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Original article

The Processing and Application of Calcium phosphate-based Bioceramics: A Review

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Abstract
This review provides a comprehensive overview of the processing, properties, and applications of calcium phosphate (CaP)-based bioceramics in dentistry. It focuses on key materials such as hydroxyapatite (HA), fluorapatite (FAp), and tricalcium phosphates (α-TCP and β-TCP), which are central to modern restorative and regenerative strategies due to their compositional and structural similarity to natural bone and enamel. The paper examines the fundamental properties of bioceramics, including their biocompatibility, osteoconductivity, and bioactivity. Concurrently, it addresses their inherent mechanical limitations, primarily brittleness, which restricts their use in high-stress, load-bearing applications. Strategies to overcome these challenges are detailed, including the development of composites with polymers and other ceramics, as well as chemical modifications like ion doping (e.g., Ag+, Sr2+) to impart antimicrobial properties and fluorine substitution to form more acid-resistant fluorapatite. A wide range of dental applications is discussed, from their use in remineralizing toothpastes and serving as bioactive coatings on titanium implants to enhance osseointegration, to their fabrication into porous scaffolds for bone tissue engineering and drug delivery. The outlook suggests the development of multifunctional, customized materials through advanced fabrication techniques, such as 3D printing and nanotechnology, to create active therapeutic systems that can heal, prevent disease, and withstand the demanding oral environment.
Keywords: Bioceramics, Calcium Phosphate, Dental.

Introduction

Teeth are mineralized structures composed of enamel, dentin, and pulp, with enamel being almost entirely hydroxyapatite (~96 wt%), while dentin contains a mixture of hydroxyapatite, collagen, water, and salts [1]. The acidic environment generated by bacterial metabolism of dietary carbohydrates leads to progressive demineralization of enamel and dentin, ultimately causing caries [2]. Since teeth cannot regenerate on their own, restoration requires the use of biomaterials. Biomaterials, as defined by the European Society for Biomaterials, are designed to interact with biological systems to repair, replace, or augment tissues or organs [3,4]. Depending on their chemistry and properties, they are classified into polymers, metals, ceramics, and composites, with key requirements including biocompatibility, bioresorbability, bioactivity, and adequate mechanical stability [5–9]. Among them, bioceramics, and particularly calcium phosphates (CaPs), are highly relevant to dentistry due to their compositional similarity to natural hard tissues, ability to release remineralizing ions, and excellent compatibility with host tissues [10,11].

Hydroxyapatite (HA), the principal mineral of teeth and bone, is widely applied in dental and orthopedic materials owing to its osteoconductivity and bioactivity, while α-tricalcium phosphate (α-TCP) serves as a precursor that converts into HA in physiological fluids, enabling remineralization [12]. Fluorapatite (FAp), formed by fluoride substitution in HA, provides greater acid resistance and durability, and has been incorporated into dental composites and calcium phosphate cements to tailor biological and mechanical performance [13–19]. Beyond single-phase materials, composites combining CaPs with polymers or oxides such as TiO_2 and ZrO_2 have been developed to optimize porosity, rheology, strength, and stability [20,21]. This review focuses on the development and application of calcium phosphate-based biomaterials in dentistry, emphasizing their structural and functional properties, strategies for improving bioactivity and mechanical strength, and recent advances in composites and cement systems. Particular attention is given to their role in tooth remineralization, restorative dentistry, and implant coatings, highlighting both current achievements and ongoing challenges.

Biomaterials and their properties

Biomaterials are defined as materials designed to interact with biological systems for the purpose of repairing, replacing, or supporting tissues and organs [3,4]. Their most critical requirement is biocompatibility, ensuring safe integration without toxic effects. Depending on their interaction with tissues, biomaterials may be bioinert, biomimetic, or bioactive, and in some cases bioresorbable, enabling gradual replacement by natural tissue [22]. Besides compatibility, they must exhibit sufficient mechanical strength, wear resistance, and chemical stability for long-term function in demanding environments [5–10].

Biomaterials are generally classified into polymers, metals, ceramics, and composites [23,24]. While polymers (e.g., PMMA, PLA, PGA) offer flexibility and biodegradability [25-27], and metals (notably

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titanium alloys) provide high strength [28-33], both face limitations in bioactivity. Dentistry, therefore, increasingly relies on ceramic-based systems, either alone or in composites.

Mechanical performance

Mechanical properties are a key consideration in the application of biomaterials, especially in load-bearing dental and orthopedic contexts. Polymers offer flexibility and processability but have low hardness, wear resistance, and fracture toughness, limiting their use under high stress [5,25]. Metals, particularly titanium and its alloys, provide high strength, impact resistance, and durability, yet they are biologically inert and cannot bond directly with tissue without surface modification [33].

Ceramics, including alumina, zirconia, and calcium phosphates, combine high hardness, compressive strength, and wear resistance with chemical stability and biocompatibility [34-41]. Among ceramics, zirconia stands out for its toughness, while alumina offers excellent hardness but lower fracture resistance. However, the inherent brittleness of ceramics limits their ability to withstand tensile or impact loads, making reinforcement strategies essential.

Composite materials address these limitations by combining ceramics with polymers or other ceramics. For example, HA/polymer composites or HA/zirconia ceramics enhance toughness, reduce brittleness, and improve resistance to wear, while retaining bioactivity and compatibility. Nanoscale ceramic fillers can significantly improve tensile and compressive strength and reduce polymerization shrinkage in dental composites [16]. Thus, careful selection and combination of matrix and reinforcement enable tailoring of mechanical properties to match specific dental or orthopedic demands, balancing strength, bioactivity, and longevity.

Ceramics and calcium phosphates

Ceramics are characterized by hardness, chemical stability, and excellent wear resistance [42]. In dentistry, their main appeal lies in biocompatibility and bioactivity, although brittleness limits their load-bearing use [43]. Bioceramics include:

Bioinert ceramics, such as alumina and zirconia, are valued for strength and corrosion resistance but are unable to bond with tissue [44-47].

Bioactive ceramics form chemical bonds with bone through surface reactions. This group includes bioactive glasses (e.g., Bioglass® 45S5) and, most importantly, calcium phosphates (CaPs) [48-54].

