

Fabrication of hydroxyapatite microspheres with poor crystallinity using a novel flame-drying method

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Abstract: Three kinds of hydroxyapatite (HA) microspheres were prepared using a flame-drying method. The morphologies and selected area diffraction of HA slurries were determined by TEM. The phase composition, and morphologies were studied by TEM, X-ray diffractometer (XRD), scanning electron microscope (microstructure, SEM), respectively. The TEM result shows that the slurries are composed of nano-particle HA. With the aging time of HA slurry prolonging, the morphology of HA particle changes from spherical ACP (amorphous calcium phosphate) to rod-like acicular nano-crystal morphology. Low temperature can also cause the crystallinity degree of HA slurry decrease obviously. The XRD result shows that the crystallinity of HA microspheres prepared from three kinds of HA slurry is consistent with its corresponding slurry. The SEM result shows that the sphericity of the microspheres prepared by pure HA slurry without ammonia water is the best among three kinds of microspheres, then the HA slurry containing ammonia solution forms the hollow microspheres with open pore, and ice-water mixture slurry.

Key words: hydroxyapatite; poor crystallinity; porous microspheres; flame-drying

1 Introduction

Hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$), with similar chemical composition and crystal structure as mineral composition present in a biological hard tissue [1–3], has been widely used as an important biocompatible material. However, the use of HA with irregular morphology is limited due to its fragile nature of crystalline form. HA spheres have recently been developed because of the advantages, such as high specific surface area, good flow ability, excellent chemical and physical properties. In present, several fabricating microsphere methods, such as spray drying [4,5], high temperature melting [6], solid-in-water-in-solid emulsion and microemulsion [1,7] have been widely used, and these development have led to a renewed interest of HA powders in the high technology field [8,9]. However, the main attempt paid in the past years is to control the shape of HA powders, the crystal size, particle size distribution, porosity and crystallinity,

because both the mechanical performance and bioactivity of HA depend strongly on them.

In fact, the major component of the bone mineral is amorphous calcium phosphate (ACP) (65% (mass fraction) in young bone and 35% in adult bone), which is a precursor to crystalline HA. ACP was first synthesized in solution by POSNER et al [10,11] and it plays an important role in the biomineralization of bone because it is a precursor to crystalline bone apatite. The poor hydroxapatite and ACP can be used in various applications, such as coated implant, filler and bone cements, due to its good bioactivity and excellent biodegradability [12,13]. The formation methods of poor crystalline HA and ACP have been reported recently, such as chemical synthesis in aqueous solution with stabilizer [14], organic-water synthesis [15], organic-mediated sol-gel synthesis [16], quenching of melted calcium phosphate and physical deposited techniques. But the fabricating method of poor crystalline HA microsphere is rarely reported and the processes of these methods are complicated. In this work, a novel

flame-drying method was used to fabricate the poor crystalline HA microsphere. And the influence factors and the formation mechanism of porous HA microspheres were also researched.

2 Experimental

2.1 HA slurry synthesis

The precursor of HA microsphere phase was HA slurry prepared by wet method with diammonium hydrogen phosphate $[(\text{NH}_4)_2\text{HPO}_4]$ and calcium nitrate tetrahydrate $[\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}]$ with a Ca/P ratio of 1.67 in the presence of aqueous ammonia. During stirring, the white HA floccules could be observed in the mixed solution. Three kinds of HA slurry were fabricated and the parameters are listed in Table 1. One kind of HA slurry was heated for vaporizing the ammonia in it, which was defined as HA slurry without ammonia (NAHAs). After heating, NAHA was rinsed for eliminating the NH_4NO_3 and was aging for 48 h. HA slurry containing ammonia (CAHAs) was preserving the ammonia and NH_4NO_3 in slurry. CAHA was also aging for 72 h for using to next process. HA slurry under ice-water condition (IWHAs) was only stirring for 5 min for using to prepare the HA microsphere. The process of formation of HA phase can be described as the following reactions [17]:

