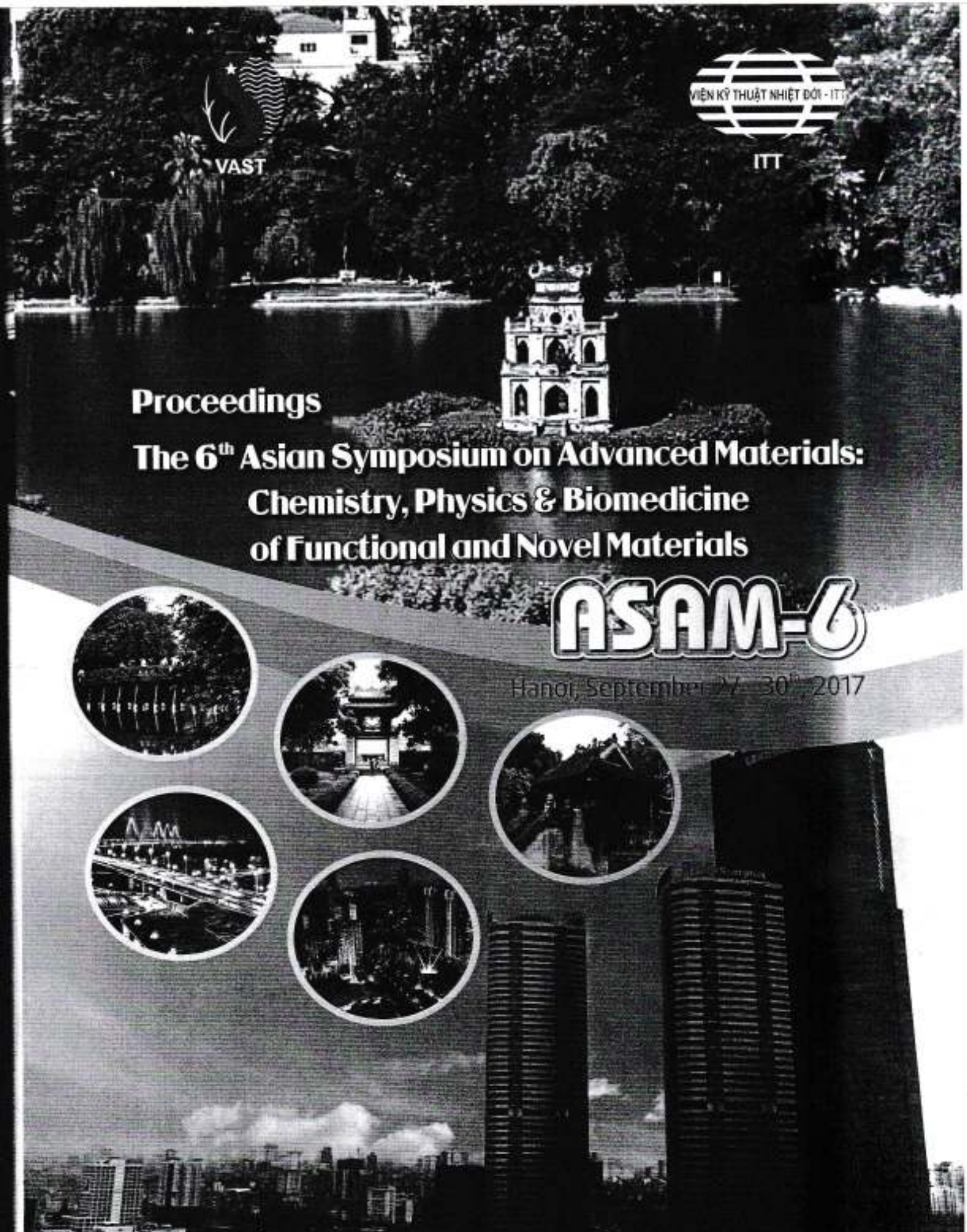

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HYDROTHERMAL SYNTHESIS OF PEG-COATED $CoFe_2O_4$ NANOPARTICLES: STRUCTURAL PROPERTIES AND HYPERTHEMIA APPLICATION

