MAGNETIC CORE-SHELL NANOSYSTEMS FOR MAGNETO-RESONANCE IMAGING

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Magnetic nanoparticles

In nanomedicine the magnetic nanoparticles provide unprecedented levels of new functionality. For example, by manipulating magnetic nanoparticles with external field gradients, applications can be opened up in guided transport/delivery of drugs and genes., as well as immobilization and separation of magnetically tagged biological entities.

For these applications, the particles must have combined properties of high magnetic saturation, biocompatibility and interactive functions at the surface. The particles with these functionalities can be considered magnetic nanosystems.

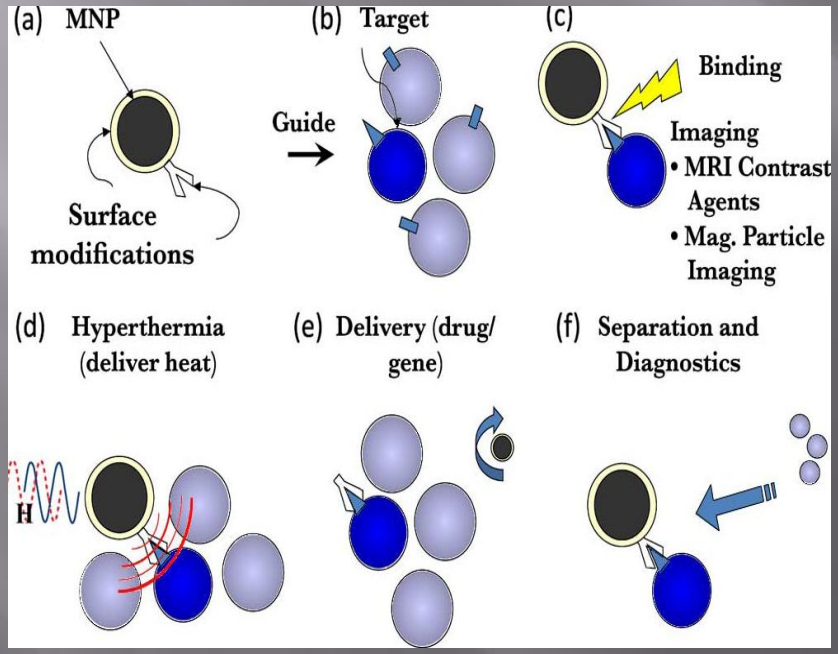

Fig. 1. Magnetic nanoparticles in nanomedicine. (a) Prior to use, the surface of the magnetic nanoparticles must be modified to provide both biocompatibility and functionality (specific binding and targeting moieties).
(b) They can then be guided to the targeting location either using tailored magnetic field gradients or by injecting into the appropriate vasculature.
(c) After localization at the target, the magnetic properties of the particles provide novel functionality. This could be as contrast agents for MRI.
(d) The dynamic relaxation of the nanoparticles, when subject to an alternating magnetic field can be used for therapeutics (hyperthermia), imaging (magnetic particle imaging) or diagnostics (biosensing).
(e) The functionalized molecule on the surface could be a drug that can be released in response to external stimuli such as pH, temperature or an alternating magnetic field.
(f) Moving the particles with magnetic field gradients allows for magnetic targeting, delivery and *in vitro* separations and diagnostics.

Magnetic nanoparticles

There are two limits to magnetic behavior of materials as a function of size and dimensionality. At one end of the spectrum (bulk) the microstructure determines the magnetic (hard and soft) behavior. At the other end, as the length scales approach the size of domain wall-widths (nanostructures), lateral confinement (shape and size) and inter-particle exchange effects dominate, until finally, at atomic dimensions quantum-mechanical tunneling effects are expected to predominate [10].As a first approximation of this characteristic size, one can set the simple magnetization reversal energy equal to the thermal energy, i.e., at room temperature, and for typical ferromagnets obtain a size 5–10 nm, below which ferromagnetic behavior gives way to superparamagnetism (Fig. 2(a)). In real materials, changes in magnetization direction occur via activation over an energy barrier and associated with each type of energy barrier is a different physical characteristic. These characteristics are the crystalline anisotropy, the magnetostatic force and the applied field.

