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Characteristics, preparation and improvement of porous hydroxyapatite bioceramic materials

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ABSTRACT

Hydroxyapatite exhibits the outstanding biocompatibility and bioactivity with bone replacement in living tissues. Porous hydroxyapatite bioceramic is able to intensity the osteoconduction and osteoinduction and suitable for artificial bone substitutes. By means of controllingporosity, size, interconnectivity and surface roughness of pores, the porous HA with optimal properties can be obtained. Variousmethods for preparing porous HA bioceramic have been introduced, such as pore-forming agent method, foaming method, conversion of natural body, colloidal template method, and freeze casting. To improve properties of porous HA bioceramic, two or several kinds of preparation methodshave beencombined to use, and designing and developing porous HA-based biocomposite materials is also acceptable.

KEYWORDS

Porous;
Hydroxyapatite;
Bioceramic.

INTRODUCTION

Hydroxyapatite ($[Ca_{10}(PO_4)_6(OH)_2]$, HA or HAP), one of the most representational bioceramic, which exhibits the outstanding biocompatibility and bioactivity with bone replacement in living tissues, has raised considerable attention in these materials as excellent candidates for orthopaedic, dental and maxillofacial applications[1,2]. The properties like osteoconductivity and osteoinductivity enhance the bone regeneration and make it an important material in tissue engineering[3,4]. However, the poor mechanical performances of synthesized HA, such as high elastic modulus and low fracture toughness have imposed limitation on its further application[5].

In recent years, research hotspots of HA bioceramic focus on preparing porous HA ceramics, tailoring the morphology of HA powders, and Designing HA composites[6]. Porous HA have been applied for cell loading, drug releasing agents, chromatography analysis, and the most extensively for hard tissue scaffolds[7,8]. It has strong abilities to intensify the osteoconduction and osteoinduction and be suitable for artificial bone substitutes, so particular attention has been paid to the preparation of HA bioceramics with porous morphology.

CHARACTERISTICS OF POROUS HA BIOCERAMIC

Porous structure of biological bone tissue can keep blood circulating, ensure bone tissue normal metabolism, and suit stress change in certain range synchronously. Accordingly, development of porous HA bioceramic is significant in bionics. Highly denseHA has high strength, but osteoblast can only attach its surface when it is implanted in vivo. Interconnected porous HA bioceramic with reticulated pore structurecan favor the ingrowth of neonatal tissue inside the pores, which can providean excellentosteointegration between the porous HA surface and the neonatal tissue, reduce its brittleness, and raise its bend strength. Consequently, porous HA bioceramic fit for repairing bone defect greatly[9–11].

Characteristics requirements of porous HA bioceramic have been concluded by Sopyan et al in literature[12]. The literature indicated that: dimension and morphology of pores are crucial factors for an excellent osteointegration. Minimum pores are desired to be about 100~150μm, through which ingrowth of the surrounding bone together with blood supply, and even osteoconduction can also occur at pores of as small as 50μm.Besides, interconnectivity of the pores and their surface roughness should be important requirements; the former for the penetration of the osteoblast-like cellsinside the pores, and the latter for theattachment of cells.The mechanical and biological properties are also affected by porosity of the porous HA. By means of controllingporosity, size, interconnectivity and surface roughness of pores, the porous HA with optimal properties can be obtained.

PREPARATION OF POROUS HA BIOCERAMIC

At present, variousmethods for preparing porous HA bioceramic have been developed, such as pore-forming agent method, foaming method, conversion of natural body, colloidal template method, and freeze casting.

Pore-forming agent method

The porous HA with Complex shape and different pore structure can be prepared by the pore-forming agent method. The pore characteristics are determined by type, amount and properties of the added pore-forming agent. At high temperature, the organic or inorganic filler in ceramic green body is removed either by physical processes like evaporation and sublimation, or by chemical reactions like combustion and pyrolysis, thus porous structure of HA bioceramic can be formed[13]. The porous HA usually have closed macropores, so interconnectivity of the pores is poor.

