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Effect of hydrolysis on mechanical properties of tricalcium phosphate/poly-L-lactide composites

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Abstract In order to investigate hydrolysis behavior and associated variation in mechanical properties of bioresorbable plastic composites, β-tricalcium phosphate (β-TCP)/poly(L-lactide) (PLLA), the immersion tests into phosphate buffered solution (PBS) with different pH were conducted. After the immersion tests, tensile, bending and compressive tests were conducted on the specimen. The significant decrease in the mechanical properties of the specimens with 5.0 wt% β-TCP contents were not observed in the $\mathrm{pH} = 7.4$ immersion tests, whereas significant decrease were observed for the specimen with 9.5 and 14.0 wt% contents after 24 weeks. In the $\mathrm{pH} = 6.4$ immersion tests, the degradation was accelerated. From the fracture surface observation, debondings between β-TCP and PLLA grew into the void shape in the ductile fracture surface before immersion tests, whereas the voids were observed in the brittle fracture surface after immersion tests. This is due to the bioresorption of β-TCP particles and/or β-TCP/PLLA interface. In order to discuss the degradation of mechanical properties, tensile modulus degradation was analyzed based on the micromechanics supposing the damaged particles as voids. Degradation tendency predicted was in good agreement with experimental results. These results suggested that the degradation in modulus was attributed to lower load capacity of β-TCP particles and lower load transfer to β-TCP particles due to the hydrolysis of the β-TCP particles and the interface between β-TCP and PLLA.

1 Introduction

Bioresorbable plastic fixation devises, such as poly-L-lactide (PLLA) have already been in clinical use to reduce patient burdens. Commercially-available bioresorbable fixation devises made of PLLA, however, have some problems: limitation of application to low-loaded location and a long period of time necessary for complete resorption (over a year). Concerning the biodegradation properties, many in vitro and in vivo tests were conducted [1–4]. Migliaresi et al. [1] conducted immersion tests on PLLA into Ringer's solution. They reported that PLLA after 327 days immersion still have the strength of 120 MPa and modulus of 3.4 GPa. Pistoner et al. [2] conducted in vivo tests on PLLA. It is clarified that the degradation periods were necessary 72 weeks for crystallized specimens and 90 weeks for amorphous specimens.

In order to improve the biocompatibility of PLLA fixation devises, PLLA composites with bioactive ceramics have been investigated. In the previous study, PLLA composites with hydroxyapatite (HA) and β-tricalcium phosphate (β-TCP) have been investigated to clarify effects of bioactive ceramics fillers on the mechanical and bioresorption properties of the composites [5–13]. Verheyen et al. [5] fabricate HA/PLLA composites by ring scission polymerization of the mixture of HA and L-lactide monomer. They found that improvement in the strength and modulus of the composite with 30 wt% HA comparing with pure PLLA. Solution tests were also conducted to examine the physico-chemical behavior of the HA/PLLA composites [6]. Shikinami and Okuno [7] developed the composites with uncalcined HA (u-HA). The composites with 50 wt% u-HA have higher mechanical properties than pure PLLA, the bending strength of 267.5 MPa, the bending modulus of 12.3 GPa, the tensile strength of

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103.0 MPa, the tensile modulus of 2.4 GPa, the compressive strength of 115.3 MPa and the compressive moduli of 6.5 GPa. This is attributed to complex orientation of PLLA during forging process. Shikinami and Okuno [8] also conducted in vitro tests on the u-HA/PLLA composites. They reported that the bending strength of u-HA/PLLA after 24 weeks immersion was more than 200 MPa and the strength became 150 MPa after 52 weeks immersion. Similar results were obtained in in vivo tests with Japanese white rabbits [10]. The u-HA/PLLA composites also have higher biocompatibility, such as no inflammatory reaction for 5–7 years implantation [9, 10].

The composites with β-TCP filler also have been studied. Kikuchi et al. prepared the composites using β-TCP and copoly-L-lactide (CPLA) [11]. The bending modulus of 8.2 GPa was achieved in case of the filler contents of 80 wt% β-TCP. Ignatius et al. fabricated the composite using PDLLA (copolymer of PLLA and poly-D-Lactide) with 10 and 30 wt% β-TCP and conducted in vitro degradation tests up to 78 weeks [12]. The composites with 30 wt% β-TCP lost half of their strength after 16 weeks. On the other hand, the composites with 10 wt% β-TCP showed very similar degradation characteristics compared to the monolithic PDLLA. Thus, many experimental characterizations have been conducted on the bioresorption behavior of the bioactive ceramics/PLLA composites. Qualitative discussions have also been conducted on the experimental results, whereas quantitative evaluations based on the precise analytical modeling are limited. Precise evaluations of the bioresorbable behavior and variation in the associated mechanical properties are very important to design the bioresorbable devices considering bioresorption process.

The purpose of the present study is experimental and analytical clarification of the variation in the mechanical properties of β-TCP/PLLA composites under simulated body environment. The effect of pH of the simulated body environment was investigated to discuss the possibility of the accelerated tests. In the present study, bioresorbable behavior was not discussed based on the chemical analytical modeling. Instead, the variation in mechanical properties of β-TCP/PLLA composites was discussed analytically based on the micromechanics [13] considering the bioresorption of β-TCP particles in order to develop the basis of bioresorbable material design.

