RUBÉN TRICAS CASTILLO

# *Synthesis and characterization of nanoparticles of $MFe_2O_4$ (M=Fe, Co, Ni) for application in magnetic hyperthermia*

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# INTRODUCTION

*NANOTECHNOLOGY AND NANOMEDICINE*

The nanotechnology constitutes the basis of the next technological revolution, is the continuation of the industrial revolutions arisen in the three last centuries: the First Industrial Revolution appeared around 1750 with the introduction of the steam machine and the obtaining of the steel, and the Second Industrial Revolution, that began at the ending of 19 century as a consequence of the electricity introduction into a industrial scale. More recently, it has appeared the Information Revolution, characterized by the development of computational systems and internet. As the development of integrated circuits employed in the information processes depends on size reduction of the individual components of the circuits until a nanometric scale, the Information Revolution has turned into a Revolution of the Nanometric world. The nanotechnology is the study, design, creation, manipulation and application of materials, devices and functional systems through the control of the matter at the nanoscale, as well as the exploitation of determinate phenomena and properties of the matter at this scale. The nanoparticles are particles with dimensions comprised between the molecules and the microscopic structures. When the matter is manipulated into a scale as tiny as atoms and molecules, the matter presents totally new phenomena and properties. In concrete, the physical properties of the nanoparticles are very different in comparison with the properties observed in a solid with macroscopic size and the same chemical composition. In this way, the investigation of matter's behavior at nanometric scale opens a promising perspective of new knowledge and applications in every scientific and/or technological field. In the avant-garde of these applications, it is found the related ones to Health Sciences (1). The medical application of nanotechnology is defined as nanomedicine and is one of the fastest growth areas in nanotechnology. In recent decades, nanotechnology has become more widely used in diagnostic and therapeutic fields. Specially, multifunctional nanoparticle platforms hold great promise for use in therapeutic applications as a target probe or carrier of biomolecules, optical dyes, anti-target molecules, and bioactive drugs (2). Many of the unique physical and biological properties of NPs are related to their small sizes (in the range of 5 to 100 nm). Furthermore, nanoscale materials and systems interact with biological systems at the molecular level so they can be used to manipulate and control behaviors and functions of biological systems.

Small particles have been in use for biomedical research and in vitro diagnostic protocols since the '50s. Among nanometer-sized objects, nanoparticles have proved to be useful as building blocks for the development of nano-biomaterials. As intermediates between the molecular and the solid states, inorganic nanoparticles combine chemical accessibility in solution with physical properties of the bulk phase (2). For any specific application in biomedical sciences, the selection of the NPs is often determined by the physical properties of the core material constituting them, as well as the chemical/biological characteristics of the functional coating. An unavoidable problem associated with nanoparticles is their intrinsic instability throughout the time. The particles tend to form conglomerates in order to reduce the energy associated with the high superficial area/volume relationship. Furthermore, particles without coating are very chemically active and easily oxidize in contact with air, producing a loss of magnetism and dispersion capability. Therefore, it is crucial in the majority of the applications to develop protection strategies, during or after the synthesis, in order to chemically stabilize the magnetic particles against degradation. These strategies comprise the insertion or covering with organic species like tensioactives or polymers, or covering with inorganic layers, like silica or coal. When the stable magnetic particles are able to easily disperse in a fluid, it is formed a ferrofluid (3).

Magnetic iron oxide nanoparticles and their dispersions in various media have long been of scientific and technological interest. The cubic spinel structured $MFe_2O_4$ represents a well-known and important class of iron oxide materials where oxygen forms an fcc close packing, and $M^{2+}$ and $Fe^{3+}$occupy either tetrahedral or octahedral interstitial sites. By adjusting the chemical identity of $M^{2+}$, the magnetic configurations of $MFe_2O_4$ can be molecularly engineered to provide a wide range of magnetic properties. Due in part to this versatility, nanometer-scale $MFe_2O_4$ materials have been among the most frequently chosen systems for studies of nanomagnetism. Depending on the chemical identity of $M^{2+}$, the densely packed solid state form of nanocrystalline $MFe_2O_4$ –based materials, on the other hand, can have either high magnetic permeability and electrical resistivity (for M representing one or the mixed components from Co, Li, Ni, Zn, etc.) or half-metallicity (for M=Fe), and may be a potential candidate for future high performance electromagnetic and spintronic devices (4).

MNPs are composed of magnetic materials such as iron, nickel, cobalt and their oxides like magnetite ($Fe_3O_4$), maghemite ($\gamma$-$Fe_2O_3$), cobalt ferrite ($Fe_2CoO_4$) or chromium di-oxide ($CrO_2$). Specially, iron-oxide nanoparticles are the most employed for biomedical applications due to their smaller toxicity when compared to other magnetic materials such as cobalt and nickel. Their application is possible due to their chemical stability and biocompatibility (5). Therefore, there are three main strategies for bio-applications of MNPs:

- The application of controlled magnetic field gradients (i.e. a magnetic force) around the desired target location for remotely positioning MNPs in organs or tissues (targeting, magnetic implants, magnetic separation applied to the sequencing of DNA, etc.)
- The utilization of the magnetic moment of the MNPs as a disturbance of the proton nuclear resonance (i.e. contrast media for Magnetic Resonance Imaging, MRI).
- The magnetic losses of nanometric particles in colloids for heating purposes (magnetic hyperthermia)

## *MAGNETIC BEHAVIOR*

The magnetism of a solid is originated from the contributions of the quantum properties of electrons constituting it. These electrons determine the magnetic behavior of the solid and the strength of the interaction between atoms in it. At macroscopic scales, these magnetic interactions between atoms, together with the crystalline structure of the solid, originate the magnetic response of materials (the response of a material when a magnetic field is applied on it). When the magnetic interactions are weak, the average magnetic moment will always be zero. However, for stronger magnetic interactions between the individual moments of the atoms, some materials exhibits magnetic order and the result is a nonzero macroscopic magnetization. These materials are known as ferromagnets. But despite this 'aligning interaction' a bulk piece of most ferromagnetic materials normally has a nearly zero macroscopic magnetic moment because the interior of the block is divided into magnetic domains (multidomain). Within a single domain all magnetic moments remain parallel, but each domain is randomly oriented so that the net magnetic moment of the sample is nearly cancelled. When the volume of a small particle is reduced below a certain value, called critical domain size (DCritical) the single-domain configuration is adopted. Within this single magnetic domain all the atomic magnetic moments will be magnetized along the same direction, adding up so they behave like a giant magnetic moment (superparamagnet). The value of critical size (DCritical) below which a particle of a given material becomes single-domain is determined by intrinsic properties of that material (i.e. magnetic anisotropy, magnetic moment and exchange anisotropy), and also by the particle shape (6). Although the actual DC values depend on some preparation features, for magnetite the critical particle size has been accepted to be within the 80-100 nm range. Below these values the MNPs would be a single magnetic domain (7).

Superparamagnetism is characterized by not keeping magnetized after the action of magnetic field, offering advantage of reducing risk of particle aggregation. Ferromagnetic NPs, whose size is bellow DC, have a single magnetic domain and maintain one large magnetic moment (high ratio of induced magnetization –M- to the applied magnetic field –H). However at sufficiently high temperature (i.e. blocking temperature, TB) thermal energy is sufficient to induce free rotation of the particle resulting in a loss of net magnetization in the absence of an external magnetic field. Lack of remnant magnetization after removal of external fields enables the particles to maintain their colloidal stability and avoids aggregation making it feasible for their use in biomedical applications (8).

Magnetic fluid hyperthermia (MFH) is one of the novel clinical nanotherapies that rely on the use of magnetic nanoparticles (MNPs) as heat generators to induce localized cell death by the application of external radiofrequency (RF) radiation. At the frequencies used for MFH (the low radiofrequency range, from approximately 100 kHz to 1 MHz), the physical basis of heat generation involves the interaction between the magnetic moment of the MNPs and the magnetic component of the applied electromagnetic wave. At these frequencies the interaction of both the electrical and magnetic components of RF waves with living organisms is not relevant and can be neglected.

As for the magnetism, only a minor fraction of the molecules that compose living organisms have a permanent magnetic moment, and none of them display long-range magnetic ordering at room temperature, making their interaction with the magnetic component of RF radiation feeble or non-existent. To achieve the kind of strong interactions that would yield cellular heating (i.e. energy transfer from the magnetic field to living organisms), a heating agent is needed, i.e. magnetic nanoparticles carrying large magnetic moment must be introduced to the intracellular space. Regarding MFH, the characteristics of the interaction between magnetic fields and living organisms constitute the source of both the potential high selectivity of this therapy and the complexity to achieve its clinical application.

The electromagnetic radiation is composed of electromagnetic waves propagating at the speed of light and carrying electric and magnetic energy. RF waves are a subset of the electromagnetic spectrum with wavelengths and frequencies within a specific range of values. When a living organism is exposed to RF waves, a fraction of the energy is absorbed from the waves, yielding heating of the radiated part of the organism. The rate at which living organisms are heated is the most accepted parameter to asses and quantify the biological effects of RF radiation.

Many theoretical models about the behavior of an assembly of single-domain magnetic nanoparticles in an external alternating magnetic field have been developed along the last years. The two main physical situations that are of importance for biomedical applications are:

(1) Single-domain MNPs that are 'physically fixed' (i.e. cannot physically rotate) within some solid medium. In this case, the magnetic moment of each single MNPS that rotates as a consequence of the alternating magnetic field, against the effective magnetic anisotropy of the nanoparticle (mainly due to the particle shape or its crystal magnetic anisotropy).

(2) MNPs that are dispersed in a magnetic colloid of a given viscosity, implying that the particles can physically rotate as a whole. In this situation both the MNPs and the magnetic moment can rotate under the influence of both the torque from the AC magnetic field and the thermal fluctuations (Brownian movement) on the small MNPs by the surrounding liquid.

In either case, the description of the power absorption process is made through the relaxation of the MNPs magnetic moment governed by the thermal fluctuations at finite temperatures, known as the Neel-Brown relaxation process. Currently, general consensus can be found in the literature on what are those physical and magnetic parameters of the nanoparticles that are important for maximising the Specific Power Absorption (SPA) of a magnetic colloid: the SPA dependence on the average MNP volume, magnetic anisotropy, size distribution and surface composition has been extensively studied.

When considering in vitro applications of this model the main results are that, for the heat generation from MNPs, at least one of the following conditions must be fulfilled: (1) superparamagnetic behaviour at the experimental frequency used and at room temperature, and/or (2) a small hydrodynamic diameter and no aggregation (9).

# MATERIALS AND METHODS

*SYNTHESIS OF MNPs THROUGH THERMAL DECOMPOSITION*

There is an increasing optimism that nanotechnology applied to medicine will bring significant advances in diagnosis, prevention, and treatment of diseases. In this sense, the minimization of magnetic nanoparticle polydispersity and heterogeneity will be essential for their use in the construction of nanopharmaceuticals.

Organometallic precursor-based synthesis has proved successful for the preparation of uniform nanoparticles. This method is widely used because of the ease and reproducibility of the synthesis, as well as the uniformity and high crystallinity of the particles. It consists of the decomposition of an organometallic precursor in the presence of capping ligands, typically long chain alkyl surfactants, such as oleic acid, bind to the particle surface and are responsible not only for the stabilization against aggregation (steric repulsion), but also have an active role during the reaction.

The decomposition of organometallic precursor's method has yielded markedly improved MNP samples with good size control, narrow size distribution, and excellent crystallinity of individual nanoparticles in comparison with more traditional methods. This method is also suitable for mass production. However, absolute control over size, shape, and distribution remains a challenge, and the formation mechanism under different conditions is not yet clear. Many different factors such as the nature of the precursor, the ligand and the solvent, the precursor ratio and the decomposition temperature affect the morphology of the resulting particles (10).

Magnetic nanoparticles can be produced by a number of physical and chemical methods which determine the final properties of the product. These properties are defined by the nanoparticle shape and size, the size distribution and the surface chemistry of the resulting particles. The final magnetic properties of an ensemble of colloidal MNPs are strongly influenced by the degree of structural defects or impurities of the particle core and surface (5).

To use $MFe_2O_4$ nanoparticles for future highly sensitive magnetic nanodevice and biomedical applications, a practical route to monodisperse nanoparticles with diameters smaller than 20 nm and a tight size distribution is needed. A commonly used approach to monodisperse iron oxide nanoparticles is via high-temperature organic phase decomposition of an iron precursor in the presence of organic solvents with high boiling

points. This reaction can be extended to the synthesis of $MFe_2O_4$ nanoparticles (M=Co, Ni) by simply adding a different metal acetylacetonate precursor to the mixture of iron precursor. The process involves high temperature (up to 300º) reaction and the size of the oxide nanoparticles can be controlled by varying the reaction temperature or changing metal precursors. Alternatively, with the smaller nanoparticles as seeds, larger monodisperse nanoparticles up to 20 nm in diameter can be synthesized by seed-mediated growth. The process does not require a low-yield fractionation procedure to achieve the desired size distribution and is readily scaled up for mass production. The nanoparticles can be dispersed into nonpolar or weakly polar hydrocarbon solvent, such as hexane or toluene. The hydrophobic nanoparticles can be transformed into hydrophilic ones by mixing with a phospholipid allowing preparation of aqueous nanoparticle dispersions (4).


**Figure 1**

Here in the project we present detailed synthesis of magnetite ($Fe_3O_4$) and related metal iron oxides of Nickel ($Fe_2$ $NiO_4$) and cobalt ($Fe_2CoO_4$). The experimental setup (figure 1) has the following characteristics:

- A heating source surrounding the mixture container
- A crystal stirrer or mixer
- A nitrogen air flow and water refrigerator.

- A temperature controller.

The reaction mixture contains:

- The organometallic precursors (metal/iron acetylacetonates or iron-oleate complex)
- The solvent/s (benzyl-ether and/or trioctylamine) and, if necessary,
- The surfactants (oleic acid, oleylamine).

Although the detailed procedures used for the synthesis of nanocrystals vary depending on the materials involved, a similar strategy is generally employed to produce uniform nanocrystals, in which high supersaturation is induced by the rapid injection of the highly reactive reactants into a hot surfactant solution. The previous extensive works on the synthesis of micrometer-scale particles revealed that the burst of nucleation and subsequent size focusing growth process are critical for the formation of monodisperse nanoparticles. A similar principle is applied to the synthesis of monodisperse nanoparticles via the 'hot injection' methods. High supersaturation induced by 'hot injection' leads to the fast homogeneous nucleation reaction that is followed by the diffusion-controlled growth process, in which 'focusing' of the particle size distribution occurs. The so-called 'heating-up' method, in which the reaction solution prepared at low temperature is heated to high temperature, has been extensively used to synthesize monodisperse nanocrystals of transition metals and metal oxides (11).

