Strontium-Infused Bioglass for Better Mineralisation and Osteointegration Properties

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**Abstract:** Studies demonstrate widespread interest in bioactive glass coatings for medical implants because Strontium shows beneficial effects on bone cell growth so it is administered to patients in strontium ranelate form when they have osteoporosis. A broad selection of bio-glasses based on silicate borate and phosphate systems doped with strontium in different manufacturing forms have been produced and studied for use in advanced therapeutic techniques that aim to handle bone irregularities and injuries.This is an in vitro study where there is a comparative analysis done between pure and strontium induced bioglass for bone tissue regeneration. TEOS and ethanol are taken , TOS is dissolved in this solution and HNO3 is added to speed up the gelation after which P2O5 and calcium nitrate are added along with sodium nitrate is added along with a 30 min interval between them. Bioglass is hence formed to which strontium is added to induce strontium bioglass. The composition is discussed further in the article. In vitro investigations have demonstrated the physicochemical properties of bioglass , their composition and the bioactive properties of strontium bioglass. Further the comparison between normal bioglass and strontium induced bioglass was made to observe the enhancement of the properties in the latter. In conclusion Sr-infused bioactive glasses represent a remarkable advancement in the field of biomaterials for bone regeneration. The incorporation of strontium into bioactive glasses enhances their mineralization and osteo integration properties, making them highly desirable for a range of biomedical applications.

**Keywords:**  Bioglass , strontium induced bioglass , bone tissue engineering , osseointegration , bone repair , mineralisation

# INTRODUCTION

Ceramic materials specifically created for use as dental and medical implants are known as bioceramics. They are often utilized to replace the body's hard tissues, like teeth and bone. Bioceramics can be classified as "bioinert" or "bioactive" based on their interaction with host tissue, with bioactive ceramics being either resorbable or non-resorbable. Bioactive ceramics interact with the body in a way that eventually leads to tissue attachment and integration into the body. Example : calcium phosphate based bioceramic. The only interaction that bioinert ceramics have with the body's surroundings is the first "fibrous tissue" response , example : alumina and zirconia. [(“Bioceramics: Past, Present and for the Future,” 2008; Harsha & Subramanian, 2022; Kaur, 2017)](https://paperpile.com/c/g9JGZj/AKma+QVsf+Ua16).

Bioglass is a group of reactive materials that can bond to bone, and it has been used to create scaffolds for bone repair and regeneration. [(“Bioactive Glass,” 2008; Deepika et al., 2022)](https://paperpile.com/c/g9JGZj/AU5m+uU2F). Bioactive glasses were discovered by Larry Hench, a Research Professor in the Department of Materials Science and Engineering at the University of Florida and then Director of the Bioglass Research Centre at the same University. [(Baino et al., 2018; Solanki et al., 2022)](https://paperpile.com/c/g9JGZj/6MJr+sT5d) The primary use of bioactive bioceramics is in the treatment of bone deficiencies, which can result from illness, trauma, or congenital abnormalities such osteoporosis or tumor excision. [(Ajay, Rakshagan, et al., 2022; Rajeshkumar, 2021; “Review of Bioactive Glass: From Hench to Hybrids,” 2013)](https://paperpile.com/c/g9JGZj/CLhk+aJO0+RfCF) . In the 80’s it was discovered that these bioglasses can be used to stimulate osteogenesis and hence led to tissue regeneration. It was also discovered that the ions dissolved in these glasses behave like growth factors which provide signals to the cells. [(Ajay, Sasikala, et al., 2022; Hench & Jones, 2015)](https://paperpile.com/c/g9JGZj/Cukx+XpdI). Glass-ceramic materials have two distinct benefits over other materials. The first is that because they are formed from a parent glass that can be moulded using a variety of well-known affordable procedures , GCs can be obtained in highly complicated shapes . The second significant benefit is that GCs often have a very fine microstructure with few or no residual pores, leading to better mechanical characteristics. GCs have an unusual combination of qualities, including biological, electrical, thermal, and mechanical capabilities. [(Ajay, Suma, et al., 2022; Fernandes et al., 2018; Hench & Jones, 2015)](https://paperpile.com/c/g9JGZj/Cukx+6UGc+h1Xa). Strontium is an element that has gained attention for its beneficial effects on bone health. Studies have shown that strontium can enhance osteogenesis, stimulate bone formation, and improve bone mineral density. [(“Early Osseointegration of a Strontium Containing Glass Ceramic in a Rabbit Model,” 2013; Katyal et al., 2021)](https://paperpile.com/c/g9JGZj/7obr+Y8fT). Strontium (Sr) has been used for the treatment of osteoporosis in the form of strontium ranelate (SrR) for several decades, and it has been found to improve bone density by enhancing osteoblast activity and inhibiting osteoclast function.[(Maliael et al., 2021; Maiti, 2021)](https://paperpile.com/c/g9JGZj/83fs+Crsl) In addition, strontium has been used in toothpaste to repair decayed teeth due to its restorative capability.[(Jabin et al., 2021)](https://paperpile.com/c/g9JGZj/iMzD) Strontium-containing bioactive glasses have also been developed for bone tissue engineering, and they have been found to have promising applications in bone repair and regeneration . The incorporation of Sr2+ ions in these glasses can enhance the density of bone tissue, resulting in a significant reduction in fracture risk in mammals. [(Balaji Ganesh S & Sugumar, 2021; Fernandes et al., 2018)](https://paperpile.com/c/g9JGZj/6UGc+QvHK).