2 Experimental methods

2.1 Materials

Poly-L-lactide, Lacty®#5000 (Shimadzu Co. Ltd., Japan) and β-tricalcium phosphate, β-TCP (Taihei Chemical Industrial Co. Ltd., Japan) were used as the matrix and the filler materials, respectively. The diameter of β-TCP particle is less than 2.0 μm with spherical shape. Specific surface area is 50–60 m^2/g. The PLLA pellets and β-TCP powder were mixed in a polyethylene bottle in dry condition. The target β-TCP/PLLA mix proportions were 5/95, 10/90, and 15/85 in weight. Rectangular specimens (100 mm × 10 mm × 4 mm) of the β-TCP/PLLA composites were then fabricated from the mixtures by injection molding under the conditions listed in Table 1. The actual weight fractions, W_{fa} of β-TCP particles contained in the composites were given by the following equation:

$$W_{fa} = \frac{W_f - W_r}{W_m + W_f - W_r} \times 100, \tag{1}$$

where W_f is the initial weight of β-TCP particles, W_r is the residual β-TCP weight in the polyethylene bottle used for mixing of β-TCP powder and the PLLA pellets, and W_m is weight of PLLA pellets. In the present study, the specimens were molded with two batches so that the actual weight fraction of the specimen was slightly different. For the immersion tests in the simulated body environment as mentioned below, the specimens with β-TCP contents shown in Table 2 were used.

2.2 Immersion tests

In the present study, 1/15 mol/l phosphate buffered solution (PBS) was selected as simulated body environment. The pHs of PBS were 7.4 and 6.4. A schematic view of immersion tests is shown in Fig. 1. Five hundred milliliters of PBS were used for 15 samples, which results in 6.6 ml per g samples. PBS was poured into a tray and the specimens were placed on the aluminum plates in order to immerse the whole of the specimen. The trays were located in an incubator. Temperature in the incubator was kept at 37°C. The immersion periods were 8, 16, 20 and 24 weeks.

Table 1 Molding conditions

Mold clamping force (kN)	69
Injection pressure (MPa)	114
Fusion temperature (°C)	200
Mold temperature (°C)	50
Injection time (s)	40
Cooling time (s)	30

Table 2 Weight fraction of β-TCP for each experiment

	Weight fraction of β-TCP/(%)		
pH:7.4	5.0	9.5	14.0
pH:6.4	5.2	9.1	13.6

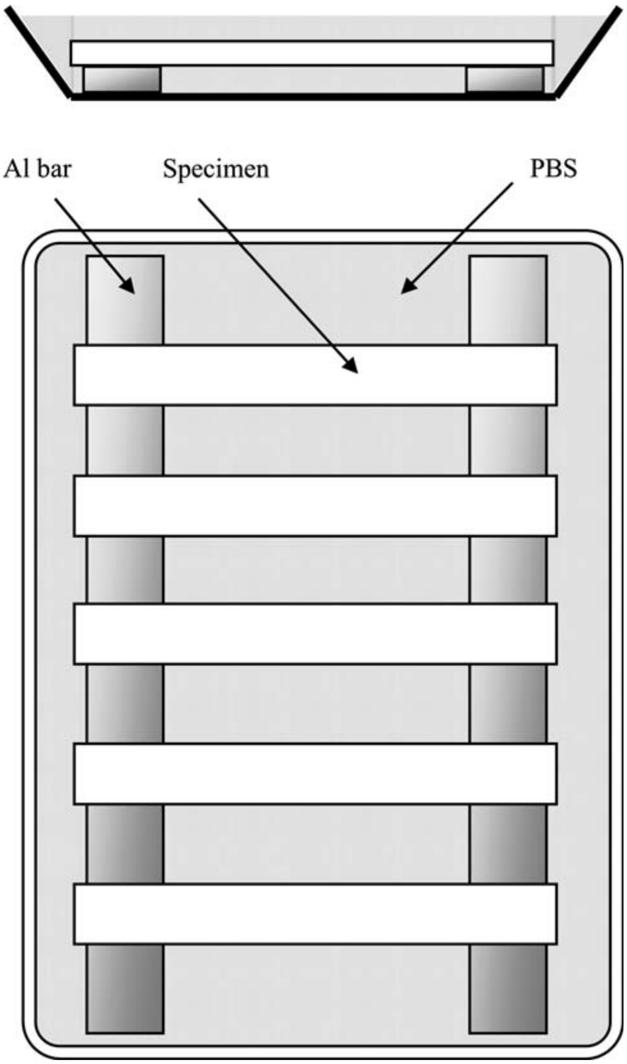


Fig. 1 Schematic view of immersion test

After immersion tests PBS solution at the surface of the specimen was wiped up and tests were conducted immediately.

2.3 Tensile, bending and compressive tests

For the tensile tests, the aluminum tabs were glued on the end of the injection molded specimens to prevent the stress concentration at the grips. The length of the tabs was 20 mm, which result in the reduced length of 60 mm. Strain gauges were also glued on the both surface of the specimen to monitor strain during tests. The tensile tests were conducted with a universal testing machine (AG-10 kNE, Shimadzu Co. Ltd., Japan) at a cross-head speed of 1 mm/min under room temperature.

