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Ferrite Nanoparticles for Biomedical Application

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Abstract: *Ferrite nanoparticles have gained a lot of attention in recent years due to their applications in diverse fields and particularly in the biomedical field where their enhanced magnetic properties offer diversity in imaging, diagnosis and treatment. The ferrite nanoparticles have been widely used for biomedical applications for their inherent biocompatibility and good binding properties with most of the chemicals. The significant magnetization and superparamagnetic behaviour of the ferrite nanoparticles suggest the usage of streptokinase coated ferrite nanoparticles as potential candidates for targeted drug delivery systems. These biological studies require supporting physical characterization studies on ferrite nanoparticles. This work examines the magnetization and FTIR spectroscopy on a batch of chemically synthesized ferrite nanoparticles.*

Keywords: Nanoparticles; Magnetization; Superparamagnetic; Streptokinase

I. INTRODUCTION

Since ancient Greek time, lodestone, i.e., bulk magnetite (Fe_3O_4), has been used in the treatment of common ailments. Ferrites are ferrimagnetic ceramic compounds derived from iron oxides such as hematite (Fe_2O_3) or magnetite(Fe_3O_4) as well as oxides of other metals. Ferrites are classified as soft and hard which refers to their low or high coercivity of their magnetism. Iron oxide in small concentrations can be ingested by living cells. Biodegradation of iron oxide nanoparticles releases free iron that is incorporated into the haemoglobin making the body free of residual iron oxide nanoparticles. Hence iron oxide nanoparticles are preferred in biomedical application. With the advancement in nano-biotechnology, such magnetic ferrite nanoparticles (MFNPs)have become popular due to their applications in biomedical field.

II. METHODOLOGY

Ferrite nanoparticles were synthesized by a wet chemical route of co-precipitation of acidic solution of ferrous and ferric chlorides by slow addition of a base (NaOH) under continuous stirring. The reaction temperature was maintained at 80ºC and the pH of the solution was above 12. The resultant black precipitate was washed several times with acetone and centrifuged at 5000 rpm for 10 minutes. The powder obtained after discarding the supernatant was dried at 50ºC for 24 hours and stored at room temperature for immobilization and analysis. Stock solutions of the enzymes were prepared in a phosphate buffer and stored at 4ºC. These solutions were mixed with the nanoparticles using carbodiimide as binding agent by incubating under shaker conditions for 24 hours at room temperature [1].

III. RESULTS AND DISCUSSIONS

3.1 XRD Analysis

The structural properties of ferrite were analysed by X-ray powder diffraction (XRD) with a JDX-8030 X-ray diffractometer using the monochromatized X-ray beam from the nickel-filtered CuK$\propto$ radiation. The average size of the crystals (D; Å) was estimated using Scherrer's formula $D = K \lambda L / \beta \cos \theta$.

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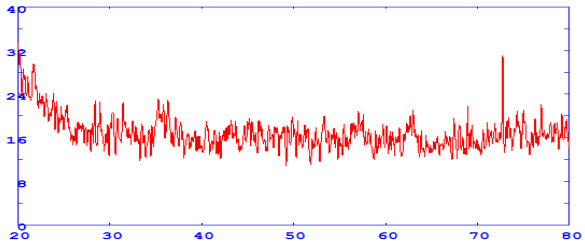

