Mesoporous Bioactive Glass Doped with Inorganic Compounds: A Promising Approach for Osteosarcoma Applications. Review Article

Nikoleta IVANOVA [1] *, Stoyan IVANOV [2], Galina YANEVA [1], Stefan PEEV [3], Tsanka DIKOVA [4]

[1] *Department of Biology, Faculty of Pharmacy, Medical University of Varna, 9000 Varna Bulgaria*
[2] *Department of Orthopaedics and Traumatology, Faculty of Medicine, Medical University of Varna, 9000 Varna Bulgaria*
[3] *Department of Department of Periodontology and Dental Implantology, Faculty of Dental Medicine, Medical University of Varna, 9000 Varna Bulgaria*
[4] *Department of Dental Materials Science and Prosthetic Dental Medicine, Faculty of Dental Medicine, Medical University of Varna, 9000 Varna Bulgaria*

http://doi.org/10.5755/j02.ms.43043

Received 13 October 2025; accepted 22 December 2025

Osteosarcoma treatment requires a multidisciplinary team approach. Standard therapy for localized osteosarcoma includes a combination of chemotherapy and surgical intervention. Survivors require specialized long-term follow-up, as both chemotherapy and surgery may lead to significant and lasting adverse effects on patients' quality of life. This article aims to explore the potential of innovative osteosarcoma treatment strategies involving bioactive glass. To review the scope of existing studies on the applicability of mesoporous bioactive glass doped with inorganic compounds in osteosarcoma, scientific publications from global sources were analyzed. The literature search was conducted in February and March 2025 using the electronic databases PubMed, Google Scholar, and ResearchGate. A total of 42 full-text articles were identified, with a substantial increase in publications over the past five years, reflecting the growing scientific interest in this topic. Mesoporous bioactive glass represents a specialized class of bioactive materials with excellent capacity for controlled drug release in malignant tumors. This type of glass exhibits structural characteristics similar to mesoporous silicate materials while retaining the compositional features typical of conventional bioactive glasses. The combination of traditional therapy with the synergistic bone-regenerative potential of mesoporous bioactive glass provides a strong foundation for the development of new treatment approaches for bone cancer. Evidence indicates that ions released from mesoporous bioactive glasses demonstrate high therapeutic efficacy in cancer treatment and tissue engineering.
Keywords: mesoporous bioactive glass, osteosarcoma, bone regeneration, innovation, treatment.

1. INTRODUCTION

Osteosarcoma (also called osteogenic sarcoma) is the most common type of cancer that originates in the bones. The cancer cells in these tumors resemble early forms of bone-forming cells, which normally contribute to the development of new bone tissue; however, the bone tissue produced in osteosarcoma is not as strong as that of healthy bone. Osteosarcoma most frequently occurs in teenagers and young adults, although it may also develop in younger children and older adults. It is most commonly found in the long bones.

Osteosarcoma typically arises in areas where bone growth is most rapid. The majority of tumors develop in the bones around the knee, in the distal femur or proximal tibia. The proximal humerus is the next most common site. Nevertheless, osteosarcoma can occur in any bone, including those of the pelvis, shoulder, and jaw [1, 2]. Signs and symptoms may include swelling near a bone, bone or joint pain, a bone injury, or a fracture occurring without an obvious cause.

The exact cause of osteosarcoma remains unknown. Factors that increase the risk include prior radiation therapy, other bone disorders such as fibrous dysplasia, and certain hereditary or genetic conditions, including hereditary retinoblastoma and Bloom syndrome. Osteosarcoma can spread from its primary site to other parts of the body, complicating treatment and recovery. Metastasis most often occurs in the lungs or other bones.

The aggressive chemotherapy required to treat osteosarcoma can lead to significant short- and long-term side effects. Nevertheless, advancements in treatment have substantially improved the prognosis for patients over the years. Lifelong follow-up is recommended after completion of therapy to monitor for potential late effects of intensive treatment [3, 4].

Bioactive glasses are increasingly used in osteosarcoma treatment due to their unique physical and materials-science properties, which allow for both the elimination of tumor cells and the stimulation of bone regeneration. Their precisely tunable composition and structure make them highly versatile, enabling applications in the repair of bone defects, treatment of infections, and targeted delivery of drugs or therapeutic ions. These properties collectively determine the bioactivity, biocompatibility, solubility, mechanical behavior, and overall therapeutic potential of bioglass. Bioglass can be synthesized with varying ratios of SiO_2, CaO, Na_2O, P_2O_5, and other oxides, allowing precise

* Corresponding author: N. Ivanova
E-mail: *nikoleta.ivanova@mu-varna.bg*

control over bioactivity, solubility, and mechanical properties, while the incorporation of ions such as Mg, Zn, Sr, Cu, Ag, Fe, Ga, and rare earth elements further enhances osteogenesis, angiogenesis, antibacterial, and antitumor effects [5 – 7].

The high porosity and large specific surface area of mesoporous and nanostructured bioglasses provide substantial space for loading drugs and therapeutic molecules, enabling high loading efficiency and controlled release. The release rate can be finely adjusted through pore size, chemical composition, and surface functionalization. These mesoporous structures allow the simultaneous incorporation of different drugs and ions, whose release can be regulated by changes in pH, temperature, enzymatic activity, or other external stimuli [8 – 10]. In addition, the high surface area promotes rapid formation of a hydroxyapatite layer upon contact with body fluids, which is essential for osteoinduction and successful integration with bone tissue. The surface topography and nanoscale architecture further enhance cell adhesion, proliferation, and differentiation of bone cells, thereby accelerating bone regeneration [11].

Doping bioglass with specific metals (e.g., iron, bismuth, ruthenium, tellurium) enables the application of photothermal or magnetic hyperthermia, which relies on localized heat generation capable of inducing tumor cell ablation when the material is subjected to infrared irradiation or an alternating magnetic field [12 – 15]. The porous structure and controlled release of therapeutic ions such as Ca, P, Si, Ga, and Fe stimulate osteogenesis and may exert selective cytotoxic effects on osteosarcoma cells [16, 17]. Chemotherapeutic agents, genes, or polyphenols can also be loaded and released in a controlled manner, specifically targeting tumor cells. Collectively, these features enable bioglass to provide photothermal/magnetic effects, selective cytotoxicity, and stimulation of bone regeneration, making multifunctional bioglasses a promising platform for simultaneous tumor treatment and bone defect repair [16, 18].

Bioglass is applied in osteosarcoma treatment due to its capacity for physicochemical modification, which provides photothermal/magnetic effects, selective cytotoxicity, and the stimulation of bone regeneration. Multifunctional bioglasses represent a promising platform for the simultaneous treatment of tumors and the repair of bone defects.

The incorporation of various inorganic dopants into mesoporous bioactive glasses induces significant changes in the glass network structure, porosity, and bioactivity. Dopants such as Cu, Sr, Fe, and others can occupy positions of network modifiers, leading to changes in silicate network connectivity and the creation of defects or pore enlargement [19 – 21]. Modeling the structure and properties of mesoporous bioactive glasses plays a key role in understanding and enabling rational design. Multiscale approaches, including molecular dynamics simulations, density functional theory, and continuum models, allow analysis of the relationships between chemical composition, network structure, and functional properties, enabling predictions of solubility, ion exchange, porosity, and mechanical behavior [22].

