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Hydroxyapatite spheres with controlled porosity for eye ball prosthesis: processing and characterization

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Porous hydroxyapatite spheres were prepared by a modified gelcasting method producing a ceramic prosthesis with controled porosity. The spheres are approximately 2.2 cm in diameter with a relatively homogeneous pore size distribution from 10 to 40 μm in diameter. The samples were characterized by X-ray powder diffractometry (XRD) and Fourier transform infra-red spectroscopy (FTIR) to identify the phases both prior to and after the gelcasting process. Surface morphology analysis and porosity evaluations were performed with scanning electron microscopy (SEM), while surface area measurements were carried out by the BET technique.

1. Introduction

Although the use of ceramic materials is well known in dentistry [1–6], their application to other medical uses such as implants is relatively new [7–17]. The main advantage of ceramics over other implant materials is their ‘‘inertness’’ or biocompatibility, which is fundamentally due to their low chemical reactivity. However, certain ceramics are made reactive on purpose to induce direct bonding to hard tissues. Some ceramics are also conveniently made so as to be absorbed *in vivo* after their original function is fulfilled [18]. The inertness of ceramics is also useful in creating polymer + ceramic composites for a variety of applications.

In ocular implants [16, 17] there has been enormous progress since the first orbital implant by Frost in 1896. After that pioneer work, a number of materials including wax, silk, glass, wool, silicone, polyethylene, polymethyl metacrylate, etc., have been tested [19].

While some of the materials named above have been used to eliminate the facial bone deformation, they provided only a temporary solution to the problem. These materials exhibit incompatibility with the host. Hydroxyapatite (HAp) has been widely used for many years now in different applications such as filling bone defects, bone ingrowth, coverings onto metallic implants, etc. [20–39]. More recently porous HAp spheres have been used with good results as eye ball prosthesis. The porous materials act as a scaffold for the rapid ingrowth of vascularized connective tissue and bone [16, 17] and they are non-toxic and hypoallergenic. HAp spheres have been approved for this use by the Food and Drug Administration (FDA) in the United States since 1989 [17].

When a porous HAp sphere is implanted into a living organism, it acts as a passive structure or framework that allows fibrovascular growth, resulting in a wrapped prosthesis with fibrous tissue which provides stability, allowing the suture with the six extraocular muscles providing a natural movement of the prosthesis [16, 17]; complete vascularization also occurs within few weeks. Once the muscles have been sutured to the HAp sphere, an iris of polymethyl metacrylate (PMMA) can be mechanically attached to the HAp sphere for the final aesthetic appearance. As a result, this eye ball prosthesis has, besides the appearance of a natural eye, all its natural movements.

Many additional advantages over other ocular implants are provided by HAp spheres [19–38]: (a) a significant decrease in the time required to reach a complete vascularization [20–24]; (b) low rate of reabsorption [25–34]; (c) virtually no evidence of rejection over the long-term of the actual implant (longer than 48 months) [35, 36]; and (d) high biocompatibility that renders a reduction in the risk of infection and inflammation [37]. For those patients who must be subjected to an irradiation treatment, this prosthesis is also stable with respect to the irradiation. Finally, and not least important, is the fact that the aesthetical appearance can be drastically improved by the natural movements these HAp spheres can have, which means a complete prosthesis integration, of great value for both patient and surgeon.

The most common method to produce these sphere consists in phosphatizing coral madrepores to convert their carbonate skeletons into a phosphate material [20]. The processing, however, requires high pressure and high energy consumption. Furthermore, from the ecological point of view, the damage to the coral reefs has not been addressed. About 25 000 people around the world now have an ocular implant made of HAp from coral. The current price in the market of one such sphere is several hundred US dollars.

In this paper we report a novel method for producing prosthesis from HAp ceramic powders with shaping into the desired spherical form and a control of the porosity. Not only a new technology but also significant reduction in the final cost is attained.

