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Review

Baghdadite: A Novel and Promising Calcium Silicate in Regenerative Dentistry and Medicine

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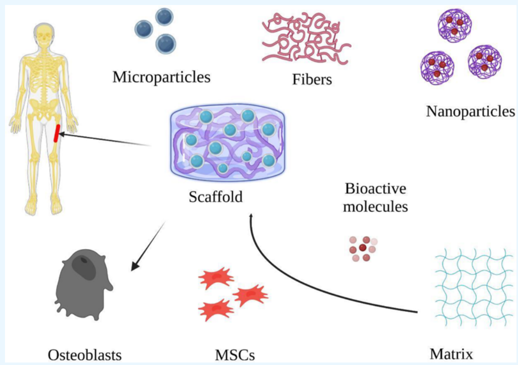
ABSTRACT: For several years, ceramic biomaterials have been extensively utilized to rebuild and substitute for body tissues. Calcium silicates have been proven to exhibit excellent bioactivity due to apatite formation and cell proliferation stimulation, in addition to degradability at levels adequate for hard tissue formation. These ceramics' excellent biological characteristics have attracted researchers. Baghdadite is a calcium silicate incorporating zirconium ions that enhances human osteoblast multiplication and development, increasing mineralization, and ossification. It has currently received much interest in academic institutions and has been extensively explored in the form of permeable frameworks, varnishes, bone adhesive and gap fillings, microparticles, and nanospheres, particularly in a wide range of biomedical applications. This review article aims to summarize and analyze the most recent research on baghdadite's mechanical characteristics, apatite-forming capability, dissolution pattern, and physiochemical qualities as a scaffold for dentofacial tissuè regeneration purposes.



1. INTRODUCTION

Reconstructive surgery is made more difficult by bone abnormalities. With the aging of the population and increased life expectancy, there is a growing desire for biomaterials that can replace missing or damaged bone. The principal measure for bone defect rehabilitation, autologous substitutes, has substantial limitations, like restricted availability, donor site operation, and donor site complications, which result in longer hospitalization.[1−4] Allografting also has various drawbacks that restrict its application, including decreased bioactivity and a higher likelihood of bacterial contamination.

Scaffold-based treatments, which use a porous material, provide an alternate method for stimulating bone development in bone lesions.[4−8] Considerable attempts have been made to create a superb artificial scaffolding, which mimics structural properties of bone while also providing the required porosity, interconnectivity, biocompatibility, and mechanical properties.[8−10] Given the popularity of these operations, there is no perfect bone transplant alternative.[11] The need for biosynthetic substances for the restoration and healing of bone tissue loss caused by injury or illness has expanded dramatically in the last 10 years.[12]

With the advancement of ceramics to cure illnesses as well as wounds for the objective of body rehabilitation and repair during the last 40 years, a breakthrough in the use of ceramics to enhance the standard of living has occurred.

Bioceramics are ceramics that are utilized for this function. Bioceramics and bioglasses are biocompatible substances.[13] Bioceramics are among the biocompounds.[14,15] From the ceramics to the remainder of the absorbable chemicals that the body eventually substitutes after assisting in healing, bioceramics are biocompatible.[16,17] Bioceramics are employed in a range of biomedical applications.

Customized bioreactors and extracorporeal circulation devices frequently use bioceramics.[18] They are valuable due to the fact that they are inefficient in the human body, and their rigidity and corrosion tolerance make them excellent for osseous and dental restorations.[19,20]

Bioceramics can be utilized in calcium silicate-derived constructions thanks to their strong capacity to create apatite and encourage cell growth and biodegradation at acceptable dense tissue regeneration frequencies because of their physicochemical resemblance to these kinds of tissues.[21−23] Silicates frameworks are critical for treating bone defects.