The combination of theoretical modeling and experimental solid-state NMR analyses reveals the mechanisms by which doping with various inorganic components modifies the glass network and bioactivity. Phosphorus oxide facilitates apatite nucleation, strontium reduces network connectivity and stimulates osteogenesis, while copper and cobalt introduce redox-active centers associated with angiogenic and anticancer effects. The incorporation of boron increases structural heterogeneity and accelerates degradation. These structural modifications correlate directly with ion release profiles and biological responses, enabling the engineering design of mesoporous bioactive glasses with targeted functionality for osteosarcoma-related applications [23, 24].

Experimental studies are essential for evaluating mesoporous bioactive glasses doped with Cu, Zn, Sr, Co, Fe, and B. These materials are primarily synthesized via sol–gel and microemulsion methods, which provide precise control over composition, morphology, and pore structure. Structural characterization is performed using XRD, SEM, TEM, and FTIR analyses, while BET measurements quantitatively determine specific surface area and porosity, which are directly related to bioactivity and ion release kinetics [25, 26]. Bioactivity and biocompatibility are demonstrated through in vitro tests, including hydroxyapatite layer formation in simulated body fluid and favorable cellular compatibility with osteoblasts, mesenchymal stem cells, and fibroblasts. Doping with ions such as Cu, Zn, Ag, and Fe imparts antibacterial and anticancer properties via reactive oxygen species generation, while mechanical properties can be tailored through boron incorporation, enhancing strength and hardness while simultaneously accelerating degradation and ion release [27].

This article aims to investigate the potential of using bioactive glass as an innovative treatment approach for osteosarcoma.

2. MATERIALS AND METHODS

2.1. Search strategy and selection criteria

A structured literature search was conducted in PubMed, Google Scholar, and ResearchGate using advanced search options. Two groups of keywords were applied:

1. osteosarcoma-related terms (“development of the disease osteosarcoma”, “risk groups”, “innovations in treatment”, “treatment”, “long-term treatment effects”); and
2. bioactive glass terms (“mesoporous bioactive glass”, “inorganic doping”, “bioactive glass doped with inorganic compounds”, “biomedical application”).

Filters were applied when available: full-text access, English language, peer-reviewed articles, and relevance to biomaterials, oncology, or biomedical engineering. The search covered January 2018 – March 2025. To refine the results and ensure the relevance of the material, several filters were applied when available within the databases:

— full-text availability;
— language: English;
— publication type: peer-reviewed journal articles;

— subject focus: biomaterials, oncology, biomedical engineering, nanotechnology;
— access type: open access or open archive (when possible).

2.2. Inclusion and exclusion criteria

Inclusion criteria. Studies were included if they:
— addressed osteosarcoma development, treatment, or disease-related factors, and/or investigated mesoporous bioactive glass doped with inorganic compounds or its application in bone regeneration;
— were full-text, peer-reviewed journal articles (reviews or in vitro/in vivo studies);
— were written in English or Bulgarian and published within 2018 – 2025;
— provided sufficient methodological information for scientific evaluation.

Exclusion criteria. Studies were excluded if they:
— did not focus on osteosarcoma or on doped mesoporous bioactive glass;
— examined unrelated biomaterials, polymers, or nanostructures;
— lacked full-text access or were non–peer-reviewed (e.g., abstracts, conference summaries, theses);
— were published in languages other than English or outside the 2018–2025 time frame;
— provided insufficient methodological detail.

2.3. Statistical analyses and presentation

Descriptive statistical analysis and graphical representations of the extracted data were prepared using MS Excel 2016.

3. RESULTS

Following the literature search, a total of 312 records were initially identified. After removing duplicates and screening titles and abstracts for relevance, 198 articles were excluded due to a lack of focus on osteosarcoma, insufficient relevance to mesoporous bioactive glass, or the absence of full-text availability.

A full-text assessment was then conducted for 114 articles. During this stage, 72 records were excluded based on predefined criteria, including non-peer-reviewed publications, insufficient methodological detail, lack of connection to doped mesoporous bioactive glass, or lack of relevance to osteosarcoma-related therapeutic applications.

After this multistep selection process, 42 studies met all inclusion criteria and were included in the final qualitative synthesis. The main themes identified in these studies are summarized in Table 1.

Table 1. Main themes found in the articles

Topic	Articles	Purpose of the study
Evolution of diagnosis and therapeutic Strategies in Osteosarcoma	28, 29, 30, 31	The studies present the evolution of osteosarcoma diagnosis and treatment, from standard surgical and chemotherapeutic approaches to contemporary targeted and immunotherapeutic strategies, with an emphasis on early diagnosis, a multidisciplinary approach, therapeutic resistance, and improvements in survival and quality of life.
Osteosarcoma treatment and bone regeneration: therapeutic strategies and biomaterial innovations	28, 30, 31, 32, 33, 34	The studies provide an integrated overview of osteosarcoma, encompassing standard and innovative therapeutic approaches, advances in diagnosis and treatment, including targeted and immunotherapies, the role and complexity of the tumor microenvironment, emerging molecular targets identified through single-cell transcriptomics, and the development of novel biomaterials for bone regeneration, with an emphasis on multidisciplinary management and the need for improved therapeutic strategies.
Osteosarcoma pathogenesis, tumor microenvironment, and emerging therapies	2, 28, 31, 33	The objective is to provide an overview of osteosarcoma pathogenesis, diagnosis, and treatment, highlighting the role of the tumor microenvironment in metastasis and drug resistance, and discussing current and emerging therapies, including targeted and immunotherapeutic strategies, with emphasis on metastatic and resistant cases.
Current and emerging therapies in pediatric osteosarcoma: tumor microenvironment and novel therapeutic targets	28, 29, 31, 32, 35	The objective is to review current and emerging therapies for pediatric osteosarcoma, including standard and targeted approaches, highlighting challenges in metastatic and resistant cases, the role of the tumor microenvironment, and the identification of novel therapeutic targets and metabolic vulnerabilities.
The study focuses on Eu-doped mesoporous bioactive glass nanospheres for controlled doxorubicin release and inhibition of MG-63 osteosarcoma cells.	36	Development and evaluation of the efficacy of europium-doped mesoporous bioactive glass nanospheres for osteosarcoma treatment.
Development of PHBV microspheres with mesoporous bioactive glass nanoparticles, PLA-co-GA antibacterial coatings on magnesium, and evaluation of PSME2 as a biomarker influencing osteosarcoma malignancy.	37, 38, 39	The study aims to develop antibacterial and bone-regenerative microspheres, optimize electrophoretic coatings for magnesium implants, and assess PSME2 as a biomarker influencing osteosarcoma malignancy.
Molecular mechanisms of chemoresistance in osteosarcoma and biomaterials for bone regeneration and antimicrobial protection	37, 40	Investigation of PRKDC in doxorubicin resistance via GNAS stabilization and AKT activation, and development of PHBV microspheres with mesoporous bioactive glass nanoparticles loaded with cinnamaldehyde for antibacterial and bone-regenerative applications.
Study of tellurium-doped bioactive glass on osteosarcoma cells, focusing on ferroptosis induction and its potential for bone regeneration.	41	The study aims to develop a novel biomaterial that simultaneously eliminates residual tumor cells and supports bone tissue regeneration.

