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Green Synthesis, Characterization and Evaluation of Antimicrobial Activity of Copper Oxide Nanoparticles Using Natural Extract of Ginger (Zingiber officinale)

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Abstract- The green synthesis of CuO nanoparticles using plant extracts, specifically ginger (Zingiber officinale) was studied for its affordability and eco-friendly traits. The CuO NPs were analyzed via Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), field emission scanning electron microscopy coupled with energy dispersive X-ray spectroscopy (FESEM-EDX) and TEM. Their antimicrobial effectiveness was evaluated against two bacterial strains Escherichia coli (E. coli) and Staphylococcus aureus (S. aureus) and two fungal species Fusarium oxysporum (F. oxysporum) and Fusarium graminearum (F.graminearum) using the disk diffusion technique. The biosynthesized CuO nanoparticles were evaluated alongside chemically synthesized CuO nanoparticles to assess how the synthesis method influences their structural, optical, morphological properties, as well as their antibacterial and antifungal efficacy. The topological characteristics including dimensions, shapes, aggregation behavior, and basic structural arrangements of green-synthesized CuO nanoparticles are critical determinants of their biological activity. Investigations serve as valuable methods for studying these properties. TEM analysis confirmed that the biosynthesized CuO nanoparticles have a spherical shape. Particle size distribution analysis showed a size range of 4 to 28 nm, with an average diameter of 16.2 nm.

Key words: Nanocomposites, Green Synthesis, Natural, Extracts Ginger, Antibacterial and Antifungal Activity.

I. INTRODUCTION

Metal and metal oxide nanoparticles have become some of the most advanced materials in nanotechnology due to their modified and adjustable morphology, small size, large surface area, and unique physicochemical properties [1, 2]. They have diverse applications in agriculture, pharmaceuticals, biology, and environmental fields. These nanoparticles offer benefits such as low toxicity, high chemical and thermal stability, compatibility, easy synthesis, variable nano scale morphology, high specific surface area, enhanced oxygen adsorption capacity, and low cost [3-5]. A growing trend in green nanotechnology focuses on developing practical, non-toxic, and natural methods for producing metal oxide nanoparticles in aquatic environments [6].

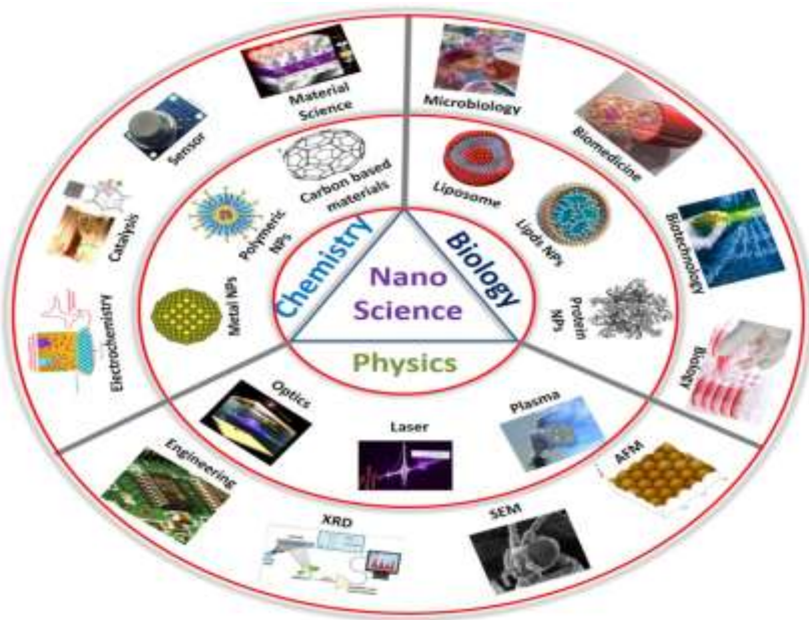

Fig:1 Graphical Abstract of Nano Science and nanotechnology

As a viable alternative to chemical and physical processes, the use of plants in the green synthesis of metal oxide nanoparticles has attracted a growing amount of attention [7]. The bio-resources (plants, fungi, algae, and microorganisms) that can serve as reducing agents, stabilizers, and capping agents in the formation of nanoparticles are used in the green synthesis approach for the synthesis of metal nanoparticles [8-10]. This approach outperforms conventional methods for the synthesis of metal nanoparticles because it is simple, cost-effective, and friendly to the environment]. As a result, researchers are working to develop cost-effective, clean, and nontoxic methods that completely eliminate the use of hazardous chemicals [11-13].

