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Materials Science and Engineering A 430 (2006) 341–345

MATERIALS SCIENCE & ENGINEERING A

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Short communication

A novel in situ synthesis of dicalcium phosphate dehydrate nanocrystals in biodegradable polymer matrix

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Received 15 February 2006; received in revised form 10 April 2006; accepted 18 May 2006

Abstract

In the paper, we found a novel method to synthesize dicalcium phosphate dehydrate (DCPD) nanocrystals by in situ reaction in biodegradable PDLLA matrix. Calcium hydrid was selected as calcium source of DCPD, which is different from general methods. The method is not only simple and effective to synthesize Ca–P particles, but also can avoid the aggregation of inorganic nanoparticles in the course of their being dispersed into polymer matrix.

Keywords: Chemical synthesis; Crystal growth; Polymer; Composites; Ceramics

1. Introduction

In the last decade, totally resorbable composite bone substitute materials have been the subjects of hot study in surgical reconstruction and bone tissue engineering [1,2]. Especially, calcium phosphate biomaterials have wide clinical application for repair of bone defects, bone augmentation, and coatings for metal implants. Calcium phosphates of biological significance mainly include amorphous calcium phosphate (ACP), brushite or dicalcium phosphate dehydrate (DCPD, $CaHPO_4{\cdot}2H_2O$), monetite or dicalcium phosphate anhydrous (DCPA, $CaHPO_4$), octacalcium phosphate (OCP, $Ca_8H_2(PO_4)_6{\cdot}5H_2O$), whitlockite or tricalcium phosphate (TCP, $Ca_3(PO_4)_2$), calcium pyrophosphate dehydrate (CPPD, $Ca_2P_2O_7$) and calcium-OH-apatite (HAP, $Ca_{10}(PO_4)_6(OH)_2$) [3]. Calcium phosphates/poly(lactic acid) (PLA) composites become an important representative of these composite bone substitute materials since they combine the ostesconductivity and bone bonding ability of calcium phosphate with the biodegradation, biocompatibility and the easy processing property of the polymer matrix [4]. For these composites, the interfacial strength between calcium phosphate fillers and PLA matrix is a critical factor to determine the mechanical properties of the composites. Several methods have been developed to improve adhesion between calcium phosphate fillers and PLA matrix, such as utilization of surface modification of calcium phosphate ceramics [5,6], and direct graft-polymerization of polymer on HA surfaces [7–9]. Among the existing methods, in situ formation of nanocomposites by forming nano-size of calcium phosphate crystals in the presence of polymers is one of the most attractive routes, since it avoids extensive particle agglomeration while a mechanical mixing between nanopowder and selected polymer is adapted [10]. However, it is a challenging work to make such homogeneous nanocomposites as calcium phosphate nanoparticles are synthesized in aqueous environment and especially tend to agglomeration. Furthermore, hydrophobic PLA polymer will be precipitated from PLA organic solution in the aqueous environment. Thus, it often results in poor uniformity for composite materials between calcium phosphate particles and polymer matrix. In order to resolve above problems, in this communication, we focused on the in situ synthesis of DCPD ($CaHPO_4{\cdot}2H_2O$) nanocrystals in biodegradable polymer matrix and directly obtained biodegradable sub-micron composite powder based on DCPD and poly-D,L-lactide (PDLLA) with a modified water-in-oil emulsion method. The chemical composition and morphology of resultant products were characterized by FT-IR, EDAX, XRD and SEM.

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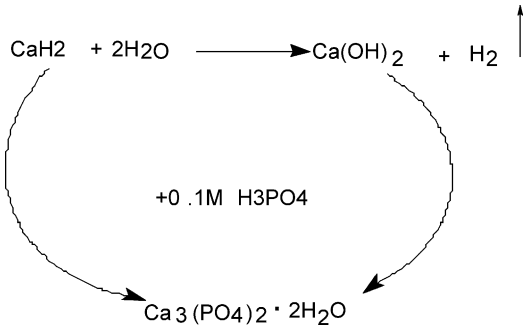
doi:10.1016/j.msea.2006.05.065

2. Experimental

Poly(D,L-lactide) (PDLLA, MW:144 kDa) was synthesized by ring-opening polymerization of cyclic lactide monomer as described previously [11]. H_3PO_4 and calcium hydrid both of an extra pure grade were purchased from Chengdu Kelong Chemical Reagents Department of China. All other chemicals and solvents were of reagent grade or better. Solvents were dried and purified in the usual manner.

