Asian Journal of Applied Science and Technology (AJAST)
Volume 10, Issue 1, Pages 37-47, January-March 2026

Hydroxyapatite from Fish Bone Waste: Synthesis, Characterization, and Multidisciplinary Applications

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DOI: https://doi.org/10.38177/ajast/2026.10103

Article Received: 11 November 2025 *Article Accepted: 15 January 2026* *Article Published: 25 January 2026*

ABSTRACT

Hydroxyapatite (HAp), $Ca_{10}(PO_4)_6(OH)_2$, is a calcium phosphate ceramic extensively used in biomedical, dental, and environmental applications due to its excellent biocompatibility, osteoconductivity, and chemical stability. In recent years, increasing attention has been directed toward biogenic hydroxyapatite derived from fish bone waste as a sustainable and biomimetic alternative to conventionally synthesized hydroxyapatite. Fish bones, a major by-product of the global seafood processing industry, are naturally rich in calcium phosphate minerals with chemical composition, crystallinity, and trace element profiles closely resembling biological apatite. This review provides a comprehensive and critical overview of hydroxyapatite derived from fish bone waste, covering raw material characteristics, synthesis and extraction strategies, physicochemical characterization techniques, biological performance, and multidisciplinary applications. Comparative discussion with synthetic hydroxyapatite is provided to highlight advantages and inherent limitations. Key challenges related to raw material variability, standardization, scalability, and clinical translation are discussed, and future research directions are proposed. The review aims to support the development of sustainable biogenic hydroxyapatite materials within the framework of waste valorization and circular economy.

Keywords: Biogenic Hydroxyapatite; Fish Bone Waste; Calcium Phosphate; Bioceramics; Biomaterials; Sustainability; Circular Economy; Waste Valorization; Bone Tissue Engineering; Environmental Remediation; Osteoconductive; Thermal Calcination.

1. Introduction

The global fisheries and aquaculture sectors have experienced rapid growth over the past decades, driven by increasing demand for protein-rich food sources. According to the Food and Agriculture Organization (FAO), global fish production exceeded 180 million tons annually, with a substantial proportion processed industrially [1]. During processing, a significant amount of solid waste is generated, accounting for approximately 30–50% of the total fish biomass. This waste mainly consists of heads, skins, viscera, scales, and bones, among which fish bones represent one of the largest fractions [2]. Fish bone waste is commonly discarded, landfilled, or utilized for low-value applications such as animal feed or organic fertilizers. Improper disposal of fish bone waste may result in environmental pollution, unpleasant odors, proliferation of pathogenic microorganisms, and contamination of soil and water bodies [3]. In the context of sustainable development and circular economy principles, there is growing interest in transforming fish bone waste into value-added products, thereby reducing environmental burden while creating economic benefits. Hydroxyapatite (HAp), with the chemical formula $Ca_{10}(PO_4)_6(OH)_2$, is the principal inorganic component of human bone and teeth. Due to its close chemical and crystallographic similarity to biological apatite, hydroxyapatite exhibits excellent biocompatibility, osteoconductivity, and bioactivity [4]. Consequently, it has been widely investigated and applied in biomedical fields, particularly as bone graft substitutes, tissue engineering scaffolds, implant coatings, and dental materials [5]. In addition to biomedical applications, hydroxyapatite has demonstrated promising potential in environmental remediation, catalysis, and adsorption-based technologies [6]. Conventional hydroxyapatite is typically synthesized using wet chemical precipitation, sol–gel processing, hydrothermal synthesis, or solid-state reactions employing high-purity chemical reagents [7]. While these methods allow good control over phase purity and stoichiometry, they often involve high production costs, significant energy consumption, and limited biomimetic characteristics. As a result, naturally derived or biogenic hydroxyapatite obtained from biological sources such as mammalian bones, coral, shells, and fish bones has attracted increasing attention [8]. Among these sources, fish bones offer several advantages. They are abundant, inexpensive, and widely available as industrial waste. Unlike mammalian bone sources, fish bones pose minimal ethical concerns and a lower risk of disease transmission [9]. Moreover, fish bone-derived hydroxyapatite inherently contains trace elements and carbonate substitutions that closely resemble biological apatite found in human bone, potentially enhancing its biological performance [10].

