Multidisciplinary Reviews

REVIEW ARTICLE
Published Online: August 13, 2024
https://doi.org/10.31893/multirev.2024286

# Recent advances in antimicrobial and biosynthesis properties of bioglass and nanoparticles: A narrative review

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**Abstract** Oral hard and soft tissue engineering using bioactive substances that trigger other proteins or the immune system is the main focus of biomaterials research. Long-lasting tissues and tissue components develop due to this natural ground ingredient. Bioactive glass (BAG) is one type of biomaterial that is currently used. BAG is utilized in soft-tissue restoration, orthopedics, air abrasion, pulp capping, root canal therapy, dental implant coating materials, mineralizing agents and dental restorative materials, among other medical specialities, due to its bioactive properties, which make it suitable for use in a range of clinical settings, including dentistry and medicine, where issues with complex tissue regeneration arise.Bioglass is used in dentistry for permanent restoration, intracanal medication or temporary restorative purposes. This article extensively explores the applications of Bioglass in dentistry, explicitly focusing on elucidating its mechanisms of action and biological effects. Emphasizing the uniqueness of Bioglass, this article underscores its role as a transformative tool in modern dental care.

**Keywords:** regenerative, bioactive, nanotechnology, nanoscience

## 1. Introduction

The origins of bioactive glasses were traced back to 1969 when Larry Hench introduced them as potentially advantageous biomaterials for tissue regeneration (Hench, 2006). Hench and his colleagues at the University of Florida formulated these materials, marking their creation in the same year (Hench, 2006). Hench's research team at Imperial College London and other researchers globally have made subsequent advancements and refinements. It is crucial to note that the term "Bioglass" has a specific trademark application referencing the 45S5 composition. Consequently, it is inappropriate to use "Bioglass" as a general term for all bioactive glasses; instead, it should only be employed in connection with the 45S5 composition (Navarro & Serra, 2016). The initiation of this pursuit can be attributed to Larry.

L. Hench, who recognized the limitations of inert metal and plastic materials commonly used in amputation cases, as they are prone to rejection by the host (Carvalho et al., 2019; Choe et al., 2022). Melt quenching is a method that has historically been used to create glasses such as Bioglass® 45S5 (Chen et al., 2012). Melt quenching is the process of rapidly cooling a mixture of powdered materials to a high temperature, usually over 1300°C, to cause the atomic structure to freeze. Although this method has several advantages, it is not without drawbacks. These include reduced bioactivity observed at elevated sintering temperatures and the inability to produce porous scaffolds (Peitl Filho et al., 1996).

To address these issues, heat treatment is commonly employed to mitigate the thermomechanical stresses that result from the rapid cooling of glass (Prasad, 2017).

The sol-gel process, a groundbreaking glassmaking technique introduced in the early 1970s, (Wilson et al., 1981) offers a solution to these challenges. This technique produces diverse glass compositions and forms, including scaffolds, coatings, fibers, and nanoparticles (Fernandes et al., 2018). Midha et al. (2013) successfully crafted bioactive glass scaffolds (70S30C, composed of 70% SiO2 and 30% Ca) in an innovative application of the sol-gel foaming process. These scaffolds are considered suitable matrices for bone tissue regeneration, demonstrating the versatility and potential of the sol-gel method in addressing limitations associated with conventional approaches.

At the beginning of the 1970s, a novel glassmaking method was developed: the sol-gel process.(Wilson et al., 1981) Bioactive glasses, also referred to as original bioactive glass or Bioglass, are a class of surface-reactive glass-ceramic biomaterials employed as implant devices within the human body to address or replace diseased or damaged bones because of their exceptional biocompatibility and bioactivity. (Boccaccini et al., 2016) Predominantly composed of silicate, a substance soluble in physiological fluids, these glasses release ions that facilitate healing.(Sawant & Pawar, 2020) Bioactive glass

 Received: April 4, 2024 | Accepted: June 13, 2024

distinguishes itself from traditional synthetic bone grafting biomaterials such as hydroxyapatite, biphasic calcium phosphate, and calcium sulfate due to its unique anti-infective and angiogenic properties.

Bioglass is used in dentistry because of its unique antibacterial and regenerative properties.

