WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP
Impact Factor 8.63
Volume 15, Issue 5, 951-985.
Research Article
ISSN 2277–7105

BIOGLASS AND ITS ROLE IN ENHANCING IMPLANT MATERIALS FOR ORTHOPEDIC AND DENTAL USE

***Saurabh Dubey, Dr. Sunil Kumar Prajapati, Ambuj Pandey, Dr. Alok Mahor, Jyoti Maurya**

Deprtment of Pharmaceutics, Institute of Pharmacy, Bundelkhand University, Jhansi-284128, Uttar Pradesh, India.

Article Received on 03 Feb. 2026,
Article Revised on 23 Feb. 2026,
Article Published on 01 March 2026,

https://doi.org/10.5281/zenodo.18802997

***Corresponding Author**
Saurabh Dubey
Deprtment of Pharmaceutics, Institute of Pharmacy, Bundelkhand University, Jhansi-284128, Uttar Pradesh, India.

How to cite this Article: *Saurabh Dubey, Dr. Sunil Kumar Prajapati, Ambuj Pandey, Dr. Alok Mahor, Jyoti Maurya. (2026). Bioglass And Its Role In Enhancing Implant Materials For Orthopedic And Dental Use. World Journal of Pharmaceutical Research, 15(5), 951–985.

ABSTRACT

Bioglass, a bioactive glass material primarily composed of silica, calcium, and phosphorus, has emerged as a revolutionary material in the field of biomedical implants, particularly in orthopedic and dental applications. Due to its unique ability to bond with natural bone tissue and promote cellular activity, bioglass has become a key component in enhancing the performance of implants. In orthopedics, bioglass is used in bone repair, promoting rapid healing and osseointegration in fractures and joint replacements. In dentistry, it aids in improving the integration of dental implants, promoting bone growth around the implant, and reducing the risk of infection. This article explores the role of bioglass in enhancing the materials used in both orthopedic and dental implants, focusing on its advantages, clinical applications, and future potential. We will examine its benefits over traditional materials, its ability to promote tissue healing, and the challenges that remain in fully harnessing its capabilities.

KEYWORDS: Bioglass, Bioactive glass, Orthopedic implants, Dental implants, Bone regeneration, Osseointegration, Tissue engineering, Biocompatibility, Bone healing, Implant materials.

INTRODUCTION

Implants have become an essential component of modern medicine, especially in the fields of orthopedics and dentistry, where they are used to replace or repair damaged bones and teeth. Traditional implant materials, such as metals and synthetic polymers, have demonstrated significant functionality but are often limited by issues like poor integration with the body, risk of infection, and wear over time. In response to these challenges, bioglass has emerged as a promising alternative due to its unique bioactive properties.[1]

Bioglass, first developed in the late 20th century, is a type of silica-based glass that is capable of forming strong chemical bonds with bone tissue. It not only supports bone healing but also stimulates the body's natural processes for tissue regeneration, making it an ideal material for use in orthopedic and dental implants. Its ability to release ions such as calcium and phosphate enhances the bioactivity of the surrounding tissue, accelerating bone formation and improving the integration between the implant and the natural bone.

This article aims to explore the role of bioglass in enhancing implant materials, particularly focusing on its application in orthopedic and dental implants. By examining its mechanisms of action, advantages, clinical applications, and future potential, we will highlight how bioglass is poised to revolutionize implant technology and improve patient outcomes. As we move forward, ongoing research and technological advancements will continue to expand the scope of bioglass in implantable devices, positioning it as a vital material for the future of medical treatments.

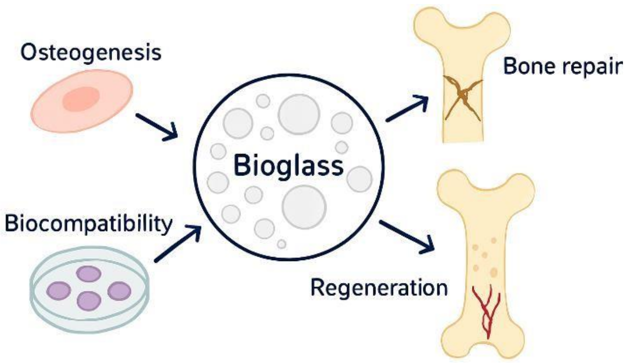


Figure 1: Schematic Representation of Bioglass Functions in Bone Repair and Regeneration.[3]

The development of advanced biomaterials has significantly transformed modern medicine, particularly in the fields of orthopedics and dentistry. Implants are widely used to restore the function of damaged bones and missing teeth, improving both mobility and quality of life for millions of patients worldwide. Conventional implant materials such as titanium alloys, stainless steel, cobalt–chromium alloys, and certain polymers have demonstrated excellent mechanical strength and durability. However, these materials are generally bioinert, meaning they do not actively interact with surrounding biological tissues. As a result, challenges such as poor osseointegration, inflammation, infection, and long-term implant failure may arise.[2,5]

To address these limitations, researchers have focused on developing bioactive materials that can form strong bonds with living tissues and stimulate natural healing processes. Among these materials, bioglass—also known as bioactive glass—has gained considerable attention. Bioglass is a silica-based material typically composed of silicon dioxide (SiO_2), calcium oxide (CaO), sodium oxide (Na_2O), and phosphorus pentoxide (P_2O_5). Unlike traditional implant materials, bioglass is not merely a passive structural support; it actively participates in biological processes. When implanted, it releases biologically active ions that stimulate osteoblast activity, promote the formation of hydroxyapatite, and enhance bone regeneration. This unique property enables bioglass to chemically bond with bone, improving implant stability and long-term performance.

In orthopedic applications, bioglass is used as a coating material, bone graft substitute, and scaffold for bone tissue engineering. It enhances bone repair in cases of fractures, bone defects, spinal fusion, and joint replacement procedures by accelerating healing and strengthening the interface between implant and host bone. In dental applications, bioglass supports jawbone regeneration, improves osseointegration of dental implants, and reduces the risk of post-surgical complications such as infection and peri-implantitis.

This article explores the role of bioglass in enhancing implant materials for orthopedic and dental use. It examines the mechanisms underlying its bioactivity, its advantages over conventional materials, and its current and future clinical applications. As research in biomaterials and regenerative medicine continues to advance, bioglass holds significant promise in improving implant success rates and shaping the next generation of medical and dental treatments.[6,8]

Composition of Bioglass

Bioglass (bioactive glass) is a **silica-based biomaterial** specifically designed to interact with biological tissues and promote bone regeneration. Its composition is carefully controlled to achieve bioactivity, biocompatibility, and controlled degradation within the body.[9]

1. **Basic Chemical Components**

The most well-known bioglass composition is **45S5 Bioglass**, developed by Larry Hench. It consists of four primary oxides:

Component	Chemical Formula	Typical Weight % (45S5)	Function
Silicon dioxide	SiO_2	~45%	Forms the glass network (structural backbone)
Sodium oxide	Na_2O	~24.5%	Increases solubility and ion release
Calcium oxide	CaO	~24.5%	Promotes bone bonding and hydroxyapatite formation
Phosphorus pentoxide	P_2O_5	~6%	Supports hydroxyapatite layer formation

2. **Role of Each Component**

1. **Silicon Dioxide (SiO_2)**

I. Acts as the **network former** in the glass structure.

II. Provides mechanical strength.

III. Controls degradation rate.

IV. Higher silica content → slower dissolution.

2. **Sodium Oxide (Na_2O)**

I. Acts as a **network modifier**.

II. Increases glass reactivity.

III. Helps in rapid ion exchange when implanted.

IV. Enhances bioactivity but reduces mechanical strength if excessive.

3. **Calcium Oxide (CaO)**

I. Essential for bone bonding.

II. Releases calcium ions that stimulate osteoblasts.

III. Contributes to the formation of a **hydroxyapatite (HA) layer**, similar to natural bone mineral.

4. **Phosphorus Pentoxide (P_2O_5)**

I. Supplies phosphate ions.

II. Helps form calcium phosphate and hydroxyapatite.

III. Supports strong chemical bonding with bone tissue.

3. Modified Bioglass Compositions

Modern bioglass formulations may include additional elements to enhance properties

a) **Magnesium (MgO)** – improves mechanical strength

b) **Strontium (SrO)** – enhances bone formation

c) **Zinc (ZnO)** – antibacterial and promotes healing

d) **Boron (B_2O_3)** – increases degradation rate

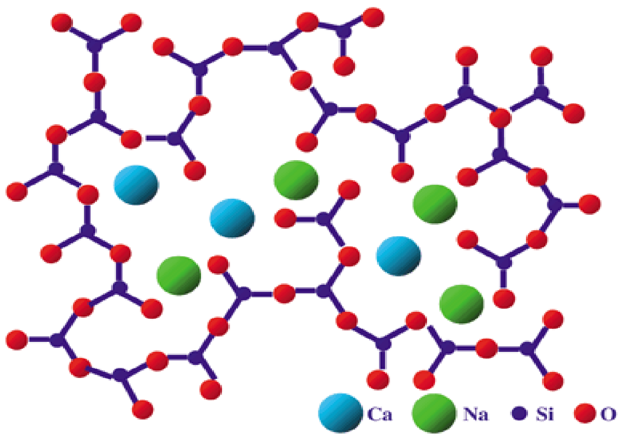
e) **Silver (Ag_2O)** – provides antimicrobial properties

These modifications allow customization for orthopedic implants, dental applications, or drug delivery systems.

