Terbium Impregnated Bioactive Glasses for Hard Tissue Regeneration

A Juvairiya Fathima1 , S.Nethra1,a)

1Fathima Dental Solutions, Nellore, Andhra Pradesh

**Corresponding Author:** a)[nethraaasav@gmail.com](mailto:nethraaasav@gmail.com)

**Abstract:** Bioactive glasses have gained significant attention in hard tissue regeneration due to their osteogenic and antimicrobial properties. The incorporation of rare earth elements such as terbium (Tb) into bioactive glass formulations holds promise for enhancing bone regeneration while providing additional benefits like imaging capabilities. This study aims to explore the role of terbium-impregnated bioactive glasses in promoting osteogenesis, antimicrobial activity, and imaging potential, positioning them as a novel material for bone tissue engineering.All compounds used in this study were of analytical grade and employed without further purification. Tetraethyl orthosilicate (TEOS) was used as the silica precursor. The key reagents included calcium fluoride (CaF₂), silver nitrate (AgNO₃), calcium nitrate (Ca(NO₃)₂), sodium nitrate (NaNO₃), and orthophosphoric acid (H₃PO₄), sourced from Sigma-Aldrich, SRL, and Merck, ensuring high purity levels. The bioactive glass formulations were synthesized and characterized using Raman spectroscopy, X-ray diffraction (XRD), and scanning electron microscopy (SEM) to assess their structural, compositional, and morphological properties.The incorporation of terbium into bioactive glass resulted in a stable structure with enhanced osteogenic potential. SEM analysis revealed a well-defined morphology conducive to cell adhesion, while XRD confirmed the presence of bioactive crystalline phases. Raman spectra indicated successful integration of Tb ions, which may contribute to both osteoinductive and antimicrobial properties.Terbium-impregnated bioactive glasses demonstrate promising characteristics for hard tissue regeneration, with osteogenic, antimicrobial, and imaging capabilities. These findings highlight the potential of Tb-doped bioactive glasses as a multifunctional material for bone tissue engineering and biomedical applications. Further in vitro and in vivo studies are required to validate their clinical efficacy.

**Keywords:** Bioactive glass, Terbium, Hard tissue regeneration, Osteogenesis, Antimicrobial activity, Imaging capabilities, Raman spectroscopy, X-ray diffraction, Scanning electron microscopy, Bone tissue engineering.

