Production of Degradable Microcarriers with Pore Channels for the Skeletal Treatment

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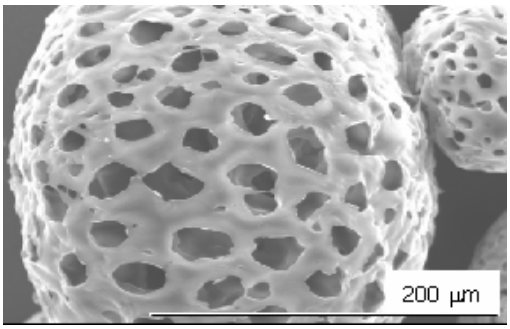
Purpose of Study: Microparticulate polymers are currently used as efficient carriers for delivery of proteins, genes and cells, for therapeutic treatment and tissue engineering applications. The delivery of osteogenic / stem cells though the mediation of microparticulates is now considered as a promising way of treating the skeletal defects. For this application, the composition and structure of the particulates are thus of highly importance. Herein the authors produced degradable polymeric microspheres with highly interconnected pore channels and addressed briefly their performance in the treatment of skeletal defects.

Methods: As a degradable polymer, polycaprolactone (PCL) was chosen. PCL dissolved in chloroform was formulated into microparticulates using a surfactant. In particular, organic porogen was introduced to generate pore channels within the microparticulates. The concentration of PCL (2.5~10%) and the ratio PCL to porogen (1:1~1:8) were controlled to produce well-shaped microparticulates. The PCL solution was poured into a surfactant-containing water bath (1:50) and stirred gently, and followed by filtration and washing. The produced microparticulates were dried under a laminar flow for 24 h. The morphology of the microparticulates was characterized with scanning electron spectroscopy. For the cell compatibility tests, rat bone-marrow mesenchymal cells (BMSCs) were used after isolation and cultivation. Aliquots of the purified cell suspension (30000 ~ 300000) were seeded onto the microparticulates to assess the cell attachment, proliferation and differentiation into osteoblasts (2,3).

Results / Discussion: The obtained microparticulates were shown to be spherical in shape and to contain numbers of pores within them due to the introduction and removal of the porogen (shown in Fig. 1). The diameter of microparticulates was adjusted to around hundreds of micrometers. The pores were observed to be highly interconnected, allowing the cells to migrate and populate. The size of the pores could be tuned within the range of tens to hundreds of micrometers by varying the composition. The cultured BMSCs were shown to attach and grow favorably over the surface and within the pore channels of the microparticulates. Moreover, the BMSCs were shown to elicit osteogenic properties with culturing, by secreting bone-associated genes, including alkaline phosphatase, osteopontin and type I collage. In particular, the culturing conditions such as cell density and microparticulate concentrations were observed to affect the expression of genes, and thus are considered to be carefully controlled for the reliable results. In depth studies are to be done on the osteogenesis for longer periods and in vivo performance in animal model.

Conclusions: In this study degradable polymeric microparticulates with highly interconnected pores were produced. The microparticulates were shown to populate mesenchymal stem cells and differentiate them into osteoblastic cells. Although more work is required to confirm their potential, the current study suggests the porous microparticulates may be useful in the treatment of skeletal defects.



Acknowledgement: The author thanks undergraduate students, Kim SY and Lee ST, for their experimental assistance.

References:

[1] Mann S, Ozin GA. Nature,1996;365:499-505.
[2] H.-W. Kim et al. Adv. Funct. Mater. 2006, 16, 1529.
[3] H.-W. Kim et al. Biomaterials, 2005, 26, 5221.