1.1. Study Objectives

The study objectives of this review are as follows:

(i) To evaluate the chemical and mineralogical characteristics of various fish species as natural sources for Fish bone hydroxyapatite (FB-HA), (ii) To compare different extraction and synthesis strategies, including thermal calcination, alkaline hydrolysis, and hydrothermal processing, (iii) To analyze the physicochemical properties of FB-HA using advanced characterization techniques such as X-ray diffraction (XRD) and Scanning Electron Microscopy (SEM), (iv) To assess the biological performance and biocompatibility of FB-HA in both in vitro and in vivo environments, (v) To explore the multidisciplinary applications of FB-HA in fields ranging from orthopedics and dentistry to environmental remediation and catalysis, (vi) To identify current technical and regulatory challenges and propose future directions for the sustainable development of FB-HA.

░ 2. Fish Bone Waste as a Natural Source of Hydroxyapatite

Fish bones are hierarchical biological composites composed of an organic matrix and an inorganic mineral phase. The organic component consists mainly of type I collagen and minor non-collagenous proteins, while the inorganic fraction is dominated by calcium phosphate minerals, primarily hydroxyapatite or hydroxyapatite-like phases [11]. The inorganic content of fish bones typically accounts for 60–70 wt.% of the dry mass, although this value can vary depending on species, age, and environmental conditions [12]. The Ca/P molar ratio of fish bone-derived hydroxyapatite generally ranges between 1.60 and 1.72, which is close to the stoichiometric value of hydroxyapatite (1.67) and comparable to natural human bone mineral [13]. This compositional similarity is one of the key factors underlying the excellent biocompatibility of biogenic hydroxyapatite.

2.1. Species-Dependent Variability

The chemical and mineralogical composition of fish bones is strongly influenced by fish species, habitat (marine or freshwater), diet, and physiological conditions. Marine fish bones often contain higher levels of trace elements such as magnesium (Mg), sodium (Na), strontium (Sr), potassium (K), and zinc (Zn) compared to freshwater fish [14]. These trace elements are known to play important roles in bone metabolism, mineralization, and cellular signaling pathways. Strontium, for example, has been reported to stimulate osteoblast activity while inhibiting osteoclast-mediated bone resorption, thereby enhancing bone formation [15]. Magnesium is involved in regulating crystal size and lattice disorder in biological apatite and has been shown to influence cell adhesion and proliferation [16]. The presence of these elements in fish bone-derived hydroxyapatite may contribute to improved biological performance compared to stoichiometric synthetic hydroxyapatite.

2.2. Carbonate Substitution and Biological Apatite

Another distinctive feature of fish bone-derived hydroxyapatite is the presence of carbonate substitution within the apatite lattice. Carbonate ions can replace either hydroxyl groups (A-type substitution) or phosphate groups (B-type substitution), or both, leading to carbonated apatite structures [17]. Fish bone-derived hydroxyapatite predominantly exhibits B-type or mixed A/B-type carbonate substitution, similar to biological apatite in human bone. Carbonate substitution results in lower crystallinity, increased lattice strain, and higher solubility compared to stoichiometric hydroxyapatite [18]. These characteristics are considered advantageous for bone regeneration, as they facilitate controlled dissolution and reprecipitation during bone remodeling processes.

░3. Synthesis and Extraction of Hydroxyapatite from Fish Bone Waste

The extraction of hydroxyapatite from fish bone waste primarily aims to remove organic components while preserving or tailoring the inorganic mineral phase. Several synthesis and extraction methods have been reported, each offering distinct advantages and limitations.

3.1. Pretreatment of Fish Bones

Prior to hydroxyapatite extraction, fish bones typically undergo pretreatment steps such as washing, boiling, solvent extraction, or enzymatic treatment to remove residual flesh, lipids, and proteins [19]. Effective pretreatment is crucial for achieving high purity and reproducibility in the final hydroxyapatite product.

