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Solution combustion synthesis of calcium phosphate particles for controlled release of bovine serum albumin

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ABSTRACT

Four different phase compositions of calcium phosphate (CaP) particles were prepared via a solution combustion method. X-ray diffraction (XRD) and Rietveld analysis results revealed that the variations in the nominal Ca/P (molar) ratios were found to provide a favorable control in the different proportions of CaP materials. Bovine serum albumin (BSA) was used as a model protein to study the loading and release behavior. The release profile indicated that the BSA release rates depended on the phase compositions of the CaP particles, and showed an order of TCP-BSA > BCP-1-BSA > BCP-2-BSA > HA-BSA. The results suggested that the BSA protein release rate can be controlled by varying the phase compositions of CaP carriers. Moreover, the release process involved two stages: firstly surface diffusion via ion exchange and secondly intraparticle diffusion.

1. Introduction

In recent years, many inorganic nanoparticles, such as silicon oxide [1], iron oxide [2,3], carbon materials [4,5], layered double hydroxide [6,7] and calcium phosphate (CaP) [8], have been studied as various drug delivery systems (DDS). Among them, CaP is one of the most promising materials due to its excellent biocompatibility, bioactivity and biodegradability.

CaP materials, such as hydroxyapatite (HA, $Ca_{10}(PO_4)_6(OH)_2$), β-tricalcium phosphate (TCP, $Ca_3(PO_4)_2$) and biphasic calcium phosphate (BCP, HA/TCP composites), have been widely used in tissue engineering (TE) and drug delivery applications due to their excellent biocompatibility, bioactivity and biodegradability [9]. Among the various CaP phases, synthetic HA is one of attractive materials for bone regeneration owing to its similarity in composition to the mineral phase of native bone. Meanwhile, HA has excellent affinity to biological substances, such as proteins, enzymes, cells and viruses. Recently, the design and synthesis of different particle morphologies and sizes of HA for drug delivery applications have attracted considerable attention [10–19]. In similar circumstances, β-TCP is another ideal material for biomedical applications because of its excellent biological characteristics, such as osteoconductivity, bioresorbability and bone-bonding ability. Moreover, recent scientific reports have indicated that β-TCP offers significant opportunities to be used as a carrier for the controlled release of drugs and biomolecules [20,21]. The BCP materials consisting of a mixture of HA and β-TCP have very different dissolution properties due to their different chemistry and crystalline structures. As a consequence, they may provide different drug loading and release properties. Previous studies have demonstrated that BCP consisting of HA and β-TCP has better adsorption properties and osteoinduction than single phase HA and β-TCP due to its controllable degradation rate and more effective bone regeneration ability [22,23]. Therefore, BCP also offers significant opportunities to be used as a carrier for the controlled release of drugs.

To the best of our knowledge, the use of CaP particles with different compositions as a controlled release system has not been reported in literature. Since the dissolution properties of CaP carriers varied depending on their phase purity and composition, it is interesting to study how protein loading and release from HA, BCP and β-TCP can be controlled. The purpose of this study was to prepare CaP (HA, β-TCP and BCP) powders with different phase compositions by a solution combustion method. Then the effects of phase compositions on drug loading and release capacities were further investigated.

2. Materials and methods

2.1. Synthesis of CaP particles

The synthesis of CaP particles via the solution combustion method was modified from our previous research [24]. All chemicals used

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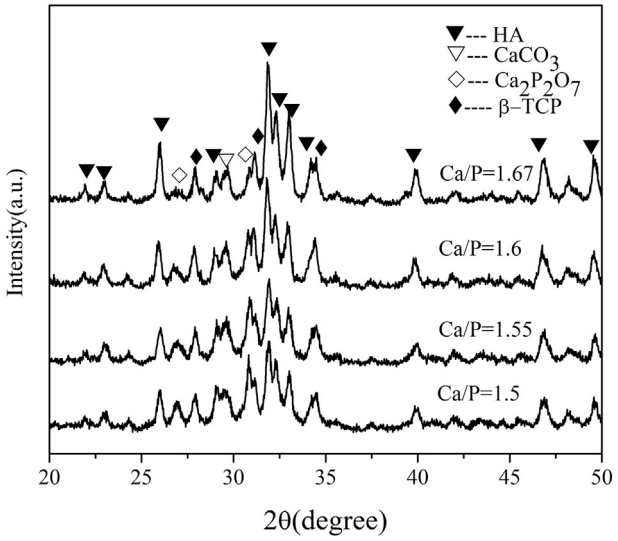

Fig. 1. XRD pattern of combustion products obtained without further sintering.

