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Towards a comprehension of Zinc oxide nanoparticles behavior in inorganic and biological fluids / Canta, Marta; Dumontel, Bianca; Racca, Luisa; Chiodoni, Angelica; Cauda, Valentina. - STAMPA. - (2016), pp. 118-118. ((Intervento presentato al convegno Merck Young Chemists Symposium (MYCS 2016) tenutosi a Rimini nel 25-27 novembre 2016.

Availability:

This version is available at: 11583/2654837 since: 2017-06-13T12:44:10Z

Publisher:

Società Chimica Italiana

Published

DOI:

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Towards a comprehension of Zinc oxide nanoparticles behavior in inorganic and biological fluids

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In recent years nanomedicine emerged as a preferred treatment option for many diseases. Zinc oxide nanoparticles (ZnO NPs) for their unique properties have received much attention for their implications in cancer therapy [1]. Recently, many efforts have been devoted to study ZnO NPs as diagnostic and therapeutic tools; however there is still a lack of knowledge about toxicity mechanisms and stability in the biological context. For clinical applications dispersed and stable nanoparticles are ideal and their aggregation behavior strongly depends on physico-chemical and surface properties.

In many studies ZnO NPs cytotoxicity is related to the production of Zn²⁺ ions [2], whose availability strongly depends on the extent of ZnO NPs dissolution and interaction with ionic species in solution.

In this scenario we decided to study ZnO NP stability in various solvents and biological media, focusing on NP aggregation and biodegradation. We synthesized ZnO NPs and characterized their morphological, chemical and physical properties [3]. In addition, we studied the stability behavior of ZnO NPs in different media, investigating parameters (particle concentrations, functionalization with aminopropyl groups and solvent nature) that would influence their hydrodynamic size, zeta potential and thus aggregation and degradation.

For this reason, we performed long term biodegradation analysis (up to one month) of these NPs in common cell culture media (EMEM) and in a simulated body fluid (SBF) mimicking human plasma. We demonstrated that our ZnO NPs aggregate rapidly when suspended in any media, independently from the synthetic batch. The rate of aggregation is however different depending on solution composition and ZnO concentration, reaching the maximum in SBF and EMEM. Long term biodegradation analysis showed that this aggregation is accompanied by small dissolution that does not affect the crystalline structure.

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

[2] J. Liu, X. Feng, L. Wei, L. Chen, B. Song, and L. Shao, *Crit. Rev. Toxicol.* **46** (2016) 46:4, 348-384.

[3] V. Cauda, R. Gazia, S. Porro, S. Stassi, G. Canavese, I. Roppolo, and A. Chiolerio, "Handbook of Nanomaterial Properties. XXVII" 1464 pages, Springer Verlag, Berlin Heidelberg, 2014.