

Syzygium cumini leaf extract mediated green synthesis of ZnO nanoparticles: A sustained release for anticancer, antimicrobial, antioxidant, and anti-corrosive applications

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ABSTRACT

ZnO nanoparticles (NPs) were synthesized with leaf extract of *Syzygium cumini* and spectroscopic (UV–Vis, FTIR, and NMR), microscopic (TEM), and structural characterization techniques (XRD) were used. Phyto-chemicals in leaf extract act as a capping agent which aids in the sustained release of ZnO NPs for anticancer, antioxidant, and antibacterial activities. An IC₅₀ concentration of 49.83 µg/ml is found in the cytotoxicity of ZnO NPs versus the HepG2 cancerous cell lines. NPs exhibited significant zones of inhibition, measuring 11.66 mm, and demonstrated minimal inhibitory concentrations (MIC) of 8.0 and 0.1 µg ml⁻¹ against *A. niger* fungus and *P. aeruginosa*, bacteria, respectively. ZnO NPs also exhibited significant antioxidative action, with an IC₅₀ of 10.54 µg ml⁻¹. ZnO NPs exhibited paramagnetic character and good anti-corrosive properties, with an impressive inhibition efficiency of 90 % at 100 ppm concentration in 1.0 M H₂SO₄ solution.

1. Introduction

The major threat to living beings is rapidly expanding pollution primarily due to industrial waste and human activities especially chemical methods of synthesis which predominately contaminate air and water bodies resulting in hazardous environmental conditions [1,2]. Scientists have utilized medicinal plant extracts, algae, and biomolecules for the synthesis which is proven to be eco-friendly, non-toxic, inexpensive, and low maintenance [3–6]. Nanotechnology has been extensively utilized in numerous scientific domains due to the eminent attributes of nanoparticles (NPs) [7–9]. NPs have prominent advantages such as tunable morphology, nano size range, high ratio of surface to volume, and functionalization of these NPs one can obtain enhanced properties that offer a foundation for an extensive uses [10–12]. The development of different metal oxide-based NPs was done by following different routes such as physical, biological, and chemical [13–16]. Another widely used is the chemical approach based on the bottom-up method because of its high yield [17–21]. As chemical method uses toxic chemicals and also ends up in hazardous by-products so limits their application in the clinical field [22–26]. The biological approach is

gaining much attention nowadays because this method utilizes micro-organisms, biodegradable polymers, and extracts from plants to create metal NPs [27–30]. The plant extracts contain phytochemicals that behave as reducing agents for the production of NPs which avoid the use of toxic chemicals to reduce the metal ions present in metal salt [31–34].

In 2013, Iravani and Zolfaghari reported that NPs synthesized by using plant extracts possess greater stability [35]. Janet al. synthesized CeO NPs from a liquid *Aquilegia pub flora* extract. These NPs were then investigated for several biological uses such as antimicrobial, anticancer, antidiabetic, antioxidant, and biocompatibility tests [36]. Birusanti et al. in 2018 utilized *Ficus Racemosus* extract to develop ZnO NPs which showed good antibacterial activity [37]. The CuO NPs' photocatalytic activity was reported which was synthesized using *Annona muricata* leaf extract [38–40]. Apart from these, metal NPs show magnetic, biosensing, wastewater treatment, anticorrosive, catalytic activity, dye degradation, and many more applications [41–47]. By optimizing the time, pH, outside temperature, and volume of the extract from plants and metal salt solution, it is possible to alter the form and quality of metal NPs [48,49]. We have selected ZnO NPs in our study because ZnO NPs are frequently employed in biological contexts because

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they exhibit high excitation binding energy and large bandwidth, as sensors because of their semi-conductor nature [54–56], and also show good antifungal and antimicrobial activity [57,58].

Syzygium cumini is a traditional medicinal tree that has been used for many years to prevent human health, natural food coloring agent, and in aroma industries [50–53]. *S. cumini* exhibits therapeutic potentials that are, anti-pyretic, anti-inflammatory, anti-oxidant, anti-cancer, antimalarial, analgesic, etc. owing to different constituents like amino acids, terpenoids, flavonoids, alkaloids, etc. [50]. The biologically active compounds that are leaves, stem, seed, and fruit pulp impart many interesting properties to the ZnO NPs [52]. The bioactive substances attach to the ZnO NPs' surface atoms and function as a surface-capping agent. These capping agents (terpenoids, and flavonoids) not only aid in getting the reduced Zinc ion to make ZnO NPs but also contribute to the overall stability factor of the resulting NPs of ZnO [53]. The bioactive compounds in *S. Cumini* including Ellagic acid, Quercetin, and Tannins mainly contribute to the antimicrobial efficacy against bacteria, fungi, and parasites [50].

Based on these facts, first-time, anticancer, antioxidant, anti-corrosive, antibacterial, antifungal, and magnetic studies of phytochemical-capped ZnO NPs were reported. First-time, we are reporting six applications of biologically synthesized ZnO NPs. We employed the *S. Cumini* leaf extract for synthesizing the ZnO NPs. To identify the structure, crystallinity, and size of NPs, these are characterized with the help of TEM, FTIR, XRD, NMR, and UV-visible methods [59]. We investigated different applications of ZnO NPs such as anti-cancer, antioxidant, anti-corrosive, antibacterial, antifungal, and magnetic behavior. Fig. 1 depicts the scheme of synthesis of ZnO NPs.

2. Materials and procedures

2.1. Chemicals and green materials

AR grade chemicals like Zinc acetate dehydrate (CAS No. 5970-45-6) and Sodium Hydroxide (CAS No. 1310-73-2) were purchased from SRL Chemicals Pvt. Ltd. *S. Cumini* leaf were gathered from the herbal yard on the campus of the Central University of Haryana, India. Zinc acetate and NaOH pellets were purchased and distilled water was used for preparing leaves extract. All the needed glassware was cleaned and oven-dried before use. The antibacterial and antifungal efficacy was examined by the Zone of Inhibition method (Kirby-Bauer method).

2.2. *S. cumini* Leaf extract preparation

The collected leaf of *S. cumini* were rinsed with double-distilled H₂O many times to eliminate the dust and other pollutants from their surface. After washing, leaves were put under the shade until completely dried and crushed into a fine powder. 3 g of leaf powder was mixed in 100 ml of double-distilled H₂O and warmed to 40 °C for 30 min. After filtering the prepared aqueous extract, the filtrate was refrigerated at 4 °C [60].

2.3. Synthesis of ZnO NPs

Five milliliters of aqueous leaf extract and 50 mL of 0.1 M Zinc acetate solution were combined, and followed by agitation for two hours at 60 °C. The pH was maintained around 11.0 which caused whitish, grey-colored precipitates to develop. Precipitates were centrifuged at 8000 rpm and then oven-dried at 100 °C for 12 h and further used for characterization [61].

2.4. Characterization by UV-visible, FTIR, TEM, p-XRD techniques

UV-visible absorption study was carried out on UV-2600, Shimadzu, Toshvin Analytical, Mumbai. FTIR study was carried out on Bruker alpha-II, FTIR, Germany. ATR (Attenuated Total Reflection) form of the module was used, the Spectral range selected was 400 to 4000 cm⁻¹, at 2 cm⁻¹ resolution and the detector used was DTGS (Deuterated Triglycine Sulfate). Powder XRD was performed on the Rigaku Smart lab instrument, Rigaku cooperation, Japan, 3.0 kW, Cu-K α source. The surface characterization of ZnO NPs was done by Joel TEM, 300 kV.