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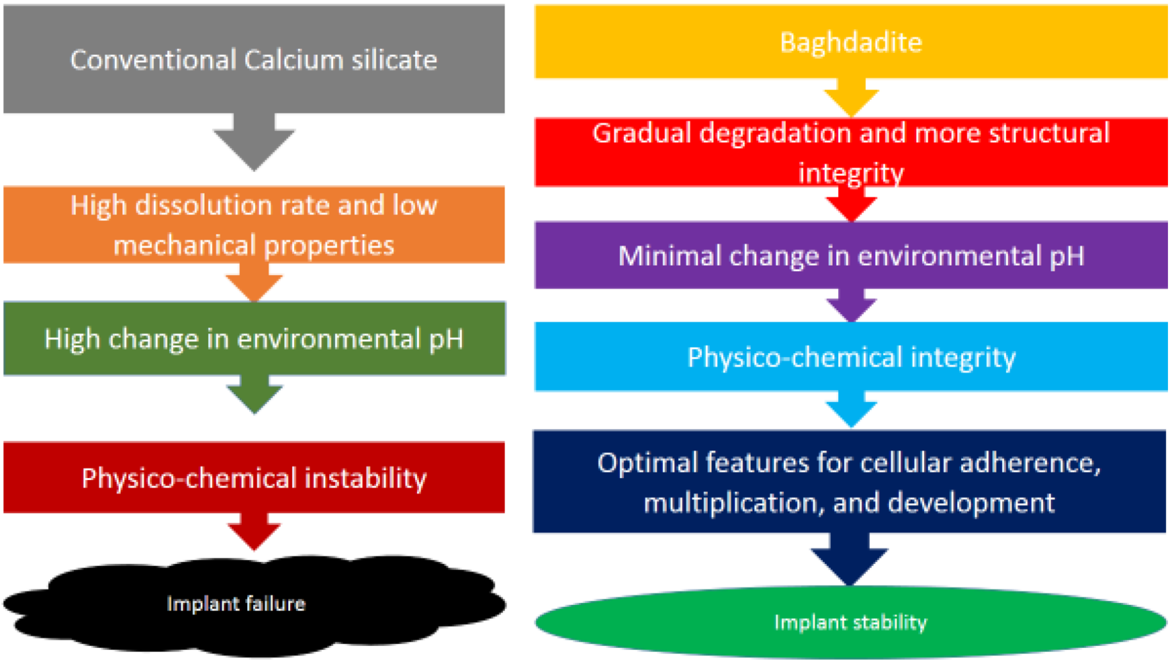

Figure 1. Biomechanical features of calcium silicates and baghdadite.

This category of bioceramics is notable for its outstanding in vitro bioactivity, as evidenced by their elevated mineral deposition capacity in physiologic environments, as well as their capacity to liberate SiO_4^{4-} ions, which boost the development and multiplication of periodontal cells, osteoblasts, and adipose-derived progenitor cells.[24−27] Silica has been found in bones at 100 ppm and extracellular matrix components at 200− 550 ppm. According to reports, Si is found in bone calcination sites and has a direct impact on the calcification process of bone formation.[12] One of the issues with these scaffolds is their inherent fragility and high degradability.

The application of degradable and reactive polymer-coating systems on the platform's surface resulted in increased mechanical properties as well as the capacity to control the pace of decomposition. Other studies reveal that bioactive ions, such as zirconium, significantly increased the bioactivity of Ca−Si ceramics.[28−30] Zirconium-based compounds, like zirconia ceramics (ZrO2), are frequently utilized in orthopedic and dental implants.[31] It has been claimed that Zr implants have excellent osseointegration, as well as Zr-containing materials including zirconia ceramic materials and their coatings, and have high potential for use as bone implant biomaterials. Figure 1 shows biomechanical features of calcium silicates and baghdadite. This coating has chemical stability and the potential to generate apatite.[32]

2. BAGHDADITE

Baghdadite is a novel calcium−zirconium−silicate mineral discovered in Iraq. As a result, this substance was given the name baghdadite, which is a unique mineral belonging to the cuspidine class. It is a ternary phase in the CaO−SiO2−ZrO2 system with a monoclinic structure as shown in Figure 2.

Baghdadite microparticles have formerly been employed to boost the strength, radiopacity, and bioactivity of polymer composites.[33] Baghdadite, like tricalcium phosphate, is somewhat soluble in biologically relevant aqueous solutions.[11,31]

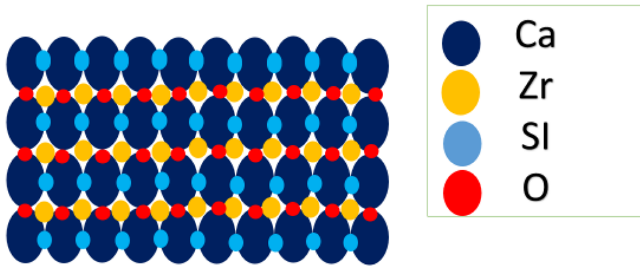

Figure 2. Schematic representation of the structure of baghdadite.