To improve the pore interconnectivity, some effective measures have been taken. Tadic et al. used mixing salt crystals and water-soluble polymers as pore-forming agents[14]. Pores are formed through leaching the salt crystals, and the pores can be well interconnected by channels resulted from the polymeric fibers. Furthermore, the process needn't any heat treatment because of good water solubility of these agents. Tsioptsias et al.[15] proposed a novel method which had beensuccessfully applied to chitin-hydroxyapatite composites. In this process, water-insoluble [poly (methyl methacrylate) (PMMA)] was selected as pore-froming agent, and a mixture of N,Ndimethylacetamide and LiClwas used as the solvent for chitin. The solvent removalwas made by bad-solvent (methanol) exchange, and PMMA particles were leached by dichloromethane. The produced scaffolds exhibited high interconnectivity and controllable pore size distribution, as shown in Figure 1.

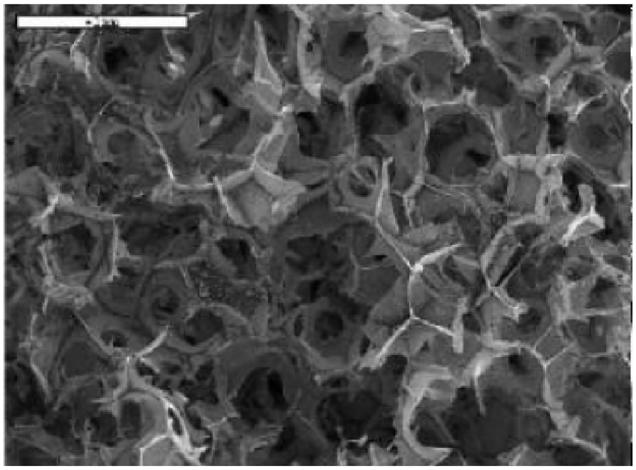

Figure 1 : Cross section of porous chitin-hydroxyapatite

Foaming method

Some foaming agents, such as hydrogen peroxide[16], carbonate salt[17], and surfactant[18], were added into the ceramic slurries or green bodies. Therefore, bubbles were produced via gas evaporating or chemical reactions, and the porous HA was obtained followed by drying and sintering. The literature[19] reported that a novel and easy process had been developed for the fabricationof a unidirectional porous HA body using ethanol bubbles forpore formation. Viscous slurry contained HA powders, methylcellulose, ethanol anddistilled water. During the heating of the slurry, bubbles wereformed at 70~80!and the unidirectional porousgreen body was produced. After sintered, the total porosity of the porous HA body was 70%, and thecompressive strength was about 10 MPa,which was comparable to that ofcancellous bone.A novel porous n-HA/PU scaffold was also prepared by a foamingmethod[20]. Castor oil as a raw material in formation of PU exhibitednot only good degree of cross linking but also excellent foamingability at definite temperature. The interconnected porousstructure and high porosity of the scaffold (its SEM photograph was shown in Figure 2[21]) could provide good microenvironmentfor cell seeding and proliferation and for growth oftissues.

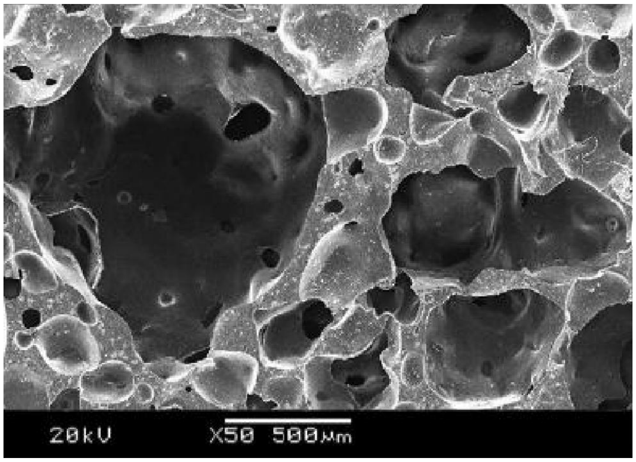

Figure 2 : SEM photograph of the porous n-HA/PU produced by water-insoluble PMMA particulatesscaffold (500-710mm): magnification bar 1 mm

