SYNERGISTIC ANTIBACTERIAL EFFECTS OF CEFOTAXIME CAPPED METAL DOPED ZINC OXIDE NANOSTRUCTURES

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ABSTRACT

Objectives: The study describes the synthesis of ZnO nanostructures doped with metals including Ca, Mg, Mn, Ag and Cu using a co-precipitation method.

Methodology: The nanostructures were examined through Scanning Electron Microscopy (SEM) analysis and X-ray diffraction (XRD) assessment The antibacterial efficacy of these nanostructures was evaluated using a modified disk diffusion Kirby Bauer method.

Results: Nanostructures displayed effective antimicrobial activity against a variety of bacterial strains. The most effective nanostructures were found to be those made with Ca-Cefotaxime and Ag-Cefotaxime doped ZnO.

Conclusions: The study demonstrates that the combination of ZnO and Cefotaxime with different metal ions has an impact on the antibacterial activity against various bacterial strains. To the best of our knowledge, nanoparticles with cefotaxime have not been studied in the literature before. Further studies should investigate the mechanism of action.

Keywords: Cefotaxime; Zinc Oxide Nanoparticles; Antibacterial Activity; Doping; Capping

INTRODUCTION

Antibiotic resistance has become a significant public health concern globally and there is an urgent need for the creation of novel antibacterial agents. Nanoparticles, particularly metal-doped ZnO, have emerged as a potential alternative to traditional antibiotics because of their distinctive physicochemical characteristics. The synergistic interactions of metal-doped ZnO nanoparticles and antibiotics explores new areas of research, as they have the potential to enhance the antibacterial activity of antibiotics, reduce the dosage required and overcome the emergence of antibiotic resistance.[1] Cefotaxime (CFX) is a third-generation cephalosporin antibiotic sanctioned by the FDA for addressing infections caused by a broad spectrum of bacteria, encompassing both gram-negative and gram-positive strains, along with anaerobic bacteria.[2] Cefotaxime is commonly used as a first-line treatment for Primary bacterial peritonitis (SBP) in patients with cirrhosis. Despite its widespread use, there has been no research done to identify the factors that can accurately diagnose this type of infection in patients with serotonergic disorders.[3,4] Recently, research has focused on using cefotaxime-capped metal nanoparticles to enhance its antibacterial activity. Cefotaxime-capped metal nanoparticles have been shown to exhibit a synergistic effect, which results in a significant increase in antibacterial activity against various strains of bacteria.[5,6] However, to the best of our knowledge, ZnO nanoparticles with cefotaxime capping have not been studied in the literature before. The environmental impact of excess antibiotics use has become a major concern. Several reports describe a novel adsorption method using Fe/Co bimetallic nanoparticles loaded with antacid on biochar (MB/Fe/Co) to remove cefotaxime from a water solution.[7] There are various techniques for synthesizing capped and doped ZnO nanostructures, as well as simple nanostructures. These methods can be broadly categorized as chemical and physical methods. Some of the common techniques include sol-gel, hydrothermal and co-precipitation methods.[8] Of these methods, co-precipitation is considered to be the most efficient and straightforward approach for creating nanoparticles.[9] Experimental results on bacteria revealed that treating Clostridium perfringens with a dosage of 10 mg/kg of Cefotaxime for 7 days was not effective. However, using Cefotaxime in combination with chitosan or exosomes with the administration of 10 mg/kg was discovered to be remarkably efficacious in therapeutic applications.[10] Research has shown that nanoparticles can effectively eliminate bacterial cells even at low concentrations and in different pH conditions.[11] The results of a meta-analysis indicate that antibiot-

ics can be removed by various nanoparticles with a 61% efficiency rate.[12] Nanoparticles play a crucial role in eliminating or killing bacteria from aqueous solutions.[13] Extended spectrum beta lactamases (ESBLs) are now found globally in all classes of enteric bacteria, including those that are resistant to the medication Cefotaxime (CFX), particularly in Escherichia coli and Klebsiella pneumoniae.[14] In this investigation, the production of ZnO nanoparticles (NPs) was achieved through co-precipitation and characterized using powder crystallography X-ray diffraction (XRD) and scanning electron microscopy (SEM).

The current study aims to investigate the effectiveness of using nanoparticles that are coated with antibiotics and infused with metal ions in eliminating bacterial cells. Our goal is to investigate the synergistic antibacterial effects of cefotaxime-capped metal-doped ZnO nanostructures for various bacteria types. We hypothesize that the combination of cefotaxime and metal-doped ZnO nanoparticles will exhibit a synergistic effect, resulting in enhanced antibacterial activity. We will also investigate the mechanism of action of the combined therapy to provide insight into the underlying biological mechanisms. By understanding the synergistic effects of cefotaxime-capped metal-doped ZnO nanoparticles, our objective is to make contributions for the advancement of novel antibacterial agents capable of addressing antibiotic resistance with increased effectiveness.

