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THERMOKINETIC ANALYSIS OF THE HYDRATION PROCESS OF CALCIUM PHOSPHATE CEMENT

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A microcalorimeter (Setaram c-80) was used to study the thermokinetics of the hydration process of calcium phosphate cement (CPC), a biocompatible biomaterial used in bone repair. The hydration enthalpy was determined to be 35.8 J g^{-1} at 37.0°C when up to 80 mg CPC was dissolved in 2 mL of citric buffer. In the present study, parameters related to time constants of the calorimeter were obtained by fitting the recorded thermal curves with the function $\theta = Ae^{-\omega_1 t}(1-e^{-\omega_2 t})$. The real thermogenetic curves were then retrieved with Tian function and the transformation rate of the hydration process of CPC was found to follow the equation $\alpha=1-[1-(0.0075t)^3]^3$. The microstructures of the hydrated CPC were examined by scanning electron microscopy. The nano-scale flake microstructures are due to crystallization of calcium phosphate and they could contribute to the good biocompatibility and high bioactivity.

Keywords: *calcium phosphate cement, hydration process, rebuilding thermogenetic curve, thermokinetics*

Introduction

Calcium phosphate cements (CPC) are a family of biomaterials used clinically in bone repair for filling non-load bearing bone defects. Being prepared with similar element composition and pore size to natural bone, the cements have good biocompatibility. The cement formation is usually based on acid-base reactions between several calcium orthophosphate combinations and set in situ in the presence of an aqueous phase [1, 2]. At pH>4.2, hydroxyapatite (HA) is formed by combining crystalline calcium phosphates such as α/β-tricalcium phosphate (TCP) with slightly acidic compounds such as dicalcium phosphate dihydrate (DCPD) [3]. In this work, a CPC preparation, a mixture of α-TCP and DCPD with mole ratio of 1:1, was examined by a microcalorimeter and the kinetic properties of the hydration process of the CPC were obtained. The microstructure of the hydrated CPC was examined with a scanning electron microscope (SEM). The results are important in optimizing the design of the cement and thus its clinical applications.

Conductive microcalorimetry is a powerful tool for investigating the kinetic properties of chemical reactions and physical processes involving thermal changes, and has received wide applications in many fields [4–8]. The kinetics and mechanism of hydration in cementitious systems have been successfully investigated by calorimetry [9–13].

For slow reactions, many thermokinetic research methods have been developed [7, 8, 14], in which the kinetic parameters can be evaluated directly from the measured thermogenetic curve. For fast reactions, however, the measured curve cannot be used directly for kinetic analysis due to hysteresis in heat transfer or dispersion. Hydration process of CPC is a fast reaction, it is thus necessary to reconstruct the real thermogenetic curve before analysis of the kinetic parameters.

According to literature [15, 16], there are two important parameters, ω_1 and ω_2, in reconstructing real thermogenetic curves, representing the rates of thermogenesis and thermal diffusion, respectively. Through several steps of function fitting and extrapolating, the values of the two parameters can be determined.

In this study, a function in the form of $\theta = Ae^{-\omega_1 t}(1-e^{-\omega_2 t})$ was employed directly to describe the apparent heat flow curves. The two parameters could then be determined in a single step using the Origin software package. With the help of the obtained real thermogenetic curves of the hydration process of the CPC preparations, the kinetic properties of the hydration process were studied.

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Experimental

Reagents

DCPD and calcium carbonate were purchased from the Beijing Chemical Reagents Company (China). α-tricalcium phosphate (α-TCP) was prepared from DCPD by reacting it with calcium carbonate. CPC, consisting of equal mole fraction of α-TCP and DCPD, was prepared by grinding them in anhydrous ethanol, and subsequent drying and sifting (the grain size approximately 2 μm). The buffer was citric acid buffer (pH=6.0).

Instrumental

A c-80 microcalorimeter (Setaram, France) was used in this work. Its working principle and proper operation have been described in detail previously [16]. All measurements were performed at 37.0°C. Inversing mixing cells were used in this experiment. A thermogenetic curve of solid–liquid mixing process could thus be generated by reversing the calorimeter body containing the CPC preparation in the inner cell and buffer in the outer cell. In this paper, a set of thermogenetic curves were generated by mixing various amounts of CPC (5, 10, 20, 30, 50, 60 and 80 mg) and 2.0 mL buffer. The reference cell was filled with 2.0 mL buffer.

An environmental scanning electron microscope (Philip XL30 ESEM) was used to examine the microstructure of hydrated CPC. The sample was prepared by mixing the CPC with the setting buffer (1 g mL^{-1}). After 4 h setting time at 37°C, the microstructures were examined.