CaPs closely resemble the mineral phase of teeth and bone, ensuring excellent compatibility and osteoconductivity. Their ability to release Ca^{2+} and PO_4^{3-} ions support remineralization, making them especially promising for dental applications such as alveolar bone repair, implant coatings, and cements [13, 55]. Porosity further enhances vascularization, cell migration, and bioresorbability, while also enabling drug delivery.

Calcium phosphates: composition and relevance

Calcium phosphates (CaPs) encompass several phases distinguished by their Ca/P molar ratio, crystallinity, and solubility, which directly influence their biological performance [11,55]. The most soluble forms are monetite (Ca/P = 1.0) and brushite (Ca/P = 1.0), typically used in fast-resorbing bone cements. Tricalcium phosphates (TCPs, Ca/P = 1.5) occur in two polymorphs: β-TCP, with moderate solubility, widely applied in bone grafts and coatings, and α-TCP, which rapidly converts to hydroxyapatite in vivo, making it suitable for cements and dentin repair.

The most stable phase, hydroxyapatite (HA, Ca/P = 1.67), closely mimics enamel and bone mineral, providing high biocompatibility, osteoconductivity, and bioactivity, though with slow resorption. Substituted apatites, such as fluorapatite (FAp), display improved acid resistance and lower solubility, aligning with enamel composition and offering enhanced durability for restorative dentistry [13-15]. Calcium phosphates vary in mechanical performance depending on phase and porosity. Dense hydroxyapatite provides good compressive strength but is brittle, while porous structures improve biointegration at the expense of mechanical stability. α- and β-tricalcium phosphate offer intermediate strength, suitable for cements and scaffold applications where gradual load transfer is desired [11]. Different CaPs, including brushite, monetite, α/β-TCP, and hydroxyapatite, offer tunable solubility and mechanical behavior depending on their Ca/P ratio [11].

In summary, low Ca/P phases (monetite, brushite) are advantageous for resorbable cements, TCPs provide a balance between solubility and stability, while apatites serve as long-term bioactive scaffolds or coatings, supporting both remineralization and mechanical reinforcement in dental applications.

Hydroxyapatite

Hydroxyapatite (HA) is a dominant dentine and bone constituent, which indicates high biocompatibility of synthetic apatite-based materials and implants. With excellent osteoconductive and bioactive properties, HA is favored as the biomaterial of choice in both dentistry and orthopedics [56,57].

Composition, structure, and properties of HA

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Among calcium phosphates, hydroxyapatite (HA, $Ca_{10}(PO_4)_6(OH)_2$) is the most widely studied and utilized due to its close resemblance to the mineral components of bone and teeth [58]. It's ideal chemical composition includes 39.6 wt% calcium and 18.5 wt% phosphorus, yielding a Ca/P weight ratio of 2.15 and a molar ratio of 1.667 [59]. The crystal structure of HA is commonly hexagonal with $P6_3/m$ symmetry (Figure 1) [60-62].

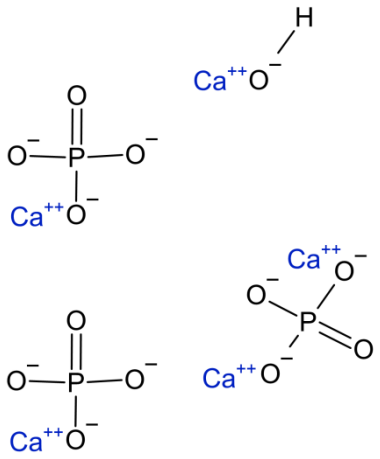

Figure 1. Structure of HA

Natural HA, found in bone, dentin, and enamel, is typically non-stoichiometric, containing additional elements such as Na, Mg, Zn, K, and F, which can partially replace calcium or hydroxyl groups, influencing both solubility and biological behavior [63]. This non-stoichiometric nature also contributes to its biodegradability, allowing osteoclast-mediated remodeling in vivo, whereas synthetic HA with a strict Ca/P ratio of 1.67 is more chemically stable. The composition of HA closely resembles that of natural hard tissues. Enamel, dentin, and bone contain approximately 35–37 wt% calcium and 15–18 wt% phosphorus, with Ca/P ratios between 1.61 and 1.71. Trace elements such as sodium, magnesium, potassium, carbonate, fluoride, and chloride are present in natural tissues but absent in pure HA. This similarity underpins HA's excellent biocompatibility and osteoconductivity, making it suitable for dental and orthopedic applications [59]. Despite its favorable bioactivity, HA shares the mechanical limitations of ceramics, including brittleness and relatively low tensile and bending strength, particularly in porous forms. Dense HA exhibits significantly higher mechanical performance, with tensile strength ranging from 38–300 MPa, compressive strength of 120–900 MPa, and bending strength of 38–250 MPa, while porous HA, which is required for effective cell infiltration and tissue growth, shows much lower values (tensile ~3 MPa, compressive 2–100 MPa, bending 2–11 MPa) [60]. This trade-off between porosity for bioactivity and mechanical strength represents a central challenge in the design of HA-based biomaterials, especially for load-bearing applications.

Synthesis of HA

The phase composition and bioactivity of hydroxyapatite (HA) strongly depend on the Ca/P molar ratio. Various synthesis techniques have been developed and are generally classified into high-temperature, dry, and wet methods (Figure 2).

