

Metal Oxide Doped Calcium Silicate Material Having Biomedical Application

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Abstract

Calcium silicate material has immense bio-medicinal potential for their remarkable osteogenic properties, biocompatibility and bioactivity led to a further enhancement in their functionality and a wider range of potential applications. Investigating recent advancements in metal oxide doped calcium silicate materials for use in biomedical applications is the aim of this comprehensive research. This article discusses the production processes and characterization techniques. This review also provides insights that are helpful for both researchers and physicians by discussing the challenges that are now being encountered as well as possible future advances in this rapidly evolving sector.

Keywords: Calcium silicate; Metal oxide doping; Biomedical applications; Bone tissue engineering; Drug delivery; Dental materials; Antibacterial properties

1. INTRODUCTION

The growing need for advanced materials in medical applications advancements in the field of biomaterials during the last several years. Calcium silicate-based biomaterials have become attractive choices among the wide range of biomaterials [1]. These materials have found numerous uses in the realm of biomedicine, including antimicrobial coatings [2, 3].

Materials made of calcium silicates are used in biomedical applications. The main components of these materials are silicon dioxide and calcium oxide [4]. They are able to form a covering of bioactive hydroxyapatite when exposed to physiological fluids, which strengthens their interaction with bone tissue. Moreover, the byproducts of their disintegration, such as calcium and silicate ions, are important in their capacity to promote osteoblast differentiation and proliferation, which in turn raises bone synthesis [5].

Despite these advantageous properties, pure calcium silicate materials have certain limitations, such as relatively low mechanical strength and inadequate biological performance for some specific applications [6]. To overcome these limitations and further enhance their properties, researchers have explored the strategy of doping calcium silicates with various metal oxides [7]. Metal oxide doping has proven calcium silicate materials, expanding their potential in biomedical applications [8].

We will discuss the various synthesis methods, characterization techniques,. Furthermore, we will explore the wide range of biomedical applications, highlighting the key findings and potential future directions in this rapidly evolving field.

2. Synthesis Methods for Metal Oxide Doped Calcium Silicate Materials

The process of producing calcium silicate materials doped with metal oxide ultimate characteristics and functionality of these materials in the context of biomedical applications. Many of these materials, and each has advantages and disadvantages of its own. This section of the essay will discuss the most common synthesis techniques and how they affect the materials that are generated.

2.1 Sol-Gel Method

One of the most often utilized processes for synthesizing metal oxide doped calcium silicate materials is the sol-gel high-purity products with controlled composition and microstructure [9]. This is a result of the approach's adaptability. In this approach, the development of a gel network comes after the formation of a colloidal solution (sol) [10] inorganic salts are necessary for this approach.

Precursors such tetraethyl orthosilicate (TEOS) for silicon, calcium nitrate for calcium, and suitable metal salts or alkoxides for the dopants are combined in a solvent (typically ethanol or water) in a conventional

sol-gel synthesis of metal oxide doped calcium silicate materials [11]. Precursors and dopants are combined to complete this procedure. Several factors, such as pH, temperature, and the ratio of water to precursors, are taken into account to control the hydrolysis and condensation reactions [12].

Metal oxide doped calcium silicate compounds, such as the following:

In terms of dopants, uniform distribution The uniform distribution of metal oxide dopants throughout the calcium silicate matrix is ensured by the molecular mixing of precursors [13].

Processing using low heat in conjunction with: The sol-gel technique is beneficial for the integration of bioactive chemicals or thermally sensitive dopants because it allows materials to be synthesised at relatively low temperatures [14].

Control the material's porosity and surface area: The porosity and surface area of the finished materials can be tailored by modifying the synthesis parameters, which is important for applications like tissue engineering and drug delivery [15]. Adaptability across product formats: Powders, fibres, coatings, and monoliths are just a few of the materials that may be created using the sol-gel process [16].

However, Some precursors and the potential for residual organic components to remain in the final product [17].

2.2 Hydrothermal Method

It is another popular synthesizing metal oxide doped calcium silicate material, especially when crystalline products are desired [18]. This method involves the crystallization of substances from aqueous solutions at elevated temperatures and pressures, typically in a sealed autoclave [19].

In a typical hydrothermal synthesis, precursor materials (e.g., calcium hydroxide, silica, and metal oxide dopants) are mixed with water and placed in a Teflon-lined autoclave [20]. The reaction mixture is then heated for several hours or days, depending on the desired product characteristics [21].

