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Synthesis and Characterization of Copper Oxide Nanoparticles from Plantago Ovata Seeds Mucilage and Its Application in Drug Delivery

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ABSTRACT

This paper has outlined an environment friendly and sustainable method of synthesis and characterisation of copper oxide nanoparticle (CuO NPs) employing mucilage of Plantago ovata (psyllium) to serve as the reducing and stabilizing agent, with special emphasis on their usage in delivering drugs. P. ovata seeds were used to extract the mucilage that was used to reduce copper sulfate to CuO nanoparticles in mild thermal conditions in the absence of toxic chemicals. This confirmation was done through a change in color and the further characterisation with regards to UV-Visible spectroscopy, Fourier Transform Infrared Spectroscopy (FTIR), and Scanning Electron Microscopy (SEM) on the formation of nanoparticles followed. The UV-Vis spectrophotometry followed by a strong absorption peak at 290 nm, which is the formation of CuO nanoparticles, and FTIR spectrophotometry observed some sharp Cu-O stretching applications, the presence of hydroxyl and carbonyl as evidence of the involvement of mucilage biomolecules in reducing and stabilizing. SEM micrographs revealed that most of the nanoparticles were spherical with an average size of 9 to 20 nm indicating homogenous morphology and capping. A high loading efficiency (c. 73.7) of the antibacterial drug cefadroxil with a synthesized CuO NP was then attained.

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Experiments of in-vitro drug release showed that it possessed an interactive pH-dependent controlled release behavior with 47 and 34 percent drug release at 6.8 and 7.4 pH over 24 hours, respectively and consequently was suitable to be used in intestinal and systemic delivery. Besides, the antibacterial activities against *Staphylococcus aureus* and *Escherichia coli* showed a remarkable inhibitory area, and it justified synergistic antibacterial ones between CuO and cefadroxil. Generally, the results confirm that *P. ovata* mucilage is an effective, biodegradable, and biocompatible green system that can be utilised in the production of nanocarrier in pharmaceutical and biomedical practice due to its effectiveness in the biosynthesis of CuO nanoparticles.

Keywords: Plantago Ovata, Copper Oxide Nanoparticles, Green Synthesis, Mucilage, Cefadroxil, Drug Delivery, Ftir, Sem, Uv–Vis Spectroscopy, Antibacterial Activity, Biocompatibility, Ph-Responsive Release, Nanocarriers, Eco-Friendly Nanotechnology, Controlled Release.

Introduction

Nanotechnology has been rapidly developed to transform various scientific and industrial processes especially in the area of materials science, chemistry and medicine. With a diameter of one to hundred nanometers, nanoparticles (NPs) can be described as having very different physical, chemical, and biological characteristics compared to their bulk counterparts because of high surface area-volume and quantum effects (Ramesh et al., 2021). Metal oxide nanoparticles have received much interest among the variety of nanomaterials because of their catalytic, antimicrobial, optical, and biomedical capabilities (Khalil et al., 2020). The copper oxide nanoparticles (CuO NPs), in particular, have become a promising category of materials that have significant prospective areas of use in biosensing, drug delivery, photothermal therapy, catalysis, and remediation of the environment (Reddy et al., 2022).

Nanoparticles can be synthesized in different ways using physical, chemical and biological processes. Nevertheless, traditional chemical and physical methodologies of synthesis frequently use toxic materials, use a lot of energy, and costly equipment that presents environmental and health risks (Yugandhar and Savithramma, 2018). To address these shortcomings, scientists have turned to green synthesis procedures which employ plant extracts, microbes and other biological factors as naturally natural reducing and stabilizing agents (Singh et al., 2021). It is an eco-friendly technique, and it reduces the application of hazardous chemicals, along with biocompatible nanoparticles that can be used in biomedical purposes (Amin et al., 2021). In particular, it is possible to note that plant-based synthesis has many advantages since it contains bioactive substances including flavonoids, alkaloids, terpenoids, and phenolic acids that help reduce metal ions and stabilize nanoparticles (Bouafia et al., 2020).

Hydrogels are currently the most popular natural polymers owing to their networking characteristics, bioactivity and ability to retain water (Ahmed, 2015). Natural polysaccharide hydrogel (cellulose, chitosan, mucilage, etc.) is of particular interest to biomedical applications because of its biodegradability and non-toxicity (Calo and Khutoryanskiy, 2015). These substances are capable of receiving massive amounts of water or biological fluids and not dissolve, which is why they are applicable to

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controlled drug delivery and tissue engineering (Li et al., 2020). In this aspect, a potent source of mucilage polysaccharide is *Plantago ovata* that is popularly called psyllium and has great gel-forming, swelling, and biocompatible properties (Azam et al., 2022). *P. ovata* seeds have been utilized heavily in the pharmaceutical industry as Medicinal binding or stabilization and drug release modifier through its mucilage extract (Yari et al., 2022).

The use of *Plantago ovata* seed mucilage as a nanoparticle produces an alternative sustainable pathway towards the synthesis of biogenic metal oxide nanoparticles. The mucilage will serve as an agent that reduces, caps, and stabilizes agents, thus, avoiding the use of other dangerous chemicals (Githala et al., 2022). Besides, it has a natural polymeric backbone that facilitates the stabilization of nanoparticles and inhibits their aggregation, thus increasing the functional stability of nanoparticles to be used in biomedical purposes (Sharma et al., 2019). Cu^{2+} ions can be chelated by the hydroxyl and carboxyl groups of psyllium mucilage to reduce the Cu^{2+} to CuO NPs under mild conditions (Awwad et al., 2020). Therefore, the cooperation between natural mucilage and green nanotechnology opens the way to sustainable synthesis approaches to designing pharmaceutical nanomaterials.

The nanoparticles of copper oxide can be used especially in the field of biomedical systems because they have a large spectrum of antimicrobial activity, cancer cell cytotoxicity, and the ability to easily load drugs (Chowdhury et al., 2020). CuO NPs have great redox properties allowing the generation of reactive oxygen species (ROS), and this property makes them useful in antibacterial and anticancer (Bao et al., 2016). Also, it makes them an interesting candidate to the targeted drug delivery system since they are highly surface-reactive and electrically conductive, meaning that drugs can be adsorbed, encapsulated, or conjugated on their surface (Radhakrishnan et al., 2021). In medicine, therapeutic efficacy can only be achieved and minimization of side effects accomplished on controlled discharge of therapeutic agents is crucial in drug delivery. This can be done by hydrogels and CuO NPs that when combined with the polymer matrix swelling capacity and the high surface reactivity of the nanocarrier (Vidovich et al., 2019).

