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Preparation and characterization of nano-hydroxyapatite/poly(vinyl alcohol) hydrogel biocomposite

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Nano-hydroxyapatite (n-HA) was used to make a new hydrogel biocomposite with poly(vinyl alcohol) (PVA) by a unique technique. Fourier transform infrared absorption spectra (IR), transmission electron microscopy (TEM), X-ray diffraction (XRD), thermogravimetric analysis (TG) and burning test were used to test the physical and chemical characteristics of the composite. Chemical binding between inorganic n-HA and poly(vinyl alcohol) was investigated and discussed. The results showed that the composite had good thermal stability and homogeneity. The n-HA crystals were uniformly distributed in the polymer matrix. The improved n-HA/PVA hydrogel could be used as an artificial articular cartilage, showing a promoting prospect. © *2004 Kluwer Academic Publishers*

1. Introduction

One of the most prevalent approaches to treat severe cartilage degeneration is joint replacement. Other methods are debridement, transplantation of osteochondral allografts or chondrocytes [1]. The success of total joint arthroplasty during the past 30 years is largely due to the use of ultra-high molecular weight polyethylene (UHMWPE) as a bearing surface. However, wear does occur in UHMWPE and sometimes can be excessive in younger and more active patients [2].

PVA hydrogels (PVA-H) resemble organic tissue and have biocompatibility as well as a high elastic modulus even though their water content is very high. PVA hydrogels have been employed in several biomedical applications including drug delivery, contact lenses, artificial organs, wound healing, and cartilage etc. [3–7]. PVA-H has been proposed as promising biomaterials to replace diseased or damaged articular cartilage. However, regarding its clinical application, some problems still remain. The first problem is the durability of PVA-H [8]. Attempts to improve hydrogel properties for load-bearing biomedical applications have included the introduction of composite materials such as rubber or glass, the use of cross-linking agents, and the use of freeze thawing procedures to induce partial crystallinity [9–11]. The other major problem in clinical application is the articular cartilage fixation method. Since PVA-H itself does not adhere to tissue, long-term fixation of PVA-H implant by sutures is difficult [8].

Therefore, a complex type artificial articular cartilage consists of PVA-H and a tissue-inducing material. Hydroxyapatite (HA) ceramic has already been used in the clinic for filling of bone defects due to its good biocompatibility and bioactivity. It can form bone-bonding with living tissue through osteoconduction mechanism [12–14]. However, the brittleness and low fatigue strength in the physiological environment limit its use [15, 16].

In this paper, nano-hydroxyapatite/poly(vinyl alcohol) hydrogel (n-HA/PVA-H) is prepared. This biomaterial will be easy to adhere to tissue and fix in site for a long-term. This biomaterial can be easily molded into customized anatomic shapes because it is gelatinous prior to the freeze/thaw processing. This composite is a very promising material for use in artificial articular cartilage.

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2. Materials and methods

2.1. Preparation of n-HA

$$10Ca(NO_3)_2 + 6(NH_4)_3PO_4 + 8NH_4OH \longrightarrow Ca_{10}(PO_4)_6(OH)_2 + 20NH_4NO_3 + 6H_2O$$

Calcium nitrate and ammonium phosphate were separately dissolved in aqueous solution. Calcium nitrate solution was dropped slowly into the ammonium phosphate solution with stirring and heating at 70°C. The pH value of solution was kept between 10 and 12 by adding ammonium hydroxide. The apatite precipitation in water solution was treated hydrothermally in an autoclave at 140°C under 0.3 MPa for 3 h. After treatment, the apatite precipitation became n-HA crystals [17].

2.2. Preparation of composite

n-HA/PVA-H was produced as follows: PVA was added into n-HA crystal slurry (from 5 to 20 wt%) with heating and stirring for 6–8 hrs to get the n-HA and PVA composite solution. The n-HA /PVA-H were prepared by exposing n-HA and PVA composite solutions to repeated cycles of freezing at −20°C and thawing at room temperature for crystallization and cross-linking of PVA molecules. The obtained composite gel was milk white. The n-HA:PVA:H_2O ratios (wt%) of prepared composites can be changed. After drying in a vacuum oven at 80°C for 48 h and pulverizing, n-HA/PVA-H composite particles were obtained.

Poly(vinyl alcohol) (PVA) is manufactured by Chongqing Beipei Chemical Co. Ltd., P. R. China. (Hydrolysis degree 99%, residual acetate groups content 0.13%, and a degree of polymerization of 1700 ± 50). The calcium nitrate, ammonium hydroxide and ammonium phosphate were from Chengdu Chemical Agent Co. Ltd., P. R. China, AR grade.

