Lanthanide-doped CaF₂ and SrF₂ nanoparticles for biomedical applications: in vivo and in vitro experimental studies

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Among the wide range of nanoparticles (NPs) studied for diagnostic and therapeutic applications lanthanide-doped nanosystems have raised special interest [1]. Their very small dimension (10 nm) and upconversion emission property have increased the range of their applications from contrast agent probes in bioimaging to drug delivery systems [2,3]. Here, the cytotoxicity of rare earth (Yb and Er)-doped CaF₂ and SrF₂ NPs has been investigated both in vitro and in vivo. In vitro studies have been conducted in a motoneuron cell line as model of neuronal interaction, and in a line of human dendritic cells which play a key role in the immune response. In the motoneuron cell line, a weak response was observed at early time points while the cell viability showed an increment, except for the highest concentration of lanthanide-doped NPs. The levels of cytokines released from human dendritic cells were low and dose-dependent. The NP biodistribution was investigated after a single peripheral administration in mice. Aggregates of NPs were shown, with different techniques, mostly in peripheral organs (spleen and liver) after one day. A limited penetration of both CaF_2 and SrF_2 NPs was seen in the brain parenchyma, associated with a mild astrocytic activation. Since the present *in vitro* findings indicate that lanthanide-doped NPs are safe, and the *in vivo* data show that they can enter the brain parenchyma crossing the blood-brain barrier, these NPs may represent promising tools for diagnostic and therapeutical applications.

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References

- Chatterjee et al. (2008) Upconversion fluorescence imaging of cells and small animals using lanthanide doped nanocrystals. Biomaterials 29; doi:10.1016/j.biomaterials.2007.10.051.
- [2] Bae et al., (2012) Endocytosis, intracellular transport, and exocytosis of lanthanide-doped upconverting nanoparticles in single living cells. Biomaterials 33, doi:10.1016/j.biomaterials.2012.08.039.
- [3] Ni et al., (2014) Dual-targeting upconversion nanoprobes across the blood-brain barrier for magnetic resonance/fluorescence imaging of intracranial glioblastoma. ACS Nano 8; doi: 10.1021/ nn406197c.

Keywords

Lanthanide ions; Nanoparticles; Cell viability; Biodistribution.