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Preparation of nanosized β-tricalcium phosphate particles with Zn substitution

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Abstract Nanosized *β*-ZnTCP powders with different Zn contents were prepared through coprecipitation of ACP out of the $CaCl_2$-$ZnCl_2$-Na_3PO_4-PEG system, and calcination of the ACP precursor at 800 °C for 3 h. The characterizations of the products showed that the products belong to *β*-TCP phase, and the particles sizes of them are about 300 nm, smaller than that of *β*-TCP (500 nm). Both the Zn_{2p} binding energy and lattice parameter variations of *β*-TCP evidenced that Zn had substituted for Ca in the lattice. Such nanosized *β*-ZnTCP powders could be used as bone repair materials with desired and sustained release of Zn.

Introduction

As an essential trace element in human body, zinc ion can stimulate enzyme activity, nucleic acid metabolism and protein synthesis [1]. In the case of bone repairing, the presence of zinc ion improves the activity of osteoblasts and promotes bone regeneration [2]. Since bone regeneration usually takes several months, the regeneration surrounding needs only a low zinc concentration. The incorporation of Zn into bone repair material has been practiced as a feasible and effective approach to facilitate bone regeneration.

Several bone repair materials have been developed as zinc carriers [3–5]. *β*-tricalcium phosphate (*β*-TCP) is one of best choices because of its good bioactivity and biodegradability [6–8]. Zinc-containing *β*-TCP (*β*-ZnTCP) is expected to be a promising bone repair material allowing zinc to play the significant role in enhancing osteoblast activity and promoting bone generation.

For bone repair, *β*-ZnTCP is usually used as bulk [3], coating [9] and particles in composites [10]. Most of these applications are based on the preparation of *β*-ZnTCP particles. In order to create high performance biomaterials, it is required for *β*-ZnTCP particles to have small particle size and uniform substitution of Zn for Ca in *β*-TCP lattice. Fine particles benefit densification of bulk ceramics, and lead to an even dispersion in coating layer or composites, while zinc substitution for Ca in *β*-TCP lattice guarantees its sustained release.

Several methods to prepare *β*-ZnTCP particles [3, 11] have been developed, among which the solid reaction route is the most popular. However, the method usually needs high temperature, which may lead to large particle size and low purity. Although *β*-ZnTCP particles could also be obtained through aqueous coprecipitation followed by 800 °C calcination, it is not easy to control the crystalline phase and the state of Zn, which may result in undesirable zinc release.

In this work, Zn containing amorphous Ca phosphate (ZnACP) with molecular homogeneity is prepared as the precursor to assure zinc substitution during *β*-ZnTCP formation at a relatively low calcination temperature. The crystallization of *β*-ZnTCP from ZnACP, influence of different zinc concentration and zinc existence status in ZnTCP were investigated and discussed.

Experiment

Materials

$CaCl_2$ (AR, Nanjing Chem. Co. China), $ZnCl_2 \cdot 6H_2O$ (AR, Hangzhou Chem. Co. China) and Na_3PO_4 (AR, Nanjing

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Chem. Co. China) were used as starting materials providing the main constituents of *β*-TCP. Poly (ethylene glycol) (PEG, AR, Shanghai Chem. Co. China) was an additive for forming ACP precursor. Deionized water was used as the solvent.

Synthesis of zinc substituted *β*-TCP

$ZnCl_2$ (0.5 mol/L) solution was first mixed with $CaCl_2$ (0.5 mol/L) solution in Zn/(Ca + Zn) molar ratios of 0.01, 0.05 and 0.1, respectively. Then, PEG solution was added to form 0.100 M (Ca + Zn) solutions with a PEG/(Ca + Zn) molar ratio of 12. Designed amount of 0.133 M Na_3PO_4 solution was dropped into the starting solution to reach the (Ca + Zn)/P molar ratio of 1.5, and maintaining the pH value of 9 using ammonia. The temperature was kept at 5 °C until the designed amount of Na_3PO_4 was completely added. After stirring for 30 min, the precipitates were rinsed by icy water to remove Cl^- and Na^+ ions, infiltrated, and lyophilized for 48 h to obtain white powder, which was ZnACP identified later. After the white powder was calcined at 800 °C for 3 h, Zn containing *β*-ZnTCP powders was obtained. Detailed sample information was tabulated in Table 1.

