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Collagen-based layer-by-layer coating on electrospun polymer scaffolds

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ABSTRACT

Preparation of microfibre constructs of collagen by electrospinning has been problematic due to the instability of collagen in volatile solvents, such as 1,1,1,3,3,3-hexafluoro-2-propanol, so that electrospinning leads to a substantial amount of gelatin fibres. In the present study we have demonstrated the production of collagen-based microfibre constructs by use of a layer-by-layer coating process onto a preformed synthetic polymer microfibre base. Soluble native collagen, which has a basic isoelectric point, has been used with modified triple-helical collagens that have acidic isoelectric points. These modified collagens have been prepared as deamidated, succinylated, maleylated and citraconylated derivatives. Together, the acidic and basic collagens have successfully coated polyacrylonitrile and poly(DL-lactide-co-glycolide) fibres, as shown by spectroscopy and microscopy. These coatings allow good cell attachment and spreading on the fibres. The native, triple helical form of the collagen has been confirmed through use of a conformation dependent monoclonal antibody.

1. Introduction

Collagen is an effective and widely used material for biomedical applications and has gained broad clinical and consumer acceptance as a safe material [1,2]. Its properties can be adapted to meet a range of different clinical applications, so that reliable commercial products are now readily available for use in a variety of medical disciplines. As a commercial medical product, collagen can be part of natural, stabilised tissue that is used in the device, such as in a bioprosthetic heart valve, or it can be fabricated as a reconstituted, purified product from animal sources, such as in wound dressings [1,2]. An important area for further development is, for example, in tissue engineering, where a collagen-based scaffold for cell and stem cell expansion on an accurate, functional matrix is important.

Collagens are characterised by the presence of a triple-helix structure that is supercoiled from three polyproline-II-like helices [3]. The steric constraints for this structure lead to the presence of glycine as every third amino acid in the sequence to allow for close packing of the three polypeptide chains, while a high content of the imino acids proline (Pro) and hydroxyproline (Hyp) promote the polyproline-II-like conformation of individual chains and provide stability [3]. When native collagen is denatured it forms gelatin; the individual chains in gelatin do not readily reform into the original aligned structure, although shorter segments of triple-helix lacking the native alignment can assemble, providing junctional domains that allow the gel network of gelatin to form [4].

Current technologies for designing tissue engineered constructs have difficulty reproducing the complexity of native tissues and organs. Electrospinning has become an increasingly popular method for fabricating nano- to micrometre diameter fibres and scaffolds for various tissue engineering applications [5–7]. Electrospun collagen would be an ideal tissue engineering scaffold as it could promote cell attachment and growth and allow penetration of cells into the fibre matrix. Electrospinning approaches have been described for collagen [8,9] using, for example, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) as the solvent for the collagen. However, concerns have been raised that this approach using HFIP leads to significant denaturation of the collagen, resulting in a loss of the triple helical structure to give gelatine or a gelatin/collagen composite. The extent of this denaturation is probably large, at least 50% [10], and possibly complete [11] leading to loss of reproducibility and of certain positive properties that native collagen can provide. Various other solvent systems have subsequently been examined. In some cases collagen has been electrospun with a copolymer in a single phase, including poly(ε-caprolactone) [12] or poly(ethylene oxide) [13]. Alternatively, other solvent systems have been examined, of which binary mixtures of phosphate buffered saline (PBS) and EtOH have emerged as the most promising [14].

In the present study, we have examined a method that limits the risk of collagen denaturation through production of collagen

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