Journal of Composites and Compounds 8(2026) 1-11

Available Online at www.jourcc.com

Journal homepage: www.JOURCC.com

CrossMark

Journal of Composites and Compounds

Recent advances in cobalt-based alloy and nano bioactive glass composites: Synthesis, characterization, and biomedical applications

Christine Narumbe Jore [a]***, Mahsa Mohammadpour Beneh Khalkhal*** [b*]***, Parisa Izadi*** [c*]

[a] *Department of Dentistry, Tbilisi state medical university, Tbilisi, Georgia*

[b] *Faculty of Dentistry, Volgograd state medical university, Volgograd, Russia*

[c] *Nanotechnology Engineering, Sapienza university of Rome, Rome, Italy*

A B S T R A C T

Cobalt-based alloys and bioactive glasses are known as biomaterials used for orthopedic and dental applications because of their mechanical and biological properties. Due to the acceptable mechanical strength, fatigue resistance, and corrosion stability of cobalt-based alloys in physiological environments, these metallic alloys are suitable for load-bearing implants. However, they have faced some limitations in osseointegration and biological performance because of their high elastic modulus, limited bioactivity, and concerns about metallic ion release in long-term use. In contrast, nano bioactive glasses (nBGs) have shown excellent bioactivity, osteogenic potential, angiogenesis and antibacterial responses through surface reactivity and controlled ion release, but their brittleness and low fracture toughness limited their load-bearing application. This review provides an overview of recent advances in cobalt-based alloy/nano bioactive glass composites as a multi-component system which is designed to overcome the limitations of single-phase systems. The structural, mechanical, and chemical properties of cobalt-based alloys and nBGs are discussed, followed by the synergistic effects achieved at the metal–glass interface. Several synthesis and compositional strategies, such as melt-derived, sol–gel processing, powder metallurgy, additive manufacturing and surface coating techniques have been explored. The in vitro biological performance of these composites, including cytocompatibility, osteogenic differentiation, angiogenic stimulation, and antimicrobial activity, is discuss in relation to their potential applications in orthopedic and dental implants. Finally, key challenges such as mechanical compatibility, long-term stability, cobalt-related regulatory concerns, and future research directions are outlined.

Peer review under responsibility of UGPH.

A R T I C L E   I N F O R M A T I O N

Article History:
Received 03 December 2025
Received in revised form 08 February 2026
Accepted 18 February 2026

Keywords:
Cobalt-based alloys
Bioactive glasses
Multi-component system
Bioactivity
Mechanical properties
Load-bearing applications

Table of Contents

* *Corresponding authors: Mahsa Mohammadpour Beneh Khalkhal & Parisa Izadi, Emails:* *mahsamohammadpour99@gmail.com*, *paisa.sp@gmail.com*
https://doi.org/10.61882/jcc.8.1.1

1. Introduction

A bioactive material is known by its surface biological response ability to form new bone and bond with host tissue [1]. Since professor Larry Hench's development of bioglass in the late 1960s, bioactive silicate glasses have become a foundational material in bone tissue engineering due to their capacity to combine with other substances like calcium to help bond with living tissues and activate genetic pathways that regulate osteogenesis [2, 3].

The benefits of bioglass over hydroxyapatite and other allografts include its biological fixation and the ability to bond with soft and hard tissues, while hydroxyapatite is limited to bonding only with hard tissues [4]. The 45S5 bioglass (45 wt% SiO_2, 24.5 wt% Na_2O, 24.5 wt% CaO, 6 wt% P_2O_5) exhibits rapid hydroxycarbonate apatite (HCA) formation upon exposure to physiological environments through rapid Na^+/Ca^{2+} exchange with H^+/H_3O^+, formation of a silica-rich gel, and subsequent HCA crystallization, releasing osteogenic ions (Si, Ca, P) that stimulate osteoblast differentiation and vascularization [5].

Despite the bioactivity and osteoinductive potential of bioglasses, they face poor mechanical strength (fracture toughness and brittleness) which restrict their application in load-bearing environments [6, 7].

To overcome these limitations, recent research has focused on using metallic systems such as stainless steel, titanium, and cobalt-chromium alloys in bioactive glass compositions [8, 9], which could effectively be used in dental and medical prostheses because of their durability, resistance to corrosion and compatibility with biological systems [2]. Among metallic systems, cobalt-based alloys provide mechanical strength, fatigue resistance, and corrosion stability, which make them more attractive than other metallic alloys, like ti-based systems which are costly and is volunteer to failure in the dynamic environment of the oral cavity [2, 10].

Studies show that addition of boron in Co-Cr alloys improves wear resistance and provide strong tissue compatibility without inflammation [11]. Moreover, cobalt has natural antimicrobial characteristics but combining this alloy with tungsten and copper has shown more efficacy against bacteria such as E. coli [12]. Research also suggest that cobalt may improve osteogenic and angiogenic properties, which is crucial for bone healing [2, 13, 14]. Also, researchers at School of Mechanical and Electrical Engineering of the Autonomous University of Nuevo Leon reported that not only incorporating boron into the Co-Cr alloy would increase mechanical strength, wear-resistance, and hardness of composition but also shows biocompatibility and osteogenic differentiation characteristics in an in vitro model [15, 16].

This review outlines the recent advances in the synthesis, characterization, and biomedical applications of cobalt-based alloy/nano bioactive glass composites, and discusses materials properties, composite fabrication (powder metallurgy, additive manufacturing, sol-gel coating methods), in vitro biological properties (cytocompatibility, osteogenesis, antimicrobial performance), in orthopedic and dental applications and bone tissue engineering.

2. Cobalt-based alloys in biomedical applications

Cobalt-based alloys are one of the significant metallic biomaterials with high mechanical and biological stability which provide excellent wear and corrosion resistance in comparison with stainless steel in clinical uses [17]. These biomedical alloy family such as ASTM F75, F799, F90, and F562 differ in alloying additions and thermo-mechanical histories which affect their microstructure, strength, and long-term implant performance [18].

ASTM F75 (Co-28Cr-6Mo) is the most established Co-based alloy for orthopedic and removable dental prostheses applications based on the formation of passive chromium-rich surface layer which causes high wear and corrosion resistance [19-21].

However, as a cast alloy, its microstructure is highly sensitive to the casting route and solidification conditions where interdendritic areas face high levels of carbides and solute elements (Mo, Cr, Co), while primary dendrites are enriched in cobalt and free from chromium, which causes large grain formation, anisotropic mechanical behavior and increases the risk of casting defects and fatigue fracture, therefore the alloy will experience a reduction in tensile strength in load-bearing applications [20, 22].

ASTM F799 (Co-28Cr-6Mo) has the same composition with F75 but is reinforced via controlled thermo-mechanical processing. High-temperature hot-working increases ductility and followed cold work induces strain hardening, as a result F799 exhibits higher yield and tensile strengths with improved ductility and fatigue resistance compared to cast F75 alloy [18, 19].

ASTM F90 (Co-20Cr-15W-10Ni) is a wrought alloy which has improved its microstructure and machinability by addition of tungsten and nickel. In the annealed state, its mechanical properties are comparable to cast F75; however, cold working can increase its strength to the level of F799. Nevertheless, achieving microstructural homogeneity during processing is important to prevent stress concentrations and fatigue failure [19, 20, 23].

ASTM F562 (Co-35Ni-20Cr-10Mo), commercially known as MP-35N, is a multiphase wrought alloy developed for applications such as cardiovascular devices and high-strength orthopedic components, which provides tensile strength up to 1,795 MPa, excellent corrosion resistance and plastic deformability, and ranks among the strongest biomedical metals available [20, 24, 25].

Clinically, because of its high wear resistance and well-documented clinical history of Co-28Cr-6Mo (ASTM F75), this alloy is widely used for removable dental prostheses and conventional joint replacement[19, 26]. In contrast, Co-35Ni-20Cr-10Mo (ASTM F562), is preferred where tensile strength and corrosion resistance are needed over long-term service [19].

2.1. Properties of Co-based alloys

Because of the mechanical strength, corrosion resistance, and biocompatibility of Cobalt-based alloys in load-bearing environments (orthopedic, dental, and cardiovascular implants) they are considered as an important class of metallic biomaterials [27].

Their chemical stability in orthopedic and dental applications depends on the formation of a chromium oxide (Cr_2O_3) as a passive layer in physiological environments [27, 28].

Based on the importance of interaction between corrosion and mechanical wear in applications such as joint prostheses, optimization of corrosion resistance is essential for the lifetime of implants, so that the addition of alloying elements such as molybdenum and nickel to Co-based alloys affects the corrosion resistance and control metal ion release [29].

