Gravity: Jurnal Ilmiah Penelitian dan Pembelajaran Fisika

http://jurnal.untirta.ac.id/index.php/Gravity

ISSN: 244-515x; e-ISSN: 2528-1976

Vol. 10, No. 1, February 2024, Page 71-77

Comparison of microstructures and magnetic characteristics of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG for drug delivery system application

Joko Utomo[1]* and Hafiz Sub'han[1]

[1]Department of Physics, Universitas Negeri Malang, Indonesia
**E-mail: joko.utomo.fmipa@um.ac.id*

(Received: 02 January 2024; Accepted: 14 February 2024; Published: 20 February 2024)

ABSTRACT

$CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG materials have been successfully prepared using the coprecipitation method with a synthesis temperature of 90 °C. Doxorubicin (DOX) was successfully loaded and released in both samples. Based on the XRD results, the crystal structure of $CoFe_2O_4$/PEG is cubic spinel while the structure of $MnFe_2O_4$/PEG is hematite with the lattice parameters for $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG is 8.40 nm and 8.41 nm, respectively. Based on the SEM results, the morphology of the two samples is quite homogenous and the particle size of $CoFe_2O_4$/PEG is smaller than $MnFe_2O_4$/PEG's. There is a vibrational spectrum of Fe – O in both samples at wave numbers of 600 - 690 cm^{-1}. Based on VSM characterization, $CoFe_2O_4$/PEG is included in hard magnetic materials with a saturation magnetization of 54.85 emu/g and coercivity of 788 Oe. Meanwhile, $MnFe_2O_4$/PEG is classified as soft magnetic materials with lower saturation magnetization of 11 emu/g and coercivity of 7.42. In addition, based on the UV-Vis characterization obtained the efficiency of drug loading of $CoFe_2O_4$/PEG is higher (98.8 %) than the $MnFe_2O_4$/PEG sample (96.3 %). It is the opposite for the drug release percentage that $CoFe_2O_4$/PEG has 30.6 % which is lower than the $MnFe_2O_4$/PEG (51.6 %).

Keywords: Co Ferrite, drug loading, drug release, Ni Ferrite, and PEG

DOI: 10.30870/gravity.v10i1.28748

INTRODUCTION

The development of an effective drug delivery system for patients diagnosed with tumors is still a big challenge for researchers in many related fields, including materials engineering and health. Modified magnetic nanoparticles have become of current interest as an agent of the drug due to their high surface area and stability, cost-effectiveness, and good biocompatibility (Septian Dwitya et al., 2024). Ferrite is a type of magnetic nanoparticle that is a good candidate to be considered because of its advantages in magnetic targeting (Chen et al., 2017). Furthermore, cobalt ferrite and manganese ferrite are examples of potential types of ferrite

which can be used for drug delivery system applications. Cobalt ferrite possesses great chemical stability and favorable magnetic characteristics (Weldekirstos et al., 2024). Meanwhile, the manganese ferrite is a soft magnetic material having low coercivity and magnetic anisotropy (Nguyen et al., 2023). Also, manganese ferrite has good biocompatibility and chemical stability so it is suitable to be applied in biomedical applications, particularly in drug delivery systems (Dippong et al., 2021).

However, cobalt ferrite and manganese ferrite are easily oxidized and their particle size is quite difficult to adjust which can reduce performance as an agent in drug delivery. In addition, on drug delivery systems, coating magnetic nanoparticles is highly recommended to produce non-toxic nanoparticles, and increase solubility and biocompatibility. As a consequence, the ideal properties of either cobalt ferrite or manganese ferrite has not been found in its entirely those materials so they need to be modified to get the desired characteristics. Cobalt ferrite and manganese ferrite encapsulated with polymer provide better biocompatibility and bioconjugation between nanoparticles with drugs and increase acceptance in the human body. Therefore, manganese ferrite and cobalt ferrite need to undergo a composition modification process through coating with the polymer to overcome the drawback, one of the polymers is PEG (Ghanbari et al., 2021; Moorthy et al., 2016; Rezvantalab et al., 2018). Previous research studying the PEG has been conducted by Thi et al informing that PEG can enhance circulation time and therapy stability biologically (Thi et al., 2020). Summing up, this research focuses on studying the microstructure and magnetic characteristics of cobalt and manganese ferrites modified by PEG to know fundamental information to the application. The efficiency of drug loading and drug release is also discussed in detail.

