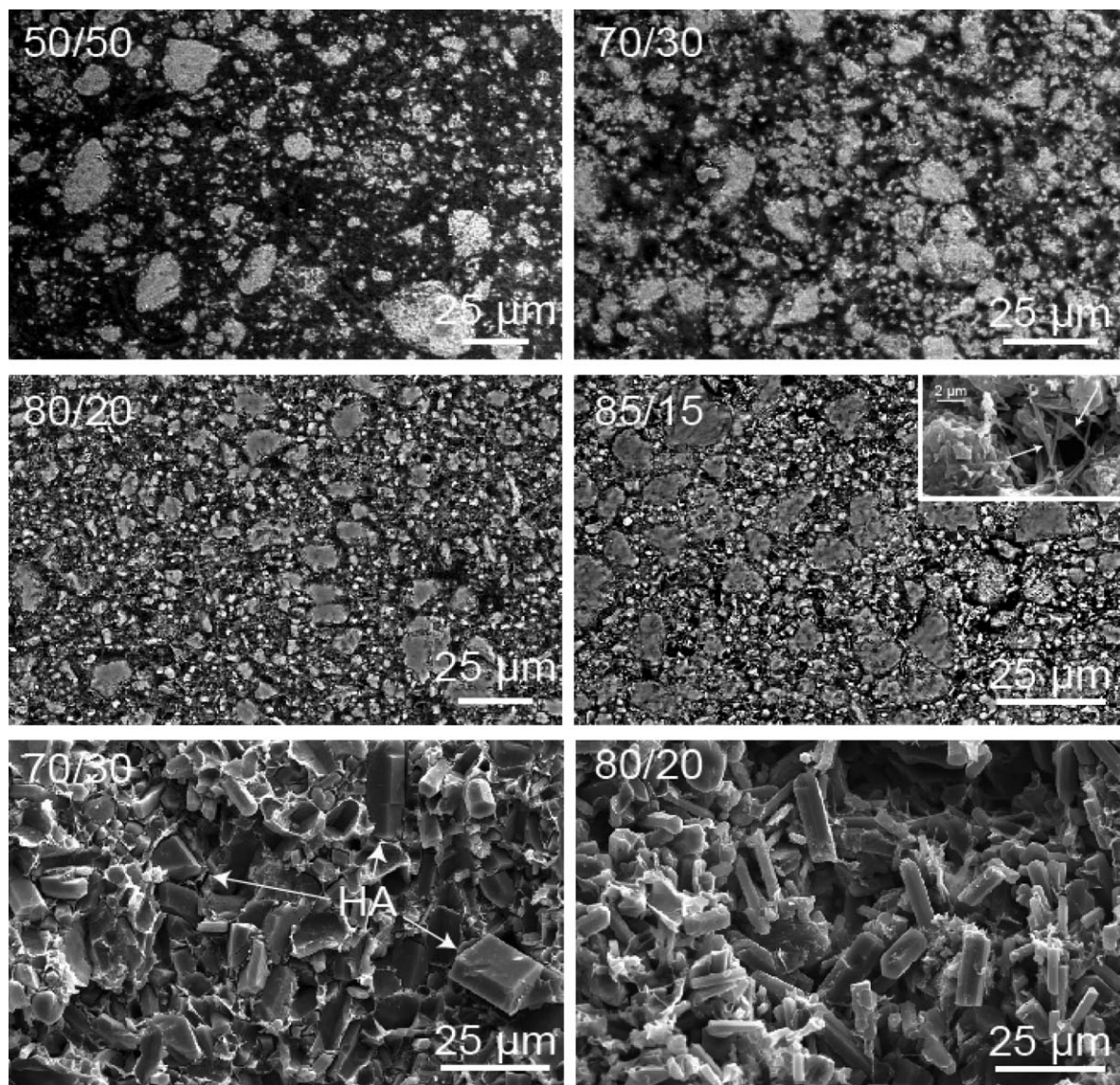

Fig. 3. Scanning electron micrographs showing the typical microstructures obtained for the composites. The composition (HA/PLA wt.%) is shown in each picture. The top four pictures correspond to composites fabricated using calcined HA powders, whereas the two bottom ones correspond to materials containing HA whiskers. The insert in the 85/15 micrograph shows the presence of polymer filaments (white arrows) bridging the ceramic particles in samples with large inorganic content.