2.3. Test of n-HA and composites

According to the n-HA content, the gel samples were classified into three groups (I, II, III). Samples were dehydrated in a vacuum oven at 80°C for 48 h and then weighed with a standard laboratory balance to determine the water content. The water content of n-HA/PVA-H was calculated using the expression:

$$H_2O\ (\text{wt\%}) = \frac{(\text{Weight of hydrated gel}) - (\text{Weight of dried gel})}{(\text{Weight of hydrated gel})}$$

After samples were dried in a vacuum oven, the pyrolysis experiment was conducted in a muffle furnace at 900°C for a period of 4 h. After the sintering, the samples were immediately cooled to room temperature inside the desiccator. The n-HA content of n-HA/PVA-H was calculated from the equation:

$$\text{n-HA (wt\%)} = \frac{\text{Weight of n-HA}}{\text{Weight of hydrated gel}}$$

The n-HA content of dried n-HA/PVA-H was calculated from the equation:

$$\text{n-HA (wt\%)} = \frac{\text{Weight of n-HA}}{\text{Weight of dried gel}}$$

Transmission electron microscopy (TEM) was employed to detect the morphology of the n-HA crystal and that in composite particles. Fourier transform infrared absorption spectra (FT-IR) were used to determine the bonding between the inorganic phase and the polymer phase. X-ray diffraction (XRD) was used to detect the phase composition and crystallinity of composite particles. Thermogravimetric analysis (TG) was carried out on 10 mg samples, flowing nitrogen at 100×10^{-6} m^3/min and heating rate of 10°C/min between 25 and 600°C using Seiko EXTAR6000 TG/DTA630 (Seiko Instruments Inc.).

3. Results and discussion

3.1. n-HA content by burning test

The n-HA contents are given in Table I. It can be seen that the content variation obtained for each test specimen was very small. For this reason, n-HA crystals can be regarded as essentially randomly distributed within the composites.

3.2. Water content

The water content test was carried out by placing the specimens in a vacuum oven at 80°C for 48 h. Table II presents the water content data.

Articular cartilage is, in fact, a natural fiber-reinforced hydrogel composed of proteoglycans, type II collagen, and approximately 75% water by weight. It is the water, ions, and proteoglycans within the extracellular matrix that endow cartilage with its load-bearing properties. The n-HA/PVA-H composite may be synthesized to mimic the water content of articular cartilage and possess a low coefficient of friction, which is an important characteristic for lubrication of articular joints.

TABLE I n-HA content (wt%) in gel and dried gel

	I Group		II Group		III Group	
	Gel	Dried gel	Gel	Dried Gel	Gel	Dried gel
1	5.64	32.28	9.48	46.44	19.61	65.03
2	5.65	32.36	9.51	46.55	19.73	65.41
3	5.68	32.55	9.50	46.51	19.60	64.97
av.	5.66	32.40	9.50	46.50	19.65	65.14

TABLE II H_2O content (wt%) of n-HA/PVA-H composites

	I Group	II Group	III Group
1	82.54	79.51	69.81
2	82.58	79.50	69.88
3	82.50	79.51	69.84
av.	82.54	79.51	69.84

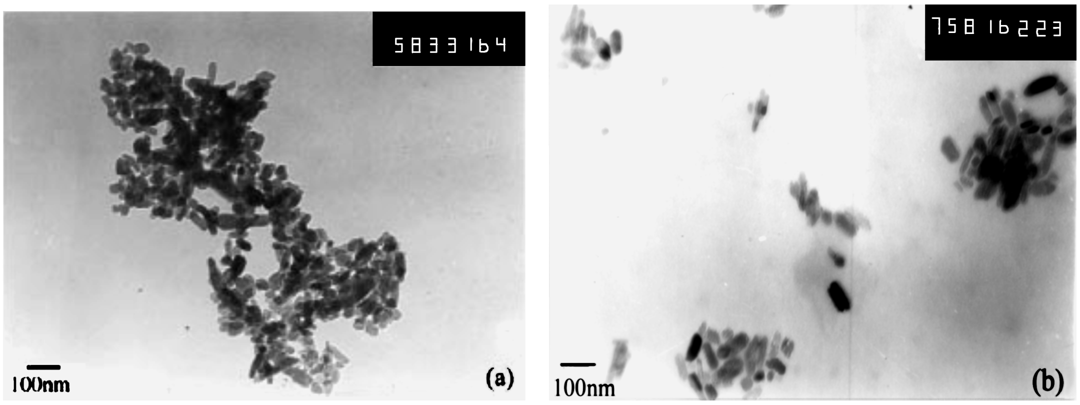

Figure 1 TEM photographs of n-HA crystals (a) and dried gel composites (b).

