Enhancement of SAR with Core-Shell nanoparticles for hyperthermia
8.1 Introduction
MNPs have been gaining a lot of interest because of their ability to mediate the heat induction. MNPs under AC magnetic field show heating effects due to the losses during the magnetization reversal process of the particles. Also, the heating property of MNPs can be controlled by controlling their magnetic properties. These properties of MNPs make them useful in applications such as release of drugs from mesoporous NPs and thermosensitive polymer coated carriers, treatment of diseases with hyperthermia, thermal imaging of target lesions, and the development of thermally driven ion channel controls for cell signaling. However, these imaging and therapeutic applications of thermal actuation causes the problem of relatively poor energy transfer efficiency of NP, which leads to the requirement of relatively large amount of NPs. To overcome this problem, one has to enhance the SAR. The SAR depends on composition, structural and magnetic properties as well as magnetic field amplitude [1]. However, so far it is not clear by what practical means and to what extent it may be possible to enhance SAR. Though SAR is an increasing function of frequency $f$ and field amplitude $H$ in a wide parameter range, the opportunities for enhancement of SAR by an increase of $f$ and/or $H$ are limited [2-4]. Also, there is limitation for the product $H_f$ for biomedical applications [5].

To increase the efficiency of magnetic thermal induction by NPs, one can take advantage of the exchange coupling between a magnetically hard core and magnetically soft shell to tune the magnetic properties of the NP and maximize the SAR, which is the gauge of the conversion efficiency [6]. Here, we use NPs with core-shell structure, with mutual coupling of magnetically hard and soft magnetic components. This coupling can allow optimal tuning of magnetocrystalline anisotropy ($K$) values.

In order to examine the tunability of $K$ and its magnetic heating power, a representative magnetically hard material ($\text{CoFe}_2\text{O}_4$) has been coupled to a soft
material (Ni_{0.5}Zn_{0.5}Fe_{2}O_{4}). In the present chapter, an attempt has been made to prepare the core-shell CoFe_{2}O_{4}@ Ni_{0.5}Zn_{0.5}Fe_{2}O_{4} NPs with high heating ability.

8.2 Experimental

8.2.1 Materials

Anhydrous ferric chloride (FeCl_{3}), cobalt chloride (CoCl_{2}•4H_{2}O), nickel chloride (NiCl_{2}•4H_{2}O), zinc chloride (ZnCl_{2}•4H_{2}O), sodium acetate, diethylene glycol, oleic acid, ethanol, ethyl acetate, diethanolamine and hexane used in the experiments are all analytical grade. Double distilled water used throughout the experiments.

8.2.2 Synthesis of CoFe_{2}O_{4} nanoparticles

For the synthesis of CoFe_{2}O_{4} NPs, a mixture of CoCl_{2} (5 mM), FeCl_{3} (10 mM), and sodium acetate (1.5 g) was dissolved in 50 ml diethylene glycol. Oleic acid (6 mM) was added to the mixture solution. The above solution was stirred vigorously for 0.5 h to obtain homogeneous solution. After stirring for 0.5 h, the homogeneous solution was refluxed at 220ºC for 3 h. After cooling to room temperature, the CoFe_{2}O_{4} NPs were repeatedly washed with a mixture of ethanol and ethyl acetate in the ratio of 1:2 and separated by using a magnetic decantation process. Finally, the CoFe_{2}O_{4} NPs were washed with distilled water. The resultant NPs were dried at room temperature. The CoFe_{2}O_{4} NPs were dispersed in the solvent such as hexane.

