

Thermosensitive Hydrogel Development for Its Possible Application in Cardiac Cell Therapy

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Abstract : Ischemic events can culminate in acute myocardial infarction by irreversible cardiac lesions that cannot be restored due to the limited regenerative capacity of the heart. Cell therapy seeks to replace these injured or necrotic cells by transplanting healthy and functional cells. The therapeutic alternatives proposed by tissue engineering and cardiovascular regenerative medicine are the use of biomaterials to mimic the native extracellular medium, which is full of proteins, proteoglycans, and glycoproteins. The selected biomaterials must provide structural support to the encapsulated cells to avoid their migration and death in the host tissue. In this context, the present research work focused on developing a natural thermosensitive hydrogel, its physical and chemical characterization, and the determination of its biocompatibility in vitro. The hydrogel was developed by mixing hydrolyzed bovine and porcine collagen at 2% w/v, chitosan at 2.5% w/v, and beta-glycerolphosphate at 8.5% w/w and 10.5% w/w in magnetic stirring at 4°C. Once obtained, the thermosensitivity and gelation time were determined, incubating the samples at 37°C and evaluating them through the inverted tube method. The morphological characterization of the hydrogels was carried out through scanning electron microscopy. Chemical characterization was carried out employing infrared spectroscopy. The biocompatibility was determined using the MTT cytotoxicity test according to the ISO 10993-5 standard for the hydrogel's precursors using the fetal human ventricular cardiomyocytes cell line RL-14. The RL-14 cells were also seeded on the top of the hydrogels, and the supernatants were subculture at different periods to their observation under a bright field microscope. Four types of thermosensitive hydrogels were obtained, which differ in their composition and concentration, called A1 (chitosan/bovine collagen/beta-glycerolphosphate 8.5%w/w), A2 (chitosan/porcine collagen/beta-glycerolphosphate 8.5%), B1 (chitosan/bovine collagen/beta-glycerolphosphate 10.5%) and B2 (chitosan/porcine collagen/beta-glycerolphosphate 10.5%). A1 and A2 had a gelation time of 40 minutes, and B1 and B2 had a gelation time of 30 minutes at 37°C. Electron micrographs revealed a three-dimensional internal structure with interconnected pores for the four types of hydrogels. This facilitates the exchange of nutrients, oxygen, and the exit of metabolites, allowing to preserve a microenvironment suitable for cell proliferation. In the infrared spectra, it was possible to observe the interaction that occurs between the amides of polymeric compounds with the phosphate groups of beta-glycerolphosphate. Finally, the biocompatibility tests indicated that cells in contact with the hydrogel or with each of its precursors are not affected in their proliferation capacity for a period of 16 days. These results show the potential of the hydrogel to increase the cell survival rate in the cardiac cell therapies under investigation. Moreover, the results lay the foundations for its characterization and biological evaluation in both in vitro and in vivo models.

Keywords : cardiac cell therapy, cardiac ischemia, natural polymers, thermosensitive hydrogel

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