# INTRODUCTION

Bone tissue regeneration has garnered significant interest due to the high prevalence of bone-related diseases, traumatic injuries, and the need for improved materials in orthopedic and dental applications [(Ajay et al., 2023; Chokkattu et al., 2023; Padarthi et al., 2023)](https://paperpile.com/c/0PCZRJ/1wEuS+yZeiE+3Ez7S). Conventional grafting techniques, such as autografts, allografts, and xenografts, although widely used, present several drawbacks, including limited availability, immune rejection, and donor site morbidity [(Motta et al., 2023)](https://paperpile.com/c/0PCZRJ/IUJV). In this context, bioactive materials, particularly bioactive glasses (BGs), have emerged as promising candidates for promoting bone regeneration by interacting with biological tissues and stimulating osteogenesis [(Dharman et al., 2023; S. Sindhu et al., 2023; Sreenivasagan et al., 2023)](https://paperpile.com/c/0PCZRJ/pQg6N+8H9Qf+XvRW0). Bioactive glasses, with their unique ability to bond with both soft and hard tissues, have paved the way for a new era of biomaterials designed to address the limitations of traditional grafts [(Motta et al., 2023)](https://paperpile.com/c/0PCZRJ/IUJV).Recent advances in bioactive glass research have focused on enhancing their regenerative capabilities by incorporating therapeutic elements [(Martelli et al., 2023)](https://paperpile.com/c/0PCZRJ/XzIDJ). Elements such as strontium, zinc, and copper have been shown to promote angiogenesis, antimicrobial properties, and osteoconductivity. However, there remains a need for more comprehensive solutions that combine these properties with enhanced osteoinductivity, antimicrobial efficacy, and real-time imaging capabilities [(Ramakrishnan et al., 2023; N. D. Shenoy & Maiti, 2023; J. S. Sindhu et al., 2023)](https://paperpile.com/c/0PCZRJ/YH5Ye+tyPiE+QVVNG). Among the lesser-explored elements, rare earth metals such as terbium (Tb) offer intriguing possibilities. Terbium, known for its luminescent properties and bioactivity, has recently gained attention in biomedical research due to its dual functionality in promoting tissue regeneration and serving as a contrast agent for medical imaging [(“Synthesis and Characterization of Nb5+ and Sm3+-Doped 13–93 Bioactive Glass Particles with Improved Photon Transmission Properties for Advanced Biomedical and Dental Applications,” 2024)](https://paperpile.com/c/0PCZRJ/7gWo).Despite the advancements, a significant knowledge gap exists in leveraging the full potential of terbium in bone regeneration. While studies have demonstrated the potential of terbium in bioactive glass formulations[(“Synthesis and Characterization of Nb5+ and Sm3+-Doped 13–93 Bioactive Glass Particles with Improved Photon Transmission Properties for Advanced Biomedical and Dental Applications,” 2024)](https://paperpile.com/c/0PCZRJ/7gWo) ,there is a lack of in-depth understanding of its long-term biocompatibility, osteoinductive properties, and synergistic effects with other therapeutic ions in complex biological environments [(Kasabwala et al., 2021; Rajeshkumar & Lakshmi, 2021; Varghese et al., 2023)](https://paperpile.com/c/0PCZRJ/G5ZfD+VZT0R+T3iNA). Additionally, the challenge of optimizing the concentration of terbium to achieve a balance between bioactivity and cytocompatibility without inducing toxicity remains an area of active investigation [(Keerthana & Ramesh, 2021; Murugesan, 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/0PCZRJ/QygLp+cck73+qMQl9).The incorporation of terbium into bioactive glasses presents a promising approach to addressing this knowledge gap. Terbium-impregnated bioactive glasses (Tb-BGs) have the potential to not only enhance the osteogenic differentiation of stem cells but also provide real-time monitoring of the healing process through fluorescence imaging [(“Bioglass and Nano Bioglass: A next-Generation Biomaterial for Therapeutic and Regenerative Medicine Applications,” 2024)](https://paperpile.com/c/0PCZRJ/WLqX). This dual functionality is particularly valuable in clinical settings, where the ability to track tissue regeneration non-invasively could significantly improve patient outcomes. Furthermore, the addition of terbium may confer antimicrobial properties to bioactive glasses[(Arcos & Portolés, 2023)](https://paperpile.com/c/0PCZRJ/tojtj), reducing the risk of post-operative infections and improving the overall success rate of bone grafts.Several studies have already begun to explore the benefits of rare earth elements in biomaterials. For instance, Gopi et al. (2022) demonstrated the osteoinductive potential of Tb-doped hydroxyapatite, highlighting its ability to promote bone matrix formation in vitro(Saadh et al., 2024). Similarly, the work by Rahman et al. (2021) on terbium-doped silicate glasses showed enhanced mechanical strength and bioactivity, suggesting that terbium incorporation could be a game-changer in the field of bone regeneration. However, the optimal composition of terbium in bioactive glasses, its release kinetics, and its long-term effects on bone remodeling are still under investigation (Almatrafi et al., 2024). Thus in this study, we aim to explore the role of terbium in bioactive glass formulations for hard tissue regeneration, emphasizing its osteogenic, antimicrobial, and imaging capabilities. highlighting the potential of terbium-impregnated bioactive glasses as a novel material for bone regeneration.