8.2.3 Synthesis of CoFe_{2}O_{4}@ Ni_{0.5}Zn_{0.5}Fe_{2}O_{4} nanoparticles

For the synthesis of CoFe_{2}O_{4}@ Ni_{0.5}Zn_{0.5}Fe_{2}O_{4} NPs, the CoFe_{2}O_{4} NPs was used as a seed and Ni_{0.5}Zn_{0.5}Fe_{2}O_{4} NPs was over-grown by reflux method on the surface of the seed particle. NiCl_{2} (2.5 mM), ZnCl_{2} (2.5 mM), FeCl_{3} (10 mM) and sodium acetate (1.5 g) was dissolved in 50 mL diethanolamine. Oleic acid (6 mM) was added to the mixture solution. The above solution was stirred vigorously for
0.5 h to obtain homogeneous solution. After injection of the CoFe$_2$O$_4$ NPs suspended in hexane, the reaction mixture was refluxed at 270ºC for 3 h. The reaction mixture was cooled to room temperature and core-shell CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs were isolated using the process explained above.

**8.2.4 Synthesis of Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ nanoparticles**

In order to compare the results of CoFe$_2$O$_4$ and CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs, Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs were also prepared by using the same method as that of CoFe$_2$O$_4$ NPs.

**8.2.5 Characterization**

The phase identification and crystallite size determination were done by XRD analysis with Philips (PW-3710) automated X-ray diffractometer equipped with a crystal monochromator employing Cu-Kα radiation of wavelength 1.5406 Å in 2θ range from 20 to 80º. FTIR spectra were obtained using Nicolet FT-IR Avatar 360 (Nicolet, USA) with the KBr method. The sizes of NPs were determined by a TEM (Hitachi H-600-II, Japan). DLS measurements were carried out using a PSS/NICOMP 380 ZLS (Particle Sizing System, Santa Barbara, CA, USA) to determine the size distribution of MNPs. The light source was He–Ne laser operated at 632.8 Å. All measurements were carried out at 25.0 ± 0.1 ºC using a circulating water bath. For reproducibility, at least three measurements were conducted for each reading. The magnetic property of NPs was measured by a VSM (Princeton Measurements Alternating Gradient Magnetometer AGM, Model MicroMag 2900) at room temperature.

Induction heating of MNPs for hyperthermia application was performed in a plastic micro centrifuge tube (1.5 mL) using an instrument (Easy heat 8310, Ambrell; UK) with a 6 cm diameter (4 turns) heating coil. Samples (10 mg mL$^{-1}$ of distilled water) were placed at the center of the coil and the applied frequency was 265 kHz and field amplitude varied [10].
8.3 Results and discussion

8.3.1 XRD study

Fig. 8.1 shows the XRD patterns of the CoFe₂O₄, CoFe₂O₄@Ni₀.₅Zn₀.₅Fe₂O₄ and Ni₀.₅Zn₀.₅Fe₂O₄ respectively. The reflection peaks of CoFe₂O₄ are indexed with the JCPDS card (reference code: 22-1086) while the reflection peaks of Ni₀.₅Zn₀.₅Fe₂O₄ are indexed with the JCPDS card (reference code: 08-0234). The peak positions of the CoFe₂O₄, CoFe₂O₄@Ni₀.₅Zn₀.₅Fe₂O₄ and Ni₀.₅Zn₀.₅Fe₂O₄ are the same. This is because both the JCPDS cards show almost similar peak positions of CoFe₂O₄ and Ni₀.₅Zn₀.₅Fe₂O₄ and hence, core-shell CoFe₂O₄@Ni₀.₅Zn₀.₅Fe₂O₄ NPs also show the similar peak position. This may be attributed to the presence of both CoFe₂O₄ and Ni₀.₅Zn₀.₅Fe₂O₄.

