U.P.B. Sci. Bull., Series B, Vol. 79, Iss. 3, 2017 ISSN 1454-2331

MESOPOROUS FERRITES OBTAINED IN THE PRESENCE OF PLURONIC COPOLYMER FOR POTENTIAL BIOMEDICAL APPLICATIONS

Doina GEORGESCU[1], Cristian MATEI[2], Nicolae STANICA[3],
Daniela BERGER[4]*

The mesoporous magnetite and cobalt ferrite nanopowders were synthesized by coprecipitation method in the presence of Pluronic P123 copolymer at room temperature and 60 °C, respectively. The synthesized ferrite nanopowders were characterized by X-ray diffraction, N_2 adsorption-desorption isotherms, FT-IR spectroscopy, scanning and transmission electron microscopy, as well as magnetic measurements. Magnetite and cobalt ferrite presented spinel structure with cubic symmetry as XRD patterns showed and the nitrogen adsorption-desorption isotherms of both spinel ferrites are characteristic for mesoporous materials. The FTIR spectra of prepared oxide nanopowders evidenced that Pluronic copolymer did not interact strongly with ferrites surface being removed during the samples washing step. The magnetite sample exhibited a superparamagnetic behavior, whilst cobalt ferrite presented ferrimagnetic properties.

Keywords: magnetite; cobalt ferrite; mesoporous materials; magnetic properties

1. Introduction

Although the saturation magnetization of ferrites with spinel structure, MFe_2O_4 (M=Fe, Co, Mn, Zn), is lower than of ferromagnetic alloys, they have several advantages because of their higher corrosion resistance and possibility to be applied at higher frequencies. Ferrites with spinel structure have many applications in biomedicine [1-4], magnetic separation in molecular biology[5], catalysis, especially in wastewaters treatment[6-8] etc.

For biomedical applications are required ferrite nanoparticles (NPs) with narrow size distribution, high magnetization values, uniform shape and

---

[1] PhD Student, Dept. of Inorganic Chemistry, Physical Chemistry and Electrochemistry, University POLITEHNICA of Bucharest, Romania

[2] Prof., Dept. of Inorganic Chemistry, Physical Chemistry and Electrochemistry, University POLITEHNICA of Bucharest, Romania, e-mail: cristi_matei@yahoo.com

[3] PhD, Romanian Academy, Institute of Physical-Chemistry “Ilie Murgulescu”, Bucharest, Romania

[4] Prof., Dept. of Inorganic Chemistry, Physical Chemistry and Electrochemistry, University POLITEHNICA of Bucharest, Romania, * corresponding author, e-mail: danaberger01@yahoo.com

superparamagnetic behavior at room temperature. Another condition for ferrite NPs is their biocompatibility and in this regard, many research efforts were focused to study *in vitro* cytocompatibility and *in vivo* toxicity of different ferrite NPs demonstrating their dose-dependent toxicity. Only superparamagnetic iron oxides (magnetite, Fe_3O_4 and maghemite, γ-Fe_2O_3) are clinically approved as magnetic NPs. However, it was found that the particle size influences their toxicity and safe employment in biomedical applications. Superparamagnetic iron oxide nanoparticles (SPION), which have the hydrodynamic diameter between 10 and 100 nm are considered optimal for intravenous administration, while particles higher than 200 nm or smaller than 10 nm are sequestered by the spleen or kidney[9].

Among biomedical applications of ferrite with spinel structure, a lot of interest presents the hyperthermia treatment of cancer based on superparamagnetic or ferrimagnetic nanoparticles with high heating ability and Curie temperature in the range of 42 °-60 °C. The treatment of tumors by hyperthermia is based on the higher resistance to temperature of the healthy cells than the tumor ones, being possible to selectively kill the tumor cells by increasing temperature. Pradhan et al. [10] reported that $MnFe_2O_4$ and Fe_3O_4 ferrofluids containing lauric acid and magnetic NPs of 9-11 nm diameter exhibiting good heating ability could be used for hyperthermia applications, while $CoFe_2O_4$ based on the measured specific absorption rate value and its higher toxicity at a dose of 0.2 mg/mL both *in vitro* and *in vivo* was considered inappropriate for this kind of biomedical application. However, Sabale et al. [11] reported a very low toxicity on A549 (human adenocarcinoma lung cancer) cell line of $CoFe_2O_4$ NPs with 4 nm diameter, obtained by polyol method. Based on their superparamagnetic properties, $CoFe_2O_4$ and $ZnFe_2O_4$ NPs are able to reach the threshold hyperthermia temperature and could be applied for the treatment of tumor cells by hyperthermia.

