INDIAN JOURNAL OF SCIENCE AND TECHNOLOGY

ORIGINAL ARTICLE

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OPEN ACCESS

Received: 01/10/2025

Accepted: 23/11/2025

Published: 31/12/2025

Citation: Md Asad Khan , Farheen , Nafees S, Anas A, Khan I (2025) Fluorine-Doped ZnO Nanoparticles: Structural Insights and Antibacterial Innovation in Orthodontic Resins. Indian Journal of Science and Technology 18(47): 3769-3777. https://doi.org/10.17485/IJST/v18i47.1654

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Funding: None

Competing Interests: None

Published By Indian Society for Education and Environment (iSee)

ISSN
Print: 0974-6846
Electronic: 0974-5645

Fluorine-Doped ZnO Nanoparticles: Structural Insights and Antibacterial Innovation in Orthodontic Resins

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Abstract

Objectives: This study aimed to develop a bioactive orthodontic composite resin incorporating fluorine-doped zinc oxide (F-ZnO) nanoparticles and to evaluate its mechanical, cytotoxic, biocompatibility and antimicrobial properties. **Method**: F-ZnO nanoparticles were synthesized using a chemical solution method and characterized through X-ray diffraction (XRD), Fourier Transform Infrared Spectroscopy (FTIR) and Scanning Electron Microscopy (SEM). The nanoparticles were integrated into composite resins and evaluated for antimicrobial efficacy against *S. mutans*, mechanical strength, and cytotoxicity. Antibacterial activity was assessed using a zone of inhibition assay, while shear bond strength and biocompatibility were also analyzed. **Findings**: Composite resins containing F-ZnO nanoparticles exhibited significantly enhanced antibacterial properties compared to control resins ($P < 0.05$), with the inhibition zone reaching up to 10.0 ± 0.31 mm at higher nanoparticle concentrations. Structural characterization confirmed the successful doping of fluorine into ZnO, contributing to improved surface charge and bioactivity. **Novelty**: No research has been done on developing a bioactive orthodontic composite resin incorporating fluorine-doped zinc oxide (F-ZnO) nanoparticles in recent times. This novel composite resin shows potential for preventing dental caries during orthodontic treatments, representing a promising advance in biomaterial innovation.

Keywords: Dental caries; F-ZnO nanoparticles; Resins; Antibacterial activity; X-ray diffraction

1 Introduction

Dental caries is a primary healthcare issue, as it is a common disease worldwide. It has been evaluated that dental caries affects 100 percent of the adult population globally. The disease is found in organizations with low socioeconomic status and regardless of being effortlessly preventable, its occurrence has not significantly decreased over the last thirty years [1]. This condition arises primarily from the metabolic activities of cariogenic bacteria such as *Streptococcus mutans*, which flourish in the dental. The consumption of carbohydrates and the subsequent acidic environment created by their fermentation, causes an increase in acid-tolerant microorganisms. Once caries bacteria proliferate, they shape a plaque biofilm, leading to loss of tooth shape and in extreme cases, capacity contamination and teeth loss [(2)]. Numerous filling materials are presently used clinically to repair dental defects as a result of caries, consisting of bioceramics, hydroxyapatite, resin restorations, and amalgam restorations [(3)]. Consequently, there is a growing need for superior restorative substances that not only restore functionality but also offer antimicrobial safety.

Resin-based substances have currently been confirmed to be powerful as fillings for the treatment of dental caries. Resin-based materials have significantly stepped forward in dentin remineralization and antimicrobial properties by means of enhancing the practice technique and uncooked material ratios. Additionally, inside the preclinical research degree, numerous polymer materials for filling defects were advanced [(4)].

However, there are some issues associated with using nanoparticles to treat oral diseases. There is a significant concern regarding the potential toxicity of nanoparticles to human cells, organs, and the entire body, which necessitates extensive biocompatibility testing. Additionally, the oral environment is a complex system that involves a delicate balance between various biological, chemical, and mechanical factors. Ensuring the stability of nanoparticles in the oral environment can be challenging. As a result, various delivery systems are developed by researchers for the specific application of nanoparticles in dentistry, resulting in improved treatment of various oral infections and diseases. Antimicrobial nanoparticles can be loaded into these delivery systems by researchers and delivered directly to the infection site, improving the stability of the nanoparticles, lowering the likelihood of antibiotic resistance, and minimizing adverse effects [(5)], [(6)].

Among those, zinc oxide (ZnO) nanoparticles have garnered massive attention due to their broad-spectrum antimicrobial properties and biocompatibility. ZnO nanoparticles have an interaction with bacterial membranes, inducing oxidative stress and disrupting critical cell functions, thereby inhibiting bacterial growth [(7)].