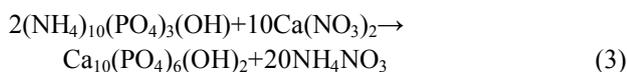


Table 1 Parameters of preparation of HA slurries

Samples	Stirring time/min	Aging time/h	Temperature of preparation/°C
NAHAs	120	48	Room temperature
CAHAs	120	72	Room temperature
IWHAs	5	–	Zero

NAHAs—HA slurry without ammonia; CAHAs—HA slurry containing ammonia; IWHAs—HA slurry under ice-water condition

2.2 Fabrication of HA microspheres

Flame-drying method was used to fabricate the HA microspheres. The flame denoted the fire of liquefied petroleum gas and oxygen. The HA slurries were directly sprayed into the flame via compressed air by a nozzle. The parameters of flame-drying are listed in Table 2.

2.3 Characterization

The microstructure morphologies and relevant

selected area diffraction (SAD) of the HA slurries were analyzed by H-800 transmission electron microscopy (TEM) operated at 200 kV. Phase composition of HA microspheres was determined by a D/max-γB X-ray diffractometer (XRD) operated at 40 kV, 100 mA and a scan speed of 4 (°)/min. JSM-6380 scanning electron microscope (SEM) with an acceleration voltage of 20 kV after Au film was deposited onto the samples was used to obtain the particle shape and surface morphologies of HA microspheres.

Table 2 Parameters of flame-drying method

Input slurry velocity/ ($\text{mL} \cdot \text{min}^{-1}$)	Nozzle diameter/ mm	Atomizing air pressure/ MPa	Flame pressure/ MPa	Flame temperature/ °C
120–150	2.5	0.6–0.8	0.2–0.4	About 500

3 Results and discussion

3.1 Microstructure of HA slurries

Figure 1 demonstrates the microstructures and relevant SAD patterns of different kinds of HA slurries. The microstructure of IWHAs, as shown in Fig. 1(c), is mainly the spherical particles with size of less 50 nm. The relevant SAD pattern shows that spherical particles are ACP [18]. While, the microstructures of HA slurry aged for a period of time (NAHAs and CAHAs) are rod-like acicular nano-particles. The relevant SAD patterns indicate that those nano-particles are low crystalline HA. And the bright rings of Figs. 1(a) and (b) can be indexed to (211) and (213), respectively. The results show that the aging time is the main parameter that affect the microstructures and crystallinity of HA slurry, which is consistent with some reports. For instance, several literatures proved that the crystallinity of HA increased with the aging time of HA slurry prolonging, and the morphology of HA particle was changed from spherical ACP to rod-like acicular nano-crystal morphology [18–20]. On the other hand, the preparation temperature maybe also affect the crystallinity of HA. It is concluded by Ref. [21] that the crystallinity of HA synthesized at 5 °C was lower than that of HA fabricated at 60 °C. These results illustrate that the low temperature can result in the slow diffusion of atoms and impede the HA crystal growth, which prevents the formation of crystalline HA or make it be minimum. Figure 1 also shows that the crystallinity of NAHAs and CAHAs has no obviously difference, but the length of acicular particles of CAHAs is increasing compared with that of NAHAs. It demonstrates that aging time of HA slurries can promote the HA crystal growth.

