Bone regeneration by bioactive glass fibrous threads and glass beads: Narrative review

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Abstract

Before the emergence of biomedical engineering, organ transplantation was considered the ideal treatment option for survival. Still, with the advent of bioactive materials, regenerative medicine was revolutionized by utilising the basic knowledge of repairing soft and hard tissues. Bioactive glass fibres possess a large surface area and provide efficient cellular attachment, while micro-spherical beads can be used as a potent drug delivery and protein vehicle. According to the composition, they are categorised as silicate, phosphate, and borate bioglasses. Their mechanism begins while in contact with body fluids, and results in an ionic interchange and formation of a hydroxyapatite layer at the implantation site. Bioglasses have several applications in regenerative medicine and dentistry, like bone graft surgeries after tumour resections, osteomyelitis and tibial fracture rehabilitations, craniofacial, pulmonary, cardiac, and skin surgeries. They are also widely used in various operative dentistry and paediatric dental procedures.

Keywords: Bioglass 45s5, Bioactive glass S53P4, Microspheres, NovaMin, Osteoconduction, Osteointegration, Growth factors.

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Introduction

The natural phenomenon of recovery, rebuilding, and improvement in the growth of affected tissues or diseased organs to restore the normal physiological functions of the human or animal body is called regeneration. Living beings have an inbuilt potential to regrow their injured body parts and tissues either through complete or partial rejuvenation.[1] Tissue repair encompasses bone remodelling during the growth of the musculoskeletal system, followed by structural organisation in adulthood. Bone remodelling occurs in episodes that restore the musculoskeletal configuration and functions.[2] Miscellaneous medical treatments and surgical modalities are currently applied for bone regeneration in cases of enormous contusive injuries. In particular, large osseous defects and maxillofacial traumas are usually restored by contemporary bone-grafting methods that are associated with implantation site morbidity, along with graft tissue insufficiency and rejection in case of autoimmune reactions. Such complications encourage the element of tissue engineering in biomedical sciences, which has returned promising results when used in conjunction with bioactive materials.

Biomedical engineering combines modern medicine and regenerative medicine, based on foundational knowledge of repairing soft tissues and bone defects.[3] Before tissue regeneration was introduced, organ transplantation was the only option for survival, but acute immunological reactions in the host body replaced organ transplants with tissue regeneration. This shift caused a paradigm change in bioengineering, and ultimately, 'regeneration' was recognized as a diverse field focussed on re-growing tissues to restore the functions of injured organs using cells with reproductive potential,[4] thereby reducing the risk of immunological reactions.

Bioactive materials inherently can repair damaged tissues and support tissue regeneration by acting as a core for three-dimensional (3D) cellular grafting.[5] Biomaterials are naturally inert and tissue-compatible, which not only delays the immediate immune response but also allows them to degrade directly at the cellular level. This makes them compatible with normal physiological functions and helps prevent in vivo teratogenic effects. The advanced bioactivity within the scaffold has led to the fourth era of biomaterials, known as "Bio-mimetic" or smart biomaterials. These materials can be natural or synthetic and are used in acellular 3D scaffold systems.

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Material and Methods

The current narrative review was conducted in July 2022 and comprised a search on Google, Google Scholar, Science Direct, PubMed, Semantic Scholar, Biomed, and other databases for studies published in the Brazilian and German languages. The data was collected, and a Gantt chart was generated to proceed with the project schedule.

Results

Scaffolding platforms are interim models needed for bone rejuvenation. These are materials that are set up to commence cellular interactions and proliferation at the microscopic level, resulting in the formation of new functional tissues.[3] A perfect scaffold should be 3D in structure and composition, exhibit uniformity in porosity and pore configuration/geometry, have a potential of carrying away metabolic wastes and nutrients, possess stress shielding property, be bio-degradable at the cellular level, and should be non-toxic and simulate biological systems in vivo, hence resulting in ideal regeneration. For effective proliferation and osteogenesis, the porosity of the scaffold plays a key role. The osteoblasts with a diameter of 10-50µm effortlessly penetrate through scaffolds of wider pores ranging 100-200µm.[4]

The primary materials for scaffolds, commonly utilized in various therapeutic and surgical interventions in regenerative medicine, are macropolymers with high molecular weight. However, in 1969, Larry Hench revolutionized tissue engineering with his ground-breaking innovation, the "Bioactive glass",[5] which later became known as bioglass (BG). He was the first to examine bioactive glass using a scanning electron microscope (SM), revealing its polymeric macrostructure along with distinctive micro-porosities (Figure 1).[6] Bioactive glass exerts its action by biologically binding to the dense, mineralized bone tissues in a normal physiological environment and promoting local bone formation. They could be sol-gel derived or melt-driven, and therefore attain two geometrical forms: fibrous threads and micro-spherical beads (Figure 2).[7,8]

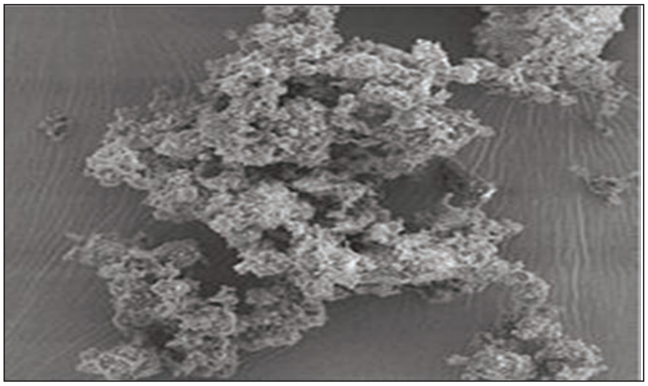

Figure-1: Scanning electron microscopy of bioglass demonstrating its polymeric macrostructure with characteristic micro-porosities.