Fluorine-doped zinc oxide (F-ZnO) nanoparticles constitute a progressive development in dental materials. The incorporation of fluorine into ZnO enhances its antimicrobial efficacy via altering its floor charge and promoting the sustained release of fluoride ions. Fluoride, a cornerstone in caries prevention, aids in tooth remineralization and inhibits bacterial metabolism, as a result providing dual safety against caries [(8)]. Furthermore, F-ZnO nanoparticles showcase outstanding esthetic compatibility, making them appropriate for applications in dental composites and adhesives without compromising visual appeal [(9)]. When incorporated into dental resins, F-ZnO nanoparticles substantially enhance antibacterial efficacy in opposition to S. Mutans and other oral pathogens. Moreover, the managed launch of fluoride from F-ZnO nanoparticles extends their defensive consequences, reducing the need for frequent dental interventions [(10)].

It is possible to improve orthodontic appliances antibacterial properties by incorporating nanoparticles. However, the studies displayed significant heterogeneity therefore, further research with standardized protocols for factors like nanoparticle size, concentration, and incorporation techniques across various orthodontic materials is crucial to guide future clinical applications [(11)].

Our study aims to evaluate the potential of F-ZnO nanoparticles in orthodontic composite resins. By synthesizing and characterizing F-ZnO nanoparticles, this study investigates their structural and purposeful properties, which specialize in their antimicrobial efficacy, cytocompatibility, and mechanical performance.

Our observations provide valuable insights into the development of superior biomaterials for restorative dentistry and additionally pave the way for next-generation materials that combine healing efficacy with structural integrity. Such innovations hold the capability to convert dental exercise, reducing the burden of caries and improving patient outcomes.

2 Methodology

The primary materials used in this study included zinc acetate dihydrate ($Zn(CH_3COO)_2{\cdot}2H_2O$), sodium fluoride (NaF), and ethanol, all of analytical grade and obtained from Merck (Darmstadt, Germany). *Streptococcus mutans* (MTCC No. 890) was sourced from the Microbial Type Culture Collection (MTCC), India. Brain Heart Infusion (BHI) broth, glucose, and agar for bacterial culture were purchased from HI Media, India.

2.1 Synthesis of Fluorine-Doped Zinc Oxide Nanoparticles

F-ZnO nanoparticles were synthesized via a chemical solution method. The precursor solution was prepared by 0.2 M of zinc nitrate hexahydrate ($Zn(NO_3)_2$ was dissolved in 0.5 M ethanol solution. Ammonium fluoride (NH4F) as dopant precursor ratio with 0, 1, 3 and 5 mol % was dropped and stirred in zinc precursor solution for 10 min. After that, ammonium hydroxide solution (NH_4OH) was dropped into the solution until pH 9 to obtain white colloids in solution. The colloids were washed with distilled water until pH 7 and dried at 100 °C under hot air oven for 24 h. Finally, F doped ZnO nano-powders by this method were obtained after calcination at 400-500 °C for 2 h[12].

2.2 Physicochemical Characterization

2.2.1. *Particle Size and Zeta Potential Analysis:*

The particle size and polydispersity index were analyzed using dynamic light scattering (DLS) with a DynaPro-TC-04 instrument. F-ZnO nanoparticles (1 mg/mL) were dispersed in Milli-Q water and sonicated for 25 seconds before measurement. The zeta potential was measured to determine surface charge stability, an important factor for nanoparticle interaction with bacterial membranes[13].

2.2.2. *X-ray Diffraction (XRD):*

Crystallographic analysis was conducted using an XRD system (Siemens D5000) with Cu Kα radiation (λ = 1.5418 Å). The diffraction peaks were matched to the JCPDS database to verify the incorporation of fluorine into the ZnO lattice structure[14].

2.2.3. *Fourier Transform Infrared Spectroscopy (FTIR):*

FTIR spectra were recorded using a Bruker Tensor 27 spectrometer in ATR mode over the range of 4000–500 cm^{-1}. Characteristic peaks corresponding to Zn–O and C=O bonds confirmed successful doping[15].

2.2.4. *Scanning Electron Microscopy (SEM):*

Morphological characterization was performed using a Nova NanoSEM 450. Energy-dispersive X-ray spectroscopy (EDX) confirmed the elemental composition of F-ZnO, specifically highlighting the presence of fluorine[16].

2.3 Preparation of Orthodontic Composite Resin

F-ZnO nanoparticles were incorporated into orthodontic composite resins at varying concentrations (0.5%, 1%, 2%, and 4% by weight). Composite discs (8 mm diameter × 2 mm thickness) were prepared and cured with an LED dental curing light for 20 seconds on each side. These specimens were polished to uniformity and stored in distilled water at 37°C for 24 hours before testing[17].