We conducted the 4-points bending tests to evaluate the bending properties of the β-TCP/PLLA composites. For the bending tests, the specimens as injection molded were used. A strain gauge was glued on the compressive surface of the specimen. The outer and inner span length of the 4-point bending tests were 66 and 22 mm (JIS K7171), respectively. The tests were conducted with a lower capacity universal testing machine (LSC-05/30, JT Toshi Co., Japan) at a cross-head speed of 1 mm/min under room temperature.

For the compressive tests, the injection molded specimens were cut into the geometry of 10 × 10 × 4 mm using a micro cutting machine (MC-201, Maruto Co., Japan). Strain gauges are glued on the both surface of the specimen to monitor the strain during tests. The compressive tests were conducted with a universal testing machine (AG-10 kNE, Shimadzu Co. Ltd., Japan) instrumented with a support jig at a cross-head speed of 1 mm/min under room temperature. In the compressive tests, since failure cannot be observed clearly, 0.2% proof strength, which determined using the 0.2% strain offset method, were used instead to compressive strength to evaluate the load bearing capacity of the composites.

Five specimens were tested for each tests condition. The fracture surfaces of the specimens were examined using a scanning electron microscope (S2500CX, Hitachi Co., Japan).

3 Experimental results

Figure 2 shows the tensile tests results of the specimen after immersion tests. In the pH = 7.4 immersion tests, no effect of immersion was observed up to 20 weeks in the specimen with 5.0 wt% β-TCP contents, whereas the significant decreases in tensile strength and modulus after 20 weeks immersion occurred in the specimen with 9.5 and 14.0 wt% β-TCP contents. In particular, tensile moduli of the specimens with 9.5 and 14.0 wt% β-TCP contents after 20 weeks immersion became lower than that of the specimens with 5.0 wt% β-TCP contents. The decrease in the tensile modulus had already occurred in the specimen with 14.0 wt% β-TCP contents after 16 weeks. In the pH = 6.4 immersion tests after 20 weeks, the decreases in tensile strength and modulus were observed for all specimens. Tensile moduli became almost the same value in all specimens after 16 weeks and became lower in the specimen with 9.1 and 13.6 wt% β-TCP contents after 20 weeks. Figure 3 shows the tensile stress-strain curves of β-TCP/PLLA composites after pH = 7.4 immersion tests. As shown in Fig. 3, the decrease in tensile modulus with immersion period was observed for the specimen with 9.5 and 14.0 wt% β-TCP contents in the pH = 7.4 immersion tests. For the specimen with 14.0 wt% β-TCP contents, elongation also decreased with immersion period. On the other hand, elongation in all specimens decreased with immersion period in the pH = 6.4 immersion test.

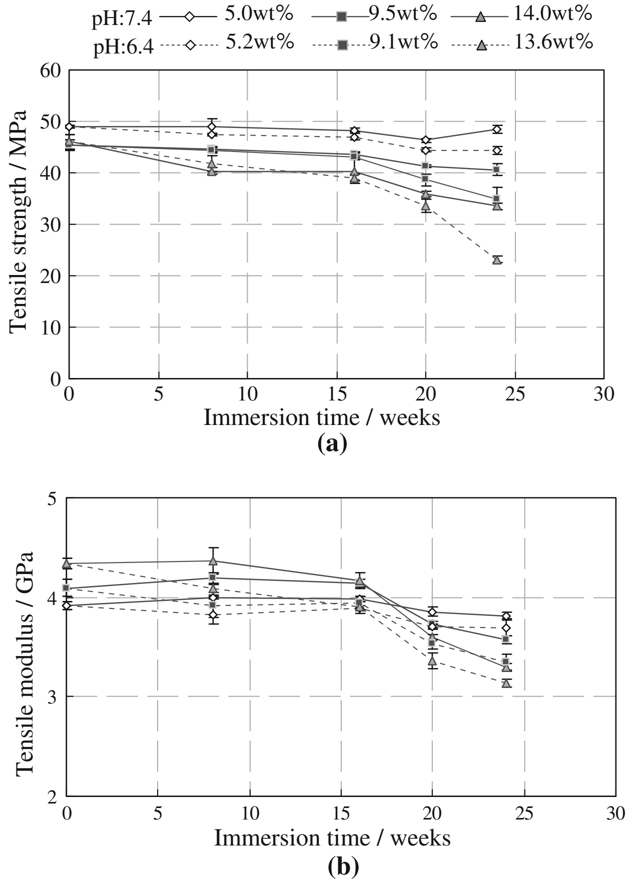


Fig. 2 The results of tensile tests of β-TCP/PLLA composites with immersion time in PBS. (**a**) Strength and (**b**) modulus