Four gram of PDLLA and one gram of calcium hydrid powder were added into 12.0 ml dry ethyl acetate in a previously flamed flask under stirring at room temperature and at the same time nitrogen gas was bubbled into the mixture at a flow rate of 200 ml/min. After the PDLLA was dissolved completely, 100 ml H_3PO_4 (0.1 M) was drop-wise added in the solution with strong stirring. After the mixture reacted under stirring for about 5 h, a white emulsion was formed. The resultant composite sub-micron powder was collected by centrifugation (Beckman Coulter Inc., USA). The powder was rinsed with distilled water and centrifuged three more times, then lyophilized overnight and stored at 4 °C.

The microstructures of the composite powder, the sample obtained after PDLLA was removed from the composite powder by dissolving, and the sample obtained after the composite powder was sintered at 1200 °C for 2 h were examined by scanning electron microscopy (SEM) (FEI, Quanta 200, Philips, The Netherlands). Crystals produced were characterized by X-ray powder-diffraction (XRD) (Phlips, X'Pert PRO, The Netherlands). The XRD patterns were recorded using Cu Kα radiation ($\lambda = 1.54056$ Å) generated at 40 kV and 40 mA, in the $10° < 2\theta < 70°$ range at a scan speed of 2.5°/min. Energy dispersive X-ray spectroscopy (EDXS) (EDAX Inc., USA) attached to a Quanta 200 SEM was carried out to analyze the chemical composition. Fourier transform infrared spectrometer (FT-IR) (Nicolet 5700, Japanese) was chosen to monitor the spectral evolution of chemical bonding.



Scheme 1. Reaction equilibria for DCPD crystals formation.

3. Results and discussion

It is well known that the method to synthesize calcium phosphate is usually by addition of Ca^{2+} solution into a stirring solution containing ammonium or sodium phosphate under some pH conditions. DCPD can be also obtained by seeded growth [12]. However, we found a novel method, namely in situ reaction in the polymer matrix with a modified water-in-oil emulsion method, to synthesize nano-size of DCPD crystal, and at the same time we could obtain the sub-micron composite powder containing DCPD and PDLLA. Previously the water-in-oil emulsion method was studied in detail in drug controlled release system [13,14]. The method was successfully borrowed to prepare DCPD nanoparticles/PDLLA composite in the experiment. The reason that calcium hydrid powder is selected as the source of calcium in our experiment is that it can easily be mixed with PDLLA polymer solution and some channels can be formed in polymer matrix due to hydrogen gas bubbling off resulted from

