RESEARCH PAPER

BIOMINERALIZATION OF ZnO-HAP FOR BONE CEMENT

Sanjay Varshan[1], Dr. Abilasha[2*]
[1]Department of Pathology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai-600077, Tamil Nadu, India
Email: 152001060.sdc@saveetha.com
[2*]Assistant Professor, Department of Oral Pathology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai-600077, Tamil Nadu, India
Email: abilasha@saveetha.com
Corresponding Author:
Dr. Abilasha
Assistant Professor, Department of Oral Pathology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai-600077, Tamil Nadu, India

ABSTRACT

Background: Biomineralization involves the deposition and growth of mineral phases that mimic the composition and structure of natural bone, offering tremendous potential for improving orthopedic implant materials. ZnO, with its unique physicochemical properties, exhibits antimicrobial effects and promotes osteogenesis, while HAP, the main mineral component of natural bone, provides excellent biocompatibility and osteoconductivity.

Aim: To assess the biomineralization property of ZnO-HAP for bone cement.

Methodology: ZnO and HAP nanoparticles were synthesized via chemical precipitation and co-dispersion techniques. Morphological analysis and functional group identification were evaluated using SEM, EDS, XRD, and FTIR. The hybrid nanoparticles were incorporated into standard bone cement. Antibacterial testing against *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus*) was carried out using the agar well diffusion method at varying concentrations (50 mg and 100 mg). Finally, statistical analyses are performed on the gathered data to derive conclusions about the biomineralized cement's potential applications in orthopedic settings.

Results: FTIR analysis confirmed successful chemical interaction and blending of the ZnO-HAP phases. SEM imaging demonstrated an interconnected, highly crystalline porous microstructure optimal for cellular anchorage. Well diffusion assays revealed potent, concentration-dependent zones of inhibition diameters against both pathogens. The 100 mg experimental group showed robust bactericidal clear zones compared to the 50 mg group and the unmodified control.

Conclusion: By incorporating ZnO and HAP nanoparticles into the bone cement matrix, we successfully achieved biomineralization, simulating the natural mineralization process of bone. Further studies are warranted to explore the long-term performance, in vivo biocompatibility, and regenerative capacity of the biomineralized cement, paving the way for its clinical translation in orthopedic applications.

Keywords: Hydroxyapatite, Biomineralization, Zinc Oxide, nanoparticles.
How to cite this article: Varshan S, Abilasha. Biomineralization of ZnO-HAP for Bone Cement. Int J Drug Deliv Technol. 2026;16(52s): 780-784. DOI: 10.25258/ijddt.16.52s.96
Source of support: Nil.
Conflict of interest: None

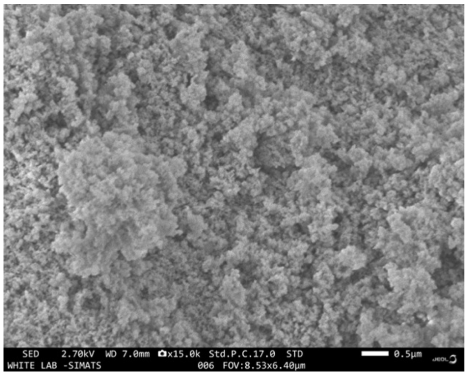
.INTRODUCTION:

The realm of medical science and biotechnology continually strives to innovate and pioneer solutions that revolutionize patient care and recovery. Among these groundbreaking advancements lies a promising avenue known as biomineralization, a process harnessing nature's wisdom to enhance medical materials. Biomineralisation, inspired by nature's intrinsic ability to create complex and resilient structures, has become a focal point in material science, especially in the domain of orthopedic implants and bone tissue engineering(1). Biomineralization involves the deposition and growth of mineral phases that mimic the composition and structure of natural bone, offering tremendous potential for improving orthopedic implant materials(2). It plays a crucial role in the field of biomaterials, particularly in the development of bone cement.