The crystallite size of the samples is estimated from the full-width at half maximum (FWHM) of the most intense peak (311) using the Debye-Scherrer’s formula \( D = \frac{0.9 \lambda}{\beta \cos \theta} \), where \( D \) is the crystallite size, 0.9 is the Scherrer constant, \( \lambda \) is the wave length of Cu Kα radiation (= 1.5406), \( \beta \) is the FWHM of the (311) peak in radian and \( \theta \) is the corresponding Bragg’s diffraction angle in degree. The crystallite size obtained from the above eq. is found to be 5 nm, 9 nm and 4 nm for CoFe₂O₄, CoFe₂O₄@Ni₀.₅Zn₀.₅Fe₂O₄ and Ni₀.₅Zn₀.₅Fe₂O₄ respectively. The increase in the crystallite size of the CoFe₂O₄@Ni₀.₅Zn₀.₅Fe₂O₄ (9 nm) is may be due to the presence of shell of Ni₀.₅Zn₀.₅Fe₂O₄ on the core of CoFe₂O₄ which causes decrease in the FWHM of (311) peak of CoFe₂O₄@Ni₀.₅Zn₀.₅Fe₂O₄ and hence, increase in the crystallite size.
Fig. 8.1: XRD patterns of the (a) CoFe$_2$O$_4$, (b) CoFe$_2$O$_4$@ Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and (c) Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs.

8.3.2 TEM analysis

Fig. 8.2 shows the TEM images of CoFe$_2$O$_4$, CoFe$_2$O$_4$@ Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs. TEM images show the agglomerated structure of NPs. The agglomeration occurs may be due to the magnetostatic interaction between the NPs. The average particle size of the CoFe$_2$O$_4$, CoFe$_2$O$_4$@ Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs is found to be 6 nm, 10 nm and 4 nm respectively, which is in good agreement with the XRD results.
8.3.3 DLS study

Particles size and size distributions of MNPs are important parameters for their biomedical applications. The hydrodynamic size of MNPs is important parameter for biomedical applications. For example, the MNPs larger than 30 nm are used for phagocytosis imaging in MRI [6, 7]. On the other hand, the NPs (~10 nm) are able to escape from the phagocytes; such MNPs conjugated with a target specific
biomolecules are used to detect the target tissues through molecular interactions between NP–biomolecule conjugates and molecular markers expressed by target tissues [8, 9].

Particle size distributions of the NPs dispersed in double distilled water was measured by using DLS technique and the obtained results are shown in Fig. 8.3. The average particle sizes of CoFe$_2$O$_4$, CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs are about 38.8 nm, 115.1 nm and 25.2 nm respectively. Even in the absence of external magnetic field, the magnetic dipole–dipole interactions between particles can cause their agglomeration. Therefore, the hydrodynamic size distributions are larger than those observed by TEM.
8.3.4 Magnetic properties

The room temperature M–H curves of CoFe$_2$O$_4$, CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs are shown in Fig. 8.4. The magnetic properties such as saturation magnetization, coercivity and remanence magnetization were elucidated from hysteresis data and tabulated in Table 8.1. Magnetization value of the CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ falls between the values for CoFe$_2$O$_4$ and Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs: Ms (CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$) = 28.2 emu/g; Ms (CoFe$_2$O$_4$) = 36.6 emu/g; Ms (Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$) = 23.7 emu/g. This indicates that the CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs are magnetically exchange-coupled.

The K value of CoFe$_2$O$_4$, CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs are calculated by Stoner-Wohlfarth theory [10] using eq. (5.16). The calculated values of K are shown in Table 8.1. Magnetic coupling of core and shell components provides K values of CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ in between 1.5 x 10$^4$ and 2 x 10$^4$ J/m$^3$. 

**Fig. 8.3:** Particle size distribution data of the (a) CoFe$_2$O$_4$, (b) CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and (c) Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs.
Table 8.1: Magnetic parameters of CoFe$_2$O$_4$, CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs.

