Journal of Advanced Sciences and Engineering Technologies (2025); 8(1):1-19

DOI: http://doi.org/10.32441/jaset.8.1.2

Journal of Advanced Sciences and Engineering Technologies

www.jasetj.com

Journal of Advanced Sciences and Eng. Technologies

JASET

Synthesis and characterization of bioactive glass Nanoparticles by sol-gel method. Review Article.

Asmaa J. AL-Lamei, *Athraa S.Ahmed*

Chemistry Department/College of Science/Al-Mustansiriyah University, Iraq

Keywords:

Bioactive glass nanoparticles, sol-gel synthesis, bone regeneration, antibacterial applications, surface characterization, regenerative medicine.

Highlights:

- *This review has presented the synthesis and characterization of bioactive glass nanoparticles (BGNs) by the sol-gel method and examined the factors that affect the synthesis of bioactive glass nanoparticles.*
- *Characterization: This analysis will delve into the characterization techniques employed to evaluate BG nanoparticles, focusing on their structural, morphological, and bioactivity-related properties. Key techniques such as X-ray diffraction (XRD), Fourier-transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), and bioactivity assays will be discussed to demonstrate how each method aids in assessing the nanoparticles' potential for biomedical applications.*
- *Biomedical Applications: The review will explore both current and potential biomedical applications of bioactive glass nanoparticles, especially in areas such as bone tissue engineering, drug delivery, and antibacterial treatments.*
- *Fields of usage of BGN are bone regeneration, drug delivery, antimicrobial coatings, and wound healing, in which they are bioactive and biocompatible, allowing for stimulating tissue repair and targeted treatment.*

ARTICLE INFO

Article history:

Received	01 Dec	2024
Received in revised form	15 July	2025
Accepted	21 July	2025
Final Proofreading	10 Aug.	2025
Available online	14 May	2025

*Corresponding author:

Asmaa J. AL-Lamei

Department of Chemistry, College of Science, University of AL-Mustansiriyah, Iraq.

Abstract: Bioactive glass nanoparticles (BGNs) are potentially significant in the biomedical field because of their bioactive, biocomposite, and versatile nature of applications in various therapeutic fields. This review discusses the synthesis of BGNs through the sol-gel method, which is a low-temperature process, offering the opportunity to achieve a controlled composition of the BGNs for their application in medicine. The morphological, structural, and chemical characterization methods are explained to show how these properties affect the bioactivity of BGN and its fitness for a particular application. BGNs have been effectively used in bone regeneration, drug delivery, antibacterial treatments, and wound healing due to their ability to combine with bone tissue, release therapeutic ions, and deliver the drug accordingly. It also points to future possibilities of BGNs in more sophisticated areas, such as cancer treatment and bioimaging, and calls for more design in strengthening their applications in healthcare-related fields. This evaluation highlights the role of BGNs in promoting the progress of biomedical science and substantiates the possibility of providing a substantial contribution to personalized and regenerative medicine.

INTRODUCTION

Bioactive glass (BG) is an outstanding material in the biomedical field since its discovery in the late 1960s by Larry Hench. BG's ability to bond with bone tissue, promote osteogenesis, and stimulate tissue formation has led to its widespread use in orthopedics and bone tissue engineering [1]. This property paved the way for the use of BG in orthopedics together with regenerative medicine, especially in bone tissue engineering, as it has the potential to promote new tissue formation. After decades of development, BG nanoparticles have been born and penetrated other areas such as tissue engineering and drug delivery, where bioactivity, biocompatibility, and controllable degradation performance are closely related. The latest decades have seen the development of nanotechnologies that expand the application of bioactive glass to the nanoscale [2].

Bioactive glass nanoparticles are valued for the extent to which they may engage with biological environments substantially beyond the capacities of bulk materials. For instance, in bone regeneration, these nanoparticles enhance the osteogenic differentiation of mesenchymal stem cells by enhancing the adhesion of bone cells and aiding in the deposition of minerals that facilitate healing [3]. Due to the fact that nanoparticles have a large surface area, a greater number of ions can be released from them, which is valuable for generating cellular reactions. Moreover, in pharmaceutical applications, the porosity of the BG nanoparticles allows for the loading and delivery of therapeutic agents in a controlled manner, enhancing their therapeutic value [4]. In tissue engineering, it can be used as the scaffold or the composite of the material that provides support for cellular growth and tissue development, which is an essential requirement for constructing bioengineered tissues [3].

As mentioned above, the reactivity and the size of the BG nanoparticles enhance several properties compared to the bulk material. One of the most important advantages is the high bioactivity promoted by the growth of the surface area to volume ratio. This enables a faster ion exchange if the material comes into contact with body fluids, and enhances the creation of hydroxyapatite, a bone-like mineral that clinches the connection to living bone [5]. This property is important in uses such as bone grafts or implant materials; an ideal material must integrate well into the body’s system. Furthermore, the small size and high surface charge of nanoparticles

increase cellular uptake and interaction and thus are more compatible with the surrounding tissues [6]. At the same time, the adjustable surface characteristics also make it possible to employ subsequent biomolecular decorations, which will enhance their performance in certain roles, like drug delivery systems or bactericidal layers [7].