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Abstract

Cobalt ferrite nanoparticles functionalized with polyethylene glycol (PEG) were synthesized by hydrothermal method to prepare magnetic fluid. The resulting nanoparticles (NPs) were characterized using X-ray diffraction, Fourier transform infrared spectroscopy, transmission electron microscopy, zeta potential measurements, thermogravimetric analysis and vibrating sample magnetometry (VSM). The average particle size was 12 - 20 nm. The presence of characteristic functional groups of PEG covered on the surface of cobalt ferrite NPs was confirmed by FTIR spectroscopy while the amount of PEG shell was estimated by TGA analysis. Room-temperature magnetic measurements were conducted with a VSM which demonstrated the superparamagnetic nature of the NPs with high saturation magnetization of 60.67 emu/g. The magnetic induction heating data showed that the temperature attained by the PEG coated $CoFe_2O_4$ ($CoFe_2O_4$/PEG) NPs of 15 nm and concentration of about 10 mg/ml was 68.13 °C. The heat generating capacity of NPs gave a specific absorption rate (SAR) of 68.27 W/g at concentration of 6 mg/ml and 80 Oe.

Keywords. Cobalt ferrite, polyethyleneglycol (PEG), hydrothermal synthesis, magnetic fluid, nanoparticles, hyperthermia.

1. INTRODUCTION

In recent years, nanocrystalline materials are becoming a subject of intense research because of their unique properties. Magnetic NPs have been of interest for their typical physical and chemical properties as well as their potential applications in various fields such as information technology, environmental treatment, catalysis, biomedicine (extraction of biomolecules, targeted drug delivery, magnetic resonance imaging (MRI) contrast enhancement and thermal magnetic therapy) [1-4]. In particular, magnetic spinel ferrites ($M_xFe_{3-x}O_4$, where M = Fe, Co, Ni, Mn, or Zn) are emerging as innovative nanostructures for many biological applications, where a superparamagnetic behavior, a high magnetization value, a diameter smaller than a critical value (typically around 10-20 nm), a narrow size distribution, and an appropriate surface coating are required. Among magnetic spinel ferrite NPs, $CoFe_2O_4$ has received a lot of attention for its unique magnetic properties, such as a large anisotropy energy, tunable coercivity, and high saturation magnetization that make $CoFe_2O_4$ NPs good candidates to be used for MRI and hyperthermia treatment. There are several common ways to synthesize $CoFe_2O_4$ nanoparticles, including co-precipitation, sol-gel or hydrothermal methods [5-8]. Among these techniques, hydrothermal synthesis is an attractive method for the high rate of production and simplicity. In this paper, we reported the structural properties, magnetic properties and magnetic heating effect of $CoFe_2O_4$ samples, prepared by hydrothermal process.

2. EXPERIMENTAL

2.1. Chemicals

Chemicals: ferric chloride hexahydrate, cobalt chloride tetrahydrate and sodium hydroxide were purchased from Merck. Polyethylene glycol (6000 g/mol) was ordered from Sigma-Aldrich. All chemical are at analytical pure grade. Ultra-pure nitrogen gas (99.99 %) was used to provide anaerobic condition in solution. Distilled deionized water was used to prepare all the solutions.

2.2. Synthesis of $CoFe_2O_4$ magnetic fluid

The chlorides of cobalt (II) and iron (III) were dissolved in deionized water at the molar ratio (Fe/Co = 2:1) under N_2 with stirring at 400 rpm for 25 minutes. Aqueous solution of NaOH 3M was used as the precipitating agent. The obtained solution was added by dropwise into 15 ml sodium hydroxide (NaOH 3M) solution with rate of 3 ml/min, under vigorous stirring in an N_2 atmosphere, after which the color of the mixture turned to black and the pH value was higher than 12. High pH values (above 12) were used because it controls the nucleation rate and reduces the particles sizes. The obtained solution was maintained at a fixed temperature for 2 hours under vigorous stirring with a magnetic stirrer in an N_2 atmosphere [5, 8]. This precursor, (denoted A) was used for hydrothermal synthesis.