Numerous scientific researchers have recently focused on BAG, which has been widely researched in porous scaffolds, microparticles and nanomaterials, musculoskeletal, dental, and craniofacial coatings, and bone cement and fillers applications, as shown in Figure 3.[23,34,35]

Unlike hydroxyapatite ceramics, baghdadite offers higher biomechanical characteristics.[11,36,37] The baghdadite framework has also been identified as a biodegradable and biocompatible material that stimulates cell growth, development, and cytoskeleton remodeling.[38,39] Some of the major disadvantages of this material are its poor strength, intrinsic brittleness, and fast degradability.[40−43] Table 1 shows mechanical features of BAG-based scaffolds in the manufacturing of multicomponent nanostructures, a well-known way to improve both physicochemical and biological characteristics of bioceramics,. We can attain this aim by generating ceramic-reinforced composites or biocomposites.[44−48]

3. BIOLOGICAL CAPABILITIES OF CALCIUM, ZIRCONIA, AND SILICA IN OSSEUOS REMODELING

To highlight the potential of baghdadite as a bone replacement material, a complete study of the physiological roles of calcium, zirconia, and silica particles in osseous turnover is first examined.

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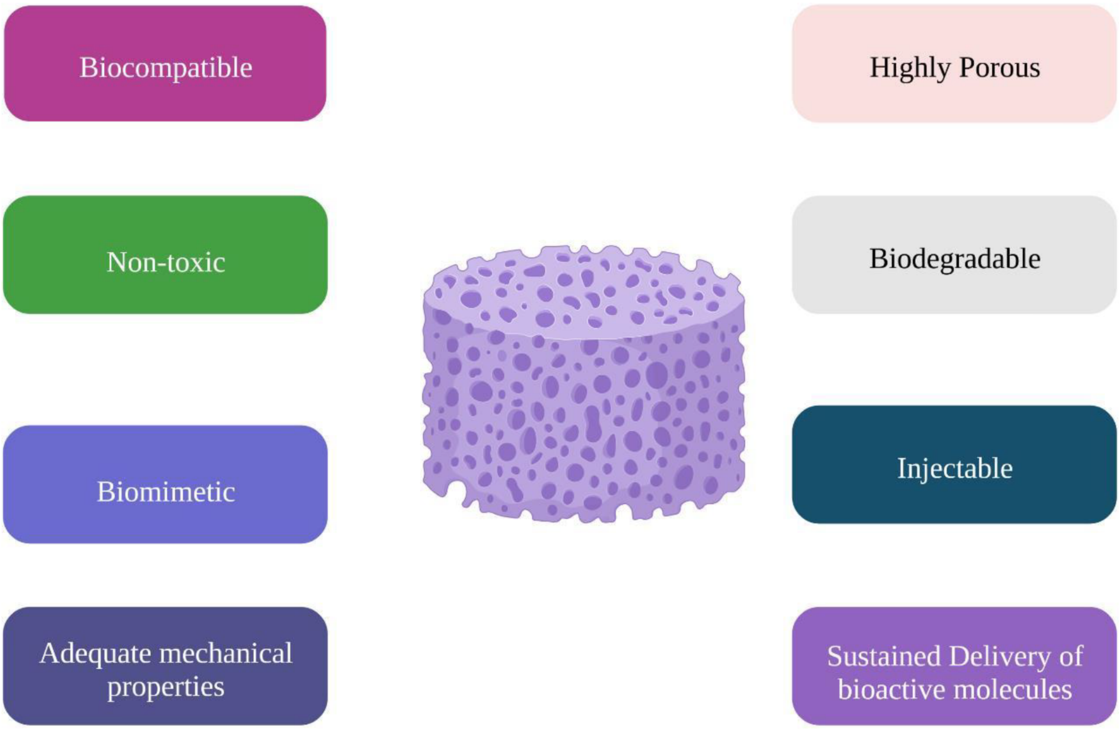

Figure 3. Benefits of baghdadite scaffolds.

Table 1. Mechanical Features of BAG-Based Scaffolds

structure	porosity (%)	pore size (μm)	compressive strength (MPa)	compressive modulus (MPa)	reference
BAG	85	500	0.27	15.3	28
BAG/nylon-6 (10/90 wt %)	70	153−253	1.41	6.23	46
BAG/vancomycin	80−82	300−400	0.86−0.88		47
TCP/HA (60/40 wt %)	85		0.12	10.5	48

Table 2. Strategies of Generation of Porous Ceramic Scaffolds

manufacturing process	benefits	limitations	reference
space holder	low cost with favorable material characteristics	obtaining a porous architecture with excellent interconnectivity is challenging	63
polymer sponge	intercommunication and permeability	inadequate replicability and material performance, as well as a lack of porous structure	64
freeze-drying	high porosity	time and energy consuming	65
solvent casting and particulate leaching	cost effective with high porosity	it is challenging to create a porous geometry with interconnectivity, and the leaching agent is highly toxic	66
electrospinning	high surface area, high porosity	lack of macropores, low mechanical properties	67
3D printing	replicability through better control of permeability and pore magnitude	energy consuming, lack of microspores	68

Ca makes up around 2% of the human body, with bones accounting for 98%. Ten to fifteen milligrams per 100 mg are found in bodily fluids and cells.