**Dynamic light scattering (DLS)**

This technique is one of the most popular methods used to determine the size of particles (hydrodynamic diameter). Shining a monochromatic light beam, such as a laser, onto a solution with spherical particles in Brownian motion causes a Doppler Shift when the light hits the moving particle, changing the wavelength of the incoming light. This change is related to the size of the particle. It is possible to compute the sphere size distribution and give a description of the particle's motion in the medium, measuring the diffusion coefficient of the particle and using the autocorrelation function. This method has several advantages: first of all the experiment duration is short and it is almost all automatized so that for routine measurements an extensive experience is not required. Moreover, this method has modest development costs. Commercial "particle sizing" systems mostly operate at only one angle (90°) and use red light (675 nm). Usually in these systems the dependence on concentration is neglected. The advantage of using dynamic scattering is the possibility to analyze samples containing broad distributions of species of widely differing molecular masses, and to detect very small amounts of the higher mass species (<0.01% in many cases). (12)

**Vibrating Sample Magnetometer (VSM)**

A vibrating sample magnetometer operates on Faraday's Law of Induction, which tells us that a changing magnetic field will produce an electric field. This electric field can be measured and can tell us information about the changing magnetic field. A VSM is used to measure the magnetic behavior of magnetic materials. A VSM operates by first placing the sample to be studied in a constant magnetic field. If the sample is magnetic, this constant magnetic field will magnetize the sample by aligning the magnetic domains, or the individual magnetic spins, with the field. The stronger the constant field, the larger the magnetization will be. The magnetic dipole moment of the sample will create a magnetic field around the sample, sometimes called the magnetic stray field. As the sample is moved up and down, this magnetic stray field is changing as a function of time and can be sensed

by a set of pick-up coils. The alternating magnetic field will cause an electric field in the pick-up coils according to Faraday's Law of Induction. This current will be proportional to the magnetization of the sample. The greater the magnetization, the greater the induced current. The induction current is amplified by a transimpedance amplifier and lock-in amplifier. The various components are hooked up to a computer interface. Using controlling and monitoring software, the system can tell you how much the sample is magnetized and how its magnetization depends on the strength of the constant magnetic field.

**UV/visible spectroscopy studies for total Iron determination:**

Total iron concentration determination needs complete dissolution of particles. Ferrous ions present in the solution were oxidized to ferric ions by HNO3 prior to reacting with thiocyanate salt to form the iron- thiocyanate complex ([Fe (SCN) 6] 3- (aq)). Nanoparticles were completely dissolved in 1:1 v/v HCl 6M-HNO3 (65%) for 2 h at elevated temperatures (50°C–60°C). Potassium thiocyanate was added to the Fe3+ solution and then the iron concentration was determined by spectrophotometric measurements at 478 nm using a CARY-50 Probe UV-visible recording spectrophotometer.

**DM100 Series**

DM100 Series is the only integral, immediate and reliable solution to the instrumentation needs of magnetic hyperthermia through all its stages: from magnetic characterization to clinical application. This commercial model is an alternate magnetic field applicator that measures the heating efficacy of magnetic nanoparticles throughout the SPA index. The design conceptualization of the DM100 series emerges from the real need of the Magnetic Hyperthermia lab of the Institute of Nanosciences of Aragón (Spain). The specific needs involved in the process of applying a magnetic field, measuring and analyzing the results were thoroughly examined and approached one by one, leading to an integrated and final solution that guarantees the highest standards in Magnetic Hyperthermia research. The results achieved with DM100 Series are now endorsed by published results on characterization of nanostructured materials, experiments with cellular cultures, parasithology, among other fields.

DM100 Series devices apply a user-adjustable magnetic field from 0 to 300/600 gauss, on user selectable frequencies, and perform in situ temperature measurements through an advanced optical fiber system, without metallic parts and with a negligible thermal mass. Information on temperature, time, magnetic field and incidences is collected and stored up, and it can be processed with a computer. Specially designed software allows also for programming and scheduling automated tests on intensity curves, sampling frequency, pauses, etc. (13)

**Transmission electron microscopy (TEM)**

MNPs average size, distribution and morphology were analyzed by transmission electron microscopy (TEM) using a FEI Tecnai T20 microscope and operating at 200 keV. TEM samples were prepared by placing one drop of a dilute suspension of magnetite nanoparticles in water/hexane on a carbon-coated copper grid and allowing the solvent to evaporate at room temperature. The average particle size (DTEM) and distribution were evaluated by measuring the largest internal dimension of 200 particles.

# EXPERIMENTAL RESULTS

*MORPHOLOGY AND STRUCTURE OF MNPs*

The influence of several parameters, such as concentration of base and iron salt, reaction time or the use of mixed solvents was studied by TEM to explore their influence on the morphology, size and crystallinity of the sample. This is the previous step before selecting the optimum nanoparticles for the study of their magnetic properties.

According with previous work, the reaction of organometallic precursors with surfactants at high temperature leads to monodisperse metal/iron oxide nanoparticles, which can be easily isolated from reaction byproducts and the high boiling point solvents. The studies says that as the boiling point of trioctylamine (365-367ºC) is higher than that of benzyl-ether (298ºC), the larger sized nanoparticles obtained from trioctylamine solution seems to indicate that high reaction temperature will yield larger particles. However, regardless of the size of the particles, the key to the success of making monodisperse nanoparticles is to heat the mixture to 200ºC first and remain at that temperature for some time before it is heated to reflux at ~365ºC in trioctylamine or at ~300ºC in benzyl-ether. Directly heating the mixture to reflux from room temperature would result in nanoparticles with wide size distribution, indicating that the nucleation and the growth of the nuclei under these reaction conditions is not a fast process (4).

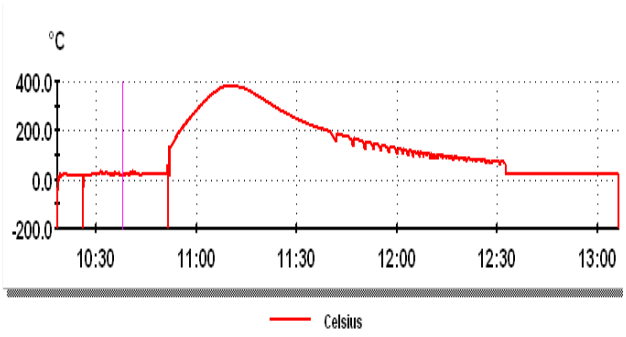
The goal of this experimental work is to agree the previous theory, and subsequently, choose the MNPs that accomplish the principal features for obtain good results of monodispersity, hydrodynamic size, and magnetic properties.

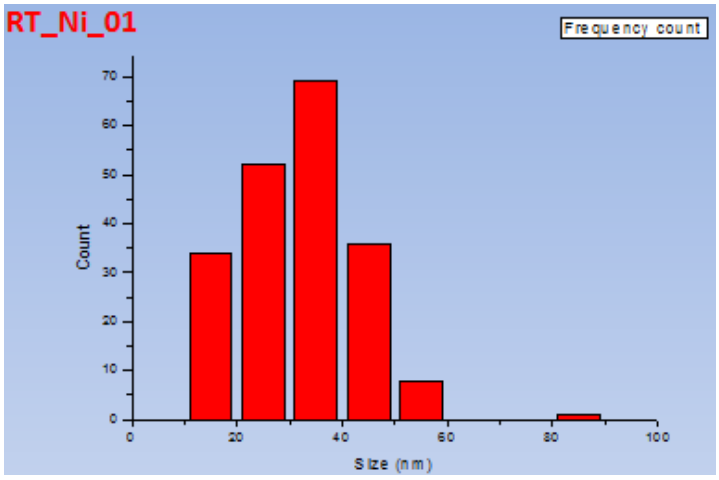
First of all, we present the data corresponding to the whole of synthesis carried out by thermal decomposition: 8 $Fe_2NiO_4$, 5 $Fe_2CoO_4$ and 3 $Fe_3O_4$. This data are summarized in *Table 1* and they will be described below.

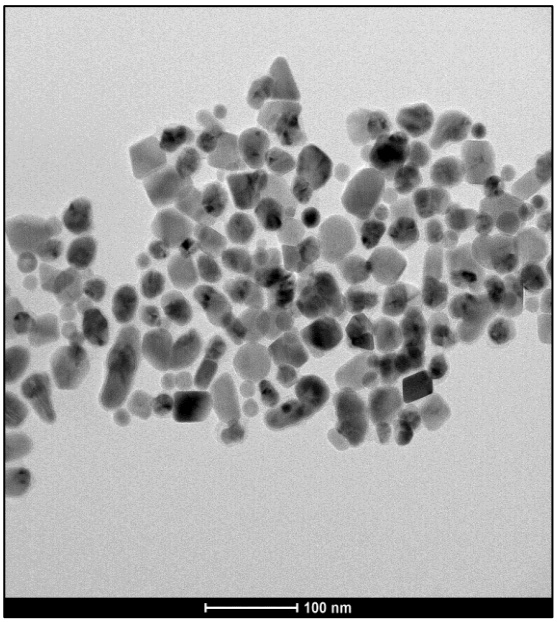
| | trioctylamine | Benzyl-ether | Oleylamine | Oleic acid | Dodecanodiol | T nucleaction | T rx – t$^a$ max |
|---|---|---|---|---|---|---|---|
| Ni-01 | 100mL | | | 15mL | | | 7' 350-380ºC |
| Ni-03 | 100mL | | | 15mL | | | 8' 320-375ºC |
| Ni-04 | 100mL | | | 15mL | | 30'-200ºC | 7' 330-375ºC |
| Ni-05 | 80mL | 20mL | 5mL | 15mL | 1,8g | 30'-200ºC | 10' 350ºC |
| Ni-06 | 50mL | 50mL | 5mL | 15mL | 1,8g | 30'-200ºC | 30' 320ºC |
| Ni-07 | | 100mL | 5mL | 15mL | 1,8g | 30'-200ºC | 1h-300ºC |
| Ni-08 | 30mL | 120mL | | | | 30'-200ºC | 1h 300-320ºC |
| Co-01 | 80mL | 20mL | 5mL | 15mL | 1,8g | 30'-200ºC | 10' 330-350ºC |
| Co-03 | 80mL | 20mL | 5mL | 15mL | 1,8g | 30'-200ºC | 10' 350ºC |
| Co-04 | 50mL | 50mL | 5mL | 15mL | 1,8g | 30'-200ºC | 10' 320ºC |
| Co-05 | | 150mL | 17,5g | 14,66g | 17,5g | 30'-200ºC | 1h 280-315ºC |
| HK-20 | 80mL | 20mL | | 1g+1mL | | | 20' 300-360ºC |
| HK-24 | 80mL | 70mL | 17,93g | 14,65g | 17,48g | 1h-200ºC | 30'-320ºC |
| HK-25 | 80mL | 20mL | | | | | 25' 310-330ºC |

Table 1. Summary table showing the compounds employed in each synthesis reaction and their quantities. It also shows the time spent for the two principal steps in the process (nucleation and growth of metal/iron oxide nanocrystals)

1. $Fe_2NiO_4$ / Ni-01

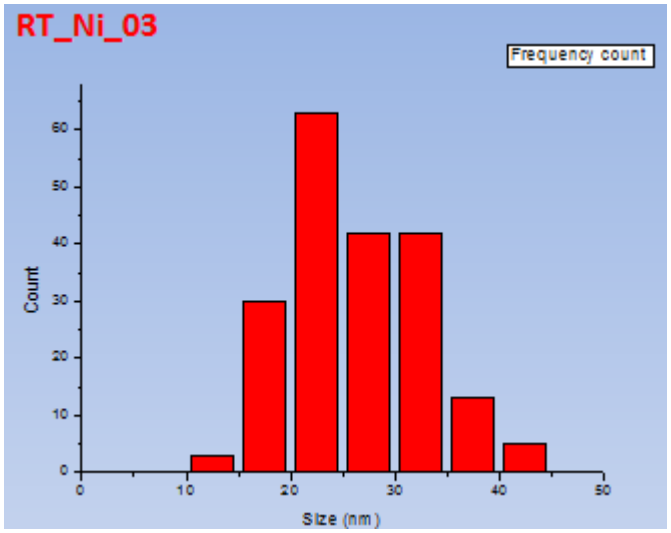


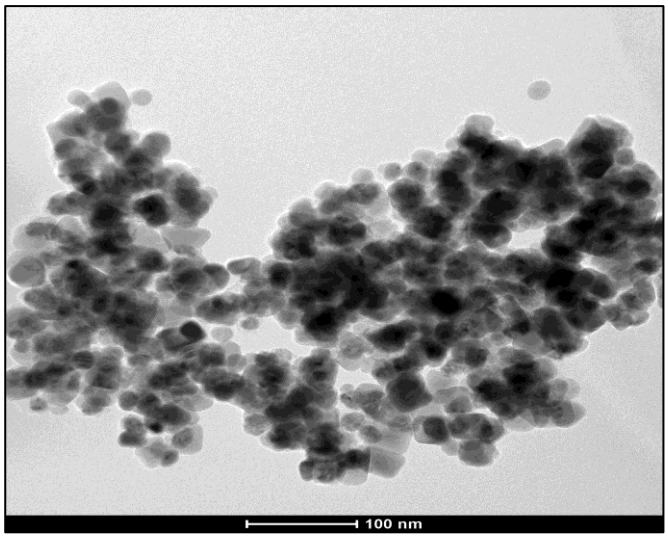



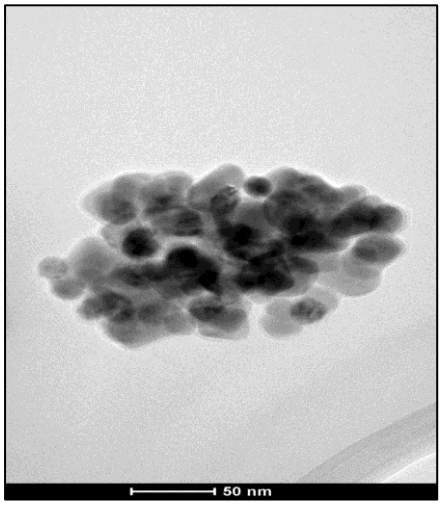



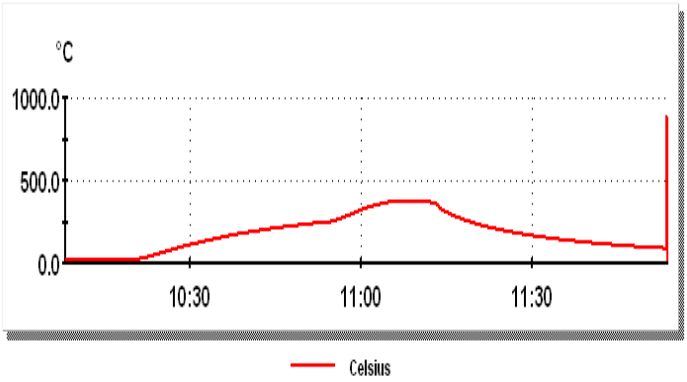

- It is only employed trioctylamine as solvent (100 mL) and oleic acid as surfactant.
- Very fast synthesis (30 minutes of total time; constant variac 7,5) with 7 minutes at boiling temperature (350-380ºC).
- Non violent reaction (it is not observed explosions), but a steamy environment.
- The resulting magnetic material dissolved in hexane is transferred to water medium throughout lauric acid aggregation. Two passages are done following each other in different weeks, but there is agglomeration of particles in both (maybe in the passage of the first week the attraction between them is higher).(Appendix)
- The average size of the particles oscillates between 20 and 40 nm and they are not homogeneous. They are too big but, even this way; they are stable enough in hexane. However, they precipitate in water (agglomeration provokes sedimentation).
- The particles do not present a regular form or structure.