Types of Bioglass

Bioglass (bioactive glass) can be classified based on its **composition, structure, and application.**[10,15] Over time, different types have been developed to improve mechanical strength, bioactivity, degradation rate, and clinical performance in orthopedic and dental uses.

1. Silicate-Based Bioglass (Traditional Bioglass)



Example: 45S5 Bioglass

- First developed type
- Contains SiO_2–Na_2O–CaO–P_2O_5
- Highly bioactive
- Forms hydroxyapatite rapidly

Applications

1. Bone grafts

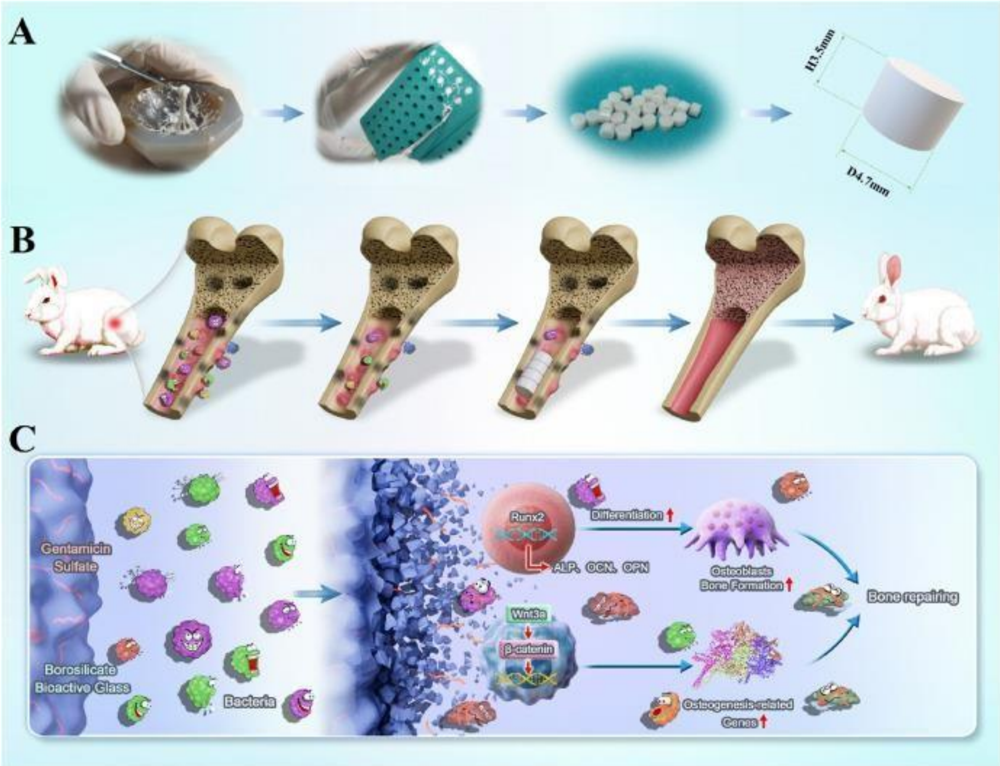
2. Orthopedic coatings

3. **Dental bone regeneration**

✔ Advantages: Excellent bone bonding

✖ Limitation: Relatively low mechanical strength

2. **Borate-Based Bioglass**



- Silicon is partially or fully replaced by **boron (B_2O_3)**
- Faster degradation rate
- Converts more quickly to hydroxyapatite

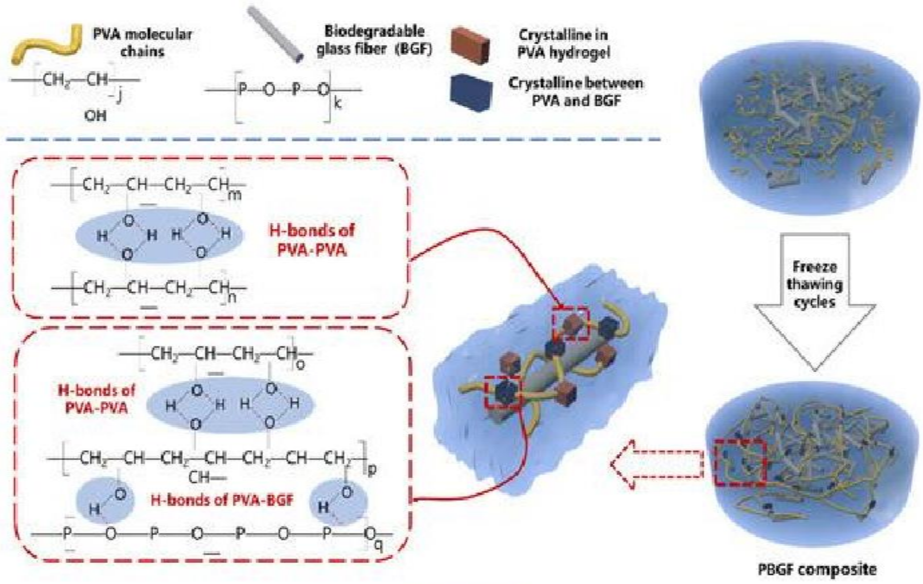
Applications

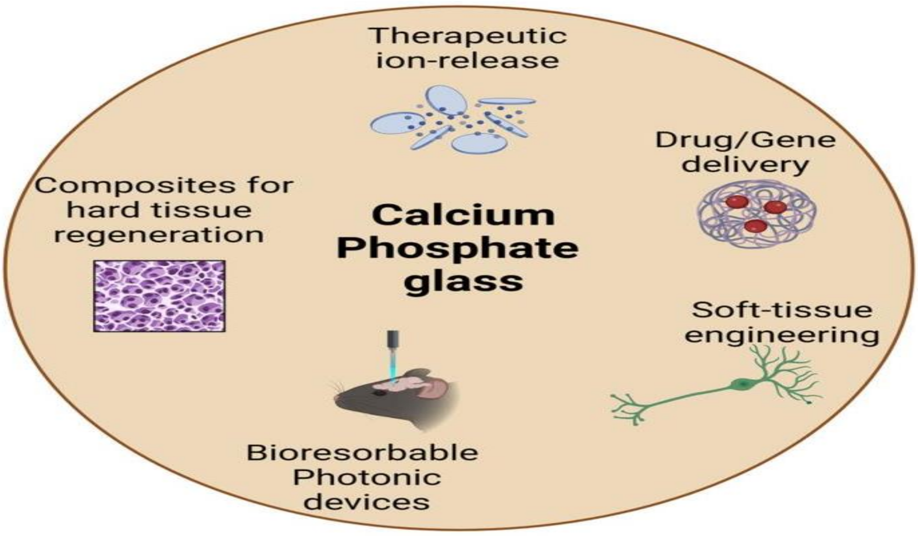
1. Soft tissue repair
2. Wound healing
3. Faster bone regeneration cases

✔ Advantage: Controlled, faster resorption

✖ Limitation: May degrade too quickly for load-bearing implants

3. Phosphate-Based Bioglass





- Based mainly on P_2O_5
- Fully biodegradable
- Degradation rate can be precisely controlled

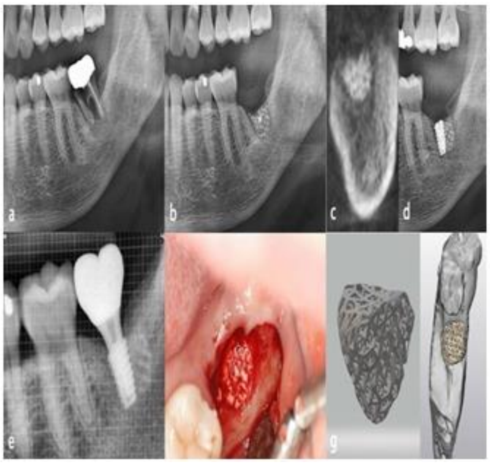
Applications

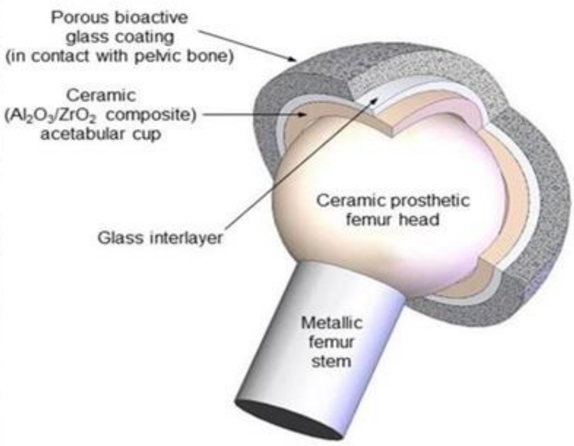
1. Temporary implants
2. Drug delivery systems
3. Tissue engineering scaffolds

✔ Advantage: Complete resorption in the body

✖ Limitation: Lower bioactivity compared to silicate glass.

