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The Potency of Noni Leaves Extract (*Morinda citrifolia* L.) as a Bioreductor in the Synthesis of Copper Nanoparticles and Its Effectiveness as an Antibacterial against *Streptococcus pyogenes*

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Abstract

The noni (*Morinda citrifolia L*) is one of Indonesia's traditional medicinal plants, which people have widely used to treat dysentery, hypertension, diabetes, and heart attacks, and prevent cancer. The noni contains phenolic compounds, namely flavonoids, anthraquinones, alkaloids, and tannins, which have the potential to act as bioreductors. The research aims to synthesize copper nanoparticles (CuNPs) using noni leaves extract as a bioreductor and assay their antibacterial activity. CuNPs were synthesized by mixing noni leaf extract and copper sulfate in a 1:1, 1:2, 1:3, and 1:4 ratio. It was characterized using UV-Vis, PSA, FTIR, and XRD. Antibacterial activity was tested using the disc diffusion method on *Streptococcus pyogenes*. The results showed that the optimum synthesis of CuNPs was at a ratio of 1:3 and pH 10. CuNPs had a maximum UV-Vis absorption wavelength at 305 nm, an average particle size of 5.46 nm with a polydispersity index (PDI) of 0.2048, and the Cu-O peak was observed at 560 cm^{-1} in the FTIR spectrum. XRD measurements revealed peaks at 2θ angles of 43.38°, 50.50°, and 74.43°. CuNPs showed good potential as an antibacterial agent against *Streptococcus pyogenes* with an average inhibition zone diameter of 17.3 mm. Thus, copper nanoparticles synthesized using noni leaf extract bioreductor had the potential to be developed as an antibacterial agent for *Streptococcus pyogenes.*

1. Introduction

Developing an environmentally friendly process for synthesizing copper nanoparticles (CuNPs) is a new aspect in nanotechnology. In recent years, secondary metabolites found in plant extracts have been widely used as natural reductants in the green synthesis process of various nanoparticles. This method is cheap, simple, and can be applied on a larger scale. Nanoparticles are small solid particles with diameters ranging from 1 to 100 nm [1]. Nanoparticles have several advantages, including being able to penetrate the intercellular space that is only the size of a colloidal particle, it has a greater ability to penetrate cell walls through diffusion and opsonization and can be flexibly combined with several other technologies to open up new opportunities for wider development opportunities for various needs and purposes. Another advantage of nanoparticles is the increased affinity of the system due to the same amount of contact surface [2].

Metal nanoparticles are among the most extensively developed nanomaterials, with copper nanoparticles being a prominent example [3]. These nanoparticles have attracted significant attention from researchers due to their various applications, such as antibacterial agents, and several advantages, including their non-toxic nature as conductive materials, ease of synthesis, and relatively low and affordable production costs. Copper nanoparticles can be synthesized through physical and chemical methods. However, both approaches often require substantial time, energy, and financial resources and may pose environmental risks. With advancements in technology, metal nanoparticles can now also be synthesized using chemical methods that align with the principles of green synthesis, commonly referred to as biological methods.

Green synthesis utilizes natural materials such as plants, microorganisms, fungi, and algae as reducing agents and stabilizing agents in nanoparticle synthesis [4]. Compared to chemical and physical methods, biological synthesis offers several advantages: it is cost-effective, environmentally friendly, suitable for large-scale production, and does not require high pressure, energy, temperature, or toxic chemicals [5].

In this study, copper nanoparticles were synthesized using *Morinda citrifolia* leaf extract as a bioreductant, as this specific synthesis has not been previously reported. *Morinda citrifolia*, commonly known as noni, mengkudu, tibah, wakudu, ach, or pace, is one of Indonesia's traditional medicinal plants, widely used to treat conditions such as dysentery, hypertension, diabetes, and heart disease, as well as for cancer prevention [6]. *Morinda citrifolia* L. is a plant that contains various types of bioactive compounds, such as flavonoids, anthraquinones, saponins, antrapolyphenols, triterpenes, alkaloids, and tannins [7]. These bioactive compounds, especially phenolic compounds, allow the reduction of Cu^{2+} ions into copper nanoparticles (Cu^0).