Ca is found in the active zone of natural bone and is required for blood vessel and bone formation.[49] Ca levels as low as 2−4 mmol encourage osteoblast transformation and multiplication, whereas medium Ca dosages of 6−8 mmol favor matrix calcification, and Ca amounts of more than 10 mmol are hazardous to cells.[50] Furthermore, extracellular calcium regulates bone regeneration independently of hormones by stimulating cation-sensing ligands.[51] Extracellular Ca, for example, can boost the efficiency of insulin-like growth factor (IGF) II, precisely regulating osteoblast multiplication.[52]

Extracellular Ca levels can also increase osteoblast glutamate secretion.[53]

Previous studies proved that silica has a beneficial role in bone activities and osseous development.[54] Carlisle[55] demonstrated a possible function for silicon in osteoid tissues, and various other research studies over the past few years have also been done to study the involvement of silica in bone formation.

Si is often absorbed as metasilicate, which is widely distributed in connective tissue.

Si is required for the bone homeostasis linked with bone calcification and is beneficial for increasing bone mass and preventing osteoporosis.[56,57] Furthermore, during the early stages of osseous tissue densification, Si levels in nascent bone can promote osteogenesis.[58] Aqueous Si was capable of precipitating the inorganic component of bone, namely hydroxyapatite.[59] According to several studies, Si can also

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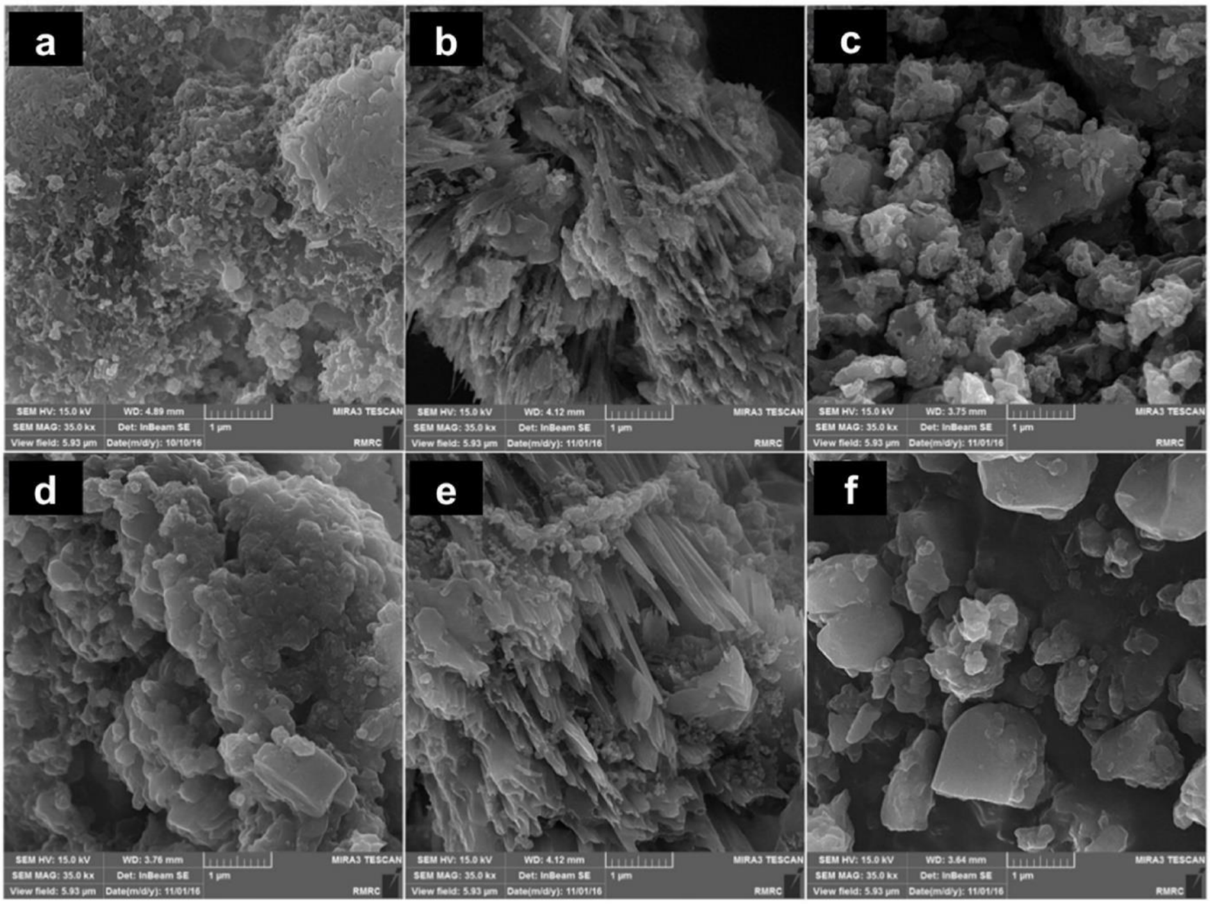

