ISSN (e) 2520-7393
ISSN (p) 2521-5027
www.estirj.com

Magnetic Iron Oxide Nanoparticles: An Effective Approach to Reduce Cholesterol

Nisar Ali Othi [1], M I Abro [2], MA Bhutto [3]

[1,2,]*Department of Metallurgy and Materials Engineering Mehran University of Engineering and Technology, Jamshoro*
[3] *IBGE, University of Sindh ,Jamshoro*

Abstract: Cholesterol is a lipid molecule in lipoprotein and cell membrane and precursor of bile acids, steroids hormones and vitamin D. There are two types of cholesterol in human blood HDL (high density lipoprotein) referred to as good cholesterol and LDL (low density lipoprotein) referred to bad cholesterol. Higher levels of cholesterol, especially LDL, become a cause of cardiovascular disease (CVD). In this research iron oxide (Fe_3O_4) nanostructures were used as selective adsorption materials for cholesterol. Iron oxide nanoparticles were synthesized using a hydrothermal method then coated with lysine amino acid ($C_6H_{14}N_2O_2$). The uncoated (Fe_3O_4-P) and coated (Fe_3O_4-L) iron oxide nanoparticles samples were characterized by XRD, FTIR and DLS analysis. The particles were then analyzed for adsorption of cholesterol using uv-visible spectroscopy. Outstanding adsorption capacity (13.63%) was observed for Fe_3O_4-L in just 20 minutes.

Keywords: *Cholesterol, Cardiovascular disease, Iron oxide nanoparticles, Lysine*

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide accounting for 32% of death from chronic disease in the world[1] [2]. Cardiovascular disease are heart disease and related disorder such as arrhythmia, rheumatic heart disease, atherosclerosis, coronary heart disease, peripheral arterial disease, congenital heart disease, thrombosis, and pulmonary embolism, all are due to changes in the normal functioning of the heart and its associated structures. The main explanation for this reported disease is a sedentary lifestyle with little or no which has been identified as the main cause of CVD in human[3] [4] . Cardiovascular disease occurs due to cholesterol in human blood, Cholesterol is the waxy, fat-like material present in each cell of the body. Body needs some cholesterol to make hormones, food processing substance and nutrient D. Body will produce all the cholesterol that it requires. If there is an excess of cholesterol in the blood, plaque might be delivered by blending in with other substance in the blood. Plaque sticks in blood vessel dividers it might cause illness of the coronary course, where coronary conduits become restricted or obstructed. In sound human serum 200 mg/dL measure of cholesterol is alluring. There are two type of cholesterol, High-density lipoprotein (HDL) and Low-density lipoprotein (LDL). High density lipoprotein (HDL) also known as good cholesterol and Low-density lipoprotein also known as bad cholesterol [5]. Methods for cholesterol reduction from human body are physical exercise, medication, and LDL-Apheresis therapy[6]. In this research amino acid coated on iron oxide nanostructures and used for Cholesterol treatment. although several drugs are available for the treatment of hyperlipidemia. Iron oxide (Fe_3O_4) Nanoparticles play crucial role in the field of nanotechnology and in drug delivery[7]. Iron oxide (Fe_3O_4) NPs dependents upon their smallest size and as compared to other transition metal iron is rich in the earth crust[8]. Attractive Iron oxide (Fe_3O_4) NPs focus due to their properties, for example, superparamagnetic properties, surface territory and volume proportion, low poisonousness, size, shape, crystallization, and engineered technique. Iron oxide (Fe_3O_4) NPs have been used in biomedical field such as drug delivery, thermal therapy, diagnostic, and magnetic resonance imaging (MRI) [9][10]. Synthesis of iron oxide (Fe_3O_4) nanostructures is critical for its novel attractive properties, especially super-paramagnetic behavior, and biomedical applications, Magnetite nanostructures are utilized in different vital gadgets and have applications in mechanical and restorative supplies. Magnetite is one of the vital part of Ferrites that appear extraordinary innovative and logical intrigued[11]. Magnetite has a cubic converse spinal structure with Fe cations involving tetrahedral destinations and octahedral locales and oxygen shaping an 'FCC' closed packing. Iron oxide (Fe_3O_4) NPs has coating with PEG for enhance the biocompatibility and incorporate efficiency of NPs[12].

