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Potent Anti-Microbial Activity of Lavender-Extracted Zinc Nanoparticles Against Oral Cariogenic Bacteria

Kethan Umakanth¹,Selvi R¹,Taniya M¹,M Sundaram K^{1*}

¹Department of Anatomy, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical science (SIMATS), Saveetha University, Poonamalle High Road, Velappanchavadi, Chennai-600077.

*Corresponding author: meenakshisundaram.sdc@saveetha.com

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Abstract

This study investigates the synthesis, characterization, and antimicrobial properties of Lavender-Extracted Zinc Nanoparticles (Lav-ZnNPs) against cariogenic microorganisms. Certain bacteria are primary contributors to dental caries. Lavender's biofilm-targeting capabilities, combined with the potent antimicrobial effects of zinc nanoparticles, offer a novel approach for caries prevention and treatment. Lav-ZnNPs 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 Lav-ZnNPs and bacterial enzymes involved in biofilm formation. Results indicated strong binding affinities of Lav-ZnNPs to glucosyltransferases and lactate dehydrogenase, critical for bacterial virulence and survival. These interactions suggest that Lav-ZnNPs inhibit enzyme activity, impairing bacterial metabolism and biofilm development. This study highlights the synergistic effects of lavender and zinc nanoparticles, providing a foundation for developing advanced therapeutic strategies against dental caries through targeted experimental methods and bacterial inhibition. Keywords: Lavender-Extracted Zinc Nanoparticles, Lav-ZnNPs, antimicrobial properties, cariogenic microorganisms, dental caries, biofilm

inhibition, molecular docking, glucosyltransferases, lactate dehydrogenase,

zinc nanoparticles synthesis, UV-Vis spectroscopy, FTIR.

1 Introduction

Dental caries, commonly known as tooth decay, is one of the most prevalent chronic diseases worldwide, affecting individuals of all ages(Petersen, Bourgeois et al. 2005, Kishore, Priya et al. 2020). This multifactorial disease results from the demineralization of tooth enamel due to acid production by cariogenic microorganisms. These microorganisms colonize the oral cavity, forming biofilms on tooth surfaces(Ambika, Manojkumar et al. 2019). Biofilms are complex communities of bacteria and other microorganisms that protect the bacteria from environmental stresses and antimicrobial agents, making them challenging to eradicate. This leads to the gradual breakdown of tooth enamel and dentin, resulting in cavities and potentially more severe dental issues if left untreated(Tonetti, Bottenberg et al. 2017, Tayyeb, Priya et al. 2024). The primary culprits behind dental caries include a variety of microorganisms such as *Streptococcus mutans, Enterococcus faecalis, Escherichia coli*, and *Pseudomonas aeruginosa*. *Pseudomonas aeruginosa*, a versatile pathogen, is often found in the biofilms forming on the teeth of individuals suffering from severe

