

Fabrication and Characterization of SPIONs for Drug Loading and Release Applications

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Abstract. Superparamagnetic iron oxide nanoparticles (SPIONs) were synthesized for metformin and probiotic drug delivery agents. In this work, the lattice parameter of SPIONs formation was 8.351, constructing an inverse spinel cubic with a crystallite size of 10.18 nm, respectively. The SPIONs formation was also detected by the presence of Fe–O functional groups, which were Fe–O tetrahedral and octahedral functional groups at 625–700 cm^{-1} and 418–500 cm^{-1} , respectively. In this experiment, SPIONs exhibited spherical particles with a size of 35.12 nm and presented superparamagnetic character with a saturation magnetization of 41.45 emu/g. Interestingly, SPIONs exhibited loading activity for metformin and probiotics with loading efficiencies of 67.51% and 80.67%, respectively.

1 Introduction

In the last decade, investigations in the health sectors, especially related to nanotechnology, such as drug delivery systems, have been intensively developed [1]. The intention is related to the great potential to solve issues, particularly in the progression of a disease condition [2]. In this context, drug delivery performance is strongly correlated with nanoparticles, controlling direct drug targets. Superparamagnetic iron oxide nanoparticles (SPIONs) with particle sizes of 10–100 nm become one of the most commonly used as drug delivery agents. SPIONs exhibited interesting properties such as stability, biocompatibility, and environmental sustainability [3]. A previous work has shown that SPIONs exhibit beneficial properties for more even loading and release of drugs, leading to serving as drug delivery agents. However, there are limited investigations related to the use of SPIONs as delivery agents for metformin and probiotics.

Metformin has been frequently used to reduce inflammatory cell infiltration, steatosis, and fibrosis in the liver. Furthermore, probiotics have been employed in providing an alternative complementary therapy to increase good microbes and treat liver problems [4]. Previous research has shown that the combination of probiotics and metformin was able to significantly reduce inflammation and adipose tissue in patients [5]. This was also proven in research conducted by Sophia et al., that metformin and probiotics can be released simultaneously without disrupting kidney function, and can reduce glomerular hypertrophy and glomerulosclerosis [6]. Interestingly, metformin and probiotics are drugs that can be

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classified as oral medications [10],[11]. In this context, oral drug delivery significantly reduces the frequency of drug administration and the total amount of medication compared to conventional oral medications. Previous research has shown that nanotechnology-based oral drug delivery can improve drug solubility and enhance drug absorption through cellular membranes, prerequisites for oral drug delivery. Therefore, the use of SPIONs as drug delivery agents is highly promising in nanotechnology-based drug delivery systems, both in terms of drug loading and release, until the drug is received by the target fat in the liver [9]. This study aims to synthesize and characterize SPIONs to be used as an effective drug delivery system, as well as to evaluate physicochemical characterization and the effectiveness of the loading and release of metformin and probiotics.

2 Methods

In this study, SPIONs were synthesized using the coprecipitation method, following the steps outlined in our previous study [10]. The SPION was characterized using X-ray Diffraction (XRD), Fourier Transform Infrared Spectroscopy (FTIR), Scanning Electron Microscope (SEM), Vibrating Sample Magnetometer (VSM), drug loading test, and drug release test. The results of the drug loading were tested using UV-Vis characterization to determine the absorption value. The data were analyzed qualitatively and quantitatively to be correlated among the characterization results.

3 Results and Discussion

The SPION diffraction pattern from the XRD characterization results is shown in Figure 1. Based on this figure, it is known that diffraction peaks were detected at $2\theta = 30.2^\circ$, 35.7° , 43.2° , 57.2° , 62.9° . These results are consistent with the Fe_3O_4 database, namely AMCS D 0000945, associated with the respective hkl planes (220), (311), (400), (422), (511), and (440). These peaks are characteristic of the SPION phase with an inverse spinel crystal structure arranged in a face-centered cubic structure [11]. Furthermore, the analysis results show that SPIONs have a crystallite size of 10.18 nm with a lattice parameter of 8.351 Å.