2.5. Spectroscopic study of *S. cumini* leaf extract

Spectroscopic characterization was carried out using ¹HNMR, ¹³CNMR, and FTIR spectroscopy. Fig. S1 (ESI) shows ¹HNMR and ¹³CNMR of leaf extract. Fig. S2 (ESI) shows FTIR spectra of *S. cumini*. A singlet sharp peak in the ¹HNMR spectrum (Fig. S1 A) suggests that all protons are equivalent and decoupled protons. This may be due to a single type of hydrogen environment, (-CH₃) groups, or a hydrogen atom attached to an aromatic ring. In the case of *S. cumini*, this can be a part of a flavonoid or phenolic group. Three small peaks in the range of 75–78 ppm in the ¹³CNMR spectrum (Fig. S1 B) can be associated with C atoms bonded to electronegative atoms (O), indicating the presence of either alcohols, ethers, or esters. NMR signals of leaf extract of *S. cumini* represent C atoms in flavonoids, polyphenols, or glycosidic structures,

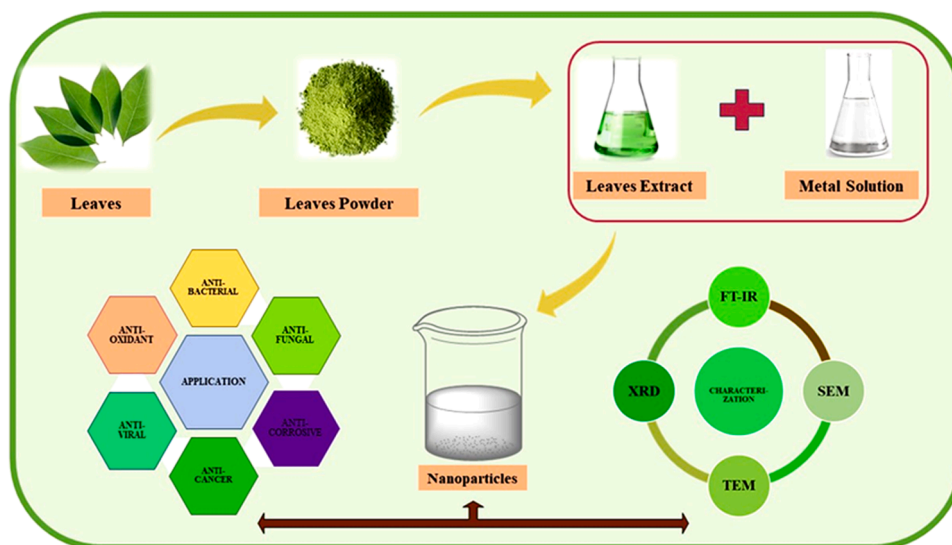


Fig. 1. Green synthesis of ZnO NPs using *S. Cumini* leaf extract.

where C atoms are bonded to O atom.

The FTIR spectrum of *S. cumini* leaf extract shows specific peaks that correspond to different functional groups and a broad peak at 3000–3600 cm⁻¹ results due to O–H stretching. This suggests the presence of polyphenols, flavonoids, or moisture. A sharp peak at 1636 cm⁻¹ represents C=C stretching vibrations, which are often associated with alkenes or aromatic compounds. In plant extracts, this may also correspond to amide I bands, suggesting the presence of proteins or secondary metabolites like flavonoids and phenolics. Fingerprint Region (633, 573, and 534 cm⁻¹) may correspond to C–H bending vibrations, bending modes (out-of-plane) of aromatic rings, or metal-oxygen bonds if any metallic elements are present. This can be due to glycosides, alkaloids, or even trace metal complexes naturally present in the *S. Cumini* leaf.

2.6. Anticorrosive study

To examine the anti-corrosive nature, 06 MS coupons having dimensions 3.1 by 1.5 cm² were mechanically polished. ASTM standard test procedure (ASTM D6980) was followed for weight loss study. Sandpaper of different markings that is 100, 200, 300, 400, and 600 µm, was used to polish MS coupons. After thoroughly cleaning the mild sheets with water and acetone, these were dried and accurately weighed. The MS was submerged in the 1.0 M H₂SO₄ acid solution at an ambient temperature and left for 4 h. After completion of exposure time, the mild steel sheet was washed, dried, and accurately weighed. Table 1 depicts data from the anticorrosive study of ZnO NPs in the dilute sulfuric acid medium at room temperature. Based on the wt. loss, both the CR and the percentage of corrosion inhibition efficiency (CIE) were calculated [62].

2.7. Cytotoxicity study

Using MTT assay, the sample's cytotoxicity on the HepG2 cell line was assessed. The 10,000 cells/well were grown in 96-well plates for 24 h at 37 °C and 5 % carbon dioxide in a culture medium that contained 1 % antibiotics solutions and DMEM enhanced with a 10 % concentration of fetal bovine serum (FBS). The following day, the procedure was applied to the cells with formulations which are ranging from 1 to 1000 µg/ml. Cells without mannered were considered as controls. MTT solution was added to the cell culture and incubated for an additional two hours at a final concentration of 250 µg/ml following a 24-hour incubation period. Following the experiment, 100 µl of DMSO was employed to break down the cell layers matrix and eliminate the culture supernatant and measured at 540.0 and 660.0 nm wavelength with the help of Elisa plate-reader (I Mark, Biorad). Using Graph Pad (Prism-6) computation, the IC50 was determined.

2.8. Antifungal activity against fungal culture- *Aspergillus niger*

The fungal culture *Aspergillus niger* produces a variety of bioactive compounds and secondary metabolites like organic acids. These compounds exhibit antifungal properties. Also, *A. Niger* is considered as safe according to FDA and its wide readability makes it a promising fungal culture for laboratories. Similarly, *P. aeruginosa* is also the most

Table 1
Anticorrosive study of ZnO NPs synthesized by green synthetic route.

Concentration (ppm)	Initial wt. (in g)	Final wt. (in g)	Weight-loss (g)	Corrosion Rate (CR)	IE (%)
200	1.5948	1.1854	0.4094	9647.60	59.18
400	1.4613	1.1568	0.3045	7175.67	69.64
600	1.4925	1.2364	0.2561	6035.10	74.46
800	1.4519	1.2885	0.1634	3850.59	83.68
1000	1.8264	1.7289	0.0975	1590.66	90.01
Blank	1.9150	0.0912	1.003	2363.60	–

spreading Gram-negative bacteria and also produces secondary metabolites which show antimicrobial properties. Because of this, we have selected a particular culture for our experiment.

To check the antifungal activity of the ZnO NPs, after dispersing 100 µl of *A. niger* fungal culture across the PDA plates, discs comprising varying concentrations (varies from 0.0 – 100.0 mg/ml) set on top of the inoculation. Amphotericin B (50 µg) was used as an agent of positive control, and one disc per plate contains solvent solely to act as control. For 48 h, the *A. niger* plates were maintained at the temperature of 37 °C in an incubation chamber. After treatment, the clear zones created around the disc were observed.