Plants like Punica granatum peel [14], Cedrus deodara [15], Ailanthus altissima leaf [16], Bougainvillea flower [17], Cucumis sativus (cucumber) [18], and Brassica oleracea var. italic [19] have demonstrated the CuO NPs' biosynthesis processes. The Euphorbiaceae family includes the E. alata plant, which is mostly found in China and the majority of Arab nations. Traditionally, this plant has been used to treat edema, allergies, nasal congestion, the flu, asthma, colds, chills, fever, coughs, and headaches. In addition, the dried stems of the plant have long been used medicinally by the community, particularly for their anti-cancer, anti-asthmatic, and bronchodilator properties.

There are a number of active metabolites in ginger extract, including volatile and nonvolatile compounds like gingerol, paradols, shogaol, alkaloids, flavonoids, and zingerone, all of which are thought to have distinct biological and medicinal properties [20]. The bioactive compounds in ginger extract have the potential to slow down and stabilize the synthesis of nano materials [21-23]. A green synthesis approach is supported by the use of ginger extract, which is in line with environmentally friendly and sustainable practices. It has fewer adverse environmental effects than conventional synthesis and uses fewer harsh chemicals [24]. Ginger extract is a good option for biomedical applications due to the biocompatibility and low toxicity of its bioactive compounds [25]. Therefore, Ginger extract, chosen as the raw material for the synthesis of nano materials, offers several distinct advantages owing to its unique chemical composition and functional properties.

Copper's electrical, optical, catalytic, biomedical, and antifungal and antibacterial applications make it the most widely used material in the world, followed by gold, silver, palladium, zinc, and so on. Copper nanoparticles are used as an antimicrobial in a variety of applications. Copper is considered an effective bactericidal metal because it is highly toxic to bacteria like E. coli, S. aureus, and P. aeruginosa but nontoxic to animal cells.

To enhance the surface reactivity and properties of nanoparticles, numerous well-defined CuO nanostructures have been synthesized in recent years, including nano spheres [26], nano flowers [27], micro machines [28], nano leaves [29], nano rods [30], nanotubes [31], nano sheets [32], and nano rings [33]. CuO NPs are produced through a variety of physical and chemical processes. However, these methods are not environmentally friendly, come at a high cost, necessitate long-term expansion, and require multiple steps.

Sensors [34], electrochemical [35], solar cells [36], optoelectronics [37], medical and pharmacy [38], industrial [39], and agricultural [40] are just a few of the many fields in which CuO NPs can be used. Degradation and removal of dyes and biological activity from wastewater to lessen their environmental impact have also piqued their interest [41]. Numerous textile industries, including food production, agricultural research, pharmaceuticals, paper manufacturing, cosmetics, and leather [42], rely heavily on dye. Among the chemically synthesized dyes, cationic dyes (MB) are the most commonly produced in larger quantities [43]. They can cause serious risks to human health and the natural environment due to their low biodegradability, stability, toxicity, and hazardous potential [44]. UV and solar radiation are utilized in a number of water treatment processes, including adsorption, reverse osmosis, foculation, coagulation, evaporation, electro-precipitation, and photocatalytic degradation [45]. Photocatalysis has proven to be an important wastewater treatment method thanks to these methods. Due to the process's cost-effectiveness by utilizing a renewable solar energy source, the development of the photocatalytic technique typically focuses on sunlight irradiation rather than artificial UV radiation [46]. In addition, because sunlight is naturally available, the goal is to use it to remove dyes, which is efficient, cost-effective, simple, and endless [47]. CuO is one of the most significant catalysts utilized in the process of removing industrial waste from the environment. The oxygen surface lattice of CuO is thought to be involved in the catalytic reaction, which appears to be a structure-sensitive mechanism. CuO nanostructures' form and exposed crystal planes influence their catalytic reactivity. Therefore, the structurally controlled synthesis of CuO structures may help develop novel structures with the needed improved performance [48-49].