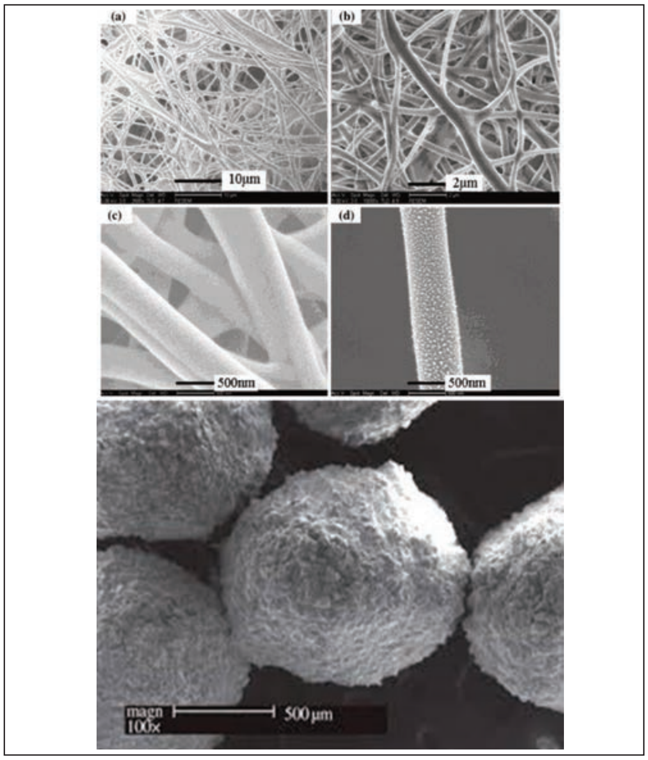

Figure-2: Basic architectural forms of bioglass (threads and microspheres) as seen on scanning electron microscope (SEM).

The bioglass threads strengthen the tissue engineering scaffold complex due to their enhanced mechanical and osteoconductive properties, upon which the fundamental cellular units of the human body can be grown and cultured to analyze the susceptibility of living cells in 3D scaffolds. However, the rigid and crystalline configuration of bioactive fibres has narrowed their medical applications. The formation of microsphere beads has advanced biomedical engineering due to their layering ability and proficient drug delivery.[6] Usually, 1.2% and 3.6% of cerium oxide (CeO_2) carrying glass beads are considered the finest 3D bioactive scaffolds for coping with oxidative strain in the course of osseous regeneration. Despite the eminent role of CeO_2, several studies highlighted[7] the osteoblasts stimulation by bioactive fibres/beads in the presence of several bioactive agents, like metal ions, surface active agents, and antioxidants, in the artificial environment.[8,9] But to date, no study has pinpointed the function of ascorbic acid/Vitamin C incorporated bioglass for successful bone regrowth.

Biologically active glasses

Glass is an unstructured solid material that can reduce its consistency upon a rise in the temperature of the substance, owing to which it becomes mouldable into numerous figures and forms.[10] Generally, bioglasses are the rigid configuration-based materials readily used as scaffolds. One of their rapid bonding attributes with the bone and cellular stimulation at the gene level makes them bond very rapidly with the bone compared to other bioactive ceramic materials. These materials could be melt-driven, but sol-gel-synthesised bio glasses render more promising results due to nanometer-scale porosity. They are available under numerous commercial brands established based on[7] their combinations that include Barium 45S5, S53P4 (contain 53% of silicone dioxide) and other ion-doped glasses,[11] like Copper-doped 45S5, silver-doped 45S5, Calcium and Potassium dopped bioglasses, 13-93 type of bioglasses, Strontium-Bioglass, 70S30C (contain 70% silicon dioxide and 30% of calcium oxide), 77S (bioglass contain 77% of silicon dioxide), Zinc-doped sol-gel-derived mesoporous glasses.[12]

Microscopic structure of bioactive glass

The BGs generally comprise a triad of network formers (silica, Silicone dioxide/SiO_2, Phosphate dioxide/PO_2, and boron trioxide/BO_3),[13] network modifiers, and intermediate oxides that have been modified gradually over the years. Multiple alternative forms of bioactive glass and their prosthetic implants have been launched for several bio-engineered and regenerative applications, such as a prosthesis for the middle ear, called Middle Ear Prosthesis (MEP), which was invented ages ago for repairing defective ears, and it was later replaced with CeraVital. In addition, newer bioglass materials, including Endosseous Ridge Maintenance Implant (ERMI), Extracochlear Percutaneous Implant (EPI), Nova Bone, PerioGlas, StroneBone, Biogran, BoneAlive, Arglaes, NovaMin, Corglaes, and Medpor, etc., have been used for miscellaneous regenerative treatments. The recent Thera Glass powders are effectively utilised for bone regeneration.[5]