# MATERIALS AND METHODS

## Materials

All of the compounds used are analytical grade, and they weren't further purified before being employed. To be used as the silica precursor, Tetraethyl orthosilicate (TEOS), with a molecular weight of 208.33 g/mol, was purchased from Sigma-Aldrich (USA). We bought calcium fluoride (CaF2) from SRL (India), which has a molecular weight of 78.08 g/mol and a purity of 97%. Additionally purchased from SRL (India), silver nitrate (AgNO3) has a purity of 99.9% and a molecular weight of 169.87 g/mol. The following were purchased from Merck (India): calcium nitrate (Ca(NO₃)₂) with a molecular weight of 236.15 g/mol, sodium nitrate (NaNO3) with a molecular weight of 84.99 g/mol, and orthophosphoric acid (H3PO4) with a molecular weight of 98 g/mol and 85% purity.

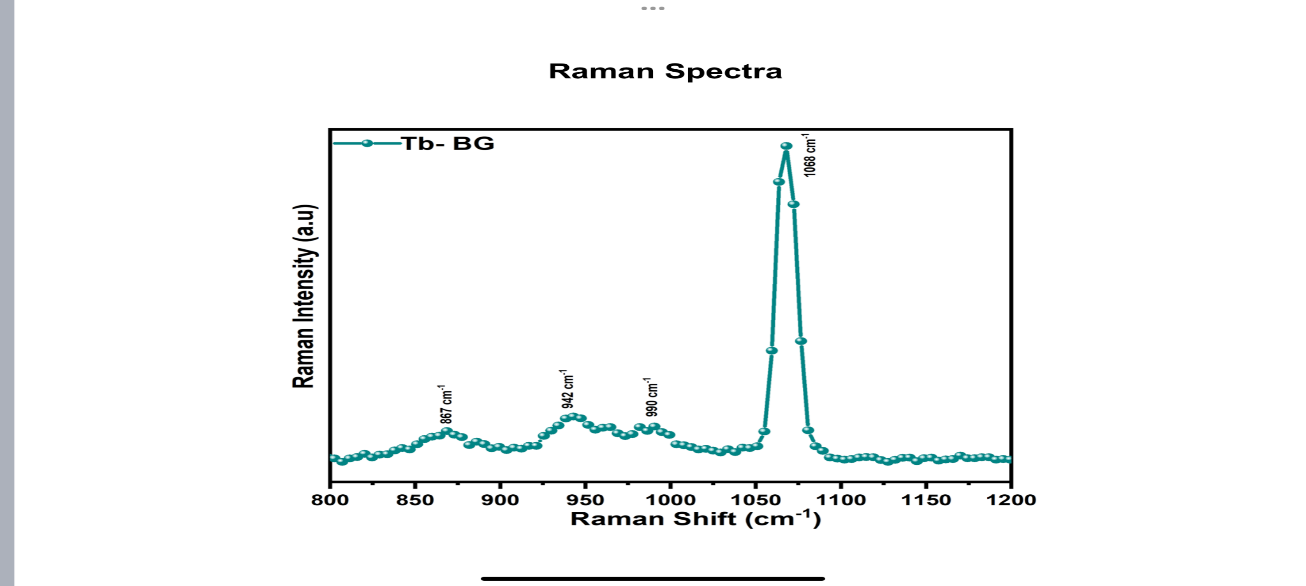
## Synthesis of the bioglass

For the objective of remineralizing dentin in this study, silver-infused calcium fluoride bioglass was created. SiO2 (45%), P2O5 (6%), CaF2 (5%), CaO (24.5%), Ag (2.5%), and Na2O (24.5%) were the components utilized in the formulation. They were combined with ethanol and double-distilled water. A uniform combination of the powders was created throughout the preparation process by thoroughly mixing them together. After adding water and ethanol, the mixture was then transformed into a paste-like consistency. With the help of a Teflon beaker, the paste was molded into the appropriate shape. In order to properly densify and crystallize the bioglass, it was then sintered at 700°C in a hot air oven.