4. Glass-Ceramics (Crystallized Bioglass)





- Produced by controlled crystallization of bioglass
- Higher mechanical strength
- Lower degradation rate

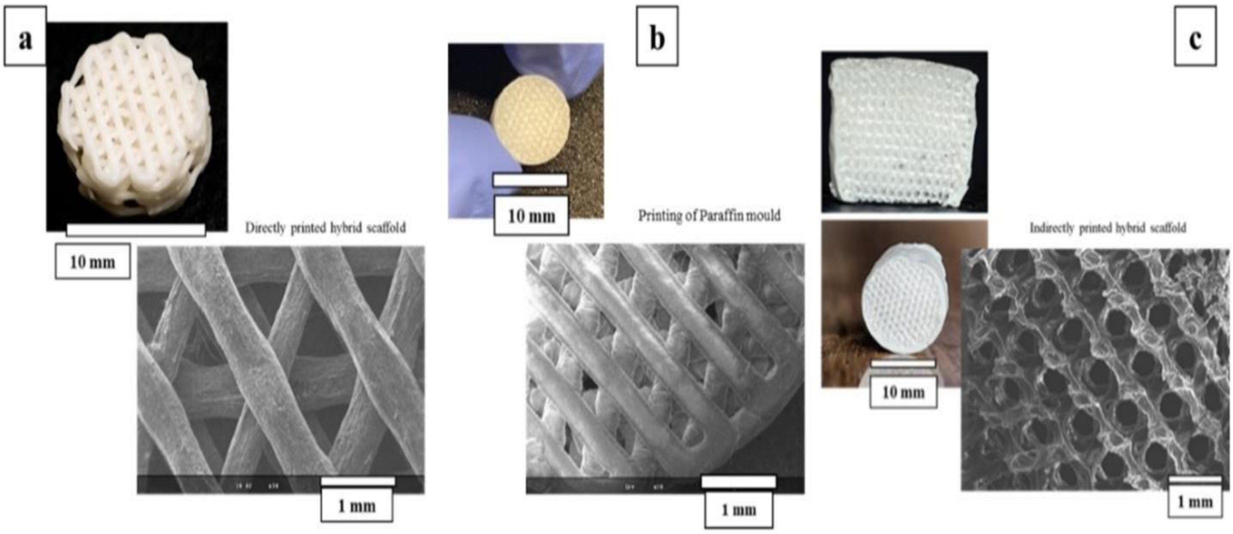
Applications

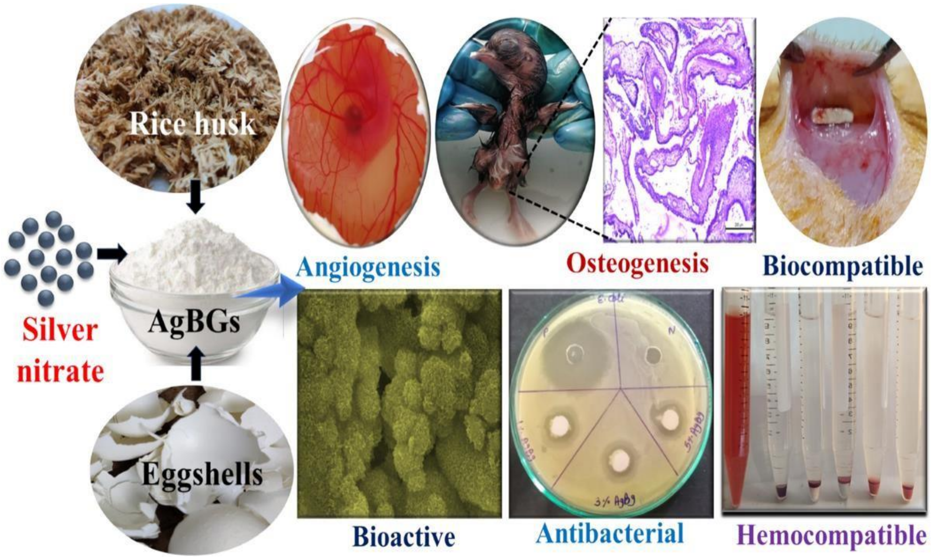
1. Load-bearing orthopedic implants
2. Spinal fusion devices

✔ Advantage: Stronger than traditional bioglass

✖ Limitation: Slightly reduced bioactivity

5. Doped or Modified Bioglass





Contains additional therapeutic ions such as

- **Strontium (Sr)** – enhances bone formation
- **Silver (Ag)** – antimicrobial
- **Zinc (Zn)** – promotes healing
- **Magnesium (Mg)** – improves strength

Applications

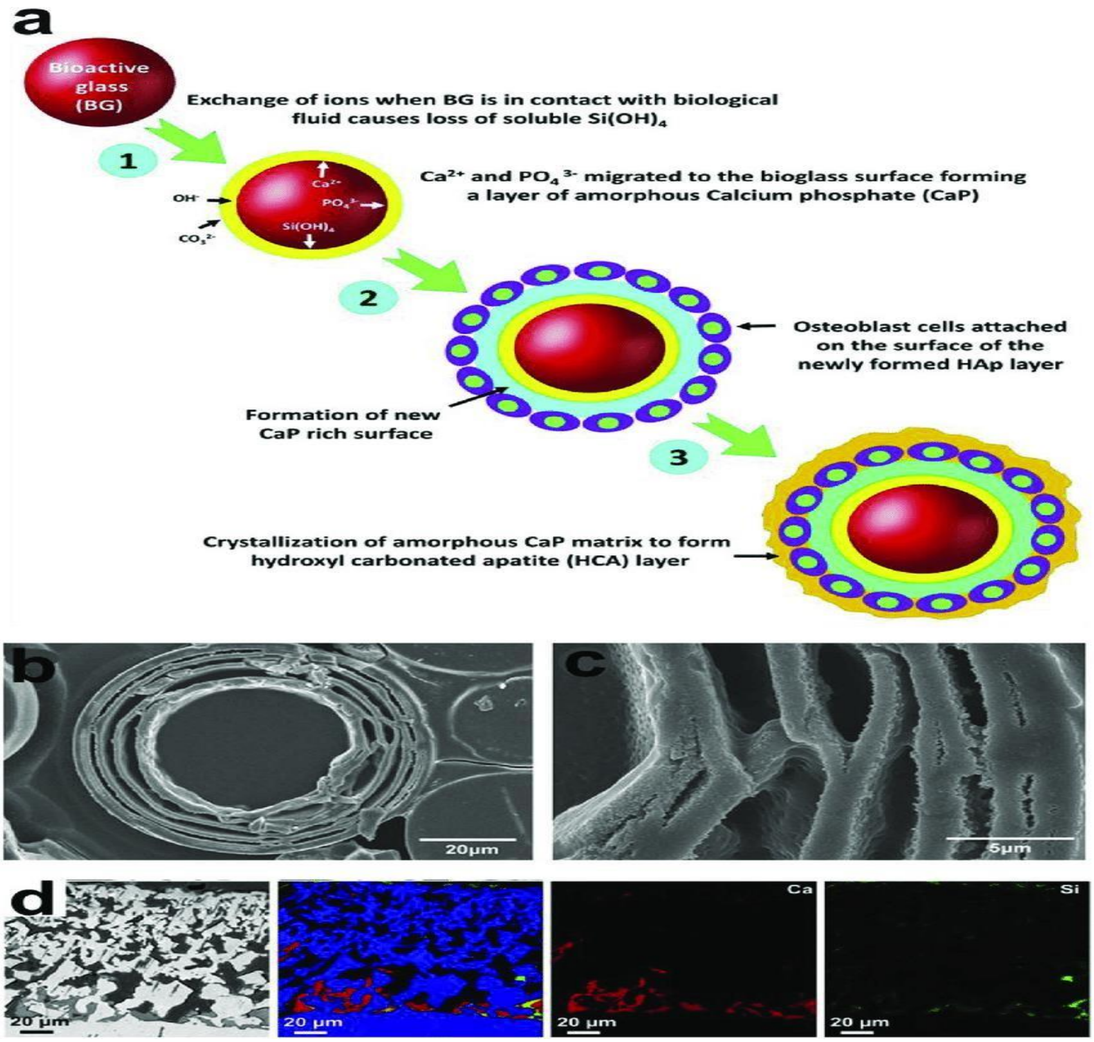
1. Infection-resistant implants
2. Enhanced orthopedic and dental implants
3. Drug delivery systems

✔ Advantage: Tailored biological response

✔Growing focus in modern implant research

Mechanism of Bioglass

Bioglass is considered **bioactive** because it does not remain inert inside the body. Instead, it undergoes a sequence of surface reactions that lead to the formation of a strong chemical bond with bone. This mechanism occurs at the interface between the implant material and physiological fluids (such as blood plasma).[16,20]



The bioactivity process can be divided into five major stages

Stage 1: Ion Exchange (Initial Reaction)

Immediately after implantation:

- Sodium (Na^+) and calcium (Ca^{2+}) ions from bioglass exchange with hydrogen (H^+) or hydronium (H_3O^+) ions from body fluids.
- This increases the local pH around the material.
- The glass network begins to break down at the surface.

