STM JOURNALS

International Journal of
Cheminformatics

Volume 3, Issue 2, 2025
July-December
DOI (Journal): 10.37591/IJCI

https://journals.stmjournals.com/ijci/

Review JoEAM

Iron Oxide/Chitosan Nanocomposite: Properties and Design for AI-Enhanced Immunotherapy and Regenerative Medicine

Gizachew Diga[1,*]

Abstract

Biopolymers are valuable complex materials. They attract the attention of many scientists, engineers, and medical professionals due to their distinguished properties for various applications. In this research, emphasis is given to Fe_3O_4/chitosan nanocomposite, which has desirable biophysical properties compared to pure chitosan nanoparticles. Following green synthesis procedures and characterization methods, including thermogravimetric analysis, an AI-assisted biomedical application of Fe_3O_4/chitosan nanocomposite is presented. The effect of alkali, KOH, in purifying chitosan during the green synthesis process is presented. Moreover, the effect of photon energy on the biodegradation of Fe_3O_4/chitosan nanocomposite in conjunction with varying Fe concentration is discussed in the synthesis procedure. In this regard, AI-based approaches, such as deep learning and machine learning, in data generation, analysis, and stimulating the biomedical function of Fe_3O_4/chitosan composite are seen. It is expected that doping Fe_3O_4/chitosan with Fe and Graphene Quantum Dot (GQDs) has an influence on the properties, such as biodegradation, biocompatibility, sensitivity, and fluorescence. AI is also investigated for optimizing the functionality of Fe_3O_4/chitosan and predicting the outcome of medical procedures. Moreover, the impact of increasing Fe concentration application of Fe_3O_4/chitosan composite in immunotherapy and regenerative medicine is observed. Finally, the possibility of optimizing the biophysical properties of Fe_3O_4/chitosan nanocomposite for AI-assisted immunotherapy, drug delivery, and regenerative medicine is observed.

Keywords: Biopolymers, Fe_3O_4/Chitosan nanocomposite, green synthesis, drug delivery, immunotherapy, regenerative medicine

INTRODUCTION

Polymer composite materials are prepared by combining a polymer matrix with fiber or filler materials to achieve desirable biophysical properties. The best model of polymer nanocomposite is the Fe_3O_4/chitosan nanocomposite. Chitosan is a natural biopolymer, and Fe_3O_4 is a superparamagnetic nanoparticle, which is a filler material. In this study, the Fe_3O_4/chitosan nanocomposite is studied because of its distinguished biophysical properties and pronounced biomedical applications.

***Author for Correspondence**
Gizachew Diga
E-mail: Phygidg@gmail.com

[1]Professor, Department of Physics, Jimma University, Jimma, Ethiopia

Received Date: June 23, 2025
Accepted Date: October 08, 2025
Published Date: October 20, 2025

Citation: Gizachew Diga. Iron Oxide/Chitosan Nanocomposite: Properties and Design for AI Enhanced Immunotherapy and Regenerative Medicine. International Journal of Cheminformatics. 2025; 3(2): 22–32p.

Fe_3O_4/chitosan nanocomposite was in a solid/liquid phase. The crystal size of the Fe_3O_4/chitosan nanocomposite was nearly 10 nm-12 nm. It had a cubic crystal structure. Fe_3O_4/chitosan nanocomposites are a family of biodegradable biopolymers. It combines the magnetic properties of Fe_3O_4 with the mechanical properties of chitosan nanoparticles. These properties include biocompatibility, biodegradation, enzyme immobilization, superparamagnetism, and the predictable zeta potential of the Fe_3O_4/chitosan bilayer.

As suggested by Cuana et al. (2022) [1], Fe_3O_4/chitosan can be synthesized from plant extracts. Huong et al. (2023) [2] also revealed that Fe_3O_4/CuO/chitosan can be synthesized by an ultrasound-assisted green method. Besides, Fe_3O_4/chitosan can be characterized using various instruments. As verified by M. Antony Arockiaraj et al. (2022) [3], Fe_3O_4 and Fe_3O_4/chitosan can be characterized by XRD, SEM, and UV spectroscopy.

Polymer nanocomposites have several applications. Their varied biophysical properties, biodegradability, compatibility, sensitivity, and stability to external fields, light, and heat make them valuable biomaterials for medical and industrial applications. Fe_3O_4/chitosan nanocomposites have a multitude of applications, including bioelectronics, biomedicine, energy storage media, photocatalysis, water treatment, and environmental health. In biomedicine, Fe_3O_4/chitosan nanocomposites are primarily used in AI-assisted immunotherapy, magnetic fluid hyperthermia, wound healing, and targeted drug delivery. Fe_3O_4/chitosan nanocomposites are a family of biodegradable biopolymers, which is the focus of this study.

BIOPOLYMER NANOCOMPOSITE

Biopolymer nanocomposites are comprised of organic and non-organic counterparts. They consist of continuous and discontinuous phase (filler) materials. In such structures, the filler materials are nanoparticles (NPs). Typical examples of biopolymer nanocomposites are superparamagnetic Fe_3O_4/chitosan nanoparticles with a size of 10 nm ~ 12 nm and a cubic spinel structure.

Therefore, this research aimed to determine the properties and applications of Fe_3O_4/chitosan nanocomposite in biomedicine, particularly AI-assisted immunotherapy, drug delivery, and healing. Hence, the effects of photon energy, Fe concentration, and alkali and enzymatic activities were observed in the green synthesis of chitosan. Moreover, the impact of Fe concentration and AI has been studied in enhanced biomedicine, including targeted drug delivery, immunotherapy, and wound healing.