The field of biomaterials has witnessed significant advancements, and our research focuses on harnessing the power of biomineralization to enhance the performance and biocompatibility of bone cement(3). Among the various biomaterials used in bone cement, Zinc Oxide (ZnO) and Hydroxyapatite (HAP) have gained significant attention due to their unique properties and potential for enhancing bone regeneration(4). ZnO-HAP, a novel composite, presents itself as a remarkable milestone in this domain, combining the biocompatibility and mechanical strength of hydroxyapatite with the unique properties of zinc oxide nanoparticles. The synthesis of ZnO-HAP involves intricate processes aimed at achieving an optimal balance between the inherent properties of both zinc oxide and hydroxyapatite(5). This amalgamation aims not only to enhance mechanical strength but also to introduce antibacterial features, crucial in preventing post-surgical infections. Researchers are meticulously fine-tuning the composition and structure of ZnO-HAP to ensure its compatibility with the human body, paving the way for safer and more effective orthopedic interventions(6).

Bone cement serves as a critical component in orthopedic surgeries, playing a pivotal role in stabilizing implants and facilitating the regeneration of damaged bone tissue(7). Traditional bone cements face limitations concerning mechanical strength, biocompatibility, and antibacterial properties. However, the integration of ZnO-HAP into bone cement formulations holds the promise of overcoming these constraints, marking a significant leap forward in orthopedic material science(8). Moreover, the incorporation of ZnO-HAP into bone cement formulations exhibits promising characteristics, including improved biocompatibility and bioactivity, promoting cell attachment and tissue regeneration. Its inherent antibacterial properties contribute significantly to reducing the risk of infections, a common concern in implant-related surgeries(9). Additionally, the enhanced mechanical strength of ZnO-HAP-infused bone cement offers greater stability and longevity to orthopedic implants, potentially minimizing the need for revision surgeries.

As ongoing research and clinical trials continue to validate the efficacy of ZnO-HAP in bone cement applications, the horizon of orthopedic medicine is undergoing a transformative shift. The prospect of leveraging biomineralization techniques to tailor materials specifically for the human body's needs is reshaping the landscape of orthopedic surgeries, promising more durable, infection-resistant, and biocompatible solutions for patients in need of bone repair and augmentation. The evolution of ZnO-HAP-infused bone cement heralds a new era in orthopedic materials, propelling the field toward safer, more efficient, and patient-centric approaches to bone reconstruction and healing(10). This article delves into the intriguing realm of biomineralization with ZnO-HAP, exploring its synthesis methodologies, the impact on bone cement properties, and the potential implications for orthopedic surgeries.



MATERIALS AND METHODS:

Materials:

Calcium nitrate tetrahydrate (Ca(NO3)2·4H2O), diammonium hydrogen phosphate (NH4)2HPO4 (DAHP), ammonia solution (25%) and triethanolamine (TEA) were purchased from Merck (Germany). Chitosan (75% degree of deacetylation) and sodium alginate were purchased from Sigma-Aldrich (St Louis, MO). Ammonium chloride (NH4Cl) was purchased from Fluka (Buchs, Switzerland). The infrared spectra of the nanocomposites were recorded on a Perkin Elmer 983 infrared spectrophotometer (Perkin Elmer, Boston, MA) at room temperature.

Synthesis of Nano-Hydroxyapatite (n-HA)

In this work, HA nanoparticles were synthesized using a chemical precipitation method (CitationHarris 1984, CitationKumar 2006). According to this method, 6.5 g of Ca(NO3)2·4H2O (0.033 mol) and 4.3 g of diammonium hydrogen phosphate (0.035 mol) were dissolved in 50 and 45 mL of deionized water, respectively, with ratio Ca/P = 1.7. Triethanolamine (TEA; 1.8 g) (0.013 mol) was used in conjunction with Ca(NO3)2·4H2O solution (Ca2+:TEA = 1:0.6). The pH of both calcium nitrate and DAHP solutions was maintained at ∼11–12. (NH4)2HPO4 solution was added drop-wise to the mixture of Ca(NO3)2·4H2O and TEA, stirred using a mechanical stirrer for 5 h. The pH of the reacting mixture was also maintained at ∼11–12 by adding NH4OH solution. A white gelatinous precipitate was formed, which was filtered by a centrifugal filtration process and washed with deionized water and NH4Cl solution, so dried at 85°C for 20 h.

