IN SITU GELLING SYSTEMS TO PROLONG THE INTAMURAL DELIVERY OF SECRETOMA IN THE TREATMENT OF ACUTE MYOCARDIAL INFARCTION

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PURPOSE: the aim of the present work was the development of in situ gelling scaffold based on Methylcellulose (Me) and Sodium Alginate (SA), associated with Chondroitin sulfate (CS), to prolong the intramural delivery of secretoma in the treatment of acute myocardial infarction (MI). Secretoma, released by γ-irradiated apoptotic cord blood-derived mononuclear cells (CB-MNCs), contains many growth factors and cytochines involved in *wound healing,* collagen remodeling, inflammation and in activation of monocythes, macrophages and neutrophils.
METHODS: Me and CS, respectively at 1% and 4%, were hydrated in physiological solution (0.9% w/w). SA and CS were hydrated in isotonic mannitol aqueous solution (5.07% w/w), and CS and SA concentration were 2% (w/w). The systems were characterized for mechanical properties, in term of viscosity and viscoelasticity, mechanical resistance and siringability. Moreover protection against hypoxic and oxidative stress was evaluated in vitro on fibroblasts and HUVEC (Human Umbelical Vein Endothelial Cells).
RESULTS: the formulation based on Me/CS was characterized by an increase of G' value in the range of 31 e 36° according to the physiologic application. The formulation based on SA/CS was characterized by an increase of viscosity after contact with physiological concentration of Ca^{2+} ions. Both formulation were characterized by a good siringability at 25°C (administration temperature). Secretoma loaded SA and CS based formulation was able to induce cell proliferation after oxidative and hypoxic stress as much as the cell substrates not exposed to induced damages. Moreover if its proliferation properties were less than that of pure secretoma probably due to a controlled release of bioactive molecules.
CONCLUSION: Even further evaluation are needed, on the basis of these results in situ gelling systems based on SA/CS seems promising for the intramural delivery of secretoma in the treatment of MI to prevent the apoptotic response and the consequent fibrosis.