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Preparation of nanosized hydroxyapatite particles at low temperatures

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Hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$, HAp] has been used to manufacture biomaterials for hard tissue repair and replacement, because of its excellent biocompatibility with the human organism as well as its close similarity to the main inorganic constituent of bone in both composition and structure [1, 2]. Numerous processes have been developed for the preparation of HAp powders, which include chemical co-precipitation [3], sol–gel process [4], spray-pyrolysis [5], hydrothermal syntheses [6] and emulsion techniques [7]. The preparation of HAp powders via the above methods is usually carried out at the condition of heating or with the help of after-heat-treating, which excludes the application of these methods to preparing hydroxyapatite/collagen (HAp/Col) composites, because collagen will lose its bioactivity at the temperature higher than 40 °C.

Collagen is the major organic component of bone tissue. It has an improved bioactivity and osteoconduction compared with HAp. The combination of collagen with HAp particles can enhance the mechanical properties and bioactivity of the composite formed. So, many researchers tried to synthesize the HAp/Col composite at low temperatures [8, 9]. The key step in HAp/Col composite synthesis is the growth of HAp on a collagen matrix in aqueous medium. Up to now, most of researchers have synthesized crystallite HAp particles using the reaction of calcium hydroxide ($Ca(OH)_2$) and phosphoric acid (H_3PO_4) at temperatures ≤ 40 °C [8, 10]:

$$10Ca(OH)_2 + 6H_3PO_4 = Ca_{10}(PO_4)_6(OH)_2 + 18H_2O$$

In this method, water suspension of $Ca(OH)_2$ and H_3PO_4 aqueous solution were simultaneously and gradually added into a reaction system, and the pH of which was maintained at a fixed value. HAp particle formation occurred during the mixing process. Although there is no other subsidiary product formed except water in this process, the pH of the reaction system must be controlled strictly during the course of preparation.

In the present work, a simple precipitation process, using ammonium hydrogen phosphate ($(NH_4)_2HPO_4$) instead of phosphoric acid (H_3PO_4), was proposed to prepare nanosized crystallite HAp particles at low temperatures (<40 °C). The effect of mole ratio of $Ca(OH)_2$ to $(NH_4)_2HPO_4$ used on the Ca/P ratio of HAp particles obtained was examined and the product was characterized.

$Ca(OH)_2$ and $(NH_4)_2HPO_4$ were used as starting materials. Pure $Ca(OH)_2$ was synthesized from hydration of calcium oxide (CaO) obtained from heat decomposition of calcium carbonate ($CaCO_3$) at 1050 °C for 3 hr. $Ca(OH)_2$ was dispersed in distilled water to form 0.5 mol l^{-1} suspension, into which 0.3 mol l^{-1} $(NH_4)_2HPO_4$ aqueous solution was added dropwise in a given mole ratio of $Ca(OH)_2$ to $(NH_4)_2HPO_4$ under stirring. The precipitation was carried out at the temperature of 37 ± 0.5 °C with the final pH of the resulting slurry being higher than 10. The system was further stirred for another 2 hr after completion of the precipitation. The as-prepared powder was filtrated, thoroughly washed with deionized water and then dried at room temperature under vacuum.

The Ca/P ratio in as-dried HAp powders was calculated from the mass contents of Ca and P in the powders determined by chemical analysis. The HAp powders were dissolved in a HCl aqueous solution. The P content was determined using quinoline phosphomolybdate ($(C_9H_7N)_3H_3PO_4{\cdot}12MoO_3$) volumetric method, and the Ca content was determined via $KMnO_4$–titrating $C_2O_4{}^{2-}$ contained in CaC_2O_4 precipitation formed by adding $(NH_4)_2C_2O_4$ aqueous solution. Characterization of the as-dried HAp powders was carried out by X-ray diffraction (XRD) with CuKα (35 kV, 30 mA, scanned at 6° min^{-1}) radiation using a Rigaku D/MAX-IIIB diffractometer, infrared (IR) analysis on HAP/KBr pellets with a Nicolet Nexus 470 FTIR spectrometer, and transmission electron microscopy (TEM) imaging using a Jeol JEM-2010 transmission electron microscope. The specific surface area of the as-dried powder was determined by nitrogen absorption analysis (BET) using a NOVA 1000e Surface Area & Pore Size Analyzer. Samples were degassed at 150 °C for 2 hr under vacuum prior to analysis.