In this study we aim to investigate the bioceramic for their tissue regenerative properties and to further conduct a comparative analysis of pure and strontium infused bioglass by investigation of structural and in vitro biological properties of the following materials for their regenerative application.[(Dharman, 2021; Ramamurthy, 2021; Tiwari & Jain, 2023)](https://paperpile.com/c/g9JGZj/1dWz+nQ0o+tsrx) Further, The fundamental aspects of Sr-doped glasses, such as their physicochemical qualities and reactivity when in contact with biological fluids, are described and contrasted. The crystal structure and the other physicochemical structure and their reaction to biological fluids along with its application has been discussed further in the article.

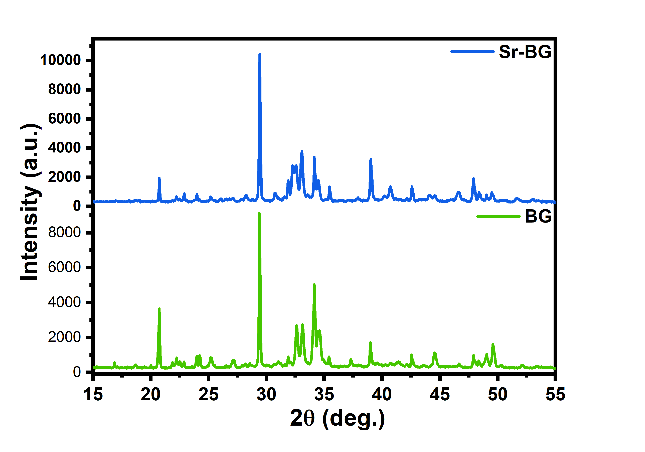
## MATERIALS AND METHODS

The study employed reagents and chemicals in analytical grade form that required no purification prior to use. 98% pure tetraethyl orthosilicate was acquired from Alfa Aesar and orthophosphoric acid at 88% purity as well as 99% pure strontium nitrate and nitric acid (70%) from spectrum reagents and chemicals Pvt. Ltd. (Kerala, India) while sodium hydroxide with 98% pure was obtained from Sisco research laboratory (Tamil Nadu, India). Bioactive glass was prepared through sol-gel method which incorporated SiO2 (45%), P2O5 (6%), CaO (24.5%), Na2O (24.5%). The fabrication process included Na2O reduction by integrating 0.5%, 1.5% and 2.5% Sr(NO3)2 content. Sodium concentration was reduced by adding 1.5% strontium nitrate in specific solution sites during preparation. The reaction process involved dissolving all components including tetraethyl orthosilicate and orthophosphoric acid with ethanol and nitric acid and double-distilled water through one-hour stirring which resulted in gel formation. A solution received strontium nitrate together with sodium hydroxide. The bioglass has different compositions with 5% Sr-BG having Na2O (19.5%) . All the precursors were added individually to the solution through weight percentages during 30-minute periods. The research took place at room temperature until a total gel structure developed. The drying process occurred at 80 °C for overnight during which the samples dried completely. All the samples underwent hot air oven drying at 100 °C for 24 hours to remove moisture followed by heat treatment at 600 °C for 3 hours [(“Impact of Copper on in-Vitro Biomineralization, Drug Release Efficacy and Antimicrobial Properties of Bioactive Glasses,” 2020)](https://paperpile.com/c/g9JGZj/Aww3) [(S. & S., 2021)](https://paperpile.com/c/g9JGZj/59t1).