2. $Fe_2NiO_4$ / Ni-03



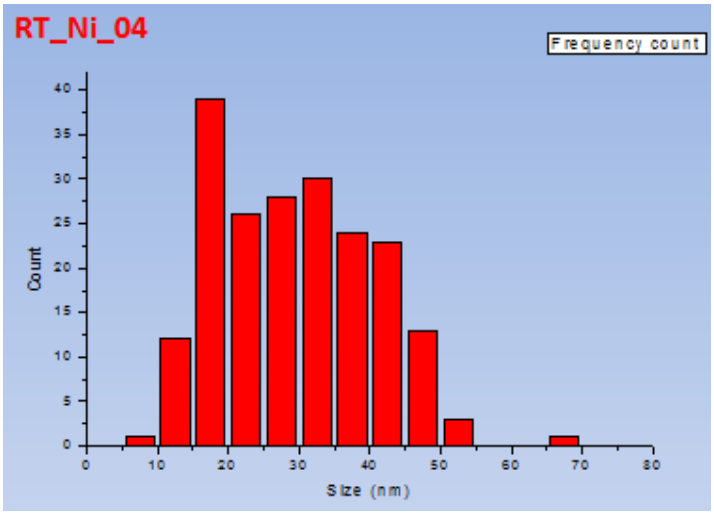



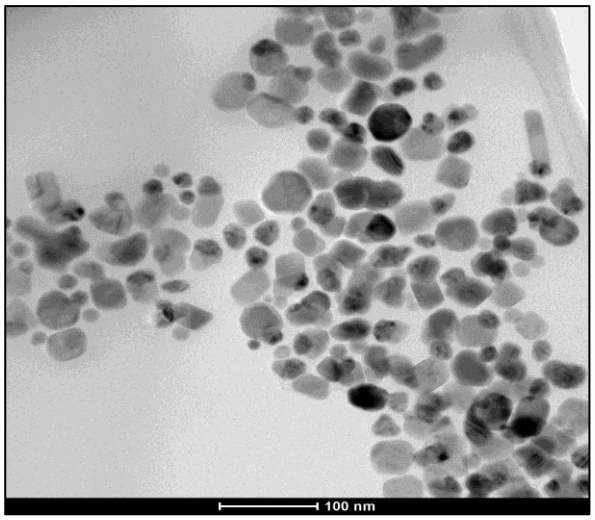



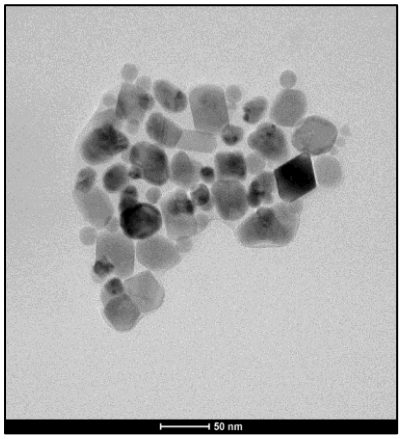



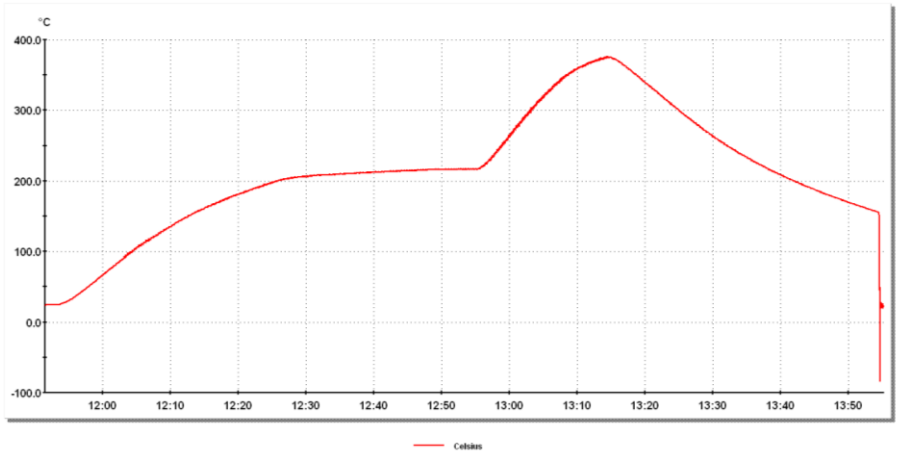

- 100 mL of trioctylamine and 15 mL of oleic acid.
- A bit longer synthesis than the two first ones (50 minutes total time). Non nucleation step and 8 minutes at boiling temperature (320-375ºC).
- When the heating source is switched off, the sample is transferred to a cold blanket, but this does not improve the results.
- The average size of the particles is a little bit smaller than in Ni-01, approximately 25 nm (it varies from 15 to 35 nm). They are not homogeneous and do not exhibit a regular form.
- The particles are not stable and easily precipitate.

3. $Fe_2NiO_4$ / Ni-04



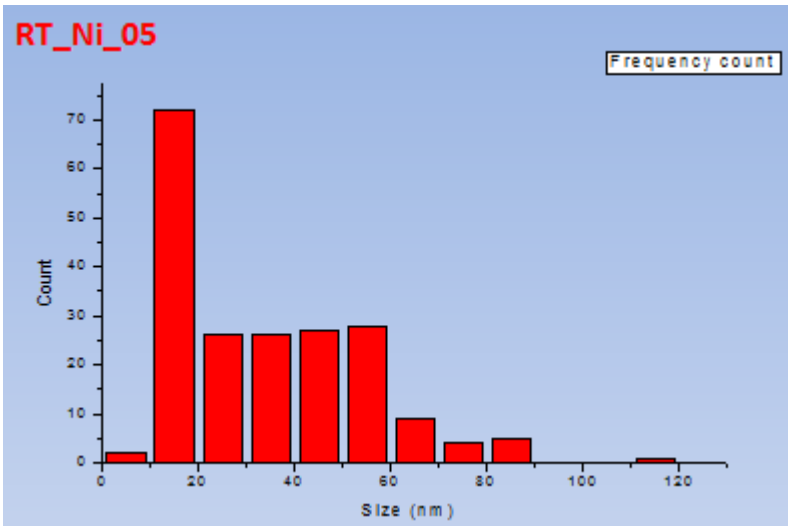



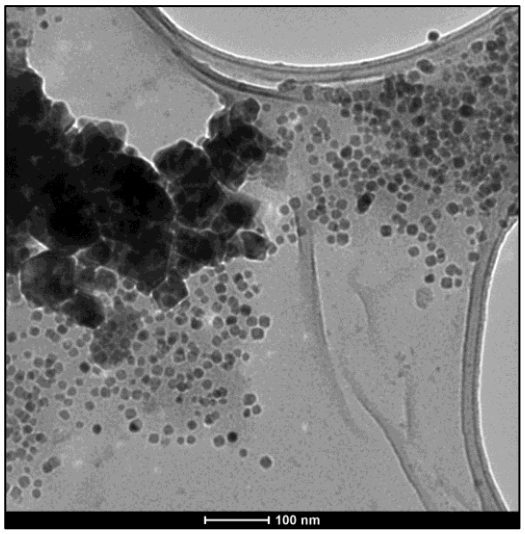



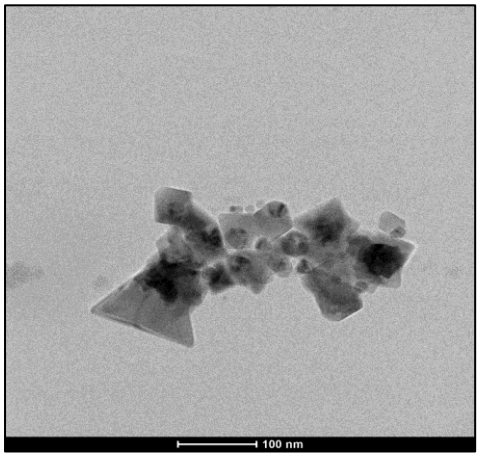



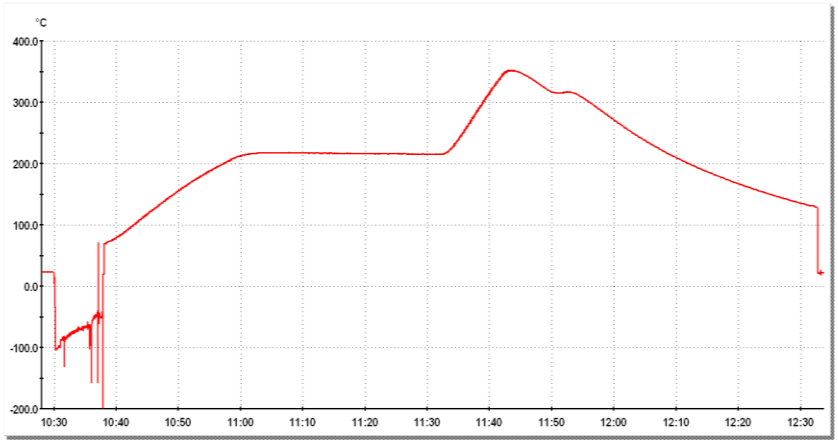

- 100 mL of trioctylamine and 15 mL of oleic acid.
- Synthesis still longer than the previous ones (1 hour 20 minutes of total time). The temperature slowly increases, it is kept 30 minutes at 200ºC (nucleation time) and, finally, 7 minutes at 330-375ºC (boiling point).
- Unexplosive synthesis without big explosions.
- The change in the temperature curve does not offer improvements in the resulting particles: they are irregular, inhomogeneous (from 10 to 50 nm), and also unstable.

4. $Fe_2NiO_4$ / Ni-05



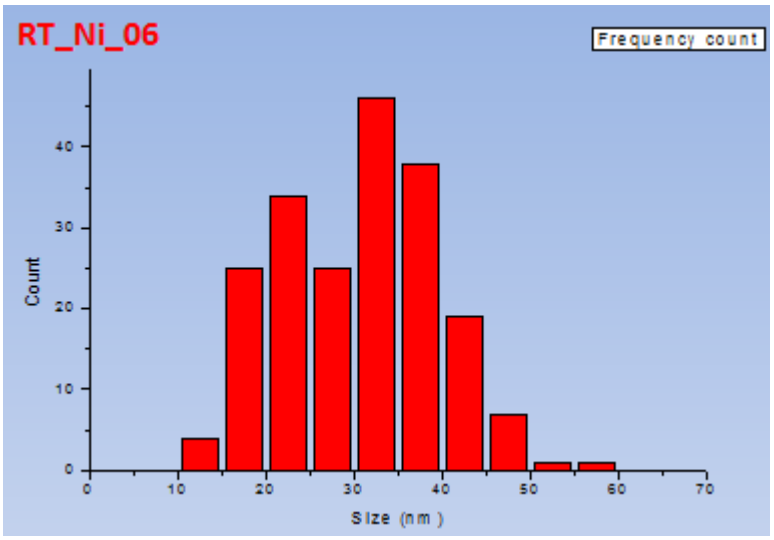



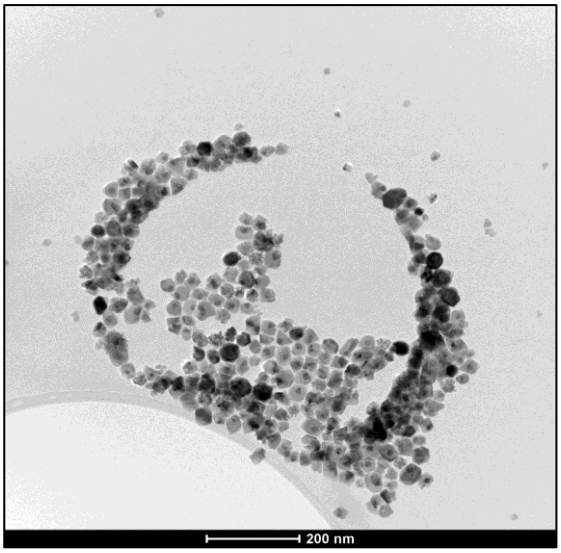



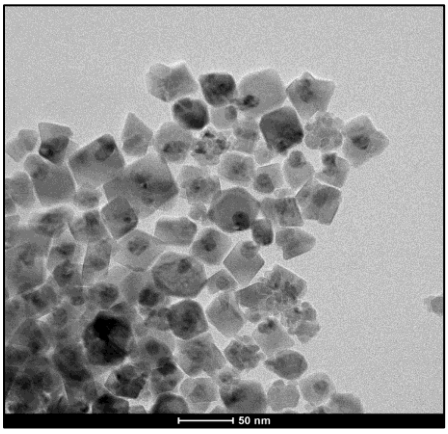



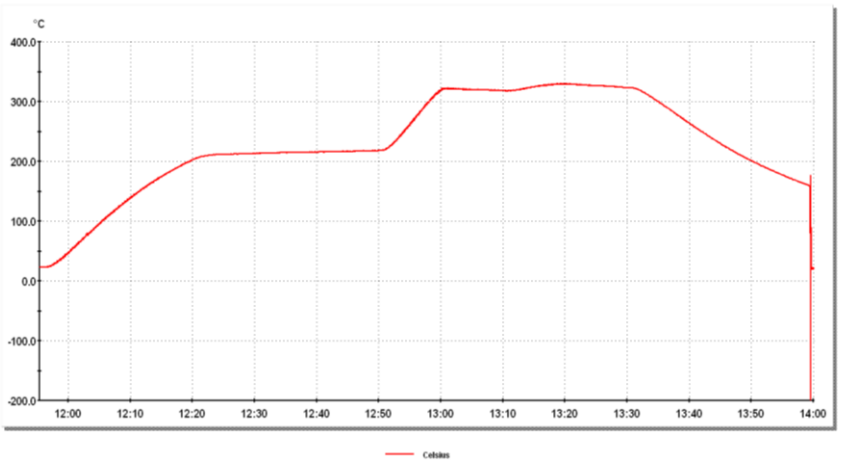

- Nickel iron oxide synthesis with the conditions applied to cobalt synthesis route: 80 mL of trioctylamine plus 20 mL of benzyl-ether (mixture of solvents). 15 mL of oleic acid and 5 mL of oleylamine (another stabilizer surfactant), and 1,8g of 1,2-dodecanediol.
- 1 hour 10 minutes of total duration: 30 minutes at 200ºC, 10 minutes at maxim temperature (350ºC).
- Non violent synthesis
- Irregular and heterogeneous particles: very huge particles that tend to agglomerate. The size of the particles varies between 10 and 60 nm, but it is found the major part of them between 10 and 20 nm.
- They are not stable.