Characterizations

The crystalline phases of the as prepared and calcined powders were determined in an X-ray diffractometer (RIGAKUD/MAX-C), with a step of 0.02° at a speed of 2° per minute. For transmission electronic microscopy (TEM, JEOL 1200) observation, the samples were prepared by suspending particles in ethanol and collecting them by copper grids with carbon-supporting-film. The thermal evolutions of the as-prepared powders were characterized by thermogravimetry (TG) and differential thermal analysis (DTA, SDT Q600, TA, American). Also, the calcined powders were characterized by X-ray photoelectron spectroscopy (XPS, AXIS His 165 Ultra). High-resolution spectra of Zn2p in ZnTCP were obtained using Al Kα radiation, with steps of 0.1 eV. All spectra were calibrated with C1s binding energy at 284.6 eV.

Table 1 Annotation and composition of the samples

As-lyophilized precipitates	Powders after calcined at 800 °C	Molar ratio of Zn/(Ca + Zn) during precipitation reaction
ACP	TCP	0
ZnACP1	ZnTCP1	0.01
ZnACP5	ZnTCP5	0.05
ZnACP10	ZnTCP10	0.10

Results

The as-lyophilized ZnACP powders listed in Table 1 are all composed of aggregates with the average diameter of about 60 nm, which is almost the same as the ACP prepared in this study and in previous study [12]. After 800 °C calcinations for 3 h, ZnACP transformed to ZnTCP and at the same time the particle size grew. Figure 1 shows the TEM images of the TCP and ZnTCP after calcinations. The particle size of typical ZnTCP is 300 nm (Fig. 1a), which is smaller than that (500 nm) of TCP powders (Fig. 1b). The XRD patterns show that the as-lyophilized powder is amorphous, and all the calcined powders with different Zn content are *β*-TCP phase (Fig. 2). The XRD peaks of ZnTCP obviously shift with Zn content. The lattice parameter of ZnTCP as a function of Zn content is plotted in Fig. 3. The *c* parameter decreases with increasing Zn content, while *a* and *b* are almost unchanged.

In XPS survey spectra (Fig. 4a), ZnTCP powders with high Zn content (ZnTCP5 and ZnTCP10) have obvious signals related to Zn. In high-resolution spectra of Zn2p (Fig. 4b), two peaks at 1021.7 eV and 1044.8 eV appear, and they become more obvious in ZnTCP10 than those in ZnTCP5. The two peaks are attributed to $Zn2p_{3/2}$ and $Zn2p_{1/2}$, respectively.

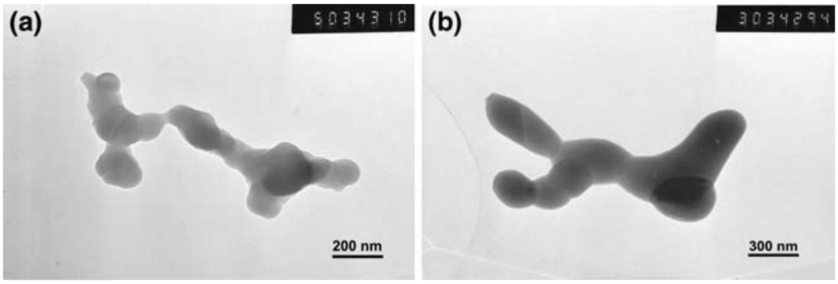
The DTA and TG curves of ZnACP and ACP in this study have found almost the same. Only the DTA and TG curves of ZnACP5 are shown in Fig. 5. An endothermic peak at about 100 °C with 15.8 wt% weight loss, an exothermic peak at 241 °C with 10.4 wt% weight loss and an exothermic peak at 700 °C without weight loss are observed.

Discussion

The lyophilized ZnACP and ACP precipitated from $CaCl_2$-$ZnCl_2$-Na_3PO_4-PEG system are amorphous evidenced by the XRD pattern in Fig. 2. The ACP with different Zn contents transform to *β*-TCP phase after 800 °C calcination (Fig. 2). The average particle sized of *β*-ZnTCP is 300 nm, which is smaller than that (500 nm) of *β*-TCP. The decrease in *β*-ZnTCP particle size may be attributed to the presence of Zn, which acted as an obstacle to diffusion and thus hinder the *β*-TCP particle growth.