The so-called gelcasting [39] is a relatively new method to produce ceramic objects with almost any geometry; the method presents many advantages over the usual procedures. The process separates the mold-filling operation from the setting operation, and uses a solution-based vehicle instead of a 100%- or polymer-based vehicle. The basis of the process is the use of a monomer solution that can be polymerized *in situ* to form a strong, cross-linked polymer-solvent gel, and this provides a mechanism for permanently immobilizing the ceramic slurry in the desired shape after it has been poured into a mold. To achieve our objectives, in this work we introduce some modifications to the standard gelcasting method.

2. Experimental procedure

2.1. Sphere preparation

Fig. 1 shows schematically the traditional gelcasting method for processing of ceramic bodies. Fig. 2 shows a diagram of our process of obtaining HAp spheres with controled porosity by modifying the traditional method.

Synthetic HAp powders were prepared by the precipitation method [39] performing hydrolysis of brushite at 60 °C and pH = 8.0 according to the following scheme:

$$\begin{aligned}&\mathrm{CAHPO_4} + 2\mathrm{H_2O}\ (\mathrm{DCPD, brushite})\\&\mapsto \mathrm{HAp}(\mathrm{Ca/P} < 1.67)\end{aligned} \tag{1}$$

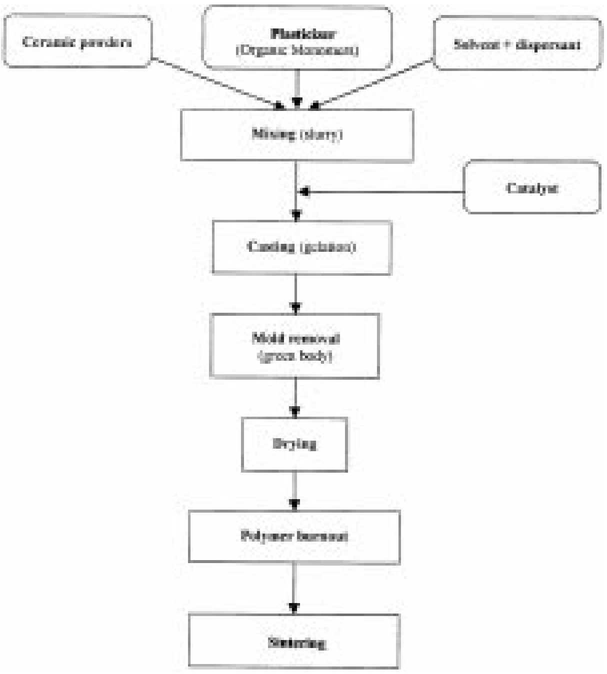

Figure 1 Schematical diagram of the traditional gelcasting method.

Figure 2 Controlled pore size HAp spheres formation through a modified gelcasting method.

$$\mathrm{HAp}(\mathrm{Ca/P} < 1.67) \mapsto \mathrm{HAp}(\mathrm{Ca/P} = 1.67) \tag{2}$$

As can be seen from reaction (1), simple hydrolysis produces Ca-defficient HAp. Thus, it is necessary to subject the powder to a heat treatment for 3 h at 40 °C and pH ≈ 9 in the presence of CaCl as the calcium source. This procedure leads to stoichiometric HAp [30].

The polymer-based vehicle (binder + plastifier) was prepared by using a method elaborated by us before [39]. Commercial poly(vinyl butyrate) from Merck was mixed with HAp in the weight ratio of HAp : polymer equal to 10 : 1. The solvent, which must be chosen considering the functional groups of the polymers as well as the flocculation characteristics of the HAp, was also developed in Arita *et al.* [39]. The polymeric component (binder and plastifier) and the dispersant were mixed in a flask containing the solvent and a cross-linked polymer-based vehicle was formed. Then HAp powders and the pore-forming agent were added to the above solution and mixed in the first step (batch preparation) which takes place at room temperature. Once mixing was completed, the resulting mixture was poured into a spherical-shaped mold and dried at room temperature (cold shaping step).

Once the sphere dries into a green body, the polymers are burned out while the porosity-forming steps take place at the same time. This is done in two stages, respectively, at 450 °C and at 850 °C, for 2 h. The drying process requires careful execution because the vapor pressure in the pores may fracture the sphere. Finally, consolidation by sintering to improve the mechanical properties of the sphere is performed. This process is carried out at a temperature above 1100 °C for at least 2 h.