Fracture toughness testing was performed in general accordance with the ASTM Standard E-399 for Plane-Strain Fracture Toughness [17] under the four conditions mentioned previously. Beams $\sim 1 \times 2.5 \times 12$ mm were sectioned from each composite and notched to a depth of ~ 1.25 mm using a regular slow-speed saw and then sharpened with a razor blade. The samples were loaded to failure at a rate of 0.01 mm/s under three-point bending (center-to-end loading span = 5.15 mm) using the ELF® 3200 series voice-coil mechanical testing machine. The load-displacement data thus obtained were analyzed to assess the fracture resistance which was reported in terms of the strain energy release rate, G.

3. Results and discussion

3.1. Microstructural characterization

Figs. 1 and 2 show the particle sizes and shapes for the starting hydroxyapatite powders and the whiskers. The calcined powders consisted of roughly spherical, sintered aggregates with a bimodal size distribution (Figs. 1a and 2), while the whiskers were $\sim 25-30$ μm long and ~ 5 μm in diameter (Fig. 1b). X-ray diffraction analysis performed on the powders and the whiskers (see insets in Fig. 1) showed only peaks corresponding to hydroxyapatite, confirming their chemical composition.

The microstructure of the calcined HA composites consisted mainly of a distribution of HA particles in the polymer matrix, with some instances of agglomeration of the HA being observed (Fig. 3). The high ceramic burden composites showed a less uniform polymer matrix as evidenced by the thin polymer filaments bridging the HA particles that were observable at higher magnifications (Fig. 3). The microstructure of the whisker HA composites, on the other hand, was more uniform in appearance for the compositions investigated, with the whiskers being distributed in a matrix of the PLA (Fig. 3). Inclusions from the potassium salts used during the manufacture of the whiskers were also observed surrounding the whiskers.

The relative densities of samples containing calcined HA pressed at 180 °C for 15 min and at 220 °C for 5 min as obtained by Archimedes' method are compared in Fig. 4. The final density of the composites did not appear to depend strongly on the pressing conditions. However, there is a marked decrease ($\sim 10-15\%$) in the relative density of the samples with HA content greater than 80 wt.%. It is plausible that due to the lack of sufficient polymer to create a more uniform matrix (see Fig. 3), composites with such high ceramic content do not densify as much as those with lower HA burden. Indeed, the final materials have poor mechanical properties (see below). The whisker HA-containing composites had densities of 92% and 86% for the 70 and 80 wt.% HA composites, comparable to the values that were obtained for the calcined HA-based composites.

3.2. Mechanical characterization

3.2.1. Elastic modulus in as-received condition

The elastic modulus of the calcined HA composites strongly depended on the HA content (Fig. 5). It was observed to peak
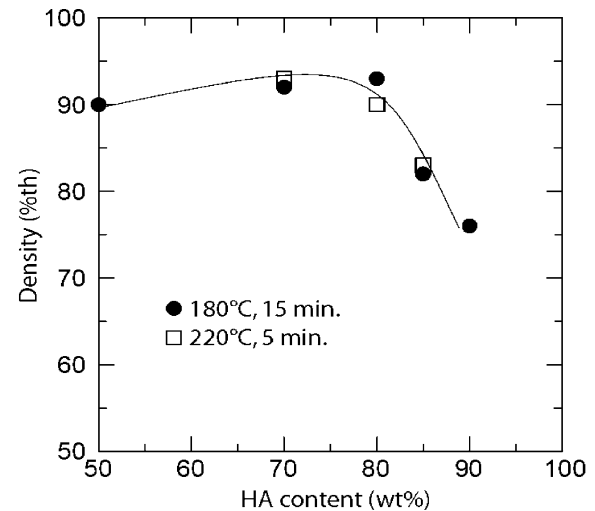

Fig. 4. Density evolution of the hot pressed materials is shown for the calcined HA composites processed. Note the drop in density for the calcined HA composites above ~ 80 wt.% HA.

at around 80 wt.% of HA at a value slightly above 10 GPa, usually considered the lower limit for human cortical bone [18]. It should be noted that the moduli obtained for the composites with 90 and 95 wt.% of HA are not "true" elastic moduli as there was evidence that the material behavior was not elastic during the recovery phase upon unloading. For the whisker HA composites with 70 and 80 wt.% of the ceramic phase, similar values of the elastic moduli were obtained as compared to the corresponding calcined HA composites (Fig. 5). As mentioned previously, one of the more important conditions for an ideal bone substitute, in particular those that are to be used for load-bearing applications, is to have mechanical properties that match those of the bone tissue that they are intended to substitute [7]. Matching the elastic modulus, as we have been able to achieve here, is very important since one of the main factors that limits the life of current metallic implants is the mismatch of elastic modulus with the surrounding bone and the resulting stress shielding that ends, causing tissue necrosis leading to osteoporosis [7] and implant failure [6].