The resulting suspension A was transferred into a teflon-lined stainless steel autoclave with a capacity of 50 ml. The autoclave was sealed and treated at 180 °C for 20 hours. After the hydrothermal reaction time, the autoclave was taken out and cooled to room temperature naturally. The synthesized $CoFe_2O_4$ NPs were washed by decanting with assistant of magnet, using deionized distilled water until neutralization. The prepared $CoFe_2O_4$ NPs were dispersed into poly-ethylene glycol (PEG) solution at temperature 70 °C under N_2 with ultrasonic vibration for 30 minutes, after that filtered off the product of PEG coated NPs, washed by decanting with assistant of magnet, using deionized distilled water until neutralization.

2.3. Measurements

The crystal structure of the samples before and after coating with PEG was determined by XRD technique using the X-ray diffraction D8 Advance Bruker with Cu-Kα radiation (λ=1.5406 Å). The core-shell bonding was analyzed by Fourier transform infrared spectroscopy FT-IX (Nicolet 6700), while the amount (%) of PEG shell was estimated by TGA analysis. The morphology (size and shape) of the NPs was obtained by field emission scanning electron microscopy FESEM (Hitachi S-4800). The saturation magnetization value of the samples at room temperature was measured using a VSM. Size distribution and stability of magnetic fluids were examined by the Zetasizer instrument (Nano ZS - Malvem - UK). The magnetic induction heating effect was performed on the magnetic fluid based on the $CoFe_2O_4$ NPs with the highest saturation magnetization and uniform particle size under an alternating magnetic field in the range of 50-80 Oe and frequency of f = 178 kHz, provided by the commercial generator (RDO HFI 5 KW).

3. RESULTS AND DISCUSSION

3.1. Properties, morphology and particle size

The X-ray diffraction patterns of the $CoFe_2O_4$ and $CoFe_2O_4$/PEG NPs are shown in Fig. 1(a, b). It can be seen that the typical peaks of (220), (311), (400), (422), (511) and (440) correspond to pure phase with spinel structure of $CoFe_2O_4$ (JCPDS Card No: 22-1086). The crystallite size D of the samples was calculated from data of peak at 2θ= 35.5° with Miller indices by (311), using Scherrer equation:

$$D_{XRD} = \frac{0.89\lambda}{\beta\cos\theta} \quad (1)$$

In which D is the grain diameter, β is half intensity width of the relevant diffraction, λ is X-ray wavelength and θ is the diffraction angle. The lattice parameter was calculated according to the Eq. (2):

$$a = d_{hkl}(h^2+k^2+l^2)^{1/2} \quad (2)$$

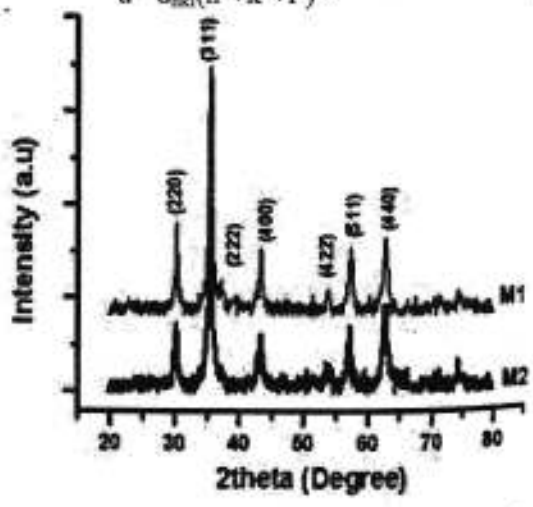

Figure 1. XRD patterns of the $CoFe_2O_4$ and $CoFe_2O_4$/PEG

Table 1. The unit cell parameter (a), averaged crystal size (D_{XRD}), averaged particle size (D_{FEEM}), magnetization measured at 10 kOe (M_{10kOe}), coercivity (H_c) of prepared samples