Properties of Fe_3O_4/Chitosan Nanocomposite

Biopolymers and polymer nanocomposites exhibit different properties depending on their sources, stimuli, and structures. Nano-sized biopolymers are highly degradable. Natural biopolymers and Fe_3O_4/chitosan offer enhanced biocompatibility and biodegradability. Particularly, Fe_3O_4/chitosan exhibits good biophysical properties.

Fe_3O_4/chitosan exhibits electrical, magnetic, mechanical, optical, and thermal properties. Fe_3O_4/chitosan nanoparticles are semiconductors that exhibit conductivity up to 1.5×10^{-2}S/m. The conductivity increased with increasing iron (Fe) content. Unlike normal semiconductors, the electrical conductivity of Fe_3O_4/chitosan decreases with increasing temperature. Fe_3O_4/chitosan nanocomposite exhibits superparamagnetism, low coercivity, magnetic remanence, and high saturation magnetization. Chitosan coating of iron oxide nanoparticles did not significantly affect their magnetic properties.

Chitosan exhibits low optical absorption and refractive index in the visible electromagnetic spectrum. Consequently, coating with chitin or Fe_3O_4 nanoparticles can improve the optical absorption. Magnetic nanoparticles, such as Fe_3O_4, can also enhance optical properties, including light trapping and surface plasmon resonance. As revealed by Rona Cuana et al. (2022) [4], coating chitosan with Fe_3O_4 increases its optical properties, such as surface plasmon resonance. To modify the surface plasmon resonance of chitosan, doping with Fe_3O_4 nanoparticles is expected to form a composite. Eventually, the chitosan doping of the Fe_3O_4/chitosan nanocomposite increases its refractive index. Hence, the surface plasmon resonance and optical absorption peak increased.

METHODS

Synthesis Methods

The functional properties of polymer nanocomposites can be influenced by the synthesis procedure and method used. The synthesis of biopolymers includes enzyme-catalyzed polymerization of active

monomers. It occurs within the cells as a product of complex metabolic processes. Biopolymers can be industrially synthesized by the action of photons. It can also be synthesized by dark fermentation of sugar (glucose) by microorganisms.

Freire et al. (2016) [5] demonstrated that chitosan/Fe_3O_4 nanocomposite can be synthesized by fast ultrasound-assisted methods. As Louis et al. (2015) [6] demonstrated, chitosan nanoparticles can be prepared by emulsion, ionic gelation, reverse micelle, and self-assembly. However, the green synthesis method was the focus of this study. As Soares P.I. et al. (2016) [7] demystified, Fe_3O_4/chitosan nanocomposite can be synthesized using two methods: chemical precipitation and thermal decomposition. In this study, green synthesis methods are emphasized. The green synthesis method is greatly anticipated, as it fosters environmental safety and reduces costs. Green synthesis methods involve the use of enzymatic hydrolysis to produce gelatin. The procedural steps of this biocatalytic synthesis method are simple, controllable, and can be further modified. It involves the synthesis of biopolymers and polymer composites from viruses, bacteria, algae, fungi, plankton, leaves, and stems by enzymatic action. The sequential process of chitosan formation is shown in Figure 1.

To accelerate the degradation rate, solid fungi should be exposed to a light (photon) of optimum energy, $\hbar\omega$. The photon-activated fungi are then fed with active enzymes, such as yeast cells, which further increases the degradation rate. This enzyme has great significance in fungal degradation. Fungal metabolites were used to reduce iron ions and stabilize the resulting Fe_3O_4 nanoparticles. In this synthesis procedure, chitinases can help break down chitin, while lipases, proteases, esterases, and various oxidative enzymes can enhance the degradation process. It is then converted into plant protein. Proteins extracted from fungi by the action of enzymes are then allowed to react with potassium hydroxide and KOH to form ethylene alcohol. The mixture was then allowed to react with hydrochloric acid (HCL). Then, any chromatic pigments were removed by washing with KOH to form chitin. This product was then deacetylated to form chitosan with the desired characteristic properties.

During the deacetylation process, the acetyl groups (CH_3CO) that appear on the N-acetyl glucosamine units of chitin are removed. Subsequently, it must be exposed to amino groups (NH_2). In this process, chitin is treated with alkali oxides, such as NaOH, KOH, or enzymes, and then exposed to steam to form chitosan. Islam et al. (2017) [8] verified that chitosan, β-(1-4) linked 2-amino-2-deoxy-β-D-glucopyranose, is an N-deacetylated derivative of chitin.

