Magnetic studies of polylactic-*co*-glicolic acid nanocapsules loaded with selol and γ-Fe_2O_3 nanoparticles

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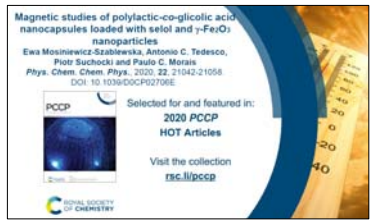


Motivation

Polylactic-co-glicolic acid (PLGA), maghemite (γ-Fe_2O_3) nanoparticles and selol (Se^{4+} – based anticancer drug) were used to fabricate selol-loaded PLGA magnetic nanocapsules in order to use them as a potential magnetic drug delivery system for cancer therapy.

In vitro antitumor activity of the nanocapsules was evidenced using neoplastic murine melanoma (B16-F10), oral squamous carcinoma (OSCC), pulmonary adenocarcinoma (A549), murine (4T1) and human (MCF-7) breast cell lines. Further exposure of these cell lines to an alternating magnetic field increased the antitumor effect of the nanocapsules. Moreover, the nanocapsules presented the antitumor effect while not affecting normal cells. The association of the nanocapsule's surface with folic acid increased its cell uptake (by specific tumors cell receptors) and toxicity against cancer cells. Additionally, nanocapsules with the shell conjugated to doxorubicin showed a significantly increased cytotoxicity against breast adenocarcinoma (4T1) cells which is suggestive of additive or synergic effect of selol and doxorubicin.

The nanocapsules show also unique magnetic properties presented here.

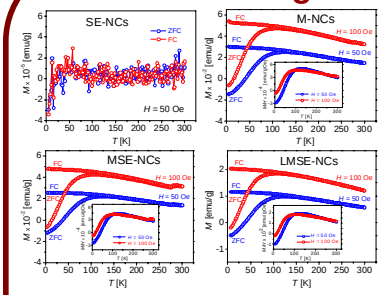
Experimental details

All magnetic measurements were performed on the PLGA-based nanocapsules containing selol only (SE-NCs sample), maghemite nanoparticles only (M-NCs sample) or maghemite nanoparticles and selol before (MSE-NCs sample) and after lyophilization (LMSE-NCs sample).

Dc magnetization and ac magnetic susceptibility data were collected using a Quantum Design PPMS extraction magnetometer in a wide temperature range (4 – 300 K).

ESR spectra were collected by means of a standard X-band spectrometer (Bruker EMX – 10/12) operating around 9.46 GHz with 100 kHz field modulation.

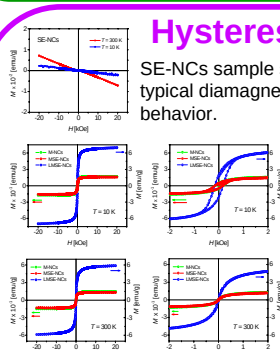
ZFC-FC magnetization measurements



SE-NCs sample shows a diamagnetic behavior. M-NCs, MSE-NCs and LMSE-NCs samples show a superparamagnetic behavior, i.e. the splitting of the ZFC and FC curves below the irreversibility temperature T_{irr} = 150 K and a well-defined maximum in the ZFC curve at the blocking temperature T_B = 126 K. The maximum of the ZFC curve is very broad and a clear Curie-Weiss law behavior is not observed above T_B. This indicates the existence of non-negligible magnetic dipole-dipole interaction among maghemite nanoparticles.

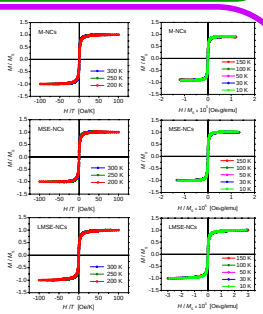
Increasing H leads to a shift of the ZFC peak to lower temperatures, accompanied by a slight decrease in magnitude of the dc susceptibility (see insets in figures), whereas for non-interacting superparamagnetic particles the magnitude should be field independent. Below T_{irr}, the FC curve splits from the ZFC curve and increases very slowly with decreasing temperature, not following the Curie-Weiss law, which also reveals the presence of a non-negligible dipole-dipole interaction among the maghemite nanoparticles.

Hysteresis curves



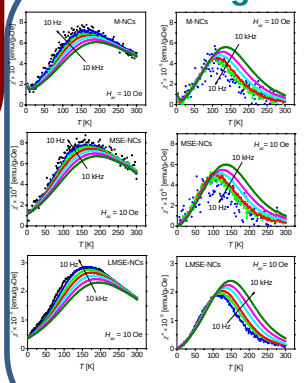
SE-NCs sample shows typical diamagnetic behavior.

M-NCs, MSE-NCs and LMSE-NCs samples show superparamagnetic behavior, meaning no hysteresis above the blocking temperature T_B.



Classical superparamagnetic scaling (the M/M_S versus H/T) holds for 200 K < T < 300 K. At T < 200 K M/M_S scales with H/M_S. This indicates the gradual emergence of the interacting superparamagnetic regime of magnetic nanoparticle systems.