Nanosized ferrite particles can also be applied as contrast agents in magnetic resonance imaging (MRI), one of the most powerful imaging technologies due to its noninvasive character and multidimensional tomographic capabilities. Yang et al. suggested that tetraethylene-stabilized manganese ferrite nanoparticles could be used as MRI contrast agents for liver imaging because they were preferentially accumulated in the liver after 4h from intravenous injection. [12]

Spinel ferrite NPs can be applied in angiogenesis process which consists in the formation of new blood vessels from preexisting ones, being involved in wound–healing process and tumor growth. Among amine-functionalized MFe_2O_4 (M=Ni, Co, Mn) NPs that all exhibited an improvement of angiogenesis, the best results being obtained for $CoFe_2O_4$ NPs. [13] $CoFe_2O_4$ could also be applied in magnetic separation, being able to bind DNA molecules with 59% efficiency, at pH=8.5 in Tris-HCl buffer. [5]

Among ferrites, $CoFe_2O_4$, a hard magnetic material has a high coercivity (about 4.3 kOe) at room temperature for the 40 nm size single domains and higher anisotropy constant ($K_1=19\cdot10^{-5}$ erg/cm^3) than Fe_3O_4 ($K_1=-1.2\cdot10^{-5}$ erg/cm^3). [15]

Here, we report the properties of mesoporous magnetite and cobalt ferrite nanoparticles obtained by coprecipitation method at low temperature. As either stabilizing agent or mesopores generator was chosen the triblock copolymer Pluronic P123, which is a pharmaceutical excipient listed in the British Pharmacopoeia, being used in various pharmaceutical formulations. [16]

2. Experimental

2.1. Materials

Poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) (Pluronic P123, average MW 5800, Sigma), ammonia solution 25% (Scharlau), iron (II) sulfate heptahydrate (≥ 99%, Sigma-Aldrich), cobalt chloride hexahydrate (≥ 98%, Sigma-Aldrich) and iron (III) chloride hexahydrate (≥ 97%, Sigma-Aldrich) and sodium hydroxide (≥ 98% anhydrous, Sigma-Aldrich) were used as received.

2.2. Synthesis of spinel ferrite nanopowders

Fe_3O_4 and $CoFe_2O_4$ nanopowders were synthesized in the presence of triblock copolymer Pluronic P123 as capping agent, by co-precipitation method. In a solution containing 0.1875 g Pluronic P123 g in 30 mL 1:1 (vol) water : ethanol mixture, 4.9819 g iron (III) chloride and 2.5668 g iron (II) sulfate were dissolved under magnetic stirring, at 40 °C and argon atmosphere. After 1 h, 20 mL of 25% (wt.) aqueous ammonia solution were poured into the solution containing iron ions under inert atmosphere to avoid the oxidation of Fe^{2+} ions and the formation of maghemite as secondary phase. The reaction mixture was mechanical stirred for 1 h, at 40 °C and the resulted black solid was recovered and washed with water and ethanol by magnetic decantation. Cobalt ferrite was obtained similarly by using cobalt chloride (2.1968 g) and 10 mL 10 M aqueous solution NaOH as precipitating agent instead of iron (II) sulfate and ammonia solution, respectively. In the case of cobalt ferrite, a longer ageing step at 60°C for 20 h was necessary to obtain crystalline oxide powder.

2.3. Materials characterization

X-ray powder diffraction (XRD) analyses were performed on a Rigaku Miniflex II diffractometer, equipped with CuKα radiation in 2θ range of 10°-70°, a scanning rate of 1°/min and 0.02°/step. FTIR spectra were recorded on Bruker Tensor 27 spectrometer (KBr pellets technique). In order to determine the textural parameters of spinel ferrite nanopowders, the nitrogen adsorption-desorption isotherms were carried out at 77K on a Quantachrome Autosorb iQ_2 gas physisorption analyzer. Scanning and transmission electron microscopy (SEM and TEM) performed on a Tescan Vega 3 LMH microscope coupled with EDX spectrofotometer and a FEI Tecnai G2-F30 high resolution electron transmission microscope equipped with a field emission electron gun and a maximum accelerating voltage 300 kV were used to investigate the morphology of ferrite nanomaterials. The magnetic properties were measured at room temperature recording the magnetization function of applied magnetic field, in the range of -10000÷10000 G on a LakeShore 7404 vibrating sample magnetometer.