2.2. Characterization techniques

Prior to as well as after the processing, the spheres are characterized by a number of techniques to compare the composition of the starting material to that of the final

T A B L E I Elemental composition of the raw HAp powders and final spheres obtained by EDX

Element %	Raw materials	Final product
C	0.91	0.78
O	27.85	33.95
P	20.45	21.02
Cl	3.06	1.64
Ca	47.74	42.61
Ca/P	1.80	1.57

product. Microanalysis (EDX) was carried out in a Philips XL–30 scanning electron microscope (SEM) with an EDAX detector. X-ray powder diffractometry (XRD) was performed with a Siemens D5000 diffractometer with Cu$-$K$_\alpha$ radiation. Fourier transform infra-red (FTIR) reflection spectroscopy was performed with a Nicolet FT-Raman 910 apparatus. SEM observations were carried out in a JEOL-5200 machine and BET analysis was made in a Micromeritics ASAP–2000 analyzer.

3. Results and discussion

The elemental analysis obtained by EDX shows that the composition is practically the same from the very beginning until the end of the whole process-as shown in Fig. 3 and Table I. These results show that there is a reduction in the amount of carbon in the thermal treatment which induces the desorption of CO_2 (at around 850 °C) out of the sphere. Since the sintering is carried out in air, the amount of oxygen in the final material increases. The phosphorus contents remains practically constant, within the experimental error, throughout the whole process. An important result is the reduction in the content of chlorine. This can be responsible for a reduction in the calcium content in the sphere and consequent lowering of the Ca/P ratio from 1.80 to 1.57. Since the stoichiometric HAp has the ratio Ca/P = 1.67, the sphere so produced has the desired Ca/P stoichiometry of the hydroxyapatite.

Fig. 4 corresponds to the FTIR spectra of the ceramic body both before (a) and after (b) the processing. The spectrum for the final material shows a small absorption band at 2450 cm^{-1} which corresponds to the P-OH stretching vibration. This band is due to the sintering process which increases the crystallinity of the sample. Additionally, the peaks in the spectrum of the final material show stronger bands, indicating that the sintering and all the thermal processes increase the amount of crystalline HAp in the sample.

Fig. 5 shows the corresponding X-ray powder diffraction patterns of the phases present before (a) and after (b) the gelcasting and sintering processes. As can be seen, the characteristic apatite bands and crystalline structure remain the same in spite of the thermal treatment. From these diffractograms one also infers that the amount of the crystalline phase has increased slightly – due as before to the thermal treatment. The size of the crystallites remains practically the same, however. These are very encouraging results indeed; they show that the apatite properties remain unchanged through the process developed in this work, i.e. the HAp remains chemically stable during the modified gelcasting process.

Fig. 6 shows the final shape of the hydroxyapatite prosthesis after the modified gelcasting process and ready for implantation. As observed, no macroscopic fractures are present in the sphere, indicating that the drying process was successful.

Figs 7–9 show SEM micrographs of the sphere surface at different magnifications. As observed in Figs 7 and 8, the pores have two average sizes in a bimodal distribution, centered around 1 μm and 30 μm. Fig. 9 shows the surface of the sphere at a higher magnification demonstrating graphically that the sintering process was performed successfully; at this magnification pores smaller than 100 nm are not visible. We note relatively large interfacial areas between the HAp granules.

The BET results show a relatively small surface area for the final product (4.68 m^2/g), but still considerably higher than in the case of commercial coralline hydroxyapatite (1.4 m^2/g) [35]. This implies that the biodegradability in this case is substantially lower, thus allowing a better interaction between the host and the prosthesis.