To evaluate its enhanced properties, the original bioactive glass, or bioglass made of silicon and calcium—is mixed with a dental material that has been used extensively for a few decades. Some of these improved properties include the ability to stick to the tooth, seal against micro leaks, release fluoride, have antimicrobial and anti-infective properties, prevent secondary caries, and —most importantly—replicate the tooth's natural tissues or encourage its regeneration. Contrary to popular belief, tissue engineering has a historical foundation that has extended beyond recent times, demonstrating practical success in various dentistry applications, including dentine, pulp tissue scaffolds, templates, periodontal membranes, and bone cement. (Carvalho et al., 2019) Bioactive glass (BAG) has emerged as a crucial material in these endeavours. It was found that this material could bind to soft and hard tissues without rejecting them, and it also precipitated hydroxyapatite in aqueous solutions. Because of its bioactive properties, BAG has changed the medical industry. It regenerates hard tissue in various clinical settings, such as dentistry and medicine (Najeeb et al., 2016; Skallevold et al., 2019). Nanotechnology has proven instrumental in synthesizing bioactive glass (BAG) at the nanoscale, facilitating its application in coating the surfaces of dental, spinal, and orthopedic implants (Zafar et al., 2020). The widespread use of Bioglass® 45$5, with over 1.5 million patients treated globally to date, attests to the success of this nanotechnological approach (Baino et al., 2018).

In response to the burgeoning interest in biomaterials that can endure the challenging oral environment and foster biomimetic dentistry, there has been a surge in research (Carvalho et al., 2019; Jones et al., 2016; Simila & Boccaccini, 2023). Academic studies have highlighted the effectiveness of antibacterial nanoparticles (NPs) across diverse domains, including biomedicine, dentistry, and agriculture (Arun et al., 2020; Saqib et al., 2022).

Originally sold under the trade name Bioglass® 455, this specific BAG formulation comprised 45% SiO2, 24.5% Na20, 24.5% CaO, and 6% P205 (Oztekin et al., 2022).

## 2. Material and Method

This project aims to examine pertinent research on the antimicrobial and regenerative applications of BAG in dentistry. A review of the literature was conducted in electronic databases using the following keywords: Bioglass, nanoparticles, copper doping, zinc doping, calcium, strontium, boron, and doping. The papers' titles and abstracts were scrutinized to eliminate those that lacked context or were unrelated to the review. Fifty-two documents judged to have full texts relevant to the context and of excellent quality were selected after this first filter. The papers were published after 1978, and all of them were written in English.

## 3. Review of Literature

### *3.1. Zinc*

Five grams of copper were dissolved in 120 mL of alkaline methanol (with a pH of 12.5), followed by the addition of calcium nitrate tetrahydrate. Simultaneously, in a separate batch, tetracthylorthosilicate was dissolved in 30 mL of absolute methanol (with a pH of 12.5). This second solution was added to the initial copper-containing solution while ultrasonic homogenizers were used. This process was part of a research study focusing on the biological and mechanophysical characteristics of therapeutic dental cement that integrates Bioglass nanoparticles doped with copper; it was observed that the inclusion of Cu-bgn in zinc phosphate cement (ZPC) did not yield a significant (NS') difference in mechanophysical properties compared to those of ZPC without Cu-bgn. However, noteworthy distinctions emerged when analyzing the extracts from the Cu-ZPC group. These extracts significantly increased odontoblastic differentiation, alkaline phosphate (ALP) activity, and cell viability compared to those of the ZPC group. This finding underscores the potential of copper-doped bioglass nanoparticles to enhance specific biological aspects when integrated into dental cement. It was also found that the ZPC extracts did not perform as well as the Cu-ZPC extracts in the antibacterial test. (Choe et al., 2022) Cu, Ca, and Si are among the therapeutic ions that Cu-bgn may release. (Boccaccini et al., 2016) Using different extracts, Cu-ZPC performed better biologically than the ZPC group. Compressive testing revealed no discernible variation. Baccaccini et al., 2016) The use of Cu-kgn incorporated dental cement or Cu-ZPC has enormous potential in biomedical engineering and dental tissue regeneration. (Boccaccini et al., 2016) According to a different study titled "Polymeric Zinc-Doped Nanoparticles for High Performance in Restorative Dentistry," bioactive materials should encourage intrafibrillar and interfibrillar remineralization to restore dentin. (Osorio et al., 2016) As the monomer and initiator reach the desired molecular weight, a polymerization chain is formed by the precipitation polymerization process. In this method, a continuous phase arises from dissolving a monomer and an initiator in a solvent without the use of a stabilizer or additive, resulting in insolubility:

(Medina-Castillo, 2020; Slomkowski et al., 2011)The foundation of this model lies in the interactions between the expanding polymeric chains and solvent molecules (Medina-Castillo, 2020).