Besides composition, microstructural characteristics including grain size, the balance between γ-fcc and ε-hcp phases, and carbide morphology have an influence on the strength and stiffness of Co-based alloys[30]. Recent advances in processing techniques, such as additive manufacturing, and powder metallurgy, offer different ways to control these microstructural parameters and optimize the performance of cobalt-based biomaterials [30, 31].

Biological properties of cobalt alloys are generally well tolerated by host tissues, and demonstrate favorable biocompatibility, low cytotoxicity, and hemocompatibility for applications involving blood contact [27]. It is important to note that the biological response is sensitive to surface chemistry, topography, and the physicochemical nature of degradation products or wear particles. To promote osseointegration, tissue regeneration, and minimize inflammatory or immunological reactions associated with metal ion dissolution, strategies include surface modification, controlled ion release, and hybridization with bioactive phases such as nano bioactive glass [32].

The performance of cobalt-based biomaterials is influenced by their composition, microstructural features, mechanical integrity, electrochemical behavior, and biological interactions, therefore achieving a balanced optimization among these factors is essential for the functional requirements of next-generation orthopedic, dental, and cardiovascular implants [32].

2.2. Clinical perspectives (Advantages and limitations)

Co alloys, especially Co-Cr alloys, have been widely used in orthopedics and restorative dentistry because of their high strength, good wear and corrosion resistance, and generally acceptable biocompatibility based on long-term clinical experiences compared with many other base-metal systems [33].

Within the current European regulation, cobalt is classified as a carcinogenic, mutagenic and reprotoxic(CMR) substance, and medical devices containing substances classified as CMR at concentrations above 0.1% (w/w) are subject to strict justification requirements, and in some cases may be omitted from marketing [33]. This is especially critical for Co-Cr dental alloys in which cobalt is typically the major constituent (often around one-third to more than half of the alloy composition) [33].

Despite these high concentrations, such alloys can still be placed on the market if manufacturers demonstrate that no suitable alternative materials exist and provide a strong scientific and clinical justification, which must be accepted by notified bodies, under strict compliance with Medical Device Regulation (MDR) and Classification, Labelling and Packaging(CLP) requirements, including mandatory labeling and risk communication [33].

As an example, although Co-Cr alloys being considered non-cytotoxic or low-cytotoxic under clinical conditions, in vitro studies report measurable Co and Cr ion release from Co-Cr dental alloys and cast Co-Cr-Mo implants, which could cause allergic contact dermatitis (ACD) and concentration-dependent cytotoxic and inflammatory responses in fibroblasts and osteoblasts (Fig. 1). The systemic impact of this ion release from dental alloys on cancer development in humans remains unclear [33, 34].

However, from an industrial and clinical perspective, finding replacement biomaterials that match the mechanical strength, corrosion resistance, and long clinical history of Co-Cr alloys in such a short time frame is challenging. One proposed strategy is to develop new alloy compositions with ultra-low levels of the problematic metals while preserving key functional properties, optimizing processing routes (e.g., Selective Laser Melting(SLM)/Direct Metal Laser Sintering(DMLS)) to minimize corrosion and ion release, and using hybrid systems such as cobalt-based substrates modified with nBGs or other biofunctional coatings to achieve mechanical performance from the surface biological interactions [35].

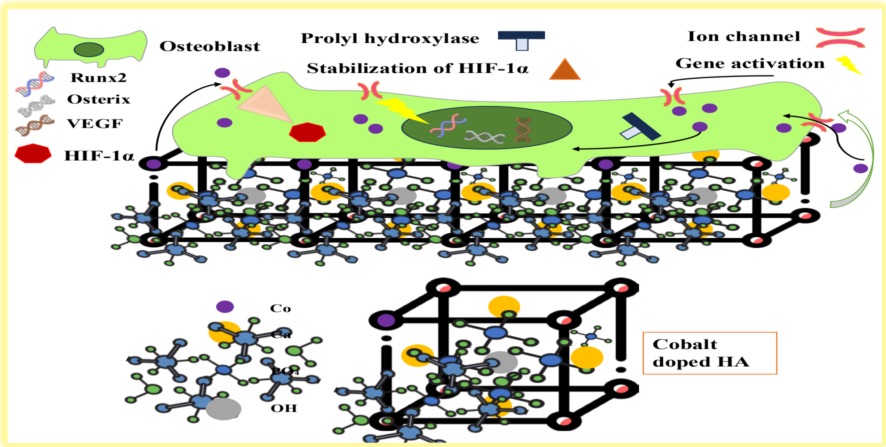

Fig. 1. Interaction of cobalt doped on HA when attached to osteoblast bone cells in bone tissue.

3. Nano bioactive glasses (nBGs): Structure and functionality

nBGs are promising biomaterials, offering enhanced potential for bone tissue engineering due to their nanoscale dimensions, high surface area, and controlled ion-release profiles which allow rapid interaction with bone tissue and promote new bone formation [36-38]. These silica-based materials rapidly form a HCA layer upon immersion in physiological fluids, chemically bond to bone and provide an ideal substrate for osteoblast adhesion and proliferation [39, 40]. The controlled release of bioactive ions (Si^{4+}, Ca^{2+}, PO_4^{3-}) in nBGs can promote osteogenesis by stimulating the growth factor production and cell proliferation, as well as gene expression associated with bone regeneration in osteoblasts that leads to bone regeneration [41]. In vitro studies on human dental pulp stem cells report extracts of nBGs can promote alkaline phosphatase (ALP) activity and collagen type I (Col I) expression which are crucial for osteogenic differentiation in bone and dentin formation [41], and these materials are one of the most important candidates for pulp-dentin regeneration and endodontic therapies [42].

3.1. Composition and structural features

Physical and chemical reactivity, controlled ion release, and biological performance of bioactive glasses are determined by their composition and nanoscale morphology. NBGs structures typically contain a silica-based (SiO_2) matrix which is modified by Na_2O, CaO and P_2O_5, where the degree of N_4 silica network connectivity, adjusted by the Si/O ratio and dopant additions, directly influenced dissolution kinetics and apatite formation potential [6]. The high specific surface area of nBGs improves interfacial effects in physiological fluids which leads to HCA nucleation and promotes bioactivity [41].

Beyond size effects, particle morphology has a great impact on physicochemical stability, protein adsorption, and cellular responses. Comparative studies have shown that spherical hydroxyapatite nanoparticles compared to rod-like counterparts, support osteoblast adhesion, proliferation, and mineralization due to more isotropic surface chemistry [41]. The physicochemical and biological behavior of bioactive glasses is influenced not only by chemical composition but also by structural organization, particle morphology, and surface properties, which are strongly determined by synthesis and processing parameters such as melting history, precursor chemistry, and post-processing conditions. Thus glasses with the same composition can provide different structural features and biological responses when produced by different fabrication strategies [43].

3.2. Surface reactivity and ion release of nano bioactive glasses

45S5 nBGs particles, compared to their micron-sized ones, show greater surface reactivity due to their higher specific surface area. During immersion of nBGs in simulated body fluid (SBF), the silicate network begins to hydrolyze, leading to the release of SiO_2, Ca^{2+} and PO_4^{3-} , which causes nucleation and growth of hydroxyapatite (HAp) layers on the surface of the glass, a characteristic of bioactivity [44]. In vitro studies by Brunner et al. (2012) showed HAp nucleation and formation of calcite on nBG surfaces after seven days of immersion in SBF. These phases were characterized using Raman spectroscopy, scanning electron microscopy (SEM), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), and Transmission electron microscopy (TEM). These findings show that nBGs can form HAp within one day of immersion, whereas the same micron-sized glasses require several days for comparable layer development [44]. During HAp mineralization, ion release increases local pH and osmotic pressure, and this chemical microenvironment inhibits bacterial adhesion and biofilm establishment. On the other hand, the addition of therapeutic ions including Zn^{2+}, Cu^{2+}, Ga^{3+}, Ce^{4+}, or Ag^{+}, increases these bactericidal effects and supports tissue regeneration [45].

3.3. Bioactivity and osteogenic potential of nano bioactive glasses

Ajita et al. reported that reduction of bioactive glass particles to nanoscale improved osteoconductivity, dissolution behavior, and biomineralization of bioactive glasses, due to their nanostructured surface, which promotes cell adhesion, osteoblast proliferation, and differentiation. This work also highlighted the size-dependent cellular response, where smaller nBG particles induced higher mesenchymal stem cell (MSC) proliferation [46].

