# Abstract

The magnetic fluid hyperthermia is the heating of a suspension containing magnetic nanoparticles in presence of an alternating magnetic field due to the magnetic losses with the subsequent conversion into heat. Its efficiency is determined by the specific power absorption ($SPA$), equivalent to the heating rate normalized by the mass of nanoparticles. The key point in the magnetic fluid hyperthermia is the dephasing between the magnetic moment, thermally relaxing, and the applied field. The two main thermal relaxation mechanisms of the magnetic monodomain (nanoparticles ($NPs$)) acting in a medium with finite viscosity are the viscous mechanism (Brown) and that one associated to the reversion of the magnetic moment against the energy barrier (Néel). The predominant mechanism is defined by the intrinsic properties of the particles, such as effective anisotropy ($K_{\text{eff}}$), saturation magnetization ($M_s$) and volume ($V$), together with the viscosity of the medium ($\eta$) where they are dispersed and the hydrodynamic volume ($V_{\text{hyd}}$) in this medium.

Ferrite nanoparticles are interesting systems for biomedical applications, with several potential applications in this field, especially in magnetic fluid hyperthermia. A main motivation of this thesis is the growing interest in to optimize the morphological and magnetic properties of the ferrite $NPs$, as well as their behavior in the dispersion medium, specially focused on its use in magnetic fluid hyperthermia. For this, *Zn* and *Mn* ferrite $NPs$, synthesized by the thermal decomposition of organometallic compounds of the involucrate ions in organic solvents assisted by surfactants, were study in terms of the chemical composition, morphology, structure and magnetic properties. For this, we look for the relation between the change in the chemical composition (incorporation of *Zn* and *Mn*) with the magnetic properties of the $NPs$, specifically the effective anisotropy. The composition, morphology and magnetic properties of the $NPs$ were analyzed with different experimental techniques: particle induced x-ray emission ($PIXE$), x-ray diffraction ($DRX$), transmission electron microscopy ($TEM$), thermogravimetric analysis ($TGA$) together with differential thermal analysis ($DTA$) and magnetization measurements as function of the applied field and temperature. According to this, the synthesized $NPs$ has different amounts of *Zn* or *Mn* incorporated in the ferrite structure with different diameters, presenting a high saturation magnetization and different effective magnetic anisotropy. These nanoparticles were dispersed in distinct media with different viscosities: organic solvents (hexane and toluene), water, clarified butter oil (*CBO*) and paraffin.

The dominant mechanism of magnetic relaxation in the *Zn* ferrite samples is the Néel one ($\tau_N$) for all samples dispersed in any medium used. For three *Mn* ferrite samples dispersed in any medium used, the dominant relaxation mechanisms is the Brown one ($\tau_B$). However, one of the Mn ferrite *NPs* sample, with a specific composition, botyh relaxation mechanisms are important when the *NPs* are dispersed in *CBO* and paraffin. Based on the previous analysis of the properties of the samples and on the dominant relaxation mechanism identified for each sample dispersed in each medium, magnetic fluid hyperthermia experiments were performed for all samples with using an applied field with frequency in the range of 350 kHz and 817 kHz, and amplitude between 200 Oe and 300 Oe, allowing to study the heating efficiency of the *NPs* according with their morphological and magnetic properties. The measurements showed values of *SPA* in a broad range: from samples with any heating efficiency to sample with *SPA* of hundreds of W/g. Evaluation of the *SPA* based on the composition (incorporation of *Zn* or *Mn*), diameter, field frequency and concentration of *NPs* in different media, shows the preponderance of the diameter and the energy barrier of the *NPs* in its *SPA*, at least in an initial time. This dependence was studied in terms of a graphical analysis comparing the experimental value of the *SPA* and that one calculated with using the linear response theory (*LRT*), both as function of the measured diameter and the effective magnetic anisotropy constant.

To verify the real efficiency of selected systems with better performance in themagnetic fluid hyperthermia experiments mentioned previously, they were used in *in vitro* magnetic fluid hyperthermia experiments with BV2 cells. For this, the *NPs* of the selected samples were functionalized with DEXTRAN and PEG. These *NPs* present low or absent toxicity. Magnetic fluid hyperthermia experiments were performed during 30 minutes with 570 kHz and 300 Oe. *Zn* ferrite *NPs* present a high temperature increment in this experiment, while *Mn* ferrite *NPs* present a moderate one. For all sample, the higher temperature allowed for the system was 46 °C, which was attempted for the *Zn* sample, but not for the *Mn* one. Despite this limitation of maximum temperature, avoiding the ablation, a cell death process was induced after the hyperthermia treatment, not immediately after the treatment, but starting 4 hours after. This effect was not observed in control systems, without nanoparticles, but also exposed to the same applied field.

Although the role of magnetism in magnetic fluid hyperthermia has been extensively studied, the thermal properties of the medium with *NPs* and their changes during hyperthermia experiments have been underestimated until now. In this work, a novel phenomenon was observed in the study of *SPA* as a function of viscosity, which is based on the intrinsic dependence of viscosity with temperature. For that, the *Zn* ferrite $NPs$ were dispersed in medium with phase transition in the temperature range of the hyperthermia experiment: $CBO$ and paraffin. These systems show a non-linear behavior of the heating rate within the temperature range of the experiments. For $CBO$, a rapid rise to $\sim$ 33 °C associated with changes in viscosity ($\eta(T)$) and heat specific ($c_p(T)$) of the medium below and above its melting temperature. This increase in heating rate occurs around $\sim$ 45 °C for paraffin. The magnetic and morphological characterizations of the $NPs$ together with the agglomeration observed above $\sim$ 33 °C ($CBO$) and $\sim$ 45 °C (paraffin) indicate that the rapid increase of the curves of heating could not be associated with a change in the magnetic relaxation mechanism, with Néel relaxation being the dominant one. In fact, successive experiments runs performed up to temperatures below and above the melting point $CBO$ resulted in different heating curves due to agglomeration of $NPs$ driven by inhomogeneity of the magnetic field during experiments. Similar effects were seen for paraffin. Our results highlight the relevance of the thermodynamic properties of the medium with $NPs$ for an accurate measurement of heating efficiency for environments such as in vitro and in vivo, where the thermal properties are largely variable within the temperature window of magnetic fluid hyperthermia experiments.

**Keywords:** MAGNETIC NANOPARTICLES, FERRITES, MAGNETISM, MAGNETIC FLUID HYPERTHERMIA