The hydrothermal method offers several advantages for the synthesis of metal oxide doped calcium silicate materials:

1. **Enhanced crystallinity:** The high-temperature and high-pressure conditions promote the formation of well-crystallized products [22].
2. **Control over particle size and morphology:** By adjusting the synthesis parameters (temperature, pressure, pH, and reaction time), it is possible to control the size and shape of the resulting particles [23].
3. **Environmentally friendly:** The hydrothermal method often uses water as the reaction medium, making it a relatively green synthesis approach [24].
4. **One-step synthesis:** Complex compositions can often be synthesized in a single step, reducing the need for multiple processing stages [25].

However, the hydrothermal method also has some limitations, such as the need for specialized equipment (autoclaves) and the potential for inhomogeneous product distribution due to temperature gradients within the reaction vessel [26].

2.3 Solid-State Reaction Method

It is synthesizing metal oxide doped calcium silicate materials, particularly when high-temperature phases are desired [27]. This method involves the direct reaction of solid precursors at elevated temperatures, typically above 1000°C [28].

In a typical solid-state synthesis, stoichiometric amounts of calcium oxide (or calcium carbonate), silica, and metal oxide dopants are thoroughly mixed and ground together [29]. The mixture is then pressed into pellets and heated at high temperatures for several hours or days, often with intermediate grinding and re-pressing steps to ensure complete reaction [30].

The solid-state reaction method offers several advantages:

1. **Simplicity:** The method is straightforward and does not require complex equipment or procedures [31].
2. **Scalability:** Solid-state reactions can be easily scaled up for large-scale production [32].
3. **High-temperature phases:** This method is particularly suitable for synthesizing high-temperature phases that may be difficult to obtain through other techniques [33].

However, the solid-state reaction method also has some limitations:

1. **High energy consumption:** The high temperatures required for solid-state reactions result in significant energy consumption [34].
2. **Inhomogeneity:** Achieving a homogeneous distribution of dopants can be challenging, especially for low dopant concentrations [35].

3. Limited control over particle size and morphology: The high-temperature processing often results in large, irregularly shaped particles [36].

2.4 Precipitation Method

For the manufacture of metal oxide doped calcium silicate materials, the precipitation process offers a simple and affordable method, especially when fine particles are required [37]. This method makes use of the precipitation of calcium, silicon, and dopant ions from aqueous solutions [38].

Aqueous solutions containing calcium ions (calcium nitrate, for example), silicate ions (sodium silicate, for example), and dopant ions are combined in a precipitation synthesis under controlled pH and temperature settings [39]. The final product is then obtained by filtering, washing, and drying the precipitate that is formed [40].

The precipitation process offers several advantages in the production of metal oxide doped calcium silicate compounds, such as the following:

1. **Low-temperature processing:** The precipitation method can be carried out making it suitable for incorporating temperature-sensitive dopants [41].
2. **Fine particle size:** This method typically produces fine particles [42].
3. **Homogeneous dopant distribution:** The co-precipitation of all ions ensures a uniform distribution of dopants within the calcium silicate matrix [43].
4. **Cost-effectiveness:** The precipitation method often uses inexpensive precursors and does not require specialized equipment [44].

However, the precipitation method also has some limitations:

1. **Amorphous products:** The precipitated products are often amorphous and may require additional heat treatment to achieve crystallinity [45].
2. **Impurities:** The final product may contain impurities from the precursor solutions, necessitating thorough washing steps [46].
3. **Limited control over particle morphology:** Achieving specific particle shapes can be challenging with the precipitation method [47].

2.5 Comparison of Synthesis Methods

To provide a clear overview of the different synthesis methods discussed, we present a comparative table highlighting the key features, advantages, and limitations of each method.

Table 1: Comparison of synthesis methods for metal oxide doped calcium silicate materials.

Method	Key Features	Advantages	Limitations
Sol-Gel	Molecular-level mixing Low-temperature processing Versatile product formation	Homogeneous dopant distribution Control over porosity and surface area Suitable for thermally sensitive dopants	High cost of some precursors Potential residual organics Complex process control
Hydrothermal	High temperature and pressure conditions Aqueous medium Crystalline products	Enhanced crystallinity Control over particle size and morphology Environmentally friendly	Requires specialized equipments Potential homogeneity due to temperature gradients Limited Scalability

Solid-State Reaction	High temperature processing Direct reaction of solid precursors Simple procedure	Simplicity Scalability Suitable for high temperature phases	High energy consumption In homogeneous dopant distribution Limited control over particle characteristics
Precipitation	Room temperature or low temperature processing Aqueous medium Fine particle production	Low temperature processing Fine particle size Homogeneous dopant distribution Cost-effectiveness	Often produces amorphous products Potential impurities Limited control over particle morphology

For the specific requirements of the intended biomedical application. Researchers often combine or modify these methods to achieve optimal results for their specific needs.

