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Uptake and Cytotoxicity of Silica Nanoparticles of Different Charges and Sizes

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Extended Abstract

Silica nanoparticles have a great potential for diagnostic and therapeutic applications in medicine because of the high inertness and chemical stability of silica material. However, at the nanoscale, particles possess novel properties and potential unusual biological effects. Nanoparticle physico-chemical features seem to have a direct impact on their biological activity. The aim of this study was to determine the influence of two of these parameters: size and surface functionalization on cellular uptake and cytotoxicity. To that purpose, well-characterized fluorescent silica nanoparticles with a diameter around 60 nm were synthetized. RAW 264.7 murine macrophages, the main target cells of the respiratory system responsible for the phagocytosis of the exogenous particles were incubated for 20 hours with each kind of particles. Nanoparticles uptake by cell and membrane adsorption were assessed by fluorimetric assays and cellular responses were evaluated in terms of cytotoxicity (Lactate DeHydrogenase LDH release), pro-inflammatory factor (Tumor necrotic factor TNFα) production and oxidative stress (Reactive Oxygen Species ROS generation).

(1) In order to observe the impact of surface functionalization, nanoparticles with different coatings (negative COOH functionalization, positive NH_2 functionalization, neutrally Poly Ethylene Glycol charge) were used. Neutrally stabilized nanoparticles were significantly more internalized but less pro-inflammatory than charge stabilized nanoparticles. However, these latter, and more particularly positively charged nanoparticles, triggered more cytotoxicity and were more adsorbed at the cell surface.

(2) In order to observe the impact of particle size, the behavior of 60 nm nanoparticles was compared to that of sub-micronic particles of same coating of 130 nm in diameter. Particles uptake by cells was investigated by fluorimetry and by time-lapse microscopy. Compared by mass, submicronic particles were the less cytotoxic particles and the less significantly uptaken, suggesting that nanoparticles cytotoxicity might be related to their uptake. Importantly, our findings expressed by surface area instead of mass suggest that biological activity of particles might be related to the particle specific surface. But both particles were cytotoxic at the highest dose.

Further investigations are needed to better understand how nano-scale may impact biological responses of silica particles in order to provide a “safer by design” approach for the engineering of new nano-objects. This model of particles may be helpful for a better understanding of uptake mechanisms, a key issue of nanotoxicology.