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# Multifunctional biomaterials based on biomimetic apatite core-shell particles: towards smart antibacterial/osteogenic bone substitutes.


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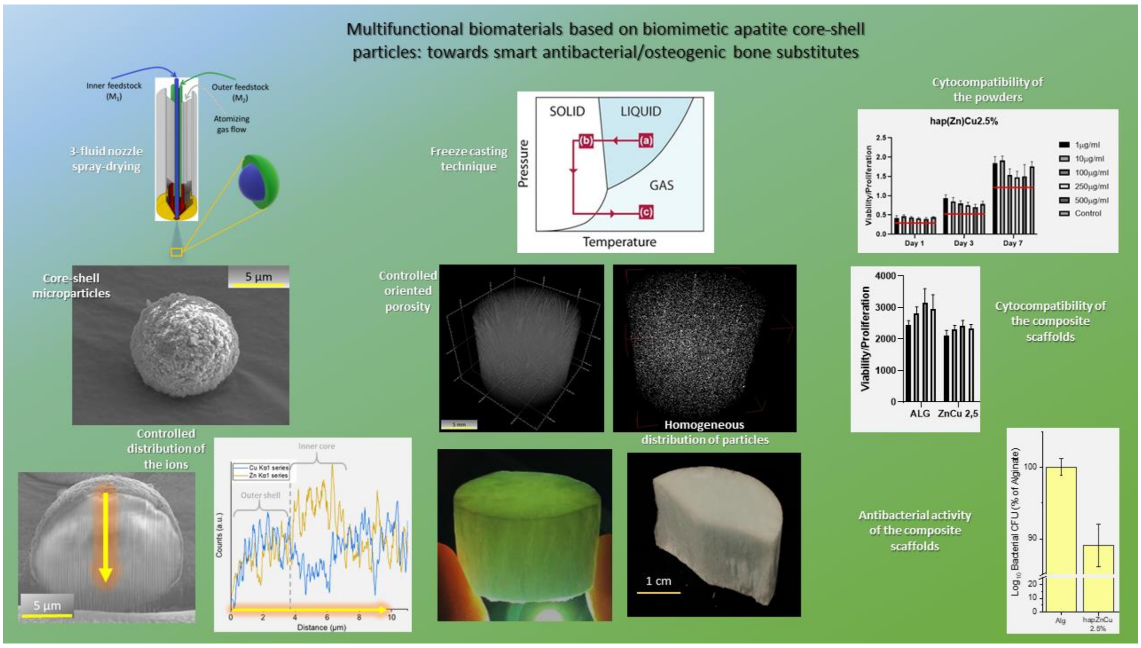
**Project:** Antimicrobial Integrated Methodologies for Orthopaedical Applications



## Abstract

Antimicrobial Resistance (AMR) related diseases are a major concern for the medical community and the society. Their general impact is especially worrying in orthopaedics, leading to the rising threat of nosocomial infections, complexified by the porous structure of bone. It is foreseen by the ECDC that, by 2050, AMR will be responsible of more deaths than cancers. Furthermore, the World Bank predicts that AMR will have an economic impact on healthcare comparable to the 2008 economic crisis. This scenario enhanced the research of alternatives to traditional antibiotics, which is the scope of the AIMed (Antimicrobial Integrated Methodologies for orthopaedic applications: www.aimed-itn.eu) European Innovative Training Network (H2020). This network, that includes this work, focuses on the development of innovative materials with antibacterial properties for use as orthopaedic bioactive implants.

This work aimed at obtaining some innovative antibacterial biomaterials based on bio-inspired apatites exhibiting a spatial control of ionic substituents, in view of displaying subsequent biological actions after implantation. The substituted biomimetic apatites were synthesized, using either copper, zinc or silver cations. The metals were selected not only for their antimicrobial potential but also for their potential angiogenicity and/or osteogenicity. These apatites were then used as the feedstock to generate, through a 3-fluid nozzle spray dryer, several core-shell apatite particles with a dual, spatially organized, ionic substitution and a control of size and morphology.

The particles were then used as charges in apatite-alginate composite scaffolds, the latter is a biopolymer known for its biocompatibility and regularly used in medical devices. Since the goal of the project is bone repair, the 3D-scaffolds were fabricated using the freeze-casting technique, allowing us to obtain a controlled oriented porosity, suitable for bone substitutes. The scaffolds were also cross-linked to enhance their mechanical properties and behaviour in aqueous media.

In vitro biological evaluations were carried out to assess the cytocompatibility and antibacterial behaviour of the compounds. No sample was found cytotoxic, and a gradual cell growth was observed in the scaffolds, showing that the pore size is suitable for this purpose. Depending on the structure and on the substitution ratio in antibacterial ions $Cu^{2+}$ and $Ag^{+}$, the samples also showed antibacterial activity toward E. Coli and/or S. Aureus.

By proposing, for the first time, a core-shell concept based on biomimetic apatites – and 3D scaffolds containing them – to allow subsequent biological actions (first antibacterial, then osteogenic), this work enters in the appealing generation of dynamically-bioactive bone substitutes of clinical relevance.