In particular, nBGs particles stabilize extracellular signal-regulated kinase (ERK) activation and adjust cyclin gene expression, facilitate cell cycle progression from the G0/G1 phase to the S and G2/M phases. These findings offer a design strategy for controlling nBG particle dimensions that enhance cellular proliferation and osteogenic activity for dental and orthopedic biomaterials [46].

Gong et al. reported that ionic products released from nano-sized bioactive glasses activate mitogen-activated protein kinase (MAPK) signaling pathways, specifically ERK and P38. This pathway activation promotes the expression of Runx2, a key transcription factor that leads to osteoblast differentiation, followed by upregulation of osteogenic markers such as osteocalcin (OCN) and bone sialoprotein (BSP), ultimately leading to enhanced matrix mineralization (Fig. 2). Notably, nano-sized 58S bioactive glass exhibited stronger MAPK phosphorylation and osteogenic gene activation than conventional 45S5 compositions [47].

Finally, these studies have demonstrated that nanoscale engineering of bioactive glasses not only increases bioactivity but also enables molecular-level regulation of osteogenic signaling pathways.

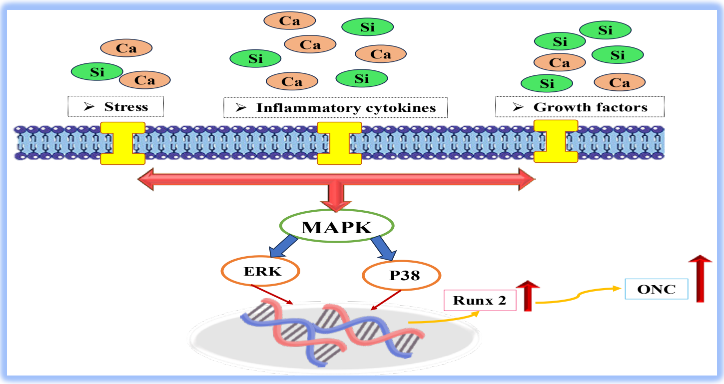

Fig. 2. Schematic illustration of cell signaling pathways involved in bioactive glass induced osteogenic gene activation.

4. Cobalt-based alloy/nBG composites

Since vascularization is a key limiting factor in regenerative therapies, especially in large bone defects and dental implants, where insufficient angiogenesis disturbs healing [48], cobalt-doped bioactive glasses provide a promising strategy by combining osteogenic and bone-bonding properties of bioactive glasses with cobalt-mediated angiogenic signaling [48].
In this case, controlled release of Co^{2+} ions activate hypoxia-mimetic pathways, stabilizing hypoxia-inducible factor-1α (HIF-1α) and upregulating angiogenic factors such as VEGF, bFGF, and SDF-1α in osteoblasts, endothelial cells, and mesenchymal stem cells. Similarly, bioactive glass matrix supports osteogenesis through HCA formation and release of Si, Ca, and P ions, which regulate Runx2, ALP, and osteocalcin expression [48].
This combination allows implants to provide both structural support with cobalt-based metallic alloys (Co-Cr, Co-Cr-B, Co-Cr-Mo) and biological activity, through the controlled ion release from nBGs [48]. These cobalt-doped bioactive glasses show excellent biocompatibility, angiogenic activity and minimal cytotoxicity in relevant in vitro and in vivo models [48, 49].
Moreover, cobalt-releasing bioactive glasses are being developed in various forms, including micro and nanoparticles, polymer composites, fibers, and porous scaffolds, in applications beyond bone regeneration, including wound healing and cancer therapy. However optimizing cobalt dosage, ion-release kinetics, and long-term safety to maximize angiogenesis while minimizing potential cytotoxicity remains challenging [50].

5. Synthesis and fabrication approaches

Cobalt-doped bioactive glasses are synthesized through melt-derived and sol-gel methods (including template-directed approaches), while their composites with Co-based alloys are fabricated via powder metallurgy, additive manufacturing, and coating techniques for load-bearing biomedical applications. These strategies are discussed separately in the following sections [48].

5.1. Bioactive glass synthesis routes

5.1.1. Melt-derived bioactive glasses

Melt-derived bioactive glasses, first developed by Hench in 1969, are produced by melting oxide precursors (SiO_2, CaO, Na_2O, P_2O_5) at high temperatures (≈1300-1500 °C) followed by rapid quenching to produce an amorphous structure with a disordered networks and high surface reactivity [37, 51].
Despite high bioactivity of melt-derived bioactive glasses, their brittleness has limited their performance in load-bearing applications. To overcome this limitation, cobalt-doped bioactive glasses are increasingly used to combine structural toughness with biological functionality [48].
In melt-derived cobalt-doped bioactive glasses, cobalt is commonly added as cobalt oxide (CoO), acting as a network modifier that changes the thermal and rheological behavior of the glass [48]. Incorporation of cobalt, influences melt viscosity and crystallization kinetics, and generally lowers the glass transition temperature (Tg) while shifting the onset of crystallization (Tx) to higher values compared with undoped glasses [48].
It is noticeable that controlled concentrations of cobalt can prevent undesirable crystallization during cooling and subsequent heat treatments. This enables the fabrication of amorphous powders, fibers, or porous glass precursors without phase separation. However, uncontrolled cobalt content can disrupt the glass network, increase crystallization risk, and reduce microstructural uniformity [48]. As a result, careful control of composition and processing parameters such as homogeneous mixing of precursors, rapid quenching, and optimized heat-treatment parameters are essential [52].

5.1.2. Sol-gel derived bioactive glasses

Sol-gel synthesis is a low-temperature, wet-chemical method, based on hydrolysis and condensation reactions which allow adjustment of both composition and nanostructure [53, 54].
The sol-gel process involves alkoxide-based precursors such as tetraethyl orthosilicate (TEOS), triethyl phosphate (TEP), and calcium salts to form an amorphous silica-based network. In the process, the sol converts to a crosslinked gel, followed by drying and calcination, which results in a high specific surface area and an interconnected mesoporous architecture [43].
This structure improves ion exchange and HCA nucleation compared to melt-derived glasses, resulting in faster bioactivity and more efficient release of therapeutic ions [43, 55]. The system also offers a controllable platform for cobalt addition as a network modifier into bioactive glass networks. Unlike melt quenching, cobalt can be doped at the molecular level of bioactive glasses during sol preparation using soluble salts such as $Co(NO_3)_2{\cdot}4H_2O$ or $CoCl_2{\cdot}4H_2O$, and the cobalt incorporation effectiveness depends on both precursor chemistry and dopant concentration [48].
At doping levels around 2-2.5 mol%, cobalt ions are fully integrated into the amorphous network structure without the formation of crystalline secondary phases and preserve the mesoporous structure [55]. In contrast, higher cobalt addition levels around 4-5 mol% may promote the formation of cobalt oxide crystallites, which have a negative impact on nanoscale homogeneity and biological performance [48].
The choice of precursor can also be important because nitrate-based precursors lead to complete incorporation and controlled ion release, whereas chloride salts are more prone to incomplete integration and secondary phase formation [48].
Beyond composition, sol-gel processing parameters such as sol pH, hydrolysis and calcination temperature critically influence particle size, pore connectivity, and cobalt distribution [56].
In general, sol-gel processing provides a strategy for producing cobalt-doped nBGs with controlled nanostructure and bioactivity, supporting their application in advanced dental and orthopedic composites [6].

5.1.2.1. Template-directed sol-gel bioactive glasses

As shown in Fig. 3 template-directed bioactive glasses (TGs) are a class of sol-gel derived materials with arranged mesoscale structure (2-50 nm) in an amorphous atomic network, which is separated by thin amorphous SiO_2-CaO-P_2O_2 walls [43, 57].
It is noteworthy that the ordered pore architecture of TGs is made through sol-gel processing where surfactants or solid templates guide mesoporous formation during gelation, enabling control over pore size, connectivity, and surface area [43]. The mesoporous arrangement of TGs improves ion release, HCA formation, and bioactivity [58].

