PEG-coated Mesoporous Silicas to Release Large Biomolecule in Acidic Environment and Their Use in 3D Printed Collagen Scaffolds

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Introduction During the resorption phase of bone remodelling, active osteoclasts (OCs) generate a local acidic microenvironment that, in combination with the secreted enzymes, causes the bone matrix degradation and the release of the encased growth factors (GFs) [1]. In the field of biomolecule/drug release, mesoporous silica particles (MSs) are well known due to their excellent biocompatibility and high loading capability [2] due to the presence of nanopores in the range of 2–8 nm [3]. In order to host large biomolecules such as GFs, the nanopores need to be enlarged. The present study aimed at developing smart MSs with large-pores (LP-MSs) able to upload GFs, coated with a pH-responsive polymer, poly(ethylene glycol) (PEG), to release the cargo in response to a pH decrease thus mimicking the GF release during bone resorption. The smart carrier system was then incorporated in a type I collagen solution to 3D print bone-like scaffolds.

Experimental methods LP-MSs were obtained combining the traditional sol-gel method with a hydrothermal treatment, assessing the influence of temperature and time over the final mesostructure. Horseradish peroxidase (HRP) was used as model protein to evaluate the ability of LP-MSs to adsorb and release large biomolecules. These carriers were then coated with a silane functionalized PEG and the release kinetics were investigated up to 24 h at different pHs. Finally, PEG-coated LP-MS particles were incorporated into a type I collagen solution to enable 3D printing of bone-like scaffolds that were enzymatically crosslinked with transglutaminase and analysed.

Results and discussion The synthetised LP-MSs presented micrometric dimensions and a cage-like mesoporous structure with accessible pores of diameter up to 23 nm. LP-MSs produced at 140 °C for 24 h showed the best compromise in terms of specific surface area (428 m^2/g), pores size (17–23 nm) and volume (1.09 cm^3/g) and hence, were selected for further experiments. HRP was successfully adsorbed into LP-MS mesopores with an adsorption efficiency of about 81.1%. PEG-coated carriers tested at acidic pH enabled a faster release compared to those observed under physiological conditions after 24 h, due to the protonation of PEG at low pH that catalyses polymer hydrolysis reaction. In the 3D printed scaffolds, PEG-coated LP-MSs were homogeneously distributed and embedded in the

collagenous matrix.

Conclusion Our findings indicate that LP-MSs can host large molecular weight molecules as GFs and that PEG can be an effective pH-responsive coating. The obtained collagen-based hybrid formulation is a suitable biomaterial ink and was used to design 3D printed scaffolds able to release GFs for bone tissue engineering applications.

References

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