We have thus shown that it is possible to fabricate PLA/HA materials using a simple hot-pressing procedure with elastic modulus properties close to that of bone. However, the ceramic contents required for our composites (over 70 wt.%) are somewhat higher than that seen typically in human bone (up to $\sim 60-70$ wt.% [19]). Indeed, they are much higher than those that could be expected from a simple rule of mixtures; since the Young's moduli of pure HA and PLA are $\sim 80-175$ GPa [20] and $\sim 4-5$ GPa [7], respectively, one could expect that HA burdens of the order of $10-40$ wt.% would be sufficient to achieve the required modulus (typically, between 10 and 20 MPa for human cortical bone [18]). Our observations are consistent with those by others for similar polymer–ceramic composites (e.g., [21]). In addition to the fact that the composites did have some inherent porosity (even the densest compositions had about $7-8\%$ porosity—see Fig. 4), one additional possible source of this discrepancy could lie in the fact that HA used was not fully
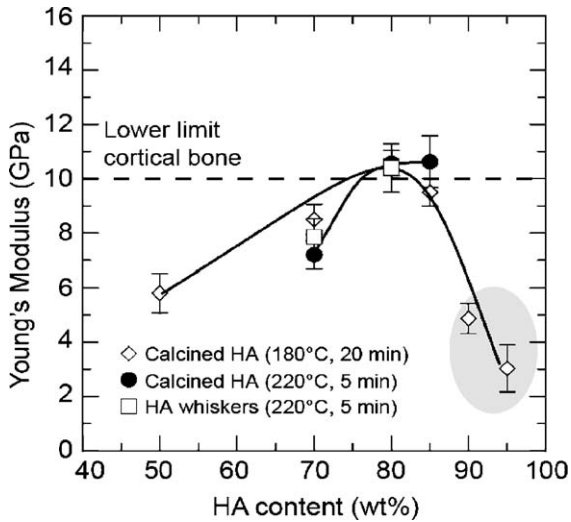
Fig. 5. Evolution of the Young's modulus with HA content; the points in the gray area correspond to materials with large ceramic content that are porous and show extensive damage during the indentation process.

defect-free and, hence, had a lower modulus than used in the above calculations; efforts are currently underway to improve our starting materials.

3.2.2. Elastic modulus after in vitro degradation

The calcined HA composites processed at 180 °C for 15 min typically did not survive in vitro degradation in HBSS with extensive cracking being observed after as little as 1 day in HBSS. On the other hand, the calcined HA composites processed at 220 °C for 5 min did not show as much degradation, presumably as the shorter processing time span was less damaging to the polymer phase. Only composites with 70–85 wt.% HA were evaluated in this case as they were considered promising based on the high initial elastic modulus values ($\sim$7–11 GPa) obtained. For these composites, the elastic modulus did decrease gradually for all cases ($\sim$8–17% reduction over a period of 20 days in HBSS) with such a reduction being more pronounced for the samples with the higher ceramic content (Fig. 6). Similar trends were observed

for the composites with whisker HA, albeit with more gradual ($\sim$3–5%) rates of decrease (Fig. 6).

3.2.3. Bending strength and fracture resistance

The bending strengths and strain energy release rates, G, were measured for the composites with 70–85 wt.% calcined HA and the whisker HA compositions. While the calcined HA composites processed at 180 °C for 15 min generally showed as-received strength and strain energy release rates comparable to that of human cortical bone (composition-dependent bending strengths of $\sim$60–130 MPa and toughness values of $\sim$100–275 J/m^2, as compared to lower bound values of 35 MPa and 100 J/m^2 for human cortical bone [18]), they typically did not survive in vitro degradation in HBSS with extensive cracking being observed. The calcined HA composites processed at 220 °C for 5 min showed similar properties in the as-received state, but were much less degraded upon exposure to HBSS; data for the in vitro degradation of the strength and fracture resistance are included in Fig. 7. As in the case of the Young's modulus, these properties did degrade with immersion in HBSS, with such degradation being more pronounced for samples with larger hydroxyapatite contents. Indeed, strengths and toughness values of the composites with 80 and 85 wt.% HA deteriorated to values lower than that of bone over the period studied. The composite with 70 wt.% HA did not show as much degradation, and the strength and toughness appears to asymptote to values of $\sim$70 MPa and $\sim$135 J/m^2 over the period of 20 days in HBSS. For the whisker HA composites, similar properties and in vitro degradation trends were observed, albeit with a slightly slower rate of degradation being observed for both the compositions examined (Fig. 7).