2.4 Antibacterial Activity

Antibacterial efficacy against *Streptococcus mutans* was assessed using the agar diffusion method. BHI agar plates were inoculated with a standardized suspension of *S. mutans* (OD600 = 0.5). Specimens of the F-ZnO composites were placed onto the agar, and zones of inhibition were measured after incubation at 37°C for 48 hours. The experiments were performed in triplicate[18]. As a reference control, standard antibiotic discs of chlorhexidine (0.2%) and ampicillin (10 μg) were used for comparison of antibacterial activity against *Streptococcus mutans*. These were placed on BHI agar plates alongside the test specimens. Zones of inhibition were measured in millimeters after 48 hours of incubation.

2.5 Fluoride Ion Release Study

Fluoride ion release from F-ZnO composites was measured using a fluoride ion-selective electrode (Orion 9609BNWP, Thermo Scientific) connected to an ion meter. Composite resin discs (n = 3 for each group) were immersed in 10 mL of deionized water and stored at 37 °C. Aliquots were collected at predetermined time intervals (1, 3, 7, and 14 days) and replaced with fresh deionized water. Each sample was mixed with a total ionic strength adjustment buffer (TISAB III) in a 1:1 ratio prior to measurement to maintain constant pH and ionic strength. Fluoride concentrations (ppm) were determined using a standard calibration curve. The protocol was adapted from previously reported methodologies that employed the Orion 9609BNWP electrode with similar immersion, buffering, and measurement conditions[19].

2.6 Cytotoxicity Assay

The cell viability activity of carboplatin and nanocarboplatin was assayed by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT). The MTT assay is a quantitative and rapid colorimetric method, based on the development of a yellow tetrazolium salt to insoluble purple formazan crystals by the mitochondrial succinate dehydrogenase enzymes of viable cells. The MTT assay was carried out as previously described. Briefly, human gingival fibroblast (HGFs) cell line was seeded overnight with a cell count of 1×10^5 per well and then incubated with various concentrations of fluorine-doped zinc oxide for 24. At the end of the treatment, the media was removed, and cells were incubated with 20 μl of MTT (5 mg/ml in PBS) in fresh medium (50 μl) for 4 h under a CO_2 incubator. After 4 h, formazan crystal was formed and solubilized in DMSO (150 μl/well), and the absorbance was read at 570 nm after 10 min incubation on the iMark Microplate Reader (Bio-Rad, USA). Percent cytotoxicity was expressed as IC_{50}. The percentage of cell viability was calculated, and the result was also expressed as mean percent of viability $\pm$ standard error of mean (SEM)[20].

2.7 Statistical Analysis

The reviewer emphasized the need to specify the sample size (n value) and statistical tests used. All experimental measurements were conducted in triplicates (n = 3) to ensure reproducibility. One-way ANOVA followed by Tukey's post hoc test was applied to determine statistical significance, with $p \leq 0.05$ considered significant. This uniform statistical approach was used across all datasets, including cytotoxicity, antibacterial activity, and fluoride ion release studies, ensuring consistent and reliable interpretation of results.

3 Results and Discussion

For structural characterisation we performed the procedure of enamel and dentin slicing. We collected extracted teeth, which are discarded as biological waste. These teeth were collected from the faculty of Dentistry, Jamia Millia Islamia, New Delhi. The tooth was placed in a sample holder and with the help of a sharp circular saw, we cut enamel and dentin slices with a 5$\pm$2 mm side and 0.8$\pm$0.1 mm thickness. These slices have been soaked in 15 ml of 17% EDTA for two hours at room temperature and then were analyzed by the ATR mode of FT-IR to study the effect of EDTA treatment. These slices were used further for the remineralization study of our synthesized nanomaterials.

To study the surface charges, Zeta Potential analysis was performed of synthesized nanomaterials using Zetasizer Nano ZS instrument. When a particle is dispersed in a liquid, functional groups of this material start reacting with the surrounding medium, resulting in the accumulation of oppositely charged particles. These measurements bring insight into the causes of dispersion, aggregation, and flocculation. Surface charges of enamel and dentin were always negative as per the reported data. Hence, it would be preferable to study the surface charge of synthesized nanomaterials for a better understanding of the binding interaction between dentin and synthesized nanomaterials. Typically, undoped ZnO nanoparticles exhibit zeta potential values around -10 mV to -15 mV, while the F-ZnO nanoparticles in this study showed a more negative potential of -23.3 mV, reflecting enhanced surface charge and colloidal stability. This improvement can be attributed to fluorine doping, which increases surface electronegativity and minimizes aggregation, as shown in Figure 1(a). *Polydispersity Index (PDI)* is a measure of the distribution of particle sizes in a given sample. It indicates the uniformity of the nanoparticle size distribution, where a lower PDI (close to 0) reflects a more homogeneous dispersion and higher stability, while a higher PDI suggests a broader range of particle sizes and possible agglomeration. In our study, the PDI of F-ZnO nanoparticles was relatively high, indicating some degree of polymorphism, which was consistent with the observed SEM images. The Such a range is common for doped ZnO nanorods and supports the SEM observations showing partial aggregation of rod-shaped structures.

