Key Engineering Materials Vol. 218-220 (2002) pp 287-290
online at http://www.scientific.net

Synthesis of Sol-Gel Derived Bioactive Foams

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Keywords: Bioactive, Foams, Sol-Gel, Genes, Bone, Porous, Tissue Engineering

Abstract. Certain compositions of Na_2O-CaO-P_2O_5-SiO_2 bioactive glasses have been successfully used clinically to regenerate bone for many years, because they will form a mechanically strong bond to bone. Recent research at the Imperial College has shown that bioactive glass dissolution products exert a genetic control over osteoblast cell cycle and rapid expression of genes that regulate osteogenesis and the production of growth factors. These findings provide a scientific foundation for design of new generation of resorbable bioactive materials for tissue engineering and in situ tissue regeneration and repair. This work describes a novel method of producing 3D bioactive scaffolds using bioactive glasses through foaming of sol-gel systems. A hierarchical structure is obtained, with mesopores (2-50 nm) for enhanced reactivity and cell attachment and an interconnected array of macropores (10-500 μm) for tissue ingrowth. The macro-porous glasses provide the potential properties for applications in tissue engineering and in situ bone tissue repair and regeneration.

Introduction

Bioactive glasses have been long known to regenerate bone, because of their osteoconductive and osteoinductive abilities. *In vivo* results have demonstrated the greater ability of 45S5 bioactive glasses in producing faster healing, compared to other types of bioactive materials such as hydroxyapatite and glass-ceramics. [1] Highly porous sol-gel glasses are known to exhibit even greater bioactivity than melt-derived ones, such as 45S5, and can be produced in resorbable compositions.[0] Furthermore, Xynos *et al* [3] have shown that bioactive glass dissolution products exert a genetic control over the cell cycle of primary human osteoblasts, promoting rapid expression of genes that regulate osteogenesis and the production of growth factors, resulting in rapid osteoblast proliferation and 3-D nodule formation. However, the creation of suitable macro-porous structures with the bioactive glasses is required to support further cell organisation in the 3D form for tissue engineering applications.

This work describes a novel process for making a macro-porous 3D scaffold of bioactive glass compositions, using foaming of sol-gel systems, to provide a template to support tissue growth in bone repair and tissue engineering applications.

Methods

The novel process was developed through foaming [0] applied to the sol-gel technology. A detailed description of the process is given reference [0]. Foams were prepared in three different compositions, including pure silica, the binary 70 mol% SiO_2 and 30 mol% CaO, and the 58S composition (60 mol% SiO_2, 36 mol% CaO, 4 mol% P_2O_5) to test the applicability of the process. Sol-gel precursors were tetraethoxyl orthosilicate (TEOS), triethoxyl orthophosphate (TEP), and

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calcium nitrate, hydrolysed in the presence of nitric acid. A sol was foamed with the addition of surfactants and by vigorous agitation. An acidic catalyst was added for fast condensation. As the gelling point was approached the solution was cast into moulds. Ageing, drying and thermal stabilisation was carried out at 600°C according to established procedures. Scanning electron microscopy (JEOL, JSM T220A) was used to examine the morphological and textural features of the foams. Larger pore size ranges were assessed by intrusion mercury porosimetry (PoreMaster 33, Quantachrome), whereas the porosity in the framework and specific surface area were determined by nitrogen adsorption technique (Autosorb AS6, QuantaChrome).

Results and Discussions

Flawless foamed glasses were successfully produced with various compositions in a wide range of shapes and sizes (Figure 1). Although agitation of sols containing surfactant typically leads to low and unstable foam formation, the viscosity increase that results from the initial stages of condensation is the key factor that enables generation of a stable foam and higher foam volumes. Therefore, the catalyst amount has to be adjusted to produce rapid gelation, usually within periods of approx. 5-10 minutes. After this initial viscosity increase, the agitation procedure must be kept as short as possible to avoid breakage of the gel structure. Contrary to what is observed to production of monoliths in sol-gel technology, drying of sol-gel foams can be accomplished without problems because of the easier solvent evaporation through the open macro-pores.

