Exploration of Yttrium Infused Bioactive Glasses for Bone Regeneration

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**Abstract**:​​ Bioactive glasses (BGs) have gained significant attention in bone tissue engineering due to their exceptional bioactivity, biocompatibility, and osteoconductive properties. The incorporation of yttrium (Y) into bioactive glasses presents a promising strategy to enhance their mechanical strength, biological performance, and therapeutic potential. Yttrium, a rare earth element, is known for its ability to stabilize glass structures, improve radiopacity, and exhibit antimicrobial effects, making it a valuable dopant for biomedical applications. This review explores the role of yttrium-infused bioactive glasses (Y-BGs) in bone regeneration, focusing on their structural, physicochemical, and biological properties. The addition of yttrium enhances the mechanical resilience of BGs, supports controlled ion release, and promotes osteogenesis while potentially reducing bacterial colonization. Moreover, Y-BGs have demonstrated the ability to stimulate cellular responses, including increased osteoblast proliferation and differentiation, as well as angiogenesis, crucial for bone repair. Recent in vitro and in vivo studies indicate that Y-BGs could serve as superior scaffolds for bone defect healing, offering a multifunctional approach to bone regeneration. Future research should focus on optimizing yttrium concentrations to balance bioactivity and cytocompatibility, ensuring their clinical translation. The development of Y-BGs represents a significant advancement in biomaterials for orthopedic and maxillofacial applications.

**Keywords**: Bioactive glass, yttrium, bone regeneration, osteogenesis, biomaterials, scaffolds

# Introduction

Bone regeneration is a complex biological process aimed at restoring the structure and function of lost or damaged bone tissue. Over the last few decades, advances in materials science have introduced a range of bioactive materials for bone regeneration, with a particular focus on bioactive glass (BG) due to its osteoinductive properties[(Fred et al., 2024)](https://paperpile.com/c/NmWI7W/2aSa)[(Ajay et al., 2023; Chokkattu et al., 2023; Padarthi et al., 2023)](https://paperpile.com/c/NmWI7W/2fx3D+cTe7c+Zs5kL)[(Dharman et al., 2023; S. Sindhu et al., 2023; Sreenivasagan et al., 2023)](https://paperpile.com/c/NmWI7W/pRINm+egF5o+zUCp9)[(Ramakrishnan et al., 2023; Shenoy & Maiti, 2023; J. S. Sindhu et al., 2023)](https://paperpile.com/c/NmWI7W/TrODC+T62Tx+3dZWU)[(Kasabwala et al., 2021; Rajeshkumar & Lakshmi, 2021; Varghese et al., 2023)](https://paperpile.com/c/NmWI7W/HueiM+8D5Se+aBhtA).The unique ability of bioactive glass to bond with both bone and soft tissues has made it a preferred material for regenerative applications. Traditional BG, such as 45S5, is known to release ions that enhance osteoblast activity, facilitate hydroxyapatite formation, and promote cellular differentiation, which are all essential for bone healing and integration[(Fukushina et al., 2023)](https://paperpile.com/c/NmWI7W/qUNz). However, challenges such as the limited mechanical strength of bioactive glass and the need to tailor its degradation profile for specific clinical applications [(“The Effect of Tricalcium Silicate Incorporation on Bioactivity, Injectability, and Mechanical Properties of Calcium Sulfate/bioactive Glass Bone Cement,” 2023)](https://paperpile.com/c/NmWI7W/vf6R) highlight a gap in optimizing bioactive glass for widespread use in bone regeneration.Recent innovations in bioactive glass technology have focused on doping BG with various metal ions to enhance its bioactivity, antibacterial properties, and mechanical strength. Metals like zinc, silver, copper, and strontium have been explored for their ability to modify the physicochemical properties of bioactive glass[(Al-Ghamdi et al., 2023)](https://paperpile.com/c/NmWI7W/UWKX). Among these, the incorporation of yttrium ions (Y³⁺) has gained attention due to their potential to improve both the biological and mechanical properties of bioactive glass. Yttrium is known for its role in enhancing osteogenesis and has been shown to support cellular activities crucial for bone regeneration, including promoting the proliferation and differentiation of osteoblasts [(Smolyak et al., 2023)](https://paperpile.com/c/NmWI7W/92oN). Additionally, yttrium-doped materials are recognized for their ability to increase the mechanical stability of scaffolds, which is critical in load-bearing applications[(Deliormanlı et al., 2024)](https://paperpile.com/c/NmWI7W/Y7MA)[(Keerthana & Ramesh, 2021; Murugesan, 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/NmWI7W/PJl5T+xBBdO+F7JEp)[(Keerthana & Ramesh, 2021; Murugesan, 2021; Subramanian et al., 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/NmWI7W/PJl5T+xBBdO+F7JEp+EdxjP)[(Evaluation Composite Restoration Posterior Teeth Proanthocyanidin Pretreatment Liner Using Fédération Dentaire Internationale Criteria: Split-Mouth Randomized Controlled Trial, n.d.; Pranati et al., 2021; Sakthi 2021)](https://paperpile.com/c/NmWI7W/xg4WG+rQTNX+9kLrH)[(G. & Ganapathy, 2022; Kumar & Ramesh, 2021)](https://paperpile.com/c/NmWI7W/nXTbl+AZA8x))Despite these promising developments, a critical gap exists in fully understanding the interaction mechanisms between yttrium ions and bone tissues. While preliminary studies suggest that yttrium has osteogenic potential, there is a need for deeper investigation into how yttrium-doped bioactive glass influences the cellular microenvironment, specifically the signaling pathways that mediate bone formation and resorption. Moreover, yttrium’s influence on angiogenesis [(Chawla et al., 2023)](https://paperpile.com/c/NmWI7W/vPN6), an essential process for effective bone regeneration—remains underexplored. This knowledge gap hinders the full exploitation of yttrium-infused bioactive glass in clinical settings, particularly in complex bone defects where vascularization plays a crucial role in regeneration (Almatrafi et al., 2024).To address these challenges, we aim to focus on developing yttrium-infused bioactive glass with optimized ion release profiles.By addressing the limitations of conventional bioactive glass and filling critical knowledge gaps in understanding yttrium's role in osteogenesis and angiogenesis, this novel material could offer significant advancements in the treatment of bone defects(Saadh et al., 2024).