3. Characterization Techniques for Metal Oxide Doped Calcium Silicate Materials

Proper characterization of metal oxide doped calcium silicate materials is crucial for understanding their properties and evaluating their potential for biomedical applications. A wide range of analytical techniques is employed. we will discuss the most commonly used characterization techniques and their significance in the context of metal oxide doped calcium silicate materials.

3.1 X-ray Diffraction (XRD)

XRD fundamental analyzing structure and phase composition of metal oxide doped calcium silicate materials [48]. XRD provides information about:

1. Crystal structure and lattice parameters
2. Phase identification and quantification

Metal oxide doped calcium silicates, XRD is particularly useful for:

- Confirming the formation of desired calcium silicate phases (e.g., β -Ca₂SiO₄, Ca₃SiO₅)
- Detecting the presence of secondary phases or unreacted precursors
- Investigating the incorporation of dopants into the calcium silicate lattice
- Monitoring phase transformations during heat treatment or in vitro testing

3.2 Fourier Transform Infrared Spectroscopy (FTIR)[49].

It provides information about:

1. Chemical bonds and functional groups
2. Structural changes due to doping
3. Surface hydroxyl groups and adsorbed species

For metal oxide doped calcium silicates, FTIR is particularly useful for:

- Identifying characteristic Si-O, Ca-O, and M-O (M = dopant metal) vibrations
- Detecting the formation of silanol (Si-OH) groups on the material surface
- Monitoring hydroxyapatite during bioactivity testing
- Investigating drugs, proteins

3.3 Scanning Electron Microscopy (SEM) and Energy Dispersive X-ray Spectroscopy (EDS)

It is coupled with EDS is a powerful technique of metal oxide doped calcium silicate materials [50]. This technique provides information about:

1. Particle size and morphology
2. Surface topography and porosity
3. Elemental composition and distribution

For metal oxide doped calcium silicates, SEM-EDS is particularly useful for:

- Investigating the formation of surface features (e.g., pores, crystals) during processing or in vitro testing
- Confirming the presence and distribution of dopant elements within the material
- Analyzing the elemental composition of specific regions or features

3.4 Transmission Electron Microscopy (TEM)

TEM provides information about internal structure of metal oxide doped calcium silicate materials [51].

1. Crystal structure and lattice defects
2. Particle size and shape at the nanoscale
3. Elemental mapping with high spatial resolution

For metal oxide doped calcium silicates, TEM is particularly useful for:

- Investigating the nanostructure and crystallinity of the materials
- Analyzing the distribution of dopants within individual particles
- Studying hydroxyapatite nanoscale
- Examining the material and biological entities (e.g., cells, proteins)

3.5 X-ray Photoelectron Spectroscopy (XPS) [52].

XPS offers insights into:

1. Surface elemental composition
2. Chemical state of elements
3. Depth profiling of composition

For metal oxide doped calcium silicates

- Analyzing the surface composition and oxidation states of dopant elements
- Investigating changes in surface chemistry during in vitro testing or cell interactions
- Studying the formation of calcium phosphate layers during bioactivity testing
- Examining the adsorption of biomolecules on the material surface

3.6 Brunauer-Emmett-Teller (BET) Surface Area Analysis

Metal oxide doped calcium silicate materials technique [53]:

1. Specific surface area Pore size distribution
2. Total pore volume
3. Surface texture

For metal oxide doped calcium silicates, BET analysis is particularly useful for:

- Evaluating the effect of dopants on the surface area and porosity of the materials
- Assessing the suitability of materials for drug delivery applications
- Investigating changes in surface characteristics during in vitro degradation
- Correlating surface properties with biological performance (e.g., protein adsorption, cell attachment)

3.7 Thermogravimetric Analysis (TGA) and Differential Scanning Calorimetry (DSC)

TGA and DSC are thermal analysis techniques used to study the thermal behavior and phase transitions of metal oxide doped calcium silicate materials [54]. These techniques provide information about:

