The Potential of Clustered Core Magnetic Particles for MPI

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Introduction

To date, an ideal MPI tracer has not been identified and the structure-efficacy relation is not yet fully understood. Iron oxide nanoparticles with comparably large mono-crystalline cores as obtained by organic synthesis are predicted to exhibit high MPI efficacy. However, empirical investigations show that particles with cores comprised of small clustered crystallites as obtained by aqueous synthesis show surprisingly high MPI performance[1-3]. Hence, further research is required to evaluate and understand the full potential of both particle types for MPI. Here, we present an investigation comparing various clustered core particles, namely novel polymer-coated iron oxide nanoparticles synthesized *via* the aqueous route, Resovist® (Bayer Pharma AG) and FeraSpin™ R (Viscover™, Miltenyi Biotec GmbH).

Materials and Methods

The different polymer-coated iron oxide nanoparticles were synthesized *via* basic precipitation in aqueous medium. Their mean hydrodynamic diameters (intensity weighted) were obtained by dynamic light scattering using a NICOMP Submicron Particle Sizer Model 370 (Particle Sizing Systems; USA).
TEM images were obtained with a Tecnai G2 Spirit BioTWIN (FEI) using 200 mesh copper grids coated with a carbon film (Plano GmbH; Germany).
The magnetic particle spectra (MPS) were recorded at a drive field of 25 mT and f_0=25 kHz with a commercial MPS system (Bruker BioSpin MRI GmbH; Germany).
The *M*(*H*)-curves were measured with a commercial susceptometer (MPMS, Quantum Design). The distribution $f(d_m)$ of the effective magnetic diameters of (single domain) spheres with the saturation magnetisation M_S was estimated by fitting $M(H) = \phi M_S \frac{1}{\bar{V}} \int f(d_m) \frac{\pi}{6} d_m^3 L \, \mathrm{d}d + M_p$ to the M(H)-data with ϕ, M_S and $\bar{V}$ being the volume fraction of magnetite, the saturation magnetisation and the mean volume of the magnetic nanoparticles (MNP), respectively. We had to add a magnetisation M_p allowing for weakly magnetic structures, which are evident by the absence of a typical saturation behaviour. M_P is not a simple paramagnetic signal and its origin is still unknown. Therefore, we have approximated M_p phenomenologically by $M_p = A_p L(d_p)$, with the amplitude A_P and a relative small diameter d_P.

Results

Among the various iron oxide nanoparticles synthesized here we observed even for those with very similar particle structures, i.e. same polymer coating and same or similar hydrodynamic size as well as crystallite size within the clustered cores (Fig. 1a), remarkable differences between their magnetic particle spectra (MPS, Fig. 2). The MPS amplitude differs by a factor of up to 6 in the lower, and 11 in the higher harmonics between the particles with the highest and lowest observed MPI efficacy (denoted as particle #1 and #2), respectively. In comparison to Resovist and FeraSpin R, this means an improvement by a factor of about 3 in the lower, and 2 in the higher harmonics in case of the high efficacy particle #1. This does not represent the theoretical limit, but so far similar performance was only found for size-optimized particles obtained from the best state-of-the-art clustered core MPI tracers, Resovist and FeraSpin R[1-3], as well as certain mono-crystalline core particles from organic synthesis[4].

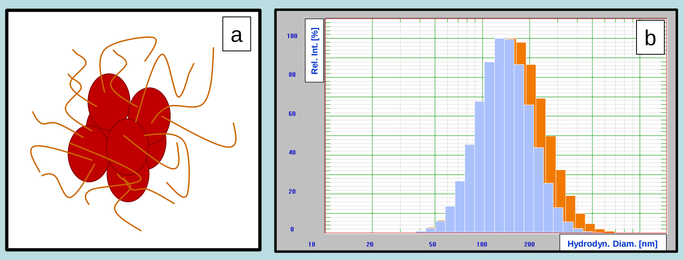

Fig. 1 (a) Schematic illustration and (b) intensity weighted hydrodynamic size distribution; blue: particle #1, orange: particle #2.

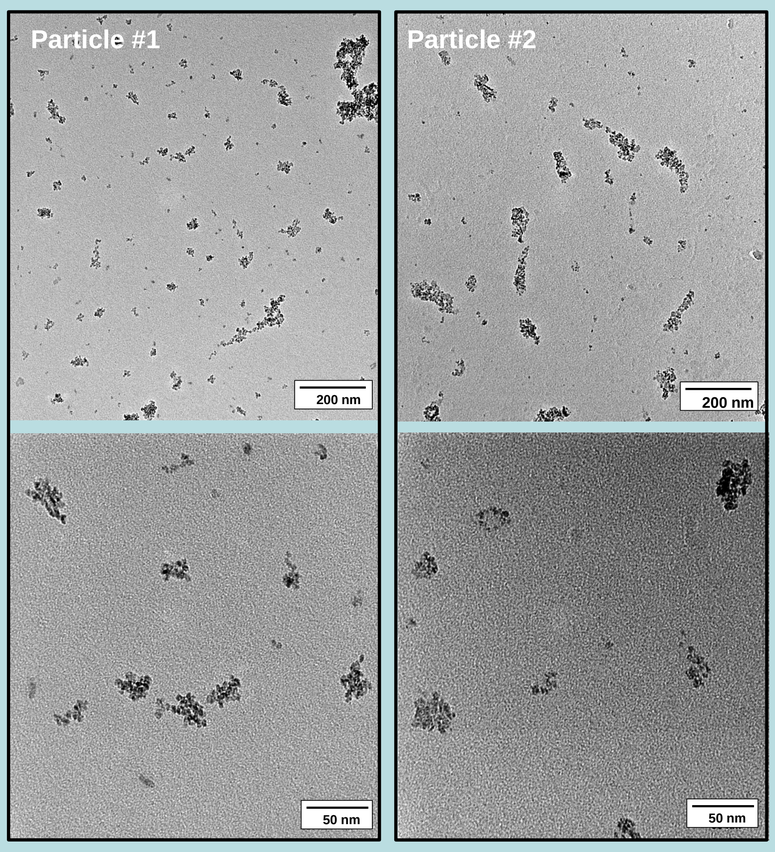

Fig. 3 TEM images of the highest (#1) and lowest (#2) MPI efficacy particles synthesized here.