Substituting Zn-ups with Zn-doped polymeric nanoparticles has been shown to reduce the toxic effects of zinc (Osorio et al., 2016). Moreover, it has been shown to inhibit the formation and growth of bacterial biofilms and to exhibit antimicrobial properties in previous in vitro analyses. Zinc-doped dentin adhesives, therefore, have the potential to stabilize dentin hybrid layers therapeutically or protectively (Alam et al., 2022).

*3.2. Calcium*

Calcium hydroxide (0.28 g or 0.28 g of ZnO:1.0Ca) was combined with 240 uL of PRG or 240 uL of the vehicle mixture (120 uL of PEG and 120 uL of PRG) in a laminar flow chamber. This process was repeated to produce the pastes under controlled conditions within the laminar flow chamber (Oztekin et al., 2022). When comparing calcium hydroxide to ZnO:1.0Ca, it was observed that calcium hydroxide exhibited higher pH and cell viability values. Interestingly, compared with calcium hydroxide nanocrystals, ZnO:1.0Ca nanocrystals associated with a low-surface-tension vehicle demonstrated increased radiopacity, permeability, and cell viability. However, calcium hydroxide nanocrystals showed higher pH and cell viability values. The vehicle had no discernible impact on any parameters (PRG or PEG-PRG) (Hench, 2006).

*3.3. Strontium*

Strontium nitrate (0.4 M, Sr(NO3)2) was dissolved in 30 mL of deionized water to produce F-doped material. The solution was stirred for 30 minutes using a magnetic stirrer (Oztekin et al., 2022). In addition to promoting preosteoblast replication, lowering the expression of osteoclastic markers, guaranteeing osteoblast differentiation, increasing alkaline phosphatase activity, and displaying major antiresorptive and osteoblastic activities in vivo, strontium also facilitates mineralization without harming bone tissue (Oztekin et al., 2022). With strontium replacement, its ability to promote remineralization and increase antibacterial activity is expected to improve. Studies have shown that the high radiopacity of strontium-doped nanohydroxyapatite (srnhap) ceramics allows for a deeper curing depth when they are used in dental composites cured by ultraviolet light-emitting diode (UV-LED) curing systems (Ravi et al., 2012). The study's results suggest that strontium ions may form a Stern layer that shields enamel from rust and lessens the likelihood that it will corrode in an acidic environment (Wang et al., 2019). The author also cited a study demonstrating how strontium-containing toothpaste could increase the amount of strontium in enamel and decrease its brittleness. The study revealed that using toothpaste containing Sr, F-, and Sr-HAP allowed the white spot lesion on the tooth to return to its original state of mineralization after six months of use (Athanassouli et al., 1983; Curzon & Losee, 1978). Combining Sr-doped nhap with other remineralizing materials, such as F, may enhance its capacity to heal enamel lesions. There is much potential for improving dental health and preventing dental disease with the development of Si-doped nanoparticles in dentistry (Rajendran et al., 2023).

*3.4. Lithium*

Tricalcium silicate and mesoporous bioactive glass nanoparticles were formed with different concentrations of lithium (Li), namely, 0%, 5%, 10%, and 20%. The morphology and chemical structure of these materials were thoroughly analyzed. Subsequently, powders at a concentration of 1.5 mg/mL were incubated in artificial saliva, Hank's balanced saline solution, or simulated body fluid at 37°C for 28 days. The pH evolution and apatite formation were closely monitored throughout the incubation period.

The regenerative potential of multifunctional Li-doped mesoporous nanoparticles, referred to as Li-MNPs, was evaluated in vivo using a mouse model.(Zhang et al., 2019) Lithium, a well-known activator of the ß-catenin signaling pathway (Clément-Lacroix et al., 2005), plays a crucial role in this process. In a study, it was discovered that glass fillers prereacted on the surface and infused with lithium could stimulate odontogenic differentiation in human dental pulp stem cells. Furthermore, these fillers promoted dentin synthesis through the B-catenin signaling pathway in a pulp capping rat model (Ali et al., 2019).

The interest in lithium stems from its potent antibacterial qualities and resistance to bacteria, rendering it an appealing component for pulp capping agents to combat infections in pulp tissue (Lieb, 2004). Lithium-doped bioactive glass-based magnetic nanoparticles have been identified as having the potential to serve as efficient antibacterial bioactive pulp-capping agents while simultaneously promoting dentin regeneration. Moreover, research indicates that Li-MNPs significantly suppress the growth of S. mutans, underscoring their ability to stimulate dentin regeneration in a manner comparable to that of mineral trioxide aggregate (MTA). Restorative dentistry using sol-gel synthesized tricalcium silicate and lithium-doped mesoporous bioactive glass nanoparticles. Glass ceramics based on lithium have long been used as dental prosthesis materials. (Mao et al., 2020) On the other hand, a comparative study of the physicochemical structure, biocompatibility, and antibacterial susceptibility of Hazel O. Simila & Aldo R. Boccaccini revealed that BG doped with 5% lithium inhibited multidrug-resistant S. aureus more than 10% lithium.