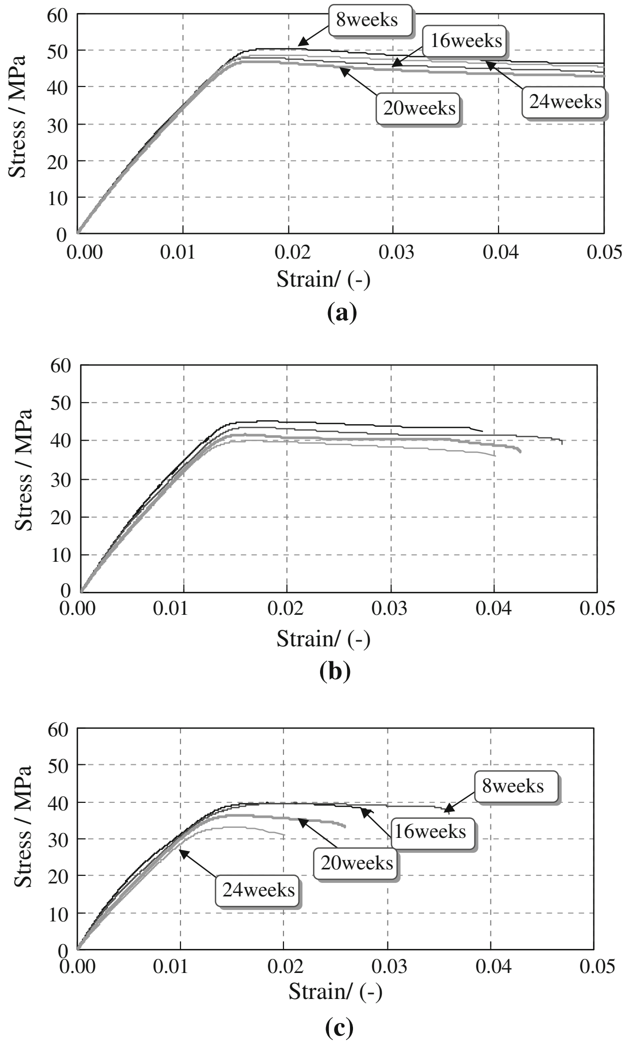


Fig. 3 Tensile stress-strain curves of β-TCP/PLLA composites with different β-TCP contents after immersion in PBS (pH:7.4). (**a**) 5.0 wt%, (**b**) 9.5 wt%, and (**c**) 14.0 wt%

Figure 4 shows the bending tests results after the immersion tests. Similar to the tensile tests results, although little effect of immersion was observed for the specimen with 5.0 wt% β-TCP contents up to 20 weeks in the pH = 7.4 immersion tests, significant decrease in bending strength and modulus were observed for the specimen with 9.5 and 14.0 wt% β-TCP contents. The bending tests results after pH = 6.4 immersion tests had the same tendency to the tensile tests. The strength reduction rate with immersion was larger in the bending tests comparing to the tensile tests. Figure 5 shows the bending stress-strain curves of β-TCP/PLLA composites after pH = 7.4 immersion tests. As shown in Fig. 5, the ultimate strain in all specimens decreased after 24 weeks pH = 7.4 immersion tests. On the other hand, the ultimate strain decreased with immersion period in pH = 6.4 immersion tests.

Figure 6 shows the compressive tests results after the immersion tests. Compressive moduli decreased in the specimens with larger β-TCP contents in both immersion tests, similar to the tensile and bending tests results. On the other hand, 0.2% proof strength did not decrease up to 20 weeks. Decreases in compressive 0.2% proof strength were observed for the specimen with 14.0 wt% β-TCP contents in the pH = 7.4 immersion tests and for the specimens with 9.1 and 13.6 wt% β-TCP contents in the pH = 6.4 immersion tests. These results were confirmed in the compressive stress-strain curves as shown in Fig. 7. From these results, the larger strength reduction in the bending tests is attributed to the decrease in the compressive 0.2% proof strength, since the bending loading consists of tensile and compressive loading in the sectional area of a specimen.

4 Discussion

4.1 Fracture process

In the previous study, it was confirmed that the fracture surface of β-TCP/PLLA composite consists of two types of

