**Cell uptake and cytotoxicity studies of Metal Oxide Nanoparticles**

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Metal oxide and metal NPs are widely used in various industrial processes and common products. Some examples of these are $TiO_2$ and ZnO as catalysts and UV protectors, CuO in anti-fouling paints, $Al_2O_3$ as a surface protector, $CeO_2$ in polishing, indium-tin oxides forming anti-electrostatic coatings and various rare earth oxides in electronics manufacturing.

Metal and metal oxide NPs may be toxic for two reasons:

1) They may possess increased catalytic activity due to nanoscale structure or chemical modification of their surface. These catalytic properties may interfere with numerous intracellular biochemical processes.

2) The decomposition of NPs and subsequent ion leakage may result in a continuous formation of free radicals and metal ions, and, in this way, may heavily interfere with the intracellular free metal ion homeostasis, which is essential for cell metabolism and requires that metal ions are kept at extremely low levels in the cytoplasm. [1]

A key issue regarding the study of the toxicological effects of metal oxides NPs is their localization and biological fate at cellular level and the quantification of their uptake by cells. Confocal Scanning Laser Microscopy (CLSM) and Flow Cytometry are normally applied for NPs uptake studies but require the labelling of cell interior and as well as the NPs, which may change their properties and their toxicological end points.

We will show that intracellular localization of NPs is possible by means of Spontaneous Confocal Raman Spectroscopy. Both NP and cells have characteristic Raman spectra [2] that can be employed for their detection avoiding labelling. [3] In parallel, NP localization has also been studied by TEM to provide a reference for the Raman Studies (Figure 1).

Besides localization, Raman can be used to asses changes in the cellular machinery after exposition to the NPs like DNA fragmentation or protein conformation that can be related to the toxicity of the NPs. As control cell viability studies were conducted with MTT.

In addition, Metal oxide NPs have been characterized by Transmission Electron Microscopy (TEM), Dinamic Light Scattering (DLS), UV-Visible Spectrophotometry, Confocal Raman Microscopy, Energy-dispersive X-ray Spectroscopy (EDX) and X-ray photoelectron Spectroscopic (XPS). The size/aggregation and charge of NPs were characterized in cell culture by means of DLS.

## References

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## Figures

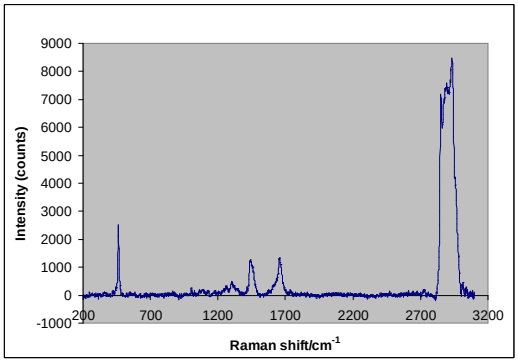


*Figure 1. Spectrum recorded from a cell (HepG2 line) wich was incubated together with $CeO_2$ NPs during 48h. Here it is possible to see NP characteristic peak (at 460) and the rest of peaks coming from different compounds of the cell.*