TCS particles were associated with increased alkalinizing effects and improved bioactivity following immersion in various fluids.

As detailed in a study titled "In Vivo Effects of Nanotechnologically Synthesized and Characterized Fluoridated Strontium

Apatite Nanoparticles in the Surgical Treatment of Endodontic Bone Lesions", a notable transformation in the shape of nanoparticles occurred, transitioning from nanorods to nearly spherical forms with the introduction of fluorine (F) doping. (Oztekin et al., 2022) This fluorine doping not only altered the morphology of the nanoparticles but also facilitated their agglomeration. Additionally, an intriguing observation was the reduction in the size of the nanoparticles following F doping. These changes in shape, aggregation, and size suggest the significant impact of fluorine doping on the characteristics and behavior of strontium apatite nanoparticles, highlighting the importance of this modification in the context of endodontic bone lesion treatment. The ionic radius of F is smaller than that of OH, which causes the size of the nanoparticles to decrease. It is believed that when the surface area and crystallinity increase, the nanoparticles will tend to cluster together (Jiang et al., 2022; Wang et al., 2019). Studies conducted by other researchers have also demonstrated that F doping results in a decreased particle size and increased accumulation (Karunakaran et al., 2022; Saqib et al., 2022; Wang et al., 2019).

### *3.5. Magnesium*

Magnesium acetate was dissolved in deionized water with thorough mixing. This solution was carefully added dropwise to a zinc acetate solution. Next, the combined solution was added to a sodium carbonate solution and continuously mixed for thirty minutes. The resulting residue was subjected to ultrasonic washing, followed by drying at 80°C and subsequent heating at three hundred degrees Celsius for 2 hours (Tanweer et al., 2022).

In a study conducted by Tahreem Tanweer on magnesium dental composites featuring magnesium-doped zinc oxide nanoparticles, noteworthy antibacterial efficacy was observed. This effect was particularly evident in the prevention of secondary caries in an alloxan-induced diabetic model. The following are the key findings from the study:

1. Bacterial Growth Inhibition:

- Under optimal conditions, the buffering effect of specific concentrations of Mg-doped ZnO NPs hindered the growth of anaerobic bacteria (Tanweer et al., 2022).
- Composites containing 1% Mg-doped nO demonstrated greater efficacy against saliva-derived microcosms, E. faecalis, and S. mutans than those with 1% ZnQ NPs (Tanweer et al., 2022).

2. Concentration-dependent Antibacterial Activity:

- The antibacterial activity against E. faecalis, S. mutans, and saliva-derived microcosms significantly increased with increasing concentrations of Mg-doped ZnQ NPs (Tanweer et al., 2022).

3. pH Changes:

An increase in pH is observed, although it varies according to the percentage ratio (Tanweer et al., 2022).

4. Synthesis and Antibacterial Properties of Mg-Doped ZnO NPs:

- The successful synthesis of Mg-doped ZnO NPs was highlighted, showing their role as antibacterial agents effective against various bacteria while preserving the mechanical properties and aesthetic appeal of the resulting resin composite (Tanweer et al., 2022). In addition, a study by Alaa M. Abdel Aziz et al. emphasized the enhanced antibacterial action of magnesium oxide nanoparticles (MgO NPs) in their nanoform. As functional nanometallic oxide particles, MgO NPs exhibit bactericidal properties due to their large surface area. They interact strongly with bacterial cell walls and spores, demonstrating antibacterial activity against both gram-positive and gram-negative bacteria, as well as viruses (Gopi et al., 2014; Huang et al., 2005; Leung et al., 2014). Because the cell walls of bacteria are made of surface proteins that make it easier for materials such as teichoic acid and polysaccharides to attach and colonize, which offers protection against environmental factors and host defense, metal oxide nanoparticles primarily target bacteria. 1. Alaa M. Abdel Aziz et al. reported that MGO has better antibacterial activity when it is in the nano form.2. Ultrasonic activation is a significant factor in the antimicrobial activity of irrigants, independent of their chemical composition.

### *3.6. Boron*

For organisms that aid in the formation and maintenance of bones, boron is a vital source of nutrients. The hydrothermal method has proven successful in producing boron-doped strontium apatite nanoparticles.

