Preparation and characteristics of zinc and strontium co-doped hydroxyapatite whiskers

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Abstract. Zn and Sr ions co-doped hydroxyapatite (Ca₁₀(PO₄)₆(OH)₂, HA) whiskers were synthesized by a hydrothermal homogeneous precipitation method. The morphology, structure and the phase composites of the products were characterized by XRD and SEM. The results showed that Zn²⁺ and Sr²⁺ partially substituted for Ca²⁺ in the HA crystal, resulting in lattice distortion and low crystallinity. When the doping ratio of Zn²⁺ in the solution containing Zn²⁺ and Sr²⁺ was more than 3 mol%, the shorter whiskers with low crystallinity appeared in the products.

1. Introduction

Hydroxyapatite (Ca₁₀(PO₄)₆(OH)₂, HA) is an ideal substitute for hard tissue due to its composition that is similar to human bone and teeth [1]. Compared with other materials for hard tissue substitute, such a material has good biocompatibility and bioactivity [2-4], showing a strong corrosion resistance and good osseointegration behavior with bone tissue. It can also enhance healing ability of bone tissue without toxic side effects. However, the mechanical strength of hydroxyapatite is poor. Thus, the preparation of HA whiskers has been expected to provide an effective route to improve its application performance through whisker toughening technique [5].

Biological apatites are usually calcium-deficient, the hydroxyapatite crystals in natural bone therefore has lattice defects, in which Ca ions along a six-fold c-axis are easily replaced by divalent metal ions, such as Zn²⁺, Cu²⁺, Sr²⁺ and so on [6]. The crystallinity and structural stability of synthetic HA materials are higher than those of natural bone apatite, which is not conducive to the growth of bone and the degradation of synthetic materials [7]. Adding these trace elements contained in the natural bone into the synthetic hydroxyapatite can reduce the crystallinity and structural stability of HA, and also improve the degradation and biological performance of HA. Sr²⁺ is a necessary trace element in bone, which can stimulate the formation of bone collagen, increase the proliferation of osteoblasts, decrease the number and activity of osteoclasts, reduce bone resorption and stimulate new bone formation. Substitution of Sr²⁺ for Ca²⁺ has been proved to enhance bone regeneration ability [8]. Zn²⁺ is the most abundant trace metal in bone, and can also promote proliferation of osteoblasts and selectively inhibit the activity of osteoclasts [9,11]. Zn²⁺ doped with HA has been found to be able to cause the lattice distortion, greatly giving rise to the change in the crystallinity, solubility and biodegradability of the HA materials, which effectively improve the biological properties and antibacterial capacity of Zn-HA [12]. Therefore, the preparation and characteristics of HA whiskers
doped with Zn$^{2+}$ and Sr$^{2+}$ ions is of great significance to develop a novel biomaterials with good bone inducing and antibacterial activity and to expand the clinical application of HA-based bioactive ceramics. Although the single doping of these two elements has been systematically studied, no literature on double ion doped HA was found. This paper mainly studies the preparation technology of Sr$^{2+}$, Zn$^{2+}$ co-doped HA whiskers, and explores the influence of Sr$^{2+}$, Zn$^{2+}$ doping on the crystal structure and morphology of HA whiskers.

2. Materials and Methods

2.1. Preparation of metal ions doped HA.
The whiskers doped with Sr and Zn ions were prepared by hydrothermal homogeneous precipitation according to the reaction equation as follows:

$$(10-x)\text{Ca}^{2+} + x\text{M}^{2+} + 6\text{PO}_4^{3-} + 2\text{H}_2\text{O} \rightarrow \text{Ca}_{(10-x)}\text{M}_x(\text{PO}_4)_6(\text{OH})_2 + 2\text{H}^+ \ (0 \leq x \leq 10)$$

In the formula: M$^{2+}$ = Sr$^{2+}$, Cu$^{2+}$

According to the stoichiometric ratio of (Ca + Me)/P = 1.67, aqueous solution containing 0.1 mol/L NH$_4$H$_2$PO$_4$ and 0.06 mol/L mixing solution of Ca(NO$_3$)$_2$·4H$_2$O and strontium and zinc nitrate were firstly prepared under constant stirring with teflon-coated magnetic stirring bar. 1 mol/L C$_2$H$_5$NO was added into the mixed solution and its pH was adjusted to 3.00 by addition of 1 mol/L HNO$_3$ and 1:1 ammonia under constant stirring. The prepared solution was put into a high-pressure reactor, and kept for 10 hours at 180 ℃ to obtain Sr/Zn-HA whiskers. Sr&Zn-HA whiskers were obtained by filtrating, washing several times and drying at 80 ℃.