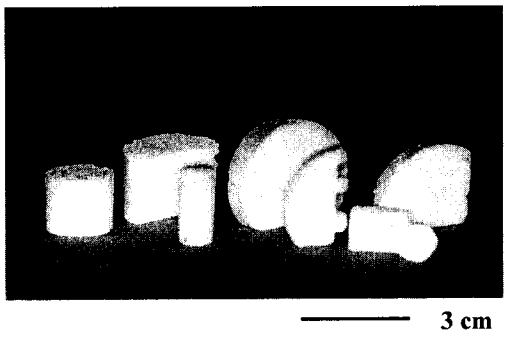

Figure 1. Bioactive 58S sol-gel foams produced in a variety of shapes and sizes.

After thermal stabilisation, the bioactive foams exhibit a hierarchical structure of small and large pores and porosity fractions in the range of 50% to 90% vol, depending on the foam volume produced. Macropores in broad distributions with diameters in the range of 10-200 μm were measured by mercury porosimetry. Larger pores are also noted under SEM observation, in the range of 500 μm (Figure 2.a). The bioactive foam framework presents a texture typical of gel-glasses, as shown in Figure 2.b. Nitrogen sorption analysis revealed framework pores in the mesoporous range of 10-28 nm average and very high specific surface areas in the range of 106-283 m^2/g.

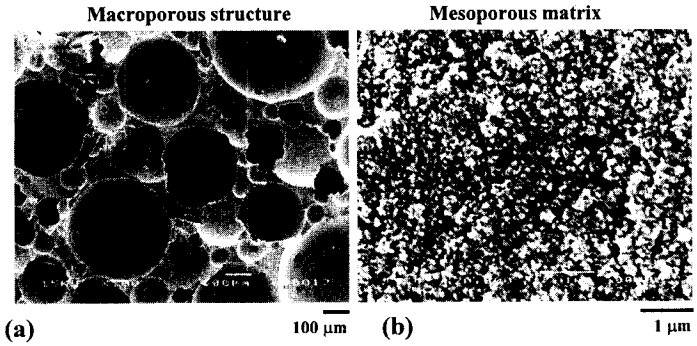

Figure 2. Bioactive foam structure observed under scanning electron microscopy, showing the macroporous network (a) and mesoporous matrix at higher magnification (b).

The hierarchical structures of bioactive foams combine many of the requirements for potential use as tissue engineering scaffolds, and for in situ repair and reconstruction of damaged tissue. The mesoporosity supplies the high surface area, sites for cells to attach and for adsorption of chemical substances, while the intricate framework and open macropores can potentially support 3D organisation of cells and tissue ingrowth. Bioactive compositions supply ions that provide biological stimuli to enhance cellular differentiation and proliferation via gene activation and also the ability of tissue bonding. The glasses can be produced in resorbable compositions and desired pore size ranges to dissolve at controlled rates, therefore, with potential to match rates of tissue growth in tissue repair applications, creating a novel 3-dimensional tissue similar to natural tissues and organs.

Conclusions

A novel process for producing 3D bioactive scaffolds has been developed by foaming sol-gel systems. This new class of material combines macro and mesopores with the properties of bioactive materials. Therefore, these matrices can potentially support 3D organisation of cells, tissue ingrowth, enhance cellular differentiation and proliferation and resorb by controlled rates creating a novel three–dimensional tissue similar to natural tissues and organs.

Acknowledgements

The authors wish to thank FAPESP, Brazil (Grant number 99/02172-4) and the EPSRC (UK) for their support to this research.

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doi:10.4028/0-87849-889-3
Synthesis of Sol-Gel Derived Bioactive Foams
doi:10.4028/0-87849-889-3.287