Preparation and mechanical properties of calcium phosphate/copoly-L-lactide composites

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New artificial bone materials were prepared using calcium phosphates, hydroxyapatite and β-tricalicum phosphate, and copoly-L-lactide, CPLA. Calcium phosphate powder and CPLA were mixed at 453 K for 10 min with various mixing ratios. Scanning electron microscope observations indicated that the composites of β-tricalicum phosphate and CPLA were homogeneously dispersed and highly adhesive. Young's modulus of the composites was the same as bone, and bending strength was over half that of bone. The improvement of Young's modulus compared to the original two materials was due to a composite effect. The composites are expected to be usable as artificial bone materials.

1. Introduction

Hydroxyapatite (HAp) and β-tricalcium phosphate (β-TCP) are well known as bioactive ceramics and are used in medical and dental fields in the form of blocks and particles [1]. These ceramics, implanted into bone, are gradually substituted with bone by an osteoconduction process; however, these ceramics are brittle and not suitable for medical use as structural materials. On the other hand, polylactide-based polymers are known as biodegradable materials and are used as bone plates and pins [2, 3]; however, these polymers are soft and have no osteoconductivity.

A composite of these two materials was prepared by Gen *et al.* [4]. They dipped a porous hydroxyapatite block into a melted poly-L-lactic acid, an oligomer of -L-lactic acid, and reported that the composite obtained had osteoconductivity and biocompatibility. Chen *et al.* [6] implanted the composite described by Gen into a rat parietal bone for 12 weeks; however, no osteoconduction was observed. Tencer *et al.* [5] showed a similar result to Gen *et al.* for a hydroxyapatite porous body prepared using a coral. Further, Jansen *et al.* [7] prepared a sheet of poly(ethyleneglycol terephthalate)/poly(butylene terephthalate) coated with hydroxyapatite powder and found good properties for guided tissue regeneration membrane. However, these kinds of composite were not easily cast; therefore, their applications were limited.

In the present study, the authors prepared composites of calcium phosphate and CPLA [8] (copolymer of L-lactide acid with fatty polyesters) in order to find a new, easily-cast artificial bone which is not only osteoconductive but also suitable for a structural material.

2. Experimental procedure

Calcium phosphates, HAp and β-TCP, were prepared by a wet method using $Ca(OH)_2$ suspension and H_3PO_4 solutions. The pH of the mixtures was controlled at 9 for HAp and 7 for β-TCP. The precipitates obtained were dried at 333 K for 24 h and calcined at 1073 K for 3 h.

CPLA was provided by Dainippon Ink Chemicals, Inc. The mechanical properties of CPLA were controlled by regulating the amounts and species of added fatty polyesters. Hard (CPLA-H) and soft (CPLA-S) types of CPLA had a mean molecular weight of about 150 000.

Calcium phosphates and CPLA were mixed by the following three methods:

(1) Chloroform-solvent method: A calcium phosphate powder was added into a chloroform solution of CPLA and dried at 293 K in vacuum.

(2) Heating mortar method: CPLA was put in a mortar and heated at 453 K for 30 min in a drying oven. Then, the mortar was taken out and heated on a mantle heater at the same temperature. Calcium phosphate, also heated at 453 K, was added to the mortar and mixed with melted CPLA for 15 min. After mixing, the composite was removed from the mortar and cooled in air to room temperature.

(3) Thermal kneading method: CPLA was fed into a plastomill(Toyo Seiki) at 453 K for 1 min, and the

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calcium phosphate powder heated at 453 K was gradually added into CPLA over 3–4 min. Then, the mixture was kneaded for 10 min at 50 rpm for CPLA-S and at 20 rpm for CPLA-H.

These three types of composites were formed into plates by thermal pressing at 453 K and kept at 373 K for 30 min to crystallize CPLA. The molecular weight change of CPLA was measured after the thermal treatment with gel permeation chromatography. Plates were cut into $3 \times 5 \times 20$ mm blocks with a diamond saw in ethanol.

Three-point bending strength was measured with a universal testing machine at a crosshead speed of 500 μm/min with a span of 15 mm. Fracture surfaces were observed by a scanning electron microscope.

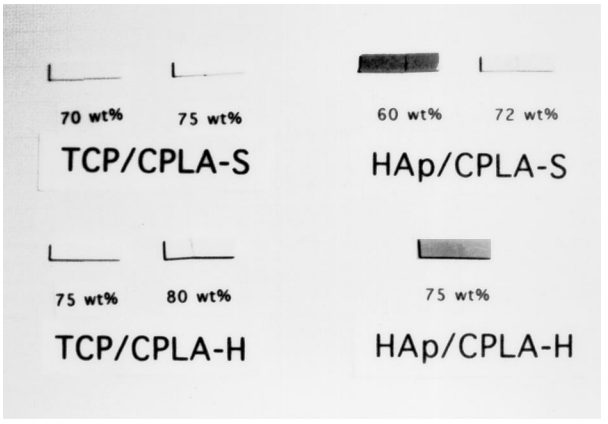


Figure 1 Composites of calcium phosphates and CPLA.