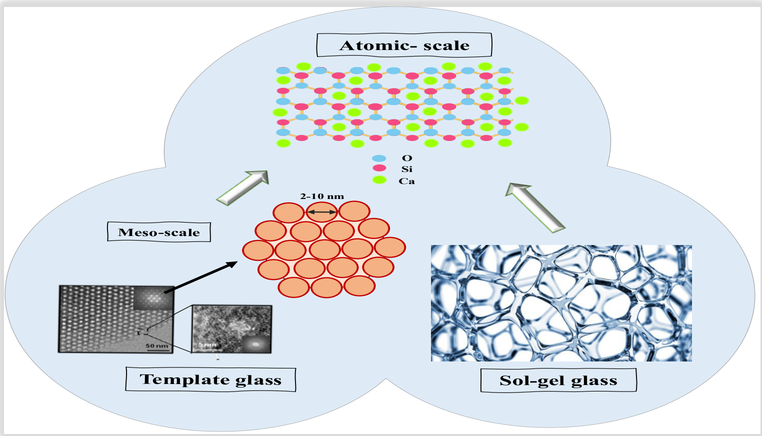

Fig. 3. The key differences between sol–gel glasses and templated bioactive glasses (TGs).

5.2. Composite fabrication techniques

5.2.1. Powder metallurgy and sintering

Powder metallurgy (PM) is one of the methods for fabricating metal glass composites, in which metallic and glass powders are homogeneously mixed, then the mixture is compacted by pressing and sintered under a protective atmosphere. This controlled environment prevents oxidation and enables the particles to bond, and create the dense composite with a well-defined microstructure [59].

The densification process in these composites occurs through two mechanisms: solid-state sintering and liquid-phase sintering. In solid-state sintering, atoms move slowly through the surface of particles and cause reduction in surface energy Filling voids between particles. This process strengthens the structure while preserving compositional uniformity. In contrast, liquid-phase sintering occurs during heating when part of the glass melts and forms a liquid phase that improves rearrangement of particles, accelerates densification and fills pores more efficiently. It is important to notice that the effectiveness of liquid-phase sintering requires careful matching of the thermal expansion of metal and glass to avoid interfacial stresses or cracks [60].

A practical example of this system is the combination of cobalt-doped bioactive glass into Co-Cr-Mo matrices using PM with liquid-phase sintering. Researchers achieved This combination provides composites with excellent densification, improved mechanical performance, and strong interfacial bonding [59].

Notably, when accurate composition is considered, solid-state sintering is a good choice because it provides a controlled consolidation, while liquid-phase sintering allows faster densification and better particle-glass contact, so process selection directly affects the final properties of the composite [61].

5.2.2. Additive manufacturing

Additive manufacturing (AM) is a fabrication method that provides designing biomaterials with controlled geometries. Techniques such as Selective Laser Melting (SLM), Selective Laser Sintering (SLS), and Fused Deposition Modeling (FDM) in AM are based on layer-by-layer integration of metal powders derived from CAD models, allowing the creation of internal structures, surface topographies, and mechanical gradients. In SLM and SLS techniques densification is achieved through laser sintering, whereas in FDM, the metal-polymer composite is extruded, followed by debinding and sintering. These fabrication methods enable the capability to design porosity, lattice structures, and surface roughness at micro and meso scales [62, 63].

In a case study, Bafandeh et al. successfully fabricated Co-Cr/nBG composites via SLM, and reported that they achieved uniform glass distribution with enhanced bioactivity [6].

Laser cladding in AM is another technique to provides additional control over surface properties and allows deposition of thin metallic layers with strong metallurgical bonding. In this technique, powder is delivered through a nozzle aligned with the laser beam, and melting allows a defect-free interface. This method offers a good connection between bioactive coatings and alloyed surface layers [64, 65]. As an example, Comesaña et al. used laser cladding to deposit bioactive glass coatings on Co-Cr substrates, and reported that strong metallurgical bonding with HCA formation was achieved within 3 days [63].

In general, the combination of AM with laser cladding offers a strategy to fabricate metallic biomaterials with optimized bulk and surface properties, enabling control of densification, microstructure, mechanical performance, and interfacial bonding for biomedical constructs [62, 63].

5.2.3. Sol–gel coating methods

In sol–gel coating, metal or metalloid precursors undergo hydrolysis to form a cross-linked matrix. There are two ways to form a sol-gel coating, the inorganic route, which involves converting colloidal oxide suspensions into a gel, and the organic route, which is usually based on the formation of metal alkoxide precursors in low-molecular-weight organic solvents [66].

During hydrolysis, by-products such as alcohol and water are released, this is followed by drying, which the network shrinks to form the final coating structure which is influenced by pH, temperature, reactant ratios, and solvent composition [67, 68].

Spraying and electrodeposition are modern techniques used in sol-gel coatings, while conventional methods like dip-coating and spin-coating are also widely use [68, 69].

Electrodeposition, as a controllable method for sol-gel coatings, can be used even on complex geometries. In this technique, parameters such as solution pH, colloid concentration, deposition voltage, and time are carefully controlled. For example, researchers reported that SiO_2 coating on galvanized steel using electrodeposition were crack-free, and show highly corrosion-resistant [68].

Time-consuming nature of sol-gel synthesis could be a challenge; for example, aging time can take several hours to days, which is not suitable for industrial use. On the other hand, phase separation is common during heat-treatment [70]. After deposition, the solvent starts to evaporate, leading to internal stress and volume contraction in the coating. If the processing conditions are not carefully controlled, cracking would appear. So optimizing the synthesis process and developing new gelation and heat-treatment strategies based on the microstructure and application are essential for sol-gel coating systems [70].

6. Biological performance

6.1. In vitro cytocompatibility and osteogenic response

In vitro studies on cobalt-based bioactive systems show that cellular responses are influenced by cobalt concentration, release kinetics, and local exposure time. Therefore, controlled cobalt ion release support cytocompatibility, as well as normal cell attachment and growth [13, 71, 72].

In some studies, materials by controlled levels of Co^{2+} ions release show acceptable cytocompatibility, osteoblast and mesenchymal stem cell viability, while supporting cell adhesion and proliferation [73].

In cobalt-based bioactive system, hypoxia-mimicking pathways are activated, while the glass matrix provides osteoconductive cues through its dissolution products. This interaction promotes vascular support and bone formation without relying on external biological agents [74]. As evidence of their biological performance, cobalt-modified collagen and bioactive scaffolds, have shown the stabilization of HIF-1α, increased VEGF secretion, and regulation of bone-related gene expression in bone marrow stromal cells which results in vascularized bone formation with cellular compatibility [75].

The biological performance of cobalt-based bioactive materials is design-dependent, and is controlled by composition, nanostructure, and processing parameters [75].

6.2. Antimicrobial behavior

Cobalt-based materials have shown antimicrobial activity in addition to their osteogenic and angiogenic properties, which is an important factor in implant applications. In this mechanism, Cobalt ions interact with bacterial membranes, and induce oxidative stress, so essential cellular processes blocked, which cause a reduction in bacterial adhesion and viability [75].

For instance, Co-Cr-W-Cu as a cobalt-based alloy shows inhibitory activity against Escherichia coli, while preserves biocompatibility [76].

Also, surface functionalization strategies have been explored to increase the antimicrobial performance of cobalt-containing substrates. In a report, formation of self-assembled monolayers (SAMs) based on cobalt and cationic metallosurfactants on stainless steel (SS 316L) has shown antibacterial efficiency while improving corrosion resistance. This antibacterial behavior is linked to the nature and length of hydrophobic chains which affect bacterial membrane interactions and biofilm formation [76].

6.3. Hemocompatibility and tissue interactions

Surface treatment with ion addition is a method to achieve hemocompatibility and electrochemical stability in Co-based biomedical alloys. The method decreased blood-material interactions by reducing in hemolysis rate and increasing dynamic clotting times. In a case study on Co-based alloys, CoCr and Co_3Ti as primary phases, along with TiC and TiO, form a disordered layer which provide both hemocompatibility and corrosion resistance. These modifications is a strategy to use Co-based alloys for cardiovascular and orthopedic implants, where blood compatibility and material stability are essential [77].

7. Biomedical applications

Biomaterial scaffolds containing cobalt-based alloys with bioactive glasses are known as multi-component system reported a strategy in orthopedic and dental implants, bone tissue engineering, and antibacterial coatings especially in large or vascular defects where both mechanical support and biological stimulation are required [48].

7.1. Orthopedic and dental implants

Cobalt-based alloy/nano-bioactive glass composites are candidate for orthopedic and dental implants, combining mechanical durability and biological functionality [78]. In orthopedic applications, recent studies have shown that 82S5 silica-based nano-bioactive glass coated by Co-Cr-Mo scaffolds, show improved bioactivity and corrosion resistance which is crucial for load bearing applications [79].