RESEARCH METHODS

$CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG samples have been successfully synthesized using the coprecipitation method with the synthesis temperature of 90 °C and further heating of annealing has been conducted. The used precursor materials in this research include cobalt (II) chloride, manganese (II) chloride, iron (III) chloride, sodium hydroxide, HCl, and PEG. In making the $CoFe_2O_4$/PEG sample, the stage was started by dissolving cobalt (II) chloride and iron (III) chloride separately in 25 ml of distilled water for 3 minutes. The solutions were then mixed and HCl was added to speed up the reaction (solution X). Separately, a NaOH solution was also prepared by dissolving 6 M NaOH in 25 ml of distilled water for 5 minutes. In the next stage, solution X was added to NaOH drop by drop and kept at 90 °C for 1 hour. The obtained precipitate from the previous stage was washed 6 times using distilled water. Next, the product was dried using a furnace at 90 °C for 4 hours and the powder of $CoFe_2O_4$ was produced. Afterwards, the $CoFe_2O_4$ powder and PEG were mixed into 25 ml aquades with the mass composition of $CoFe_2O_4$ powder and PEG which was 1: 1. In the following step, the mixture was washed several times and dried using a furnace at 45 °C. In the final stage, the obtained powder was characterized using some type of equipment i.e. XRD, SEM, FTIR, VSM, and UV-Vis spectroscopy to see the microstructures, magnetic properties, and effectiveness of drug loading and drug release. Similar stages were also carried out to make $MnFe_2O_4$/PEG samples.

RESULTS AND DISCUSSION

$CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG materials have been synthesized using the coprecipitation method and characterized using XRD, SEM, FTIR, VSM, and UV-Vis to investigate microstructures, magnetic properties, and percentage of drug loading and drug release of samples. Based on the XRD analysis, the diffraction pattern of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG materials is shown in Figure 1.

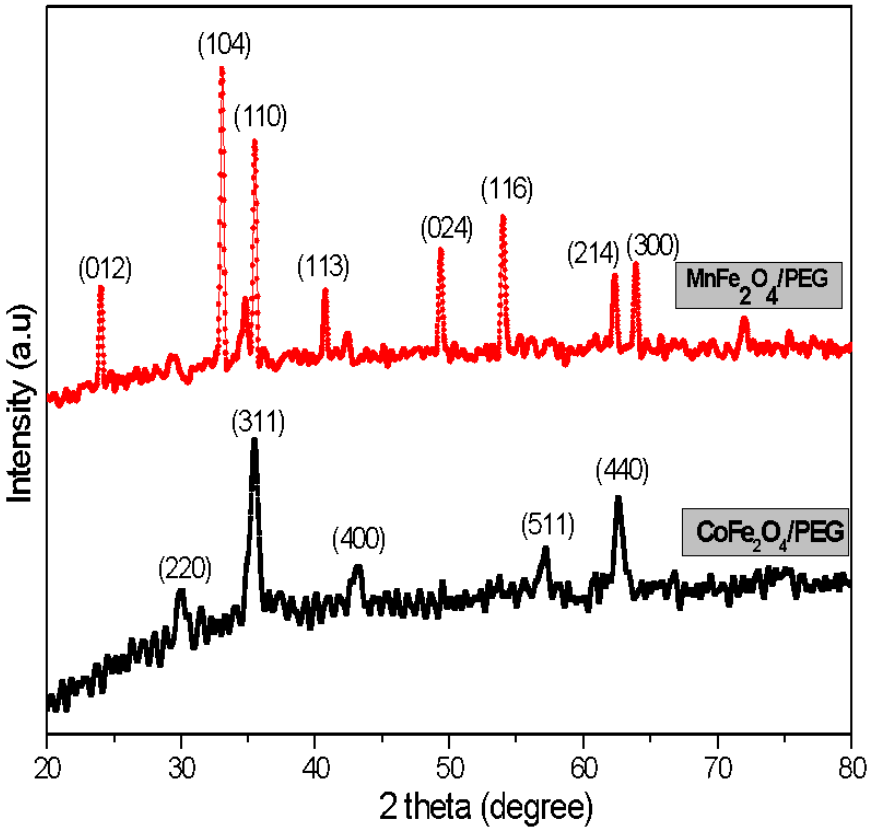

Figure 1. Diffraction pattern of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG materials