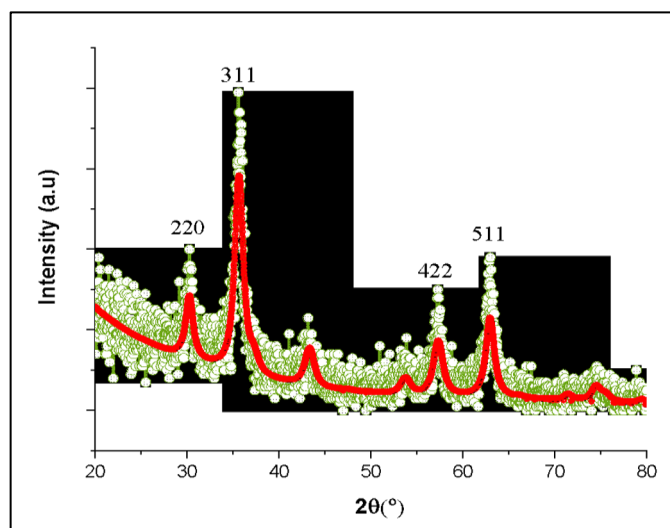


Fig. 1. Diffraction pattern of SPIONs

Figure 2 shows the FTIR spectrum of SPIONs in the range of 400–4000 cm^{-1} . Based on the FTIR spectrum, there are Fe-O tetrahedral and octahedral functional groups at 625–700 cm^{-1} and 418–500 cm^{-1} , respectively. These results are similar to previous studies [12]. In addition to Fe–O, the FTIR spectrum also detects O–H groups at 2832–3800 cm^{-1} and 1300–1650 cm^{-1} , which are related to stretching and bonding vibrations, respectively [13].

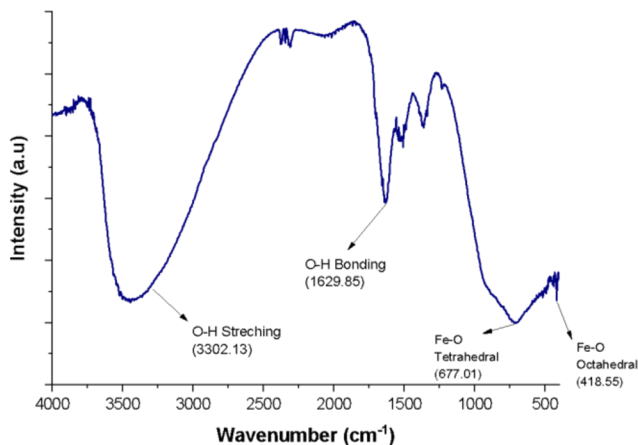


Fig. 2. FTIR spectrum of SPIONs

The surface morphology and particle size distribution of SPIONs were analyzed using a scanning electron microscope at 150,000 \times magnification, as shown in Figure 3. Based on Figure 3 (a), it is known that SPIONs have a spherical shape and tend to form homogeneous particle sizes, which generally form a more regular crystalline structure. Based on the data analysis, SPIONs have a particle size distribution of 35.12 nm.

