Inorganic and Organic-Based Carriers to Vehicle And Release Growth Factors For Bone Regeneration Applications

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Biomaterial synthesis and characterisation

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INORGANIC AND ORGANIC-BASED CARRIERS TO VEHICLE AND RELEASE GROWTH FACTORS FOR BONE REGENERATION APPLICATIONS

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Introduction: Bone is a dynamic tissue that undergoes a lifelong process, known as bone remodelling, where bone resorption by osteoclast (Oc) and new bone deposition by osteoblast (Ob) are synergistically coupled. During this process, the resorption of bone portions involves the excretion of enzymes that are able to digest the collagenous fibers and cause the release of biomolecule as growth factors (GFs) stored in the bone matrix[1]. GFs are responsible for regulating several cellular processes, including the stimulation of Ob migration and activity[1]. This study aims to design and characterise different carriers able to incorporate and vehicle GFs. In this context, two possible routes have been explored: the development of mesoporous silica particles with large-pores (LP-MSs) able to incorporate the GFs inside their pores and the encapsulation of GFs using resorbable polymeric particles as carriers. With the final purpose to design a biomimetic 3D printed scaffold able to reproduce the natural bone architecture and biology, the developed carriers are incorporated in a type I collagen matrix in order to develop a bioactive composite system able to gradually release the GFs and support bone regeneration.

Experimental methods:

Inorganic-based carriers

Mesoporous particles were synthesised by combining the sol-gel method with the use of surfactants. Large pore dimensions were obtained by the addition of 1,3,5-trimethyl benzene as a swelling agent and setting the aging temperature at 140°C. Horseradish Peroxidase (HRP) was used as model protein due to molecular size and charge properties similar to those of biological growth factors[2] in order to evaluate the ability of LP-MSs to adsorb and release proteins.

Organic-based carriers

Transforming growth factor βeta1 (TGFβ1) was used in this study and PLGA was selected as carrier thanks to its biocompatibility and tuneable degradation enabling a controlled spatial-temporal release of TGFβ1. PLGA containing TGFβ1 particles were synthesised through double evaporation technique.

Release tests at physiological conditions (Phosphate Buffered Saline pH 7.4, 37°C) were carried out on both carriers to obtain their release kinetics.

Bioactive composite system

LP-MSs or PLGA particles were incorporated in a 0.5M acetic acid solution of type I collagen obtaining a suspension and the viscoelastic properties of the systems were investigated with rheological tests.

Image:

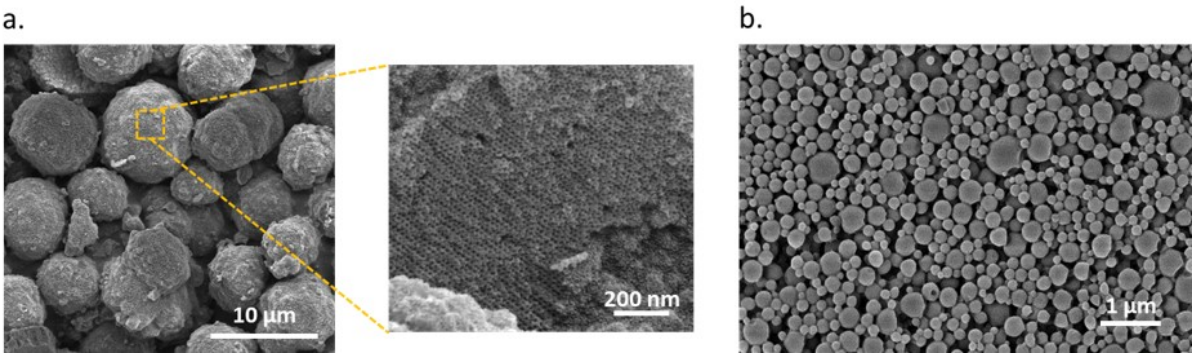

Table: Fig.1: Field emission scanning electron microscopy images of (a.) LP-MSs and (b.) PLGA particles

Results and discussions: Nitrogen physisorption analysis showed that LP-MBGs have a high exposed surface area and uniform accessible pores. Preliminary release test has shown that loaded HRP was almost fully released in the first 5 hours while PLGA particles provided a more gradual release of TGFβ1. The viscoelastic properties assessment of the composite systems and the release tests from the composite are currently ongoing.

Conclusions: This study has shown two different approaches to successfully vehicle GFs and obtain different release kinetics for bone regeneration applications. The swelling of LP-MSs pore dimension resulted to be a good strategy to host large molecular weight molecules as GFs. LP-MSs work is currently ongoing with TGFβ1 and Western Blot analysis will be performed to assess GFs functionality with both carriers.

References/Acknowledgements:

1. Florencio-Silva R et al., Biomed Res Int. 2015
2. Banci L et al., Biochemistry 1994, 33, 41

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