Interestingly, as the level of B doping increased, the lengths of the nanorods decreased. This observation suggested that the shape of the nanoparticles resembled that of the nanorods, indicating that the doping process has a notable impact on the morphology of the nanoparticles (Öztekin et al., 2022) This ability to tailor the shape and characteristics of nanoparticles through doping demonstrates the versatility and potential of nanotechnology in biomaterial design and synthesis.

## 4. Discussion and Result

The following table 1 comprises the review of references:

**Table 1** Summary of references.

| Sr no | Title of article | Author & year | Nanoparticle | Material and method | Findings of article |
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| 1 | "Preparation and In Vitro Osteogenic Evaluation of Biomimetic Hybrid Nanocomposite Scaffolds Based on Gelatin/Plasma Rich in Growth Factors (PRGF) and Lithium-Doped 45 s5 Bioactive Glass Nanoparticles"(Farmani et al., 2023) | Ahmad Reza Farmani et al. | Lithium | by combining a solid and a liquid phase PSC/calcium sulfate was prepared | Lithium when doped with biglass has excellent bone formation and anti-inflammatory properties |
| 2 | "Development of a Bioactive Flowable Resin Composite Containing a Zinc-Doped Phosphate-Based Glass"(Lee et al., 2020) | Myung-Jin Lee et al. | Zinc | The study comprises preparation , mechanical and antibacterial properties evalutation. | Enhancement of antibacterial activity and prevention of secondary caries was observed by Zinc doping |
| 3 | "The Efficacy of an Aqueous Solution of Magnesium Oxide Nanoparticles and Its Ultrasonic Activation on Root Canal Enterococcus Faecalis Biofilm (In Vitro Study)"(Abdelaziz et al., 2022) | Alaa M. Abdel Aziz et al. | Magnesium oxide | 3 groups for irrigation Group 1 MgO nanoparticles, Group 2 NaOCL 5.25% Group 3 saline. Antimicrobial efficacy was detected | enhanced antibacterial action by ultrasonic activation. |
| 4 | "In Vivo Evaluation of the Effects of B-Doped Strontium Apatite Nanoparticles Produced by Hydrothermal Method on Bone Repair" (Oztekin, Gurgenc, Dundar, Ozercan, Yildirim, et al., 2022) | Faruk Oztekin et al. | Boron | The doped and undoped groups were investigated for bone formation. | Boron group shows Osteoblast density biocompatibility and the new bone formation |
| 5 | "Multifunctional Lithium-Doped Mesoporous Nanoparticles for Effective Dentin Regeneration in vivo"(Liang et al., 2023) | Zitian Liang et al. | Lithium | The study encompassed the quantification and analysis of various parameters. | Lithium-loaded Magnetic Nanoparticles (Li-MNPs) were found to possess the ability to promote dentin regeneration and effectively inhibit the growth of *S. mutans.* |
| 6 | "Dental Composites with Magnesium Doped Zinc Oxide Nanoparticles Prevent Secondary Caries in the Alloxan-Induced Diabetic Model" (Tanweer et al., 2022) | Tahreem Tanweer et al. | Magnesium | The material was synthesized using the coprecipitation method and subjected to comprehensive characterization employing various analytical techniques. | Mg-doped ZnO has demonstrated efficacy in preventing secondary caries. |
| 7 | "In Vivo Effects of Nanotechnologically Synthesized and Characterized Fluoridated Strontium Apatite Nanoparticles in the Surgical Treatment of Endodontic Bone Lesions"(Oztekin, Gurgenc, | Faruk Oztekin et al. | Fluoridated Strontium | The investigation of biocompatibility was conducted by embedding the materials as biomaterials into bone defects | new bone formation and osteoblast levels was witnessed |