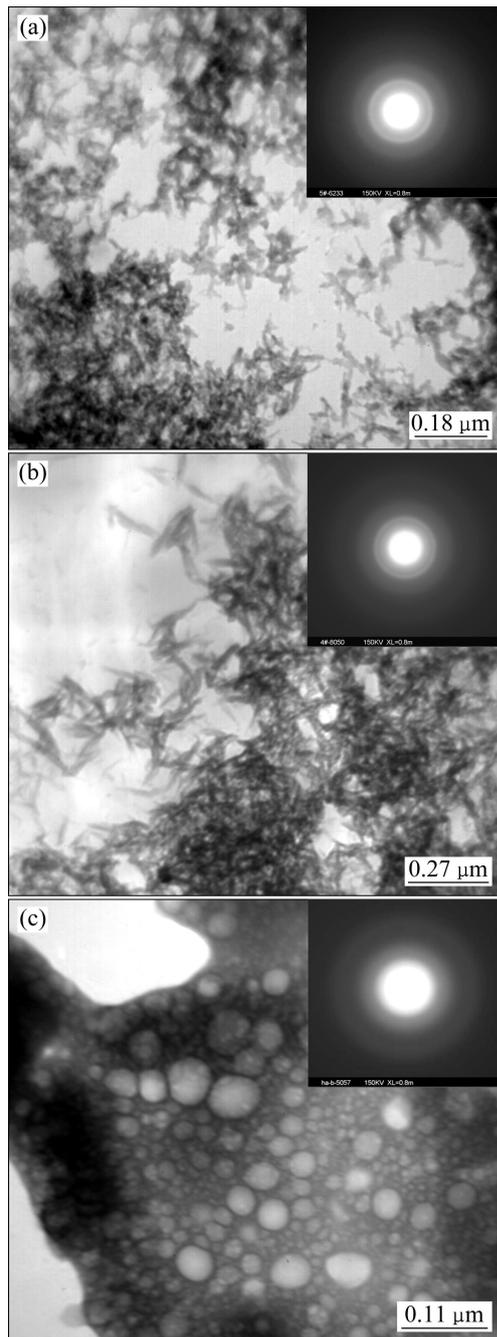


Fig. 1 TEM images and relevant SAD patterns of NAHAs (a), CAHAs (b) and IWHAs (c)

3.2 Phase composition of HA microspheres

Figure 2 shows the XRD patterns of HA microspheres fabricated by the flame-drying method. The diffraction of NAHAs (Fig. 2(a)) has narrower peak and higher intensity, indicating that the crystallinity of HA microsphere prepared by NAHAs (defined as NAHAM) is the lowest compared with that of the other two kinds of samples (defined them as CAHAM and IWHAM, respectively). The IWHAM has the lowest crystallinity, as shown in Fig. 2. These results show that

the crystallinity of HA microspheres prepared from three kinds of HA slurries is consistent with their corresponding slurries, as shown in Figs. 1 and 2. The reasons of these results can be explained by the formation mechanism of HA microspheres during the drying process. The formation of a solid HA microsphere involves three processes: 1) precipitation from solution (formation of solid phase); 2) crystallization (building up long-range order) within the solid, the two processes can be shown in reactions (4) and (5); 3) formation of agglomerates of HA microspheres by atomizing HA slurry into a flame zone. This process can cause instantaneously two phenomena: (a) Evaporation of the solvent contained in the slurry in the form of microdroplets by drying, (b) The formation of spherical agglomerates of HA microspheres by solidification. During the third process, the crystallization will simultaneously occur [22].

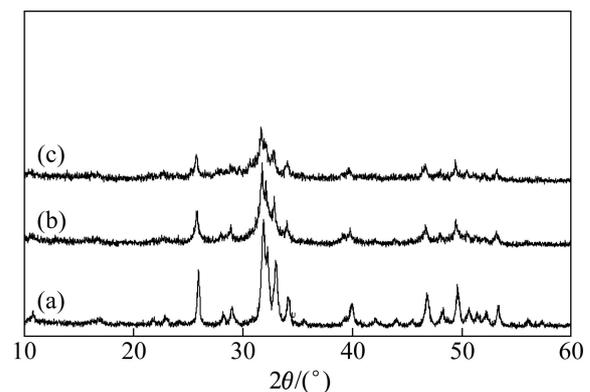
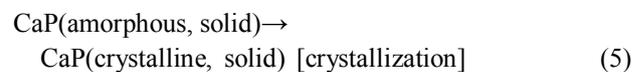
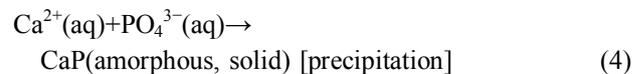


Fig. 2 XRD patterns of HA microspheres fabricated by flame-drying method from NAHAs (a), CAHAs (b) and IWHAs (c)