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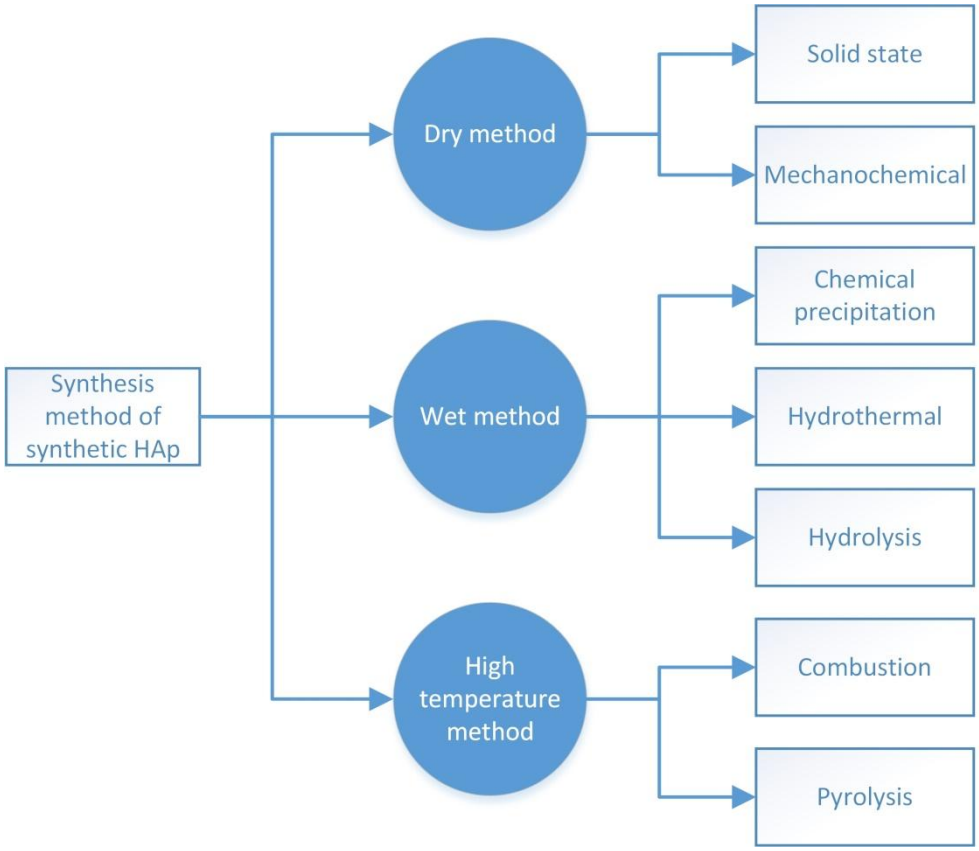

Figure 2. HA synthesis techniques

Chemical modification of HA

Doping

Hydroxyapatite (HA) ion doping has garnered significant interest among researchers because it allows for the incorporation of various ions into the crystal lattice of HA without compromising its structural integrity. To enhance antimicrobial efficacy and mitigate the risk of infection during the integration of dental implants into osseous tissue, hydroxyapatite (HA) was doped with silver (Ag^{+}) and copper (Cu^{2+}) ions [22]. Numerous studies have integrated strontium (Sr^{2+}), cobalt (Co^{2+}), magnesium (Mg^{2+}), manganese (Mn^{2+}), and ferric (Fe^{3+}) ions to augment the resemblance to the natural bone composition [61-66].

Substitution with fluorine

Fluorine constitutes a critical element that plays a significant role in the process of bone mineralization, rendering it an exemplary candidate for the substitution of OH^{-} ions in hydroxyapatite (HA). Consequently, this substitution leads to the formation of fluorapatite (FA), characterized by the chemical formula $Ca_{10}(PO_4)_6F_2$. The structural configuration of FA is illustrated in (Figure 3), with lattice parameters recorded as: a=9.368 and c=6.875 [67]; notably, the a-axis exhibits a shorter length in comparison to HA, attributable to the disparity in ionic radii between F^{-} and OH^{-} ions.

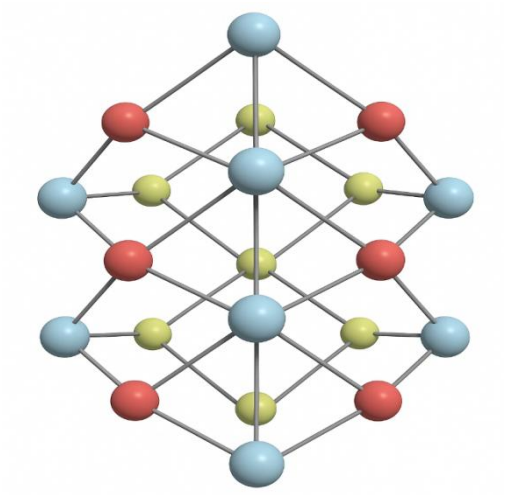

Figure 3. Structure of fluorapatite

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Fluorapatite demonstrates enhanced thermal stability and reduced solubility relative to hydroxyapatite, thereby rendering it more amenable to processing at elevated temperatures that may induce the decomposition of HA [67]. Furthermore, FA exhibits a greater resistance to acidic environments, and as such, it is employed as a protective agent against demineralization; hydroxyapatite undergoes dissolution when the pH declines below 5.5, whereas fluorapatite commences dissolution at pH levels beneath 4.5. In the context of saliva, the presence of fluorine mitigates demineralization by substituting the hydroxyl group in dissolved HA, subsequently depositing onto the enamel [6, 13-15, 68]. Synthetic fluorapatite is synthesized employing methodologies akin to those utilized in the production of hydroxyapatite. In addition to its superior chemical and thermal characteristics compared to hydroxyapatite, fluorapatite also exhibits enhanced mechanical properties. Notable features of FA ceramics include elevated hardness values, increased modulus of elasticity, and superior fatigue resistance, which confer a distinct advantage over alternative apatite materials. However, it is imperative to recognize that fluorine is a highly toxic element; therefore, meticulous research must be conducted to ascertain the optimal concentration of fluorapatite that ensures safety for utilization within the human body [66].

Application of HA and its composites

Hydroxyapatite powder has found application as a biomaterial in various parts of the human body. Some of them are bone and teeth filling, toothpastes, titanium implant coatings, and reinforcement in polymer-based materials [69-78]. The application of HA can be divided into
Commercial products,
Tissue engineering and
Drug delivery systems.

Commercial products based on HA

Due to their benefits, toothpastes and mouthwashes containing hydroxyapatite (HA) have grown significantly in popularity recently [79]. Teeth are frequently subject to demineralization caused by everyday wear, pressure, and shifts in saliva pH. While fluorine is a common oral care ingredient known for slowing this process, concerns over its toxicity and the ongoing need for daily treatment of dental hypersensitivity through enamel remineralization have focused attention on adding HA to toothpastes.

Application in dentistry

HA coatings

Dental implants, typically made from metallic titanium alloys, are used to replace missing teeth [30]. While these implants offer superior mechanical properties, including high resistance to wear and fracture compared to ceramics, they cannot directly bond with the surrounding host tissue. This necessitates applying a bioactive and biocompatible coating, like hydroxyapatite (HA) [80].
HA is preferred over other calcium phosphates (CaPs) because its structure is like natural teeth, and it exhibits low solubility [81].