2.9. Minimum inhibitory concentration (MIC) activity against- *A. niger*

0.5 Mc Farland Standard dilution of microbes (*A. niger* - MTCC-281) was used for the MIC study of ZnO NPs. Diluted the 0.5 Mc Farlands Standard culture 10X for the media required as per the below calculations. Initially, 500 µl of medium was put into the empty Eppendorf tube, and then 20 µl of mixed culture was added. 25 µl of different concentration treatment dilutions that were made to the defined tubes and incubated for 2–5 days the container and pellet were obtained after incubating and centrifugation, and after two to five days, the gross weight of the container containing the pellet was noted.

2.10. Minimum inhibitory concentration (MIC) activity- *P. aeruginosa*

0.5 Mc Farland Standard dilution of microbes was used for the study. Five microliters of treatment dilutions at varying concentrations were added to the designated tubes along with one hundred microliters of diluted log cultures of *P. aeruginosa* (MTCC 3541) bacteria, which were then incubated for twenty-four hours in the microcentrifuge tube. All material was moved to a 96-well plate after incubation, and an Elisa Plate Reader (iMark Bio-Rad) was used to measure the turbidity at 630 nm. As a positive control, 10 µg of ciprofloxacin was used.

2.11. Antioxidant study by DPPH scavenging technique

In a 96-well plate, A 70.1 mL DPPH solution of 0.1 mM was combined with 5 µl of stock chemical. The experiment had been set to proceed in triplicate, and blanks duplicated with 0.2 ml of DMSO/Methanol and 5 µl of various doses of the chemical were made. The plate was kept in the dark for thirty min. The removal of color was calculated at 495 nm by a microplate reader after the incubation. The control sample was a reaction solution with 20 µl of water that had been deionized. For the control, the rate of scavenging was displayed as "% inhibition". Scavenging activity in the sample was observed concerning standard ascorbic acid (IC-50 = 10.54 ± 1.49 µg/ml) [63,64].

2.12. Analysis of antimicrobial activity against bacterial culture - *Pseudomonas aeruginosa*

The Kirby-Bauer method was adopted to analyze the antibacterial study. After dispersing 100 µl of *P. aeruginosa* bacterial culture, over the MHA plates, discs comprising 10.0 µl of different doses (0.0 – 100 mg/ml concentrations) were added. Each of the plates had one disc that served as the vehicle control and was filled with solvent and 10 µg of ciprofloxacin referred to as positive control. *P. aeruginosa* plate was cultivated at 37 °C for a full day. Following treatment, the clear zones were reported.

2.13. Magnetic study of ZnO NPs

The produced ZnO NPs' magnetic properties were determined by using Gouy balance. To determine the magnetic properties of ZnO NPs, magnetic susceptibility (χ) was measured. For this, the fine solid powdered ZnO sample was taken in a cylindrical container. This

cylindrical container is suspended between the magnetic poles through an attached thread by applying current, a magnetic field is generated. Due to this generated magnetic field, there is variation in the weight of ZnO NPs. By increasing current, the magnetic field increases, and the corresponding change in the wt. of NPs was recorded. The magnetic susceptibility (χ) of the sample was calculated utilizing the technique outlined by Kumar et al. [46,47].

3. Results and discussions

3.1. XRD study

The structural and crystallographic information of ZnO NPs was acquired from their XRD pattern (Fig. 2). The 2θ values were assigned to the Miller indices with prominent peaks, 31.93° (100), 34.46° (002), 36.35° (101), 47.47° (102), and 56.66° (110) corresponding to Wurtzite structure of ZnO. Based on the indexing pattern, we can confirm that the XRD pattern corresponds to a hexagonal unit cell. Using the Scherrer equation, the average particle size corresponding to the highest peak was found to be 35 nm.

3.2. Spectroscopic study

3.2.1. FT-IR

As shown in Fig. 3, the stretching of the phenol and alcohol groups is the cause of a prominent absorption at approx. 3372 cm^{-1} . The peaks in the range of 1585 , 1398 , 1332 , 1017 , and 933 cm^{-1} are because of the stretching bend of the C—H bond of alkanes, C—C stretch, and N—H bond of amides and amines, C—N bond of aliphatic amines and aromatic ring stretch, respectively. The sharp peaks at 667 , 614 , and 504 cm^{-1} were due to the Zn—O characteristic stretch. It ensures zinc oxide NPs formation. A broad peak in the 2900 – 3600 cm^{-1} range is due to O—H stretching vibrations. The broadening of the peak indicates H-bonding. In ZnO NPs, the OH groups on their surface influence their surface properties, such as their interaction with bacterial cell walls during antibacterial activity.

3.2.2. UV-visible characterization

In Fig. 4, the sharp resonance peak at 373 nm verifies the successful synthesis of ZnO NPs and a broad peak at 294 nm is probably due to the aromatic compounds which are the major constituents of leaf extract of *S. cumini*. A shift in the absorbance peak from the UV region to the visible region is due to complete capping by the phytochemical molecules present in the surface layer of Zinc-oxide NPs. The same information was obtained from TEM images of ZnO NPs.

3.2.3. TEM study

The surface study of NPs which are synthesized by reduction with the leaves extract of *S. cumini* was done by TEM microscopy techniques. Fig. 5 (a to f) depicts TEM images. NPs are seen to be embedded in the

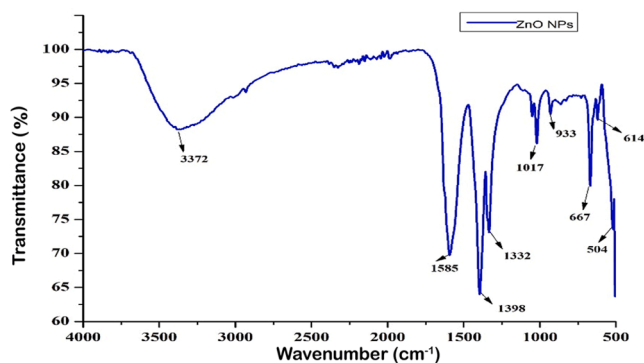


Fig. 3. FT-IR spectra of green-produced ZnO NPs.

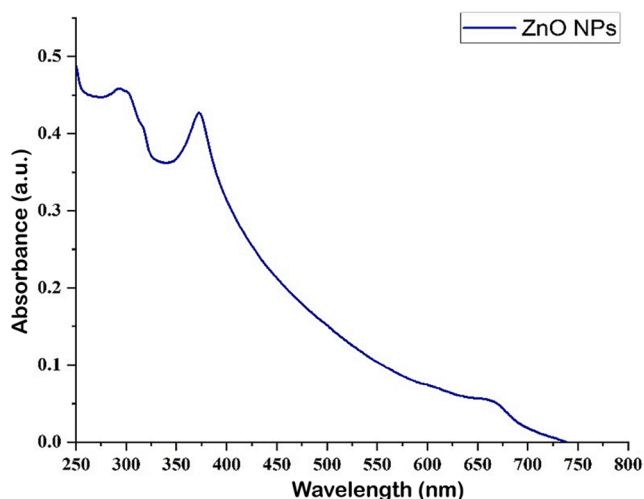


Fig. 4. UV-visible spectrum of produced Zinc oxide NPs.

phytochemicals of *S. cumini* leaves. The powder-like quantum dots of ZnO NPs were seen in the matrix of phytochemicals. It turns out that the average size $< 20\text{ nm}$. Clearly in the TEM pictures of ZnO NPs, black specks in the form of powder are readily apparent (Fig. 5).