1. Thermal stability
2. Phase transitions
3. Decomposition temperatures
4. Heat capacity and enthalpy changes

For metal oxide doped calcium silicates, TGA and DSC are particularly useful for:

- Investigating the influence of dopants on the thermal stability of calcium silicates
- Studying the decomposition of precursors during material synthesis
- Analyzing the formation and transformation of different calcium silicate phases
- Assessing the presence of residual organic components or adsorbed water

3.8 Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES)

It is quantitative elemental metal oxide doped calcium silicate materials [55]. This technique provides information about:

1. Elemental composition
2. Trace element analysis
3. Ion release kinetics

For metal oxide doped calcium silicates, ICP-OES is particularly useful for:

- Determining the exact composition of synthesized materials
- Quantifying dopant elements calcium silicate matrix
- Studying the release kinetics of various ions (Ca, Si, dopants) during in vitro degradation
- Assessing the uptake of elements by cells during biological testing

Table 2: Summary of characterization techniques for metal oxide doped calcium silicate materials.

Technique	Key Information	Relevance to Metal Oxide Doped Calcium Silicates
XRD	Crystal structure, phase composition	Phase identification, dopant incorporation, crystallinity
FTIR	Chemical bonding, functional groups	Surface chemistry, bioactivity, molecular interactions
SEM-EDS	Morphology, elemental composition	Particle characteristics, dopant distribution
TEM	High-resolution structure, nanostructure	Nanostructure, dopant distribution at nanoscale
XPS	Surface composition, chemical states	Surface chemistry, oxidation states of dopants
BET	Surface area, porosity	Drug delivery potential, degradation behavior
TGA/DSC	Thermal behavior, phase transitions	Thermal stability, phase transformations
ICP-OES	Elemental composition, ion release	Composition verification, ion release kinetics

The combination of these of the physicochemical properties of metal oxide doped calcium silicate materials, which is essential for optimizing their performance in various biomedical applications.

4. Influence of Metal Oxide Dopants on Calcium Silicate Properties

The incorporation of metal oxide dopants into calcium silicate materials can significantly alter their physicochemical and biological properties. This section calcium silicates relevant to biomedical applications.

4.1 Magnesium Oxide (MgO) Doping .

Effects of MgO doping on calcium silicate properties:[56]

1. Mechanical properties: MgO doping generally improves the compressive strength and hardness of calcium silicates by promoting densification and reducing porosity [57].
2. Bioactivity: Low levels of MgO doping (< 5 wt%) can enhance the bioactivity of calcium silicates by promoting the formation of a bone-like apatite layer. However, higher concentrations may inhibit apatite formation [58].
3. Degradation rate: MgO doping typically increases the degradation rate of calcium silicates, which can be beneficial for controlled release of therapeutic ions and scaffold resorption [59].
4. Cell response: Mg²⁺ ions released from doped calcium silicates have been shown to promote osteoblast proliferation and differentiation, enhancing bone formation [60].

4.2 Zinc Oxide (ZnO) Doping

Zinc in bone metabolism widely studied as a dopant in calcium silicate materials [61].

Effects of ZnO doping on calcium silicate properties:

1. Antibacterial properties: ZnO doping imparts strong antibacterial properties to calcium silicates, which is particularly useful for preventing implant-associated infections [62].
2. Osteogenic activity: Zn²⁺ ions released from doped calcium silicates stimulate osteoblast proliferation and differentiation, promoting bone formation [63].

3. Mechanical properties: ZnO doping can improve the compressive strength and fracture toughness of calcium silicates, especially at low concentrations (< 3 wt%) [64].

4. Degradation rate: ZnO doping generally decreases the degradation rate of calcium silicates, which can be advantageous for long-term implant stability [65].

4.3 Strontium Oxide (SrO) Doping

Strontium has gained significant attention as a dopant in calcium silicate materials [66].

Effects of SrO doping on calcium silicate properties:

1. Osteogenic and anti-osteoclastic activity: Sr^{2+} ions released from doped calcium silicates stimulate osteoblast activity while inhibiting osteoclast function, leading to enhanced bone formation [67].

2. Bioactivity: SrO doping can improve the bioactivity of calcium silicates by promoting the formation of a Sr-substituted hydroxyapatite layer [68].

3. Mechanical properties: Low levels of SrO doping (< 5 wt%) can enhance the compressive strength and elastic modulus of calcium silicates [69].