Copper oxide nanoparticles have been the subject of much interest from researchers looking for agents with antimicrobial, antifungal, and Gram-positive and Gram-negative bacteria activity. In a previous study [50], Selvam et al. discovered that copper oxide nanoparticles in the leaves of Canthium coromandelicum degraded MB by 91% in 180 minutes. Calotropis procera leaf extract-biosynthesized CuO NPs has recently demonstrated antibacterial and antifungal activity [51]. Karuppannan, S.K. et al. have reported that the Cardiospermum halicacabum aqueous extract-mediated synthesized CuO NPs were examined under Gram +ve bacteria and MB dye was degraded by 93% in about 210 min [52].

This study presents a simple, cost-effective, and eco-friendly method for synthesizing copper oxide nanoparticles (CuO NPs) using the natural extract of ginger (Zingiber officinale). The structural properties of the ginger root extract were analyzed with Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), field emission scanning electron microscopy combined with energy dispersive X-ray spectroscopy (FESEM-EDX), and transmission electron microscopy (TEM). The extract is rich in phenolic and flavonoid compounds, which act as reducing, stabilizing, and capping agents in the synthesis process. The biosynthesized CuO NPs demonstrated antimicrobial activity against bacterial strains Escherichia coli and Staphylococcus aureus, as well as fungal strains Fusarium oxysporum and Fusarium graminearum. These novel CuO nanoparticles show promising potential for biomedical and environmental applications.

II. EXPERIMENTAL SECTION

Materials and method

The fresh ginger (Z. officinale) roots came from the Botanical Herbal Garden on our college campus in the District of Balaghat, MP, India. All of the chemicals were supplied by Sigma-Aldrich, including copper nitrate trihydrate ($Cu(NO3)2.3H2O$), copper sulfate pentahydrate ($CuSO4.5H2O$), deionized water (DI), nutrient agar granulated (95 %), agar-agar type 1 (95 %), bacteria pure culture (100 % ethanol ($C2H5OH$, 98 %), nutrient broth, and antibiotics. The chemicals were all analytical grades and were used without additional purification.

Preparation of the Ginger Root Extract

Using an electric grinder, the gathered and dried ginger roots were ground into a fine dust and stored in plastic containers. Ginger root powder extracts were made by combining 10 gm with 100 mL of 70% acetone while vigorously stirring for 15 minutes. The mixture was then allowed to sit at room temperature for 48 hours before being filtered through Whatman No. 1 filter paper. After removing the acetone by heating the extract to 70 °C for 20 minutes, it was cooled to room temperature. After that, the filtrate was kept in a refrigerator at 4 °C so that it could be utilized for additional research [53].

Chemical Synthesis of CuO NPs

CuO NPs were created in this study using the hydrothermal method. To create a homogenous, blue-colored solution, 1 gm of copper sulfate ($CuSO4$, $5H2O$) was dissolved in 50 milliliters of deionized water (DIW) in a round-bottom flask and stirred for a few minutes using a magnetic stirrer. Next, 100 ml of DIW was used to dissolve 1 gm of potassium hydroxide (KOH), which was then added drop by drop until the pH reached 10. The color of the solution begins to change when the KOH is injected. At 90 °C, the mixture was agitated for two hours. The blue solution turns into a precipitate with a dark hue. Furthermore, the precipitate was centrifuged three times for ten minutes at 3500 rpm before being cleaned with doubly distilled water (DDW). The black product was dried for eighteen hours at 80 °C. Lastly, the powder was calcined for four hours at 400 °C [54].

Green synthesis of CuO NPs

0.1M $Cu(NO3)2.3H2O$ was used to create copper oxide nanoparticles. To reduce copper ions to their copper oxide nanoparticles, 25 mL of the Zingiber rhizome extract was gradually added to 100 mL of the copper nitrate trihydrate in a 250 mL Erlenmeyer flask. Stirring continuously, 10 mL of 2M NaOH solution was added to bring the pH up to 11. For two hours, the solution was constantly stirred at 80°C. The blue solution instantly turned green, and a dark brown precipitate formed after about two hours. The formation of a dark brown precipitate signified the reduction of all copper ions and the formation of CuO NPs [55]. After centrifuging the precipitate at 10000 rpm for 10 minutes and repeatedly washing it with ethanol and distilled water to remove contaminants, the sample was dried for two hours at 80°C.