2.2. Materials characterization.
The crystal structure and phase composition were analyzed by X-ray diffractometer (D8 Advance, Brook AXS, Germany) and Fourier transform infrared spectroscopy (FTIR, Nicolet 6700, Thermo electron Scientific Instruments, USA); the morphology of the samples was observed by field emission environment scanning electron microscope (FE-SEM, Quanta FEG 450*, FEI, Hong Kong, China).

3. Results and discussion

3.1. Effect of Zn$^{2+}$/Sr$^{2+}$ doping ratio.
Fig. 1 showed the XRD pattern of Sr and Zn doped HA (Sr&Zn-HA) with a total doping concentration at 8 mol%. When [Zn$^{2+}$] ≤ 4 mol%, the diffraction peak of the samples was consistent with those of the standard XRD pattern of HA (PDF 09-0432), and there was no impurity phase; the fewer second phase that was assigned to CaZn$_2$(PO$_4$)$_2$·2H$_2$O appeared in the products, when [Zn$^{2+}$] ≥ 5 mol%. Compared with the standard XRD pattern of HA, the strongest peak appeared on (300) crystal plane instead of (211) crystal plane, indicating that the Sr&Zn-HA crystal grew along the c axis, which accorded with the crystal structure characteristics of HA whiskers. With the increase of doping concentration of Zn$^{2+}$, the tendency of whiskers growing along the c axis decreased first and then increased when the doping concentration of Zn$^{2+}$ was more than 6 mol%, and the XRD diffraction intensity ratio of (300) crystal plane and (211) crystal plane (I$_{(300)}/I_{(211)}$) was the smallest when Zn$^{2+}$ doping was 6 mol%.

The morphology of Sr&Zn-HA with a total doping concentration at 8 mol% was showed in Fig.2. With the decrease of Zn$^{2+}$ content, the percentage of whiskers in the field of vision increased. The degree of agglomeration also decreased, which corresponds to the result of XRD in Fig. 1.

3.2. Effect of doping amount of Sr and Zn ions.
As shown in Fig.3, the main phase of the sample remained HA, but the X-ray diffraction intensity ratio of I$_{(300)}/I_{(211)}$ of Sr&Zn-HA obviously changed with the ions doping concentration. With the increase of ions co-doping concentration, the intensity of the diffraction peak gradually decreased and the position of the diffraction peak gradually offset to a small angle due to the relatively large concentration of Sr$^{2+}$. 

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Since the radius of Sr\(^{2+}\) was larger than those of Ca\(^{2+}\) and Zn\(^{2+}\), which resulted in an increase in lattice constant after incorporating into the crystal lattice. In addition, the diffraction intensity of the (300) crystal plane was found to be weakened gradually with the increase of doping amount, indicating that the tendency of Sr&Zn-HA whiskers growing along the c axis was weakened. The crystallinity of 5mol%, 8 mol% and 10 mol% Sr&Zn-HA is 89.25 %, 77.93 % and 71.58 %, respectively. This may be due to the incorporation of ions into the crystal lattice, which inhibits the crystallinity of the HA crystals.

SEM observation showed that the length of Sr&Zn-HA whiskers doped with 5 mol%, 8 mol% and 10 mol% Sr and Zn ions were about 39-167 μm, 40-146 μm, 29-117 μm, respectively, and the proportion of whiskers decreased with the increase of ion co-doping concentration. This indicated that the incorporation of Sr\(^{2+}\) and Zn\(^{2+}\) into HA whiskers not only caused lattice distortion, but also affected the crystallinity and morphology.

![XRD patterns of 8 mol% doped Sr&Zn-HA whiskers](image1)

![SEM images of 8 mol% doped Sr&Zn-HA whiskers](image2)

Fig.1 XRD patterns of 8 mol% doped Sr&Zn-HA whiskers

Fig.2 SEM images of 8 mol% doped Sr&Zn-HA whiskers

a: Zn-7; b: Zn-6; c: Zn-5; d: Zn-4; e: Zn-3; f: Zn-1
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4. Summary
Sr&Zn-HA whiskers could be prepared through hydrothermal homogeneous precipitation. The phase composition and morphology of Sr&Zn-HA whiskers were affected by both the concentration and ions doping ratio of the Sr$^{2+}$ and Zn$^{2+}$ ions. When the total amount was 8 mol%, and Zn$^{2+}$ doping ratio less than 4 mol%, Sr&Zn-HA whiskers without a heterophase can be obtained. As the doping concentration increased, the crystallinity of the sample decreased and the percentage of whiskers decreased.

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