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Biomimetic collagen scaffolds with anisotropic pore architecture

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ABSTRACT

Sponge-like matrices with a specific three-dimensional structural design resembling the actual extracellular matrix of a particular tissue show significant potential for the regeneration and repair of a broad range of damaged anisotropic tissues. The manipulation of the structure of collagen scaffolds using a freeze-drying technique was explored in this work as an intrinsically biocompatible way of tailoring the inner architecture of the scaffold. The research focused on the influence of temperature gradients, imposed during the phase of crystallisation of collagen suspensions, upon the degree of anisotropy in the microstructures of the scaffolds produced. Moulding technology was employed to achieve differences in heat transfer rates during the freezing processes. For this purpose various moulds with different configurations were developed with a view to producing uniaxial and multi-directional temperature gradients across the sample during this process. Scanning electron microscopy analysis of different cross-sections (longitudinal and horizontal) of scaffolds revealed that highly aligned matrices with axially directed pore architectures were obtained where single unidirectional temperature gradients were induced. Altering the freezing conditions by the introduction of multiple temperature gradients allowed collagen scaffolds to be produced with complex pore orientations, and anisotropy in pore size and alignment.

1. Introduction

Every tissue and organ has its own specific three-dimensional (3-D) extracellular matrix (ECM) structure. Cells in a 3-D support for tissue engineering typically align new ECM components according to the inner architecture of the bioscaffold [1–3]. Therefore, sponge-like matrices with a specific 3-D structural design resembling the actual ECM of a particular tissue would have great potential for the regeneration and repair of a broad range of damaged anisotropic tissues.

Several approaches have been reported to date for the production of scaffolds with anisotropic arrangements, mostly with longitudinal pore alignments. Many of these procedures are based on heating and/or the use of harsh chemicals [4–8]. For example, the techniques injection moulding and solvent evaporation [4], fibre templating [5], porogen leaching [6], microfilament alignment [7] and wire heating [8] involve the incorporation, and subsequent removal, of additional chemicals, polymeric fibres or metal wires in the scaffold architecture to obtain the desired pore orientation. Such methods may be effectively applied for the production of 3-D matrices from synthetic polymers but are not to be recommended for proteins, since these would become denatured and their biological properties would be destroyed [9,10]. Hence, despite the success of the above mentioned methods in producing anisotropic scaffolds the complexity of the processes themselves and the use of additional chemicals demand that novel technologies be developed to form tissue-specific matrices.

An important technique which overcomes the above obstacles is that of freeze-drying. In this case a suspension of the water-soluble polymer is frozen, thereby creating an interpenetrating network of ice crystals [11–14]. These ice crystals are then removed by reducing the chamber pressure to induce sublimation, thus leading to the formation of a porous scaffold. Studies show that uniform conditions throughout the sample on freezing induce an isotropic pore arrangement in the lyophilised biopolymer [12–15]. O'Brien et al. [12], for example, reported the synthesis of highly uniform collagen–glycosaminoglycan (GAG) scaffolds by adjusting the mould size and cooling rate. In this work the conventional freeze-drying technique was modified to create an even more uniform contact between the pan containing the collagen–GAG suspension and the freezing shelf. At the same time the rate of cooling of the collagen–GAG suspension was slowed down in order to produce more homogeneous freezing conditions during the process of formation. These modifications led to an increase in the homogeneity of the scaffold structure.

Recently, improved methods for producing collagen-based scaffolds have been detailed where pore structure homogeneity and

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