

# Degradation Behavior of Porous Calcium Phosphates

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## Abstract

Concerning an ideal scaffold, evaluation of many factors, such as porosity, porous size and mechanical properties are needed so as to investigate degradation behavior in addition to chemistry and structure of materials used. In this study, the porous calcium phosphates were made on addition of a pore-former compound (PVA) by sinter processing. Mechanical properties, morphology, and weight change in in vitro testing were assessed. Experimental results indicated macropore sizes as large as hundreds of micrometers were generated and many micropores were also observed in the sintered body. After immersion in Hanks' solution, on the body surface there was a pitting appearance with immersion-induced micropores. The compressive strength of as-sintered bodies decreased steadily with addition of PVA. With increasing immersion time, the compressive strength and modulus of various porous bodies decreased and the weight loss increased. The biomedical uses of the present porous materials might limit to use as bone defect repair.

**Keywords:** Tissue engineering, Porous scaffold, Mechanical property, Calcium phosphate

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## Introduction

Tissue engineering is regarded as one of the bioscience for guiding body to regenerate or repair tissues, when organ and tissue lose or failure occurs [1-3]. The scaffold is a temporary supporting structure of tissue-engineered constructions and it needs to be selected carefully. The scaffold materials must be biocompatible and bioresorbable with controllable degradation rates to match tissue replacement [1-2,4-5]. Besides suitable surface chemistry, the scaffold architecture provides sufficient space and suitable mechanical properties for the tissues regeneration [1-2]. Hence, the use of biodegradable biomaterials as bone scaffolds has attracted a great deal of attention and a variety of fabrication methods have been proposed to produce porous scaffolds with interconnected pore networks [3-6]. Porous biodegradable synthetic materials, such as calcium phosphates, poly(lactic acid) (PLA), and poly(glycolic acid) (PGA), are currently tested as implants for the regeneration of damaged and diseased tissues [2-4,7].

The available synthetic biodegradable calcium phosphate ceramics for bone tissue regeneration include hydroxyapatite (HA),  $\beta$ -tricalcium phosphate ( $\beta$ -TCP), and calcium polyphosphate [3,4,6,7]. The biodegradation behavior of calcium polyphosphate materials in both in vitro and in vivo has been reported [6-10]. Utilizing solid freeform fabrication to build porous parts of calcium polyphosphate, Porter *et al.* [8] found a decline in mechanical strength in tris-buffered solution.

Lee *et al.* [9] suggested that the composite graft of marrow-derived mesenchymal cells and porous calcium polyphosphate may be useful for the repair of bone defects.

Few studies on the variations in mechanical properties of porous calcium phosphates, when immersed in simulated body fluid have been exploited. In the present study, porous calcium phosphates were prepared by sintering mixtures of monocalcium phosphate monohydrate (MCPM,  $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot \text{H}_2\text{O}$ ) and polyvinyl alcohol (PVA). To impart porosity to the ceramic body, the PVA was burned out during firing, leaving free space in the resulting body. The degradation behavior of porous bodies was characterized by monitoring changes in compressive strength, compressive modulus as well as weight loss in simulated physiological solution.

## Materials and Methods

Commercially pure MCPM and PVA powders (Showa, Tokyo, Japan) were used. The as-received MCPM powder was directly mixed with PVA in a vacuum mixer (VM-112T, J.Morita, Saitama, Japan) for 5 minutes to ensure homogeneity. Four different types of porous bodies were prepared from mixtures of MCPM and PVA powders with different ratios (75/25, 67/33, 60/40, and 50/50 by weight). For simplicity, throughout this study the green body and the sintered body derived from the same mixture are designated with the same code. For example, the specimen code "67C33V" stands for both the mixture containing 67 wt% MCPM and 33 wt% PVA