METHODOLOGY

An aqueous solution of Cefotaxime (CFX) was synthesized and combined with an aqueous solution of Zinc Oxide (ZnO). Sodium Hydroxide was added dropwise while combination was subjected to heating and agitated at room temperature for a duration of 30 minutes. Afterwards, the solution was stirred for an additional 5 hours at 80°C, leading to the formation of white precipitates. These precipitates were separated and purified by washing with ethanol and distilled water. The resultant sample was subsequently subjected to heat treatment in a preheated oven at 120°C for one hour, followed by further heating at 300°C for two hours, leading to the formation of a nanopowder.[15]

A solution was made from manganese acetate tetrahydrate (Mn(CH3COO)2•4H2O) by meticulously mixing it with water and gradually introducing into the solution of zinc acetate dihydrate, all while maintaining continuous stirring. Following this, a cefotaxime solution was gently introduced into the mixture. Subsequently, a potassium hydroxide solution was added drop by drop to induce the formation of precipitates. The pH was adjusted to 8.5 and the resulting solution was stirred for approximately 2 hours at 85°C. Following this, it was left undisturbed for about 1 hour. The precipitates that formed were carefully washed with both ethanol and distilled water. Finally, they were subjected to drying and subsequent calcination at 500°C for a duration of 4 hours to yield the desired nanoparticles.[16]

A solution of magnesium nitrate hexahydrate salt was introduced into a solution of zinc nitrate hexahydrate while maintaining continuous stirring at a temperature of 60°C. Following this, the cefotaxime solution was incorporated into the aforementioned solution. Subsequently, a sodium hydroxide solution was introduced drop by drop, resulting in the formation of white precipitates. Ultimately, the solution was continuously stirred for a period of 4 hours and underwent reflux at room temperature for the subsequent 24 hours. Following this, it was subjected to multiple washes with distilled water and ethanol to eliminate any impurities. The resulting precipitates were initially dried at 120°C and subsequently subjected to annealing at 500°C within a furnace, a process that lasted approximately 6 hours, finally leading to the formation of nanostructures.[17]

A solution of calcium nitrate tetrahydrate was gradually introduced into the solution of zinc nitrate hexahydrate while maintaining continuous stirring. Following that, a solution of Cefotaxime was carefully introduced into the pre-existing solution. Sodium hydroxide was then added drop by drop, resulting in the formation of precipitates. This final solution was initially stirred at room temperature for a duration of half an hour, followed by further stirring at 60°C for a period of 4 hours. Subsequently, it underwent refluxing for an additional 24 hours at room temperature to achieve a clear solution. This clear solution was then subjected to multiple washes with distilled water and ethanol to eliminate any impurities. The precipitates were initially dried at 120°C and then subjected to annealing at 600°C for a duration of 4 hours.[18]

An aqueous solution of copper chloride was gradually introduced into an aqueous solution of zinc chloride ($ZnCl_2$) while maintaining continuous stirring. Subsequently, a Cefotaxime solution was also added to this mixture. Aqueous ammonia was then meticulously added drop by drop to generate white precipitates. The pH was adjusted to 8, and the solution was heated and stirred. After approximately 10 minutes of stirring, the solution was filtered and underwent washing with distilled water and ethanol. The precipitates that developed were dried in an oven and subsequently subjected to annealing at 600°C for 3 hours under reflux conditions. These temperature and other parameter variations resulted in the formation of Cu and Cefotaxime-doped ZnO nanowires.[19,20]

A silver nitrate ($AgNO_3$) salt solution was gradually introduced into a zinc acetate $Zn(CH_3CO_2)_2$ solution to create a uniform mixture. Following this, a Cefotaxime solution was added to the resulting homogeneous mixture. hen, a sodium carbonate solution was slowly introduced drop by drop

to the homogeneous mixture with vigorous stirring, leading to the formation of precipitates. The resulting precipitates were thoroughly washed with both distilled water and ethanol on multiple occasions and subsequently separated. Following this, they were subjected to drying in a drying oven at 80°C and then annealed for a duration of 2 hours at approximately 300°C to yield nanoparticles.[20]

X-ray Diffraction (XRD), a laboratory-based technique, was employed to identify the crystalline components and assess the unit cell dimensions. This method was utilized to investigate the structural characteristics and momentum of materials. Furthermore, XRD analysis was employed to ascertain the average crystal size of nanoparticles, a critical factor influencing their physical and chemical properties, including their antibacterial efficacy.[21]

One of the most important techniques used for characterization was Scanning Electron Microscopy (SEM). It was utilized to get photographs from the sample by scanning the surface including a concentrated stream of electrons. SEM analysis allowed the observation of the surface of ZnO nanoparticles at high magnification and resolution, which revealed important information about the particle size, shape and surface morphology.[22]

Strains of S. marcescens ATCC 13880, P. aeruginosa ATCC 27853, E. coli K88, B. subtilis ATCC 19659, S. typhi ATCC 50013 and S. aureus ATCC 25923 were supplied by PCSIR and were kept in storage at a temperature of 4°C. A modified adaptation of the Kirby Bauer disk diffusion method was utilized for assessing the antibacterial activity. Strains of the selected bacteria were sub-cultured into fresh Müller-Hinton broth media the day prior to experimentation. Nutrient agar media was first prepared in a flask, then sterilized using an autoclave, and subsequently poured into petri plates to allow for solidification. Once solidification was achieved, these plates were incubated for 24 hours to ensure sterility. Afterwards, with the use of glass rod which was previously sterilized, fresh bacterial culture of approximately 100 µL was streaked on petri dishes. The bacterial concentration was estimated to be around 10^6 colony-forming units (CFU)/mL. The Petri dishes were left undisturbed for a short duration to facilitate the absorption of bacteria into the media. Subsequently, 8mm diameter wells were punched into the media using a cork screw. A droplet of molten agar was introduced into each well to prevent any potential leakage of the samples of nanostructures. Various concentrations of the sample (30µg, 60µg, and 90µg) were dispensed into the wells using a micropipette. Each well initially had 100µL of each sample. The plates were appropriately labeled and subsequently placed in an incubator at a temperature of 35°C ± 2°C for a duration of 12 hours. Tetracycline and Ampicillin were used as positive controls, while the negative control consisted of a blank solvent added to the wells. The measurement of the inhibition zone was conducted to assess the antibacterial efficacy of the samples.[23,24]

RESULTS

The X-ray diffractometer was used to confirm the crystalline structure of ZnO NPs. The XRD results were consistent with the synthesis of NPs. Furthermore, the size of the nanoparticles was determined through the application of the Debye-Scherrer equation, and the average size was subsequently calculated.