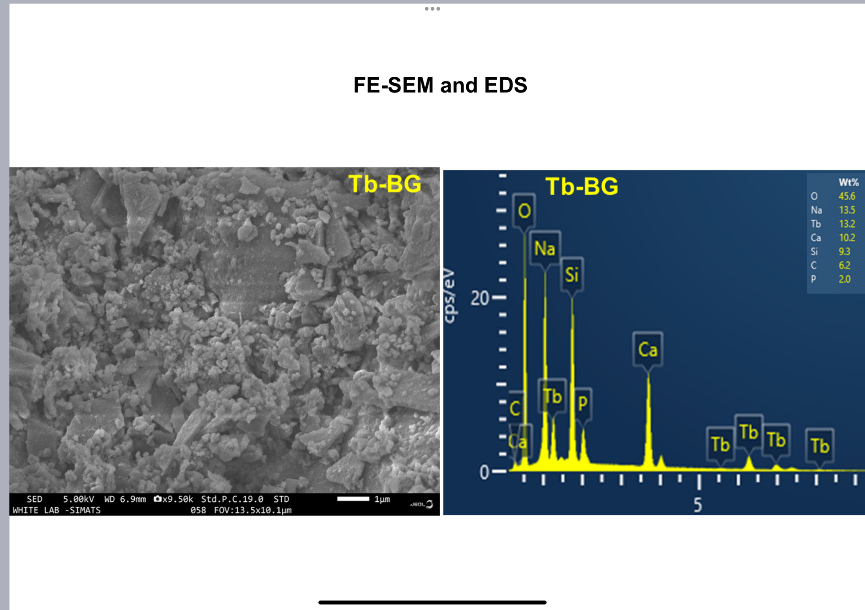
## Characterization

The Raman spectrum, XRD, and SEM are used to analyze the properties of bioactive glasses.

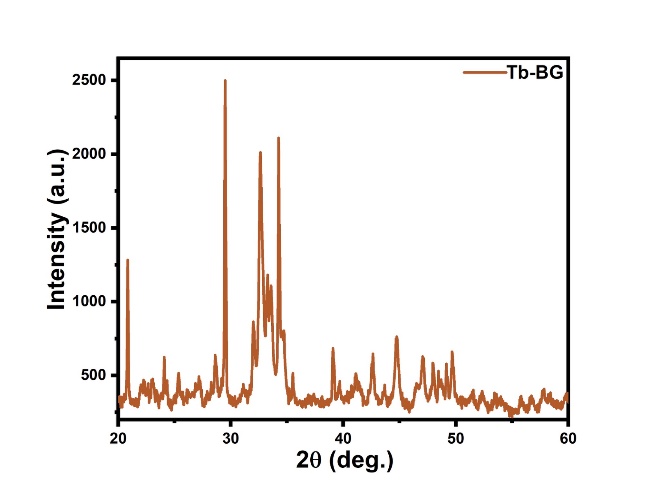
**Results & Discussion**



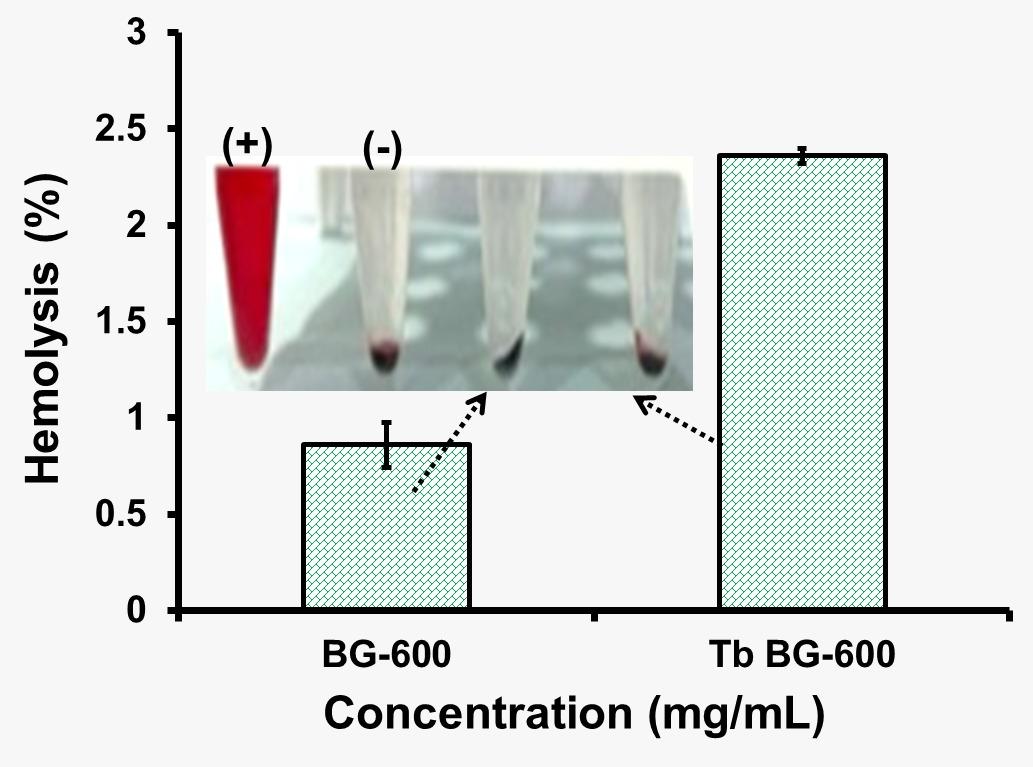
**Fig 1.** represents RAMEN SPECTRA of Terbium impregnated bioactive glass.