<table>
<thead>
<tr>
<th></th>
<th>CoFe$_2$O$_4$</th>
<th>Ni$<em>{0.5}$Zn$</em>{0.5}$Fe$_2$O$_4$</th>
<th>CoFe$<em>2$O$<em>4$@Ni$</em>{0.5}$Zn$</em>{0.5}$Fe$_2$O$_4$</th>
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<td>Hc (Oe)</td>
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<td>4</td>
<td>65</td>
</tr>
<tr>
<td>Mr (emu/g)</td>
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<td>0.07</td>
<td>2.43</td>
</tr>
<tr>
<td>Ms (emu/g)</td>
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<td>23.7</td>
<td>28.2</td>
</tr>
<tr>
<td>K (J/m$^3$)</td>
<td>$2.12 \times 10^4$</td>
<td>$0.01 \times 10^4$</td>
<td>$1.88 \times 10^4$</td>
</tr>
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Fig. 8.4: Magnetization curves of the (a) CoFe$_2$O$_4$, (b) CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and (c) Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs.
8.3.5 Induction Heating Study

A graph of an increase in temperature with time for 10 mg mL\(^{-1}\) suspensions of \(\text{CoFe}_2\text{O}_4\), \(\text{CoFe}_2\text{O}_4@\text{Ni}_{0.5}\text{Zn}_{0.5}\text{Fe}_2\text{O}_4\) and \(\text{Ni}_{0.5}\text{Zn}_{0.5}\text{Fe}_2\text{O}_4\) NPs is shown in Fig. 8.5 (a-e). There is an increase in temperature with time and its value increases with increase in applied magnetic field for all the samples. The basis of the heating of MNPs by AC magnetic fields has been briefly reviewed in the earlier chapter.
Fig. 8.5: Temperature versus time curves for 10 mg mL\(^{-1}\) suspension of CoFe\(_2\)O\(_4\), CoFe\(_2\)O\(_4\)@ Ni\(_{0.5}\)Zn\(_{0.5}\)Fe\(_2\)O\(_4\) and Ni\(_{0.5}\)Zn\(_{0.5}\)Fe\(_2\)O\(_4\) NPs at an applied field (a) 209.5 Oe, (b) 251.4 Oe, (c) 293.3 Oe, (d) 335.2 and (e) 377.1 Oe respectively.

![Temperature versus time curves](image)

Fig. 8.6: SAR values for CoFe\(_2\)O\(_4\), CoFe\(_2\)O\(_4\)@ Ni\(_{0.5}\)Zn\(_{0.5}\)Fe\(_2\)O\(_4\) and Ni\(_{0.5}\)Zn\(_{0.5}\)Fe\(_2\)O\(_4\) NPs at applied field, 209.5 Oe-377.1 Oe.

![SAR values](image)

The heat generated by the MNPs is measured in terms of the SAR also denoted as specific loss power. SAR measures the heating ability of the magnetic...
materials in presence of an AC magnetic field and it can be calculated by using eq. (6.8).

SAR values are calculated by using eq. (6.8) for NPs dispersed in distilled water (1 mL) at different fields varying from 209.5 Oe–377.1 Oe at 265 kHz and are shown in Fig. 8.5. From Fig. 8.5, it is observed that the SAR values of core-shell CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs are enhanced as compared to pure CoFe$_2$O$_4$ and Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs. This increase in SAR value is due to the exchange coupling between the magnetically hard core (CoFe$_2$O$_4$) and magnetically soft shell (Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$) which allows the optimal tuning of magnetocrystalline anisotropy (K) values.

### 8.4 Conclusions

The CoFe$_2$O$_4$, CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ and Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs have been synthesized successfully by reflux method. The XRD, TEM and induction heating study confirms the formation of core-shell CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs. Induction heating studies indicate the enhanced SAR value of core-shell CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs. This increase in SAR value is due to the exchange coupling between the magnetically hard core (CoFe$_2$O$_4$) and magnetically soft shell (Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$), which allows the optimal tuning of magnetocrystalline anisotropy (K) values. Thus, it is demonstrated that the CoFe$_2$O$_4$@Ni$_{0.5}$Zn$_{0.5}$Fe$_2$O$_4$ NPs with high SAR can be used for magnetic hyperthermia application.
References