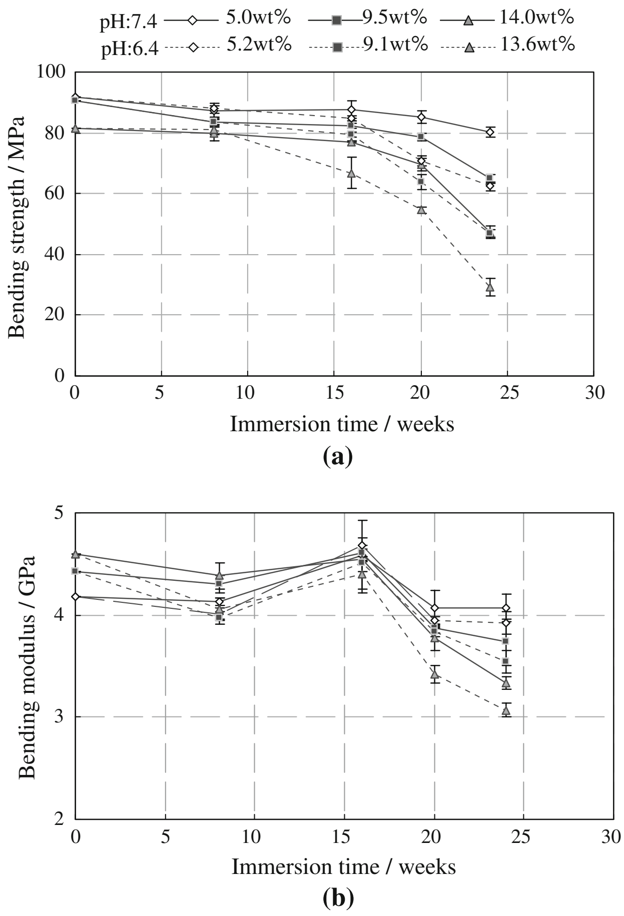


Fig. 4 The results of bending tests of β-TCP/PLLA composites with immersion time in PBS. (**a**) Strength and (**b**) modulus

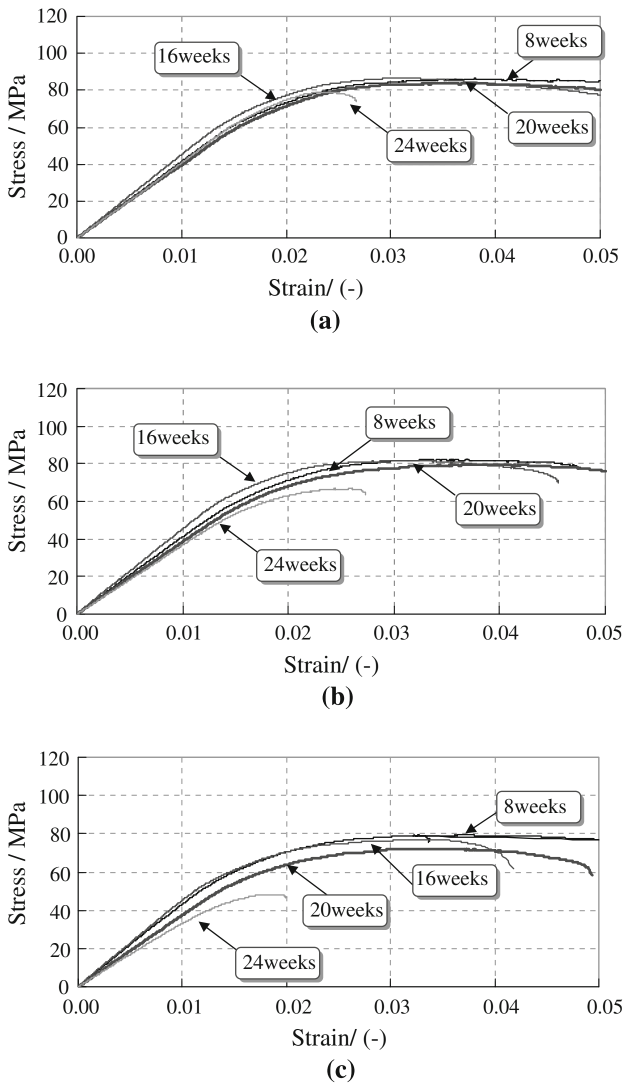


Fig. 5 Bending stress-strain curves of β-TCP/PLLA composites with different β-TCP contents after immersion in PBS (pH:7.4). (**a**) 5.0 wt%, (**b**) 9.5 wt%, and (**c**) 14.0 wt%

fracture surfaces, such as ductile and brittle regions [13]. This difference in the fracture surfaces depends on the crack growth rate. That is, the debondings between β-TCP/PLLA grew into the void-shape in the ductile region, whereas the matrix failed in the catastrophic manner before the energy release rate associated with void formation reaches the critical values in the brittle region so that β-TCP/PLLA interfaces keep intact. Figure 8 shows the brittle regions in the tensile fracture surface of composite with 14.0% β-TCP contents in pH = 7.4 immersion tests and with 13.6 wt % β-TCP contents in pH = 6.4 immersion tests observed by scanning electron microscopy. From the fracture surfaces in pH = 7.4 immersion tests, as shown in Fig. 8a, it is observed that the β-TCP/PLLA interfaces kept intact after 8 and 20 weeks. After 24 weeks, the interfacial debondings were observed. From the fracture surfaces in pH = 6.4 immersion tests, the interfacial debondings after 20 weeks and the voids around the β-TCP particles after 24 weeks were observed. In the brittle regions of the bending fracture surface, the debondings were also observed in the pH = 7.4 immersion tests after 24 weeks and in the pH = 6.4 immersion tests after 20 weeks. In the pH = 6.4 immersion tests after 24 weeks, however, it is very difficult to distinguish the ductile and brittle regions and the voids were observed all over the fracture surface.

