A REVIEW OF CERAMIC BIOMATERIALS USED IN BONE TISSUE ENGINEERING

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Abstract

Bioceramics, recognized for their exceptional bioactivity, have become integral in applications across medicine, surgery, dentistry, and tissue engineering. Their inherent biocompatibility, combined with both osteoconductive and osteoinductive properties, offers significant advantages over traditional graft materials in bone regeneration therapies. This review specifically focuses on ceramics, glasses, and glass-ceramics applied within bone tissue engineering, emphasizing porous scaffold systems. These materials not only provide mechanical support but also actively stimulate healing by facilitating cell migration, tissue integration, and the exchange of nutrients and metabolic products. In this paper, the structural properties, clinical applications, and recent advancements in these biomaterials are critically examined, with particular emphasis on enhancing mechanical strength, bioactivity, and antiseptic functionalities.

Keywords: bioceramics, bioglass, glass-ceramic materials, bone tissue engineering, bioceramic scaffolds

1. INTRODUCTION

Bioceramics are a class of materials widely applied in medicine, dentistry, orthopedics, and tissue engineering due to their high biocompatibility, corrosion resistance, and stability under compressive loads. However, despite these advantageous properties, their inherent brittleness and low fracture toughness significantly limit their use, especially in load-bearing applications. To overcome these limitations, bioceramic materials are often engineered into porous forms or combined with other phases to improve their mechanical performance while preserving their biological functionalities.

Bioceramics can be broadly classified into three categories based on their biological interactions with tissues [1]:

- Bioinert ceramics, such as alumina and zirconia, are biologically passive and integrate with tissues via morphological fixation without provoking an immune response. However, this interaction often leads to the formation of a fibrous capsule that mechanically isolates the implant from the surrounding biological environment. The thickness of this fibrous layer can serve as an indirect indicator of the degree of bioinertness of the material.
- Surface-bioactive ceramics, including sintered hydroxyapatite (s-HA), bioglasses, and glass-ceramics, can form a strong chemical bond with tissues. This is achieved through the formation of a hydroxycarbonate apatite (HCA) layer on their surface when exposed to body fluids, which closely mimics the mineral phase of bone. This surface-driven bioactivity allows for stable integration with bone tissue. It should be noted, however, that the degree of bioactivity and the rate of bioresorption of these materials can vary depending on in vivo conditions and the biological environment.
- Bioresorbable ceramics, such as non-sintered hydroxyapatite (HAp), tricalcium phosphate (TCP), and octacalcium phosphate (OCP), are designed to degrade gradually in the body and be replaced by native bone tissue. Their chemical composition and crystallographic structure are closely aligned with the mineral components of natural bone, ensuring high biocompatibility, osteoconductivity, and the capability to bond directly with bone. The physical form of these materials-whether solid, porous,

granular, or powder does not inherently affect their bioactivity. However, the rate of biodegradation is influenced by multiple factors, including chemical composition, porosity, specific surface area, degree of crystallinity, presence of structural defects, as well as local environmental parameters such as pH and saturation.

In recent years, the development of bioceramic materials has advanced beyond the traditional boundaries of materials science [2]. Current research not only focuses on enhancing their bioactivity and resorbability but also seeks to improve their mechanical strength and multifunctionality, particularly for applications in bone tissue engineering. This includes materials such as hydroxyapatite (HAp) [3], tricalcium phosphate (TCP) [4], bioactive glasses [5], and bioactive glass-ceramics [6]. For example, the possibility of precise shaping of porous scaffolds [7, 8] can be supported by advanced laser processing techniques [9, 10] known from other fields of materials science. Moreover, the pursuit of optimizing the manufacturing processes and functional properties of bioceramics is in line with the principles of quality management [11] and the concept of circular economy [12], by searching for materials with long service life and the potential for recycling or safe biodegradation. In the context of energy saving [13, 14], research on energy-efficient methods of synthesis and sintering of bioceramics is crucial for sustainable development. Moreover, in the aspect of managing the design and implementation [15] of new biomaterials, it is becoming important to take into account the aspects of environmental sustainability. An interdisciplinary approach, combining knowledge from the field of bioceramics with advanced models of computational materials engineering [16] in the development of new technologies and broader trends of the economy [17] can accelerate the transfer of innovations from laboratories to practical clinical and industrial applications.