2.EXPERIMENTAL WORK

Chemicals

Iron(iii) chloride anhydrous ($FeCl_3$), Polyethylene glycol (PEG 400), Hydrazine (N_2H_2), Deionized water, L-lysine ($C_6H_{14}N_2O_2$) was purchased and used in this study.

Synthesis of Iron Oxide (Fe_3O_4) NPs

Synthesis of iron oxide nanoparticles was carried out by using hydrothermal method. Polyethylene glycol (PEG) 10 ml was added to 60 ml deionized water followed by addition of 320 mg of Iron chloride anhydrous ($FeCl_3$), and prepared under magnetic stirrer, subsequently 1 ml Hydrazine (N_2H_2) was added dropwise, the synthesis shown in Figure.1.

After stirring reddish solution was obtained, which then transfer into Teflon autoclave and heated at 120°C temperature in muffle furnace for 4hr. Finally, iron oxide (Fe_3O_4) magnetic nanoparticles were collected using magnetic separation and washed three times with deionized water, then dried at 90°C for 8hr before further characterization and use.

Iron Oxide (Fe_3O_4) NPs Coated with Lysine Amino Acid ($C_6H_{14}N_2O_2$)

Iron oxide (Fe_3O_4) was then further modified by using amino acid (lysine). For this, 100 mg lysine was dissolved in 10 ml deionized water, after that 50 mg of synthesized iron oxide (Fe_3O_4) nanoparticles were suspended in the solution followed by heating at 800C for 1 hr. Then the particles were collected, washed, and dried for further characterization and use. The pristine iron oxide nanoparticles were termed as Fe_3O_4-P and after lysine coating it is termed Fe_3O_4-L in the document.

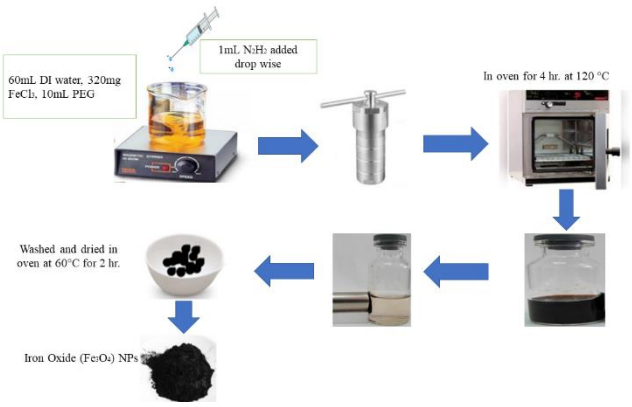

Figure 1: Synthesis of iron oxide NPs

Characterization

X-Ray Diffraction (XRD) was used to investigate the crystallographic structure of iron oxide nanoparticles. Fourier transformed infrared spectroscopy (FTIR) was done of pristine and coated iron oxide (Fe_3O_4) nanoparticles by using PerkinElmer (Model: Spectrum Two) instrument in the wave number region of 3500-400 cm^{-1} to obtain the characteristic peaks of samples. FTIR was also done after cholesterol removal investigation. Morphology of iron oxide NPs were investigated by using scanning electron microscopy (Model: JEOL6380L). Dynamic light scattering (DLS) was done by using Malvern (Model: Nano-ZS) instrument to determine the particle size of nanoparticles. UV Visible Spectroscopy was done by using PerkinElmer (Model: Lambda 365) instrument to investigate the cholesterol removal efficiency of the nanoparticles.

4. Results and Discussion

The XRD patterns of Fe_3O_4-P and Fe_3O_4-L demonstrated the characteristic peaks of magnetite and match with JCPDS card number 19-0629, as shown in Figure.2. The intense peaks at the values expressed in 2$\boldsymbol{\theta}$ degrees of 31.6º, 35.7º, 43.4º, 57.5º, and 63.8º corresponding to 220, 311, 400, 422 and 511 crystal planes respectively [13]. Using Bragg's law, the lattice parameter, a, and interplanar spacing, d, were estimated. The XRD pattern reveals the formation of a magnetite crystalline structure with a lattice parameter about a = 0.839nm and d_{311} = 0.242 nm, respectively.

