Gadolinium Infused Bioactive Glasses for Biomedical Application

Sriraj Gannamaneni1 , S.Suresh1,a)

1Sri Health solutions, Guntur, Andhra Pradesh, India

Corresponding Author: a)[yamschoci0322@gmail.com](mailto:yamschoci0322@gmail.com)

**Abstract:** Bioactive glass research benefits greatly from the addition of gadolinium as it marks a significant advancement in biomedical science. Various advanced materials give promising opportunities in multi-functional biomedical technology. Researchers are using gadolinium properties within bioactive matrices to develop improved therapeutic and diagnostic approaches in healthcare as well as biomedical engineering.The researchers began their study by developing bioactive glasses combined with gadolinium through a detailed synthesis method. Each material received tests through spectroscopic methods and microscopic observations to understand their chemical structure. The rat bone marrow-derived osteoblastic cells were used to explore both biocompatibility and bioactivity in various in vitro experiments. The evaluation included both cell line experiments and tests of ionic substances to verify the appropriateness of these substances for healthcare and biomedical applications.A bioactive glass formulation with gadolinium infusion showed better biocompatibility and bioactivity properties for innovative biomedical application use in medical diagnosis and treatment.Experimental research demonstrates that gadolinium-infused bioactive glasses are well-suited for biomedical purposes because of their improved bioactivity features and compatibility properties. Bioactive glasses containing gadolinium present promising prospects as therapeutic remedies and diagnostic equipment which demonstrate progress in healthcare innovation although additional research is required for effective practical use.

**Keywords**: Gadolinium, bioactive glasses, biomedical applications, bioactivity, biocompatibility, healthcare innovation, therapeutic materials, diagnostic tools.

# INTRODUCTION

Larry Hench invented bioactive glass in 1969. This glass is recognized as a novel chemical that causes a good reaction from the body and bone to the host tissue, which is frequently bone.[(Galiatsatos et al., 2021)](https://paperpile.com/c/rQfZGr/hfHEv) It served as the first bioactive substance..Because bioglass dissolves and forms an apatite coating on the surface of the host bone, it is thought to be osteoinductive[(Ajay, Suma, et al., 2022)](https://paperpile.com/c/rQfZGr/8YUpL) [(Katyal et al., 2021)](https://paperpile.com/c/rQfZGr/9IS12). The bioglass's dissolving byproducts, such as silica and calcium ions, encourage the cells to produce a bone matrix.[(Kaur, 2018)](https://paperpile.com/c/rQfZGr/76HJL)

The investigation of gadolinium-infused bioactive glasses is the focus of this study, which opens up new possibilities for biological applications [(Jabin et al., 2021)](https://paperpile.com/c/rQfZGr/ZUCc9)[(Balaji Ganesh S & Sugumar, 2021)](https://paperpile.com/c/rQfZGr/3xltR) [(Govindaraj & Dinesh, 2021)](https://paperpile.com/c/rQfZGr/YhgCL) . It has long been known that bioactive glasses can interact with biological tissues to encourage cell proliferation and support tissue regeneration. By combining therapeutic and diagnostic functions, gadolinium—a rare earth element with unique magnetic and radiographic properties—expands the usefulness of these glasses.[(Ylänen, 2017)](https://paperpile.com/c/rQfZGr/wb51q)

​​The regulated release kinetics of bioactive materials employed for in situ tissue regeneration or scaffolds for tissue engineering must match the sequence of cellular changes that occur during wound repair .[(Hench et al., 2012)](https://paperpile.com/c/rQfZGr/VYYPF) Ionic concentrations are too high to be useful if dissolving rates are too quick [(Tiwari & Jain, 2023)](https://paperpile.com/c/rQfZGr/1mONu)[(Graf et al., 2023)](https://paperpile.com/c/rQfZGr/GGn1t). The concentrations won't be high enough to promote cellular differentiation and proliferation if the rates are too sluggish. The two concepts of bioactive materials and resorbable materials have given rise to a new, third generation of biomaterials: bioactive materials are being made resorbable, and resorbable polymers are being made bioactive.Molecular changes of resorbable polymers and bioactive composite systems elicit specific interactions with cell integrins, which in turn regulate cell proliferation, differentiation, and the development and structure of extracellular matrix.[(Niinomi et al., 2015)](https://paperpile.com/c/rQfZGr/bXtBu)