RESULT

Rapid dissolution starts, creating a reactive surface.

Stage 2: Hydrolysis of the Silica Network

- The Si–O–Si bonds in the glass break.
- Silanol groups (Si–OH) form on the surface.
- Soluble silica ($Si(OH)_4$) is released into the surrounding fluid.

RESULT

A hydrated silica-rich layer begins forming.

Stage 3: Formation of Silica Gel Layer

- The silanol (Si–OH) groups condense.
- A porous, negatively charged silica gel layer forms on the surface. This layer acts as a template for calcium and phosphate deposition. **Importance:**

This layer is crucial for bone bonding.

Stage 4: Calcium–Phosphate Layer Formation

- Calcium (Ca^{2+}) and phosphate (PO_4^{3-}) ions accumulate on the silica gel layer.
- An amorphous calcium phosphate (ACP) layer forms. This layer gradually thickens.

Stage 5: Crystallization into Hydroxyapatite (HA)

- The amorphous layer crystallizes into **hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$)**.
- This hydroxyapatite is chemically and structurally similar to natural bone mineral.

Final Result

Bone cells (osteoblasts) attach to this layer and begin producing new bone matrix.

Cellular Response Mechanism

Beyond surface chemistry, bioglass also stimulates biological activity

1. Ion Release Stimulates Cells

- Released Si, Ca, and P ions activate genes in osteoblasts.
- Promotes collagen production.
- Enhances bone matrix formation.

2. Angiogenesis Stimulation

- Silicon ions help promote blood vessel formation.
- Improves nutrient supply to healing tissue.

3. Antibacterial Effect

- Increased local pH inhibits bacterial growth.
- Ion release can create an unfavorable environment for pathogens.

Literature review

Singh Manisha et al; 2025

The implant technology is undergoing significant transformation, with a strong emphasis on the creation of advanced and aesthetically refined devices that enhance both functionality and patient experience. This evolution is driven by advances in tissue engineering, materials science, and nanotechnology, enabling the development of implants that more effectively mimic the structure and function of natural bone and teeth. Whilst metal implants offer desirable mechanical strength, biocompatibility concerns have spurred the investigation of alternative materials, most significantly Bioglass and zirconia. Bioglass demonstrates exceptional biocompatibility and osseointegration capabilities, and its bioactivity can be further enhanced through the incorporation of bioactive agents, including antibacterial, anti-inflammatory, and growth factor delivery systems. The combination of Bioglass with biodegradable polymers is emerging as a promising strategy for creating sustainable implant solutions with controlled degradation and drug release profiles.

Hammami et al; 2025

Dental implants are fundamental to contemporary restorative dentistry, providing an exceptional solution for individuals experiencing tooth loss due to aging, trauma, or disease. The global demand for dental implants has increased significantly, driven by an aging population, increased awareness of oral health, and advancements in implant technology. These implants are essential for restoring oral function, aesthetics, and overall quality of life, making them a primary focus in biomedical research (Addy, 2024; Cociuban et al., 2024). Despite significant progress, the long-term efficacy of dental implants remains uncertain. Osseointegration, the biological process through which the implant integrates with surrounding bone tissue, is crucial for stability and functionality.

Mihaela Dinu et al; 2025

The development of bioactive coatings for metallic implants is essential to enhance osseointegration and improve implant longevity. In this study, composite thin films based on bioactive glass and melittin were synthesized using the matrix-assisted pulsed laser evaporation technique and deposited onto titanium substrates. The coatings were characterized using physicochemical analysis methods, including scanning electron microscopy, atomic force microscopy, contact angle measurements, Fourier transform infrared spectroscopy, energy-dispersive X-ray spectroscopy, and electrochemical impedance spectroscopy. Simulated body fluid immersion tests were also conducted to assess bioactivity over time. Scanning electron microscopy and atomic force microscopy revealed dense, irregular surface textures with nanoscale features and an average roughness of ~120 nm, favorable for cell adhesion.

Diana Georgiana Filip et al; 2022

Inorganic biomaterials, including different types of metals and ceramics are widely used in various fields due to their biocompatibility, bioactivity, and bioresorbable capacity. In recent years, biomaterials have been used in biomedical and biological applications. Calcium phosphate (CaPs) compounds are gaining importance in the field of biomaterials used as a standalone material or in more complex structures, especially for bone substitutes and drug delivery systems. The use of multiple dopants into the structure of CaPs compounds can significantly improve their in vivo and in vitro activity. Among the general information included in the Introduction section, in the first section of this review paper, the authors provided a background on the development of hydroxyapatite, methods of synthesis, and its applications. The advantages of using different ions and co-ions for substitution into the hydroxyapatite lattice and their influence on physicochemical, antibacterial, and biological properties of hydroxyapatite are also presented in this section of the review paper.

Oluwatosin David Abodunrin et al; 2022

Because of their excellent biologically active qualities, bioactive glasses (BGs) have been extensively used in the biomedical domain, leading to better tissue–implant interactions and promoting bone regeneration and wound healing. Aside from having attractive characteristics, BGs are appealing as a porous scaffold material. On the other hand, such porous scaffolds should enable tissue proliferation and integration with the natural bone and neighboring soft tissues and degrade at a rate that allows for new bone development while preventing bacterial colonization. Therefore, researchers have recently become interested in a different BG composition based on borate (B2O3) rather than silicate (SiO2). Furthermore, apatite synthesis in the borate-based bioactive glass (BBG) is faster than in the silicate-based bioactive glass, which slowly transforms to hydroxyapatite. This low chemical durability of BBG indicates a fast degradation process, which has become a concern for their utilization in biological and biomedical applications.

Sílvia Rodrigues Gavinho et al; 2023

The use of implantable medical devices, such as orthopedic or dental implants, has become common practice in almost all fields of medicine. However, foreign bodies are associated with a significant risk of bacterial infections. These infections are a significant concern in healthcare settings, and can lead to serious complications. The biofilms, which are communities of bacteria encased in a protective matrix, can form on the surface of the implants, and trigger an inflammatory response in the surrounding tissue, leading to further complications. In the case of dental implants, biofilm formation plays a significant role in the development of peri-implantitis, which is a chronic inflammatory disease caused by anaerobic Gram-positive and Gram-negative bacteria that gradually leads to bone loss and implant failure

Role of Bioglass in Orthopedic Implants

Orthopedic implants are widely used to restore function in damaged bones and joints caused by trauma, degenerative diseases, tumors, or congenital defects. Common implant materials such as titanium alloys, stainless steel, and cobalt–chromium alloys provide excellent mechanical strength but are biologically inert.

The introduction of **Bioglass 45S5**, developed by **Larry Hench**, revolutionized implant materials by introducing bioactivity—the ability to form a direct chemical bond with bone. Bioglass enhances implant integration, accelerates healing, and reduces implant failure rates.[20,27]

Applications of Bioglass in Orthopedic Implants: 1 Implant Coatings

Bioglass is commonly used as a coating over:

- Titanium hip implants
- Knee joint prostheses
- Spinal fixation devices Benefits:
- Improved bonding strength
- Reduced micromovement at interface
- Better long-term stability

2 Bone Graft Substitute

Bioglass granules or scaffolds are used to fill:

- Bone defects from trauma

- Tumor resection cavities
- Non-union fractures

Advantages over traditional bone grafts:

- No donor site morbidity (unlike autografts)
- Unlimited availability
- Osteoconductive and osteostimulative properties

3 Fracture Repair

Bioglass particles can be placed in fracture gaps to:

- Stimulate bone regeneration
- Accelerate callus formation
- Improve mechanical healing

Role of Bioglass in Dental Implants

Dental implants are widely used to replace missing teeth and restore oral function and aesthetics. Most dental implants are made of titanium due to its excellent mechanical strength and corrosion resistance. However, titanium is biologically inert and relies mainly on mechanical interlocking for stability.

