Abstract-PhD Thesis

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Title: The Use of Cross-Flow Membrane Emulsification to Fabricate Large, Porous Polymeric Microparticles for Tissue Engineering Applications

A common approach in tissue engineering strategies is to deliver living cells together with supporting scaffolds to damaged or injured body parts and then induce cell proliferation and differentiation for the purpose of regenerating functional tissues. Porous polymeric microparticles (Por-MPs), as scaffolds have recently received extensive interest for their pores, facilitating exchange of nutrients throughout the scaffolds and, sizes (micrometre scale) and shapes (spherical), offering delivery of the cell-scaffold system via narrow bore needle with minimally invasive surgical intervention to repair irregularly shaped tissue defect. For fabrication of MPs, conventional emulsion-solvent evaporation (CE) methods are most commonly used; however the size distributions of the prepared MPs are broad, which could bring negative impacts on the efficiency of the scaffolds as cell-delivering vehicles. On the other hand, cross-flow membrane emulsification (X-ME) is a promising technique for preparation of uniform-sized MPs.

One of the aims of this study was to develop a robust protocol for preparing uniform-sized, large and porous poly (lactide-co-glycolide) (PLGA) MPs using the X-ME method. The method development process started with fabrication of solid polycaprolactone (PCL) MPs (Sol-MPs). Different process and formulation parameters, such as working pressure (P_w), membrane pore diameter (D_0), viscosity of disperse phase (η_{DP}) and emulsifier concentration ($Conc._{CP}$) were optimised for preparing Sol-MPs with mean diameter of approximately 100 µm. Span factor was used as a criteria of degree of monodispersity of the MPs; in general the lower the span factor, the narrower the size distribution. The same emulsion conditions were taken into account for preparation of monodisperse porous PLGA MPs (Por-ME MPs) with mean dimeter of approximately 100 µm. The further aim of this study was to assess the performance of the novel porous MPs (Por-ME MPs) as scaffolds for delivery of stem cells in

bone tissue regeneration. Immortalised human mesenchymal stem cells (ihMSCs) were seeded with Por-ME MPs and the attachment, viability, proliferation and osteogenic differentiation of the cells were assessed.

Under the optimal emulsification conditions, such as at certain P_w, D_0, η_{DP}, $Conc._{CP}$, Sol-MPs with mean diameter of 109 µm (± 20.75) and span factor of 0.52 (± 0.04) were prepared via the ME method. On the other hand, the mean diameter and span factor of Por-ME MPs prepared via X-ME were 114 µm (± 19) and 0.43 (± 0.02), respectively. The size distributions of the Por-ME MPs, prepared via X-ME were substantially narrower than those of the Por-CE MPs, prepared via conventional high shear homogenizer. The mean diameter and span factor of Por-CE MPs were 78 µm (± 25) and 0.70 (± 0.07), respectively. On the other hand, the novel porous MPs were biocompatible with ihMSCs in terms of viability, proliferation and osteogenic differentiation of the cells.

Via this study, a new platform for fabrication of porous PLGA MPs was introduction. The strategy used to prepare these MPs, could be applied for preparing MPs with other biodegradable polymers. The newly developed scaffold system (Por-ME MPs) has the potential to regenerate bone tissues; however, further research is necessary in order to establish the scaffold system as a reliable stem cell delivering vehicle.