# RESULTS AND DISCUSSION

## XRD Pattern

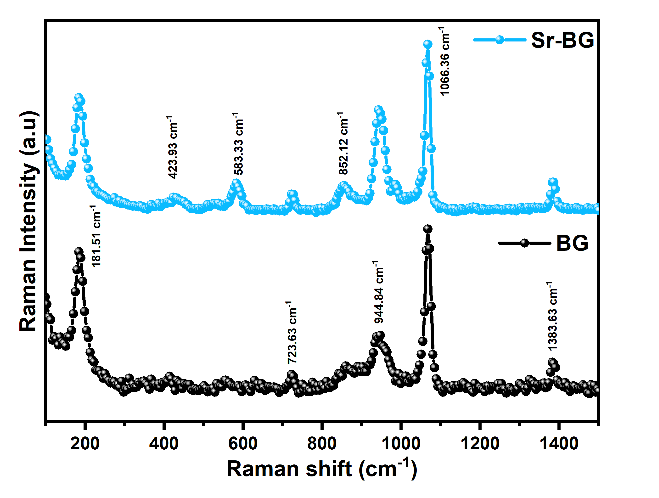
The XRD pattern of the bio glass reveals the crystalline structure of the material in order to observe the formation of bioglass. Bioglass showed CaCO3 and NaCaPO4 crystalline phases; in the case of Sr-BG strontium peak was observed around 33°. The crystallinity was also increased in Sr-BG than BG [(S et al., 2022)](https://paperpile.com/c/g9JGZj/lQ20).



**Fig 1:** XRD pattern of BG and Sr-BG.

## Raman Spectroscopy

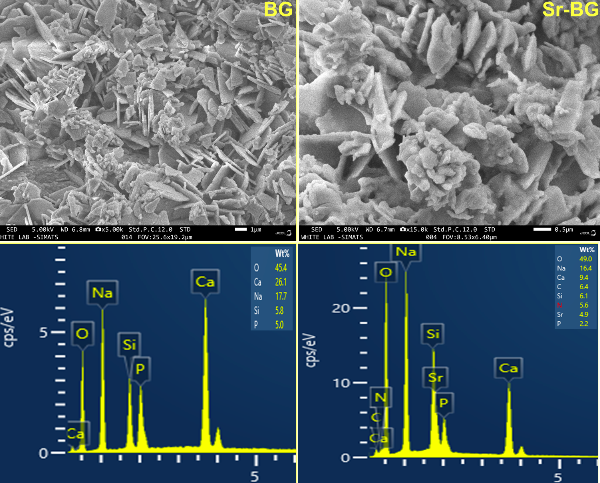
Raman spectra have been observed with the help of silica and phosphate vibration and were checked in order to observe the mineralisation of the material and to see if it supports the above data collected from xrd. Elevated phosphate vibration was observed in Sr-BG than pure bioglass.



**Fig 2:** Raman Spectra of BG and Sr-BG.

## FE-SEM andEDS

Field emission scanning electron microscopy is majorly used to study the surface morphology of the bioglass and further helps in analyzing the quality and the microstructures found in the material. Flake-like structures were found in pure BG and the dimension of flakes was increased in Sr-BG. And respective Si, Ca, P, Na, O, C were found in pure BG; along with these elements Sr was observed in Sr-BG that authenticates the formation of bioglass.

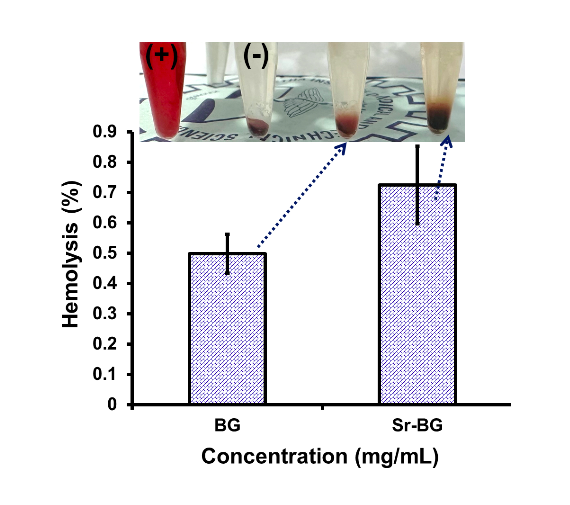


**Fig 3:** FE-SEM and EDS of BG and Sr-BG.

## Hemolysis assay

The blood compatibility , antibacterial and the biomineralization tests of strontium bioglass reveals that it is well tolerated by cells and aids in great bonding and integration of bone hence leading to enhanced bone regeneration and repair which hence concludes that these properties can make strontium bioglass a potent solution for treating bone disorders and diseases(Rafi et al., 2024). A similar study done on the effects of strontium incorporated into gelatin bioglass (*in vitro* and *in vivo*) revealed that strontium containing bioglass enhance the mechanical and biological properties of the matrix and furthermore ionic dissolution and their effects on the environment will help refine the properties of glass and fabricate it for tissue engineering. [(“The Effects of Strontium Incorporation on a Novel Gelatin/bioactive Glass Bone Graft: In Vitro and in Vivo Characterization,” 2018)](https://paperpile.com/c/g9JGZj/uE1A). Another study revealed that Incorporating Sr into BGs might be a useful tactic to provide aged osseous defect areas with a consistent flow of Sr2+ ions (Tuluwengjiang et al., 2024)