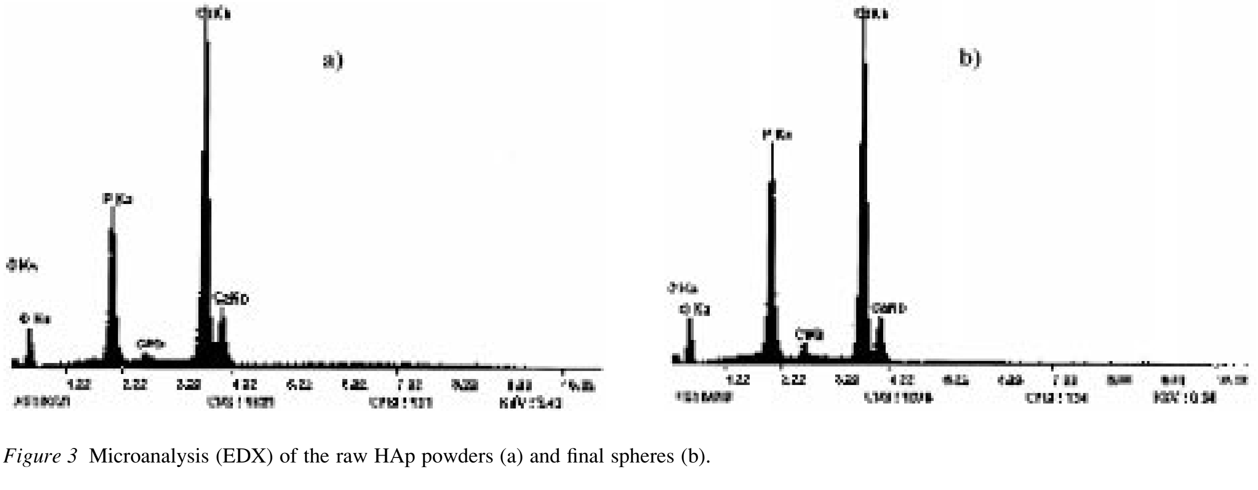

Figure 3 Microanalysis (EDX) of the raw HAp powders (a) and final spheres (b).

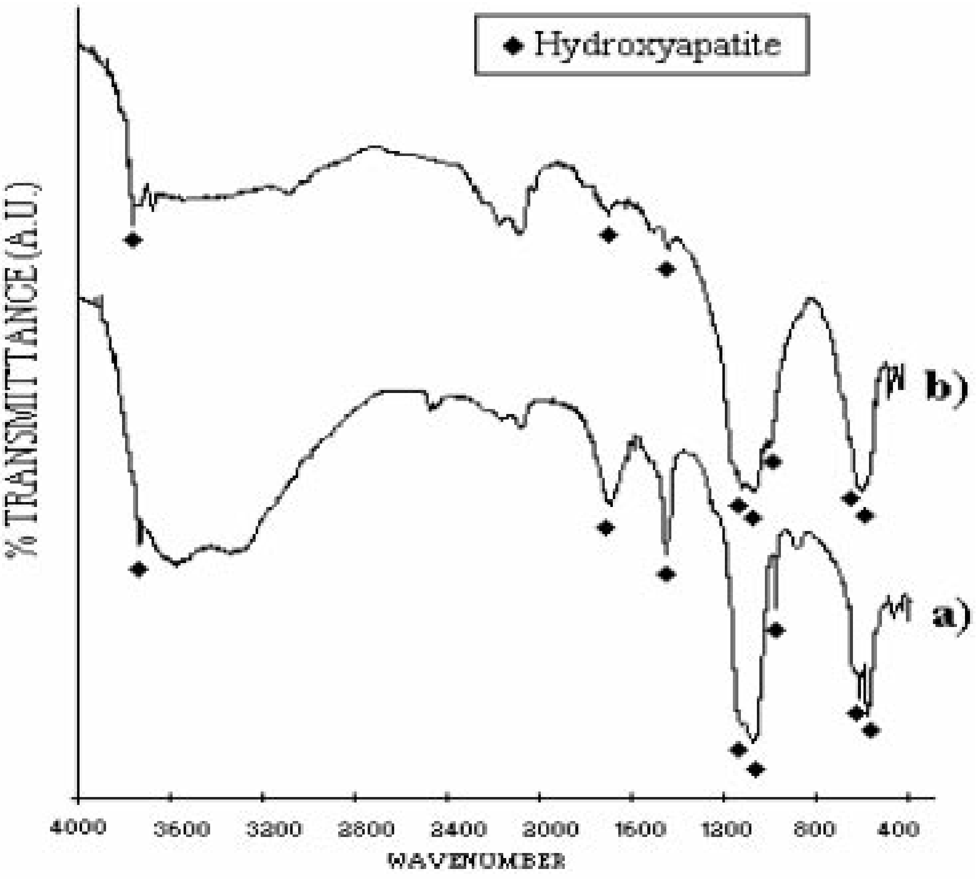

Figure 4 FTIR spectra of (a) HAp powders before gelcasting and (b) a final HAp sphere.

