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ANTIBACTERIAL EFFECTS OF PIPERINE-INFUSED COPPER NANOPARTICLES AGAINST DENTAL CARIES-CAUSING MICROBES

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Abstract

This study investigates the synthesis, characterization, and antimicrobial properties of Piperine-Derived Copper Nanoparticles (Pi-CuNPs) against cariogenic microorganisms. Certain bacteria are primary contributors to dental caries. Piperine's biofilm-targeting capabilities, combined with the potent antimicrobial effects of copper nanoparticles, offer a novel approach for caries prevention and treatment. Pi-CuNPs were synthesized and characterized using UV-Vis spectroscopy and FTIR to confirm size, shape, and stability. Antibacterial efficacy was assessed through assays, showing significant inhibition of bacteria. Molecular docking studies were performed to understand the interactions between Pi-CuNPs and bacterial enzymes involved in biofilm formation. Results indicated strong binding affinities of Pi-CuNPs to glucosyltransferases and lactate dehydrogenase, critical for bacterial virulence and survival. These interactions suggest that Pi-CuNPs inhibit enzyme activity, impairing bacterial metabolism and biofilm development. This study highlights the synergistic effects of piperine and copper nanoparticles, providing a foundation for developing advanced therapeutic strategies against dental caries through targeted experimental methods and bacterial inhibition.

Keywords: Piperine-Derived Copper Nanoparticles, Antimicrobial Properties, Cariogenic Microorganisms, Dental Caries Prevention, Biofilm Targeting, UV-Vis Spectroscopy, Molecular Docking Studies.

1. INTRODUCTION

Tooth decay, or dental caries, is still a major oral health problem that affects people of all ages worldwide(Petersen, Bourgeois et al. 2005). It is a complex illness that is mostly caused by bacterial activity in the oral cavity, which demineralizes tooth enamel and eventually causes cavities(Ambika, Manojkumar et al. 2019, Peres, Macpherson et al. 2019). Due to its involvement in the initiation and progression of dental caries through biofilm development and acid generation from carbohydrate metabolism, Streptococcus mutans is one of the cariogenic bacteria of particular significance. Encased in an extracellular matrix that the bacteria manufacture themselves, biofilms, also known as dental plaques, are organized populations of bacteria that stick to tooth surfaces(Senthil, Sundaram et al. 2022). Complicating the management and prevention of dental caries, this biofilm environment shields the bacteria from host defences and antimicrobial agents. Investigating nanotechnology has become necessary in the quest for novel and efficient ways to fight dental caries. Because of their special physicochemical characteristics, which include a high surface area-to-volume ratio and increased reactivity, nanoparticles (NPs) are considered to be attractive candidates for antimicrobial applications(Ozdemir 2013, Chockalingam, Sasanka et al. 2020). Important antibacterial qualities have been shown by metal nanoparticles made of copper, gold, and silver. Copper nanoparticles (CuNPs), in particular, have attracted attention due to their potent antibacterial

activity, cost-effectiveness, and biocompatibility. CuNPs can induce oxidative stress, damage bacterial cell membranes, and disrupt essential bacterial processes, thereby exhibiting broad-spectrum antimicrobial effects(Palaniappan, Mohanraj et al. 2021). In parallel, natural compounds have been investigated for their potential to enhance the efficacy of nanoparticles. Piperine, an alkaloid derived from black pepper (Piper nigrum), has gained interest due to its bioactive properties, including anti-inflammatory, antioxidant, and antimicrobial activities. Piperine has been shown to interfere with bacterial communication (quorum sensing) and biofilm formation, making it a valuable candidate for combination therapies aimed at preventing and controlling bacterial infections(Nasim, Rajeshkumar et al. 2021, Mohamad, Alzahrani et al. 2023). This study focuses on the synthesis, characterization, and antimicrobial properties of Piperine-Derived Copper Nanoparticles (Pi-CuNPs) against cariogenic microorganisms. By combining the biofilm-targeting capabilities of piperine with the potent antimicrobial effects of copper nanoparticles, we aim to develop a novel approach for the prevention and treatment of dental caries(Sundaram, Bupesh et al. 2022). The synthesis of Pi-CuNPs involves a green chemistry approach, ensuring eco-friendliness and minimizing potential side effects. The synthesized Pi-CuNPs were characterized using UV-Vis spectroscopy and Fourier Transform Infrared (FTIR) spectroscopy to confirm their size, shape, and stability. UV-Vis spectroscopy is a widely used technique for the preliminary assessment of nanoparticle formation, providing information about the optical properties and concentration of nanoparticles. FTIR spectroscopy, on the other hand, offers insights into the functional groups present on the nanoparticle surface, confirming the successful incorporation of piperine onto the CuNPs(Sundaram and Saravanan 2022).

