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RESARCH ARTICALE

RARE EARTH ELEMENT-DOPED BIOGLASS FOR PERIODONTAL REGENERATION; AN IN VITRO INVESTIGATION OF BIOCOMPATIBILITY AND REGENERATIVE POTENTIAL

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ABSTRACT

Background: Periodontitis is a chronic inflammatory disease that causes progressive destruction of periodontal structures, including the alveolar bone, cementum, and periodontal ligament. Restoring these tissues remains a key challenge in periodontal therapy. Bioactive glass has shown potential for periodontal regeneration due to its osteoinductive and osteoconductive properties. Recently, ion doping has been explored to enhance its regenerative effects, with erbium-doped bioglass (Er-BG) gaining attention for promoting osteogenic differentiation. This study evaluates the physicochemical properties, biocompatibility, and regenerative potential of Er-BG for periodontal tissue repair.

Material and Methodology: Er-BG was synthesized using the sol-gel method. Structural and compositional characterization was performed using Scanning Electron Microscopy (SEM), Energy Dispersive X-ray Spectroscopy (EDS), X-ray Diffraction (XRD), and Attenuated Total Reflectance Infrared Spectroscopy (ATR-IR). Biocompatibility and osteogenic potential were assessed using human periodontal ligament stem cells (PDLSCs) through MTT, Alkaline Phosphatase (ALP), collagen estimation, and calcium deposition assays. Zebrafish embryo models were used for toxicity evaluation.

Results: SEM revealed a porous surface facilitating cell attachment. EDS confirmed erbium integration, while XRD indicated an amorphous structure. Er-BG enhanced ALP activity (~130%), collagen synthesis (~105%), and calcium deposition (~145%). Zebrafish studies confirmed minimal cytotoxicity.

Conclusion:Er-BG demonstrated excellent biocompatibility, osteogenic potential, and low toxicity, making it a promising candidate for periodontal regeneration. Further in vivo studies are needed.

Keywords: **Erbium-doped bioglass, periodontal regeneration, osteogenesis, biocompatibility, bioactive glass, tissue engineering.**

INTRODUCTION

Periodontitis, a chronic inflammatory disease affecting the supporting structures of the teeth, is a major cause of tooth loss in adults. Effective treatment requires not only controlling infection but also promoting the regeneration of damaged periodontal tissues, including the alveolar bone, cementum, and periodontal ligament.[1]Various biomaterials have been explored for their potential to enhance periodontal regeneration. Among these, bioactive glasses (BGs), particularly those designed to stimulate bone regeneration, have shown great promise due to their ability to induce osteogenesis, enhance tissue regeneration, and support periodontal cell growth.[2]

The principal anatomical consequence of periodontitis is the loss of alveolar bone support. The extent and severity of periodontal osseous lesions are typically assessed through clinical and radiographic methods.[1,2] Periodontal defects are categorized as suprabony (horizontal), infrabony (vertical), and interradicular (furcation) defects. According to Goldman (1958)[2], suprabony defects have a pocket base coronal to the alveolar crest, whereas infrabony defects extend apically beyond the bone crest. Intrabony defects, which affect a single tooth root surface, and crater defects, which involve adjacent root surfaces, are classified based on remaining bony walls as 1-wall, 2-wall, or 3-wall defects.[3-5] Achieving complete regeneration of infrabony defects remains a significant clinical challenge.

Autografts are considered the gold standard for bone and periodontal regeneration due to their osteogenic, osteoconductive, and osteoinductive properties. However, drawbacks such as limited availability, donor site morbidity, and extended operative time have led to the development of bone tissue engineering strategies. Despite advancements, achieving complete periodontal regeneration remains unpredictable.[6-8] Among various biomaterials, BGs have attracted attention for their ability to form a highly reactive carbonate hydroxyapatite layer.[9]