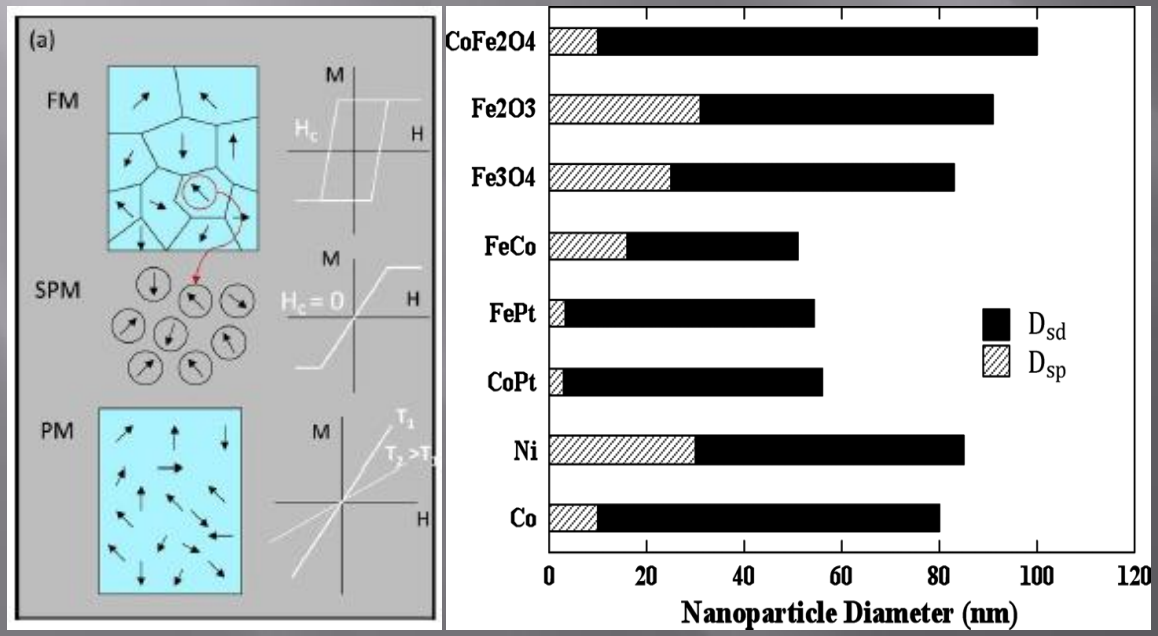

Fig. 2. (a) Materials show a wide range of magnetic behavior. The non-interacting spins in paramagnetic materials (bottom) characterized by a linear susceptibility that is inversely dependent on the temperature (Curie law). The ferromagnetic materials (top), characterized by exchange interaction, hysteretic behavior and a finite coercivity, HC. If reduce the size of the ferromagnetic material to ultimately reach a size where thermal energy (*kB*T=4x10-21 J, at 300 K) can randomize the magnetization, such that when there is no externally applied field the magnetization measured in a finite time interval (typically, 100 s) is zero. Such nanoparticles show no coercivity and behave as paramagnets with a large moment, or as superparamagnets. (b) On the nanometer scale magnetic materials, at a given temperature, show distinctly different behavior as a function of size. Critical sizes for the observation of superparamagnetism is Dsp and for single-domain is Dsd [13].

Obtaining of nanosystems

Preparation of magnetic nanoparticles

The technique of microemulsion acting as "nanoreactor" inside which salt reduction and particle growth occurs, has allowed to obtain monodisperse particles which may display a define shape. For the dispersion and to prevent aggregation in other reducing methods are used typical ligands or capping agents like: sodium citrate, polymers, long chain thiols or amines [19, 20, 21].

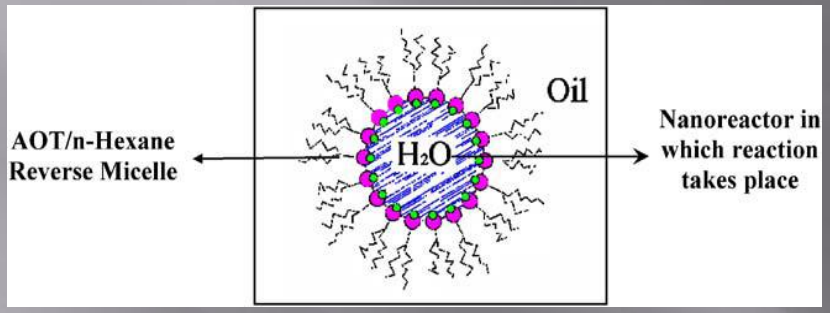

Fig. 3. Structure of reverse micelles formed by dissolving AOT, a surfactant, in n-hexane. The inner core of the reverse micelle is hydrophilic and can dissolve water-soluble compounds. The size of these inner aqueous droplets can be modulated by controlling the parameter Wo (Wo ¼ [water]/[surfactant]).