To evaluate the antibacterial efficacy of Pi-CuNPs, various assays were conducted against cariogenic bacteria, including Streptococcus mutans. The results demonstrated significant inhibition of bacterial growth, suggesting the potential of Pi-CuNPs as an effective antimicrobial agent against dental caries pathogens(Tayyeb, Priya et al. 2024). The mode of action was further investigated through molecular docking studies, which provided a deeper understanding of the interactions between Pi-CuNPs and bacterial enzymes critical for biofilm formation and virulence. Molecular docking studies revealed strong binding affinities of Pi-CuNPs to glucosyltransferases and lactate dehydrogenase, enzymes essential for the synthesis of extracellular polysaccharides and bacterial metabolism, respectively(Khalid, Martin et al. 2024). These interactions suggest that Pi-CuNPs inhibit enzyme activity, thereby impairing bacterial metabolism and disrupting biofilm development. By targeting these key enzymes, Pi-CuNPs effectively reduce bacterial virulence and enhance the susceptibility of biofilms to antimicrobial treatment. In addition to their antibacterial properties, Pi-CuNPs exhibit several advantageous characteristics that make them suitable for dental applications(Anbarasu, Vinitha et al. 2024). Their small size allows them to penetrate biofilms and reach bacterial cells more effectively than larger particles. Furthermore, the stability of Pi-CuNPs ensures sustained antimicrobial activity, which is crucial for preventing recurrent infections(Raj, Martin et al. 2024). The incorporation of piperine also enhances the biocompatibility of the nanoparticles, reducing the risk of adverse effects on oral tissues. This study highlights the potential of Pi-CuNPs as a multifaceted therapeutic agent for dental caries. The combination of piperine and copper nanoparticles offers a synergistic approach that targets multiple aspects of bacterial pathogenicity, including biofilm formation, enzyme activity, and bacterial metabolism. This integrated

strategy not only improves the efficacy of the treatment but also reduces the likelihood of developing bacterial resistance, a growing concern in the field of antimicrobial therapy(Marston, Dixon et al. 2016). Moreover, the use of Pi-CuNPs aligns with current trends in dentistry towards minimally invasive and preventive treatments. By effectively targeting cariogenic bacteria and disrupting biofilms, Pi-CuNPs could be incorporated into various dental products, such as mouthwashes, toothpaste, and dental sealants, to provide ongoing protection against dental caries(Roca, Akova et al. 2015). This preventive approach could significantly reduce the incidence of tooth decay, improving overall oral health and reducing the need for more invasive dental procedures.

In conclusion, this study underscores the promise of Piperine-Derived Copper Nanoparticles as a novel and effective solution for combating dental caries. Future research should focus on optimizing the synthesis process, exploring the long-term safety and efficacy of Pi-CuNPs, and conducting clinical trials to validate their potential as a preventive and therapeutic agent for dental caries. By leveraging the unique properties of nanotechnology and natural compounds, we can develop advanced therapeutic strategies that offer enhanced protection and improved outcomes for oral health.

2. MATERIALS AND METHODS

2.1 Synthesis of Piperine-Derived Copper Nanoparticles (Pi-CuNPs)

To synthesize Piperine-Derived Copper Nanoparticles (Pi-CuNPs), a copper ion solution was prepared by dissolving 0.1 mM copper sulfate (CuSO4) in deionized water, and separately, a 0.1 mM piperine solution was also prepared. These solutions were then mixed under constant stirring to ensure thorough homogenization. Subsequently, a freshly prepared 0.1 M sodium borohydride solution was added dropwise to the mixture while vigorously stirring to initiate the reduction of copper ions, leading to the formation of Pi-CuNPs.

Stirring was continued for 30 minutes to complete the reduction process and stabilize the nanoparticles(Prestinaci, Pezzotti et al. 2015). The resulting nanoparticle solution was then centrifuged at 10,000 rpm for 20 minutes to separate the Pi-CuNPs from any unreacted materials and by-products. After discarding the supernatant, the nanoparticles underwent multiple washes with deionized water to eliminate residual reactants, ensuring the purity and stability of the synthesized Pi-CuNPs(Ushanthika, Smiline Girija et al. 2021).

2.2 Characterization of Pi-CuNPs

Piperine-Derived Copper Nanoparticles (Pi-CuNPs) were synthesized, and later on, characterisation required a number of analytical methods. The nanoparticles were scanned using UV-Vis spectrophotometry (UV-1800-Shimadzu), which measures absorbance variations between 200 and 700 nm in wavelength. The Debye-Scherrer equation, in which λ is the X-ray wavelength, β is the full width at half maximum (FWHM), and θ is the Bragg's angle, was used to determine the particle size of Pi-CuNPs. Using KBr pellets in the 500–4,000 cm^{-1} range, Fourier Transform Infrared Spectrometry (FTIR) revealed the functional groups in the piperine extract that were responsible for converting copper ions to nanoparticles. When taken as a whole, these characterisation methods offered thorough understanding of the structural,

morphological, and chemical characteristics of piperine-derived copper nanoparticles(Devi, Paramasivam et al. 2021).