2. CALCIUM PHOSPHATE BIOMATERIALS

The CaP family materials used in regeneration include: tricalcium phosphate (TCP), hydroxyapatite (HAp), amorphous calcium phosphate (ACP), octacalcium phosphate (OCP), dicalcium phosphate anhydrous (DCPA), dibasic calcium phosphate dihydrate (DCPD), and tetracalcium phosphate (TTCP) [1].

Hydroxyapatite (HAp) – $Ca_{10}(PO_4)_6(OH)_2$ – constitutes about 70% of the dry mass of bone and strongly binds to bone tissue. It demonstrates osteoconduction, stability in body fluids (fluoroapatite is more durable), and biocompatibility. Its properties depend on composition, microstructure, and porosity. HAp is the final mineral phase of bone, and other CaPs (ACP, OCP) are precursors. HAp properties change with the Ca/P ratio; it reaches its mechanical optimum at Ca/P = 1.67, and strength decreases above this value [3]. There are three forms of HAp: solid, porous, and granular. Solid HAp ceramics, which are high-strength, are used for loaded implants and manufactured by pressing or casting with sintering. Its key features are bending, tensile strength, and fracture resistance. It is used in long-term subcutaneous implants and monitoring devices [4]. Porous HAp ceramics are preferred for bone implants/shells and drug delivery systems. Bimodal porosity (100-135 µm and smaller pores) supports tissue ingrowth and vascularization. It is obtained by firing pore-forming organic substances or foaming with H_2O_2, obtaining 50-60% porosity [7]. HAp ceramic pellets (e.g., Interpore® 200, Osteogen®, Pro Osteon®) are commonly used in periodontal reconstructive surgery, cysts, and drug delivery systems [18].

Tricalcium phosphate (TCP), with two crystalline phases (α-TCP and β-TCP), is one of the best-studied CaP biomaterials. Crystalline β-TCP is formed at about 800 °C from thermal decomposition of CDHA and transforms into α-TCP above 1125 °C. Therefore, α-TCP is a high-temperature phase of β-TCP [4]. Clinically, β-TCP is superior to HAp in terms of osteoconductivity, osteoinduction, biodegradability, and resorption, finding application in bone cements and bioceramics [19]. The nanoporous structure of β-TCP supports biomineralization, adhesion, and cell proliferation. The α-TCP phase is mainly used in cements due to its transformation into HAp in contact with water.

Amorphous calcium phosphate (ACP) is the initial phase of HAp and a key element of bone mineralization [3]. ACP exhibits high osteoconductivity and biodegradability, making it suitable for bone cements, scaffolds, bone repair biomaterials, and dental implants. It is also a good drug carrier due to its high surface area nanoclusters and pH-dependent biodegradability.

Tetracalcium phosphate (TTCP) is a highly alkaline, metastable phase of CaP, which gradually hydrolyzes to HAp and $Ca(OH)_2$ in a moist environment. There are three types of TTCP bone cement: single-, multi-, and polymeric. TTCP is used in self-curing bone cements, composites, and root canal sealers.

Octacalcium phosphate (OCP) is a precursor of HAp crystallization and is important in bone formation and biomineralization. It exhibits good osteoinduction and is used for bone repair, as a coating for metal implants, in bone cements, and in composite scaffolds for bone tissue regeneration [20].

3. CLASSIFICATION OF BIOGLASSES

The name of the glass most often comes from the main oxide that forms the network: network former.