4. Radiopacity: SrO doping increases the radiopacity of calcium silicate materials, improving their visibility in X-ray imaging [70].

4.4 Copper Oxide (CuO) Doping

Copper has been investigated as a dopant in calcium silicate materials primarily for its angiogenic and antibacterial properties [71].

Effects of CuO doping on calcium silicate properties:

1. Angiogenic activity: Cu^{2+} ions released from doped calcium silicates stimulate the formation of new blood vessels, which is crucial for bone regeneration [72].

2. Antibacterial properties: CuO doping imparts antibacterial properties to calcium silicates, helping to prevent implant-associated infections [73].

3. Osteogenic activity: Low concentrations of Cu^{2+} ions have been shown to promote osteoblast proliferation and differentiation [74].

4. Mechanical properties: CuO doping can improve the compressive strength of calcium silicates, especially at low concentrations (< 2 wt%) [75].

4.5 Iron Oxide (Fe_2O_3) Doping

Iron oxide doping has been explored in calcium silicate materials for its potential to impart magnetic properties and enhance osteogenic activity [76].

Effects of Fe_2O_3 doping on calcium silicate properties:

1. Magnetic properties: Fe_2O_3 doping can impart magnetic properties to calcium silicates, allowing for potential applications in magnetic-guided drug delivery and hyperthermia treatment [77].

2. Osteogenic activity: Fe^{3+} ions released from doped calcium silicates have been shown to promote osteoblast proliferation and differentiation [78].

3. Mechanical properties: Fe_2O_3 doping can improve the compressive strength and fracture toughness of calcium silicates [79].

4. Degradation rate: Fe_2O_3 doping generally decreases the degradation rate of calcium silicates, which can be advantageous for long-term implant stability [80].

4.6 Multi-element Doping

The co-doping of calcium silicates with multiple metal oxides to achieve synergistic effects and tailor the material properties for specific applications [81].

Effects of multi-element doping on calcium silicate properties:

1. Enhanced biological performance: Co-doping with elements like Mg, Zn, and Sr can lead to improved osteogenic activity, antibacterial properties, and overall biological performance [82].

2. Tailored degradation rates: Combining dopants with different effects on degradation (e.g., Mg and Zn) allows for fine-tuning of the material's resorption rate [83].

3. Optimized mechanical properties: Multi-element doping can help achieve a balance between strength, toughness, and elasticity to match the properties of natural bone [84].

4. Multifunctional materials: Co-doping enables the development of multifunctional materials that combine properties such as osteogenesis, angiogenesis, and antibacterial activity [85].

Table 3: Summary of the effects of metal oxide dopants on calcium silicate properties.

Dopant	Mechanical Properties	Bioactivity	Degradation Rate	Biological Effect	Other Properties
M (Magnesium)	↑ Strength Hardness ↑	Low Conc. ↑ ↓ High Conc.	(Increase) ↑	Osteogenesis ↑	
Z (Zinc)	Strength ↑	(No Significant Change)	(Decrease) ↓	↑ Osteogenesis Antibacterial ↑	
Sr (Strontium)	↑ Strength Modulus ↑	(Increase) ↑	(No Significant Change)	↑ Osteogenesis Osteoclast activity ↓	Radiopacity ↑
Cu (Copper)	↑ Strength	(No Significant Change)	(No Significant Change)	Angiogenesis ↑ ↑ Antibacterial	
Fe (Iron)	↑ Strength Toughness ↑	(No Significant Change)	↓ (Decrease)	↑ Osteogenesis	Magnetic Properties

↑: Increase, ↓: Decrease, ↔: No significant change or variable effect

The choice of dopant(s) and their concentration(s) should be carefully considered various metal oxide dopants on calcium silicate properties, researchers can design and optimize

5. Biomedical Applications of Metal Oxide Doped Calcium Silicate Materials

Metal oxide doped calcium silicate materials have tailored for specific requirements. This section explores the major biomedical applications of these materials, highlighting key research findings and potential future directions.

5.1 Bone Tissue Engineering

Prominent applications of metal oxide doped calcium silicate materials. These materials serve as scaffolds to support bone regeneration and repair [86].

Key applications and findings:

1. Porous scaffolds: Metal oxide doped calcium silicate scaffolds with controlled porosity and interconnected pore structures [87].
2. Composite scaffolds: Combinations of metal oxide doped calcium silicates with biodegradable polymers (e.g., polycaprolactone, poly(lactic-co-glycolic acid)) have been explored to improve the mechanical properties and degradation behavior of scaffolds [88].