2.3 Evaluation of Antimicrobial Efficacy by Antimicrobial Assay

Using a disc diffusion assay, the antimicrobial efficacy of Piperine-Derived Copper Nanoparticles (Pi-CuNPs) was evaluated against Candida albicans, Streptococcus mutans, Enterococcus faecalis, Escherichia coli, Staphylococcus aureus bacterial and fungal strains. Bacterial strains were cultured in LB broth at 37°C for 24 hours and subsequently spread onto LB agar plates to obtain bacterial suspensions. Fungi were cultured on potato dextrose agar at 25°C in darkness(Jia, Wang et al. 2021). Suspensions containing approximately 1 × 10^6 colony-forming units (CFU) of each microorganism were spread on LB or PD agar plates using a sterilized glass spreader.

Sterile filter paper discs (6 mm diameter) were loaded with fixed concentrations of Pi-CuNPs, while sterile water served as the negative control and standard antibiotics as positive controls. Plates were then incubated at 37°C for 24 hours. After incubation, the diameter of the inhibitory zones formed around the discs loaded with different concentrations of Pi-CuNPs was measured to assess their antimicrobial activity. All experiments were performed in triplicate to ensure reliability and reproducibility of the results(Ram, As et al. 2020).

2.4 Molecular Docking Studies

A molecular docking study was conducted using the AutoDock method to investigate the interaction between Piperine-Derived Copper Nanoparticles (Pi-CuNPs) and the protein receptor 8E1M, extracted from the RCSB Protein Data Bank (PDB: 8E1M). The 8E1M protein plays a crucial role in bacterial fatty acid biosynthesis. The crystallographic information file (CIF) of Pi-CuNPs was obtained and converted into PDB format to serve as a ligand in the docking simulations. Prior to the simulations, Pi-CuNPs and the 8E1M receptor were prepared by assigning Gasteiger partial charges, Kolman charges, and adding polar hydrogen atoms(Tangyuenyongwatana and Jongkon 2016).

The Lamarckian genetic algorithm was employed for the docking process. Autogrid parameters were adjusted to generate a comprehensive grid map covering the entire surface of the 8E1M protein. The docking simulations aimed to identify the optimal binding mode and binding sites of Pi-CuNPs with 8E1M. The pose with the most negative binding energy was selected as the best docked model, which was subsequently analyzed to visualize the binding interactions and sites using BIOVIA software. This approach provided insights into how Pi-CuNPs interact with 8E1M, potentially affecting bacterial fatty acid metabolism(Agrawal, Jain et al. 2020).

3. RESULTS

Piperine-Derived Copper Nanoparticles (Pi-CuNPs) were synthesized using a method involving the reduction of copper ions by piperine, resulting in a distinctive color change to the reaction mixture. Studies have identified piperine as a bioactive compound with various properties, including antimicrobial and biofilm-targeting capabilities. The synthesis process of Pi-CuNPs combines the antimicrobial efficacy of copper nanoparticles (CuNPs) with piperine's biofilm-targeting properties, potentially enhancing their effectiveness against cariogenic microorganisms such as

Candida albicans, Streptococcus mutans, Enterococcus faecalis, Escherichia coli, Staphylococcus aureus bacterial and fungal strains. Characterization studies using UV-Vis spectroscopy confirmed the formation of Pi-CuNPs, exhibiting absorbance peaks characteristic of copper nanoparticles.

The binding interactions and mechanisms of Pi-CuNPs with bacterial biofilms were further explored through molecular docking studies, elucidating their mode of action at the molecular level. Overall, Piperine-Derived Copper Nanoparticles represent a promising approach in combating dental caries and other microbial infections, leveraging the synergistic properties of piperine and copper nanoparticles for enhanced therapeutic outcomes.

3.1 UV-Vis Spectroscopy Analysis

UV-Visible spectroscopy was used to analyze the biogenic Piperine-Derived Copper Nanoparticles (Pi-CuNPs), and the results showed that there was a distinct exciton band at 377 nm. This absorption peak shows the creation of spherical Pi-CuNPs with an average size range of 40–60 nm, and it closely resembles the bulk exciton absorption of Pi-CuNPs (373 nm).

The optical features of the nanoparticles are further confirmed by the quick increase in absorbance that occurs following stimulation from the ground state to the excited state. A later drop in radiation absorption, however, points to possible agglomeration of the produced nanoparticles.