5. $Fe_2NiO_4$ / Ni-06



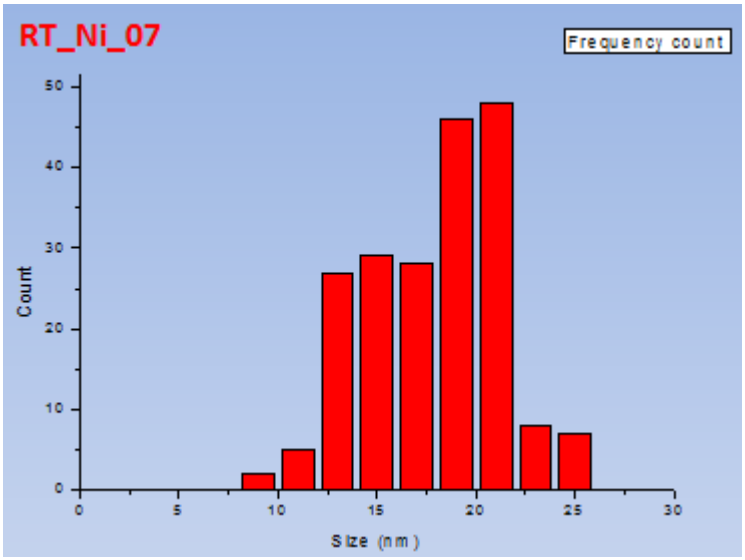



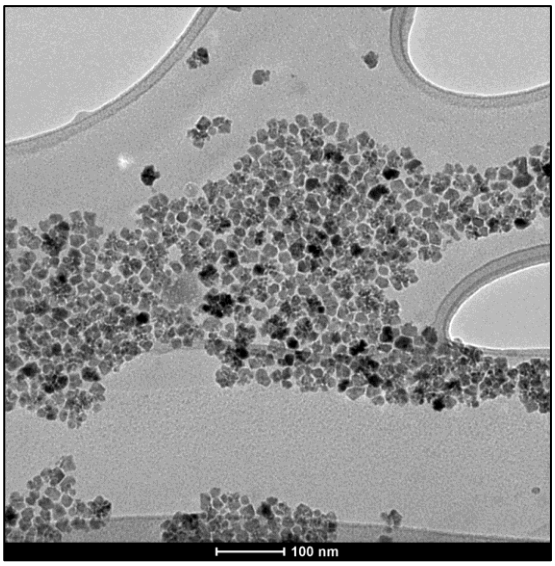



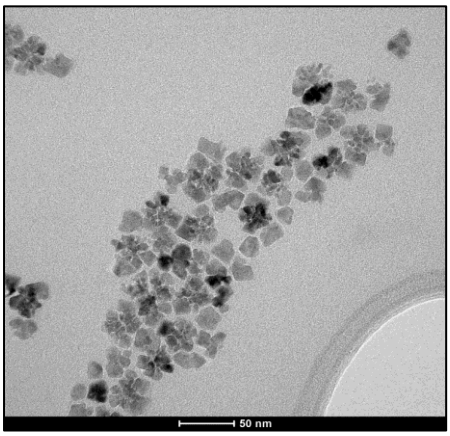



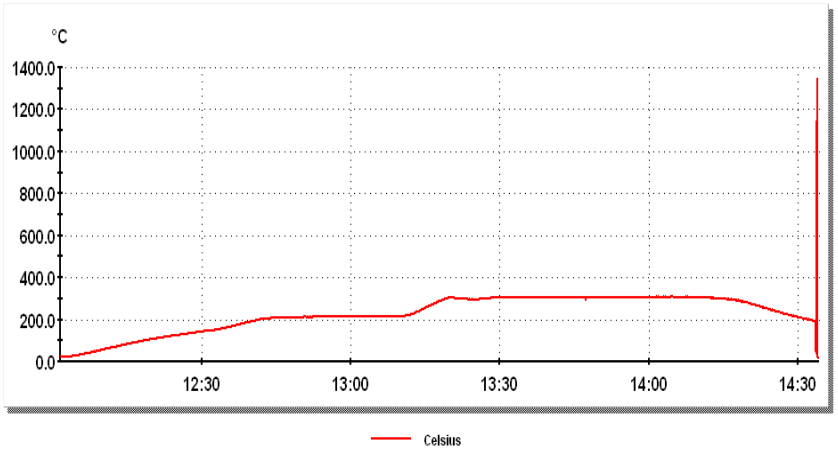

- In this case, it is employed a mixture of solvents in equal proportions: 50 mL of trioctylamine and 50 mL of benzyl-ether. In addition, 15 mL of oleic acid, 5 mL of oleylamine, and 1,8g of 1,2-dodecanediol.
- 1 hour 35 minutes total duration: 30 minutes at 200ºC, 30 minutes at 320-330ºC.
- Unexplosive synthesis.
- Not very homogeneous particles with different shapes: the size oscillates between 10 and 50 nm.
- The particles are too big but stable enough in hexane during a long period of time.

6. $Fe_2NiO_4$ / Ni-07



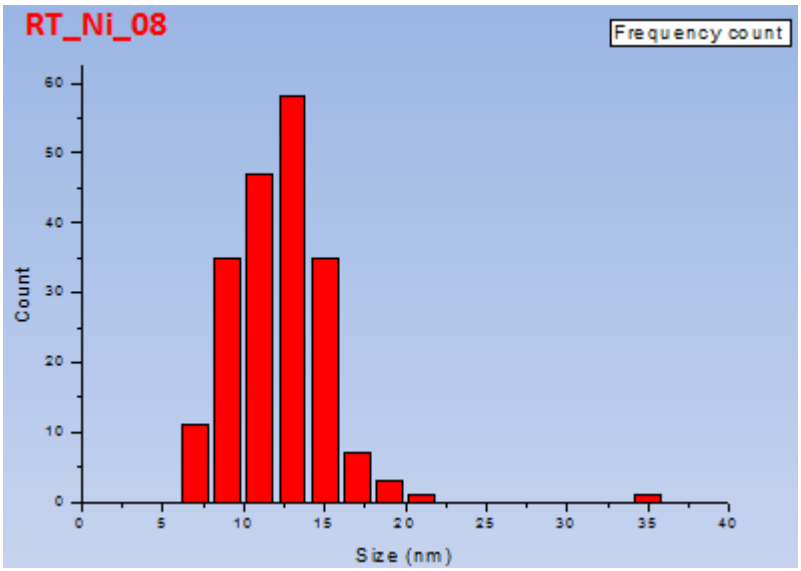



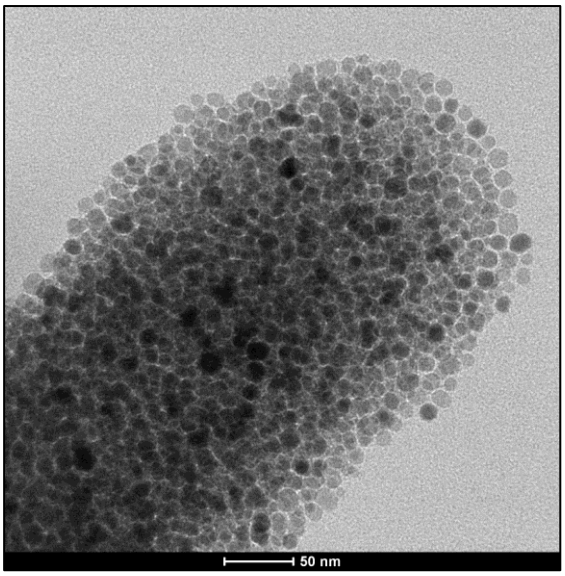



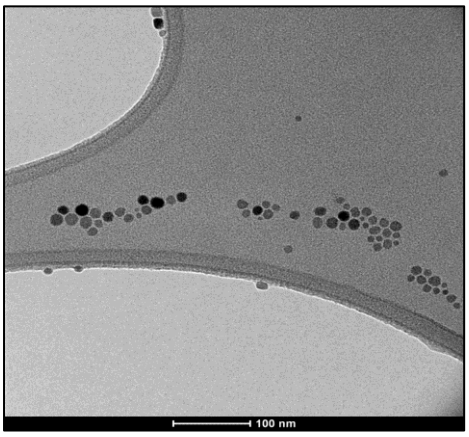



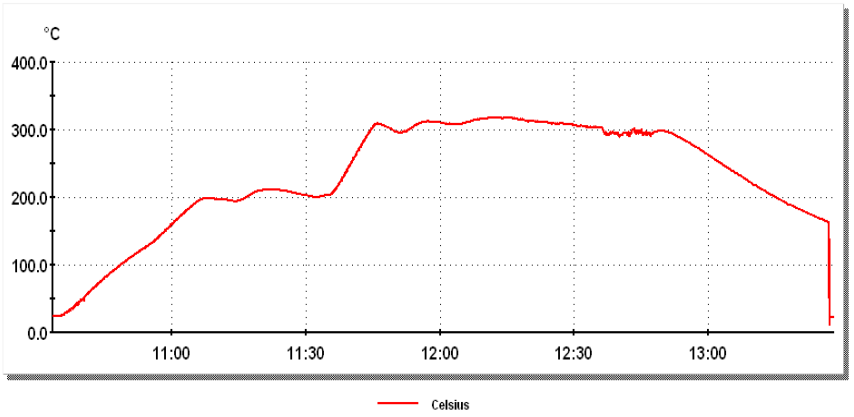

- In this synthesis it is employed 100 mL of benzyl-ether as unique solvent in the mixture. Furthermore, it is included 15 mL of oleic acid, 5 mL of oleylamine and 1,8g of 1,2-dodecanediol.
- Long duration synthesis (2 hours, 15 minutes): 30 minutes at 200ºC, 1 hour at 300ºC.
- Unexplosive synthesis but with a bubbly environment.
- Homogeneous enough particles: between 15 and 20 nm the major part of them. They present very irregular forms.
- They exhibit the best stability until now, so in hexane as in water.

7. $Fe_2NiO_4$ / Ni-08



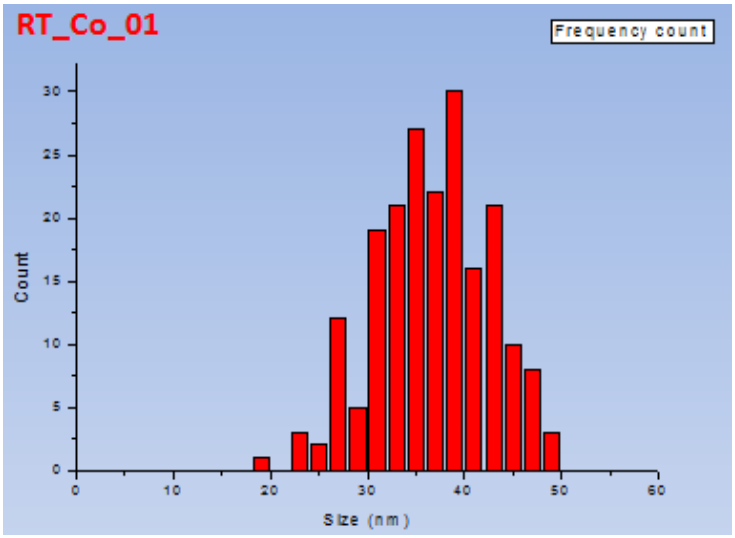



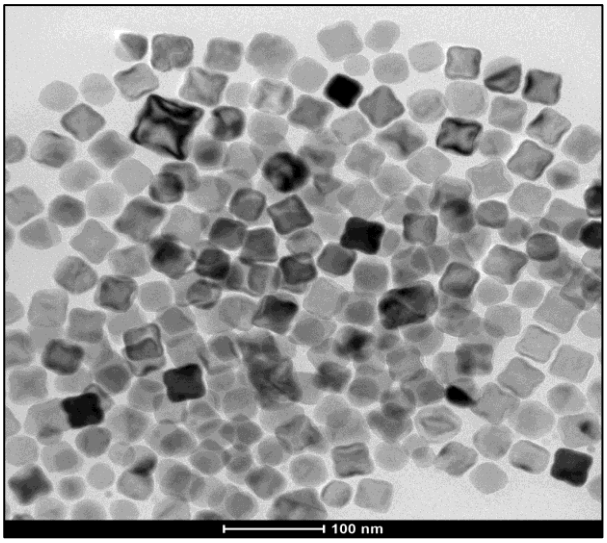



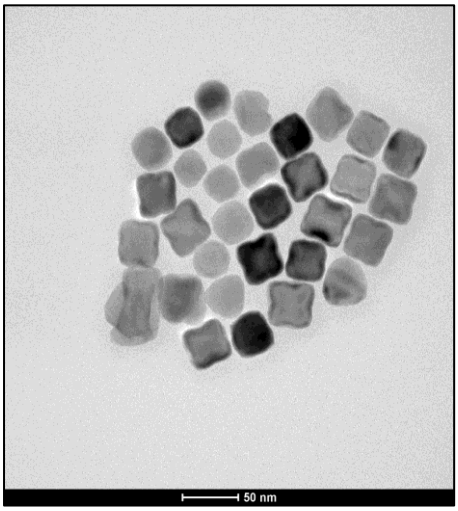



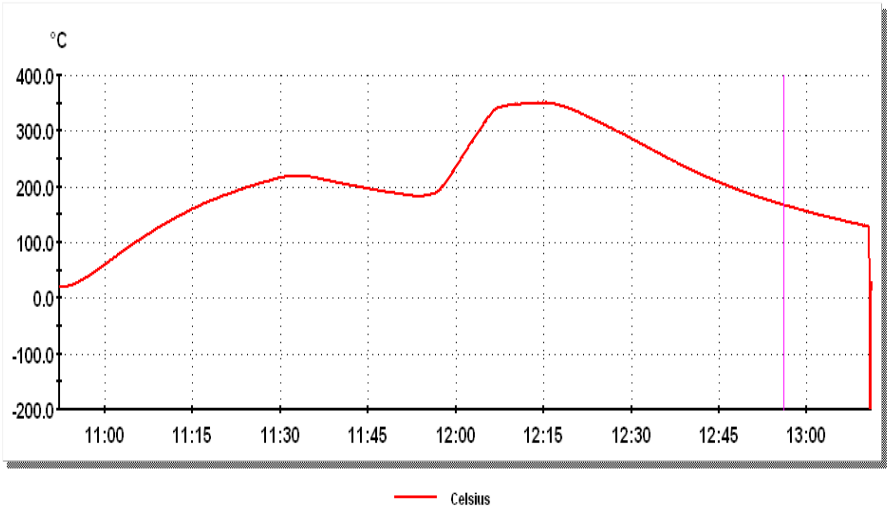

- The last synthesis of nickel ferrites is carried out with more quantity of benzyl-ether than trioctylamine. In this case, the proportion is 4:1. It is added 120 mL of benzyl-ether and 30 mL of trioctylamine.
- It is not employed surfactants in this reaction.
- Very violent synthesis with visible explosions.
- Very homogeneous small particles: between 10 and 15 nm. They present round regular shapes.
- Stable enough particles.

8. $Fe_2CoO_4$ / Co-01



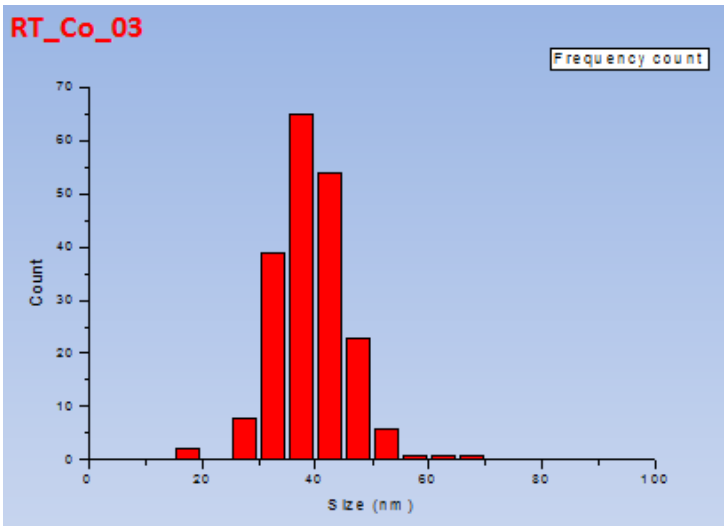



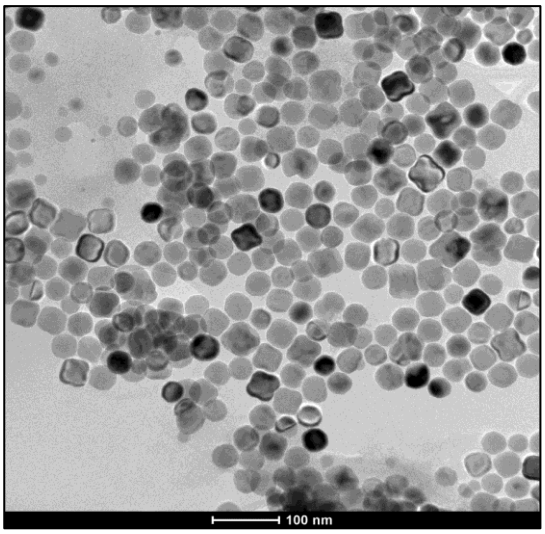



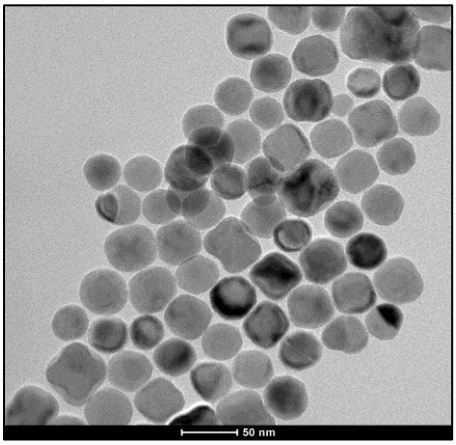



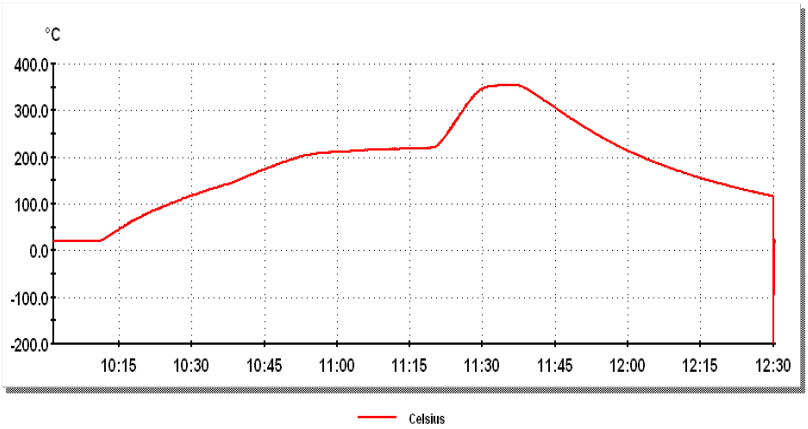

- 80 mL of trioctylamine plus 20 mL of benzyl-ether, 15 mL of oleic acid, 5 mL of oleylamine and 1,8g of 1,2-dodecanediol.
- Synthesis duration about 1 hour and 20 minutes of total time: 30 minutes at 200ºC, 10 minutes at 330-350ºC. The temperature rapidly increases.
- Unexplosive synthesis.
- Not very homogeneous particles (between 30 and 45 nm) and uniform in their shape (round and cubic forms).
- They precipitate (unstable particles).