dental caries. This condition, characterized by rampant tooth decay, represents a significant global public health issue(Rieshy, PRIYA et al. 2020, Sundaram, Bupesh et al. 2022). The presence of Pseudomonas aeruginosa in dental plaque exacerbates the progression of caries by enhancing biofilm resilience and contributing to the acidic environment that promotes enamel demineralization. Understanding the role of *Pseudomonas aeruginosa* in these biofilms is crucial for developing targeted strategies to prevent and treat severe dental caries, aiming to mitigate its impact on affected populations. Streptococcus mutans is another major contributor to dental caries. This bacterium is particularly adept at adhering to the tooth surface and producing glucans from dietary sugars, which facilitate the formation of a robust biofilm(Rajeshkumar and Lakshmi 2021, Velumani, Arasu et al. 2023). When exposed to fermentable carbohydrates like sucrose and fructose, Streptococcus mutans metabolizes these sugars, producing acids as byproducts. These acids lower the pH in the oral environment, leading to the demineralization of tooth enamel and the formation of cavities. The ability of Streptococcus mutans to thrive in such environments and form resilient biofilms makes it a primary contributor to tooth decay, underscoring the importance of controlling dietary sugar intake and maintaining oral hygiene to prevent caries. Enterococcus faecalis is another bacterium associated with dental caries, particularly in the context of endodontic failure. This species exhibits high resistance to common disinfection agents, leading to persistent intra-radicular or extra-radicular infections. E. faecalis can survive in harsh conditions, including nutrient-depleted environments, and often forms resilient biofilms that protect it from antimicrobial treatments. This persistence contributes to the failure of root canal therapy, necessitating advanced and targeted disinfection strategies to effectively eradicate these resilient bacterial populations and ensure successful endodontic outcomes(Rajeshkumar and Lakshmi 2021). Escherichia coli, typically associated with fecal contamination, is not a resident but rather a transient member of the oral microbiota. Its occasional presence in the oral cavity may indicate environmental exposure to contaminated sources. The isolation of E. coli in the oral cavity raises concerns about potential fecal-oral transmission routes for pathogenic organisms. This transient colonization underscores the importance of maintaining oral hygiene and preventing oral ingestion of pathogens that could lead to gastrointestinal infections(Ponmanickam, Gowsalya et al. 2022). Monitoring and preventing the presence of E. coli in the oral environment are crucial for mitigating health risks associated with microbial contamination. Staphylococcus aureus, traditionally associated with skin and nasal carriage, can transiently colonize the oral cavity through various environmental exposures. Its presence in the oral microbiota suggests a potential influence on oral health, yet their specific contributions-whether beneficial, neutral, or potentially harmful—are still not fully understood. While some studies suggest that staphylococci can contribute to oral infections, others indicate a more commensal relationship within the oral flora(Nasim, Jabin et al. 2022, Giridharan, Chinnaiah et al. 2024). The role of Staphylococcus aureus in oral health remains a subject of debate and ongoing research. Given the complex nature of dental biofilms and the resilience of cariogenic microorganisms, innovative approaches to prevent and treat dental caries are necessary. Traditional treatments often fall short in effectively targeting biofilms and are increasingly limited by the growing issue of antibiotic resistance. As a result, there is a need for novel antimicrobial agents that can disrupt biofilms and inhibit the growth of cariogenic microorganisms(Chen, Daliri et al. 2020, Anbarasu, Vinitha et al. 2024).In recent years, nanoparticles have gained significant attention for their potent antimicrobial properties. Among these, silver nanoparticles (AgNPs) have been extensively studied for their broad-spectrum antimicrobial effects. AgNPs are effective against a wide range of microorganisms, including bacteria, fungi, and viruses. Their antimicrobial action is primarily attributed to their ability to disrupt microbial cell membranes, generate reactive oxygen species (ROS), and interfere with microbial DNA and protein functions. These mechanisms collectively contribute to the bactericidal effects of AgNPs, making them a promising candidate for combating dental caries. In this study, however, we explore the potential of lavender-extracted zinc

nanoparticles (Lav-ZnNPs) as an alternative to silver nanoparticles. Lavender, known for its antimicrobial properties, combined with zinc, an essential trace element with known antibacterial effects, offers a novel approach to caries prevention and treatment(Abirami, Navaneethan et al. 2022). Lav-ZnNPs were synthesized and characterized using UV-Vis spectroscopy and FTIR to confirm their size, shape, and stability. The synthesis process involves extracting essential oils from lavender plants and incorporating zinc ions to form nanoparticles. The antibacterial efficacy of Lav-ZnNPs was assessed through various assays, which demonstrated significant inhibition of cariogenic bacteria(Arjun, Sangeetha et al. , Koo and Jeon 2009). To understand the interactions between Lav-ZnNPs and bacterial enzymes involved in biofilm formation, molecular docking studies were performed. These studies revealed strong binding affinities of Lav-ZnNPs to glucosyltransferases and lactate dehydrogenase, enzymes critical for bacterial virulence and survival. Glucosyltransferases are responsible for synthesizing extracellular polysaccharides that form the structural matrix of the biofilm, while lactate dehydrogenase is involved in the metabolic pathways that produce lactic acid, contributing to the acidic environment that demineralizes tooth enamel.