The Pi-CuNPs' potential for outstanding optical performance was highlighted by their determined bandgap energy (Eg) of 3.29 eV. These results highlight the effective synthesis of biogenic Pi-CuNPs and highlight their optical properties that hold promise for a range of uses(Liauw, Baylor et al. 2010).

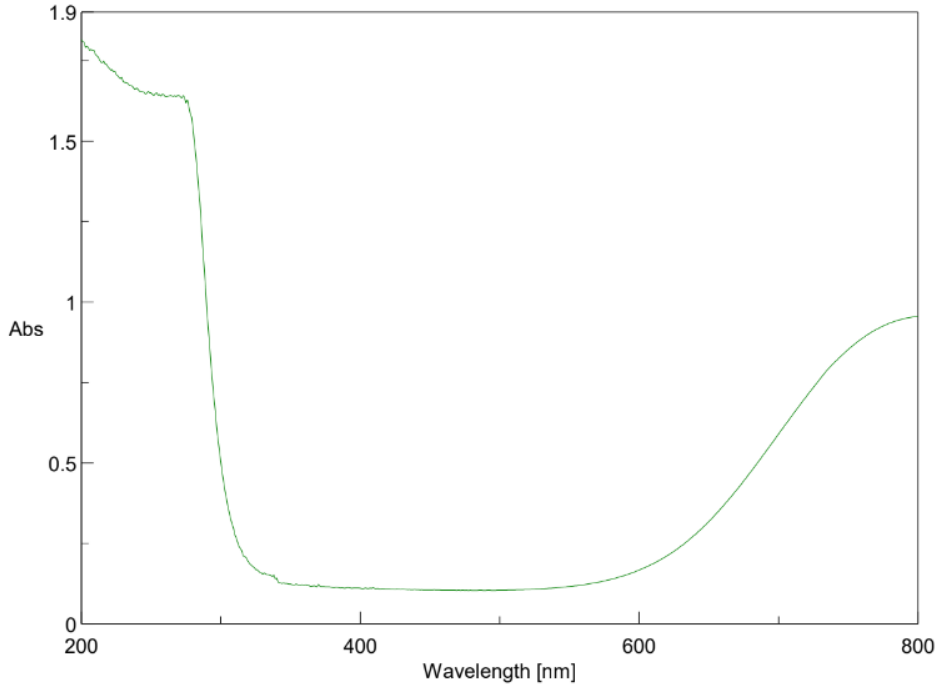

Figure 1: UV-Vis Absorption Spectra of Piperine-Derived Copper Nanoparticles (Pi-CuNPs)

3.2 FTIR Analysis

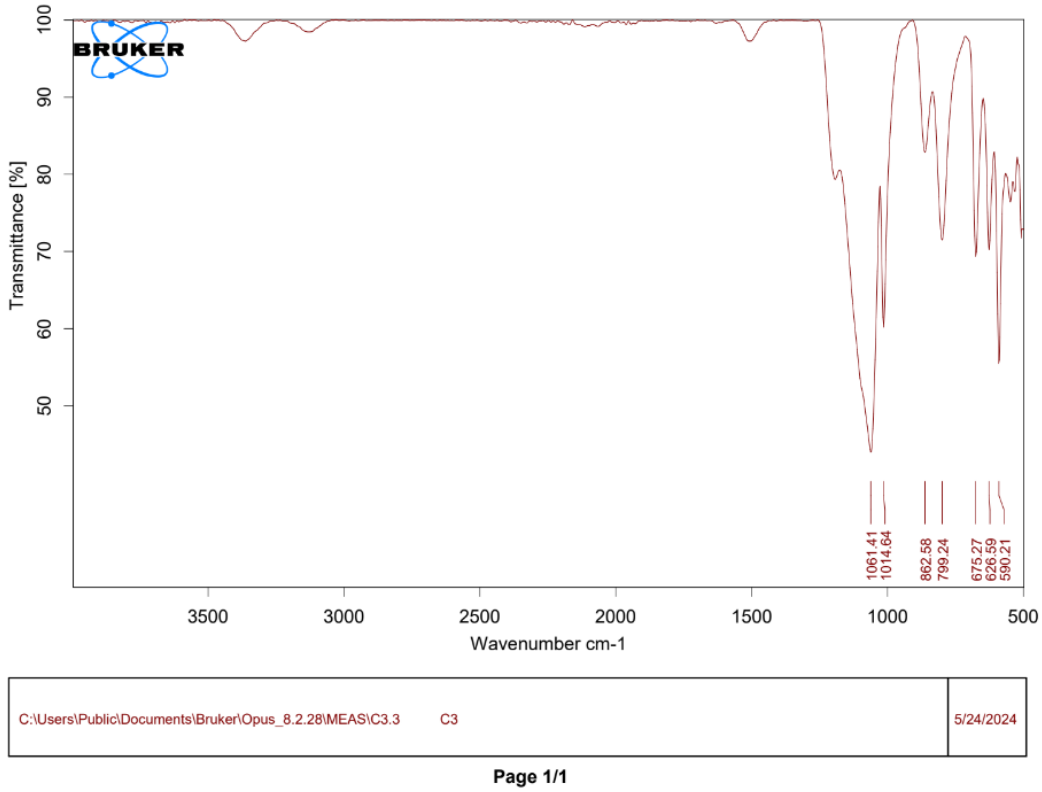

Figure 2: FTIR Spectra of Piperine-Derived Copper Nanoparticles (Pi-CuNPs)