Sixteen of the articles analyzed are related to the course of the disease, risk factors, treatment and innovations in the treatment provided. Of the 16 studies, 14 are literature reviews and 2 are related to clinical studies of patients. The results found that osteosarcoma is the most common and severe bone malignant tumor, characterized by a high degree of metastasis, which in most cases affects the lungs. A higher peak of the disease is found in children and adolescents [28, 29]. Timely diagnosis is a challenge for specialists, because nonspecific symptoms are observed, mimicking musculoskeletal injuries, which reflects a low suspicion for osteosarcoma on the part of physicians [33, 35].

It has been established that the overall survival of patients with localized osteosarcoma is approximately five years, while in cases with metastatic disease, survival decreases proportionally to the extent of metastatic involvement [28, 42]. In the context of developing new therapeutic strategies to improve patient outcomes, there is a recognized need for a deeper and more comprehensive analysis of the complex osteosarcoma microenvironment [32, 43]. Furthermore, resistance to chemotherapy has been identified as a major challenge and one of the leading causes of poor prognosis in affected patients [36, 44]. Efforts are currently underway to introduce personalized therapeutic approaches for osteosarcoma through the identification and analysis of new biomarkers in high-risk patients, enabling more precise treatment strategies. With the advancement of modern technologies, including artificial intelligence, researchers have demonstrated the potential to analyze groups of clinical factors to enhance the accuracy of prognostic assessments [33, 35].

Various studies also explore options for screening and monitoring in children, emphasizing the need for reliable disease markers within this vulnerable population [34, 45]. Screening practices are found to focus predominantly on groups at elevated risk of osteosarcoma, such as individuals with a genetic predisposition to cancer development [33, 37]. The impact of fluoride exposure in childhood on the development of multiple diseases, including osteosarcoma, has also been investigated; however, current evidence remains insufficient to establish a definitive link or to confirm predictive value regarding future disease development [46, 47].

New therapeutic possibilities for osteosarcoma, such as neoadjuvant chemotherapy, immunotherapy, and immune checkpoint inhibitors, have been proposed, yet they still lack validation through robust clinical trials and comprehensive research [31, 39, 48].

Twenty-six of the analyzed articles focus on the specific properties of bioactive glass and its medical applicability. Among them, 14 are literature reviews, while the remaining studies are based on clinical or experimental data involving patients. In 24 of the 26 studies, the effectiveness of mesoporous bioactive glass doped with inorganic compounds for applications in osteosarcoma treatment is demonstrated. In the remaining two studies, the authors highlight the need for additional research to further clarify its therapeutic potential.

Regarding the application of mesoporous bioactive glass doped with inorganic compounds in osteosarcoma, numerous benefits have been identified, the most significant of which are summarized in Fig. 1.

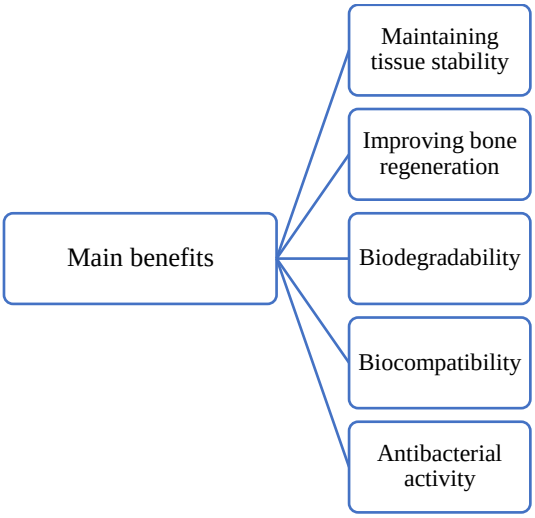

Fig. 1. Main benefits of the application of Mesoporous bioactive glass doped with inorganic compounds in osteosarcoma identified [31, 41, 46, 49, 50, 51]

The analysis of the reviewed articles revealed that osteosarcoma is a rare tumor that primarily affects the long bones and is associated with a very poor prognosis. Standard interventions for diagnosing and treating the disease include radiotherapy and chemotherapy, often combined with surgical resection of the primary tumor. These procedures, however, have a substantial negative impact on patients' quality of life.

Because surgical removal of osteosarcoma involves significant bone resection, biomaterials are employed to stabilize the remaining tissue and support bone regeneration [41]. Furthermore, the majority of studies highlight the key difference between traditional treatments and bioactive glass applications, as illustrated in Fig. 2. While conventional therapies mainly focus on tumor elimination, bioactive glass can simultaneously target cancer cells and promote local bone regeneration.

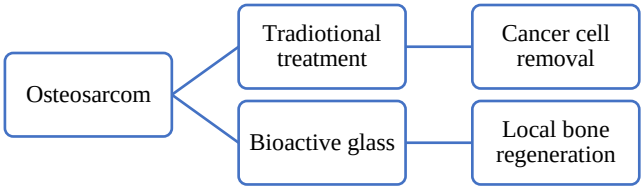

Fig. 2. Main differences in outcomes between traditional treatment and bioactive glass-based therapy, adapted from Souza et al. [52]

As shown in Fig. 2, traditional osteosarcoma treatments primarily focus on the elimination of cancer cells, whereas the use of bioactive glass not only targets tumor cells but also promotes local bone regeneration. Conventional therapies often fail to support bone regeneration due to a lack of selective targeting, affecting both cancerous and healthy cells. In contrast, bioactive glasses have been demonstrated to selectively destroy human osteosarcoma cells while exhibiting no systemic or local toxicity [52].

4. DISCUSSION

Osteosarcoma treatment requires a multidisciplinary team approach involving medical and pediatric oncologists, general and orthopedic surgeons, radiologists, pathologists, and specialized nurses [33]. Standard therapy for localized osteosarcoma includes chemotherapy and surgical resection [49]. Although these treatments can improve clinical outcomes, none of them is free from adverse effects. Therefore, it is essential not only to halt disease progression and limit the high risk of metastasis, but also to reduce the negative side effects associated with conventional chemotherapy [28].

Osteosarcoma survivors often experience long-term physical limitations, chronic pain, and an elevated risk of chronic conditions, particularly cardiovascular disease and osteoporosis. Consequently, specialized long-term medical follow-up is required, as the combination of chemotherapy and surgery can lead to substantial and lasting impairments in patients' quality of life [33]. A review of recent research shows that, despite progress in chemotherapeutic modalities, the overall effectiveness of osteosarcoma treatment has not significantly improved in recent years [31].

