## Magnesium, manganese and cobalt substituted nanocrystalline apatites obtained by hydrothermal transformation of biogenic calcium carbonate

Cano-Plá SM<sup>1\*</sup>, Fernández-Penas R<sup>1</sup>, Triunfo C<sup>2</sup>, Verdugo-Escamilla C<sup>1</sup>, Gärtner S<sup>3</sup>, Maoloni G<sup>4</sup>, Cölfen H<sup>3</sup>, Falini G<sup>2</sup>, Gómez-Morales J<sup>1\*</sup>

Fishery industry waste seashells represent an important environmental issue and imply the loss of potentially useful biomaterials [1]. They are composite materials made of CaCO<sub>3</sub> and an organic matrix (1-5 wt.%) formed mainly of proteins and polysaccharides. Fabrication of functional calcium phosphates (eg. doped nanoapatites) using this type of biogenic CaCO<sub>3</sub> as a calcium source may partially alleviate the ecological problem and be an alternative source of biocompatible materials intended for biomedical uses. In this work, the one-pot hydrothermal method [2] has been used in the preparation of biocompatible Mg<sup>2+</sup>, Mn<sup>2+</sup>, and Co<sup>2+</sup>-doped apatites. These divalent transition metal ions fulfill different roles in skeletal metabolism and may stimulate bone tissue regeneration [3-5]. The experiments were performed in a hydrothermal multitube set-up as well as in an autoclave, using oyster shell calcium carbonate particles from the species Crassostrea gigas, the KH<sub>2</sub>PO<sub>4</sub> as a P reagent (P/CaCO<sub>3</sub> 0,6), and temperatures from 25°C to 200°C. Full transformation of CaCO<sub>3</sub> was obtained at 160 °C, yielding platy-shaped apatite nanoparticles doped with either 0.22 mol% Mg<sup>2+</sup>, 0.012 mol% Mn<sup>2+</sup>, or 0.16 mol% Co<sup>2+</sup>, and sizes within the range 75-90 nm. All samples showed a high cytocompatibility/biocompatibility when incubated with human mesenchymal stem cells for 1 and 3 days, and a small decrease in cell viability after 7 days of incubation in a dose-dependent concentration. Overall, the method was demonstrated to be promising in the preparation of doped biocompatible apatite nanocrystals with osteogenic features, and the biogenic CaCO<sub>3</sub> a huge and unexplored calcium source for the preparation of apatite-based biomaterials.

Acknowledgements: Grant ref. PCI2020-112108 is funded by MCIN/AEI/10.13039 /501100011033 (Spain) and the European Union "NextGenerationEU"/PRTR". PCI2020-112108 is part of the project CASEAWA of ERA-NET Cofund BlueBio H2020.

## References

- [1] Morris J P. Shells from aquaculture: a valuable biomaterial, not a nuisance waste product, Revs. in Aquaculture 2019,11,42.
- [2] Fernández-Penas R et al. One-step hydrothermal transformation of oyster shell Mg-calcite to nanocrystalline apatite and their osteoinductive properties, 2023 (to be submitted).
- [3] Andrés NC et al. Manipulation of Mg<sup>2+</sup>–Ca<sup>2+</sup> switch on the development of bone mimetic hydroxyapatite, ACS Appl Mater Interf 2017, 9, 15698.
- [4] Kulanthaivel S et al. Cobalt doped proangiogenic hydroxyapatite for bone tissue engineering application, Mater Sci Eng C 2016, 58, 648.
- [5] Huang Y et al. Characterisation, corrosion resistance and in vitro bioactivity of manganese-doped hydroxyapatite films electrodeposited on titanium, J Mater Sci Mater Med 2013, 24, 1853–1864.

<sup>\*</sup>lead presenter: sandra.cano@csic.es (S. Cano-Pla)

<sup>&</sup>lt;sup>1</sup>LEC, IACT (CSIC-Univ. Granada), Avda. Las Palmeras, nº 4, 18100 Armilla (Spain).

<sup>&</sup>lt;sup>2</sup>Dpt. Chemistry "G. Ciamician", Univ. of Bologna, via F. Selmi 2, 40126 Bologna (Italy)

<sup>&</sup>lt;sup>3</sup>Physical Chemistry, Dpt. Chemistry, Univ. Konstanz, Universitätsstrasse 10, Box 714, D-78457 Konstanz (Germany).

<sup>&</sup>lt;sup>4</sup>Plant Ascoli Piceno, Finproject S.p.A., 3100 Ascoli Piceno, Italy.