Drawing conclusions from the XRD results, it can be inferred that Cefotaxime doping did not significantly affect the crystalline nature of Zinc Oxide Nanostructures, as confirmed by the XRD pattern as represented by Figure 1A. The average crystal size of the Cefotaxime doped Zinc Oxide Nanostructures was found to be 31.31 nm. In comparison, Mn and Cefotaxime doped ZnO nanostructures showed a smaller average crystal size of 11.27 nm as illustrated in Figure 2A, while Mg and Cefotaxime doped ZnO nanostructures had an even smaller average crystal size of 5.99 nm can be seen in Figure 3A. On the other hand, Ca and Cefotaxime doped ZnO nanostructures had an average crystal size of 28.28 nm depicted in Figure 4A and Ag and Cefotaxime doped ZnO nanostructures had an average crystal size of 23.67 nm shown in Figure 5A. It is noteworthy that Cu and Cefotaxime doped ZnO nanostructures had the smallest average crystal size of 0.73 nm outlined in Figure 6A. This phenomenon could potentially be attributed to the impact of Cu doping on the nanoparticle size. In summary, the XRD results confirmed the successful synthesis of Cefotaxime doped ZnO nanostructures with varying average crystal sizes depending on the type of dopant used. The average crystal size of the nanoparticles was calculated using the Debye-Scherrer equation.

The morphology and configuration of the nanoparticles, synthesized through the co-precipitation method, were scrutinized using Scanning Electron Microscopy (SEM). The micrographs displayed that the Mn-doped ZnO nanoparticles exhibited spherical shapes with certain levels of aggregation. It was likely due to the magnetic properties of the NPs arising from the interplay of repulsive and attractive interactions among the nanostructures. The average size of these nanoparticles was determined to be 130 ± 97 nm by use of of Image J software.

The nanostructures of Cefotaxime-capped ZnO via SEM showed a spherical morphology with some level of aggregation. The average size was determined to be in the range of 10 to 20 nm. The SEM micrographs also showed that these NPs had a variety of shapes including roughly spherical, rod-like, circular, fibrous and spherical with

some degree of aggregation. The average size of these NPs were calculated to be 50-100 nm, 30-50 nm, 50-200 nm, 10-50 nm and 20-50 nm, respectively (Figures 1B, 2B, 3B, 4B, 5B and 6B). The small size of the capped ZnO crystals is believed to contribute to the aggregation, which alters their physicochemical and biological properties.

Table 1 presents the results of an investigation into the antibacterial activity of various samples on three different bacterial strains: S. marcescens (B1), E. coli (B2) and P. aeruginosa (B3). The samples are described by their composition, such as "ZnO + Cefotaxime," "ZnO + Cefotaxime +Mn," "ZnO + Cefotaxime +Mg," and so on. The samples were evaluated at three distinct concentrations (30 µg/ml, 60 µg/ml, and 90 µg/ml) and the extent of inhibition of bacterial growth was quantified in millimeters (mm).

The results show that sample ZnO + Cefotaxime+ Mn did not show any antibacterial activity against all three bacterial strains while ZnO + Cefotaxime was active only against E. coli. ZnO + Cefotaxime+ Mg exhibited antibacterial potential against strains E. coli, P. aeruginosa and S. marcescens only at higher concentrations.

ZnO+ CFX+ Ag showed the best antibacterial activity against all three bacterial strains at all three concentrations. Samples ZnO + Cefotaxime +Ca and ZnO + Cefotaxime +Cu showed the second best antibacterial activity against all three bacterial strains at all three concentrations.

Table 2 represents the results of an antibacterial activity assay for different nanostructures against three types of bacteria: Salmonella typhi (B4), Staphylococcus aureus (B5) and Bacillus subtilis (B6). The samples tested include a combination of ZnO+ Cefotaxime along with other substances, including Mn, Mg, Ca, Cu and Ag. The assay measured the inhibition of bacterial growth in millimeters at three different sample concentrations (30µg/ml, 60µg/ml and 90µg/ml).

From the results, it can be observed that ZnO when combined with Cefotaxime, the sample showed inhibition against S. aureus and B. subtilis at different concentrations but not against S. typhi. The sample ZnO + Cefotaxime + Mn showed the highest inhibition (32mm) against S. aureus at 90 µg/ml concentration. Other than that, it was ob-

Table 1: Results of Antibacterial Activity of nanostructures against S. marcescens, E. coli and P. aeruginosa.

Nanostructures	S. marcescens inhibition in mm (B1)			E. coli inhibition in mm (B2)			P. aeruginosa inhibition in mm (B3)		
	30 µg/ml	60 µg/ml	90 µg/ml	30 µg/ml	60 µg/ml	90 µg/ml	30 µg/ml	60 µg/ml	90 µg/ml
ZnO + Cefotaxime	0	0	0	13	15	16	0	0	0
ZnO + Cefotaxime +Mn	0	0	0	0	0	0	0	0	0
ZnO + Cefotaxime +Mg	0	0	15	0	13	14	0	14	15
ZnO + Cefotaxime +Ca	15	17	19	0	11	13	18	19	20
ZnO + Cefotaxime +Cu	`20	15	18	0	0	0	23	24	25
ZnO + Cefotaxime +Ag	20	23	25	19	20	22	20	22	24

Table 2: Results of Antibacterial Activity of nanostructures against S. typhi, S. aureus and B. subtilis.