Because bioactive glass is already routinely applied for bone repair, interest in its potential for targeted bone cancer therapy has grown considerably. Bioactive glass offers dual therapeutic benefit. First, gallium incorporated into the glass is chemically similar to iron; rapidly dividing cancer cells absorb gallium because they require large amounts of iron. Unlike healthy cells, osteosarcoma cells accumulate gallium, making them highly susceptible to its cytotoxic effects. Laboratory experiments have demonstrated that bioactive glass containing 5 % gallium oxide reduces osteosarcoma cell viability by 99 % without harming healthy osteoblasts, the cells responsible for bone formation [18, 31].

Second, bioactive glass actively supports bone healing. When exposed to simulated body fluids, laboratory solutions that mimic the composition of human blood plasma, the glass forms a calcium phosphate layer within seven days, which stimulates new bone growth. This is particularly important for osteosarcoma patients, as tumor removal often leaves substantial bone defects requiring regeneration. By reinforcing the affected bone and accelerating tissue repair, bioactive glass may also help reduce the risk of fractures commonly seen in bone cancer patients [3, 31].

Bioactive glass is increasingly employed in bone tissue engineering due to its biodegradability and biocompatibility [37]. Studies have investigated its composite coatings, antibacterial activity, bioactivity, biodegradability, and corrosion resistance, revealing that composite coatings can regulate the rate of substrate degradation in physiological conditions, while bioactive glass coatings promote the growth of healthy tissue [38].

Menshikh demonstrated that during bone healing, angiogenesis and osteogenesis are closely interconnected, highlighting the importance of using mesoporous biomaterials that do not interfere with angiogenesis [53]. Furthermore, Pańczyszyn showed that bioactive glass doped with tellurium ions represents a novel therapeutic approach that is highly effective both in eliminating residual malignant cells and promoting bone regeneration. In this study, bioactive glass selectively targeted cancer cells while preserving the viability of healthy cells and enhancing overall bone tissue regeneration [41].

De Oliveira et al. reported that biocomposite macrospheres of Sr-bioactive glass, combined with chitosan, polymeric acid, and sodium alginate, are effective as bone fillers. The study also found that biocomposite macrospheres, as well as polylactic acid-based bioactive glass composites, were most effective in increasing cell viability [46].

Despite advancements in the treatment of various diseases, osteosarcoma therapies still face significant challenges, including severe side effects of radiation and chemotherapy, high tumor recurrence rates, and low overall survival. Fellenberg et al. investigated the therapeutic potential of mesoporous bioactive glass and found a substantial reduction in tumor cell viability, resulting in an overall decrease in tumor burden. According to these researchers, bioactive glasses hold considerable promise for developing new osteosarcoma therapies, as they exhibit minimal cytotoxicity toward healthy cells while simultaneously supporting bone regeneration [50, 31].

An interesting study investigated the applicability of bioactive glasses doped with silver and gold, synthesized using a semi-solid state technique, in the treatment of osteosarcoma. The study found that gold-doped bioactive glasses enhance the uptake of substances by healthy cells, whereas silver-doped glasses can be employed for rapid tissue healing and are significantly more cost-effective [51].

Prevention of cancer recurrence in osteosarcoma patients typically involves surgical removal of the malignant tumor followed by postoperative therapy. Vergnaud et al. examined the use of magnetic hyperthermia both as a standalone treatment and in combination with radiotherapy and chemotherapy, reporting significant therapeutic success. The combination of bone-healing biomaterials with the benefits of hyperthermia demonstrated rapid repair of critical bone defects resulting from tumor resection [54].

A fundamental characteristic of bioactive glasses is their ability to form a bone-like apatite layer on their surfaces. The formation of this apatite layer is influenced by multiple factors, including pH, the choice of starting materials, glass composition, soaking solutions, and synthesis parameters. For instance, the incorporation of titanium has been shown to significantly enhance the physicochemical properties of bioactive glass. Mabrouk et al. reported that titanium not only improves physicochemical characteristics but also enhances physical properties such as molar volume, density, glass transition temperature, and coefficient of thermal expansion [55].

Similar findings were reported by Bian et al., who demonstrated that bioactive glasses can positively impact postoperative management of osteosarcoma by simultaneously inhibiting tumor recurrence, reducing the risk of periprosthetic infection, and promoting bone regeneration [42]. Importantly, the materials used in bioactive glasses selectively target cancerous cells without adversely affecting normal cells [56, 57].

Due to their ability to bond directly with living bone, bioactive glasses are widely applied in hard tissue

engineering [58]. The specific properties of various bioactive glasses are summarized in Table 2.

Table 2. Specific properties of bioactive glasses [43]

Property	Characteristics
High biocompatibility	The substances in bioactive glasses have been scientifically proven to be highly effective as implantable materials in the human body for repairing and replacing bones damaged or altered because of chronic disease.
Solubility	Bioactive glass dissolves more rapidly in acidic environments than in neutral or slightly alkaline environments. Thus, upon interaction with an acidic environment resulting from the digestion of sugars by bacteria or the consumption of acidic beverages, the bioparticles dissolve more rapidly, increasing the pH and releasing phosphate, calcium and fluoride ions to minimize the acidic dissolution of apatite crystals from the enamel.
Solid tissue engineering	High efficiency due to the ability of bioactive glasses to bond with living bone.

Bioactive glasses possess the unique property of exhibiting specific surface reactivity upon contact with biological aqueous fluids, leading to the formation of a strong bond between living bone and the biomaterial. This property, known as bioactivity, is crucial when evaluating the potential of new biomaterials for bone regeneration [59, 60].

To further enhance the properties of bioactive glasses, specialized synthesis methods are employed. Based on supramolecular and sol-gel chemistry principles, surfactants are incorporated during synthesis to control the glass nanostructure. These surfactants facilitate the formation of mesophases, guiding the creation of mesoporous channels with uniform pore diameters. Unlike conventional bioactive glasses, mesoporous bioactive glasses feature smaller and well-controlled particle sizes, which enhance their capacity for biomolecule delivery. The mesopores in these nanoparticles typically range from 5 to 10 nm in diameter, and the overall particle size can be adjusted by varying the surfactant concentration [3, 54].

Zambanini et al. reported that bioactive glasses are highly effective in osteosarcoma treatment because the holmium contained in them can be activated by neutrons, providing therapeutic benefits when used in brachytherapy. Their study demonstrated that bioactive glasses with a high holmium content (approximately 5 %) achieved the most favorable outcomes in bone cancer therapy [61].

In another study, it was shown that functional ions play a significant role in stimulating bone tissue regeneration. Mesoporous bioactive glass nanospheres containing europium were found to maintain a long-term inhibitory effect on tumor cell viability, while simultaneously promoting mineralization of anatite and enhancing bone tissue regeneration [40, 62].

Boanini et al. synthesized mesoporous bioactive glass nanospheres to serve as carriers for one of the most potent aminobiophosphonates, alendronate. Structural and chemical characterization revealed that even low concentrations of alendronate incorporated into the nanospheres effectively reduced tumor cell viability. These findings indicate that the topical application of alendronate via functionalized mesoporous bioactive glass nanospheres holds high therapeutic potential for osteosarcoma due to their combined antitumor and bone-regenerative properties [44].

