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Effect of self-assembled nanofibrous silk/polycaprolactone layer on the osteoconductivity and mechanical properties of biphasic calcium phosphate scaffolds

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ABSTRACT

We here present the first successful report on combining nanostructured silk and poly(ε-caprolactone) (PCL) with a ceramic scaffold to produce a composite scaffold that is highly porous (porosity ~85%, pore size ~500 μm, ~100% interconnectivity), strong and non-brittle with a surface that resembles extracellular matrix (ECM). The ECM-like surface was developed by self-assembly of nanofibrous structured silk (20–80 nm diameter, similar to native collagen found in ECM) over a thin PCL layer which is coated on biphasic calcium phosphate (BCP) scaffolds. The effects of different concentrations of silk solution on the mechanical and physical properties of the scaffolds were also comprehensively examined. Our results showed that using silk only (irrespective of concentration) for the modification of ceramic scaffolds could drastically reduce the compressive strength of the modified scaffolds in aqueous media, and the modification made a limited contribution to improving scaffold toughness. Using PCL/nanostructured silk the compressive strength and modulus of the modified scaffolds reached 0.42 MPa (compared with 0.07 MPa for BCP) and ~25 MPa (compared with 5 MPa for BCP), respectively. The failure strain of the modified scaffold increased more than 6% compared with a BCP scaffold (failure strain of less than 1%), indicating a transformation from brittle to elastic behavior. The cytocompatibility of ECM-like composite scaffolds was investigated by studying the attachment, morphology, proliferation and bone-related gene expression of primary human bone-derived cells. Cells cultured on the developed scaffolds for 7 days had significant up-regulation of cell proliferation (~1.6-fold higher, $P < 0.001$) and osteogenic gene expression levels (collagen type I, osteocalcin and bone sialoprotein) compared with the other groups tested.

1. Introduction

While commercially available ceramic scaffolds such as β-tricalcium phosphate (β-TCP), hydroxyapatite (HA), biphasic calcium phosphates (BCP), bioactive glasses (BG) and calcium silicates (CS) are bioactive [1–5], their use in load-bearing applications is limited by the inherent brittleness of ceramics. The weakness of ceramic scaffolds is particularly evident at the optimal porosity (>80%), interconnectivity (~100%) and pore size (200–900 μm) required for bone regeneration [6,7]. During routine fabrication ceramic scaffolds are exposed to high temperatures for long periods of time in order to increase their mechanical integrity, which can compromise their bioactivity. Moreover, the lack of fibrillar proteins in these scaffolds results in poor surface reactivity and interaction with biological entities [7,8]. Silk fibroin, a naturally occurring structural protein with excellent mechanical properties, biocompatibility and biodegradability [9–14], has been widely used in tissue engineering applications. Recent studies reported the efficacy of silk in bone tissue regeneration, both as a single material or in combination with other constituents [15–19]. Silk fibroin scaffolds can be prepared using various methods [19–25]. Although these scaffolds excel amongst polymer-based scaffolds for bone regeneration, their mechanical strength is significantly less than that of ceramic scaffolds with similar physical characteristics, due to partial degradation of the protein structure. Combining silk with ceramics (in particle or scaffold form) remains a major challenge in the field due to the poor adhesion of silk to ceramic materials, which limits its application in drug delivery devices [26–30]. The use of silk to address the brittleness of ceramic scaffolds also requires further investigation. Polycaprolactone (PCL), a semi-crystalline linear ali-

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