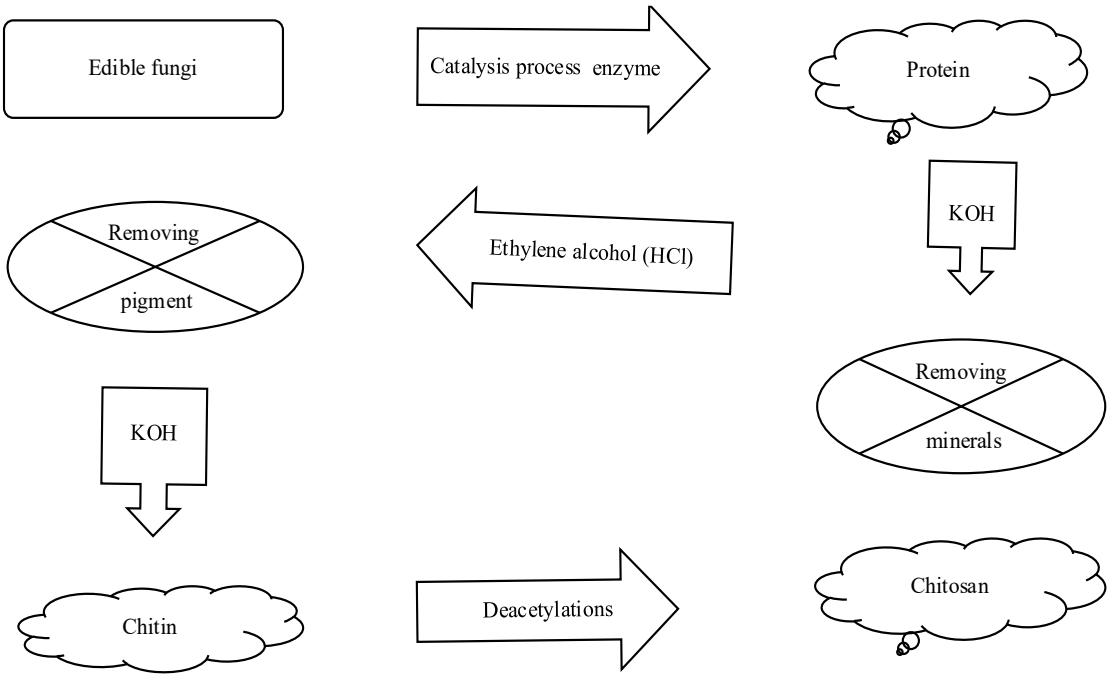

Figure 1. Green synthesis of chitosan.

Finally, Fe_3O_4 nanoparticles were mixed with the chitosan nanofluid and sonicated. After drying, the resulting nanocomposite will yield Fe_3O_4/chitosan. AI approaches such as deep learning and machines can accelerate the synthesis process by optimizing synthesis parameters and predicting outcomes. AI can also help detect possible pitfalls during the synthesis procedure and help test fatigue. To increase mechanical strength, bio-nanopolymers are doped with green nanoparticles like graphene nanoparticles. In addition, to increase the molecular weight and degree of depolymerization, the chitosan nanoparticles were treated with Fe_3O_4 nanoparticles to form Fe_3O_4/chitosan nanocomposite.

Characterizations

The biophysical properties of biopolymers must be tested, analyzed, and characterized to determine their elemental composition, size, and toxicity. The characteristic behavior of Fe_3O_4/chitosan can be studied using experimental methods, theoretical approaches, and simulations. As Nathan R. Zaccai et al. (2017) [9] presented, some of the experimental methods for characterizing Fe_3O_4/chitosan are mass spectrometry, hydrodynamics, and nuclear magnetic resonance (NMR). To determine their physical, chemical, and biological properties, various instruments are required. As verified by Vo et al. (2024) [10], the structural and morphological properties of Fe_3O_4/chitosan can be characterized by XRD, SEM, and EDX spectroscopy. According to Sarojini et al. (2023) [11], the Fe_3O_4/chitosan nanocomposite synthesized from Azolla Pinnata can display a highly porous structure that exhibits higher absorption activity. Fe_3O_4/chitosan nanocomposite was also characterized by thermogravimetric analysis.

As verified by Dufresne et al. (2013) [12], the size, charge distribution, hydrophobicity, and morphology of biopolymers can be determined by physicochemical characterization methods. A common biopolymer, such as chitosan, can be converted into a hydrogel by modifying its ionic characteristics and PH value. Biopolymers, including proteins, possess primary, secondary, and tertiary structures. These structures can be characterized by crystallographic methods such as X-ray diffraction and neutron diffraction. Measuring the zeta potential of Fe_3O_4/chitosan by either laser Doppler velocimetry (LDV) or electrophoretic mobility can help identify the type and amount of particle charge. This is advisable, as the zeta potential measures the stability of the Fe_3O_4/chitosan nanocomposite and the interaction of Fe_3O_4 nanoparticles with chitosan.

Computationally, chitosan and Fe_3O_4/chitosan nanocomposite can be simulated by molecular dynamics simulations. Molecular dynamics (MD) simulations can be used to help study the interactions between Fe_3O_4 surfaces and chitosan molecules. This enabled the adsorption of chitosan onto the Fe_3O_4 crystallographic plane. MD enables the simulation of the interaction of nanocomposites with body cells, providing valuable information for designing drug delivery systems based on Fe_3O_4/chitosan nanocomposites. Moreover, the Derjaguin–Landau–Verwey–Overbeek (DLVO) theory can help determine the surface interactions and zeta potential of the Fe_3O_4/chitosan bilayer.

DISCUSSION

Sensitivity and Solubility of Fe_3O_4/Chitosan

Polymer nanocomposites exhibit several properties that can be exploited in biomedical applications. Among polymer nanocomposites, Fe_3O_4/chitosan exhibits distinguished and unique biophysical properties, including biodegradation, biocompatibility, sensitivity, solubility, and stability, which can be tailored for biomedicine. Chitosan and Fe_3O_4 nanoparticles are both hydrophilic nanomaterials. As a composite material, Fe_3O_4/chitosan is also hydrophilic and water-soluble; however, the solubility of Fe_3O_4/chitosan depends on the molecular weight, degree of acetylation, pH, temperature, and crystallinity. In this study, three important strategies were identified to increase the solubility of Fe_3O_4/chitosan nanocomposite. These are acylation, increasing Fe_3O_4 concentrations by further coating, and resizing and reducing particle size to increase the surface area to volume ratio.

