XXXVIII Reunión Bienal de la Sociedad Española de Química (RSEQ), Granada, 2022
ISBN: 978-84-09-42159-6
https://intranet.pacifico-meetings.com/amsysweb/faces/publicacionOnlineLIBRO.xhtml?id-661

BIOMIMETIC LUMINESCENT APATITE NANOPARTICLES FOR DICLOFENAC DELIVERY IN INFLAMMATORY ENVIRONMENTS

S. M. Cano-Plá[a], A. D´Urso[b], J. F. Fernández-Sánchez[c], D. Colangelo[b], D. Choquesillo-Lazarte[a], M. Prat[b,d,e,f], J. Gómez-Morales[a]

[a]*Laboratorio Estudios Cristalográficos, IACT, CSIC-UGR. 18100 Armilla, Granada, Spain*

[b]*Dpto Scienze della Salute, Univ. Piemonte Orientale, 28100 Novara, Italy*

[c]*Dpto. Química Analítica, Facultad de Ciencias Univ. Granada, 18071 Granada, Spain*

[d]*Centro Biotecnologie per la Ricerca Medica Applicata (BRMA), 28100 Novara, Italy*

[e]*Consorzio Interuniversitario per Biotecnologie (CIB), Località Padriciano 99, 34149 TS, Italy*

[f]*Consorzio Interuniv. Nazionale Scienza e Tecnologia Materiali (INSTM), 50121 Firenze, Italy*

E-mail: jaime@lec.csic.es

Keywords: *diclofenac; apatite; Tb-apatite; luminescence; cytocompatibility, inflammation*

Today bone tissue pathologies, such as osteoporosis, osteoarthritis and rheumatoid arthritis represent important health problems with considerable socio-economic burden, linked to the general population aging [1]. These musculo-skeletal disorders are characterized by a clinical condition of inflammation. For all these pathologies the available therapeutic strategies are still unsatisfactory, namely because of the associated side effects. Sodium diclofenac (DF) is a non-steroidal anti-inflammatory drug (NSAID) with analgesic, anti-inflammatory and anti-pyretic activities, exerting its activity by competitively blocking cyclooxygenases-2 (COX-2) enzymatic activity responsible for the synthesis of inflammatory mediators, e.g., prostaglandin E_2 (PGE_2) [2]. As all the NSAIDs, DF has adverse systemic side effects, such as gastrointestinal ulceration and bleeding, hepato-renal dysfunction, disorders in the cardiovascular and central nervous systems, and skin reactions [3]. Local delivery of this drug via luminescent nanoparticles (NPs) would offer a method of bypassing these inconveniences, while allowing their localization by luminescence emission. In this context, apatite (Ap) NPs, which consist of calcium phosphate and closely mimic bone apatite nanocrystals both from chemical and structural points of view, when doping with a lanthanide ion (Eu^{3+}, Tb^{3+},..) become luminescent, thus being particularly suited for therapeutic and diagnostic applications. In this work [4] we explored the loading/release ability of diclofenac in both undoped Ap and luminescent (Tb^{3+})-doped citrate-coated carbonated apatite (Tb^{3+}:Ap) NPs at different temperatures (25, 37, 40 ºC) and pHs (7.4, 5.2). Adsorption isotherms fitted the Langmuir-Freundlich model. The maximum adsorbed amounts at 37 ºC were higher than at 25 ºC, and particularly when using Tb^{3+}:Ap NPs. DF-release efficiencies were higher at pH 5.2, a condition simulating a local inflammation. The luminescence properties of DF-loaded Tb^{3+}:Ap NPs were affected by pH, being the relative luminescence intensity higher at pH 5.2, but not influenced either by the temperature or by the DF-loaded amount. Both Ap and Tb^{3+}:Ap NPs were cytocompatible on two osteosarcoma cell lines and primary human osteoblasts. In addition, DF release increased COX-2 mRNA expression and decreased PGE_2 production in an *in vitro* osteoblast's cytokine–induced inflammation model. These findings evidence the potential of these NPs for osteo-localized delivery of NSAIDs and the possibility to localize the inflammation by changes in luminescence.

Acknowledgements: Spanish Grant "Bioscaffold" Ref. PGC2018-102047-B-I00 (MCIU/AEI/FEDER, UE) and Italian Ricerca Fondi di Ateneo per la Ricerca—FAR 2018 funded this work.

References

[1] M.A. Clynes; N.C Harvey, et al. *Br. Med. Bull*. **2020**, 133, 105–117.
[2] T.J. Gan, *Curr. Med. Res. Opin*. **2010**, 26, 1715–1731.
[3] K.D. Rainsford, *Am. J. Med*. **1999**, 107, 27–35.
[4] S.M. Cano-Plá, A. D'Urso et al. *Nanomaterials* **2022**, 12, 562.