Green synthesis of CuO NCs

Zingiber rhizome extract has been successfully used to create an environmentally friendly NP. 25 mL of Zingiber rhizome extract and 100 mL of deionized water were combined with 0.5 gm of copper nitrate trihydrate to create a 20% CuO nanocomposite. After adjusting the pH of the solution to 11 with a drop-wise addition of an aqueous solution of NaOH (2 M) the precipitate was cleaned and dried after being centrifuged for 10 minutes at 10000 rpm [57].

Instrumentation

FTIR (Fourier Transform Infrared) Spectrophotometer, SN 340, BRUKER OPTIK GmbH, GERMANY was used to record IR spectra of the prepared samples. Pellets containing 10 mg of sample and 200 mg of spectroscopic grade KBr were used to obtain the FTIR spectra in the 450-4000 cm-1 wave length. The structure of the samples was analyzed by a Powder XRD, X-Ray Diffractometer, D-8 Advance 206890, BRUKER AXS GmbH, GERMANY with CuKa1 radiation (l = 1.5418 Å). The diffraction peak at 25.9º was selected for calculating crystallite size using Scherrer's formula because it is sharper and distinct from the surrounding peaks. This peak, associated with Miller's plane family (002), indicates the growth of hydroxyapatite crystals along the axis of the crystalline structure. FESEM was used to examine the materials' morphology with a SEM (Scanning

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Electron Microscope) NOVA NANO SEM 450, FEI CO. OF USA (S.E.A.) PTE LTD., SINGAPORE, scanning electron microscope and TEM (Transmission Electron Microscope), Tecnai G2 30 S-TWIN, FEI CO. OF USA (S.E.A.) PTE LTD., SINGAPORE.

Characterization Techniques

FTIR analysis was used to determine the functional groups guiding the synthesis and stabilization of CuO NPs. The presence of multiple functional groups in the material was verified by FTIR analysis. FTIR analysis was used to find potential biomolecules with bio-reducing properties in the plant extract. CuO NPs' spectra showed prominent bands at 3413, 1570, 1406, 1116, 868, and 617 cm−1, respectively Fig. 1. The presence of alcohols or phenolic compounds from the extract is indicated by a broad absorption band near 3413 cm^{-1} in the FTIR analysis of CuO NPs made using a plant extract, which is attributed to hydroxyl (O–H) stretching vibrations [58].] Furthermore, the >C=O stretching vibrations of carboxylic groups are linked to a clear peak at 1570 cm^{-1}, indicating that bioactive molecules in the extract were involved in both the reduction and stabilization of the nanoparticles [59]. The peaks at 1406 cm−1 were indicative of the C-N stretching vibrations of aromatic amines [60]. The peaks at 1116 cm−1 were indicative of the C-O stretching vibrations [61].

Biosynthesized CuO NPs exhibit absorption bands at 868 and 617 cm–1, which are attributed to the metal oxide [62]. Consequently, the FTIR data indicated that the biomolecules in the extract, including terpenoids, flavonoids, and phenolic compounds, might be in charge of the prolonged stability of CuO NPs by reducing and capping them. Additionally, the participation of phenol and flavonoid sites in the binding process of CuO NPs is indicated by the decrease in intensity of these functional group bands after a decrease in Cu2+ ions [63]. Together, the results show that CuO can be effectively reduced to CuO NPs. Our findings are consistent with previous studies on the characteristics of green synthesized CuO NPs [64].