BGN refers to the sol-gel developed nanoparticles of bioactive glass, which have subsequently received immense interest in biomedical uses because of their characteristics and easier synthesis process [8]. It is noteworthy that BGN prepared using the sol-gel technique can be easily and reproducibly tailored to have desired characteristics, specifically size, shape, pore structure, and composition. This method has been employed to coat a wide range of materials used in biomedical implants as well as drug delivery systems [9]. The structural features and elemental concentration of bioactive sol-gel-derived glasses that make up the porous structure play a key role in their biological performance, explaining why the synthesis process should be well controlled for application in biomedical engineering [10]. Various methods, like microemulsion and acid-catalyzed synthesis, have been used to synthesize BGN with certain properties. These materials contain potential for use in bone tissue engineering and other biomedical sectors such as soft tissue repair and wound healing applications [8, 10].

Significance of the Sol-Gel Method in Nanoparticle Synthesis

The sol-gel route is acknowledged as one of the best approaches toward synthesizing bioglass nanoparticles because of its high flexibility and purity of materials with desired composition and morphology [8, 11]. Compared to conventional melt-quenching techniques, this method has a couple of advantages: better bioactivity and better control over the processing conditions [11]. The synthesis technique of sol-gel is used to stabilize the BGNs and control their size, shape, pore size, and composition, as they are critical factors for their performance in the biomedical industry, according to Zheng and Boccaccini[8]. These applications are not limited to the promotion of bone regeneration alone but also in soft tissue repair, wound healing, and in the targeted delivery of drugs [8, 9]. Several approaches for the fabrication of sol-gel have been invented, involving different catalysts, templates, and dopants to enhance the properties of BGN [9, 12].

Sol-gel process entails the conversion of a sol solution containing the precursors to a gel, then to solid nanospheres through hydrolysis and polycondensation reactions. This approach provides multiple advantages:

- Another advantage of the sol-gel method is that it performs its function at substantially lower temperatures, usually below 200°c, and for this reason, volatile organic components may be preserved, while heat-sensitive biomolecules or therapeutic agents can be integrated into the nanoparticles during the process. This method of synthesis is excellent in the preparation of bioactive glass nanoparticles for use in biomedical applications because high temperature may affect some properties of these glasses [13].

- The sol-gel process is a versatile method with the ability to create perfect control over the composition of nanoparticles. Through proper control of choices of the precursors and reaction conditions, it is possible to incorporate specific ions (such as calcium, phosphorus, or even therapeutic ions such as silver or zinc) that increase the bioactivity and specific biological reactions [14, 15]. Furthermore, the sol-gel method is followed by a pleasant control over the size, morphology, and porosity of the nanoparticles that can directly affect the biological performance of the scaffold and interaction with adjacent tissues [15, 16].

- The solution-bred characteristic of the sol-gel method allows the incorporation of the precursors at the molecular level, thus good dispersion of elements within the nanoparticles [17]. This homogeneity is actually enrichment for homogenous bioactivity through the particle, because all the particles in the material possess the same composition and properties of structure. Also, the sol-gel process normally generates high-purity materials, whereby there is a reduced number of impurities that may hinder either the bioactivity or the compatibility of the nanoparticles [18].

Even with these benefits, creating consistent, bioactive glass nanoparticles through the sol-gel method poses various challenges that researchers are currently striving to address.

- Achieving consistent nanoscale particle sizes can be challenging with the sol-gel method due to factors such as rapid gelation and the tendency of nanoparticles

to clump together during the drying phase [15]. This aggregation can impede the bioactivity of the nanoparticles by decreasing their effective surface area, which in turn limits ion exchange and interaction with biological environments [19]. Researchers need to carefully optimize synthesis parameters—like pH, precursor concentration, and drying conditions—to produce well-dispersed, uniform particles.

- The sol-gel method allows for the inclusion of bioactive ions, but reaching the desired bioactivity level can be difficult. Minor changes in reaction conditions can affect the material's composition and, in turn, its bioactivity. Furthermore, fine-tuning the sol-gel process to create bioactive glass nanoparticles that can effectively form hydroxyapatite—the bone-like mineral essential for bonding with bone tissue—demands careful control over the synthesis parameters [14].