Based on the result of XRD analysis from Figure 1, a sample of $CoFe_2O_4$/PEG has a spinel cubic structure with the miller index of (220) (311) (400) (511) (440). This is in line with the previous research conducted (Azab et al., 2024; Kapur et al., 2024). Meanwhile, $MnFe_2O_4$/PEG material depicts the different phase which is hematite (α-Fe_2O_3) with the miller index of (012) (104) (110) (113) (024) (116) (214) (300). This result is similar to the previous work conducted by several researchers (Dippong et al., 2022; Zhang & Wu, 2013). The appearance of hematite in $MnFe_2O_4$/PEG materials is caused by the high annealing temperature of that material which is up to 400 °C. In addition, every sample has no impurities indicating that both samples have a single phase.

In addition, the results of the structural analysis for both samples are shown in Table 1. The lattice parameters of the $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG samples are 8.40 nm and 8.41 nm, respectively. Meanwhile, the size of the crystallites of the $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG is in the range of 5.41 – 6.72 nm. From Table 1, it can be seen that the strain of $CoFe_2O_4$/PEG is higher than $MnFe_2O_4$/PEG. This is attributed to the defect of the crystal in that material.

Table 1. Structural parameters of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG materials

Sample	Lattice Parameter (Å)	Crystallite Size (nm)	Strain
$CoFe_2O_4$/PEG	8.40	5.41	0.046
$MnFe_2O_4$/PEG	8.41	6.72	0.037

The morphology of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG is depicted in Figure 2. Based on Figure 2, the particle size distribution in both samples is in the range of 67 – 73 nm. The particle size of $CoFe_2O_4$/PEG is smaller than $MnFe_2O_4$/PEG. This is in good agreement with the results obtained from XRD analysis. In addition, the $CoFe_2O_4$/PEG material appears to be more agglomerated and lighter than $MnFe_2O_4$/PEG.