# MATERIALS AND METHODS:

## Synthesis of Materials

The research utilized analytical grade reagents that operated without purification procedures. The chemicals 98% pure tetraethyl orthosilicate originated from Alfa Aesar whereas 88% orthophosphoric acid, 99% pure calcium nitrate and nitric acid (70%) originated from spectrum reagents and chemicals Pvt. Ltd. (Kerala, India) bought together with 98% pure sodium hydroxide obtained from Sisco research laboratory (Tamil Nadu, India). A sol-gel approach produced bioactive glass through the combination of SiO2 (45%), P2O5 (6%), CaO (24.5%), and Na2O (24.5%) along with 0.5%, 1.5%, and 2.5% copper nitrate in particular sections during the preparation process (Rafi et al., 2024). 5% Gadolinium was introduced at specific sodium locations. A mixture of tetraethyl orthosilicate together with orthophosphoric acid achieved complete dissolution through an hour of stirring in an ethanol and nitric acid and double-distilled water solution which subsequently produced a gel-like network. The solution containing sodium hydroxide and calcium nitrate received the pre-described ingredients. The sodium content in solution was replaced with 5 % Gadolinium (Tuluwengjiang et al., 2024). The experimental group included products labeled as 5% Gd-BG using Na2O (19.5 %). The solution received new precursors every thirty minutes following the complete dissolution of independent precursors (all precursors were measured through weight percentage). The reaction occurred at room temperature until the gel solution became completely formed. The researchers kept the samples in a drying condition at 80 °C throughout the complete night. A hot air oven dried all samples for 24 hours at 100 °C before exposing them to 600 °C heat for 3 hours to eliminate moisture content [(Chitra et al., 2020; S et al., 2022)](https://paperpile.com/c/rQfZGr/gqW78+Q6HH).

## Materials Characterization

characterization methods such as energy-dispersive X-ray spectroscopy (EDX), scanning electron microscopy (SEM), and X-ray diffraction (XRD) are utilized.

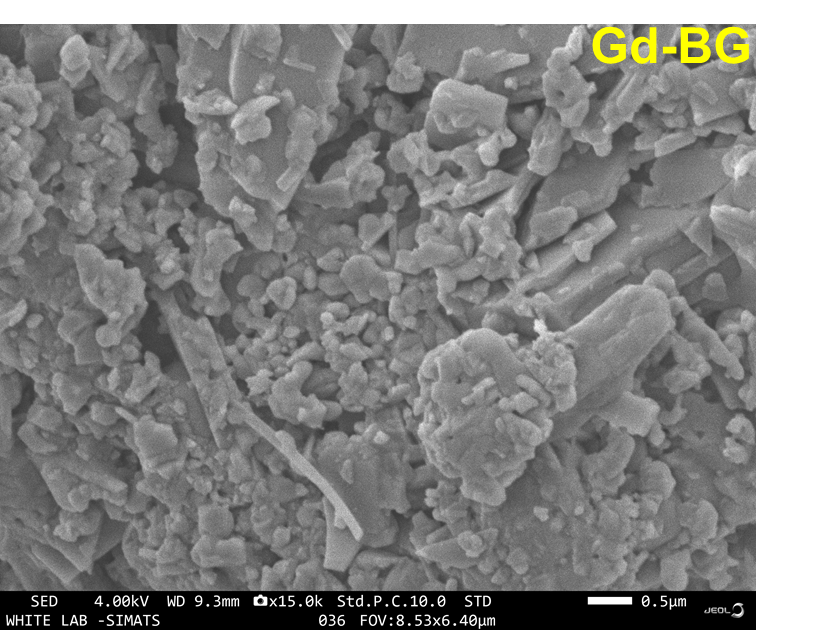
## Blood Compatibility

Viability and interactions between relevant cell lines are evaluated in vitro as part of biocompatibility testing. Hemocompatibility used based on the following protocol [(Shivalingam et al., 2020)](https://paperpile.com/c/rQfZGr/MNB5). Antimicrobial protocol was followed by Chitra et al., [(Chitra et al., 2020)](https://paperpile.com/c/rQfZGr/Q6HH)