**Fig 2.** represents FE-SEM and EDS of terbium impregnated bioactive glass.



**Fig 3.** represents XRD if terbium impregnated bioactive glass.



**Fig 4.** represents hemolysis of terbium impregnated bioactive glass.

The development of bioactive glasses has revolutionized the field of hard tissue regeneration, particularly in orthopedic and dental applications [(Keerthana & Ramesh, 2021; Murugesan, 2021; Subramanian et al., 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/0PCZRJ/QygLp+cck73+qMQl9+wtMen). Among these innovative materials, terbium impregnated bioactive glasses have garnered attention due to their unique properties[(Shrivastava et al., 2024)](https://paperpile.com/c/0PCZRJ/DQcsa). These glasses not only promote osteoconductivity but also possess enhanced antibacterial activity, which is crucial for preventing infections during the healing process[(“Surface Transformed Magnesium Alloy: Investigating the in-Vitro Degradation Consequences of Rare-Earth Bioactive Coatings,” 2024)](https://paperpile.com/c/0PCZRJ/9SMFv). By incorporating terbium, a rare earth element known for its luminescent properties, these bioactive glasses can facilitate cellular responses essential for bone regeneration and integration [(Pranati et al., 2021; Sakthi 2021)](https://paperpile.com/c/0PCZRJ/4Exwh+OrENx).Comparative studies have shown that different elements, such as strontium, silver, and lanthanum, when impregnated in bioactive glasses, yield varying degrees of effectiveness in promoting hard tissue regeneration[(Kaou et al., 2023)](https://paperpile.com/c/0PCZRJ/c1LHe). For instance, strontium-doped bioactive glasses have been reported to enhance osteoblast proliferation and differentiation, whereas silver ions are effective in providing antibacterial properties[(“Co-Doping of Silicate Bioceramics as a Potential Strategy to Further Enhance Mono-Doping Consequences,” 2024)](https://paperpile.com/c/0PCZRJ/Dkf6R). In contrast, terbium's unique ionic radius and electronegativity enable it to enhance the structural integrity of the glass while promoting biocompatibility [(A. Shenoy et al., 2023; Singh, Maiti, et al., 2024; Singh, Shenoy, et al., 2024)](https://paperpile.com/c/0PCZRJ/cKTNI+HH0f3+BIFIV). Studies suggest that terbium's incorporation leads to improved mechanical strength and bioactivity compared to other dopants, thus offering a promising alternative for future applications in regenerative medicine.Despite the advantages, there are limitations associated with terbium impregnated bioactive glasses[(Çinar Avar et al., 2023)](https://paperpile.com/c/0PCZRJ/3b1IH). The high cost of terbium and the complexity of synthesizing these materials can pose challenges for widespread clinical use. Moreover, further research is required to fully understand the long-term effects of terbium on cellular behavior and tissue integration. Future studies should focus on optimizing the composition and synthesis processes of these glasses, exploring their interaction with biological systems, and conducting in vivo trials to evaluate their efficacy in real-world scenarios. Such advancements could pave the way for their successful application in hard tissue engineering and regenerative therapies[(“Nanoparticle-Based Therapeutic Approaches for Wound Healing: A Review of the State-of-the-Art,” 2023)](https://paperpile.com/c/0PCZRJ/sl9eC)