Conversion of natural body

Natural bodies include marine coral, cuttlefish bone, cancellous bone and so on. In this method, hydrothermal exchange reaction convertscalcium carbonate in the natural body into HA in thepresence of phosphate ions, then its skeleton structure can be hold as a template for porous HA bioceramic[22]. After hydrothermal-treatment of cuttlefish bone ($NH_4H_2PO_4$ solution, 200°c, 48 h), aragonite ($CaCO_3$) monoliths from the cuttlefish bonewere completelytransformed into hydroxyapatite, while its interconnected channeledstructure (as shown in Figure 3) was retained[23]. The specific surface area and total pore volume of the obtained porous HA increased and its mean poresize somewhat decreased.A disadvantage of the method is that porosity is restricted by the structure of natural body, and moreover, limited mount of natural body is also an obstacle.

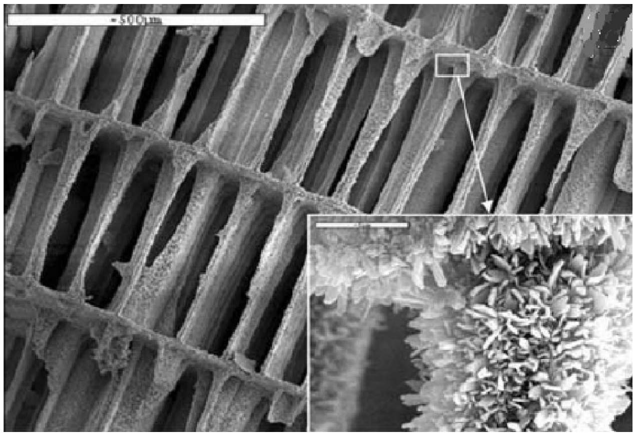

Figure 3 : The cuttlefish bone after hydrothermal

Colloidal template method

This method has been successfully used for fabricating highly ordered macroporous hydroxyapatite[24]. Zhou et al. have investigated the related issue as follow: Colloidal template was firstprepared with SiO_2 spheres by gravitational sedimentation, which was then infiltrated withhydroxyapatite precursor prepared by the sol-gel process. After removal of the template by immersing inNaOH solution, the resulting hydroxyapatite replicatedthe three-dimensionally ordered macroporous structure of SiO_2, which was shown in Figure 4[25]. The arrangement ofthe pore structure was hexagonal close-packed and pore sizes could be controlled by the sizes ofSiO_2 spheres.Modified by H_2O_2, the SiO_2spheres could be packed into better ordered template.

Freeze casting

The mainprocessing steps of freeze casting have been summarized by Sylvain, as shown in Figure 5[26]. In the process, ceramic suspension is completelyfrozen and then sublimated, so the frozen solvent crystals induce unique porous architectures[27,28]. Water[29] and camphene[30] as freezing vehicle (i.e. solvent) have been applied to prepare porous HA bioceramic. The porousHA scaffolds with a lamellar morphology and aligned channels were produced using aqueous HAslurries[31]. The freezing characteristicsof the HA slurries affectthe pore structures of theporousHA scaffolds. Yoonet al.[32] demonstrated how large pore channels could beachieved using the camphene-based freeze casting method,which should allow porous HA scaffolds to find very useful applicationsfor bone tissue engineering. A major problem offreeze-casting is the low strength of the green bodies; when thefrozen suspension is volatilized, the green bodies become veryfrangible and difficult to handle, and further efforts are underwayto improve the green bodies'strength[28].

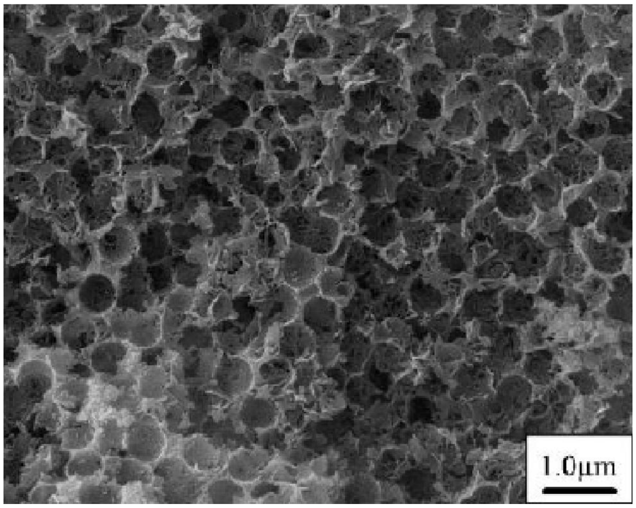

Figure 4 : Medium magnification SEMimage conversion at 200°c/24 hshowing plate- and of highly ordered macroporous HAneedle-like HAP crystals (inset)