Recent research has shown the possibility of CuO NPs, prepared through plant extracts, to be used in drug delivery and antimicrobial purposes. As an example, copper oxide nanoparticles prepared using extracts of *Aerva javanica* and *Leucas aspera* had a considerable antibacterial and antioxidant effect (Amin et al., 2021; Radhakrishnan et al., 2021). Likewise, green-synthesized CuO NPs have demonstrated effectiveness in biosensing and biodegradation of the environment and degradation of dyes, which supports their catalytic and biocompatible characteristics (Sorbiun et al., 2018). Nevertheless, the use of CuO NPs produced by planting *ovata* mucilage to deliver various drugs is still rather unexpressed. Considering the polymeric properties of the *P. ovata* mucilage and biomedical compatibility with many drugs as natural sources, it is an encouraging matrix upon which nanoparticles can be encapsulated and free drug delivery systems can be controlled (Azam et al., 2022).

This paper synthesized copper oxide nanoparticles with sample mucilage of *Plantago ovata* seed as a natural reducing and stabilizing agent. Each of the resulting nanoparticles was analyzed in terms of their structure and morphology by means of UV

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spectral analysis, Fourier Transform Infrared Spectroscopy (FTIR) and Scanning Electron Microscopy (SEM). Cfdroxil, one of the antibacterial drugs, was subsequently adsorbed onto the CuO nanoparticles to determine their drug-loading capability and releasing properties at physiological pH. It is one of the pieces of work in the developing body of biogenic nanomaterials on pharmaceutical applications due to the green synthesis methodology used in the study that considers the values of sustainability, cost effectiveness, and eco safety. In addition, the paper examines how naturally prepared mucilage can be combined to nanostructured drug delivery systems to increase their therapeutic benefits at a minimized environmental toxicity.

Literature Review

Overview of Nanoparticle Research in Biomedical Applications

Nanoparticles have brought a revolution to biomedical sciences because of their physicochemical properties that are tunable and their high surface reactivity that is used in delivery of drugs, imaging and diagnosis. Their small nanoscale allows them to be internalized by the cell and increases the pharmacokinetics compared to traditional formulations (Mahmoudi et al., 2022). Nanoparticles made of metals, specifically, have good possibilities under the antimicrobial, anticancer, and catalytic properties due to their high level of surface energy and redox potential (Yoon et al., 2021). One of them is copper oxide nanoparticles (CuO NPs), which have been of increasing interest due to their low cost, stability, and versatile uses in biology (Pérez-Miranda et al., 2023). The recent developments show that it is possible to design CuO NPs into a productive nanocarrier, antioxidant, and catalyst with relatively high biocompatibility during green synthesis (Liu et al., 2022).

Evolution of Green Synthesis Approaches

Commonly used synthesis routes to nanoparticles such as sol-gel, chemical vapor deposition tend to generate dangerous byproducts, and demand complicated reaction kinetics. Green synthesis on the other hand provides a green pathway and uses biological resources into reducing and stabilizing agents that include plant extracts, bacteria, fungi, and algae (Sundaram et al., 2020). In addition, this technique can remove toxic reagents and also improve the stability of particles by capping them with biomolecules (Narasimha et al., 2021). The phytochemicals can be flavonoids, terpenoids, and polysaccharides that are reducing agents that bioreduce metal ions into nanoparticles in mild temperatures and pH conditions (Rastogi et al., 2022). Such syntheses with the aid of plants have been found to generate controlled morphology, homogenous size distribution, and improved biological performance nanoparticles in comparison to chemically synthesized nanoparticles (Basavegowda and Kim, 2020). Most lately, other plants like *Moringa oleifera*, *Aloe vera* and *Azadirachta indica* have been effectively used to prepare CuO NP that has the ability to kill bacteria and also exhibit photo reactive activities (Jain et al., 2021). Hydroxyl and carboxyl functional groups enable the stabilization of the surface of these extracts which explains why they are applicable specifically in biomedical (Ezhilarasu et al., 2021). These strategies underscore the fact that green nanotechnology addresses the connection between material chemistry and biological sustainability.

Green Synthesis of Copper Oxide Nanoparticles

The application of copper oxide nanoparticles has become the focus of attention because of its semiconducting behavior, low bandgap energy, and high biological activity (Yousefi et al., 2022). It has been noted that several studies have used different extracts like *Camellia sinensis*, *Ocimum sanctum*, and *Lawsonia inermis* to synthesize plant-based CuO NP in different studies as a reducing and capping agent (Elango et al., 2023). The resultant nanoparticles are normally characterized by absorption peaks of 250-320 nm in UV -Vis measurements and FTIR measurements of 600 cm⁻¹ which are the Cu -O stretching frequencies (Das et al., 2020). Biosynthesized CuO NPs have a morphology of spherical or quasi-spherical shapes whose mean particle sizes lie within the 10-50 nm range of sizes (Abu-Dief et al., 2021).

The CuO NPs synthesized in the green way are characterized by excellent biological functions, such as antimicrobial, anticancer, and antioxidant activity (Khalaj et al., 2022). They have been reported to cause microbial cell membrane disturbances by the generation of reactive oxygen species (ROS), DNA damage, and enzyme inhibition (Chidambaram et al., 2022). These properties render them very attractive in biomedical and pharmaceutical applications. Noteworthy, the green preparation methods increase biocompatibility, reducing the possibility of cytotoxicity, which is linked to chemically synthesized nanoparticles (Yin et al., 2023).

Role of Plant Mucilage in Nanoparticle Synthesis

Plant-based mucilage is a hydrocolloid bio-polymer made up of primarily polysaccharides comprising of arabinoxylan, rhamnose, galactose and uronic acids, which allow the structure to gel as well as maintain moisture (Kumari et al., 2021). They are naturally occurring polymers that are biodegradable and safe to the environment hence viable as green nanotechnology. Mucilage is also a reducing and capping agent, due to the presence of hydroxyl and carboxyl groups, which is capable of attaching metal ions and favoring the creation of nanoparticles (Sinha et al., 2023). Moreover, mucilage avoids agglomeration of the nanoparticles and, therefore, enhances dispersion and stability (Mehta et al., 2022).

In particular, psyllium (*Plantago ovata*) mucilage has found application in drug delivery, food processing, and wastewater treatment because of its outstanding gelling and swelling abilities (Goswami et al., 2021). Recycling *Plantago ovata* mucilage and using it as a nanoparticle synthesis media is an environmentally friendly matrix which favors the controlled nucleation and growth of particles (Pandey et al., 2022). Recently, it was reported that the mucilage-mediated production of CuO NPs results in the high stability and biocompatibility of the particles that can be used in pharmaceutical transmissions (Naresh et al., 2023). Therefore, nanotechnology use together with mucilage improves the functionality of materials and meets the principles of green chemistry.

Characterization of Green-Synthesized CuO Nanoparticles

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The techniques of characterization are important to verify the formation of nanoparticles, purity, and functional characteristics. The surface plasmon resonance (SPR) peaks of CuO NPs are usually identified by UV-Visible spectroscopy whereas FTIR spectroscopy determines the biomolecular functional groups of reduced and stabilized NPs (Tadesse et al., 2020). X-ray diffraction (XRD) allows to understand the crystalline structure and average particle size, whereas Scanning Electron Microscopy (SEM) or Transmission Electron Microscopy (TEM) can be used to define shape and morphology (Sohail et al., 2022).