Copper nanoparticles have good antimicrobial properties, including antibacterial and antiviral activities [8]. These properties arise from the interaction between microbial membranes and metal ions released into the surrounding solution. As the nanoparticles gradually oxidize, they release copper ions and generate reactive oxygen species (ROS), which lead to membrane denaturation, lipid peroxidation, protein oxidation, and DNA degradation [9, 10]. Due to their small size, copper nanoparticles can penetrate bacterial cell walls and disrupt intracellular biochemical pathways by damaging cellular organelles. This multi-targeted mechanism makes it highly challenging for bacteria to develop resistance against copper nanoparticles.

Synthesis of CuNPs has been reported using bioreductors from several plant extracts, including *Phragmanthera austroarabica* [11], *Garcinia mangostana* [12], *Eryngium caucasicum* [13], and *Carica pubescens* [14]. However, no research has reported using noni (*Morinda citrifolia* L.) leaf extract for CuNPs synthesis, nor has it had any antibacterial activity against *Streptococcus pyogenes*. Therefore, this study aims to synthesize CuNPs using noni leaf extract through a green synthesis approach. The materials used in the synthesis include $CuSO_4.5H_2O$ as the copper precursor and noni leaf extract as the bioreductant and stabilizing agent. The synthesized copper nanoparticles were characterized using UV-Vis spectrophotometry, Fourier-transform infrared spectroscopy (FTIR), particle size analyzer (PSA), and X- ray diffraction (XRD). Furthermore, their antibacterial activity was evaluated against *Streptococcus pyogenes*, a primary causative agent of pharyngitis that remains prevalent among the Indonesian population.

2. Experimental

2.1. Materials and Instruments

The materials used in this study were noni leaves (*Morinda citrifolia L.*) obtained from Bugul Kidul Village, Bugul Kidul District, Pasuruan City, East Java, $CuSO_4.5H_2O$ (Merck), distilled water (Otsuka), filter paper, aluminum foil, warp, disc paper, Nutrient Agar media, *Amoxicillin*, NaCl, $BaCl_2$, H_2SO_4 (Merck), and bacterial suspension (*Streptococcus pyogenes*).

The instruments used in this study were a UV-Vis spectrophotometer (Shimadzu UV-1600), a PSA (Malvern), an XRD (Shimadzu XRD-6000), and an FTIR spectrophotometer (Perkin Elmer).

2.2. Extraction of Noni (*Morinda citrifolia* L) Leaves

Sample extraction was carried out using the infusion method. Noni leaves powder (10 g) was dissolved using deionized water (100 mL). The solution was covered with aluminum foil to avoid light effects and then stirred using a magnetic stirrer for 30 minutes at a temperature of 70°C. Afterward, it was allowed to cool to room temperature for approximately one hour. The mixture was then filtered using Whatman No. 1 filter paper to separate the filtrate from the residue. The resulting filtrate was stored at 4°C and later used as a bioreductant to synthesize copper nanoparticles [15, 16].

2.3. Preparation of 0.1 M $CuSO_4.5H_2O$

A total of 2.4969 g of $CuSO_4.5H_2O$ crystals was weighed to prepare a 0.1 M solution. The salt was placed into a 100 mL beaker and dissolved in approximately 95 mL of distilled water. The mixture was stirred using a magnetic stirrer until a homogeneous, clear blue solution was obtained. The solution was then transferred into a 100 mL volumetric flask and diluted with distilled water up to the calibration mark. Finally, the prepared solution was stored in a glass bottle for further use [17].

2.4. Noni (*Morinda citrifolia* L.) Leaves Extract

2.4.1. Synthesis of CuNPs with Comparison of Bioreductor Concentrations

Synthesis of CuNPs was carried out by mixing noni leaf extract with a 0.1 M $CuSO_4.5H_2O$ solution in varying ratios: 1:1, 1:2, 1:3, and 1:4 (30 mL:30 mL, 20 mL:40 mL, 15 mL:45 mL, and 12 mL:48 mL), maintaining a total volume of 60 mL for each mixture. The solutions were stirred using a magnetic stirrer at 70°C and 1500 rpm for 30 minutes. After stirring, the mixtures were allowed to stand for 24 hours, during which a visible color change to greenish-brown was observed, indicating nanoparticle formation. The resulting solutions were analyzed using UV-Vis spectrophotometry in the range of 200–800 nm to determine the maximum absorbance wavelength and identify the optimal ratio between the noni leaf extract and the $CuSO_4.5H_2O$ precursor [12, 17].