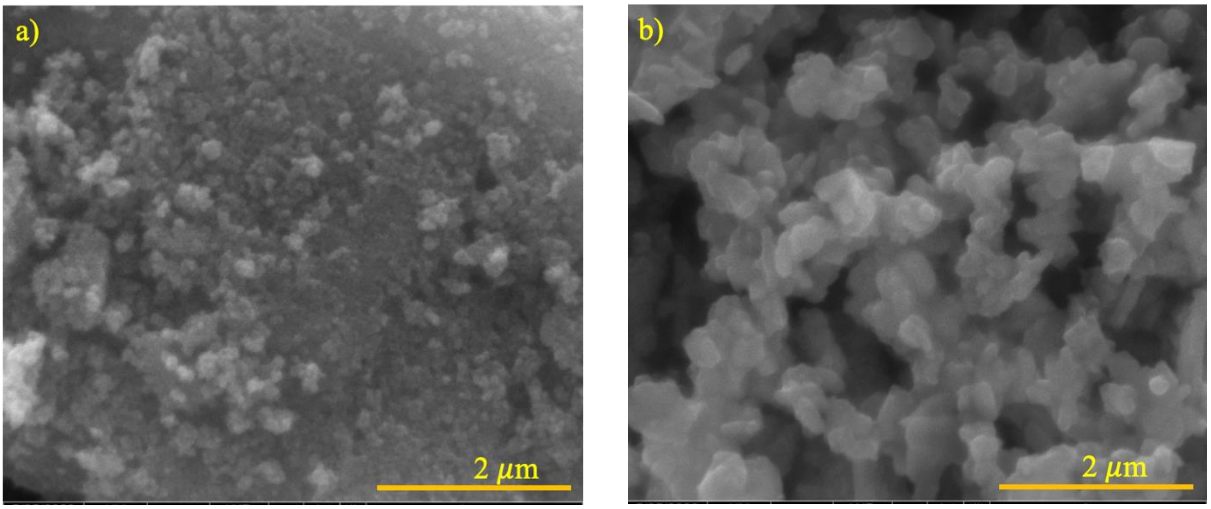

Figure 2. The morphology of a) $CoFe_2O_4$/PEG and b) $MnFe_2O_4$/PEG materials

The FTIR spectra of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG are displayed in Figure 3. Based on Figure 3, the vibrational mode of Fe – O tetrahedral appears on the wave number of 600 – 690 cm^{-1}. Also, there is a bonding of M – O (M = Co and Mn) octahedral investigated in the wave number of 400 – 460 cm^{-1}. In addition, vibrational stretching of C – O – C is appeared on the wave number of 900 – 1150 cm^{-1}. This is attributed to the result of bonding between $CoFe_2O_4$ or $MnFe_2O_4$ with PEG. Another bonding is investigated which is O – H bonding, confirming water molecules absorbed on the surface of the material when the synthesis process is conducted.

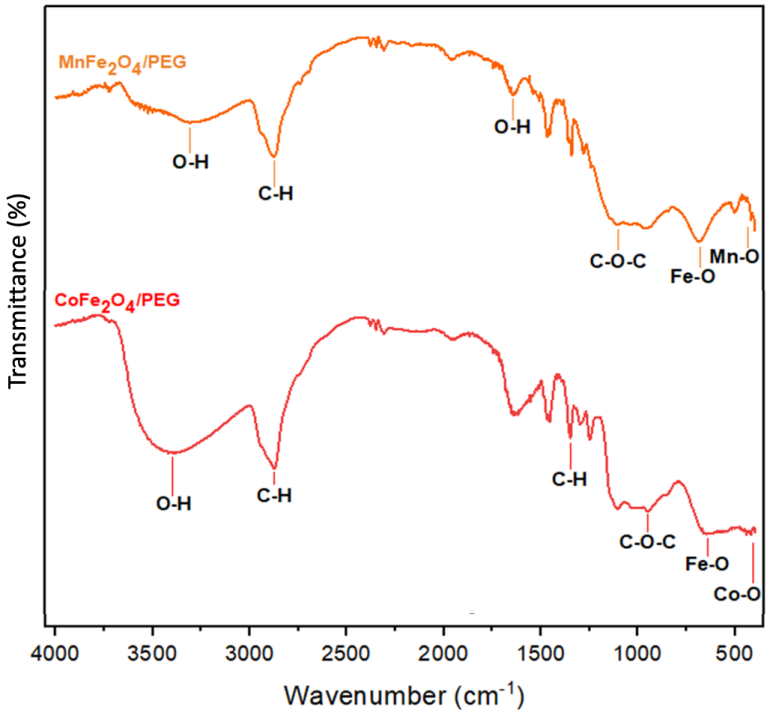

Figure 3. The FTIR spectra of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG materials

Magnetic properties of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG are investigated by the VSM instrument, and the result of the sample is depicted in Figure 4. Based on Figure 4, loop hysteresis of $CoFe_2O_4$/PEG is broader than $MnFe_2O_4$/PEG, indicating that $CoFe_2O_4$/PEG is hard magnetic while $MnFe_2O_4$/PEG is included in soft magnetic materials.