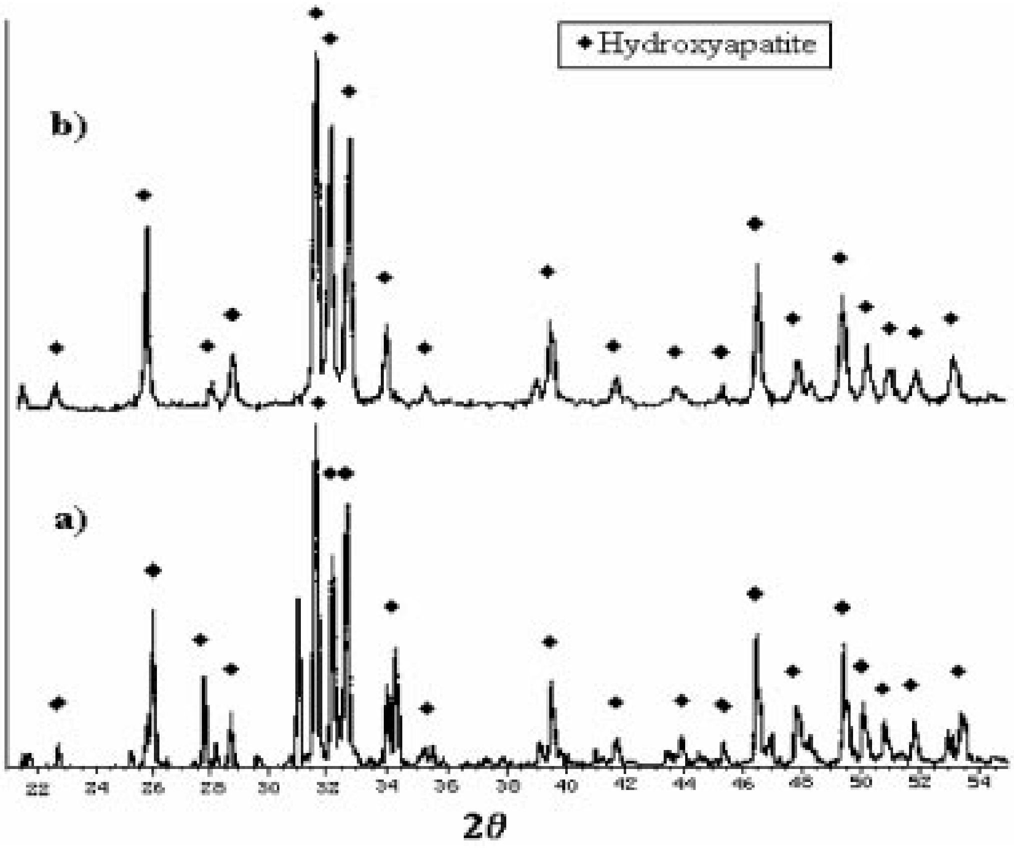

Figure 5 X-ray powder diffractometry of (a) HAp initial powder and (b) HAp powders of the prosthesis after gelcasting.

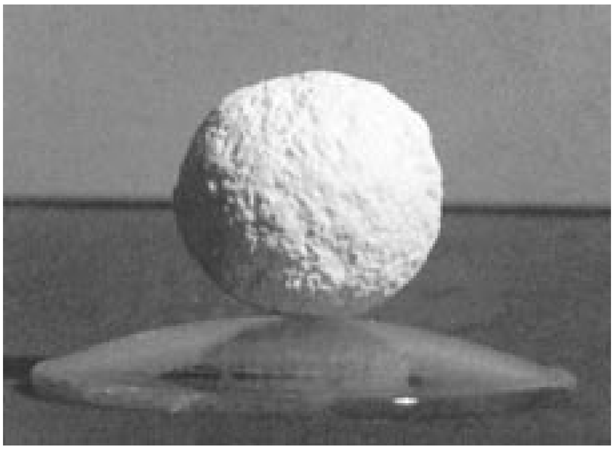

Figure 6 Actual HAp prosthesis.