Nanostructures	S. typhi inhibition in mm (B4)			S. aureus inhibition in mm (B5)			B. subtilis inhibition in mm (B6)		
	30 µg/ml	60 µg/ml	90 µg/ml	30 µg/ml	60 µg/ml	90 µg/ml	30 µg/ml	60 µg/ml	90 µg/ml
ZnO + Cefotaxime	0	0	0	17	19	27	16	19	20
ZnO + Cefotaxime +Mn	0	0	12	20	27	32	11	14	15
ZnO + Cefotaxime +Mg	0	0	0	0	19	20	0	11	17
ZnO + Cefotaxime +Ca	0	17	21	20	22	24	28	29	35
ZnO + Cefotaxime +Cu	15	16	17	0	0	0	0	0	0
ZnO + Cefotaxime +Ag	20	22	24	30	32	35	19	20	21

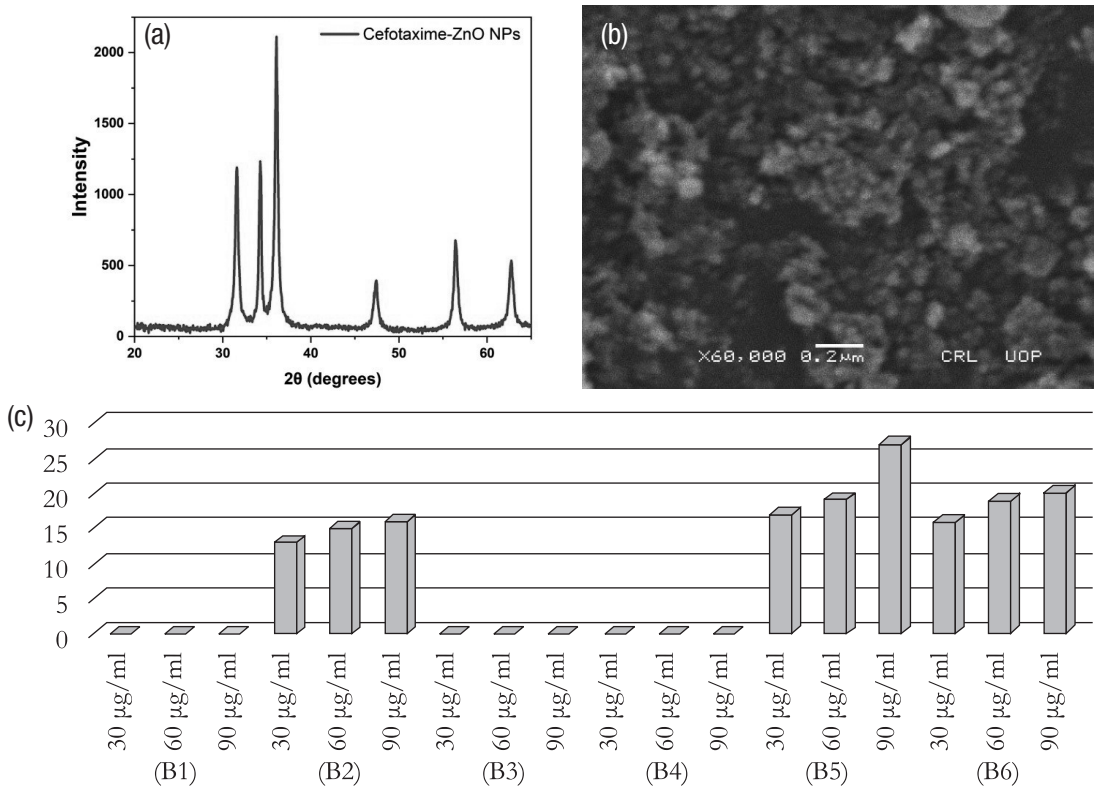

Figure 1: (a) XRD for Cefotaxime capped ZnO nanostructures; (b) SEM image of CTX capped ZnO nanostructures, (Morphology: Irregular; Size: 10-20 nm); (c) Antibacterial activity of Cefotaxime capped ZnO nanoparticles.