4. Applications study of ZnO NPs

4.1. Cytotoxicity test against HepG2 cancer cell line

The MTT Assay was used in the cytotoxicity investigation. Using the “MTT (3-(4,5-dimethyl-thiazol-2-yl)-2,5-diphenyl-tetrazolium-bromide) study”, the cytotoxicity of the material was investigated on the HepG2 cell line. This assay measures the amount of MTT dye that is reduced by mitochondrial enzymes in viable cells, producing a purple formazan product that can be measured spectrophotometrically. This allows one to estimate the viability of the cells. Fig. 6 depicts cytotoxicity on the HepG2 cancer cell line. HepG2 cancer cell line is Hepatocellular Carcinoma cell-line employed as a model for liver toxicity studies. HepG2 cells are widely utilized in cytotoxicity assays due to their relevance to liver-related toxicity and their availability.

In cytotoxicity investigations, the IC₅₀, or half-maximal inhibitory concentration, is a critical parameter used to quantify the potency of a substance in reducing cell viability or inhibiting cell proliferation. It shows the amount of material (ZnO NPs in this case) needed to 50 % reduce cell viability. The IC-50 was observed using Graph Pad Prism –6 software and found to be approximately $49.83\text{ }\mu\text{g ml}^{-1}$, as depicted in Fig. 6. This indicates the concentration of ZnO NPs needed to induce cytotoxic effects on HepG2 cells. The cytotoxicity of ZnO NPs on HepG2c

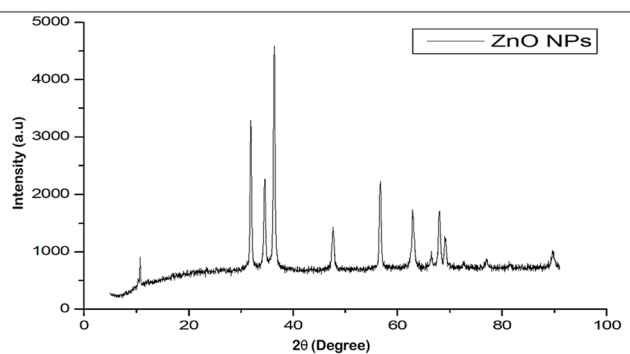


Fig. 2. X-ray diffraction pattern of ZnO NPs.

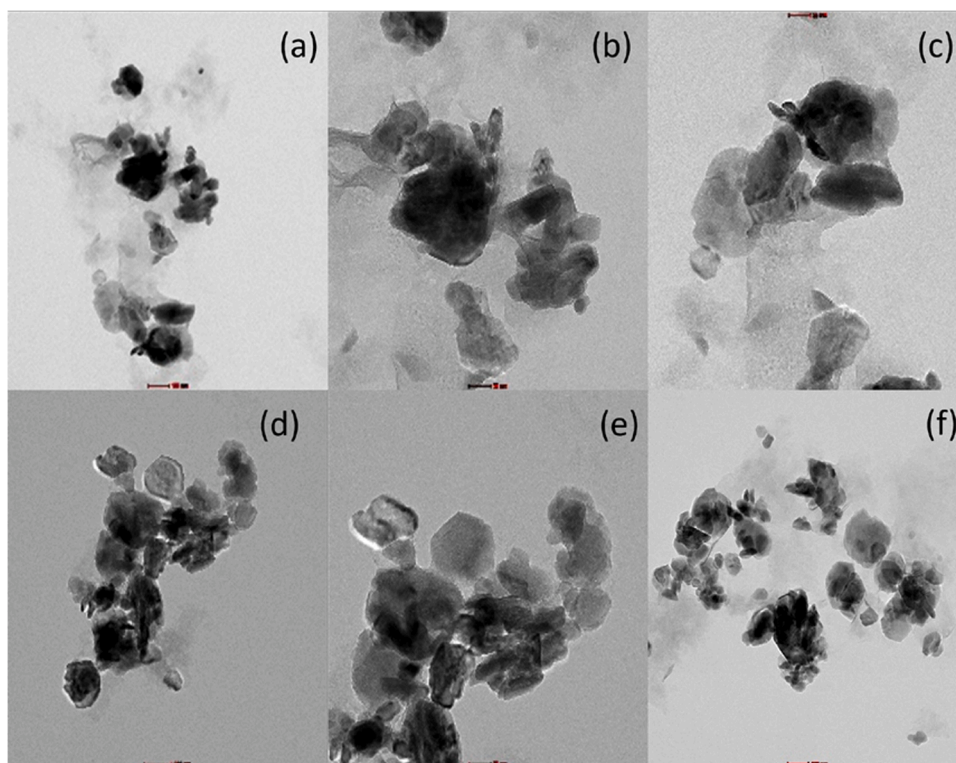


Fig. 5. TEM pictures of synthesized Zinc-oxide NPs.

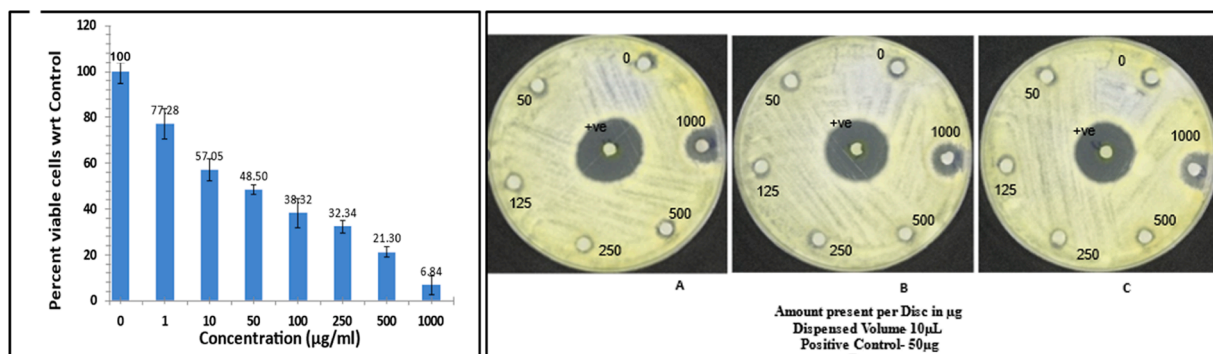


Fig. 6. Cytotoxicity on HepG2 cancer cell line (A), ZnO NPs zone inhibition against *A. niger* fungal culture (B).

cells is depicted in Fig. 6. The graph shows a dose-response curve, where increasing concentrations of ZnO NPs correlate with a decrease in cell viability. The IC₅₀ value serves as a quantitative measure of the cytotoxic potency of ZnO NPs on HepG2 cells. A lower IC₅₀ value indicates higher cytotoxicity, meaning that lower concentrations of ZnO NPs are needed to induce detrimental effects on cell viability. Sharmila et al. used a green synthesis approach for synthesizing ZnO NPs using *T. castinofolia* leaf extract and evaluated anticancer activity A549 cell line and showed 65 $\mu\text{g/ml}$ anticancer activity [66]. Dimita et al. synthesized ZnO NPs by green synthesis approach using *C. formosum* for skin cancer cells and showed 300 $\mu\text{g/ml}$ for HepG2 cell line [67]. Arumugam et al. prepared ZnO using a green synthesis route from leaf extract of *S. cumini* and showed an anticancer activity against A 549 cell line of 72.5 $\mu\text{g/ml}$ [69].