In our work, the magnetic particles have been obtained by co-reducing of the metallic salts using microemulsion technique and dispersion in a capping agent. The preparation of cobalt nanoparticles has made using cobalt nitrate hexahydrate, in concentration 0.01M – 0.02 M dissolved in 10 ml of sodium bis (2-ethylphenyl) sulfosuccinat / toluene solution. The particles of cobalt-nickel alloy with the composition $Co_{0.9}Ni_{0.1}$ have been obtained by boiling in reflux of an ethylene glycol solution of cobalt and nickel acetates, dissolved in 10 ml of ethylene glycol, refluxed with continuous stirring. At the end of the reaction, the particles were precipitated by adding 20 ml water and isolated by centrifugation. Combinations of myristic acid (MA), oleic acid (OA) were used for coating magnetic nanoparticles in order to be dispersed in water.

Synthesis of magnetite nanosystem

The strategies developed for the synthesis of c*ore-shell structures* in homogenous solution can be generalized by separating the stages of particle nucleation from its subsequent growth.

The particles of magnetite were prepared by boiling in reflux of a mixture formed by γ-Fe_2O_3 and Fe(II) salt . An aqueous solution of γ- Fe_2O_3 and FeC_2O_4 (2 Fe_2O_3: 1 FeC_2O_4 molar ratio) was boiled, 100^oC, in reflux for two hours with vigorous stirring. From the magnetite particles of we prepared a core-shell nanosystem: magnetite-PVP-saccharide. The synthesis of magnetite nanosystem is described elsewhere [22].

Results and disscusion

Magnetic NiCo nanoparticles (Fig. 4) have soft ferromagnetic behavior, with saturation magnetization: 60 emu/g at relative high magnetic field (H_S) of 3000 Oe. Fig. 5 shows the hysteresis loop of Co nanoparticles. This sample has small ferromagnetic behavior at room temperature: saturation magnetization of 0.6 emu/g, saturation magnetic field (H_S) of 4500 Oe and the coercivity (H_c) is 50 Oe. Magnetic behavior of Co particles sample suggest that cobalt particles are covered with cobalt oxide.

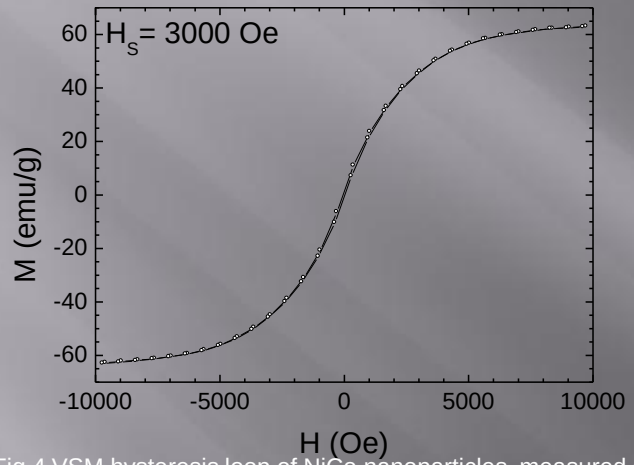

Fig.4 VSM hysteresis loop of NiCo nanoparticles, measured at room temperature.