BGs are bioactive materials composed of silicon dioxide, sodium oxide, calcium oxide, and phosphorus pentoxide. First introduced by L. L. Hench in 1969, BGs revolutionized biomaterials by providing bonding interfaces with both bone and soft tissues [9]. The original 45S5 Bioglass formulation (45% SiO2, 24.5% CaO, 24.5% Na2O, and 6% P2O5) was the first synthetic material to bond with bone. A significant effect of BG is the release of biologically active silicon (Si^{4+}) and calcium (Ca^{2+}) ions, which stimulate osteoblast proliferation and bone growth around the implant interface. Additionally, BG 45S5 enhances vascular endothelial growth factor (VEGF) secretion, promoting angiogenesis in vitro and vascularization in vivo.[10,11]

Bioglasses have gained significant attention in tissue engineering due to their osteoinductive and osteoconductive effects, making them suitable for regenerating hard and soft tissues. Different types, including calcium, silicon, borate, and phosphate-based BGs, have been explored for tissue repair.[12] Though brittle, bioglasses facilitate hydroxyapatite formation. Recent research focuses on doping BG with various ions to enhance its surface properties and regenerative potential. Ions such as calcium, strontium, silica, silver, and lithium have been studied for their osteogenic effects.[13]

Erbium-doped bioglass (Er-BG) has recently gained interest for periodontal applications. Erbium ions improve bioactivity through antimicrobial and anti-inflammatory properties, which are beneficial for periodontal treatment.[14] Erbium ions can reduce bacterial colonization, inflammation, and enhance osteoblast proliferation and differentiation,[15] Additionally, Er^{3+} exhibits luminescent properties in the near-infrared (1.54 µm) and visible regions, enabling bioimaging and real-time tracking of biomaterial interactions with tissues, which aids in monitoring osteogenesis.[16] These combined properties make Er-BG a promising candidate for periodontal regeneration.

This study aims to evaluate the efficacy of erbium-doped bioglass as a biomaterial for periodontal regeneration. The material was characterized using SEM, ATR-IR, and XRD analyses. Its regenerative potential was assessed by measuring alkaline phosphatase activity, collagen content, and calcium deposition. The biocompatibility of Er-BG was evaluated through an MTT assay, while toxicity assessments were conducted using zebrafish models to ensure its safety.

MATERIALS AND METHODOLOGY

Material Characterization

- SEM Analysis: Surface morphology and porosity were examined using field emission SEM at varying magnifications (500×–50,000×).
- EDS Analysis: Elemental composition and dopant distribution were assessed to confirm rare-earth incorporation.

- XRD Analysis: Crystalline and amorphous phases were identified to determine structural stability.
- ATR-IR Spectroscopy: Functional groups and bioactive features of the doped bioglass were analyzed.

Biocompatibility and Regenerative Potential

- MTT Assay: Cell viability was assessed on human periodontal ligament stem cells (PDLSCs) cultured with different bioglass concentrations (12.5–100 µg/mL).
- Alkaline Phosphatase (ALP) Activity: Osteogenic differentiation was evaluated through ALP expression.
- Collagen Estimation: Extracellular matrix deposition was analyzed via Sirius Red staining.
- Calcium Content Analysis: Alizarin Red S staining was used to measure mineralization levels.

Toxicity Assessment

- Zebrafish Embryo Assay: The in vitro toxicity of the bioglass was examined by monitoring embryo development over 120 hours. Cell viability, hatching rates, and morphological abnormalities were recorded.

RESULTS

1. Surface Morphology and Structural Analysis

Scanning Electron Microscopy (SEM) Analysis
The SEM images of erbium-doped bioglass (Er-BG) revealed a highly porous, rough, and irregular surface texture with a well-interconnected network. The pore sizes varied between 1 to 5 µm, which facilitates cell attachment, proliferation, and nutrient exchange, essential for bone regeneration. Additionally, small spherical aggregates (1–3 µm) were observed, likely formed due to erbium doping affecting the sintering process. These aggregates contribute to increased surface roughness, which may enhance osteoconductivity, providing a favorable environment for bone cell attachment and differentiation (Figure 1).