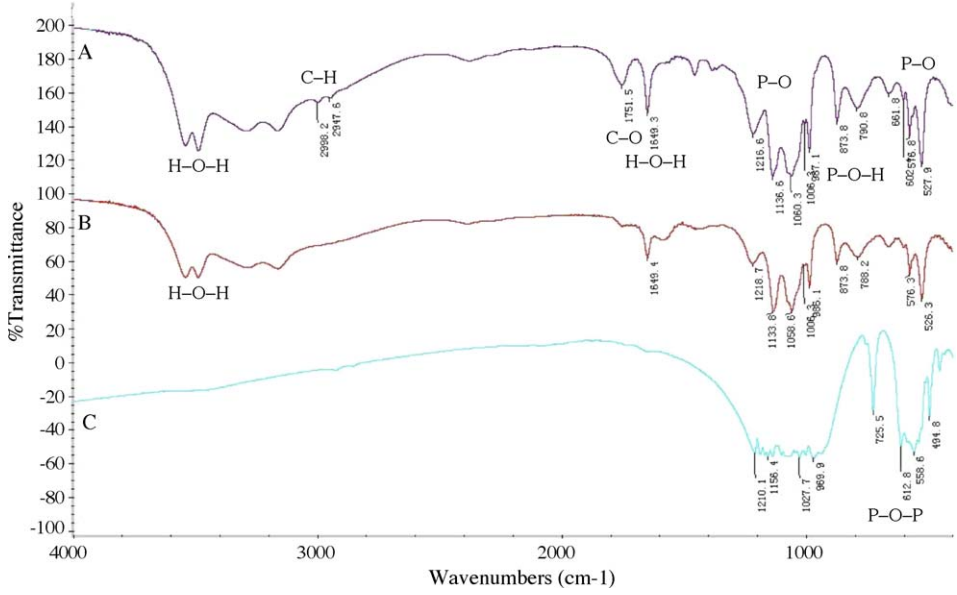


Fig. 1. FT-IR spectra of PDLLA/DCPD composite powder (A), DCPD nanoparticles obtained after PDLLA was removed (B), and the sample obtained after the composite powder was sintered at 1200 °C for 2 h (C).

the chemical reaction of CaH_2 with H_2O and H_3PO_4 (shown in Scheme 1). The formed channels may be very important to help H_3PO_4 penetrate into polymer matrix. Thus, CaH_2 powder in polymer matrix could react completely and nano-size of CDPD crystal could form by the in situ reaction. Therefore, the modified water-in-oil emulsion method is different from general methods to synthesize calcium phosphate reported previously. With the method, we can directly obtain biodegradable composites containing DCPD nanoparticles and PDLLA polymer.

In order to confirm chemical compositions of DCPD, FT-IR was first employed in the paper. From Fig. 1, it can be seen that some differences exist among the spectra of PDLLA/Ca–P inorganic particles composite powder (A), Ca–P inorganic particles obtained after PDLLA was removed (B), and the sample obtained after the composite powder was sintered at 1200 °C for 2 h (C). In the A FT-IR spectrum, the absorption bands at 2998, 2947 and 1751 cm^{-1} are attributed to the C–H stretching vibrations of the methyl (CH_3) and methine (CH) and the C=O stretching vibrations of the ester carbonyl group for the PDLLA, respectively. The absorption bands at 3450 and 1649 cm^{-1} are attributed to the H–O–H vibrations of H_2O of crystallization. The absorption bands at 1210–986 and 660–520 cm^{-1} are attributed to the P–O vibrations, and the absorption bands at 870 and 790 cm^{-1} are attributed to the P–O–H vibrations for inorganic Ca–P component. According to the appearance of above absorption peaks, we can conclude primarily that the inorganic Ca–P component obtained by in situ reaction was DCPD. In order to further confirm the formation of DCPD, the spectrum of pure Ca–P inorganic particles obtained after PDLLA was removed from the composites by solvent dissolution is shown in Fig. 1B. The absorption bands for PDLLA are disappeared, whereas absorption bands for DCPD are saved in Fig. 1B, which is identical with previous reports [15,16]. At the same time, we prove the formation of DCPD indirectly, namely, the sample obtained after the composite powder was sintered at 1200 °C for 2 h is analyzed with FT-IR shown in Fig. 1C. Li et al. reported that CPPD ($Ca_2P_2O_7$) could be obtained by sintering of DCPD under high-temperature conditions [17]. The H–O–H vibrations and P–O–H vibrations all disappeared, but the absorption bands at 1210–986 and 725 cm^{-1} are assigned to the P–O vibrations and P–O–P for CPPD, respectively. Therefore, it also can be concluded that DCPD is obtained from the formation of CPPD.

Fig. 2 shows the EDXS spectra of PDLLA/Ca–P inorganic particles composite powder (A), Ca–P inorganic particles obtained after PDLLA was removed (B). In the A spectrum, the peak of carbon element belongs to PDLLA in the composite, whereas phosphor element peak with 47.75% of mol ratio and calcium element peak with 52.25% of mol ratio attribute to Ca–P inorganic particles. The B spectrum also shows the peak of P element and Ca element with almost same intensity. The Ca/P mol ratio is close to 1:1, which also indicates that the Ca–P inorganic articles should be DCPD.