3. 3D-printed scaffolds: Advanced manufacturing techniques employed to create patient-specific scaffolds with precise geometries and controlled internal structures [89].

4. Growth factor delivery: Metal oxide doped calcium silicate scaffolds have been used as carriers for bone regeneration [90].

5. Cell-laden constructs: Pre-seeding of metal oxide doped calcium silicate scaffolds with stem cells or osteoblasts has shown promise in accelerating bone formation in vivo [91].

Table 4: Examples of metal oxide doped calcium silicate materials for bone tissue engineering.

Dopant(s)	Material Form	Key Findings	Reference
Mg, Zn	Porous scaffold	Enhanced osteogenesis and angiogenesis	[92]
Sr	3D-printed scaffold	Improved mechanical properties and bone formation	[93]
Cu	Composite scaffold	Antibacterial activity and stimulated vascularization	[94]
Fe	Magnetic scaffold	Magnetic-responsive drug delivery and enhanced osteogenesis	[95]

5.2 Drug Delivery Systems

The unique properties of metal oxide doped calcium silicate materials, drug delivery applications [96].

Key applications and findings:

1. Antibiotic delivery: Metal oxide doped calcium silicate materials have been used as carriers for antibiotics to treat bone infections, providing sustained release and local high concentrations of drugs [97].

2. Anti-cancer drug delivery: These materials have shown potential in delivering anti-cancer drugs for bone cancer treatment, combining the benefits of local drug delivery with osteogenic properties [98].

3. Growth factor delivery: Controlled from metal oxide doped calcium silicates has been explored to enhance bone regeneration and vascularization [99].

4. Multi-drug delivery systems: Co-delivery of multiple therapeutic agents (e.g., antibiotics and growth factors) has been achieved using metal oxide doped calcium silicate carriers [100].

5. Stimuli-responsive drug delivery: Incorporation of magnetic (Fe_3O_4) or thermosensitive elements into calcium silicate materials has enabled the development of stimuli-responsive drug delivery systems [101].

Table 5: Examples of metal oxide doped calcium silicate materials for drug delivery.

Dopant(s)	Drug(s)	Key Findings	Reference
Zn	Vancomycin	Sustained antibiotic release and enhanced osteogenesis	[102]
Sr	Doxorubicin	Controlled release for bone cancer treatment	[103]
Cu	VEGF	Angiogenic factor delivery and antibacterial properties	[104]
Fe	BMP-2	Magnetic-responsive growth factor delivery	[105]

5.3 Dental Materials

Metal oxide doped calcium silicate materials have gained significant attention in dentistry, particularly for endodontic applications and dental cement formulations [106].

Key applications and findings:

1. Root canal sealers: Metal oxide doped calcium silicate-based sealers have shown excellent sealing ability, biocompatibility, and potential for promoting tooth regeneration [107].
2. Bone grafting materials: Metal oxide doped calcium silicates have been explored as bone grafting materials for periodontal and maxillofacial applications [109].
3. Dental implant coatings: Coatings based on metal oxide doped calcium silicates have been developed to enhance osseointegration of dental implants [110].
4. Remineralizing agents: Incorporation of these materials into toothpastes and mouthwashes has been investigated for their potential to promote enamel and dentin remineralization [111].

Table 6: Examples of metal oxide doped calcium silicate materials for dental applications.

Dopant(s)	Application	Key Findings	Reference
Zn, Cu	Root canal sealer	Enhanced antibacterial properties and bioactivity	[112]
Sr	Pulp capping material	Improved reparative dentin formation	[113]
Mg	Bone grafting material	Accelerated bone regeneration in periodontal defects	[114]
Fe	Dental implant coating	Improved osseointegration and antibacterial properties	[115]

5.4 Antibacterial Coatings

The incorporation of metal oxide dopants with antibacterial properties (e.g., Zn, Cu, Ag) into calcium silicate materials has led to the development of effective antibacterial coatings for various biomedical applications [116].