The chemical reaction for this synthesis process may be expressed as follows,

$$10Ca(OH)_2 + 6(NH_4)_2HPO_4 = Ca_{10}(PO_4)_6(OH)_2 \downarrow + 12NH_3 + 18H_2O$$

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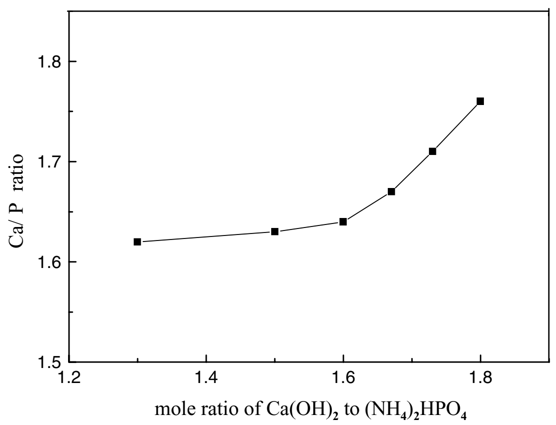

Figure 1 Variation of Ca/P ratio of as-dried HAp powders with the mole ratio of $Ca(OH)_2$ to $(NH_4)_2HPO_4$.

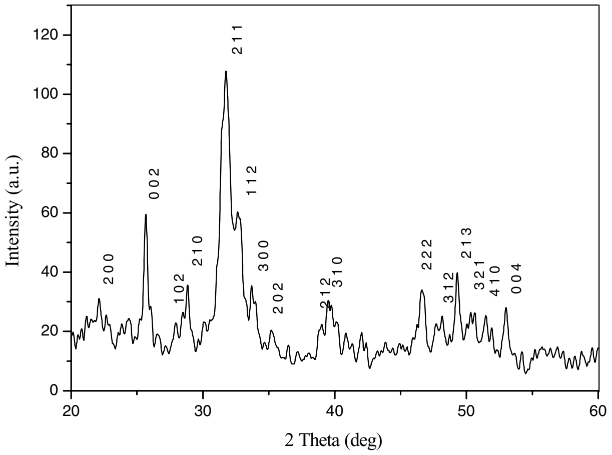

Figure 2 XRD pattern of as-dried HAp powder.

The mole ratio (R) of $Ca(OH)_2$ to $(NH_4)_2HPO_4$ used in the process of precipitation has significant influence on the Ca/P ratio of HAp powders formed. As shown in Fig. 1, the Ca/P ratio increased slowly with R increased from 1.3 to 1.6 and rapidly with R increased from 1.6 to 1.8. When the R was 1.67, the HAp powders obtained had the Ca/P ratio of 1.67, which is consistent with the Ca/P ratio in stoichiometric HAp. The Ca/P ratios of the HAp powders synthesized at $1.3 < R < 1.67$ were less than the stoichiometric ratio, which indicated that the HAp particles formed at these conditions were calcium deficient. The HAp powders synthesized at $1.67 < R < 1.80$ had the Ca/P ratios higher than 1.67, which was caused by the presence of unreacted calcium hydroxide contained within the HAp powders.

Fig. 2 shows the XRD pattern of the as-dried HAp powders synthesized at $R = 1.67$. It can be seen that the as-dried powders have a crystallized apatite structure and exhibit a diffraction pattern that matches the standard for HAp [11]. No X-ray evidence can be found for the existence of other calcium phosphate phases in the powders. Peak analysis of the (2 1 1) reflection using the Scherer formula ($L = 0.9\lambda/B\cos\theta$, where λ is the wavelength of the X-ray, B the full-width at half maximum, and θ the Bragg angle) predicts the crystallite size of 15 nm.