3. Results

3.1. Comparison of the three preparation methods

The composites prepared by the chloroform-solvent method were heterogeneous and brittle. This method was therefore not practical; in addition, chloroform is toxic for a mammalian.

The composites prepared by the heating mortar method were brown (Fig. 1, upper right). This colouring was due to a high-temperature hydrolysis reaction of CPLA as the molecular weight of CPLA decreased to 10 000 or less (Table I). The hydrolysis reaction was most notable in HAp/CPLA composites in which a hydroxyl group of HAp acted as a basic catalyst for the hydrolysis reaction of CPLA.

In contrast, the TCP/CPLA composites prepared by the thermal kneading method were homogeneously dispersed without colouring or obvious degradation (Fig. 1, left). The hydrolysis reaction was extensively reduced for the thermal kneading method in comparison to the heating mortar method; in particular, the decomposition of CPLA was very slight in the TCP/CPLA composite. Thus, the thermal kneading method was adopted for the preparation of the present composite.

Fig. 2 indicates X-ray powder diffraction patterns of calcium phosphates before and after mixing with CPLA. No effect of thermal treatment with CPLA on crystal structures of calcium phosphates, HAp and β-TCP, was detected by X-ray powder diffractometry.

TABLE I Molecular weight of CPLA after mixing

Material	Mixing ratio (wt/wt %)	M_w	M_w/M_n
TCP/CPLA-H	75/25	111000	1.83
TCP/CPLA-S	75/25	100000	1.73
HAp/CPLA-H	75/25	60300	2.16
HAp/CPLA-S*	72/28	44300	2.41

* Heating mortar method.
M_w: weight-average molecular weight, M_n: number-average molecular weight.

3.2. Mechanical properties of composites

Table II gives the mechanical properties of the composites prepared by the thermal kneading method. The mechanical strength of the HAp/CPLA composites was low, however, TCP/CPLA composites had good mechanical properties; the maximum bending strength was 54 MPa which was nearly equal to that of CPLA and half the value for cortical bone, and Young's modulus was 8.2 GPa, which is the same as cortical bone. In this system, Young's modulus for TCP/CPLA composites was especially enhanced in comparison to the original CPLA.

Fig. 3 shows the mechanical properties of the composites as a function of mixing ratio of calcium

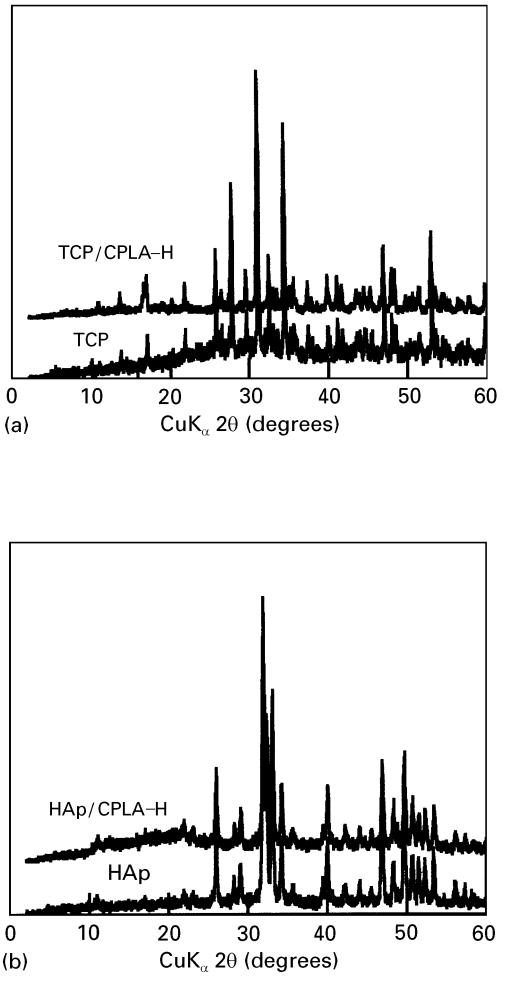


Figure 2 X-ray powder diffraction patterns of calcium phosphates before and after thermal kneading treatment: (a) β-TCP; (b) HAp.