Bioactive glass composition

BGs embody numerous constituents that render special characteristics to smart glasses. In general, bio active glass mainly carry 40-52% of silicon dioxide/SiO_2 in their network, 10-50% calcium-oxide, 20-24.4% sodium oxide/Na_2O, 2-8% phosphorus pentaoxide/P_2O_5, 0-25% Calcium Flouride/CaF_2, and 0-10% Boron Trioxide/B_2O_3, while traces metals like Potassium, Magnesium and Lithium also constitutes glass matrix.[14] According to the chemical composition, bioglasses are categorised into subgroups as silicate, phosphate, and borate forms according to the presence of elements.[15,16]

Silicate Bioglass

Silicate bioglass (45S5) was the introductory bioactive glass fibre and considered as class-A bioglass material, which mainly comprised 46.1% Silicon dioxide/SiO_2, 24.4% Sodium Oxide/Na_2O, 26.9% Calcium Oxide/CaO, and 2.6-6% Pentoxide/P2O5 by weight.[6] The principal constituent of these glasses is SiO_4, called Orthosilicate Tetrahedron, where the tetrahedron configuration is encircled by four oxygen atoms joined via Silicon and oxygen (Si-O-Si) nexus. The dissolution rate of premium glasses is quite steady, so complete in vivo dissolution occurs in 1-2 years.

Phosphate Bioglass

Phosphate-based glasses containing Calcium, Oxygen-Sodium and Phosphate/Na_2O-P_2O_5 are widely used in tissue engineering applications. Atoms are usually ortho-phosphate in configuration, with 8% of Si-O-P (Silicon, Oxygen, and Phosphate) also being part of their chemistry along with a minute quantity of pyrophosphates that contribute to their internal chemistry, and strengthen their network.[17]

Borate Bioglass

These mainly consist of Boron Trioxide/B_2O_3 (46.1 %).[18] Although these bioglasses are highly cytotoxic due to the liberation of Boron ions, doping of such glasses with strontium ions overcomes their cytotoxic effects and enhances their biocompatibility with living tissues. Borate glasses are generally chemically resistant and resemble silicate bioglass in terms of chemical longevity.

Ideal properties of Bioglasses

Bioactivity within tissues

The rate of dissolution of bioactive glass fibres is the prime factor behind their biological reactivity. Conventional glasses acquire a lower dissolution rate and stronger durability, and, hence, they are devoid of bioactive properties, contrary to BGs.[19] Biological activity is normally achieved by the integration of network modifiers within the glass network. For instance, Calcium Oxide and Sodium Oxide modifiers increase the surface reactivity and strengthen the silica network of BGs. Instant contact of these glasses with body fluids interchanges Hydrogen/H^+, Sodium/ Na^+, and Calcium/Ca_2^+ ions within tissues, which brings about ionic dissolution and glass degradation at the site of implantation.[14]

Genesis of the hydroxyapatite layer

The formation of a gel layer between bioglass and the tissue helps in the genesis of the hydroxyapatite layer/HAL, which acts as a potent vehicle for the adsorption and transportation of bone-forming growth factors over the surface of bioglass. Furthermore, it facilitates the binding and multiplication of osseous progenitor cells, which participate in the repair and regeneration of osseous tissues (Figure 3). The nascent bone starts replacing bioglass due to the inward extensions of the hydroxyapatite layer/HAL, which proceeds to osteo

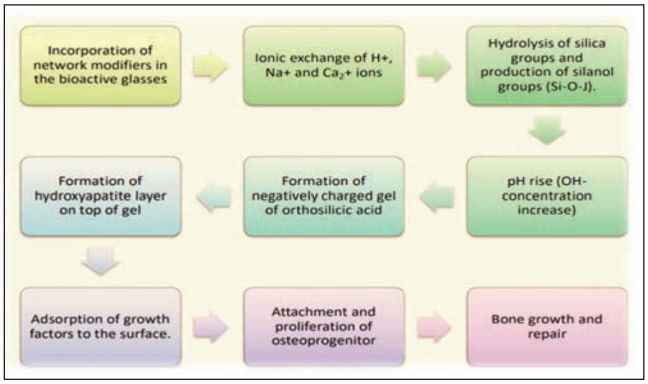

Figure-3: Steps of bone repair and growth. The formation of gel layer between bioglass and the tissue helps in the genesis of hydroxyapatite layer that acts as a potent vehicle for the adsorption and transportation of bone forming growth factors over the surface of bioglass. It facilitates the binding and multiplication of osseo-progenitor cells which participate in the repair and regeneration of osseous tissues.

regeneration.[20] The universal concept concerning bioactive glass surfaces indicates that a larger surface area results in a greater dissolution rate and potency in its hydroxyapatite emergence.