Fig. 3 shows the FT-IR spectrum of the as-dried powders synthesized at $R = 1.67$. The bands at around 1092, 1042 and 602, 566 cm^{-1} correspond to the asymmetrical stretching (υ_3) and bending (υ_4) modes of PO_4^{3-} ions, respectively, while the bands at around 962 and 472 cm^{-1} correspond to the symmetric stretching modes (υ_1 and υ_2) of the PO_4^{3-} ions, respectively [1]. The bands at $1412{\sim}1450$ cm^{-1} could be due to CO_3^{2-} ions incorporated during synthesis. The band at 1630 cm^{-1} and the broadband centered at 3440 cm^{-1} are indicative of crystal water and surface absorbed water. The bands at around 3571 and 631 cm^{-1} are derived from stretching and vibrational modes of OH in HAp [12], the intensities of which are weak in the spectrum, suggesting that the as-dried HAp powders are poorly crystallized.

Fig. 4 shows the TEM micrograph of the as-dried HAp powders synthesized at $R = 1.67$. The powders are composed of aggregates of nanosized HAp particles of about 10–20 nm in size. The BET specific surface area of the HAp powders synthesized at $R = 1.67$ is 136 $m^2\ g^{-1}$, based on which the average particle size of 14 nm was estimated through the empirical equation $d = 6/(\rho S)$ (where d is the average grain size in micron, ρ, the density in grams per centimeter cube, and S the specific surface area in meter square per

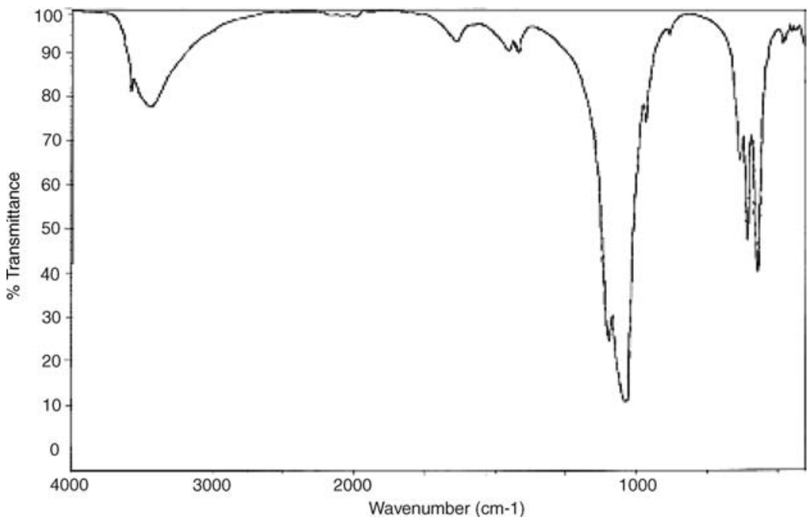

Figure 3 Infrared spectra of as-dried powder.

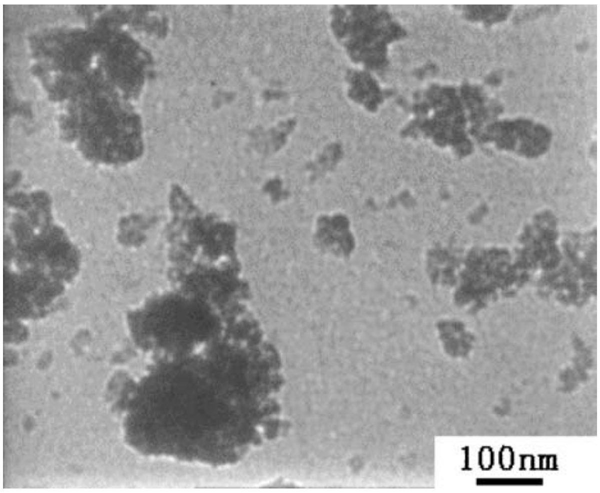

Figure 4 TEM micrograph of the as-dried HAp powder.

gram). This size value is in reasonable agreement with the results of the TEM observation and the crystallite size estimation by XRD.

In summary, nanosized crystallite hydroxyapatite powders, with particle size in the range of 10–20 nm and a BET specific surface area of 136 m^2 g^{-1}, can be prepared through the reaction of $Ca(OH)_2$ and $(NH_4)_2HPO_4$ at temperature of 37 °C. This method, which has the characteristic of easy control of preparing conditions, provides a new way to synthesize nanosized HAp particles at low temperatures and may find application in manufacturing HAp/Col composites.

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