In another study, microstructural analyses of electrophoretic deposition of nBG on a 3D-printed Co-Cr-Mo substrate show apatite layer formation for bone bonding and osteointegration. These coatings could be a choice in long term load-bearing applications compared with uncoated implants [79]. In other coating strategies, bioactive glass has been applied to titanium orthopedic implants to overcome osseointegration challenges [80]. For example, bioactive glass coated on Ti6-Al-4V substrates by electrophoretic deposition and vacuum sintering show a uniform coverage and strong mechanical adhesion (≈41 ± 11 MPa tensile bond strength). This structure is suggested for use in load-bearing implants such as joint components and fixation devices as well as dental fixtures [80]. Bioactive glass coatings are widely used in dental implantation because of their biocompatibility. Co-Cr-Mo-Ti alloys modified with bioactive glass coatings show rapid osseointegration around dental implants and support soft-tissue attachment. This feature is crucial for dental applications such as implant-supported crowns and bridges [81].

These studies have shown that cobalt-chromium-based compositions with bioactive glass surface coatings enhance clinical functionality and improve biological interactions in load-bearing devices. Selected examples of orthopedic and dental implants systems are summarized in Table 1.

Table 1
Cobalt-based bioactive glasses and metallic platforms applied in orthopedic and dental implants.

Material / Scaffold	Key Features / Properties	Application / Specific Outcome	Reference
(Ag-Co-Ti) doped 58S bioactive glass coating on Ti implants	Multi-element pore-rich coating; enhanced surface nano hardness and biocompatibility; antibacterial activity	**Dental implants** Co-doped BG promotes apatite formation in vitro, antibacterial effects against P.gingivalis, improved implant surface properties	[82]
Bioactive glass coating on Co-Cr and Ti alloy substrates	Bioactive glass coatings improve bioactivity and biocompatibility of inert metal implants	**Orthopedic & dental implants** BG coatings on metallic implants enhance integration via apatite layer formation and tissue bonding	[78]
Electrophoretic 45S5 BG on oxidized Co-Cr-W alloy	Improved corrosion resistance; enhanced surface bioactivity compared with uncoated alloy	**Orthopedic & dental structural** applications: Co-Cr-W alloy coated with 45S5 BG shows better electrochemical behavior, suggesting improved implant longevity	[83]
(Sr/Co) -doped mesoporous bioactive glasses (MBGs)	Co + Sr co-doping provides pro-osteogenic ion release, potential pro-angiogenic benefit	**Bone repair & regeneration models** Co/Sr MBGs promote osteogenesis and may support bone regeneration	[84]

Table 1
Continued.

Material / Scaffold	Key Features / Properties	Application / Specific Outcome	Reference
Cu-bearing Co-Cr-W-Ni alloy	Copper incorporated into Co-Cr-W-Ni alloy matrix; sustained Cu^{2+} ion release; slight increase in corrosion current density facilitating antibacterial ion availability; surface biofilm inhibition	**Load-bearing orthopedic implants** requiring infection resistance Strong antibacterial activity against E. coli and S. aureus; antibacterial efficacy increased with Cu content; significant suppression of bacterial biofilm formation on alloy surface	[85]

7.2. Bone tissue engineering scaffolds

The main goal in bone tissue engineering is not simply structural replacement, but to provide a bioactive microenvironment for guiding cellular behavior and supporting tissue progression [86]. In this context, cobalt-based bioactive glasses systems as a multi component system, enable controlled ionic release, with adjustable degradation kinetics, which allows activation of osteogenic responses at the defect site [87].

In sol-gel mesoporous bioactive glasses (MBGs), replacement of traditional network modifiers with cobalt ion affects gene expression related to osteogenesis and angiogenesis. For instance, addition of 2-5 mol% Co to SiO_2-CaO-P_2O_5 mesoporous glass scaffolds, increased osteogenic genes expression such as ALP, angiogenic factors like VEGF, and osteocalcin in bone marrow stromal cells compared to the undoped control groups. These properties are dependent on compositional control in scaffold design and optimal Co-alloy concentration in biological responses [48].

In vivo evidence in a sheep model of bone grafting, reported that mesoporous bioactive glasses doped with Co^{2+} ions promoted bone regeneration activity, despite the cytotoxic potential of higher cobalt concentrations, localized effects of controlled ion release cause new bone formation, through synergistic osteogenic and angiogenic mechanisms [74]. Other studies show that addition of 1% Co-alloy in a 3D-printed scaffold based on BG/β-tricalcium phosphate matrices, improved osteogenic outcomes with strong cytocompatibility and proved the ability of Co^{2+} to enhance extracellular matrix deposition and osteoblast differentiation in human adipose-derived stem cells [88]. These studies have shown that cobalt-doped bioactive glass is not only osteoconductive carriers but also they are active modulators of the bone healing environment [74]. Selected examples of bone tissue engineering systems are summarized in Table 2.

Table 2
Cobalt-based bioactive glasses and metallic platforms applied in bone tissue engineering.

Material / Scaffold	Key Features / Properties	Specific Outcome	Reference
Injectable hydrogel with Co-doped BG microspheres	Homogeneous Co distribution, upregulation of COL1A1, ALPL, OCN, RUNX2, HIF1A/VEGF; improved bone and cartilage repair in calvarial rat model	Promotes angiogenesis and osteogenesis in vivo	[89]
Li-Co -doped mesoporous bioactive glass nanoparticles	Sustained release of Co^{2+} and Li^{+}, increased osteogenic and angiogenic activity, antibacterial effect against S. aureus & E. coli	Enhances osteogenesis and vascularization while providing antibacterial function	[90]
- 3wt% Cobalt-Doped Borosilicate Bioactive Glass (($36B_2O_3$, 22CaO, $18SiO_2$, 8MgO, $8K_2O$, $6Na_2O$, $2P_2O_5$; mol%) + 3wt % CoO)	Controlled Co^{2+} release, increased ALP activity and osteogenic gene expression, promoted vascular network formation	Significantly improved bone regeneration and angiogenesis in rat model after 8 weeks	[91]
Electrospun SilkMA/silicate-chlorinated cobalt-doped bioactive glass composite	High cytocompatibility with aBMSCs, strong antibacterial activity, limited calcium deposition	Biocompatible scaffold Antibacterial properties; potential bone tissue engineering application in dentistry	[50]
Borate bioactive glass co-doped with Co^{2+}, Cu^{2+}, Zn^{2+}	Melt-derived borate glass network incorporating therapeutic metallic ions; controlled multi-ion release (Co^{2+}, Cu^{2+}, Zn^{2+}); enhanced degradation rate typical of borate systems; antibacterial ion-mediated membrane disruption	Infection control capability Clear inhibition halos against Staphylococcus aureus; maintained in vitro bioactivity; potential for simultaneous angiogenic stimulation (Co^{2+}) and antibacterial protection	[92]

8. Research gaps and future perspectives

Co-based nano-bioactive glasses Offer good preclinical results, but they also face some challenges that impact their clinical applications. Ion release (especially Co^{2+}) affects the activation of signaling pathways of vascularization and osteointegration, however long-term ion release is still challenging because it could cause local cytotoxicity and long term dissolution of Si, Ca, and P ions weakens structural integrity [93].

Co-based alloys have higher elastic modulus than cortical bone, which can lead to stress shielding, peri-implant bone resorption and implant fracture under load-bearing conditions [20, 93-95].

Co-Cr alloys are considered non or low-cytotoxic under clinical conditions, but in vitro studies on cast Co-Cr-Mo implants report the measurable Co and Cr ion release from dental alloys, which could cause allergic contact dermatitis (ACD) and concentration-dependent cytotoxic and inflammatory responses in fibroblasts and osteoblasts. The systemic impact of this ion release from dental alloys on cancer development in humans continues to be challenging [33, 34].

To address these limitations, the material design and fabrication strategies should be promoted. Multi-scale structural engineering offers this potential to fabricate the scaffold from dense cores to porous surfaces which could decrease stress shielding while support localized ion release supporting angiogenesis and osteogenesis [96, 97].

Molecular-level control over composition and processing would produce scaffolds with adjustable microporosity, mesoporosity, and surface chemistries which align with the electrochemical environment of bone repair and accelerate cell proliferation and differentiation [79].

These developments on Co-based nano bioactive glasses not only restore its structural integrity but also activate genetic repair mechanisms, which could reduce the gap between allografts and autografts. Future research will need to solve the current gap between experimental innovation and practical orthopedic and dental applications [98, 99].

9. Conclusion

Cobalt-based alloy/nano bioactive glass composites are known as multi-component system which combines the mechanical strength and fatigue resistance of Co alloys with the rapid apatite formation and therapeutic ion release of bioactive glasses. This system overcomes the high modulus of cobalt alloys while supporting strength limitation of nBGs.