Antibacterial properties

Osseous and soft tissue originated infections are arduous to treat due to the emerging strains of multidrug-resistant (MDR) microbes.[21] Currently, bioactive glasses are effectively employed as drug delivery systems to address infections caused by drug-resistant microbes using three new strategies: the release of ionic compounds when bioactive glasses are introduced into an aqueous solution; the incorporation of biocidal metals into bioactive glass; and the promotion of antibiotic delivery from the surfaces of these materials. The widely used 45S5 bioactive glass exhibits antibacterial properties due to its strong ability to generate an alkaline environment that is detrimental to microbes. As a result, both 45S5 and S53P4 typically sustain a balance between alkalinity (with a pH of 7.9) and osteogenic properties to enhance bone regeneration. Furthermore, their effectiveness against biofilms is bolstered by the incorporation of various antimicrobial nanoparticles and fragments within the glass structure. Elements such as Silicon, Phosphate, Strontium, Copper, Silver, Zinc, Galium, Cobalt, and Iron are primarily embedded within the porous framework to inhibit microbial growth. At present, Copper-enriched mesoporous silicon dioxide and Calcium Oxide-based Bioglass are yielding superior regenerative outcomes in osteomyelitis cases due to their strong bactericidal effects against Staphylococcus Aureus, Escherichia Coli, and Staphylococcus. Epidermis. As a result, these materials are advantageous in treating soft tissue infections. Likewise, alkali-free Zinc Oxide and Strontium Oxide-doped bioactive glass effectively reduce *E. coli* and *S. aureus* in vivo.[22]

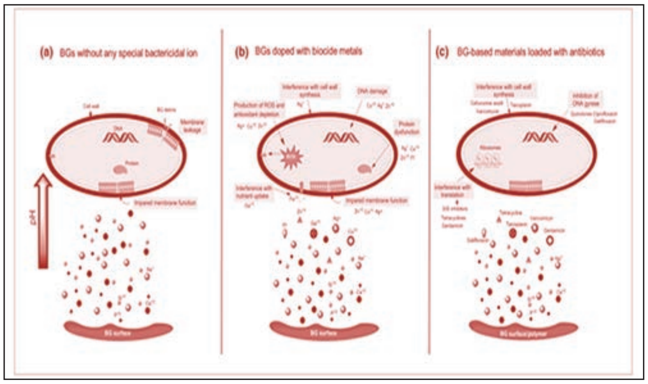

Figure-4: Antibiotic delivery from bioglass surface. (a) The mode of action of bioglass bits while disintegrating at the cellular level; (b) The mode of action of bacteriocidal ions liberating from metal-ion-doped bioglass; (c) The mode of action of bioglass packed with antimicrobial drugs.

Systemic and dental uses of Bioactive glass

The BGs are readily pre-owned for treating numerous oro-systemic pathologies, fracture rehabilitations, and regrowth. The silicon-based bioglass has several applications in clinical, therapeutic, and biomedical areas, like bone graft surgeries after tumour resections, osteomyelitis, and tibial fracture rehabilitations, craniofacial, pulmonary, cardiac, and skin surgeries.[23] Besides, these materials have a diverse usage in dentistry. For example, they are incorporated in toothpastes, dentifrices, and dental restorative materials to conquer caries-induced dissolution and to suppress dentine hypersensitivity. They can be sprayed over oral implants for better osseointegration. Fluoride-based bioglass is used for the symptomatic treatment of gingival and periodontal diseases. Additionally, they are also used in dentin-pulp capping and endodontic treatment. Currently, Novamin-potent bioglass is used in enamel re-mineralisation, which combats dentine hypersensitivity. Mostly, sol-gel-derived bioglass renders promising results than melt-driven ones in pulp capping therapies among deciduous dentition. PerioGlass brought fruitful outcomes in restoring infra-bony and interproximal bone defects due to its efficient osteoblastic proliferation and fixation properties. Biogran is preferred in maxillofacial traumas and for repairing the defects of the jawbone.[5]

Bioactive glass challenges

Despite being characterised as a smart material, BGs still have certain issues. For example, Bioglass 45S5 has in vivo cytotoxic effects that disrupt its usage in regenerative medicine. The cytotoxicity starts with an ionic burst of Sodium and Calcium ions within the network, which holds back hydroxyapatite layer genesis and osteoblastic proliferation during bone regrowth. Besides, 45S5 glass is mechanically very rigid, so it remains unsuitable for synthesising 3D porous scaffolds. Several fabrication methods of bioactive glass lead to denaturation of biomolecules,[24] like fractionation of protein molecules in ethanol during the sol-gel-derived technique, in the presence of organic solvents, and hamper their usage. Due to their rapid dissolution, they destabilise endosseous implants within tissues within no time, hence resulting in peri-implantitis. Therefore, bio-ceramics are found to be more suitable for implant coatings and osseointegration. In dentistry, the major disadvantage of bioglasses is their rapid degradation due to glazing over dental implants. This downside can be attributed to the significant difference in values between the thermal expansion coefficients of glazing materials and the dental implant substrate on which it is coated.[21]

Discussion

Disadvantages of 3D porous scaffolds

The premier wide-pore 45S5 glass scaffolds, fabricated by the sponge replication method, are extremely rigid for implantation. The soaring brittleness and deficient sintering ability of a particular bioactive glass create hollow struts within the scaffold's network. Further, sol-gel-obtained meso-porous scaffolds are also brittle and hold 1MPa (Megapascals) compressive strength, which is quite low, hence challenging their usage in load-bearing areas. The additive manufacturing technologies (AMTs), which gave stronger compressive strength to scaffolds up to 16 MPa, overcame the challenge smartly. But still, AMT-manufactured scaffolds exhibit a major drawback of a weak 3D complex that should be ruled out to gear up for the future developing challenges in regenerative medicine.[25]