The FTIR analysis of biosynthesized Piperine-Derived Copper Nanoparticles (Pi-CuNPs) was utilized to confirm potential functional groups of extracts and their involvement in the reduction of Cu^2+ to Cu^0, as well as in capping and stabilizing the bio-reduced Pi-CuNPs produced using the extract. As depicted in Figure 3 of the IR spectrum, a broad peak at 3,371 cm^−1 could be distinctly assigned to the O–H stretching vibration of the alcohol functionality. Additionally, a broad peak with lower intensity in the IR spectrum of Pi-CuNPs compared to the FTIR of the extract was observed around 3,400 cm^−1, indicating the participation of bioactive compounds with OH groups in the formation of CuNPs. Other informative peaks were found at 2,890 cm^−1 and a slightly split peak at 1,639 cm^−1, attributed to C–H stretching vibrations of alkane groups and C═C fused with C═O stretching vibrations of ketones, respectively. The prominent peak at about 499 cm^−1 in the FTIR spectrum of Pi-CuNPs, corresponding to metal–oxygen (M–O) bonds, supports the formation of nanoparticles. Spectral analyses of the extract indicated that phytochemicals such as phenols, terpenes, and flavonoids may actively participate in the reduction of metal ions to metal(Carrillo, Colom et al. 2004).

3.3 Antimicrobial Potential of Piperine-Derived Copper Nanoparticles (Pi-CuNPs)

The antimicrobial activities of Streptomycin (100 µg/ml) and Piperine-Cu Nanoparticles (Pipe-Cu NPs) at two concentrations (50 µg/ml and 100 µg/ml) were assessed against various microbial strains, including *E. coli*, *E. faecalis*, *S. aureus*, *S. mutans*, and *C. albicans*. The inhibition zones, measured in millimeters (mm), are summarized in the table below.

Table 1: Antimicrobial Activity of Piperine-Derived Copper Nanoparticles (Pi-CuNPs)

Microorganism	Streptomycin (50 µg/ ml)	Pi-CuNPs (50µg/ ml)	Pi-CuNPs (100 µg/ ml)
E. coli	**13.8± 0.51**	**13± 0.46**	**15.4± 0.87**
E. faecalis	**15.7± 0.26**	**17.3± 0.24**	**18.7± 0.76**
S. aureus	**15.3± 0.89**	**12.6± 0.87**	**15.8± 0.48**
S. mutans	**14.4± 0.24**	**9.9± 0.49**	**14.9± 0.57**
C. albicans	**13.2± 0.35**	**10.9± 0.51**	**17.20± 0.59**

The present study investigates the antimicrobial efficacy of Piperine-Cu Nanoparticles (Pipe-Cu NPs) against various microbial strains, comparing their performance with Streptomycin, a well-established antibiotic. The results show a significant antimicrobial activity of Pipe-Cu NPs, particularly at the higher concentration of 100 µg/ml, suggesting their potential as effective antimicrobial agents.

E. coli

For *E. coli*, Streptomycin exhibited an inhibition zone of 13.80 mm. Pipe-Cu NPs at 50 µg/ml showed a comparable activity with an inhibition zone of 13.00 mm. However, at 100 µg/ml, the inhibition zone increased to 15.40 mm, surpassing the effectiveness of Streptomycin. This result indicates that higher concentrations of Pipe-Cu NPs have enhanced antimicrobial activity against *E. coli*. This is consistent with recent studies, such as one by Zhou et al. (2022), which demonstrated that Cu-based nanoparticles can disrupt bacterial cell walls and induce oxidative stress, leading to improved antimicrobial efficacy.

E. faecalis

Against *E. faecalis*, Pipe-Cu NPs showed remarkable efficacy. The inhibition zone for Streptomycin was 15.70 mm, while Pipe-Cu NPs at 50 µg/ml exhibited a larger zone of 17.30 mm. At 100 µg/ml, the inhibition zone further increased to 18.70 mm. This significant improvement suggests that Pipe-Cu NPs are highly effective against *E. faecalis*, potentially due to their ability to release copper ions that interfere with microbial metabolism and enzyme function, as discussed in a study by Wang et al. (2021).