The literature review indicates that bioactive glasses have numerous biomedical applications, particularly in the regeneration of soft and hard tissues. Their unique properties, including biocompatibility and bioactivity, make them suitable for the fabrication of bone scaffolds and various pharmaceutical applications. It is important to note that the properties of bioactive glasses depend on their composition and synthesis methods. By carefully controlling the elemental composition, the biocompatibility, bioactivity, degradation rate, and overall applicability of the glasses can be precisely tuned.

Despite their clear advantages, bioactive glasses have certain limitations, primarily related to fragility, low mechanical strength, and limited fracture resistance [63]. These constraints reduce their use as a pure material; however, doping with other substances can significantly improve their properties [1].

In recent years, attention has increasingly focused on mesoporous bioactive glasses, which combine the bioactive behavior of conventional bioactive glasses with the structural advantages of mesoporous materials. Key features of mesoporous bioactive glasses include a porous architecture with uniform pore shapes and consistent surface area and pore volume. The nanoscale structure enhances reactivity and surface energy, improving interactions with biological cells.

The small particle size of mesoporous bioactive glasses allows for versatile biomedical applications, including coatings, scaffolds, and composites, making them highly adaptable for bone tissue regeneration. These materials support both bone tissue growth and angiogenesis. Moreover, mesoporous bioactive glasses are particularly valuable in osteosarcoma therapy due to their customizable surface area, pore size, and volume, which enable the targeted delivery of small therapeutic molecules, such as antitumor drugs, as well as larger biomolecules, including growth factors [64].

5. CONCLUSIONS

Biomaterials, such as mesoporous bioactive glasses, have been widely studied for their applicability in various bone defects, because their ability to bind to the bone and, by releasing biologically active ions, stimulate osteogenesis has been proven. It is important to specify that when implanting biomaterials, an inflammatory state may occur, which may require prolonged treatment with various medications. In recent years, the possibilities for developing biomaterials with antioxidant properties have increasingly begun to be investigated to reduce possible complications during implantation. Bioactive glass has proven its effectiveness in terms of regenerative medicine, due to its ability to improve bone tissue regeneration, as well as its

integrative properties. Mesoporous bioactive glass is a specific class of bioactive glass that has excellent ability for controlled drug release in malignant tumors. A specific feature of this type of glass is that it has similar structural characteristics to mesoporous materials, which are based on silicate, but also shares a similar composition to other bioactive glasses. In summary, it can be stated that the combination of traditional therapy and synergistic bone regeneration based on mesoporous bioactive glass is a prerequisite for the application of new approaches for the treatment of bone cancer. It has been proven that the ion released from mesoporous bioactive glasses has high efficiency in cancer therapy and tissue engineering.

Acknowledgments

This study is financed by the European Union-NextGenerationEU through the National Recovery and Resilience Plan of the Republic of Bulgaria, Project No. BG-RRP-2.004-0009.

REFERENCES

1. **Ahmed, M.M., Omar, A.E., Zayed, H.S.** Bioactive Glass Doped With Zinc-Based Metal–Organic Frameworks (Zn/Mof) Nanoparticles for Antibiotic Delivery Applications *Applied Physics A* 130 (209) 2024: pp. 1 – 17. https://doi.org/10.1007/s00339-024-07363-4
2. **Yang, C., Tian, Y., Zhao, F., Chen, Z., Su, P., Li, Y., Qian, A**. Bone Microenvironment and Osteosarcoma Metastasis *International Journal of Molecular Sciences* 21 (19) 2020: pp. 6985. https://doi.org/10.3390/ijms21196985
3. **Arcos, D., Portolés, M.** Mesoporous Bioactive Nanoparticles for Bone Tissue Applications *International Journal of Molecular Sciences* 24 2023: pp. 3249. https://doi.org/10.3390/ijms24043249
4. **Shoaib, Z., Fan, T.M., Irudayaraj, J.M.K.** Osteosarcoma Mechanobiology and Therapeutic Targets *British Journal of Pharmacology* 179 (2) 2022: pp. 201 – 217. https://doi.org/10.1111/bph.15713