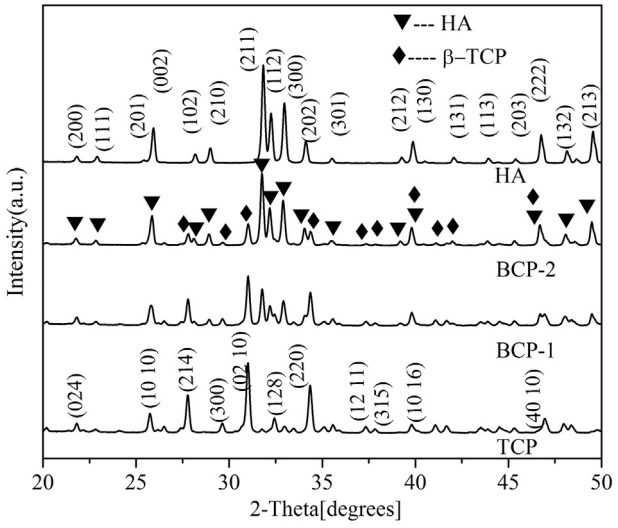

Fig. 2. XRD patterns of the samples sintered at 1150 °C.

in this research were analytical grade and used without future purification. In a typical synthesis, 0.01 mol of $Ca(NO_3)_2 \cdot 4H_2O$ and different amounts of $NH_4H_2PO_4$ were first dissolved in 20 mL of deionized water with a Ca/P molar ratio of 1.5, 1.55, 1.6, and 1.67 (marked as TCP, BCP-1, BCP-2 and HA, respectively). 0.01 mol of $C_6H_8O_7$ and 0.05 mol of NH_4NO_3 were added into the mixture solution and continuously stirred and evaporated at 80 °C to form a colloidal transparent solution. With sustained heating, the colloidal solution swelled rapidly and introduced the vigorous combustion reaction. The spontaneous combustion lasted for about 10–20 s and gave rise to the fluffy products. The combustion products were collected and then sintered at 1150 °C for 3 h.

2.2. Characterization of CaP samples

The phase analysis was described by X-ray diffraction (Dmax-2200PC) with CuKα radiation (40 kV, 40 mA), a step size of 0.02° and a present time of 4 s. The Rietveld analysis was performed on the diffraction patterns via the program MAUD. The morphology was monitored by a field emission scanning electron microscope (FEI nova nano-SEM 450). Transmission electron microscopy (TEM) was obtained by a JEOL JEM-2100 electron microscope.

2.3. Drug loading and release

Bovine serum albumin (BSA) was selected as the model drug. Typically, 0.625 g of each sample was added into 50 mL of the BSA solution with a concentration of 28 mg mL^{-1}, and dispersed at 30 °C for 24 h with a shaking bath. The BSA loaded samples were separated by centrifugation, washed with distilled water, then dried under vacuum for 48 h, and marked as TCP-BSA, BCP-BSA-1, BCP-BSA-2 and HA-BSA, respectively. The in vitro delivery of BSA was performed by immersing 0.45 g of the sample into 45 mL of simulated body fluid (SBF) with slow stirring under the immersing temperature of 37 °C. The release medium solution (4 mL) was taken out for UV–vis analysis at given time intervals and replaced with the same volume of fresh SBF which was preheated to 37 °C. FTIR spectra (Nicolet 380) were used to determine the protein secondary structure within the scanning range 400–4000 cm^{-1}. The amounts of BSA adsorbed onto the samples were monitored by TG analyzer (TGA/SDTA851^e) in an ambient atmosphere with the heating rate of 10 °C/min. The concentration of BSA released at certain set times was determined

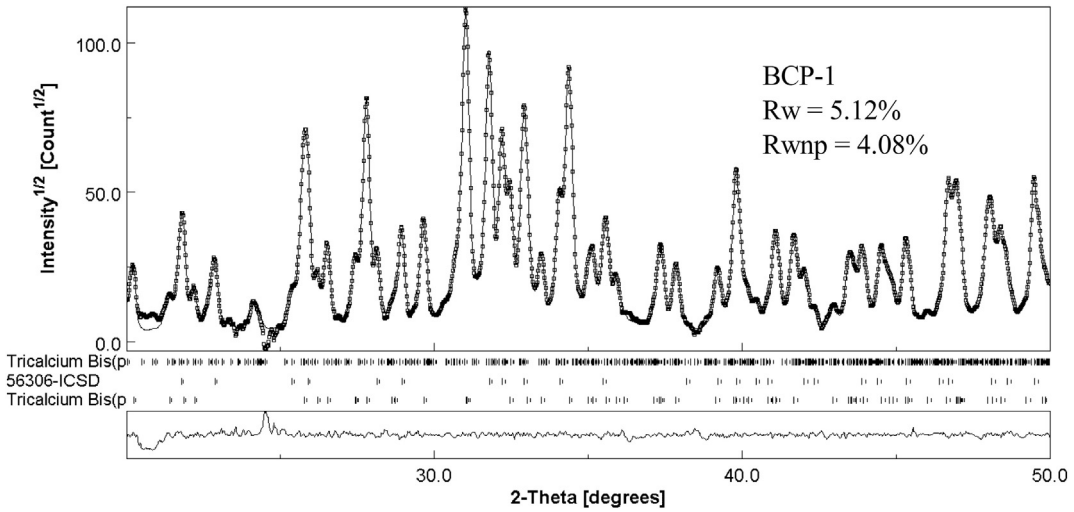

Fig. 3. Rietveld analysis of sample BCP-1.