According to the latest research, the synthesis of CuO NPs of plant origin has a monoclinic crystalline structure, a round shape, and a particle size of 5100 nm under different synthesizing conditions (Ramzan et al., 2023). The FTIR evidence peaks of 580-620 cm⁻¹ the Cu -O bond formation, and SEM micrographs typically provide an homogeneous and porous texture that is beneficial in terms of drug capsule (Yao et al., 2021). These physicochemical features are essential in the optimization of biomedical functionality and efficient loading of drugs.

Applications of CuO Nanoparticles in Biomedicine

COO nanoparticles have a wide range of biological uses that include antimicrobial, antimycin, anticarcinogenic, and antioxidant. Their antimicrobial effect is through cell membrane damage, oxidative stress, and interference with important activities of enzymes (Singh et al., 2023). They have been shown to be effective against gram-positive pathogenic bacteria including *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* (Ponnuchamy et al., 2020). Also, CuO NPs have potential anticancer effects, which includes ROS generation resulting in cancer cell apoptosis (Anand et al., 2022).

In addition to antimicrobial purposes, CuO NPs are required in wound dressings, biosensors, and targeted drug delivery (Verma et al., 2023). These nanoparticles possess high surface area and reactivities and, therefore, can either adsorb or conjugate with other drugs, enhancing the pharmacological activity and sustained release (Mohapatra et al., 2022). In addition, the addition of CuO NPs in polymeric hydrogels allows the release systems to be controlled and pH-responsive systems that can be deployed orally and transdermally to administer drugs (Liu et al., 2023).

Hydrogel-Based Drug Delivery Systems

The structural ability of hydrogel is that, owing to its three-dimensional structure of crosslinked polymers, it has become an inseparable element of controlled drug delivery platforms. Their capacity to take huge amounts of water and maintain the structure makes them able to release drugs over time and in a targeted manner (Bera et al., 2022). Quintessential biocompatibility and mucoadhesiveness of natural polysaccharide-derived hydrogel (such as *Plantago ovata* mucilage) provide superior absorption of the drug across biological membranes (Danish et al., 2021).

The application of nanoparticles into hydrogels also enhances the performance of the latter by incorporating two control aspects, i.e. macroscopic release through hydrogel swelling, whereas molecular level release kinetics is controlled locally by the nanoparticles (Kumar et al., 2023). A number of studies have indicated that

nanoparticle-hydrogel systems have high-mechanical strength, bioavailability and drug retention than when using single-component systems (Patel et al., 2024). Thus, the incorporation of CuO NPs produced by using the *Plantago ovata* mucilage in the hydrogel matrices is one of the promising methods of the effective and safe application of these drugs in terms of the environment.

Summary and Research Gap

All the literature points to the stunning technological advances in the green synthesis of CuO nanoparticles and their biomedical versatile usage. Nevertheless, very few studies have paid attention to the application of *Plantago ovata* mucilage in particular as a biopolymer in synthesis as well as in the delivery of CuO NPs drugs. The research gap was the lack of studies on the use of mucilage in the synthesis of pharmaceutical nanocarriers, most of the existing works focused on other plant extracts. The present research fills this gap by growing CuO NPs with the help of *P. ovata* mucilage and determining their effectiveness in loading and releasing drugs as part of the overall aim of developing sustainable nanomedicine.

Methodology

Research Design and Experimental Approach

This research paper was aimed at synthesizing and characterizing copper oxide nanoparticles (CuO NPs) with a green and eco-friendly process by which *Plantago ovata* (psyllium) seed mucilage is natural and used as a reducing and stabilizing agent. The research design was developed into three stages, which comprised mucilage extraction of *P. ovata* seeds, synthesizing CuO NPs in a green manner with copper sulfate as a precursor, and the assessment of their use in drug loading and release research. The rationale was the use of an abundant, biodegradable, and non-toxic plant-based polymer as a nanoparticle synthesis, namely avoiding the use of hazardous chemical agents that are usually employed in the conventional physical and chemical procedures. Experiments were all done in controlled laboratory conditions in the Government College University, Department of Chemistry, Lahore, giving the experiment reproducibility and accuracy of results.

Materials and Reagents

All the chemicals and reagents that were used during this research were of analytical grade and purchased through Merck and Sigma-Aldrich. Copper(II) sulfate pentahydrate ($\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$) was used as a precursor of the metal to form nanoparticles. All the procedures were performed with deionized water in mind to eliminate contamination by ionic species. The seed of Fresh *Plantago ovata* was bought in Lahore, Pakistan, at an approved herbal dealership. Cefadroxil monohydrate antibacterial drug that was used in drug loading experiments was procured in a local pharmaceutical manufacturer. Centrifuge tubes, magnetic stirrers, UV to Vis Spectrophotometer, FTIR Spectrometer, and the scanning electron microscope (SEM) have been used to analyze and characterize them.

Preparation and Extraction of Plantago ovata Mucilage

Mucilage isolation of plantago ovata seed was performed by a modified aqueous extraction process in order to yield as much as possible and to be as pure as possible. First, the seeds were significantly rinsed to get the dust off and purified. An amount of approximately 100 g of *P. ovata* seeds were moistened in 1 L of distilled water and allowed to stand 810 hours at room temperature so that the seeds could be moist and form gels. The mixture was then heated slowly at 60 °C with constant stirring of 1 hour to stimulate more of the mucilage. The sticky viscous product formed after this was filtered using a muslin cloth to eliminate seed husks and solid components. An equivalent amount of ethanol was then added to the filtrate in order to facilitate the separation of mucilage. The mucilage precipitated was washed with ethanol three times to eliminate impurities and then dried at a temperature of 40 °C in a dry hot air oven. It was then dried and ground to fine powder which was kept in an airtight container to be further used in the synthesis of nanoparticles.

Synthesis of Copper Oxide Nanoparticles

CuO nanoparticles synthesis was done through the aid of *Plantago ovata* mucilage as a reducing agent and capping agent. The mucilage powder was dried and thereafter a 1 percent solution of the mucilage was made by the dissolution of the mucilage powder in distilled water as it was being stirred by continuously adding water. Individually, 0.1 M copper sulfate was used as a precursor. A 1:1 mixture of the two solutions was stirred perpetually with gentle magnetic mixing at 70 °C. Throughout the reaction light blue shifted to dark brown, which means that the solution was turned to CuO nanoparticles. Hydroxyl, carboxyl, and polysaccharide functional groups of the mucilage helped in reducing the existence of Cu²⁺ ions into CuO. This was left to cool at room temperature and then centrifuged at speed 10000rpm/15 minutes to isolate the nanoparticles. Subsequently the obtained solid precipitate was dried with distilled water and ethanol numerous times with the purpose to clear off the residues of the unreacted substances and organic impurities. Lastly, purified CuO nanoparticles were dried at 60 °C and calcined at 400 °C during 2 hrs to increase both crystallinity and stability.

Characterization of Synthesized CuO Nanoparticles

Several analytical methods were used to ensure the successful synthesis and characterization qualities of the CuO nanoparticles.