Key applications and findings:

1. Orthopedic implant coatings: Metal oxide doped calcium silicate coatings on orthopedic implants have shown the ability to prevent implant-associated infections while promoting osseointegration [117].
2. Wound dressings: These materials have been explored as components of advanced wound dressings, providing antibacterial protection and promoting wound healing [118].
3. Catheters and medical devices: Coatings based on metal oxide doped calcium silicates have been developed to reduce catheter-associated infections and biofilm formation on medical devices [119].
4. Dental materials: Antibacterial coatings have been applied to dental implants, orthodontic appliances, and restorative materials to prevent oral infections and improve long-term outcomes [120].
5. Tissue engineering scaffolds: Incorporation of antibacterial metal oxide dopants into calcium silicate scaffolds has enabled the development of infection-resistant tissue engineering constructs [121].

Table 7: Examples of metal oxide doped calcium silicate materials for antibacterial coatings.

Dopant(s)	Application	Key Findings	Reference
Zn, Cu	Orthopedic implant coating	Dual antibacterial and osteogenic effects	[122]
Ag	Wound dressing	Sustained antibacterial activity and enhanced healing	[123]

Cu, Fe	Catheter coating	Reduced biofilm formation and long-term effectiveness	[124]
Zn, Mg	Dental implant coating	Improved osseointegration and antibacterial properties	[125]

5.5 Bioactive Glass and Glass-Ceramics

Metal oxide doped calcium silicate-based emerged as promising materials for various biomedical excellent bioactivity and tailorable properties [126].

Key applications and findings:

1. Bone grafts: Metal oxide doped bioactive glasses have been used as synthetic bone graft materials, promoting rapid bone bonding and regeneration [127].
2. Soft tissue engineering: These materials have shown potential in soft tissue applications, such as wound healing and nerve regeneration, due to their ability to release therapeutic ions [128].
3. Cancer treatment: Some compositions of metal oxide doped bioactive glasses have demonstrated selective cytotoxicity towards cancer cells, opening up possibilities for cancer therapy [129].
4. Dental applications: Bioactive glass-ceramics have been used in dental restorations, endodontic sealers, and remineralizing agents for enamel and dentin [130].
5. Drug delivery: The high surface area and controlled degradation of these materials make them suitable carriers for various therapeutic agents [131].

Table 8: Examples of metal oxide doped calcium silicate-based bioactive glasses and glass-ceramics.

Dopant(s)	Application	Key Findings	Reference
Sr, Mg	Bone graft substitute	Enhanced osteogenesis and angiogenesis	[132]
Cu, Zn	Wound healing	Antibacterial activity and stimulated soft tissue regeneration	[133]
Ce	Cancer therapy	Selective cytotoxicity towards osteosarcoma cells	[134]
F, Sr	Dental restoration	Improved mechanical properties and remineralization potential	[135]

5.6 Theranostic Applications

The combination of therapeutic and diagnostic functionalities in metal oxide doped theranostic platforms for various biomedical applications [136].

Key applications and findings:

1. Magnetic resonance imaging (MRI): Incorporation of magnetic elements (e.g., Fe, Gd) into calcium silicate materials enables their use as MRI contrast agents while maintaining therapeutic functions [137].
2. Photodynamic therapy: Doping with elements like Ce or Eu has been explored to create materials capable of photodynamic therapy for cancer treatment [138].
3. Hyperthermia treatment: Magnetic metal oxide doped calcium silicates have shown potential for localized hyperthermia treatment of cancer [139].
4. Drug delivery monitoring: The incorporation of fluorescent or radiopaque elements allows for real-time monitoring of drug delivery and material degradation [140].
5. Multimodal imaging: Combination of multiple imaging modalities (e.g., MRI, CT, optical imaging) has been achieved through careful selection of dopants [141].

Table 9: Examples of metal oxide doped calcium silicate materials for theranostic applications.

Table 9: Examples of metal oxide doped calcium silicate materials for theranostic applications.

Dopant(s)	Application	Key Findings	Reference
Fe, Gd	MRI-guided drug delivery	Enhanced contrast and targeted drug release	[142]
Ce	Photodynamic therapy	ROS generation and cancer cell apoptosis	[143]
Fe ₃ O ₄	Hyperthermia treatment	Magnetic-induced heating and controlled drug release	[144]
Eu	Fluorescence imaging	Real-time monitoring of scaffold degradation	[145]

6. Challenges and Future Perspectives

Metal oxide doped calcium silicate materials for biomedical applications, several challenges remain to be addressed. This section discusses the current limitations and future research directions in this field.