3.2. Thermal Calcination

Thermal calcination is the most widely employed method for producing hydroxyapatite from fish bones. In this approach, pretreated fish bones are heated at temperatures ranging from 600 to 900 °C in air to decompose organic matter and obtain hydroxyapatite-rich powders [20]. Calcination at lower temperatures (600–700 °C) generally yields hydroxyapatite with lower crystallinity and smaller crystallite size, while higher temperatures (>800 °C) increase crystallinity but may lead to grain growth and partial phase transformation into tricalcium phosphate [21]. The main advantages of calcination include simplicity, scalability, and the ability to produce phase-pure hydroxyapatite. However, high energy consumption and limited control over particle morphology remain significant drawbacks.

3.3. Alkaline Hydrolysis

Alkaline hydrolysis involves treating fish bones with strong alkaline solutions such as sodium hydroxide (NaOH) or potassium hydroxide (KOH) to remove organic matter at relatively low temperatures [22]. This method can produce nano-sized hydroxyapatite with high surface area and low crystallinity, which are advantageous for biomedical applications. However, extensive washing is required to remove residual alkali ions, and improper control may introduce lattice defects.

3.4. Hydrothermal and Combined Chemical–Thermal Methods

Schematic illustration of synthesis routes for hydroxyapatite derived from fish bone waste is presented in Figure 1. The diagram presents the comprehensive workflow from raw fish bone waste through mandatory pretreatment steps (washing, drying, defatting, and milling) to three distinct synthesis pathways: calcination (800–1000 °C), alkaline hydrolysis (NaOH treatment at 80-100 °C), and hydrothermal processing (high pressure) to produce the final biogenic HAp powders for characterization. Hydrothermal treatment enables controlled recrystallization of hydroxyapatite under elevated temperature and pressure, allowing fine control over particle size, morphology, and crystallinity [23]. Combined chemical–thermal methods, which integrate alkaline treatment with subsequent calcination, have also been reported to optimize purity and microstructure. Although these approaches yield high-quality hydroxyapatite, their complexity and cost may limit large-scale industrial application.