The cytotoxicity of NPs on HepG2 cells has significant implications for their potential biomedical applications, particularly in cancer therapy. While the cytotoxicity shown by ZnO NPs towards cancer cells can be advantageous for anticancer treatments, it also raises concerns regarding their potential toxicity towards healthy cells. Assessing the

cytotoxicity in other cell lines and in vivo models can deliver a more inclusive understanding of their safety profile and facilitate their safe utilization in various biomedical applications. Moreover, strategies to mitigate the cytotoxic effects of ZnO NPs, such as surface modification or controlled release approaches, may be explored to enhance their biocompatibility and therapeutic efficacy.

4.2. Analysis of antifungal activity against fungal culture- *Aspergillus niger*

ZnO NPs' antifungal property was assessed on a Potato-dextrose-agar (PDA) plate using the disk diffusion method. A standardized amount of *A. niger* fungal culture (100 μL) was spread uniformly on the agar surface, and then paper discs loaded with varying concentrations of NPs were placed on the agar surface. Clear zones of inhibition surrounding the discs can be seen in this experimental configuration, demonstrating the ZnO NPs' antifungal action. The diameters of the clear zones that were seen surrounding the discs that were loaded with various ZnO NPs concentrations (Fig. 6). Concerning antifungal activity, clear zones

measuring 6.33, 6.33, 5.66, 6.0, and 11.66 mm were noted at 50, 125, 250, 500, and 1000 $\mu\text{g}/\text{disc}$ [62]. These sizes were in contrast to a positive control of 22.66 mm. These clear zones represent areas where fungal growth was inhibited due to the presence of ZnO NPs. A larger clear zone indicates greater inhibition of fungal growth, indicating higher antifungal activity. The antifungal activity was compared to that of a positive control, likely a standard antifungal agent known to inhibit the growth of *A. Niger*. The positive control exhibited a clear zone of 22.66 mm, indicating strong antifungal properties. By comparing the sizes of the clear zones around the ZnO NP-loaded discs to control, the relative antifungal efficacy of the ZnO NPs can be assessed. The results suggest that ZnO NPs possess antifungal properties against *A. niger*, with the extent of inhibition depending on the concentration of NPs. At higher concentrations (500 $\mu\text{g}/\text{disc}$ and 1000 $\mu\text{g}/\text{disc}$), larger clear zones were observed, indicating greater inhibition of fungal growth. This concentration-dependent antifungal activity suggests that ZnO NPs may disrupt fungal growth and development through various mechanisms, such as membrane damage, ROS generation, and interference with cellular processes. Jamdagni et al. employed an environment-friendly synthesis approach for synthesizing zinc oxide NPs using *N. arbor-tristis* extract and investigated antifungal properties against *A. niger* fungi and showed 16 $\mu\text{g}/\text{ml}$ [65].

The antifungal properties of NPs hold promise for different applications in agriculture, medicine, and materials science. In agriculture, ZnO NPs can be used as eco-friendly fungicides in crops. In medicine, they may find applications in antifungal coatings for medical devices or as components of antifungal formulations.

4.3. Minimum inhibitory concentration (MIC) activity- *A. niger*

A. niger and *P. aeruginosa* are selected for antibacterial and antifungal studies using ZnO NPs for reasons like *P. aeruginosa* is a Gram-negative bacteria. It shows high resistance to many of the antibiotics. *A. niger* is a fungus that causes infection and hence weakens the immune system. *P. aeruginosa* possesses a complex wall consisting of Gram-negative bacteria. *A. niger* is a eukaryotic organism having a chitin-containing cell wall that is a challenge for different antimicrobial agents. This combination of *A. niger* and *P. aeruginosa* will help to access the versatility of ZnO as an antimicrobial against different pathogenic organisms.

The MIC study of ZnO NPs was conducted using a 0.5 McFarland Standard dilution of *A. niger* microbial culture (strain MTCC-281). The McFarland Standard is a turbidity standard used to adjust the density of microbial suspensions to a level suitable for antimicrobial susceptibility testing. In this case, a standardized concentration of *A. niger* was prepared to ensure consistency in the assay conditions. Minimum MIC of ZnO NPs required to prohibit the growth under defined conditions. The MIC of ZnO was approximately 8 $\mu\text{g}/\text{ml}$, as depicted in Fig. 7. This indicates that at concentrations equal to or above 8 $\mu\text{g}/\text{ml}$, the growth of *A. niger* was inhibited, while at concentrations below this threshold, growth was observed.

The MIC value of 8 $\mu\text{g}/\text{ml}$ suggests that ZnO NPs exhibit potent antimicrobial activity against *A. niger*. This finding is significant as it provides quantitative evidence of the efficacy of ZnO NPs as antimicrobial agents. The ZnO inhibits the growth of *A. niger* at such low concentrations indicating their potential utility in controlling fungal infections or contaminations. The observed MIC of ZnO NPs against *A. Niger* has important implications in different fields, including, medicine, agriculture, and materials science. In medicine, ZnO NPs could be explored as antimicrobial agents for treating fungal infections, either alone or in combination with existing antifungal drugs. In agriculture, they may find applications as eco-friendly fungicides for protecting crops against fungal diseases.

While the MIC study gives a valuable understanding of the antimicrobial efficacy of ZnO against *A. Niger*, further research is required to explore different aspects. This elucidates the antimicrobial activity of ZnO NPs, against *A. Niger*, assessing their cytotoxicity towards mammalian cells, investigating their stability and biocompatibility in different environments, and optimizing their synthesis methods to enhance their antimicrobial potency and application versatility.

4.4. Analysis of antimicrobial activity against bacterial culture - *Pseudomonas aeruginosa*

The antibacterial properties of ZnO were observed against *P. aeruginosa* using the Kirby-Bauer method. It involves placing paper discs loaded with different concentrations of ZnO NPs onto an agar plate inoculated with the bacterial culture (Fig. 8). The plates are then incubated, allowing the diffusion of ZnO NPs into the agar and subsequent inhibition of bacterial growth around the discs. Clear ZOI was observed around the discs loaded with ZnO NPs at different concentrations. The sizes of these clear zones indicate the extent of inhibition of bacterial growth by the ZnO NPs. Clear zones with sizes of 7.3, 7.6, 7.3, 9.3, and 11.66 mm were observed at concentrations of 50, 125, 250, 500, and 1000 $\mu\text{g}/\text{disc}$, respectively. The positive control is likely a standard antibacterial agent known to retard the growth of *P. aeruginosa*. The clear zone observed around the positive control was 33.66 mm, indicating strong antibacterial properties. By comparing the sizes of the inhibited zones around the ZnO NP-loaded discs to control, the relative antibacterial efficacy of the ZnO was assessed.