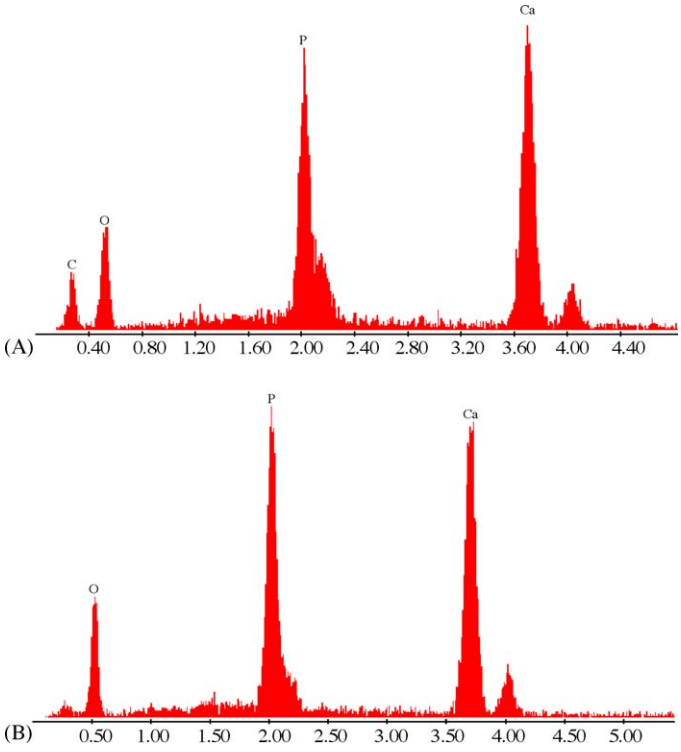


Fig. 2. EDXS spectra of PDLLA/DCPD composite powder (A) and DCPD nanoparticles obtained after PDLLA was removed (B).

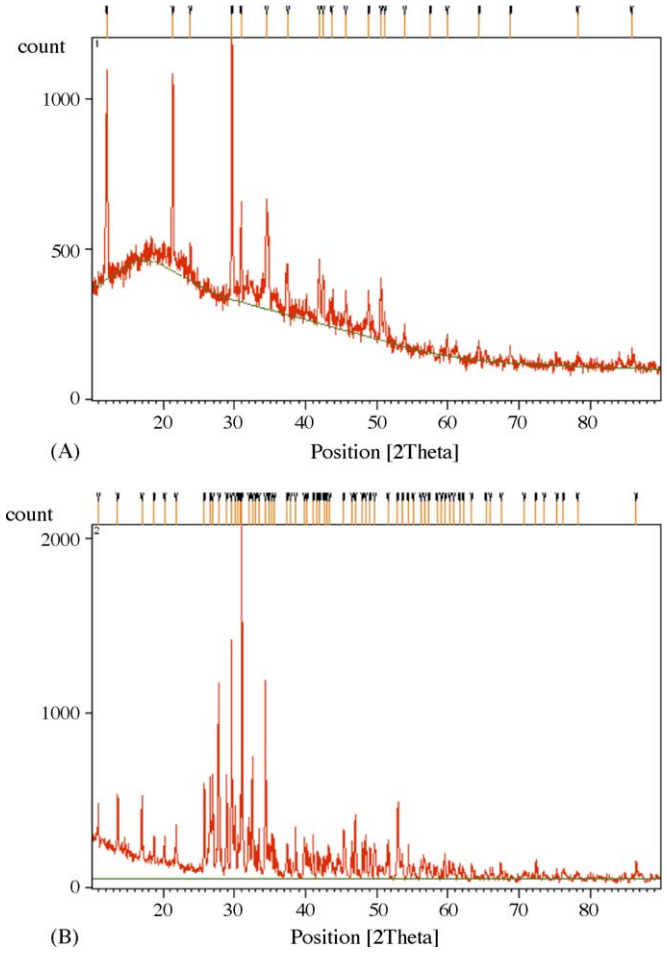


Fig. 3. XRD patterns of PDLLA/DCPD composite powder (A) and the sample obtained after the composite powder was sintered at 1200 °C for 2 h (B).