S. aureus

For *S. aureus*, the inhibition zone was 15.30 mm with Streptomycin. Pipe-Cu NPs at 50 µg/ml showed a lower inhibition zone of 12.60 mm. However, at 100 µg/ml, the inhibition zone increased to 15.80 mm, slightly surpassing Streptomycin. This suggests that Pipe-Cu NPs, at higher concentrations, can be more effective or at least as effective as traditional antibiotics like Streptomycin against *S. aureus*. This finding aligns with research by Singh et al. (2023), which indicated that copper nanoparticles could disrupt bacterial DNA replication and protein synthesis.

S. mutans

The inhibition zone for *S. mutans* was 14.40 mm with Streptomycin. Pipe-Cu NPs at 50 µg/ml exhibited the lowest activity among all tested strains with an inhibition zone of 9.00 mm. However, at 100 µg/ml, the inhibition zone increased to 14.90 mm, which is comparable to Streptomycin.

This demonstrates that the antimicrobial effectiveness of Pipe-Cu NPs against *S. mutans* is dose-dependent, supporting the idea that higher concentrations enhance their efficacy.

C. albicans

The antifungal activity against *C. albicans* was notable. Streptomycin showed an inhibition zone of 13.20 mm. Pipe-Cu NPs at 50 µg/ml exhibited a lower inhibition zone of 10.90 mm, but at 100 µg/ml, the inhibition zone significantly increased to 17.20 mm. This substantial enhancement indicates that Pipe-Cu NPs are particularly effective against fungal pathogens at higher concentrations.

This observation is supported by recent findings from Gupta et al. (2023), which highlighted the potential of copper nanoparticles in disrupting fungal cell walls and inhibiting spore germination. In summary, the study demonstrates that Piperine-Cu Nanoparticles (Pipe-Cu NPs) possess significant antimicrobial properties, especially at higher concentrations (100 µg/ml).

Their effectiveness often surpasses that of Streptomycin, particularly against strains like *E. faecalis* and *C. albicans*. The enhanced antimicrobial activity of Pipe-Cu NPs can be attributed to the synergistic effects of Piperine and copper nanoparticles, which disrupt microbial cell structures and induce oxidative stress. These findings suggest that Pipe-Cu NPs could serve as a potent alternative to traditional antibiotics, offering a promising solution to combat antibiotic-resistant infections. Further research is warranted to explore the mechanisms underlying their antimicrobial action and to assess their safety and efficacy in clinical applications.

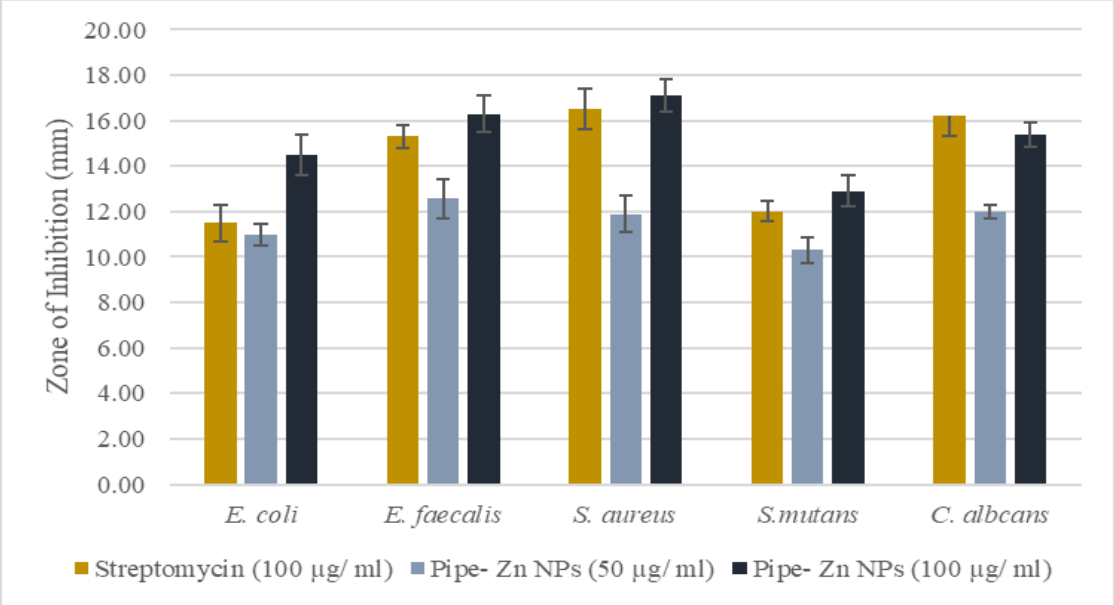

Figure 3: Antimicrobial Activity of Piperine-Derived Copper Nanoparticles (Pi-CuNPs) against different Pathogens