With increasing amount of Zn in the reaction system, the *c* parameter of the resulting *β*-TCP phase decreases, and *a* and *b* parameters are almost same (Fig. 3), which implies that Zn has substituted for Ca in *β*-TCP lattice. If Zn enters into *β*-TCP lattice and occupies Ca site, $(Zn,Ca)_3(PO_4)_2$ solid solution is formed and chemical bonds of Zn–O–P are constructed. The chemical circumstance of Zn in the solid solution is different from that in ZnO and $Zn_3(PO_4)_2$. The

Fig. 1 Typical TEM photographs of ZnTCP5 (**a**) and TCP (**b**)



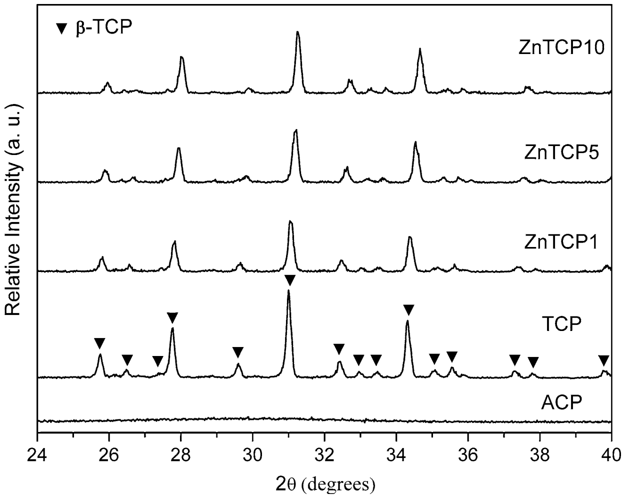


Fig. 2 XRD patterns of ACP, TCP and ZnTCP

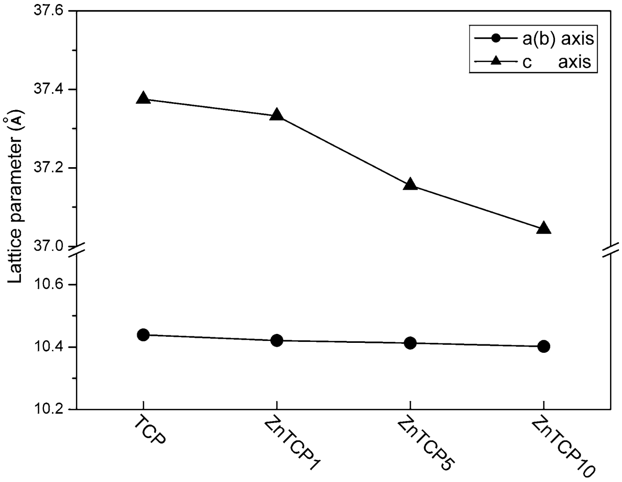


Fig. 3 Lattice parameters of TCP and ZnTCP

$Zn2p_{3/2}$ and $Zn2p_{1/2}$ in $Zn_3(PO_4)_2$ appear at 1,024.8 eV and 1,047.7 eV, with calibration of P2p binding energy at 135.0 eV, respectively [13], but in ZnO, they are located at 1,021.4 eV and 1,044.5 eV [14]. While the peaks at 1,021.7 eV and 1,044.8 eV from $Zn2p_{3/2}$ and $Zn2p_{1/2}$ in β-ZnTCP (Fig. 4) lie between those of ZnO and $Zn_3(PO_4)_2$. On the other hand, the peak intensity of Zn2p in β-ZnTCP increase with the increase in Zn content (Fig. 4), meanwhile, the symmetries and the full-width half-maximum (FWHM) of Zn2p peaks remain the same, which indicates that no impurity phase appear with increase of Zn content. The XPS results (Fig. 4) confirm that Zn has substituted for Ca, and no segregation appears on the surface of the nanosized particles.