3. Results and discussion

The oxide nanopowders obtained by coprecipitation method in the presence of triblock copolymer Pluronic P123 were analysed by XRD, FTIR spectroscopy, N_2 adsorption-desorption isotherms and magnetic measurements recorded at room temperature.

Both magnetite and cobalt ferrite powders synthesized by coprecipitation method and capped in Pluronic P123 present inverse spinel structure with cubic symmetry demonstrated by powder X-ray diffraction analysis (Fig. 1). The mgnetite sample and cobalt ferrite nanopowder were indexed according ICDD 79-0418 and ICDD 22-1086, respectively. The unit cell parameter of magnetite was 70.137 Å, while for $CoFe_2O_4$, a lower value was obtained, 69.813 Å. The crystallite size was computed using Rigaku PDXL software based on Sherrer's equation from all diffraction peaks. The crystallite size was smaller for magnetite (9 nm) than for $CoFe_2O_4$ (12 nm).

The oxide nanopowders were also investigated by FTIR spectroscopy in order to assess the formation of inverse spinel structure characteristic for ferrites and the interactions between oxide nanoparticles and the polymer used as capping agent. The characteristic stretching vibrations of Fe-O bonds in FTIR spectrum of Fe_3O_4 nanopowder can be noticed at 450, 580 and 630 cm^{-1} (Fig. 2, black curve) and correspond to Fe(II)-O and Fe(III)-O bonds in both octahedral and tetrahedral geometries. [16-18] The polymer bands are hardly visible in the FTIR spectrum of Fe_3O_4. In the FTIR spectrum of $CoFe_2O_4$ sample (Fig. 2, red curve), besides the band at 580 cm^{-1} corresponds to the stretching vibration mode of Fe-O bond in tetrahedral geometry, characteristic for ferrite with inverse spinel structure, other weak bands are noticed at: 1390 cm^{-1} attributed to C-C stretching vibrations, 1090 cm^{-1} assigned to Fe-O-C bonds and 980 cm^{-1} corresponding to methylene rocking deformation band, which confirm the presence of the capping agent on cobalt ferrite NPs surface. Both ferrite nanopowders present the characteristic deformation band of adsorbed water at 1650 cm^{-1} and the O-H stretching vibrations in 3200 -3600 cm^{-1} range characteristic for surface hydroxyl groups associated by hydrogen bonding. These two bands are more intense in the case of cobalt ferrite sample that could be explained by the additional contribution of Pluronic P123 groups as result of stronger interaction of $CoFe_2O_4$ NPs with Pluronic P123 than in the case of Fe_3O_4.