3.1. Silicate bioglasses

Silicate bioglasses are the basic type of bioactive glasses in which the basic octahedra $(SiO_4)^{4-}$ are connected to each other by corners, creating empty spaces between the anionic layers. This makes the glass susceptible to corrosion in a biological environment and releases ions responsible for bioactivity from its structure.
The first known silicate glass is Bioglass 45S5 (45% SiO_2, 24.5% Na_2O, 24.4% CaO, 6% P_2O_5 by weight). Its surface releases silicon, calcium, sodium, and phosphorus ions. Ion exchange has a positive effect on cellular reactions, making the glass osteoinductive. In vitro studies have shown that Bioglass 45S5 has a positive effect on the expression and secretion of VEGF [21]. Slowly released silica is excreted in urine and does not accumulate. The transformation of glass into HCA results in the presence of fragments of unprocessed glass in the new tissue, which is quickly rebuilt. Bioglass 45S5 crystallizes during sintering and has poor mechanical properties [5]. Glasses based on Bioglass 45S5 have better processing and forming properties, but similar bioactivity and biodegradability. Currently, there are two bioglasses based on 45S5 Bioglass® available on the market, differing in particle fraction [22]:

- PerioGlas® - NovaBone – 90 - 170 µm
- BioGran® - BIOMET2i™ – 300 - 355 µm

These glasses are used in dentistry, with the difference that BioGrain® bioglass particles are combined with autogenous bone, and PerioGlas® bioglass particles are used alone. A small amount of autogenous bone ensures proper immunohistochemical response, osteoblastic activity, and vascularization process during bone repair [22].

Bioglass S53P4, which permanently bonds to bone, can replace bone tissue. It is osteoconductive, osteostimulating, and antibacterial. It is used in bone regeneration, vascularization, cartilage repair, and the treatment of osteomyelitis. Its bioactivity is similar to other silicate glasses, but the release of alkaline ions during dissolution increases pH and osmotic pressure, inhibiting bacteria [22]. It is most often found in the form of granules. Small granules are used in hand and maxillofacial surgery, larger ones in orthopedic, trauma, and the treatment of bone infections. Nonporous glass plates and implants in the shape of a kidney, heart, or round are used in the regeneration of orbital fractures [23].

3.2. Borosilicate bioglasses

The first biomedical borosilicate glass was designed by Brink in 1990 [24]. Boron glasses are reactive and chemically unstable, which accelerates the formation of HCA (rich in borates) on their surface, similarly to Bioglass 45S5. The rate of degradation is controlled by the B_2O_3 content. Boron facilitates sintering [22]. Boron glass, due to its pH, is an efficient in vitro culture medium, increasing cell proliferation. In vivo, it shows high cell infiltration. The toxicity of boron ions requires control of their release so as not to exceed the body's ability to remove them. Boron glasses are enriched with silver and cerium ions. Cerium relaxes the glass structure for silver ions, which have antibacterial and anti-inflammatory effects, supporting the degradation and bioactivity of the glass [25,26].

3.3. Phosphate bioglasses

P_2O_5-based glasses were introduced in 1980. Asymmetric tetrahedra [PO_4] in phosphorus (V) oxide causes low durability and easy hydration of P–O–P bonds in phosphate glasses. Due to their high solubility, P_2O_3-based bioglasses are used in regenerative medicine. The dissolution rate is modified by oxide additives (TiO_2, CuO, NiO, MnO, Fe_2O_3). Ease of forming and spinning makes phosphate bioglasses useful in soft tissue engineering, especially for muscle and nerve regeneration. Positive results of *in vivo* studies using glass tubes or neural nets confirm their material intelligence. In bone tissue engineering, they are valued in the form of masses or powders with polymers due to their regenerative potential [27].

3.4. Doped bioglasses

Additives to bioactive bioglass (partial or complete replacement of the main components) allow the production of glasses with different bioactivity and biodegradability [22]. Each doping element and each oxide in the composition of bioglass affects its properties. Silicon and calcium are crucial for homeostasis, while boron, fluorine, lithium, magnesium, phosphorus, strontium, niobium, and zinc stimulate bone mineralization. Calcium, phosphorus, silicon, fluorine, lithium, magnesium, silver, strontium, and zinc improve the activity, adhesion, and proliferation of osteoblasts. Collagen synthesis and angiogenesis are supported by silicon, magnesium, and zinc. Cobalt stimulates osteoclasts and inhibits osteoblasts [28].

3.5. Mesoporous bioactive glasses (MBG)

Mesoporous bioactive glasses (MBG), called template glasses, have a composition similar to gel glasses and controlled porosity (5-50 nm). MBGs are characterized by ordered mesoporous channels, stable structure, large pore volume and surface area, regular nanopores, and uniform morphology (hexagonal/cubic). MBGs are used in catalysis, adsorption, separation, filtration, and biomedicine, mainly as drug delivery systems [8].