# Materials and Methods

## Materials

All chemicals used in this study were of analytical grade and were applied without any further purification. Tetraethyl orthosilicate (TEOS), with a molecular weight of 208.33 g/mol, was sourced from Sigma-Aldrich (United States) to act as the silica precursor. Among the chemical compounds, calcium fluoride (CaF₂), with a purity of 97% and a molecular weight of 78.08 g/mol, was obtained from SRL (India). Silver nitrate (AgNO₃), also acquired from SRL (India), has a molecular weight of 169.87 g/mol and a purity of 99.9%. Sodium nitrate (NaNO₃), with a molecular weight of 84.99 g/mol, phosphoric acid (H₃PO₄) with a molecular weight of 98 g/mol and a purity of 85%, and calcium nitrate (Ca(NO₃)₂), with a molecular weight of 236.15 g/mol, were all purchased from Merck (India).

## Synthesis of bioglass

For the objective of alveolar bone regeneration in this study, Yttrium-infused bioglass was created. SiO2 (45%),P2O5 (6%), CaNO3(24%), NaNO3 (24.5%),Yttrium (2.5%), 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 tools

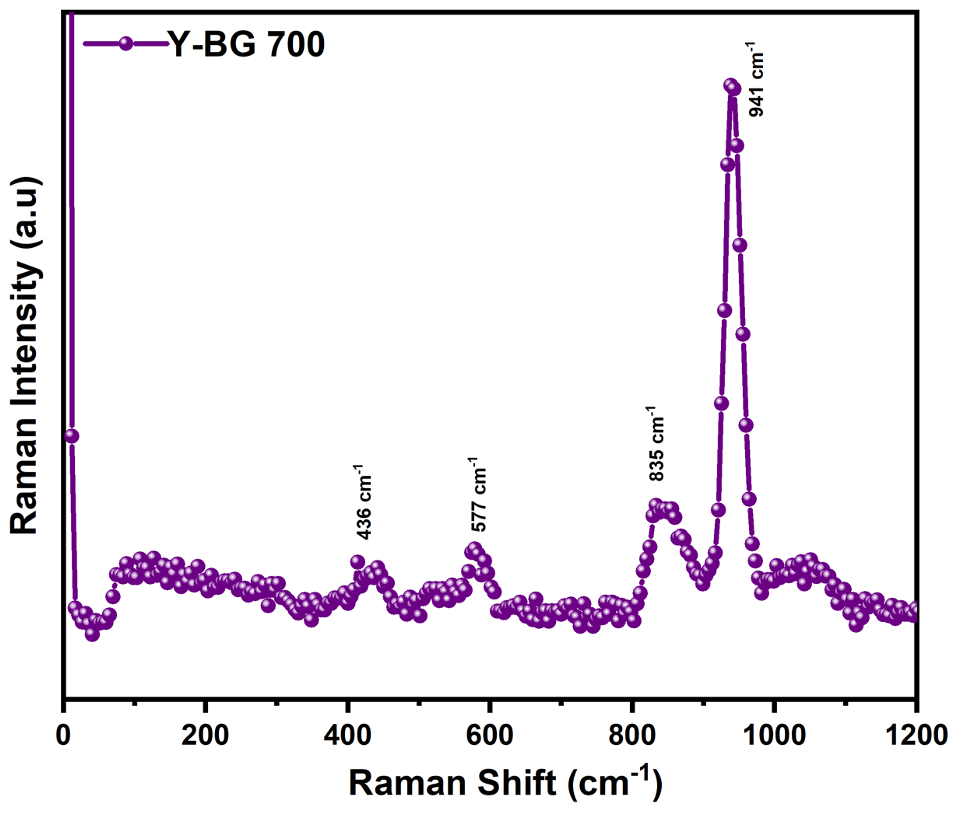
Scanning electron microscopy (SEM), X-ray diffraction (XRD), Raman spectra, Fourier-transform infrared spectroscopy (FT-IR), Blood compatibility test were employed to analyze the morphology, crystal structure, functional group and biocompatibility features in the bioglass infused with yttrium after the cooling process.