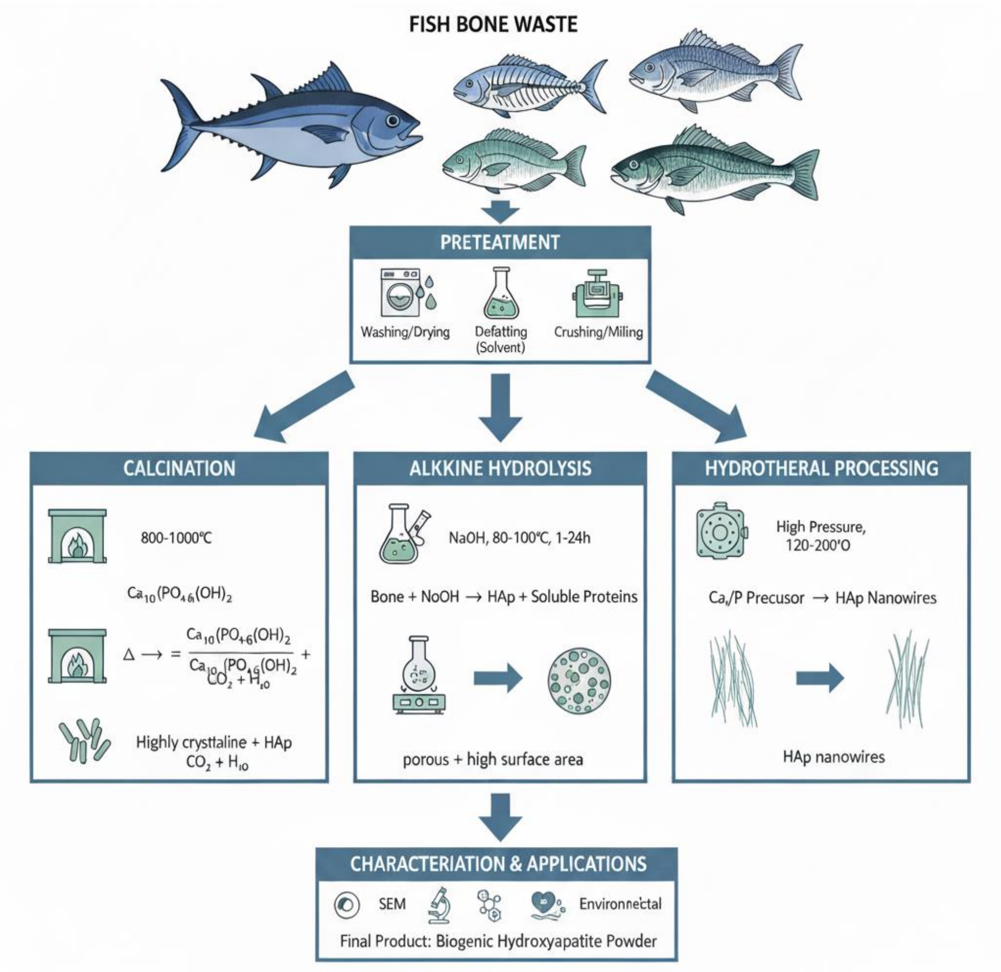

Figure 1. Schematic illustration of synthesis routes for hydroxyapatite derived from fish bone waste, including pretreatment, calcination, alkaline hydrolysis, and hydrothermal processing.
This image was constructed based on references [20-23].

4. Physicochemical Characterization

Figure 2 represents XRD patterns, FTIR spectra, and SEM images of biogenic hydroxyapatite compared with synthetic hydroxyapatite. Comprehensive physicochemical characterization is essential to understand the structure–property relationships of fish bone-derived hydroxyapatite and to evaluate its suitability for various applications. X-ray diffraction (XRD) is the most commonly used technique to identify crystalline phases and assess crystallinity. Fish bone-derived hydroxyapatite typically exhibits diffraction peaks corresponding to hexagonal apatite, although peak broadening indicates lower crystallinity compared to synthetic hydroxyapatite [24]. Fourier transform infrared spectroscopy (FTIR) and Raman spectroscopy are widely used to identify functional groups and lattice substitutions. Characteristic phosphate and hydroxyl bands confirm the formation of hydroxyapatite, while carbonate bands indicate biological apatite characteristics [25].