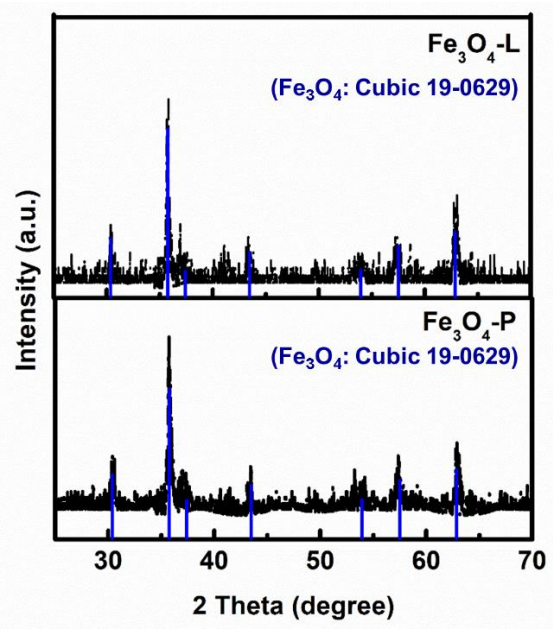

Figure 2: XRD of Fe_3O_4-P and Fe_3O_4-L

FTIR absorption spectra of pristine iron oxide (Fe_3O_4-P) and lysine coated iron oxide (Fe_3O_4¬L) are shown in Figure.3. The analysis of the infrared (IR) spectra confirms the monomer obsession of iron oxide (Fe_3O_4) nanoparticles. The bonds appear at 3438cm^{-1} may be attributed to the O-H vibrating stretching. Moreover, the existence of peaks at 1633cm^{-1} and 1426cm^{-1} are assigned to C-H bending C-O stretching bands respectively. Peaks at 878 cm^{-1} and 464 cm^{-1} are contributing to Fe–O bond and 574.24 579 $cm^{-1}$are the identical peak for Fe_3O_4. Which nearly coincides with the reported peak values. After the amino acid coating Fe-O absorption band at 428cm^{-1} stretch is diminished, that indicating acidic medium coated[14] [15] [16] [17].

Morphology of iron oxide (Fe_3O_4) nanoparticles was confirmed by using SEM analysis as shown in Figure.4. The obtained results using scanning electron microscopy analysis clearly show the pristine and coated nanoparticles have spherical shape. Slight increase in size was also observed after the coating of amino acid.

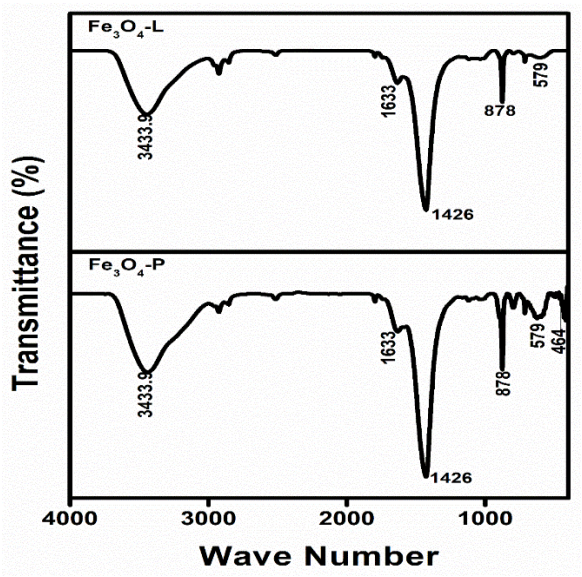

Figure 3: FTIR of Fe_3O_4-P and Fe_3O_4-L

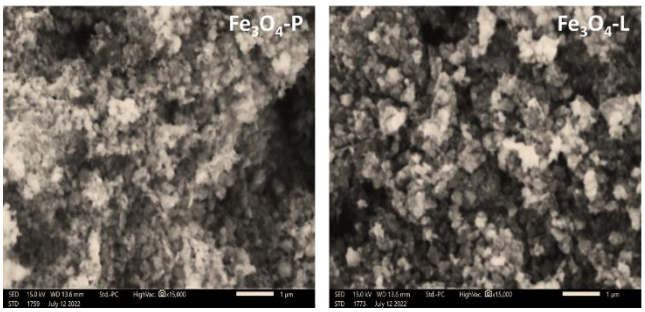

Figure 4: SEM of Fe_3O_4-P and Fe_3O_4-L

Particle size was determined by dynamic light scattering measurement as shown in Figure.5. Pristine iron oxide nanoparticles show mean particles size of 116.5 nm while lysine coated iron oxide shows mean particle size of 135 nm. The increase in size of the nanoparticles verifies that amino acid coating which is attributed to the cholesterol removal.