# Results

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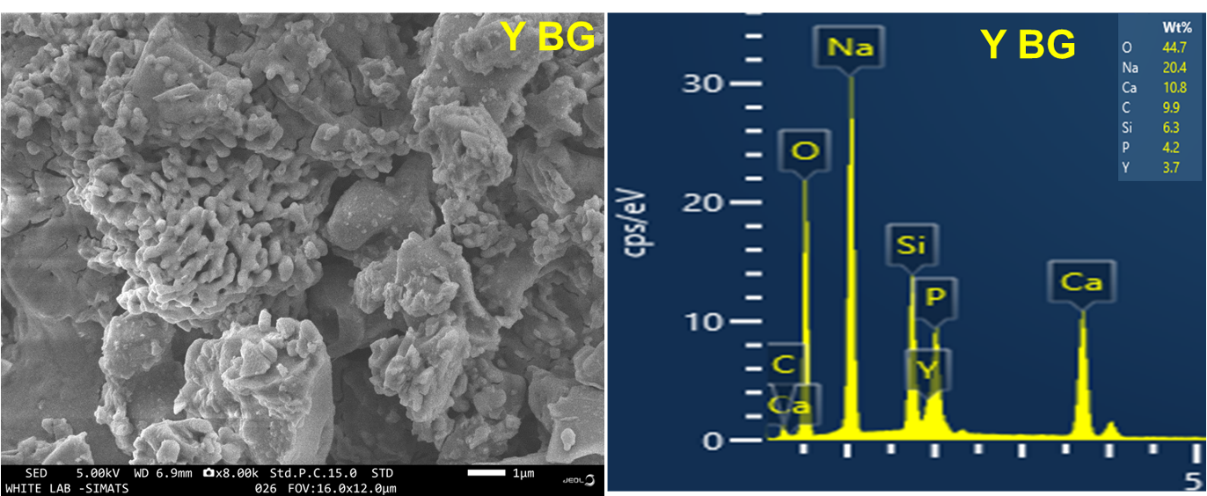
**Figure 1** represents the XRD patterns of yttrium infused bioglass

## RAMAN SPECTRUM



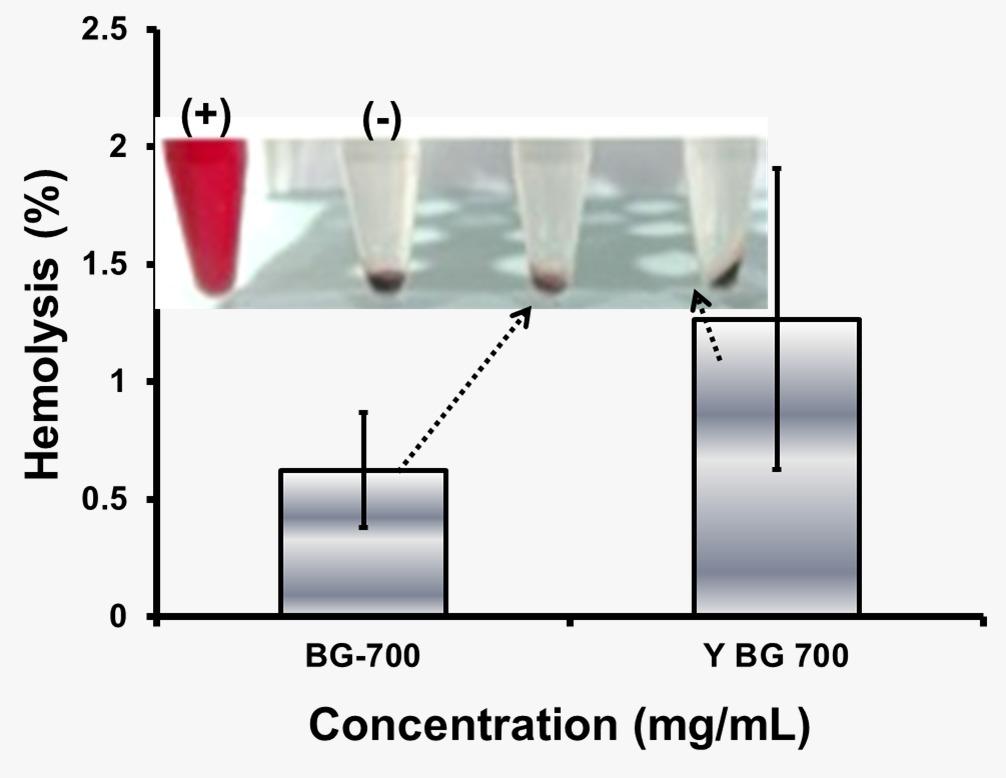
**Figure 2** represents the raman spectrum of yttrium infused bioglass

