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The shielding effect of phospholipidic bilayers on zinc oxide nanocrystals for biomedical applications

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Zinc oxide nanocrystals (ZnO NCs), thanks to their unique properties, are receiving much attention for their use in nanomedicine, in particular for therapy against cancer [1]. To be efficiently employed as diagnostic and therapeutic (yet theranostic) tools [2], highly dispersed, stable and non-toxic nanoparticles are required. In the case of ZnO NCs, there is still a lack of knowledge about cytotoxicity mechanisms and stability in the biological context, as well as immunological response and haemocompatible features.

Most of these above-mentioned behaviours strongly depends on physico-chemical and surface properties of the nanoparticles. We thus propose a novel approach to stabilize the ZnO NCs in various biological media, focusing on NC aggregation and biodegradation as a function of the surface functionalization.

We synthesized bare ZnO NCs, amino-propyl functionalized ones, and lipid bilayer-shielded NCs, and we characterized their morphological, chemical and physical properties. The stability behavior of the three different samples was evaluated, comparing their biodegradation profiles in different media, i.e. organic solvents, water, and different simulated and biological fluids. The studies aim to investigate how the particle surface functionalizations, and thus chemistry and charge, could influence their hydrodynamic size, zeta potential and consequent aggregation and degradation in the different solvents. We demonstrated that bare and amino-functionalized ZnO NCs strongly and rapidly aggregate when suspended in both simulated and biological media. Long-term biodegradation analysis showed small dissolution into potentially cytotoxic Zn-cations, also slightly affecting their crystalline structure. In contrast, high colloidal stability and integrity was retained for lipid-shielded ZnO NCs in all media, rendering them the ideal candidates for further theranostic applications [3].

[1] P. Zhu, Z. Weng, X. Li, X. Liu, S. Wu *Adv. Mater. Interfaces* **3** (2016) 1500494.

[2] E. Lim, T. Kim, S. Paik, S. Haam, Y. Huh, and K. Lee, *Chem. Rev.* **115** (2015) 327–394.

[3] B. Dumontel, M. Canta, H. Engelke, A. Chiodoni, L. Racca, A. Ancona, T. Limongi, G. Canavese and V. Cauda, *J. Mater. Chem. B*, under review

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