Figure 1: Intensity (Count) vs 2θ forferrite at pH 7.5

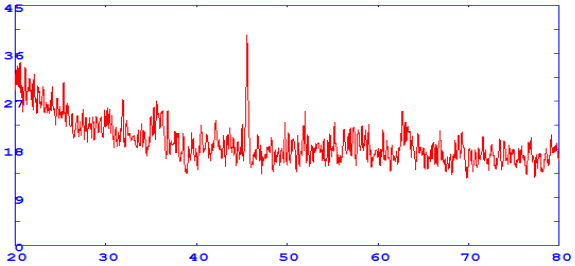

Figure 2: Intensity (Count) vs 2θfor ferrite at room temperature, pH 9

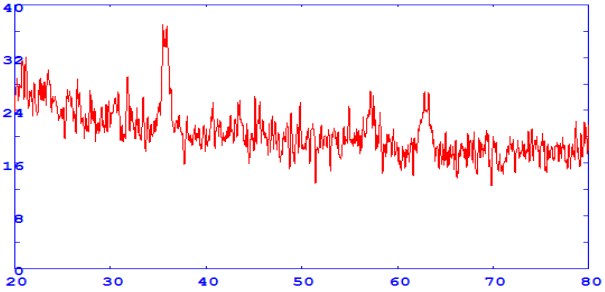

Figure 3: Intensity (Count) vs 2θfor ferrite at 80ºC, pH 9

The size of ferrite at pH 7.5 could not be estimated using Scherrer's formula. The absence of the peaks indicates improper formation and amorphous nature of the sample. The broadening of the peak indicates the small size. At room temperature ferrite nanoparticles formed were 25nm in size. It is observed that reaction temperature affects the particle size, phase, and reaction time. At 80ºC highly magnetic, black ferrite nanoparticles were formed approximately 28nm in size. The exercise of varying the reaction parameters of synthesis, pH of reactants clearly shows that the Fe_3O_4 phase is formed for pH above 10 and temperature of about 80ºC.

3.2 SQUID Analysis

The magnetization studies on the particles before and after enzyme immobilization was carried out on a SQUID magnetometer.

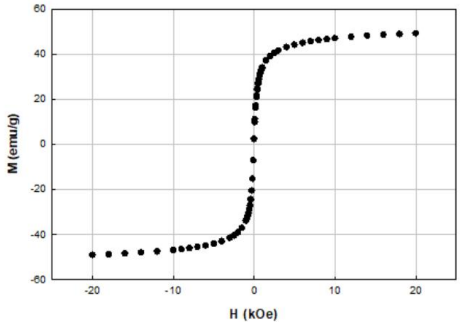

Figure 4: Free ferrite nanoparticles

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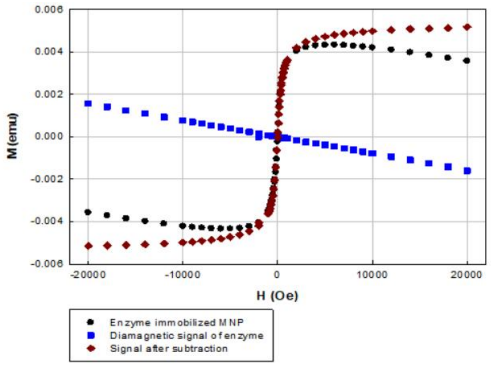

Figure 5: Enzyme streptokinase coated ferrite nanoparticles

The free ferrite nanoparticles have a high magnetization of 50 emu/g and very low coercivity, indicative of superparamagnetic behaviour. The magnetization of the immobilized suspensions after subtracting the diamagnetic signal of the blank enzyme shows a similar superparamagnetic behaviour with a minor reduction in magnetization as compared to the ferrite nanoparticles[2]. This data is of value in the desired medical application of formulating targeted drug delivery systems.

3.3 FTIR Spectroscopy

FTIR spectroscopy of the uncoated ferrite nanoparticles and enzyme streptokinase coated ferrite nanoparticles was carried out at Dept of Chemistry, University of Mumbai. It was used to confirm the binding of CHO to the particles.