## FE-SEM and EDS



**Figure 3** represents the FE-SEM and EDS of yttrium infused bioglass

## BLOOD COMPATIBILITY



**Figure 4** represents the blood compatibility test of yttrium infused bioglass

# Discussion

Alveolar bone regeneration is essential for dental health, particularly in cases where bone loss occurs due to trauma, infection, or tooth extraction. Alveolar bone serves as the structural support for teeth, and its regeneration is crucial for the successful placement of dental implants and the restoration of function[(Li et al., 2023)](https://paperpile.com/c/NmWI7W/Z75i). Bioglass releases therapeutic ions that stimulate cellular responses, enhancing bone regeneration. Yttrium-infused bioactive glasses represent a recent advancement in this field, with yttrium playing a role in improving the bioactivity and mechanical properties of the glass[(“Bioglass and Nano Bioglass: A next-Generation Biomaterial for Therapeutic and Regenerative Medicine Applications,” 2024)](https://paperpile.com/c/NmWI7W/xWRF).In comparison to other studies using different dopants in bioactive glasses, such as strontium, zinc, or magnesium, yttrium-infused bioactive glasses show distinct advantages. Strontium has been widely used for its ability to enhance bone formation and reduce resorption[(Silva et al., 2023)](https://paperpile.com/c/NmWI7W/eg7E). while zinc contributes to enzyme regulation and bone mineralization[(Rajzer et al., 2023)](https://paperpile.com/c/NmWI7W/a9Q8). Magnesium, on the other hand, is crucial for bone metabolism and cell proliferation[(Gavinho et al., 2023)](https://paperpile.com/c/NmWI7W/dJIG). However, yttrium offers a unique combination of benefits, such as enhanced mechanical strength and the ability to release ions that promote bone tissue healing, while also exhibiting some radioprotective properties not found in the other dopants. Recent studies have shown that yttrium can improve the overall performance of bioactive glasses by promoting osteoblast differentiation and enhancing new bone formation, making it a competitive option for alveolar bone regeneration in comparison to traditional materials like strontium or magnesium-infused glasses[(Say et al., 2024)](https://paperpile.com/c/NmWI7W/RaUb).Despite the promising results, there are limitations to the use of yttrium-infused bioactive glasses. One major challenge is the need for precise control over the release of yttrium ions to avoid potential cytotoxicity at high concentrations. Additionally, while the initial studies show positive outcomes, long-term in vivo studies are required to fully understand the biocompatibility and degradation behavior of these glasses in complex biological environments. Moreover, there are concerns regarding the potential accumulation of yttrium ions in the body, which might pose risks for certain patient populations.In terms of future scope, further research is needed to optimize the yttrium concentration within bioactive glass formulations, ensuring a balance between bioactivity and safety. Investigating the combination of yttrium with other therapeutic ions, such as calcium or silicon, could offer synergistic effects, enhancing the osteoconductive and angiogenic properties of bioactive glasses.

# Conclusion

Yttrium-infused bioactive glasses show promising potential for bone regeneration due to their enhanced biocompatibility, osteoconductive properties, and ability to promote cell proliferation. The incorporation of yttrium improves the material's mechanical strength and bioactivity. These glasses also exhibit effective antibacterial properties, contributing to better healing outcomes. Future research should focus on optimizing yttrium concentrations for improved clinical performance. Overall, yttrium-infused bioactive glasses represent a valuable advancement in bone tissue engineering.

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