Figure 4. FESEM micrographs of nanoporous baghdadite, reprinted with permission from Elsevier.[69]

increase osteogenic differentiation and influence the stimulation of bone-related transcriptional factors.[60] Nielsen and Poellot[61] highlight Si's biochemical involvement in bone development processes before the crystallization process, impacting osseous collagen and extracellular matrix peptides, such as osteopontin.[62] According to the findings, physiological quantities of soluble Si can promote collagen type 1 production in osteoblast-like human cells.

Zirconium (Zr) has long been utilized to make prosthetic devices due to its nontoxicity and structural integrity. Zr ions could be employed to enhance biological characteristics and structural integrity in a variety of bioactive systems. Zr ions have good osseointegration, according to in vivo studies. As synthetic bone implants, zirconium-derived substances such as zirconia coatings and ceramics have been employed.

4. FABRICATION METHODS AND CHARACTERISTICS OF BAGHDADITE

There are many methods to fabricate bioceramic scaffolds, such as sol–gel, solid-state, etc., as shown in Table 2

Generally, there are two techniques for synthesizing BAG powder: the sol–gel technique and the direct solid-state process. The sol–gel method is the most prevalent and has been utilized in numerous investigations, as shown in Figure 4.[8,28,36]

Tetrahydrate of calcium nitrate ($Ca[NO_3]$), Ca, Si, and Zr sources included tetraethyl orthosilicate (TEOS, $Si[C_2H_5O]_4$) and zirconia oxide nitrate ($ZrO[NO_3]_2$). To solubilize TEOS, it is combined and agitated for half an hour with ethanol and 2 M nitric acid (HNO_3). The Zr and Ca sources are then added to the solution in the molar ratio 1:3:2 = $ZrO[NO_3]_2$:$Ca[NO_3]Si[C_2H_5O]_4$:$2.4H_2O$. The reagents are agitated at ambient temperature for 5 or 6 h, and the clear solution is dried at 60–100 °C for several days before being autoclaved above 900 °C. In the solid-state reaction pathway,[33,7071] $Ca_3ZrSi_2O_9$ is generated by blending calcium oxide (CaO) or calcium carbonate ($CaCO_3$),[72] silicon dioxide (SiO_2), and zirconium dioxide (ZrO_2) as initiating compounds with proportions of 3:2:1, respectively. The mixture is then sintered at temperatures more than 1000 °C.

The structure of BAG ceramics generated with a density of 3.48 g/cm^3[19,73] was explored with diameters less than 100 nm[74] through electron microscopy images. Spheric structures were also investigated in other studies.[3472] Doostmohammadi et al.[75] detected the diameter of BAG particles in the range of 80–150 nm by utilizing field emission scanning electron microscopy (FE-SEM). They also found the agglomeration of particles, which could be because of the high surface energy of nanoparticles.[76] Moreover, in transmission electron microscopy (TEM) pictures, the average size of BAG components was shown to be 32 nm,[48] which may occur due to the relatively lower particulate aggregation. Ottman et al.[72] characterized single-phase synthetic BAG. Their thorough spectrum analysis revealed that BAG has unique physical and chemical properties and is a single-phase substance with multiple crystals.