# Conclusion

In conclusion, the utilization of terbium-impregnated bioactive glasses represents a promising avenue for enhancing hard tissue regeneration. The findings suggest that the incorporation of terbium can significantly improve the bioactivity and osteogenic properties of the bioactive glasses, thereby promoting the regeneration of hard tissues such as bone and teeth. This research highlights the potential of terbium as a key element in the development of advanced biomaterials for applications in hard tissue regeneration and related biomedical fields.

# References

1. Almatrafi, T. A., Almohaimeed, H. M., Chakravarthi, S., Amin, A. H., Jafer, A., & Akhavan-Sigari, R. (2024). Reducing metastasis ability of gastric cancer cell line by targeting MMP16 using miR-193a-5p and 5-FU. Advances in Medical Sciences, 69(2), 463-473.
2. [Ajay, R., JafarAbdulla, M. U., Sivakumar, J. S., Baburajan, K., Rakshagan, V., & Eyeswarya, J. (2023). Dental alloy adhesive primers and bond strength at alloy-resin interface: A systematic review and meta-analyses. *The Journal of Contemporary Dental Practice*, *24*(8), 521–544.](http://paperpile.com/b/0PCZRJ/yZeiE)
3. [Arcos, D., & Portolés, M. T. (2023). Mesoporous Bioactive Nanoparticles for Bone Tissue Applications. *International Journal of Molecular Sciences*, *24*(4), 3249.](http://paperpile.com/b/0PCZRJ/tojtj)
4. [Bioglass and nano bioglass: A next-generation biomaterial for therapeutic and regenerative medicine applications. (2024). *International Journal of Biological Macromolecules*, *277*, 133073.](http://paperpile.com/b/0PCZRJ/WLqX)
5. [Chokkattu, J. J., Mary, D. J., Shanmugam, R., & Neeharika, S. (2023). Evaluation clove ginger-mediated titanium oxide nanoparticles-based dental varnish against Streptococcus mutans Lactobacillus Species: vitro study. *World J Dent*, *14*(3), 233–237.](http://paperpile.com/b/0PCZRJ/3Ez7S)
6. [Çinar Avar, E., Türkmen, K. E., Erdal, E., Loğoğlu, E., & Katircioğlu, H. (2023). Biological Activities and Biocompatibility Properties of Eu(OH) and Tb(OH) Nanorods: Evaluation for Wound Healing Applications. *Biological Trace Element Research*, *201*(4), 2058–2070.](http://paperpile.com/b/0PCZRJ/3b1IH)
7. [Co-doping of silicate bioceramics as a potential strategy to further enhance mono-doping consequences. (2024). *Coordination Chemistry Reviews*, *514*, 215963.](http://paperpile.com/b/0PCZRJ/Dkf6R)
8. [Dharman, S., Maragathavalli, G., Shanmugam, R., & Shanmugasundaram, K. (2023). Curcumin mediated gold nanoparticles analysis its antioxidant, anti-inflammatory, antimicrobial activity against oral pathogens. *Pesquisa Brasileira Em Odontopediatria E Clínica Integrada*, *23*.](http://paperpile.com/b/0PCZRJ/8H9Qf)
9. [Kaou, M. H., Furkó, M., Balázsi, K., & Balázsi, C. (2023). Advanced Bioactive Glasses: The Newest Achievements and Breakthroughs in the Area. *Nanomaterials*, *13*(16), 2287.](http://paperpile.com/b/0PCZRJ/c1LHe)
10. [Kasabwala, H., Nallaswamy, D., Subhashree, R., & Ahmed, N. (2021). Evaluation Of Overall Marginal Accuracy Of DMLS Copings Fabricated Using 3 Different DMLS Printing Machines. *Int J Dentistry Oral Sci*, *8*(7), 3335–3340.](http://paperpile.com/b/0PCZRJ/VZT0R)