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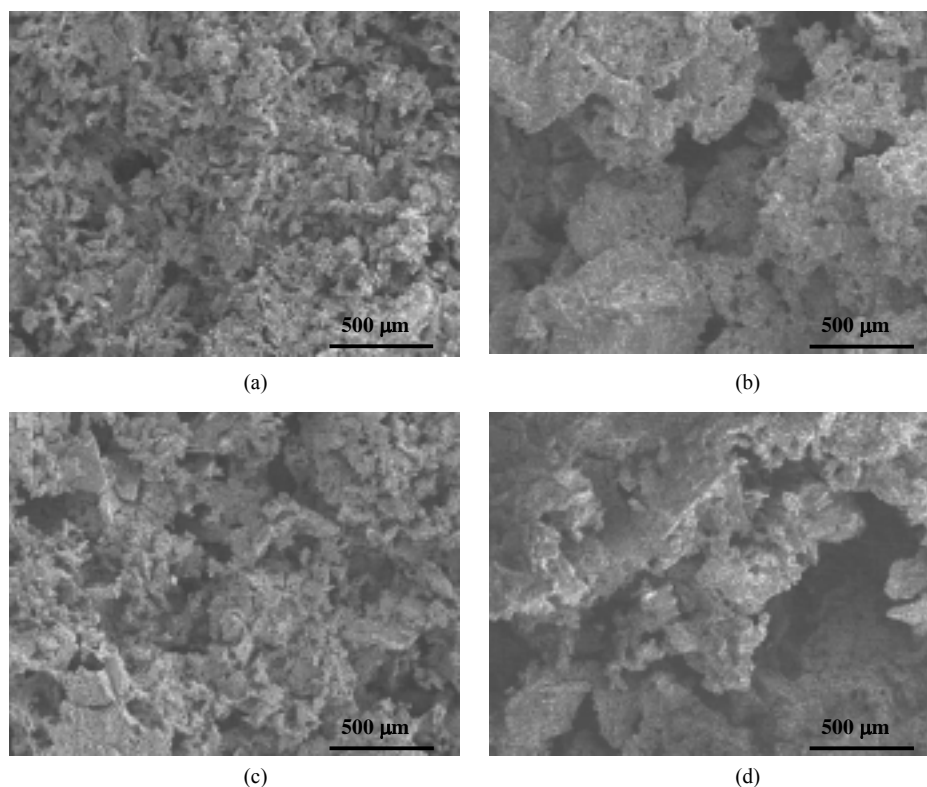


Figure 1. SEM micrographs of as-sintered porous bodies prepared with the weight fractions of PVA particulates of (a) 25%, (b) 33%, (c) 40%, and (d) 50%.

Table 1. Chemical composition of Hanks' physiological solution.

Constituent	g/L
NaCl	8.00
NaHCO <sub>3</sub>	0.35
KCl	0.40
MgCl <sub>2</sub> · 6H <sub>2</sub> O	0.10
CaCl <sub>2</sub>	0.14
Na <sub>2</sub> HPO <sub>4</sub> · 2H <sub>2</sub> O	0.06
MgSO <sub>4</sub> · 7H <sub>2</sub> O	0.06
KH <sub>2</sub> PO <sub>4</sub>	0.06
Glucose	1.00

and the sintered body. The mixture was pressed using a stainless steel mold at a pressure of 10 MPa. The green bodies were heated to 900°C in air and held for 3 hr, and then furnace-cooled to room temperature. The morphology was observed using a scanning electron microscope (SEM, Hitachi S-4200, Japan).

The extracellular solution with an ionic composition similar to that of human plasma, Hanks' balanced salt solution (Table 1), was used for the immersion test. The solution had an initial pH of 7.4. The specimens were immersed in 10 ml of the solution for the predetermined periods of time at  $37 \pm 0.5^\circ\text{C}$ . After immersion, the specimens were removed from the vials and placed in a container with fresh Hanks' solution to evaluate the mechanical properties. Immersion-induced changes in sample weight were also determined. Prior to the

weight measurement using a 4-digital balance (Ael-40sm, Shimadzu, Tokyo, Japan), the immersed specimens were dried at 120°C for 3 hr in an oven. At least seven samples were tested for each measurement. The compressive testing was conducted on an EZ-Test machine (Shimadzu, Kyoto, Japan) at a loading rate of 0.5 mm/min. The compression load at failure was obtained from the recorded load-deflection curves. The Young's modulus of the samples was determined from the slope of the initial linear elastic portion of the load-deflection curve. One-way ANOVA statistical analysis was used to evaluate the significance of the strength data. Scheffé multiple comparison testing was used to determine the significance of the deviations. In all cases, the data were considered statistically different when  $p < 0.05$ .

## Results and discussion

### Morphology

The morphologies of a series of as-sintered porous bodies are shown in Fig. 1. The SEM micrographs showed the pore structure of calcium phosphate bodies can essentially be considered as an assembly of the macropores and micropores. Macropore sizes as large as hundreds of micrometers were generated and many micropores ( $< 10 \mu\text{m}$ ) were also observed in the sintered body. It is obvious that introduction of PVA in the ceramic powder resulted in sintered bodies with macropores and micropores as desired.