The mean hydrodynamic diameters of the mentioned particles #1 and #2 obtained by DLS are 147 nm and 178 nm, respectively, both exhibiting a relatively broad size distribution (Fig.1b). TEM images reveal a clustered particle core structure as expected from aqueous synthesis, with a crystallite size below 5 nm for both particle types, #1 and #2 (Fig. 3). Considering these similar structural features, the huge differences of their MPS is indeed unexpected.

Our results from static magnetization measurements help to understand the MPS quantitatively: The curvature of the M(H)-data of particle #1, i.e. the onset of non-linearity at smaller field strengths (Fig. 4) is indicative of an improved MPS signal as compared to Resovist/FeraSpin R. It has to be noted that M(H) represents the moments only, and neglects the dynamics. The MPS, however, is determined also by the mobility and thus, depends on the particle magnetic anisotropy. According to prior findings for Resovist[5] we applied a bimodal size distribution $f = (1\text{-}b_2)\, f_1 + b_2\, f_2$ to the data. In case of Resovist, the mode of the smaller sizes, f_1, could be identified with a single core fraction (i.e. one crystallite within the core), while f_2 with b=30%, was attributed to clusters. In case of particle #1 and #2 the apparent size mode f_1 with a mean magnetic size (diameter of the effective mean magnetic volume) of 5.5 and 7 nm, respectively, might be not associated with an individual small MNP but might be part of the clustered core. This interpretation is consistent with TEM-images, where only a very small fraction is identified as single core MNP. Considering the drawbacks of TEM images, namely potential drying artefacts and poor statistical information, our hypothesis is mainly supported by our recent studies where clustered core particles with narrow size distribution (FeraSpin™ S to XXL, Viscover™) were shown to bear two effective magnetic sizes within one and the same core[6].

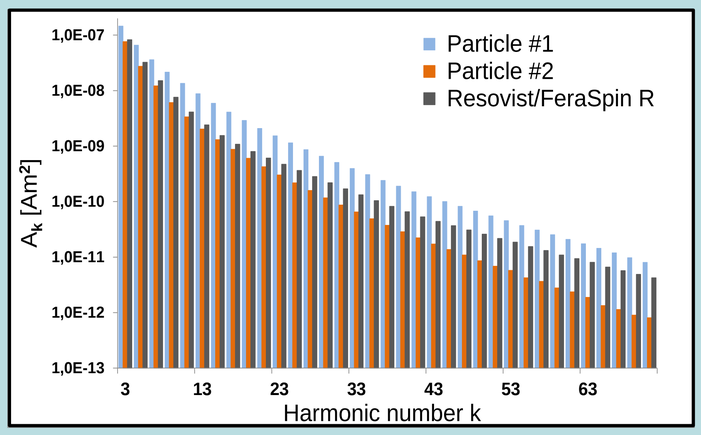

Fig. 2 MPS of the highest (#1) and lowest (#2) MPI efficacy particles synthesized here in comparison to Resovist and FeraSpin R normalized to the iron concentration (drive field 25 mT, f_0=25 kHz).

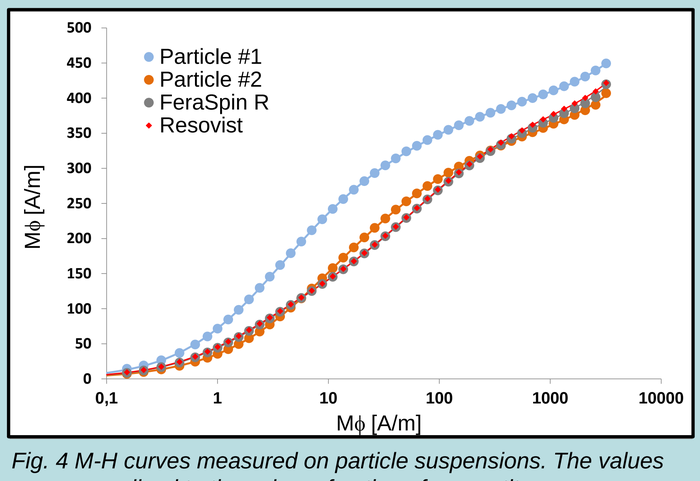

Fig. 4 M-H curves measured on particle suspensions. The values were normalized to the volume fraction of magnetite.

We conclude that similar effects might be of relevance here and that differences in the interactions of the crystallites within the clustered cores of particles #1 and #2 cause their different MPS. Thus, the arrangement of crystallites within clusters is a promising approach for the optimisation of particles for MPI.

Conclusion

We synthesized different iron oxide nanoparticles which show no obvious differences between their structures, yet their MPI efficacy varies significantly. Our results indicate that the structural feature of clustered particle cores and thus, the aqueous synthesis route, indeed holds a currently unknown potential for MPI, which still remains to be explored. Our findings lead us to conclude that the presence of crystallite clusters, their size and the crystallites´ interaction inside the clusters is a determining parameter for a particle´s MPI performance. It will be a matter of further studies to investigate these interactions in more detail in order to allow for an understanding of the structure-efficacy relation and the directed optimisation of iron oxide nanoparticles for MPI applications.

References

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