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| | Dundar, Ozercan, Eskibaglar, et al., 2022) | | | | |
| 8 | "A Systematic Review on the Effect of Strontium- Doped Nanohydroxyapatite in Remineralizing Early Caries Lesion"(Rajendran et al., 2023) | Ratheesh Rajendran et al. | Strontium | A synthesis of five studies utilizing extracted human maxillary premolars revealed a collective focus on remineralizing dental structures. Specifically, four studies concentrated on remineralizing enamel, while one study specifically targeted the remineralization of dentin. | Sr-doped nHAP enhance F- effectiveness in repairing enamel lesions. |
| 9 | "Calcium-doped zinc oxide nanocrystals as an innovative intracanal medicament: a pilot study"(G. L. de Souza et al., 2022) | Gabriela Leite de Souza et al. | Calcium | The pastes were prepared, and the pH levels were assessed after day1 and day 4 of storage in deionized water. | ZnO:1.0Ca in a medicament shows more radiopacity, penetrability & cell viability compared to Ca(OH)2. |
| 10 | "Polymeric zinc-doped nanoparticles for high performance in restorative dentistry"(Toledano et al., 2021) | Manuel Toledano et al. | zinc | The proper generation of the randomization sequence and concealment of sample allocation were assessed. | Nanoparticles infused with zinc aided in preserving collagen, promoting remineralization, and enhancing mechanical properties at the resin-dentin interface. |
| 11 | "Investigating the mechanophysical and biological characteristics of therapeutic dental cement incorporating copper doped bioglass nanoparticles"(Choe et al., 2022) | Young-Eun Choe et al. | copper | evaluated the mechanophysical properties and biological behaviors | In the extracts from the Cu-ZPC group, a higher level of stimulation was observed compared to the ZPC group. This heightened stimulation was evident in terms of cell viability and odontoblastic differentiation, as well as in alkaline phosphatase (ALP) activity and alizarin red S (ARS) staining. |
| 12 | "Sol-gel synthesis of lithium doped mesoporous bioactive glass nanoparticles and tricalcium silicate for restorative dentistry: Comparative investigation of physico-chemical structure, antibacterial susceptibility and biocompatibility"(Simila & Boccaccini, 2023) | Hazel O. Simila et al. | Lithium | Tricalcium silicate and mesoporous bioactive glass nanoparticles were formed with varying lithium (Li) concentrations (0%, 5%, 10%, and 20%). The morphology and chemical structure of these materials were subsequently determined. | realistic data on bioactive compounds targeting dental applications may be achieved by varying the immersion media. |
| 13 | "Polyetheretherketone surface modification by lithium-doped bioglass nano- spheres to regulate | Xin-Jin Su et al. | Lithium | The surface morphology of PEEK, SPK, 0.1Li-SPK, and 0.5Li-SPK was | The bone-promoting capabilities of Li-SPK are linked to its ability to |

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| | bone immunity and promote osseointegration"(Su et al., 2024) | | | observed using field-emission scanning electron microscopy. Additionally, an X-ray diffractometer (D8 ADVANCE) was employed to conduct X-ray diffraction (XRD) analysis. | stimulate macrophage polarization toward the M2 phenotype. |
| 14 | "Effect of copper-doped silicate 13–93 bioactive glass scaffolds on the response of MC3T3-E1 cells in vitro and on bone regeneration and angiogenesis in rat calvarial defects in vivo" (Lin et al., 2016) | Yinan Lin et al. | copper | the release of Cu ions from bioactive silicate glass scaffolds on the response of cell, bone regeneration & angiogenesis were studied. | Incorporating BMP2 (1 μg per defect) into both undoped and Cu-doped scaffolds notably improved their ability to promote bone regeneration. |
| 15 | "Electrospun polylactic acid scaffolds with strontium- and cobalt-doped bioglass for potential use in bone tissue engineering applications"(De Souza et al., 2023) | Joyce Rodrigues et al. | Strontium & cobalt | Solutions of 7% PLA was added in three different bioglass,<br><br>4% of 58S bioglass<br><br>4% bioglass-doped strontium<br><br>4% bioglass-doped cobalt (PLA-BGCo). | The bioglass demonstrates favorable outcomes, including cell viability exceeding 70%, along with notable total protein production and alkaline phosphatase activity. |
| 16 | "In vitro bioactivity of titanium-doped bioglass"(Asif et al., 2014) | Imran M. Asif et al. | titanium | We utilized scanning electron microscopy (SEM) images to assess surface morphology development, while energy dispersive X-ray measurements were employed to analyze elemental ratios | Additional research is necessary to ascertain whether the inclusion of titanium in silicate glasses derived from melt-quenching processes can yield comparable advantageous outcomes in alternative bioactive glass systems. |
| 17 | "In Vivo Analysis of the Immune Response to Strontium- and Copper-doped Bioglass" (Barbeck et al., 2022) | MIKE BARBECK et al. | Strontium- and Copper | Four distinct bioglass alkali compositions were created using the melt-quenching method. | The introduction of copper and strontium doping in Bioglass did not demonstrate a significant impact on the foreign body response or vascularization of the implantation bed in vivo. |
| 18 | "Gadolinium-doped bioglass scaffolds promote osteogenic differentiation of hBMSC via the Akt/GSK3β pathway and facilitate bone repair in vivo"(Zhu et al., 2019) | Zhu et al. | Gadolinium | The in vitro effects and underlying mechanisms were evaluated using various methods, including Cell Counting Kit-8 (CCK-8) for cell viability assessment, scanning electron microscopy for observing surface morphology, alkaline phosphatase activity assay, Alizarin red staining for | Gd-BG scaffolds were observed to enhance both the proliferation and osteogenic differentiation of human bone marrow-derived mesenchymal stem cells . |