The BG threads are fibrous scaffolding platforms with their diameter, thickness, and tensile strength strongly influencing their performance at the tissue level. Usually, the thickness of 9-93 glass fibre threads ranges from 20µm to 140µm. Secondly, the mean diameter of 13-93 glass fibres is 34µm, whereas S53P4 glass fibres are 39µm in width. The tensile strength of fibres strongly depends upon the fibres' width: thin fibres have more strength compared to thick fibres. A study suggested that thinner 9-93 fibres possess massive tensile strength of 1625 MPa, whereas the thicker ones bear 617 MPa tensile strength, hence weak in bearing forces.[26] Besides, the total surface area of fibres also contributes to their efficacy. The thinnest nano-fibers are highly beneficial in tissue engineering applications because of the enormous surface area and uniform meso-porous configuration, which makes them suitable for efficient cellular multiplication and in vivo attachment.

The degradation of bioactive glass threads is another salient feature that influences their in vivo performance and functions. Fibre's dissolution rate depends upon their width and methods of fabrication, like the phosphate-based bioglass fibres have a higher dissolution rate than the degradation rate of bulk glasses due to greater overall surface area.[25]

Challenges for bioactive glass fibres and glass beads

One of the crucial challenges linked with fibres is the strict control of their thickness, which directly impacts their overall performance and function. The altered diameter is linked with the electro-spinning method of drawing fibres. The electro-spun bioactive fibres with a small diameter result in a smaller pore size and lesser cellular infiltration within the scaffolds. Secondly, fibre crystallisation also changes their bioactivity in vivo. This problem is mostly associated with melt-driven 45S5 bioglass, enriched with calcium and sodium, which hampers fibre fabrication due to crystallisation.[27]

Microsphere bioglass is a unique form of bioactive material. Microsphere beads are widely used in bone repair and regrowth, and are also used as a potent drug delivery and protein vehicle under a controlled physiological environment. The bioglass beads are ball-shaped particles ranging from 1µm to 1,000µm in diameter[28] with an average pore size of 3.02nm. Generally, beads hold less pore volume and have a higher surface area compared to irregular bioglass beads (IBGs). Therefore, they enhance cellular proliferation and adhesion in 3D scaffolds at a faster pace. For example, mesenchymal stem cells (MSCs) of human bone marrow fixate and proliferate over microspherical surfaces quickly than rough fibrous facets.[29] Usually, they are synthesised by the melt-quenching method following flame spheroidization of glass balls in which powdered glass particles are added in the presence of an oxygen flame, and are gathered subsequently. Moreover, a few latest fabrication techniques, like heat sinterisation, super-saturation processes, solvent and non-solvent vaporisation, and sintering methods, have also been used for synthesising bioactive glass beads with better physical and mechanical properties. These sintering systems upgrade the mechanical attributes of microspherical beads. Poly lactic-co-glycolic acid (PLGA) is one of the most interconnected, well-structured, and uniformly porous sintered microspheric scaffold systems (SMSs) with better dissolution in vivo, high biocompatibility, and coherent drug loading capacity.[30]

Despite the numerous advantages and effective therapeutic uses of microspherical beads, they encounter several obstacles. To begin with, their high production costs limit their widespread application in therapy. Additionally, variations in environmental conditions (such as temperature, pH, and solvent) can impact their stability and efficiency during the encapsulation process. One significant drawback of these injectable beads is their tendency to move away from the injection site and become dispersed.[31]

Bone regeneration: Latest trends

Miscellaneous modern treatment modalities have come up for efficient osseous healing and extra-skeletal deformities, which concede a multitude of approaches used for bone regeneration. Some of the quality procedures popular for bone regeneration include the bone transport method (filling osseous defects resulting from infections and traumas), distraction osteogenesis (artificial construction of longer bones from smaller bones), and grafting techniques for bone repair.[2] Many grafting procedures, like autologous grafts, allografts, xenografts, and graft substitutes, are used for forming new bones. For example, autologous bone grafts are mostly used in maxillofacial and orthopaedic surgeries. They render highly efficient results because they include three processes simultaneously: osteo-induction, osteo-genesis, and osteo-conduction.[32] Due to successful sequels, surgical bone grafting with distraction osteogenesis is considered the gold standard for osseous regeneration. In addition, a few cellular therapies are also popular for bone healing and repair by implanting osteoprogenitor cells at the desired area, for which mesenchymal stem cells represent the best option. They are procured from human bone marrow as mesenchymal stem cells, adipocytes, and placental cord blood, which bear the potential for forming new bone and give positive results if used in conjunction with biomaterials.[33]

Limitations of current strategies

The latest treatment strategies used for bone tissue engineering have proved to be highly effective for patients. However, modern bone engineering methods still have some limitations. For example, many of the newer approaches are not cost-effective for the patients. Secondly, the dearth of heterologous bone substitutes resembling natural bone is another setback for successful osseointegration and regeneration. Therefore, well-structured and efficacious bone regeneration modalities need highly efficient alternative approaches that can alleviate the shortfalls of contemporary bone healing and remodelling techniques in the era of regeneration.