# RESULTS AND DISCUSSION

## Morphological Analysis

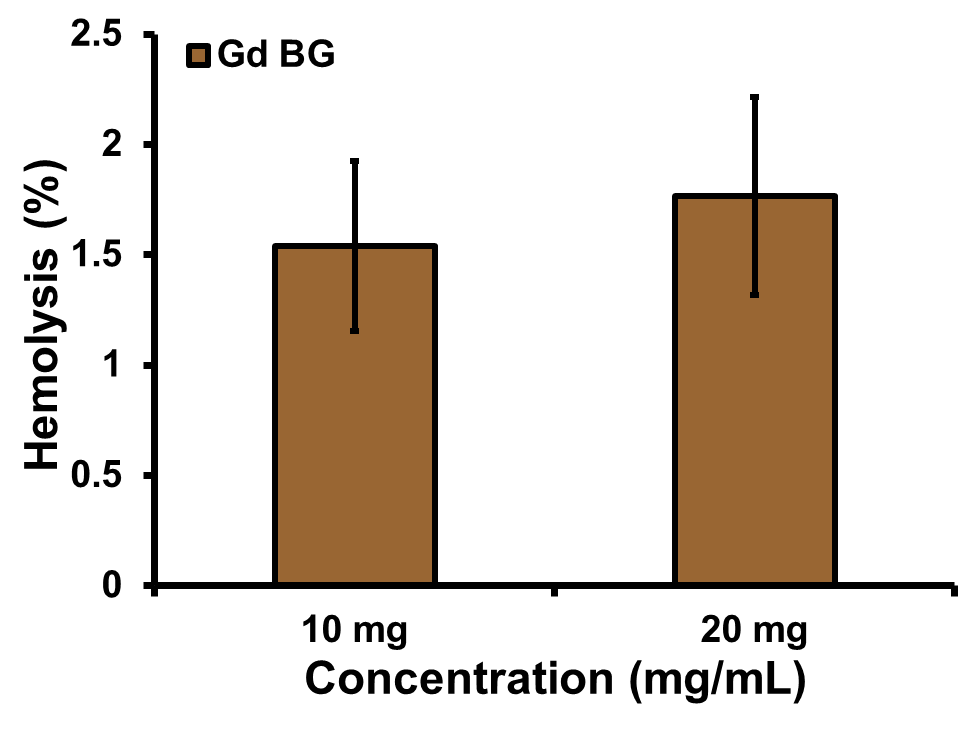
Small spherical and flake-like morphology was observed from Gd-bioglass. Flakes aggregated on top of that small globule like structure was perceptible.