Similarly, in the case of Fluorine-doped ZnO nano-powder, we have obtained a mean particle size in microns, as can be seen in Figure 1(b). Here, the PDI of the material is quite high, indicating polymorphism in the material. On correlating with FESEM data, we can see higher agglomeration in the nanorods of the synthesized material.

The findings from this study emphasize the significant potential of fluorine-doped zinc oxide (F-ZnO) nanoparticles in enhancing the antimicrobial efficacy of dental materials. The incorporation of fluorine into ZnO alters its surface charge and enables the controlled release of fluoride ions, which are crucial for inhibiting *Streptococcus mutans*. These mechanisms align with prior studies highlighting the synergistic role of dopants like fluorine in enhancing ZnO's antibacterial properties[21]. Additionally, fluorine doping enhances the hydrophilicity and bioactivity of ZnO, facilitating better interaction with microbial cells and contributing to its antimicrobial potency[22].

Figure 2(a) depicts the FT-IR spectrum of the synthesized fluorine-doped ZnO nanopowder. This spectrum reveals bands around 3370 $cm^{-1,}$ which indicates the presence of OH stretching bonds. Symmetric and asymmetric stretching bands of acetate species have been observed at 1618 cm^{-1}, 1313 cm^{-1} and 824 cm^{-1}. A strong peak at 614 cm^{-1} is attributed to ZnO bond of the metal oxide. Figure 2(b) depicts the XRD spectrum of the synthesized fluorine-doped ZnO nanoparticles. On peak identification with the standard data, different sharp peaks at (100), (101), (100), (110), (101), (111), (210), (211), and (220) were observed. On peak identification with the standard data, a mixed phase of ZnF_2 is also noticed. The diffraction peaks of calcined powder are sharp which indicates high crystallinity with low intensity of the synthesized material. The diffraction peaks of calcined nano-powder match well with ZnF_2 as indexed to JCPDS 895014 with major grains orientation

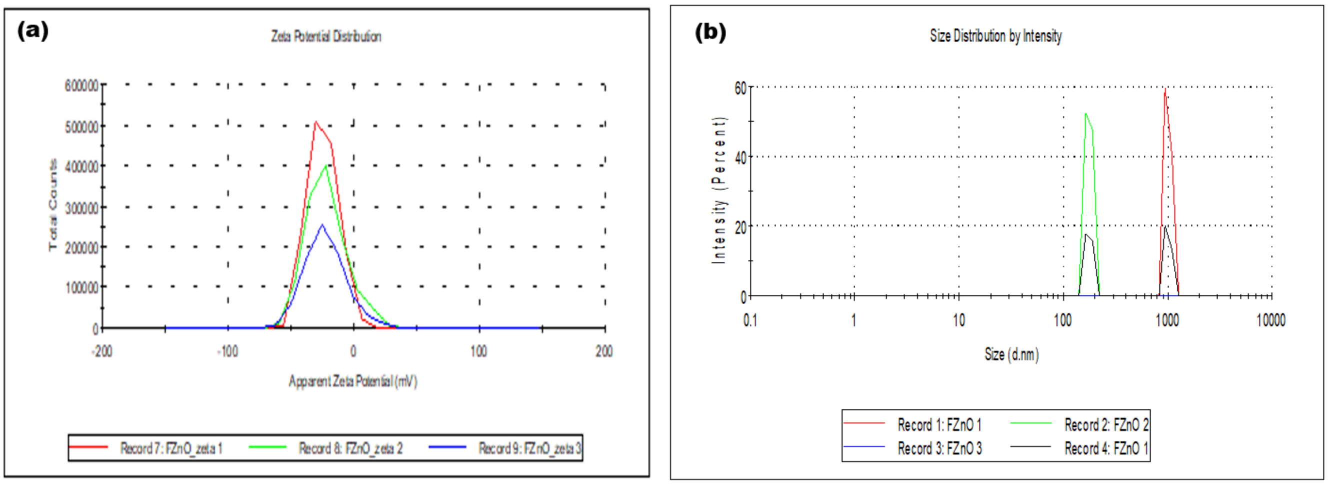

Fig 1. Synthesized F doped ZnO nanoparticles showed (a) Zeta potential (b) Particle size distribution by DLS

to (100) plane of ZnO. From a structural perspective, XRD and FTIR analyses confirmed successful fluorine integration into the ZnO lattice, as supported by previous works exploring the physicochemical impacts of fluorine doping on ZnO [23]. These structural modifications provide insights into the robust antibacterial performance exhibited by the nanoparticles at higher concentrations. The composite resins embedded with F-ZnO nanoparticles demonstrated superior mechanical properties, as indicated by shear bond strength. This suggests that the inclusion of nanoparticles did not compromise the structural integrity of the composites, a critical consideration for orthodontic applications which is in agreement with the previous studies [24].