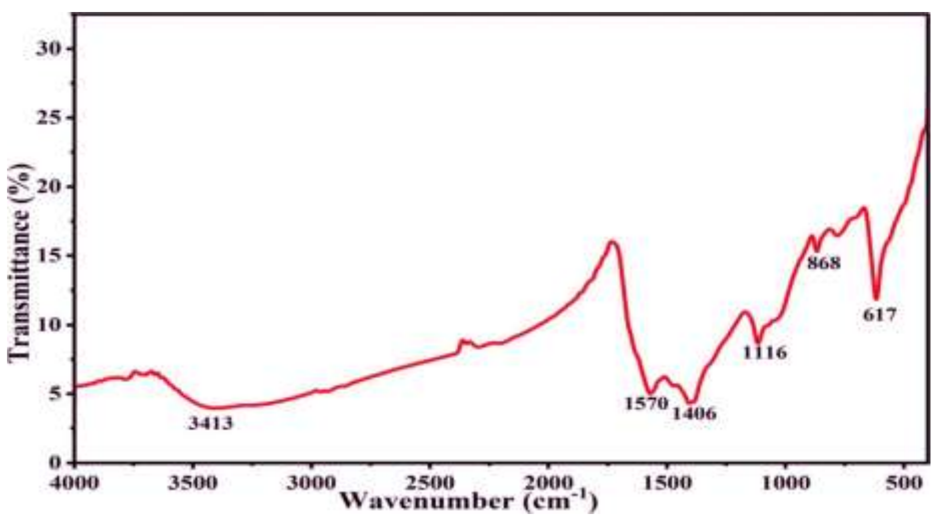

Fig.1: The FTIR spectra of IR spectra of CuO NPs

The XRD-pattern results shown in Fig. 2 revealed clear, strong peaks at the following 2θ-angles: 28.3°, 36.4°, 40.5°, 43.3°, 50.4°, 58.6°, 61.3°, 66.4°, and 74.1°. These correspond to the crystallographic planes 110, 002, 111, 202, 020, 113, 311, and 222, confirming the formation of crystalline CuO consistent with the standard pattern for bulk copper (II) oxide. The absence of extra peaks from other phases and the alignment of all diffraction peaks with a monoclinic crystal structure confirm the exceptional purity of the CuO NPs. Moreover, the distinct and sharp CuO reflections indicate a well-crystalline nanoparticle structure [65]. The detected peak within the 2θ range of 35–39° further supports the synthesis of CuO NPs, consistent with earlier studies [66].

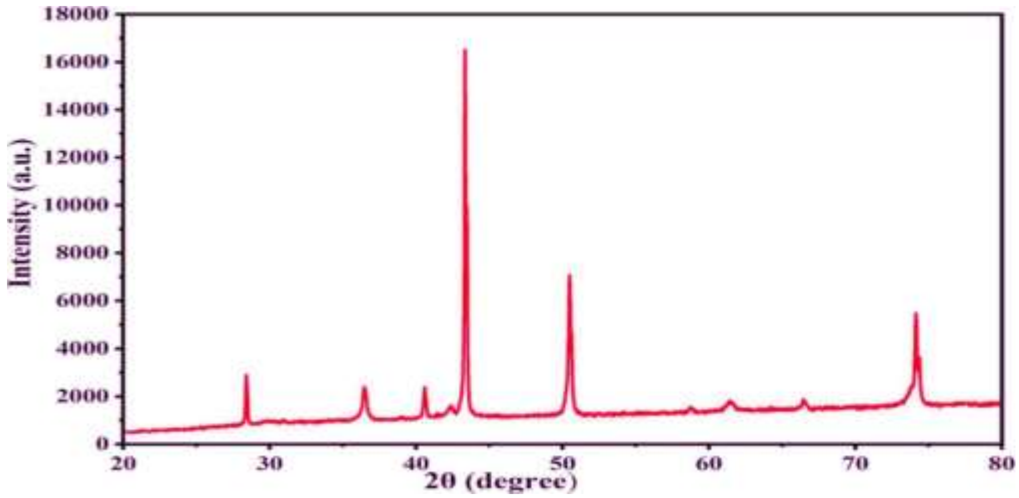

Fig. 2: X-ray diffraction of CuO NPs

Consistent with the EDX analysis, the absence of additional peaks in the XRD image confirmed the exceptional purity of the produced CuO NPs. The collected data was in good agreement with several studies on green synthesized CuO NPs [67]. Green synthesized CuO NPs' topological characteristics, including their sizes, shapes, accumulations, and basic patterning, are crucial elements affecting their biological activity [68]. Investigations using TEM, SEM, and EDX are useful techniques for analyzing these characteristics. The spherical shape of the biosynthesized CuO NPs was verified by TEM analysis (Fig. 3). An average diameter of 16.2 nm and a size range of 4 to 28 nm were found by particle size distribution analysis.

