Review
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Hydroxyapatite in Contemporary Dentistry: Functional Versatility, Formulation Advances, and Clinical Relevance

Ştefania Dinu [1,2], Adrian Moldoveanu [3,4], Camelia Szuhanek [5,6], Raluca Milutinovici [6,*], Diana Haj Ali [7,8] and Şerban Talpoş [9]

[1]Department of Pedodontics, Faculty of Dental Medicine, Victor Babes University of Medicine and Pharmacy, 9 No., Revolutiei 1989 Bv., 300041 Timisoara, Romania; dinu.stefania@umft.ro
[2]Pediatric Dentistry Research Center, Faculty of Dental Medicine, Victor Babes University of Medicine and Pharmacy, 9 No., Revolutiei 1989 Bv., 300041 Timisoara, Romania
[3]Doctoral School, Victor Babeş University of Medicine and Pharmacy, 300041 Timişoara, Romania; iosifadi23@yahoo.com
[4]Department of Surgery I, Victor Babeş University of Medicine and Pharmacy, 300041 Timişoara, Romania
[5]Orthodontic Research Center (ORTHO-CENTER), "Victor Babeş" University of Medicine and Pharmacy Timişoara, 300041 Timişoara, Romania; cameliaszuhanek@umft.ro
[6]Faculty of Dental Medicine, "Victor Babeş" University of Medicine and Pharmacy from Timişoara, 9 Revoluţiei 1989 Ave., 300070 Timişoara, Romania
[7]Faculty of Pharmacy, "Victor Babeş" University of Medicine and Pharmacy, 2 Eftimie Murgu Square, 300041 Timişoara, Romania; diana.haj-ali@umft.ro
[8]Research Centre for Pharmacotoxicologic Evaluations (FARMTOX), "Victor Babeş" University of Medicine and Pharmacy Timişoara, 2 Eftimie Murgu Square, 300041 Timişoara, Romania
[9]Discipline of Oral and Maxillo-Facial Surgery, Faculty of Dental Medicine, "Victor Babes" University of Medicine and Pharmacy Timisoara, Revolutiei Boulevard 9, 300041 Timisoara, Romania; talpos@yahoo.com
*email: balan.raluca@umft.ro

Abstract

1. Background/Objectives: Calcium phosphate biomaterials (CPBs), including hydroxyapatite (HA), are among the most commonly used biomaterials in dentistry due to their biocompatibility and similarity to the body's hard tissues. This review aims to highlight the clinical applications of CPBs in dentistry, focusing mainly on hydroxyapatite and its modern formulations. 2. Methods: A literature search was conducted by analyzing data published up to May 2025 in databases such as PubMed, Web of Science, and Google Scholar using keyword combinations such as "Biomaterials", "dentistry", "calcium phosphate", and "hydroxyapatite". 3. Results: The findings of this work reveal the wide clinical use of HA, including tooth remineralization, implant coating, bone grafting, and the treatment of dental hypersensitivity. Furthermore, the novel formulations of hydroxyapatite have substantially improved its therapeutic and physicochemical characteristics. 4. Conclusions: The clinical relevance of HA and its modern formulations emphasizes the need for continuous research that will contribute to further enhancement of HA's therapeutic outcomes.

Keywords: *biomaterials; dentistry; calcium phosphate; hydroxyapatite*

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1. Introduction

In dentistry, biomaterials are naturally derived or synthetic substances designed to interact with biological structures to preserve, support, improve, or replace damaged tissues such as enamel, dentin, pulp, and periodontal structures [1]. Although biomaterials have been used in dental practice since ancient times [2], significant advancements have mainly occurred in recent decades, leading to increased interest in modern dentistry due to their remarkable properties, such