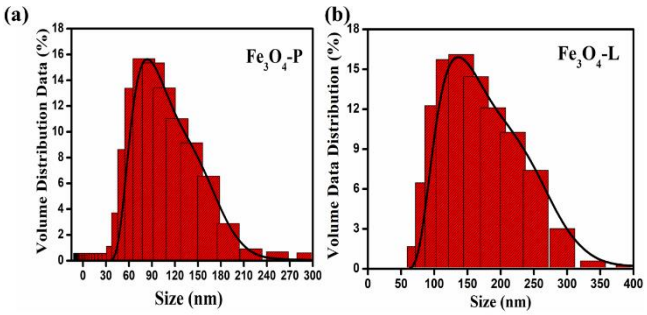

Figure 5: Size distribution of (a) Fe_3O_4-P (b) Fe_3O_4-L

Cholesterol (100µL) was added in 20ml phosphate buffer solution in three different beakers. After that 5 mg each Fe_3O_4-P and Fe_3O_4-L were added to two separate beakers and no particle was added to third beaker and the beakers were incubated at 37^0C under uv-light. Sample was collected after different time intervals and investigated using uv-visible spectroscopy for determination of cholesterol level and the results are shown in Figure.6. cholesterol level decreasing in different medium. It is observed that only uv-visible light does not remove the total cholesterol while the addition of nanoparticles lowers the cholesterol level in the PBS solution. It is evident from the result that lysine coated iron oxide shows better cholesterol removal (13.63%) after 20 min exposure time. This is due to ionic interaction between positively charged region of the cholesterol and negatively charged region of lysine[18].

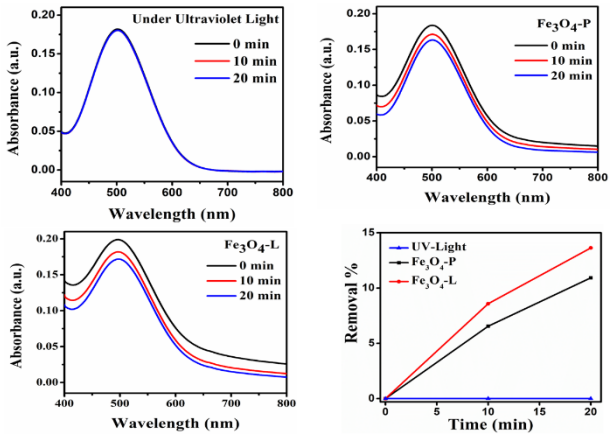

Figure 6: Cholesterol removal by (a) uv-light (b) Fe_3O_4-P (c) Fe_3O_4 -L and (d) Removal percentage efficiency

5. Conclusion

In this study, hydrothermal approach for the synthesis of lysine coated nano iron oxide nanoparticles was utilized. The particles were analyzed using XRD, FTIR, SEM, DLS and uv-visible spectroscopy. XRD and FTIR study confirms the formation of Fe_3O_4 nanoparticles and spherical morphology was determined by using SEM. Lysine coated nano iron oxide nanoparticles has demonstrated excellent cholesterol removal efficiency than pristine iron oxide nanoparticles. About 13.63% cholesterol removal was observed in 20 minutes for Fe_3O_4-L. Potentially and promisingly the advance strategy for the design of iron oxide nano particles would be an alternative roadmap to cholesterol removal application.

References

[1] M. Bansal, "cardiovascular disease and COVID-19," *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, vol. 14, no. 3, pp. 247–250, May 2020, doi: 10.1016/j.dsx.2020.03.013.

[2] Y. Shi *et al.*, "Epigenetic regulation in cardiovascular disease: mechanisms and advances in clinical trials," *Sig Transduct Target Ther*, vol. 7, no. 1, p. 200, Jun. 2022, doi: 10.1038/s41392-022-01055-2.

[3] N. J. Wald and M. R. Law, "A strategy to reduce cardiovascular disease by more than 80%," vol. 326, 2003.

[4] H. Chopra *et al.*, "Nanomaterials: A Promising Therapeutic Approach for Cardiovascular Diseases,"

Journal of Nanomaterials, vol. 2022, pp. 1–25, Feb. 2022, doi: 10.1155/2022/4155729.

[5] N. R. Nirala, S. Abraham, V. Kumar, A. Bansal, A. Srivastava, and P. S. Saxena, "Colorimetric detection of cholesterol based on highly efficient peroxidase mimetic activity of graphene quantum dots," *Sensors and Actuators B: Chemical*, vol. 218, pp. 42–50, Oct. 2015, doi: 10.1016/j.snb.2015.04.091.