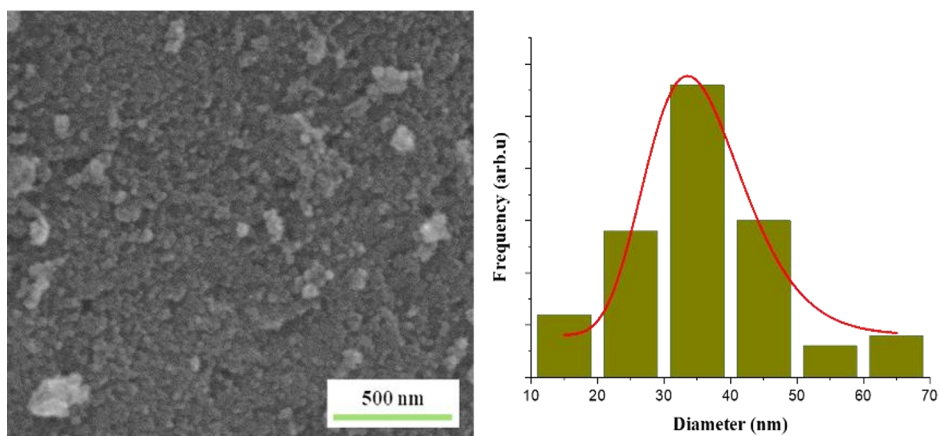


Fig. 3. Morphology and particle size distribution of SPIONs

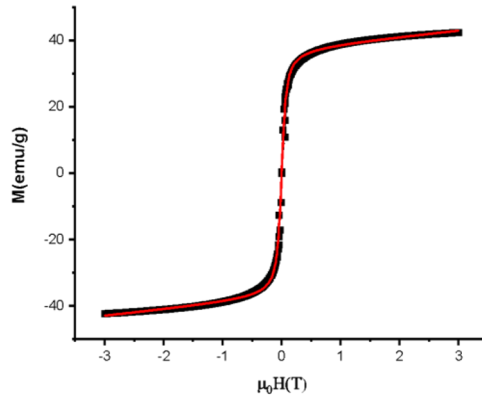


Fig. 4. Hysteresis curve of SPIONs

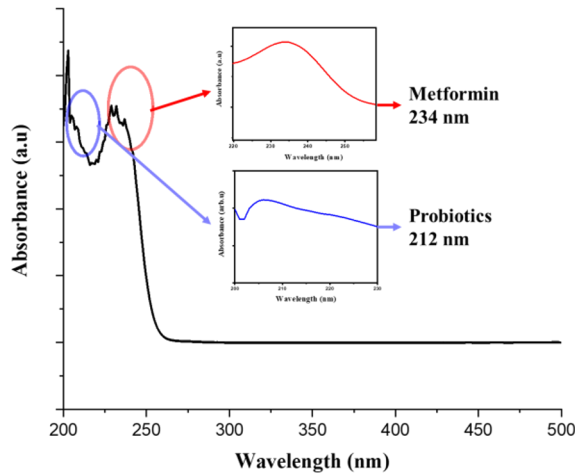


Fig. 5. Drug loading of SPIONs for metformin and probiotics

The hysteresis curve of SPIONs shown in Figure 4 has an S-shape, which is characteristic of superparamagnetic behavior. Furthermore, the hysteresis curve was also analyzed using the Langevin method with susceptibility (Equations 1–2) [14].

$$M = M_r + M_s \times \left(\coth(C \times H) - \frac{1}{C \times H} \right) + \chi \times H \quad (1)$$

M , M_r , and M_s are magnetization (emu/g), remanent magnetization (emu/g), and saturation magnetization (emu/g).

$$C = \frac{\mu}{k_B T} \quad (2)$$

H is the magnetic field (T), χ is the susceptibility, and k_B is the Boltzmann constant with the value of 1.38×10^{-23} J/K. The magnetic property parameters obtained were saturation magnetization of 41.45 emu/g and remanent magnetization of 0.0199 emu/g. Qualitatively, SPIONs exhibit superparamagnetic properties with coercive field and magnetic remanence values that are very small, approaching zero.

In this study, the performance of SPIONs as a loading agent for metformin and probiotics was tested, with the results shown in Figure 5. Based on the figure, it can be seen that there are absorbance peaks at wavelengths of 233 nm and 212 nm, which represent the absorbance peaks of metformin and probiotics. These results are in line with previous studies reporting that the absorbance peaks of metformin and probiotics are in the range of 221–241 nm [15].

The drug loading test requires prior calibration of metformin and probiotic concentrations. The calibration identified the wavelength with the highest absorption, which is important to determine the drug loading percentage. In this experiment, SPIONs exhibited drug loading for metformin with an efficiency of approximately 67.51%. On the other hand, SPIONs also exhibited drug loading for probiotics with an efficiency of approximately 80.67%. These findings suggest that SPIONs show high potency as drug delivery agents for metformin and probiotics.

4 Conclusion

SPIONs have been fabricated for metformin and probiotics drug delivery agents. The formation of SPIONs was confirmed by XRD analysis, where SPIONs had an inverse spinel cubic with a lattice parameter of 8.351 Å. Furthermore, the FTIR spectrum indicated the presence of octahedral and tetrahedral Fe–O stretching vibration at 625–700 cm⁻¹ and 418–500 cm⁻¹, respectively, which are characteristic functional groups of SPIONs. SPIONs had an average particle size of 35.12 nm with supermagnetic behavior. Interestingly, SPIONs exhibited drug delivery performance with good loading capacity for both metformin and probiotics. Based on these results, SPIONs are highly effective as a carrier system for delivering metformin and probiotics.

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