HA scaffolds and drug delivery

As mentioned before, HA is not suitable for load-bearing applications due to poor mechanical properties. However, they can be valuable to produce scaffolds, to enhance cell proliferation and integration in the structure [82]. Scaffold is presented in (Figure 4).

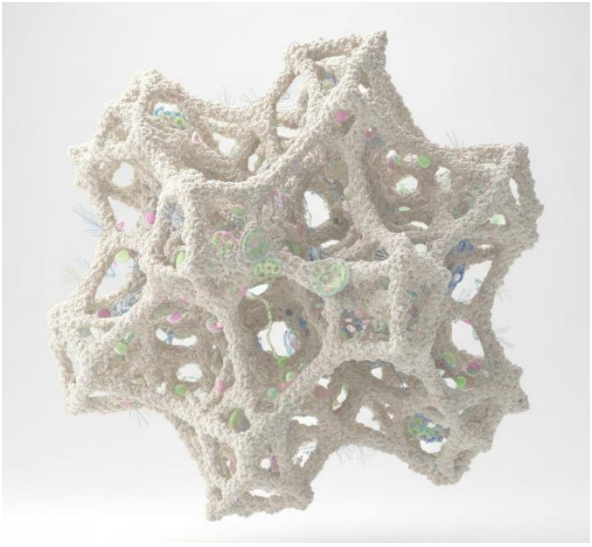

Figure 4. HA-based scaffold

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HA-based scaffolds are extensively researched for bone tissue engineering and regeneration. Using a replication technique, HA scaffolds with pores up to 300mm were created; these scaffolds exhibited bone-like compressive strength and supported the proliferation and migration of SASO2 cells [83]. The 3D printing technique has also proven useful for making HA scaffolds with interconnected channels, showing a high capacity to support the growth of MC3T3-E1 cells, positioning these materials as strong candidates for bone repair [84].

Composite Scaffolds

Significant research has also focused on composite scaffolds made from HA combined with natural or synthetic polymers.
Nano-HA/collagen scaffolds have been successfully used to deliver stem cells, leading to effective bone regeneration [85,86].
Nano-HA combined with gelatin and chitosan created porous composite scaffolds that promoted the proliferation and growth of MC3T3-E1 cells, making them suitable for tissue engineering [87].
A highly biocompatible composite scaffold was prepared using HA derived from biological sources, combined with gelatin, chitosan, fibrin, and bone ash; this material showed excellent compatibility with MG-63 cells and is considered safe for use as a bone substitute [88].
Electrospun nanofiber composites of insulin-modified HA and PLGA (poly(lactic acid-co-glycolic acid)) demonstrated high osteogenesis potential, suggesting a promising pathway for artificial bone creation [27].

Drug Delivery Applications

HA-based materials are also being employed as local drug delivery systems:
A scaffold made of HA doped with Ag^{+}, and modified with sodium alginate and chitosan, has been reported as an effective vehicle for releasing the anesthetic drug lidocaine [89].
Chitosan/HA scaffolds are effective for loading gentamicin sulfate, a drug used to treat and prevent infections during the regeneration process [90].
More recently, a nano-HA/graphene oxide nanocomposite was identified as a promising material for delivering anti-cancer drug doxorubicin [91].

A- AND ß- tricalcium phosphate

Tricalcium phosphates (TCP - $Ca_3(PO_4)_2$) are biodegradable ceramic materials that exist in four crystalline forms (allotropes), with α- and β-TCP being the most common [9, 30]. Since TCP dissolves in water, it holds great potential for use in bone tissue regeneration. However, its resorption rate can vary significantly based on factors like its calcium-to-phosphate (Ca/P) ratio, purity, and porosity. If the rate is too fast, the new tissue won't have time to regenerate, making the material unsuitable as a scaffold.

ß-Tricalcium Phosphate (ß-TCP)

The allotrope β-TCP (β-$Ca_3(PO_4)_2$) has been extensively researched and used as a bone substitute [16, 24]. Like HA, β-TCP is not naturally occurring and must be synthesized using high-temperature techniques [92]. It is more thermally stable than HA and resorbs faster due to its higher solubility. However, the β-TCP's bioresorbability is heavily influenced by its porosity and surface roughness; high-density forms have sometimes been reported as having low bioactivity [92].

α-Tricalcium Phosphate (α-TCP)

The other significant polymorph is α-tricalcium phosphate (α-TCP), which is recognized as a material for bioceramics and bone cement [12]. Although α-TCP (α-$Ca_3(PO_4)_2$) (Figure 5) shares the same chemical formula as β-TCP, they have distinct crystal structures. β-TCP has a more ordered structure, which results in it being less soluble than α-TCP [12].

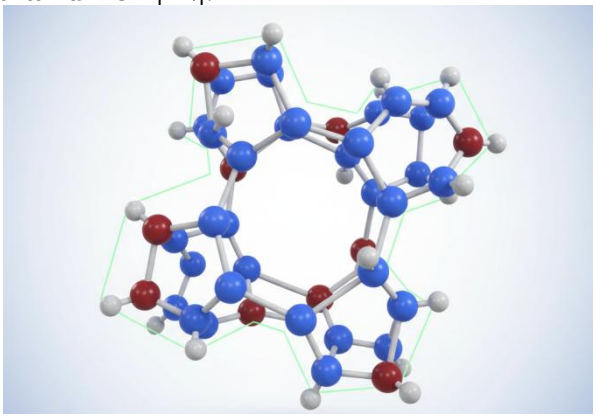

Figure 5. α-TCP structure: blue spheres: Calcium (Ca), white spheres: Phosphorus (P), red spheres: Oxygen (O)

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Major drawback in TCPs' use lies in their brittleness, which could be overcome by a combination with more ductile materials [24].

Future outlook

The field of calcium phosphate bioceramics is rapidly evolving towards multifunctional and highly customized materials designed for site-specific dental and orthopedic challenges. The future outlook centers on integrating advanced material science with biological function:

Precision Nanotechnology and Targeted Remineralization: Future efforts will concentrate on perfecting the use of nano-HA and nano-Fluorapatite **(**FAp**)**, leveraging their small size for highly efficient, biomimetic remineralization of enamel and dentin. Research is moving toward creating 'smart' dental materials, such as FAp-reinforced acrylate composites, that actively release therapeutic ions in response to local pH changes, mimicking natural defense mechanisms.