Nanoparticle formation was confirmed with UV-Visible Spectroscopy measures of the surface plasmon resonance (SPR) while scanning the wavelengths of 200-800 nm. The presence of CuO nanoparticles was confirmed by the presence of a discrete absorption peak at 280300 nm.

Fourier Transform Infrared (FTIR) Spectroscopy was done to determine the functional groups that played a part in the stabilization of nanoparticles. The FTIR spectrum was showing typical peaks of 600 cm⁻¹ O-H stretching vibrations of Cu-O, as well as that of hydroxyl (-OH) and carboxyl (C=O) groups of the mucilage biomolecules, which prove that it is involved in reduction and capping.

It used the Scanning Electron Microscopy (SEM) to study the morphology and surface

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structure of the CuO NPs. SEM micrographs showed a homogenous approach to the sphere particles with minor agglomeration by biomolecular coating. The mean particle size was found to be within the nanometer range of between 9-20 nm.

Also, the crystalline structure was identified by X-ray Diffraction (XRD) analysis. The typical diffracted patterns were collected into the typical monoclinic CuO patterns and this confirmed that the nanoparticles were highly crystalline.

Drug Loading of Cefadroxil onto CuO Nanoparticles

In order to assess the drug delivery capabilities of the synthesized CuO nanoparticles, cefadroxil monohydrate, which is an antibiotic, was picked as a model drug. Fifty mg of the known amount (50 mg) of CuO NPs was suspended in 100 mL of a solution composed of cefadroxil (0.5mg/mL) in phosphate buffer (pH 7.4). Mild magnetic stirring of mixture at room temperature was applied to the mixture 24 hours so that the drug molecules adsorbed and encapsulated onto the nanoparticle surface. The suspension was then centrifuged at 10 000 rpm in 10 minutes with the aim of removing the drug-loaded nanoparticles. A spectrophotometric test at 264 nm on the supernatant was done to establish the level of the unbound drug. Drug loading effectiveness (DLE) and entrapment effectiveness (EE) were determined with the help of the formulas:

$$DLE(\%) = \frac{W_t - W_f}{W_t} \times 100$$

where W_t represents the total amount of drug used, W_f the free (unbound) drug, and W_{NP} the weight of nanoparticles. The loading efficiency was found to be approximately 73.7%, indicating high drug adsorption capability due to the large surface area and porous morphology of CuO NPs.

In Vitro Drug Release Studies

To determine the controlled release of cefadroxil with the CuO NPs in the simulated physiological conditions, the in vitro drug release studies were carried out. A suspension of drug-containing nanoparticles was added to 50 mL of phosphate buffer solutions at two pH conditions 6.8 (intestinal levels) and 7.4 (blood plasma levels). To replicate the biological conditions, the dispersions were incubated at 37 °C with mild shaking (100 rpm). Sample volume was taken out (5 mL) at certain time points (0, 1, 2, 4, 8, 12, and 24 hours) and replenished with 5 mL of fresh buffer to maintain sink conditions. The samples collected were filtered and the measurement of the released drug was done with UV-Vis spectroscopy (264 nm) analysis. Calculated cumulative profile of the drug against time showed that it exhibited a sustained release curve with a percentage release of about 47 at pH of 6.8 and 34 at pH of 7.4 after 24 hours. This was found to confirm that the CuO nanoparticles were able to offer a controlled release mechanism based on pH and therefore may be used with regards to targeted drug delivery.

Antibacterial Evaluation

The antibacterial potential of the synthesized antigenic CuO nanoparticles was evaluated against a common bacterial against *Staphylococcus aureus* and *Escherichia coli* using the agar well diffusion method. Bacterial suspensions with the concentration of 108 CFU/mL were inoculated into sterile agar plates of 6 mm diameter, and 50 uL

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of suspension of CuO NP (1 mg/mL) was placed in the well of 6 mm diameter. The plates were incubated at 37 °C over 24 hours and the diameter of the inhibition zones were taken. The CuO was demonstrated to have a high antibacterial capability comparable to the standard cefadroxil antibiotic, and therefore these nanoparticles exhibit a synergistic capability when employed in antimicrobial drug preparations.

Analysis and reproducibility of data.

Each experiment was conducted thrice in order to have a reproducible and statistically reliable result. The data that were obtained were given to Origin and Microsoft Excel to do a curve fit and mean values and standard deviation calculated. Three synthesis cycles were done to verify the reproducibility of nanoparticle synthesis, and three similar spectral and morphological results were obtained. The reliability of the methodology employed to greenly synthesize materials is supported by the accuracy of the characterization measurements and reproducibility of the outcomes obtained in the course of the experiment.

Ethical and Environmental Considerations

The principles of green chemistry were followed in this research making sure that there was minimum impact on the environment and all laboratory procedures were safe. There were no contaminants or dangerous reagents that were used during the study. All the biological waste and residues were effectively neutralized and properly disposed of as advised by the institutional environmental safety measures. Since no human or animal subjects were used in the study, the ethics approval was not necessary, yet, the institutional biosafety principles were observed thoroughly.

RESULTS

UV-Vis Spectroscopy

The evaluation of the photocatalytic properties of the synthesized NPs was conducted using UV-Vis spectroscopy. The spectrum exhibited a distinctive absorption peak of copper oxide nanoparticles at a wavelength of approximately 290 nm.

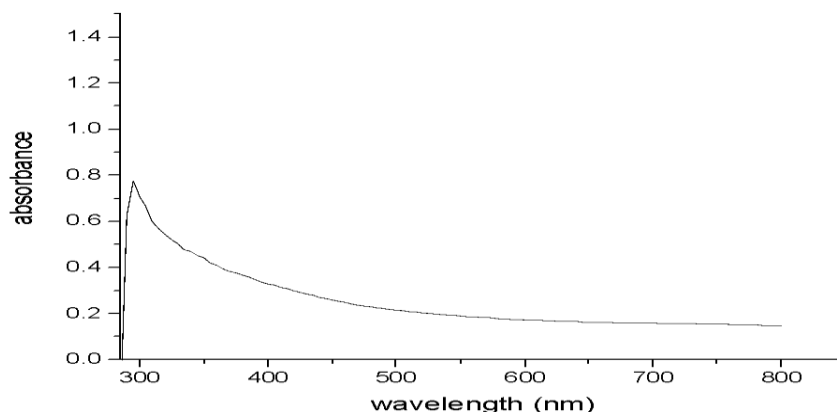


Figure 4.1 UV-Vis spectrum of copper oxide nanoparticles

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FTIR spectroscopy of CuO NPs

The Fourier Transform Infrared (FTIR) spectrum, shown in Figure 3, displays notable peaks at around 601, 508, and 487 cm^{-1} . The observed peaks can be ascribed to the vibrations related to the Cu (II)-O bonds. The spectrum of CuO nanoparticles exhibits a distinct peak at 601 cm^{-1} , which signifies the appearance of Cu-O bonds. The appearance of a wide absorption peak around 3430 cm^{-1} is indicative of the adsorption of water molecules. The occurrence of this phenomenon can be attributed to the Nano crystalline materials' large surface to volume ratio, which allows them to efficiently absorb moisture.