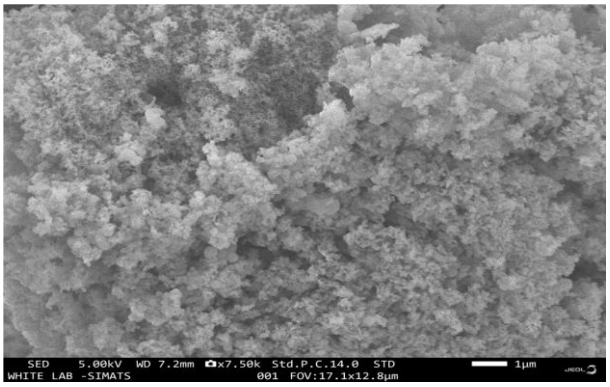

Figure 1. Represents the SEM of prepared erbium doped bioglass

Energy Dispersive X-ray Spectroscopy (EDS) Analysis

The EDS analysis confirmed the successful incorporation of erbium (Er) into the bioglass matrix, along with silicon (Si), calcium (Ca), and phosphorus (P), which are crucial for bioactivity. The homogeneous distribution of erbium ions ensures uniformity within the material, supporting its potential for periodontal and orthopedic applications. The elemental composition analysis further validates that erbium doping did not alter the fundamental bioglass composition, but rather enhanced its bioactivity (Figure 2).

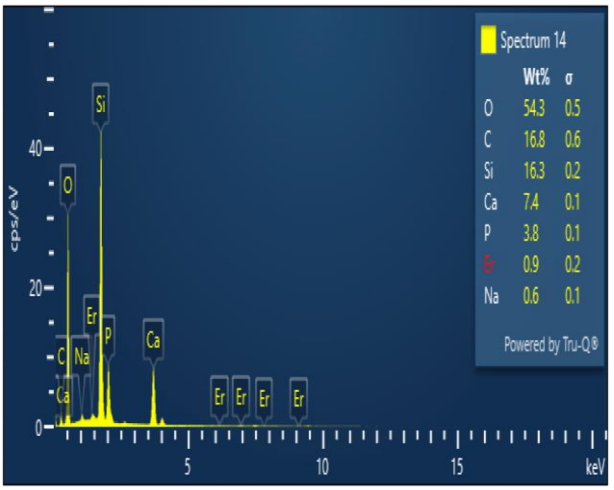

Figure 2. Represents the presence of various elements using the EDS analysis

Attenuated Total Reflectance Infrared Spectroscopy (ATR-IR) Analysis

The ATR-IR spectra confirmed the presence of key functional groups associated with bioglass bioactivity. A strong Si-O-Si stretching vibration was observed at 1035 cm^{-1}, indicating the formation of a stable silicate network. Additionally, phosphate (P-O)

stretching bands at 565.59 cm^{-1} and 603.23 cm^{-1} confirmed the presence of phosphate groups essential for hydroxyapatite formation. Slight shifts in peak intensities were noted due to erbium incorporation, suggesting that Er-doping may influence the structural properties of the bioglass matrix (Figure 3).

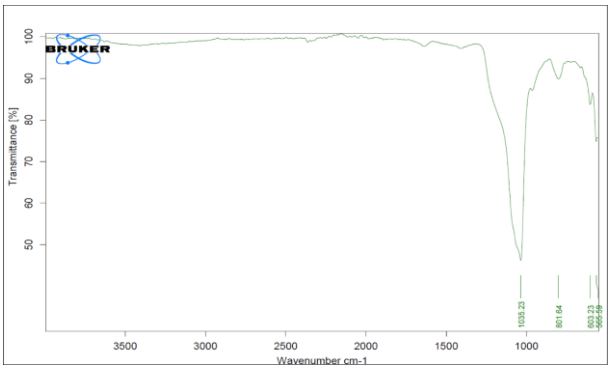

Figure 3. Represents the ATR-IR of prepared erbium doped bioglass

X-ray Diffraction (XRD) Analysis

The XRD pattern exhibited a broad diffraction hump between 20°–35° 2θ, characteristic of an amorphous bioglass structure. However, minor crystalline peaks were observed around 30° and 50°, indicating partial crystallization due to erbium doping. The predominantly amorphous nature of Er-BG ensures excellent bioactivity and ion exchange capability, both of which are critical for bone tissue regeneration (Figure 4).