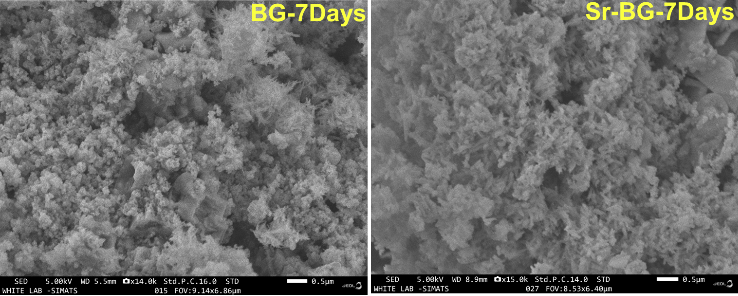
. However, in individuals with osteoporosis, excessive osteoclast suppression may postpone bone remodeling and, therefore, tissue regeneration. [(Kargozar et al., 2019)](https://paperpile.com/c/g9JGZj/KMt7). An in vitro study conducted on a similar topic shows that incorporating strontium into glass promotes rat calvarial osteoblastic cell proliferation. [(“The Effects of Strontium Incorporation on a Novel Gelatin/bioactive Glass Bone Graft: In Vitro and in Vivo Characterization,” 2018)](https://paperpile.com/c/g9JGZj/uE1A).



**Fig 4.** Blood compatibility of BG and Sr-BG.

## Biomineralization

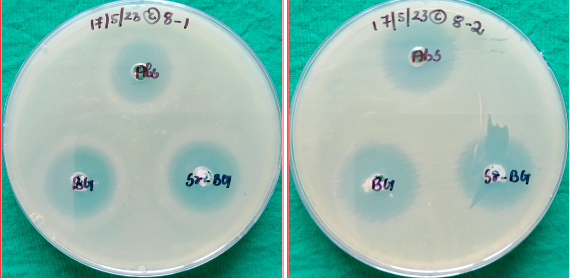
Spike-like structures were observed in pure BG and branched flower-like morphology was prominent in Sr-BG at the incubation of 7 days that enunciates the proper mineralization behaviour of the bioactive materials.



**Fig 5:** Biomineralization of BG and Sr-BG via FE-SEM.

## Antibacterial Activity

Bioglass generally showed antimicrobial activity. The results explain that both the materials are inhibiting the growth of *E.coli* and *pseudomonas aeruginosa .* Compared to BG, Sr-BG showed upregulated antimicrobial activity.



**Fig 6:** Antibacterial potentiality of BG and Sr-BG.

One of the most difficult challenges in tissue engineering was simulating the extracellular matrix. Scaffolds made of biocomposite nanofibers and nanohydroxyapatite were inherently porous, allowing for optimal cell occupancy, vascularity, and the transport of nutrients and metabolic waste products. Increased osteoblast proliferation and differentiation was seen in studies comparing bioinert to bioactive glass ceramic templates.[(Graf, S.,Thakkar, D., Hansa, I., Pandian, S.M., Adel, S.M., n.d.; Krishnan & Lakshmi, 2013)](https://paperpile.com/c/g9JGZj/RQVM+u2dK). Sr2+ ions can increase bone tissue density by increasing osteoblast activity and decreasing osteoclast activity. Additionally , bioglass can also be used as air abrasives , along with restorative materials , also used in pulp capping and other endodontic therapies. [(Chidambaram et al., 2022; Skallevold et al., 2019)](https://paperpile.com/c/g9JGZj/pop5+k2zx). Sr-infused bioactive glasses offer great promise for achieving better mineralization and osseointegration properties in biomedical applications. [(Lakshmi, 2021; Dharman , 2021)](https://paperpile.com/c/g9JGZj/KwJK+JgXH) Their ability to enhance mineralization, stimulate osteogenesis, modulate inflammation, and provide controlled ion release makes them a valuable biomaterial for promoting successful bone healing and integration. Future research efforts in this area will enable scientists to improve both the properties and possible applications of Sr-infused bioactive glasses which will lead to better solutions for patients requiring bone healing implants.

# CONCLUSION

The exciting potential of Sr-infused bioactive glass for better mineralization capabilities and osseointegration applications extends to bone healing processes and tissue engineering along with dental implants applications. The formation of new bone tissue occurs at enhanced volumes with better quality through Sr-infused bioglass at faster rates when compared to other biomaterials. Research needs to expand to improve mechanical strength, fracture toughness and biocompatibility features of Sr-infused bioactive glass. The application of Sr-infused bioactive glass coatings and other bioactive glass versions shows excellent promise for better integrating metallic implants in host tissue and accelerating tissue regenerative processes.

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