as tissue repair, enhancement of functionality, regeneration, and advantageous biocompatibility [3]. Whereas both synthetic and natural biomaterials aim to restore function and facilitate healing, they differ significantly in terms of their structure, interaction with the biological environment, and clinical applications [4]. For example, natural origin biomaterials such as collagen derived from animal tissues, chitosan derived from crustaceous species, hyaluronic acid naturally occurring in human extracellular matrices, alginate extracted from brown seaweed, and autologous fibrin derived from blood are widely employed as scaffolding materials alongside their common use as components in guided tissue regeneration (GTR) membranes due to their capacity to facilitate cell recognition, adhesion, and chemotactic migration, in addition to the advantage of low immunogenicity [5]. While natural biomaterials provide many advantages, they also have some limitations, such as serial variability, quick deterioration, inferior mechanical properties, and limited processing capacity, which impede their large-scale use in clinical practice [6, 7]. Synthetic biomaterials such as calcium compounds (e.g., hydroxyapatite, alpha-tricalcium phosphate, and beta-tricalcium phosphate ceramics), bioactive glasses (e.g., silicon dioxide, calcium oxide, calcium sodium phosphosilicate), and polymer-based bone substitutes (e.g., polymethyl methacrylate, polycaprolactone) [8] exhibit a series of advantages such as biocompatibility, formability, and a lower potential of complications concerning the risk of infection. Another important advantage to consider is the broad accessibility of these materials, which is primarily due to the relatively simple manufacturing processes of some of them compared to other types of biomaterials [9]. Synthetic materials can also have disadvantages, the most important one being the lack of ability of some of these materials to induce osteogenesis, unlike those of natural origin [9, 10]. However, recent advancements in biotechnologies have substantially improved dental biomaterials through the integration of nanotechnologies and biofunctionalization approaches, thus enhancing their tissue regeneration and osseointegration properties. These new approaches aim to develop biomimetic surfaces that interact closely with biological structures, resulting in better clinical outcomes [11, 12]. This review aims to explore the relevance and uses of calcium phosphate biomaterials in dentistry, focusing mainly on hydroxyapatite and its novel formulations, briefly highlighting their therapeutic properties, biological activity, and clinical applications.

2. Materials and Methods

This review was conducted by analyzing and collecting data published up to May 2025 from peer-reviewed journals and databases, including PubMed, Web of Science, and Google Scholar, using keyword combinations such as “biomaterials”, “dentistry”, “calcium phosphate”, and “hydroxyapatite”. Articles that focused on both natural and synthetic biomaterials used in dentistry, particularly calcium phosphate and hydroxyapatite biomaterials, were selected. Articles with insufficiently detailed methodologies or confusing or conflicting results were excluded.

3. Results and Discussions

Recently, calcium phosphate biomaterials (CPBs) have gained increasing interest in dentistry given the chemical similarity of these compounds to bone and teeth and their satisfactory safety profile [13]. Evidence from the literature suggests that CPBs stimulate and promote the proliferation of osteogenic cells and the formation of chemical bonds with bone and dental structures. This process is biochemically mediated by the adsorption of osteogenesis-inducing proteins onto the surface of these materials [13, 14]. Nowadays, CPBs, particularly calcium phosphate cements (CPCs), are employed as implant coating materials, bone graft substitutes in dental augmentation procedures, structural support for tissues and regeneration, and as vehicles for drugs and growth factors [15]. Ongoing research on CPBs continues, with the aim of identifying additional functions such as antibacterial activity, the potential to induce angiogenesis, and the ability to upregulate the genes involved in osteogenic processes, as well as their impact on microRNA (miRNA) regulation and the signaling pathways responsible for mediating these effects [16]. Among the main CPBs used in dentistry are hydroxyapatite, tricalcium phosphate, calcium phosphate cements, octacalcium phosphate, and amorphous calcium phosphate [17, 18]. **Figure 1** illustrates the classification of these CPBs.

Hydroxyapatite, with the chemical formula Ca10(PO4)6(OH)2, is naturally found in the structure of bone and teeth, representing approximately 70% of the weight of bone, constituting the primary mineral phase of these tissues. From a structural point of view, bone can be considered a nanocomposite material consisting of an organic part dominated by type I collagen and an inorganic part represented by HA crystals interwoven between collagen fibers. This generates mineralized collagen, the fundamental unit of hard tissues in the body. Unlike bones, teeth do not contain collagen; instead, amelogenin and enamelin serve as a matrix for hydroxyapatite, thus contributing to the mineralization of teeth [19]. Within these structures, HA significantly contributes to mechanical strength and the mineralization process [20]. HA can originate from natural sources or can be synthetically produced. Natural sources of HA include animal and fish bones, as well as eggshells [21]. Whereas HA from natural sources offers excellent biocompatibility and satisfactory biological activity, along with the advantage of being derived from sustainable natural sources, it also presents certain limitations,

such as variability in composition and the potential presence of impurities. In contrast, synthetic HA exhibits superior mechanical strength, and its compositional consistency makes it the preferred choice in clinical applications, despite being associated with higher production costs [22].

