BIODEGRADABLE MICROPARTICLE FOR STEM CELL DELIVERY AND DIFFERENTIATION

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ABSTRACT

The formation of three-dimensional (3D) models for tissue engineering purpose provides a more conducive environment to enable complex biological interactions and processes between cells, biomaterials and bioactive molecules. Microparticles (MP) can be used as supporting matrix for 3D construct in cells and a carrier to deliver bioactive agents for cell development and differentiation, particularly for bone tissue engineering. Poly(glycerol adipate) (PGA) is a potential polymer for tissue engineering purposes as it is biodegradable and has biocompatibility with several cells. The aim of this study is to modify PGA polymer for MP with well-defined properties for drug encapsulation and release, promote cell-MP interaction and evaluate the osteogenic differentiation with MP incorporation in mouse embryonic stem (mES) and osteoblast cells. The PGA polymer has been modified by substituting 40% pendant hydroxyl groups onto the polymer backbone with stearoyl (C_{18}) groups to increase encapsulation efficiency of drug within MP. Further modification was tethering one carboxyl terminus in PGA polymer with maleimide-poly(ethylene glycol) (MIHA-PEG-NH_2) linker for ligand attachment on the surface of MP. Collagen, as a ligand, was modified by attaching iminothiolane to give a functional thiol group for interaction with maleimide group on the surface of 40%C_{18}-PGA-PEG-MIHA MP. The microparticles were prepared using an emulsification method. Dexamethasone phosphate (DXMP) and simvastatin (SIM) were encapsulated within the MP. The MP-cell aggregate formation was evaluated as well as cell metabolism activity. The effect of polymer modification on drug release from MP was evaluated in the cells by analyzing osteogenic differentiation in cells. The MP prepared from modified PGA polymer exhibited high encapsulation efficiency of SIM in MP. By adjusting the formulation parameters, the release of SIM from MP could be extended to 21 days. The collagen attachment on the surface of 40%C_{18}-PGA-PEG-MIHA MP promoted cell metabolic activity and produced more extensive markers related to osteogenic differentiation.