3.3. Particle size of n-HA and composite

Fig. 1 shows the TEM photographs of the n-HA crystals (a) and the composite powders (b). Fig. 1a indicates that n-HA crystals are in nanometer grade. The n-HA crystals in the composite particles shown in Fig. 1b also are in nanometer grade. PEG was used to modify n-HA crystals and improve their dispersion in the solution [18]. PVA and PEG are similar in chemical structure, which has many hydroxyl groups. PVA was used as modifier and dispersant. When using the n-HA/PVA composite to make gel products, the n-HA crystals can be ensured to disperse uniformly in the poly(vinyl alcohol) matrix.

3.4. XRD analysis

Fig. 2 shows relevant XRD patterns, in which 2a is for n-HA crystals, 2b is for PVA, and 2c is for n-HA/PVA-H composite particles. It is known that PVA is a semi-crystalline polymer in which high physical interactions present between the polymer chains, due to hydrogen bondings between the hydroxyl groups exist. Pure PVA in Fig. 2b, has an obvious diffraction peak at $2\theta = 20°$, and is characteristic for an orthorhombic lattice. After forming the composite, the crystallinity of the PVA phase decreased as shown in Fig. 2c, indicating that the crystal structure of PVA was changed after forming the composite with n-HA crystals. The hydrogen bondings in PVA contribute to its crystallinity. When forming the composite, the interface bonding formed between n-HA and PVA may result in a decrease in the number of hydrogen bonds, thus lessened PVA crystallinity.

3.5. IR analysis

FT-IR spectrum in Fig. 3a shows the presence of –OH (3571.14 and 632.93 cm^{-1}), H_2O (3600–2500, 1637.68 cm^{-1}) and HPO_4^{2-} (871.12 cm^{-1}) as well as CO_3^{2-} (1400–1500 cm^{-1}) in the n-HA crystals. For pure PVA in Fig. 3b, a broad band at 3400–3100 cm^{-1} due to O—H stretching vibration and another band at 2930 cm^{-1} assigned as C—H stretching vibration were observed. The adsorption peaks of 918 and 854 cm^{-1} represent C—C stretching [19]. The 1200–1000 cm^{-1} region contains a number of modes, which have been shown to be sensitive to the degree of crystallinity in PVA. The peak at 1147 cm^{-1} is crystallinity–dependent [20]. From the

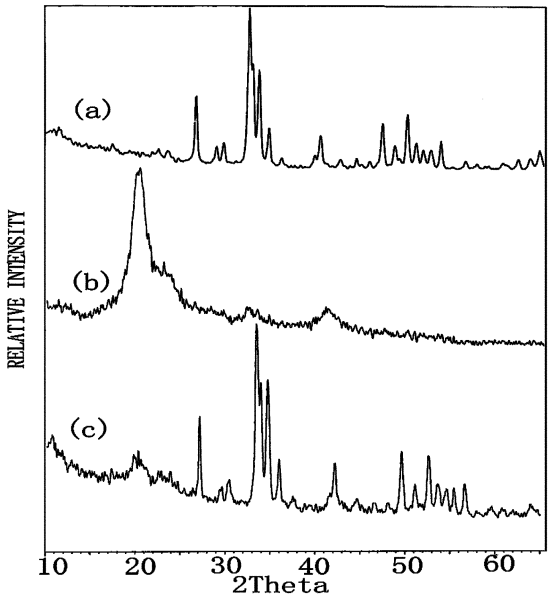

Figure 2 XRD patterns of n-HA crystals and dried gel composites: (a) n-HA crystals, (b) PVA, and (c) n-HA/PVA composite.