From the previous study, voids were hardly observed in the brittle region of the fracture surface of the β-TCP/PLLA specimen without immersion. This is because the energy release rate in matrix surpass the fracture toughness and matrix crack progresses rapidly without void formation. In addition, pure PLLA, same type of the present study, less degraded up to 24 weeks in the previous study [8]. From the consequence, for the sake of the debondings and/or the voids formation in the brittle region, the critical energy release rates associated with β-TCP/PLLA debonding and void formation are necessary to decrease with

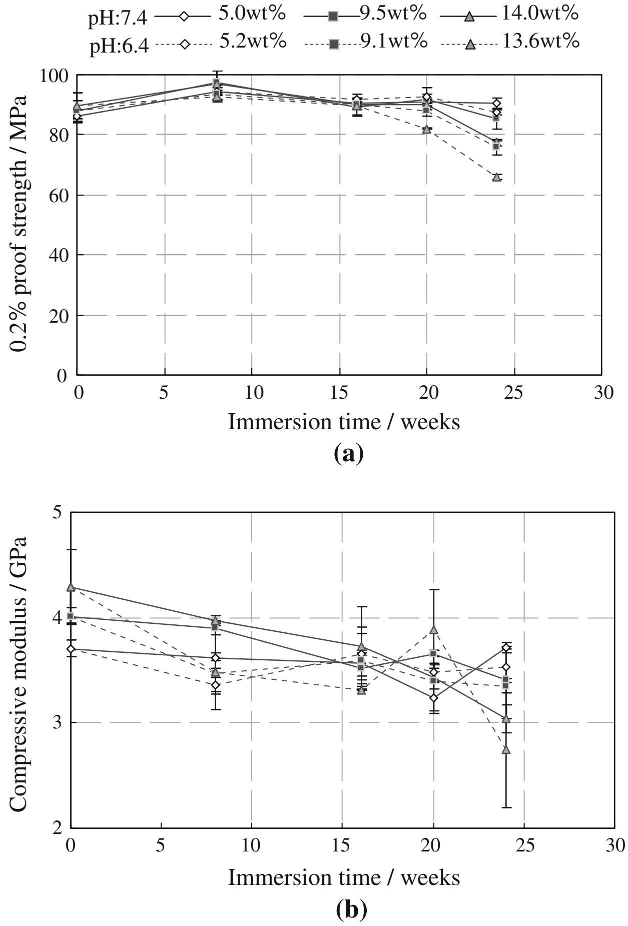


Fig. 6 The results of compressive tests of β-TCP/PLLA composites with immersion time in PBS. (**a**) Strength and (**b**) modulus

the immersion periods. That is, β-TCP/PLLA interface and/or β-TCP particles in the β-TCP/PLLA composite fabricated in the present study were hydrolyzed and the nominal critical energy release rate associated with debonding and void formation decreased with immersion period.

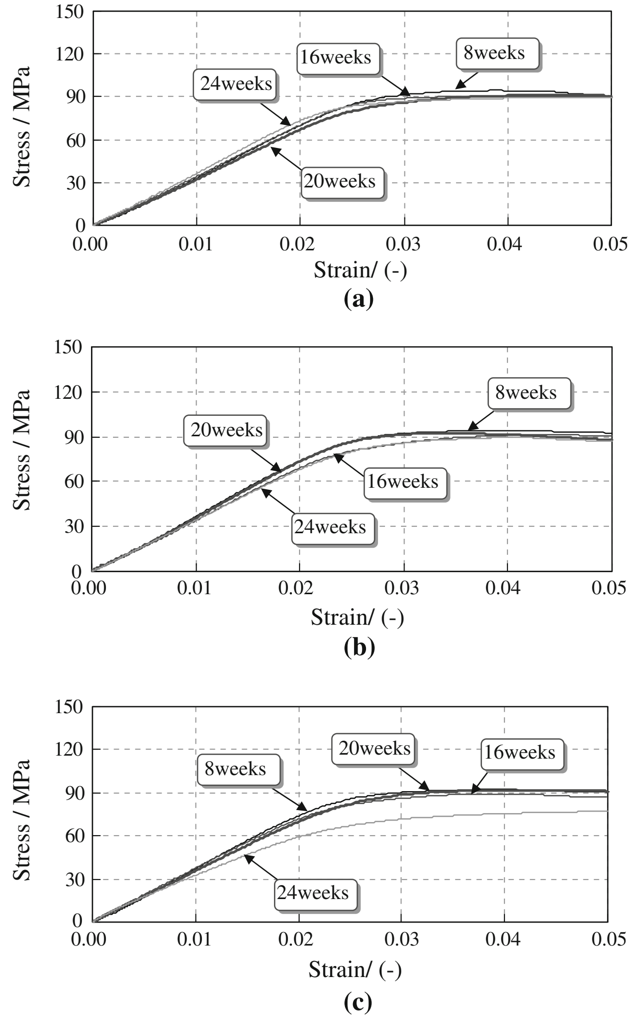


Fig. 7 Compressive stress-strain curves of β-TCP/PLLA composites with different β-TCP contents after immersion in PBS (pH:7.4). (**a**) 5.0 wt%, (**b**) 9.5 wt%, and (**c**) 14.0 wt%