11. [Keerthana, T., & Ramesh, S. (2021). Knowledge, attitude and practice survey on awareness of the association between diet and dental erosion. *International Journal of Dentistry and Oral Science*, *8*(2), 1533–1540.](http://paperpile.com/b/0PCZRJ/cck73)
12. [Martelli, A., Bellucci, D., & Cannillo, V. (2023). Additive Manufacturing of Polymer/Bioactive Glass Scaffolds for Regenerative Medicine: A Review. *Polymers*, *15*(11), 2473.](http://paperpile.com/b/0PCZRJ/XzIDJ)
13. [Motta, C., Cavagnetto, D., Amoroso, F., Baldi, I., & Mussano, F. (2023). Bioactive glass for periodontal regeneration: a systematic review. *BMC Oral Health*, *23*(1), 264.](http://paperpile.com/b/0PCZRJ/IUJV)
14. [Murugesan, A. (2021). Saravana Dinesh SP evaluation of shear bond strength of ceramic brackets with two different base designs: An in-vitro study. *Int J Dentistry Oral Sci*.](http://paperpile.com/b/0PCZRJ/qMQl9) <https://www.academia.edu/download/72981941/IJDOS_2377_8075_08_304.pdf>
15. [Nanoparticle-based therapeutic approaches for wound healing: a review of the state-of-the-art. (2023). *Materials Today Chemistry*, *27*, 101319.](http://paperpile.com/b/0PCZRJ/sl9eC)
16. [Padarthi, L. C., Anumula, L., Chinni, S. K., Sannapureddy, S., & Govula, K. (2023). Evaluation Composite Restoration Posterior Teeth Proanthocyanidin Pretreatment Liner Using Fédération Dentaire Internationale Criteria: Split-mouth Randomized Controlled Trial. *International Journal Prosthodontics Restorative Dentistry*, *13*(4), 191–200.](http://paperpile.com/b/0PCZRJ/1wEuS)
17. [Pranati, T., Ranjan, M., & Sandeep, A. H. (2021). Marginal adaptability custom made cast post made different techniques-a literature review. *Int J Dentistry Oral Sci*, *8*(8), 3954–3959.](http://paperpile.com/b/0PCZRJ/OrENx)
18. [Rajeshkumar, S., & Lakshmi, T. (2021). Biomedical potential of zinc oxide nanoparticles synthesized using plant extracts. *Int J Dent Oral Sci*, *8*, 4160–4163.](http://paperpile.com/b/0PCZRJ/T3iNA)
19. [Ramakrishnan, M., Shanmugam, R., Neeharika, S., Chokkattu, J. J., Thangavelu, L., & Khanna, N. (2023). Anti-inflammatory activity and cytotoxic effect of ginger and Rosemary-mediated titanium oxide nanoparticles-based dental varnish. *World Journal of Dentistry*, *14*(9), 761–765.](http://paperpile.com/b/0PCZRJ/tyPiE)
20. [Sakthi, S. (2021). Thymus vulgaris mediated selenium nanoparticles, characterization and its antimicrobial activity - an in vitro study. *International Journal of Dentistry and Oral Science*, 3516–3521.](http://paperpile.com/b/0PCZRJ/4Exwh)
21. [Shenoy, A., Rohinikumar, S., Maiti, S., Sivaswamy, V., & Rajaraman, V. (2023). Evaluation of Peri-Implant Crestal Bone Loss with Different Implant Systems, Primary Stability, Bone Density and Soft Tissue Thickness: A Retrospective Study. *Journal of Long-Term Effects of Medical Implants*, *33*(4), 53–58.](http://paperpile.com/b/0PCZRJ/BIFIV)
22. Saadh, M. J., Rasulova, I., Khalil, M., Farahim, F., Sârbu, I., Ciongradi, C. I. (2024). Natural killer cell-mediated immune surveillance in cancer: Role of tumor microenvironment. Pathology-Research and Practice, 254, 155120.