Substitutes for bone regeneration

The latest bone repairing and healing methods have a few drawbacks, which led to the inception of some contemporary techniques. For instance, distraction osteogenesis has the downside of being a lengthy and time-consuming treatment. So, the Masquelet technique has been introduced as the latest method for reconstruction of large osseous defects.[34] It is a two-step procedure, which is initiated by the formation of a biological membrane, followed by the insertion of non-vascularised autografts.[35] In addition, other modalities, like pulsed electromagnetic fields (PEMF) and low-intensity pulsed ultrasound (LIPUS), are readily applied in bone regeneration methods.[36] Due to several pitfalls of autologous and allografts, new synthetic biomaterials have been introduced for better treatment outcomes.

Gaps in the literature

Bioactive glasses have countless useful properties that make them a flawless material for therapeutic, clinical, biomedical, and regenerative applications. Despite being popular materials, some areas still need the attention of researchers and clinicians for future usage of these smart biomaterials in the modern era of tissue regeneration.

For instance, the rate and speed at which these smart glasses undergo surface dissolution in vivo are still unclear. Further, no study has pinpointed the effect of edible acids (citric acid and lactic acid) on the osteoblastic activity when incorporated into the bioactive network. Also, several surface coating/glazing and metal ions have antibacterial actions in vivo, but the layering of human body lysozyme (intracellular enzyme) over bioglass surfaces deserves the attention of biomedical engineers to evaluate the outcomes when inserted into the human body.[37] Moreover, the role of vitamin E-integrated bioactive glass in effective osteoblast stimulation and proliferation is still ambiguous and needs to be thoroughly explored.[38] Besides, the role of ascorbic acid-incorporated bioactive glass fibres and beads needs extra attention, because it efficiently escalates bone regeneration due to matrix development and maturation by enhancing chemical, physical, and biological features of active glasses at room temperature. Negligible data is available on the powerful Osseo integrative role of ascorbic acid during bone regrowth when embedded into the bioactive glass network. The action of vitamin C in tissue engineering shall further expand on experimental platforms, keeping in view three important factors that alter ascorbic acid activities in vivo and in vitro. The first factor is the glass systems. Plain glass is deficient in its bioactive potential, and, for assessing the bioactivity of vitamin C-induced BG fibres or microspheres, and vitamin C-induced plain glass, comparative studies can help understand this attribute of ascorbic acid-induced BG for assessing the biological potential within the host body. The second factor relates to temperature changes.[39] It is a crucial factor in ascorbic acid functionality. Temperature >30^{0}C denatures vitamin C, so it is critical to maintain a temperature suitable for effective osteoblastic cells stimulation and proliferation. Finally, the third such factor is moisture control.[40] The effect of humidity on the bone regeneration by ascorbic acid-treated bioactive glass is an important factor that shall be explored in tissue regeneration forums. Moisture is a critical variable that chemically destabilises ascorbic acid at implantation sites.

Prospects of the future

The emergence of bioactive glass revolutionized the medical field, paving the way for the advancement of modern regenerative medicine driven by biomaterials. The challenges lie in the extensive range of potential applications for BGs. There is a need to encourage discussions on future investigations and pave the way for novel medical applications.[39] Various bioactive elements play an essential role in cellular proliferation, differentiation, and overall development, and are crucial in deoxyribonucleic acid (DNA) replication, growth factor synthesis, and enzyme activity, all of which are fundamental to regenerative dentistry.[40] Besides, the clinical outcomes of 45S5 bioglass, S53P4 bioactive glass, and borate-based glass 19-93B3 bioglass have been evaluated in the treatment of various human diseases, especially in dentistry, reconstructive osteo surgery, infection management, and venous ulcers.[41]

Further, various novel glass formulations have been introduced in recent years, incorporating what are known as rare therapeutic ions. These systems are expected to be the focus of ongoing and future clinical studies for their versatile applications in numerous medical fields.[42]

Conclusion

Even though microporous spherical glass beads render promising results in biomedical and therapeutic applications, like potent drug delivery, powerful loading ability, sufficient mobilisation of nutrients and toxins, implicit control over the liberation of biological growth factors and other biocompatible elements, better cellular adhesion and proliferation due to greater surface area, the surface reactivity and bioactive potentials of bioactive glass fibres make them a more favourable material in biomedical applications due to uniformity in their geometry and porosity. Overall, bioglass fibres have emerged as a smart class of 3D structural materials and are considered an ideal commodity over conventional materials for bone regeneration due to their superior mechanical, thermal, and biological attributes.