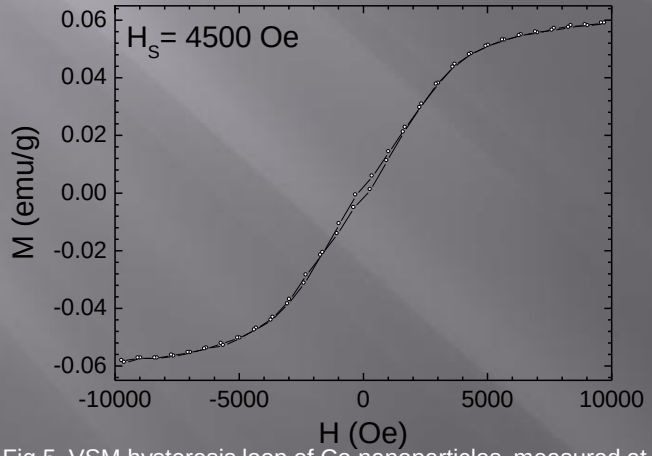

Fig.5. VSM hysteresis loop of Co nanoparticles, measured at room temperature.

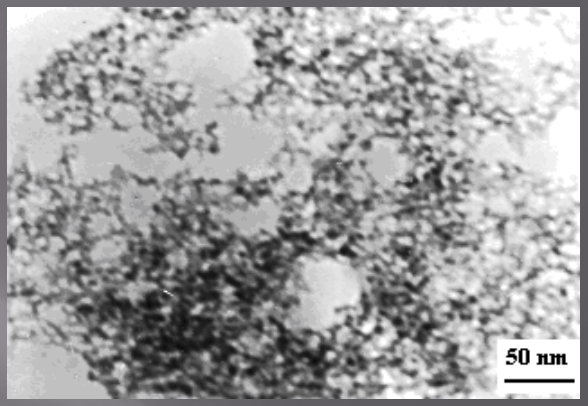

Fig. 7 TEM image of sample NiCo nanoparticles, the average size of 5-10 nm

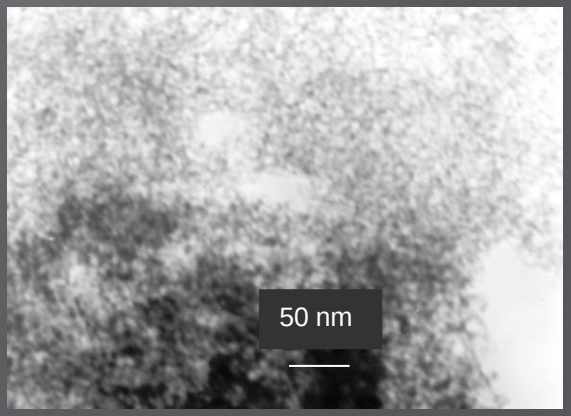

Fig. 8 TEM image of Co nanoparticles, the average size of 2-5 nm

Results and disscusion

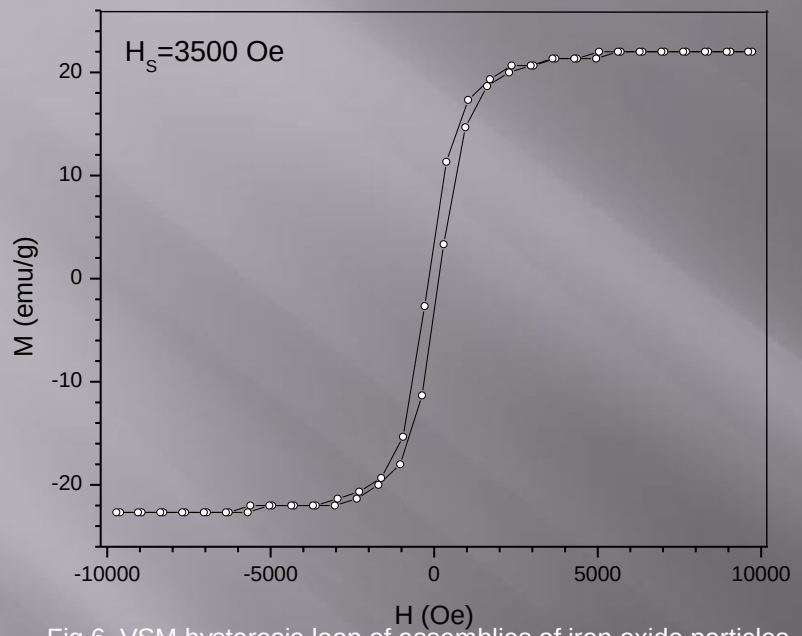

Fig.6. VSM hysteresis loop of assemblies of iron oxide particles, measured at room temperature