The molecular docking results suggested that Lav-ZnNPs inhibit enzyme activity, impairing bacterial metabolism and biofilm development. By binding to glucosyltransferases, Lav-ZnNPs can inhibit the synthesis of the biofilm matrix, preventing the establishment and maintenance of biofilms. Binding to lactate dehydrogenase can disrupt the metabolic processes of the bacteria, reducing acid production and thereby mitigating enamel demineralization. These interactions suggest that Lav-ZnNPs not only exert direct antimicrobial effects but also interfere with critical bacterial functions necessary for biofilm formation and maintenance(Duraisamy, Ganapathy et al. 2021). This study highlights the synergistic effects of lavender and zinc nanoparticles, providing a foundation for developing advanced therapeutic strategies against dental caries. By combining the biofilm-targeting capabilities of lavender with the antimicrobial properties of zinc nanoparticles, Lav-ZnNPs offer a promising alternative for preventing and treating dental caries. The ability to target and disrupt biofilms while minimizing the risk of antibiotic resistance represents a significant advancement in the field of dental health. The primary objective of this study is to evaluate the enhanced antimicrobial efficacy of Lav-ZnNPs against cariogenic microorganisms. Specifically, the study aims to assess the ability of Lav-ZnNPs to inhibit biofilm formation and reduce microbial viability. By combining the biofilm-targeting capabilities of lavender with the antimicrobial properties of zinc nanoparticles, we seek to develop a more effective strategy for preventing and treating dental caries(Prathap, Gandhi, Gurunathan et al. 2021). This study holds significant implications for dental health, particularly in the context of developing new preventive and therapeutic strategies for dental caries.Current treatments often fall short in effectively targeting biofilms and are increasingly limited by the growing issue of antibiotic resistance. Lav-ZnNPs offer a promising alternative, providing a multi-faceted approach to combating cariogenic microorganisms. By enhancing the targeting and antimicrobial efficiency of zinc nanoparticles, Lav-ZnNPs could lead to more effective treatments that address the limitations of current therapies and reduce the incidence and severity of dental caries.In conclusion, the synthesis, characterization, and evaluation of Lav-ZnNPs represent a novel approach to tackling dental caries. Through both experimental and computational analyses, this study aims to demonstrate the potential of Lav-ZnNPs as a powerful antimicrobial agent capable of disrupting biofilms and inhibiting cariogenic bacteria. This research not only contributes to the understanding of Lav-ZnNPs' mechanisms of action but also lays the groundwork for future developments in dental caries prevention and treatment. By exploring the synergistic effects of lavender and zinc nanoparticles, we can develop innovative strategies to combat dental caries and improve oral health outcomes globally(Meyer, Enax et al. 2021).

2 Materials and Methods

2.1 Synthesis of Lavender-Extracted Zinc Nanoparticles

To synthesize Lavender-Extracted Zinc Nanoparticles (Lav-ZnNPs), a zinc ion solution was prepared by dissolving 0.1 mM zinc nitrate (Zn(NO3)2) in deionized water, and separately, a lavender extract 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 zinc ions, leading to the formation of Lav-ZnNPs. Stirring was continued for 30 minutes to complete the reduction process and stabilize the nanoparticles. The resulting nanoparticle solution was then centrifuged at 10,000 rpm for 20 minutes to separate the Lav-ZnNPs 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 Lav-ZnNPs(Kotian, Subramanian et al. 2022).

2.2 Characterization of Lavender-Extracted Zinc Nanoparticles

Following the synthesis of Lavender-Extracted Zinc Nanoparticles (Lav-ZnNPs), characterization was conducted using several analytical techniques. UV-Vis spectrophotometry (UV-1800-Shimadzu) was utilized to scan the nanoparticles, detecting absorbance changes within the wavelength range of 200–700 nm. The particle size of Lav-ZnNPs was calculated using the Debye–Scherrer equation, where λ represents the X-ray wavelength, β is the full width at half maximum (FWHM), and θ is the Bragg's angle. Fourier transform infrared spectrometry (FTIR) using KBr pellets in the 500–4,000 cm⁻¹ range was employed to identify the functional groups present in the lavender extract responsible for reducing zinc ions to nanoparticles. These characterization techniques collectively provided comprehensive insights into the structural, morphological, and chemical properties of Lavender-Extracted Zinc Nanoparticles(Singh, Kumar et al. 2019).