Multifunctional Composites and Bio-Doping: A key trend is the development of second-generation implants and scaffolds by integrating multiple functionalities. Ion doping (e.g., Sr^{2+} or Ce^{3+} doped FAp) is crucial for simultaneously improving osteoconductivity and imparting essential antimicrobial properties to combat post-implantation infections. Moreover, the combination of HA with novel materials like graphene oxide shows immense promise for targeted delivery of highly potent drugs, such as doxorubicin, for localized anti-cancer therapy.

Advanced Fabrication and Injectable Cements: The widespread use of additive manufacturing technologies like 3D printing will enable the creation of customized HA-based scaffolds with precisely controlled, interconnected channel microstructures, optimizing cell migration and vascularization for regeneration. For CPCs, research will continue to optimize rheological properties (flow, setting time) through sophisticated polymer additions (e.g., HPMC, PEG, chitosan) to ensure superior handling and complete sealing in endodontic procedures, without compromising their inherent biocompatibility and bioactivity.

Bioactivity and Morphological Control: Future materials will focus on accelerating the natural healing process. For instance, the modification of α-TCP with compounds like triazole, which promotes the rapid formation of a plate-like HA morphology more akin to natural bone, represents a significant step forward in developing superior bone substitutes.

Ultimately, the future of CaP bioceramics in dentistry lies in designing materials that are not merely passive replacements, but truly active therapeutic systems capable of healing, preventing disease, and enduring the demanding mechanical and chemical environment of the oral cavity.

Conclusions

Calcium phosphate (CaP) bioceramics, particularly hydroxyapatite (HA) and the tricalcium phosphates (α- and β-TCP), have cemented their indispensable role in modern restorative and regenerative dentistry. Their fundamental advantage lies in their compositional and structural similarity to natural hard tissues (enamel and bone), ensuring high biocompatibility and osteoconductivity. This review highlighted the diverse applications of HA, ranging from consumer products like toothpastes for dentin hypersensitivity and remineralization to critical roles as bioactive coatings on metallic dental implants to enhance osteointegration. While bulk HA is limited by low mechanical strength for load-bearing applications, its utility as a scaffold material for bone tissue engineering, often in polymer composites (HA/collagen, HA/chitosan), remains high due to its capacity to support cell proliferation and drug delivery. Furthermore, α-TCP and β-TCP offer tunable solubility and resorption kinetics, making them essential components in calcium phosphate cements (CPCs). α-TCP's spontaneous transformation into HA in physiological fluids is key for effective bone and root canal repair. Despite existing challenges, such as the inherent brittleness of ceramics and issues with coating uniformity, research has successfully demonstrated that chemical modification (ion doping with Ag^{+}, Zn^{2+}, Sr^{2+}) and composite formation are effective strategies to improve mechanical strength, control bioactivity, and add crucial functionalities like antimicrobial action. The ongoing focus on controlling the properties of CPCs through liquid and powder phase modification further solidifies CaP's position at the forefront of dental biomaterials research.

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Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Nanci A. Ten Cate's Oral Histology: Development, Structure, and Function. 8th ed. St. Louis (MO): Elsevier Mosby; 2017.