Numerous additional investigations employed FTIR analysis as a characterization method to study the crystalline nature of

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Table 3. Studies on Baghdadite Application in Bone Regeneration

framework	experiment	duration of the study	outcomes	reference
baghdadite	rat	8 weeks	improved osteogenesis	82
baghdadite	sheep	26 weeks	angiogenesis and neovascularization	83
baghdadite	rabbits radial segmental defect model		baghdadite is capable of bridging large bone deformities	28
baghdadite/PCL/BG	sheep	26 weeks	filling of the defect	84
baghdadite ($Ca_3ZrSi_2O_9$)	human osteoblast-like cells, osteoclasts, and endothelial cells		exhibited good cytocompatibility and adherence of cells such as osteoblasts, osteoclasts, and endothelial cells; baghdadite ceramics promoted increased multiplication and specialization of osteoblast-like cells	8
nylon-6−baghdadite	in vitro and in vivo analysis utilizing the MG63 cell-line		optimal degradation rate, enhanced cellular activity	85

produced BAG powders.[74,72,77,46,72] Thermal investigation of BAG powder using concurrent differential thermal analysis (DTA) and thermogravimetry (TG) revealed that sintering at temperatures over 900 °C is required to generate crystalline BAG.[72] Najafinezhad et al.[78] studied the thermal nature of BAG in relation to other ceramics. As stated by their findings, nitrate is removed from zirconium nitrate at 540 °C and calcium nitrate at 710 °C, correspondingly. At 800 °C, an exothermic peak indicating BAG crystallization developed.

Ramaswamy et al. investigated the biological characteristics of BAG nanostructures and their potential uses in bone regeneration in 2008.[11] BAG was created synthetically by incorporating Zr into calcium−silicate (Ca−Si) frameworks.

Aside from the capacity of BAG ceramic to generate apatite, SEM and inverted fluorescence microscopy pictures of grown human osteoblast cells (HOB) demonstrated a better cell spread on BAG discs in relation to calcium silicate. BAG samples showed enhanced HOB cellular multiplication and specialization levels as measured by the methoxyphenyl tetrazolium salt (MTS) test, as well as measures of rates of alkaline phosphatase (ALP) activities and mRNA transcription. Similarly, experimental tests on human mesenchymal bone marrow stem cells revealed cytocompatibility and the osteoinduction capability of nanobaghdadite.[72]

Furthermore, encapsulating ibuprofen, the sustained drug release capacity of BAG nanostructures was evaluated in vitro.

According to the findings of research conducted by Doostmohammadi et al.,[75] BAG nanoparticles were biocompatible and could enhance bone marrow-originated mesenchymal stem cell growth.

Six weeks after generating a hole and packing it with BAG nanostructures, nearly full regeneration of rabbit tibia was described. Until 2014, essentially no data on the mechanical characteristics of artificial or natural BAG has been documented. Schumacher and colleagues[35] pioneered this research in order to broaden the possible uses of BAG in the biomedical realm.

They found that bulk BAG ceramic had the best mechanical characteristics when sintered at 1400 °C; the fracture toughness and hardness were higher than those of hydroxyapatite (HA). BAG was proposed as an acceptable option for nonload-bearing implementation, like bone fillers and coatings, with a bending strength of 98.16 MPa.

In a research study that examined the compressive strength of different types of silicate bioceramics, BAG outperformed akermanite and diopside.[78] In another study conducted by Khandan et al.,[79] when using a second phase, the cold crushing strength (CCS) of HA samples rose as the quantity of BAG was elevated from 0 to 30 wt %. The CCS ratio increased by up to 50% (max. 2.8 MPa) in samples containing 30% BAG, whereas the porosity of these samples dropped by 60% to 49%. Notably, doping strontium (Sr) into the architecture of BAG enhanced its tensile characteristics while having no effect on the microstructure.[33]

5. BAGHDADITE IN PERIODONTAL REGENERATION

Baghdadite ($Ca_3ZrSi_2O_9$) has PDLC-specific in vitro cementogenic activation.[80] This study found that baghdadite ceramic discs might boost PDLC attachment and multiplication while also significantly increasing the transcription of cementogenic/osteogenic biomarkers.

Ionic compounds derived from baghdadite powders shown remarkable pro-cementogenic/osteogenic properties, which may be attributed to Wnt/b-catenin pathway activation by the released Ca, Zr, and Si ions.