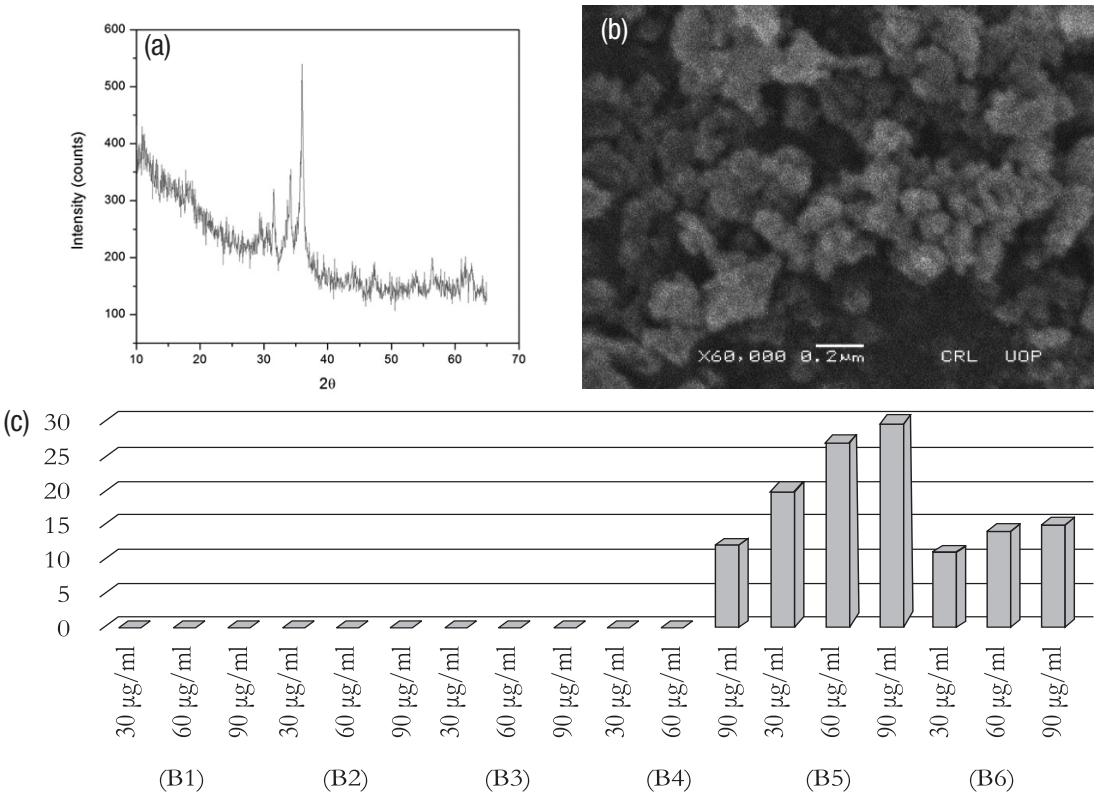

Figure 2: (a) XRD for Cefotaxime capped and Mn doped ZnO nanostructures; (b) SEM image of Mn doped and CTX capped ZnO nanostructures. (Morphology: roughly spherical, size 50-100 nm); (c) Antibacterial activity of Cefotaxime capped Mn doped ZnO nanoparticles.

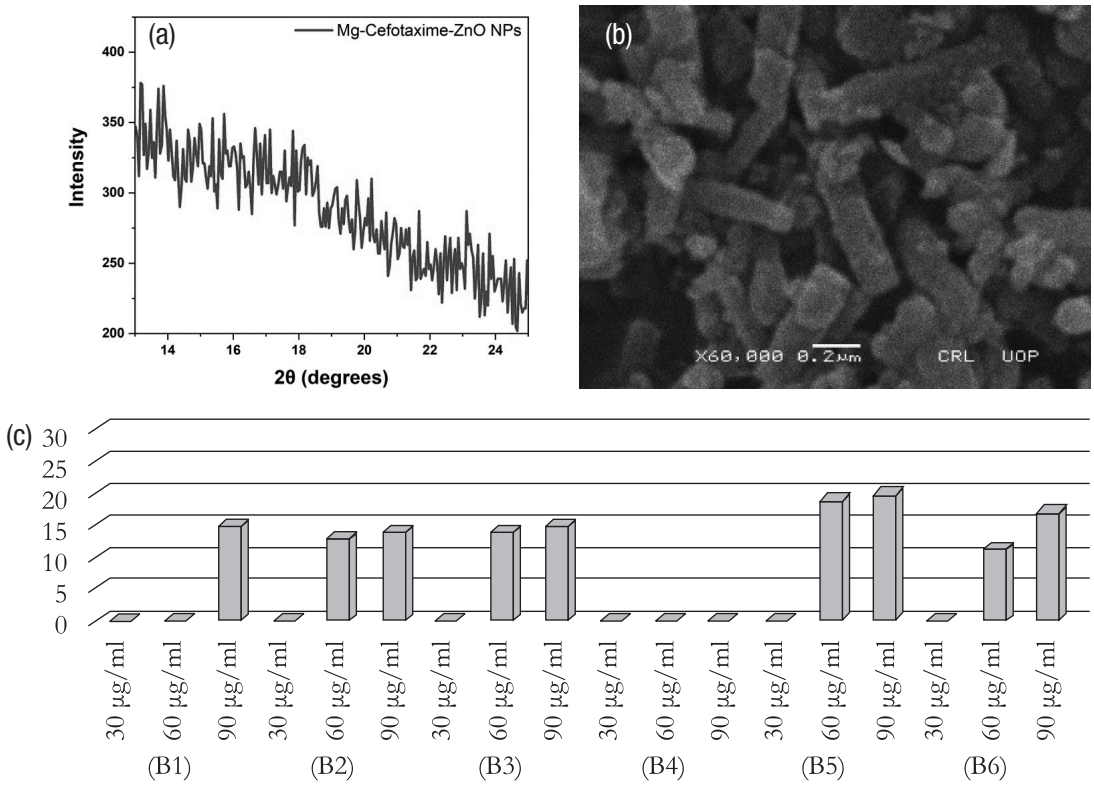

Figure 3: (a) XRD for Mg doped and cefotaxime capped ZnO nanostructures; (b) SEM image of Mg doped and CTX capped ZnO nanostructures. (Morphology: Rod shaped, size 30-50 nm); (c) Antibacterial activity of Cefotaxime capped Mg doped ZnO nanoparticles.