IMPROVEMENT OF POROUS HA BIOCERAMIC

Currently, two or several kinds of preparation methodshave beencombined to improve properties of porous HA bioceramic[33,34], for example, gelcasting process was modified using polyethylene sphere as pore forming agent[35]. Yook et al demonstrated that the significant improvement in the compressive strength of porousHA scaffolds could be achievedthrough adding PSpolymer as a binder into the HA/camphene slurries[36], which was mainly attributed to both the suppression of the cracking of the green sampleduring freeze drying and the mitigation of the formation of micro-pores in the HA walls. In addition, pore morphology and microstructure of freeze-cast porous HA bioceramic could be adjusted by polyvinylalcohol (PVA) and gelatin. The open porosity and pore connectivitywere improved because of the addition of PVA[37]. The pore morphology was changed from a two-dimensional flat pore to a three-dimensionalreticulated pore after gelatin addition[38].

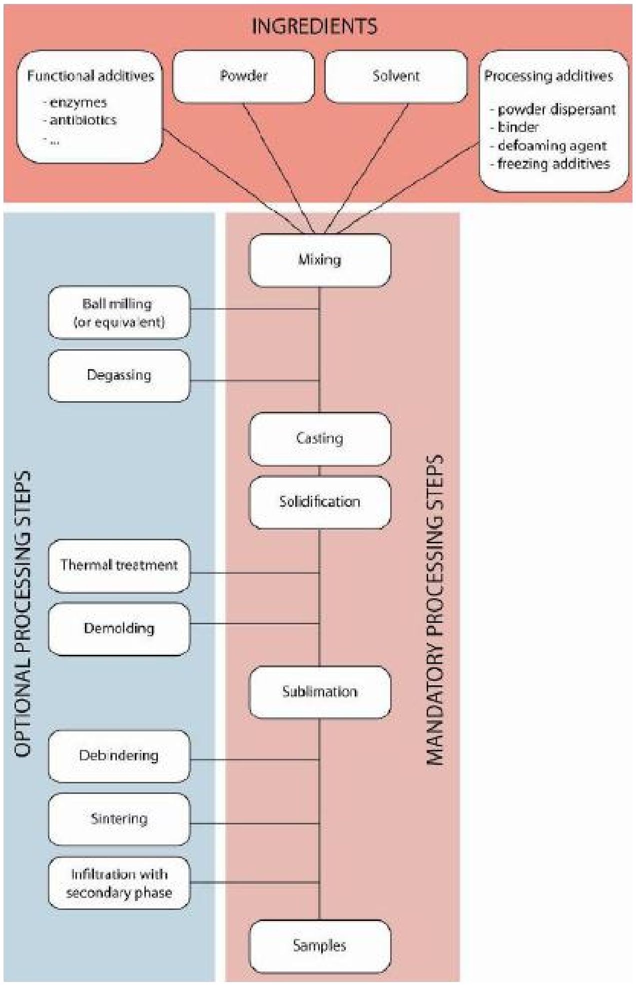

Figure 5 : The mainprocessing steps of freeze casting

Freeze-gelcasting is a novel technique for fabricating porous HA bioceramic, which can combine advantages of freeze-casting and gelcasting. Highly porous HA scaffolds with a unique pore structure (as shown in Figure 6) anddesirable compressive strength could be prepared by theTBA-based freeze/gel-casting technique[39]. It was proved that the combined processing route played an important role in controlling the optimumfabrication conditions corresponding to a specific requirement. The freeze-gelcasting method was also combined with polymer spongetechnique to fabricate porous HA scaffolds with controlled "designer" porestructures and improved compressive strength for bone tissueengineering applications[40].