Fe_3O_4/chitosan nanocomposite is sensitive to pH, and its activity can be expressed as a function of time and number density. Because chitosan is highly sensitive to pH, it must be improved by doping

with Fe or GQD for medical purposes. Doping Fe_3O_4/chitosan with Fe or GQDs creates a suitable microenvironment that is sensitive to pH and can be used for the treatment of cardiovascular diseases and as a scaffold for drug delivery. It can also be tuned for targeted drug delivery to specific tissues or organs, such as the gastrointestinal tract. The sensitivity of Fe_3O_4/chitosan nanocomposite to changes in pH can also be modified with acidic or alkaline media for targeted drug delivery. Fe_3O_4/chitosan nanocomposite can also be used in nanobiosensors, which are sensitive to various analytes, including gastric acids. As Tiama et al. (2023) [13] indicate, a chitosan/Fe_3O_4 nanocomposite with Fe_3O_4, 0.25 at %, exhibits better sensitivity compared to pure chitosan. Fe_3O_4/chitosan nanocomposite can interact with cell membranes and is absorbed by body cells. It has good cytocompatibility with gynecological cells and does not influence cell viability in vitro.

Thermal Stability of Fe_3O_4/Chitosan

The thermostability of biopolymers can be determined by visualizing their responses to electric and magnetic fields, light, and temperature. This was also determined by measuring the coefficient of thermal expansion. Polymers with a high coefficient of thermal expansion are considered thermally stable. Moreover, Biopolymers with high specific heat capacity are thermally stable. For example, Meyer B. Jackson (2006) [14] determined the thermostability of lysozyme from T_4 bacteriophage by observing the temperature sensitivity of the mutants.

Testing the thermostability of Fe_3O_4/chitosan involves observing the behavior of the composite by exposing it to heat and increasing the temperature. This was achieved using thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). This device can detect changes in weight or temperature during heating. The TGA measures the changes in weight as the temperature varies. However, DSC detects the direction of heat flow during the heating or cooling processes, regardless of whether it conflicts with 2nd law of thermodynamics. Chitosan exhibits thermal stability in the range 200–220°C. Hence, it is considered a good stabilizer compared with the stability of the composite. As Geddes (1999) [15] noted, thermogravimetric (TG) analysis is valuable in determining the content of volatile species, fillers, and polymer degradations. This also indicates phase transformations and changes in states as the temperature changes.

Moreover, as Qu et al. (2010) [16] revealed, the binding of chitosan to the Fe_3O_4 nanoparticles was also demonstrated by the measurement of FTIR spectra and TGA. Gustavo Adolfo Muñoz Ruiz et al. (2016) [17] determined that the molecular weight of chitosan is between 1×10^5 Da and 5×10^5 Da. The percentage of depolymerization is given by

$$\delta = \frac{W_p}{W_s} x100\%$$

Where, δ is the degree of depolymerization or degradation, W_P is the molecular weight of the polymer, and W_s is the molecular weight of a single polymer. The following pie chart illustrates the degree of depolymerization or degradation of chitosan as a function of the Fe concentration.

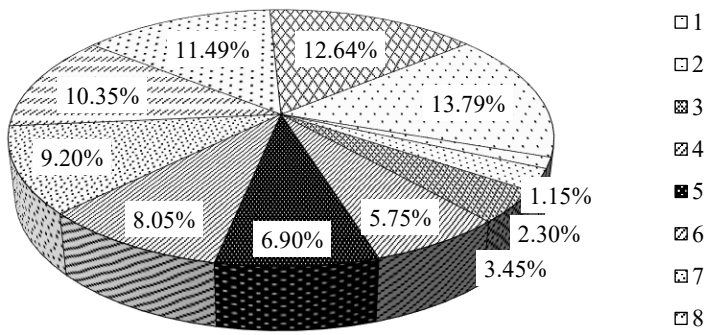

Figure 2. The degree of depolymerization of chitosan as a function of Fe.

As Figure 2, the depolymerization rate increased as a function of Fe. However, the degree of polymerization decreased as the Fe_3O_4 concentration increased. Fe_3O_4 accelerated the breakdown (degradation) of chitosan into small nanoparticles.

Hydrolysis of Fe_3O_4/Chitosan

Like any other polysaccharide, chitosan hydrolysis is treated by an aqueous solution of acids to break the bond between functional groups and hydroxyl groups. This process was performed to create instability in the bonds of the Fe_3O_4/chitosan composites. As Siti Hajar Othman et al. (2014) [18] realized, biodegradation of biopolymers results in CO_2 and H_2O. The hydrolysis process can be equally applied to the Fe_3O_4/chitosan nanocomposite. The hydrolysis of the Fe_3O_4/chitosan composite undergoes breakdown of the chitosan component, which results in the formation of minute chitosan nanoparticles. This also led to the separation of chitosan and Fe_3O_4 nanoparticles.

Micro- and nano-capsule biopolymers exhibit good biocompatibility and biodegradability. These biopolymers and their composites can be optimized for drug delivery via hydrolysis or enzymatic degradation. Hydrolysis is necessary for surface modification, enzyme immobilization, and drug delivery. This process can also enhance the enzyme-loading capacity of the Fe_3O_4/chitosan nanocomposite and its ability for targeted drug delivery.

Design of Fe_3O_4/Chitosan for AI-Enhanced Immunotherapy

Immunotherapy strategies aim to maximize the potential of Fe_3O_4/chitosan nanocomposite to develop the immune system. These strategies include immune checkpoint blockage, surface engineering cell microstates, and integrating AI systems for generating data and analyzing it. Another strategy involves incorporating nanomedicine and nanobiosensors for therapy, drug delivery, and cancer vaccines.

