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FE_3O_4 NANOPARTICLES FOR MRI CONTRAST ENHANCEMENT.

J. Salado[1], M. Insausti[1], L. Lezama[1], T. Rojo[1], J.J. Echevarria[2], I. García-Alonso[3], I. Aguirre Urcelay[4], J.S.Garitaonandia[5] and F. Plazaola[6]

(1) Dpto. Química Inorgánica, U.P.V.-E.H.U., Apdo. 644, 48080, Bilbao, Spain

qipinpem@ehu.es

(2) Servicio de Radiodiagnóstico. Hospital de Galdakao-Usánsolo, Vizcaya

(3) Departamento de Cirugía y Radiología. Facultad de Medicina EHU/UPV. Leioa, Vizcaya

(4) OSATEK-RM

(6) Física Aplikatua II Saila, UPV-EHU, P.K. 644, 48080 Bilbao

(5) Elektrizitatea eta Elektronika Saila, UPV-EHU, P.K. 644, 48080 Bilbao

The great interest of magnetic nanomaterials arises from their novel mesoscopic properties, which are associated with their large surface-to-volume ratio [1]. Magnetic nanoparticles have attracted great attention in the field of medicine for many reasons [2]. They can be functionalized with biological molecules to make them interact with or bind to a biological entity. They can be manipulated by an external magnetic field, which opens up many applications involving the transport and/or immobilization of the nanoparticles. Finally, they can be made to resonantly respond to a time-varying magnetic field, leading to its use as hyperthermia agents. What is more, superparamagnetic nanoparticles have also been developed as contrast agents for both standard and functional MR imaging [3].

Taking into account these facts, the aim of our study is to optimize the preparation of Fe_3O_4 and core-shell Fe_3O_4@Au nanoparticles in order to concentrate them inside tumorous tissue in the liver and make them heat through energy absorption. Indeed, in this communication we present the preparation and magnetic study of Fe_3O_4 nanoparticles and their application in *in vivo* experiments as contrast agents.

The synthesis of the magnetic nanoparticles has been developed from $Fe(acac)_3$ in the presence of 1,2-hexadecanodiol, oleic acid and oleylamine [4]. The synthesis method, the iron concentration and the nature of the solvents used for separation have been changed in order to optimize the preparation method. In this way, nanoparticles with sizes in the 3.8(6) – 7.1(9) nm range, surrounded by the organic ligands have been obtained. The characterization of the samples was performed by means of X-ray diffraction (XRD), transmission electron microscopy (TEM) and thermogravimetric analysis (TGA). Magnetic properties have been investigated using electron paramagnetic spectroscopy (EPR) and SQUID magnetometer.

Depending on the synthesis method the content of organic ligands surrounding the nanoparticles varies from 18% to 40%, mainly composed by oleic acid. TEM micrographs show nanoparticles with a narrow size distribution (Fig. 1). The smaller size of the nanoparticles seems to be related with the larger content of the organic ligand. X-ray diffraction and electron diffraction confirmed the presence of Fe_3O_4 in all cases.

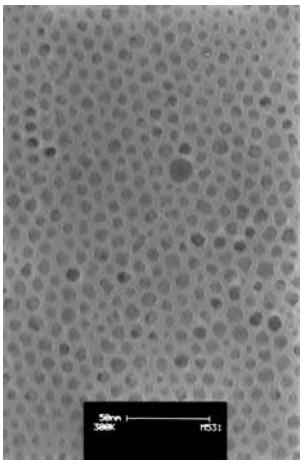

Fig. 1. TEM picture of Fe_3O_4 NPs.

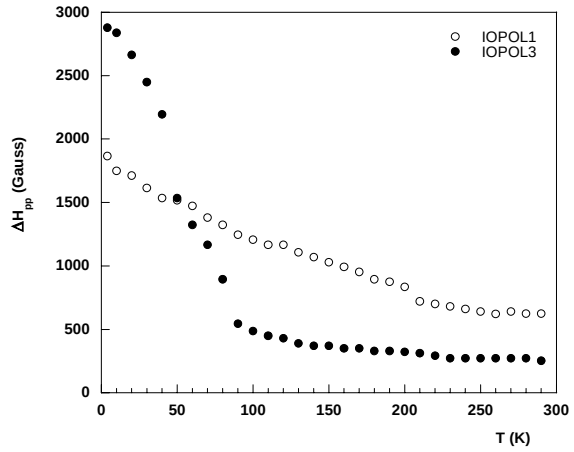

Fig. 2. EPR resonance field versus temperature for two different samples.

The expected superparamagnetic behaviour for nanoparticles below the critical size has not been observed in all cases. In fact, at room temperature, coercive fields between 30 and 130 Oe characteristic of ferromagnetic behavior have been calculated from hysteresis cycles. In order to complete this study, electron paramagnetic resonance spectra with temperature have been performed.

The spectra show strong and broad signals with effective g values from 2.0 to 2.38, depending on the sample. In all samples, while the linewidth increases, the resonance field decreases with temperature. However, the behavior of $\Delta H_{p.p.}$ and Hr vs T is rather different for the samples (Fig. 2). A relative smooth increase of $\Delta H_{p.p.}$ (decrease of Hr) with decreasing temperature is typical of ferromagnetic samples while for superparamagnetic ones a change in the slope is observed at the blocking temperature, T_B, of the nanoparticles.

Finally, Fe_3O_4 samples were dissolved in lipiodol and injected into the liver to WAG rats in order to register MR images. These samples were supplied through ileo-colic vein, and no vascular embolic phenomena were developed. It has been proved that very small quantities are enough to visualize the images (Fig. 3). Finally, in pathologic analysis of liver specimens, only few inflammatory changes were detected.

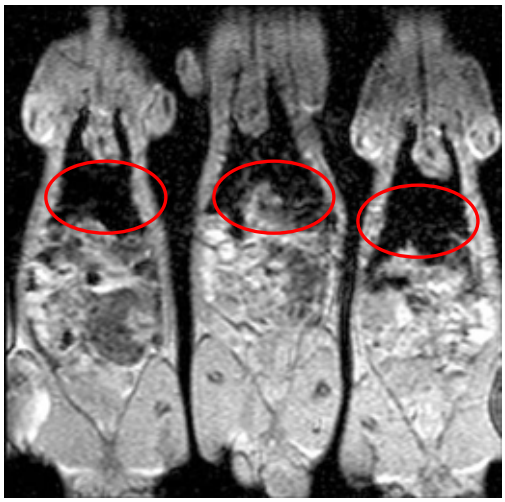

Fig. 3. Magnetic resonance image of rats' coronal planes showing the localization of magnetite nanoparticles in the liver.

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