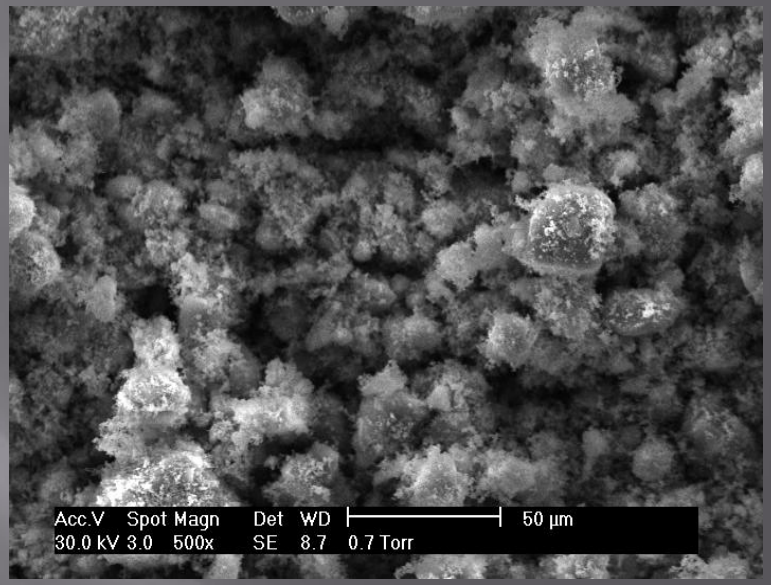

Fig.9 SEM image of Fe_3O_4 particles assemblies, the average sizes of 100-200 nm

Figure 6 shows the hysteresis loop of magnetite nanoparticles assemblies. This sample has ferromagnetic behavior: saturation magnetization of 20 emu/g , saturation magnetic field (H S) of 3500 Oe, the coercivity (Hc) of 100 Oe. Magnetic behavior of Fe3O4 nanoparticles suggest that assemblies of magnetic multi-domains are formed. Electronic microscopy reveals spheroidal morphology of magnetite particles.

Results and disscusion

Figure 10 shows our model of „magnetite-biocompatibil polymer (PVP)-saccharide nanosystem". Superparamagnetic iron oxide **, magnetite**, is strong enhancers of proton relaxation. **Polyvinylpyrrolidone (PVP)** enhances the blood circulation time and stabilizes the colloidal solution. Saccharide: **2-Deoxy-D-glucose** is a glucose molecule which has the 2-hydroxyl group replaced by hydrogen, so that it cannot undergo further glycolysis. This substance traps in most cells so that it makes a good marker for tissue glucose use and hexokinase activity. Many cancers have elevated glucose uptake and hexokinase levels. 2 deoxy-D-glucose is used as „vehicle" to target the malignant cells.

