Bioactive injectable triple acting thermosensitive hydrogel enriched with nano-hydroxyapatite for bone regeneration: in-vitro characterization, Saos-2 cell line cell viability and osteogenic markers evaluation.

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Abstract

Hydrogels forming in-situ have gained great attention in the area of bone tissue engineering recently, they were also showed to be a good and less invasive alternative to surgically applied ones. The primal focus of this study was to prepare chitosan-glycerol phosphate thermosensitive hydrogel formed in-situ and loaded with risedronate (bone resorption inhibitor) in an easy way with no requirement of complicated processes or large number of equipment. Then we investigated its effectiveness for bone regeneration. In-situ forming hydrogels were prepared using chitosan cross-linked with glycerol phosphate and loaded with risedronate and nano-hydroxyapatite as bone cement. The prepared hydrogels were characterized by analyzing their gelation time at 37¡ÁC, % porosity, swelling index, in-vitro degradation, rheological properties, and in-vitro drug release. Results showed that the in-situ hydrogels prepared using 2.5% (w/v) chitosan cross-linked with 50% (w/v) glycerol phosphate in the ratio (9:1, v/v) reinforced with 20¡mg/mL and nano-hydroxyapatite possessed the most sustained drug release profile. This optimized formulation was further evaluated using DSC and FTIR studies, in addition to their morphological properties using scanning electron microscopy. The effect on Saos-2 cell line viability was evaluated also using MTT assay on the optimized hydrogel formulation in addition to their action on cell proliferation using fluorescence microscope. Moreover, calcium deposition on the hydrogel and alkaline phosphatase activity were evaluated. Risedronate-nano-hydroxyapatite loaded hydrogels significantly enhanced the Saos-2 cell proliferation in addition to enhanced alkaline phosphatase activity and calcium deposition. Such results suggest that risedronate-nano-hydroxyapatite loaded hydrogels present great biocompatibility for bone regeneration. Proliferation of cells, as well as deposition of mineral on the hydrogel, was an evidence of the biocompatible nature of the hydrogel. This hydrogel formed in-situ present a good less invasive alternative for bone tissue engineering.

Journal Drug Development and Industrial Pharmacy 2019, February