Fe_3O_4/chitosan nanoparticles were designed for AI-based immunotherapy by magnifying their biophysical properties, such as biocompatibility, biodegradation, cell viability, and optical absorption. These measurable properties help to amplify its activity for targeted drug delivery and immune cell modulation. Because chitosan is both a biocompatible and biodegradable polysaccharide, it creates a suitable ecosystem for therapeutic action. Moreover, Fe_3O_4 nanoparticles exhibit superparamagnetic physical behavior, which helps to induce optimum heat/temperature for the cell, which enhances drug release, drug release, and immune cell therapy. Pourmadadi (2023) [19] demonstrated that flow cytometry analysis of Fe_3O_4/chitosan/agarose loaded with curcumin showed a high apoptosis percentage when the designed drug delivery system was programmed properly. This action can increase the risk of cancer, including toxicity.

Fe_3O_4/chitosan nanocomposite should be designed and suited for properly visualizing the cells, tissues, and parts of these organs. To this end, Fe_3O_4/chitosan doped with quantum dots, such as graphene quantum dots, stimulates fluorescence light. GQD-Fe_3O_4/chitosan enables the visualization of the structures and kinetics of cells and tissues. Consequently, the doping of Fe_3O_4/chitosan with GQDs increased cell viability. This action is promising for magnetic fluid hyperthermia, cancer therapy, and targeted drug delivery applications. In addition, quantum computing can simulate fluorescence in Fe_3O_4/chitosan nanocomposite. This process can influence the functionality of Fe_3O_4/chitosan for drug delivery, fluorescence imaging, and magnetic fluid hyperthermia. In such a process, AI provides useful information regarding the design, prediction of fault operations, and feedback.

AI-ASSISTED MEDICAL APPLICATIONS OF Fe_3O_4/CHITOSAN

Fe_3O_4/chitosan nanocomposites have several applications. Most importantly, these nanocomposites are widely used in biomedical applications, including magnetic fluid hyperthermia, nano-biosensors, targeted drug delivery, and AI-assisted immunotherapy. Similar to magnetic nanoparticles, Fe_3O_4/chitosan can be used to cross the blood–brain barrier (BBB) for delivery, tumor therapy, and wound healing. Bio-nanopolymer increases the effectiveness of cancer treatment. By activating its

sensitivity with photons of optimum energy, the Fe_3O_4/chitosan nanocomposite can be used to enhance drug delivery. It also accelerates biodegradation and improves drug kinetics.

Studies such as Noura El-Ahmady El-Naggar et al. (2022) [20] indicate that biologically synthesized chitosan nanoparticles can be used for medical treatments and food preservation. Green synthesized chitosan nanoparticles triggered antitumor, antimicrobial, diagnostic, drug delivery, soft tissue imaging, and skin effects. In addition, chitosan nanoparticles can enhance immune and oncological therapies.

Fe_3O_4/chitosan nanocomposite is a valuable nanomaterial for theranostic medicine, cancer treatment, and precision medicine. Thus, they offer a versatile nanoplatform for theranostic medicine. This mechanism helps accurately and precisely target, deliver, and monitor therapeutic agents. It also enables simultaneous imaging and tissue and cell repair. In the subsequent section, AI enables the biomedical application of the Fe_3O_4/chitosan nanocomposite to be discussed.

Drug Delivery and Kinesis

The functional groups of polyelectrolyte polymers form an electrostatic equilibrium because their charges are equal and opposite to each other. These compounds have potential applications in drug delivery. Gomes et al. (2017) [21] show that chitosan can be used as an antimicrobial film and an antifungal agent. Belen Begins et al. (2020) [22] used natural polymers, such as dextran, gelatin, guar gum, collagen, and CH, in oncology and drug release. Körhegyi et al. (2019) [23] verified that self-assembled nanoparticles of chitosan-based polyelectrolyte complexes can be used as drug delivery systems. As indicated by Tia Y et al. (2022) [24], chitosan has been used as a drug carrier in the form of hydrogels and nanoparticles. Chitosan nanoparticles can be used to treat melanoma and sarcoma of the skin and soft tissues.

Teichoic acids (TAs) are surface copolymers that are phosphate-rich molecules found in gram-positive bacteria and pathogens. These interactions are suitable for electrostatic interactions. These interactions can be expressed in terms of electric charge, lung constant, and separation distance, R. This interaction reinforces the destruction of the bacterial cell wall or cell death. Research by Kim et al. (2020) [25] indicates that chitosan colloids can help in developing food ingredients or drug carrier templates that are stable over a wide pH range. Owing to their good antimicrobial properties and stiffness, hydrogels, sponges, nanoparticles, and thin films of chitosan can serve as nanocarriers for drug delivery to treat injuries and lesions of the skin, muscles, blood vessels, and nervous system. AI-based analysis and delivery enable controlled drug release and targeted delivery to the tumor microstate. Nanocomposites of Fe_3O_4/chitosan are functional in both drug kinetics and magnetic drug targeting. This can be achieved in the presence of superparamagnetic Fe_3O_4 nanoparticles.

AI-Enhanced Immunotherapy

AI can help to optimize the properties of nanopolymers for specific therapeutic goals, such as immunotherapy. Immune cell therapy is a process of isolating the patient's own or AI-derived immune cells, which can be improved by chitosan composites. It is then re-infused into the patient’s cell at the point of care, and immune cells that have been modified by means of Fe_3O_4/chitosan composites are then assisted by AI machines, such as nanorobots, to kill cancerous cells and generate memory-type immunity. This AI-enabled therapeutic system can prevent tumor cells, malignant cancers, and metastases. CAR-T, TCR-T, TIL, and CAR-NK are widely used immunotherapies.