- The sol-gel synthesis of bioactive glass nanoparticles (BGNs) allows for precise control over their composition and properties, which is essential for biomedical applications [8]. However, achieving the desired level of bioactivity can be difficult, as even minor changes in reaction conditions can impact the material's composition [8]. Various factors, including the type of solvent, the order of reagent addition, stirring duration, and catalyst concentration, play a role in ion incorporation and particle size [14]. While the calcium content is known to affect bioactivity, its influence may not be significant within certain compositions [15]. The sol-gel method is versatile, enabling the creation of different bioactive materials, such as nanoparticles for cancer treatment and drug delivery systems [13]. To optimize the sol-gel process for producing BGNs that can effectively form hydroxyapatite—critical for bonding with bone tissue—careful control over the synthesis variables is necessary [8, 14].

Objective and Focus of the Review

This review provides an in-depth analysis of bioactive glass (BG) nanoparticles created through the sol-gel method, emphasizing their synthesis, characterization, and potential uses in the biomedical sector. BG nanoparticles have demonstrated significant promise in promoting bone regeneration, facilitating drug delivery, and serving other biomedical purposes due to their distinctive properties and favorable interactions with biological environments. Considering the benefits of the sol-gel

method, such as its ability to precisely control particle composition and structure, this review will explore the specific techniques employed to optimize the synthesis of BG nanoparticles and how their bioactivity can be enhanced for various applications.

The review will focus on three key aspects:

Synthesis: The discussion will delve into the principles of the sol-gel method and examine the factors that affect the synthesis of bioactive glass nanoparticles. This includes aspects like reaction conditions, the selection of precursors, and the ability to control particle size and structure. Special attention will be given to strategies aimed at addressing challenges related to uniformity and scalability in the sol-gel process.

Characterization: This analysis will delve into the characterization techniques employed to evaluate BG nanoparticles, focusing on their structural, morphological, and bioactivity-related properties. Key techniques such as X-ray diffraction (XRD), Fourier-transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), and bioactivity assays will be discussed to demonstrate how each method aids in assessing the nanoparticles' potential for biomedical applications.

Biomedical Applications: The review will explore both current and potential biomedical applications of bioactive glass nanoparticles, especially in areas such as bone tissue engineering, drug delivery, and antibacterial treatments. It will discuss how BG nanoparticles contribute to tissue regeneration, enhance therapeutic efficacy, and support various medical interventions, highlighting the importance of these materials.

SYNTHESIS OF BIOACTIVE GLASS NANOPARTICLES USING SOL-GEL METHOD

1. Principles of the Sol-Gel Process

The sol-gel process is a wet-chemical technique employed to fabricate solid materials with precise compositions at the nanoscale. This method is commonly utilized to produce advanced materials like bioactive glass (BG) nanoparticles [14]. The process consists of several important stages:

Preparation of the Initial Solution (Sol): The First step involves the dissolution of an

organometallic precursor, generally a metal alkoxide, such as silica or calcium alkoxides, in a suitable solution. This creates the solution from which the reaction will start – it has liquid precursors that will yield a solid network [20].

Chemical Reactions (Hydrolysis and Condensation): The sol gets set as a chemical reaction by the addition of dilute water content with an optional addition of acid or alkaline catalyst. This leads to the hydrolysis and condensation reactions, which enable the formation of cross-linkages with the formation of an interconnected network of the precursor molecules (the reactions are described below)[21].

Gelation: As the condensation reactions proceed to completion, the sol turns into a semi-solid, partly fluid state within the system known as the gel. The gel is an interconnected particle network that is formed at a later stage of the reaction of the interlinkage of the precursors [22].

Drying: Subsequent cross-linking is followed by solvent evaporation, and this makes the gel shrink into a more competent solid mass with improved homogeneity in terms of composition. The drying stage facilitates the regulation of pore characteristics since the number of pores, pore size, and pore distribution in the final solid are significantly less than those of the initial gel [23].

Aging and Calcination: Finally, the dried gel is treated with respective temperatures to avoid remaining traces of organic matter and also enhance its mechanical and thermal strength. This results in a highly pure, nanostructured glass material [17].

Key Reactions Involved (Hydrolysis and Condensation)

Hydrolysis**:** The sol-gel mechanism is launched by hydrolysis. Water molecules also interact with the metal alkoxide (for example, tetraethyl orthosilicate) in a manner that displaces the alkoxide functional groups (-OR) with the hydroxyl functional groups (-OH) [24]. The general equation for hydrolysis can be represented as:

$$M(OR)_2 + xH_2O \rightarrow M(OH)_x + xROH \qquad eq.1$$

Here, the meaning of M is the metal (for instance, silicon), and R is the organic group that is bonded to M. Hydrolysis yields hydroxyl functions that are useful in the latter condensation process. Hydrolysis results in the formation of hydroxyl groups

of significance in the subsequent condensation reaction.