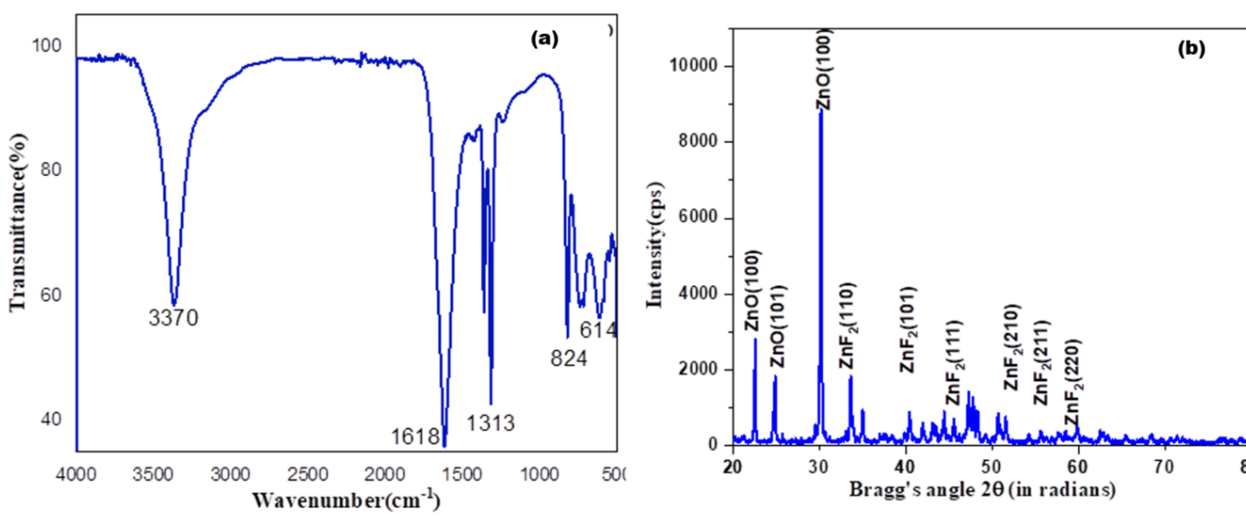

Fig 2. Synthesized Fluorine doped ZnO nanopowder (a) FT-IR spectrum (b) X-Ray diffraction pattern

Scanning Electron Microscopy (SEM) is an advanced imaging technique that provides high-resolution surface morphology images of nanomaterials. It uses a focused beam of electrons emitted by a field emission source to scan the surface of the sample. The morphology of the synthesized material, Fluorine-doped ZnO was observed using SEM (NOVA NANOSEM-450). Typical SEM images of the deposited material under different magnifications i.e., 20μm, 2μm, 1μm, and 500 nm, are shown in Figure 3(a-d). These images confirm the formation of ZnO nanorods in a well-arranged manner. The clear regions are marked with circles. Different sizes of nanorods are observed from the SEM images, as shown in Figure 3(a, b). In this study, SEM helped visualize the shape, size, and aggregation behavior of the synthesized F-ZnO nanoparticles, confirming the formation of nanorods and their structural integrity.