In addition to the scientific and technical relevance of the above results, the production cost is also important. That cost, by using our method, represents a significant reduction as compared to commercial methodologies.

4. Conclusions

Let us list here differences between the standard gelcasting method and our modification of that method. We use different polymers to form a cross-linked structure that supports the HAp ceramic particles. Moreover, we use a pore-forming agent to assure controlled pore sizes – and we achieve this without modifications of the chemical structures of the final spheres. Our modification of the traditional gelcasting method has several advantages: faster gel formation; the molds can be made from a large variety of materials such as metals, glass, wood, polymers, etc.; and the mold cleaning procedure used is not critical for producing high quality materials.

The starting ceramic phase (HAp), remains practically unchanged during the modified gelcasting process, allowing production of a ceramic object with a predetermined shape. This demonstrates the feasibility of manufacturing through the method proposed here porous ceramic objects starting with HAp powders with no change of their physical and chemical properties. The control of porosity achieved by the use of a pore-forming agent during the modified gelcasting method is clearly succesful. Higher porosity allows a better interaction between the host and the prosthesis, which in turn allows vascularization to occur within a shorter time period. The surface areas obtained are higher than in coralline commercial samples. At the same time, we have a narrower distribution of pore sizes. Thus, very large pores are absent which ensures lower biodegradability of our materials. While the method has been applied to hydroxyapatite spheres, clearly it can be applied to produce other materials with predefined porosity.

This work belongs to a larger program of developing polymers, ceramics, and polymer + ceramic composites with predefined properties. In related developments, we have created a procedure of making HAp from eggshells by a reaction at an elevated temperature [40]. We have also developed polymer + ceramic composites of the polyelectrolyte cement type for high temperature service [41].