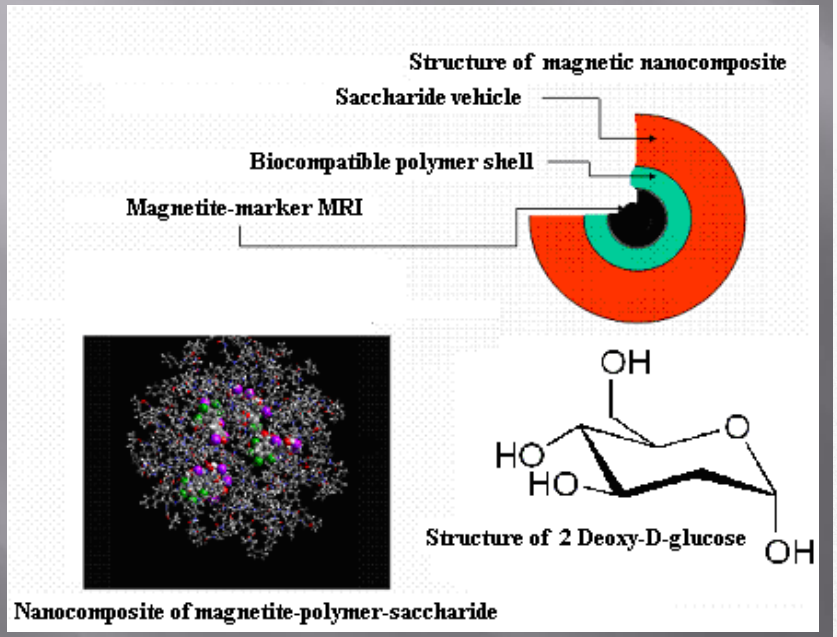

Fig. 10 Model of magnetite- polymer (PVP)-saccharide nanocomposite

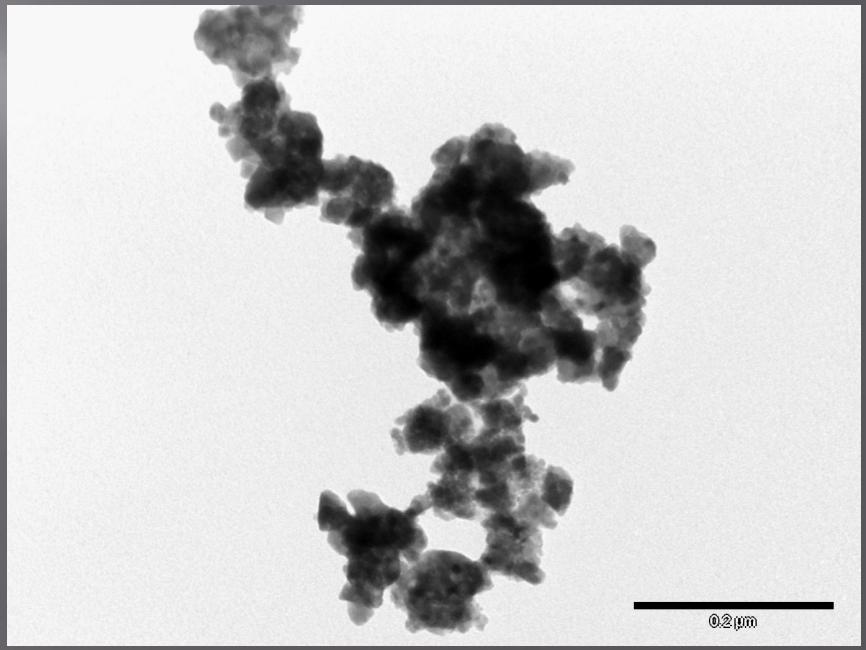

Fig. 11 TEM image of magnetite- (PVP)-2 Deoxy Dglucose.
The sizes of nanoparticles are 2-10nm.

Conclusions

- All biomedical applications of magnetic nanoparticles arise from the combination of their magnetic properties with biological relationships and phenomena. Naturally, the convergence of these two areas is most pronounced at the surface of the magnetic nanoparticle where it interfaces with its biological environment. By manipulating the nanoparticle surface it is possible to induce a wide range of biological responses, and the importance of the surface functionalization of the magnetic nanoparticles, especially for *in vivo* biomedical applications.
- Soft chemical methods are versatile techniques that can be used to prepare and organise any type of magnetic particles. The magnetic properties of magnetic nanoparticles have good quality for diagnostic tools and targeting treatment in cancer. Magnetic properties obtained for NiCo nanoparticles and for magnetite core-shell nanosystem answer to magnetic field strengths required to manipulate nanoparticles have no deleterious impact on biological tissue. NiCo nanoparticles have a magnetic behavior that magnetizing strongly under an applied field, but retaining no permanent magnetism once the field is removed.
- The synthesis [22] and properties obtained for magnetic core-shell nanosystem: *magnetite- (PVP)-2 Deoxy-D-glucose* achieved one's end to find a biomedical imaging method unradioctive for diagnosis of malignant cells. The classical Positron Emission Tomography (PET) used high energy γ-rays radiation.

	Radiation Used	Spatial Resolution	Temporal Resolution	Sensitivity	Quality of contrast agent used	Comments
Positron Emission Tomography (PET)	high energy γ-rays	1-2 mm	10 sec to minutes	10^{-11}-10^{-12} Mole/L	Nanograms	Sensitive, Quantitative, Needs cyclotron
Magnetic Particle Imaging (MPI)	Radiowaves	200-500 μm	Seconds to minutes	10^{-11}-10^{-12} Mole/L	Nanograms	Good sensitivity, Quantitative, Fast, Good resolution, No tissue contrast.

ACKNOWLEDGMENT

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