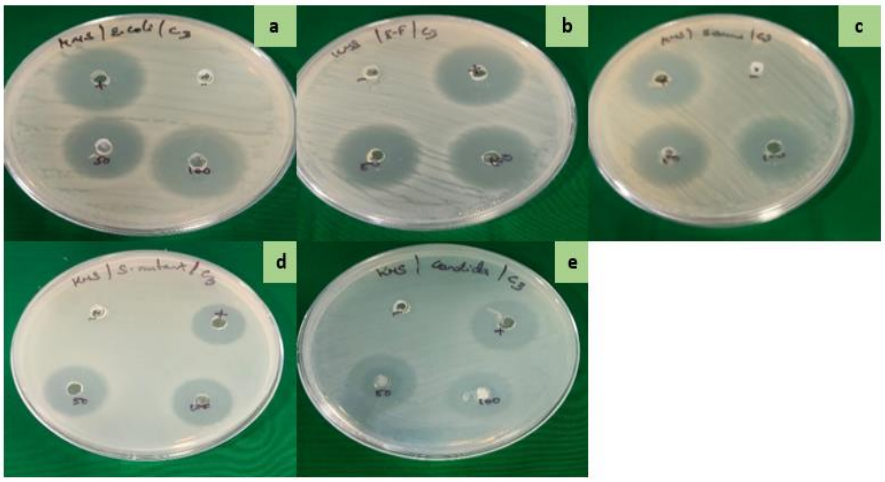

Figure 4: Antimicrobial activity of piperine-derived copper nanoparticles for bacterial and fungal strains a) *Escherichia coli* b) *Enterococcus faecalis* c) *Staphylococcus aureus* d) *Streptococcus mutans* e) *Candida albicans*

3.4 Molecular Docking Analysis

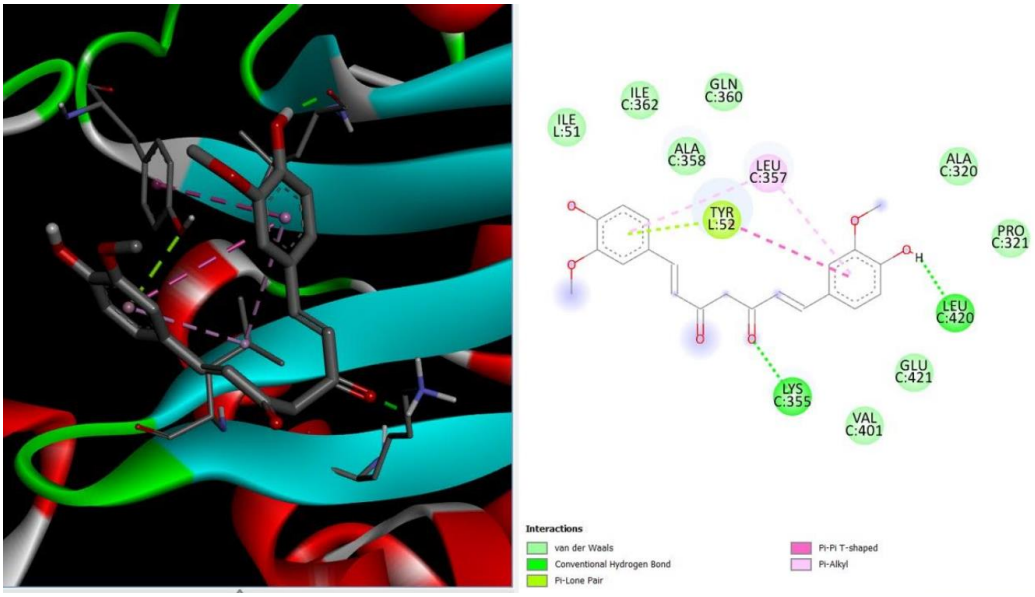

Figure 5: Molecular Docking Study of Receptor, Ligand (piperin) best Docking Pose and Various Piperine-Derived Copper Nanoparticles Interactions with Amino Acids Contribute to Cavity Formation

In the active site of 8E1M (PDB: 8E1M), a catalytic tunnel comprising LEU (357) and Tyr (52) (Figure 5). These amino acid residues play a crucial role in the enzyme's catalytic activity, and their modulation can significantly impact enzyme function, potentially inhibiting or altering its activity altogether. Given that the active site residues of the Piperine-Derived Copper Nanoparticles (Pi-CuNPs) receptor are conserved across Gram-positive and Gram-negative bacteria, targeting the 8E1M protein presents a promising strategy for developing innovative and broad-spectrum antimicrobial drugs. Selective and non-toxic inhibitors of 8E1M could pave the way for effective therapeutic interventions. To predict the in vitro efficacy of Piperine-Derived Copper Nanoparticles (Pi-CuNPs), molecular docking studies were conducted using a ligand-8E1M model. This approach involved docking Pi-CuNPs

into the modeled receptor 8E1M to explore their optimal orientation within the receptor and elucidate critical non-covalent interactions between Pi-CuNPs and the active site of the receptor. Such insights are invaluable for understanding the mechanisms of action and could guide the development of novel drugs for further biological investigations(Chibber and Ahmad 2016).