Co-nBGs are promising materials in load-bearing applications while promoting osteogenic, angiogenic, and antibacterial functionality. Fabrication of nBGs composite through melt-derived to sol-gel processing could bring Co into the structure to gain vascularization alongside bone repair.

These composites support biological performance with rapid HCA layer formation, bacterial inhibition against pathogens, and enhanced bone-implant contact in infection environments.

While long-term release, high elastic modulus of Co alloy and systemic impact of ion release remain challenging, emerging solutions like multi-scale structural engineering and molecular-level control of composition can be helpful.

Cobalt–nBGs composites show strong potential for future generations, establishing a new standard for next-generation load-bearing implants in orthopedic and dental applications.

Author contributions

Christine Narumbe Jore: Conceptualization, Writing – original draft, Writing – review & editing; **Mahsa Mohammadpour Beneh Khalkhal:** Writing – original draft, Writing – review & editing; **Parisa Izadi:** Writing – original draft, Writing – review & editing.

Funding

No funding was received for this study.

Conflict of interest

The authors declare no conflict of interest.

Data availability

None.

REFERENCES

[1] M.N. Rahaman, D.E. Day, B.S. Bal, Q. Fu, S.B. Jung, L.F. Bonewald, A.P. Tomsia, Bioactive glass in tissue engineering, Acta biomaterialia 7(6) (2011) 2355-2373.

[2] M.C. Garcia-Mendez, V.H. Urrutia-Baca, C.A. Cuao-Moreu, E. Lorenzo-Bonet, M. Alvarez-Vera, D.M. Ortiz-Martinez, M.A. de la Garza-Ramos, In vitro biocompatibility evaluation of a new Co-Cr-B alloy with potential biomedical application, Metals 11(8) (2021) 1267.

[3] L.L. Hench, The story of Bioglass®, Journal of materials science: materials in medicine 17(11) (2006) 967-978.

[4] A.F. Mavrogenis, P.J. Papagelopoulos, G.C. Babis, Osseointegration of cobalt-chrome alloy implants, Journal of long-term effects of medical implants 21(4) (2011).

[5] L.L. Hench, J. Wilson, Biocompatibility of silicates for medical use, Ciba Foundation Symposium 121-Silicon Biochemistry: Silicon Biochemistry: Ciba Foundation Symposium 121, Wiley Online Library, 2007, pp. 231-253.

[6] M.R. Bafandeh, R. Gharahkhani, M.H. Fathi, Characterization of fabricated cobalt-based alloy/nano bioactive glass composites, Materials Science and Engineering: C 69 (2016) 692-699.

[7] V.P.S. Sidhu, R. Borges, M. Yusuf, S. Mahmoudi, S.F. Ghorbani, M. Hosseinikia, P. Salahshour, F. Sadeghi, M. Arefian, A comprehensive review of bioactive glass: synthesis, ion substitution, application, challenges, and future perspectives, Journal of Composites and Compounds 3(9) (2021) 247-261.

[8] Q. Fu, E. Saiz, M.N. Rahaman, A.P. Tomsia, Bioactive glass scaffolds for bone tissue engineering: state of the art and future perspectives, Materials Science and Engineering: C 31(7) (2011) 1245-1256.

[9] L. Wondraczek, E. Bouchbinder, A. Ehrlicher, J.C. Mauro, R. Sajzew, M.M. Smedskjaer, Advancing the Mechanical Performance of Glasses: Perspectives and Challenges, Advanced Materials 34(14) (2022) 2109029.

[10] Q. Wang, Y. Ren, M.B. Shahzad, W. Zhang, X. Pan, S. Zhang, D. Zhang, Design and characterization of a novel nickel-free cobalt-base alloy for intravascular stents, Materials Science and Engineering: C 77 (2017) 565-571.

[11] N. Sedighi-Pirsaraei, A. Tamimi, F. Sadeghi Khamaneh, S. Dadras-Jeddi, N. Javaheri, Boron in wound healing: a comprehensive investigation of its diverse mechanisms, Frontiers in bioengineering and biotechnology 12 (2024) 1475584.

[12] M.A. Alshehri, Application of Chemically and Physically Synthesized Metal Nanoparticles to Staphylococcus aureus, Journal of Pharmaceutical Research International 34(28A) (2022) 36-59.

[13] W. Gregorowicz, L. Pajchel, The role of cobalt ions in angiogenesis—a review, International Journal of Molecular Sciences 26(15) (2025) 7236.

[14] J. Li, C. Zhao, C. Liu, Z. Wang, Z. Ling, B. Lin, B. Tan, L. Zhou, Y. Chen, D. Liu, Cobalt-doped bioceramic scaffolds fabricated by 3D printing show enhanced osteogenic and angiogenic properties for bone repair, Biomedical engineering online 20(1) (2021) 70.

[15] M.A. Hernandez-Rodriguez, D.A. Laverde-Cataño, D. Lozano, G. Martinez-Cazares, Y. Bedolla-Gil, Influence of boron addition on the microstructure and the corrosion resistance of CoCrMo alloy, Metals 9(3) (2019) 307.

[16] W. Fu, S. Liu, J. Jiao, Z. Xie, X. Huang, Y. Lu, H. Liu, S. Hu, E. Zuo, N. Kou, Wear resistance and biocompatibility of Co-Cr dental alloys fabricated with CAST and SLM techniques, Materials 15(9) (2022) 3263.

[17] J. Wilson, Metallic biomaterials: State of the art and new challenges, Fundamental Biomaterials: Metals (2018) 1-33.

[18] G. Radenković, D. Petković, Metallic biomaterials, Biomaterials in Clinical Practice: Advances in Clinical Research and Medical Devices, Springer2017, pp. 183-224.

[19] M.C. Tanzi, S. Farè, G. Candiani, Foundations of biomaterials engineering, Academic Press2019.

[20] L.H. Antunes, C.R. de Lima, Cobalt-chromium alloys–properties and applications, (2018).

[21] T. Narushima, K. Ueda, Alfirano, Co-Cr alloys as effective metallic biomaterials, Advances in metallic biomaterials: tissues, materials and biological reactions, Springer2015, pp. 157-178.

[22] S. He, Z.F. Li, X. Liu, X.M. Liu, C. Zhang, J.S. Wang, Carbide Precipitation Behavior of High-Alloy Steel During Solidification and Cooling Process, steel research international 95(8) (2024) 2400130.

[23] K. Ueki, K. Ueda, T. Narushima, Microstructure and Mechanical Properties of Heat-Treated Co-20Cr-15W-10Ni Alloy for Biomedical Application, Metallurgical and Materials Transactions A 47(6) (2016) 2773-2782.

[24] J.E. Zerwekh, M.J. Nicar, T. Shimizu, W.J. Stith, The effect of pulsed electromagnetic fields on the corrosion of a chromium-cobalt-nickel alloy orthopaedic implant, Biomaterials 7(4) (1986) 243-246.

[25] J. Schaffer, An examination of fatigue initiation mechanisms in thin 35Co-35Ni-20Cr-10Mo medical grade wires, Journal of ASTM International 5(7) (2008) JAI101567.

[26] Y.S. Al Jabbari, Physico-mechanical properties and prosthodontic applications of Co-Cr dental alloys: a review of the literature, The journal of advanced prosthodontics 6(2) (2014) 138.

[27] B.E. Nagay, J.M. Cordeiro, V.A.R. Barão, Alloy materials for biomedical applications, Alloy Materials and Their Allied Applications (2020) 159-189.

[28] C. Spicer, Chemistry of Inorganic Biomaterials, Royal Society of Chemistry2021.

[29] Z. Guo, X. Pang, Y. Yan, K. Gao, A.A. Volinsky, T.-Y. Zhang, CoCrMo alloy for orthopedic implant application enhanced corrosion and tribocorrosion properties by nitrogen ion implantation, Applied surface science 347 (2015) 23-34.

[30] H. Li, M. Wang, D. Lou, W. Xia, X. Fang, Microstructural features of biomedical cobalt–chromium–molybdenum (CoCrMo) alloy from powder bed fusion to aging heat treatment, Journal of Materials Science & Technology 45 (2020) 146-156.

[31] J. Kandasamy, S. Arulvel, P. Jeyapandiarajan, M. Murugan, R. Prayer Riju, Recent Trends and Future Prospects in Metallic Implants for Biomedical Applications, Challenges and Innovations in 3D Printed Bio-Organs and Their Materials, Springer2025, pp. 223-253.

[32] A. Bandyopadhyay, I. Mitra, S.B. Goodman, M. Kumar, S. Bose, Improving biocompatibility for next generation of metallic implants, Progress in materials science 133 (2023) 101053.