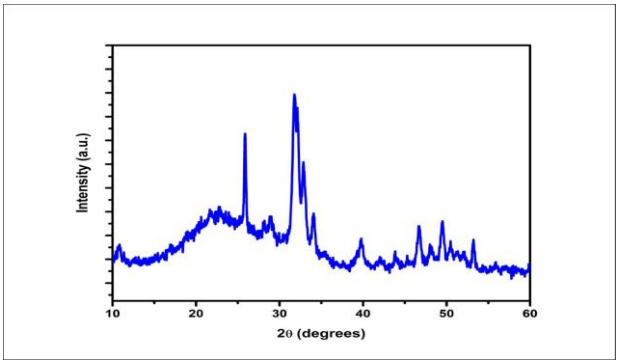

Figure 4. Represents the XRD of prepared erbium doped bioglass

Biocompatibility and Osteogenic Potential

Cell Viability (MTT Assay)

The biocompatibility of Er-BG was assessed through the MTT assay, which demonstrated high cell viability (>90%) across all tested concentrations (12.5–100 µg/mL). The control group consistently exhibited slightly higher viability than the Er-doped bioglass samples, but no significant cytotoxic effects were observed. These results indicate that Er-BG supports cellular function and proliferation, making it a promising biomaterial for bone regeneration (Figure 5).

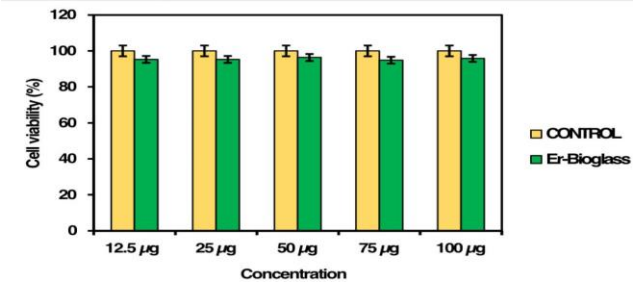

Figure 5. This graph represents the percentage of cell viability in different concentrations of control and Erbium doped bioglass.

Collagen Content Estimation

Collagen synthesis, an essential component of the extracellular matrix and bone maturation, was analyzed in the control and Er-BG-treated groups. The Er-doped bioglass samples exhibited an approximate 105% increase in collagen content compared to the control group, suggesting that erbium incorporation plays a role in promoting collagen production. The presence of an enriched collagen matrix further supports bone formation and tissue regeneration, reinforcing Er-BG's potential as a scaffold material (Figure 6).

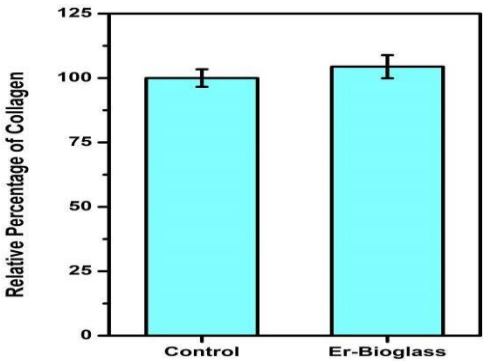

Figure 6. This graph represents the relative percentage of Collagen in control and Erbium doped bioglass

Alkaline Phosphatase (ALP) Activity

Alkaline phosphatase (ALP) is a key osteogenic marker that signifies early osteoblast differentiation. The Er-BG samples demonstrated a 130% increase in ALP activity compared to the control group, confirming its enhanced osteoinductive potential. The increased ALP expression indicates that Er-BG facilitates bone matrix mineralization and osteoblast maturation, which are essential for effective bone regeneration (Figure 7).