Designing and developing porous HA-based biocomposite materials should be another route to improve its properties[41-44]. The literature[45] reported, a novel degradable n-HA/CS/CMC compositescaffold had desirable physico-chemical propertiesdue to the strong ionic cross-linking interactionsbetween CS and CMC. The scaffold had irregular porous structure with highly complicated interconnected network, as shown in Figure7. Yang et al prepared Poly (L-lactic acid) PLLA/HA porouscomposite using HA particles which were modified with long-chain organic silane-Octadecyltrichlorosilane (OTS)[46]. The more OTSdosage was, the more obviously the mechanicalproperties of the compositesincreased. Comparingwith unmodified HA, OTS-modified HA can lead to the composite with three times higher elastic modulus andtwo times higher compressive strength. Moreover, OTS modification can effectively improve theinterface compatibility between HA surface and PLLA. It has been suggested that porous HA scaffold can gained an improved compressive strength by coating with gelatin[47] or polycaprolactone (PCL)[48]. Some inorganics, for example bioglass, can be used for reinforcing porous HA bioceramic[49,50]. Despite the porosity of the porous HA was reduced, its mechanical properties can be imporved through good densificationÿ

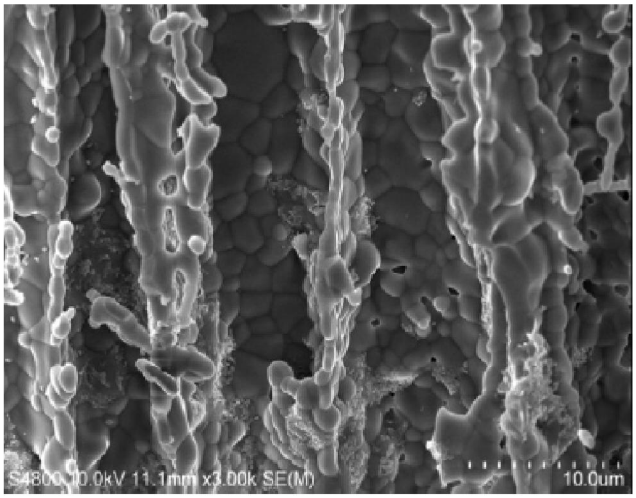

Figure 6 : SEM photo of crosssection perpendicular

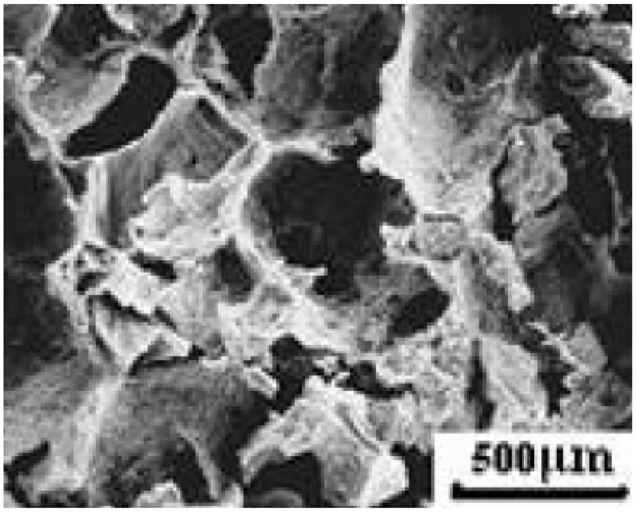

Figure 7 : The SEM microstructure of n-HA/CS/CMC

CONCLUSIONS

Porous hydroxyapatite, a promising material inbiomedical application, has been used as bone scaffolds anddrug carriers. Many works have focused on themicrostructure design and pore morphology adjustment ofporous HA bioceramic. Characteristics requirements of porous HA bioceramic are controlled porosity, good pore interconnectivity, mechanical strength, and surface roughness. By means of controllingporosity, size, interconnectivity and surface roughness of pores, porous HA with optimal properties can be prepared by variousmethods, such as pore-forming agent method, foaming method, conversion of natural body, colloidal template method, and freeze casting. To improve properties of porous HA bioceramiccorresponding to requirement of bone tissue engineering, two or several kinds of preparation methodshave beencombined to use, and designing and developing porous HA-based biocomposite materials is also another effective route.

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