3.3. Fractographic examination

To obtain a micromechanistic understanding of the processes involved, the microstructures and fracture surfaces of the composites were examined before and after in vitro degradation using optical and scanning electron microscopy.
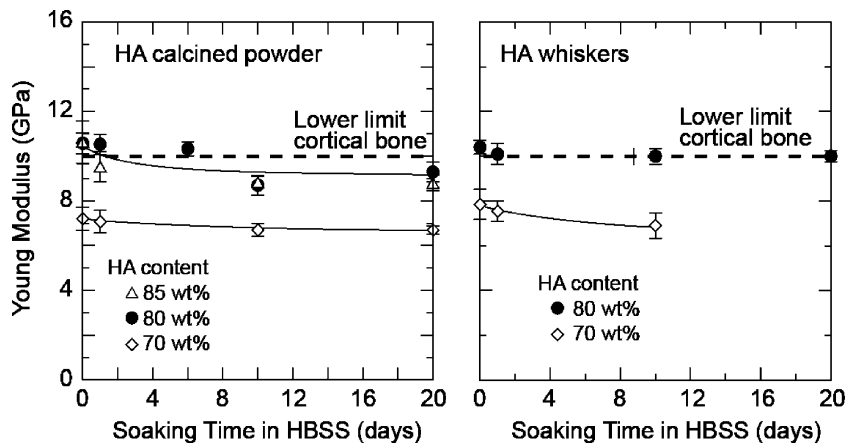

Fig. 6. Evolution of the Young's modulus after soaking in HBSS for different times. A decrease (more pronounced for samples with larger ceramic loads) can be clearly observed.
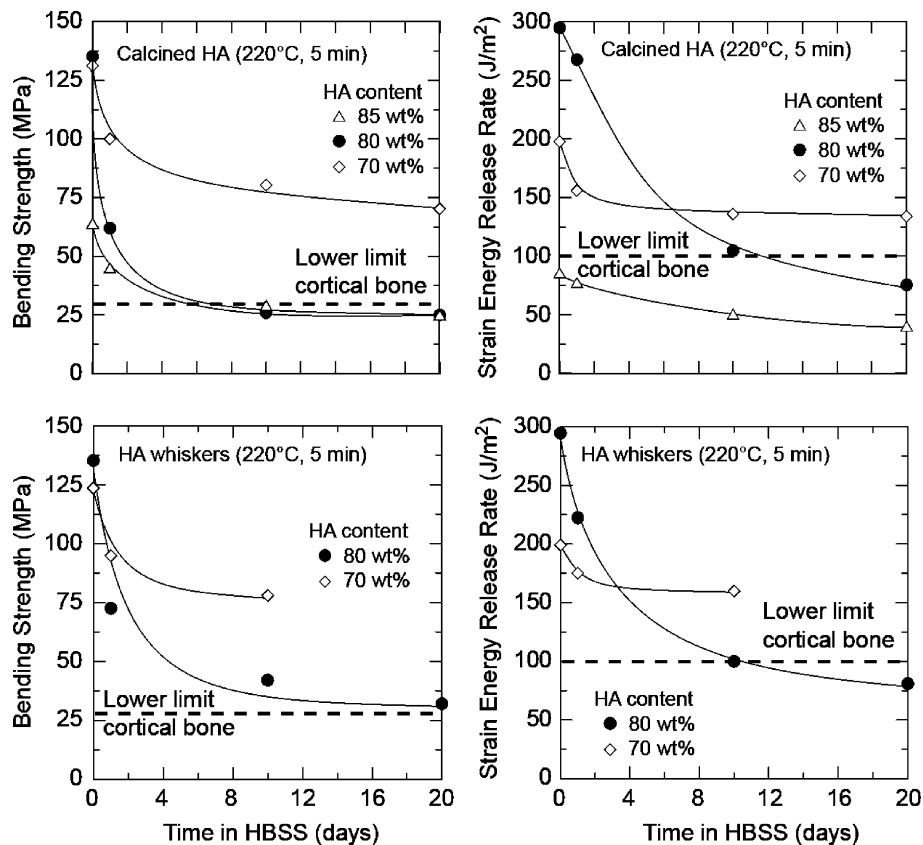
Fig. 7. Strength and fracture resistance properties of composite materials pressed at 220 °C for 5 min. The initial properties match those of cortical bone but were observed to degrade with time in HBSS.