4. GLASS-CERAMIC BIOMATERIALS

Glass-crystalline/glass-ceramic materials are created as a result of controlled crystallization of primary glasses, during which crystalline phases precipitate in the amorphous matrix (which can also occur during the production of bioglasses, e.g., sintering). Glass-crystalline materials based on bioglass are characterized by high bioactivity and better mechanical properties than the parent glass (hardness, bending strength, fracture toughness). The classification of bioactive glass-ceramics is based on the type of crystalline phases and their applications. The most well-known and commercially available glass-crystalline materials on the medical market include [29]:

- Ceravitals® – CaO-P_2O_5 apatite in a glass matrix of Na_2O–K_2O–MgO–CaO–SiO_2–P_2O_5 (1973) - osteoconductive material used for phalangeal prostheses.
- Cerabones® – apatite and wollastonite (A-W) in a MgO–CaO–SiO_2– P_2O_5 glass matrix (1980) - manufactured in a variety of shapes and used as a bone substitute.
- Bioverits® – apatite and mica in a glass matrix of Na_2O–MgO–CaO–Al_2O_3–SiO_2–P_2O_5–F (1985) - easy to process and shape material used for prostheses and middle ear implants.
- Biosilicates® – apatite-free ceramics (1996) with the following composition: 23.75Na_2O–23.75CaO–48.5SiO_2–24P_2O_5 (wt%) - high bioactivity index and workability, used for coatings, disc-shaped implants, orbital and phalangeal implants, and ossicular implants.

Other glass-ceramic materials showing bioactivity can be divided, depending on the phases present in the materials, into: apatite-mullite, kanansite-apatite, rananite, calcium-pyrophosphate, k-fluorichterite and alkali-free ceramics [30].

Glass bioceramics are used in load-bearing implants, as glassy coatings improve their fracture toughness. In zirconia implants, a composite intermediate layer (glassy phase surrounding zirconia) is formed, providing continuous thermomechanical properties. Ceramic composites reinforced with crystalline glass increase flexural and fracture toughness, and magnetic bioactive glass ceramics are used in cancer therapy (hyperthermia destroys cancer cells through heat generated in an alternating magnetic field by ferri-/ferromagnetic materials, e.g. lithium, magnesium, zinc, magnesium-zinc ferrites, and iron oxides). Bioactive glass scaffolds are produced by sintering (nucleation and growth of crystalline phases in an amorphous matrix). Technologies for the production of porous glass ceramics include phase separation, leaching, sol-gel, sintering, and foaming. Crystalline phases are biocompatible and improve scaffold mechanics. Porous glass-ceramic materials have shown better in vivo results in bone formation, mineralization and implant-bone strength compared to bioglass (powders/fine particles), HAp and TCP [6]. So far, bioactive glass-crystalline materials have been used as middle ear implants, implant coatings after tooth extraction, filling of bone defects (including maxillofacial bone), tissue scaffolds and porous drug delivery systems [30].

5. CONCLUSION

Bioceramics have been widely studied since the 1970s, and over the last half-century, numerous advances have been achieved, addressing many of the early limitations associated with these materials. Over this period, the field has evolved from the development of bioceramics intended solely to replace damaged bone fragments to the design of materials capable of promoting regeneration and restoring function to damaged or missing tissues. Current technologies enable the development of materials with improved antimicrobial properties and enhanced mechanical strength, while maintaining their inherent biocompatibility, bioactivity, and biodegradability. Ongoing research in the area of bone tissue regeneration, as well as in drug delivery applications, focuses on both the optimization of manufacturing processes and the precise tailoring of chemical compositions, aiming to simultaneously control porous structure parameters and biological performance. Given the significant achievements of bioactive ceramics in bone tissue engineering, these materials are now increasingly being explored and applied in soft tissue engineering applications.