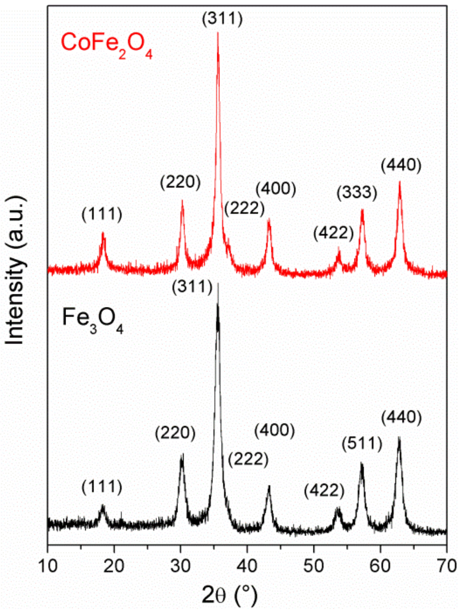

Fig. 1. XRD patterns of synthesized magnetite and cobalt ferrite nanopowders

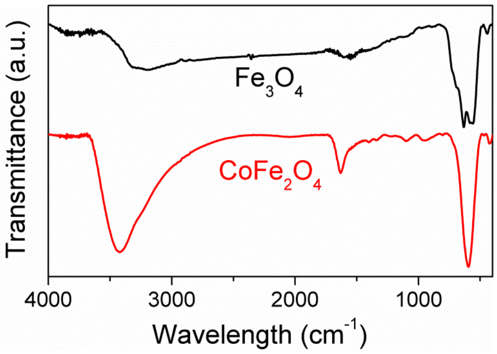

Fig. 2. FTIR spectra of Fe_3O_4 and $CoFe_2O_4$ samples

The morphology of Fe_3O_4 and $CoFe_2O_4$ samples was investigated by scanning electron microscopy. The samples present similar morphology having nanosized spherical particles, with narrow size distribution having the tendency to form spherical agglomerates (Fig. 3). TEM investigation of $CoFe_2O_4$ nanopowder showed the presence of small particles with the diameter in the range of 8-16 nm. One can notice that the porosity of the sample results due to interparticle pores (Fig. 4).

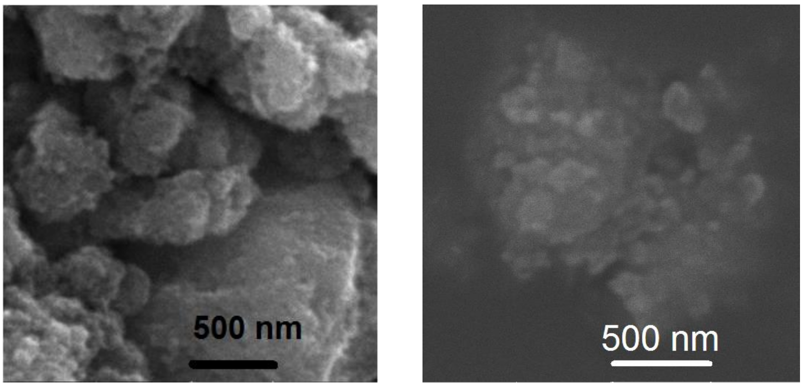

Fig. 3. SEM micrographs of Fe_3O_4 (left) and $CoFe_2O_4$ (right)

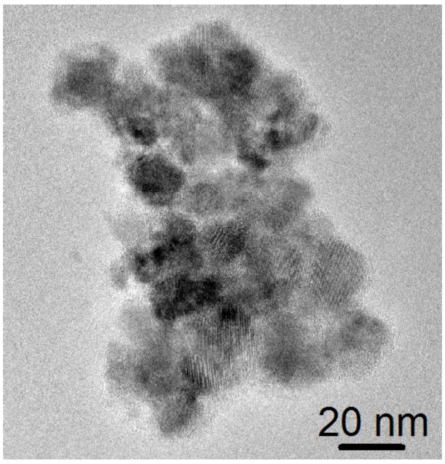

Fig. 4. TEM micrograph of $CoFe_2O_4$ prepared in the presence of P123

The N_2 adsorption-desorption isotherms for both ferrites synthesized in the presence of Pluronic P123 are type IV with H1 hysteresis loop typical for mesoporous materials (Fig. 5). The textural parameters of ferrite samples (specific surface area, S_{BET}, total pore volume, V_{p} and average pore diameter, d_{BJH}) are listed in Table 1. The total pore volumes were determined at relative pressure, P/P_0=0.9900, specific surface area values were computed using Brunauer–

Emmett–Teller (BET) method from multi-point regression in the 0.05-0.30 relative pressure range, while the pore size distribution curves were computed by Barrett-Joyner-Halenda model based on Kelvin equation from the isotherm desorption branch. Both samples exhibited unimodal pore size distribution, lower value of average pore diameter (8.34 nm) being determined for $CoFe_2O_4$ than for magnetite (12.40 nm). Both samples have the pores dimension in the range of mesopores. Also, Fe_3O_4 and $CoFe_2O_4$ have high values of specific surface area (120 and 155 m^2/g, respectively).