For IWHAM, the process of crystallization (reaction (5)) is very short because the slurry is only stirred about 5 min and no aging time and then immediately used to atomize into the flame. On the other hand, the low temperature also can prevent crystallization of HA. In the third process, the ACP particles instantaneously formed the microsphere and the crystallinity of HA had a little increase because of the high temperature of flame. The ammonia and NH_4NO_3 containing in the CAHAs will be changed into gases due to high temperature. These decomposed gases maybe affect the crystallization of HA microspheres during formation of agglomerates. For NAHAM, its crystallinity is markedly increasing

compared with relevant slurry.

3.3 Morphologies of HA microspheres

The SEM images of HA microspheres prepared by different HA slurries are shown in Fig. 3. It shows that the particles are mainly spherical in shape, but the sphericity of the NAHAM (Fig. 3(a)) is the best compared with those of the CAHAM and IWHAM. Some hollow microspheres with open pore exist in the sample of CAHAM (arrows), as shown in Fig. 3(c). Its corresponding high magnificant image indicates that the sphere is an agglomerate of HA particles. The reason of formation of these microspheres with pore can be explained from the decomposed gases during flame-drying process. NH_4NO_3 and ammonia were decomposed due to high temperature, which can be

described as the following reactions:



At the beginning, for the CAHAM, the decomposed gases were distributed inside the dropwise liquid particle and the gases began to aggregate inside the liquid drop with the evaporation of the water content. When the aggregation reached a certain degree, the aggregated gases released suddenly and thus opening air holes were formed. The application of this microsphere with open pore will be further studied in the future. Besides, the sphericity of IWHAM is not very well, but some spheres in it are also very compacted like others, as shown in Fig. 3(f). It may be because the water containing in the HA slurry bead was evaporated quickly as the regional