2.4.2. Determination of Optimum pH

The synthesis using the optimum extract-to-precursor ratio was further optimized by adjusting the pH to 6, 7, 8, 9, and 10. This was achieved by adding 0.1 M

NaOH dropwise during stirring on a magnetic stirrer. The resulting solutions were then analyzed using UV-Vis spectrophotometry to measure the maximum absorbance wavelength and determine the optimal pH for CuNPs synthesis [17].

2.5. Characterization of Synthesized CuNPs

2.5.1. UV-Vis Spectrophotometer

Characterization using a UV-Vis spectrophotometer was conducted by first setting the wavelength range from 200 to 800 nm. A blank solution was placed into the cuvette to perform the baseline calibration. Subsequently, the test sample-diluted with deionized water-was placed into the cuvette and inserted into the spectrophotometer. The measurement was initiated by selecting the "Start" function, allowing the instrument to record the absorbance at the specified wavelength range [18].

2.5.2. Fourier Transform Infrared Spectroscopy (FTIR)

The synthesized CuNPs were characterized using FTIR to identify the shift of functional groups in the reduction and stabilization processes during synthesis. The analysis was performed by preparing the solid CuNPs with KBr pellets and analyzing them using the FTIR instrument within a wavelength range of 450-4000 cm^{-1}. The analysis showed the peaks and functional groups acting as reducing or stabilizing agents. These results were then compared with standard reference spectra [19].

2.5.3. Particle Size Analyzer (PSA)

The synthesized CuNPs were characterized using PSA to determine their size. The particle size distribution analysis was based on the maximum size obtained for a specific percentage of the sample volume. For this purpose, 0.1 grams of CuNPs were dissolved in 5 mL of distilled water and sonicated for 15 minutes. The resulting solution was then transferred into a portable cuvette and analyzed using the PSA instrument [19].

2.5.4. X-ray diffraction (XRD)

CuNPs were analyzed using an XRD equipped with a Cu Kα radiation source and a Ni filter, operated at 30 kV and 30 mA. All XRD data were collected under the same experimental conditions within the angular range of $20° \leq 2\theta \leq 80°$ [20].

2.6. Antibacterial Activity Test

The antibacterial activity of CuNPs was evaluated against Gram-positive *Streptococcus pyogenes* using the disc diffusion method and compared with the activity of the noni leaf extract. Both the CuNP and extract solutions were prepared at a concentration of 100%. Bacterial cultures were standardized to match the turbidity of a 0.5 McFarland solution. The test began by inoculating the bacterial suspension onto solid agar media, followed by the placement of sterile paper discs soaked with the CuNP and extract solutions onto the agar surface. The petri dishes were then incubated at 37°C for 24 hours. After incubation, the inhibition zones were observed and measured based on the clear zones surrounding the discs, indicating the area of bacterial growth inhibition [3].

3. Results and Discussion

3.1. Characterization of CuNPs using UV-Vis Spectrophotometer

CuNPs were characterized using a UV-Vis spectrophotometer to confirm their formation. The characteristic peaks, which indicate the presence of CuNPs, were observed within the wavelength range of 300-400 nm. In this study, the absorption spectrum was recorded in the range of 200–800 nm.

3.1.1. Optimization of CuNPs with Comparison of Bioreductor Concentrations

The concentration of the bioreductant is a key factor influencing nanoparticle formation. An optimal volume of noni leaf extract enhances the reduction of Cu^{2+} ions, facilitating their conversion into copper nanoparticles. Increasing the concentration of the leaf extract improves its reducing capability, leading to more efficient reduction of Cu^{2+} to Cu^0, resulting in a higher yield of CuNPs [21].