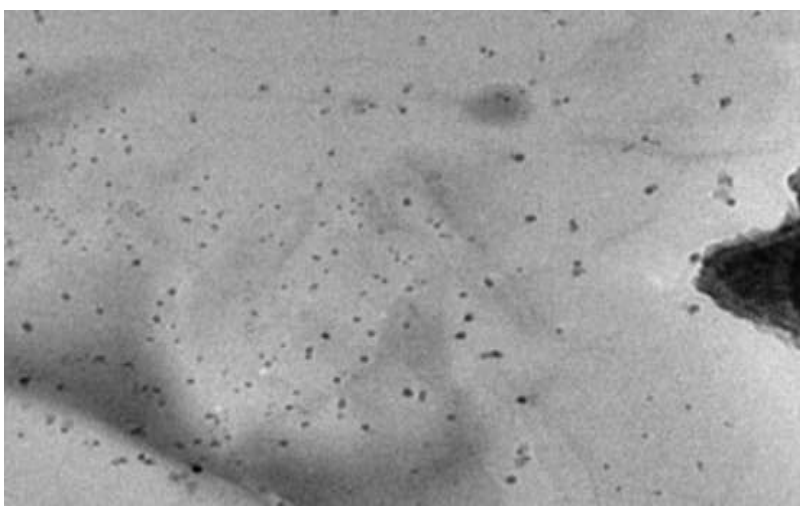

Fig. 3: The TEM analysis of CuO NPs

A homogeneous synthesis process is characterized by a relatively narrow size distribution, as shown by the histogram in Fig. 4. The spherical CuO NPs produced using the water-soluble extract of Zingiber rhizome had a mean particle size of 16-31 nm in a similar study [69].

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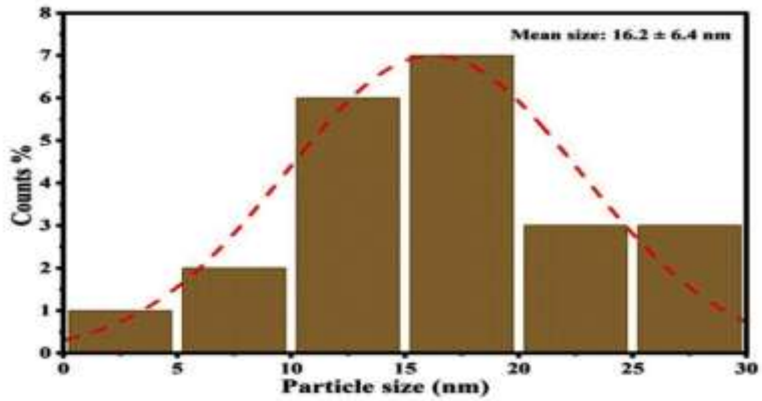

Fig. 4: Histogram for particle size analysis of CuO NPs

The sizes and shapes of nanostructures directly affect their biological characteristics. CuO NPs' cytotoxic potential varies depending on their diameters, which range from 4 to 24 nm. Despite the latter's superior capacity to dissolve toxic ions (Cu2+) more quickly than their larger counterparts, reports show that CuO NPs measuring 24 nm are significantly more toxic to A549 adenocarcinoma cells than those measuring 4 nm [70]. In comparison to spherical forms, the antibacterial efficacy of rod and platelet-shaped CuO NPs made from ginger root extract against E. coli and S. aureus was higher [84]. The increased surface energy linked to surface active regions of different fundamental morphologies may be the cause of this variation in activity [71]. Additionally, SEM analysis was used to examine the morphological features of plant-derived CuO NPs Fig. 5.