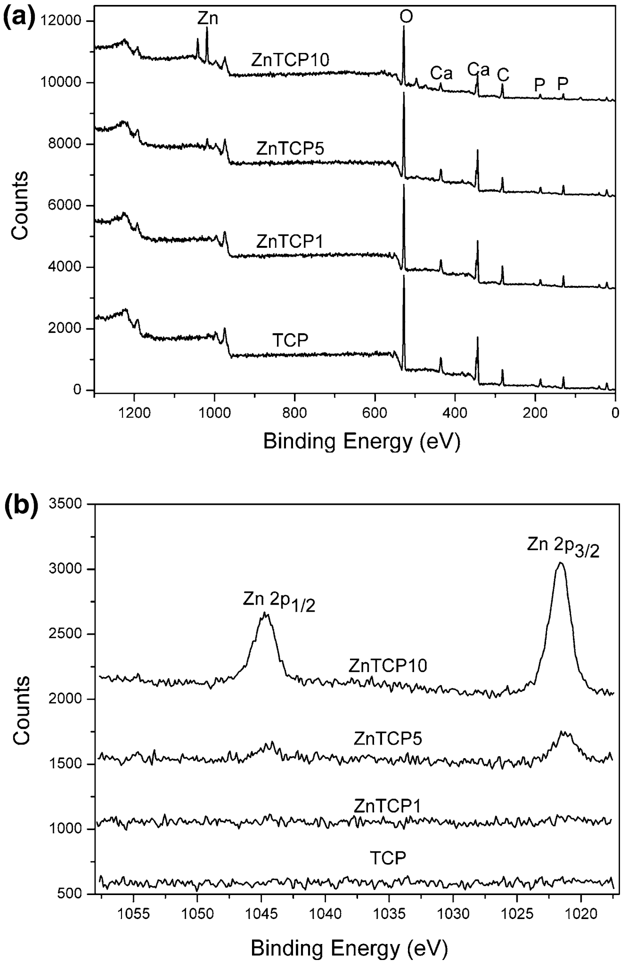


Fig. 4 XPS survey spectra (**a**) and high-resolution spectra of Zn2p (**b**) in TCP and ZnTCP

In the present work, the Zn substitution in β-TCP at relatively low temperature could be attributed to ZnACP with high level composition homogeneity. While the attaining of

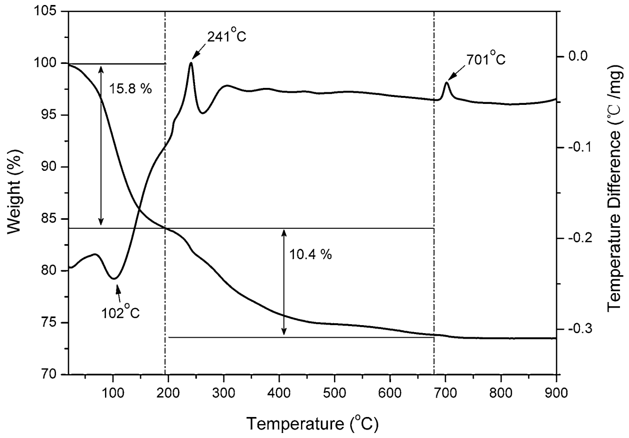


Fig. 5 DTA and TG curves of ZnACP5

homogeneity comes from a coprecipitation reaction because Ca phosphate and Zn phosphate have similar solubility product, $Ca_3(PO_4)_2$ with Ksp of 2.0×10^{-29} and $Zn_3(PO_4)_2$ with Ksp of 9.0×10^{-33} [15]. After a series of reactions during heat treatment, ZnACP tends to crystallize into thermodynamically stable state. DTA and TG results provide more details of such process: an endothermic peak at about 100 °C with 15.8% weight loss is due to removal of water in the ZnACP, exothermic peaks at 241 °C with 10.4% weight losses is due to PEG decomposition, and an exothermic peak at 700 °C without weight loss is due to crystallization of β-TCP. Hence, the changes in phase during heating ZnACP could be formulated as below:

$$Ca_{(9-\chi)}Zn_{\chi}(PO_4)_6 \cdot (PEG)_m \cdot (H_2O)_n$$
$$\xrightarrow{100\,^{\circ}C} Ca_{(9-\chi)}Zn_{\chi}(PO_4)_6(PEG)_m + H_2O\uparrow$$
$$\xrightarrow{300\,^{\circ}C} Ca_{(9-\chi)}Zn_{\chi}(PO_4)_6 + CO_2\uparrow + H_2O\uparrow$$
$$\xrightarrow{700\,^{\circ}C} Ca_{(9-\chi)/3}Zn_{\chi/3}(PO_4)_2$$

Conclusions

Pure and nanosized β-ZnTCP particles can be prepared by 800 °C calcination of ZnACP precursor, which was coprecipitated from $CaCl_2$-$ZnCl_2$-Na_3PO_4-PEG system. The process guarantees that Zn occupies Ca site in the lattice and its content could be tailored by varying $ZnCl_2$ content. The chemical composition homogeneity in ZnACP is considered as a main reason for the low temperature formation of $(Zn,Ca)_3(PO_4)_2$ solid solution. The nanosized Zn substituted β-TCP (β-ZnTCP) without Zn segregation could give a stable and sustained Zn release behavior, which is required in bone repair.

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