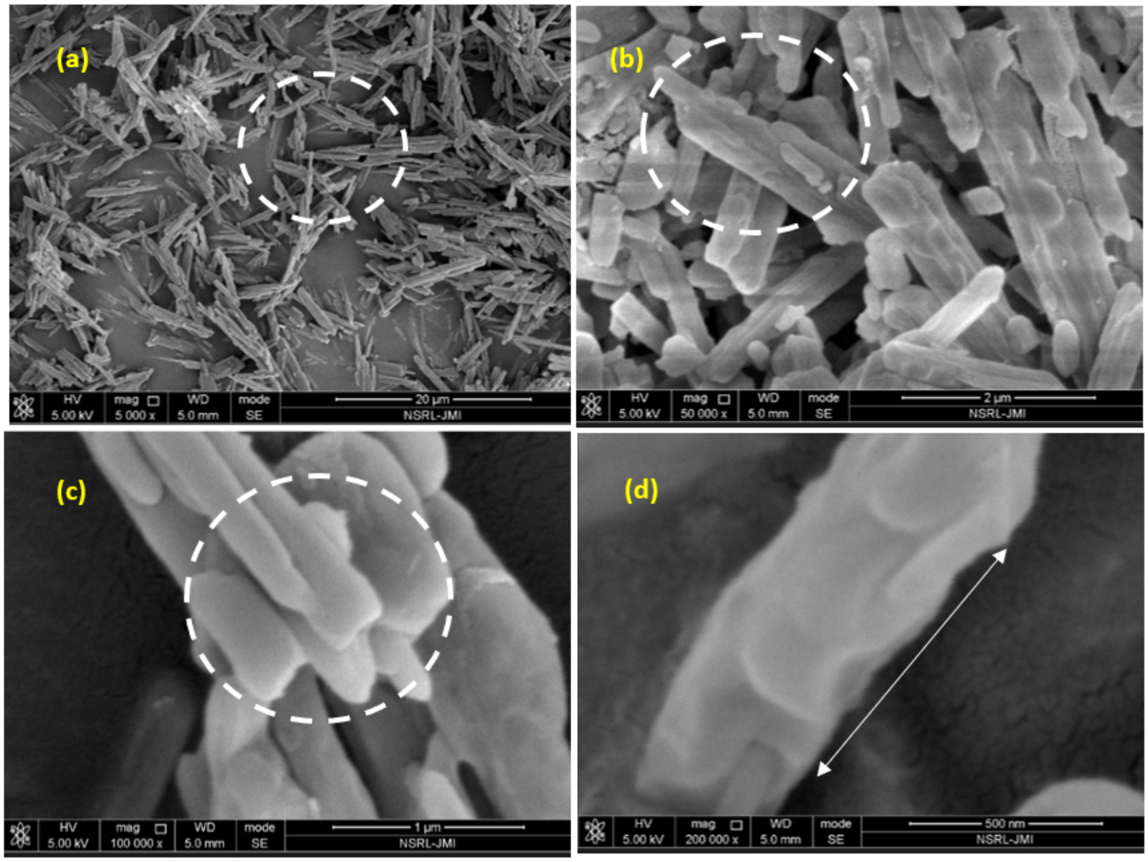

Fig 3. SEM micrographs Fluorine doped ZnO nanoparticles

Cytotoxicity assays revealed that F-ZnO-modified composites are biocompatible, with cell viability exceeding 85% even at higher nanoparticle concentrations. These findings align with recent reports emphasizing the biocompatibility of ZnO-based nanomaterials for biomedical applications[10]. The MTT assay revealed in HGFs cells that F-ZnO composites exhibited excellent biocompatibility, with cell viability remaining above 85% across all tested concentrations at 24 hrs (Figure 4). A slight dose-dependent decline in viability was observed, but values remained statistically non-significant ($p > 0.05$), confirming the biosafety of the composites. These results align with earlier reports demonstrating the non-toxic nature of doped ZnO nanoparticles in dental applications. Our results indicated that the fluorine-doped zinc oxide nanoparticles were non-toxic at the given dose and time of exposure.

The safety profile of F-ZnO composites, combined with their antibacterial efficacy, underscores their potential as next-generation dental materials capable of preventing secondary caries during orthodontic treatments. The *S. mutans* strain was purchased in dried form from MTCC Chandigarh. *S. mutans* has been cultured in brain-heart infusion (BHI) broth[25]. For media preparation, we have added 5.0 g BHI, 10.0 g tryptone, 10.0 g Yeast extract, 10.0 g glucose, 10.0 g agar, and 1 L of distilled water, then stirred this solution properly. The pH of the Solution was adjusted to 7.2 to 7.5. This media was autoclaved for further use. After the cooling of the media, plating was done. The same protocol was used for broth (without agar). This broth was stored at room temperature. ZnF nanocomposite was screened for its anti-microbial activity against gram-positive bacteria, *Streptococcus mutans* (*S. mutans*), which resides in the human oral cavity and is a major etiological agent of human dental caries. A zone of inhibition assay was performed to check the inhibitory effect of ZnF nanocomposites on the growth of *S. mutans* bacteria. A clear zone of inhibition was observed, and the diameter of zone was presented in mm and taken as mean $\pm$ SD of triplicates. It was observed that an increase in the concentration of ZnF leads to an increased inhibition as reflected by enhancement in diameter (Table 1). It is clearly observed from Figure 5(a,b) that ZnF nanocomposites show inhibitory activity against *S. mutans* which is dose-dependent. The zone of inhibition for F-ZnO composites was compared to that of standard antibiotics. Chlorhexidine exhibited an inhibition zone of 16.2 ± 0.4 mm, and ampicillin showed 14.5 ± 0.5 mm, while the

