Enhancing the osteogenic potential of the polymeric nanofibrous scaffolds by the incorporation of ceramic nanofillers for Bone Tissue Engineering Applications

Abstract

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In this study, we report our work on the incorporation of ceramic nanofillers, within a poly(caprolactone) (PCL) nanofibrous scaffold by electrospinning and their advantages over the native PCL scaffold for bone tissue engineering applications. PCL is biocompatible, biodegradable, FDA approved biomaterial. It is one of the strong candidates for bone tissue engineering. It is bioinert and has good mechanical strength as compared to polymers like PLGA and chitosan. This thesis focuses on the incorporation of different ceramic nanofillers in nanofibrous PCL scaffolds and the changes caused due to its incorporation in the properties of the scaffold, in terms of their hydrophobicity, biocompatibility, mechanical strength and osteogenic potential. Ceramics are hard and brittle materials, mostly known to be osteoconductive. Ceramics while in a composite give the mechanical strength to polymers. They can also increase the biological response especially the bioactivity of the scaffold. Nanofillers used in our study were namely, silica nanopowder (nSiO₂), halloysite nanoclay (NC), nano hydroxyapatite (nHAp) and multifunctional nano hydroxyapatite (MF-nHAp). Such a study involving these four particular PCL/nanofiller composite scaffolds for assessing their regenerative potential for the purpose of bone tissue engineering may not have been done ever before in our opinion.

Here, in our study, we wanted to take advantage of properties of nanoceramics (nSiO₂, NC, nHAp and MF-nHAp) for reducing the hydrophobicity of PCL and enhancing the scaffold properties like strength and osteogenic potential for bone tissue engineering. Also, we wanted to exploit the magnetic resonance (MR) contrast enhancement ability of the MF-nHAp. These MF-nHAp incorporated scaffolds were engineered in order to enhance the osteogenic potential as well as its MR functionality for its application in bone tissue engineering. All three above mentioned ceramics, known to promote bone formation, were incorporated in nano-form into a PCL nano-construct for bone tissue engineering. This thesis
study, in our opinion for the first time investigates in detail the comparative effects of these nano-filler additions to PCL nano-fibrous scaffold in terms of toxicity, osteogenesis, stem cell proliferation, mechanical strength, protein absorption, etc. Additionally another unique aspect of this study is the investigation of magnetic resonance (MR) contrast nHAp, previously developed in this laboratory, which potentially could allow the monitoring of the progress of bone tissue regeneration.

All the nano-composite scaffolds along with pristine PCL were evaluated physico-chemically and biologically in vitro, in the presence of human mesenchymal stem cells (hMSC). The incorporation of 4 and 8% nSiO$_2$, showed an increase in scaffold strength, protein adsorption and osteogenic potential. The bare nSiO$_2$ was found to cause toxicity by entering the cells, hence we tried using NC as a replacement filler. It is an alluminosilicate and known to be non-toxic and osteogenic. The scaffolds containing NC showed increased mechanical strength and osteogenic potential. The incorporation of 30-40nm sized MF-nHAp within the nanofibers showed a substantial increase in scaffold strength, protein adsorption, proliferation and osteogenic differentiation of hMSCs along with enhanced MR functionality. This preliminary study was performed to eventually exploit the MR contrast imaging capability of MF- nHAp in nanofibrous scaffolds for real time imaging of the changes in the tissue engineered construct during bone regeneration.