**Fig:1** FE-SEM analysis of Gd-bioactive glass.

## Blood compatibility Analysis

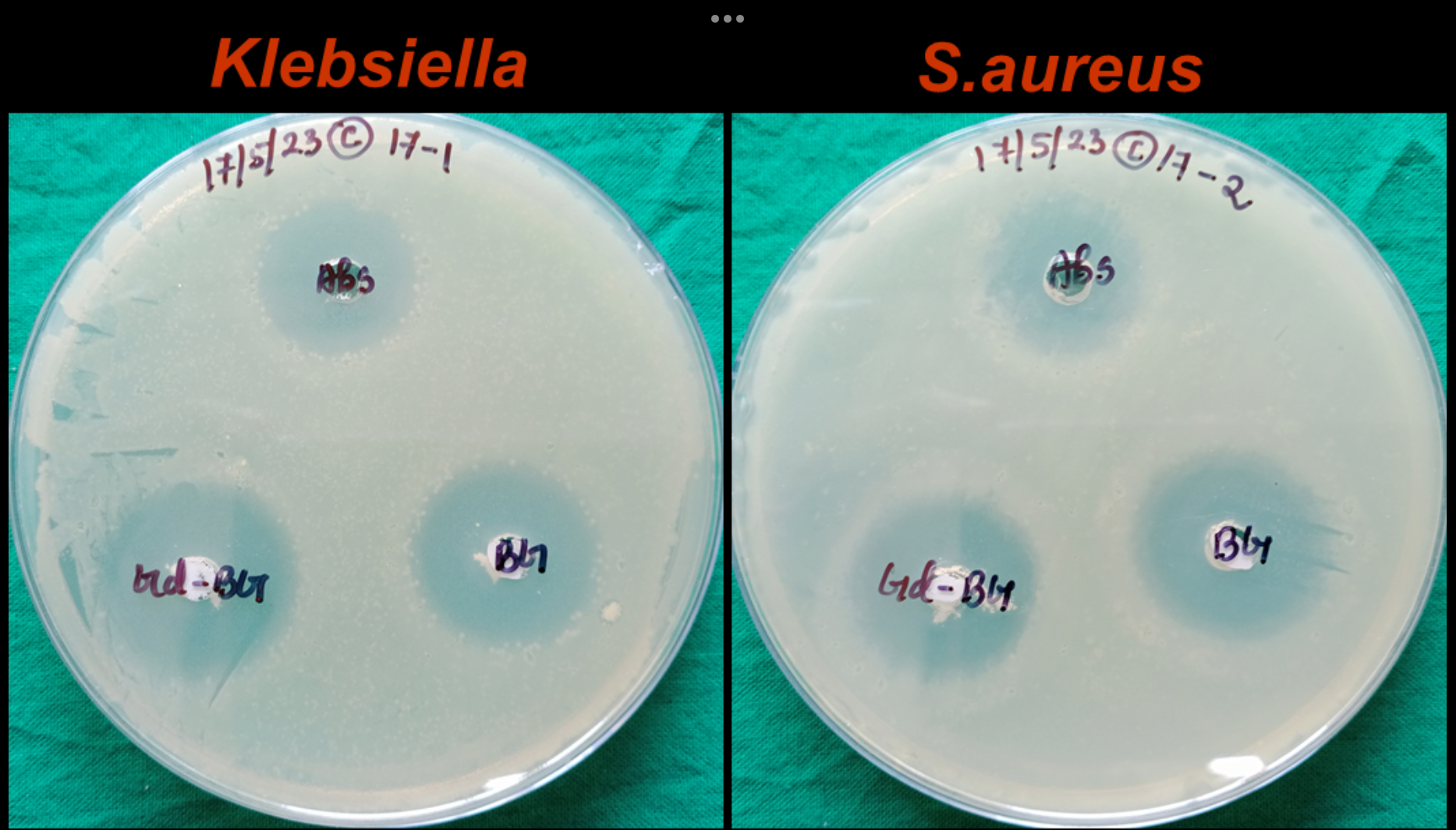
According to international standards up to 5% blood lysis is acceptable. In this direction here, we obtained very minimal lysis of below 2% and that is significantly acceptable for biomedical application.



**Fig:2** Blood compatibility of Gd-bioactive glass.

## Antibacterial Activity

Antibacterial activity of the synthesized materials was assessed against E. coli and S. mutans. Compared to antibiotics, significant inhibition of zones were perceptible with the treatment of bioactive glass. Elevated inhibitory action was observed in both the microbes and among which Gd-BG showed enhanced activity than pure bioglass.



**Fig:3** Zone of inhibition of Gd-bioactive glass.

Table 1: materials

|  |  |  |  |
| --- | --- | --- | --- |
| MATERIALS | ZONE OF INHIBITION | MATERIALS | ZONE OF INHIBITION |
| Ab | 19 | Ab | 15 |
| BG | 20 | BG | 19 |
| Gd-BG | 22 | Gd-BG | 22 |