Results and discussion

The apparent thermogenetic curves of the hydration process from different amount of CPC are shown in Fig. 1. By integrating the thermogenetic curve, the total heat generated during hydration of the CPC samples can be obtained. With increasing quantity of CPC, a linear relationship was observed as shown in Fig. 2. The enthalpy was determined to be 35.8 J g^{-1} at 37.0°C. The enthalpy of hydration could be of help in optimizing the design of the cement and thus the practical applications. When the ratio of CPC to buffer solution is less than 1:20, the heat evolved can only raise the temperature slightly, less than 0.5°C. When the ratio reaches to 1:2 or 1:1, the temperature increase in the mixture could be up to 4 or 5°C. This temperature change cannot be ignored during application of CPC.

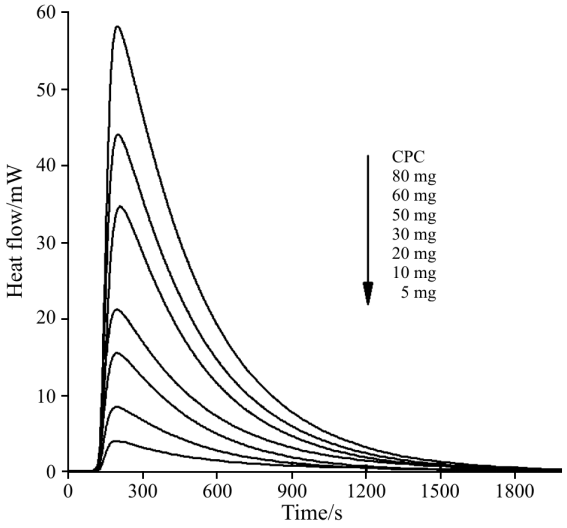

Fig. 1 The thermogenesis curves from mixing different amounts of CPC and 2 mL buffer at 37.0°C

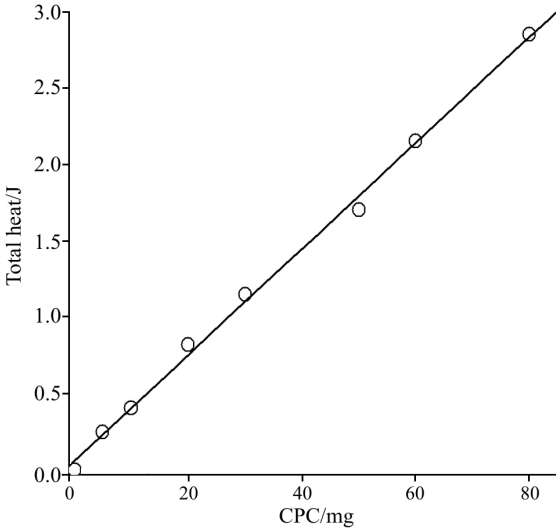

Fig. 2 The linear relationship between the total heat of hydration process and the mass of CPC

Rebuilding the actual thermogenetic curve

The hydration process of the calcium phosphate cement is quite fast, all the curves return to baseline within half an hour (Fig. 1). Apparently, the thermogenetic processes only last for several minutes. It is thus necessary to retrieve the actual thermogenetic curve by means of a theoretic model before performing kinetic analysis.

A well-documented method [16] describes the curve by a series of exponentials as in Eq. (1):

$$\theta = \Delta Q(a_1 e^{-\omega_1 t} + a_2 e^{-\omega_2 t} + \cdots) \quad (1)$$

where θ is heat flow of the calorimeter, ΔQ the heat generated by exothermic reaction, ω_i the time constant, and a_i the coefficient of thermal process. In

general, only the first two terms of the series are needed to give a satisfactory account of the apparent thermogenetic curve for a typical calorimeter.

Due to the fast reaction rate of hydration process of the CPC, the heat was generated and accumulated in a short time. Therefore, the two processes of heat generation and heat diffusion could be approximately considered as successive events. Here, a mathematic model (similar to a pulse function) was used as shown below:

$$\theta = A\mathrm{e}^{-\omega_1 t}(1-\mathrm{e}^{-\omega_2 t}) \quad (2)$$

where A is a constant. In the case we consider only the first two terms in Eq. (1), $\omega'_1 = \omega_1$, and $\omega'_2 = \omega_1 + \omega_2$. If ω_1 is very small in comparison to ω_2, the two parameters will bear the same meaning in Eqs (1) and (2). In the present work, Eq. (2) was used directly to fit the measured thermal curve, and the constants ω_1 and ω_2 were obtained by a single step using the Origin software package, shown in Table 1. Thus, ω_1=0.00296±0.00004 and ω_2=0.035±0.001. The former is less than one tenth of the latter. Comparison of one original thermal curve with the fitted data is shown in Fig. 3, which indicated a well agreement in the whole time range.