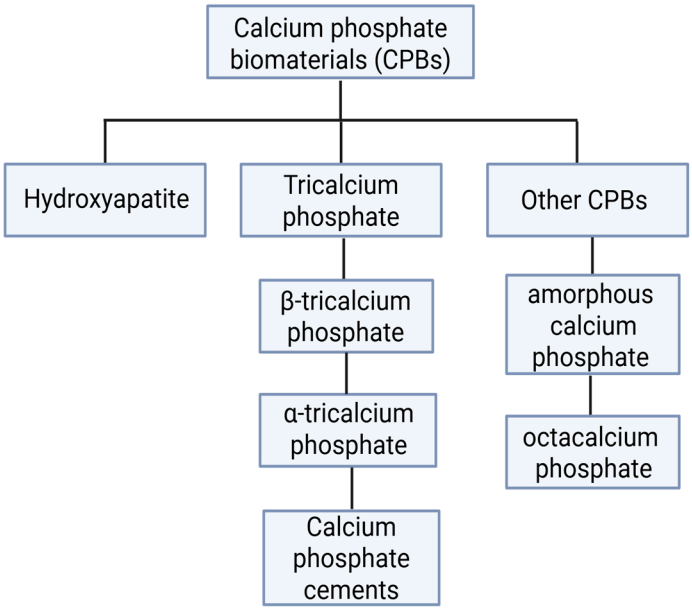

Figure 1. The main calcium phosphate biomaterials used in dentistry. This figure was created with https://BioRender.com (accessed on 15 June 2025).

Recent advances in dental biomaterial engineering have led to the design of novel hydroxyapatite formulations aimed at enhancing its therapeutic properties and minimizing its limitations. These new formulations include nanoparticles, ion-substituted formulations, and composite systems. The development of such advanced forms has significantly improved the key biological functions of hydroxyapatite, including bone remineralization, antibacterial activity, and tissue regeneration [23]. Examples of new hydroxyapatite formulations and their main therapeutic actions are mentioned in **Table 1**.

Table 1. The main hydroxyapatite formulations and their characteristics.

HA formulation	**characteristics**
Nano-hydroxyapatite (nHA)	Among the different forms of hydroxyapatite, nano-hydroxyapatite is distinguished by its wide range of applications in dental practice, notably in the remineralization of enamel. It is also applied in orthodontics for the purpose of reducing microleakage beneath orthodontic bands. Furthermore, nano-hydroxyapatite is utilized as a bone grafting in addition to its indications in implantology [24].
Fluoridated hydroxyapatite	Exhibits good penetrability into the dentinal tubules, enhances the antibacterial effect of hydroxyapatite, and contributes to the reduction in dental sensitivity [25].
Magnesium-doped hydroxyapatite	Enhances the physicochemical properties of HA and its biological activity, promoting tissue regeneration and osteoconductivity [26].
Zinc-doped hydroxyapatite	Promotes the antibacterial activity of HA and periodontal tissue regeneration [27].
Strontium-doped hydroxyapatite	Exhibits better physicochemical characteristics and improves the angiogenic and osteogenic effects of HA [28].
Silver-doped hydroxyapatite	Presents a high antibacterial effect, particularly in implant coatings [29].
Chitosan-based hydrogels combined with nHA and sodium fluoride	Presents better dentin and enamel mineralization [30].
Bioactive glass–nHA–fluoride gels	Significantly improves mechanical bone strength and dentin remineralization [31].
nHA combined with iontophoresis	Provides better delivery of nHA and prolonged effectiveness in reducing hypersensitivity [32].

Beyond all these well-established applications, hydroxyapatite in toothpaste form has been increasingly utilized for preventive purposes and as an adjuvant in managing various conditions such as dental caries, enamel and dentin demineralization, and dental hypersensitivity. Additionally, it has been explored for cosmetic purposes, including its use as a whitening agent for teeth [33].

4. Conclusions

Hydroxyapatite continues to be among the most used biomaterials in dental practice, whether for preventive purposes or for the treatment of various dental diseases and tissue replacement. This can be attributed both to its excellent biocompatibility and its similarity to biological tissues. Moreover, the emergence of new formulations of HA has significantly improved both its therapeutic performance and its physicochemical characteristics, which in turn encourages further research aimed at identifying new innovative formulations, contributing to the development of solutions to the current limitations of existing variants.

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Author contributions

Conceptualization, Ș.D. and A.M.; Software, D.H.A.; Validation, Ș.T., Writing—Original Draft Preparation, R.M. and C.S. Writing—Review and Editing, Ș.D. and C.S.; Visualization, D.H.A.; Supervision, Ș.D. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

Additional information

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