The decrease in mechanical properties reported in the previous section was accompanied by a definite degradation of the underlying microstructure. For the calcined HA composites, there was definitive evidence of some dissolution of the polymer matrix between the ceramic particles. This degradation was particularly observable in the case of the higher HA wt.% containing composites where, upon dissolution of the PLA, the filamentous structure that bonds the ceramic particles together was often eliminated (Fig. 8). The polymer matrix binds together the ceramic phase and provides the material its strength and toughness, but it is also easily accessible to the in vitro environment and consequently, susceptible to environmental degradation. As a result, the

strength and toughness properties were observed to degrade rapidly in the aqueous environment. On the other hand, the ceramic phase is the major contributor to the elastic modulus and would be expected to be relatively unaffected by the in vitro degradation, as was the case here (Fig. 6). For the whisker HA composites, examination of the fracture surfaces revealed some evidence of dissolution of the polymer in the aqueous environment, supporting the degradation of the mechanical properties. Future effort will also be directed towards understating such microstructural changes.

One of the interests of using PLA-based materials is that poly-L-lactic is a bioresorbable polymer, and these materials can be slowly replaced by bone. Unfortunately, the resorption
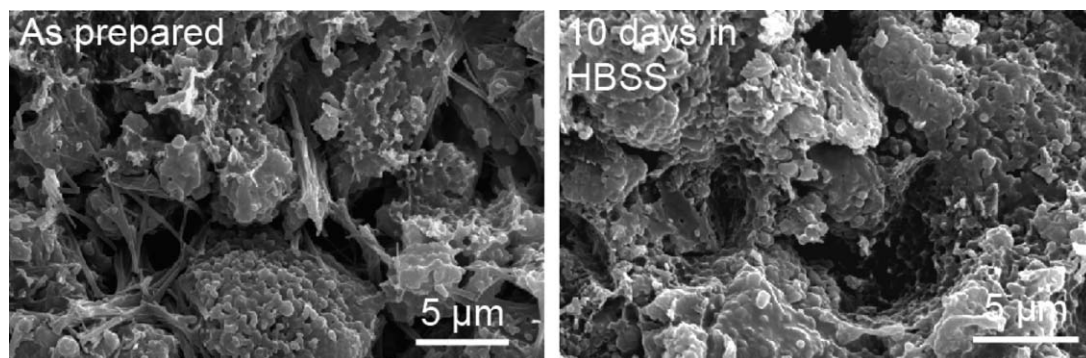

Fig. 8. Microstructure of the 85/15 calcined-HA composite (hot pressed at 220° for 5 min, under a pressure of 45 MPa) before and after immersion in HBSS. After soaking in HBSS, the polymer bridges have degraded or disappeared, causing a significant degradation of the mechanical properties.

of PLA can also degrade the mechanical response of the implant. It is hence important to design microstructures where the degradation rate matches the rate at which bone is formed at the implant site so that the material remains stable during its useful life. While we were able to achieve two very different microstructures for the composites using a simple processing route, both materials showed some degradation in the mechanical properties in a simulated environment. It is hence necessary to look at alternative microstructures that provide for slower in vitro degradation. In an attempt to do this, we are currently investigating another processing route where HA particles are encapsulated into PLA microspheres that will serve as the building blocks for the fabrication of dense composites. The objective is to design a denser polymer phase that will slow degradation, with a distribution of HA particles to provide the modulus levels required.

4. Conclusions

A simple processing route based on the casting and hot pressing of polymer-containing slurries has been designed for the fabrication of PLA/HA composites. Materials with HA contents close to 80 wt.% and mechanical properties that match those of bone can be prepared. However, the microstructure of these materials formed by the ceramic particles distributed in a polymer matrix makes them quite susceptible to environmental degradation. An alternative fabrication route that uses dense microscopic PLA/HA spheres as the building block for the materials is being investigated.

Acknowledgement

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