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Engineered core-shell nanoparticles: synthesis, characterization, and biocompatibility studies

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ABSTRACT

Superparamagnetic iron oxide nanoparticles (SPIONs) have emerged as promising contrast agents for Magnetic Resonance Imaging (MRI). Some SPIONs are already approved for clinical use. Coating of these nanoparticles with an additional biocompatible layer serves to improve the colloidal stability and biocompatibility. The present thesis is focused on the synthesis, characterization, and in vitro biocompatibility assessment of SPIONs as well as the assessment of the potential impact of the so-called bio-corona on the surface of these nanoparticles on their behavior. In addition, synthesis and magnetic evaluation of novel nanocomposites was also performed.

In Paper I, the production of mono-dispersed, necking-free, single-core iron oxide-silica shell nanoparticles with tunable shell thickness was achieved by a carefully optimized inverse microemulsion method. The development of novel nanomaterials for biomedical applications need to be accompanied by careful scrutiny of their biocompatibility with a particular focus on the possible interactions with the primary defense system against foreign invasion, the immune system. Consequently, in Paper II, our efforts in synthesizing high quality core–shell nanoparticles with superparamagnetic character and sufficiently high magnetization were coupled with in vitro biocompatibility assessment and studies of cellular internalization using primary human macrophages and dendritic cells. The silica-coated nanoparticles were nontoxic to primary human monocyte-derived macrophages at all doses tested whereas dose- and size-dependent toxicity was observed for primary monocyte-derived dendritic cells exposed to smaller silica-coated nanoparticles, but not for the same-sized, commercially available dextran-coated iron oxide nanoparticles. Furthermore, the silica-coated iron oxide nanoparticles were taken up in both cell types through an active, actin cytoskeleton-dependent process to a significantly higher degree when compared to the dextran-coated nanoparticles, irrespective of size. This has potentially useful implications for labeling of immune cells for visualization, diagnosis or treatment of inflammatory processes.

When nanomaterials confront physiological media, the formation of a “corona” of proteins by adsorption to the surface of nanomaterials occurs which will influence how the particles will interact with a biological system and consequently will affect the fate of the particles. The potential effect of the protein corona on the magnetic and biological behavior of silica- versus dextran-coated SPIONs was addressed in Paper III. A thorough physical characterization of SPIONs without and with a protein corona as well as in vitro biocompatibility and cellular internalization using human primary macrophages was performed. Modulation of the magnetization and relaxivity signals of the SPIONs was noted following interaction with human plasma proteins. Macrophage viability was influenced by the presence or absence of a protein corona on silica-coated SPIONs but in the case of the dextran-coated SPIONs. Macrophage production of pro-inflammatory TNF-α was not triggered by SPIONs with or without a corona. Moreover, comprehensive assessment of the protein corona using mass spectrometry and bioinformatics tools revealed distinctive compositions on the two types of nanoparticles. Further studies need to be performed to understand the interrelationship between the acquired protein corona on the SPIONs and their function as MRI contrast agents.

In Paper IV, incorporation of iron oxide nanoparticles homogeneously dispersed in a polymeric matrix and assessment of the magnetic and optical properties of the resulting structured nanomaterials are presented. Magnetic evaluation of the nanocomposite revealed its ferromagnetic properties while the low loading of nanoparticles with very good distribution in the nanostructure yielded materials with good magneto-optical properties. These materials have potential applications as micro actuators, sensors, relays and magneto optical devices based on the Faraday effect.

Overall, this thesis attempts an interdisciplinary approach to the synthesis and characterization of nanomaterials and their biocompatibility assessment, with the aim to enable future applications in nanomedicine.

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