Based on Figure 1, the lowest absorbance was observed at the 1:1 ratio (E1C1), with a value of 0.985 at a wavelength of 311 nm, while the highest absorbance was recorded at the 1:3 ratio (E3C1), with a value of 1.857 at a wavelength of 314 nm. These results are consistent with the findings reported by Suprapto *et al.* [22], who stated that copper nanoparticles synthesized using *Caromoliana odorata* L. leaf extract exhibited a maximum wavelength of 305 nm. The variation in maximum wavelength is influenced by the secondary metabolites present in the bioreductant, which affect the structure, size, and stability of the resulting nanoparticles. Smaller nanoparticles typically exhibit a Surface Plasmon Resonance (SPR) peak at shorter (blue-shifted) wavelengths, whereas larger nanoparticles tend to show a red-shift toward longer wavelengths [23].

3.1.2. Optimization of CuNPs by pH Determination

Following the identification of the optimal bioreductant-to-precursor volume ratio, pH optimization was carried out to determine the most favorable pH condition for synthesizing copper nanoparticles. This step aims to produce CuNPs with relatively smaller and more stable sizes under optimal conditions [24].

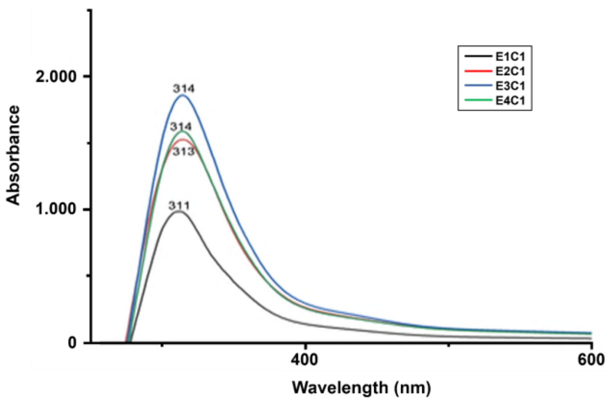

Figure 1. UV-Vis spectra of CuNPs with varying volume ratios

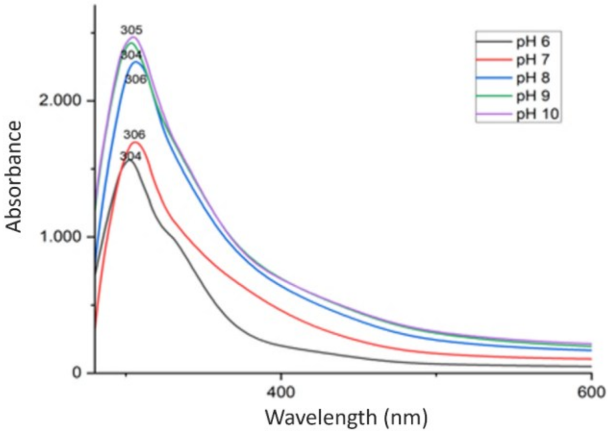

Figure 2. UV-Vis spectra of CuNPs at varying pH values

Figure 2 shows that the lowest absorbance was observed at pH 6, with a value of 1.564 at a wavelength of 304 nm, while the highest absorbance occurred at pH 10, with a value of 2.469 at a wavelength of 305 nm. These findings are consistent with the study reported by Alahdal *et al.* [11], which demonstrated that copper nanoparticles synthesized using *Phragmanthera austroarabica* extract exhibited optimal formation at pH 10. Variations in wavelength and absorbance are influenced by the pH of the reaction medium.

At higher pH levels, the functional groups of secondary metabolites in the bioreductant become deprotonated, enhancing their ability to stabilize and reduce copper ions. This leads to the formation of a larger number of nanoparticles with more uniform sizes, resulting in a narrower SPR band with higher intensity [25]. Rajeshkumar and Rinitha [26] also reported that alkaline conditions facilitate a greater reduction of copper ions, promoting the synthesis of smaller nanoparticles. In contrast, acidic conditions tend to induce nucleation aggregation, resulting in larger, non-uniform nanoparticles forming and producing a broader SPR band with lower intensity [23, 25].