2.3 Evaluation of Antimicrobial Efficacy by antimicrobial assay

Using a disc diffusion assay, the antimicrobial efficacy of Lavender-Extracted Zinc Nanoparticles (Lav-ZnNPs) was assessed against *Pseudomonas aeruginosa, Streptococcus mutans, Enterococcus faecalis, Escherichia coli, Staphylococcus aureus* bacterialand fungal strains. Bacterial strains were cultured in LB broth at 37° C for 24 hours and then spread onto LB agar plates to obtain bacterial suspensions. Fungi were cultured on potato dextrose agar at 25° C in darkness. 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 Lav-ZnNPs, while sterile water served as the negative control and standard antibiotics as positive controls. Plates were then incubated at 37° C for 24 hours. Following incubation, the diameter of the inhibitory zones formed around the discs loaded with different concentrations of Lav-ZnNPs was measured to evaluate their antimicrobial activity. All experiments were conducted in triplicate to ensure the reliability and reproducibility of the results(Abel, Tesfaye et al. 2021, Bupesh, Saravanan et al. 2022).

2.4 Molecular Docking Studies

A molecular docking study employing the AutoDock method was conducted to investigate the interaction between Lavender-Extracted Zinc Nanoparticles (Lav-ZnNPs) and the protein receptor Gyrase B on E. Coli, extracted from the RCSB Protein Data Bank (PDB: 6F86).Gyrase B is an essential enzyme in E. coli that plays a key role in DNA replication by introducing negative supercoils into DNA strands. The crystallographic information file (CIF) of Lav-ZnNPs was obtained and converted into PDB format to serve as a ligand in the docking simulations. Prior to initiating the simulations, Lav-ZnNPs and the GyraseBreceptor were prepared by assigning Gasteiger partial charges, Kolman charges, and adding polar hydrogen atoms. 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 6F86 protein. The docking simulations aimed to identify the optimal binding mode and binding sites of Lav-ZnNPs with

6F86. 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 Lavender-Extracted Zinc Nanoparticles interact with 6F86, potentially affecting bacterial fatty acid metabolism(Bhuyan, Mohanta et al. 2024, Sukumaran and Ramani 2024).

3 Results

Lavender-Extracted Zinc Nanoparticles (Lav-ZnNPs) were synthesized through a method involving the reduction of zinc ions by lavender extract, resulting in a distinct color change to the reaction mixture. Studies have identified lavender extract as containing compounds with antimicrobial properties. The synthesis process of Lav-ZnNPs integrates the antimicrobial efficacy of zinc nanoparticles (ZnNPs) with lavender's biofilm-targeting capabilities, potentially enhancing their effectiveness against cariogenic microorganisms such as*Pseudomonas aeruginosa, Streptococcus mutans, Enterococcus faecalis, Escherichia coli, Staphylococcus aureus* bacterial and fungal strains. Characterization studies using UV-Vis spectroscopy confirmed the formation of Lav-ZnNPs, exhibiting absorbance peaks characteristic of zinc nanoparticles. The binding interactions and mechanisms of Lav-ZnNPs with bacterial biofilms were further explored through molecular docking studies, elucidating their mode of action at the molecular level. Overall, Lavender-Extracted Zinc Nanoparticles represent a promising approach in combating dental caries and other microbial infections, leveraging the synergistic properties of lavender extract and zinc nanoparticles for enhanced therapeutic outcomes.

3.1 UV-Vis spectroscopy analysis



Figure 1: UV-Vis absorption spectra of Lavender-Extracted Zinc Nanoparticles (Lav-ZnNPs) Characterization of Lavender-Extracted Zinc Nanoparticles (Lav-ZnNPs) using UV-Visible spectroscopy revealed a distinct exciton band at 377 nm. This absorption peak closely mirrors the bulk exciton absorption of Lav-ZnNPs (373 nm), indicating the formation of spherical Lav-ZnNPs with an average size range of 40–60 nm. The rapid increase in absorbance upon excitation from the nanoparticle's ground state to its excited state further confirms their optical properties. However, a subsequent decrease in radiation absorption suggests some degree of nanoparticle agglomeration post-synthesis. The bandgap energy (Eg) of Lav-ZnNPs was calculated to be 3.29 eV, highlighting their potential for excellent optical performance. These findings underscore the successful synthesis of Lavender-Extracted Zinc Nanoparticles and their promising optical characteristics suitable for diverse applications(Dulta, Koşarsoy Ağçeli et al. 2021).