Fe_3O_4/chitosan synthesized by the green method has a variety of applications. Fe_3O_4/chitosan can be used to prevent viruses or bacteria from penetrating the cell wall and membrane. Chitosan nanocarriers can be used as diagnostic imaging agents. AI can be used in a variety of applications, including analyzing and predicting the value of the zeta potential at the Fe_3O_4/chitosan bilayer. The zeta potential is greatly influenced by biophysical parameters, including the pH, Fe concentration, electric field, and magnetic field. AI-based computing enables real-time analysis of these potentials, models particle interactions, and identifies the surface charge density. Consequently, AI can modify the biomedical

applications of Fe_3O_4/chitosan for drug delivery, immunotherapy, magnetic fluid hyperthermia, and wound dressings.

Zahra Fakhroueian et al. (2018) [26] indicated that ZnO co-assisted nano polymers are used for cancer therapy and prevent psychological patient stress from the injection. Ding J. and Guo Y. (2022) [27] realized that chitosan-based vehicles can be used for the encapsulation of chemotherapeutic drugs, therapeutic genes, and targeted therapy for cancer.

Bio-nanopolymer can be used in AI-enhanced immunotherapy to improve the design, delivery, and targeting of immunotherapeutic agents. AI can improve Fe_3O_4/chitosan systems for immunotherapy by optimizing various aspects of the design and application. Iron oxide-suspended chitosan nanoparticles are used for cell, gene, and immunotherapy applications. It can help predict the most effective strategies for enhancing immunotherapy, simulating data, and helping in gene sequencing. AI analyzes the immune responses of Fe_3O_4/chitosan nanoparticles.

Regenerative Medicine

Fe_3O_4/chitosan nanocomposite is useful for biomedical applications. As Carmen P. Jiménez-Gómez and Juan Antonio Cecilia (2020) [28] revealed, chitosan is valuable in skin, bone, tissue engineering, artificial kidneys, nerves, livers, and wound healing. As Kakani and Amit Kakani (2004) [29] discussed, polymers can be adapted for repairing damaged kidneys or hearts. Krepsztul et al. (2019) [30] also revealed that chitosan nanofibers and oil particles can serve as anti-pathogenic agents against Pseudomonas aeruginosa.

Chitosan nanoparticles are useful bio-nanomaterials for reducing cholesterol levels and hypertension. Fe_3O_4/chitosan composites can be fabricated into scaffolds that provide physical support for cell growth and tissue regeneration. Magnetic Fe_3O_4/chitosan scaffolds can improve bone tissue by providing suitable microenvironments and nutrients for tissue growth. In this circumstance, AI can help design Fe_3O_4/chitosan scaffolds that guide neural cell generation, signal transport, and nerve cell growth. Chitosan-coated Fe_3O_4 can be used to prevent the hurts and damages of blood–brain barrier (BBB). However, brain cell repairing using Fe_3O_4/chitosan remains a challenge.

Gum Arabica, an edible biopolymer, is used as an antimicrobial agent to inhibit plaque formation and improve dental remineralization. Like any biopolymer, Fe_3O_4/chitosan nanocomposite can combine the remineralization properties of chitosan and the magnetic properties of Fe_3O_4 for enhanced bone and tooth repair.

Zhang et al. (2015) [31] verified that chitosan is used in wound dressings to decrease bleeding, treat chronic disease, and diabetic wounds. Chitosan can produce a nanofilm on the cell surface, which blocks the entry of oxygen and pathogens into the cell. AI systems, including machine learning (ML), can significantly enhance the application of Fe_3O_4/chitosan composites in wound healing by optimizing their material properties. AI can improve the capacity of Fe_3O_4/chitosan for skin repair, tissue repair, and drug delivery to predict healing outcomes and increase precision. These techniques can foster and shape the frontier of regenerative medicine.

Although the validity of Fe_3O_4/chitosan in immunotherapy and regenerative medicine encounters certain challenges related to stability, sensitivity, and solubility to some molecules, the remedy can be corrected by further reducing the size of the composites and maximizing their magnetic properties. Dwivedi et al. (2019) [32] suggested that the diagnosis and surgery of infection using biomaterials like Fe_3O_4/chitosan is a great challenge. However, the pitfall can be resolved by doping bionanopolymers either with MesoGold nanoparticles or with silver nanoparticles. In addition, Gökçen Yaşayan (2020) [33] indicated that silver sulfadiazine loaded in films was designed for wound healing because of its antimicrobial properties.

