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Prof. Dr. Mika Lindén (Universität Ulm)

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Mika Lindén

Inorganic Chemistry II, Ulm University, Albert-Einstein-Allee 11, Ulm
89075, Germany



Mesoporous silica nanoparticles (MSNs) have evolved as a new class of nanoscopic drug carriers and/or contrast agents during the last decade or so. There are many positives associated with this class of drug carriers, including parallel control of mesopore diameter, particle size and shape, and the flexibility of surface functionalization, the latter also allowing covalent attachment of different additional functions to the particles, including targeting ligands for addressing surface receptors on specific cells or different types of imaging agents (fluorophores, positron emitting or radioactive isotopes, etc.) Furthermore, the particles are biodegradable and largely biocompatible at clinically relevant doses. A bulk of studies report successful cell-specific drug delivery in vitro, and an increasing number of studies also give evidence for enhanced therapeutic outcomes in vivo when MSNs are used as drug carriers in comparison to using the free drug. However, detailed design criteria for MSNs to be used as drug carriers are largely missing. The knowledge about the factors influencing the biodistribution of MSNs is relatively shattered due to the relatively limited numbers of studies where serum protein adsorption, particle dissolution in serum, and (semi)-quantitative biodistribution experiments have been performed using the same particles. Furthermore, the variation in experimental design between the different biodistribution studies is broad (different animal models, differences in particle size and shape, different surface functionalization, varying particle dissolution rates, different protein corona compositions, and different administered doses). The presentation will attempt to summarize the current state-of-the-art in terms of the factors influencing the biodistribution of MSNs, and also discuss possible design aspects in relation to targeted drug delivery using MSNs.