RESULTS:

Fig 1: Represents the high-magnification surface topography of the cured matrix, showing a rough, interconnected nanostructured network ideal for cellular anchorage and growth.

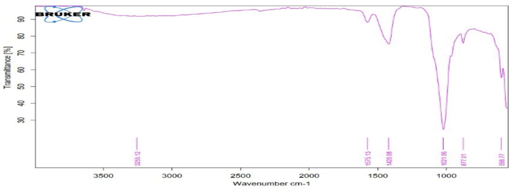


Fig 2: Represents the molecular architecture and chemical functional bands of the ZnO-HAP system, confirming successful integration and chemical blending without material decomposition.

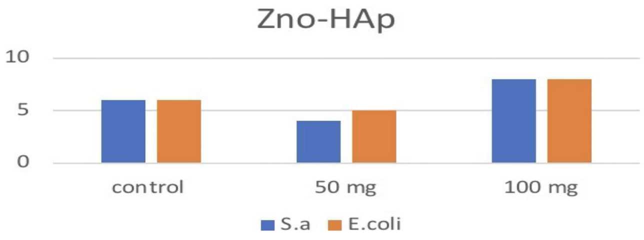


Fig 3: Represents the biological zones of inhibition, demonstrating concentration-dependent bactericidal efficacy where the 100 mg well shows the strongest clearing against E. coli and S. aureus compared to the 50 mg well and the inactive control.

DISCUSSION:

The long-term stability and degradation behavior of the ZnO-HAP composite within the physiological environment would likely be a focal point(11). Understanding how the material behaves over time, both structurally and functionally, is crucial for assessing its potential clinical translation and its ability to support bone healing in various patient populations. This research investigates the synthesis and application of Zinc Oxide (ZnO) incorporated with Hydroxyapatite (HAP) for bone cement, exploring its biocompatibility, mechanical properties, and osteogenic potential, which likely delves into the process of synthesizing the ZnO-HAP composite and its structural characterization through techniques such as X-ray diffraction (XRD), scanning electron microscopy (SEM), or Fourier-transform infrared spectroscopy (FTIR)(12). These analyses would elucidate the crystalline structure, morphology, and chemical composition of the composite, providing insights into its suitability for bone repair and regeneration. Moreover, this article addresses the challenges associated with traditional bone cements, such as their inability to fully integrate with the surrounding tissue or the risk of bacterial infections. ZnO-HAP's potential for biomineralization might offer a solution by promoting the formation of hydroxyapatite on its surface, mimicking the natural mineralization process in bones and facilitating better osseointegration(13).

Comparing this study with similar articles, research on biomaterials in orthopedics emphasizes the significance of enhancing bone regeneration and the mechanical integrity of implants. Some articles highlight the use of different materials like calcium phosphate, bioactive glasses, or polymers for bone substitutes(14). What sets the ZnO-HAP composite apart is its potential for controlled biomineralization, allowing for tailored degradation rates, which is crucial for bone healing. Moreover, some studies delve into the role of nanoparticles in bone tissue engineering, citing their potential for controlled drug release and improved mechanical strength. The integration of ZnO nanoparticles in HAP could offer a dual advantage of antibacterial properties along with promoting osteogenesis, addressing infection risks in orthopedic applications(15). Comparative studies may highlight the importance of controlling the release of ions or growth factors from biomaterials. For instance, while calcium phosphate-based materials are known for their similarity to the mineral phase of bone tissue, the addition of ZnO might provide additional advantages, such as imparting antimicrobial properties, modulating cellular functions, or aiding in angiogenesis, which are critical aspects of successful bone regeneration(16). Furthermore, the article likely discusses in vitro and in vivo evaluations, such as cell viability assays or animal studies, to demonstrate the material's efficacy and biocompatibility. The comparison with other studies might elucidate the advantages of ZnO-HAP in terms of biomineralization kinetics, cytocompatibility, and its ability to support bone regeneration while maintaining mechanical stability(17). Additionally, the research might discuss the feasibility of scaling up production, considering factors like cost-effectiveness, scalability, and regulatory aspects crucial for its clinical adoption. Addressing these aspects early in the research phase ensures a smoother transition from the lab bench to clinical trials and, eventually, to widespread clinical use.