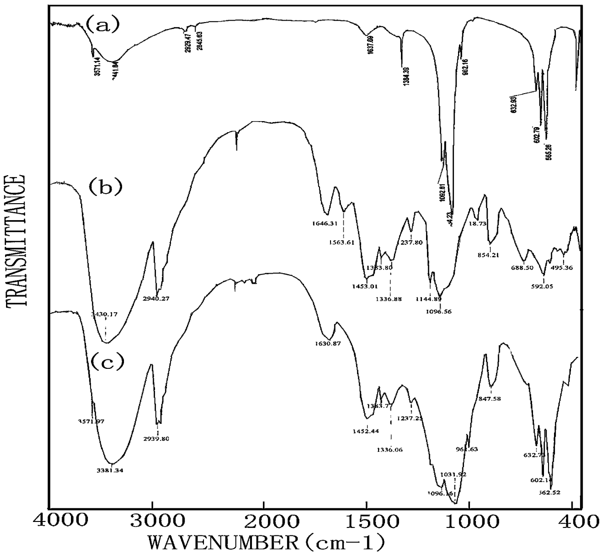

Figure 3 IR spectra of n-HA crystals and dried gel composites: (a) n-HA crystals, (b) PVA, and (c) n-HA/PVA.

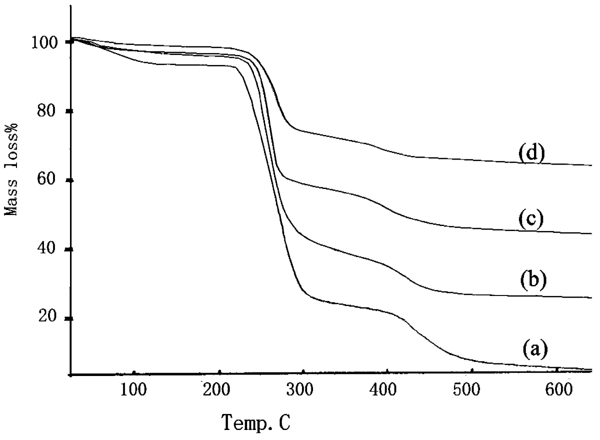

Figure 4 TG curves of PVA (a) and dried gel composites, (b) n-HA 32 wt%, (c) 46 wt%, and (d) 65 wt%.

FT-IR spectrum in Fig. 3a, a peak at 1144 cm^{-1} is observed. The 1144 cm^{-1} mode is due to C—C stretching and C—O stretching [19].

The IR spectra show the following three sets of changes in the composite: (1) the peak at 3300–3400 cm^{-1} shifted and variation of the intensities of absorption bands. (2) The crystallinity-dependent 1144 cm^{-1} peak of PVA disappeared. (3) The adsorption peak of 918 cm^{-1} of PVA disappeared and the peak of 854 cm^{-1} shifted.

The disappearance and shift of the characteristic absorption bands may result from the interaction of different –OH groups in the n-HA and PVA, the calcium ion in the n-HA and the —OH groups in PVA. So, it may be deduced from these results that the n-HA was linked with PVA by hydrogen binding and/or by the formation of hydroxy-calcium-hydroxy linkage [HO-] –Ca^{2+}–[—OH]. This kind of linkage has great effect on interface behavior and mechanical properties.

3.6. Thermal analysis

The TG plots of pure PVA and three sets of composites with PVA are shown in Fig. 4. In Fig. 4a decomposition behavior of pure PVA is shown. The n-HA content is calculated from the residual weight in TG curves at 600°C. However, since it is very difficult to control absorbed water content in the composites, this n-HA content is only an approximate value. In the TG curves several steps are observed. The first step, showing a small decrease in weight, is associated with adsorbed water-removing when heated above 90°C. The second step from 200 to 280°C may be due to the dehydration reaction of —C—OH groups in PVA chains. This temperature shifts to a higher temperature, when the n-HA content increases. The third step was degradation of PVA matrix releasing CO$_2$ gas. This temperature shifts to a lower temperature in the TG curves caused by the increasing n-HA content. The fact that the second step is initiated at slightly higher temperature and the third step occurs at slightly lower temperature than in pure PVA is suggestive of the presence of chemical interaction between PVA and the n-HA.

4. Conclusion

The formation of chemical bonding between n-HA and PVA, such as hydrogen bonding and/or hydroxyl-calcium-hydroxyl ([HO–]–Ca^{2+}–[–OH]), allows the uniform dispersion of n-HA in poly(vinyl alcohol) hydrogel matrix. The solution-blending technique adopted in this study also contributes to the uniform dispersion and prevents the aggregation of n-HA. Interface bonding, uniform dispersion and high content of HA are important for enhancement of mechanical properties and bioactivity of the composite. The n-HA/PVA-H composite will be easier to adhere to tissue and fix in the long-term than pure PVA-H. The n-HA/PVA-H composite provides an opportunity to produce high-performance materials for artificial articular cartilage.

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