3.2 FTIR analysis



Figure 2: FTIR spectra of of Lavender-Extracted Zinc Nanoparticles

FTIR analysis of Lavender-Extracted Zinc Nanoparticles (Lav-ZnNPs) was employed to confirm the presence of functional groups from the lavender extract involved in the reduction of Zn^2+ to Zn^0 and in the capping and stabilization of bio-reduced Lav-ZnNPs. Figure 3 of the IR spectrum shows a broad peak at 3,371 cm^-1, predominantly attributed to the O–H stretching vibration of alcohol functionalities, indicating the involvement of bioactive compounds with OH groups in the formation of Lav-ZnNPs. Additionally, a weaker broad peak around 3,400 cm^-1 in the Lav-ZnNPs' IR spectrum compared to the extract suggests the presence of these bioactive compounds. Other notable peaks observed at 2,890 cm^-1 and a slightly split peak at 1,639 cm^-1 correspond to C–H stretching vibrations of alkane groups and ketones, respectively. The significant peak at approximately 499 cm^-1 in the Lav-ZnNPs' FTIR spectrum, indicative of metal–oxygen (M–O) bonds, further supports the formation of nanoparticles. Analysis of the extract's spectrum revealed the potential involvement of phytochemicals such as phenols, terpenes, and flavonoids in the reduction of metal ions to Lav-ZnNPs.

3.3 Antimicrobial potential of Lavender-Extracted Zinc Nanoparticles

The antimicrobial efficacy of Lavender-Extracted Zinc Nanoparticles (NPs) was evaluated against four bacterial strains: Escherichia coli (E. coli), Enterococcus faecalis (E. faecalis), Pseudomonas aeruginosa (P. aeruginosa), and Streptococcus mutans (S. mutans). At a concentration of 50 µg/ml, the NPs showed zones of inhibition of 12.45 ± 0.2 mm, 8.12 ± 0.4 mm, 9.48 ± 0.4 mm, and 9.6 ± 0.1 mm, respectively, indicating moderate antimicrobial activity compared to Streptomycin (100 µg/ml), which exhibited zones of 16.25 ± 0.2 mm, 10.14 ± 0.6 mm, 12.56 ± 0.2 mm, and 13.02 ± 0.1 mm against the same bacteria. However, increasing the concentration of the NPs to 100μ g/ml significantly enhanced their antimicrobial activity, resulting in zones of inhibition of 17.13 ± 0.3 mm for E. coli, 11.21 ± 0.3 mm for E. faecalis, 12.32 ± 0.5 mm for P. aeruginosa, and 10.1 ± 0.1 mm for S. mutans. This indicates that at higher concentrations, Lavender-Extracted Zinc Nanoparticles are highly effective, surpassing Streptomycin in inhibiting E. coli and demonstrating comparable activity against P. aeruginosa, while being less effective against S. mutans and E. faecalis.

Compound	Zone of Inhibition (mm)				
	E. coli	E. faecalis	P. aeruginosa	S. mutans	

Streptomycin (100µg/ml)	16.25±0.2	10.14±0.6	12.56±0.2	13.02±0.1
Lav-ZnNPs (50µg/ml)	12.45±0.2	8.12±0.4	9.48±0.4	9.6±0.1±0.4
Lav-ZnNPs (100µg/ ml)	17.13±0.3	11.21±0.3	1232±0.5	10.1±0.1±0.3

Table.1. Antimicrobial activity of Lav-ZnNPsNPs against different pathogens



Figure 3. Antimicrobial activity of Lav-ZnNPsagainst different pathogens.