Condensation: After the hydrolysis step, the hydroxyl groups present on the polymer chain tend to react with each other or with the remaining alkoxide groups and thus newly formed oxide bonds, or links (M-O-M) are generated between the molecules. This leads to the formation of the solid network while the thiosemicarbazones and the complexes are obtained as the products [25]. The condensation reactions can occur as follows:

Condensation between two -OH groups:

$$M(OH) + M(OH) \rightarrow M - O - M + H_2O \qquad eq.2$$

Condensation between -OH and -OR groups:

$$M(OR) + M(OH) \rightarrow M - O - M + ROH \qquad \text{eq.3}$$

As we know, the sol-gel process depends on hydrolysis and condensation reactions whereby the molecules link up and form a multiple network. This stepwise assembly finally leads to the formation of a solid nanostructured material with predetermined characteristics.

2. Precursors and Reagents

Common Precursors In the sol-gel synthesis of bioactive glass nanoparticles, common precursors include:

Alkoxysilanes (e.g., Tetraethyl Orthosilicate, TEOS): The alkoxysilanes are generally employed as a silica source in the manufacturing process of bioactive glass; it is an important structural component in its framework. Among various alkoxysilanes, TEOS is the most common, which results in a siloxane network through hydrolysis and condensation[26].

Calcium Sources (e.g., Calcium Nitrate, Calcium Chloride): According to previous studies, bioactivity and osteoconductivity of calcium ions are crucial for bioactive glasses. Calcium sources cause the incorporation of calcium ions with the sol-gel solution, and they behave as substituent ions within the glass matrix in the entire sol-gel process. When the material comes into contact with water in biological fluids, ion exchange and bioactivity occur [27].

Phosphorus Sources (e.g., Triethyl Phosphate, TEP): Phosphorus has significance in the creation of hydroxyapatite, which is a ceramic phase that resembles the composition of bone. TEP and other phosphorus sources supply phosphate groups that may further the bioactive nature of the glass to form a bio-socially favorable surface layer in physiological conditions[28].

Function of Each Component in the Sol-Gel Process

Silica Source: In the case of well-known alkoxysilanes, such as TEOS, the primary matrix for the bioactive glass is already formed through hydrolysis and condensation reactions [29].

Calcium Source: The rate of the glass hydrolysis depends on the ability of calcium precursors to modulate bioactivity. Fluorescence studies indicate that in physiological environments, the bioactive glass releases calcium ions, which coordinate with natural bone tissues for bonding [27].

Phosphorus Source: The present phosphate precursors allow the bioactive glass to promote the formation of a hydroxyapatite layer of natural bone, which is critical in the adhesion process [30].

Each component is chosen to achieve the highest possible performance and harmony of bioactive glass nanoparticles to create materials for multiple biomedical purposes, such as bone tissue reconstruction and tissue engineering.

3. Influence of pH, Solvent Type, Temperature, Aging, and Drying on the Structure and Size of BGNs

- pH:

pH influences the rate of hydrolysis and condensation in the sol-gel process, altering the structure and size of bioactive glass nanoparticles (BGNs) [8].

The rationale for the slower condensation rates being preferred for acidic conditions is that such conditions yield. Smaller, uniform particles, while basic conditions can spur condensation; thus, petroleum coke with bigger sizes and potentially different porosity [31].

- Solvent Type:

The volatility of solvents affects the dispersion of solutes that, in this case, are precursors in the formation of the particular particles. The definition of the green solvent should consider low toxicity and the ability to distribute precursors evenly, such as polar solvents, including ethanol[32].

The polarity, dielectric constant, and viscosity of the solvent can all affect particle size and morphology, and higher solvent polarity tends to give more uniform nanoparticles [33].

- Temperature:

Higher synthesis temperatures normally enhance the rates of hydrolysis and condensation, thus leading to larger particle sizes. Nevertheless, aggregation is seen at very high temperatures [34].

Regulation of temperature can be used to adjust the particle size and porosity; moderate temperature gives well-distributed nanoparticles [35].

- Aging:

This is the time they refer to as aging and is the time the gel is allowed to continue with the condensation reactions required to strengthen the network. Normal aging is at least characterized by an improvement of the network connection in addition to the enhanced porosity density, resulting in more compact structures of BGNs [8].

- Drying:

The stage of drying impacts solvents, shrinkage, and even porosity, and the stability of particles. This enables controlled drying to help achieve homogeneity in size and shape, while an overexposure may lead to cracking and disruption of the particles' shape [36].

Some of the Approaches for Regulating the Shape of Nanoparticles

Use of Surfactants: Antistatic agents are employed to regulate particle size and to avoid aggregation. Other reagents, such as CTAB, participate in stabilizing mechanisms through the formation of an interparticle layer. At the surface of growing particles, surfactant molecules form a layer, which assists in preventing a particle

from growing too large and in defining its shape, mostly spherical or some other well-defined form [37].

Templating Techniques: Templating, therefore, requires the use of a pre-structured material that guides the formation of the growing nanoparticles. For example, soft templates such as micelles or hard templates, such as polymer beads, generate structures that define the formation of nanoparticles. In the case of the sol-gel process, the template can be eliminated while a structure remains well-defined and of a certain size. This method can be useful for creating BGNs of definite shapes, for example, hollow or porous nanoparticles, which may be desirable for drug delivery [38].