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2. Hart PS, Hart TC. Disorders of human dentin. Cells Tissues Organs. 2007;186(1):70-7. PubMed PMID: 17627121.
3. Biswal T, BadJena SK, Pradhan D. Sustainable biomaterials and their applications: A short review. Mater Today Proc. 2020;30(Pt 2):274-82.
4. Naderi H, Matin MM, Bahrami AR. Critical issues in tissue engineering: biomaterials, cell sources, angiogenesis, and drug delivery systems. J Biomater Appl. 2011 Jul;26(1):383-417. PubMed PMID: 21148409.
5. Sheikh Z, Najeeb S, Khurshid Z, Verma V, Rashid H, Glogauer M. Biodegradable materials for bone repair and tissue engineering applications. Materials (Basel). 2015 Sep;8(9):5744-94. PubMed PMID: 28793542.
6. Pajor K, Pajchel L, Kolmas J. Hydroxyapatite and Fluorapatite in Conservative Dentistry and Oral Implantology-A Review. Materials (Basel). 2019 Sep;12(17):2683. PubMed PMID: 31443527.
7. Przekora A. A Concise Review on Tissue Engineered Artificial Skin Grafts for Chronic Wound Treatment: Can We Reconstruct Functional Skin Tissue In Vitro? Cells. 2020 Jul;9(7):1-29. PubMed PMID: 32630147.
8. Khan AS, Aamer S, Chaudhry AA, Wong FS, Rehman IU. Synthesis and characterizations of a fluoride-releasing dental restorative material. Mater Sci Eng C Mater Biol Appl. 2013 Aug 1;33(6):3458-64. PubMed PMID: 23706233.
9. Koutsopoulos S. Synthesis and characterization of hydroxyapatite crystals: a review study on the analytical methods. J Biomed Mater Res. 2002 Dec 15;62(4):600-12. PubMed PMID: 12402315.
10. Hench LL. Sol-gel materials for bioceramic applications. Curr Opin Solid State Mater Sci. 1997 Oct;2(5):604-10.
11. Huang J, Best SM. Ceramic biomaterials. In: Boccaccini AR, Gough JE, editors. Tissue Engineering Using Ceramics and Polymers. Cambridge: Woodhead Publishing; 2007. p. 3-30.
12. Ayoub G, Veljovic D, Zebic ML, Miletic V, Palcevskis E, Petrovic R, et al. Composite nanostructured hydroxyapatite/yttrium stabilized zirconia dental inserts – The processing and application as dentin substitutes. Ceram Int. 2018 Oct 15;44(15):18200-8.
13. Cury JA, Tenuta LM. Enamel remineralization: controlling the caries disease or treating early caries lesions? Braz Oral Res. 2009;23 Suppl 1:23-30. PubMed PMID: 19838555.
14. Neel EA, Aljabo A, Strange A, Ibrahim S, Coathup M, Young AM, et al. Demineralization–remineralization dynamics in teeth and bone. Int J Nanomedicine. 2016;11:4743-63. PubMed PMID: 27785025.
15. Altaie A, Bubb N, Franklin P, German MJ, Marie A, Wood DJ. Development and characterisation of dental composites containing anisotropic fluorapatite bundles and rods. Dent Mater. 2020 Aug;36(8):1071-85. PubMed PMID: 32564971.
16. Elghazel A, Taktak R, Elleuch K, Bouaziz J. Mechanical and tribological properties of tricalcium phosphate reinforced with fluorapatite as coating for orthopedic implant. Mater Lett. 2018 Feb 15;215:53-7.
17. Barandehfard F, Kianpour Rad M, Hosseinnia A, Khoshroo K, Tahriri M, Jazayeri HE, et al. The addition of synthesized hydroxyapatite and fluorapatite nanoparticles to a glass-ionomer cement for dental restoration and its effects on mechanical properties. Ceram Int. 2016 Nov;42(15):17866-75.
18. Jmal N, Bouaziz J. Fluorapatite-glass-ceramics obtained by heat treatment of a gel synthesized by the sol-gel processing method. Mater Lett. 2018 Feb 15;215:280-3.
19. Kazuz A, Radovanović Ž, Veljović D, Kojić V, Miletić V, Petrović R, et al. α-Tricalcium phosphate/fluorapatite based composite cements: Synthesis, mechanical properties, and biocompatibility. Ceram Int. 2020 Nov;46(16):25149-54.
20. Jeong J, Kim JH, Shim JH, Hwang NS, Heo CY. Bioactive calcium phosphate materials and applications in bone regeneration. Biomater Res. 2019;23:4. PubMed PMID: 30820282.
21. Al-Sanabani JS, Madfa AA, Al-Sanabani FA. Application of Calcium Phosphate Materials in Dentistry. Int J Biomater. 2013;2013:876132. PubMed PMID: 24324552.
22. Böstman OM, Laitinen OM, Tynninen O, Salminen ST, Pihlajamäki HK. Tissue restoration after resorption of polyglycolide and poly-laevo-lactic acid screws. J Bone Joint Surg Br. 2005 Nov;87(11):1575-80. PubMed PMID: 16260682.
23. Callister WD Jr. Materials Science and Engineering: An Introduction. 5th ed. New York: John Wiley & Sons; 1999.
24. Hasirci V, Hasirci N. Fundamentals of Biomaterials. New York: Springer Nature; 2018.
25. Ruyter IE, Oeysaed H. Composites for use in posterior teeth: composition and conversion. J Biomed Mater Res. 1987 Jan;21(1):11-23. PubMed PMID: 3553203.
26. Arora M, Chan EK, Gupta S, Diwan AD. Polymethylmethacrylate bone cements and additives: A review of the literature. World J Orthop. 2013 Apr 18;4(2):67-74. PubMed PMID: 23610750.
27. Athanasiou KA, Agrawal CM, Barber FA, Burkhart SS. Orthopaedic applications for PLA-PGA biodegradable polymers. Arthroscopy. 1998 Oct;14(7):726-37. PubMed PMID: 9788366.
28. Desai S, Bidanda B, Bártolo PJ. Metallic and Ceramic Biomaterials: Current and Future Developments. In: Bártolo PJ, Bidanda B, editors. Bio-Materials and Prototyping Applications in Medicine. Berlin: Springer; 2008.
29. Williams DF. Orthopedic implants: Fundamental principles and the significance of biocompability. In: Williams DF, editor. Biocompatibility of Orthopedic Implants. Vol. 1. Boca Raton (FL): CRC Press; 1982. p. 1-50.
30. Prasad K, Bazaka O, Chua M, Rochford M, Fedrick L, Spoor J, et al. Metallic Biomaterials: Current Challenges and Opportunities. Materials (Basel). 2017 Jul;10(8):884. PubMed PMID: 28773240.
31. Lin D, Li A, Li W, Zhou S, Swain MV. Design optimization of functionally graded dental implant for bone remodeling. Compos Part B Eng. 2009 Oct;40(7):668-75.
32. Verma RP. Titanium based biomaterial for bone implants: A mini review. Mater Today Proc. 2020;26(Pt 2):3148-51.

Received*: 11-08-2025 -* ***Accepted****: 08-10-2025 -* ***Published****: 16-10-2025*