[6] Y. Wang *et al.*, "Pollens derived magnetic porous particles for adsorption of low-density lipoprotein from plasma," *Bioactive Materials*, vol. 6, no. 6, pp. 1555–1562, Jun. 2021, doi: 10.1016/j.bioactmat.2020.11.015.

[7] B. H. J. Gowda *et al.*, "Current trends in bio-waste mediated metal/metal oxide nanoparticles for drug delivery," *Journal of Drug Delivery Science and Technology*, vol. 71, p. 103305, May 2022, doi: 10.1016/j.jddst.2022.103305.

[8] A. Hemben, I. Chianella, and G. J. T. Leighton, "Surface Engineered Iron Oxide Nanoparticles Generated by Inert Gas Condensation for Biomedical Applications," *Bioengineering*, vol. 8, no. 3, p. 38, Mar. 2021, doi: 10.3390/bioengineering8030038.

[9] S. M. Dadfar *et al.*, "Iron oxide nanoparticles: Diagnostic, therapeutic and theranostic applications," *Advanced Drug Delivery Reviews*, vol. 138, pp. 302–325, Jan. 2019, doi: 10.1016/j.addr.2019.01.005.

[10] M. G. Montiel Schneider *et al.*, "Biomedical Applications of Iron Oxide Nanoparticles: Current Insights Progress and Perspectives," *Pharmaceutics*, vol. 14, no. 1, p. 204, Jan. 2022, doi: 10.3390/pharmaceutics14010204.

[11] K. Hedayati, M. Goodarzi, and D. Ghanbari, "Hydrothermal Synthesis of Fe3O4 Nanoparticles and Flame Resistance Magnetic Poly styrene Nanocomposite," *jns.kashanu.ac.ir*, vol. 7, no. 1, Jan. 2017, doi: 10.22052/jns.2017.01.004.

[12] M. M. Yallapu, S. P. Foy, T. K. Jain, and V. Labhasetwar, "PEG-Functionalized Magnetic Nanoparticles for Drug Delivery and Magnetic Resonance Imaging Applications," *Pharm Res*, vol. 27, no. 11, pp. 2283–2295, Nov. 2010, doi: 10.1007/s11095-010-0260-1.

[13] S. Rostami, F. Tafvizi, and H. R. Kheiri Manjili, "High efficacy of tamoxifen-loaded L-lysine coated magnetic iron oxide nanoparticles in cell cycle arrest and anti-cancer activity for breast cancer therapy," *Bioimpacts*, vol. 12, no. 4, pp. 301–313, Jul. 2022, doi: 10.34172/bi.2021.23337.

[14] A. A. Gadgeel, S. T. Mhaske, C. Duerr, and K. L. Liu, "In-Situ Preparation and Characterization of Aconitic Acid Capped Fe3O4 Nanoparticle by Using Citric Acid as a Reducing Agent," *J Inorg Organomet Polym*, vol. 29, no. 5, pp. 1688–1700, Sep. 2019, doi: 10.1007/s10904-019-01131-1.

[15] Z. I. Takai, M. K. Mustafa, S. Asman, and K. A. Sekak, "Preparation and Characterization of Magnetite (Fe3O4) nanoparticles By Sol-Gel Method," vol. 12, no. 1, pp. 37–46, 2019.

[16] S. Liu, K. Yao, L.-H. Fu, and M.-G. Ma, "Selective synthesis of Fe_3O_4, γ-Fe_2O_3, and α-Fe_2O_3 using cellulose-based composites as precursors," *RSC Adv.*, vol. 6, no. 3, pp. 2135–2140, 2016, doi: 10.1039/C5RA22985E.

[17] Y. P. Yew *et al.*, "Green Synthesis of Magnetite (Fe3O4) Nanoparticles Using Seaweed (Kappaphycus alvarezii) Extract," *Nanoscale Res Lett*, vol. 11, no. 1, p. 276, Dec. 2016, doi: 10.1186/s11671-016-1498-2.

[18] K. H. Weisgraber, T. L. Innerarity, and R. W. Mahley, "Role of lysine residues of plasma lipoproteins in high affinity binding to cell surface receptors on human fibroblasts.," *Journal of Biological Chemistry*, vol. 253, no. 24, pp. 9053–9062, Dec. 1978, doi: 10.1016/S0021-9258(17)34284-9.