Future research avenues might explore refining the composite's composition, exploring different ratios of ZnO and HAP, or even incorporating other bioactive compounds to further enhance its properties. Furthermore, understanding the specific cellular and molecular mechanisms underlying the biomineralization process induced by this composite could unlock new strategies for targeted bone regeneration and personalized orthopedic treatments. Moreover, assessing the long-term safety profile of

ZnO-HAP through rigorous biocompatibility studies and in-depth analyses of potential systemic effects remains crucial(18). This would involve investigating the material's behavior not only at the site of application but also in circulation and interactions with other bodily systems. Collaboration between multidisciplinary teams comprising materials scientists, biologists, clinicians, and regulatory experts will be pivotal for advancing this technology. Their collective expertise can drive innovation, address challenges, and ensure a comprehensive approach toward developing clinically viable bone cements based on the principles of biomineralization.

Ultimately, this research area stands at the intersection of materials science, biotechnology, and medicine, aiming to design advanced biomaterials that not only repair but actively participate in the regeneration and integration of damaged bone tissue. The comprehensive analysis and comparison with other studies help in understanding the unique advantages and potential challenges associated with the ZnO-HAP composite, paving the way for future advancements in orthopedic biomaterials. In summary, this study holds promise in the field of orthopedics by offering a novel composite with potential benefits in controlled degradation, antibacterial properties, and enhanced osteogenesis compared to other biomaterials used in bone tissue engineering.

CONCLUSION:

In conclusion, the biomineralization of zinc oxide hydroxyapatite for bone cement holds immense promise in the field of orthopedics. This innovative approach not only enhances the mechanical properties and biocompatibility of bone cement but also facilitates better integration with the host tissue, promoting faster healing and reducing the risk of implant failure. While these in vitro results are highly promising, further long-term evaluations are needed to fully characterize the material's extended performance, in vivo biocompatibility, and regenerative capacity under functional loads. These steps will be essential to guide this biomineralized bone cement toward successful clinical translation in orthopedic and maxillofacial surgery. Further research and clinical trials are warranted to validate its long-term efficacy and safety for widespread application in improving bone repair and regeneration therapies.

ACKNOWLEDGEMENT:

The authors would like to thank Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University for providing research laboratory facilities to carry out the work.

CONFLICT OF INTEREST:

All the authors declare that there was no conflict of interest in the present study

REFERENCES:

1. Cera A, Verdugo-Escamilla C, Marín JA, Palacio S. Calcium sulphate biomineralisation: Artefact of sample preparation? Physiol Plant. 2023 Sep-Oct;175(5):e14017.
2. Sleight VA. Cell type and gene regulatory network approaches in the evolution of spiralian biomineralisation. Brief Funct Genomics. 2023 Nov 17;22(6):509–16.
3. Jones TR, Poitras J, Levett A, Langendam A, Vietti A, Southam G. Accelerated carbonate biomineralisation of Venetia diamond mine coarse residue deposit (CRD) material - A field trial study. Sci Total Environ. 2023 Oct 1;893:164853.
4. Guerfi Z, Kribaa OK, Djouama H. Chemical-physical behavior of Hydroxyapatite: A modeling approach. J Mech Behav Biomed Mater. 2023 Nov 21;150:106229.
5. Han Q, Cai L, Huang P, Liu S, He C, Xu Z, et al. Fast Ionic Conducting Hydroxyapatite Solid Electrolyte Interphase Enables Ultra-Stable Zinc Metal Anodes. ACS Appl Mater Interfaces. 2023 Oct 18;15(41):48316–25.
6. Ullah I, Ali S, Ahmad Z, Khan A, Siddiqui MA, Jiang Y, et al. Physicochemical Properties and Simulation of Magnesium/Zinc Binary-Substituted Hydroxyapatite with Enhanced Biocompatibility and Antibacterial Ability. ACS Appl Bio Mater [Internet]. 2023 Nov 13; Available from: http://dx.doi.org/10.1021/acsabm.3c00599
7. Choi KU, Park JI, Nam JH, Lee CH, Son JW. Sharp foreign body causing hemopericardium: Bone cement fragment. Eur Heart J Cardiovasc Imaging [Internet]. 2023 Nov 24; Available from: http://dx.doi.org/10.1093/ehjci/jead322
8. Kotha AK, Nicholson JW, Booth SE. Biological Evaluation of Zinc Phosphate Cement for Potential Bone Contact Applications. Biomedicines [Internet]. 2023 Jan 18;11(2). Available from: http://dx.doi.org/10.3390/biomedicines11020250
9. Kanwal N. Novel Zinc Containing Phosphate Glasses for Glass-ionomer Cements for Bone Cement Applications. 2014.