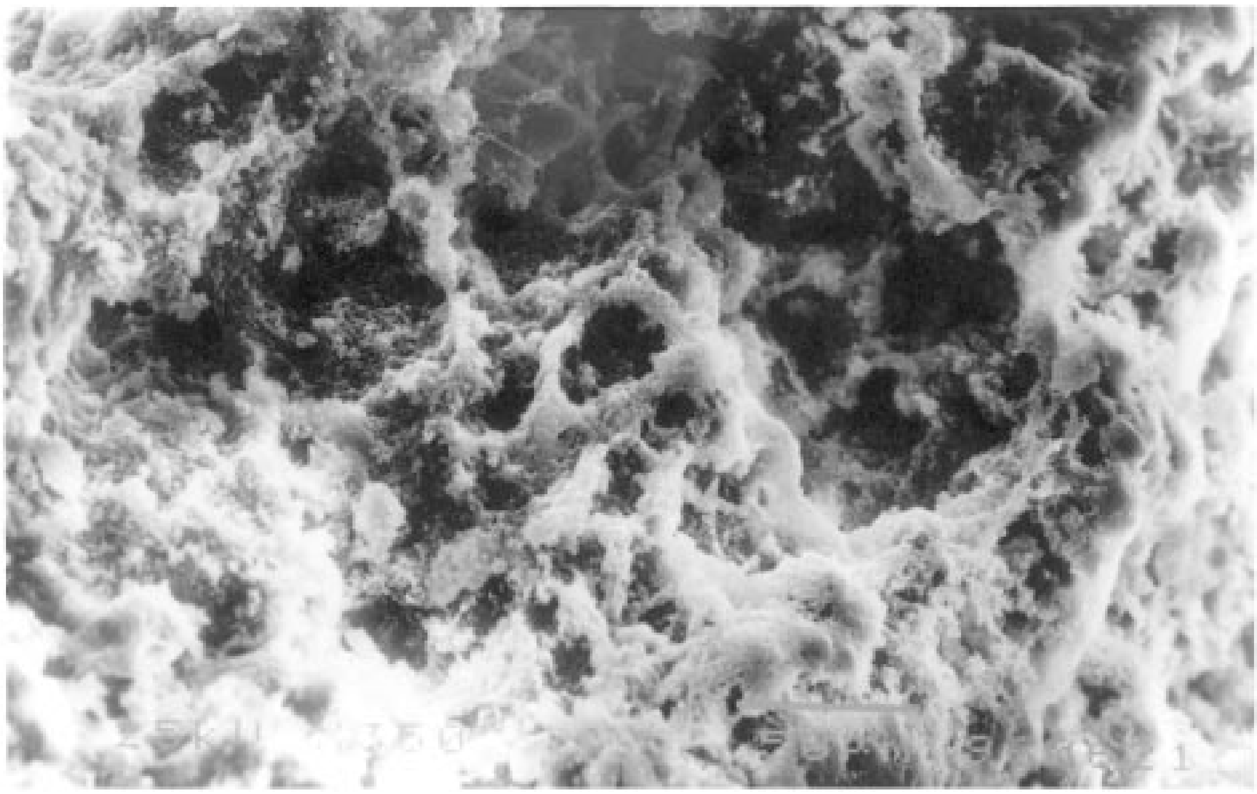

Figure 7 SEM micrograph showing the porosity distribution in the HAp spheres.

