Abstract

The increasing number of bone defects caused by diseases, congenital defects or by accidental fracture urge to formulate innovative strategies to repair the defective bones. However, the slow rate of auto osteoinduction, improper osteo-reconstruction and bacterial colonization at the fracture site are the foremost reasons for developing innovative approaches to augment bone regeneration. The objective of the present thesis is to fabricate the novel segmented polyurethane (PU) or polyurethane-urea (PUU) based 3D porous scaffolds for accelerated bone tissue regeneration. The PU or PUU is synthesized using various biodegradable and biocompatible soft segments such as polyethylene carbonate diol (PCD) and polycaprolactone diol (PCL-OH). The biomolecule spermine, which acts as a natural growth factor for most of the eukaryotic cells, is used as a chain extender along with the conventional chain extender, butanediol (BDO). The integrated biomolecule within the polymer chain is envisaged to reduce the risk of various side effects such as nerve pain, post-operative inflammation, ectopic bone formation etc.

To improve the physico-mechanical properties, imparting antibacterial activity and osteogenic bioactivity, the decorated nanohydroxyapatite (nHA) is synthesized and incorporated within the polymer matrix by in situ technique. The nanorod like nHA is decorated with other nanomaterials such as graphene oxide (GO), carboxyl functionalized carbon nanotube (CCNT) and titanium phosphate (TP) to further accelerate the osteogenic bioactivity of the scaffolds. The 3D porous scaffolds are initially fabricated by salt leaching and electrospinning techniques. Afterward, the 3D porous scaffolds are also fabricated by 3D printing technique giving rise to the porous scaffold with controlled hierarchical architecture, mimicking the native extracellular matrix. In order to achieve superior bioactivity, the surface of the 3D printed scaffolds is modified by immobilized polydopamine, which promoted cell adhesion and proliferation on the scaffold. The synthesized materials and the fabricated scaffolds are characterized by NMR, XPS, FTIRATR, XRD, FESEM, HRTEM, AFM, DSC and TGA. The decorated nHA incorporated scaffolds show significant improvements in physico-mechanical properties with decent antibacterial activity against human pathogen. In vitro studies including biomineralization, MTT assay, cell proliferation, qRT-PCR indicated the superior osteogenic bioactivity of the decorated nHA incorporated nanohybrid scaffolds. After assessing the osteogenic bioactivity of the scaffolds by in vitro study, the scaffolds are implanted at the tibial site of Sprague Dowley rat for in vivo evaluation. Micro-CT study and the histological evaluation of the operated bone section imply accelerated bone regeneration of implanted nanohybrid scaffolds compared to the control sample without exhibiting any organ toxicity as confirmed by histopathology study. The detailed study indicates that the decorated nHA incorporated PU or PUU based nanohybrid scaffolds with improved physico-mechanical properties and superior osteoconductive bioactivity can be a promising alternative platform for bone tissue regeneration applications.

Keywords: Polyurethane-urea, Polycarbonate diol, Polycaprolactone diol, Spermine, Nanohydroxyapatite, Nanohybrid scaffold, Electrospinning, 3D printing, Polydopamine, Bone healing, Histology.