The results suggest that NPs display concentration-dependent antibacterial activity for *P. aeruginosa*. At higher concentrations (500 $\mu\text{g}/\text{disc}$ and 1000 $\mu\text{g}/\text{disc}$), larger clear zones were observed, indicating greater inhibition of bacterial growth. This concentration-dependent effect is consistent with the mechanism of action of ZnO NPs, where higher concentrations lead to increased contact between the NPs and bacterial cells, resulting in enhanced antibacterial properties.

The observed antibacterial property, of ZnO against *P. aeruginosa* has significant implications in different fields, including medicine, health-care, and materials science. In medicine, ZnO NPs could be explored as antimicrobial agents for treating bacterial infections, either alone or in

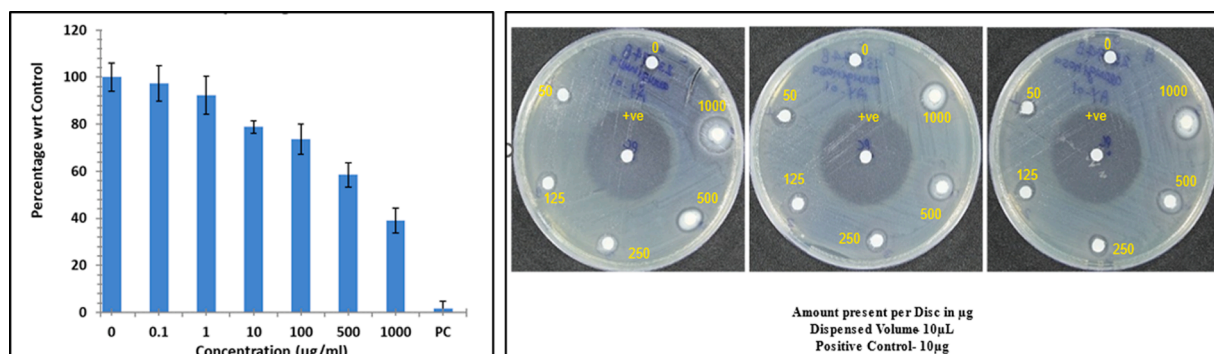


Fig. 7. MIC study of ZnO NPs against *A. niger* fungal culture (A), ZnO NPs zone inhibition against *P. aeruginosa* bacterial culture (B).

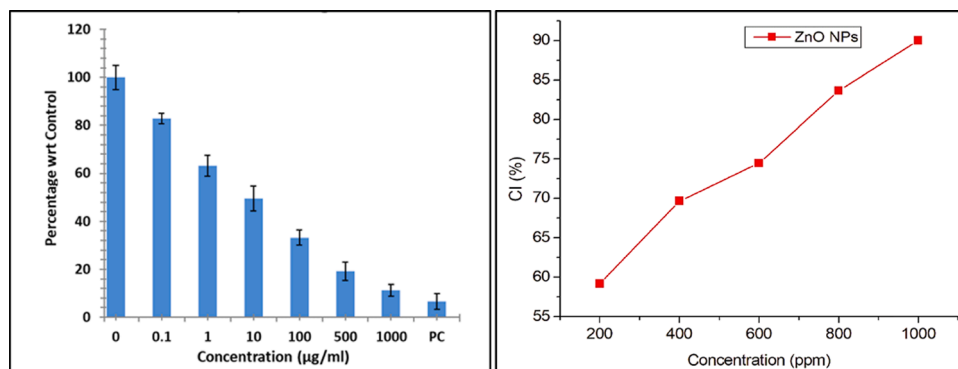


Fig. 8. ZnO NPs MIC study against *P. aeruginosa* culture (A), Corrosion Inhibition Efficiency (CIE) of synthesized ZnO NPs (B).

combination with existing antibiotics. Furthermore, in materials science, ZnO NPs could be incorporated into antibacterial textiles, packaging materials, or paints to inhibit bacterial growth and contamination.

4.5. Minimum inhibitory concentration (MIC) activity- *P. aeruginosa*

0.5 Mc Farland Standard dilution of microbes was used for the study. The micro-centrifuge tube was filled with 100 µl diluted log cultures of *P. aeruginosa* (MTCC 3541) bacteria. Five µl of created treatment dilutions at varying concentrations were added to the designated tubes, and the mixture was incubated for twenty-four hours. Following incubation, all material was moved to a 96-well plate, and an Elisa Plate Reader (iMark Bio-Rad) was used to measure the turbidity at 630 nm. Ten milligrams of ciprofloxacin acted as a positive control. The MIC of produced ZnO is displayed in Fig. 8 at 0.1 µg/ml.

4.6. Antioxidant activity by DPPH scavenging assay

Scavenging activity in the sample was observed concerning ascorbic acid (IC-50 value of ZnO NPs was very low i.e., 10.54 ± 1.49 µg/ml) [63, 64]. Almost 50 % percentage inhibition was achieved against control at a 10-ppm concentration of ZnO NPs. Abdelbaky et al. prepared ZnO NPs using *P. odoratissimum* extract and showed antioxidant properties of 28.1 µg/ml [68]. Arumugam et al. prepared ZnO by green synthesis route using *S. cumini* leaf extract and showed an antioxidant property of 70.85 µg/ml [69]. Faisal et al. prepared ZnO by an environment-friendly approach using *M. fragrans* extract and showed an antioxidant property of 71.1 µg/ml [70].

Mechanism of antioxidant properties of ZnO NPs

ZnO NPs exhibit antioxidant properties through an unknown mechanism. One probable mechanism is their ability to scavenge free radicals, particularly ROS like the 2,2-diphenyl-1-picrylhydrazyl, (DPPH) radicals. DPPH is a popularly known method to evaluate the antioxidant properties of Metal oxide NPs. In this assay, antioxidants donate electrons to the DPPH radical, thereby neutralizing its free radical nature and producing a color change purple to yellow, observed by UV-visible spectroscopy. The antioxidant property of ZnO NPs observed concerning standard ascorbic acid and is a well-known natural antioxidant. The midpoint maximum inhibitory concentration (IC50) of ZnO NPs was 10.54 ± 1.49 µg/ml. This indicates the amount of ZnO NPs compulsory to scavenge 50 % of the DPPH in the assay. Comparing the IC50 value of ZnO NPs provides insights into the relative antioxidant potency as compared to a standard antioxidant. An almost 50 % percentage inhibition was achieved against the control at a concentration of 10 ppm (parts per million) of ZnO. This indicates the ability of ZnO to inhibit the formation of DPPH radicals in the assay system. The concentration of 10 ppm is often used in antioxidant assays to evaluate the efficacy of antioxidant NPs. The observed antioxidant activity of ZnO NPs is

significant from both scientific and practical perspectives. Scientifically, it adds to our understanding of the antioxidant properties of NPs, particularly metal oxide NPs like ZnO NPs. It highlights the potential of ZnO NPs as alternative antioxidant agents or supplements.