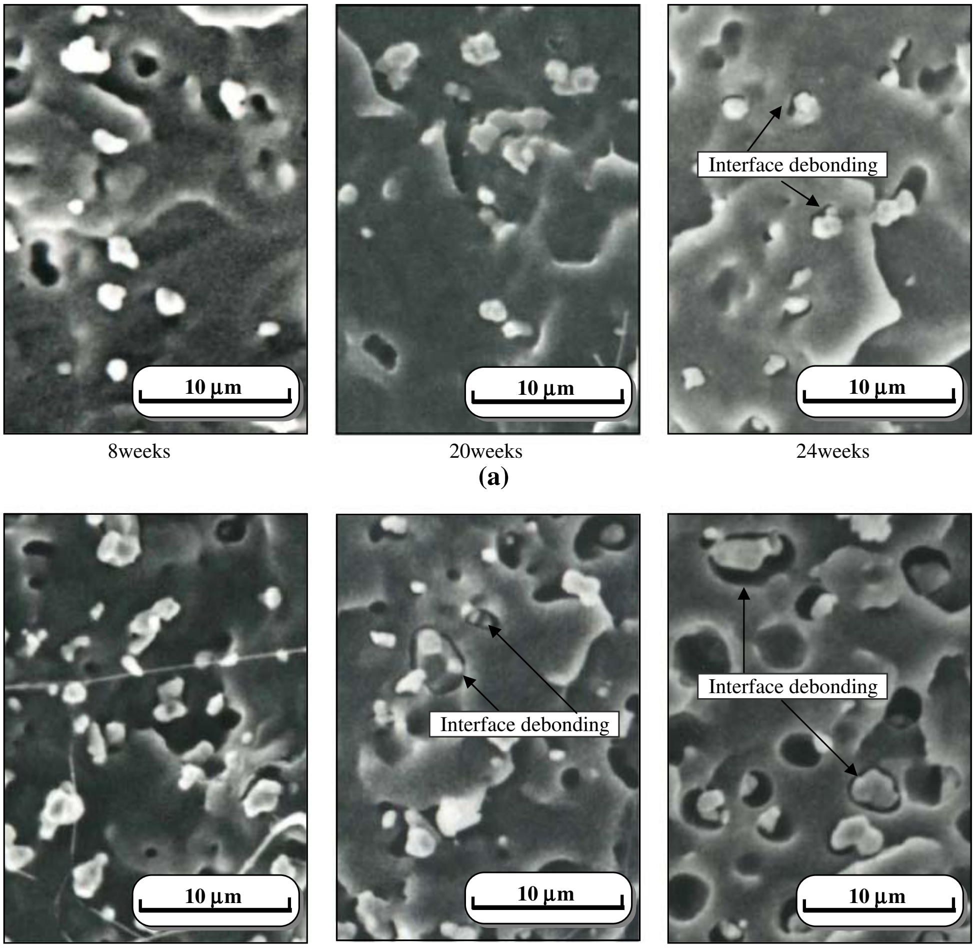
4.2 Analytical prediction of modulus reduction

Modulus and strength of β-TCP/PLLA composite fabricated in the present study decreased after 24 weeks immersion tests. Degradation rates of modulus and strength were larger in composite with larger β-TCP contents at each pH condition and were accelerated in pH = 6.4 immersion tests. These were due to the decrease in critical energy release rate associated with β-TCP/PLLA debondings and decrease in stress transfer to the β-TCP particles caused by the hydrolysis of β-TCP/PLLA interface and β-TCP particles, especially in acidic solution. In the present study, the decrease in the tensile modulus attributed to the decrease in load bearing capacity of β-TCP particles are analyzed with micromechanics for 3-phase particle reinforced composites [13]. The effective rigidity, $\mathbf{C}$, is given by

$$\mathbf{C} = \mathbf{C_0}\Big[\mathbf{I} + c_1\Big[(\mathbf{1}-c_1)\mathbf{S_1} + \mathbf{A} - c_2\mathbf{S_2}[\mathbf{S_2}+\mathbf{B}]^{-1}[\mathbf{S_1}+\mathbf{A}]\Big]^{-1} + c_2\Big[(\mathbf{1}-c_2)\mathbf{S_2} + \mathbf{B} - c_1\mathbf{S_1}[\mathbf{S_1}+\mathbf{A}]^{-1}[\mathbf{S_2}+\mathbf{B}]\Big]^{-1} \tag{2}$$

where $\mathbf{C}_o$ is the rigidity of matrix, $\mathbf{I}$ is the 4th-rank unit tensor, $\mathbf{A} = [\mathbf{C}_1 - \mathbf{C}_0]^{-1}\mathbf{C}_0$, $\mathbf{B} = [\mathbf{C}_2 - \mathbf{C}_0]^{-1}\mathbf{C}_0$ and c_i and $\mathbf{S}_i$ (= $\mathbf{C}_i^{-1}$) are the volume fraction and the compliance of ith phase, respectively. In the analysis, β-TCP particles without load bearing capacity were treated as voids and the properties of PLLA kept constant after 24 weeks immersion tests. Tensile modulus and Poisson's ratio of β-TCP and PLLA used in the analyses are 95 GPa and 0.22, and 3.7 GPa and 0.44, respectively. The volume fraction of β-

Fig. 8 Tensile fracture surfaces of β-TCP/PLLA composites with highest β-TCP contents after different immersion period in PBS (pH:7.4). (**a**) pH 7.4 and (**b**) pH 6.4



8weeks 20weeks 24weeks

(a)

8weeks 20weeks 24weeks

(b)