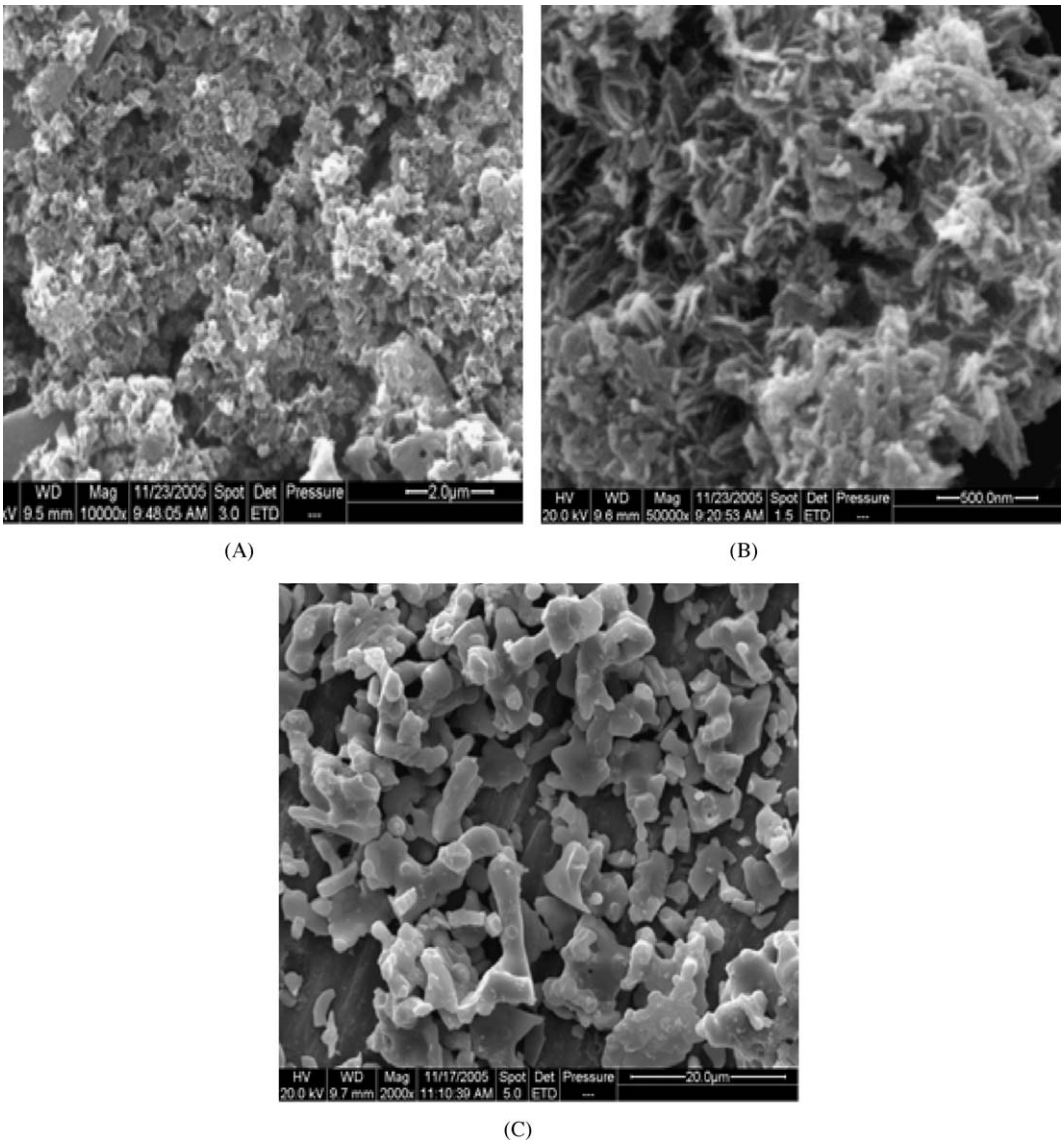


Fig. 4. SEM micrographs of PDLLA/DCPD composite powder (A), DCPD nanoparticles obtained after PDLLA was removed (B), and the sample obtained after the composite powder was sintered at 1200 °C for 2 h (C).

The XRD patterns of PDLLA/Ca–P inorganic particles composite powder (A) and the sample obtained after the composite powder sintered at 1200 °C for 2 h (C) are shown in Fig. 3. In the A pattern, the wide diffraction peak in the $10^\circ < 2\theta < 30^\circ$ range attributes to amorphous PDLLA in the composites, whereas the other shape diffraction peaks are almost identical with standard graphics of DCPD (reference code: 00-001-0395), which further indicates DCPD formed indeed. Also, the B pattern is almost identical with normal graphics of CPPD (reference code: 01-071-2123), which indirectly proves the formation of DCPD.