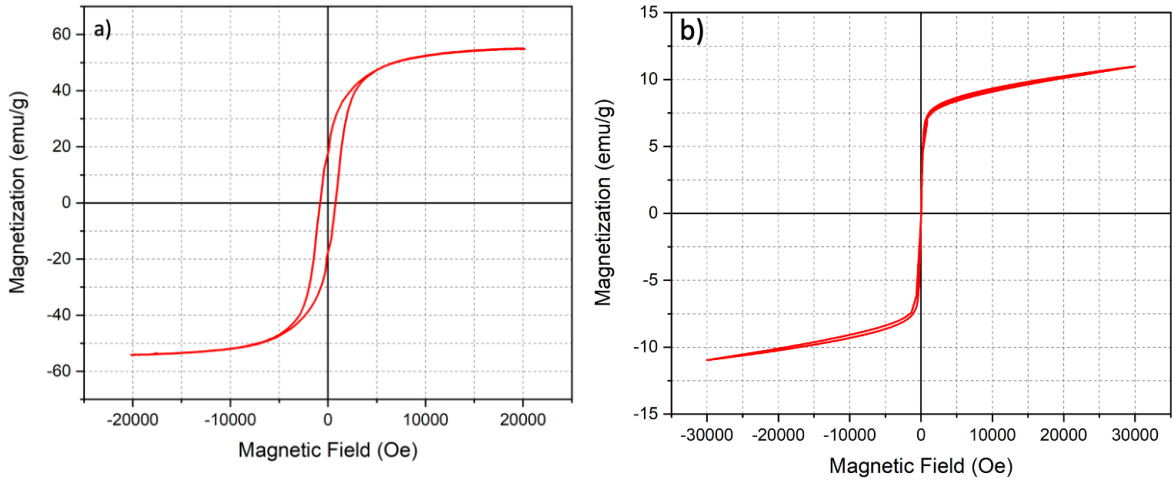

Figure 4. Magnetic Properties of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG materials

Based on the hysteresis shown in Figure 4, the saturation magnetization of $CoFe_2O_4$/PEG is 54.85 emu/g which is higher than $MnFe_2O_4$/PEG (11 emu/g). This is followed by the trend of remanent magnetization that $CoFe_2O_4$/PEG possesses higher remanent magnetization (17.44 emu/g) compared to $MnFe_2O_4$/PEG (0.17 emu/g). Meanwhile, the value of the coercivity field of $CoFe_2O_4$/PEG is 788 Oe which is also higher than $MnFe_2O_4$/PEG having the coercivity field of 7.42 Oe. The higher value of saturation magnetization, remanent magnetization, and coercivity of $CoFe_2O_4$/PEG is attributed to the type of magnetic properties,

namely ferromagnetic. In addition, $MnFe_2O_4$/PEG is included in the paramagnetic materials so that it has low magnetic properties. The detailed magnetic parameters of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG are provided in Table 2.

Table 2. Magnetic parameters of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG materials

Sample	Saturation magnetization (emu/g)	Remanent magnetization (emu/g)	Coercivity (Oe)
$CoFe_2O_4$/PEG	54.85	17.44	788
$MnFe_2O_4$/PEG	11	0.17	7.42

The efficiency of drug loading and drug release of the Doxorubicin (DOX) is analyzed by UV-VIS spectroscopy. The wavelength around 480 nm is observed with the appearance of the absorbed peak for both samples. Based on the drug loading analysis, it is found that the drug loading of $CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG is 2.881 mg DOX/g NP with the efficiency of 98.8 % and 2.811 mg DOX/g NP with the efficiency of 96.3 %, respectively. This is in good agreement with the result of XRD and SEM analysis that the drug loading of $CoFe_2O_4$/PEG is higher than $MnFe_2O_4$/PEG. This is because $CoFe_2O_4$/PEG has a smaller particle size so it has a larger surface area informing better drug loading. Meanwhile, the percentage of release cumulative of $CoFe_2O_4$/PEG is found 30.6 % which is lower than the $MnFe_2O_4$/PEG reaching up to 51.6 %

CONCLUSION

$CoFe_2O_4$/PEG and $MnFe_2O_4$/PEG materials have been successfully prepared using the coprecipitation. The crystal structure of $CoFe_2O_4$/PEG is cubic spinel while the structure of $MnFe_2O_4$/PEG is hematite with a lattice parameter is about 8.40 nm. In addition, the particle size of $CoFe_2O_4$/PEG is smaller than $MnFe_2O_4$/PEG. The smaller the particle size is, the bigger the surface area is. It is attributed to the better drug loading on the drug delivery system. Meanwhile, $CoFe_2O_4$/PEG is detected included in hard magnetic material (ferromagnetic), and $MnFe_2O_4$/PEG is included in soft magnetic material having low coercivity.

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