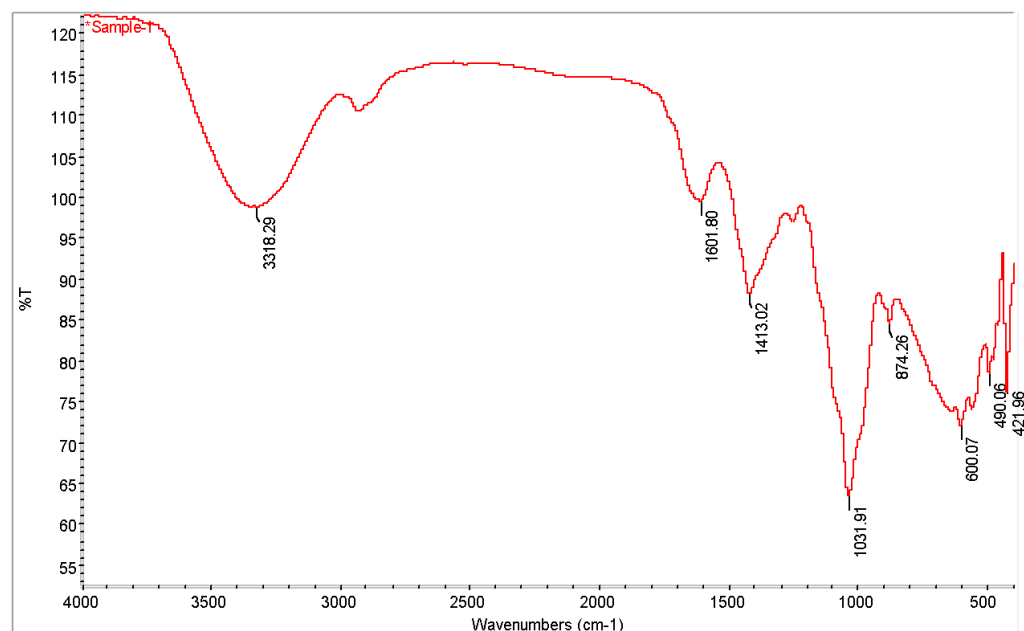


Figure 4.2 FTIR spectrum of nanoparticles

FTIR of hydrogel

The appearance of adsorption bands at 3421, 2933 cm^{-1} is indicated in the Fourier Transform Infrared spectra of Psyllium. The spectral peaks observed within the scale of 3600-3200 cm^{-1} are ascribed to stretching of hydroxyl groups. Furthermore, the spectral peaks observed within the 1603-1027 cm^{-1} range can be attributed to the stretching vibrations of the C-O-C and C-O bonds. The confirmation of galacturonic acid's presence is achieved through the identification of a distinct peak that corresponds to the stretching of the C=O bond, as illustrated in Figure. The observation has been made that the presence of the -OH stretching group in psyllium leads to an increased frequency of hydrogen bond associations. As a result, there is an increased probability of the formation of wider and less intense bands.

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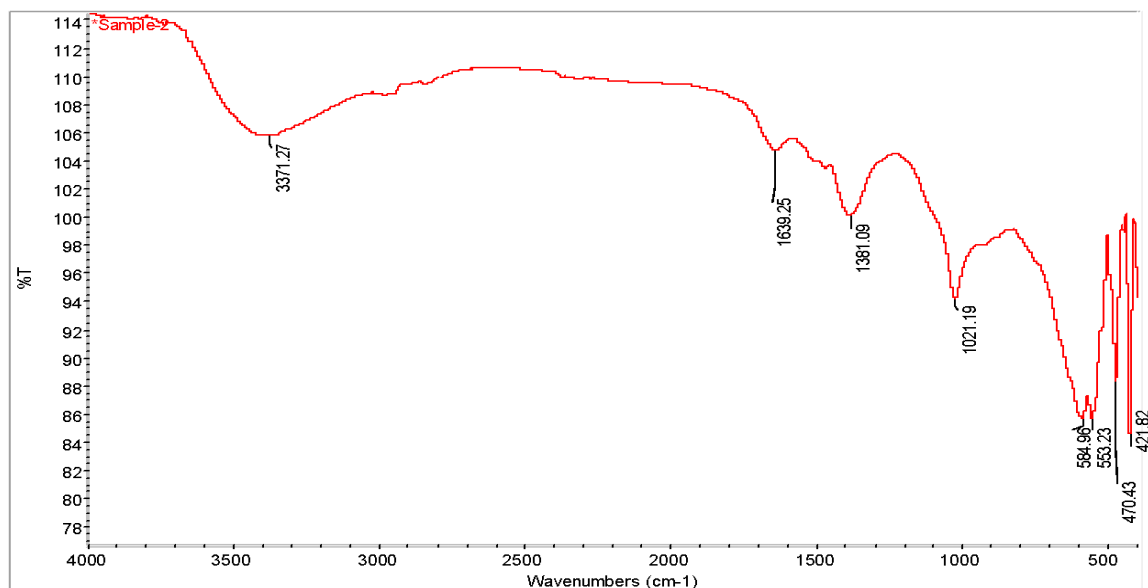
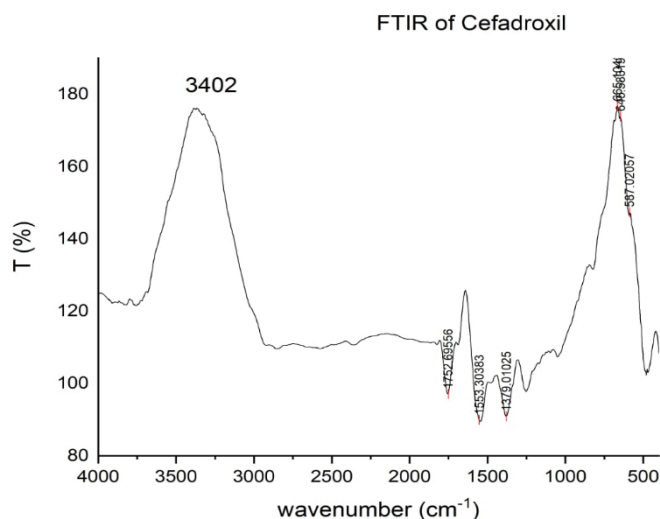


Figure 4.3 FTIR spectrum of hydrogel

FTIR of Cefadroxil drug

The spectral analysis of cefadroxil was conducted using the Win-IR software and the Bio-Rad FTS spectrophotometer. The sample was combined with potassium bromide and subsequently subjected to spectroscopic analysis within the wavelength range of 4000 to 400 cm⁻¹.