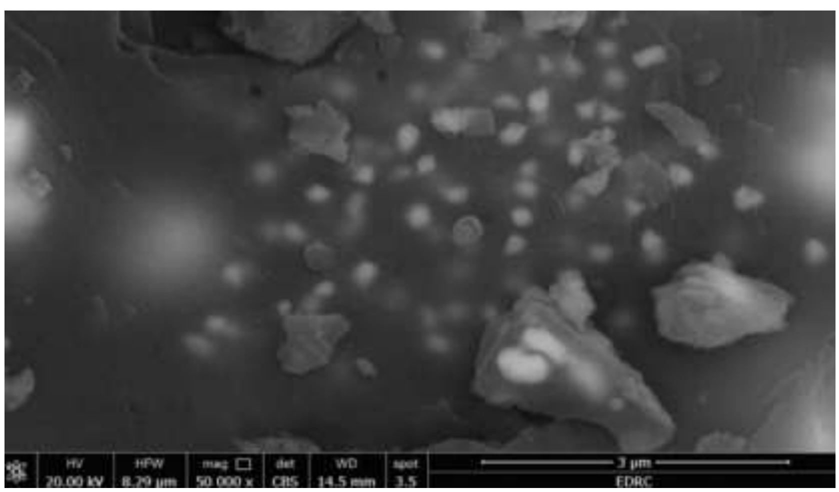

Fig. 5: The SEM analysis of CuO NPs

The CuO NPs were spherical in shape, had a smooth surface, and were arranged without agglomeration.

SEM analysis revealed the spherical shape of CuO NPs produced using extracts from Zingiber rhizome [72]. Some aggregations observed in SEM images, which may enlarge particle size compared to TEM analysis, are caused by coating agents derived from plant material. As shown in Fig. 6, EDX analysis of the green synthesized CuO NPs indicated that the biosynthesized product mainly consisted of copper and oxygen.

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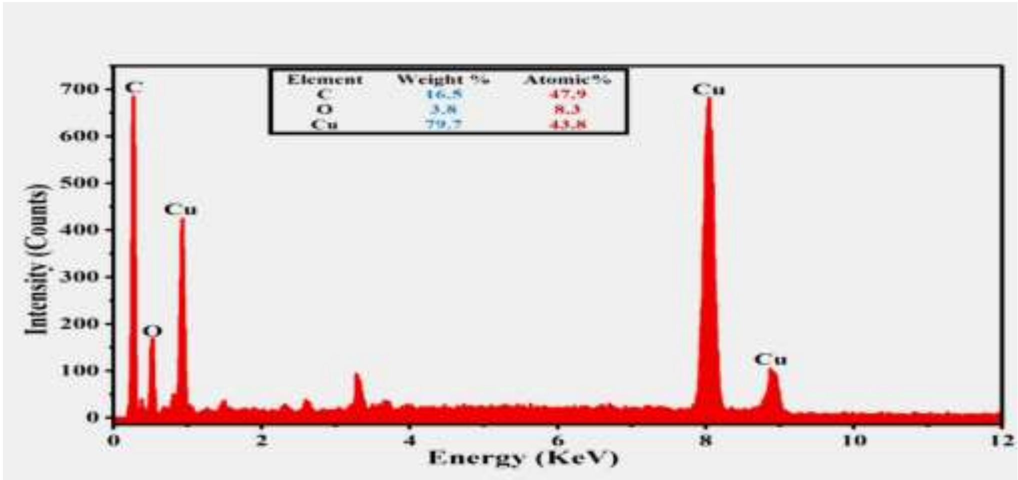

Fig. 6: The EDX analysis of CuO Nps

Oxygen was represented by the signal at 0.5 KeV, and copper was responsible for the peaks at 1.0, 8.0, and 9.0 KeV. The quantitative results showed atomic percentages of 47.9% for oxygen and 43.8% for copper, with weight percentages of 16.5% and 79.7%, respectively (Fig. 6). This signal was caused by the dispersion of phytochemicals from the plant's water-based extract coating the CuO NPs surface [73]. A previous study reported similar EDX results for plant-based CuO NPs, showing weight fractions of 20.1% oxygen and 79.9% copper [74]. Another EDX analysis of CuO NPs synthesized from Zingiber rhizome extract indicated weight percentages of 65.33% copper and 34.67% oxygen [75].

Antimicrobial Activities

The prepared CuO NPs' antimicrobial activity was tested against two pathogenic bacteria, Escherichia coli (E. coli) and Staphylococcus aureus (S. aureus), as well as two fungal strains, Fusarium oxysporum (F. oxysporum) and Fusarium graminearum (F. graminearum). Results are shown in Table 1. After 24 hours of incubation at 37 °C, bacterial growth was evaluated against the green-synthesized CuO NPs. Using the disk diffusion method, antibacterial activity was assessed by measuring the zone of inhibition. The agar well diffusion technique confirmed a dose-dependent inhibitory effect, with inhibition zones increasing in size as nanoparticle concentration rose. The inhibition zones ranged from 20 to 33.5 mm, with S. aureus showing the highest antibacterial effect (33.5 mm at 1000 μg/ml), followed by E. coli (26.1 mm), and the smallest zone observed against F. graminearum (21.4 mm).