[33] A. Vaicelyte, C. Janssen, M. Le Borgne, B. Grosgogeat, Cobalt–Chromium dental alloys: Metal exposures, toxicological risks, CMR classification, and EU regulatory framework, Crystals 10(12) (2020) 1151.

[34] M.C. Lucchetti, G. Fratto, F. Valeriani, E. De Vittori, S. Giampaoli, P. Papetti, V.R. Spica, L. Manzon, Cobalt-chromium alloys in dentistry: An evaluation of metal ion release, The Journal of prosthetic dentistry 114(4) (2015) 602-608.

[35] S. Lopez-Esteban, E. Saiz, S. Fujino, T. Oku, K. Suganuma, A.P. Tomsia, Bioactive glass coatings for orthopedic metallic implants, Journal of the European Ceramic Society 23(15) (2003) 2921-2930.

[36] L.L. Hench, Genetic design of bioactive glass, Journal of the European Ceramic Society 29(7) (2009) 1257-1265.
[37] L.L. Hench, J.M. Polak, Third-generation biomedical materials, Science 295(5557) (2002) 1014-1017.
[38] N. Jafari, K. Mikeladze, Magnesium-doped 58S bioglass: synthesis, characterization, and biomedical applications, Journal of Composites and Compounds 7(22) (2025).
[39] L.L. Hench, R.J. Splinter, W. Allen, T. Greenlee, Bonding mechanisms at the interface of ceramic prosthetic materials, Journal of biomedical materials research 5(6) (1971) 117-141.
[40] Q. Hu, X. Chen, N. Zhao, Y. Li, Facile synthesis and in vitro bioactivity of monodispersed mesoporous bioactive glass sub-micron spheres, Materials Letters 106 (2013) 452-455.
[41] Q. Hu, W. Jiang, Y. Li, X. Chen, J. Liu, T. Chen, G. Miao, The effects of morphology on physicochemical properties, bioactivity and biocompatibility of micro-/nano-bioactive glasses, Advanced Powder Technology 29(8) (2018) 1812-1819.
[42] A. Sadeghian, M. Kharaziha, M. Khoroushi, Dentin extracellular matrix loaded bioactive glass/GelMA support rapid bone mineralization for potential pulp regeneration, International Journal of Biological Macromolecules 234 (2023) 123771.
[43] M.S. Shoushtari, D. Hoey, D.R.A. Biak, N. Abdullah, S. Kamarudin, H.S. Zainuddin, Sol–gel-templated bioactive glass scaffold: a review, Research on Biomedical Engineering 40(1) (2024) 281-296.
[44] M. Mačković, A. Hoppe, R. Detsch, D. Mohn, W.J. Stark, E. Spiecker, A. Boccaccini, Bioactive glass (type 45S5) nanoparticles: in vitro reactivity on nanoscale and biocompatibility, Journal of Nanoparticle Research 14(7) (2012) 966.
[45] T. Mehrabi, A.S. Mesgar, Z. Mohammadi, Bioactive glasses: a promising therapeutic ion release strategy for enhancing wound healing, ACS biomaterials science & engineering 6(10) (2020) 5399-5430.
[46] J. Ajita, S. Saravanan, N. Selvamurugan, Effect of size of bioactive glass nanoparticles on mesenchymal stem cell proliferation for dental and orthopedic applications, Materials Science and Engineering: C 53 (2015) 142-149.
[47] W. Gong, Y. Dong, S. Wang, X. Gao, X. Chen, A novel nano-sized bioactive glass stimulates osteogenesis via the MAPK pathway, RSC advances 7(23) (2017) 13760-13767.
[48] F. Baino, M. Montazerian, E. Verné, Cobalt-doped bioactive glasses for biomedical applications: a review, Materials 16(14) (2023) 4994.
[49] A.K. Solanki, F.V. Lali, H. Autefage, S. Agarwal, A. Nommeots-Nomm, A.D. Metcalfe, M.M. Stevens, J.R. Jones, Bioactive glasses and electrospun composites that release cobalt to stimulate the HIF pathway for wound healing applications, Biomaterials research 25(1) (2021) 1.
[50] J.R. de Souza, C. Anselmi, L.M. Cardoso, L.T. Kito, A.H. dos Reis-Prado, P.H. de Oliveira, R. Dal-Fabbro, M. Rahimnejad, T.M. Campos, L.T. Cintra, Electrospun SilkMA/silicate-chlorinated cobalt-doped bioactive glass composite for bone regeneration, Journal of the Mechanical Behavior of Biomedical Materials 164 (2025) 106929.
[51] I. Izquierdo-Barba, A.J. Salinas, M. Vallet-Regí, Bioactive glasses: from macro to nano, International Journal of Applied Glass Science 4(2) (2013) 149-161.
[52] L.L. Hench, J.R. Jones, Bioactive glasses: frontiers and challenges, Frontiers in bioengineering and biotechnology 3 (2015) 194.
[53] G. Kaur, G. Pickrell, N. Sriranganathan, V. Kumar, D. Homa, Review and the state of the art: sol–gel and melt quenched bioactive glasses for tissue engineering, Journal of Biomedical Materials Research Part B: Applied Biomaterials 104(6) (2016) 1248-1275.
[54] F. Niazvand, J. Hosseinzadeh, P. Zahed, N. Azizabadi, Effect of SrO incorporation on the morphology of sol-gel derived 58S bioactive glass, Journal of Composites and Compounds 7(25) (2025).
[55] R. Li, A. Clark, L. Hench, An investigation of bioactive glass powders by sol-gel processing, Journal of Applied Biomaterials 2(4) (1991) 231-239.
[56] A. El-Fiqi, H.-W. Kim, Sol-gel synthesis and characterization of novel cobalt ions-containing mesoporous bioactive glass nanospheres as hypoxia and ferroptosis-inducing nanotherapeutics, Journal of Non-Crystalline Solids 569 (2021) 120999.
[57] X. Yan, C. Yu, X. Zhou, J. Tang, D. Zhao, Highly ordered mesoporous bioactive glasses with superior in vitro bone-forming bioactivities, Angewandte Chemie-International Edition 43(44) (2004) 5980-5984.
[58] H. Danninger, R. Calderon, C. Gierl-Mayer, Powder metallurgy and sintered materials, Addit. Manuf 19(4) (2017) pp.
[59] Z. Oksiuta, J. Dabrowski, A. Olszyna, Co–Cr–Mo-based composite reinforced with bioactive glass, Journal of materials processing technology 209(2) (2009) 978-985.
[60] V. Pavkov, G. Bakić, V. Maksimović, S. Stopić, Synthesis and characterisation of metal–glass composite materials fabricated by liquid phase sintering, Materials 18(19) (2025) 4622.
[61] T. Talapaneni, V. Chaturvedi, Consolidation of Mechanically Alloyed Powders, Mechanically Alloyed Novel Materials: Processing, Applications, and Properties, Springer2024, pp. 111-169.
[62] W. Lin, C. Chen, Characteristics of thin surface layers of cobalt-based alloys deposited by laser cladding, Surface and Coatings Technology 200(14-15) (2006) 4557-4563.
[63] R. Comesaña, F. Quintero, F. Lusquiños, M. Pascual, M. Boutinguiza, A. Durán, J. Pou, Laser cladding of bioactive glass coatings, Acta biomaterialia 6(3) (2010) 953-961.
[64] P. Monson, W. Steen, Comparison of laser hardfacing with conventional processes, Surface Engineering 6(3) (1990) 185-193.
[65] A. Hirose, K.F. Kobayashi, Formation of hybrid clad layers by laser processing, ISIJ international 35(6) (1995) 757-763.
[66] R. Ciriminna, A. Fidalgo, V. Pandarus, F. Beland, L.M. Ilharco, M. Pagliaro, The sol–gel route to advanced silica-based materials and recent applications, Chemical reviews 113(8) (2013) 6592-6620.
[67] D. Wang, G.P. Bierwagen, Sol–gel coatings on metals for corrosion protection, Progress in organic coatings 64(4) (2009) 327-338.
[68] A. Zanurin, N. Johari, J. Alias, H.M. Ayu, N. Redzuan, S. Izman, Research progress of sol-gel ceramic coating: A review, Materials today: proceedings 48 (2022) 1849-1854.
[69] M. Montazerian, F. Baino, E. Fiume, C. Migneco, A. Alaghmandfard, O. Sedighi, A.V. DeCeanne, C.J. Wilkinson, J.C. Mauro, Glass-ceramics in dentistry: Fundamentals, technologies, experimental techniques, applications, and open issues, Progress in Materials Science 132 (2023) 101023.
[70] A.M. Coco, F.A. Campos, T. Martins, B.R. Barrioni, P.L. Gastelois, D.C. Soares, M. Houmard, A.R. Boccaccini, E.H. Nunes, Synthesis and evaluation of mesoporous cobalt-doped bioactive glass nanospheres loaded with curcumin, Ceramics International (2025).
[71] A.K. Khosrowshahi, A.B. Khoshfetrat, Y.B. Khosrowshahi, H. Maleki-Ghaleh, Cobalt content modulates characteristics and osteogenic properties of cobalt-containing hydroxyapatite in in-vitro milieu, Materials Today Communications 27 (2021) 102392.
[72] A. Hoppe, N.S. Güldal, A.R. Boccaccini, A review of the biological response to ionic dissolution products from bioactive glasses and glass-ceramics, Biomaterials 32(11) (2011) 2757-2774.
[73] P. Valerio, M.M. Pereira, A.M. Goes, M.F. Leite, The effect of ionic products from bioactive glass dissolution on osteoblast proliferation and collagen production, Biomaterials 25(15) (2004) 2941-2948.
[74] J. Jiménez-Holguín, D. Lozano, M. Saiz-Pardo, D. De Pablo, L. Ortega, S. Enciso, B. Fernández-Tomé, I. Díaz-Güemes, F.M. Sánchez-Margallo, M. Portolés, Osteogenic-angiogenic coupled response of cobalt-containing mesoporous bioactive glasses in vivo, Acta Biomaterialia 176 (2024) 445-457.
[75] C. Wu, J. Chang, A review of bioactive silicate ceramics, Biomedical materials 8(3) (2013) 032001.
[76] H. Mehta, G. Kaur, G.R. Chaudhary, N. Prabhakar, S. Kaul, N.K. Singhal, Evaluation of corrosion resistant, antimicrobial and cytocompatible behaviour of cobalt based metallosurfactants self-assembled monolayers on 316L stainless steel surface, Surface and Coatings Technology 444 (2022) 128657.
[77] C. Liang, N. Huang, Study on hemocompatibility and corrosion behavior of ion implanted TiNi shape memory alloy and Co-based alloys, Journal of Biomedical Materials Research Part A: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials 83(1) (2007) 235-240.
[78] N.O. Joy-anne, Y. Su, X. Lu, P.-H. Kuo, J. Du, D. Zhu, Bioactive glass coatings on metallic implants for biomedical applications, Bioactive materials 4 (2019) 261-270.
[79] P. Munyensanga, M. Bricha, K. El Mabrouk, Enhanced bioactivity and biocorrosion resistance of porous CoCrMo implants with high-silica glass coatings, Materials Today Communications 42 (2025) 111477.
[80] A. Braem, T. Mattheys, B. Neirinck, M. Čeh, S. Novak, J. Schrooten, O. Van der Biest, J. Vleugels, Bioactive glass–ceramic coated titanium implants prepared by electrophoretic deposition, Materials science and engineering: C 32(8) (2012) 2267-2273.
[81] I. Peter, M. Rosso, A. Toppi, I. Dan, B. Ghiban, Investigation on cobalt based alloy modified by titanium for dental applications, Archives of Materials Science and Engineering 61(2) (2013) 62-68.
[82] C.Y. Lung, M.M. Abdalla, C.H. Chu, I. Yin, S.-R. Got, J.P. Matinlinna, A multi-element-doped porous bioactive glass coating for implant applications, Materials 14(4) (2021) 961.
[83] Ş.M. Tüzemen, Y.B. Bozkurt, B. Atik, Y. Uzun, A. Çelik, Electrochemical Impedance Spectroscopy Analysis of 45S5 Bioglass Coating on After Oxidation of CoCrW Alloy, Türk Doğa ve Fen Dergisi (1) (2024) 82-86.
[84] F. Kermani, S. Mollazadeh Beidokhti, F. Baino, Z. Gholamzadeh-Virany, M. Mozafari, S. Kargozar, Strontium-and cobalt-doped multicomponent mesoporous bioactive glasses (MBGs) for potential use in bone tissue engineering applications, Materials 13(6) (2020) 1348.
[85] S. Wang, C. Yang, L. Ren, M. Shen, K. Yang, Study on antibacterial performance of Cu-bearing cobalt-based alloy, Materials Letters 129 (2014) 88-90.
[86] M. Ansari, Bone tissue regeneration: biology, strategies and interface studies, Progress in biomaterials 8(4) (2019) 223-237.
[87] S.S. Shendage, G. Kamble, R. Chavan, N.R. Jadav, R.-a. Doong, J.-Y. Chang, A.V. Ghule, Bioactive Glass for Bone Tissue Regeneration: Focusing on the Key Biological Properties, ACS Biomaterials Science & Engineering 12(1) (2025) 71-89.