Bioactive glasses integrate Gadolinium as a promising material for biomedical applications [(Harsha & Subramanian, 2022)](https://paperpile.com/c/rQfZGr/02cNH)[(Deepika et al., 2022)](https://paperpile.com/c/rQfZGr/ZJ0Yd)[(Solanki et al., 2022)](https://paperpile.com/c/rQfZGr/d9MTH). The combination creates stronger gadolinium potential for diagnosis and treatment because it unites the glass properties with gadolinium unique features[(Chidambaram et al., 2022)](https://paperpile.com/c/rQfZGr/VKeBI).[(Ajay, Sasikala, et al., 2022)](https://paperpile.com/c/rQfZGr/xXszd). The study needs to extensively investigate biocompatibility as the main priority to ensure the material remains safe for the biological system over lengthy periods. Research has evaluated many different oxide effects on bioactive glasses through various studies that analyzed samples against control specimens and commercial 45S5 Bioglass[(Ajay, Rakshagan, et al., 2022)](https://paperpile.com/c/rQfZGr/OpiSz). The research findings indicate positive effects on cell adhesion and cell proliferation together with cell spreading behavior alongside osteoblast differentiation.The growth of bioactive glasses into bone tissue engineering scaffolds represents an active area of research in this field.[(Dharman et al., 2021)](https://paperpile.com/c/rQfZGr/4ubyB) . Bioactive glass manufacturers are producing different magnesium-containing variations that match required mechanical and biological along with physicochemical requirements across multiple biomedical fields[(Sabarathinam & Madhulaxmi, 2021)](https://paperpile.com/c/rQfZGr/Td8H4)[(Sushanthi et al., 2021)](https://paperpile.com/c/rQfZGr/1qznv)[(Harsha et al., 2022)](https://paperpile.com/c/rQfZGr/FvOe8). The essential component of glass science consists of magnesium which regulates numerous glass functionality characteristics. The properties of bioactive glasses are influenced by magnesium oxide (MgO) as well as other oxides that exist and occur in various concentrations in individual glass compositions.[(Neha et al., 2021)](https://paperpile.com/c/rQfZGr/Du7JE)[(Maliael et al., 2021)](https://paperpile.com/c/rQfZGr/bEO6S)[(Lakshmi, 2021)](https://paperpile.com/c/rQfZGr/xxZ97). The evaluation of Gd-containing amorphous glass capacity to induce angiogenesis requires immediate investigation because recent research supports Gd-containing polycrystalline silicates in promoting vascularization in live subjects. [(“Silicate Bioceramics Induce Angiogenesis during Bone Regeneration,” 2012)](https://paperpile.com/c/rQfZGr/Id41S)

# CONCLUSION

Gadolinium integration into bioactive glasses creates significant potential uses for biological requirements which drive advances in both imaging and therapeutic practices. Investigative studies need to address the concerns related to gadolinium release as well as the long-term effects on human tissue and material compatibility. The material shows better application through its tissue interactions and capability to deliver tailored medication. The benefits of gadolinium-infused bioactive glasses depend on finding equilibrium between their safety measures and effectiveness levels within evolving medical technology fields. These materials need both sustained study and development work to fulfill their biological potential for substantial long-term effects.