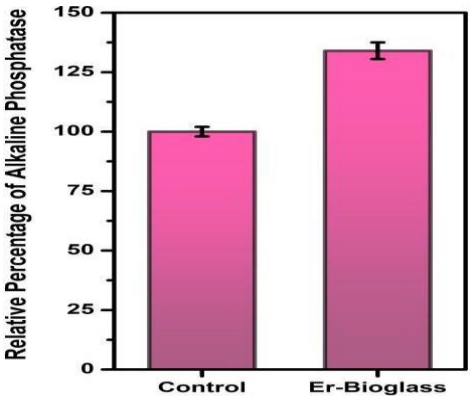

Figure 7. This graph represents the relative percentage of Alkaline Phosphatase in control and Erbium doped bioglass

Calcium Deposition (Mineralization)

Calcium deposition is a crucial indicator of bone tissue mineralization and scaffold integration. The results showed a 145% increase in calcium content in the Er-BG samples, compared to the control. This significant enhancement suggests that Er-doped bioglass promotes greater mineralization, reinforcing its role in bone remodeling and repair (Figure 8).

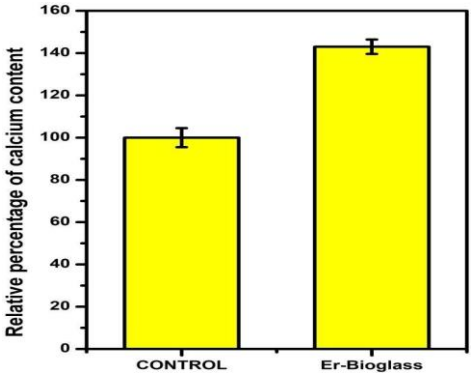

Figure 8. This graph represents the percentage of relative percentage of calcium content in control and Erbium doped bioglass

Cytotoxicity and In Vitro Toxicity Assessment

Zebrafish Embryo Toxicity Test

The potential toxicity of Er-BG was evaluated using zebrafish embryos, which were monitored at different developmental stages (24, 48, 72, 96, and 120 hours post-fertilization). The embryos exposed to Er-doped bioglass exhibited high survival rates, minimal developmental abnormalities, and normal anatomical structure formation. However, a slight delay in hatching was observed at higher concentrations, though no significant increase in mortality was noted. These findings suggest that Er-BG has a strong safety profile and does not exert significant teratogenic effects, supporting its use in biomedical applications (Figure 9).

Cytotoxicity Analysis

Cytotoxicity analysis was conducted in accordance with ISO 10993-5 standards for biomaterials. The assessment showed that cell viability remained above 80% across all tested concentrations, confirming the non-toxic nature of Er-BG. While a slight reduction in viability was noted over time, the values remained well within the non-toxic threshold, further reinforcing its excellent biocompatibility and suitability for tissue engineering applications (Figure 10).

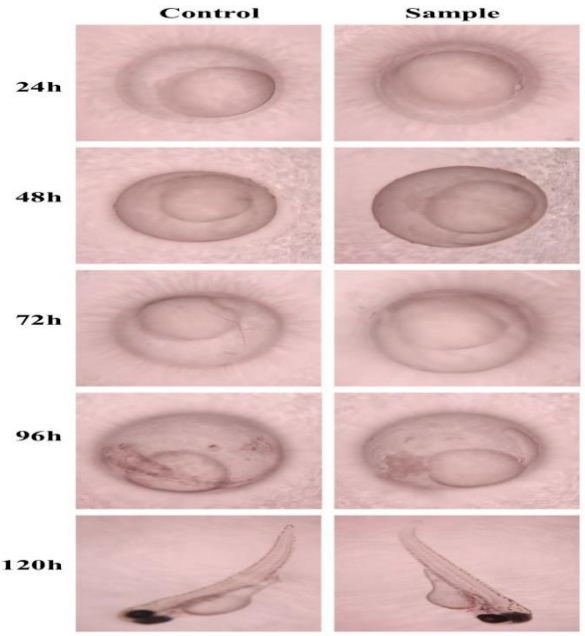

Figure 9. Represent that bioglass doped with erbium exposed eggs and matured embryos at 24,48,72,96, 120 hpf