The introduction of **Bioglass 45S5**, developed by **Larry Hench**, has significantly improved the biological performance of dental implants. Bioglass enhances osseointegration, promotes bone regeneration, and provides antibacterial benefits, making it highly valuable in dental implantology.[28,32]

Applications of Bioglass in Dental Implants 1 Implant Surface Coating

Bioglass is used as a coating over titanium dental implants to:

- Improve bioactivity
- Increase surface roughness
- Enhance bone bonding

This coating transforms an inert implant surface into a bioactive interface.

2 Bone Grafting and Ridge Augmentation

In cases of insufficient bone volume, bioglass granules are used for:

- Socket preservation after extraction

- Sinus lift procedures
- Ridge augmentation
- Treatment of peri-implant bone defects Advantages:
- Osteoconductive scaffold
- No need for donor site (unlike autograft)
- Controlled resorption
- Stimulates new bone formation

3 Periodontal Regeneration

Bioglass is widely used in periodontal therapy for

- Intrabony defects
- Furcation defects
- Guided tissue regeneration It promotes regeneration of:
- Alveolar bone
- Periodontal ligament
- Cementum

4 Treatment of Dentin Hypersensitivity

Certain bioglass formulations are incorporated into desensitizing toothpastes. The released calcium and phosphate ions occlude dentinal tubules, reducing sensitivity.

Advantages of Bioglass in Implant Technology

Bioglass is one of the most significant developments in biomaterials science. Since the discovery of **Bioglass 45S5** by **Larry Hench**, it has transformed the design and performance of orthopedic and dental implants. Unlike conventional inert materials, bioglass actively interacts with biological tissues, offering multiple clinical and biological advantages.[33,40] below is a detailed explanation of its key advantages in implant technology.

1. Superior Bioactivity

The most important advantage of bioglass is its **bioactivity**—its ability to form a direct chemical bond with bone.

How it Works

a) Releases biologically active ions (Si^{4+}, Ca^{2+}, Na^{+}, PO_4^{3-})

b) Forms a hydroxycarbonate apatite (HCA) layer

c) Bonds chemically with surrounding bone

Benefit

1. Eliminates fibrous tissue formation at implant interface
2. Ensures strong and stable fixation

This property makes bioglass fundamentally different from bioinert materials like titanium or stainless steel.

2. Enhanced Osseointegration

Osseointegration is critical for long-term implant success.

Bioglass Promotes

1. Osteoblast proliferation
2. Collagen synthesis
3. Bone mineralization
4. Faster bone maturation

Clinical Impact

1. Reduced healing time
2. Earlier implant loading
3. Improved implant stability
4. Lower risk of implant loosening

This is especially important in orthopedic joint replacements and dental implants.

3. Osteoconductive and Osteostimulative Properties

Bioglass not only provides a scaffold (osteoconduction) but also stimulates new bone formation (osteostimulation).

Osteoconductive

- Acts as a framework for bone growth

Osteostimulative

- Activates genes responsible for bone formation
- Stimulates growth factors

This dual function enhances bone regeneration more effectively than passive materials.

4. Biocompatibility

Bioglass is highly biocompatible and does not produce toxic reactions.

Advantages

1. Minimal inflammatory response
2. No rejection by host tissue
3. Safe degradation products

Its ionic dissolution products are naturally present in the body, making it safe for long-term applications.

5. Controlled Degradation and Resorbability

Unlike permanent implants, bioglass can gradually degrade in the body.[41]

Benefits

1. Degradation rate can be controlled by composition
2. Matches new bone formation rate
3. Eliminates need for secondary removal surgery

This is particularly useful in bone defect fillers and scaffolds.

6. Strong Bone–Implant Bonding

Traditional implants rely mainly on mechanical interlocking. Bioglass forms a **chemical bond** with bone.

RESULT

1. Increased interfacial strength
2. Reduced micromotion
3. Lower risk of aseptic loosening

This significantly improves long-term implant survival.

7. Antibacterial Properties

Infections are a major cause of implant failure. Bioglass offers natural antibacterial effects through.

1. Increase in local pH
2. Osmotic pressure changes
3. Ion release disrupting bacterial metabolism Additionally, it can be doped with antimicrobial ions such as:

- Silver (Ag^{+})
- Zinc (Zn^{2+})
- Copper (Cu^{2+}) This reduces:

a) Post-surgical infections
b) Biofilm formation
c) Peri-implantitis (in dental implants)[42]

8. Angiogenic Potential (Promotes Blood Vessel Formation) Recent research shows bioglass stimulates angiogenesis. **Importance:**

a) Improves blood supply at implant site
b) Enhances nutrient delivery
c) Accelerates tissue healing

Good vascularization is essential for successful bone regeneration.

9. Versatility in Application Forms

Bioglass can be used in multiple forms:

1. Implant coatings
2. Granules
3. Porous scaffolds
4. Injectable pastes
5. Composite materials
6. 3D-printed structures

This versatility makes it suitable for

a) Orthopedic implants
b) Dental implants
c) Bone graft substitutes
d) Spinal fusion devices

10. Surface Modification Capability

Bioglass can enhance implant surfaces by:

a) Increasing surface roughness
b) Improving wettability
c) Enhancing protein adsorption

These factors promote better cell attachment and faster integration.

11. Reduced Healing Time

Due to rapid HCA layer formation and stimulation of osteoblast activity:

1. Healing periods are shortened
2. Patients recover faster
3. Early functional loading becomes possible

This improves patient outcomes and satisfaction.

12. Compatibility with Composite Systems

Although pure bioglass is brittle, it works exceptionally well when combined with:

1. Titanium
2. Polymers
3. Hydroxyapatite
4. Biodegradable materials These composites combine:

a) Mechanical strength
b) Bioactivity
c) Controlled degradation

Thus overcoming mechanical limitations while retaining biological advantages.[43]

13. Improved Long-Term Implant Survival

Because of

1. Chemical bonding
2. Reduced infection
3. Enhanced bone regeneration
4. Better interfacial stability Bioglass contributes to:

- Lower revision rates

- Increased implant lifespan
- Better functional outcomes

14. Minimal Risk of Disease Transmission

Unlike allografts or xenografts

1. No donor tissue required
2. No risk of disease transmission
3. No ethical concerns

This makes it safer and more widely acceptable.

15. Future-Ready Material

Bioglass supports advanced technologies such as:

1. Nanotechnology-based coatings
2. Drug-delivery systems
3. Growth factor incorporation
4. Smart responsive implants

This ensures its continued relevance in next-generation implant design.

Limitations and Challenges

Although bioglass has revolutionized implant materials due to its bioactivity and regenerative properties, it is not without limitations. Understanding these challenges is important for improving its clinical performance in orthopedic and dental applications.

Bioglass compositions such as **Bioglass 45S5**, originally developed by **Larry Hench**, show excellent biological behavior but face mechanical, processing, and clinical challenges.[44,50]

1. Poor Mechanical Strength

1.1 Brittleness

The most significant limitation of bioglass is its **brittle nature**.

- Low tensile strength
- Low fracture toughness
- Prone to cracking under stress

Unlike metals such as titanium, bioglass cannot withstand high mechanical loads.

Clinical Impact

- Not suitable for load-bearing implants (e.g., hip or knee replacements) as a bulk material
- Risk of fracture under cyclic loading

2. Limited Load-Bearing Capacity

Bioglass lacks the mechanical strength required for high-stress applications.

Problem

- Cannot replace metallic implants in major joint replacements
- Unsuitable as a structural implant material

Current Solution

- Used as coatings on metals
- Incorporated into composites
- Combined with polymers or ceramics

3. Rapid Degradation in Some Compositions

Certain bioglass formulations dissolve too quickly in physiological environments.

Risks

- Premature loss of mechanical support
- Unpredictable degradation rate
- Local pH increase beyond optimal levels

If degradation is faster than bone regeneration, structural stability may be compromised.

4. Difficulty in Processing and Fabrication Bioglass has complex manufacturing requirements. **Challenges:**

- High melting temperatures
- Narrow sintering window
- Risk of crystallization during processing

Crystallization reduces bioactivity because amorphous glass is more reactive than crystalline forms.

5. Weak Adhesion of Coatings

When used as a coating on metallic implants

- Risk of delamination
- Thermal expansion mismatch with metal
- Cracking during implantation

Poor bonding between coating and substrate can reduce implant longevity.

6. Limited Fatigue Resistance

Orthopedic and dental implants experience repetitive loading. Bioglass

- Has low fatigue strength
- Can develop microcracks
- May fail under cyclic stress

This restricts its use in long-term dynamic load environments.

7. Risk of Excessive Ion Release

Bioglass works by releasing ions, but excessive release may cause

- High local alkalinity
- Temporary inflammatory response
- Cytotoxic effects in extreme cases

Proper composition control is essential to balance bioactivity and safety.