# REFERENCES

1. [Ajay, R., Rakshagan, V., Queenalice, A., Vinothkumar, S., Ravivarman, C., & Saravanadinesh, P. (2022). Effect of triazine comonomer substitution on the structure and glass transition temperature of monomethacrylate-based resin polymer: An in vitro study. The Journal of Contemporary Dental Practice, 23(2), 202–207.](http://paperpile.com/b/rQfZGr/OpiSz)
2. [Ajay, R., Sasikala, R., Rakshagan, V., Raghunathan, J., LalithaManohari, V., & Baburajan, K. (2022). Evaluation of cytocompatibility of thermopolymerized denture base copolymer containing a novel ring-opening oxaspiro comonomer. World Journal of Dentistry, 13(2), 127–132.](http://paperpile.com/b/rQfZGr/xXszd)
3. [Ajay, R., Suma, K., Sasikala, R., Rakshagan, V., Baburajan, K., & Kalarani, G. (2022). Evaluation of linear dimensional stability of monomethacrylate-based dental polymer containing a novel tricyclic diacrylate cross-linker using a novel surface-level index technique. World Journal of Dentistry, 13(6), 568–573.](http://paperpile.com/b/rQfZGr/8YUpL)
4. [Balaji Ganesh S, & Sugumar, K. (2021). Internet of Things—A novel innovation in dentistry. Journal of Advanced Oral Research, 12(1), 42–48.](http://paperpile.com/b/rQfZGr/3xltR)
5. [Chidambaram, S. R., George, A. M., Muralidharan, N. P., Prasanna Arvind, T. R., Subramanian, A., & Rahaman, F. (2022). Current overview for chemical disinfection of dental impressions and models based on its criteria of usage: A microbiological study. Indian Journal of Dental Research : Official Publication of Indian Society for Dental Research, 33(1), 30–36.](http://paperpile.com/b/rQfZGr/VKeBI)
6. [Chitra, S., Bargavi, P., Balasubramaniam, M., Chandran, R. R., & Balakumar, S. (2020). Impact of copper on in-vitro biomineralization, drug release efficacy and antimicrobial properties of bioactive glasses. Materials Science & Engineering. C, Materials for Biological Applications, 109, 110598.](http://paperpile.com/b/rQfZGr/Q6HH)
7. [Deepika, B. A., Ramamurthy, J., Girija, S., & Jayakumar, N. D. (2022). Evaluation of the antimicrobial effect of Ocimum sanctum L. oral gel against anaerobic oral microbes: An in vitro study. World Journal of Dentistry, 13(S1), S23–S27.](http://paperpile.com/b/rQfZGr/ZJ0Yd)
8. [Dharman, S., Kumar, R., Shanmugasundaram, K. (2021). Ecofriendly Synthesis, Characterisation and Antibacterial Activity Of Curcumin Mediated Silver Nanoparticles. International Journal of Dentistry and Oral Science, 2314–2318.](http://paperpile.com/b/rQfZGr/4ubyB)
9. [Galiatsatos, P., Galiatsatos, A., & Phillipatos, G. (2021). Characterization of the Interface of Heat-pressed Glass-Ceramic Masses on Metal Support Cr-Co in Metal-Ceramic Prosthetic Restorations. The Journal of Contemporary Dental Practice, 22(4), 335–341.](http://paperpile.com/b/rQfZGr/hfHEv)
10. [Govindaraj, A., & Dinesh, S. P. S. (2021). Effect of chlorhexidine varnish and fluoride varnish on White Spot Lesions in orthodontic patients- a systematic review. The Open Dentistry Journal, 15(1), 151–159.](http://paperpile.com/b/rQfZGr/YhgCL)
11. [Graf, S., Thakkar, D., Hansa, I., Pandian, S. M., & Adel, S. M. (2023). 3D metal printing in orthodontics current trends, biomaterials, workflows and clinical implications. Seminars in Orthodontics. https://doi.org/](http://paperpile.com/b/rQfZGr/GGn1t)[10.1053/j.sodo.2023.01.001](http://dx.doi.org/10.1053/j.sodo.2023.01.001)
12. [Harsha, L., Navaneethan, R., Acid, T., & Acid, C. A.-A. (2022). CITRIC ACID-AN VITRO STUDY. International Journal Clinical Dentistry, 15(3), 413–419.](http://paperpile.com/b/rQfZGr/FvOe8)
13. [Harsha, L., & Subramanian, A. K. (2022). Comparative assessment of pH and degree of surface roughness of enamel when etched with five commercially available etchants: An in vitro study. The Journal of Contemporary Dental Practice, 23(2), 181–185.](http://paperpile.com/b/rQfZGr/02cNH)
14. [Hench, L. L., Fenn, M. B., & Jones, J. R. (2012). New Materials and Technologies for Healthcare. World Scientific.](http://paperpile.com/b/rQfZGr/VYYPF)