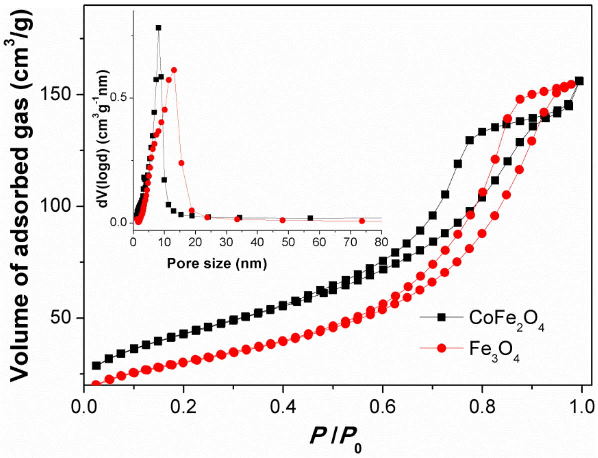

Fig. 5. N_2 adsorption-desorption isotherms of Fe_3O_4 and $CoFe_2O_4$ nanopowders

Table 1

Properties of synthesized spinel ferrites

Sample	**Ms (emu/g)**	**χ_gx10^6 (cm^3/g)**	**Mr/Ms**	**S_{BET} (m^2/g)**	**V_p (cm^3/g)**	**d_{BJH} (nm)**
Fe_3O_4	49.73	970.26	0	108	0.24	11.42
$CoFe_2O_4$	40.01	583.30	0.273	155	0.24	8.34

The magnetic properties of Fe_3O_4 and $CoFe_2O_4$ were studied by measuring magnetization as function of applied magnetic field in the range of -10000 – 10000 Oe. At a given applied magnetic field, the magnetization depends on the magnetic moment, which is influenced by the particle size. The total magnetization is a sum of three components: ferromagnetic (hysteretic magnetization), superparamagnetic (fitted by a Langevin function) and paramagnetic.[19,20] It can be noticed that either magnetite or cobalt ferrite did not reach the saturation magnetization, these values being determined by fitting the experimental data considering the ferromagnetic and paramagnetic contributions for cobalt ferrite that exhibited a ferrimagnetic behavior and the superparamagnetic component for Fe_3O_4. The magnetization loop of magnetite shows zero coercivity and zero remanence proving its superparamagnetic behavior. The saturation magnetization of Fe_3O_4 (49.73 emu/g) is lower than for magnetite obtained similarly by coprecipitation in the presence of trimethylhexadecylammonium bromide (59.70 emu/g).[21] Cobalt ferrite capped in P123 has high coercivity, H_c=468.87 Oe, and a remnant magnetization of 10.93 emu/g, demonstrating a ferrimagnetic behavior (Table 1), its saturation magnetization being 42.47 emu/g, lower value than for cobalt ferrite capped in oleic acid (52.33 emu/g), having the average particle size of 13 nm.[22]

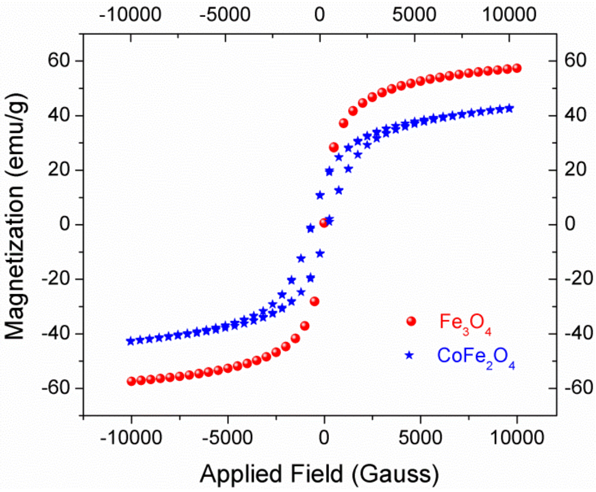

Fig. 5. Magnetization versus applied filed for mesoporous ferrite nanopowders

As expected, the saturation magnetization of magnetite and cobalt ferrite, which is a result of the sum of the unpaired spins of cations, is lower than of the corresponding bulk materials (~95 emu/g[23] and 79 emu/g[24], respectively) demonstrating the nanosize nature of synthesized spinel ferrite particles.

4. Conclusions

Mesoporous magnetite and cobalt ferrite with spinel single phase structure and cubic symmetry were successfully synthesized by coprecipitation method at room temperature and 60 °C, respectively, using Pluronic P123 copolymer as stabilizing agent. N_2 sorption analyses demonstrated the mesoporous nature of synthesized ferrites with an average pore size of 11.42 nm for magnetite and 8.34 nm for cobalt ferrite and high specific surface areas (108 m^2/g in the case of Fe_3O_4 and 155 m^2/g of $CoFe_2O_4$).