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| | | | | mineralization analysis, and polymerase chain reaction (PCR) for gene expression profiling. | |
| 19 | "Evaluation of effectiveness of 45S5 bioglass doped with niobium for repairing critical-sized bone defect in in vitro and in vivo models"(L. P. L. de Souza et al., 2020) | Lucas P L de Souza et al. | niobium | The systemic biocompatibility was evaluated by quantifying biochemical markers and conducting histopathological examinations of the liver, kidneys, and muscles. | Defects filled with BGPN2.6 glass demonstrated over 90% coverage, in contrast to only 66% coverage observed for 45S5 Bioglass. |
| 20 | "Cytocompatibility of Potential Bioactive Cerium-Doped Glasses based on 45S5"(Malavasi et al., 2019) | Gianluca Malavasi et al. | Cerium | The investigation of cytocompatibility for potential bioactive glasses, featuring diverse concentrations of CeO2 doping, was conducted by formulating three distinct glass compositions with an escalating amount of CeO2. The designed glasses aimed to incorporate cerium in both its Ce3+ and Ce4+ oxidation states. | The presence of cerium ions has been noted to enhance cell uptake and viability, with a particular emphasis on favoring cell proliferation in the case of BG_3.6. Additionally, the glass with the highest cerium content (BG_5.3) has exhibited a significant promotion of cell proliferation. |

The result of the present review states that much progress has been made in recent decades. Nanoparticles have always a promising tool for material science but their synergism with bioglass makes them much more reliable.

The literature that supports results are from the studies of nanoparticles of lithium, the results in various studies by Ahmad Reza Farmani et al., (2023), Liang et al., (2023), Simila et al., (2023), and Su et al., (2024) where osteoinductive and antimicrobial properties of Lithium have been highlighted. The formation of a Scaffold is its key property.

Zinc stands as another powerful material in the field of regenerative dentistry. In the current review the properties of zinc for preserving collagen, promoting remineralization, and enhancing mechanical properties at the resin-dentin interface (Lee et al., 2020). Magnesium oxide and Magnesium are mainly used for the prevention of the spread of caries in teeth and bacterial infection in root canals. Solution of Magnesium Oxide Nanoparticles and Its Ultrasonic Activation on Root Canal Enterococcus faecalis Biofilm have been proven effective in a study by Alaa et al. (2019) which highly indicated its use in retreatment cases (Abdelaziz et al., 2022). Enterococcus Faecalis is the main bactéria present in the rooth canals When performing retreatment. Strontium is considered a great partner compound and is mainly used in conjugation with Other material to give an extremely effective synergistic effect. Its use with copper, cobalt and fluoride have been mentioned in the studies considered for this review and states that new bone formation and osteoblast levels was witnessed.(Barbeck et al., 2022) When testing Fluoridated Strontium Apatite Nanoparticles in the Surgical Treatment of Endodontic Bone Lesions(Oztekin et al., 2022). Further when strontium- and cobalt-doped bioglass for potential use in bone tissue engineering applications the bioglass demonstrates favorable outcomes, including cell viability exceeding 70%, along with notable total protein production and alkaline phosphatase activity (De Souza et al., 2023).

However with copper the results weren't favourable as copper and strontium doping in Bioglass did not demonstrate a significant impact on the foreign body response or vascularization of the implantation bed and the results here are contradictory fron our results, this our be due to smaller sample size taken in the mentioned study (Barbeck et al., 2022).

Some Other materials that have earned light in the recent decade are Boron, it shows Osteoblast density biocompatibility and new bone formation (Oztekin et al., 2022) whereas gadolinium-doped bioglass scaffolds were observed to enhance both the proliferation and osteogenic differentiation of human bone marrow-derived mesenchymal stem cells (Zhu et al., 2019). Niobium is proven to fill defects with BGPN2.6 glass demonstrating over 90% coverage, in contrast to only 66% coverage observed for 45S5 Bioglass (de Souza et al., 2020). The presence of cerium ions has been noted to enhance cell uptake and viability, with a particular emphasis on favouring cell proliferation in the case of BG_3.6. Additionally, the glass with the highest cerium content (BG_5.3) has exhibited a significant promotion of cell proliferation (Malavasi et al., 2019).