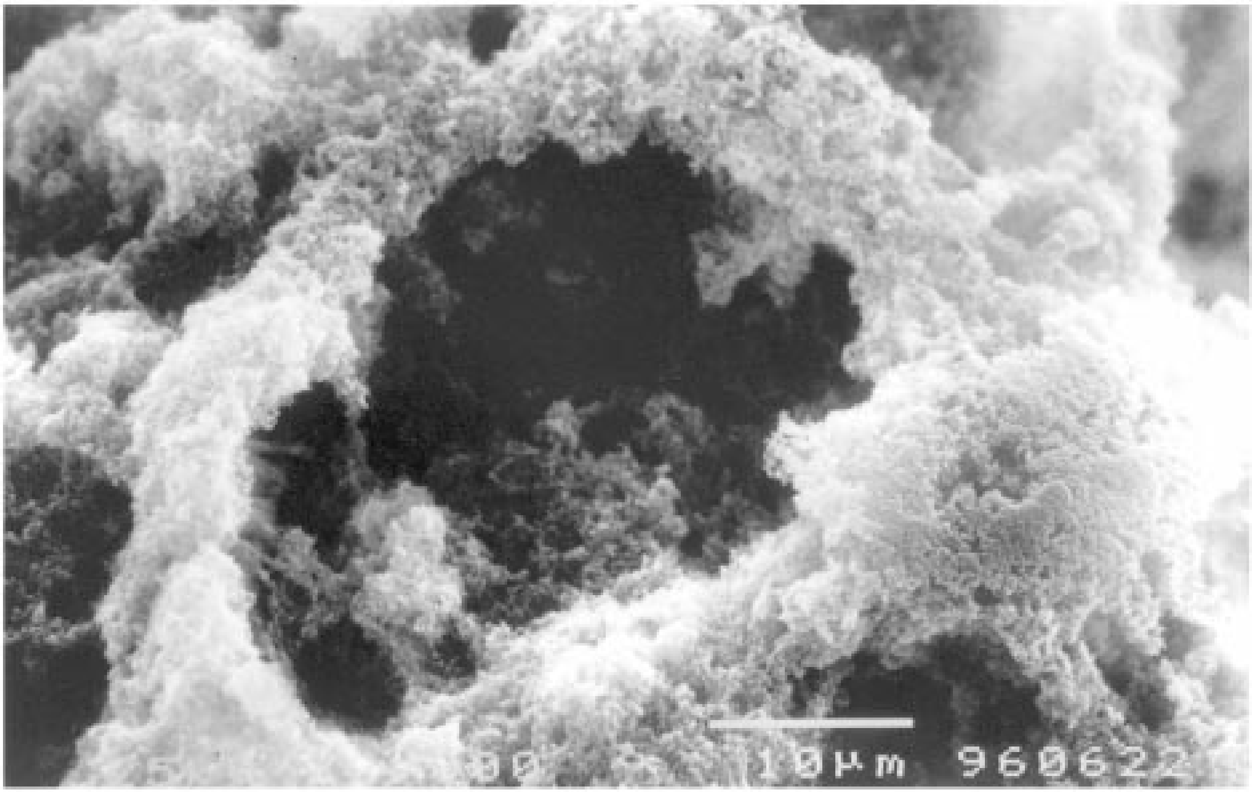

Figure 8 SEM micrograph of the final prosthesis showing a pore with a size of around 30 µm.

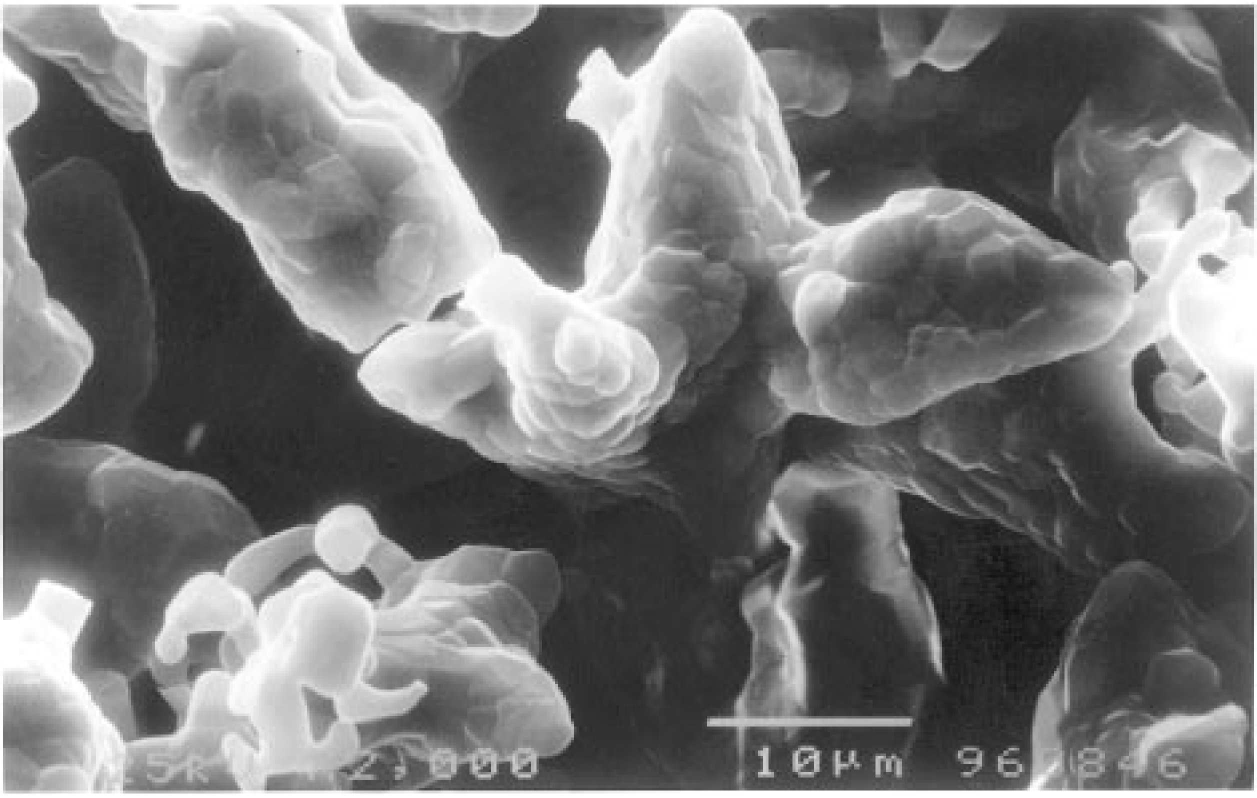

Figure 9 SEM micrograph of the final product showing successful sintering of the HAp granules and the absence of microporosity.

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