FTIR spectroscopy proved that the interactions between triblock copolymer Pluronic P123 and spinel ferrites surface were not strong because the stabilizing agent was almost completely removed during the samples isolation and washing, the polymer role being to form especially interparticle mesopores.

The measurement of magnetization versus applied magnetic field demonstrated a superparamagnetic behavior of magnetite with a saturation magnetization of 49.73 emu/g, while cobalt ferrite exhibited ferrimagnetic properties with a saturation magnetization of 42.47 emu/g, both values being lower than for the bulk materials, which proved their nanosize particles, also noticed by SEM and TEM investigation.

The magnetic properties, porosity and nanosized-particle dimensions of the synthesized spinel ferrites are optimal for biomedical applications.

R E F E R E N C E S

[1] *AK Gupta, M.Gupta* Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications, Biomaterials, **vol. 26**, 2005, pp. 3995-4021.

[2] *J. Dobson*, Magnetic nanoparticles for drug delivery, Drug Development Research, **vol. 67**, 2006, pp. 55-60.

[3] *J. Kim, H. S. Kim, N. Lee, T. Kim, H. Kim, T. Yu, I.C. Song, W.K. Moon, T. Hyeon*, Multifunctional uniform nanoparticles composed of a magnetite nanocrystal core and a mesoporous silica shell for magnetic resonance and fluorescence imaging and for drug delivery, Angew. Chem. Int. Ed., **vol. 47**, 2008, pp. 8438-8441.

[4] *S. Popescu, I.L Ardelean, D. Gudovan, M. Rădulescu, D. Ficai, A. Ficai, B.Ş. Vasile, E. Andronescu*, Multifunctional materials such as MCM-41/Fe_3O_4/folic acid as drug delivery system, Romanian Journal of Morphology and Embryology, **vol. 57**, 2016, pp. 483-489.

[5] *S. Amiri, H. Shokrollahi*, The role of cobalt ferrite magnetic nanoparticles in medical science, Materials Science and Engineering C, **vol. 33**, 2013, pp. 1–8.

[6] *S.K. Jesudoss, J.J. Vijaya, L.J. Kennedy, P. Iyyappa Rajan, H.A. Al-Lohedan, R. Jothi Ramalingam, K. Kaviyarasu, M. Bououdina*, Studies of the efficient dual performance of $Mn_{1-x}Ni_xFe_2O_4$ spinel nanoparticles in photodegradation and antibacterial activity, J. Photochem. Photobiol. B: Biology, **vol. 165**, 2016, pp. 121–132.

[7] *C. Tan, N. Gao, D. Fu, J. Deng, L. Deng*, Efficient degradation of paracetamol with nanoscaled magnetic $CoFe_2O_4$ and $MnFe_2O_4$ as a heterogeneous catalyst of peroxymonosulfate, Sep. Purif. Technol., **vol. 175**, 2017, pp. 47-57.

[8] *S. Mandal, S. Natarajan, A. Tamilselvi, S. Mayadevi*, Photocatalytic and antimicrobial activities of zinc ferrite nanoparticles synthesized through soft chemical route: A magnetically recyclable catalyst for water/wastewater treatment, J. Environ. Chem. Eng., **vol. 4**, 2016, pp. 2706-2712.

[9] *N. Singha, G.J.S. Jenkins, R. Asadi, S.H. Doak*, Potential toxicity of superparamagnetic iron oxide nanoparticles (SPION), Nano Reviews, **vol. 1**, 2010, 5358, DOI: 10.3402/nano.v1i0.5358.

[10] *P. Pradhan, J. Giri, G. Samanta, H. Dev Sarma, K. Prasad Mishra, J. Bellare, R. Banerjee, D. Bahadur*, Comparative evaluation of heating ability and biocompatibility of different ferrite-based magnetic fluids for hyperthermia application, J. Biomed. Mater. Res. Part B: Applied Biomaterials, DOI: 10.1002/jbm.b.30630 (2006) pp. 12-22.