5. **Kaou, M., Furko, M., Balázsi, K., Balázsi, C.** Advanced Bioactive Glasses: the Newest Achievements and Breakthroughs in the Area *Nanomaterials* 13 (16) 2023: pp. 2287. https://doi.org/10.3390/nano13162287
6. **Pantulap, U., Arango-Ospina, M., Boccaccini, A.** Bioactive Glasses Incorporating Less-Common Ions to Improve Biological and Physical Properties *Journal of Materials Science. Materials in Medicine* 33 (1) 2021: pp. 3. https://doi.org/10.1007/s10856-021-06626-3
7. **Ghițulică, C., Damian-Buda, A., Cucuruz, A., Voicu, G.** Synthesis and Characterization of Zno(Mgo)-Cao-Sio2-P2o5 Bioglass Obtained by Sol-Gel Method in Presence of Surfactant Agent *Gels* 7 (4) 2021: pp. 187. https://doi.org/10.3390/gels7040187
8. **Arcos, D., Portolés, M.** Mesoporous Bioactive Nanoparticles for Bone Tissue Applications *International Journal of Molecular Sciences* 24 (4) 2021: pp. 3249. https://doi.org/10.3390/ijms24043249
9. **Cui, Y., Hong, S., Jiang, W., Li, X., Zhou, X., He, X., Liu, J., Lin, K., Mao, L.** Engineering Mesoporous Bioactive Glasses for Emerging Stimuli-Responsive Drug Delivery and Theranostic Applications *Bioactive Materials* 34 2024: pp. 436 – 462. https://doi.org/10.1016/j.bioactmat.2024.01.001
10. **Gupta, J., Quadros, M., Momin, M.** Mesoporous Silica Nanoparticles: Synthesis and Multifaceted Functionalization for Controlled Drug Delivery *Journal of Drug Delivery Science and Technology* 81 2023: pp. 104305. https://doi.org/10.1016/j.jddst.2023.104305
11. **Islam, M., Macri-Pellizzeri, L., Sottile, V., Ahmed, I.** Rapid Conversion of Highly Porous Borate Glass Microspheres Into Hydroxyapatite *Biomaterials Science* 9 2021: pp. 1826 – 1844. https://doi.org/10.1039/d0bm01776k
12. **Regadas, J., Gavinho, S., Teixeira, S., De Jesus, J., Pádua, A., Silva, J., Devesa, S., Graça, M.** Influence of the Particle Size on the Electrical, Magnetic and Biological Properties of the Bioglass® Containing Iron Oxide *Magnetochemistry* 9 (209) 2023: pp. 1 – 14. https://doi.org/10.3390/magnetochemistry9090209
13. **Jian, G., Wang, S., Wang, X., Lu, Q., Zhu, X., Wan, S., Wang, S., Li, D., Wang, C., He, Q., Chen, T., Song, J.** Enhanced Sequential Osteosarcoma Therapy Using a 3d-Printed Bioceramic Scaffold Combined with 2d Nanosheets Via Nir-Ii Photothermal-Chemodynamic Synergy *Bioactive Materials* 50 2025 pp. 540 – 555. https://doi.org/10.1016/j.bioactmat.2025.04.029
14. **Dang, W., Yi, K., Ju, E., Jin, Y., Xu, Y., Wang, H., Chen, W., Wang, K., Wang, Y., Tao, Y., Li, M.** 3d Printed Bioceramic Scaffolds as a Universal Therapeutic Platform for Synergistic Therapy of Osteosarcoma *ACS Applied Materials & Interfaces* 13 (16) 2021: pp. 18488 – 18499. https://doi.org/10.1021/acsami.1c00553
15. **Wang, L., Yuan, L., Dong, Y., Huang, W., Zhu, J., Du, X., Zhang, C., Liu, P., Mo, J., Li, B., Liu, Z., Yu, X., Yu, H.** Multifunctional 3d Matrixes Based on Flexible Bioglass Nanofibers for Potential Application in Postoperative Therapy of Osteosarcoma *Regenerative Biomaterials* 11 2024: pp. rbae088. https://doi.org/10.1093/rb/rbae088
16. **Malash, A., Alesnawy, A., Ereiba, K., Bakr, A., Abdraboh, A.** An in Vitro Study of The Effects of Methotrexate Loaded Biocomposite Beads on Mg63 Osteoblast Cells *Scientific Reports* 15 (1) 2025: pp. 2231. https://doi.org/10.1038/s41598-025-85702-y
17. **Hussein, L., Moaness, M., Mabrouk, M., Farahat, M., Beherei, H.** Advancements in Mesoporous Bioactive Glasses for Effective Bone Cancer Therapy: Recent Developments and Future Perspectives *Biomaterials and Biosystems* 17 2025: pp. 100108. https://doi.org/10.1016/j.bbiosy.2025.100108
18. **Souza, L., Ferreira, F., Lopes, J., Camilli, J., Martin, R.** Cancer Inhibition and in Vivo Osteointegration and Compatibility of Gallium-Doped Bioactive Glasses for Osteosarcoma Applications *ACS Applied Materials & Interfaces* 14 2022: pp. 45156 – 45166. https://doi.org/10.1021/acsami.2c12102
19. **Anand, A., Sengupta, S., Kaňková, H., Švančárková, A., Beltrán, A., Galusek, D., Boccaccini, A., Galusková, D.** Influence of Copper-Strontium Co-Doping on Bioactivity, Cytotoxicity and Antibacterial Activity of Mesoporous Bioactive Glas *Gels* 8 (11) 2022: pp. 743. https://doi.org/10.3390/gels8110743
20. **Kermani, F., Vojdani-Saghir, A., Beidokhti, M., Nazarnezhad, S., Mollaei, Z., Hamzehlou, S., El-Fiqi, A., Baino, F., Kargozar, S.** Iron (Fe)-Doped Mesoporous 45S5