8. Handling and Brittleness During Surgery

In granular or scaffold form:

- Fragile structure
- Difficult to shape during surgery
- Risk of fragmentation

This can complicate clinical handling procedures.

9. Limited Soft Tissue Integration (Compared to Bone)

Bioglass bonds very well to bone but

- Limited long-term integration with soft tissues
- Risk of epithelial downgrowth (in dental implants) Research is ongoing to improve soft

tissue compatibility.

10. Cost and Manufacturing Complexity

Compared to conventional materials

- Production can be expensive
- Requires controlled processing techniques
- Advanced fabrication methods increase cost This may limit accessibility in some healthcare systems.

11. Incomplete Replacement of Autografts

Although bioglass is an excellent bone graft substitute:

- It may not fully match the osteogenic potential of autografts
- Lacks living cells and natural growth factors Thus, in complex cases, autografts are still preferred.

12. Long-Term Clinical Data Limitations

While short- and medium-term studies are promising:

- Limited very long-term (>20 years) data
- Need for more large-scale clinical trials
- Long-term degradation behavior still under investigation

13. Structural Limitations in 3D Printing

In advanced applications like 3D-printed scaffolds:

- Maintaining mechanical strength is challenging
- Porosity reduces structural integrity
- Balancing porosity and strength is difficult

Summary of Major Limitations[50]

Category	Limitation
Mechanical	Brittle, low fracture toughness
Structural	Poor load-bearing capacity
Biological	Rapid degradation in some forms
Clinical	Handling difficulty, coating delamination

Category	Limitation
Manufacturing	High processing complexity
Long-term	Limited long-term clinical data

Recent Advances and Future Perspectives

1. Advanced Bioactive Glass Coatings and Surface Engineering

Researchers have made major strides in **bioactive glass coatings** that improve both biological performance and mechanical integration on implant surfaces. These coatings are tailored using newer fabrication techniques (like sol-gel, electrophoretic deposition, pulsed laser deposition) to reduce cracking, enhance bonding, and provide smoother yet bioactive surfaces compatible with metallic implants such as titanium. These surface-engineered coatings help implants integrate faster with bone and reduce long-term micromotion, which enhances implant stability in both orthopedic and dental settings.[51,56]

Examples of advancements include

- Patterned or gradient bioglass coatings that better match the mechanical properties of bone.
- Combined glass–ceramic layers that balance bioactivity and structural integrity

2. Ion-Doped and Multifunctional Bioglasses

A major recent trend is *doping bioglass with therapeutic ions* such as **strontium (Sr), zinc (Zn), silver (Ag), copper (Cu), and boron (B)**. These dopants expand bioglass functionality beyond simple bone bonding

- **Strontium** enhances bone formation and increases density.
- **Zinc and silver** provide strong antibacterial effects, which reduce infection risk around implants.
- **Copper** promotes angiogenesis (formation of new blood vessels), vital for bone healing.
- **Boron** improves dissolution control and can increase regenerative response.

This multifunctional approach means bioglass can not only bond with bone but actively *modulate healing processes*, fight infection, and encourage vascularization—advances that were previously only possible using separate growth factors or drugs.

3. Injectable and Minimally Invasive Bioglass Formulations

New bioglass formulations are being developed as **injectable composites, cements, or hydrogels**. These can be delivered into complex bone defects or periodontal spaces without large incisions, reducing surgical trauma, recovery time, and the risk of infection.

Key advantages

- Uniform distribution in irregular bone defects.
- Lower risk of postoperative issues.
- Potential for simultaneous drug delivery from the injectable matrix.

This opens doors to treating defects that are difficult to reach with traditional solid implants.

4. 3D Printing and Patient-Specific Scaffolds

Additive manufacturing (3D printing) of bioglass and bioglass composites has emerged as a powerful tool. Recent studies show that *3D-printed bioglass meshes and scaffolds* can be customized to match patient anatomy while providing highly controlled porosity that supports bone ingrowth.

Techniques like **selective laser melting** and **fused deposition modeling** allow integration of bioglass with metals (e.g., Ti–6Al–4V) or polymers, resulting in implants that are optimized for both mechanical performance and bioactivity.

5. Smart and Responsive Bioglass Systems

The future of bioglass is heading toward **smart bioactive materials** that can *sense and respond* to the physiological environment. For example:

- Materials that release more antibacterial ions in infection-prone acidic conditions.
- Systems that accelerate calcium/phosphate release during active bone formation.

Integration with **sensors and external monitoring systems** (potentially even AI-assistance) could allow implants to dynamically support healing based on real-time biological feedback.[57]

6. Composite and Hybrid Systems

To overcome mechanical limitations of bioglass (especially brittleness), strategies now focus on **composite materials** where bioglass is combined with:

- Biodegradable polymers (improving flexibility)
- Hydroxyapatite or β-TCP ceramics (enhancing strength)
- Metals (improving load-bearing capacity)

These composites retain bioactivity while significantly improving structural performance, making them more suitable for load-bearing orthopedic and dental uses.

7. Nanotechnology and Drug Delivery

Nanostructured bioglass and bioglass nanoparticles are being explored as carriers for drugs, growth factors, or genetic material. This allows controlled local release directly at the implant site, aiding bone regeneration and preventing infection.

Nanostructuring also increases surface area and cellular interaction, further enhancing osteogenic (bone-forming) potential.

8. Personalized and Regenerative Medicine Integration

Modern developments are pushing bioglass into **personalized medical applications**, especially when combined with:

- Patient-derived stem cells
- Tissue-specific growth factors
- Customized scaffold designs

This aligns bioglass technology with regenerative medicine goals—where the body's own cells are guided to repair tissue

Future Perspectives[58,60]

Looking ahead, researchers foresee several transformative directions:

AI-Assisted Implant Design

Combining bioglass materials with AI-guided diagnostics and design tools could personalize implants based on patient bone quality and healing capacity.

Smart Responsive Materials

Bioglass systems that adapt in real-time to changes in pH, temperature, or biological signals—boosting healing when needed and remaining silent when not required.

Clinical Translation and Regulatory Approvals

While lab and animal results are promising, widespread clinical adoption depends on stronger long-term human trial data and smoother regulatory pathways.

Commercial and Cost Accessibility

Future research aims to reduce production costs and manufacturing complexity so that bioglass technology becomes more accessible globally.[61]

Summary of Recent Advances & Future Trends

Area	Progress	Impact
Coatings & surface engineering	Smoother, stronger bonding layers	Better implant stability
Ion-doped glasses	Enhanced antibacterial & regenerative functions	Reduced infection + faster healing
Injectable systems	Minimally invasive delivery	Broader clinical application

Area	Progress	Impact
3D printing	Customized scaffolds	Patient-specific implants
Smart materials	Responsive ion release	Adaptive tissue support
Nanotechnology	Drug delivery + high surface interaction	Controlled therapy + regeneration
AI & integration	Personalization potential	Tailored implant strategies

CONCLUSION

Bioglass has revolutionized implant material science by introducing bioactivity into traditionally inert materials. Its ability to bond with bone, stimulate regeneration, and reduce infection makes it a promising component in orthopedic and dental implants. While mechanical limitations remain, ongoing research and composite technologies continue to expand its clinical applications. Bioglass represents a significant step toward more effective, longer-lasting, and biologically integrated implant solutions.

Bioactive glasses have emerged as a transformative class of biomaterials with wide-ranging applications in regenerative medicine, dentistry, orthopedics, and soft tissue repair. Since the introduction of the original 45S5 Bioglass®, continuous advancements in composition, processing methods, and functionalization strategies have significantly expanded their clinical relevance. Their unique ability to bond with living tissues, stimulate osteogenesis and angiogenesis, and deliver therapeutic ions distinguishes bioactive glasses from conventional inert biomaterials

This review has highlighted the structural characteristics, biological mechanisms, and diverse applications of bioactive glasses, with particular emphasis on antibacterial activity, drug-delivery potential, and nano-scale formulations. The development of ion-doped and nano-bioactive glasses has enabled multifunctional behavior, allowing simultaneous tissue regeneration and infection control. Advanced fabrication techniques, including sol–gel processing and additive manufacturing, have further enhanced design flexibility and biological performance.