If these parameters and techniques are fine-tuned, researchers can thus fine-tune the characteristics of bioactive glass nanoparticles that would be useful in various biomedical applications, such as improving bioactivity.

CHARACTERIZATION OF BIOACTIVE GLASS NANOPARTICLES

Knowledge of bioactive glass nanoparticles' (BGNs) general characteristics is imperative, as physical and chemical properties determine their efficiency in biomedical usage. Appropriate estimation of morphology, structure, chemical composition, and surface properties of BGNs can aid researchers in achieving the characteristics needed for the desired applications, such as bone regeneration, drug delivery, and tissue engineering. The characterization techniques offer useful information on the size and shape of BGNs, the crystalline structure, and chemical composition of BGNs, which are essential for enhancing bioactivity, compatibility, and stability.

Morphological and Structural Characterization

Techniques for Size and Shape Analysis are that the field emission SEM affords excellent on-plane resolution of surface topographical features and particle size in the range of BGNs. It also enables the determination of the uniformity and structure of the particle, especially at the nanometer surface features of the particle [39].

TEM is higher in resolution than SEM and can also be used to show internal structure imaging of BGNs. It is also useful for comparing different end products

across the size distribution, including changes in shape and size of various particles, or for identifying whether the internal structure of the particles is porous or crystalline [40].

DLS is employed to determine the particle size of a nanoparticle in a liquid medium and also the extent of its aggregation. This method is suitable for analyzing BGNs in different biological milieus since what a particle is doing in solution may greatly influence its bioactivity and ability to interact with cells [41].

Crystal Structure Analysis: XRD identifies the crystalline or amorphous nature of BGNs; it also demonstrates that they are crystalline. This technique gives details of crystalline phases and the level of crystallinity, which is crucial for bioactivity. Bioactive glass is generally non-crystalline, but some level of crystallinity can be controlled for a desired function [42].

FTIR identifies the chemical structures and the specific chemical group of BGNs. It is beneficial for the purpose of examining the structural regularities of certain molecular configurations like Si–O–Si/ Si–O–Ca, which are responsible for the bioactivity as well as the dissolution characteristics of the created oxide glass. FTIR is usually applied for checking whether or not additions of such or such elements as calcium or phosphorus are well incorporated and for following changes on the surface [43].

Bioactivity Evaluation

A determination of the bioactivity of bioactive glass nanoparticles (BGNs) is crucial in understanding their potential for use in biomedical applications, especially in bone tissue engineering. Bioactivity means the ability of BGNs to adhere to biological tissues, usually determined by their propensity to create hydroxyapatite (HA) – a 'bone-like' mineral when exposed to liquids that mimic the human body [44]. Cytotoxicity and cell lineage-directed gene expression assays used in bioactivity tests indicate the ability of BGNs to interact appropriately with the human body, with regard to the adhesion and differentiation of cells, as well as their integration into natural bone [45].

BIOMEDICAL APPLICATIONS OF BIOACTIVE GLASS NANOPARTICLES

Synthesized inorganic bioactive glass nanoparticles (BGNs) have found numerous applications in different fields of biomedical flux due to their high bioactivity, biocompatibility, and utility. In hard tissue engineering applications, it was demonstrated that BGNs may provide effective approaches for bone regeneration, drug delivery, and antibacterial properties, while in soft tissue engineering applications, the potential application of BGNs has also been outlined [8].

1. Bone Regeneration and Tissue Engineering

Mechanisms of Interaction Between BGNs and Bone Tissue:

BGNs communicate with hard tissue by the capacity to develop an HA layer when placed in body fluids. This HA layer is a bonding interface by which BGNs adhere to and interpenetrate with natural bone. Furthermore, ions such as calcium and silicon released from BGNs can promote cell behaviors that facilitate bone formation, osteoblast differentiation, as well as improved bone remodeling [46].

Studies Showing Osteoconductive and Osteoinductive:

BGNs are acknowledged to possess osteoconductive – the capacity to promote adhesion and the subsequent division of new bone cells attached to the BGN surface. Several works have also shown that the ions released from BGNs also possess osteoinductivity: the process of activating progenitor cells into osteoblasts that form bone tissue. These properties make BGNs well-suited for use in scaffolds within the field of tissue engineering, particularly for bone injury and repair[46].

2. Drug Delivery Systems

Loading Capacity, Release Kinetics, and Controlled Drug Release Potential:

The synthesized BGNs are highly porous with a large surface area, and hence they act as a matrix to load drugs into them. Ion-exchange and degradation rates of BGNs can be regulated, thus facilitating the controlled release of drugs, fulfilling the purpose of localized therapy for extended periods. It is, therefore, most helpful in situations that require a constant programme of the drug, for instance, in cancer treatment or infection control [47]

Examples of Drugs or Biomolecules Delivered Using BGNs:

Nice examples of therapeutic agents that have been delivered using BGNs include antibiotics such as gentamicin and ciprofloxacin, anti-inflammatory drugs such as ibuprofen, and growth factors such as bone morphogenetic proteins. This flexibility enables BGNs to embellish several treatment modalities, like those that target tissues of interest or therapeutics that need slow and sustained release [48].