33. Le Guéhennec L, Soueidan A, Layrolle P, Amouriq Y. Surface treatments of titanium dental implants for rapid osseointegration. Dent Mater. 2007 Jul;23(7):844-54. PubMed PMID: 16904738.
34. Bowen RL. Properties of a silica-reinforced polymer for dental restorations. J Am Dent Assoc. 1963 Jan;66:57-64. PubMed PMID: 13999560.
35. Cao XQ, Vassen R, Stoever D. Ceramic materials for thermal barrier coatings. J Eur Ceram Soc. 2004 Jan;24(1):1-10.
36. Rouxel T. Mechanical Properties of Ceramics. In: Boch P, Niepce J-C, editors. Ceramic Materials: Processes, Properties and Applications. Newport Beach (CA): ISTE USA; 2007. p. 261-324.
37. Hench LL. Sol-gel materials for bioceramic applications. Curr Opin Solid State Mater Sci. 1997 Oct;2(5):604-10.
38. dos Santos V, Brandalise RN, Savaris M. Engineering of Biomaterials. Cham (CH): Springer International Publishing; 2017.
39. Mondal S, Pal U. 3D hydroxyapatite scaffold for bone regeneration and local drug delivery applications. J Drug Deliv Sci Technol. 2019 Oct;53:101131.
40. Khaskhoussi A, Calabrese L, Currò M, Ientile R, Bouaziz J, Proverbio E. Effect of the Compositions on the Biocompatibility of New Alumina–Zirconia–Titania Dental Ceramic Composites. Materials (Basel). 2020 Mar;13(6):1374. PubMed PMID: 32197440.
41. Sivaraman K, Chopra A, Narayan AI, Balakrishnan D. Is zirconia a viable alternative to titanium for oral implant? A critical review. J Prosthodont Res. 2018 Jul;62(2):121-133. PubMed PMID: 29289439.
42. Thamaraiselvi TV, Rajeswari S. Biological evaluation of bioceramic materials—a review. Trends Biomater Artif Organs. 2004;18(1):9-17.
43. Dorozhkin SV. Calcium Orthophosphates as Bioceramics: State of the Art. J Funct Biomater. 2010 Jun;1(1):22-107. PubMed PMID: 24956213.
44. Sidane D, Rammal H, Beljebbar A, Gangloff SC, Chicot D, Velard F, et al. Biocompatibility of sol-gel hydroxyapatite-titania composite and bilayer coatings. Mater Sci Eng C Mater Biol Appl. 2017 Apr 1;72:650-658. PubMed PMID: 28024647.
45. Josset Y, Oum'hamed Z, Zarrinpour A, Lorenzato M, Adnet JJ, Laurent-Maquin D. In vitro reactions of human osteoblasts in culture with zirconia and alumina ceramics. J Biomed Mater Res. 1999 Sep 15;47(4):481-93. PubMed PMID: 10497278.
46. Carvalho SM, Oliveira AAR, Lemos EMF, Pereira MM. Bioactive Glass Nanoparticles for Periodontal Regeneration and Applications in Dentistry. In: Subramani K, Ahmed W, editors. Nanobiomaterials in Clinical Dentistry. 2nd ed. Amsterdam: Elsevier Inc.; 2019. p. 351-83.
47. El-Ghannam A, Ducheyne P. Bioactive Ceramics. In: Ducheyne P, editor. Comprehensive Biomaterials II. Vol 1. Amsterdam: Elsevier Ltd.; 2017. p. 204-34.
48. Hench LL. Bioceramics: From Concept to Clinic. J Am Ceram Soc. 1991 Jul;74(7):1487-510.
49. Kaur G, Kumar V, Baino F, Mauro JC, Pickrell G, Evans I, et al. Mechanical properties of bioactive glasses, ceramics, glass-ceramics and composites: State-of-the-art review and future challenges. Mater Sci Eng C Mater Biol Appl. 2019 Nov;104:109895. PubMed PMID: 31500044.
50. Sadat-Shojai M, Khorasani MT, Jamshidi A. Hydrothermal processing of hydroxyapatite nanoparticles - A Taguchi experimental design approach. J Cryst Growth. 2012 Oct 1;361:73-84.
51. Clyne TW, Hull D. An Introduction to Composite Materials. 3rd ed. New York: Cambridge University Press; 2019.
52. Tsai SW, Hahn HT. Introduction to Composite Materials. Lancaster (PA): Technomic Publishing Company, Inc.; 1980.
53. Sideridou ID, Karabela MM, Vouvoudi EC. Physical properties of current dental nanohybrid and nanofill light-cured resin composites. Dent Mater. 2011 Jun;27(6):598-607. PubMed PMID: 21411143.
54. Beun S, Glorieux T, Devaux J, Vreven J, Leloup G. Characterization of nanofilled compared to universal and microfilled composites. Dent Mater. 2007 Jan;23(1):51-9. PubMed PMID: 16487660.
55. Meereis CTW, Münchow EA, de Oliveira da Rosa WL, da Silva AF, Piva E. Polymerization shrinkage stress of resin-based dental materials: A systematic review and meta-analyses of composition strategies. J Mech Behav Biomed Mater. 2018 Jun;82:268-281. PubMed PMID: 29547777.
56. Bacchi A, Nelson M, Pfeifer CS. Characterization of methacrylate-based composites containing thio-urethane oligomers. Dent Mater. 2016 Feb;32(2):233-9. PubMed PMID: 26608141.
57. Zhou X, Huang X, Li M, Peng X, Wang S, Zhou X, et al. Development and status of resin composite as dental restorative materials. J Appl Polym Sci. 2019 Nov;136(44):48180.
58. Aminoroaya A, Neisiany RE, Khorasani SN, Panahi P, Das O, Madry H, et al. A review of dental composites: Challenges, chemistry aspects, filler influences, and future insights. Compos Part B Eng. 2021 Apr;216:108852.
59. Vassal MF, Nunes-Pereira J, Miguel SP, Correia IJ, Silva AP. Microstructural, mechanical and biological properties of hydroxyapatite - CaZrO3 biocomposites. Ceram Int. 2019 May;45(7):8195-203.
60. Ooi CY, Hamdi M, Ramesh S. Properties of hydroxyapatite produced by annealing of bovine bone. Ceram Int. 2007 Sep;33(7):1171-7.
61. Orlovskii VP, Komlev VS, Barinov SM. Hydroxyapatite and hydroxyapatite-based ceramics. Inorg Mater. 2002 Oct;38(10):973-84.
62. Lin K, Chang J. Structure and properties of hydroxyapatite for biomedical applications. In: Mucalo M, editor. Hydroxyapatite (HA) for Biomedical Applications. Oxford: Elsevier Ltd.; 2015. p. 3-19.
63. Galindo TGP, Chai Y, Tagaya M. Hydroxyapatite Nanoparticle Coating on Polymer for Constructing Effective Biointeractive Interfaces. J Nanomater. 2019;2019:6495239.

Received*: 11-08-2025 -* ***Accepted****: 08-10-2025 -* ***Published****: 16-10-2025*