Bioactive Glasses: Implications for Cancer Therapy *Translational Oncology* 20 2022: pp. 101397. https://doi.org/10.1016/j.tranon.2022.101397

21. **Kandari, S., Gupta, S., Pal, S., Yadav, M., Kumar, A., Murugavel, S.** Unravelling The Dopant-Induced Hemostasis and Osteogenesis in Mesoporous Bioactive Glass Nanoparticles *ACS Omega* 10 2025: pp. 19922 – 19938. https://doi.org/10.1021/acsomega.5c01571
22. **Shearer, A., Bossen, A., Kheilnezhad, B., Du, J., Baino, F., Mauro, J., Montazerian, M.** Modeling the Structural and Functional Properties of Bioactive Glasses: Atomic to Macro-Scale Perspectives *Acta Biomaterialia* 202 2025: pp. 45 – 65. https://doi.org/10.1016/j.actbio.2025.06.048
23. **Philippart, A., Gómez-Cerezo, N., Arcos, D., Salinas, A., Boccardi, E., Vallet-Regí, M., Boccaccini, A.** Novel Ion-Doped Mesoporous Glasses for Bone Tissue Engineering: Study of Their Structural Characteristics Influenced by the Presence of Phosphorous Oxide *Journal of Non-crystalline Solids* 455 2021: pp. 90 – 97. https://doi.org/10.1016/j.jnoncrysol.2016.10.031
24. **Deilmann, L., Winter, O., Cerrutti, B., Bradtmüller, H., Herzig, C., Limbeck, A., Lahayne, O., Hellmich, C., Eckert, H., Eder, D.** Effect of Boron Incorporation on The Bioactivity, Structure, and Mechanical Properties of Ordered Mesoporous Bioactive Glasses *Journal of Materials Chemistry B* 8 (7) 2020: pp. 1456 – 1465. https://doi.org/10.1039/c9tb01805k
25. **Anand, A., Sengupta, S., Galusek, D., Beltrán, A., Galusková, D., Boccaccini, A.** A New Approach to Overcome Cytotoxic Effects of Cu by Delivering Dual Therapeutic Ions (SR, CU) *Journal of Trace Elements in Medicine and Biology: Organ of the Society for Minerals and Trace Elements* 87 2024: pp. 127565. https://doi.org/10.1016/j.jtemb.2024.127565
26. **Naruphontjirakul, P., Li, M., Boccaccini, A.** Strontium and Zinc Co-Doped Mesoporous Bioactive Glass Nanoparticles for Potential Use in Bone Tissue Engineering Applications *Nanomaterials* 14 (7) 2024: pp. 575. https://doi.org/10.3390/nano14070575
27. **Chen, Y.T., Chang, P., Chiou, Y., Chang, W., Weng, C., Chen, C., Chang, Y., Lin, C.** Synergistic Effect of Strontium Doping and Surfactant Addition in Mesoporous Bioactive Glass for Enhanced Osteogenic Bioactivity and Advanced Bone Regeneration *Polymers* 17 (2) 2025: pp. 187. https://doi.org/10.3390/polym17020187
28. **Argenziano, M., Tortora, C., Pota, E., Di Paola, A., Di Martino, M., Di Leva, C., Di Pinto, D., Rossi, F.** Osteosarcoma in Children: Not Only Chemotherapy *Pharmaceuticals (Basel, Switzerland)* 14 (9) 2021: pp. 923. https://doi.org/10.3390/ph14090923
29. **Isakoff, M.S., Bielack, S.S., Meltzer, P., Gorlick, R.** Osteosarcoma: Current Treatment and a Collaborative Pathway to Success *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology* 33 (27) 2015: pp. 3029 – 3035. https://doi.org/10.1200/JCO.2014.59.4895
30. **Ferguson, J.L., Turner, S.P.** BONE CANCER: Diagnosis and Treatment Principles *American Family Physician* 98 (4) 2018: pp. 205 – 213. https://pubmed.ncbi.nlm.nih.gov/30215968/
31. **Panez-Toro, I., Muñoz-García, J., Vargas-Franco, J.W., Renodon-Cornière, A., Heymann, M.F., Lézot, F., Heymann, D.** Advances in Osteosarcoma *Current Osteoporosis Reports* 21 (4) 2023: pp 330 – 343. https://doi.org/10.1007/s11914-023-00803-9
32. **Liu, Y., Feng, W., Dai, Y., Bao, M., Yuan, Z., He, M., Qin, Z., Liao, S., He, J., Huang, Q., Yu, Z., Zeng, Y., Guo, B., Huang, R., Yang, R., Jiang, Y., Liao, J., Xiao, Z., Zhan, X., Lin, C., Mo, Z.** Single-Cell Transcriptomics Reveals The Complexity of The Tumor Microenvironment of Treatment-Naive Osteosarcoma *Frontiers in Oncology* 11 2021: pp. 709210. https://doi.org/10.3389/fonc.2021.709210
33. **Beird, H.C., Bielack, S.S., Flanagan, A.M., Gill, J., Heymann, D., Janeway, K.A., Livingston, J.A., Roberts, R.D., Strauss, S.J., Gorlick, R.** Osteosarcoma *Nature Reviews Disease Primers* 8 (1) 2022: pp. 77. https://doi.org/10.1038/s41572-022-00409-y
34. **Islam, M., Macri-Pellizzeri, L., Sottile, V., Ahmed, I.** Rapid Conversion of Highly Porous Borate Glass Microspheres Into Hydroxyapatite *Biomaterials Science* 9 (5) 2021: pp. 1826–1844. https://doi.org/10.1039/d0bm01776k
35. **Wang, Y., Ma, X., Xu, E., Huang, Z., Yang, C., Zhu, K., Dong, Y., Zhang, C.** Identifying Squalene Epoxidase as a Metabolic Vulnerability in High-Risk Osteosarcoma Using an Artificial Intelligence-Derived Prognostic Index *Clinical and Translational Medicine* 14 (2) 2024: pp. e1586. https://doi.org/10.1002/ctm2.1586
36. **Zhang, Y., Hu, M., Wang, X., Zhou, Z., Liu, Y.** Design and Evaluation of Europium Containing Mesoporous Bioactive Glass Nanospheres: Doxorubicin Release Kinetics and Inhibitory Effect on Osteosarcoma Mg 63 Cells *Nanomaterials (Basel, Switzerland)* 8 (11) 2018: pp. 961. https://doi.org/10.3390/nano8110961
37. **Chotchindakun, K., Pekkoh, J., Ruangsuriya, J., Zheng, K., Unalan, I., Boccaccini, A.R.** Fabrication and Characterization of Cinnamaldehyde-Loaded Mesoporous Bioactive Glass Nanoparticles/Phbv-Based Microspheres for Preventing Bacterial Infection and Promoting Bone Tissue Regeneration *Polymers* 13 (11) 2021: pp. 1794. https://doi.org/10.3390/polym13111794
38. **Manzur, J., Akhtar, M., Aizaz, A., Ahmad, K., Yasir, M., Minhas, B.Z., Avcu, E., Ur Rehman, M.A.** Electrophoretic Deposition, Microstructure, and Selected Properties of Poly (Lactic-*Co*-Glycolic) Acid-Based Antibacterial Coatings on Mg Substrate *ACS Omega* 8 (20) 2023: pp. 18074 – 18089. https://doi.org/10.1021/acsomega.3c01384
39. **Li, R., Yan, L., Jiu, J., Liu, H., Li, D., Li, X., Zhang, J., Li, S., Fan, Z., Lv, Z., Zhu, Y., Wang, B.** Psme2 Offers Value as a Biomarker of M1 Macrophage Infiltration in Pan-Cancer and Inhibits Osteosarcoma Malignant Phenotypes *International Journal of Biological Sciences* 20 (4) 2024: pp. 1452 – 1470. https://doi.org/10.7150/ijbs.90226
40. **Zhang, W., Li, W., Yin, C., Feng, C., Liu, B., Xu, H., Jin, X., Tu, C., Li, Z.** Prkdc Induces Chemoresistance in Osteosarcoma by Recruiting Gde2 to Stabilize Gnas and Activate AKT *Cancer Research* 84 (17) 2024: pp. 2873 – 2887. https://doi.org/10.1158/0008-5472.CAN-24-0163
41. **Pańczyszyn, E., Lallukka, M., Gagliardi, M., Saverio, V., Monzani, R., Miola, M., Verné, E., Corazzari, M.** Tellurium-Doped Bioactive Glass Induces Ferroptosis in Osteosarcoma Cells Regardless of Fsp1 *Antioxidants (Basel, Switzerland)* 13 (11) 2024: pp. 1327. https://doi.org/10.3390/antiox13111327
42. **Bian, Y., Zhao, K., Hu, T., Tan, C., Liang, R., Weng, X.** A Se Nanoparticle/Mgfe-Ldh Composite Nanosheet as a

Multifunctional Platform for Osteosarcoma Eradication, Antibacterial and Bone Reconstruction *Advanced Science (Weinheim, Baden-Wurttemberg, Germany)* 11 (33) 2024: pp. e2403791. https://doi.org/10.1002/advs.202403791