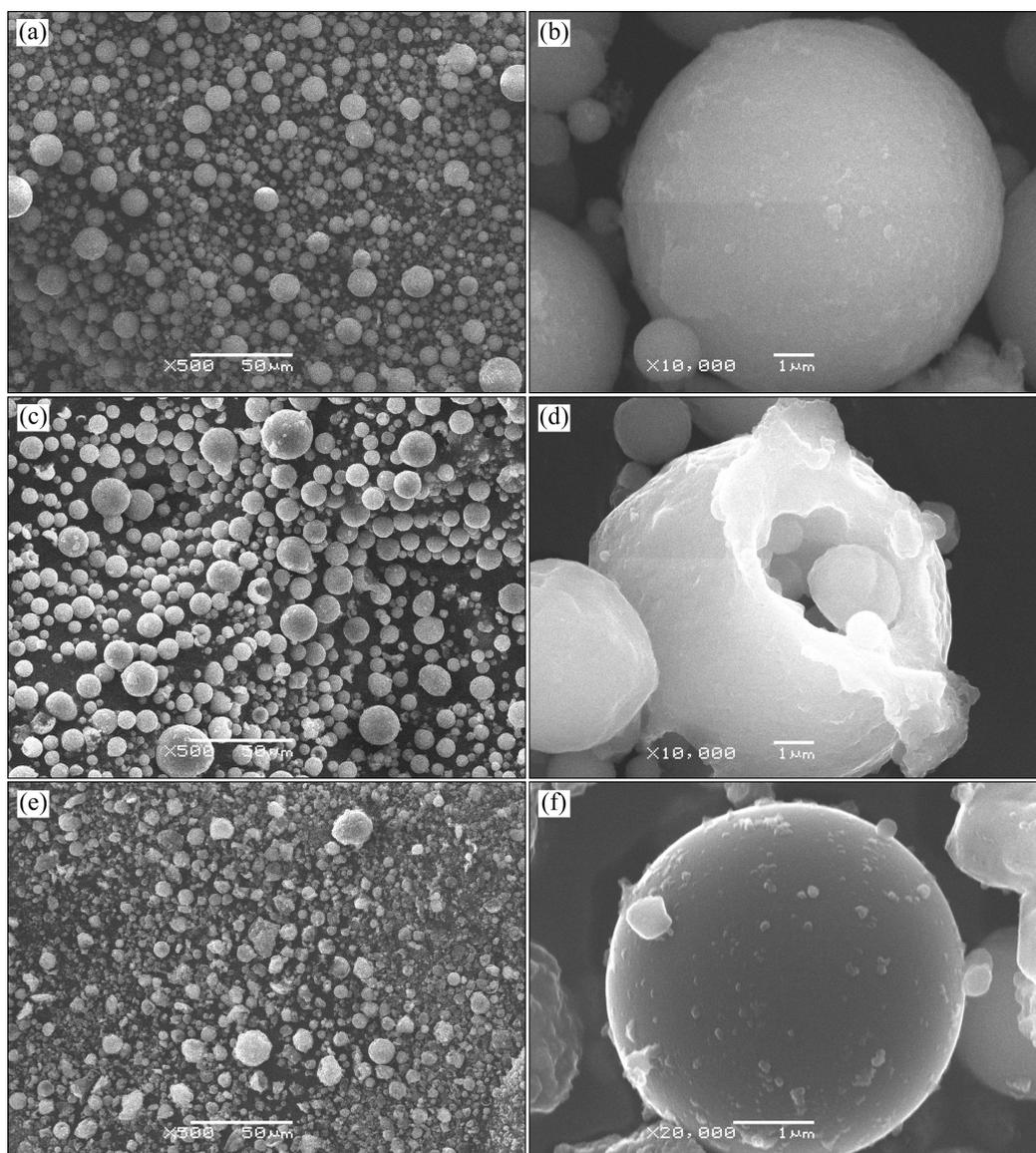


Fig. 3 SEM images of HA microspheres prepared by flame-drying method using different HA slurries: (a,b) NAHAM; (c,d) CAHAM; (e,f) IWHAM

higher temperature. However, most microspheres prepared by the IWHAs was the loose structure.

4 Conclusions

1) The HA microspheres with poor crystallinity can be fabricated by a novel flame-drying method. The reaction time of HA slurry will affect its properties, such as crystallinity and morphology. In addition, low temperature (0 °C) can result in the slow diffusion of atoms and impedes the HA crystal growth in the slurry. Hence, IWHAs contain more amorphous phase comparing with other two kinds of slurries.

2) The crystallinity of HA microspheres prepared from three kinds of HA slurry is consistent with its corresponding slurry. The crystallinity of NAHAM is the highest among the three HA microspheres, and that of IWHAM is the lowest.

3) During the flame-drying process, the gases decomposed by the impurity containing in the HA slurries can restraint crystallinity of HA microspheres, and form the hollow microspheres with open pore because of the decomposition gases evolution. The IWHAM has the loose structure because more gases are come out of from its dried slurry.

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火焰干燥法制备低结晶度羟基磷灰石微球

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摘要: 利用火焰干燥法将 3 种不同性质的羟基磷灰石(HA)料浆分别制得不同结构的微球。通过透射电镜(TEM)、X 线衍射仪(XRD)和扫描电镜(SEM)分别研究不同磷灰石料浆中颗粒的微观结构、所得 HA 微球的相组成及其表面形貌, 进而分析料浆性质及干燥工艺参数对所得 HA 微球结构的影响。TEM 结果表明, 随着磷灰石料浆反应陈化时间的延长, 其中的纳米颗粒形貌由球状的非晶态转变为针状的纳米晶态; 低温条件下 HA 料浆的结晶程度明显降低。XRD 结果表明: 火焰干燥所得 3 种 HA 微球的结晶程度和其对应料浆的结晶程度一致。SEM 结果显示: 去氨水后的纯 HA 料浆经火焰干燥所得微球的球形度最好, 含有氨水的 HA 料浆所得微球具有表面开口的空心结构, 而冰水混合物料浆所得 HA 微球球形度最差。

关键词: 羟基磷灰石; 低结晶度; 多孔微球; 火焰干燥

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