Sample	M1 ($CoFe_2O_4$)	M2 ($CoFe_2O_4$/PEG)
a(Å)	8.356	8.381
d_{311}(Å)	2.521	2.527
β (degree)	0.620	0.532
$D_{(XRD)}$ (nm)	13.31	15.51
D_{FESEM}	14.2±0.8	16.9±1.1
M_{10kOe} (emu/g)	60.07	56.12
H_c (Oe)	39	7.9

The $CoFe_2O_4$/PEG NPs exhibit similar diffraction pattern as that of $CoFe_2O_4$ NPs. This suggests that the crystalline structure of $CoFe_2O_4$ NPs did not change after the surface modification of the NPs by PEG. FESEM study was performed to understand the details of the morphology of the $CoFe_2O_4$ and $CoFe_2O_4$/PEG NPs. The FESEM images of $CoFe_2O_4$ and $CoFe_2O_4$/PEG NPs are shown in Fig. 2. From FESEM images it is observed that the uncoated $CoFe_2O_4$ nanoparticles show highly agglomerated porous foam like structure. It is possible that the dipole-dipole interaction between magnetic NPs results in the agglomeration. While coated $CoFe_2O_4$ NPs show well dispersed structure with almost no agglomerations. The grain size for $CoFe_2O_4$ NPs and$CoFe_2O_4$/PEG NPs was found to be 13 nm and 16 nm respectively. One thing is to be noted that, morphology of coated and uncoated $CoFe_2O_4$ nanoparticles is quite similar in both cases.

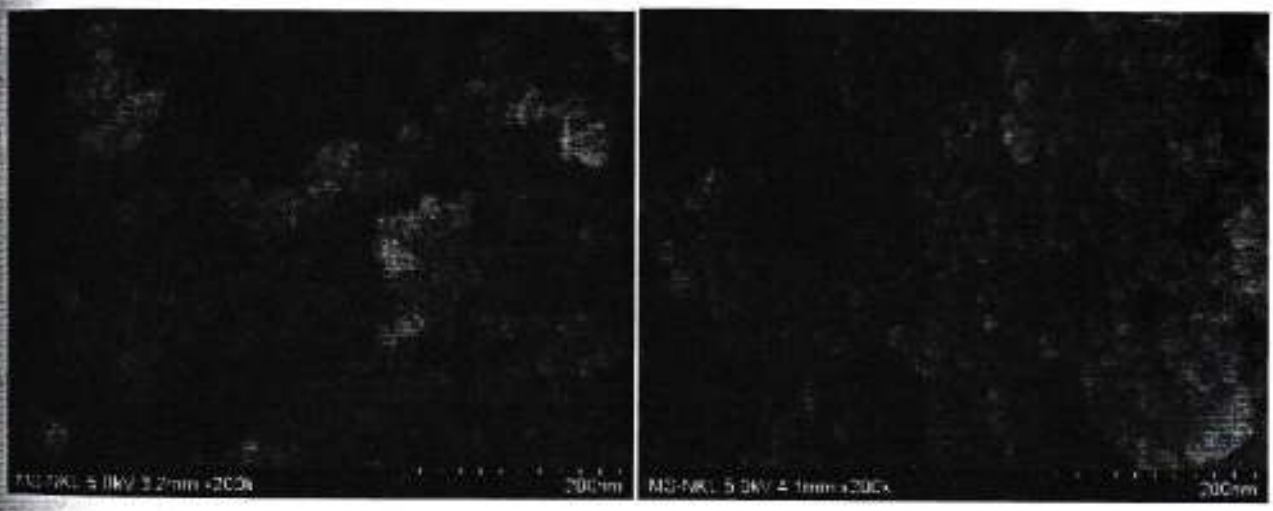

Figure 2. FESEM images of nanoparticles: $CoFe_2O_4$ (left) and $CoFe_2O_4$/PEG (right)