43. **Bigham, A., Fasolino, I., Borsacchi, S., Valente, C., Calucci, L., Turacchio, G., Pannico, M., Serrano-Ruiz, M., Ambrosio, L., Raucci, M.G.** A Theragenerative Bio-Nanocomposite Consisting of Black Phosphorus Quantum Dots for Bone Cancer Therapy and Regeneration *Bioactive Materials* 24 (35) 2024: pp. 99 – 121. https://doi.org/10.1016/j.bioactmat.2024.01.018
44. **Boanini, E., Panseri, S., Arroyo, F., Montesi, M., Rubini, K., Tampieri, A., Covarrubias, C., Bigi, A.** Alendronate Functionalized Mesoporous Bioactive Glass Nanospheres *Materials (Basel, Switzerland)* 9 (3) 2016: pp. 135. https://doi.org/10.3390/ma9030135
45. **Cersosimo, F., Lonardi, S., Bernardini, G., Telfer, B., Mandelli, G.E., Santucci, A., Vermi, W., Giurisato, E.** Tumor-Associated Macrophages in Osteosarcoma: From Mechanisms to Therapy *International Journal of Molecular Sciences* 21 (15) 2022: pp. 5207. https://doi.org/10.3390/ijms21155207
46. **de Oliveira, I.R., Dos Santos Gonçalves, I., Wallace Dos Santos, K., Lança, M.C., Vieira, T., Carvalho Silva, J., Cengiz, I.F., Reis, R.L., Oliveira, J.M., Miranda Ribeiro Borges, J.P.** Biocomposite Macrospheres Based on Strontium-Bioactive Glass for Application as Bone Fillers *ACS Materials Au* 3 (6) 2023: pp. 646 – 658. https://doi.org/10.1021/acsmaterialsau.3c00048
47. **Nakamoto, T., Rawls, H.R.** Fluoride Exposure in Early Life as The Possible Root Cause of Disease in Later Life *The Journal of Clinical Pediatric Dentistry* 42 (5) 2018: pp. 325 – 330. https://doi.org/10.17796/1053-4625-42.5.1
48. **Li, H., Shen, X., Ma, M., Liu, W., Yang, W., Wang, P., Cai, Z., Mi, R., Lu, Y., Zhuang, J., Jiang, Y., Song, Y., Wu, Y., Shen, H.** Zip10 Drives Osteosarcoma Proliferation and Chemoresistance Through Itga10-Mediated Activation of The Pi3k/Akt Pathway *Journal of Experimental & Clinical Cancer Research: CR* 40 (1) 2021: pp. 340. https://doi.org/10.1186/s13046-021-02146-8
49. **Du, J., Ding, H., Fu, S., Li, D., Yu, B.** Bismuth-Coated 80s15c Bioactive Glass Scaffolds for Photothermal Antitumor Therapy and Bone Regeneration *Frontiers in Bioengineering and Biotechnology* 10 2023: pp. 1098923. https://doi.org/10.3389/fbioe.2022.1098923
50. **Fellenberg, J., Losch, S., Arango-Ospina, M., Hildenbrand, N., Tripel, E., Deng, L., Renkawitz, T., Westhauser, F., Lehner, B., Boccaccini, A.R.** Targeting Bone Tumours with 45s5 Bioactive Glass *International Journal of Molecular Sciences* 25 (19) 2024: pp. 10830. https://doi.org/10.3390/ijms251910830
51. **Mostafa, A.A., El-Sayed, M.M.H., Emam, A.N., Abd-Rabou, A.A., Dawood, R.M., Oudadesse, H.** Bioactive Glass Doped with Noble Metal Nanoparticles for Bone Regeneration: *In Vitro* Kinetics and Proliferative Impact on Human Bone Cell Line *RSC Advances* 11 (41) 2021: pp. 25628 – 25638. https://doi.org/10.1039/d1ra03876a
52. **Souza, L., Ferreira, F.V., Lopes, J.H., Camilli, J.A., Martin, R.A.** Cancer Inhibition and in Vivo Osteointegration and Compatibility of Gallium-Doped Bioactive Glasses for Osteosarcoma Applications *ACS Applied Materials Interfaces* 14 (40) 2022: pp. 45156 – 45166. https://doi.org/10.1021/acsami.2c12102
53. **Menshikh, K., Reddy, A.K., Cochis, A., Fraulini, F., Zambon, A., Lusvardi, G., Rimondini, L.** Bifunctional Mesoporous Glasses for Bone Tissue Engineering: Biological Effects of Doping with Cerium and Polyphenols in 2d and 3d *in Vitro* Models *Biomaterials and Biosystems* 14 2024: pp. 100095. https://doi.org/10.1016/j.bbiosy.2024.100095
54. **Vergnaud, F., Kesse, X., Jacobs, A., Perton, F., Begin-Colin, S., Mertz, D., Descamps, S., Vichery, C., Nedelec, J.M.** Magnetic Bioactive Glass Nano-Heterostructures: A Deeper Insight into Magnetic Hyperthermia Properties in The Scope of Bone Cancer Treatment *Biomaterials Science* 10 (14) 2022: pp. 3993 – 4007. https://doi.org/10.1039/d2bm00319h
55. **Mabrouk, M., Beherei, H.H., Tanaka, Y., Tanaka, M.** Investigating The Intermediate Water Feature of Hydrated Titanium Containing Bioactive Glass *International Journal of Molecular Sciences* 22 (15) 2021: pp. 8038. https://doi.org/10.3390/ijms22158038
56. **Dziadek, M., Dziadek, K., Checinska, K., Zagrajczuk, B., Cholewa-Kowalska, K.** Bioactive Glasses Modulate Anticancer Activity and Other Polyphenol-Related Properties of Polyphenol-Loaded Pcl/Bioactive Glass Composites *ACS Applied Materials & Interfaces* 16 (19) 2024: pp. 24261 – 24273. https://doi.org/10.1021/acsami.4c02418
57. **Fernandes, J.S., Reis, R.L., Pires, R.A.** Wetspun Poly-L-(Lactic Acid)-Borosilicate Bioactive Glass Scaffolds for Guided Bone Regeneration *Materials Science & Engineering. C, Materials for Biological Applications* 71 2017: pp. 252 – 259. https://doi.org/10.1016/j.msec.2016.10.007
58. **Kargozar, S., Milan, P.B., Amoupour, M., Kermani, F., Gorgani, S., Nazarnezhad, S., Hooshmand, S., Baino, F.** Osteogenic Potential of Magnesium (Mg)-Doped Multicomponent Bioactive Glass: i*n Vitro* and *in Vivo* Animal Studies *Materials (Basel, Switzerland)* 15 (1) 2022: pp. 318. https://doi.org/10.3390/ma15010318
59. **Vallet-Regi, M., Salinas, A.J.** Mesoporous Bioactive Glasses for Regenerative Medicine *Materials Today. Bio* 11 2021: pp. 100121. https://doi.org/10.1016/j.mtbio.2021.100121
60. **Sharifi, E., Bigham, A., Yousefiasl, S., Trovato, M., Ghomi, M., Esmaeili, Y., Samadi, P., Zarrabi, A., Ashrafizadeh, M., Sharifi, S., Sartorius, R., Dabbagh Moghaddam, F., Maleki, A., Song, H., Agarwal, T., Maiti, T.K., Nikfarjam, N., Burvill, C., Mattoli, V., Raucci, M.G., Makvandi, P.** Mesoporous Bioactive Glasses in Cancer Diagnosis and Therapy: Stimuli-Responsive, Toxicity, Immunogenicity, and Clinical Translation *Advanced Science (Weinheim, Baden-Wurttemberg, Germany)* 9 (2) 2022: pp. e2102678. https://doi.org/10.1002/advs.202102678
61. **Zambanini, T., Borges, R., de Souza, A.C.S., Justo, G.Z., Machado, J.Jr., de Araujo, D.R., Marchi, J.** Holmium-Containing Bioactive Glasses Dispersed in Poloxamer 407 Hydrogel as a Theragenerative Composite for Bone Cancer Treatment *Materials (Basel, Switzerland)* 14 (6) 2021: pp. 1459. https://doi.org/10.3390/ma14061459
62. **Zhao, X., Wu, Q., Gong, X., Liu, J., Ma, Y.** Osteosarcoma: A Review of Current and Future Therapeutic Approaches *Biomedical Engineering Online* 20 (1) 2021: pp. 24.

https://doi.org/10.1186/s12938-021-00860-0

63. **Hussein, L., Moaness, M., Mabrouk, M., Farahat, M.G., Beherei, H.H.** Advancements in Mesoporous Bioactive Glasses for Effective Bone Cancer Therapy: Recent Developments and Future Perspectives *Biomaterials and Biosystems* 17 2025: pp. 100108. https://doi.org/10.1016/j.bbiosy.2025.100108

64. **Matic, T., Daou, F., Cochis, A., Barac, N., Ugrinovic, V., Rimondini, L., Veljovic, D.** Multifunctional Sr, Mg-Doped Mesoporous Bioactive Glass Nanoparticles for Simultaneous Bone Regeneration and Drug Delivery *International Journal of Molecular Sciences* 25 (15) 2024: pp. 8066. https://doi.org/10.3390/ijms25158066