Fig. 4 shows SEM micrographs of PDLLA/Ca–P inorganic particles composite powder (A), Ca–P inorganic particles obtained after PDLLA was removed (B), and the sample obtained after the composite powder was sintered at 1200 °C for 2 h (C). Obvious difference exists among the SEM photos of (A)–(C). Due to hydrogen gas bubbling from PDLLA matrix, there are lots of tousy and irregular particles with diameter about 500 nm containing PDLLA matrix and DCPD nanoparticles in the A photo. After PDLLA was removed from the composites by solvent dissolution, the characteristic tabular plate morphology with 50 nm of thickness looked like ribbons for the residual DCPD aggregated crystals is shown in Fig. 4(B). In order to further observe the morphology of Ca–P particles, the SEM of the sample obtained after the composite powder was sintered is shown in Fig. 4(C). The particles diameter in Fig. 4(C) is much bigger than DCPD particles diameter in Fig. 4(B) due to the DCPD nanocrystals being melted at 1200 °C and aggregating together. The morphology looks like Ca–P bioceramics [18].

4. Conclusions

In summary, Ca–P inorganic nanoparticles obtained with the in situ reaction synthesis in biodegradable polymer matrix are DCPD nanocrystals by analysis of IR, EDAX, XRD and

SEM. We can directly prepare biodegradable composites containing biodegradable polymer matrix and Ca–P nanoparticles and avoid the aggregation of nanoparticles during their dispersing. Of course, pure DCPD nanocrystals and CPPD particles also can be obtained by removing polymer from composites. The biodegradable composites powder is very potential for biomedical applications in preparation of scaffold of tissue engineering, the repair of periodontal bony defects and ridge augmentation.

Acknowledgements

This work was supported by National Natural Science Foundation of China (no. 50303018) and the Cultivation Fund of the Key Scientific and Technical Innovation Project, Ministry of Education of China.

References

[1] N. Ignjatovic, S. Tomic, M. Dakic, et al., Biomaterials 20 (9) (1999) 809.
[2] X. Deng, J. Hao, M. Yuan, J. Mater. Sci. Lett. 20 (2001) 281.
[3] Z.L. Racquel, Calcium Phosphates in Oral Biology and Medicine, S. Karger AG, 1991.
[4] Y. Shikinami, M. Okuno, Biomaterials 20 (9) (1999) 859.
[5] K. Nishizawa, M. Toriyama, T. Suzuki, Y. Kawamoto, Y. Yokugawa, F. Nagata, Chem. Soc. Jpn. 1 (1995) 63.
[6] Q. Liu, J.R. de Wijn, D. Bakker, C.A. van Blitterswijk, J. Mater. Sci. Mater. Med. 7 (1996) 551.
[7] Q. Liu, C.A. van Blitterswijk, J. Biomed. Mater. Res. 40 (1997) 358.
[8] Q. Liu, J.R. de Wijn, K. de Groot, C.A. van Blitterswijk, Biomaterials 19 (1998) 1067.
[9] Z. Hong, P. Zhang, C. He, X. Qiua, et al., Biomaterials 26 (2005) 6296.
[10] K. Kato, Y. Eika, Y. Ikada, J. Mater. Sci. Mater. Med. 32 (1997) 5533.
[11] D.K. Gilding, A.M. Reed, Polymer 20 (1979) 1459.
[12] J.C. Heughebaert, J.F. de Rooij, G.H. Nancollas, G.H. Nancollas, J. Cryst. Growth 77 (1986) 192.
[13] X. Deng, S. Zhou, X. Li, et al., J. Control Rel. 71 (2001) 165.
[14] S. Zhou, X. Deng, X. Li, et al., J. Control Rel. 75 (2001) 27.
[15] E.E. Berry, C.B. Baddiel, Spectrochim. Acta 23 (1967) 1089.
[16] R.Z. LeGeros, D. Lee, G. Quirolgico, W.P. Shirra, L. Reich, Scan. Electron. Microsc. 3 (1983) 407.
[17] S. Li, X. Chen, Bioceramics, Publication of Wuhan University of Industry, 1989, P76.
[18] H. Morgan, R.M. Wilson, J.C. Elliott, S.E.P. Dowker, P. Anderson, Biomaterials 21 (2000) 617.