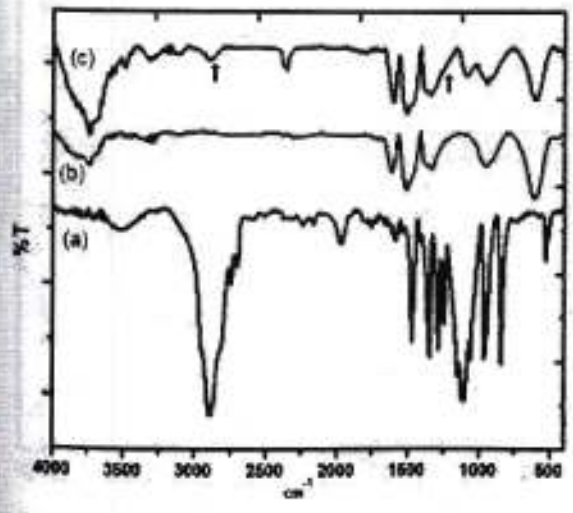

Figure 3. FTIR spectra (a) pure PEG-6000 (b) pure $CoFe_2O_4$ and (c) $CoFe_2O_4$/PEG NPs

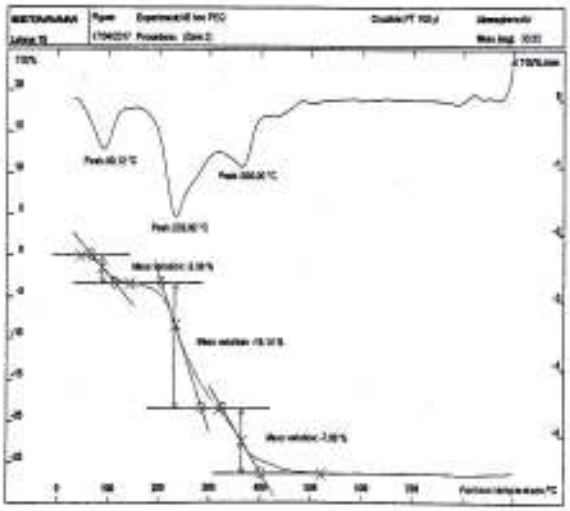

Figure 4. Thermo-Gravimetric curves of $CoFe_2O_4$/PEG NPs

3.2. FTIR and thermal gravimetric analyses

FTIR is an appropriate technique to evaluate the attachment of the polymer to the surface of the NPs. Figure 3 shows the FTIR spectra of PEG (a), uncoated (b) and coated $CoFe_2O_4$ NPs (c). It can be seen that a strong IR band at 571 cm^{-1} (Fig. 3b) is the characteristic of Fe-O octahedral vibrations, related to the ferrite core. The characteristic bands for $CoFe_2O_4$ were nearly no changed after coating, but two bands at 2885 cm^{-1}(ν_{CH}) and 1110 cm^{-1}(ν_{COC}) in Fig. 3c can be assigned to the vibrations of PEG [9, 10].

TGA data provide additional quantitative evidence on the amount of the PEG shell on the NPs. In TGA experiment, the MNPs are heated to 1000 °C under air atmosphere and the changes in the weight of sample are recorded. On the TGA curves, one can observe the samples' weight loss at two stages. The first weight loss of 1.4 %, recorded in the temperature range of 90-130 °C, likely corresponds to the moisture dehydration, followed by a second weight loss peak were observed at higher temperature (200-300 °C) which was attributed to the separation and decomposition of PEG layer giving rise to significant weight loss ~23 %. This desorption pattern is in good agreement with patterns reported in literature for PEG ligands [11]. This shows that PEG was physically adsorbed on surface of nanoparticles.

The zeta potential measurements for the two samples results in the low value of -26.8 mV for $CoFe_2O_4$ NPs (M1) while for $CoFe_2O_4$/PEG NPs (M2) these value is shifted to -40.3 mV[12].