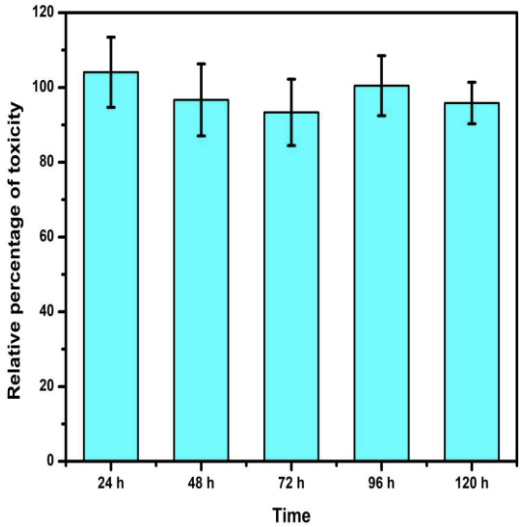

Figure 10. Represent the relative percentage of toxicity

DISCUSSION

The development of bioactive materials for bone regeneration has gained significant attention in periodontal and orthopedic research. Among these materials, bioglass has demonstrated promising potential due to its ability to stimulate osteogenesis, promote vascularization, and facilitate bone repair. Recent advancements in ion-doped bioglasses have further improved their regenerative potential, making them an ideal candidate for tissue engineering applications. In this study, erbium-doped bioglass (Er-BG) was investigated for its structural, biological, and osteogenic properties and the findings highlight the morphological, compositional, and biological advantages of Er-BG, positioning it as a superior biomaterial for periodontal applications.

The morphological and compositional characteristics of bioglass play a vital role in determining its bioactivity and regenerative properties. In this study, SEM analysis of Er-BG revealed a highly porous, rough, and interconnected surface, which is beneficial for cell adhesion, proliferation, and osteogenesis. When compared to previously studied bioglasses (BGp, BG85Sp, and BG45Sp), some key differences were observed. While BGp and BG45Sp displayed irregularly shaped particles with rough surfaces, similar to Er-BG, BG85Sp showed a higher tendency for particle agglomeration, which may limit cellular infiltration and nutrient diffusion.[17-19] In contrast, Er-BG maintained a more uniform porosity with well-defined structural integrity, allowing better vascularization and tissue integration. These morphological advantages position Er-BG as a more osteoconductive and bioactive scaffold for bone regeneration applications. Further elemental analysis (EDX) confirmed the successful incorporation of erbium in Er-BG, alongside essential components such as silicon (Si), calcium (Ca), and phosphorus (P), which are critical for bioactivity. Unlike commercially available BG45Sp, which contained high sodium levels (Na_2O: 25%), Er-BG lacked sodium, likely leading to a more controlled degradation rate and reduced cytotoxicity.

Studies on Ion modified-BG have demonstrated that low crystallization tendencies and controlled dissolution profiles contribute to better bioactivity and osteogenesis. Incorporating ions such as erbium into Ion modified bioglass could further enhance its therapeutic effects, making Er-BG a promising alternative to conventional bioglasses. Additionally, Boron (B)-doped bioglasses have been investigated for their osteogenic and angiogenic potential, but their bioactivity appears to be highly dose-dependent, with high concentrations leading to cytotoxicity. Comparatively, Er-BG maintained a stable biocompatibility profile, with high cell viability and minimal toxicity, suggesting a wider therapeutic window for clinical applications.[17-19]

The biocompatibility of Er-BG was validated through MTT assays, which demonstrated >90% cell viability across all tested concentrations. These findings align with previous bioglass studies, such as BG1 and BG2, which were well tolerated by periodontal cells without reducing viability below toxicity thresholds. While bioglass toxicity is often observed at higher concentrations (>2 µg/mL), Er-BG maintained high cell viability even at elevated concentrations, reinforcing its suitability for biomedical applications. [19] In comparison, B-doped BGs displayed variable cytotoxic effects, with high boron ion concentrations leading to a significant drop in cell viability over time. A previous study indicated that borate ion concentrations above 2.5 mM (27.03 mg/L ionized B) resulted in a 50% reduction in cell proliferation, suggesting a narrow therapeutic window for B-doped bioglasses. In contrast, erbium doping did not show any dose-dependent cytotoxic effects, making Er-BG a safer alternative.