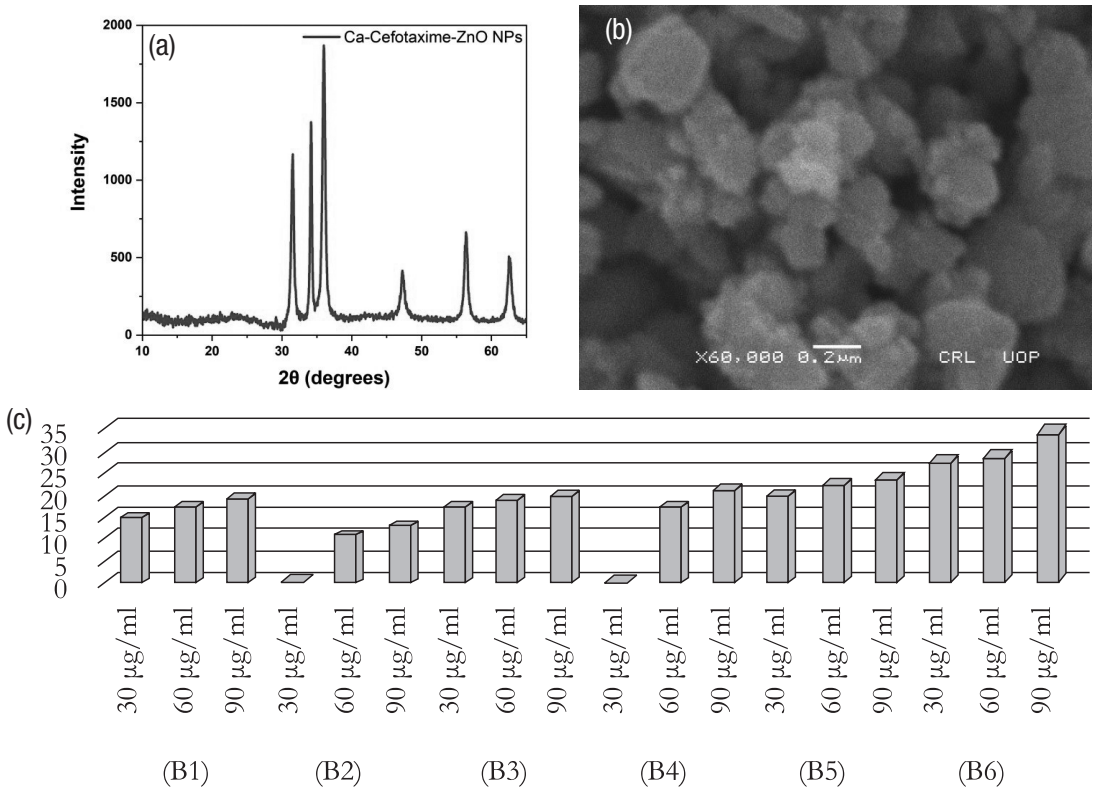

Figure 4: (a) XRD for Ca dopped and Cefotaxime capped ZnO nanostructures; (b) SEM image of Ca doped and CTX capped ZnO nanostructures. (Morphology: Roughly spherical; size 50-200 nm); (c) Antibacterial activity of Cefotaxime capped Ca doped ZnO nanoparticles.

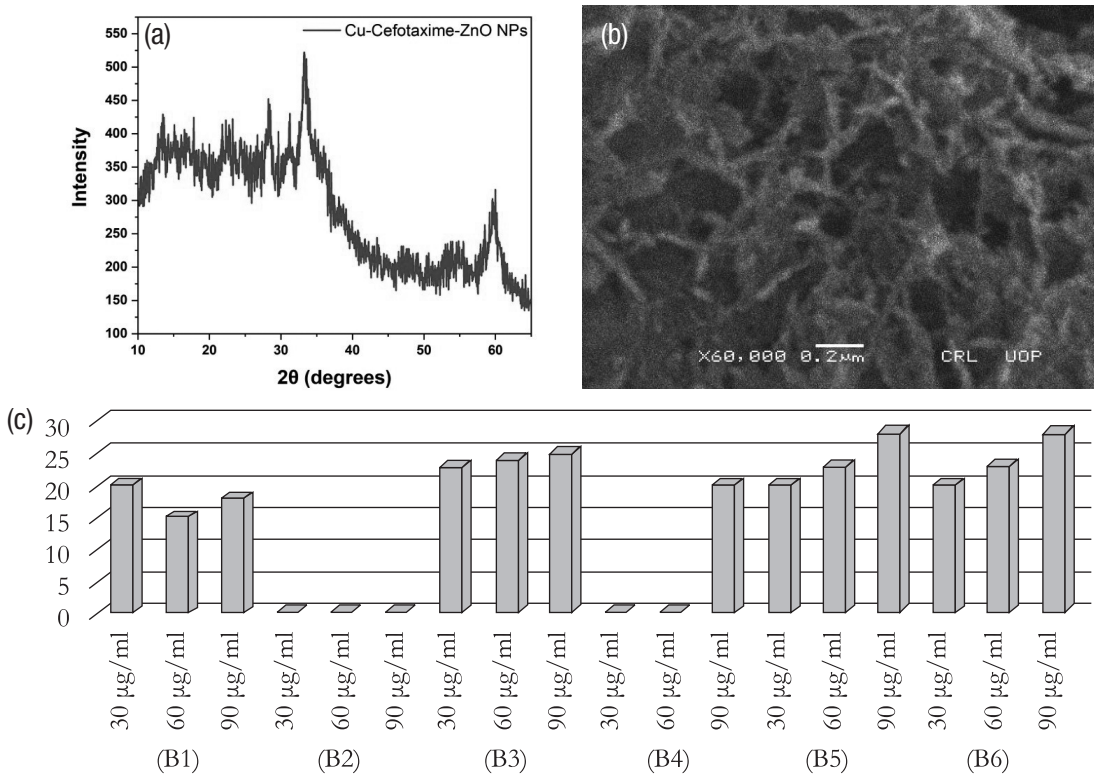

Figure 5: (a) XRD for Cu doped and Cefotaxime capped ZnO nanostructures; (b) SEM image of Cu doped and CTX capped ZnO nanostructures. (Morphology: Rod shaped (fiber like); size: 10-50 nm); (c) Antibacterial activity of Cefotaxime capped Cu doped ZnO nanoparticles.

