# Injectable Simvastatin-Loaded Micelle/Hydrogel Composites for Bone Tissue Engineering

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## Introduction

➡ Injectable hydrogels have shown broad application prospects in bone tissue engineering because of minimally invasive surgical procedure, in situ gelation, filling of complex shape defects and simulation of natural extracellular matrix. Simvastatin (SIM) is a commonly used lipid-lowering drug with the advantages of safety, stability, and low costing, shows great potential in promoting bone formation. Moreover, SIM can also provide additional functions like promoting neovascularization and possessing anti-inflammation property. However, the solubility of SIM is pretty poor in water. Besides burst release of the drug is also a common problem when SIM is loaded directly into the material matrix, which greatly impacts the maintaining of effect concerntration. In order to homogeneously disperse SIM and achieve sustained release of SIM, we designed a kind of injectable micelle/hydrogel composites based on maltodextrin and carboxymethyl chitosan.

## Experimental

➡ The composite hydrogels were fabricated by self-crosslinking between aldehyde-modified MDex-C16 micelles (micelle-CHO)-loaded oxidized maltodextrin (OMDex) solution with carboxymethyl chitosan (CMCS) solution. The preparation of micelle/hydrogel composites, drug loading, and release were investigated. The mouse osteogenic precursor cells (MC3T3-E1) were encapsulated within the composite hydrogels to evaluate their cytocompatibility and osteogenic capability (**Fig.1**).

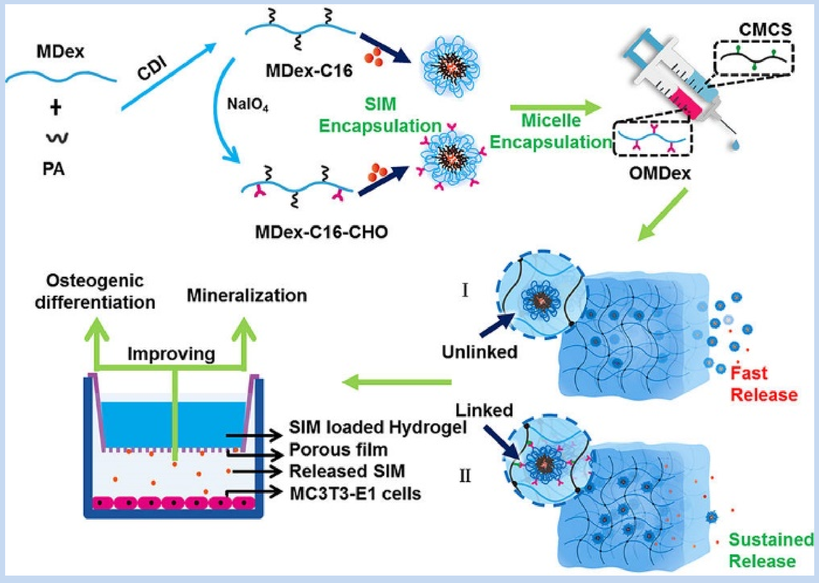


**Fig.1** Schematic illustration for the fabrication of injectable SIM-loaded micelle/hydrogel composites.

## Results

➡ Quantitative analysis of alizarin red staining and alkaline phosphatase (ALP) activity assay of MC3T3-E1 cells cultured on the hydrogels were conducted to verify the in vitro osteogenic activity of the different composite hydrogels. From the quantitative analysis of alizarin red staining, the MC3T3-E1 cells exhibited a continuously increasing mineralization after 7 and 14 days of culture. The highest mineralization degree was found in the SIM/Micelle-CHO hydrogel group. As shown in Fig.2, ALP activity was also increased with culture time and achieved the highest value on the SIM/Micelle-CHO hydrogels. These results suggested that SIM/Micelle-CHO composite hydrogel possessed great potential as an injectable system for bone tissue engineering.

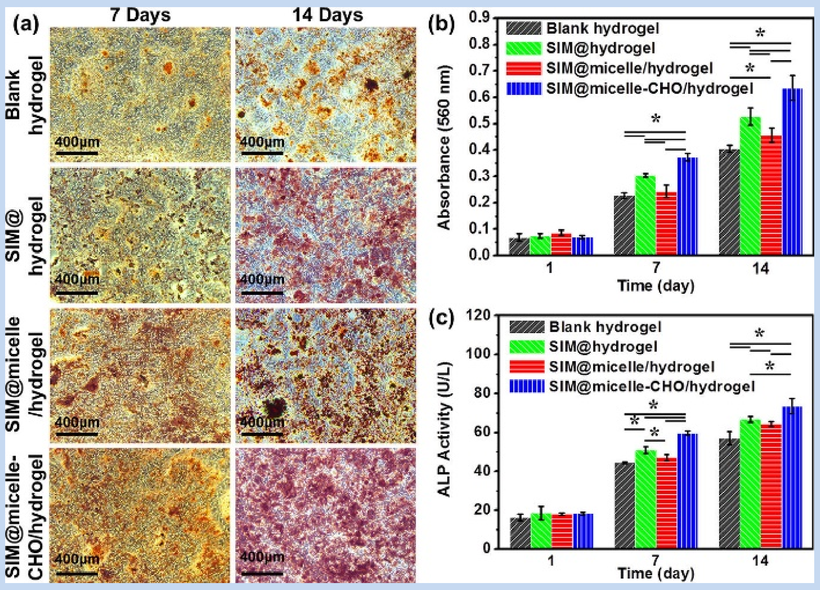


**Fig.2** Osteogenesis of MC3T3-E1 cells.
(a) Alizarin red staining at 7 and 14 days. Quantitative results of (b) alizarin red staining and (c) ALP staining.

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