64. Wang M, Chen H, Shih W, Chang H, Hon MH, Hung IM. Crystalline size, microstructure and biocompatibility of hydroxyapatite nanopowders by hydrolysis of calcium hydrogen phosphate dehydrate (DCPD). Ceram Int. 2015 Feb;41(2):2999-3008.
65. Sakamoto K, Yamaguchi S, Nakahira A, Kaneno M, Okazaki M, Ichihara J, et al. SHA-controlled synthesis of hydroxyapatite from α-tricalcium bis(orthophosphate) in organic-aqueous binary systems. J Mater Sci. 2002 Feb;37(5):1033-41.
66. Al-Noaman A, Karpukhina N, Rawlinson SCF, Hill RG. Effect of FA on bioactivity of bioactive glass coating for titanium dental implant. Part I: Composite powder. J Non Cryst Solids. 2013 Mar;364:92-8.
67. Rey C, Combes C, Drouet C, Sfihi H. Fluoride-Based Bioceramics. In: Tressaud A, Haufe G, editors. Fluorine and Health. Amsterdam: Elsevier B.V.; 2008. p. 279-333.
68. Leroy N, Bres E. Structure and substitutions in fluorapatite. Eur Cells Mater. 2001 Jul;2:36-48. PubMed PMID: 14562283.
69. Chatzistavrou X, Papagerakis S, Ma PX, Papagerakis P. Innovative approaches to regenerate enamel and dentin. Int J Dent. 2012;2012:856470. PubMed PMID: 23251135.
70. Ghosh SS, Ghosh SS, Atta AK, Pramanik N. A succinct overview of hydroxyapatite based nanocomposite biomaterials: Fabrications, physicochemical properties and some relevant biomedical applications. J Bionanosci. 2018;12(2):143-58.
71. Fukase Y, Eanes ED, Takagi S, Chow LC, Brown WE. Setting reactions and compressive strengths of calcium phosphate cements. J Dent Res. 1990 Dec;69(12):1852-6. PubMed PMID: 2175751.
72. Kamitakahara M, Ohtsuki C, Miyazaki T. Review paper: Behavior of ceramic biomaterials derived from tricalcium phosphate in physiological condition. J Biomater Appl. 2008 Jul;23(3):197-212. PubMed PMID: 18550613.
73. Afewerki S, Bassous N, Harb S, Palo-Nieto C, Ruiz-Esparza GU, Marciano FR, et al. Advances in dual functional antimicrobial and osteoinductive biomaterials for orthopaedic applications. Nanomedicine. 2020 Feb;24:102143. PubMed PMID: 31866438.
74. Fiume E, Magnaterra G, Rahdar A, Verné E, Baino F. Hydroxyapatite for Biomedical Applications: A Short Overview. Ceramics. 2021 Dec;4(4):542-63.
75. Ridi F, Meazzini I, Castroflorio B, Bonini M, Berti D, Baglioni P. Functional calcium phosphate composites in nanomedicine. Adv Colloid Interface Sci. 2017 Nov;244:281-295. PubMed PMID: 27837959.
76. Hunter KT, Ma T. In vitro evaluation of hydroxyapatite-chitosan-gelatin composite membrane in guided tissue regeneration. J Biomed Mater Res A. 2013 Apr;101A(4):1016-25. PubMed PMID: 22961979.
77. Lin K, Zhang M, Zhai W, Qu H, Chang J. Fabrication and characterization of hydroxyapatite/wollastonite composite bioceramics with controllable properties for hard tissue repair. J Am Ceram Soc. 2011 Jan;94(1):99-105.
78. Coelho CC, Grenho L, Gomes PS, Quadros PA, Fernandes MH. Nano-hydroxyapatite in oral care cosmetics: characterization and cytotoxicity assessment. Sci Rep. 2019 Jul;9(1):11050. PubMed PMID: 31363149.
79. Kim HW, Kim HE, Knowles JC. Fluor-hydroxyapatite sol-gel coating on titanium substrate for hard tissue implants. Biomaterials. 2004 Aug;25(17):3351-8. PubMed PMID: 15020108.
80. Bose S, Tarafder S, Bandyopadhyay A. Hydroxyapatite coatings for metallic implants. In: Mucalo M, editor. Hydroxyapatite (HA) for Biomedical Applications. Cambridge: Woodhead Publishing; 2015. p. 143-57.
81. Kim HW, Kim HE, Knowles JC. Fluor-hydroxyapatite sol-gel coating on titanium substrate for hard tissue implants. Biomaterials. 2004 Aug;25(17):3351-8. PubMed PMID: 15020108.
82. Tripathi G, Basu B. A porous hydroxyapatite scaffold for bone tissue engineering: Physico-mechanical and biological evaluations. Ceram Int. 2012 Jan;38(1):341-9.
83. Leukers B, Gülkan H, Irsen SH, Milz S, Tille C, Schieker M, et al. Hydroxyapatite scaffolds for bone tissue engineering made by 3D printing. J Mater Sci Mater Med. 2005 Dec;16(12):1121-4. PubMed PMID: 16362210.
84. Curtin CM. Innovative collagen nano-hydroxyapatite scaffolds offer a highly efficient non-viral gene delivery platform for stem cell-mediated bone formation. Adv Mater. 2012 Feb;24(6):749-54. PubMed PMID: 22213333.
85. Itoh S, Kikuchi M, Koyama Y, Takakuda K, Shinomiya K, Tanaka J. Development of an artificial vertebral body using a novel biomaterial, hydroxyapatite/collagen composite. Biomaterials. 2002 Oct;23(19):3919-26. PubMed PMID: 12162326.
86. Dan Y, Liu O, Liu Y, Zhang Y, Li S, Feng X, et al. Development of Novel Biocomposite Scaffold of Chitosan-Gelatin/Nanohydroxyapatite for Potential Bone Tissue Engineering Applications. Nanoscale Res Lett. 2016 Dec;11(1):487. PubMed PMID: 27807882.
87. Sathiyavimal S, Vasantharaj S, Oscar FL, Pugazhendhi A, Subashkumar R. Biosynthesis and characterization of hydroxyapatite and its composite (hydroxyapatite-gelatin-chitosan-fibrin-bone ash) for bone tissue engineering applications. Int J Biol Macromol. 2019 Jul;129:844-852. PubMed PMID: 30851361.
88. Dubnika A, Loca D, Rudovica V, Parekh MB, Berzina-Cimdina L. Functionalized silver doped hydroxyapatite scaffolds for controlled simultaneous silver ion and drug delivery. Ceram Int. 2017 Mar;43(4):3698-705.
89. Zhang YG, Zhu YJ, Chen F, Sun TW. A novel composite scaffold comprising ultralong hydroxyapatite microtubes and chitosan: preparation and application in drug delivery. J Mater Chem B. 2017;5(22):3898-906. PubMed PMID: 32263759.
90. Sang R, Chen M, Yang Y, Li Y, Shi J, Deng Y, et al. HA@GO drug delivery vehicle with dual-stimuli-triggered drug release property and efficient synergistic therapy function against cancer. J Biomed Mater Res A. 2019 Nov;107(11):2296-2309. PubMed PMID: 31328835.
91. Caldas IP, Alves GG, Barbosa IB, Scelza P, de Noronha F, Scelza MZ. In vitro cytotoxicity of dental adhesives: A systematic review. Dent Mater. 2019 Feb;35(2):195-205. PubMed PMID: 30579638.
92. Kwon SH, Jun YK, Hong SH, Lee IS, Kim HE, Won YY. Calcium Phosphate Bioceramics with Various Porosities and Dissolution Rates. J Am Ceram Soc. 2002 Dec;85(12):3129-31.

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