[11] *S. Sabale, V. Jadhav, V. Khot, X. Zhu, M. Xin, H. Chen*, Superparamagnetic MFe_2O_4 (M=Ni, Co, Zn, Mn) nanoparticles: synthesis, characterization, induction heating and cell

viability studies for cancer hyperthermia applications, J. Mater Sci. Mater. Med., **vol. 26**, 2015, pp. 127 (9 pages).

[12] *H. Yang, C. Zhang, X Shi, H. Hua, X. Du, Y. Fang, Y. Mad, H. Wu, S Yang*, Water-soluble superparamagnetic manganese ferrite nanoparticles for magnetic resonance imaging, Biomaterials, **vol. 31**, 2010, pp. 3667–3673.

[13] *M. Nooris, D. Aparna, S. Radha*, Synthesis and characterization of MFe_2O_4 (M = Co, Ni, Mn) magnetic nanoparticles for modulation of angiogenesis in chick chorioallantoic membrane (CAM), Eur. Biophys. J., **vol. 45**, 2016, pp. 139–148.

[14] *X.H. Li, C.L. Xu, X.H. Han, L. Qiao, T. Wang, F.S. Li*, Synthesis and magnetic properties of nearly monodisperse $CoFe_2O_4$ nanoparticles through a simple hydrothermal condition, Nanoscale Res Lett., **vol. 5**, 2010, pp. 1039–1044.

[15] *A.V. Kabanov, P. Lemieux, S. Vinogradov, V. Alakhov*, Pluronic block copolymers: novel functional molecules for gene therapy, Adv. Drug Delivery Rev., **vol. vol.**, 2002, pp. 223–233.

[16] *P.E.G. Casillas; C.A.M. Pérez; C.A.R. Gonzalez*, Infrared spectroscopy of functionalized magnetic nanoparticles. INTECH Open Access Publisher, 2012.

[17] *A.B. Salunkhe, V.M. Khot, N.D. Thorat, M.R. Phadatare, C.I. Sathish, D.S. Dhawale, S.H. Pawar*, Polyvinyl alcohol functionalized cobalt ferrite nanoparticles for biomedical applications, Appl. Surface Sci., **vol. 264**, 2013, pp. 598– 604.

[18] *C.I. Covaliu, C. Matei, A.C. Ianculescu, I. Jitaru, D. Berger*, Fe_3O_4 and $CoFe_2O_4$ nanoparticles stabilized in sodium alginate polymer, UPB Sci. Bull., Series B: Chemistry and Materials Science **vol. 71(4)**, 2009, pp. 53-60.

[19] *J.C. Cezar, M. Knobel, H.C.N. Tolentino*, Magnetic properties of Cu-Permalloy granular alloy, J. Magn. Mag. Mater., **vol. 226-230**, 2001 pp. 1519-1521.

[20] *M. Kuźmiński, A. Ślawska-Waniewska, H.K. Lachowicz, M. Knobel*, The effect of particle size and surface-to-volume ratio distribution on giant magnetoresistance (GMR) in melt-spun Cu-Co alloys, J. Magn. Mag. Mater., **vol. 205**, 1999, pp. 7–13.

[21] *R.A. Mitran, D. Georgescu, N. Stanica, C. Matei, D. Berger*, Coating magnetite nanoparticles with mesostructured silica shell of different pore size and geometry, Revista Română de Materiale / Romanian Journal of Materials, **vol. 46(3)**, 2016, pp. 296–302.

[22] *D. Berger, D. Georgescu, A. Znfir, L. Bajenaru, N. Stanica, C. Matei*, Properties of mesostructured silica coated $CoFe_2O_4$ versus Fe_3O_4-silica composites, J. Alloys Comp. **vol. 708**, 2017, pp. 278-284.

[23] *W. Pei; H. Kumada; T. Natusme; H. Saito; S. Ishio*, Study on magnetite nanoparticles synthesized by chemical method, J. Mag. Mag. Mater., **vol. 310**, 2007, pp. 2375–2377.

[24] *M.H. Carvalho, R.J.S. Lima, C.T. Meneses, W.S.D. Folly, V.H.V. Sarmento, A.A. Coelho, J.G.S. Duque*, Determination of the effective anisotropy constant of $CoFe_2O_4$ nanoparticles through the T-dependence of the coercive field, J. Appl. Phys., **vol. 119**, 2016; 093909, doi: 10.1063/1.4942535