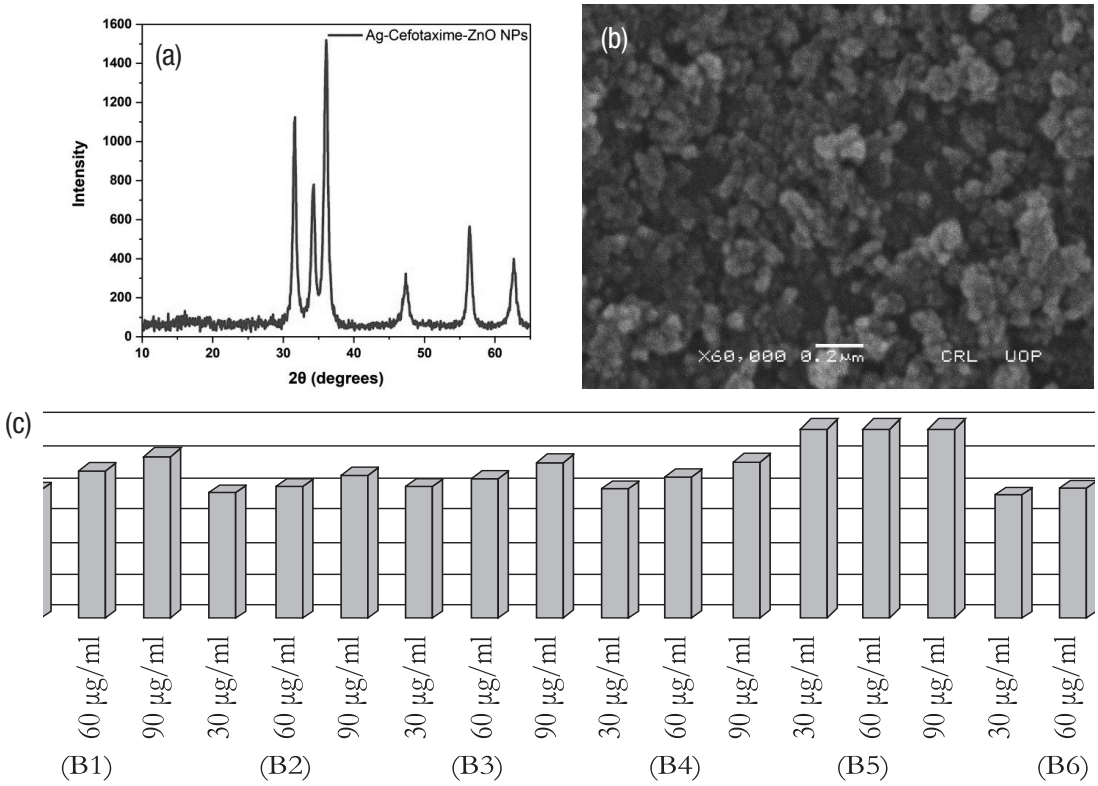

Figure 6: (a) XRD for Ag doped and cefotaxime capped ZnO nanostructures; (b) SEM image of Ag doped and CTX capped ZnO nanostructures. (Morphology: Spherical and some irregular shaped, size 20-50 nm); (c) Antibacterial activity of Cefotaxime capped Ag doped ZnO nanoparticles.

served that weak antibacterial activities were demonstrated by Zn-CFX-Mn sample in other bacteria even at higher concentrations. The sample ZnO +Cefotaxime+ Ag showed the highest inhibition (35mm) against S. aureus at 90 µg/ml concentration. This sample showed the best antibacterial potential among all the samples so far. ZnO + Cefotaxime +Mg exhibited no activity against S. typhi while in the other two bacterial species, the results were comparatively better especially a higher concentration of the sample. ZnO + Cefotaxime +Ca also showed better performance at inhibiting growth of all species of bacteria at higher concentrations. In case of ZnO + Cefotaxime +Cu in table 2, it inhibited the growth of only S. typhi and didn't work against B. subtilus or S. aureus.

It can be inferred that the addition of different metal ions (Mn, Mg, Ca, Cu, Ag) to the sample has an effect on the antibacterial activity. The sample ZnO + Cefotaxime + Mn and ZnO + Cefotaxime + Ag shows the highest inhibition against S. typhi and B. subtilis respectively. The sample ZnO + Cefotaxime + Cu and ZnO + Cefotaxime + Mg did not show any inhibition against any of the bacteria. The details can be seen in Figures 1C, 2C, 3C, 4C, 5C and 6C.

It is worth noting that the inhibition of bacterial growth at higher concentrations (60 and 90 µg/ml) is generally higher than at lower concentrations (30 µg/ml). This suggests that higher concentrations of the sample may be more effective at inhibiting bacterial growth. Additionally, it can be seen that different bacteria respond differently to the sample, with S. typhi showing the least inhibition across all sample concentrations and S. aureus showing the highest inhibition.