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References

1. Elchaninov A, Sukhikh G, Fatkhudinov T. Evolution of regeneration in animals: a tangled story. Front Ecol Evol. 2021;9:621686. doi:10.3389/fevo.2021.621686
2. Battafarano G , Rossi M , De Martino V , Marampon F , Borro L , Secinaro A, et al. Strategies for bone regeneration: from graft to tissue engineering. Int J Mol Sci. 2021; 22:1128. doi: 10.3390/ ijms 22031128.
3. Gindis E. Spotlight on: biomedical engineering. In: Gindis E, eds. Up and running with AutoCAD. Academic Press; 2017. pp-585-7.
4. Abbasi N, Hamlet S, Love RM, Nguyen NT. Porous scaffolds for bone regeneration. J Sci Adv Mater Devices. 2020; 5:1-9.
5. Montazerian M, Shearer A, Mauro JC. Perspectives on the impact of crystallization in bioactive glasses and glass-ceramics. Int J Ceramic Eng Sci. 2024;6:e10194. doi:10.1002/ces2.10194
6. Liu J, Du G, Yu H, Zhang X, Chen T. Synthesis of hierarchically porous bioactive glass and its mineralization activity. Molecules 2023;28:2224. doi:10.3390/molecules28052224
7. Abd El-Aziz AM, Serag E, Kenawy MY, El-Maghraby A, Kandil SH. Hydrothermally reinforcing hydroxyapatite and bioactive glass on carbon nanofiber scaffold for bone tissue engineering. Front Bioeng Biotechnol 2023;11:1170097. doi:10.3389/fbioe.2023.1170097
8. Elkhenany H, Alrezaki A, Alshaibi H, Alotaibi B, Alonaizan R, Alkhayal Z, et al. Emerging nanomaterials capable of effectively facilitating osteoblast maturation. Nanomedicine (Lond). 2025; 20:1603-19. doi:10.1080/17435889.2025.25114659.
9. ElBatal FH, El-Bassyouni GT. Bioactivity of Hench bioglass and corresponding glass-ceramic and the effect of transition metal oxides. Silicon. 2011; 3:185-97.
10. SK, Yee MMF, Chin KY, Ima-Nirwana S. A review of the application of natural and synthetic scaffolds in bone regeneration. J Funct Biomater 2023;14:286. doi:10.3390/jfb14050286
11. Liverani L, Reiter T, Zheng K, Neščáková Z, Boccaccini AR. Copper-doped cotton-like malleable electrospun bioactive glass fibers for wound healing applications. Mater Lett X 2022;14:100133.
12. A New Generation of Electrospun Fibers Containing Bioactive Glass Particles for Wound Healing. [Online] [Cited 2025 July 3]. Available from: URL: https://www.mdpi.com/1996-1944/13/24/5651
13. Influence of the replacement of silica by boron trioxide on the properties of bioactive glass scaffolds - Schuhladen - 2021 - International Journal of Applied Glass Science - Wiley Online Library [Online] [Cited 2025 July 13]. Available from: URL: https://ceramics.onlinelibrary.wiley.com/doi/full/10.1111/ijag.15894
14. Kumar A, Murugavel S, Aditya A, Boccaccini AR. Mesoporous 45S5 bioactive glass: synthesis, in vitro dissolution and biomineralization behavior. J Mater Chem B. 2017; 5:8786-98. doi:10.1039/C7TB01738C
15. Schumacher M, Habibovic P, van Rijt S. Mesoporous bioactive glass composition effects on degradation and bioactivity. Bioact Mater. 2021; 6:1921-31. doi:10.1016/j.bioactmat.2020.12.007
16. A review of bioactive glasses: Their structure, properties, fabrication and apatite formation - Kaur - 2014 - Journal of Biomedical Materials Research Part A - Wiley Online Library [Online] [Cited 2025 June 14]. Available from: URL: https://onlinelibrary.wiley.com/doi/abs/10.1002/jbm.a.34690
17. Li Y, Chen L, Chen X, Hill R, Zou S, Wang M, et al. High phosphate content in bioactive glasses promotes osteogenesis in vitro and in vivo. Dent Mater. 2021;37:272-83. doi:10.1016/j.dental.2020.11.017 PubMed
18. Deshmukh K, Kovářík T, Křenek T, Docheva D, Stich T, Pola J. Recent advances and future perspectives of sol–gel derived porous

bioactive glasses: a review. RSC Adv. 2020;10:33782-33835. doi:10.1039/D0RA04287K RSC Publishing+1

