Synthesis & Functionalization of Fe_3O_4 Nanoparticles for Magnetic Particle Imaging

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Magnetic Particle Imaging is a novel imaging technique recently developed by Philips to perform background-free detection of the spatial distribution of magnetic nanoparticles (MNPs) in biological tissue. Magnetic Particle Imaging (MPI) exploits the non-linear re-magnetization behavior of the particles and has the potential to surpass current methods for the detection of iron oxide in sensitivity and spatiotemporal resolution [1].

Despite much exciting progress in MPI scanner design and related image processing, relatively little effort has been devoted developing suitable MNPs. In fact, for the technique to successfully move beyond proof-of-principle experiments into the clinic or preclinical research laboratory, it will be critical to engineer MNP tracers that are optimized for MPI. Resovist® (Bayer Schering Pharma, Berlin), is, so far, the most used compound in MPI studies. However is far from being optimized for that purpose, with only 3% of the sample contributing to the signal [2]. Therefore, special interest is being placed on developing efficient tracers that depend on active targeting where each unit of tracer must generate the maximum achievable MPI signal voltage.

As well as being optimized in size, with an ideal core size about 30 nm, nanoparticles for MPI should have minimal variability in volume distribution, as well as a magnetic relaxation time that is fast enough to respond to the excitation field [3].

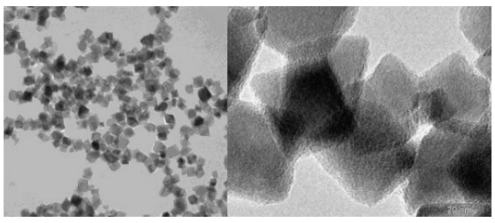
In CNIC, where the first MPI scanner for small animals in Europe it is being installed, we have started a program for the synthesis and biofunctionalization of MPI-suited tracers.

We will show our results using two new methods of synthesis, designed to obtain MNPs about 30 nm in core size and their biofunctionalization. The first approach is based on an aqueous route whereas the second one is based on the use of organic media.

Aqueous route

We present an aqueous route for the synthesis of uniform magnetite nanoparticles with sizes around the monodomain diameter (20-100 nm). The method is based on the precipitation of a Fe (II) salt in a mild oxidant in hydroalcoholic solutions, producing highly uniform and crystalline magnetic nanoparticles in a single step. Colloidal suspensions of these particles were directly obtained by simple ultrasonic treatment of the powders thanks to the presence of sulphate anions at the particle surface.

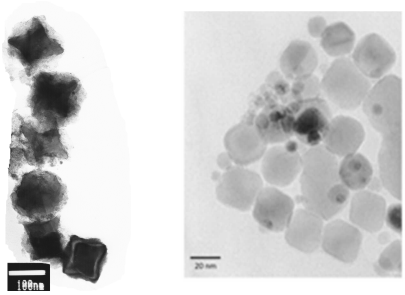
All magnetization curves saturate at much lower magnetic fields and show larger saturation magnetization than samples prepared by coprecipitation. Saturation magnetization values vary between 83 and 92 emu g−1, close to the theoretical values reported for bulk magnetite at room temperature [4].



TEM image of magnetite nanoparticles of 35 nm

Pyrolysis of Iron (III) oleate route

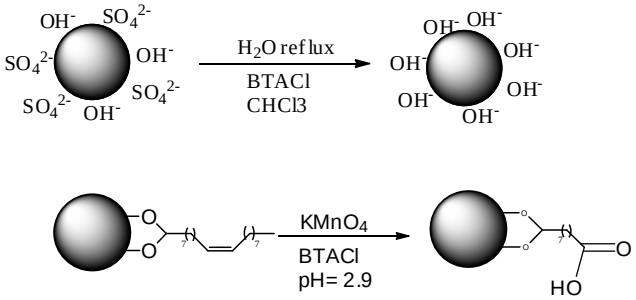
Magnetite nanoparticles were synthesized by the pyrolysis of iron (III) oleate in 1-octadecene. Iron (III) oleate was formed following the methodology described by Ferguson et al. [5]. To obtain magnetite nanoparticles a mixture of iron (III) oleate, 1-octadecene and oleic acid was heated, under argon atmosphere, and refluxed. The synthesis was performed twice with different times of reaction, obtaining different core sizes.



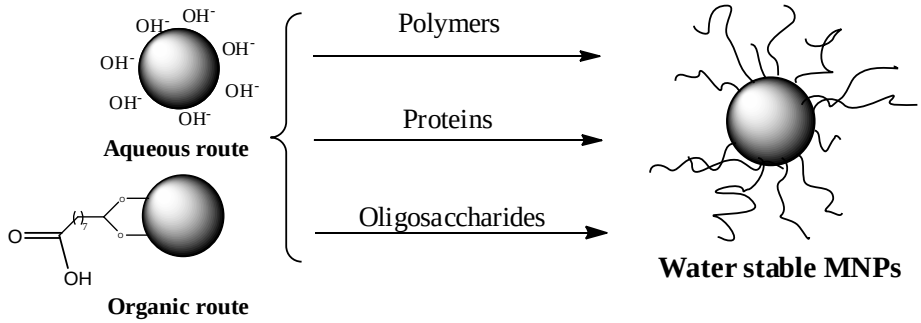
24h **6h**

Functionalization

Once obtained the nanoparticles with suitable features, we made a first functionalization to build interesting precursors.



After this, MNPs were functionalized with different biomolecules to obtain water stable and long circulating times after i,v, injection. These particles were fully characterized (TEM, DLS, VSM, FTIR and MS) and their capabilities as MPI tracers were measured.



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