CONCLUSION

In this research, a Fe_3O_4/chitosan nanocomposite was studied. Emphasis is placed on the green synthesis, properties, and biomedical applications of Fe_3O_4/chitosan nanocomposite. The study revealed that nano-sized Fe_3O_4/chitosan nanocomposite exhibits distinct mechanical, electrical, magnetic, optical, and thermal properties. The stiffness, biocompatibility, biodegradability, sensitivity, and solubility of Fe_3O_4/chitosan nanocomposite make them suitable for biomedical applications. It has been shown that the stability of chitosan can be distorted by activation with photon energy, hydrolysis, or aqueous acid. Activating edible fungi with a photon of optimum energy, $\hbar\omega$, will break the bond between constituent atoms. Post-activation was employed to enhance the biodegradation process of Fe_3O_4/chitosan to make it suitable for medical applications. In addition, controlled Fe doping may accelerate the degradation rate. AI-based approaches can enhance the synthesis procedure, predict the type and behavior of the product, and facilitate biomedical applications of nanocomposites. Moreover, molecular dynamics simulations, quantum computing, and increasing Fe concentrations can improve targeted drug delivery, immunotherapy, and regenerative medicine. It should also be noted that determining the physical parameters, such as zeta potential, is important in realizing biomedical applications and the charge of species. Fe_3O_4 and chitosan surfaces have different charges, which enable the determination of the surface charge density based on the DLVO theory and zeta potential. This is advantageous because the zeta potential accounts for parameters such as iron concentration, heat generated by nanoparticles, pH value, and their relations. Owing to its biodegradability, biocompatibility, and qualified biophysical and chemical properties, Fe_3O_4/chitosan is greatly recommended for immunotherapy, targeted drug delivery, cell/tissue imaging, and regeneration. The biomedical applications of nano-sized biopolymers like Fe_3O_4/chitosan nanoparticles can be modified by doping with Fe and GQDs. This type of doping enhances surface immobilization, induces fluorescence, and increases stability. Moreover, the AI-enabled coating of Fe_3O_4 with chitosan improved immunotherapy, targeted drug delivery, wound healing, and regenerative medicine to a greater extent. It is also promising for anticancer, cell repair, tissue repair, and growth applications in immunotherapy and regenerative medicine. AI-based analysis enables the simulation of big data, fault detection during therapeutic procedures, and the prediction of the behavior of therapeutic outcomes and patients' behavior to the drug response. Although the validity of Fe_3O_4/chitosan in immunotherapy and regenerative medicine encounters certain challenges related to stability, sensitivity, and solubility to some molecules, the remedy can be corrected by further reducing the size of the composites and maximizing their magnetic properties. In the future, Fe_3O_4/chitosan can be doped with quater die sumendum (QDs) and ZnO, which can be tailored for precision, regenerative, and personal medicine applications by leveraging its surface properties.

Acknowledgement

The researcher would like to thank Ju for their resource allocations and colleagues.

Conflict of Interest

The authors declare that there are no conflicts of interest. In addition, words, ideas, and statements added from various sources were properly acknowledged.

REFERENCES

1. Cuana R, Panre AM, Istiqomah NI, Tumbelaka RM, Sunaryono, Wicaksono ST, Suharyadi E. Green synthesis of Fe_3O_4/chitosan nanoparticles utilizing Moringa oleifera extracts and their surface plasmon resonance properties. ECS J Solid State Sci Technol. 2022;11:083015. doi:10.1149/2162-8777/ac8b36.
2. Thi Huong N, Thi Mai Huong P, Thi Kim Giang N, Thi Lan P, Thanh Dong V, Tien Dung C. Fe3O4/CuO/Chitosan Nanocomposites: An Ultrasound-Assisted Green Approach for Antibacterial and Photocatalytic Properties. ACS Omega. 2023 Nov 3;8(45):42429-42439. doi: 10.1021/acsomega.3c04956. PMID: 38024769; PMCID: PMC10652728.
3. Antony Arockiaraj M, Mani G, AlOthman ZA. Effect of chitosan-incorporated Fe_3O_4 nanocomposites on the photocatalytic removal of organic molecules. J Mater Sci Mater Electron. 2022;33:9570–9579. doi:10.1007/s10854-021-07579-7.