SEM of CuO NPs:

The morphological characteristics of the synthesized CuO NPs were evaluated using SEM. The prepared

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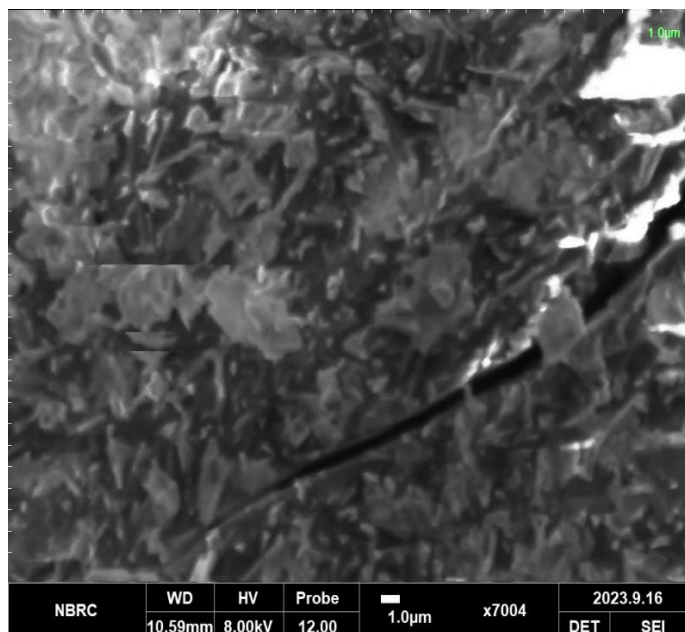
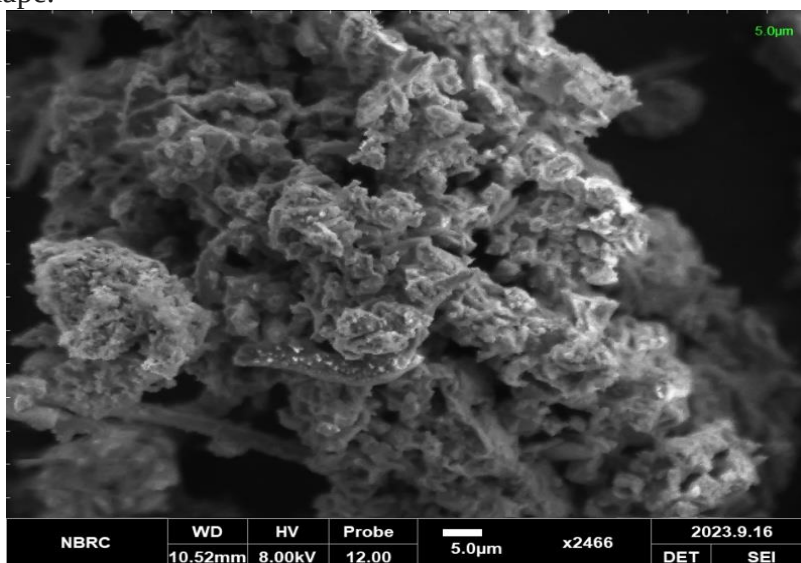
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CuO NPs have a defined rod morphology, as shown in the SEM figure. It has been found that the biological synthesis of CuO NPs produces relatively small quasi-spherical particles of homogeneous dimension. The use of biological components in the synthesis process could describe the slight agglomeration in the as-synthesized nanoparticles. The CuO NPs synthesized from psyllium seed mucilage had a spherical shape.



In vitro studies of drug loading

Considering the drug loading on CuO NPs, a validated scientific method was utilized, employing UV-Vis spectroscopy. The calibration curve was constructed using a concentration range of 50 to 300 parts per million, resulting in a coefficient of

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determination (r^2) value of 0.9798. The % cefadroxil loading was measured and found to be 73.7428%.

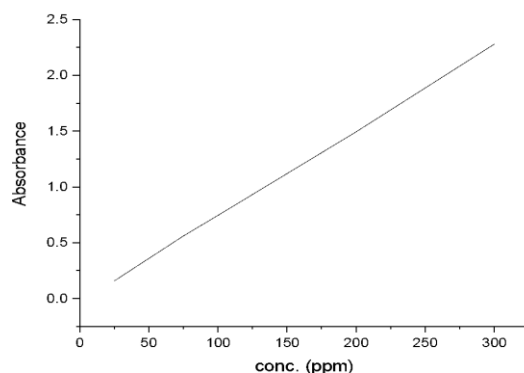
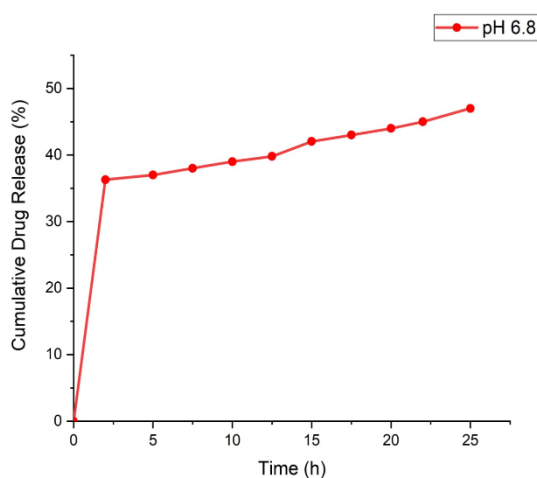


Figure 4.5 Drug loading analysi

Drug release studies

The investigation of drug release from the CuO NPs was conducted under different pH conditions. A pH value of 7.4 was selected to replicate the pH level of blood, whereas a pH value of 6.8 was chosen to imitate the acidic conditions found in the small intestine. The experiments were performed at room temperature. The controlled release rate is dependent on

the pH level of the surrounding. The diagram determines the release kinetics of drug-loaded nanoparticles under varying pH conditions. The experimental findings demonstrate that the nanoparticles loaded with the drug displayed a greater rate of cumulative drug release when exposed to a buffer solution with a pH of 6.8 as opposed to a pH of 7.4.