TABLE II Mechanical properties of composites

Materials	Mixing ratio (wt/wt %)	BS(SD) (MPa)	YM(SD) (GPa)
TCP/CPLA-H	60/40	42(2.2)	2.1(0.33)
	75/25	51(6.3)	4.2(1.1)
	80/20	46(5.5)	8.2(3.1)
TCP/CPLA-S	70/30	51(2.0)	6.1(0.34)
	75/25	54(3.5)	4.0(1.2)
HAp/CPLA-H	75/25	35(3.7)	5.6(1.0)
HAp/CPLA-S	60/40*	22(1.3)	2.3(0.12)
	72/28*	15(1.1)	2.3(0.27)
CPLA-S	–	51(6.1)	2.0(0.34)
Bone	–	120–235 [9, 10]	1.5–24 [11, 12]
Sintered HAp [13]		84–113	87–94
Sintered β-TCP[13]		118–133	87–95

* Heating mortar method.
BS: bending strength, SD: standard deviation, YM: Young's modulus.

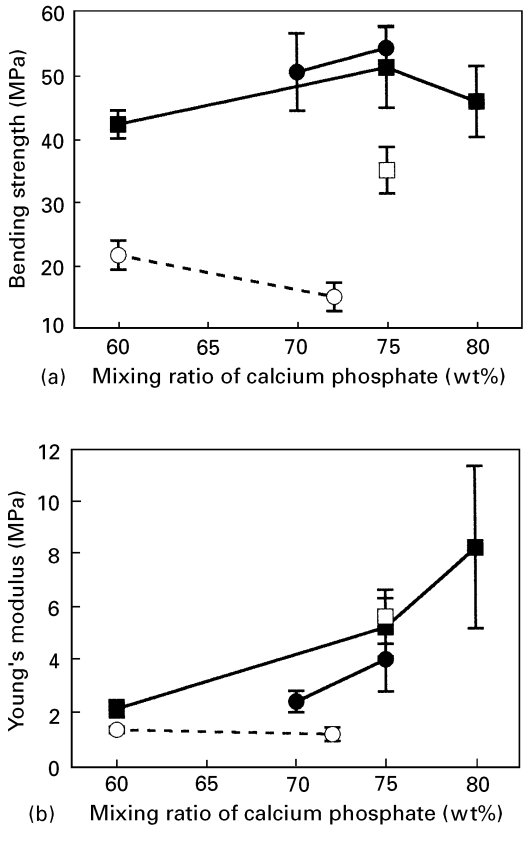


Figure 3 Mechanical properties of composites as a function of mixing ratio of calcium phosphate: (a) three-point bending strength; (b) Young's modulus: –●– TCP/CPLA-S; –■– TCP/CPLA-H; –○– HAp/CPLA-S; –□– HAp/CPLA-H.

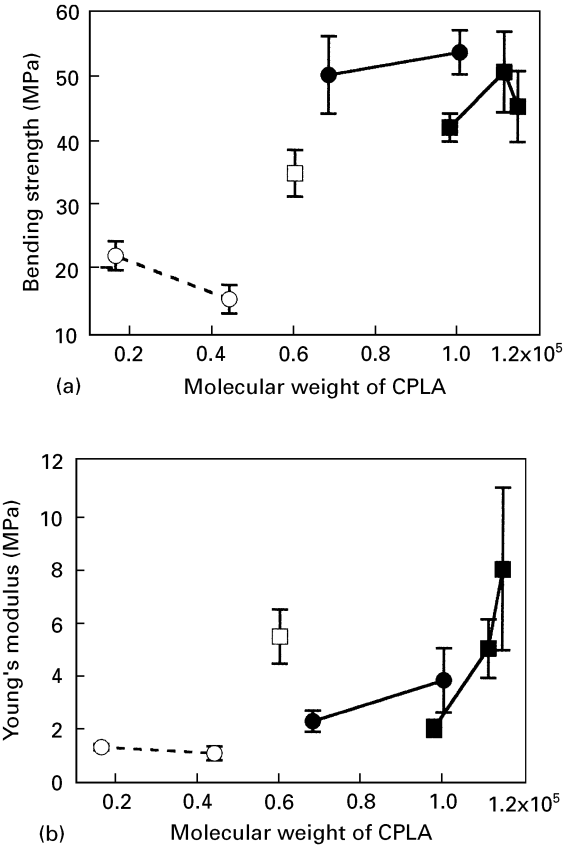
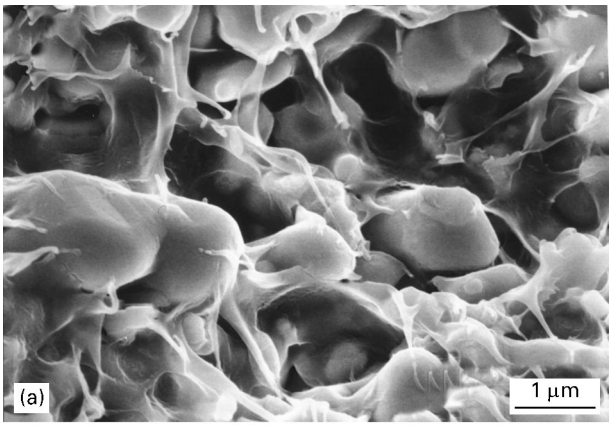


Figure 4 Mechanical properties of composites as a function of molecular weight of CPLA: (a) three-point bending strength; (b) Young's modulus: –●– TCP/CPLA-S; –■– TCP/CPLA-H; –○– HAp/CPLA-S; –□– HAp/CPLA-H.

phosphates. Young's modulus clearly had a positive correlation with the mixing ratio of composites. In this figure, some bending strength data were well scattered.