Table 1 Curve parameters fitted from the equation $\theta = A\mathrm{e}^{-\omega_1 t}(1-\mathrm{e}^{-\omega_2 t})$

CPC/mg	A/mW	ω_1/s^{-1}	ω_2/s^{-1}	R^2
5	4.5687	0.00291	0.03563	0.9988
10	11.1012	0.00298	0.03711	0.9999
20	22.5327	0.00303	0.03458	0.9998
30	27.7631	0.00293	0.03628	0.9999
50	48.0116	0.00299	0.03465	0.9999
60	57.5387	0.00295	0.03363	0.9998
80	74.7398	0.00295	0.03338	0.9998

With the help of ω_1 and ω_2, the real thermogenetic curves were retrieved through Tian function (the details can be found in [16]). Briefly, when the heat output varies sharply with time, transformation from the directly observed thermal curves $\theta(t)$ into thermal power of a sample $W(t)$ is necessary. Equation (3) is the famous Tian function.

$$W = C\left(\frac{\omega'_1\omega'_2}{\omega'_2-\omega'_1}\theta + \frac{\omega'_1+\omega'_2}{\omega'_2-\omega'_1}\frac{\mathrm{d}\theta}{\mathrm{d}t} + \frac{1}{\omega'_2-\omega'_1}\frac{\mathrm{d}^2\theta}{\mathrm{d}t^2}\right) \quad (3)$$

or

$$W = C\left(\frac{\omega_1(\omega_1+\omega_2)}{\omega_2}\theta + \frac{2\omega_1+\omega_2}{\omega_2}\frac{\mathrm{d}\theta}{\mathrm{d}t} + \frac{1}{\omega_2}\frac{\mathrm{d}^2\theta}{\mathrm{d}t^2}\right) \quad (4)$$

where C is a constant and can be evaluated through comparing the total areas underneath the original and deduced curves.

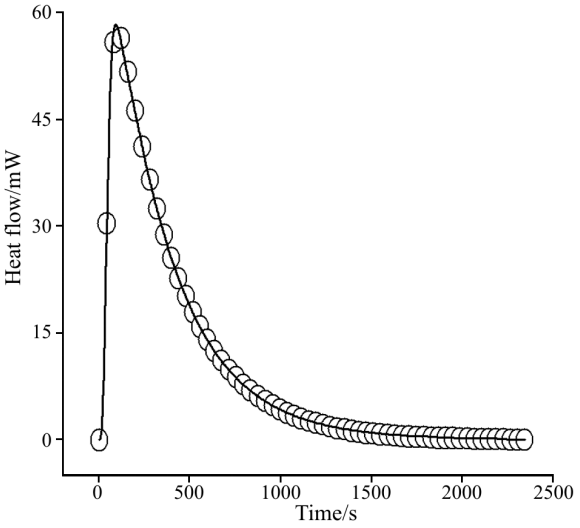

Fig. 3 A comparison of the ○ – original data with the — – fitted data derived from the mathematical model (mixture of 80 mg of CPC and 2.0 mL buffer)

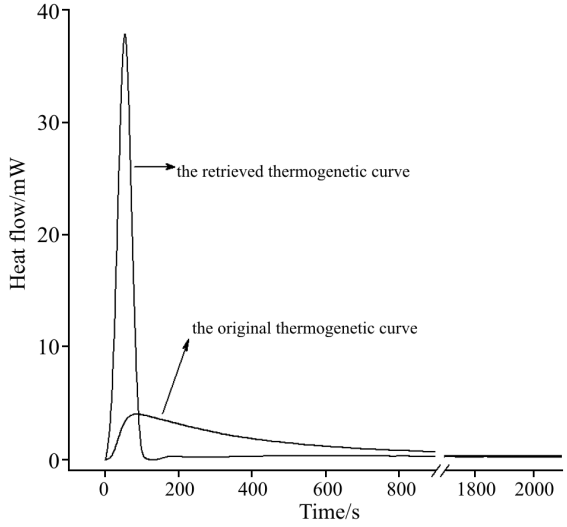

Fig. 4 Comparison of the reconstructed curve (narrow peak) and recorded thermal curve of 5 mg of CPC

The results, shown in Fig. 4, demonstrate that the period of heat generation (sharp curve) was distinctly shorter than that recorded in the original curve.