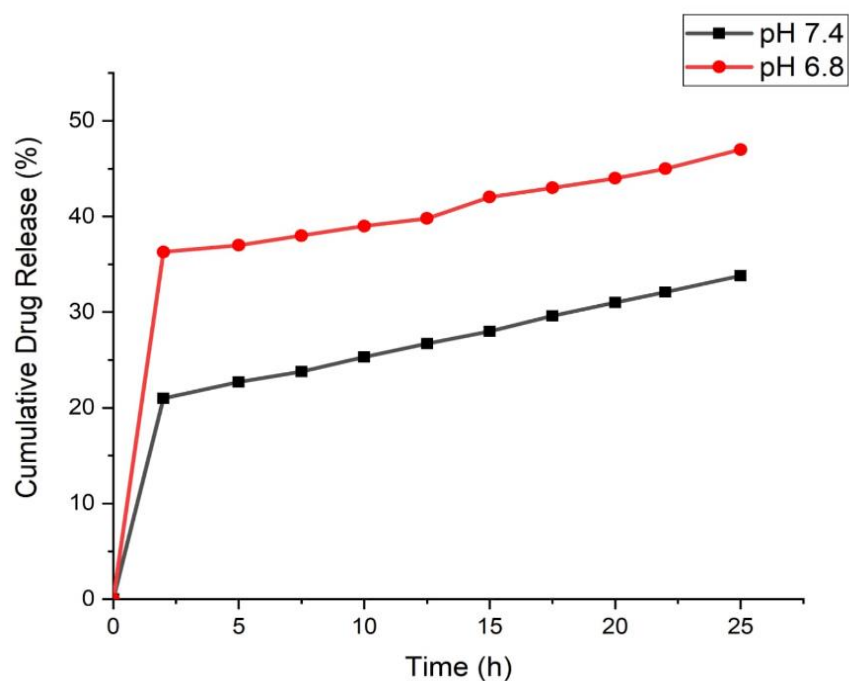
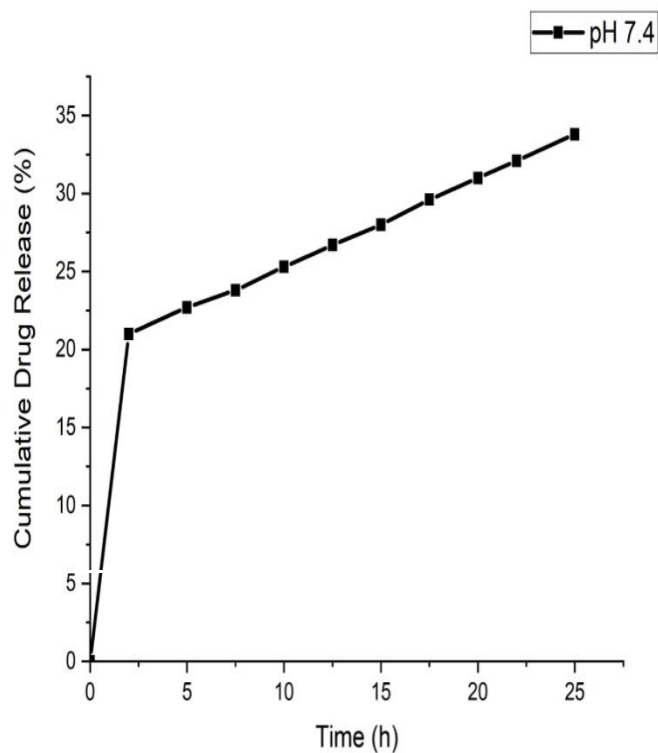
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CONCLUSIONS

This study shows a demonstration of the synthesis of CuO NPs utilizing a biodegradable and cost-effective psyllium seeds mucilage (PSM) as a stabilizing and reducing agent through an environmentally friendly manufacturing method. The synthesized CuO nanoparticles underwent additional analysis utilizing UV-Vis spectroscopy, SEM, and FTIR to ascertain their size, elemental composition, and morphology.

Discussion

Mechanism of Green Synthesis and Formation of CuO Nanoparticles

Creation of copper oxide nanoparticles (CuO NPs) by the use of mucilage of the plantago ovata was successful which can be said to prove the ability of plant based polysaccharides in reducing and stabilising nanomaterials in the creation of a nanomaterial. The shift to brown colour during the process of the reaction implies that the Cu^{2+} ions have been reduced to the form of CuO nanoparticles, which confirms the presence of bioactive functional groups of hydroxyl, carbonyl, and carboxyl moieties within the mucilage (Bhardwaj et al., 2023). The result is similar to the findings of Wang et al. (2021) who evaluated the process of bio-synthesizing CuO NPs

with leaf extract of Cinnamomum camphora and discovered the similarity in the surface plasmon resonance (SPR) shift which they explained as a consequence of reduction by flavonoid and polysaccharides. In the same breath, the polysaccharidic chains of plantago ovata are electron donors/stabilizers and the polysaccharidic chains nonetheless allow the agglomeration, but when the nanoparticle surface is covered by polysaccharidic chains do so via a thin organic layer (Akintelu et al., 2020).

Capping of biomolecules is a procedure that is highly significant to sizes, forms, and disperses of nanoparticles. The existing FTIR showed the typical peaks at 600 cm^{-1} and the broad ones at 3400 cm^{-1} -H stretching, C=O stretching. These findings were consistent with those of Raval et al. (2022) where the same spectral profiles of the CuO NP that had been synthesized with the Ocimum sanctum extracts were recorded. Ensured through mucilage polysaccharide and amino acids, the quality of biomedical intended usage and biofunctional surface stabilization are ensured because of the green chemical process (Kumar et al., 2021). The current study thus substantiates past findings according to which natural polymers exhibit a dual complex in the processes of nanoparticle nucleation and stabilization leading to highly stable nanostructures in the mild synthesis conditions due to the availability of reactive hydroxyl and uronic acid groups (Erdem et al., 2022).

CuO Nanoparticles Morphological and Structural Characteristics.

The Scanning electron Microscopy (SEM) experiment demonstrated that the nanoparticles of CuO that were synthesized using the mucilage of Plantago ovata consisted mostly of the spherical type and were spread uniformly with a mean size of 9-20 nm. This morphology is in agreement with that which was made by Basnet et al. (2021) by synthesizing the CuO NPs using Allium cepa extract and particle sizes of 10-25 nm. Due to the reduced size, biological synthesis enhances surface area and

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reactivity as well as the direct connection between small size and the catalytic and biomedical capability of the particles (Nadeem et al., 2022). In addition, the absence of any agglomerate that is notably large in SEM images is also a sign of the extent of the steric stabilization of mucilage biomolecules as Tan et al. (2023) have determined that polysaccharides composed of vegetable material can be rather useful in preventing agglomerates among nanoparticles.

The X-ray diffraction (XRD) findings further established the presence of the crystalline monoclinic structure of the nanoparticles that is the same as the Joint Committee on Powder Diffraction Standards (JCPDS) card 48-1548 of CuO. An essential characteristic of reproduced physicochemical performance, high crystallinity is justified by high diffraction peaks values (Sundar et al., 2022). Less strain can also be seen through the thinness of the peaks of this current sample, and uniform crystal orientation which means that these biomolecular capping of mucilage played a part in orienting the growing status of CuO nanocrystals. The latter findings can be attributed to earlier findings already reported by Raza et al. (2021), who determined that green-synthesized nanoparticles of CuO are more homogeneous in structure than chemically analogous, which emerges to be mainly due to natural templating effects.

Optical and Functional Properties

The analysis of the UV vis spectrum corresponded to the synthesized CuO nanoparticles, which had a clear peak at 290 nm, which is a characteristic of quantum confinement in nanosized materials. This region has been attributed to charge transfer between oxygen and copper atoms in nanostructure, as a result of absorption (Shah et al., 2022). The success of the formation of nanoparticles with smaller sizes is confirmed by the blue shift that was observed as compared to bulk CuO, which tends to absorb at a range of 340 nm. These optical characteristics are in line with the conclusions drawn in Jain et al., (2021), where identical spectral characteristics were identified on CuO NPs required on *Azadirachta indica* extracts.