REFERENCES

[1] VAIANI, L. *et al.* Ceramic materials for biomedical applications: An overview on properties and fabrication processes. *J. Funct. Biomater.* 2023, vol. 14, p. 146. https://doi.org/10.3390/jfb14030146

[2] SIWIEC, D., DWORNICKA, R., PACANA, A. Improving the process of achieving required microstructure and mechanical properties of 38mnvs6 steel. In: *METAL 2020 – 29th Int. Conf. Metall. Mater. 2020*, Ostrava, Tanger, pp.591-596. https://doi.org/10.37904/metal.2020.3525

[3] HOU, X. *et al.* Calcium phosphate-based biomaterials for bone repair. *Journal of Functional Biomaterials*. 2022, vol. 13, art.187. https://doi.org/10.3390/jfb13040187

[4] DOROZHKIN, S. V. Calcium orthophosphate-containing biocomposites and hybrid biomaterials for biomedical applications. *J. Funct. Biomater.* 2015, vol. 6, pp.708-832. https://doi.org/10.3390/jfb6030708

[5] ERASMUS, E.P. *et al.* Effects of sintering temperature on crystallization and fabrication of porous bioactive glass scaffolds for bone regeneration. *Sci. Rep.* 2017, vol. 7, art. 6046. https://doi.org/10.1038/s41598-017-06337-2

[6] MONTAZERIAN, M., ZANOTTO, E. Bioactive glass-ceramics processing, properties and applications. In: BioactiveGlasses: Fundamentals, Technology and Applications. *RSC Smart Materials.* 2016, pp. 27-60. https://doi.org/10.1039/9781782622017-00027

[7] ORLOVSKII, V.P., KOMLEV, V.S., BARINOV, S. M. Hydroxyapatite and hydroxyapatite-based ceramics. *Inorg. Mater.* 2002, vol. 38, pp.973-984. https://doi.org/10.1023/A:1020585800572

[8] IZQUIERDO-BARBA, I., VALLET-REGI, M. Mesoporous bioactive glasses: Relevance of their porous structure compared to that of classical bioglasses. *Biomed. Glas.* 2015, vol.1, pp.140-150. https://doi.org/10.1515/bglass-2015-0014

[9] RADEK, N., PIETRASZEK, J., GADEK-MOSZCZAK, A., ORMAN, L., SZCZOTOK, A. The morphology and mechanical properties of ESD coatings before and after laser beam machining. *Materials*. 2020, vol.13, art. 2331. https://doi.org/10.3390/ma13102331

[10] RADEK, N., KONSTANTY, J., PIETRASZEK, J., ORMAN, L., SZCZEPANIAK, M., PRZESTACKI, D. The Effect of laser beam processing on the properties of WC-Co coatings deposited on steel. *Materials*. 2021, vol.14, art. 538. https://doi.org/10.3390/ma14030538

[11] CZERWIŃSKA, K., PIWOWARCZYK, A. The use of combined quality management instruments to analyze the causes of non-conformities in the castings of the cover of the rail vehicle bearing housing. *Prod. Eng. Arch*. 2022, vol.28, pp.289-294. https://doi.org/10.30657/pea.2022.28.36

[12] PACANA, A., SIWIEC, D., DWORNICKA, R. Pro-quality method improving industrial products toward sustainable development with criteria of circular economy. In: *METAL 2023 – 32nd Int. Conf. Metall. Mater*. 2024, Ostrava, Tanger, pp.697-702. https://doi.org/10.37904/metal.2023.4743

[13] ORMAN, L., RADEK, N., PIETRASZEK, J., SZCZEPANIAK, M. Analysis of enhanced pool boiling heat transfer on laser-textured surfaces. *Energies*. 2020, vol.13, art. 2700. https://doi.org/10.3390/en13112700

[14] ORMAN, Ł., MAJEWSKI, G., RADEK, N., PIETRASZEK, J. Analysis of thermal comfort in intelligent and traditional buildings. *Energies*. 2022, vol.15, art. 6522. https://doi.org/10.3390/en15186522

[15] KLIMECKA-TATAR, D., NICIEJEWSKA, M. Small-sized enterprises management in the aspect of organizational culture. *Rev. Gest. Tecnol*. 2021, vol.21, pp.4-24. https://doi.org/10.20397/2177-6652/2021.v21i1.2023

[16] DWORNICKA, R., RADEK, N., KRAWCZYK, M., OSOCHA, P., POBEDZA, J. The laser textured surfaces of the silicon carbide analyzed with the bootstrapped tribology model. In: *METAL 2017 - 26th Int. Conf. Metall. Mater*. 2017, Ostrava, Tanger, pp.1252-1257.

