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Methylcellulose as a smart thermosensitive scaffold material for tissue engineering

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INTRODUCTION: Injectable thermosensitive hydrogels can be rapidly introduced into the body by injection, thus help to avoid complex and long surgeries. Methylcellulose (MC) aqueous solution, while heated up to near 37°C, as an effect of dehydration, undergoes physical two-step crosslinking [1]. Injectability of such hydrogel system at room temperature and crosslinking during subsequent heating to physiological temperature make such approach attractive for tissue engineering. The objective of this study was to investigate the crosslinking kinetics, biological properties and injection ability of MC aqueous solution, what was studied at various concentrations.

METHODS: Methylcellulose METHOCEL A15LV (Sigma Aldrich) was prepared at various (w/w %) concentrations in demineralized water.
The cross-linking kinetics was studied by differential scanning calorimetry (DSC) at the heating rate of 2 K/min, in the temperature range 20-80°C. In order to prevent water evaporation, hermetic pans were used. Biological tests of hydrogels were performed using L929 fibroblasts. MTT cytotoxicity test was carried out on extracts. Injectability tests allowed determination of the maximum force (should be lower than 30 N [2]), which is needed to carry out injection of the hydrogel into medium that simulates native tissue at 37°C.

RESULTS & DISCUSSION: DSC results show complex thermal behavior with upmost two small endothermic effects, shifting to lower temperatures with increase in MC concentration. For MC concentration higher than 6%, low temperature peak disappears, leaving only the high temperature peak. Analysis of the kinetics of the effects indicates that the rates of the two cross-linking processes increase with temperature and decrease with MC concentration. MTT cytotoxicity tests showed that this type of materials are not cytotoxic. For all MC concentrations the injectability tests showed the maximum force below 30 N.

CONCLUSIONS: Depending on MC concentration, the MC cross-linking may be two- or one-step process. Two-step cross-linking process, which takes place at lower MC concentrations, seems to proceed at higher rates, which is probably due to higher chain mobility of diluted solutions and due to higher temperature. Injectability tests prove that all of the investigated hydrogel concentrations can be easily injected.

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