Another study looked at the influence of Si ions on the osteogenesis dependency in bone marrow stromal cells, and the findings revealed that Si ions might trigger proliferation and differentiation in these cells on their own.[81]

6. BAGHDADITE IN BONE REGENERATION

Because of the established in vitro bioactivity of modified Ca−Si ceramics, BAG scaffolds were employed in bone regeneration, as shown in Table 3.[34]

6.1. In Vitro. Ramaswamy et al. studied the interplay of bone-forming and bone-resorping cells with $Ca_3ZrSi_2O_9$ and $CaSiO_3$ substances in vitro. Cells grown on baghdadite ceramics demonstrated higher multiplication and bone-dependent transcription factors levels relative to $CaSiO_3$ ceramics.[11]

Baghdadite ceramics stimulate osteoblast-like cellular proliferation more than wollastonite.[78] When compared to pure PCL, primary human osteoblasts grown on polycaprolactone (PCL)−10% baghdadite (Bag) demonstrated a substantial activation of osteogenic markers.

In conclusion, our findings suggest that PCL−10% Bag might be a suitable injectable scaffold for orthopedic and trauma applications.[30]

Karimi et al. layered baghdadite ($Ca_3ZrSi_2O_9$) on the plasma-adjusted PLLA surface and assessed the bone-forming capacity of mesenchymal stem cells generated from adipose tissue (AD-MSCs). The PLLA/baghdadite nanomaterials had increased calcium concentration and ALP activity in the cells compared to the other samples. They proposed that nanofiber

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frameworks treated with baghdadite can improve stem cell osteogenesis.[86]

Bismuth-treated baghdadite ceramics showed a considerable increase in the multiplication of primary human bone-derived cells (HOBs), with appropriate radiopacity for bone defect therapy.[87]

A unique baghdadite/PCL-graphene nanostructured framework was produced, and it stimulated the dissemination and adhesion of MG-63 osteoblast cells on the scaffolds, demonstrating vitality, cytotoxicity, good cell adhesion, and multiplication.

The findings demonstrate that this scaffolding has great promise as a transient platform for bone tissue engineering.[88]

6.2. In Vivo. Roohani-Esfahani et al. conducted promising in vivo research in which they transplanted $Ca_3ZrSi_2O_9$ and HAp/−TCP frameworks into the radii of rabbits.[31]

Baghdadite matrices produced much more new bone than HAp/−TCP composites.[28] Interestingly, cell-free permeable frameworks of baghdadite were found.[28] After 12 weeks, the rabbit was able to accomplish complete bridging and adequate regeneration of critical-sized bone lesions, with superior results as matched to calcium phosphate groups. Luo et al. reported comparable findings when they implanted $Ca_3ZrSi_2O_9$, $CaMgSi_2O_6$, and -TCP microbeads in the femurs of rats.[36]

The analysis of in vivo osteogenesis after 2 and 4 weeks demonstrated that baghdadite induced more osteogenesis and stronger transcription of type I collagen than diopside and β-TCP.[34] Baghdadite bridges critical-sized regional osseous lesions in sheep tibiae, demonstrating bone entrapment and remodeling inside the scaffolding implant.[89,84]

7. BAGHDADITE AS A SCAFFOLD FOR DELIVERY OF BIOMOLECULES

Baghdadite has low antimicrobial capabilities, which can result in implant-related pathogens and postoperative problems, as shown in Table 4.[90] To address this problem, frameworks were imbued with medications like vancomycin (Vac), an antimicrobial, which is potent against Gram positive (*Staphylococcus aureus*) pathogens and beneficial in the prevention of osteomyelitis.[90,91] 3D-printed individualized baghdadite scaffolds were produced and complexed with biodegradable coatings releasing BMP2, with or without zoledronic acid (ZA), and resulted in increased bone cellular infiltration in mice.[83]

Table 4. BAG-Based Scaffolds

structure	scaffold-manufacturing approach	BAG production strategy	reference
BAG (wt % 85) + diopside (wt % 15)	space holder	sol−gel	95
PCL + graphene + BAG	electrospinning	commercial product	96
BAG (wt % 99) + vancomycin (wt % 1)	salt leaching	sol−gel	47
BAG (wt % 10) + HA (wt % 90)	sponge replica	sol−gel	97

Furthermore, utilizing ibuprofen as a model drug, the sustained drug delivery capacity of BAG nanostructures was evaluated in vitro. The findings of research conducted by Doostmohammadi et al.[75] showed that BAG nanoparticles were biocompatible and could enhance bone marrow-derived mesenchymal stem cell growth. Six weeks after generating a hole and replacing it with BAG nanoparticles, relatively full regeneration of rabbit tibia was described.