Thermal kinetics analysis

Based on the information obtained from calorimetric methods, the kinetic properties of the hydration process were studied. The transforming ratio of thermogenetic reaction α can be calculated through Eq. (5)

$$\alpha = \frac{\int_0^t W\mathrm{d}t}{\int_0^\infty W\mathrm{d}t} \quad (5)$$

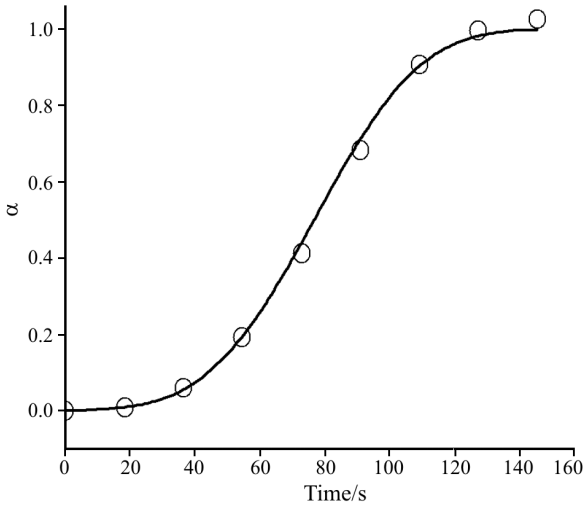

Fig. 5 Time-dependence of transforming ratio, showing the kinetic behavior of the hydration process of CPC

The dependence of α on time is shown in Fig. 5. At the beginning the value of α increases slightly, then the growth rate of α becomes fast because of the adequate contact among the reactants, and finally the rate decreases due to the reason of decreasing amount of the reactants.

Hydration kinetic analysis is dependent on setting up an appropriate mathematic model to express the processes [17]. For CPC, its hydration was mostly controlled by surface dissolution, three dimensional diffusion and calcium phosphate cement nucleation. A general reaction function (6) was deduced from these processes [17, 18]:

$$G(a)=[1-(1-\alpha)^{1/3}]^{N}=kt \qquad (6)$$

or

$$\alpha=1-[1-(kt)^{1/N}]^{3}$$

where k the rate constant of the reaction and N a constant. Using this physical model, a good agreement between the calculated transformation ratio (circles) and the fitted results (curve) was obtained (Fig. 5), with the values of k as 0.0075 s^{-1} and $1/N$ as 3. This kinetic model could be used in the design and application of CPC.

The microstructures of hydrated CPC were examined by ESEM. Shown in Fig. 6 are two representative micrograms with different magnifications. Apparently, some 100–200 μm pores and many micro-pores are formed during hydration process (Fig. 6a). Careful examination of the microgram with about 100 times higher magnification (Fig. 6b), however, shows the hydrated cement consists of homogenously distributed granules of a few micrometers in diameter. The surface of the granules

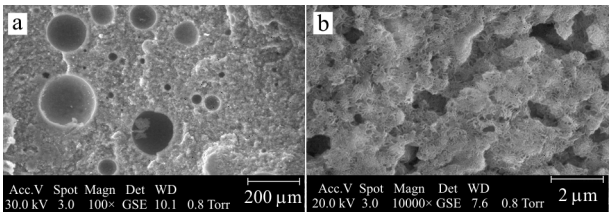

Fig. 6 SEM images of bone cement sections at two magnifications

is rough with many flower-like structures. The flake structures are the results of nucleation of calcium phosphate. In addition, the pores shown in Fig. 6a can be used to host bone cells, and the micro-pores could be used as channels to transport the body fluid and nutrient. The nano-scale flake-like microstructures shown in Fig. 6b, on the other hand, could be the results of crystallization upon hydration.

Conclusions

CPC are a family of biomaterials used clinically in bone repair for filling non-load bearing bone defects. It was found that within the range of 0–80 mg CPC per 2 mL citric acid buffer, the total heat release of the hydration process increases linearly with increasing amount of CPC. The enthalpy was determined to be 35.8 J g^{-1} at 37.0°C. So when the magnitude of CPC is too large, the thermal effects have to be considered and the effective measures should be done to protect the tissue around the repaired bone [19]. From the rebuilt thermogenetic curves of CPC, the hydration kinetic process was analyzed and the transformation rate can be expressed as $\alpha=1-[1-(0.0075t)^{3}]^{3}$.

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