9. $Fe_2NiO_4$ / Co-03



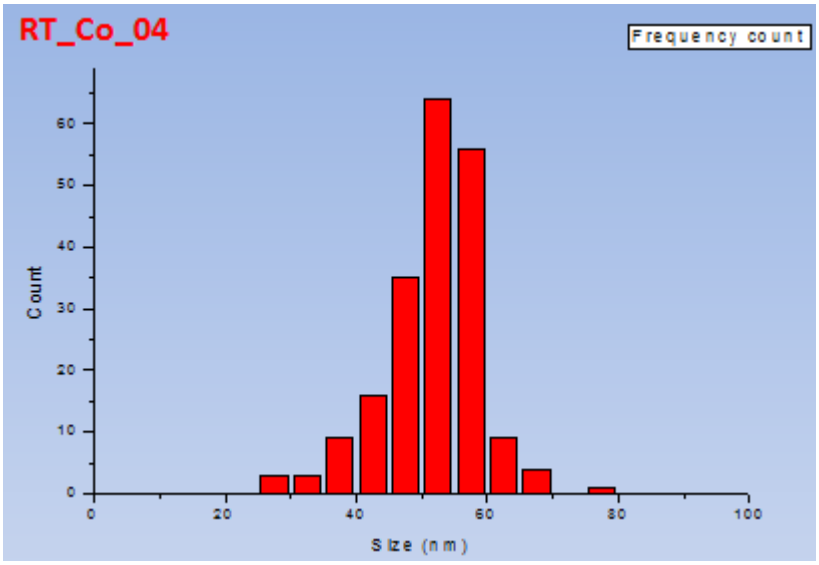



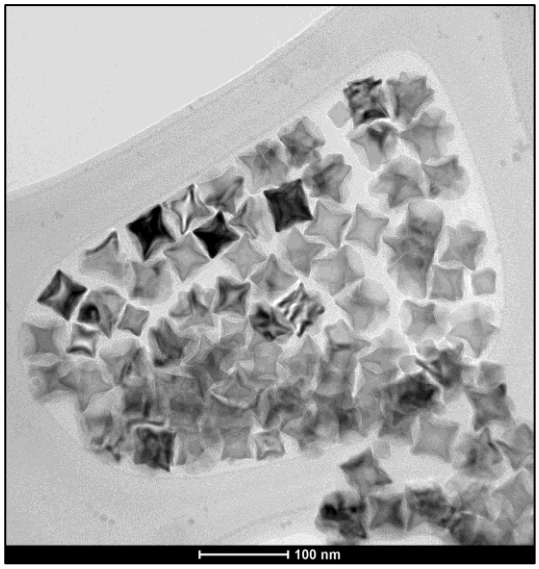



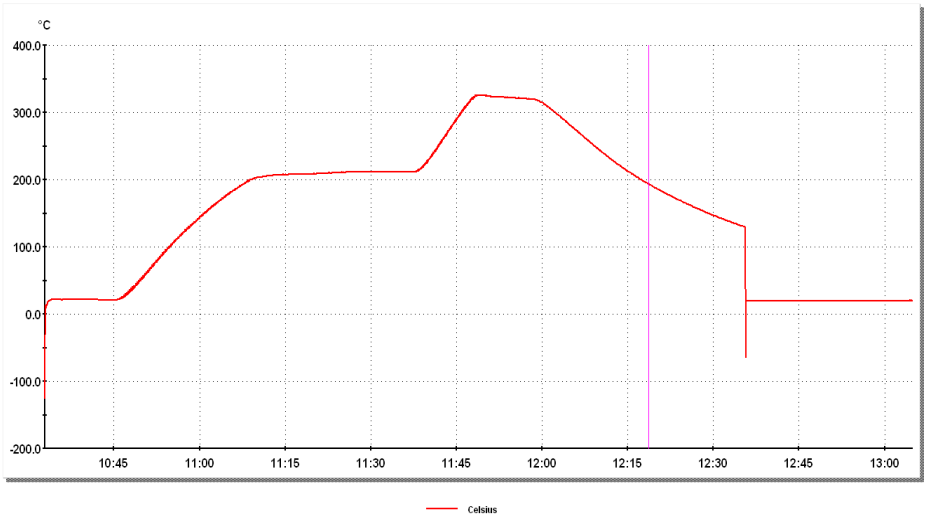




- This synthesis is the same as the previous one (Co-01). It is achieved a perfect reproduction of the first synthesis employing the same reactants and process.
- Not very homogeneous particles (30-50 nm) with regular shapes (round and cubic).
- They are too big; therefore, they precipitate.

10. $Fe_2CoO_4$ / Co-04

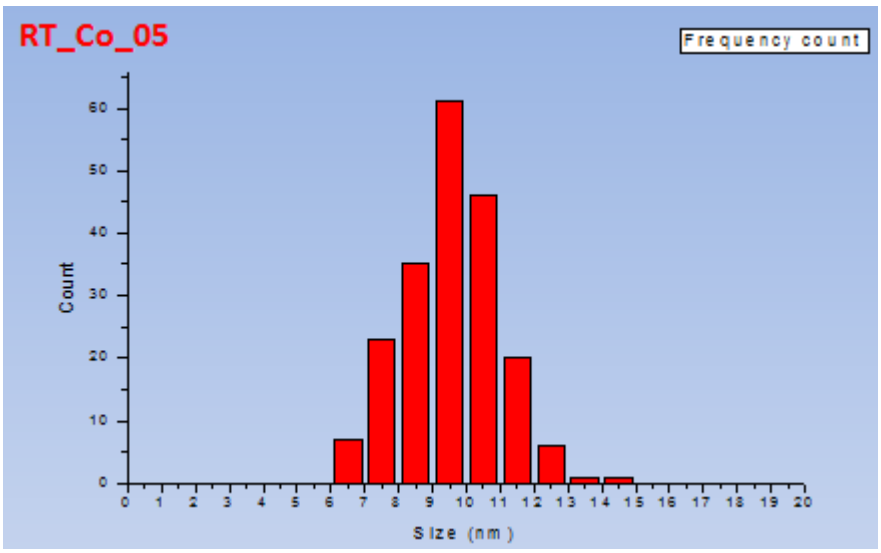


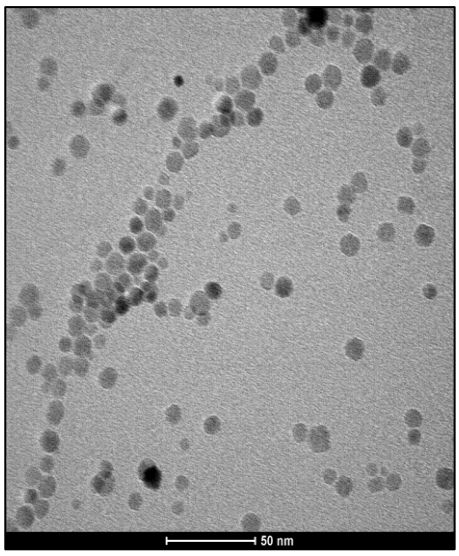



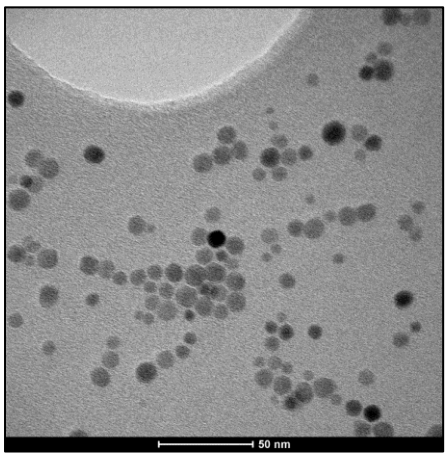



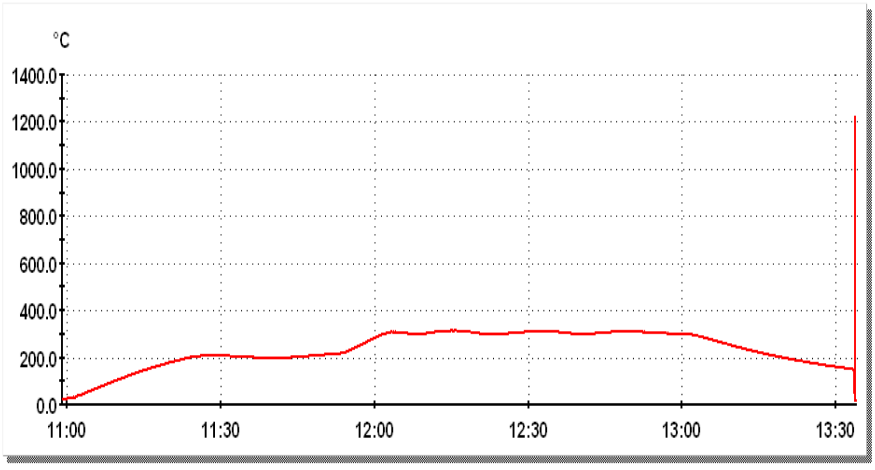

- Equal quantities of surfactants employed in this case: 50 mL of trioctylamine and 50 mL of benzyl-ether. In addition, 15 mL of oleic acid, 5 mL of oleylamine and 1,8g of 1,2-dodecanediol are added.
- Similar synthesis duration than previous ones (1 hour, 15 minutes): 30 minutes at 200ºC, 10 minutes at 320ºC. The final temperature (Tmax.) is lower in this case.
- Not very violent synthesis.
- Not very homogeneous particles (40-60 nm). The shape looks like stars.
- More stable than previous cobalt ferrites but sedimentation early occurs.

11. $Fe_2CoO_4$ / Co-05



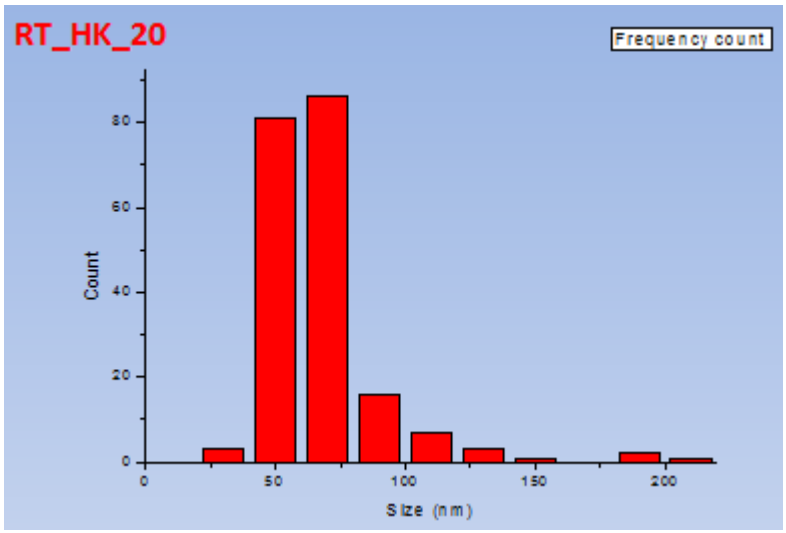



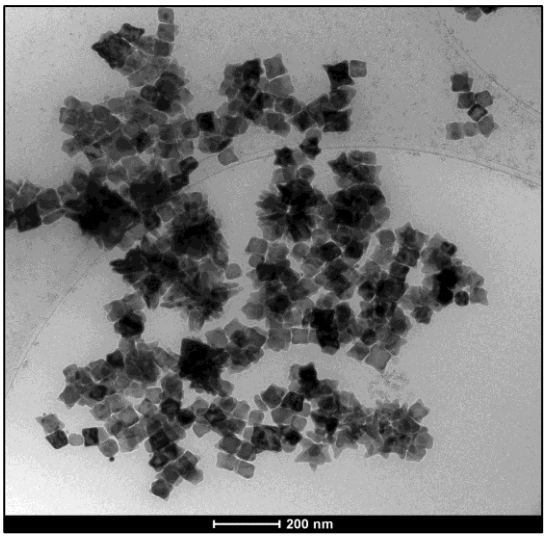



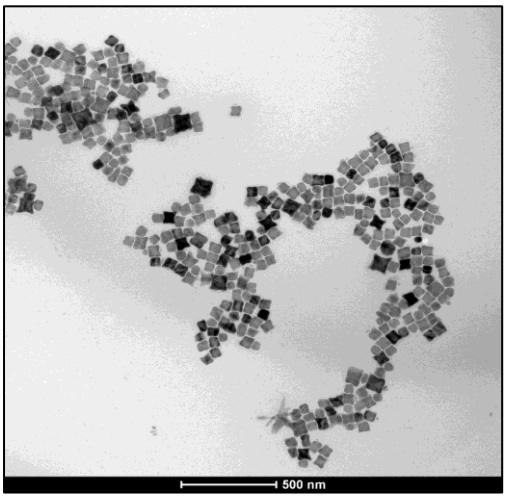



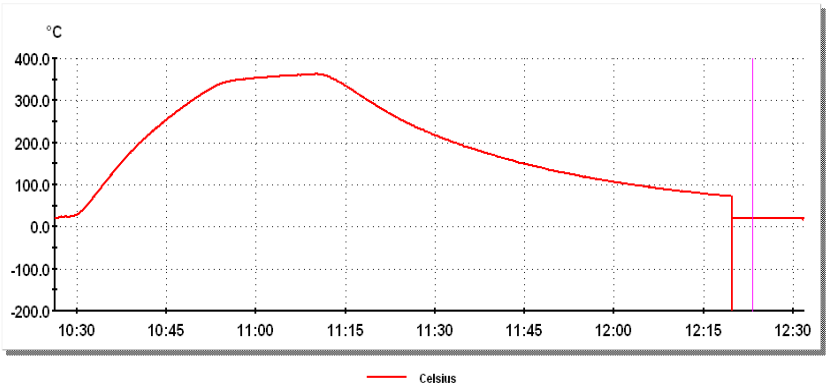

- In the last synthesis of cobalt ferrites it is only employed 150 mL of benzyl-ether; 14,66g of oleic acid, 17,5g of oleylamine and 17,5g of 1,2-dodecanediol.
- Longer synthesis than previous ones (2 hours): 30 minutes at 200ºC, 1 hour at 280-315ºC.
- Violent synthesis: bubbly reaction with a lot of explosions.
- Small homogeneous particles (from 7 to 12 nm) with round regular shape.
- The most stable particles synthesized until now. They are very stable so in hexane as in water.