By using the broth-based microdilution technique to determine the MIC and MBC, the antibacterial efficacy of CuO NPs was evaluated. S. aureus showed the lowest MIC value of 50 μg/ml, while MIC values for other strains ranged from 100 to 600 μg/ml. Variations in MIC values may be due to factors such as synthesis method, particle size, morphology, agglomeration, and surface charge [76]. The primary inhibitory mechanism involves toxic Cu^{2+} ions released after nanoparticle degradation inside bacterial cells. Enhanced antibacterial activity, like that seen in particles from Allahabad Safeda, is linked to unique surface properties and high chemical reactivity, promoting effective microbial contact [77]. The small size of these NPs facilitates greater interaction with bacterial cells, leading to structural damage of the cell envelope, compromising membrane integrity, and causing cell lysis [78]. Additionally, phytometabolites associated with the NPs disrupt bacterial quorum sensing, suppressing virulence factor expression and preventing outbreaks. Copper ions (Cu^{2+}) also play a crucial role by adhering to and penetrating bacterial membranes, enhancing bactericidal effects [79]. In summary, phyto-fabricated CuO NPs employ multiple antimicrobial mechanisms—including membrane damage, ROS-induced oxidative stress, DNA interference, and quorum sensing inhibition—making them potent agents against resistant pathogens [80].

MIC and MBC

The MIC and MBC results shown in Table 1 demonstrate clear differences in the inhibitory and bactericidal potency of the four CuO nanoparticle types CuO-ginger and CuO-synthetic using CuSO4 and Cu(NO3)2, against Gram-positive S. aureus and Gram-negative E. coli. Generally, S. aureus exhibited higher sensitivity to all CuO nanoparticles compared to E. coli, which showed higher resistance. This is consistent with previous studies and is linked to the protective outer sheath in the Gram-negative bacteria that reduces nanoparticle penetration and ion intrusion inside the bacteria [81]. CuO-ginger nanoparticles produced the strongest antibacterial inhibition and bactericidal effect among the three plant-mediated nanoparticles, with MIC values of 250 µg/mL and 500 µg/mL against S. aureus and E. coli, respectively, and an MBC value of 500 µg/mL against both bacterial strains. These superior activity results are in agreement with the literature and derive from the phytochemical composition of the ginger, which contains gingerols and shogaols that can enhance the nanoparticles' stability and improve reactive oxygen species (ROS) production, leading to higher antibacterial potency. On the other hand, CuO-synthetic using CuSO4 and CuO-synthetic using Cu(NO3)2, showed a similar antibacterial response, with values of 500 µg/mL and 1000 µg/mL for the MIC and MBC tests against S. aureus and E. coli, respectively. This could be attributed to the thicker organic capping from the plants' organics, which can limit Cu2+ and ROS production. In contrast, synthetic CuO nanoparticles gave the highest overall antibacterial inhibition, with MIC values of 250 µg/mL for both bacterial strains and MBC values of 500 and 1000 µg/mL against S. aureus and E. coli, respectively. This could be related to the higher purity and decreased surface organic coverage of the synthetic CuO, leading to greater surface reactivity and enhanced antibacterial efficiency

Table 1.: MIC and MBC values of plant-mediated and synthetic CuO nanoparticles against S. aureus and E. coli in µg/mL.

Sample	*E. Coli*		*S. aureus*	
	MIC	MCB	MIC	MCB
CuO-ginger	500	500	500	250
CuO-synthetic using $CuSO_4$	1000	500	1000	500
CuO-synthetic using $Cu(NO_3)_2$	1000	250	500	250

III. CONCLUSION

The characteristics of green-synthesized CuO NPs using Z. officinale extract and their applicability were investigated in this study. Phytochemical and GC-MS analyses of the Z. officinale extract were reported. CuO was confirmed as a nanomaterial through various characterization techniques. The CuO NPs demonstrated biofilm suppression against two biofilm-producing strains and were effective against Escherichia coli (E. coli), Staphylococcus aureus (S. aureus), as well as the fungal strains Fusarium oxysporum (F. oxysporum) and Fusarium graminearum (F. graminearum).

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