4.7. Mechanism of antimicrobial and antioxidant properties

The anti-bacterial property of zinc oxide NPs which were synthesized by reducing with *Syzygium cumini* (Jamun) leaf extract can be attributed to many factors. "Green synthesis" refers to the process of creating ZnO NPs utilizing extracts from plants, and it entails the application of bioactive molecules found in the extract of plants to aid in the metal ions' reduction to generate NPs. The probable reason for antibacterial activity shown by ZnO NPs includes, phytochemicals present in *Syzygium cumini* leaves extract. Many phytochemicals, including polyphenols, flavonoids, tannins, and other bioactive substances, are present in *Syzygium cumini* leaves. These plant-based substances behave as reducing agents. When ZnO NPs are being synthesized, Zn^{2+} is reduced to Zn^0 and to generate ZnO NPs the reducing agents help to reduce the metal salt by the phytochemicals abundantly present in the *S. cumini* leaf extract. NPs generally have a higher surface area. More contact areas for interactions with bacterial cells were possible due to this expanded surface area.

ZnO NPs release Zn^{2+} ions to the medium. Zn^{2+} ions bind with bacterial culture and lead to cellular disruption. ZnO NPs possess the ability to form a variety of reactive oxygen species (ROS), such as superoxide radicals and hydroxyl molecules. These ROS can put bacterial cells under oxidative stress, which damages and eventually kills the cells, and ZnO NPs can interact with the membranes of bacteria, changing their integrity and permeability. This disruption results in the cell death. ZnO NPs may enter bacterial cells and interact with intracellular components, disrupting vital cellular processes and leading to antibacterial effects.

4.8. Anticorrosive study of ZnO NPs

The variation in inhibitory efficacy with ZnO NP concentration is seen in Fig. 8(B). The weight loss diminishes as Zinc oxide NPs concentration rises, and rises in CIE was observed. At 100 ppm concentration of ZnO NPs, the maximum corrosion inhibition efficiency (CIE) was 90.01 percent. Fig. 9 shows the green synthetic approach of ZnO NPs and the capping of ZnO NPs by phytochemicals. The phytochemicals and ZnO NPs act synergistically in protecting the MS coupons from corrosion. Different phytochemicals present on the surface of ZnO NPs help in the sustained release of ZnO NPs.

4.9. Magnetic study of zinc oxide NPs

Table 2 depicts the data of the magnetic study of ZnO NPs. By

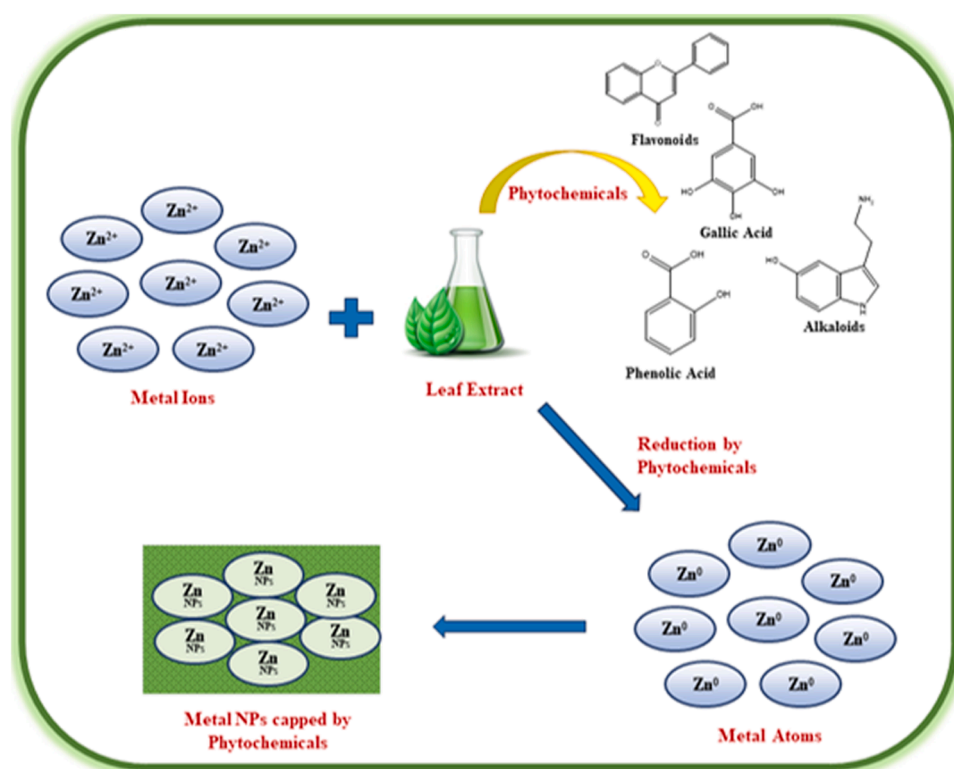


Fig. 9. ZnO NPs synthesized by green approach and capping of ZnO NPs by phytochemicals.

Table 2
Magnetic properties of ZnO NPs.

Current Applied (i)	Magnetic Field (H)	H2	Weight (g)	Change in Weight (mg)
0	18	324	12.0760	0.1
0.5	82	6724	12.0759	0.1
1.0	149	22,201	12.0758	0.3
1.5	213	45,369	12.0755	1.1
2.0	276	76,176	12.0744	1.9
2.5	373	110,889	12.0725	2.2
3.0	380	144,400	12.0703	–

increasing current, the magnetic field increases, and there is a decrease in the weight of ZnO NPs (Fig. 10A). The magnetic susceptibility (χ) of the sample was calculated i.e., 0.19. Hence, the green synthesized ZnO NPs show paramagnetic behavior and can be used for many magnetic applications.

Table 3 depicts a comparative study of green production of Zinc-

oxide NPs with literature and our reported work [65–70]. It was observed that for the first time, we are reporting antibacterial, antifungal, antioxidant, anticancer, magnetic, and anticorrosive applications of Zinc-oxide NPs produced by *Syzygium cumini* leaves extract. No other study has reported anticorrosive NPs along with antibacterial, anticancer, and antioxidant studies. IC-50 for the anticancer and antioxidant study of our ZnO NPs was found less than all other metal oxide NPs reported in the literature (Table 3).

ZnO NPs exhibit intriguing magnetic characteristics when exposed to an external magnetic field. Their magnetic properties can be further enhanced when they are doped with certain transition metals. Pure ZnO NPs itself is considered a paramagnetic material due to retention magnetization. They can be engineered to show paramagnetic behaviour through different methods, including doping with transition metals or defects engineering. Paramagnetic ZnO NPs can be widely used in magnetic resonance imaging (MRI).

In summary, ZnO NPs that are encapsulated by phytochemicals produced using a green technique function as sustained-release NPs and

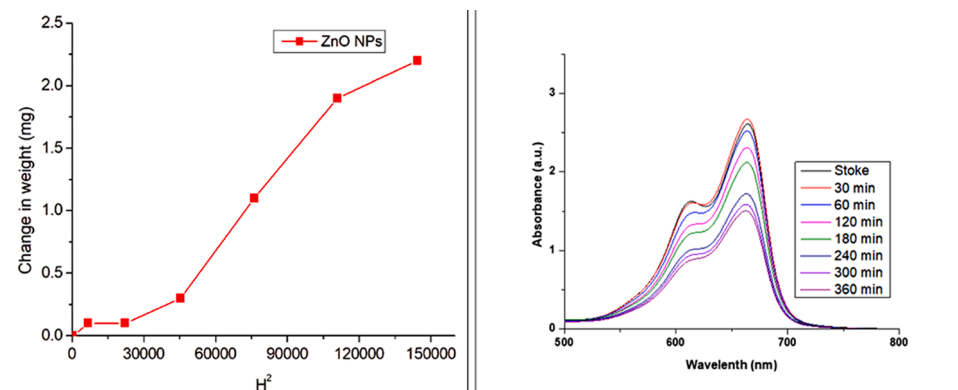


Fig. 10. Variation in weight of ZnO NPs with the applied magnetic field (A), Photocatalytic activity study of ZnO NPs against MD dye in UV light (B).