3. Antibacterial and Wound Healing Applications

Surface Modifications or Compositional Adjustments for Enhanced Antibacterial Activity:

The introduction of ions such as silver, copper, or zinc into BGNs was found to improve the antibacterial efficacy to make them relevant in dressings of wounds and implants that require controlling bacterial infections. These ions interfere with the bacterial cell membranes and their ability to reproduce, and thus, arthroplasty implant surfaces are not coated with biofilms [49].

Potential for BGNs in Wound Healing and Other Soft Tissue Applications:

In Wound healing, for instance, BGNs encourage new tissue formation by liberating ions for cellular activity and offering a suitable atmosphere for migration and proliferation of skin cells. Other examples of BGN, including those with controlled porosity and of ions, have been incorporated into wound dressings for treating chronic wounds and burns intended for soft tissue application other than for bone regeneration [50].

CONCLUSION

This review has presented the synthesis and characterization of BGNs and their various biomedical uses. Of all sol-gel techniques, the synthesis of BGNs has benefitted from a high degree of flexibility regarding its composition and structure. The healthcare applications of BGNs can be tailored through the approach that involves the complete characterization of BGNs by morphology, surface chemistry, porosity, and bioactivity [8]. Fields of usage of BGN are bone regeneration, drug delivery, antimicrobial coatings, and wound healing, in which they are bioactive and biocompatible, allowing for stimulating tissue repair and targeted treatment.

Thus, bioactive glass nanoparticles have garnered great interest in biomedical research as they have high biocompatibility, variable characteristics, and bioactivity features. These nanoparticles offer new prospects for issues that arise in tissue engineering, drug delivery, and combating bacterial infection, all of which are significant improvements in health care technology [3]. As can be seen, the property of BGNs to combine with bone tissue, stimulate cell differentiation, and deliver therapeutic agents makes them perfect for regenerative medicine and much more.

ACKNOWLEDGEMENTS

The authors are grateful to the chemistry department, College of Science, AL-Mustansiriyah University, for helping complete the research..

NOMENCLATURE

BGNs Bio glass nanoparticles
T Temperature, ℃

References

[1] Huang, C., Yu, M., Li, H., Wan, X., Ding, Z., Zeng, W., & Zhou, Z. (2021) .*Research progress of bioactive glass and its application in orthopedics.* Advanced Materials Interfaces, **8**(22): p. 2100606.

[2] Baino, F., S. Hamzehlou, and S. Kargozar. (2018).*Bioactive glasses: where are we and where are we going?* Journal of functional biomaterials, **9**(1): p. 25.

[3] Kargozar, S., Baino, F., Hamzehlou, S., Hill, R. G., & Mozafari, M. (2018). *Bioactive glasses are entering the mainstream*. Drug discovery today,**23**(10): p. 1700-1704.

[4] Anand, A., B. Kundu, and S.K. Nandi (2022). *Mesoporous bioactive glass for bone tissue regeneration and drug delivery*. Nanoengineering of Biomaterials, p. 343-370.

[5] Zhao, Y., Zhang, Z., Pan, Z., & Liu, Y. (2021). *Advanced bioactive nanomaterials for biomedical applications*. In *Exploration*. Wiley Online Library.

[6] Tomar, G. B., Dave, J. R., Mhaske, S. T., Mamidwar, S., & Makar, P. K. (2020).*Applications of Nanomaterials in Bone Tissue Engineering*. Functional Bionanomaterials: From Biomolecules to Nanoparticles, p. 209-250.

[7] Van Rijt, S., K. De Groot, and S.C. Leeuwenburgh,.(2022).*Calcium phosphate and silicate-based nanoparticles: history and emerging trends.* Tissue Engineering Part A,**28**(11-12): p. 461-477.

[8] Zheng, K. and A.R. Boccaccini. (2017). *Sol-gel processing of bioactive glass nanoparticles: A review*. Advances in Colloid and Interface Science, **249**: p. 363-373.

[9] Catauro, M. and S.V. Ciprioti. (2021). *Characterization of hybrid materials prepared by the sol-gel method for biomedical implementations. A critical review*. Materials, **14**(7): p. 1788.

[10] Deshmukh, K., Kovářík, T., Křenek, T., Docheva, D., Stich, T., & Pola, J. (2020).*Recent advances and future perspectives of sol–gel derived porous bioactive glasses: a review*. RSC advances,**10**(56): p. 33782-33835.