3.2. Characterization of CuNPs using Particle Size Analyzer (PSA)

A material can be considered a nanoparticle with a size range of 1-100 nm [27]. In Figure 3, the PSA histogram of CuNPs indicates an average particle size of 5.46 nm. This value falls within the nanoparticle size range, confirming the successful formation of copper nanoparticles. These results demonstrate the potential of aqueous noni leaf extract as an effective bioreductant for the green synthesis of CuNPs. The Poly Dispersion Index (PDI) value obtained was 0.2048, indicating that the synthesized CuNPs sample is included in the homogeneous category with a fairly high level of size uniformity [28]. This finding aligns with the study conducted by Hasheminya and Dehghannya [13], who reported that copper nanoparticles were synthesized using *Citrus medica* fruit extract with an average particle size ranging from 10–60 nm. Similarly, synthesis using *Carica pubescens* fruit extract yielded copper nanoparticles with an average size of 14.49 nm [14].

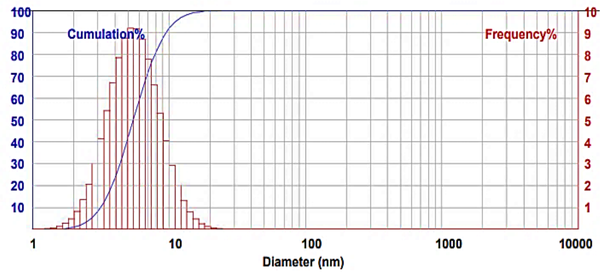

Figure 3. Characterization results of CuNPs using the PSA instrument

3.3. Characterization of CuNPs using Fourier Transform Infrared Spectroscopy (FTIR)

FTIR analysis was used to identify functional groups of chemical compounds contained in noni leaf extract, which play a role in reducing Cu^{2+} ions and stabilizing the formed CuNPs. The FTIR spectrum of Morinda citrifolia leaves extract and CuNPs is shown in Figure 4. The FTIR spectra of noni leaf extract exhibited absorption bands at 3272.38 cm^{-1}, indicating the presence of hydroxyl (–OH) groups, which are typically associated with phenolic compounds. The absorption peak detected at 2938.02 cm^{-1} corresponds to the C–H stretching vibrations. Meanwhile, the peak at 1603.52 cm^{-1} was attributed to the stretching vibration of carbonyl (C=O) groups, suggesting the presence of aldehydes, ketones, or carboxylic acids in the extract. Furthermore, a band at 1397.19 cm^{-1} was associated with the bending vibrations of alkane C–H bonds, and the absorption peak at 1050.35 cm^{-1} was linked to the C–O stretching vibrations, indicating the presence of alcohols, ethers, or esters [9, 29, 30, 31].

In contrast, the FTIR spectrum of the CuNPs showed a shift in these characteristic peaks, indicating interactions between the extract's functional groups and copper ions. The –OH group peak appeared at 3211.29 cm^{-1}, suggesting the involvement of phenolic compounds in the reduction process. The C–H stretching peak shifted to 2922.43 cm^{-1}, the C=O stretching peak to 1601.44 cm^{-1}, the C–H bending peak to 1389.67 cm^{-1}, and the C–O stretching peak to 1023.22 cm^{-1}. Additionally, a new absorption peak at 560.29 cm^{-1} appeared, corresponding to Cu–O bonds, confirming the formation of copper oxide nanoparticles [23, 29].