The article considers various available search result bioactive glasses (BAGs) indeed have versatile applications in various fields within the medical and dental domains. As you mentioned, they are currently employed in several applications:

1.Implant Coating: BAGs are utilized as coatings for implants to enhance osseointegration

2. Bone Grafting

- BAGs are commonly used as bone graft materials. Their bioactive nature stimulates bone regeneration and helps in the healing process. They can be applied in procedures where bone augmentation or replacement is needed.

3. Dentin Desensitizer

- BAGs are used in dentistry as desensitizing agents for treating sensitive teeth. The bioactive properties of these glasses can interact with the tooth structure, forming a hydroxyapatite-like layer that helps reduce tooth sensitivity.

4. Restorative Materials: BAGs have been applied in restorative materials, such as dental composites or cements. Their bioactivity and ability to bond with natural tissues make them suitable for dental restorations.

The versatility of BÄG in these applications highlights its potential as a biomaterial that provides structural support and actively interacts with the biological environment, promoting tissue regeneration and integration.

The notable developments that BAGs have made in clinical settings particularly in dentistry are examined in this paper.

A title gains its strength when it becomes essential in the research world. Undoubtedly, Bioglass is a revolutionary tool for dentistry. Its clinical benefits in conservative dentistry and endodontics include special wings. Although sufficient benefits of bioglass and nanoparticles have been discovered in the past few decades, researchers are not ready to settle on their vision of them as promising titles for research in all therapeutic branches of medicine and dentistry. The doping of different elements further represents an advance in regenerative dentistry. This review comprises zinc, copper, boron, strontium, and copper. Figure 1 summarises the Nanoparticles used in endodontics.

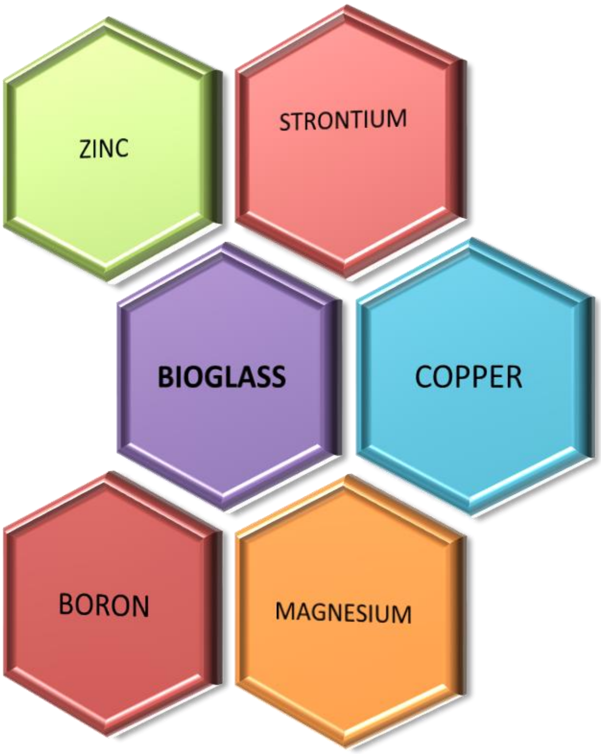


**Figure 1** The figure summarises the most useful nanoparticles in endodontice.

## 5. Final Consideration and Perspective

Research efforts in exploring the applications of Bioglass and nanoparticles in dentistry have yielded commendable results, showcasing significant benefits for both patients and clinicians. Patients experience improved treatment outcomes and faster healing processes due to the unique properties of Bioglass, while clinicians benefit from enhanced treatment efficiency and expanded therapeutic options. For instance, Bioglass-based materials demonstrate remarkable biocompatibility, fostering tissue regeneration and minimizing adverse reactions in patients. Moreover, the integration of nanoparticles enhances the mechanical properties and antimicrobial efficacy of dental materials, further improving treatment outcomes. These findings have notable practical implications for dental practice, suggesting advancements in treatment modalities such as more durable restorative materials and enhanced bone regeneration techniques. With improved biocompatibility and antimicrobial properties, patients can expect reduced treatment complications and enhanced oral health, leading to a better quality of life. Looking ahead, future research should focus on refining existing materials and exploring novel applications to address specific clinical challenges, potentially leading to transformative clinical applications and technological advancements in dental medicine.

## Ethical Considerations

Not applicable.

## Conflict of Interest

No potential conflict of interest has been disclosed by authors.

## Funding

This research did not receive any funding / financial support.

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