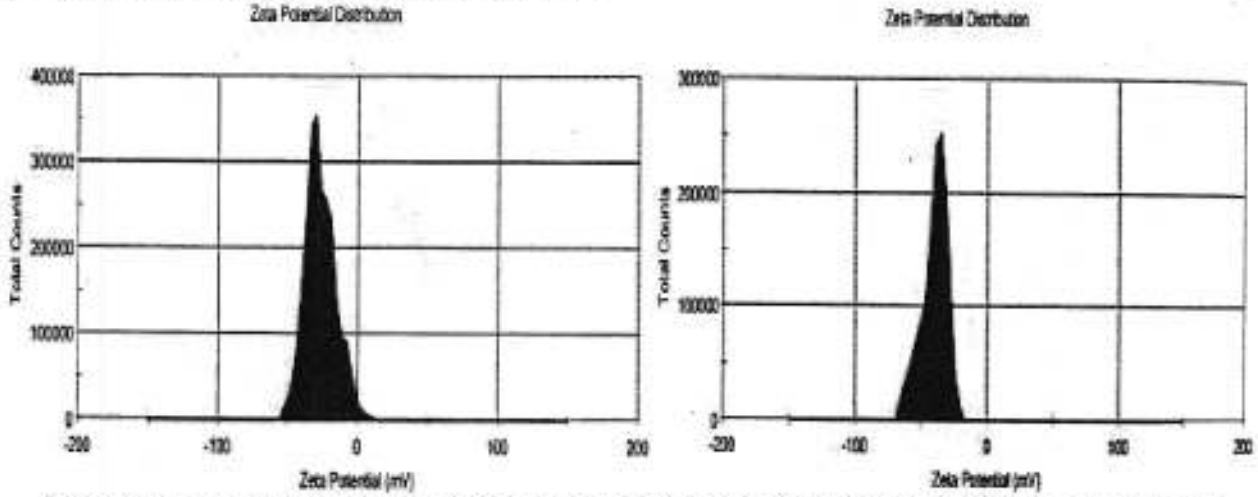

Figure 5. The zeta potential scanning $CoFe_2O_4$ nanoparticles (a) and $CoFe_2O_4$/PEGnanoparticles (b)

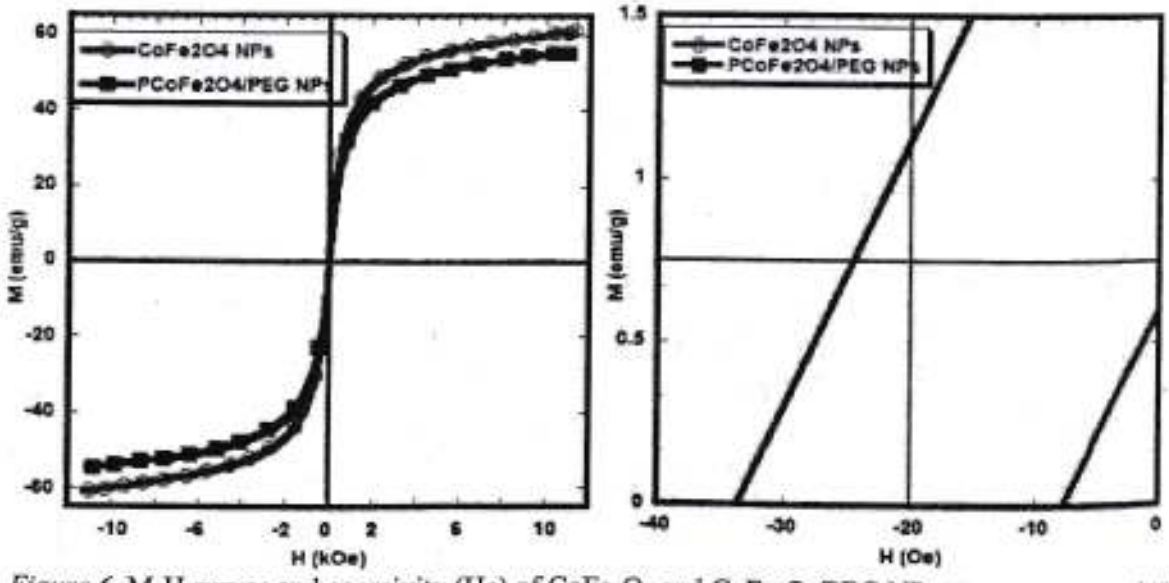

Figure 6. M-H curves and coercivity (Hc) of $CoFe_2O_4$ and $CoFe_2O_4$/PEG NPs at room temperature