12. $Fe_3O_4$ / HK-20



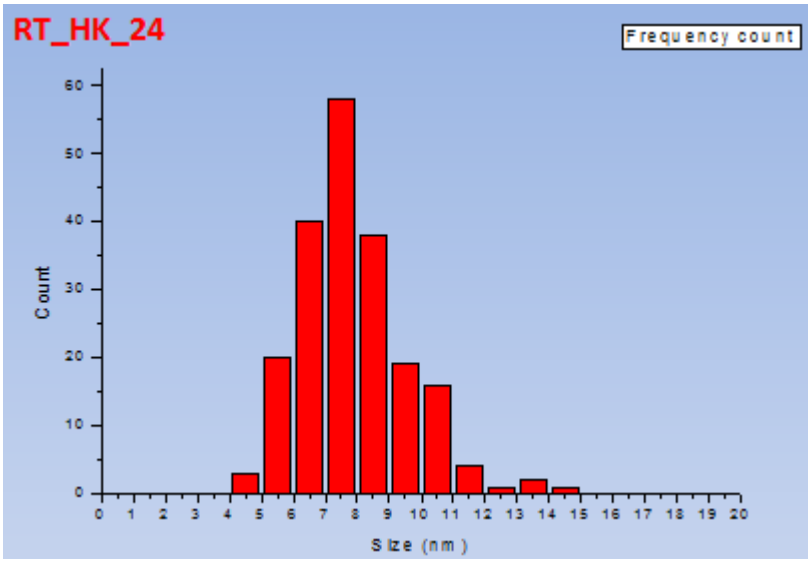



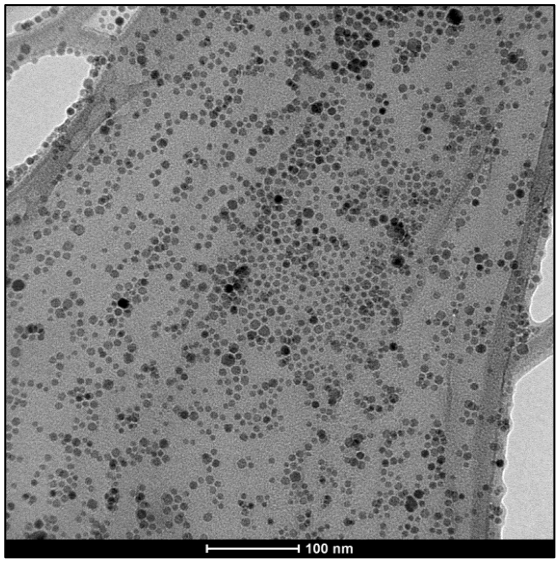



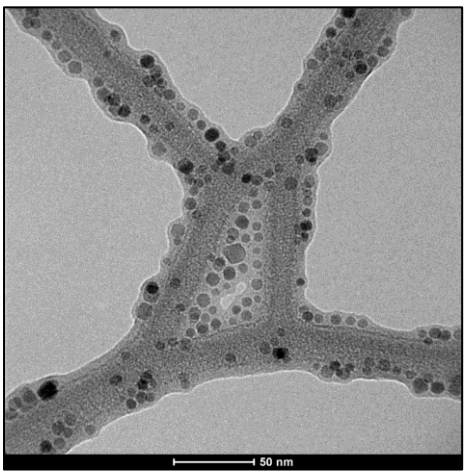



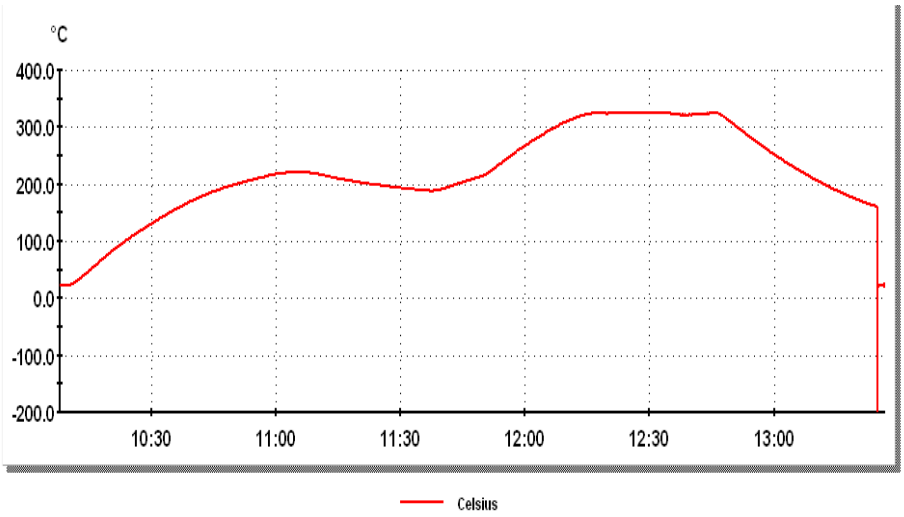

- 80 mL of trioctylamine and 20 mL of benzyl-ether, 8,6g of iron oleate and 1g of oleic acid (when the synthesis is over, it is added 1 mL more of oleic acid due to the visible sedimentation of the particles).
- Very fast synthesis (40 minutes of total time): 20 minutes at 300-360ºC. In this case, it is not necessary the nucleation step, because the precursor is iron oleate.
- Very huge particles (someone reaches 100-200 nm size) with heterogeneous size distribution between 50 and 75 nm. Cubic shaped particles are synthesized.
- They easily precipitate (unstable).

13. $Fe_3O_4$ / HK-24



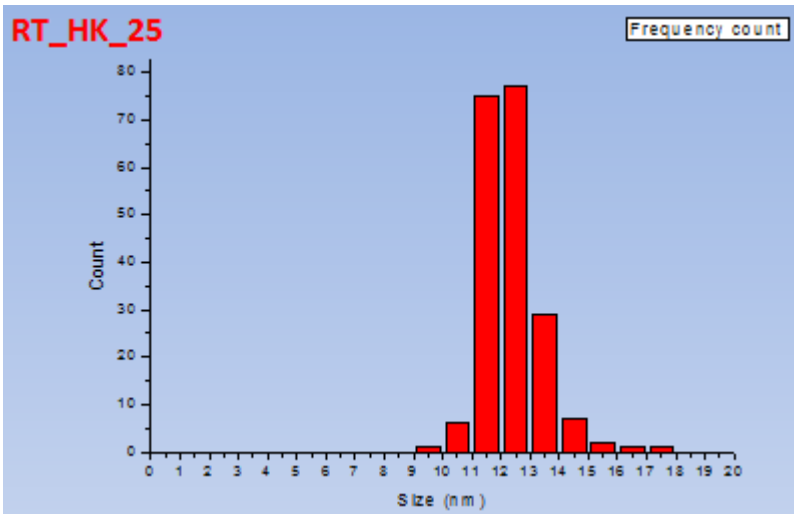



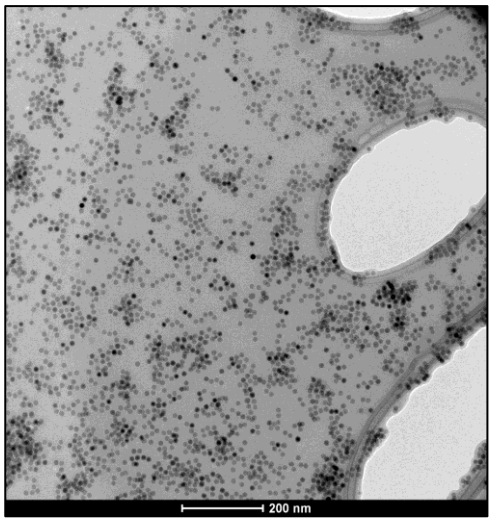



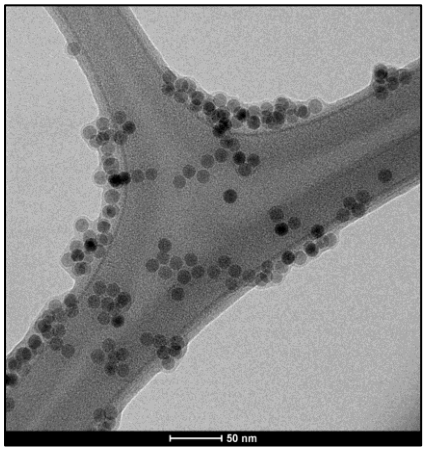



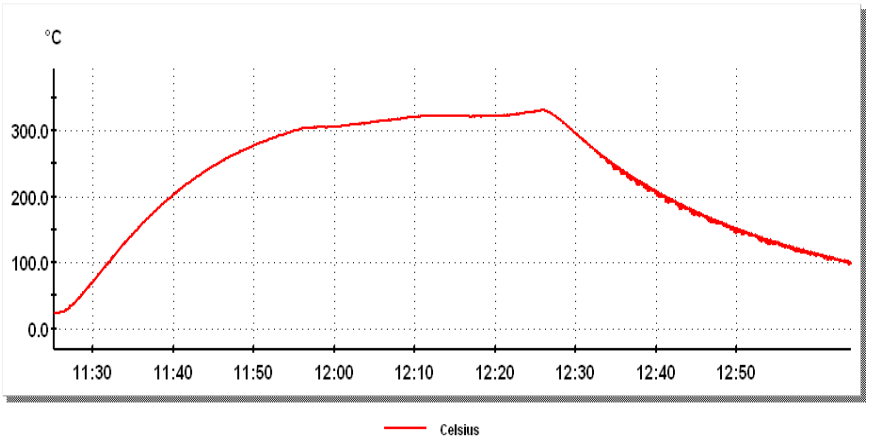

- 80 mL of trioctylamine plus 70 mL of benzyl-ether; 14,65g of oleic acid, 17,93g of oleylamine and 17,48g of 1,2-dodecanediol.
- Very long synthesis (approximately 2 hours 30 minutes): it is maintained 1 hour at 200ºC for the necessary nucleation step and 30 minutes at 320ºC.
- Explosive synthesis
- Small homogeneous particles (5-10 nm) with rounded shape.
- They exhibit the best stability index of the whole magnetite nanoparticles.

14. $Fe_3O_4$ / HK-25




- 80 mL of trioctylamine and 20 mL of benzyl-ether.
- 8,6g of iron oleate.
- It is not employed any surfactant in this last case.
- 1 hour of total synthesis reaction: it is not necessary the nucleation step due to the presence of oleate precursor; 25 minutes at boiling temperature (310-330ºC).
- Not very blast synthesis: little explosions.
- Small homogeneous particles (10-15 nm) with rounded shape.
- They sediment (unstable).

*SELECTION OF MNPs AND TRANSFER TO WATER MEDIUM*

From the whole of synthesis, it is made a selection of those ones that present better characteristics for the obtaining of good results in later studies:

- Fe2NiO4 (Ni-01)
- Fe2NiO4 (Ni-08)
- Fe2CoO4 (Co-05)
- Fe3O4 (HK-20)
- Fe3O4 (HK-24)
- Fe3O4 (HK-25)

The first step corresponds to the transfer of the selected samples to water medium through this process:

1. Measure 500 µl of sample. It is added ethanol and acetone for washing and nitrogen air flow for drying. The resulting powder is extracted in order to weigh it.
2. The powder is dissolved in chloroform (1mg/mL of concentration) in 1:1 proportions.
3. Measure the double amount of phospholipid (PEG2K-PE) respect the sample weight in order to mix them with chloroform in 1:10 proportions.
4. It is added 1 mL of the previously prepared sample in chloroform 1:1.
5. It is dried the final mixture by nitrogen air flow since a homogeneous film is formed.
6. Finally, it is added 1 mL of distilled water to each sample.

- Ni-01: Medium stability
- Ni-08: High stability
- Co-05: High stability
- HK-20: Little stability
- HK-24: Little stability
- HK-25: Medium stability

In the (appendix) it is shown the whole TEM/HRTEM images of the samples in water.

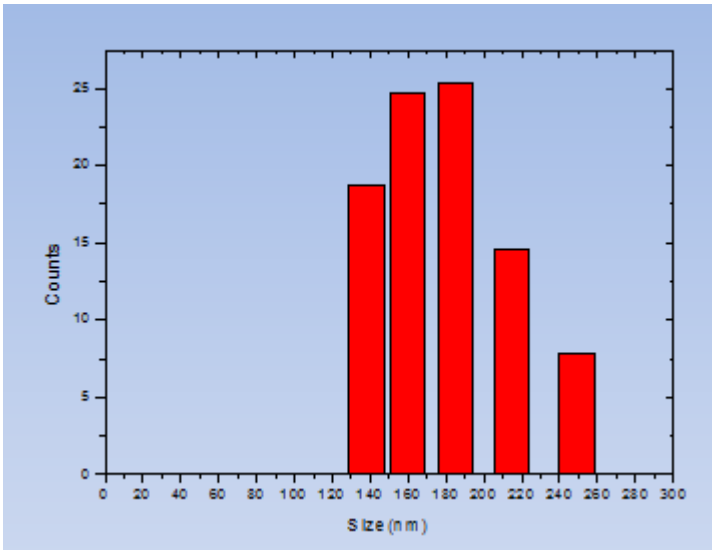
*DISPERSITY AND HYDRODYNAMIC DIAMETER OF MNPs*

This study is carried out in hexane and water by the results obtained through dynamic light scattering. This is the summary for considering correct a particle size measurement:

- Kcps (concentration): 400-500
- Baseline index ~ 9 (base line)
- Several runs with similar results of effective diameter
- Polydispersity index: <0,1 = monodisperse NPs; >0,1 = polydisperse NPs

✓ **Ni-01 ($Fe_2NiO_4$)**

Hexane

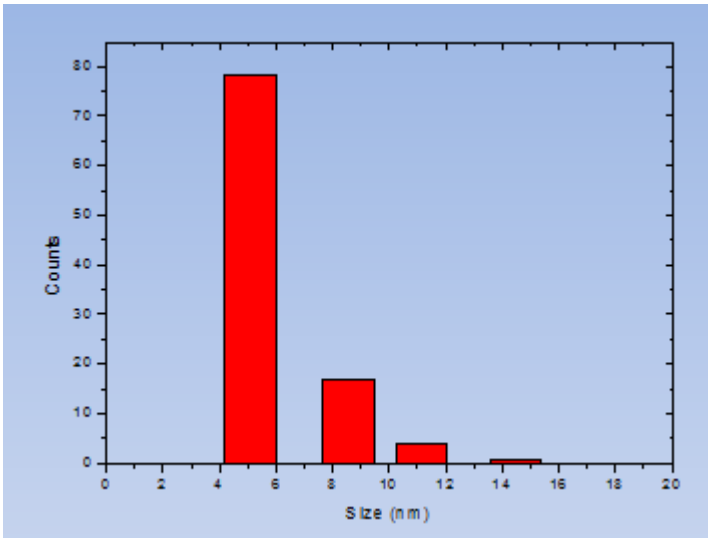



- Mean diameter: 43,2 nm
- Polidispersity: 0,172
- Avg. Count rate: 359,1 kcps
- Baseline index: 9,1 (98,03%)

