ABSTRACT

There are good prospects for bone tissue engineering and therefore researcher is aimed towards the development of cell-free scaffolds. A cell-free scaffold serves as a temporal filling for critical size defects that do not heal spontaneously. Nevertheless, a suitable scaffold composition is yet to be discovered. Moreover, modifications of cell-free scaffolds with a drug delivery system activate the internal healing capacity. Platelets occur in the healing cascade as a natural source of growth factors (GFs), chemokines and cytokines. This autologous source of bioactive compounds enables the substitution of synthetic GFs. The aim of this thesis is to develop a bioactive cell-free scaffold with a drug delivery system supporting the physiological healing of bone defects. The centrifugal spinning method was used to produce nanofibrous poly-ε-caprolactone (PCL) scaffolds. PCL scaffolds were functionalized with different platelet concentrations. Bioactive compounds released from activated platelets were trapped within the formed fibrin net, enabling their gradual release. Improved metabolic activity, proliferation and alkaline phosphatase activity of MG-63 cells and human mesenchymal stem cells (hMSCs) were detected. The release of compounds lasted for two weeks and nearly reached the plateau phase, therefore lyophilized platelet lysate (lyophilisate) was encapsulated in the core of the PCL nanofibers to prolong the bioavailability of encapsulated compounds. An amphiphilic copolymer Pluronic F-68 was used to protect the bioactivity of the lyophilisate. The release lasted for three weeks and did not reach the plateau phase. However, released concentrations of proteins were three times lower compared to platelet adhesion with no observed effect on the osteogenic differentiation of cultured cells. In view of this, further encapsulation of diverse concentrations of osteogenic supplements; β-glycerol phosphate, dexamethasone and ascorbate-2-phosphate was performed in order to induce osteogenic differentiation. The release of these supplements lasted for a month. Induced osteogenic differentiation of cultured hMSCs and promoted osteogenic marker production in Saos2 osteosarcoma cell line were detected. Such drug delivery systems, with gradual drug release, are promising for bone tissue engineering. Moreover, the 3D fibrous morphology of the PCL scaffold ensures the maintenance of natural morphology, compared to flat 2D surfaces.

KEY WORDS: drug delivery system, cell-free scaffold, centrifugal spinning, osteogenic differentiation, osteogenic supplements, platelets