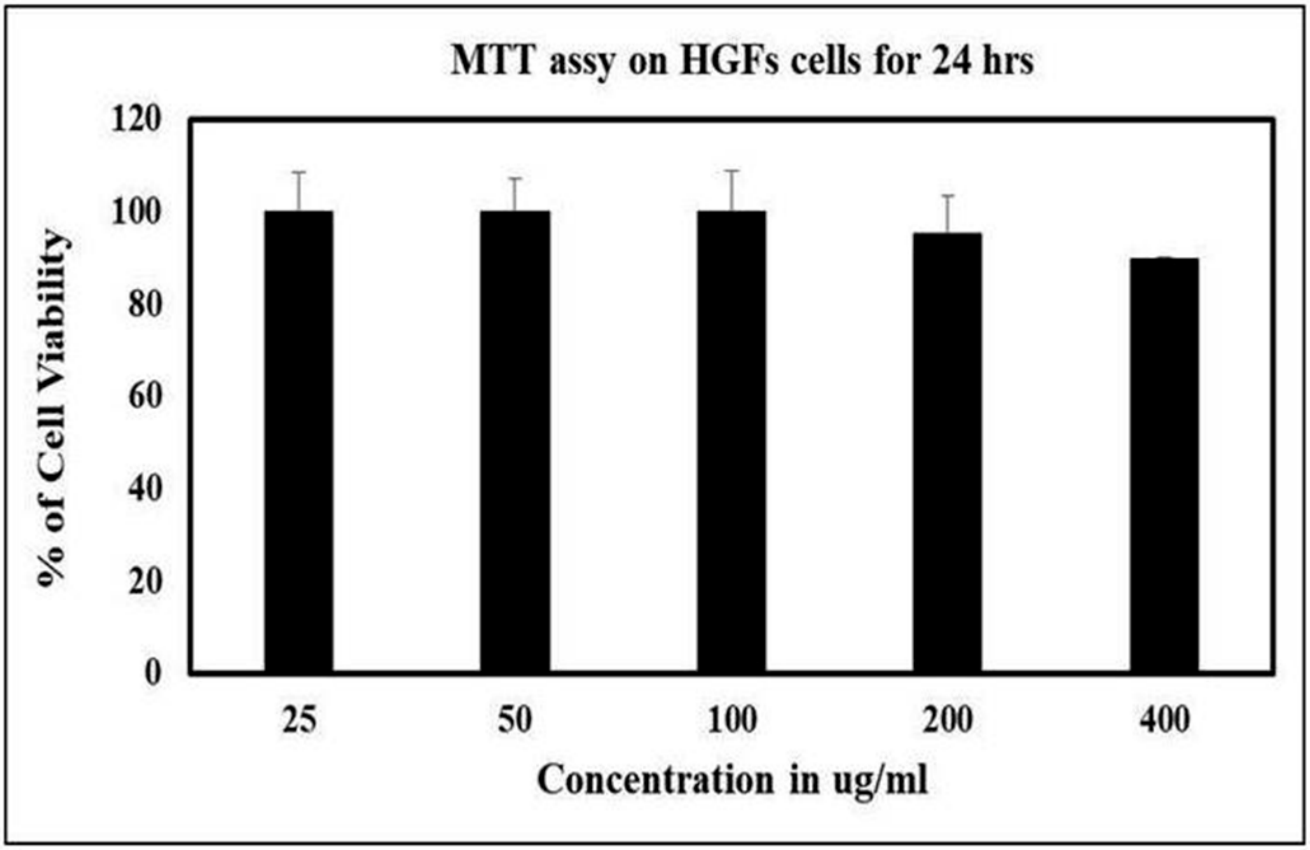

Fig 4. Cytotoxic effect of fluorine-doped zinc oxide (F-ZnO) on HGFs cell line. Cell was culture in 10% FBS medium and treated with different concentration of fluorine-doped zinc oxide (F-ZnO) at 24 h monitored by MTT assay. The percentages of viable cells were calculated in comparison to untreated cells (100%)

F-ZnO composite (4% concentration) showed a zone of 10.0 ± 0.31 mm. Although slightly lower than standard antibiotics, the F-ZnO composite exhibited dose-dependent and statistically significant antibacterial activity ($p < 0.05$), confirming its potential use as an antimicrobial biomaterial.

Table 1. Antimicrobial effects of the ZnF nanoparticles on *S. mutans*

ZnF concentration (mg/ml)	Zone of inhibition (mm)
0.2	5.3 ± 0.57
1.0	7.6 ± 0.57
2.0	9.0 ± 0.00
4.0	10.0 ± 0.31

The fluoride ion release profile demonstrated a burst release within the first 3 days, followed by a slower sustained release over 14 days. The cumulative release at day 14 reached approximately 1.8 ± 0.2 ppm for the 4% F-ZnO group. The release was concentration-dependent and confirmed the sustained availability of fluoride ions, supporting the potential anticariogenic effect of the composites.

Future studies should also explore optimizing the concentration of F-ZnO nanoparticles to balance antibacterial efficacy with cost-effectiveness and mechanical performance. The measured release of fluoride ions from the F-ZnO composites validates the fluorine doping strategy, enabling not only improved antibacterial action but also long-term remineralization potential in the oral environment, aligning with findings from previous studies.