6.1 Current Challenges

1. Mechanical properties: Toughness, and degradation rate remains a challenge, particularly for load-bearing applications [146].
2. Controlled ion release: Fine-tuning the release kinetics of therapeutic ions from metal oxide doped calcium silicates to match the physiological requirements of different tissues and healing stages is complex [147].
3. Long-term in vivo performance: More extensive long-term in vivo studies are needed to fully understand the degradation behavior, ion release, and tissue response to these materials over extended periods [148].
4. Scalability and manufacturing: Translating laboratory-scale synthesis methods to large-scale, reproducible manufacturing processes while maintaining material quality and performance is challenging [149].
5. Regulatory approval: The complex composition and multifunctional nature of metal oxide doped calcium silicate materials can complicate the regulatory approval process for clinical applications [150].

6.2 Future Research Directions

1. Advanced manufacturing techniques: Further exploration of 3D printing, electrospinning, and other advanced manufacturing techniques to create complex, patient-specific structures with optimized properties [151].
2. Smart and stimuli-responsive materials: Development of metal oxide doped calcium silicate magnetic fields for controlled drug release and tissue regeneration [152].
3. Biomimetic approaches: Integration of biological molecules (e.g., peptides, growth factors) and cell-derived components into metal oxide doped calcium silicates to create more biomimetic materials [153].
4. Multifunctional nanocomposites: Combining metal oxide doped calcium silicates with other nanomaterials (e.g., graphene, carbon nanotubes) to create multifunctional nanocomposites with enhanced properties [154].
5. Personalized medicine: Tailoring the composition and properties of metal oxide doped calcium silicate materials based on patient-specific factors (e.g., age, gender, health condition) for optimized therapeutic outcomes [155].
6. In situ real-time monitoring: Development of advanced imaging and sensing techniques for non-invasive, real-time monitoring of material degradation, ion release, and tissue regeneration in vivo [156].
7. Computational modeling: Utilization of advanced computational modeling and machine learning approaches to predict and optimize the properties and performance of metal oxide doped calcium silicate materials [157].
8. Synergistic combinations: Exploration of novel combinations of metal oxide dopants to achieve synergistic effects and multifunctional properties tailored for specific biomedical applications [158].
9. Bioactive glasses work in a number of ways to provide hemostatic effects. Their capacity to initiate the coagulation cascade, which results in the production of blood clots, is one important mechanism that has been documented. This activation is enabled by the bioactive glass composition's inclusion of ions such as

Ca²⁺ (clotting factor IV). These ions cause the clotting process and aid in hemostasis by interacting with blood proteins[159].

Table 10: Summary of challenges and future research directions for metal oxide doped calcium silicate materials.

Challenges	Future Research Directions
Mechanical properties optimization	Advanced manufacturing techniques
Controlled ion release	Smart and stimuli-responsive materials
Long-term in vivo performance	Biomimetic approaches
Scalability and manufacturing	Multifunctional nanocomposites
Regulatory approval	Personalized medicine

7. CONCLUSION

Doped calcium silicate materials with metal oxide have emerged as a potential class of biomaterials with multiple, dentistry, antibacterial coatings, and theranostics. There are numerous applications for these materials that could be pursued. Calcium silicates' physicochemical and biological characteristics can be customised. This makes it possible for the substance to satisfy the particular needs of a variety of biomedical applications.

This review has highlighted the most important advancements impact of various metal oxide dopants on important properties such the material's mechanical strength, bioactivity, rate of degradation, and biological response has been discussed in detail. These materials' adaptability and potential value are demonstrated by the vast range of applications they have found in the field of biomedicine. These applications include theranostic platforms, improved medication delivery methods, and scaffolds for bone regeneration.

However, challenges have to be addressed with regard to enhancing mechanical properties, managing ion release kinetics, and converting laboratory findings into therapeutic use. Future research directions have a lot of promise for addressing these issues and improving the properties of metal oxide-doped calcium silicate materials. These directions include the creation of stimuli-responsive intelligent materials, the advancement of advanced manufacturing methods, and the use of tailored strategies.

Collaboration across academic boundaries will be essential for materials scientists, bioengineers, clinicians, and regulatory professionals to fully realise the potential of these materials in enhancing healthcare outcomes. As the field develops further, this will remain the case. In the future of biomedicine, materials consisting of metal oxide-doped calcium silicate are expected to become more significant. These materials provide unique approaches to drug delivery, tissue regeneration, and theranostic uses. This can be attributed to the ongoing completion of research and development-related activities.

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