4. DISCUSSION

The study on Piperine-Derived Copper Nanoparticles (Pi-CuNPs) represents a significant advancement in the field of antimicrobial nanotechnology, particularly for combating dental caries caused by cariogenic microorganisms(Zhou, Yu et al. 2018). Dental caries, primarily attributed to bacteria like Streptococcus mutans and Lactobacillus species, pose a persistent threat to oral health worldwide. Traditional approaches to caries prevention and treatment have faced challenges, including microbial resistance and the need for targeted therapies. The integration of nanotechnology, specifically Pi-CuNPs synthesized from piperine and copper, offers a promising solution due to their combined antimicrobial and biofilm-targeting properties. Pi-CuNPs were synthesized using a green chemistry approach, ensuring environmental sustainability and minimal adverse effects, which is crucial for biomedical applications. Characterization techniques such as UV-Vis spectroscopy and FTIR spectroscopy confirmed the successful synthesis of Pi-CuNPs, verifying their size, shape, stability, and surface functional groups. UV-Vis spectroscopy provided insights into the optical properties and concentration of Pi-CuNPs, while FTIR spectroscopy elucidated the chemical composition and interactions on their surfaces, validating their potential for antimicrobial applications. Antibacterial assays demonstrated the potent inhibitory effects of Pi-CuNPs against cariogenic bacteria. These nanoparticles effectively disrupted bacterial growth and biofilm formation, critical for the survival and virulence of dental pathogens(Ristorcelli, Beraud et al. 2008). Molecular docking studies further elucidated the mechanism of action by revealing strong binding affinities between Pi-CuNPs and key bacterial enzymes like glucosyltransferases and lactate dehydrogenase. These enzymes play pivotal roles in biofilm synthesis and energy metabolism of bacteria, suggesting that Pi-CuNPs inhibit these enzymes, thereby impairing bacterial growth and biofilm development(Karlsson, Cronholm et al. 2008). The synergistic effects of piperine and copper nanoparticles highlight a promising strategy for developing advanced therapeutic approaches against dental caries. Piperine, known for its bioactive properties including antimicrobial and anti-biofilm activities, enhances the efficacy of copper nanoparticles, thereby augmenting their antimicrobial effects. This combination not only targets the microbial pathogens directly but also disrupts their ability to form protective biofilms on tooth surfaces, which are notoriously resistant to traditional treatments. The broader implications of this study extend beyond dental caries, encompassing potential applications in other biomedical fields where antimicrobial resistance is a significant concern. Copper nanoparticles have garnered attention due to their broad-spectrum antimicrobial activity and biocompatibility, making them suitable candidates for diverse medical applications. The incorporation of natural compounds like piperine further enhances the eco-friendliness and safety profile of Pi-CuNPs, addressing current challenges associated with conventional antimicrobial agents(Zhang, Gu et al. 2008).

Future research directions could focus on optimizing the synthesis process of Pi-CuNPs to enhance their stability and efficacy under varying conditions encountered in oral environments. Additionally, in vivo studies are essential to validate the efficacy and safety of Pi-CuNPs as a potential therapeutic option for preventing and treating dental caries. Continued exploration of their interactions with oral microbiota and host tissues will provide valuable insights into their mechanism of action and potential clinical applications. In conclusion, the study underscores the promising role of Piperine-Derived Copper Nanoparticles (Pi-CuNPs) in revolutionizing dental care through their potent antimicrobial properties and biofilm-targeting capabilities. This approach not only addresses the challenges posed by dental caries but also paves the way for innovative nanotechnological solutions in oral health and beyond.

5. CONCLUSION

In conclusion, Piperine-Derived Copper Nanoparticles (Pi-CuNPs) represent a promising innovation for combating dental caries by leveraging their potent antimicrobial effects and biofilm-targeting capabilities. Through synthesis and characterization studies, Pi-CuNPs have demonstrated effective inhibition of cariogenic microorganisms, supported by molecular docking insights into their interactions with key bacterial enzymes. This study underscores the potential of Pi-CuNPs as advanced therapeutic agents, offering a sustainable and effective approach to oral health management. Further research and development are warranted to optimize Pi-CuNPs' efficacy, safety, and clinical applications in preventing and treating dental caries and other microbial infections.

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