15. [Jabin, Z., Nasim, I., Vishnu Priya, V., & Agarwal, N. (2021). Quantitative Analysis and Effect of SDF, APF, NaF on Demineralized Human Primary Enamel Using SEM, XRD, and FTIR. International Journal of Clinical Pediatric Dentistry, 14(4), 537–541.](http://paperpile.com/b/rQfZGr/ZUCc9)
16. [Katyal, D., Subramanian, A. K., Venugopal, A., & Marya, A. (2021). Assessment of Wettability and Contact Angle of Bonding Agent with Enamel Surface Etched by Five Commercially Available Etchants: An In Vitro Study. International Journal of Dentistry, 2021, 9457553.](http://paperpile.com/b/rQfZGr/9IS12)
17. [Kaur, G. (2018). Biomedical, Therapeutic and Clinical Applications of Bioactive Glasses. Woodhead Publishing.](http://paperpile.com/b/rQfZGr/76HJL)
18. [Lakshmi, T. (2021). Medicinal value oral health aspects acacia catechu-an update. International Journal Dentistry Oral ScienceVolume, 8, 1399–1401J.](http://paperpile.com/b/rQfZGr/xxZ97)
19. [Maliael, M. T., Subramanian, A. K., & Srirengalakshmi. (2021). Effectiveness of a fluoride-releasing orthodontic primer in reducing demineralization around brackets – a systematic review. Orthodontic Waves (English Ed.), 80(4), 218–223.](http://paperpile.com/b/rQfZGr/bEO6S)
20. [Neha, N., Maiti, S., & Jessy, P. (2021). Adhesion microflora role denitrifies colour stability provisional crowns: in-vitro study. Int J Dentistry Oral Sci, 8(8), 3805–3809.](http://paperpile.com/b/rQfZGr/Du7JE)
21. [Niinomi, M., Narushima, T., & Nakai, M. (2015). Advances in Metallic Biomaterials: Processing and Applications. Springer.](http://paperpile.com/b/rQfZGr/bXtBu)
22. Rafi, D. M., Lakshmi, T. V., Shirley, C. P., Ravivarman, G., & Senthilkumar, G. (2024, April). Improving Prostate Cancer Diagnosis with Weakly Supervised Learning and Radiology-Confirmed Negative MRI Data. In 2024 International Conference on Inventive Computation Technologies (ICICT) (pp. 1183-1188). IEEE.
23. [Sabarathinam, J., & Madhulaxmi, R. (2021). Development anti inflammatory antimicrobial silver nanoparticles coated suture materials. Int J Dentistry Oral Sci, 8(3), 2006–2013.](http://paperpile.com/b/rQfZGr/Td8H4)
24. [S, C., Chandran, R., R, R., D, D., & S, B. (2022). Unravelling the effects of ibuprofen-acetaminophen infused copper-bioglass towards the creation of root canal sealant. Biomedical Materials (Bristol, England), 17(3). https://doi.org/](http://paperpile.com/b/rQfZGr/gqW78)[10.1088/1748-605X/ac5b83](http://dx.doi.org/10.1088/1748-605X/ac5b83)
25. [Shivalingam, C., Purushothaman, B., R, R. C., & Subramanium, B. (2020). Thermal treatment stimulus on erythrocyte compatibility and hemostatic behavior of one-dimensional bioactive nanostructures. Journal of Biomedical Materials Research. Part A, 108(11), 2277–2290.](http://paperpile.com/b/rQfZGr/MNB5)
26. [Silicate bioceramics induce angiogenesis during bone regeneration. (2012). Acta Biomaterialia, 8(1), 341–349.](http://paperpile.com/b/rQfZGr/Id41S)
27. [Solanki, L., Shantha Sundari, K. K., Muralidharan, N. P., & Jain, R. (2022). Antimicrobial effect of novel gold nanoparticle oral rinse in subjects undergoing orthodontic treatment: An ex-vivo study. Journal of International Oral Health: JIOH, 14(1), 47.](http://paperpile.com/b/rQfZGr/d9MTH)
28. [Sushanthi, S., Doraikannan, S., Indiran, M., & Rathinavelu, P. (2021). Rajeshkumar S. Vernonia Amygdalina. 3330–3334.](http://paperpile.com/b/rQfZGr/1qznv)
29. [Tiwari, A., & Jain, R. K. (2023). Comparative evaluation of White Spot lesion incidence between NovaMin, probiotic, and fluoride containing dentifrices during orthodontic treatment using laser fluorescence - A prospective randomized controlled clinical trial. Clinical and Investigative Orthodontics, 1–8.](http://paperpile.com/b/rQfZGr/1mONu)
30. Tuluwengjiang, G., Rasulova, I., Ahmed, S., Kiasari, B. A., Sârbu, I., Ciongradi, C. I., & Samaniego, S. S. C. (2024). Dendritic cell-derived exosomes (Dex): Underlying the role of exosomes derived from diverse DC subtypes in cancer pathogenesis. Pathology-Research and Practice, 254, 155097.
31. [Ylänen, H. (2017). Bioactive Glasses: Materials, Properties and Applications. Woodhead Publishing.](http://paperpile.com/b/rQfZGr/wb51q)