Cellular Uptake and Cytotoxicity of metal oxide Nanoparticles

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Metal oxide and metal NPs are widely used in various industrial processes as catalysts, UV protectors and so on. Interactions of the colloidal materials with biological systems and environment could lead to unintended adverse effects, which are recently recognized and attracted broad attentions [1-3]. Our goal is to study the cell uptake, intracellular distribution and the influence of the metal oxide nanoparticles on cell viability and functions. In this work, we shall introduce the interactions between TiO_2, ZnO, and Fe_3O_4 particles and NCI H460 epithelial cells, and Raw264.7 macrophage cells.

The size and surface charge properties of these nanoparticles in cell culture medium with and without serum as well as their morphology were studied by DLS, zeta potential measurements and TEM. All the particles were agglomerated to over 100nm aggregates with similar surface zeta potentials in the cell culture medium, especially in the medium containing serum. The solubility of those nanoparticles in the cell culture medium was also tested by AAS (atomic absorption spectrometry). The ZnO particles could be dissolved largely with a high Zn ions concentration (~1 μg/ml) in 4 hours. The Fe_3O_4 particles showed lower solubility (~0.01 μg/ml), while the TiO_2 particles showed very poor solubility (<0.00001 μg/ml). The difference of solubility could play an important role in the toxicity generated by the particles, e.g. the ZnO particles caused significant decrease of viability of the epithelial cells and the macrophages, while the other two types of the particles showed lower toxicity at the tested concentrations and culture time. We also found that the cytotoxicity was generated through weakening of mitochondria membrane potential (MMP) and inducing cell apoptosis. The cellular loadings of the particles were quantified by AAS, showing that the uptaken amount of the Fe_3O_4 and TiO_2 particles increased with the co-incubation time at the first 12h and reached an equilibrium state afterwards until 48h. The cellular loading of the ZnO particles increased at the initial 12h, and then the cells were dead and the final metal content in the cells was much higher than that of the other particles. Distribution of the three kinds of particles in both types of cells as a function of co-incubation time was followed by TEM. We found that all the particles entered into the NCI-H460 and raw264.7 cells and located inside the vesicles in the cytoplasm, but did not cross into the nucleus during 48 h.

References

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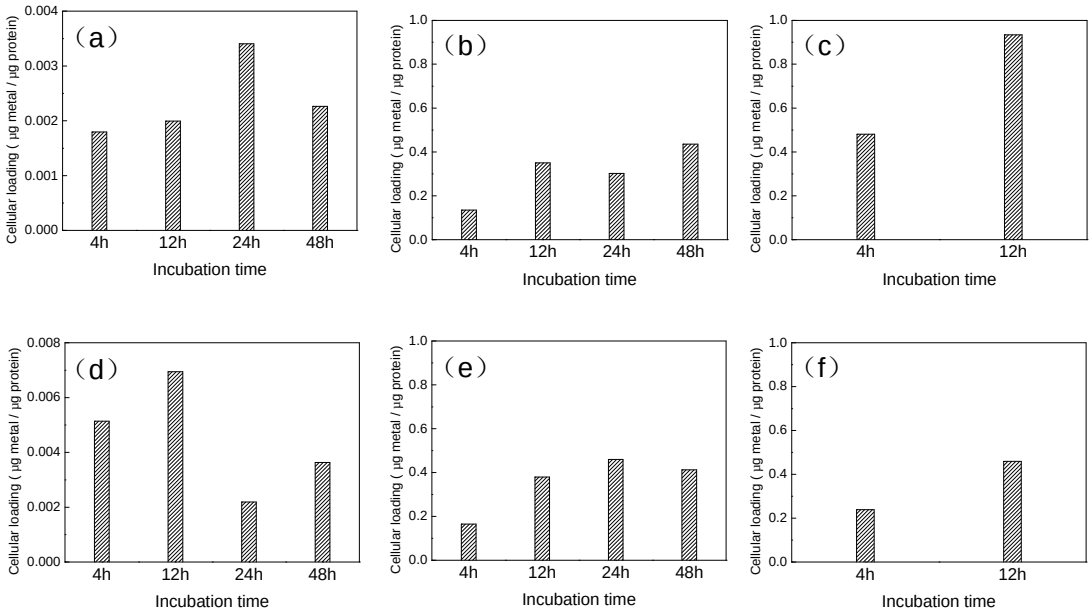
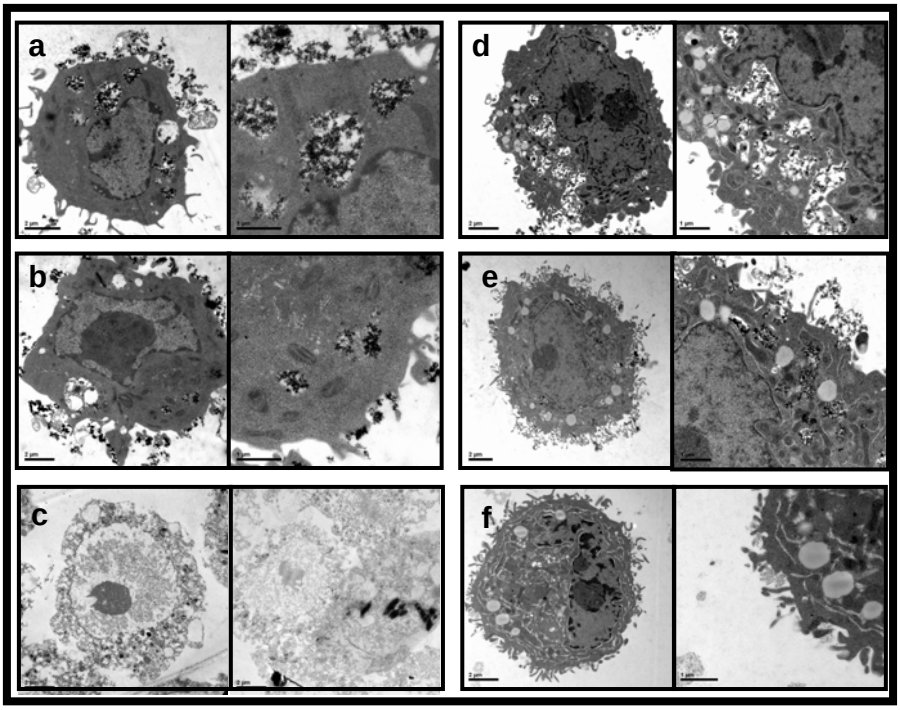


Fiugre 1 The cellular loading of metal oxide particles as a function of co-incubation time. (a-c) Raw 246.7 cells and (d-f) H 460 cells co-incubated with (a, d) TiO_2, (b, e) Fe_3O_4, and (c, f) ZnO particles.



Fiugre 2 The TEM images of the cells internalized metal oxide nanoparticles (right: corresponding magnified TEM images): (a-c) Raw 246.7 cells, (d-f) H460 cells; (a, d) Fe_3O_4, (b, e) TiO_2, and (c, f) ZnO.