DISCUSSION

The rise of antibiotic-resistant microorganisms is a worldwide issue of great concern. Research in the biomedical field has shown promising results in using ZnO nanoparticles for various applications including drug delivery systems and antimicrobial coatings. These nanoparticles have shown potential in improving targeted drug release and enhancing the antibacterial properties of medical devices, offering exciting prospects for advanced healthcare solutions such as anti-tumor medicine/gene transfer, antibacterial, cell imaging and bio-detection. However, infusing metal ions and coating the nanoparticles with antibiotics have been found to enhance the effectiveness of antibiotics against some diseases.[25] The impact of these modified nanoparticles on multidrug-resistant bacteria like E. coli, S. typhi and S. aureus is still being a subject of debate.[26]

The aim of this research was to explore the antibacterial properties of various metal-doped ZnO nanostructures capped with cefotaxime against several bacterial strains. The size and morphology of nanostructures were analyzed using SEM whereas the crystalline structure was verified through XRD. The results depicted that nanostructures of Mn-doped ZnO with cefotaxime capping had spherical shapes with some degree of aggregation, while Cefotaxime capped ZnO NPs had a spherical morphology with some degree of aggregation and a variety of shapes. The range of average size of the nanoparticles was from 10-20 nm to 50-200 nm, depending on the type of nanoparticle. This research paper shows the results of an investigation into the antibacterial activity of various nanostructures. The results recorded in tables and illustrated in graphs indicate that the samples had varying levels of effectiveness in inhibiting microbial growth. Furthermore, a significant enhancement in antibiotic activity when used in combination with ZnO nanoparticles, except for S. typhi was observed.

It appears that the addition of Ca, Cu and Ag to ZnO and Cefotaxime improved the antibacterial activity of the samples. The samples that contain Mn and Mg did not show any antibacterial activity. This might suggest that those dopants do not enhance the antibacterial activity of the samples.

Additionally, our research found that the antimicrobial effect of Cefotaxime against different bacterial strains was dependent on concentration. This study is consistent with previous work done by Usama et. al.[27] However, we used ZnO NPs instead of silver as the focal component. Several studies have reported that zinc oxide is non-toxic to somatic cells at low concentrations.[28] Furthermore, our study clearly demonstrates that Zinc oxide NPs when added to antibiotics significantly increased the killing effect of antibiotics (Cefotaxime) against E. coli. Overall, the results of this assay demonstrate that the combination of ZnO and Cefotaxime with different metal ions has an impact on the antibacterial potential against the bacterial strains. Further studies could be done to investigate mechanism of action and the most effective concentration of these samples. Additionally, it would be valuable to test the samples against a wider range of bacteria to confirm the generalizability of these results.

Prior studies have likewise documented the antibacterial properties of ZnO nanoparticles. For instance, a study by Guan et al. (2021) investigated the antibacterial potential of ZnO NPs against S. aureus and E. coli. The findings indicated that ZnO nanoparticles displayed noteworthy antibacterial effectiveness against both bacterial strains.[29] The researchers associated the antibacterial effect with the generation of reactive oxygen species (ROS) by the nanoparticles, resulting in damage to bacterial membranes and ultimately causing cell death.

Similarly, another study investigated the antibacterial properties of ZnO NPs against S. aureus and P. aeruginosa. The findings indicated that ZnO nanoparticles displayed

significant antibacterial efficacy against both bacterial strains. The researchers proposed that this antibacterial activity could be linked to the release of Zn^{2+} ions and the generation of reactive oxygen species (ROS).[30] This study's findings also provided support for our research. Another study conducted by Abdo et al. (2021) delved into the antibacterial potential of ZnO nanoparticles against various bacterial strains, including E. coli, S. aureus, and P. aeruginosa. The study's findings indicated that ZnO nanoparticles displayed notable antibacterial efficacy against all the examined bacterial strains. Additionally, the researchers proposed that this antibacterial effect could be linked to the generation of reactive oxygen species (ROS), resulting in oxidative damage and ultimately leading to cell death.[31]

In short, The present study contributes to the growing body of knowledge regarding the antibacterial properties of ZnO nanoparticles (NPs) and underscores that this antibacterial efficacy can be amplified through metal ion doping and encapsulation with Cefotaxime. The results suggest that Ag-doped ZnO NPs capped with Cefotaxime have the highest antibacterial activity against different bacterial strains, which could have potential applications in the development of antibacterial agents. Nonetheless, additional research is imperative to delve into the underlying mechanism of antibacterial action and assess the possible toxicity of these nanoparticles within biological systems.[32]

Furthermore, it is worth noting that this study is an initial step towards the development of more advanced and targeted therapy options and research is warranted to gain a comprehensive understanding of the full potential of these nanoparticles in treating bacterial infections. Such research could include in-vivo studies, as well as investigating the mode of action of these nanoparticles in combination with antibiotics. Furthermore, future combination treatment against pathogenic bacteria may also be considered due to its potential effect with major antibiotics. Such research endeavors may pave the way for the advancement of therapies targeting diseases caused by pathogenic organisms. Testing these further on multi-drug resistant bacteria is recommended because a positive outcome is anticipated

CONCLUSION

This research has shown that Zinc oxide nanoparticles made a fine synergistic impact with experimented antibiotics. This study signifies a groundbreaking approach in the realm of antimicrobial research, as it explores the use of Cefotaxime in combination with Metal-doped ZnO nanoparticles. The research aligns with prior investigations into the antibacterial properties of ZnO nanoparticles and indicates that these properties can indeed be augmented through metal ion doping and the application of Cefotaxime as a capping agent. Additional studies are imperative to delve into the specific mechanism of action underlying these effects and potential toxicity of these nanoparticles in biological systems. It is also recommended to test these further on multi drug resistant bacteria. The research serves as an initial step towards the development of more advanced and targeted therapy options.

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Author's Contribution

SL and SA Conceptualized the study, performed data analysis, and writing original draft. SFA, BT and TA helped in Revising the manuscript. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.