Water

✓ **Ni-08 ($Fe_2NiO_4$)**

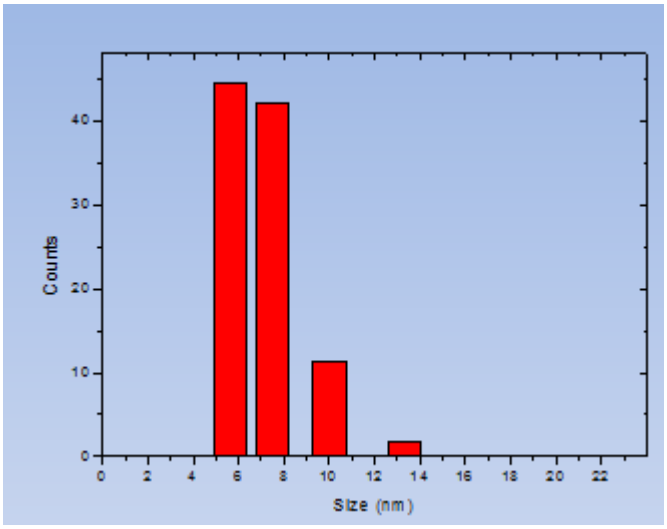
Hexane




- Mean diameter: 64,4 nm
- Polidispersity: 0,183
- Avg. Count rate: 396 kcps
- Baseline index: 9,1 (98,53%)

Water

✓ **Co-05 ($Fe_2CoO_4$)**




Hexane

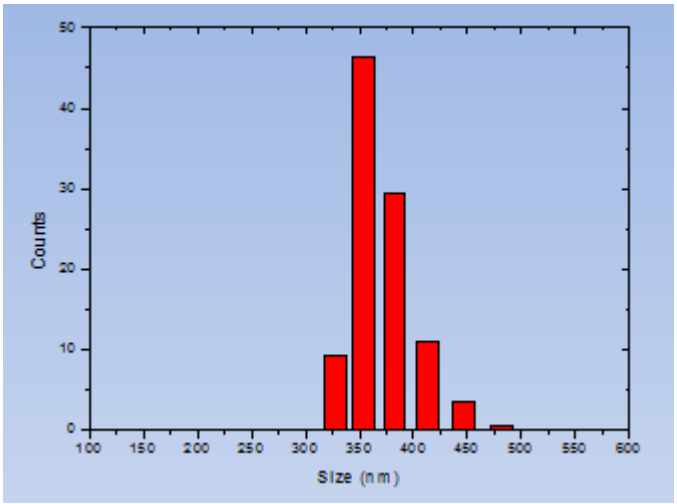
Water

- Mean diameter: 14,4 nm
- Polidispersity: 0,173
- Avg. Count rate: 288,1 kcps
- Baseline index: 7,8 (95,99%)

✓ **HK-20 ($Fe_3O_4$)**

Water

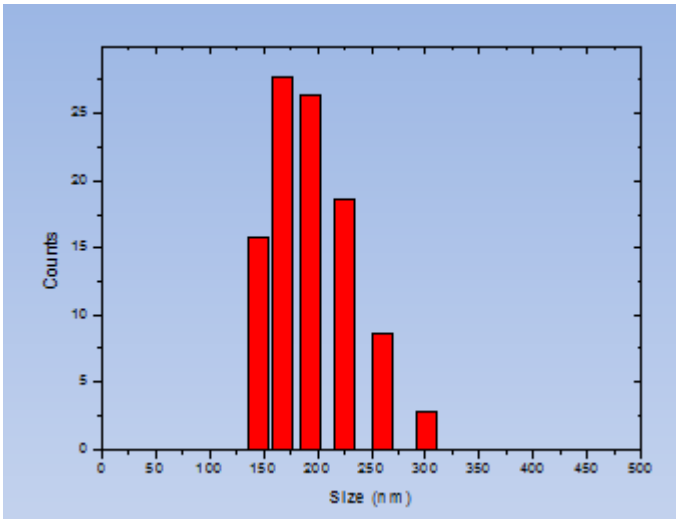
- Mean diameter: 75,1 nm
- Polidispersity: 0,280
- Avg. Count rate: 394,6 kcps
- Baseline index: 9,4 (98,18%)




Hexane

✓ **HK-24 ($Fe_3O_4$)**

Hexane

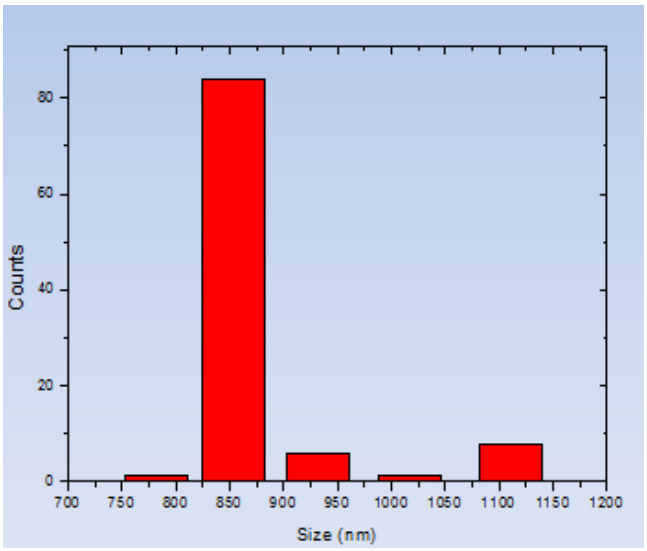



- Mean diameter: 21 nm
- Polidispersity: 0,316
- Avg. Count rate: 115,5 kcps
- Baseline index: 0 (88,67%)

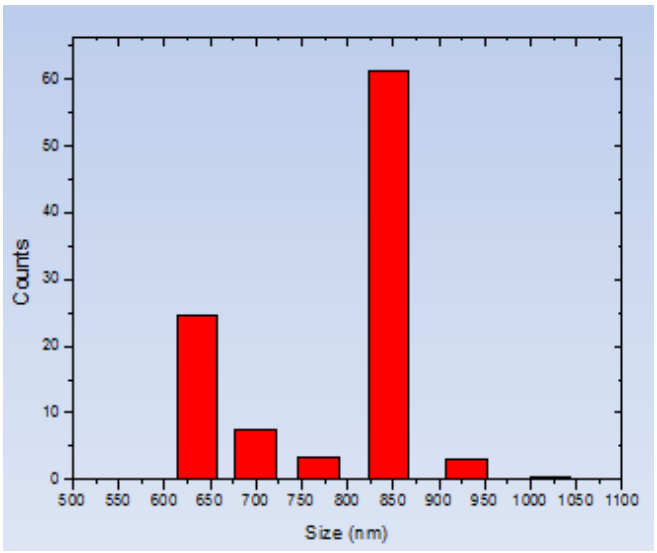
Water

✓ **HK-25 ($Fe_3O_4$)**

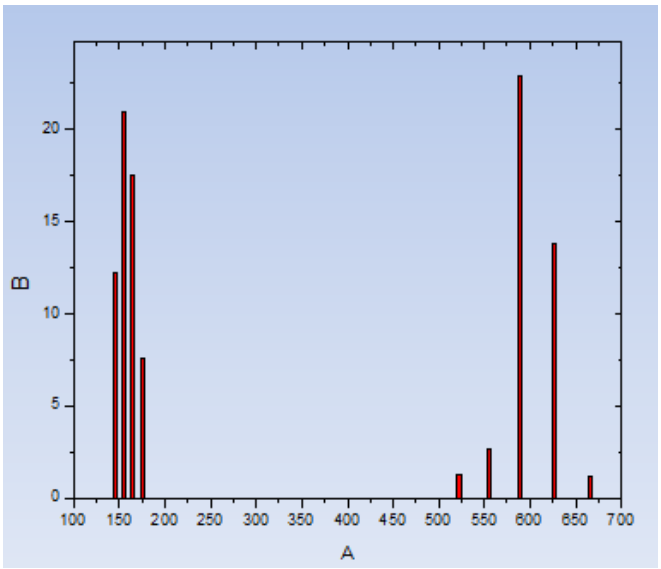
Hexane 1




Hexane 2




Hexane 3




- Mean diameter: 33,7 nm
- Polidispersity: 0,062
- Avg. Count rate: 465,4 kcps
- Baseline index: 9,8 (95,95%)

Water

## VSM

Throughout vibrating sample magnetometer it is possible to observe the magnetic behaviour of magnetic materials. It is done two different measurement probes of each selected sample, one by unknown concentrations and another by known concentration values (first ones are included in the appendix).

- Unknown concentration values: it is prepared a reference weight for each sample around 10 mg. Previously, it is dried each sample dissolved in hexane by nitrogen air flow.
- Known concentration values: It is measured known weights and concentration values in order to improve the results, trying to adjust magnetization values. For this purpose, it is decomposed each sample in nitric acid (oxidant substance) and hydrochloric acid (solvent that gives the acid environment, eliminates the surfactant and the organic byproducts: the result is nude particles). In other words, it is calculated the exact concentration of magnetic element present in the sample. Finally, it is measured the absorbance by ultraviolet (visible spectroscopy) of a conjugated complex of the particles with thiocyanate (compound that combines with iron and provokes a colour change). A correlation between the obtained absorbance and the line pattern's absorbance gives us the concentration values.

Calculations for concentration values of samples

• Fe2NiO4_01 → 50 µl de muestra: 0,5153 de absorbancia
4,87 mg/ml Fe, 10,22 mg/ml Fe2NiO4, 0,82 mg/80 µl de muestra
• Fe2NiO4_08 → 100 µl de muestra: 0,2221 de absorbancia
1,05 mg/ml Fe, 3,8 mg/ml Fe2NiO4, 0,3 mg/80 µl de muestra
• Fe2CoO4_05 → 25 µl de muestra: 0,5522 de absorbancia
10,44 mg/ml Fe, 21,89 mg/ml Fe2CoO4, 1,75 mg/80 µl de muestra
• Fe3O4_20 → 50 µl de muestra: 0,5984 de absorbancia
5,66 mg/ml Fe, 7,82 mg/ml Fe3O4, 0,63 mg/80 µl de muestra
• Fe3O4_24 → 100 µl de muestra: 0,8867 de absorbancia
4,19 mg/ml Fe, 5,79 mg/ml Fe3O4, 0,46 mg/80 µl de muestra
• Fe3O4_25 → 200 µl de muestra: 0,9341 de absorbancia
2,2 mg/ml Fe, 3 mg/ml Fe3O4, 0,24 mg/80 µl de muestra

Additions of 80 µl to VSM capsules for determining the total weight

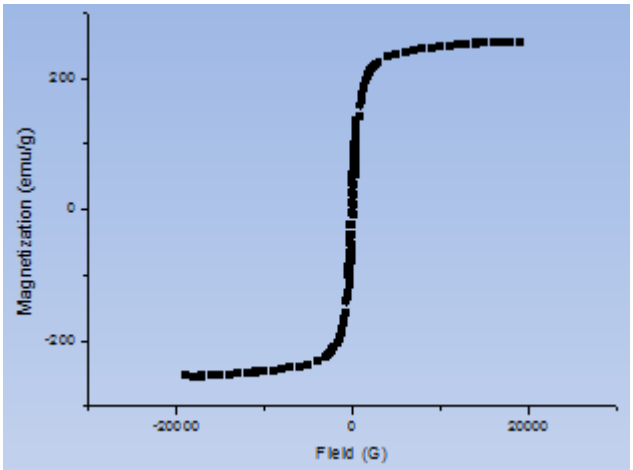
- Fe2NiO4_01: 0,82 x 7 adiciones = 5,74 mg
- Fe2NiO4_08: 0,3 x 17 adiciones = 5,1 mg
- Fe2CoO4_05: 1,75 x 6 adiciones = 10,5 mg
- Fe3O4_20: 0,63 x 9 adiciones = 5,67 mg
- Fe3O4_24: 0,46 x 12 adiciones = 5,52 mg
- Fe3O4_25: 0,24 x 22 adiciones = 5,28 mg

Final weight in each VSM capsule

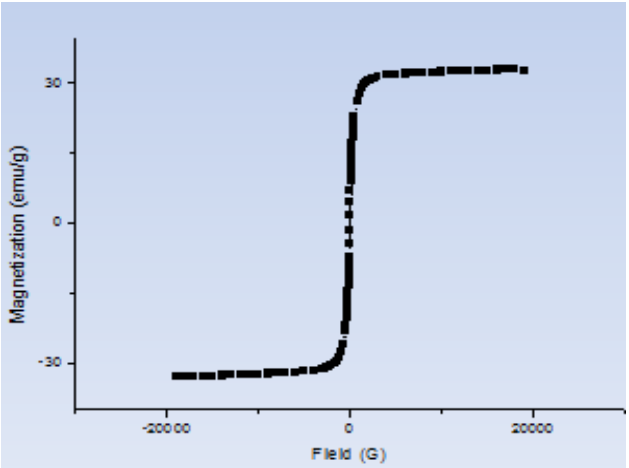
**VSM results of known concentration samples**

1. System calibration with a reference sample of nickel (6,92 emu, 5000G)
2. Centre X, Y, Z axis in their maxims.
3. Cotton utilization to immobilize the samples into the capsules (avoid the movement of the nanoparticles induced by the vibration applied by the system, and the bad orientation of the atoms when the magnetic fields are applied).
4. Cover the capsules by Teflon in order to avoid possible contamination.
5. Measurements.