Table 3

Comparative study of green production of ZnO NPs with literature and reported work.

Source of ZnO NPs	Antifungal MIC	Antibacterial MIC	Anticancer IC50	Antioxidant IC50	Anticorrosive (IE%)	References
<i>N. arborstris</i> Flower extract	16 µg/ml (<i>A. niger</i>)	NR	NR	NR	NR	[65]
<i>T. castanifolia</i> Leaf extract	NR	NR	65 µg/ml (A549 cell line)	NR	NR	[66]
<i>C. formosum</i> Leaf extract	NR	NR	300 µg/ml (HepG2 cell line)	NR	NR	[67]
<i>P. odoratissimum</i> Leaf extract	NR	NR	NR	28.1 µg/ml	NR	[68]
<i>Syzygium cumini</i> Leaf extract	NR	NR	72.50 µg/ml (A549 Cell line)	70.85 µg/ml	NR	[69]
<i>M. fragrans</i> Fruit extract	NR	17 µg/ml (<i>P. aeruginosa</i>)	NR	71.1 µg/ml	NR	[70]
Our work	8 µg/ml (<i>A. niger</i>)	0.1 µg/ml (<i>P. aeruginosa</i>)	49.83 µg/ml (HepG2 cell line)	10.54 µg/ml	90.01	

NOTE: NR stands for Not Reported.

can be used as antioxidants, antibacterial, anticorrosive, and anticancer agents. The continuous release of NPs, which improves their effectiveness and performance as antibacterial agents, is made possible by phytochemicals. To work more cooperatively and improve the effectiveness of other common antibiotics, ZnO NPs can be taken either alone or in conjunction with them.

4.10. Photocatalytic study

To evaluate the photocatalytic property of ZnO NPs, we utilized Methylene blue (MB) dye. To prepare a stock solution, 1.0 mg of MB dye was precisely measured and added to 100 mL of H₂O. The stock and working solutions were prepared with MB-colored solutions at a final concentration of 30 ppm. Additionally, 10 mg of ZnO NPs were introduced into the stock solutions. To assess the effectiveness of the produced ZnO NPs in reducing Azo dye contamination in textile dyes, MB was specifically chosen as an example. The photocatalytic action of ZnO was meticulously evaluated in UV light. Fig. 10B shows a photocatalytic activity study of ZnO NPs against MD dye in UV light. Throughout the experiment, the color of the suspension gradually diminished with response time, which indicated the decomposition of MB dye over time. The absorbance of the dye solution decreased with time at λ_{max} , especially when compared to wavelengths from 0 to 360 min. The % degradation (R) may be determined using the Eqn. (1).

$$\text{Degradation rate of dye (\%)} = (C_0 - C_t / C_0) \times 100 \quad (1)$$

C_0 and C_t represent the concentrations of the MB solution at $t = 0$ and $t = t$ min, respectively

The ZnO NPs degrade 43.94 % of dye in 360 min in UV light.

5. Future scope of the study

To improve the manufacturing processes and consequently the ZnO NPs' cytotoxicity against cancer cells, antibacterial activity, and antioxidant potential, future studies can focus on these aspects. Comprehensive biocompatibility studies are required to evaluate the safety and suitability of the synthesized ZnO NPs for antibacterial applications. This entails assessing their interactions with biological systems, possible negative effects, and toxicity profile. ZnO NPs' prolonged release, which is made possible by phytochemical capping agents, raises the possibility of their use in drug delivery systems. Subsequent investigations may examine the viability of integrating therapeutic compounds with ZnO NPs to facilitate targeted drug delivery to particular cells or regions.

ZnO NPs' antibacterial and anti-corrosive qualities make it possible to employ them in environmental remediation processes like soil and water remediation. Future research can look into how well they work to eliminate toxins and pollutants from environmental matrices. Realizing the potential societal and economic benefits of this study entails scaling

up the synthesis process and commercializing the generated materials, which in turn leads to widespread application in different industries.

6. Conclusions

The development of nanomaterials using medicinal plants proves a promising method that provides a platform for novel applications. By utilizing an aqueous extract from *Syzygium cumini* leaves, ZnO NPs were synthesized and analyzed using different spectroscopic methods. The ZnO NPs exhibit cytotoxicity for the HepG2 cancerous cell line, with IC50 of 49.83 µg/ml. They show an 11.66 mm zone of inhibition and MICs of 8 µg/ml and 0.1 µg/ml against the *A. Niger* fungus and *P. aeruginosa* bacterial culture, respectively. They also show very good antioxidant activity with IC50 of 10.54 µg/ml. When exposed to an external magnetic field, the green ZnO NPs exhibit paramagnetic activity and also act as an excellent anti-corrosive material with an inhibition efficiency of 90 % at 100 ppm in a sulfuric acid medium. The phytochemical present at the surface of ZnO NPs acts as a capping agent resulting in a sustained release for anticorrosive, antioxidant, anticancer, and antibacterial activity. However, the scalability of ZnO NPs prepared by the green approach is a challenge for industrial-scale production of NPs. Despite the promising anticancer effects of ZnO NPs, the cytotoxicity of NPs towards non-cancerous cells or tissues needs to be addressed.

The benefits of this study include the development of nanomaterials that reduce the use of harmful chemicals for mitigating the adverse consequences on mankind and environment. By using medicinal herbs to synthesize ZnO NPs, a sustainable method is presented that minimizes our dependency on synthetic chemicals, thus supporting environmental sustainability and possibly lowering health concerns related to exposure to hazardous materials. Metal NPs synthesized by a greener approach can find uses as antimicrobial agents, which might be advantageous in several industries, such as water treatment, food preservation, and medicine. Capping agents derived from phytochemicals demonstrate an environmentally friendly method for creating ZnO NPs. This promotes sustainability in material science research by decreasing reliance on artificial chemicals. Finding will certainly be beneficial for the society because we are reporting multifunctional application of phytochemicals capped ZnO NPs.

CRediT authorship contribution statement

Abhiruchi Yadav: Writing – original draft, Methodology, Conceptualization. **Harish Kumar:** Writing – review & editing, Validation, Supervision, Investigation, Conceptualization. **Parvin Kumar:** Visualization, Validation. **Gita Rani:** Visualization, Validation. **Sanjeev Maken:** Visualization, Validation.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Harish Kumar reports administrative support was provided by Central University of Haryana. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.molstruc.2024.141017](https://doi.org/10.1016/j.molstruc.2024.141017).

Data availability

No data was used for the research described in the article.

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