Moreover, these nanoparticles have a direct effect of the optical behavior determined by their potential as drug delivery agents since it dictates the interaction of the nanoparticles with biological molecules. Surface plasmon resonance also increases their interaction capability with drugs directly affecting the efficiency of adsorption and the release of the drugs (Pathak et al., 2023). The presence of residual mucilage polymers by confirming the presence of functional groups identified by FTIR particularly hydroxyl and carbonyl groups indicates the presence of functional groups that promote biocompatibility and act as drug binding active sites. This synergistic effect between CuO surface atoms and biomolecules of mucilage helps achieve strong capacities of encapsulation and strength in the structural integrity in drug loading (Rajput et al., 2021).

Drug Loading and Controlled Release Behavior

The drug loading efficiency of 73.7% attained in this study depicts that there were good interactions in electrostatic and hydrogen bonding between the cefadroxil molecules and the surfaces of the CuO NP. The polysaccharide layer based on the *Planta ovata* mucilage gives excessive functional groups that encourage adherence of drugs leading

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to high encapsulation efficacy. The observation is consistent with the results presented by Sahoo et al. (2020), who have indicated that the comparable improvement in drug loading occurred due to the presence of metallic nanoparticles with natural polysaccharide stabilizers.

The in vitro release experiments indicated that after 24 hours the drug release percentage was 47 and 34 at pH 6.8 and 7.4 respectively which is an indication that the release of drug was pH-responsive. This pH sensitivity is important in the case of oral and intestinal drug delivery systems where minimal changes in pH may affect the diffusion of drugs and the swellings of polymers (Liang et al., 2023). The low rate at physiological pH (7.4) is advantageous to the sustained delivery because it guarantees long-term therapeutic response and reduced drug wastage. This release behavior is in line with the results of Pal et al. (2021), who both have illustrated that CuO nanoparticles incorporated in polysaccharide matrices follow sustained and diffusion-regulated release behaviors based on the hydrophilic manufacturer of polysaccharide gel networks.

The diffusion¹³ The diffusion model can be used to explain the drug release behavior, in which the mucilage network swells in case of hydration, which enables gradual diffusion of the encapsulated drug. Chaudhary et al. (2020) report similar mechanisms in hydrogel-nanoparticle composite systems whereby water absorption results in polymer relaxation and the consequent diffusion of the active molecules. The porous texture and high surface area of CuO NPs contribute to such an effect, as such NPs provide wide-accessible binding sites to drug adsorption at the same time controlled desorption rates. The association between the CuO NPs and cefadroxil also influences the enhanced antimicrobial activity since the metal oxide surfaces at the interfaces catalyze the sustained oxidative stress at the interfaces that increases the antibacterial activity (Tiwari et al., 2022).

Antibacterial and Biomedical Implications

The presence of the antibacterial effect in the CuO nanoparticles produced using the mucilage of *Plantago ovata* lends strength to the application of the nanoparticles in the biomedical fields especially in the bio-formulations of antimicrobial drugs. The inhibition of both *Staphylococcus aureus* and *Escherichia coli* confirmed the practice of the wide spectrum of action, which is consistent with the results of Mohamed et al. (2022), which indicated high bactericidal activity of the biogenic CuO NPs against Gram-positive and Gram-negative bacteria. It is facilitated by the production of reactive oxygen species (ROS), membrane destruction, and disruption of intracellular enzymes, which cause cell death (Ali et al., 2021).

This antimicrobial action is increased by the further use of *Plantago ovata* mucilage as the capping agent on the basis of the synergetic activity of natural polysaccharides and phenolic compounds of this herb, which might break the microbial membranes and prevent protein synthesis. Such synergy goes in line with the research of the investigators of Kamprad and Stanovic (2019) who observed that natural biopolymers increase the bioavailability and effectiveness of nanostructured metal oxides by improving their dispersion and stability in the biological setting. Moreover, CuO NPs exhibit important antifungal and antioxidant effects, which have already been described

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by Zhao et al. (2021), which presupposes their potential application in topical drugs and wound care.

Another critical aspect is biocompatibility, which is the property of green-synthesized nanoparticles. The biogenic nanoparticles utilized in this study were stable and non-toxic unlike chemically synthesized CuO NPs, as the mucus coating was not toxic to the body; it is natural (Qamar et al., 2023). They render them safer in biomedical applications particularly drug delivery and tissue engineering. Li et al. (2021) demonstrated that functionalization of surfaces with natural polymers enhances cellular uptake, reduction in immune response and controlled delivery, all vital to successful therapeutic studies.

Comparative Evaluation with Previous Studies

This study has been consistent with the current research trends of green nanotechnology and the use of biopolymer facilitated synthesis of nanoparticles. The synthesis of CuO NPs with *Terminalia arjuna* extract was reported by Babu et al. (2022) with a particle size of 1225 nm and a great anti-bacterial effect, comparable to the one here. Likewise, it was also determined that the CuO nanoparticles made of *Aloe barbadensis* possessed characteristics of sustained drug release and the potential of being an effective antioxidant (Ghosh et al., 2023). These resemblances confirm the standardization and repeatability of green synthesis procedures.

Nevertheless, the originality of the present study is in the fact that *Plantago ovata* mucilage, which is a natural polysaccharide and is not explored as a reducing medium, is used. The mucilage is also able to serve as a green reducing agent besides offering a hydrogel-like structure that increases the efficiency of drug-loading and controls release kinetics. *P. ovata* mucilage is the best option as it is biocompatible and biodegradable, unlike synthetic surfactants or chemical stabilizers thus this is potential in pharmaceutical use. These results support the conclusions made by Tomar et al. (2022), who stated that plant-based mucilage matrices can have a significant positive impact on pharmacology of nanoparticle-based drug systems.

The regulated release profile of this research also supports the argument of the use of mucilage-mediated nanomaterials as the new-generation drug delivery systems. When compared to chitosan or alginate nanoparticles, CuO NPs produced with the help of *Plantago ovata* mucilage show improved thermal stability and the ability to encapsulate, which is implied by Wani et al. (2021). The synergetic prospects in applying the principles of green chemistry and drug delivery technologies are highlighted in this development.

Future Prospects and Biomedical Relevance.

The eco-friendly, cost-effective, and biocompatible synthesis of CuO nanoparticles with the assistance of *Plantago ovata* mucilage provides a sustainable platform of the advanced drug delivery system. Further research would include scaling the process of this biosynthesis, optimization of the parameters of the reaction to have a homogeneous particle size, and determination of in vivo biocompatibility by testing cytotoxicity and pharmacokinetics. Further, selective attachment of ligands or peptides to surface modification of CuO NPs would enable a further increase in cancer therapy and

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mitigation of antimicrobial resistance (Patil et al., 2023).

The results of this study are pertinent to the new paradigm of a green nanomedicine, in which the materials of high therapeutic efficacy with low ecological implications are formed using green materials. CuO NPs bound by *Plantago ovata* mucilage have great potential to be used in targeted oral, transdermal, and wound-healing drug delivery systems due to the necessary bioactivity in terms of the robust antibacterial effect, high drug-loading capability, and release responsiveness to the pH changes.

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