The osteogenic potential of Er-BG was further supported by enhanced ALP activity (~130%) and increased calcium deposition (~145%), surpassing the osteogenic response observed in undoped BGs. While B-doped BGs demonstrated a positive impact on osteogenic differentiation, their effectiveness was limited at higher concentrations, potentially due to cytotoxic effects. In previous studies, B-doped BGs enhanced osteogenic marker gene expression (OPN, OCN, and BMP-2), but these effects were only slightly greater than those observed in undoped BGs. In contrast, Er-BG consistently outperformed undoped BGs in terms of ALP activity and mineralization, suggesting that erbium plays a more stable role in promoting osteoblast differentiation and bone formation.[19-20] Additionally, B-doped BGs exhibited limited pro-angiogenic effects in vitro, whereas Er-BG's unique microstructure could further support vascularization in vivo.

Another crucial factor for bone regeneration is angiogenesis, which plays a fundamental role in bone repair and tissue remodeling. Studies on B-doped bioglasses have shown that low to moderate B-ion release can positively influence angiogenesis, whereas high boron concentrations may negatively impact endothelial cell viability. In contrast, Er-BG demonstrated excellent biocompatibility and sustained osteogenic properties without cytotoxic effects, making it a more reliable candidate for long-term applications. Furthermore, studies using vascular endothelial growth factor (VEGF) assays have suggested that boron-doped BGs only exhibit a limited impact on angiogenesis, requiring additional modifications to enhance vascularization.[21]

Meanwhile, Er-BG may naturally promote better vascularization due to its biocompatible and osteoinductive properties, which warrant further investigation in in vivo models.

Future research should focus on evaluating the long-term stability, degradation kinetics, and mechanical strength of Er-BG in vivo. Additionally, investigating the combined effects of erbium with other bioactive ions (e.g., strontium or magnesium) could further enhance its osteogenic and angiogenic potential. The integration of advanced biomaterial models, such as 3D cell cultures, vasculature-on-a-chip, and bioreactors, may provide deeper insights into the angiogenic-osteogenic coupling of Er-BG in complex biological environments. With continued research and clinical validation, Er-BG could revolutionize periodontal and orthopedic regenerative therapies, offering a safer and more effective alternative to currently available bioglasses.

CONCLUSION

Erbium Doped Bioglass (Er-BG) exhibits high porosity, reduced agglomeration, and enhanced osteogenic potential, making it a promising biomaterial for periodontal regeneration. Its stable biocompatibility, increased ALP activity, and higher calcium deposition support efficient bone formation and tissue integration. Additionally, Er-BG demonstrated minimal cytotoxicity and sustained bioactivity, ensuring safe and effective application in regenerative dentistry. With its ability to promote osteogenesis without dose-dependent toxicity, Er-BG holds significant potential for bone tissue engineering and clinical applications, offering a biocompatible and osteoinductive scaffold for enhanced periodontal and orthopedic regeneration.

DECLARATIONS

Conflicts of Interest

The authors declare no conflicts of interest.