When immersed in Hanks' solution, although having a similar morphology, SEM observation revealed the signs of

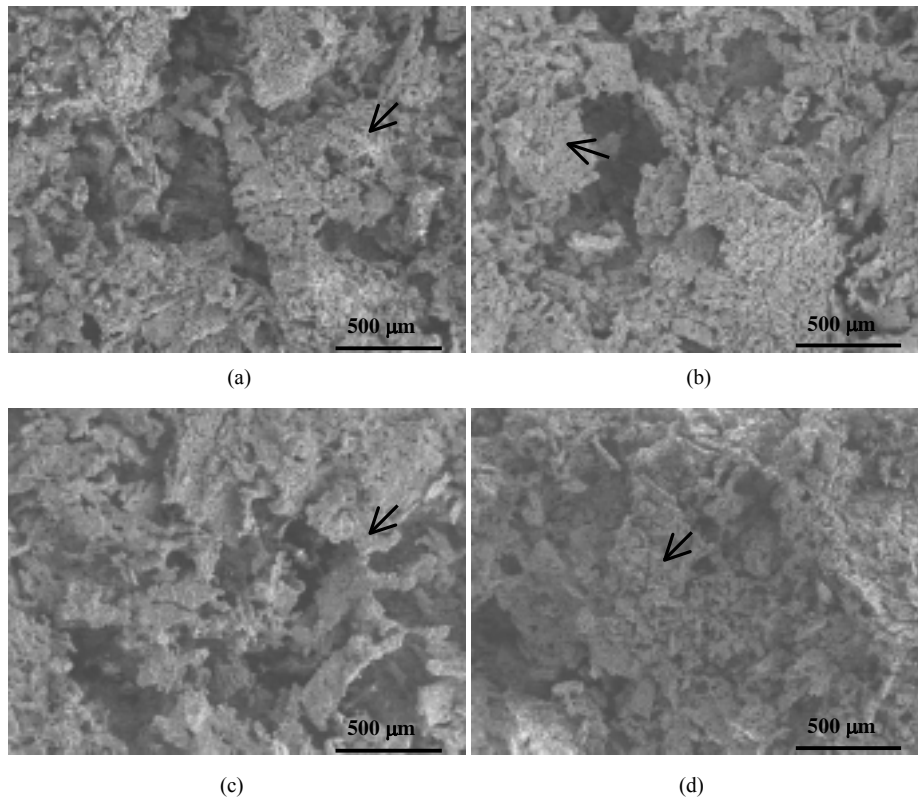


Figure 2. SEM micrographs of porous bodies prepared with the weight fractions of PVA particulates of (a) 25%, (b) 33%, (c) 40%, and (d) 50% after 90-day immersion in Hanks' solution. Arrows indicate immersion-induced micropores.

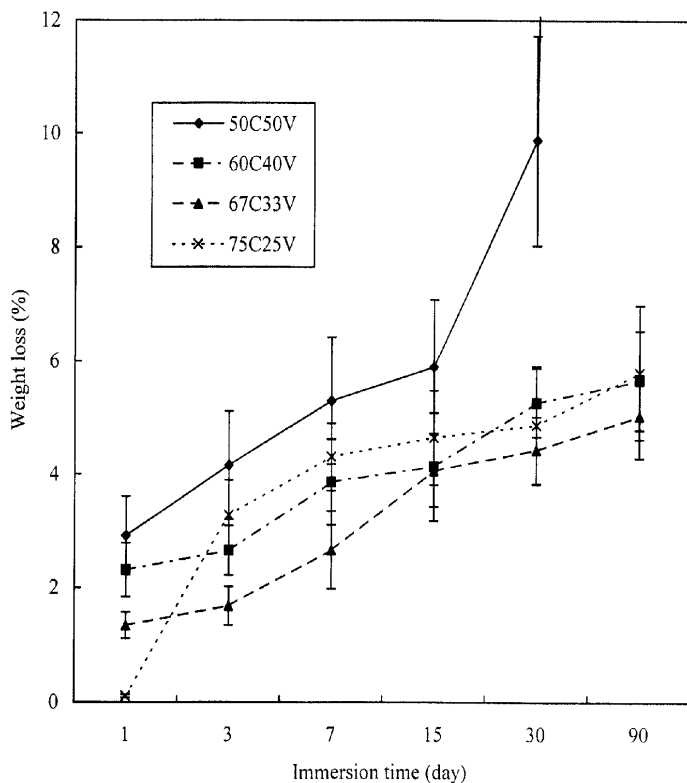


Figure 3. Weight loss variation of porous bodies after immersion in Hanks' solution. For the sample 50C50V, its weight loss was regarded as 100% after 90 days of the solution immersion because of fracture during handling.

degradation at all four samples possible due to the solution attack. The samples immersed for 90 days have a pitting appearance with large amounts of immersion-induced micropores of about several micrometers, as indicated by arrows in Fig. 2.