3.3. Magnetic properties and magnetic induction heating of PEG coated $CoFe_2O_4$ PEG NPs

Fig. 3 shows the hysteresis loops of $CoFe_2O_4$ and $CoFe_2O_4$/PEG NPs. The magnetic parameters such as coercivity (Hc) and saturation magnetization (Ms) of the $CoFe_2O_4$ and $CoFe_2O_4$/PEG NPs are given in table 1. The coercivity (Hc), saturation magnetization (Ms) of the $CoFe_2O_4$ NPs was found to be 39 Oe, 60.07 emu/g, respectively. For $CoFe_2O_4$/PEG NPs, the saturation magnetization (Ms) value was decreased from 60 emu/g for $CoFe_2O_4$ to 56 emu/g for $CoFe_2O_4$/PEG NPs. Both the samples exhibit the characteristic feature of superparamagnetic behavior. The reduction in the magnetic saturation value is attributed to the chemical combination of nonmagnetic layer of PEG in $CoFe_2O_4$/PEG NPs. The obtained structural and magnetic parameters of the PEG coated $CoFe_2O_4$ NPs can be used for biomedical application such as targeted drug delivery.

The highly stable sample (M2) was used for further study on magnetic heating effect. The maximum temperature (Tmax) and the specific absorption rate (SAR) of the samples were determined at different sample concentrations and different amplitudes of magnetic field. The SAR is defined as the variation of the temperature with time ($\Delta T/\Delta t$) of the ferro fluid in the ac magnetic field as following:

$$SAR = C\frac{m_{sample}}{m_{mnp}}\left(\frac{\Delta T}{\Delta t}\right)$$

where C is the specific heat of the fluid per weight unit (C = 4.18 J/gK), m_{sample}/m_{mnp} is the NP concentration in the fluid (with m_{sample} = 1000 mg; m_{mnp} = 1, 2, 3, 6, 10 mg), $\Delta T/\Delta t$ is the initial slope of the heating curves.

Table 2. Maximum temperature ($T_{1500\ s}$), specific absorption rate (SAR), and initial heating rate ($\Delta T/\Delta t$) of the (M2) sample at different concentrations

Concentration (mg/ml)	Magnetic field (H [Oe], f [kHz])	T_{max} (°C)	SAR (W/g)	$\Delta T/\Delta t$ (°C/s)
1	80; 178	28.52	33.98	0.011
2	80; 178	32.37	39.07	0.023
3	80; 178	37.42	48.52	0.042
6	80; 178	46.70	68.27	0.098
10	80, 178	68.13	79.00	0.189

Table 3. Maximum temperature ($T_{1500\ s}$), specific absorption rate (SAR), and initial heating rate ($\Delta T/\Delta t$) ofthe (M2) sample at 6 mg/ml concentration at different magnetic field strength values

Concentration (mg/ml)	Magnetic field (H [Oe], f [kHz])	T_{max} (°C)	SAR (W/g)	$\Delta T/\Delta t$ (°C/s)
6	50 ; 178	26.43	32.99	0.033
6	60 ; 178	30.27	36.23	0.052
6	70 ; 178	34.36	45.98	0.066
6	80 ; 178	46.70	68.27	0.098