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Ethical Approval

Not Applicable

Informed Consent

Not Applicable

Acknowledgments

Not Applicable

REFERENCES

1. Darveau RP. Periodontitis: a polymicrobial disruption of host homeostasis. Nature reviews microbiology. 2010 ;8(7):481-90.
2. Hench LL. The story of Bioglass®. Journal of materials science: materials in medicine. 2006;17(11):967-78.
3. Papapanou PN, Tonetti MS. Diagnosis and epidemiology of periodontal osseous lesions. Periodontol 2000. 2000;22:8–21.
4. Goldman HM. The intrabony pockets: classification and treatment. J periodontol. 1958;29:272–91.
5. Nibali L, Sultan D, Arena C, Pelekos G, Lin G, Tonetti M. Periodontal infrabony defects: systematic review of healing by defect morphology following regenerative surgery. J Clin Periodontol. 2021;48:101–14.
6. Wang W, Yeung KWK. Bone grafts and biomaterials substitutes for bone defect repair: a review. Bioact Mater. 2017;2:224–47.
7. Zhao R, Yang R, Cooper PR, Khurshid Z, Shavandi A, Ratnayake J. Bone grafts and substitutes in dentistry: a review of current trendsanddevelopments. Molecules. 2021;26:3007.
8. Carmagnola D, Tarce M, Dellavia C, Rimondini L, Varoni EM. Engineered scaffolds and cell-based therapy for periodontal regeneration. J Appl Biomater Funct Mater. 2017;15:e303–1
9. Hench LL. The story of Bioglass®. J Mater Sci Mater Med. 2006;17:967–78.
10. Gorustovich AA, Roether JA, Boccaccini AR. Effect of bioactive glasses on angiogenesis: a review of in vitro and in vivo evidences. Tissue Eng Part B Rev. 2010;16:199–207.
11. Krishnan V, Lakshmi T, Bioglass. A novel biocompatible innovation. J Adv Pharm Technol Res. 2013;4:78–83.
12. Jones JR. Review of bioactive glass: from Hench to hybrids. Acta biomaterialia. 2013 Jan 1;9(1):4457-86.
13. Rahaman MN, Day DE, Bal BS, Fu Q, Jung SB, Bonewald LF, Tomsia AP. Bioactive glass in tissue engineering. Acta biomaterialia. 2011 Jun 1;7(6):2355-73.
14. Hoppe A, Güldal NS, Boccaccini AR. A review of the biological response to ionic dissolution products from bioactive glasses and glass-ceramics. Biomaterials. 2011;32(11):2757-74.
15. Ayobian-Markazi N, Fourootan T, Zahmatkesh A. An in vitro evaluation of the responses of human osteoblast-like SaOs-2 cells to SLA titanium surfaces irradiated by erbium: yttrium– aluminum–garnet (Er: YAG) lasers. Lasers in medical science. 2014 Jan;29:47-53.
16. Galli C, Macaluso GM, Elezi E, Ravanetti F,

Cacchioli A, Gualini G, et al. The effects of Er:YAG laser treatment on titanium surface profile and osteoblastic cell activity: an in vitro study. *Lasers Med Sci*. 2011 Jan;26(1):19-27.

17. Skwira A, Szewczyk A, Sądej R, Prokopowicz M. Bioglass obtained via one-pot synthesis as osseointegrative drug delivery system. International Journal of Pharmaceutics. 2023 Feb 25;633:122610.
18. Korukonda H, Suresh N, K S (December 25, 2023) Fabrication and Characterization of an Innovative Silver- and Gadolinium-Doped Bioglass for Bone Regeneration. Cureus 15(12): e51086. doi:10.7759/cureus.51086
19. Clichici A, Filip GA, Achim M, Baldea I, Cristea C, Melinte G, Pana O, Tudoran LB, Dudea D, Stefan R. Characterization and In Vitro Biocompatibility of Two New Bioglasses for Application in Dental Medicine—A Preliminary Study. Materials. 2022 Dec 18;15(24):9060.
20. Tamilmani H, Srinivas BK, Suresh N, Saranya K, Saranya K. Advancing Periodontal Care: Development of a Novel Collagen-Chitosan-Bioglass Scaffold as a Substitute for Autologous Soft Tissue Grafts. Cureus. 2024 Sep 4;16(9)
21. Decker S, Arango-Ospina M, Rehder F, Moghaddam A, Simon R, Merle C, Renkawitz T, Boccaccini AR, Westhauser F. In vitro and in ovo impact of the ionic dissolution products of boron-doped bioactive silicate glasses on cell viability, osteogenesis and angiogenesis. Scientific Reports.2022;12(1):8510.