[17] BARYSHNIKOVA, N., KIRILIUK, O., KLIMECKA-TATAR, D. Management approach on food export expansion in the conditions of limited internal demand. *Pol. J. Manag. Stud*. 2020, vol.21, pp.101-114. https://doi.org/10.17512/pjms.2020.21.2.08

[18] AOKI, H. *Medical Applications of Hydroxyapatite: Bone Mineral, Drug Delivery System, Cancer \& HIV, IVH \& CAPD, Dental Implant*. Ishiyaku EuroAmerica, 1994.

[19] OWEN, G. Rh., DARD, M., LARJAVA, H. Hydoxyapatite/beta-tricalcium phosphate biphasic ceramics as regenerative material for the repair of complex bone defects. *J. Biomed. Mater. Res. B. Appl. Biomater.* 2018, vol. 106, pp. 2493-2512. https://doi.org/10.1002/jbm.b.34049

[20] SUGIURA, Y., MANUAR, M. L., ISHIKAWA, K. Fabrication of octacalcium phosphate block through a dissolution-precipitation reaction using a calcium sulphate hemihydrate block as a precursor. *J. Mater. Sci. Mater. Med.* 2018, vol. 29, art.151. https://doi.org/10.1007/s10856-018-6162-1

[21] BORDEN, M. *et al*. Controlling the bone regeneration properties of bioactive glass: Effect of particle shape and size. *J. Biomed. Mater. Res. B. Appl. Biomater.* 2022, vol.110, pp.910-922. https://doi.org/10.1002/jbm.b.34971

[22] CANNIO, M. *et al*. Bioactive glass applications: A literature review of human clinical trials. *Materials.* 2021, vol. 14, art.5440. https://doi.org/10.3390/ma14185440

[23] GIGLIO, R. *et al.* Efficacy and safety of bioactive glass S53P4 as a treatment for diabetic foot osteomyelitis. *J. Foot Ankle Surg.* 2021, vol. 60, pp.292-296. https://doi.org/10.1053/j.jfas.2020.06.029

[24] ASLAM, A. A. *et al.* Boron-based bioactive glasses: Properties, processing, characterization and applications. *Ceram. Int.* 2023, vol. 49, pp.19595-19605. https://doi.org/10.1016/j.ceramint.2023.03.164

[25] ABDALLAH, E. *et al.* Structural and antibacterial peculiarities of modified borate bioglass containing mixed dopant oxides. *J. Bio- Tribo-Corrosion*. 2022, vol. 8, art.39. https://doi.org/10.1007/s40735-022-00640-w

[26] HAJDUGA, M. B. *et al.* Analysis of the antibacterial properties of polycaprolactone modified with graphene, bioglass and zinc-doped bioglass. *Acta Bioeng. Biomech.* 2021, vol.23, pp.131-138. https://doi.org/10.37190/ABB-01766-2020-03

[27] CHRISTIE, J. K. *et al.* Structures and properties of phosphate-based bioactive glasses from computer simulation: a review. *J. Mater. Chem. B*. 2017, vol.5, pp.5297-5306. https://doi.org/10.1039/C7TB01236E

[28] O'NEILL, E. *et al.* The roles of ions on bone regeneration. *Drug Discov. Today.* 2018, vol.23, pp.879-890. https://doi.org/10.1016/j.drudis.2018.01.049

[29] MONTAZERIAN, M., ZANOTTO, E. History and trends of bioactive glass-ceramics. *J. Biomed. Mater. Res. A.* 2016, vol.104, pp.1231-1249. https://doi.org/10.1002/jbm.a.35639

[30] STANKIEWICZ-BRUDNIK, B. *et al.* Selected physico-chemical properties of composite scaffolds of sintered submicrocrystalline corundum and bioglass. *Int. J. Adv. Manuf. Technol.* 2022, vol.120, pp.1867-1876. https://doi.org/10.1007/s00170-022-08736-w