19. Hoppe A, Güldal NS, Boccaccini AR. A review of the biological response to ionic dissolution products from bioactive glasses and glass-ceramics. Biomaterials. 2011;32:2757-74. doi:10.1016/j. biomaterials. 2011.01.029
20. Karadjian M, Essers C, Tsitlakidis S, Reible B, Moghaddam A, Boccaccini AR, Westhauser F. Biological properties of calcium phosphate bioactive glass composite bone substitutes: current experimental evidence. Int J Mol Sci. 2019;20:305. doi:10.3390/ijms20020305
21. Borate Bioactive Glasses (BBG): Bone Regeneration, Wound Healing Applications, and Future Directions | ACS Applied Bio Materials. [Online] [Cited 2024 August 25]. Available from: URL: https://pubs.acs.org/doi/full/10.1021/acsabm.2c00384
22. Role of bioglass derivatives in tissue regeneration and repair: A review [Internet]. [Cited 2024 August 25]. Available from: URL: https://www.degruyter.com/document/doi/10.1515/rams-2022-0318/html
23. Pharmaceutics | Free Full-Text | Implant Surfaces Containing Bioglasses and Ciprofloxacin as Platforms for Bone Repair and Improved Resistance to Microbial Colonization [Online] [Cited 2024 August 25]. Available from: URL: https://www.mdpi.com/1999-4923/14/6/1175
24. El-Rashidy AA, Waly G, Gad A, Hashem AA, Balasubramanian P, Kaya S, et al. Preparation and in vitro characterization of silver-doped bioactive glass nanoparticles fabricated using a sol-gel process and modified Stöber method. J Non Cryst Solids. 2018;483:26-36. doi:10.1016/j.jnoncrysol.2017.12.044.
25. Skwira A, Szewczyk A, Barros J, Laranjeira M, Monteiro FJ, Sądej R, et al. Biocompatible antibiotic-loaded mesoporous silica/bioglass/collagen-based scaffolds as bone drug delivery systems. Int J Pharm. 2023;645:123408. doi:10.1016/j.ijpharm. 2023.123408
26. Therapeutic cobalt ion incorporated in poly(vinyl alcohol)/bioactive glass scaffolds for tissue engineering. [Online] [Cited 2024 August 25]. Available from: URL: https://link.springer.com/article/10.1007/s10853-020-04644-0
27. Salinas AJ, Esbrit P. Mesoporous bioglasses enriched with bioactive agents for bone repair, with a special highlight of María Vallet-Regí's contribution [Internet]. Pharmaceutics 2022;14:202. doi:10.3390/pharmaceutics14010202
28. Petrović D, Galić D, Seifert D, Lešić N, Smolić M. Evaluation of bioactive glass treatment for dentin hypersensitivity: a systematic review. Biomedicines. 2023;11:1992. doi:10.3390/biomedicines 11071992
29. Nicholson JW. Periodontal therapy using bioactive glasses: a review. Prosthesis. 2022;4:648-63. doi:10.3390/prosthesis4040052
30. Vafa E, Azizli MJ, Tayebi L, Amani AM, Kamyab H. Integrating bioactive glass with compatibilizer: a novel approach for hard tissue regeneration using PXDDA-co-PLA/PLCL/PGLA nanocomposites. Mater Chem Phys. 2024;316:129070. doi:10.1016/j.matchemphys. 2024.129070
31. Ferreira L de AQ, Lehman LFC, Diniz MG, Ferreira AJ, Silva RMF da C e, Silva TA, et al. Biogran grafting in rat tibia defects - a model of high bone metabolism site. Braz Arch Biol Technol. 2024;67:e24230003. doi:10.1590/1678-4324-babt-2023-0003
32. Ciołek L, Biernat M, Jaegermann Z, Zaczyńska E, Czarny A, Jastrzębska A, et al. The studies of cytotoxicity and antibacterial activity of composites with ZnO-doped bioglass. Int J Appl Ceram Technol 2019;16:541-51. doi:10.1111/ijac.13144
33. Maximov M, Maximov OC, Craciun L, Ficai D, Ficai A, Andronescu E. Bioactive glass—an extensive study of the preparation and coating methods. Coatings. 2021;11:1386. doi:10.3390/coatings11111386
34 Wang P, Wu Y, Rui Y, Wang J, Liu J, Ma Y. Masquelet technique for reconstructing bone defects in open lower limb fracture: analysis of the relationship between bone defect and bone graft. Injury. 2021;52:988-95. doi:10.1016/j.injury.2020.12.038
36. Xia P, Shi Y, Wang X, Li X, Zhang L, Chen Q, et al. Advances in the application of low-intensity pulsed ultrasound to mesenchymal stem cells. Stem Cell Res Ther. 2022;13:214. doi:10.1186/s13287-022-02887-z
37. Ahmed I, Kheradmandfard M, Alsharif MJ, Hamdy TM, Al-Kattan A, Nabawy A, et al. Metal-doped silicate and phosphate glasses for antibacterial dental biomaterials. TFO Collect. 2023; 3:2284372. doi:10.1080/26415275.2023.2284372 (Taylor & Francis)
38. Boaro LC, Campos TM, Valente ML, Della Bona Á, Correr-Sobrinho L, Fernandes JC, et al. Vitamin E: a review of its application and methods of detection when combined with implant biomaterials. Materials 2021;14:3691. doi:10.3390/ma14133691 (MDPI)
39. Kaur G, Kumar V, Baino F, Mauro JC, Pickrell G, Evans I, et al. Bioglass and vitamin D3 coatings for titanium implants: osseointegration and corrosion protection. Biomedicine.s 2023;11:2772. doi:10.3390/biomedicines11102772 (MDPI)
40. Ohgushi H, Okumura M, Yoshikawa T, Inoue K, Senpuku N, Tamai S, et al. Three-dimensional biocompatible ascorbic acid-containing scaffold for bone tissue engineering. Tissue Eng. 2003;9:157-65. doi:10.1089/10763270360728053
41. Vafa E, Tayebi L, Abbasi M, Azizli MJ, Bazargan-Lari R, Talaiekhozani A, et al. A better roadmap for designing novel bioactive glasses: effective approaches for the development of innovative revolutionary bioglasses for future biomedical applications. Environ Sci Pollut Res. 2023;30:116960-83. doi:10.1007/s11356-022-24176-1
42. Cortez PP, Brito AF, Kapoor S, Correia AF, Atayde LM, Dias-Pereira P, et al. The in vivo performance of an alkali-free bioactive glass for bone grafting, FastOs®BG, assessed with an ovine model. J Biomed Mater Res B Appl Biomater. 2017;105:30-38. doi:10.1002/jbm.b.33529

Author Contribution:

RA: Writing, collected previous data and made a plan to initiate the content writing.
SB: Data interpretation, collection and correction.
MRA: Revision and critically evaluated the data.
WI: Helped in gathering the articles and managed the citations along references.
SM: Finalising and proofreading.
MAGC: Managed figures and made figures legends.
RA: Collected figures data and Grammer correction.