[88] M.H. Monfared, S. Mohandesnezhad, M. Azami, S. Samani, Robocast Zn-and Co-doped bioactive glass/tricalcium phosphate scaffolds for bone regeneration, Journal of Biological Engineering 20(1) (2026) 4
[89] P. Ghiasi Tabari, A. Sattari, M. Mashhadi Keshtiban, N. Karkuki Osguei, J.G. Hardy, A. Samadikuchaksaraei, Injectable hydrogel scaffold incorporating microspheres containing cobalt-doped bioactive glass for bone healing, Journal of Biomedical Materials Research Part A 112(12) (2024) 2225-2242.
[90] X. Zhang, K. Nan, Y. Zhang, K. Song, Z. Geng, D. Shang, L. Fan, Lithium and cobalt co-doped mesoporous bioactive glass nanoparticles promote osteogenesis and angiogenesis in bone regeneration, Frontiers in Bioengineering and Biotechnology 11 (2024) 1288393.
[91] Z. Deng, B. Lin, Z. Jiang, W. Huang, J. Li, X. Zeng, H. Wang, D. Wang, Y. Zhang, Hypoxia-mimicking cobalt-doped borosilicate bioactive glass scaffolds with enhanced angiogenic and osteogenic capacity for bone regeneration, International journal of biological sciences 15(6) (2019) 1113.
[92] V.R. dos Santos, T.M.B. Campos, C. Anselmi, G.P. Thim, M.C. Bottino, A.L.S. Borges, E. de Sousa Trichês, Effect of Co, Cu, and Zn ions on the bioactivity and antibacterial properties of a borate bioactive glass, Journal of Non-Crystalline Solids 622 (2023) 122643.
[93] E. Vafa, L. Tayebi, M. Abbasi, M.J. Azizli, R. Bazargan-Lari, A. Talaiekhozani, Z. Zareshahrabadi, A. Vaez, A.M. Amani, H. Kamyab, A better roadmap for designing novel bioactive glasses: effective approaches for the development of innovative revolutionary bioglasses for future biomedical applications, Environmental Science and Pollution Research 30(55) (2023) 116960-116983.
[94] L. Wang, J. Kang, C. Sun, D. Li, Y. Cao, Z. Jin, Mapping porous microstructures to yield desired mechanical properties for application in 3D printed bone scaffolds and orthopaedic implants, Materials & Design 133 (2017) 62-68.
[95] K. Chen, X.-k. He, Z.-d. Liu, Y. Zheng, J. Ma, Effect of cooling rate on dendritic segregation and solidification structure of a Ni–Cr–Co–Mo based alloy, Journal of Iron and Steel Research International 32(10) (2025) 3555-3572.
[96] A.C. Marsh, N.P. Mellott, N. Pajares-Chamorro, M. Crimp, A. Wren, N.D. Hammer, X. Chatzistavrou, Fabrication and multiscale characterization of 3D silver containing bioactive glass-ceramic scaffolds, Bioactive Materials 4 (2019) 215-223.
[97] R. Fan, E. Guo, L. Wang, L. Wang, S. Zhao, X. Li, X. Zhang, B. Cui, Multi-scale microstructure strengthening strategy in CoCrFeNiNb0. 1Mo0. 3 high entropy alloy overcoming strength-ductility trade-off, Materials Science and Engineering: A 882 (2023) 145446.
[98] J. Jones, L. Hench, Biomedical materials for new millennium: perspective on the future, Materials Science and technology 17(8) (2001) 891-900.
[99] A.-L. Mîrț, D. Ficai, O.-C. Oprea, G. Vasilievici, A. Ficai, Current and future perspectives of bioactive glasses as injectable material, Nanomaterials 14(14) (2024) 1196.