[11] Baino, F., Fiume, E., Miola, M., & Verné, E. (2018). *Bioactive sol-gel glasses: processing, properties, and applications*. International Journal of Applied Ceramic Technology,**15**(4): p. 841-860.

[12] Widiyanti, S., (2020).*Synthesis of nano bioactive glass or bioglass*. RHAZES: Green and Applied Chemistry, **10**: p. 01-32.

[13] Catauro, M. and S. Vecchio Ciprioti, *(2019). Sol-gel synthesis and characterization of hybrid materials for biomedical applications*. Thermodynamics and Biophysics of Biomedical Nanosystems: Applications and Practical Considerations, p. 445-475.

[14] Pajares-Chamorro, N. and X. Chatzistavrou, (2020).*Bioactive glass nanoparticles for tissue regeneration*. Acs Omega, **5**(22): p. 12716-12726.

[15] Kesse, X., C. Vichery, and J.-M. Nedelec. (2019). *Deeper insights into a bioactive glass nanoparticle synthesis protocol to control its morphology, dispersibility, and composition*. Acs Omega, **4**(3): p. 5768-5775.

[16] Zheng, K., Sui, B., Ilyas, K., & Boccaccini, A. R. (2021). *Porous bioactive glass micro-and nanospheres with controlled morphology: Developments, properties and emerging biomedical applications*. Materials horizons, **8**(2): p. 300-335.

[17] Bokov, D., Jalil, A. T., Chupradit, S., Suksatan, W., Ansari, M. J., Shewael, I. H., Valiev, G. H., & Kianfar, E. (2021).*Nanomaterial by sol-gel method: synthesis and application*. Advances in materials science and engineering, **2021**(1): p. 5102014.

[18] Gonçalves, M.C., *(2018). Sol-gel silica nanoparticles in medicine: A natural choice. Design, synthesis, and products*. Molecules, **23**(8): p. 2021.

[19] Shrestha, S., B. Wang, and P. Dutta (2020). *Nanoparticle processing: Understanding and controlling aggregation*. Advances in colloid and interface science, **279**: p. 102162.

[20] Innocenzi, P. and P. Innocenzi, *(2019). The precursors of the sol-gel process*. The Sol-toGel Transition, p. 7-19.

[21] Yousif, A.H.E. and M.S.A. Eltoum, *(2020). Mechanistic Investigation of Sol–Gel Reactions Using Alkoxysilane Precursor*. Chemical Science International Journal, **29**(5): p. 25-31.

[22] Kajihara, K., K. Kanamori, and A. Shimojima (2022). *Current status of sol–gel processing of glasses, ceramics, and organic–inorganic hybrids: a brief review*. Journal of the Ceramic Society of Japan, **130**(8): p. 575-583.

[23] Kohns, R., Torres-Rodríguez, J., Euchler, D., Seyffertitz, M., Paris, O., Reichenauer, G., Enke, D., & Huesing, N. (2023). *Drying of Hierarchically Organized Porous Silica Monoliths– Comparison of Evaporative and Supercritical Drying*. Gels, **9**(1): p. 71.

[24] Polskaya, S. *Older Learners vs. Younger (2020): Who Is Better at Foreign Language Vocabulary Acquisition?* in *INTED2020 Proceedings*. IATED.

[25] Garden, J. and S. Pike, (2018). *Hydrolysis of organometallic and metal–amide precursors: synthesis routes to oxo-bridged heterometallic complexes, metal-oxo clusters, and metal oxide nanoparticles.* Dalton Transactions, **47**(11): p. 3638-3662.

[26] Meechoowas, E., Tungsanguan, O., Pamok, C., Tapasa, K., & Chaiarrekij, S. (2023). *Investigation of morphology, structure, and bioactivity of bioactive glass*. Materials Today: Proceedings.

[27] Ruiz-Clavijo, A., Hurt, A. P., Kotha, A. K., & Coleman, N. J. (2019). *Effect of calcium precursor on the bioactivity and biocompatibility of sol-gel-derived glasses*. Journal of Functional Biomaterials, **10**(1): p. 13.

[28] Pokhrel, S. (2018). *Hydroxyapatite: preparation, properties, and its biomedical applications*. Advances in Chemical Engineering and Science, **8**(04): p. 225.

[29] Durgalakshmi, D., R. Ajay Rakkesh, and B. Subramanian. (2020). *Bioactive assessment of bioactive glass nanostructures synthesized using synthetic and natural silica resources*. International Journal of Applied Ceramic Technology, **17**(4): p. 1976-1984.

[30] Li, Y., Chen, L., Chen, X., Hill, R., Zou, S., Wang, M., Liu, Y., Wang, J., & Chen, X. (2021). *High phosphate content in bioactive glasses promotes osteogenesis in vitro and in vivo*. Dental Materials, **37**(2): p. 272-283.

[31] Xiao, Y. and J.M. Hill, (2020). *Solid acid catalysts produced by sulfonation of petroleum coke: Dominant role of aromatic hydrogen*. Chemosphere, **248**: p. 125981.