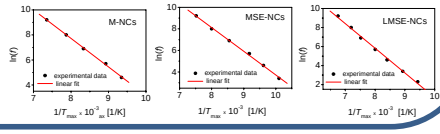
Ac magnetic susceptibility



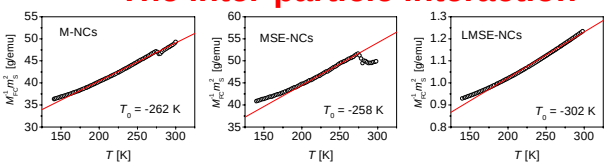
The real component $\chi'(T)$ and the imaginary component $\chi''(T)$ of the ac magnetic susceptibility exhibit the expected behavior of a superparamagnetic system, i.e. the occurrence of a maximum in both components $\chi'(T)$ and $\chi''(T)$ which shifts towards higher temperatures with increasing frequency f. Both $\chi'(T)$ and $\chi''(T)$ maxima follow the predictions of thermally activated Néel-Arrhenius model:

$$f = f_0 \exp(-E_a/k_B T)$$

where f_0 is an attempt frequency in the range of 10^9 – 10^{11} Hz for superparamagnetic systems, k_B is the Boltzmann constant and E_a is the magnetic anisotropy energy barrier



The inter-particle interaction



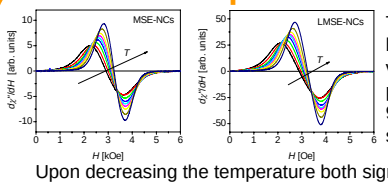
For an assembly of interacting superparamagnetic particles, the low field susceptibility is expected to be of the form:

$$\chi \sim \frac{\mu_{mean}^2}{3k_B(T - T_0)}$$

where μ_{mean} is the mean magnetic moment per particle, k_B is the Boltzman constant and T_0 is the effective temperature that is usually interpreted as a measure of the strength of the inter-particle interaction in the system. In accordance with this equation, the reciprocal of the FC susceptibility shows a linear behavior well above T_B when it is multiplied by $m_S^2(T) = M_S^2(T)/M_S^2(0)$ in order to correct for the temperature dependence of μ_{mean}.

The value of T_0 is found to be –(262 ± 10) K, –(258 ± 10) K and –(302 ± 10) K for the M-NCs, MSE-NCs and LMSE-NCs samples, respectively. This fact further supports the existence of strong dipolar inter-particle interaction with demagnetizing character.

Electron spin resonance (ESR) spectra



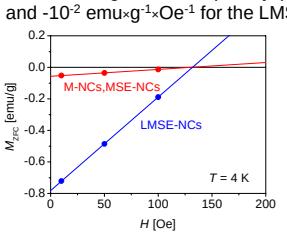
The room temperature spectra show single broad signals with an effective gyromagnetic value of about g = 2.07 and 2.06 and the peak-to-peak line width ΔH_{pp} = 792 Oe and 985 Oe for the MSE-NCs and LMSE-NCs samples, respectively.

Upon decreasing the temperature both signals shift to lower fields and gradually broaden, closely following the predictions for the ESR of superparamagnetic nanoparticles systems.

The peak-to-peak line widths considerably exceed the magnetocrystalline-anisotropy-determined minimum value, ΔH_{pp} = 400 Oe, for non-interacting single domain maghemite nanoparticles. It confirms the existence of non-negligible dipole-dipole interaction among the maghemite nanoparticles.

Giant diamagnetism at low temperatures

The initial ZFC magnetization starts with significant negative value and increases monotonically upon heating the sample up to the compensation temperature at which the magnetization direction flips positive. Even compared with usual superconductors, the order of the diamagnetic susceptibility (-10^{-3} emu×g^{-1}×Oe^{-1} for the M-NCs and MSE-NCs samples and -10^{-2} emu×g^{-1}×Oe^{-1} for the LMSE-NCs sample) is quite remarkable.



The negative magnetization decreases with increasing H and finally disappears around H = 122 Oe and 133 Oe for the M-NCs plus MSE-NCs samples and for the LMSE-NCs sample, respectively.

The giant diamagnetism can be attributed to the antiferromagnetic dipolar interaction among maghemite nanoparticles which acts like an additional internal field H_i opposite to the applied field H and hinders the response of the magnetic moments to the H field.

By slightly increasing H, the magnetization becomes zero exactly at H opposite and equal in magnitude to H_i. Hence, the value of H_i, giving a direct quantitative information about the strength of dipolar interaction among nanoparticles, can be assumed as equal to H requested for compensating the initial negative magnetization induced by the ZFC procedure.

Conclusions:

- The nanocapsules present a perfect superparamagnetic behavior at T > 200 K.
- At T< 200 K the superparamagnetic scaling is no longer observed and the nanocapsules behave as interacting superparamagnetic material.
- At low temperatures the nanocapsules show giant diamagnetism, which has not been observed earlier in this type of materials.
- The nanocapsules contain chain-like magnetic aglomerates coupled by antiferromagnetic dipolar interaction which is responsible for the magnetic behavior of the nanocapsules.
- The nanocapsules can be a new promising magnetic drug delivery system and magnetic hyperthemia inductor in antitumor therapy.
- The magnetic studies of the nanocapsules are of considerable interest also for the development of new hybrid nanomaterials showing giant diamagnetism at low temperatures.