Significance and Clinical Implications:

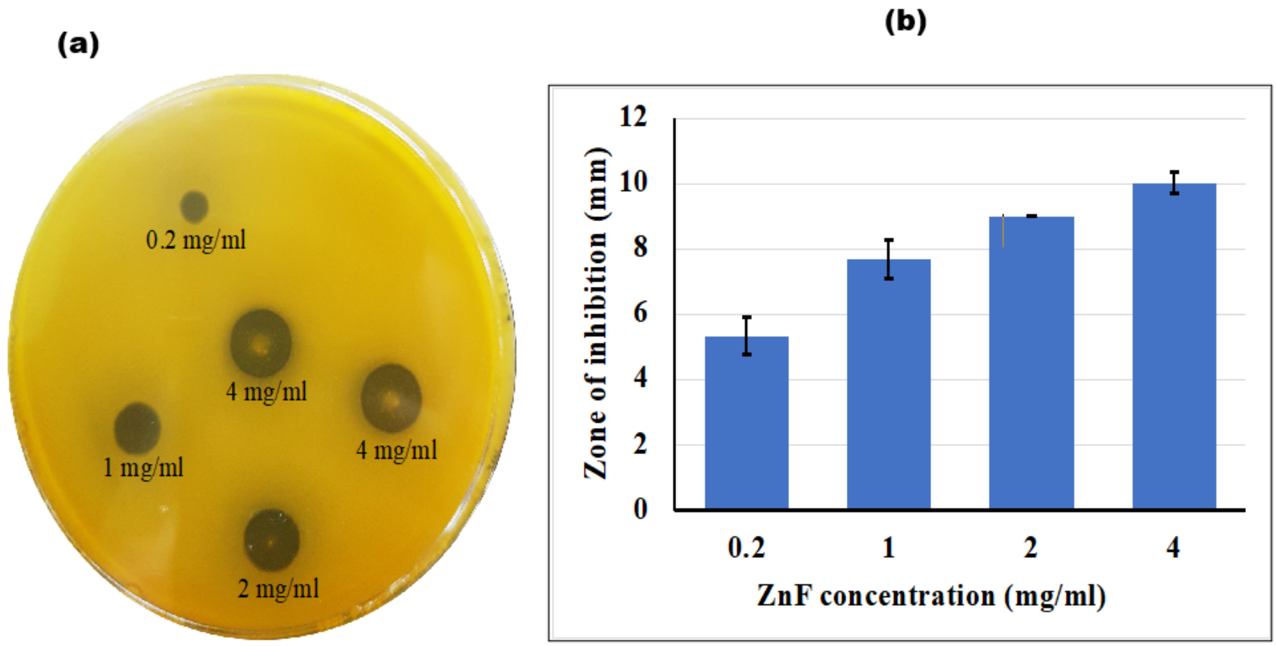

Fig 5. Effect of ZnF nanocomposites on *S. mutans.* (a) Agar zone of inhibition assay (b) Bar graph showing the zones of inhibition (in mm)

The significance of this study lies in the development of a multifunctional orthodontic resin capable of not only resisting bacterial colonization but also maintaining the required mechanical strength and biocompatibility. The use of fluorine-doped ZnO nanoparticles ensures a continuous antibacterial effect via fluoride release, which is particularly valuable in the prevention of white spot lesions and secondary caries around orthodontic brackets. This approach provides a foundation for creating more effective and preventive dental materials for clinical use.

4 Conclusion

This study successfully demonstrated the synthesis, characterization, and application of fluorine-doped zinc oxide nanoparticles in orthodontic composite resins. F-ZnO nanoparticles significantly inhibited *Streptococcus mutans*, highlighting their potential to combat cariogenic bacteria and reduce biofilm formation. The composites maintained optimal mechanical properties, such as shear bond strength, ensuring their suitability for orthodontic applications.

Cytotoxicity assays confirmed the safety of F-ZnO composites, with high cell viability across all tested concentrations. These results suggest that F-ZnO nanoparticles can play a transformative role in preventive dentistry by enhancing the antimicrobial properties of dental materials without compromising their functional and mechanical integrity. The controlled release of fluoride ions provides sustained antibacterial action, making these materials particularly effective in environments prone to bacterial colonization, such as around orthodontic brackets and wires. Future directions include exploring the long-term durability of these composites in clinical settings and expanding their application to other areas of restorative dentistry. By addressing these aspects, F-ZnO-based materials could establish a new benchmark for multifunctional dental biomaterials.

5 Acknowledgements

The authors gratefully acknowledge the work was financial supported by the Deanship of Scientific Research and the Vice Presidency for Graduate Studies and Scientific Research at King Faisal University, Saudi Arabia (Grant No. KFU 254353). This study was also supported by Jamia Millia Islamia, New Delhi, India.

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