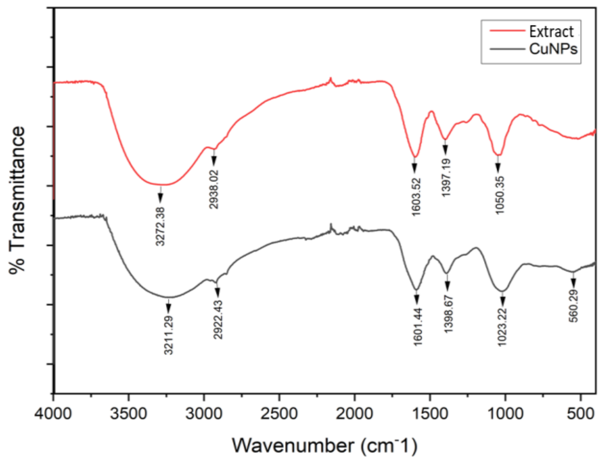

Figure 4. FTIR spectra of noni leaf extract and CuNPs

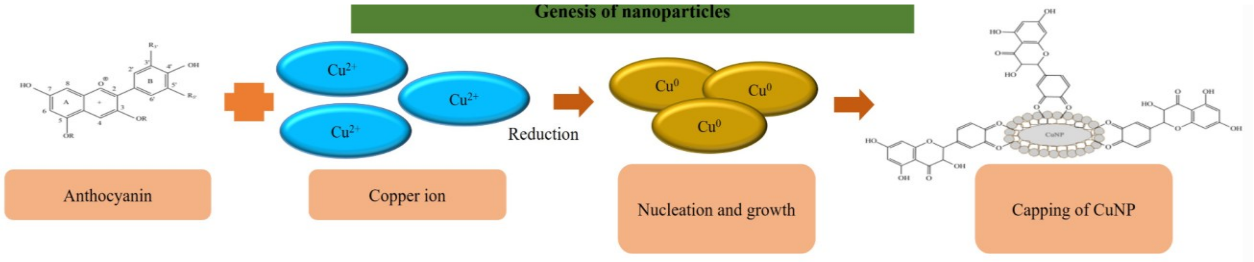

Figure 5. Reduction reaction between plant bioactive compounds and Cu^{2+} ions [32]

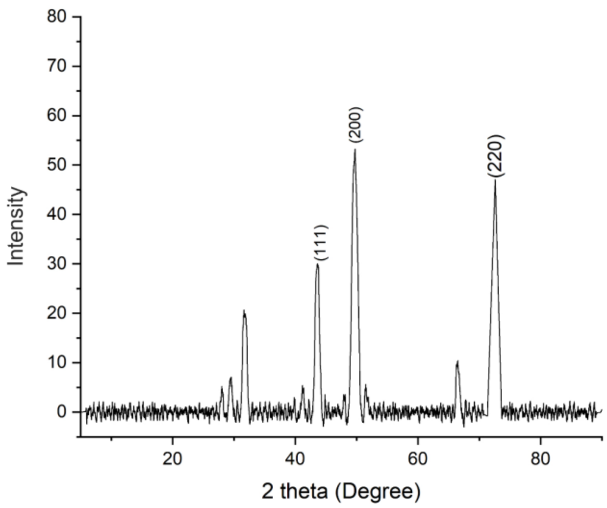

Figure 6. Diffractogram of CuNPs

The observed shifts in wave numbers and changes in absorption intensity suggest a significant interaction between the functional groups in the extract and Cu^{2+} ions, which supports the occurrence of a bioreduction process. The phenolic –OH groups, along with other functional groups present in flavonoids, tannins, saponins, and alkaloids, are likely responsible for reducing Cu^{2+} to Cu^0. The proposed mechanism for the reduction of Cu^{2+} ions from the $CuSO_4$ precursor by flavonoid compounds is illustrated in Figure 5. The phenolic –OH group in flavonoid compounds is oxidized into a quinone group, while the Cu^{2+} ion is reduced into copper nanoparticles (Cu^0). In addition, the flavonoid compound also acts as a capping agent to stabilize copper nanoparticles (CuNPs) [32].

3.4. Characterization of CuNPs using X-ray diffraction (XRD)

The synthesized CuNPs were further characterized using XRD analysis to confirm their successful formation and to examine their crystallographic structure. Figure 6 shows that the XRD patterns revealed distinct diffraction peaks that matched well with the standard reference data from the International Centre for Diffraction Data (ICDD), specifically Cu No. 01-070-3039.

The XRD results showed characteristic peaks of CuNPs at 2θ values of 43.38°, 50.50°, and 74.43°, which correspond to the cubic crystal system. The diffractogram also exhibited several additional peaks that differed from those typically associated with pure copper nanoparticles. This observation indicates that the synthesized CuNPs were not entirely pure and likely contained several impurities [33].

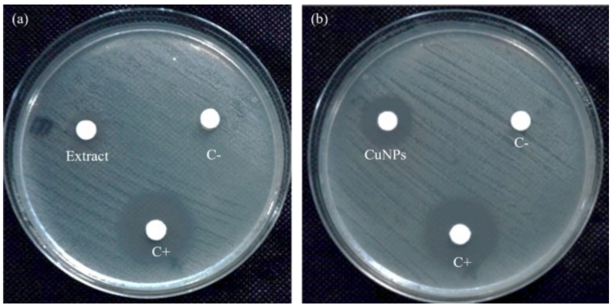

Figure 7. Antibacterial activity test of (a) noni leaf extract, (b) CuNPs against *Streptococcus pyogenes*