10. Yuan X, Wu T, Lu T, Ye J. Effects of Zinc and Strontium Doping on In Vitro Osteogenesis and Angiogenesis of Calcium Silicate/Calcium Phosphate Cement. ACS Biomater Sci Eng. 2023 Oct 9;9(10):5761–71.
11. Feng D. Composite Bone Cements Based on Hydroxyapatite and Zinc Oxide. 2002. 154 p.
12. Wulandari R, Ardiansyah A, Setiyanto H, Saraswaty V. A novel non-enzymatic electrochemical uric acid sensing method based on nanohydroxyapatite from eggshell biowaste immobilized on a zinc oxide nanoparticle modified activated carbon electrode (Hap-Esb/ZnONPs/ACE). RSC Adv. 2023 Apr 24;13(19):12654–62.
13. Fathy Abo-Elmahasen MM, Abo Dena AS, Zhran M, Albohy SAH. Do silver/hydroxyapatite and zinc oxide nano-coatings improve inflammation around titanium orthodontic mini-screws? In vitro study. Int Orthod. 2023 Mar;21(1):100711.
14. Otsuka M, Saito H, Sasaki T. Analytical Evaluation of Wet and Dry Mechanochemical Syntheses of Calcium-Deficient Hydroxyapatite Containing Zinc Using X-ray Diffractometry and Near-Infrared Spectroscopy. Pharmaceutics [Internet]. 2022 Oct 1;14(10). Available from: http://dx.doi.org/10.3390/pharmaceutics14102105
15. Akram W, Zahid R, Usama RM, AlQahtani SA, Dahshan M, Basit MA, et al. Enhancement of Antibacterial Properties, Surface Morphology and In Vitro Bioactivity of Hydroxyapatite-Zinc Oxide Nanocomposite Coating by Electrophoretic Deposition Technique. Bioengineering (Basel) [Internet]. 2023 Jun 7;10(6). Available from: http://dx.doi.org/10.3390/bioengineering10060693
16. Gopi D, Murugan N, Ramya S, Kavitha L. Retraction: Electrodeposition of a porous strontium-substituted hydroxyapatite/zinc oxide duplex layer on AZ91 magnesium alloy for orthopedic applications. J Mater Chem B Mater Biol Med. 2023 Apr 5;11(14):3262.
17. Pugliese Pereira B, Antoine C, de Barros AO da S, Pacífico L de C, Pijeira MSO, Rossi AM, et al. Evaluating Hydroxyapatite, Gold Nanoparticles, and Graphene-Copper as Bimodal Agents for X-ray and Computed Tomography. Bioengineering (Basel) [Internet]. 2023 Feb 10;10(2). Available from: http://dx.doi.org/10.3390/bioengineering10020238
18. Sivaperumal VR, Mani R, Polisetti V, Aruchamy K, Oh T. One-Pot Hydrothermal Preparation of Hydroxyapatite/Zinc Oxide Nanorod Nanocomposites and Their Cytotoxicity Evaluation against MG-63 Osteoblast-like Cells. Molecules [Internet]. 2023 Jan 1;28(1). Available from: http://dx.doi.org/10.3390/molecules28010345
19.