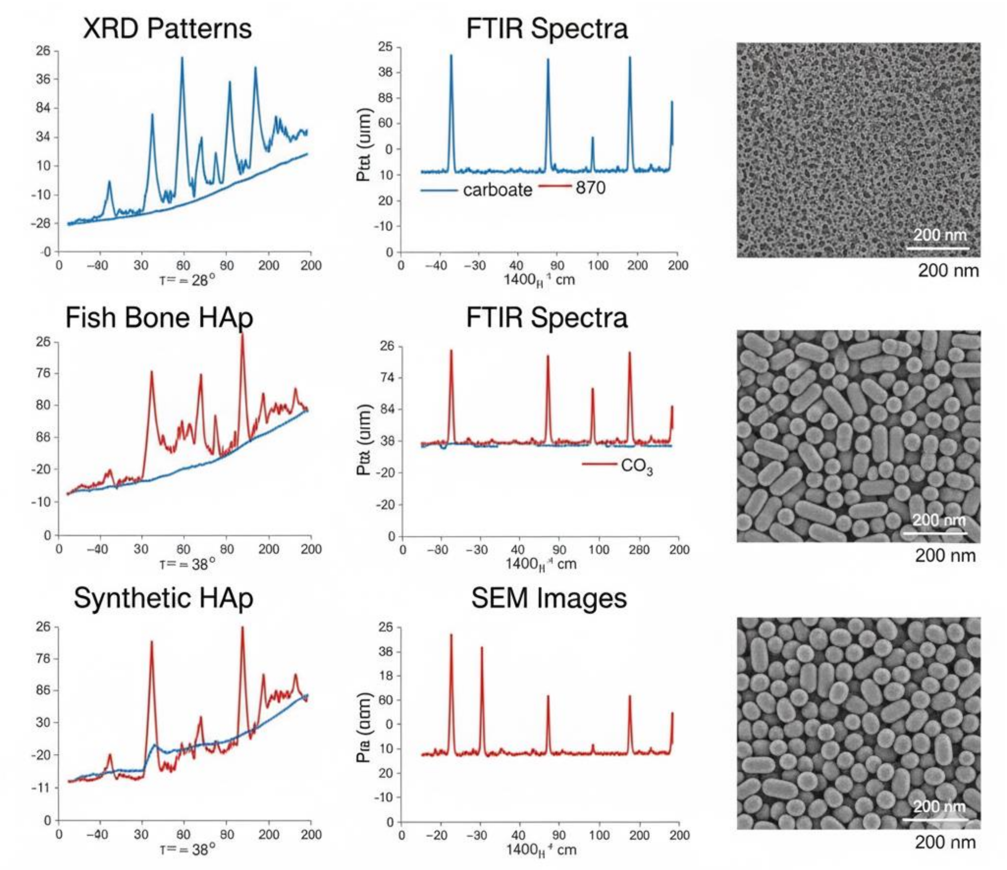

Figure 2. Representative XRD patterns, FTIR spectra, and SEM images of fish bone-derived hydroxyapatite compared with synthetic hydroxyapatite. This image was constructed based on references [15-26].

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) reveal irregular, plate-like, or rod-like morphologies with nano- to micro-scale dimensions. Brunauer–Emmett–Teller (BET) analysis often shows higher specific surface area compared to highly crystalline synthetic hydroxyapatite, which is beneficial for biological and adsorption applications [26].

5. Biological Properties and Biocompatibility of Fish Bone-Derived Hydroxyapatite

The biological performance of hydroxyapatite materials is a critical determinant for their successful application in biomedical fields, particularly in bone regeneration, dental restoration, and implantology. Fish bone-derived hydroxyapatite (FB-HAp) has attracted increasing attention due to its intrinsic biomimetic characteristics, including chemical composition, trace element incorporation, and carbonate substitution, which closely resemble natural bone mineral.

5.1. In Vitro Biocompatibility

Numerous in vitro studies have demonstrated that FB-HAp exhibits excellent cytocompatibility with various cell types, including osteoblasts, mesenchymal stem cells (MSCs), and fibroblasts. Cell viability assays such as MTT, Alamar Blue, and Live/Dead staining consistently show high cell survival rates when cultured on FB-HAp powders, coatings, or scaffolds [27]. Compared to stoichiometric synthetic hydroxyapatite, FB-HAp often promotes enhanced cell adhesion and proliferation. This improvement is attributed to its lower crystallinity, higher surface roughness, and the presence of biologically relevant trace elements such as Mg^{2+}, Sr^{2+}, and Zn^{2+} [28]. These elements are known to modulate integrin-mediated cell attachment and intracellular signaling pathways involved in osteogenesis.

5.2. Osteogenic Differentiation and Bioactivity

Beyond basic cytocompatibility, the ability of FB-HAp to stimulate osteogenic differentiation is of particular interest. Studies have reported increased alkaline phosphatase (ALP) activity, enhanced expression of osteogenic markers (e.g., RUNX2, osteocalcin, osteopontin), and accelerated mineralized nodule formation in cells cultured on FB-HAp compared to synthetic counterparts [29]. The bioactivity of FB-HAp is often evaluated using simulated body fluid (SBF) immersion tests. Rapid formation of apatite layers on the surface of FB-HAp indicates strong bioactive behavior, which is closely associated with its carbonate content and surface chemistry [30]. Such behavior is favorable for bone–implant integration.