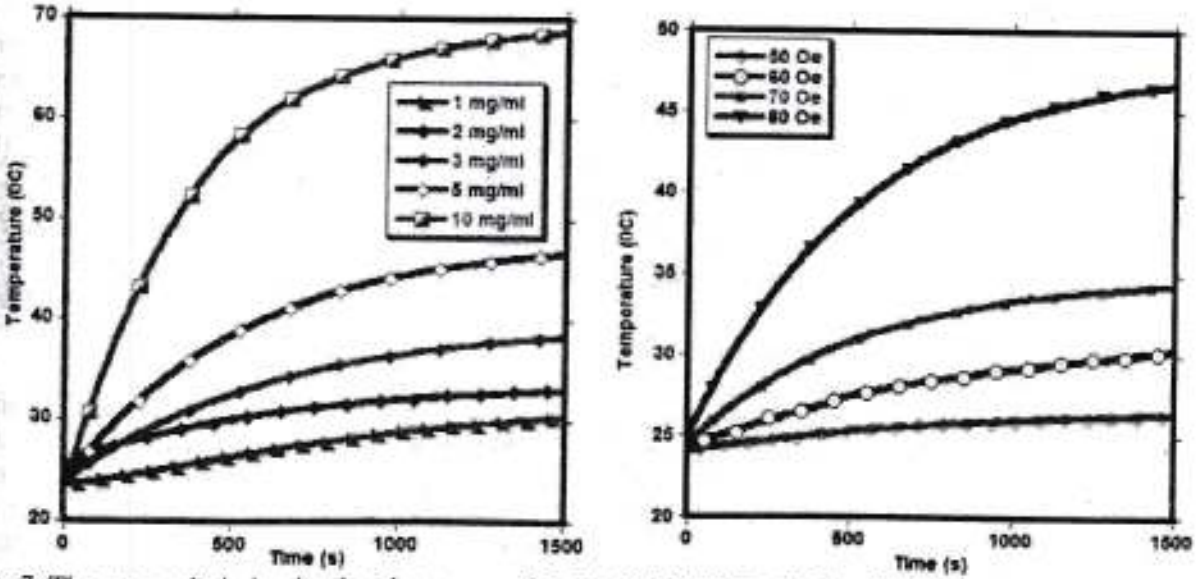

Fig. 7. The magnetic-induction heating curve of $CoFe_2O_4$/PEG NPs (M2) with different concentrations (a) and magnetic heating curves measured for suspensions of samples (M2) of 6 mg/ml at the different values of magnetic field strength (b)

The magnetic fluid M2 is highly stable and superparamagnetic at the room temperature, so it was chosen for studying the magnetic induction heating effect. For this aim, M2 with the concentration varied from 1 to 10 mg/ml were subjected to the alternative magnetic field of the frequency kHz with the strength of 80 Oe. As seen from fig. 7a, the increasing in the ferro fluid concentration has slightly improved magnetic heating effect. The maximum temperature reached 37.42 °C and SAR was only 48.52 W/g at particle concentration of 6 mg/ml. This weak heating induction is not sufficient for applications of hyperthermia treatment, while the maximum temperature reached 68 °C and SAR was 79 W/g for 25 minutes at particle concentration of 10. mg/ml. To reach 42 - 47 °C (the optimal temperature for annihilating cancer cells), the concentration of 6 mg/ml was fixed and the field strength was increased from 50 Oe to 80 Oe.

Figure 7b represents magnetic heating curves measured at different magnetic field strengths. The magnetic ferro fluid concentration was 6 mg/ml and the magnetic field frequency was 178 kHz. Unlike ferro fluid concentration, the amplitude of magnetic field strongly affected to the magnetic heating behaviors of the material (Table 3). Both the maximum temperature and SAR were increased quickly with increasing amplitude of magnetic field.

4. CONCLUSIONS

In this work, high-quality magnetic fluid cobalt ferrite nanoparticles coated by poly-ethylene glycol $CoFe_2O_4$/PEG were synthesized by hydrothermal. The PEG coating layer has improved the dispersion stability of magnetic particles in aqueous solutions. These high stable magnetic particles also owned good magnetic heating induction. The highest temperature (68 °C) was obtained for the sample concentration of 10 mg/ml when applying an alternative magnetic field with amplitude of 80 Oe and frequency of 178 kHz for 25 min. These results suggest the promising applications of magnetic nano-sized PEG coated $CoFe_2O_4$ fluid in hyperthermia cancer treatment.

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