Fig. 4 shows the same mechanical data as a function of molecular weight of CPLA. The three-point bending strength of the composite lay on a smooth curve, which dramatically decreased below a molecular weight of 75 000. In this plot, some Young's modulus data were well scattered. Thus, Young's modulus depended on the mixing ratio of calcium phosphate in the composite: in other words, it was decided by the composite effect of Young's modulus of both calcium phosphate and polymer. On the other hand, the bending strength depended on the molecular weight of polymer in the composite, that is, it was mainly regulated by the strength of the polymer.

In general, mechanical strength of resin decreases with the increase in filler material, due to weak interaction between resin and filler material. However, the bending strength of the present composites did not decrease compared to that of CPLA. This result indicates that adhesive strength between CPLA and calcium phosphate was strong.



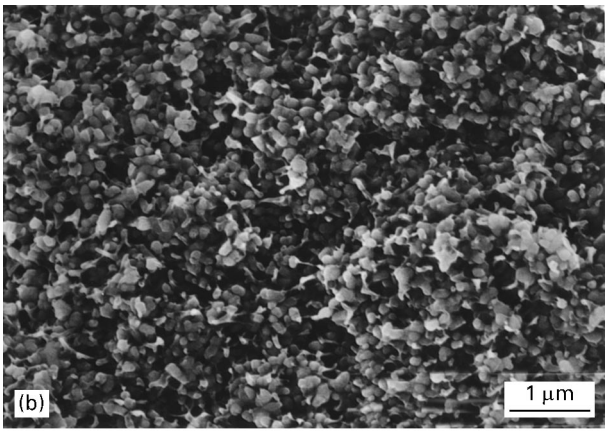


Figure 5 Fracture surfaces of composites with 75 wt % of calcium phosphate and 25 wt % of CPLA: (a) β-TCP/CPLA-H; (b) HAp/CPLA-H.

SEM images of the fracture surface of the composites are shown in Fig. 5. In HAp/CPLA composites, HAp particles were not well covered with CPLA although the primary particle size of HAp was smaller than that of TCP. The SEM images thus suggested that HAp degraded the CPLA network due to the decomposition of CPLA. On the other hand, in TCP/CPLA composites, CPLA formed a homogeneous network and covered TCP particles well. It was considered that this texture came from the adhesive strength of TCP and CPLA, resulting in no decrease in bending strength even when the amount of phosphate was high.

3.3. Thermoplasticity of composites

Fig. 6 shows various shapes of composite formed by thermal treatment. The present composites can easily deform into various shapes at temperatures between 400 K and 480 K. This thermoplastic property is very useful for medical and dental applications, which are under investigation.

4. Conclusions

TCP/CPLA and HAp/CPLA composites were prepared by a thermal kneading method. HAp accelerated the decomposition of CPLA, resulting in a deterioration in mechanical properties. TCP/CPLA composites had good mechanical properties and thermoplasticity. The mechanical properties, especially Young's modulus, were improved by strong adhesion between TCP and CPLA. Further, *in vivo* and *in vitro* testings of the composite have been carried out, and some results suggest that the composites have good bioactivity and no cytotoxicity. This composite will possibly be usable as a new type of artificial bone due to the combination of osteoconductivity of TCP and biodegradation of CPLA.

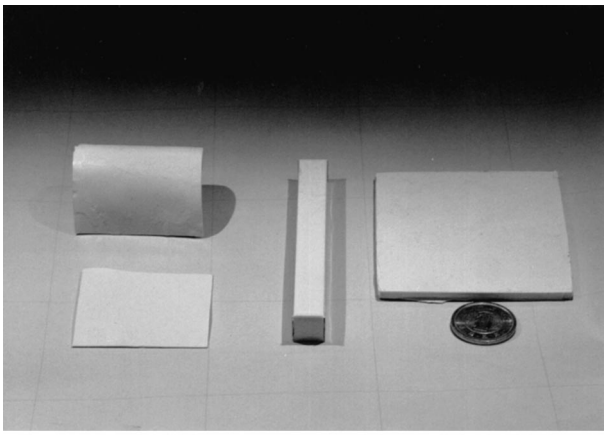


Figure 6 Various shapes of composite formed by thermal treatment.

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