

Surface Functionalization of Single Superparamagnetic Iron Oxide Nanoparticles for Targeted Magnetic Resonance Imaging (MRI)

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INTRODUCTION: Magnetic resonance imaging (MRI) is a non-invasive imaging technique often used in clinics for diagnostic purposes. However, its limited spatial resolution prevents the detection of individual cells or even molecules. Targeted MR contrast agents are thought to offer this possibility. Non-targeted commercially available negative magnetic resonance (MR) contrast agents such as Feridex often consist of multiple iron oxide cores embedded in a macromolecular matrix such as dextran. This results in clusters with a hydrodynamic diameter which is a multiple of the iron oxide core diameter and has a broad size distribution. An alternative to the reversibly binding dextran is PEG-gallol. The latter molecule has a considerably higher binding affinity towards iron oxide nanoparticles compared to dextran, leading to enhanced particle stability and smaller particle diameters.

METHODS: Superparamagnetic iron oxide nanoparticles have been synthesized by aqueous precipitation reaction and were stabilized individually using PEG-gallol. Particle size, thermal stability and magnetic properties of these individually stabilized PEGylated particles have been compared with Feridex. To functionalize the former particles, iron oxide cores were coated with a mixture of biotinylated PEG(3400)-gallol and non-biotinylated PEG(550)-gallol. Neutravidin, a biotin-binding protein, served as a linker between the PEGylated particles bearing biotin sites and biotinylated functional groups. In a first approach, these neutravidin coated PEGylated nanoparticles were targeted against atherosclerotic sites by attaching a custom-synthesized biotinylated peptide sequence known to bind to E-selectin to them¹. E-selectin is a transmembrane protein expressed on inflamed endothelial cells². It thus is an early marker for atherosclerosis.

RESULTS: The high binding affinity of gallol towards iron oxide surfaces results in a high particle stability and a well-controllable interface chemistry. Neutravidin served as an intermediate layer between the biotinylated particles and biotinylated ligands. Specific particle binding was maximized by doing binding studies with the

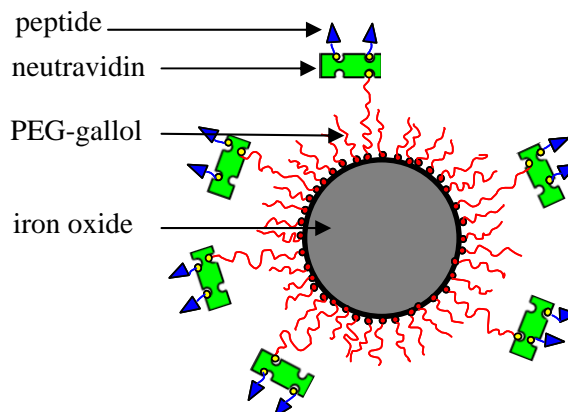


Fig. 1: Cartoon of functionalized superparamagnetic iron oxide nanoparticles. These particles were stabilized with PEG-gallol. To the biotin-bearing PEG chains, neutravidin was added, serving as a linker to attach biotinylated peptides.

quartz crystal microbalance with dissipation monitoring (QCM-D).

DISCUSSION & CONCLUSIONS: Stabilization of single superparamagnetic iron oxide nanoparticles with PEG-gallol results in high particle stability under physiological conditions and allows further functionalization of these negative MR contrast agents. Due to the smaller hydrodynamic diameter, narrower particle size distribution, enhanced particle stability, and similar r_2 -values of PEGylated particles compared to Feridex, the former particles are suited as versatile and easy-to-handle research tool for comparing binding efficiencies of ligands immobilized on these negative MR contrast agents.

REFERENCES: ¹ Martens, C.L., et al., Peptides Which Bind to E-Selectin and Block Neutrophil Adhesion. *Journal of Biological Chemistry*, 1995. 270(36): p. 21129-21136.

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