5.3. In Vivo Performance

Although fewer in number compared to in vitro studies, in vivo investigations have provided encouraging evidence for the osteoconductivity and biocompatibility of FB-HAp. Animal studies using rat calvarial defects, rabbit femoral defects, and canine models have shown that FB-HAp supports new bone formation without inducing inflammatory or immunogenic responses [31]. Compared with synthetic hydroxyapatite, FB-HAp has been reported to exhibit faster resorption rates and more active remodeling, which may be advantageous for applications requiring gradual replacement by natural bone tissue. However, excessive resorption may compromise mechanical stability, highlighting the need for controlled microstructural design.

░ 6. Multidisciplinary Applications of Fish Bone-Derived Hydroxyapatite

While biomedical applications represent the primary focus of FB-HAp research, its unique physicochemical properties have enabled its use across multiple disciplines, including dentistry, environmental remediation, catalysis, and composite materials.

6.1. Bone Tissue Engineering and Orthopedics

FB-HAp has been extensively explored as a bone graft substitute and scaffold material. It can be processed into powders, granules, porous scaffolds, and composite systems with polymers such as collagen, chitosan, gelatin, and poly(lactic acid) (PLA) [32]. Porous FB-HAp scaffolds fabricated via freeze-drying, foam replication, or additive manufacturing exhibit interconnected porosity conducive to cell infiltration and vascularization. The biomimetic composition of FB-HAp enhances osteoconduction and supports bone regeneration, making it suitable for non-load-bearing and moderate load-bearing applications.

6.2. Dental Applications

In dentistry, hydroxyapatite is widely used in toothpastes, remineralization agents, and dental fillers. FB-HAp, due to its nano-scale features and chemical similarity to enamel apatite, has demonstrated potential for enamel remineralization and dentin hypersensitivity treatment [33]. Moreover, FB-HAp coatings on dental implants have been shown to improve osseointegration and reduce healing time. The presence of trace elements may further enhance antibacterial activity, although this aspect requires more systematic investigation.

6.3. Environmental Remediation

Beyond biomedical uses, FB-HAp has gained attention as an environmentally friendly adsorbent for the removal of heavy metals, dyes, and radioactive ions from wastewater. Its high surface area, ion-exchange capability, and chemical stability make it effective for adsorbing ions such as Pb^{2+}, Cd^{2+}, Sr^{2+}, and UO$_2^{2+}$ [34]. Compared to synthetic hydroxyapatite, FB-HAp offers lower production costs and improved sustainability, aligning with circular economy principles. Studies have shown that FB-HAp can achieve comparable or superior adsorption capacities, particularly due to its defect-rich structure and surface heterogeneity.

6.4. Catalysis and Functional Materials

Figure 3 overviews of the multidisciplinary applications of fish bone-derived hydroxyapatite across various sectors. This schematic categorizes the extensive utility of FB-HA into four primary fields: Biomedical (bone tissue engineering, drug and gene delivery), Dental (enamel remineralization, fillers, and coatings), Environmental (heavy metal adsorption and pollutant removal), and Catalytic (biodiesel production and organic reaction support). FB-HAp has also been investigated as a catalyst or catalyst support in various chemical reactions, including dehydrogenation, oxidation, and transesterification processes [35]. The presence of lattice defects and trace elements can modify surface acidity/basicity, enhancing catalytic performance. Additionally, FB-HAp has been incorporated into polymer matrices to produce bio-composites with improved mechanical strength, thermal stability, and bioactivity. Such composites are promising for both biomedical implants and eco-friendly packaging materials.

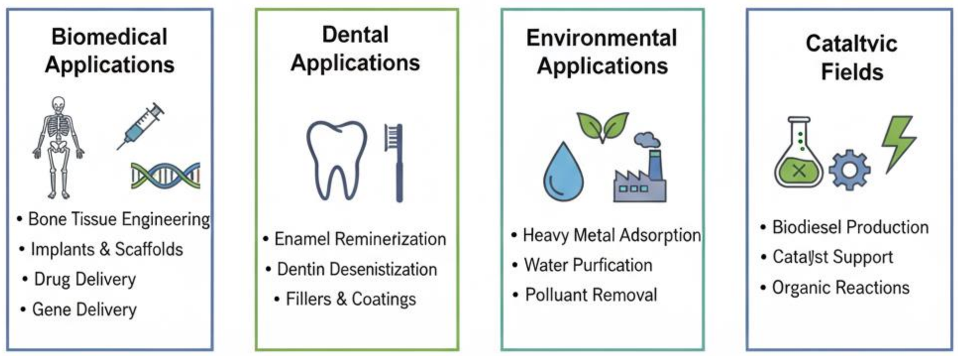

Figure 3. Overview of multidisciplinary applications of fish bone-derived hydroxyapatite in biomedical, dental, environmental, and catalytic fields. This image was constructed based on references [31-35].