Despite these advances, challenges related to mechanical limitations, degradation control, long-term safety, and large-scale manufacturing remain significant barriers to widespread clinical adoption. Addressing these issues will require interdisciplinary collaboration, rigorous standardization, and long-term clinical validation. Future research focusing on smart, responsive, and patient-specific bioactive glass systems is expected to further improve therapeutic outcomes and broaden clinical applications.[62-68]

REFERENCE

1. Eker, F., Duman, H., Akdaşçi, E., Bolat, E., Sarıtaş, S., Karav, S., & Witkowska, A. M. (2024). A Comprehensive Review of Nanoparticles: From Classification to Application and Toxicity. Molecules, 29(15): 3482. https://doi.org/10.3390/molecules29153482
2. Madival, H., Rajiv, A. A Comprehensive Review of Bioactive Glasses: Synthesis, Characterization, and Applications in Regenerative Medicine. *Biomedical Materials & Devices* (2025). https://doi.org/10.1007/s44174-025-00310-8
3. Elisa Piatti, Marta Miola and Enrica Verne Tailoring of bioactive glass and glass ceramics properties for *in vitro* and *in vivo* response optimization: a review (2024). DOI: 10.1039/D3BM01574B
4. Larry L. Hench (2013). "Chronology of Bioactive Glass Development and Clinical Applications." *New Journal of Glass and Ceramics*, 3(2): 29–47. DOI:10.4236/njgc.2013.32011
5. Vaiani, L., Boccaccio, A., Uva, A. E., Palumbo, G., Piccininni, A., Guglielmi, P., Cantore, S., Santacroce, L., Charitos, I. A., & Ballini, A. (2023). Ceramic Materials for Biomedical Applications: An Overview on Properties and Fabrication Processes. Journal of Functional Biomaterials, 14(3): 146. https://doi.org/10.3390/jfb14030146
6. Zhou, P., Garcia, B.L. & Kotsakis, G.A. Comparison of antibacterial and antibiofilm activity of bioactive glass compounds S53P4 and 45S5. *BMC Microbiol.*, 2022; **22**(212). https://doi.org/10.1186/s12866-022-02617-8
7. Hammami, I., Gavinho, S. R., Pádua, A. S., Lança, M. d. C., Borges, J. P., Silva, J. C., Sá- Nogueira, I., Jakka, S. K., & Graça, M. P. F. (2023). Extensive Investigation on the Effect of Niobium Insertion on the Physical and Biological Properties of 45S5 Bioactive Glass for Dental Implant. International Journal of Molecular Sciences, 24(6): 5244. https://doi.org/10.3390/ijms24065244
8. **Hench LL, Gaisser DM.** *The Genetic Basis for Osteogenesis Stimulation by Controlled Release of Ionic Dissolution Products.* Transactions of the Orthopedic Research Society,

Annual Meeting, San Francisco, USA, 2008.

9. **Hench LL, Polak JM.** *A genetic basis for design of biomaterials for in situ tissue regeneration.* Key Engineering Materials, 2008; 377: 151–166.
10. **Hu Y-C, Zhong J-P.** *Osteostimulation of bioglass.* Chinese Medical Journal, 2009; 122(19): 2386–2389.
11. **Oonishi H, Kushitani S, Yasukawa E, Iwaki H, Hench LL, Wilson J, Tsuji E, Sugihara T.** *Particulate Bioglass Compared with Hydroxyapatite as a Bone Graft Substitute.* Clinical Orthopaedics and Related Research, 1997; 334: 316–325.
12. Gao, Yang, Seles, Mohan Anne and Rajan, Mariappan. "Role of bioglass derivatives in tissue regeneration and repair: A review" *REVIEWS ON ADVANCED MATERIALS SCIENCE*, 2023; 62(1): 20220318. https://doi.org/10.1515/rams-2022-0318
13. Almasri, D., & Dahman, Y. (2025). Bioactive Glass Preloaded with Antibiotics for Delivery of Long-Term Localized Drug Release Exhibiting Inherent Antimicrobial Activity. Applied Sciences, 15(10): 5363. https://doi.org/10.3390/app15105363
14. Zhu Y, Zhang X, Chang G, Deng S, Chan HF. Bioactive Glass in Tissue Regeneration: Unveiling Recent Advances in Regenerative Strategies and Applications. Adv Mater, 2025 Jan; 37(2): e2312964. doi: 10.1002/adma.202312964. Epub 2024 Jul 16. PMID: 39014919; PMCID: PMC11733714.
15. dos Reis-Prado, A.H., de Souza, J.R., de Sousa Trichês, E. *et al*. Bioactive glasses for bone tissue engineering: a bibliometric study of the top 100-most cited papers. *Odontology*, 2025; 113: 488–530. https://doi.org/10.1007/s10266-024-01027-8
16. Ellakwa, D.ES., Abu-Khadra, A.S. & Ellakwa, T.E. Insight into bioactive glass and bio-ceramics uses: unveiling recent advances for biomedical application. *Discov Mater*, 2025; **5:** 78. https://doi.org/10.1007/s43939-025-00254-2
17. Filip, D. G., Surdu, V.-A., Paduraru, A. V., & Andronescu, E. (2022). Current Development in Biomaterials—Hydroxyapatite and Bioglass for Applications in Biomedical Field: A Review. Journal of Functional Biomaterials, 13(4): 248. https://doi.org/10.3390/jfb13040248
18. Fiume, E., Barberi, J., Verné, E., & Baino, F. (2018). Bioactive Glasses: From Parent 45S5 Composition to Scaffold-Assisted Tissue-Healing Therapies. Journal of Functional Biomaterials, 9(1): 24. https://doi.org/10.3390/jfb9010024
19. Babu, M.M., Rao, P.V., Govindan, N.P., Gujjala, R., Prasad, P.S. (2023). Structural and In Vitro Bioactivity of Phosphate-Based Glasses for Bone Regeneration. In: Ikhmayies, S.J. (eds) Advances in Glass Research. Advances in Material Research and Technology.

Springer, Cham. https://doi.org/10.1007/978-3-031-20266-7_4

20. Radhakrishnan Sreena, Gurusamy Raman, Geetha Manivasagam and A. Joseph Nathanael (2024) Bioactive glass–polymer nanocomposites: a comprehensive review on unveiling their biomedical applications DOI: 10.1039/D4TB01525H
21. Madival, H. Review: silicate bioactive glasses—advances in structure, bioactivity, and biomedical applications. *J Mater Sci.,* 2026. https://doi.org/10.1007/s10853-026-12217-w
22. Mi Chen, Yidan Wang, Pingyun Yuan, Lan Wang, Xiaocheng Li, Bo Lei, Multifunctional bioactive glass nanoparticles: surface–interface decoration and biomedical applications, *Regenerative Biomaterials*, 2024; 11: rbae110, https://doi.org/10.1093/rb/rbae110
23. He, L., Huang, Y., Gu, J. *et al*. Modulated Degradation Rates of Bone Mineral-Like Calcium Phosphate Glass to Support the Proliferation and Osteogenic Differentiation of Bone Marrow-Derived Stem Cells. *J Bionic Eng.,* 2024; **21:** 1960–1974. https://doi.org/10.1007/s42235-024-00540-4
24. Madival, H., Rajiv, A. Review: borate bioactive glasses—synthesis, properties, and biomedical applications. *J Mater Sci.*, 2025; **60:** 11272–11295. https://doi.org/10.1007/s10853-025-11132-w
25. Ensoylu, M., Deliormanlı, A. M., & Atmaca, H. (2023). Preparation, Characterization, and Drug Delivery of Hexagonal Boron Nitride-Borate Bioactive Glass Biomimetic Scaffolds for Bone Tissue Engineering. *Biomimetics*, 8(1): 10. https://doi.org/10.3390/biomimetics8010010
26. Mountjoy G. Comment on ‘Bond volumes in crystals and glasses and a study of the germanate anomaly’ by H.-J. Weber [J. Non-Cryst. Solids, 1999; 243: 220. J Non-Cryst Solids, 2003; 324(1-2): 177–178.
27. Hench LL, Paschall HA. Direct chemical bond of bioactive glass-ceramic materials to bone and muscle. J Biomed Mater Res., 1973; 7(3): 25–42.
28. Bose, S.; Sarkar, N.; Banerjee, D. Natural medicine delivery from biomedical devices for the treatment of bone disorders: A review. *Acta Biomater,* **2021**; *126:* 63–91.
29. Shakeel, A.; Corridon, P.R. Mitigating challenges and expanding the future of vascular tissue engineering-are we there yet? *Front. Physiol.,* 2022; 13: 1079421.
30. Wang, F.; Li, Y.; Shen, Y.; Wang, A.; Wang, S.; Xie, T. The functions and applications of RGD in tumor therapy and tissue engineering, **2013;** *14:* 13447–13462.
31. Boccaccini, A.R.; Blaker, J. Bioactive composite materials for tissue engineering scaffolds. Expert Rev. Med. Devices, 2005; 2: 303–317.
32. Xynos, I.D.; Edgar, A.J.; Buttery, L.D.K.; Hench, L.L.; Polak, J.M. Gene-expression

profiling of human osteoblasts following treatment with the ionic products of Bioglass® 45S5 dissolution. J. Biomed. Mater. Res., 2001; 55: 151–157.