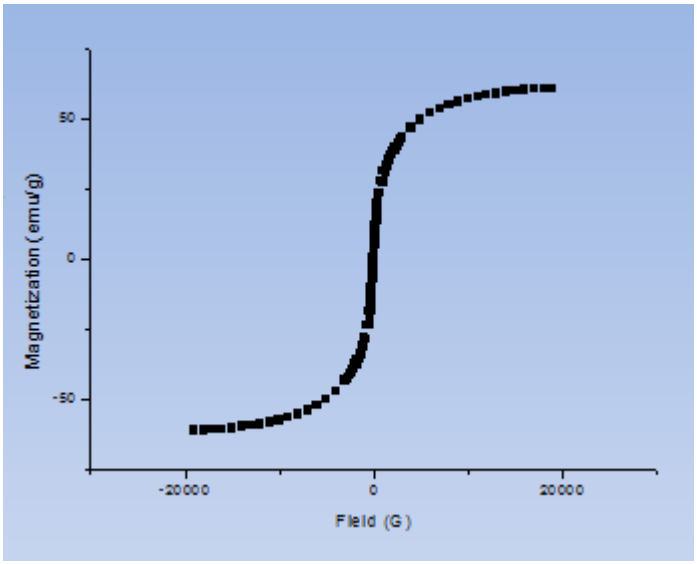
Ni-01



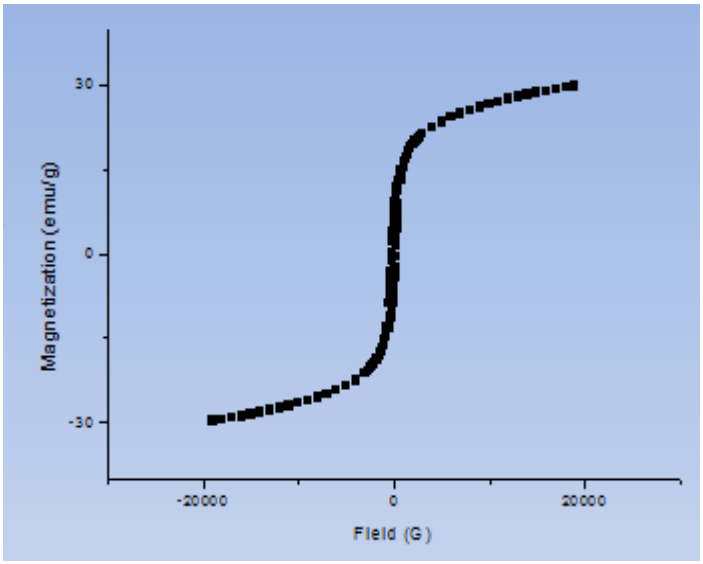

Ni-08



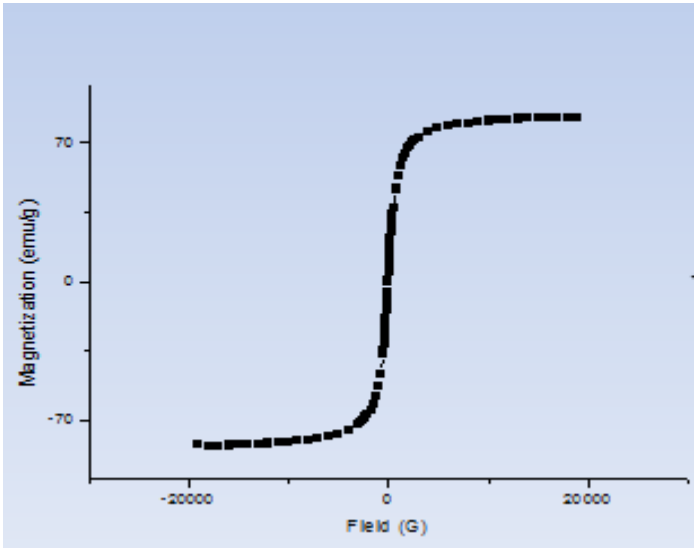
Co-05



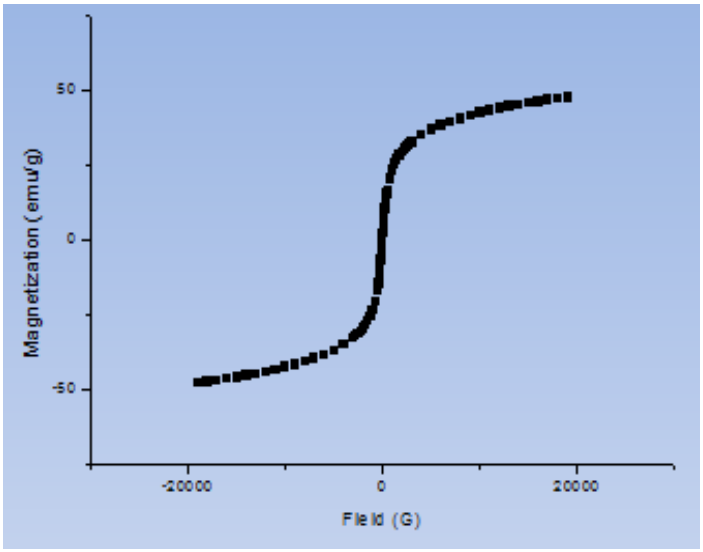

HK-20




HK-24




HK-25



**DM100 Series**

Through this equipment it is possible to obtain the SPA (specific power absorption) values for each sample at given frequency/field parameters. In this way, the results obtained with this method offer an estimate idea of MNPs as good or bad heating agents.

Here it is detailed the SPA values for each sample so in hexane as in water. The graphs of the increasing temperature versus time are shown in the 'Hyperthermia Appendix'. The slope of the ramp is used to calculate these SPA values by means of this formula:

**SPA = Calorific Capacity · Density of the medium · Slope · 1000 / Concentration**

Calorific Capacity: 2,26 in hexane; 4,18 in water
Density: 0,7 hexane; 1 water

Concentrations of samples that give us positive values in SPA:

- Ni-01 water: 1,17 mg/mL
- Ni-01 hexane: 7,20 mg/mL
- Ni-08 water: 1,087 mg/mL
- Ni-08 hexane: 2,12 mg/mL
- Co-05 water: 1 mg/mL
- Co-05 hexane: 24,33 mg/mL
- HK-24 hexane: 5,25 mg/mL

**Ni-01 water**

| Frequency/Field | SPA (W/g) |
|---|---|
| 818kHz/200G | 94,28 |
| 571kHz/200G | 65,99 |
| 440kHz/200G | 52,30 |
| 314kHz/200G | 44,41 |
| 248kHz/200G | 35,87 |
| 300G/560kHz | 209,04 |
| 270G/560kHz | 156,41 |
| 240G/560kHz | 113,04 |
| 210G/560kHz | 94,259 |
| 180G/560kHz | 55,23 |

**Ni-01 hexane**

| Frequency/Field | SPA (W/g) |
|---|---|
| 818kHz/200G | 9,57 |
| 571kHz/200G | 5,52 |
| 440kHz/200G | 4,29 |
| 314kHz/200G | 2,90 |
| 248kHz/200G | 2,04 |
| 300G/560kHz | 36,12 |
| 270G/560kHz | 16,71 |
| 240G/560kHz | 9,06 |
| 210G/560kHz | 4,69 |
| 180G/560kHz | 2,36 |

**Ni-08 water**

| Frequency/Field | SPA (W/g) |
|---|---|
| 818kHz/200G | 715,95 |
| 571kHz/200G | 449,12 |
| 440kHz/200G | 308,94 |
| 314kHz/200G | 196 |
| 248kHz/200G | 140,63 |
| 300G/560kHz | 616,12 |
| 270G/560kHz | 590,62 |
| 240G/560kHz | 540,82 |
| 210G/560kHz | 483,14 |
| 180G/560kHz | 371,20 |

**Ni-08 hexane**

| Frequency/Field | SPA (W/g) |
|---|---|
| 818kHz/200G | 127,68 |
| 571kHz/200G | 91,61 |
| 440kHz/200G | 63,96 |
| 314kHz/200G | 41,99 |
| 248kHz/200G | 28,18 |
| 300G/560kHz | 117, 25 |
| 270G/560kHz | 111,40 |
| 240G/560kHz | 102,78 |
| 210G/560kHz | 95,78 |
| 180G/560kHz | 86,59 |

**Co-05 water**

| Frequency/Field | SPA (W/g) |
|---|---|
| 818kHz/200G | 60,57 |
| 571kHz/200G | 49,95 |
| 440kHz/200G | 35,28 |
| 314kHz/200G | 30,26 |
| 248kHz/200G | 30,22 |
| 300G/560kHz | 76,87 |
| 270G/560kHz | 67,97 |
| 240G/560kHz | 44,68 |
| 210G/560kHz | 30,14 |
| 180G/560kHz | 22,57 |

**Co-05 hexane**

| Frequency/Field | SPA (W/g) |
|---|---|
| 818kHz/200G | 193,36 |
| 571kHz/200G | 132,9 |
| 440kHz/200G | 105,44 |
| 314kHz/200G | 69,84 |
| 248kHz/200G | 49,13 |
| 300G/560kHz | 244,97 |
| 270G/560kHz | 203,65 |
| 240G/560kHz | 137,15 |
| 210G/560kHz | 112,71 |
| 180G/560kHz | 110,86 |

**HK-24 hexane**

| Frequency/Field | SPA (W/g) |
|---|---|
| 818kHz/200G | 26,38 |
| 571kHz/200G | 12,98 |
| 440kHz/200G | 8,07 |
| 314kHz/200G | 4,12 |
| 248kHz/200G | 2,62 |
| 300G/560kHz | 49,4 |
| 270G/560kHz | 36,28 |
| 240G/560kHz | 28,31 |
| 210G/560kHz | 18,72 |
| 180G/560kHz | 10,94 |

# DISCUSSIONS

In general, the formation of monodispersed magnetic nanoparticles proceeds in two separated steps, nucleation and growth. Metal ions are slowly generated in the solution by progressive decomposition of the precursor or dissolution of an intermediate phase. When the concentration of ions in solution overcomes the supersaturation limit, a homogeneous nucleation takes place and the ion concentration is reduced avoiding secondary nucleations. A homogeneous and short nucleation can be induced by increasing the heating rate, giving rise to very uniform particles. The growth is controlled by the formation of certain kind of surfactant-metal complexes. Then, a diffusion mechanism, known as Ostwald ripening, slows down the growth of larger particles and accelerates the growth of the smaller ones, resulting in MNPs with a narrow particle size distribution.

Kinetic studies have shown that the formation of stable nuclei is slower than their subsequent growth so that the two phenomena are as desired temporally separated and that the reaction rate is therefore controlled by the nucleation rate. Mean particle size, shape and distribution can be modified by changing the parameters that govern the reaction mechanism in each case (10). Tuning the size of MNPs prepared by thermal decomposition is possible by adjusting experimental parameters such as the nature of the iron precursor, the nature of the stabilisers, concentration of reagents, temperature and temperature ramp or stirring rate. (14)

Organic surfactants have a key role in determining not only the size but also the shape of the products, however, the choice of surfactant remains empirical in most of the cases. Oleic acid is the most used surfactant in iron oxide nanoparticles synthesis based on the decomposition of an organometallic precursor. Nucleation and growth process are affected by the presence of the surfactant molecules in the reaction solution. First, surfactant molecules form a complex with monomer species giving rise to intermediate complexes. As a consequence of that, a delay in the nucleation takes place. Decomposition temperature of that complex increases as the oleic acid concentration also increases. Secondly, the way the surfactant molecules adhere to the surfaces of the growing nuclei is one of the most important parameters influencing crystal growth. Thus, surfactants should allow dynamic solvation, i.e. exchange on and off the crystals so that the surface is accessible for growing, but also should be strong enough to protect for aggregation.

As the boiling point of the solvent increases, the diameter of the iron oxide nanocrystals increases. This is due to the higher reactivity of the iron-complexes in the solvent with higher boiling point.

Magnetic properties of the particles show an important dependence on the particle size. The fact that oleic acid molecules are bonded to the Fe(II) or Fe(III) particle surface forming a coating layer around them has a strong influence in its magnetic behaviour, mainly at low temperature. That is, the presence of oleic acid leads to very high saturation magnetization values independent on the particle size and coercivity values which decrease as the particle size decrease. Saturation magnetization values decrease and coercivity values increase as the particle size is reduced.

It can be concluded that the oleic acid coating is responsible for the reduction in surface oxidation, particle interactions, and surface anisotropy, which seems to be neglected. The main source of magnetic anisotropy in these systems is, therefore, crystal and shape anisotropy due to the irregular shape of the particles (10).

It should be highlighted that, given the amplitude (H) and frequency (f) of an applied alternating magnetic field, the dependence of SAR with size is not necessarily linear for measurements performed over a wide enough size range. Indeed, experimental data in the literature show that, for any given frequency, SAR increases with size to reach a maximum, after which larger particles exhibit less heat dissipation efficiency. The particle size at which maximum SAR is attained increases with the amplitude of the magnetic field. Closely related with the issue of size is that of size distribution, which must be considered in order to explain hyperthermia results. Its influence on the calorific power is two-fold:
1) Samples with broad size distributions have many particles with different sizes and, consequently potentially different efficiencies for heat dissipation as discussed above, and
2) MNPs with non-similar sizes may have distinct saturation magnetization values and anisotropies, also affecting the calorific power. So, a polydispersed sample will have in general a reduced maximum SAR value but may produce calorific output over a broader frequency range. However, monodispersed samples will have enhanced SAR values but only at the right frequency.
For particles of similar average size, the SAR value significantly increases, as does the MS value when the size distribution becomes narrower.
MNP shape affects magnetic and magneto-thermal properties through its influence on the saturation magnetization and magnetic anisotropy. Spherical particles have a higher number

of defects at the surface than cubic particles, which affect both properties: saturation magnetization and magnetic anisotropy. The saturation magnetization was found to be higher for nanocubes than for nanospheres of the same volume (14).

The effect of polydispersity on the heat generation, as well as on the magnetic properties in general, is an open question. Rosensweig, and Hergt and Dutz claim that polydispersity in the size distribution of the magnetic nanoparticles will degrade the heat production of a magnetic nanoparticle system. For given field and frequency, the most heat will be generated for a specific combination of parameters (e.g. size and anisotropy). Particles away from this optimal combination will generate less (or no) heat, thereby reducing the average heat production. However, strong interactions may mitigate this effect. In the latter case, once one nanoparticle reverses, the local field it produces may be large enough to switch its neighbors, resulting in a cascade effect. Therefore, while the majority of the magnetic nanoparticles are not optimized for the field amplitude and frequency, the particles that are optimized may drive the remaining particles to produce more heat than they would by themselves. In either case, the end result is that polydispersity will, of course, produce a distribution of the heat generated per particle corresponding to the distribution(s) in the relevant magnetic properties (15).

The table 2 shows a recompilation of the results obtained by DLS, VSM and DM100 and they will be described below.

| | **Polidispersity** | **Hydrodynamic size (nm)** | **Magnetic moment (emu/g)** | **SPA (W/g)** |
|---|---|---|---|---|
| **Ni-01** | 0,172 | 43,2(w)/226(hexane) | ~ 200 | √ Water |
| **Ni-08** | 0,183 | 64,4(w)/6(hexane) | ~30 | √ Water |
| **Co-05** | 0,173 | 14,4(w)/7,1(hexane) | ~50 | √ Hexane |
| **HK-20** | 0,280 | 75,1(w)/374(hexane) | ~30 | - |
| **HK-24** | 0,316 | 21(w)/190(hexane) | ~70 | √ Hexane |
| **HK-25** | 0,062 | 33,7(w)/340(hexane) | ~50 | - |

Table 2. Summary table of DLS, VSM and DM100 Series

Regarding dynamic light scattering study, it is important to take into account that polidispersity and hydrodynamic size values can be considered as corrects if all the parameters accomplish the requirements: average count rate (between 400-500 kcps) and baseline index (~9). In this line, only nickel ferrites (Ni-01 and Ni-08) and magnetites (HK-20 in water and HK-25) offer nice results. With the exception of HK-25, that result in monodisperse particles, the rest are polidisperse particles. The hydrodynamic size values of these samples seem coherent, even though in some cases the particles tend to form aggregates, like Ni-01 and HK-25 in hexane. According to vibrating sample magnetometer results, the whole of particles exhibit good magnetic moments (between 30 and 70 emu/g). The highest magnetization value is represented by Ni-01 (approximately 200 emu/g), possibly due to its big size. The best response as a heating agent (SPA values) is carried out by Ni-08 in water, with maxims about 700 W/g. The optimum size of them (10-15nm), the narrow size distribution and the absence of surfactants in the synthesis route may be the most important reasons. However, the efficiency decreases in hexane medium, as occurs with Ni-01 particles, even though water is denser than hexane. Cobalt ferrites (Co-05) offer better results in hexane (maxims about 200-240 W/g) and the unique magnetite particles that display positive values are HK-24 (low heating response with maxims about 50 W/g), due to the same reasons of small size and size distribution.

# CONCLUSIONS

In order to obtain stable monodisperse magnetic nanoparticles able to act as heating agents, it is important to know the following concepts:

- Mean particle size, shape and distribution can be modified by adjusting experimental parameters such as the nature of the iron precursor, the nature of the stabilisers, concentration of reagents and temperature ramp (nucleation and growth steps).

- Organic surfactants have a key role in determining not only the size but also the shape of the products. Nucleation and growth process are also affected by the presence of the surfactant molecules.

- The choice of the solvent or solvents affects the boiling point of the reaction: as the boiling point of the solvent increases, the diameter of the iron oxide nanocrystals increases.

- Magnetic properties of the particles show an important dependence on the particle size and the size distribution.

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