**Weight loss**

To further study the dissolution/degradation process, a series of weight change were performed for all immersed samples. Fig. 3 shows that all samples continue dissolving after immersion in Hanks' solution. The dissolution behavior of immersed calcium phosphate materials in simulated physiological solution has been reported [10-12]. The result indicated that sample 50C50V had the fastest weight loss with degradation time. However, the weight loss remained about 6% over 90 days of immersion for all other samples. The loss in sample weight might be explained by degradation of such materials.

**Compressive strength**

The compressive strength of as-sintered calcium phosphates decreased steadily with addition of PVA, as listed in Table 2. The average compressive strengths and standard derivations of as-sintered 75C25V, 67C33V, 60C40V, and 50C50V bodies were  $1.43 \pm 0.09$ ,  $0.68 \pm 0.07$ ,  $0.44 \pm 0.05$ , and  $0.10 \pm 0.01$  MPa, respectively. One-way ANOVA analysis showed that there is significant ( $p < 0.05$ ). The samples with lower PVA contents had a higher compressive strength probably due to their less porosity. The decrease in the

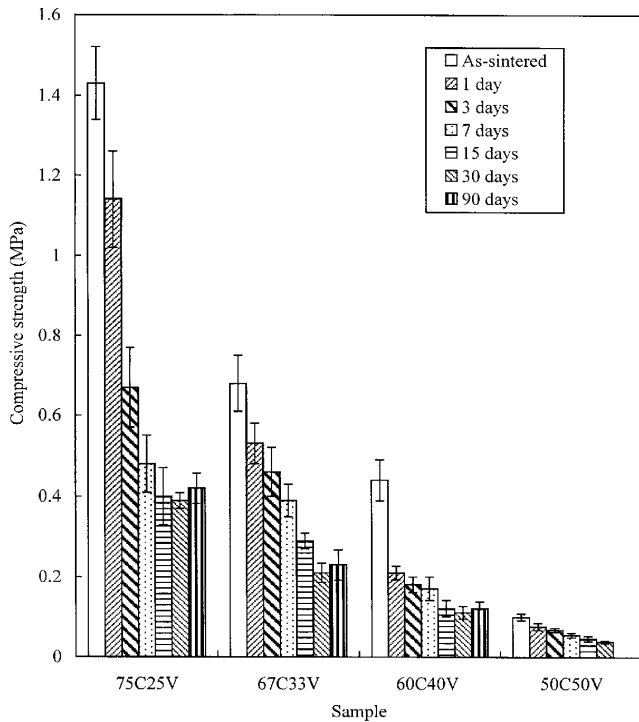


Figure 4. Compressive strengths of as-sintered and immersed samples.

compressive strength with increased porosity was not surprising and has been described elsewhere [6,13]. LeHuec *et al.* suggested that total porosity and pore size influenced mechanical strength [13], which both related to the decrease in the quantity of solid material existed in each specimen.

The variations in the compressive strength with immersion time of the series of porous bodies are presented in Fig. 4. Six immersion regimes of 1, 3, 7, 15, 30 and 90 days were selected for testing the porous bodies. The mechanical properties of 90-day-immersed 50C50V are not available due to the lack of structural integrity and fracture during handling. It is evident that the compressive strength at any immersion time was subjected to a large standard deviation, probably because of the porosity characteristics. The results revealed that, when immersed in Hanks' solution, the four different types of porous samples gradually lost their strength with increasing immersion time. For example, the initial strength of 0.68 MPa of sample 67C33V was significantly reduced down to 0.53 MPa after one-day immersion ( $p < 0.05$ ). When immersed for 15, 30, and 90 days, its strength decreased to 0.29, 0.21, and 0.23 MPa, respectively. The statistical analysis using Scheffé multiple comparison testing showed that the compressive strength of immersed calcium phosphates mixed with 25 wt% PVA in green compact (75C25V) significantly declined by about 70% after immersion for 90 days ( $p < 0.05$ ). When the green compacts comprised 33 and 40 wt% PVA, the resulting porous bodies lost 66% and 73% of their compressive strengths after 90-day immersion, respectively. This deterioration in the strength seems unavoidable for biodegradable porous ceramics immersed in simulated body fluid and has also been observed in other studies [6,8]. According to Porter *et al.*, the immersion-induced decline in

Table 2. Mechanical properties of as-sintered porous bodies.