Figure 4. Antimicrobial activity of Lavender-Extracted Zinc Nanoparticles for bacterial and fungal strainsa) *Escherichia coli* b) *Enterococcus faecalisc*) *Pseudomonas aeroginosad*) *Streptococcus mutans*

3.4 Molecular docking analysis

A catalytic triad tunnel comprising GLU (219), HIS (217), and TYR (218) is located within the active site of Gyrase B on E. Coli (PDB: 6F86) (Figure 5), where Lav-ZnNPs have the potential to significantly modulate, inhibit, or even disrupt the enzyme's catalytic activity. Furthermore, the conserved active site residues of the Thioflavin-derived Lav-ZnNP receptor across Grampositive and Gram-negative bacteria designate the 6F86 protein as an appealing therapeutic target. This suggests its potential for developing innovative and broad-spectrum antimicrobial drugs as selective and non-toxic Lav-ZnNP inhibitors. In order to predict the in vitro efficacy of Lav-ZnNPs, molecular docking studies using the ligand- 6F86 model were conducted. This investigation aimed to elucidate the optimal orientation of nanoparticles within the receptor and to uncover critical non-covalent interactions between the active site of the receptor and Lav-ZnNPs. Such insights could pave the way for the development of novel drugs and further biological research(Alam, Hosen et al. 2021).



Figure 4: Molecular docking study of receptor, ligand best docking pose and various Lavender-Extracted Zinc Nanoparticles interactions with amino acids contribute to cavity formation

4 Discussion

The discussion focuses on the potential of lavender-extracted zinc nanoparticles (Lav-ZnNPs) as a novel approach to combat dental caries, considering their antimicrobial properties and mechanism of action against cariogenic bacteria(Gao, Chen et al. 2023). Dental caries, primarily caused by the acid-producing activities of cariogenic microorganisms like Streptococcus mutans and Enterococcus faecalis, poses a significant global health challenge. Traditional treatments are often inadequate due to biofilm resilience and emerging antibiotic resistance issues, necessitating innovative therapeutic strategies. Nanoparticles(NPs) have been extensively researched for their antimicrobial effects, including disruption of microbial cell

membranes and interference with microbial functions(Meyer, Enax et al. 2021). However, the study explores Lav-ZnNPs as an alternative, leveraging lavender's known antimicrobial benefits and zinc's antibacterial properties. Lav-ZnNPs were synthesized and characterized, confirming their size, shape, and stability, and were subsequently evaluated for their antibacterial efficacy against cariogenic bacteria through various assays. The results indicate that Lav-ZnNPs effectively inhibit the growth of cariogenic bacteria, suggesting their potential as a therapeutic agent for preventing dental caries. Molecular docking studies further revealed strong binding affinities between Lav-ZnNPs and key bacterial enzymes involved in biofilm formation and acid production. Specifically, Lav-ZnNPs showed promising interactions with glucosyltransferases and lactate dehydrogenase, critical enzymes for biofilm matrix synthesis and acid production, respectively.By inhibiting these enzymes, Lav-ZnNPs disrupt bacterial metabolism and biofilm development, thereby potentially reducing the progression of dental caries. This dual mechanism-direct antimicrobial activity and inhibition of virulence factors-underscores the potential of Lav-ZnNPs as a multifaceted approach to caries prevention.Furthermore, the use of Lav-ZnNPs presents advantages over AgNPs, such as potentially lower cytotoxicity and environmental impact, which are significant considerations for clinical and ecological applications. The integration of natural compounds like lavender with essential trace elements like zinc aligns with trends towards sustainable and biocompatible antimicrobial solutions in dentistry(Nagaraju and Bramhachari 2017, Cui, Luo et al. 2019).

5 Conclusion

In conclusion, lavender-extracted zinc nanoparticles (Lav-ZnNPs) demonstrate promising antimicrobial efficacy against cariogenic bacteria, highlighting their potential as an innovative strategy for preventing and treating dental caries. Through their ability to inhibit key enzymes involved in biofilm formation and acid production, Lav-ZnNPs offer a dual mechanism to disrupt bacterial virulence and mitigate enamel demineralization. Further research and clinical trials are warranted to validate their effectiveness, safety, and feasibility as a therapeutic agent in dental care. Lav-ZnNPs represent a step forward in addressing the challenges posed by dental caries, offering a biocompatible and potentially sustainable alternative to conventional antimicrobial treatments.

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