7. Challenges and Future Perspectives

Despite significant progress, several challenges must be addressed to enable the large-scale and clinical translation of FB-HAp.

7.1. Raw Material Variability and Standardization

One of the primary challenges lies in the inherent variability of fish bone waste. Differences in species, age, habitat, and processing conditions result in variations in chemical composition, trace element content, and crystallinity. This variability complicates standardization and reproducibility, which are essential for regulatory approval and clinical use [36]. Developing standardized pretreatment and processing protocols, as well as robust quality control methods, will be crucial for ensuring consistent material properties.

7.2. Scalability and Energy Consumption

Although calcination-based methods are scalable, they are energy-intensive. Alternative low-temperature or hybrid methods may reduce energy consumption but often involve chemical reagents that introduce additional costs and environmental concerns. Life cycle assessment (LCA) studies are needed to evaluate the true sustainability of different synthesis routes.

7.3. Mechanical Limitations

Like conventional hydroxyapatite, FB-HAp is inherently brittle and exhibits limited mechanical strength. This restricts its use in load-bearing applications unless combined with reinforcing phases or polymer matrices. Advanced composite designs and hierarchical structuring strategies may help overcome these limitations.

7.4. Regulatory and Clinical Translation

The clinical translation of FB-HAp requires extensive preclinical and clinical evaluation to ensure safety, efficacy, and long-term performance. Regulatory pathways for biogenic materials derived from waste sources may be more complex than those for synthetic materials, necessitating clear documentation of processing, purity, and traceability.

8. Conclusion

Fish bone-derived hydroxyapatite represents a promising class of biogenic materials that combine excellent biological performance with sustainability and waste valorization benefits. Owing to its chemical similarity to natural bone mineral, incorporation of biologically relevant trace elements, and inherent carbonate substitution, FB-HAp often exhibits enhanced bioactivity and osteoconductivity compared to stoichiometric synthetic hydroxyapatite. This review has provided a comprehensive overview of fish bone waste as a natural source of hydroxyapatite, covering synthesis and extraction strategies, physicochemical characterization, biological properties, and multidisciplinary applications. While significant challenges remain in terms of standardization, scalability, and regulatory approval, continued advances in processing technologies and material design are expected to further expand the application potential of FB-HAp. In the context of circular economy and sustainable materials development, the conversion of fish bone waste into high-value hydroxyapatite-based products offers a compelling pathway toward environmentally responsible and clinically effective biomaterials.

Future suggestions are that: (i) Establish standardized pretreatment and quality control protocols to ensure consistency across different fish species, (ii) Conduct detailed Life Cycle Assessment (LCA) studies to evaluate and minimize the energy consumption of large-scale synthesis, (iii) Develop advanced bio-composites by incorporating FB-HAp into polymer matrices to improve mechanical strength for load-bearing implants, (iv) Systematically investigate the antibacterial potential of trace elements naturally found in FB-HAp for dental applications, (v) Streamline regulatory pathways by providing clear documentation on processing purity and traceability for clinical translation, (vi) Explore the use of FB-HAp in 3D printing and additive manufacturing to create patient-specific scaffolds with interconnected porosity.

Declarations

Source of Funding

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Competing Interests Statement

The author declares that he/she has no competing interests related to this work.

Consent for publication

The author declares that he/she consented to the publication of this study.

Authors' contributions

Author’s independent contribution.

Institutional Review Board Statement

Not applicable for this study.

Informed Consent

Not applicable for this study.

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