33. Zhao, S.; Li, L.; Wang, H.; Zhang, Y.; Cheng, X.; Zhou, N.; Rahaman, M.N.; Liu, Z.; Huang, W.; Zhang, C. Wound dressings composed of copper-doped borate bioactive glass microfibers stimulate angiogenesis and heal full-thickness skin defects in a rodent model. Biomaterials, 2015; 53: 379–391.
34. Balasubramanian, P.; Hupa, L.; Jokic, B.; Detsch, R.; Grünewald, A.; Boccaccini, A.R. Angiogenic potential of boron-containing bioactive glasses: In Vitro study. J. Mater. Sci., 2016; 52: 8785–8792. [CrossRef]
35. Naseri, S.; Lepry, W.C.; Nazhat, S.N. Bioactive glasses in wound healing: Hope or hype? J. Mater. Chem. B., 2017; 5: 6167–6174.
36. Krishnan, V.; Lakshmi, T. Bioglass: A Novel Biocompatible Innovation. J. Adv. Pharm. Technol. Res., 2013; 4: 78–83.
37. Shendage, S. S., Kamble, G., & Chavan, R. (2025). *Bioactive glass for bone tissue regeneration: focusing on key biological properties*. **ACS Biomaterials Science & Engineering.** https://doi.org/10.1021/acsbiomaterials.5c01283
38. Shendage, S. S., et al. (2024). *In situ silver-doped antibacterial bioactive glass for bone regeneration*. **Journal of Materials Science**. https://doi.org/10.1007/s10853-024-09805-z
39. Naruphontjirakul, P., et al. (2023). *Multifunctional Zn and Ag co-doped bioactive glass nanoparticles for bone regeneration*. **Scientific Reports**, 13: 34042. https://doi.org/10.1038/s41598-023-34042-w
40. Ahmed, M. M., El-Kheshen, A. A., & Moaness, M. (2025). *Strontium/copper-doped nano- bioactive glass for biomedical applications*. **Scientific Reports**. https://doi.org/10.1038/s41598-025-27551-3
41. Taye, M. B., Ningsih, H. S., & Shih, S. J. (2024). *Surface-modified bioactive glasses with enhanced angiogenic and antibacterial activity*. **Journal of Nanoparticle Research**. https://doi.org/10.1007/s11051-024-05935-2
42. Zhao, Y., Qiang, W., & Lei, B. (2025). *Advanced multifunctional bioactive glass nanoparticles*. **Advanced Healthcare Materials**. https://doi.org/10.1002/adhm.202502192
43. Yaghoubi, E., & Nourani, M. R. (2025). *MicroRNA modulation by doped bioglasses in bone regeneration*. **Journal of Applied Tissue Engineering.**
44. Balasubramanian P, Hupa L, Jokic B, Detsch R, Grünewald A, Boccaccini AR.

Angiogenic potential of boron-containing bioactive glasses: an in vitro study. **J Mater Sci.,** 2017; 52(15): 8785–8792. doi:10.1007/s10853-016-9991-1

45. Askari M, Arabuli L. Computational design of multifunctional bioactive glass nanoparticles: a multi-objective optimization approach to balance osteogenesis, anticancer activity, and antibacterial performance. **J Compos Compd.** 2025; 7(2).
46. Sreena R, Raman G, Manivasagam G, Nathanael AJ. Bioactive glass–polymer nanocomposites: a comprehensive review on unveiling their biomedical applications. **J Mater Chem B.,** 2024; 12(18): 4123–4152. doi:10.1039/D4TB01525H
47. Narayanan S, Singh M. Innovative approaches in regenerative medicine for the development of sustainable and bioactive implants. **Biomed Mater Devices,** 2025; 3: 97–118. doi:10.1007/s44174-025-00397-z
48. Zhang, Y., LeGrande, A. N., Goodkin, N., Nusbaumer, J., He, S., Schmidt, G. A., & Wang, X. (2025). *Exploring precipitation triple oxygen isotope dynamics: Insights from GISS-E2.1 simulations*. **Journal of Advances in Modeling Earth Systems**, *17*(4): e2024MS004509. https://doi.org/10.1029/2024MS004509
49. Zhu, M., Fang, Y., Jia, M., Chen, L., Zhang, L., & Wu, B. (2025). *Using machine learning models to predict the dose-effect curve of municipal wastewater for zebrafish embryo toxicity*. **Journal of Hazardous Materials**, *488*: 137278. https://doi.org/10.1016/j.jhazmat.2025.137278
50. Hench LL. The story of Bioglass®. *J Mater Sci Mater Med*., 2006; 17(11): 967–978.
51. Jones JR. Review of bioactive glass: From Hench to hybrids. *Acta Biomater*., 2013; 9(1): 4457–4486.
52. Rahaman MN, Day DE, Bal BS, Fu Q, Jung SB, Bonewald LF, et al. Bioactive glass in tissue engineering. *Acta Biomater*., 2011; 7(6): 2355–2373.
53. Xynos ID, Edgar AJ, Buttery LD, Hench LL, Polak JM. Ionic products of bioactive glass dissolution increase proliferation of human osteoblasts. *J Biomed Mater Res*., 2000; 51(2): 230–238.
54. 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): 2757–2774.
55. Lovelace TB, Mellonig JT, Meffert RM, Jones AA, Nummikoski PV, Cochran DL. Clinical evaluation of bioactive glass in the treatment of periodontal osseous defects. *J Periodontol*., 1998; 69(9): 1027–1035.
56. Wilson J, Low SB. Bioactive ceramics for periodontal treatment: comparative studies in

the Patus monkey. *J Appl Biomater*, 1992; 3(2): 123–129.

57. Fu Q, Rahaman MN, Bal BS, Brown RF, Day DE. Evaluation of 13-93 bioactive glass scaffolds for hard tissue engineering. *J Biomed Mater Res A*., 2008; 87(1): 172–179.
58. Waltimo T, Brunner TJ, Vollenweider M, Stark WJ, Zehnder M. Antimicrobial effect of nanometric bioactive glass 45S5. *J Dent Res*., 2007; 86(8): 754–757.
59. Jia W, Zheng X, Li W, Chen J, Wang Y. Bioactive glass for wound healing applications. *Adv Healthc Mater*, 2019; 8(18): e1900683.
60. Mirzaei R, Mohammadi MR, Mirzaei S. Borate bioactive glasses in soft tissue regeneration, *Ceram Int*., 2018; 44(1): 1–12.
61. Kargozar S, Baino F, Hamzehlou S, Hill RG, Mozafari M. Bioactive glasses: Sprouting angiogenesis in tissue engineering. *Trends Biotechnol*., 2018; 36(4): 430–444.
62. Campoccia D, Montanaro L, Arciola CR. The significance of infection related to orthopedic devices and issues of antibiotic resistance. *Biomaterials*, 2006; 27(11): 2331–2339.
63. Arciola CR, Alvi FI, An YH, Campoccia D, Montanaro L. Implant infection and antibiotic resistance: a mini-review. *Int J Artif Organs*., 2005; 28(11): 1119–1125.
64. Allan I, Newman H, Wilson M. Antibacterial activity of particulate bioactive glass against supra- and subgingival bacteria. *Biomaterials*, 2001; 22(12): 1683–1687.
65. Drago L, De Vecchi E, Bortolin M, Toscano M, Mattina R, Romanò CL. Antimicrobial activity and resistance selection of different bioactive glasses compared to antibiotics. *Biomaterials*, 2013; 34(26): 7020–7027.
66. Bellantone M, Williams HD, Hench LL. Broad-spectrum bactericidal activity of Ag_2O-doped bioactive glass. *Antimicrob Agents Chemother*, 2002; 46(6): 1940–1945.
67. Rai M, Yadav A, Gade A. Silver nanoparticles as a new generation of antimicrobials. *Biotechnol Adv*., 2009; 27(1): 76–83.
68. Kargozar S, Hamzehlou S, Baino F. Can bioactive glasses be useful to accelerate the healing of epithelial tissues? *Mater Sci Eng C*., 2019; 97: 1009–1020.
69. **Thomas MV, Puleo DA, Al-Sabbagh M.** *Bioactive glass three decades on* — review of Bioglass history, mechanisms of bioactivity and clinical applications. **J Long Term Eff Med Implants.,** 2005; 15(6): 585-597. doi:10.1615/jlongtermeffmedimplants.v15.i6.20
70. **Hench LL.** *Bonding mechanisms at the interface of Bioglass and tissues* — original mechanistic understanding of bioactive glass bonding in biomaterials research (covered historically in Hench reviews).
71. **Weinstein AM, Klawitter JJ, Cook SD.** *Implant-bone interface characteristics of*

bioglass dental implants — early experimental study on implant interfaces. **J Biomed Mater Res.,** 1980; 14(1): 23-29. doi:10.1002/jbm.820140104