23. [Shenoy, N. D., & Maiti, S. (2023). Evaluation marginal fit CAD/CAM crowns using CBCT digital scanners. *Annals Dental Specialty*, *11*(3-2023), 37–44.](http://paperpile.com/b/0PCZRJ/YH5Ye)
24. [Shrivastava, S., Rajak, D. K., Joshi, T., Singh, D. K., & Mondal, D. P. (2024). Ceramic Matrix Composites: Classifications, Manufacturing, Properties, and Applications. *Ceramics*, *7*(2), 652–679.](http://paperpile.com/b/0PCZRJ/DQcsa)
25. [Sindhu, J. S., Maiti, S., & Nallaswamy, D. (2023). Comparative analysis on efficiency and accuracy of parallel confocal microscopy and three-dimensional in motion video with triangulation technology-based intraoral scanner under influence of moisture and mouth opening - A crossover clinical trial. *Journal of Indian Prosthodontic Society*, *23*(3), 234–243.](http://paperpile.com/b/0PCZRJ/QVVNG)
26. [Sindhu, S., Maiti, S., & Nallaswamy, D. (2023). Factors affecting accuracy intraoral scanners-a systematic review. *Annals Dental Specialty*, *11*(1-2023), 40–52.](http://paperpile.com/b/0PCZRJ/pQg6N)
27. [Singh, P., Maiti, S., & Shenoy, A. (2024). Comparative evaluation of bond strength and color stability of polyetheretherketone and zirconia layered with indirect composite before and after thermocycling: An in vitro study. *Journal of Indian Prosthodontic Society*, *24*(3), 252–258.](http://paperpile.com/b/0PCZRJ/HH0f3)
28. [Singh, P., Shenoy, A., Nallaswamy, D., & Maiti, S. (2024). Comparative Evaluation of Microbial Adhesion on Provisional Crowns Fabricated With Milled Polymethyl Methacrylate (PMMA) and Conventional Acrylic Resin: A Prospective Clinical Trial. *Cureus*, *16*(7), e64469.](http://paperpile.com/b/0PCZRJ/cKTNI)
29. [Sreenivasagan, S., Subramanian, A. K., Mohanraj, K. G., & Kumar, R. S. (2023). Assessment of toxicity of Green Synthesized Silver Nanoparticle-coated Titanium Mini-implants with Uncoated Mini-implants: Comparison in an Animal Model Study. *The Journal of Contemporary Dental Practice*, *24*(12), 944–950.](http://paperpile.com/b/0PCZRJ/XvRW0)
30. [Subramanian, E., Ravindran, V., & Jeevanandan, G. (2021). Comparison of amount of tooth reduction in primary first molar for stainless steel, zirconia and fibre-glass crowns–in-vitro study. *International Journal of Dentistry and Oral Science*, *8*(7), 3427–3430.](http://paperpile.com/b/0PCZRJ/wtMen)
31. [Surface transformed magnesium alloy: Investigating the in-vitro degradation consequences of rare-earth bioactive coatings. (2024). *Surface and Coatings Technology*, *493*, 131260.](http://paperpile.com/b/0PCZRJ/9SMFv)
32. [Synthesis and characterization of Nb5+ and Sm3+-doped 13–93 bioactive glass particles with improved photon transmission properties for advanced biomedical and dental applications. (2024). *Ceramics International*, *50*(17), 31211–31224.](http://paperpile.com/b/0PCZRJ/7gWo)
33. [Tiwari, A., & Jain, R. K. (2021). The effect of motivational and reminder therapy on the compliance of patients wearing fixed appliances. *Int J Dent Oral Sci*, *8*(7), 3303–3305.](http://paperpile.com/b/0PCZRJ/QygLp)
34. [Varghese, R., Maliael, M., & Subramanian, A. (2023). Antibacterial activity of nanoparticle-coated orthodontic archwires: A systematic review. *Journal of International Oral Health: JIOH*, *15*(1), 1.](http://paperpile.com/b/0PCZRJ/G5ZfD)