TCP for each specimens are converted to 2.1, 4.2, and 6.3 vol% for pH = 7.4 immersion tests and 2.2, 3.9 and 6.1 vol% for pH = 6.4 immersion tests. Figure 9 shows the analytical results of tensile modulus of composites as a function of the ratio of damaged β-TCP particles (voids). The degradation rate of modulus with damaged particles is larger in composite with larger β-TCP contents. Comparing the analytical results with experimental result in the immersion tests after 24 weeks, the tendency of the modulus with β-TCP contents is coincide with the analytical results of the composites with 100% void contents. These results indicated that the decrease in modulus is attributed to decrease in load bearing capacity of β-TCP particles caused by the hydrolysis of β-TCP particles. Figure 10 shows the modulus with ratio of damaged particles as a function of β-TCP contents. For example, tensile modulus decreased to 30% with 100% damaged particles in the composites with about 30 vol% fillers contents [7]. The results in the present study suggest the possibility to fabricate the composites which degrade after a period in the living body, with β-TCP and PLLA.

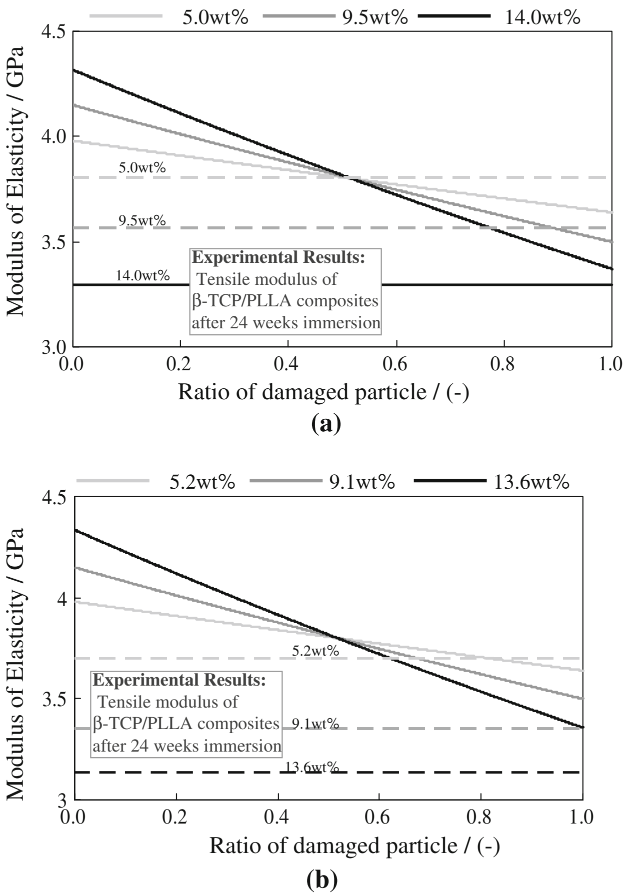
5 Conclusion

In the present study, tensile, bending and compressive tests were conducted on the β-TCP/PLLA composites after immersion tests into pH = 7.4 and 6.4 phosphate buffered solution. The conclusions are as follows.

1. In the pH = 7.4 immersion tests, mechanical properties of the composites with 5.0 wt% β-TCP contents did not decrease significantly, whereas mechanical properties of the composites with 9.5 and 14.0 wt% after 24 weeks decreased significantly. After 24 weeks, the modulus of the composites with 9.5 and 14.0 wt% became smaller than that of the composite with 5.0 wt%. Fracture of the specimens under tensile and bending loading became brittle with increasing immersion period.
2. In the pH = 6.4 immersion tests, the same tendency with the pH = 7.4 immersion tests were observed. Comparing to the pH = 7.4 immersion tests, degradation rate of the mechanical properties was larger in the

pH = 6.4 immersion tests. This is due to the acceleration of bioresorption of *β*-TCP particles and *β*-TCP/PLLA interfaces.

3. From the fracture surface observation and analytical results based on the micromechanics, modulus reduction of the composites was caused by the decrease in the load bearing capacity of the *β*-TCP particles associated with the hydrolysis of the *β*-TCP/PLLA interface and the *β*-TCP particles.



(a)

(b)

Fig. 9 Analytical results of modulus of Elasticity with damaged particle contents. (**a**) pH 7.4 and (**b**) pH 6.4

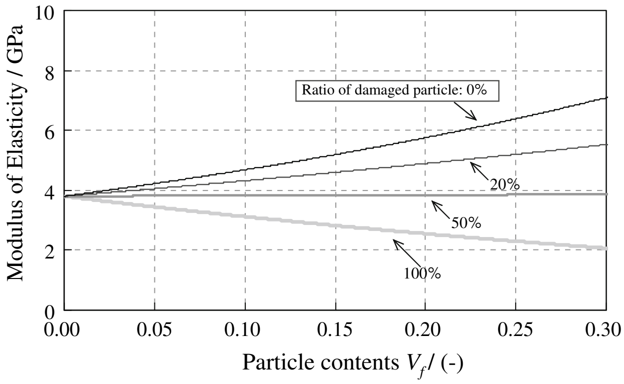


Fig. 10 Analytical results of modulus of Elasticity with particle volume fractions

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