4. Cuana R, Panre AM, Istiqomah NI, Tumbelaka RM, Sunaryono, Wicaksono ST, Suharyadi E. Green synthesis of Fe_3O_4/chitosan nanoparticles utilizing Moringa oleifera extracts and their surface plasmon resonance properties. ECS J Solid State Sci Technol. 2022;11(8):083015. doi:10.1149/2162-8777/ac8b36.
5. Freire TM, Dutra LMU, Queiroz DC, Ricardo NMPS, Barreto K, Denardin JC, et al. Fast ultrasound-assisted synthesis of chitosan-based magnetite nanocomposites as a modified electrode sensor. Carbohydr Polym. 2016;151:760–769. doi:10.1016/j.carbpol.2016.05.095.
6. Sigma-Aldrich Co. LLC. Polymeric Drug Delivery Techniques: Translating Polymer Science for Drug Delivery. St. Louis (MO): Sigma-Aldrich Co. LLC; 2015.
7. Soares PIP, Machado D, Laia C, Pereira LCJ, Coutinho JT, Ferreira IMMM, et al. Thermal and magnetic properties of chitosan–iron oxide nanoparticles. Carbohydr Polym. 2016;149:382–390. doi:10.1016/j.carbpol.2016.04.123.
8. Islam S, Bhuiyan MAR, Islam MN. Chitin and chitosan: structure, properties and applications in biomedical engineering. J Polym Environ. 2017;25:854–866. doi:10.1007/s10924-016-0865-5.
9. Vo LQ, Vu AT, Le TD, Huynh CD, Tran HV. Fe_3O_4/graphene oxide/chitosan nanocomposite: a smart nanosorbent for lead(II) ion removal from contaminated water. ACS Omega. 2024;9:17506–17517. doi:10.1021/acsomega.4c00486.
10. Sarojini G, Kannan P, Rajamohan N, Rajasimman M. Bio-fabrication of porous magnetic chitosan/Fe_3O_4 nanocomposite using Azolla pinnata for chromium removal. Environ Res. 2023;218:114822. doi:10.1016/j.envres.2022.114822.
11. Zaccai NR, Serdyuk IN, Zaccai J. Methods in Molecular Biophysics. Vol. 2. Cambridge: Cambridge University Press; 2017. doi:10.1017/9781107297227.
12. Dufresne A, Thomas S, Pothen LA. Biopolymer Nanocomposites: Processing, Properties, and Applications. Hoboken (NJ): John Wiley & Sons; 2013. doi:10.1002/9781118609958.
13. Tiama TM, et al. Structural and spectroscopic studies for chitosan/Fe_3O_4 nanocomposites as glycine biosensors. Biointerface Res Appl Chem. 2023;13:547. doi:10.33263/BRIAC136.547.
14. Jackson MB. Molecular and Cellular Biophysics. Cambridge: Cambridge University Press; 2006. doi:10.1017/CBO9780511754869.
15. Geddes UW. Polymer Physics. Berlin: Springer; 1999.
16. Qu J, Liu G, Wang Y, Hong R. Preparation of Fe_3O_4–chitosan nanoparticles used for hyperthermia. Adv Powder Technol. 2010;21:461–467. doi:10.1016/j.apt.2010.01.008.
17. Muñoz Ruiz GA, Zuluaga Corrales HF. Chitosan, chitosan derivatives and their biomedical applications. In: Shalaby E, editor. Biological Activities and Application of Marine Polysaccharides. London: IntechOpen; 2017. doi:10.5772/66527.
18. Othman SH. Bio-nanocomposite materials for food packaging applications: Types of biopolymer and nano-sized filler. Agric Agric Sci Procedia. 2014;2:296–303. doi:10.1016/j.aaspro.2014.11.042.
19. Pourmadadi M, Ahmadi M, Yazdian F. Synthesis of a pH-responsive Fe_3O_4/chitosan/agarose nanoemulsion for sustained curcumin release. Int J Biol Macromol. 2023;235:123786. doi:10.1016/j.ijbiomac.2023.123786.
20. El-Naggar NEA, Shiha AM, Mahrous H, Mohammed ABA. Green synthesis of chitosan nanoparticles and antibacterial efficacy against Acinetobacter baumannii. Sci Rep. 2022;12:19869. doi:10.1038/s41598-022-24303-5.
21. Gomes LP, Paschoalin MF, Del Aguila EM. Chitosan nanoparticles: production, physicochemical characteristics and nutraceutical applications. Rev Virtual Quim. 2017;9:387–409. doi:10.21577/1984-6835.20170022.
22. Begines B, Ortiz T, Pérez-Aranda M, Martínez G, Merinero M, Argüelles-Arias F, Alcudia A. Polymeric nanoparticles for drug delivery: recent developments and future prospects. Nanomaterials (Basel). 2020;10:1403. doi:10.3390/nano10071403.
23. Körhegyi Z, Rózsa D, Hajdu I, Bodnár M, Kertész I, Kerekes K, et al. Synthesis of ^{68}Ga-labeled biopolymer-based nanoparticle imaging agents for PET. Anticancer Res. 2019;39:2415–2427. doi:10.21873/anticanres.13359.

24. Xia Y, Wang D, Liu D, Su J, Jin Y, Wang D, Han B, Jiang Z, Liu B. Applications of chitosan and its derivatives in skin and soft tissue diseases. Front Bioeng Biotechnol. 2022;10:894667. doi:10.3389/fbioe.2022.894667.
25. Kim H, et al. Dispersion of chitosan nanoparticles stable over a wide pH range by adsorption of polyglycerol monostearate. Nanomater Nanotechnol. 2020;10:1–9.
26. Fakhroueian Z, Vahabpour R, Assmar M, Massiha A, Zahedi A, Esmaeilzadeh P, Katouzian F, Rezaei S, Keyhanvar P, Mozafari Dehshiri A. ZnO Q-dots as a potent therapeutic nanomedicine for in vitro cytotoxicity evaluation of mouth KB44, breast MCF7, colon HT29 and HeLa cancer cell lines, mouse ear swelling tests in vivo and its side effects using the animal model. Artif Cells Nanomed Biotechnol. 2018;46(Suppl 2):96–111. doi:10.1080/21691401.2018.1452023.
27. Ding J, Guo Y. Recent advances in chitosan and its derivatives in cancer treatment. Front Pharmacol. 2022;13:888740. doi:10.3389/fphar.2022.888740.
28. Jiménez-Gómez CP, Cecilia JA. Chitosan: A natural biopolymer with a wide and varied range of applications. Molecules. 2020;25(17):3981. doi:10.3390/molecules25173981.
29. Kakani SL, Kakani A. Materials Science. New Delhi: New Age International; 2004.
30. Wróblewska-Krepsztul JW, Rydzkowski T, Michalska-Pożoga I, Thakur VK. Biopolymers for biomedical and pharmaceutical applications: Recent advances and overview of alginate electrospinning. Nanomaterials. 2019;9:404. doi:10.3390/nano9030404.
31. Zhang YJ, Gao B, Liu XW. Topical and effective hemostatic medicines in the battlefield. Int J Clin Exp Med. 2015 Jan 15;8(1):10-9. PMID: 25784969; PMCID: PMC4358424.
32. Dwivedi P, Narvi SS, Tewari RP. Application of polymer nanocomposites in the nanomedicine landscape: Envisaging strategies to combat implant-associated infections. J Appl Biomater Funct Mater. 2013;11:e129–e142. doi:10.5301/JABFM.2013.11544.
33. Yaşayan G. Chitosan films and chitosan/pectin polyelectrolyte complexes encapsulating silver sulfadiazine for wound healing. Istanbul J Pharm. 2020;50. doi:10.26650/IstanbulJPharm.2020.0021.