DXP-embedded CN (DXP-CN) nanomaterials and MG 63 osteoblast-like cells were encapsulated inside the permeable scaffold of a gellan and xanthan hydrogel. Ultimately, this nanogel was layered within a porous baghdadite (BD) framework to allow for regulated cell and DXP distribution. The BD scaffold ($Ca_3ZrSi_2O_9$) was employed as a scaffolding to give a platform with the necessary rigidity and biocompatibility.[92]

Recent research has also indicated that porous baghdadite ceramics with remarkable mechanical qualities and sustained drug release capabilities may be developed to suppress postsurgery infections in bone tissue regeneration utilizing various ways such as the surfactant-directed sol−gel approach,[93] space holder method,[36,47,94] polymer sponge duplication procedure,[73] and freezing casting procedure.[35]

8. BAGHDADITE AS A COATING MATERIAL

Regenerative medicine is an approach to treating bone problems. It is a large area that covers tissue engineering and is founded on the premise of regeneration of wounded tissues with novel biomaterials.[98,99] It is widely utilized globally as a result of growing demands for bone replacements in recent years.[100] Thanks to their superior mechanical qualities, metallic inserts are regarded as one of the finest solutions used in many orthopedic applications.[100,101] The surface coating compensates for the biocompatible characteristics of metallic alloys and improves their osteointegration and osteoconduction.[102−104] Because of existing coating material constraints, such as biological destabilization[102] or a lack of adhesiveness between the coating and the matrix,[105] during the past decade, there has been a lot of attention in the advancement of new surface treatments, such as Ca−Si-derived ceramic materials.[106,107,9] Following Xie et al. initial's effort,[108] to employ zirconia/dicalcium silicate blend for layering, Linag et al.[109] implemented a new calcium zirconium silicate (BAG) coating on Ti−6Al−4V to examine its prospective orthopedic and dental uses. According to ASTM C633-01, the bonding strength between the coating layer and the substrate was 28 4 MPa, which was greater than that of formerly investigated HA coatings (∼6−16 MPa).[110,111] Furthermore, BAG-coated alloys had lesser weight loss and Ca and Si ion transfers into Tris-HCl buffer solution than Ca_2SiO_4 samples.

The generated bioactive BAG-deposited substrates' strong chemical stability proved their long-term durability. In another work, Bakhsheshi-Rad et al. discovered that BAG/ZnO-deposited (10 m) Mg alloys had superior chemical stability and mechanical strength than did ZnO-coated samples.[112] They also revealed that BG/ZnO-layered specimens are a great option for orthopedic implants due to their high surface wettability (the presence of the Si−OH group), remarkable antimicrobial functions against *Escherichia coli*, *Klebsiella*, and *Shigella*, and greater compressive toughness after 10 days of immersion in SBF, when compared to raw Mg or ZnO-coated Mg alloy. Soleymani and colleagues[113] indicated that incorporating 3 wt % BAG into PCL/chitosan coating may enhance resistance to corrosion of AZ91 Mg alloy and raise surface roughness from 4.743 to 7.026 m, facilitating cell attachment and tissue−scaffold interplay.[43] Recently in respect of physiochemical characteristics, as well as morphology, BAG and HA coatings were compared.[114]Surface roughness (Ra =

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9.9 0.6 m) was found to be more consistent in BAG coatings than in HA coatings. This may lead to greater levels of osteoblast cell adhesion.[109] BAG's increased solubility levels in comparison to highly crystalline HA can result in an increased rate of osteogenesis throughout the coating.[115] When compared to HA coating, BAG coating with a more homogeneous microarchitecture, improved microhardness, and lower modulus leads to greater adherence and proliferation of MG-63 cells.[114] Moreover, an investigation[86] revealed that the BAG coating of poly(L-lactic acid) (PLLA)-based scaffolding successfully stimulated osteogenesis of ASCs.

9. CONCLUSION

Baghdadite has been demonstrated to have strong structural and biochemical qualities that are similar to those of human bone tissue. Nevertheless, achieving regulated ion dynamics of dissociation and liberation that allow the requisite essential levels of particular ions to be discharged into the biological conditions in a controlled manner is a substantial difficulty. Future advancements should clearly investigate the kinetics of particular ion release in order to harness the favorable impact of charges released and to improve the biologic functions of baghdadite in the perspective of specific host responsiveness. Furthermore, varied production procedures and the incorporation of diverse biomolecules might boost biological function. As a result, future research on baghdadite should concentrate on two key areas: (a) improving new manufacturing techniques to increase performance and (b) using innovative bioactive molecules with therapeutic potential to promote osteoinductivity.

Ongoing effort is necessary in the development of novel calcium silicates with the goal of acquiring mechanical and biological qualities that are as near as possible to those of the osseous tissue regeneration.

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Notes

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