Code	Mechanical property	
	Compressive strength $\pm$ SD (MPa)	Modulus $\pm$ SD (MPa)
75C25V	1.43 $\pm$ 0.09	15.02 $\pm$ 1.18
67C33V	0.68 $\pm$ 0.07	12.51 $\pm$ 0.66
60C40V	0.44 $\pm$ 0.05	9.22 $\pm$ 0.44
50C50V	0.10 $\pm$ 0.01	0.96 $\pm$ 0.04

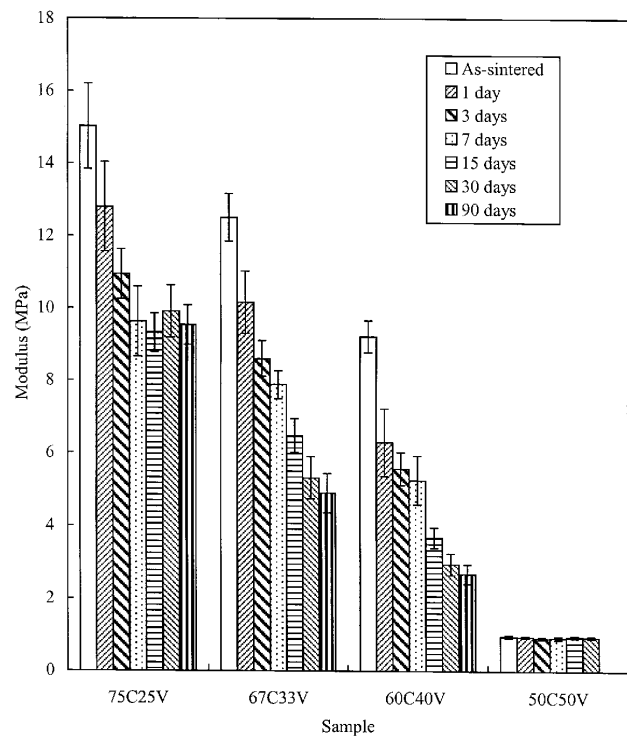


Figure 5. Compressive moduli of as-sintered and immersed samples.

mechanical strength was due to less stable zones (particle surfaces or interface regions of grains) of porous ceramic body, where the degradation occurred more rapidly [8]. Besides the resulting porous structures of calcium phosphates as described above, the dissolution of the calcium phosphate in the solution and the penetration of water/ions resulting from the solution possibly accounted for the deterioration in mechanical properties [10-11].

### Modulus

The initial moduli of porous bodies also varied with the amounts of PVA (Table 2). The Young's modulus decreased with increasing PVA content from 15.02 MPa for sample 75C25V to 0.96 MPa for sample 50C50V. As mentioned above, the samples with lower PVA contents had a less porosity and may be responsible for the greater modulus. The variations of compressive modulus against immersion time for porous bodies are shown in Fig. 5. After immersion in Hanks' solution, there was a pronounced decrease in the modulus for all porous bodies but 50C50V body, similar trends with changes in compressive strength.

### Conclusion

In this investigation, the obtained results showed the sample with lower PVA addition had a greater initial mechanical property. Hanks' solution treatment imposed in our study did have a statistically significant effect on the compressive strength. The strength and modulus values of all immersed bodies largely declined. Due to their low strength and susceptibility to solution attack, the biomedical uses of the present porous materials might limit to use as bone defect repair.

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# 多孔鈣磷酸鹽降解行為研究

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## 摘 要

理想的骨架除了考量材料本身的化性與結構外，需要評估其孔隙率、孔洞大小及機械性質等因素以研究降解行為。本實驗添加孔原形成劑(PVA)，以燒結法製作多孔鈣磷骨架，將此種材料浸泡於 Hanks 模擬體液中，研究其機械強度變化及重量損失，並觀察微結構形態。結果發現陶瓷骨架表面形成數百微米巨孔與許多微孔的結構，經浸泡於模擬體液後，出現浸蝕引起的微孔。各燒結體抗壓強度隨 PVA 添加量增加而降低，隨浸泡時間增加各陶瓷骨架之抗壓強度降低，且重量損失增加。本研究的多孔材料或許可使用在骨缺損修補。

**關鍵詞：**組織工程、多孔骨架、機械性質、鈣磷酸鹽

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