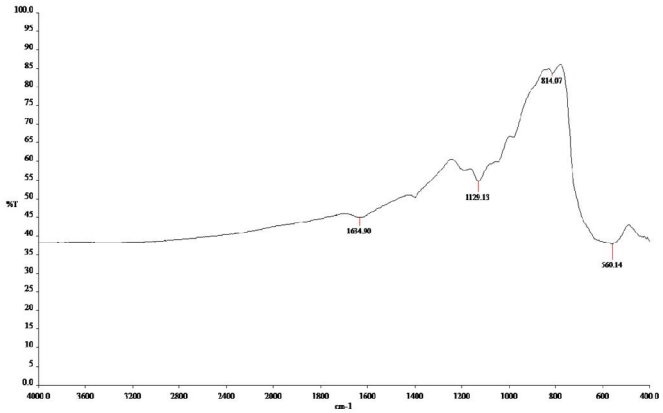

Figure 6: Uncoated ferrite nanoparticles

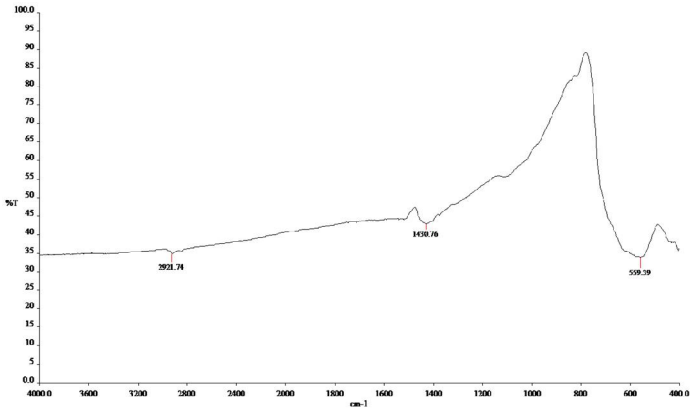

Figure 7: Enzyme streptokinase coated ferrite nanoparticles

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The FTIR spectra of both the uncoated ferrite nanoparticles and enzyme streptokinase coated ferrite nanoparticles are presented. The peak corresponding to uncoated ferrite nanoparticles has generally been reported to be in the range of 800-1000 cm-1 and we observe the peak at 814 cm-1. This peak is sharper in the enzyme streptokinase coated ferrite nanoparticles. The enhancement in the peak in the enzyme streptokinase coated ferrite nanoparticles suggests the distinct signal available from these nanoparticles and the absence of clustering. This idea receives further support from the magnetization study on these samples carried out on a SQUID magnetometer [2].

3.4 Bio-activity Studies on the Enzyme Streptokinase Coated Ferrite Nanoparticles

The lysis assay studies of the free and bound ferrite nanoparticles revealed that the stability and thrombolytic activity of the enzymes (streptokinase and urokinase) were significantly improved upon binding to the ferrite nanoparticles. Thrombolytic agents are administered to dissolve clots associated with cardiac blocks. The use of ferrite nanoparticles is to have a magnetically guided system to target the drug to the desired site and avoid side effects. This targeted delivery will also enable the reduction in dosage of the enzymes. The enhancement in thrombolytic activity [2] with the observation of significant magnetization and superparamagnetic behaviour of the ferrite nanoparticles suggest the usage of the enzyme streptokinase coated ferrite particles as potential candidates in treating thrombolysis.

IV. Conclusion

The results of the physico-chemical characterization on the ferrite nanoparticles along with the supporting biological studies suggest them to be potential candidates for various biomedical applications. The results of varying the reaction parameters of synthesis. pH of reactants etc. it is clear that the Fe3O4 phase is formed for pH above 10 and temperature of about 80ºC. The magnetization studies performed on a SQUID magnetometer shows superparamagnetic behaviour for both uncoated and enzyme streptokinase coated ferrite nanoparticles.FTIR spectroscopy of the free and enzyme streptokinase coated ferrite nanoparticles confirms the binding of CHO group of the enzyme streptokinase to the ferrite nanoparticles. The lysis assay studies of the free and bound ferrite nanoparticles revealed that the stability and thrombolytic activity of the enzymes (streptokinase and urokinase) were significantly improved upon binding to the nanoparticles. Based on these observations, the chemically synthesized ferrite nanoparticles and the subsequent enzyme streptokinase coating of ferrite nanoparticles render it suitable for biomedical application (tested for lysing of blood clots). Further, the retention of superparamagnetic behaviour after enzyme streptokinase coating on ferrite nanoparticles suggests their usage as potential candidate for magnetically guided targeted drug delivery system.

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Biography

At present Ms. Meghna A. Merchant is pursuing her PhD programme under the guidance of Prof. Vaishali A. Bambole from Department of Physics, University of Mumbai. She has obtained herdegrees M.Sc. and M. Phil from University of Mumbai.Ms. Meghna A. Merchant has worked as an Assistant Professor in Physics at Veermata Jijabai Technological Institute, Rizvi College of Engineering, Vidyavardhini College of Engineering and Technology.