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Abstract

Novel Composite Hydrogels Based on Natural Components and Akermanite Enriched with Icariin for Osteochondral Healing †

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Abstract: Osteochondral regeneration is a major challenge due to the different composition of cartilage and subchondral bone and different biochemical, biomechanical and biological properties. For this reason, a biomimetic scaffold is necessary to provide different biological signals needed to allow for osteochondral regeneration [1]. This study aims to design novel biodegradable cross-linked composite hydrogels based on gelatin and polysaccharidic components (chondroitin-4-sulphate and hyaluronic acid), mixed with akermanite and enriched with small bioactive molecule (icariin). Akermanite was used as a better alternative to conventional ceramics due to its bone-like apatite formation ability and good bioactivity [2]. Icariin (Ica) flavonoid (from traditional Chinese medicine *Epimedium* herb) was used as substitute for growth factors to enhance cell proliferation and chondrogenic and osteogenic differentiation [3]. Variants of biodegradable cross-linked composite hydrogel based on gelatin, polysaccharidic components (chondroitin-4-sulphate and hyaluronic acid), in two ratios of 2:0.8:0.2 and 2:0.08:0.02 (w/w/w), were developed and mixed with akermanite, at a ratio of 2:1 (w/w). Subsequently, both composite hydrogel variants were cross-linked with (*N*,*N*-(3-dimethylaminopropyl)-*N*-ethyl carbodiimide (EDC) and enriched with small bioactive molecule (icariin). The obtained cross-linked composite hydrogel variants enriched with Ica were characterized related to enzymatic biodegradation (type I collagenase), swelling capacity, degree of cross-linking (TNBS assay), and morphology (SEM). Their cytocompatibility was evaluated by analyses of cell viability and cellular cycle (flow cytometry), cell proliferation (Neutral Red assay), and cell adhesion to composite hydrogels (SEM) using NCTC clone L929 cell line. The final results show that both cross-linked composite hydrogel variants enriched with Ica presented optimal physicochemical and structural properties to be used as a scaffold for osteochondral healing. Our data did not reveal any toxicity of composite hydrogels in the NCTC cell line within the tested range of concentrations (10–50 mg/mL). Additionally, cells were capable of spreading and proliferating on the surface of composite hydrogels. The designed biodegradable cross-linked composites enriched with Ica are recommended for further studies as natural temporary scaffolds, which can allow both cartilage and subchondral regeneration with implications for the management of osteochondral healing.

Keywords: composites; gelatin; akermanite; icariin; osteochondral defects

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