[32] Benvenuti, J. and J.H.Z. dos Santos.(2021). *Green solvents for remediation technologies*, in *Green Sustainable Process for Chemical and Environmental Engineering and Science*. 2021, Elsevier. p. 23-30.

[33] Gholami, T., Seifi, H., Dawi, E. A., Pirsaheb, M., Seifi, S., Aljeboree, A. M., Hamoody, A. M., Altimari, U. S., Abass, M. A., & Salavati-Niasari, M. *(2024). A review on investigating the effect of solvent on the synthesis, morphology, shape, and size of nanostructures*. Materials Science and Engineering: B,**304**: p. 117370.

[34] Sigwadi, R. A., Dhlamini, M. S., Mokrani, T., & Nonjola, P. (2017). *Effect of synthesis temperature on particle size and morphology of zirconium oxide nanoparticle*. Journal of Nano Research, **50**: p.18- 31.

[35] Piñero, S., S. Camero, and S. Blanco.(2017). *Silver nanoparticles: Influence of the temperature synthesis on the particles' morphology*. In *Journal of Physics: Conference Series*. IOP Publishing.

[36] Chaves, D.H., V.S. Birchal, and E.F. Costa Junior (2024). *Particle morphology and shrinkage in spray dryers: A review focused on modeling single droplet drying*. Drying Technology, p. 1-13.

[37] Barbero, F., Moriones, O. H., Bastús, N. G., & Puntes, V. F. (2019*).Dynamic equilibrium in the cetyltrimethylammonium bromide–Au nanoparticle bilayer, and the consequent impact on the formation of the nanoparticle protein corona*. Bioconjugate Chemistry, **30**(11): p. 2917-2930.

[38] Katariya, N., Farswan, A. S., Nainwal, N., & Kumar, G. (2024). *Diagnostic and Therapeutic Role of Mesoporous Silica Nanoparticles in Combating Cancer*. Int J App Pharm, **16**(5): p. 31-37.

[39] Olbert, M., Neděla, V., Jirák, J., & Hudec, J. (2024). *Size and shape analysis of micro-to nano-particles of quartz powders using advanced electron microscopy and laser diffraction methods*. Powder Technology, **433**: p. 119250.

[40] Brodusch, N., Brahimi, S. V., Barbosa De Melo, E., Song, J., Yue, S., Piché, N., & Gauvin, R. (2021). *Scanning Electron Microscopy versus Transmission Electron Microscopy for Material Characterization: A Comparative Study on High-Strength Steels*. Scanning, **2021**(1): p. 5511618.

[41] Knysh, A., P. Sokolov, and I. Nabiev (2023). *Dynamic Light Scattering Analysis in Biomedical Research and Applications of Nanoparticles and Polymers*. Journal of Biomedical Photonics & Engineering, **9**(2): p. 020203.

[42] Nawaz, Q., et al.,(2021). *Crystallization study of sol–gel derived 13-93 bioactive glass powder*. Journal of the European Ceramic Society, **41**(2): p. 1695-1706.

[43] Tiama, T.M., et al. (2023). *Molecular and biological activities of metal oxide-modified bioactive glass*. Scientific Reports, **13**(1): p. 10637.

[44] Leite, Á. and J. Mano,(2017). *Biomedical applications of natural-based polymers combined with bioactive glass nanoparticles*. Journal of Materials Chemistry B, **5**(24): p. 4555-4568.

[45] Azizipour, E., et al., (2021). *A novel hydrogel scaffold contained bioactive glass nanowhisker (BGnW) for osteogenic differentiation of human mesenchymal stem cells (hMSCs) in vitro*. International journal of biological macromolecules, **174**: p. 562-572.

[46] Kim, J.-J., A. El-Fiqi, and H.-W. Kim *(2017). Synergetic cues of bioactive nanoparticles and nanofibrous structure in bone scaffolds to stimulate osteogenesis and angiogenesis.* ACS Applied Materials & Interfaces, **9**(3): p. 2059-2073.

[47] Dixon, D.T. and C.T. Gomillion, (2021). *Conductive scaffolds for bone tissue engineering: current state and future outlook.* Journal of Functional Biomaterials, **13**(1): p. 1.

[48] Dorati, R., et al., *(2017). Biodegradable scaffolds for bone regeneration combined with drug-delivery systems in osteomyelitis therapy.* Pharmaceuticals, **10**(4): p. 96.

[49] Taye, M.B. (2022). *Biomedical applications of ion-doped bioactive glass: A review*. Applied Nanoscience, **12**(12): p. 3797-3812.

[50] Ege, D., K. Zheng, and A.R. Boccaccini (2022). *Borate bioactive glasses (BBG): bone regeneration, wound healing applications, and future direction.* ACS applied bio materials, **5**(8): p. 3608-3622.