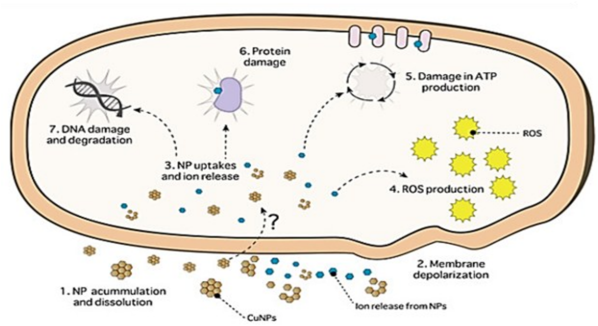

Figure 8. Antibacterial mechanism of CuNPs

3.5. Antibacterial Activity Test against *Streptococcus pyogenes*

The antibacterial activity test aimed to evaluate the effectiveness of noni leaf aqueous extract against *Streptococcus pyogenes*. The test employed the disc diffusion method, using a 100% concentration for both the extract and the CuNPs. Figure 7 and Table 1 show that the diameter of the inhibition zone for CuNPs is larger than that of the noni leaf extract against *Streptococcus pyogenes* bacteria, indicating that CuNPs exhibit stronger antibacterial activity than the noni leaf extract. The larger inhibition zone observed with CuNPs demonstrates that their antibacterial effect is enhanced in nanoparticle form. The size of nanoparticles plays a significant role in their antibacterial properties. Smaller particles increase the surface area and interaction with bacteria, thereby enhancing their antibacterial effects [13, 34].

Additionally, smaller particles promote the release of metal ions from the nanoparticle surface, contributing to their stronger antibacterial activity. Therefore, it can be concluded that the enhanced antibacterial properties of CuNPs in this study are attributed to their relatively small size [18, 35]. The antibacterial activity of CuNPs is influenced by their interaction, accumulation, dissolution, and the release of Cu^{2+} ions at the bacterial cell membrane, as depicted in Figure 8.

Table 1. Inhibition zone diameter measurements from the antibacterial activity test

Sample	Inhibition zone diameter (mm)			Average (mm)	Category
	1	2	3		
Noni leaves extract	8.15	8.29	8.12	8.18	Medium
CuNPs	17.25	17.45	17.21	17.3	Strong
Positive control (Noni leaves extract)	25.68	25.75	25.47	25.63	Very strong
Positive control (copper nanoparticles)	25.89	25.44	25.67	25.66	Very strong
Negative control	-	-	-	-	-

The accumulation and interaction of CuNPs with the cell membrane lead to a decrease in the proton motive force, causing membrane depolarization and rupture. This process facilitates the entry of nanoparticles into the cell. Once inside, the nanoparticles destabilize the cell, releasing Cu^{2+} ions. The release of Cu^{2+} ions triggers ROS formation, leading to lipid peroxidation, protein oxidation, and DNA degradation. Additionally, copper ions can damage DNA and interfere with ATP formation by interacting with phosphate and -SH groups in proteins and DNA. This results in structural disturbances, cell damage, and bacterial death [10].

In contrast, the antibacterial activity of noni leaf extract is attributed to the secondary metabolites it contains, such as flavonoids, tannins, terpenoids, and alkaloids. Each of these metabolites exhibits specific antibacterial mechanisms. For example, flavonoid compounds can disrupt cell membrane integrity and form complexes with extracellular proteins, leading to membrane damage and the leakage of intracellular contents [36].

4. Conclusion

CuNPs were successfully synthesized using noni leaf extract via a green synthesis method. The optimal synthesis conditions were achieved with a 1:3 volume ratio and pH 10. The UV-Vis spectrum revealed a peak absorption at 305 nm, while the particle size averaged 5.46 nm (PDI 0.2048). FTIR analysis showed a Cu-O peak at 560 cm^{-1}. XRD analysis identified diffraction peaks at 2θ angles of 43.38°, 50.50°, and 74.43°. Furthermore, the CuNPs demonstrated strong antibacterial activity against *Streptococcus pyogenes*, with an inhibition zone diameter of 17.3 mm.

Acknowledgments

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