



## **Bovine Bone Waste-Extracted Hydroxyapatite for Bone Regeneration: A Critical Review of Conversion Strategies and Translational Potential**

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### **Abstract:**

*The bone regenerative material, Hydroxyapatite (HAp) is the most important and basic mineral component of teeth and bonesegment of bone. It has been well vertebrates' due to its chemical and crystallographic structure resemblance to recognize that HAp nanoparticles can considerably increase the bioas of the inorganic ctivity and biocompatibility of biomaterials used for different therapeutical applications. Hence, HAp has been progressively in demand and many struggles have been made to generate many routes, including economically and scientifically new features. Many reviews articles have been published on the preparation of HAp by inorganic chemical routes. This study is the first and distinctive in presenting various methodologies of conversion of bovine bone wastes into the valuable bone regenerative material. HAp extraction from bovine bone waste is the main focus of this literature review. The purpose of this present review is to summarize and highlight all relevant literature about extraction of HAp from bovine bone, compare the physiochemical properties of each extraction method and advantages and disadvantages involved in each extraction method. By applying different extraction methodologies the properties of natural HAp can be diverse. Though, many procedures have been used to extract natural HAp for investigation, examination, and application, still slight devotion is necessary to explore the effect of various parameters on the crystallinity, size and shape of the HAp powder extracted from bovine bone waste.*



**Keywords:** *bovine bone waste, hydroxyapatite, bone regeneration, biogenic biomaterials, tissue engineering, waste valorization*

## **Introduction**

The management of important bone losses is a complicated issue since the optimal graft material should possess osteoconduction, biocompatibility, appropriate porosity, mechanical, and resorption barriers, as well as realistic availability. Hydroxyapatite (HAp), the primary mineral phase of bone has remained a popular focus of studies because of its high chemical similarity to native bone tissue and because it is compatible with osteogenic cells. Recent research has verified the primary place of HAp-based biomaterials in the field of bone tissue engineering today, especially in the presence of polymers, collagen, bioactive ions, or additive manufacturing methods (Ielo et al., 2022; Amiryaghoubi and Esfahlan, 2024; Liu et al., 2025).

The bovine bone is one of the most natural sources since it is available in abundance, very cheap and its structure is similar to that of the mineral phase of the human bone. Another important biomimetic capability of hydroxyapatite (HAp) that is extracted out of bovine bone is its ability to retain carbonate substitution and trace elements (Mg, Na, Zn, Sr) that could modulate cell behavior, mineralization and remodeling. Such a strategy is also manifested in the published work of the author, starting with the extraction of hydroxyapatite in bovine bones in the natural manner and ending with the comparison of the calcification temperature and the characterization of carbonates (Bano et al., 2017; Bano et al., 2019a; Bano et al., 2019b; Bano et al., 2020). The recent reviews of Adhikara et al. (2024) and Okpe et al. (2024) and the research dedicated to the applications by de Carvalho et al. (2024) and Ratnayake et al. (2024) suggest that bovine HAp has already stepped out of the circle of simple extraction research and has shifted to scaffold functionalization, surface modification,

Previous literature mainly focused on extraction procedures. This study prioritizes work from the last decade (2016-2025), concentrates on HAp extracted from cattle rather than non-bovine biogenic apatites in general, and addresses the subject from the perspective of the properties and performance of the process, in relation to bone regeneration and translational research on biomaterials (Londoño-Restrepo et al., 2016; Adhikara et al., 2024; Okpe et al., 2024).

## **Materials and Methods**

In this review, the literature on bovine bone waste as a source of hydroxyapatite (HAp) to be used in bone regeneration was identified by using a structured narrative approach. Database searches and publisher websites were used to identify the literature with a combination of the following terms: bovine bone hydroxyapatite, bovine HAp, calcification, hydrothermal, subcritical water, bone regeneration, scaffold, composite, fluoride-substituted, and silicate-substituted. The review has favored the literature published in 2016 to 2025 because this time frame presents the shift between the literature concerned with extraction to the literature concerned with biologically evaluated and application-oriented biomaterials.

Studies were comprised if they specifically addressed bovine bone as a precursor to hydroxyapatite or bovine bone mineral and reported at least one of the following: extraction or conversion method, physicochemical characterization, biological evaluation, ionic modification, scaffold or composite fabrication, or translational relevance to bone repair or regenerative dentistry. Non-bovine source articles were excluded unless they were recent reviews that provided broader context for hydroxyapatite-based biomaterials. Duplicate reports

and sources lacking sufficient methodological detail or of uncertain relevance to bone regeneration applications were not included.

Information regarding the manufacturing process, thermal window, phase purity, carbonate retention, Ca/P ratio, trace ion preservation, porosity, microstructure, and biological or translational outcomes was extracted qualitatively. Given the heterogeneity of the literature in terms of design, outcome measurements, and report quality, this article prioritizes a critical narrative synthesis over a formal meta-analysis. The analysis therefore focuses on process-property-performance relationships and the factors most relevant to biosafety, osteoconductive behavior, and future clinical applications.

## **Discussion**

The discussion underneath interprets the reviewed literature by correlating the regeneration strategy with material chemistry, regenerative relevance and microstructure. Instead of treating bovine bone extracted HAp as a type of material, evidence suggests that biological performance is dependent on how processing conditions shape, carbonate substitution, phase composition, porosity, trace-ion retention and the probability of incorporation into composite systems and engineered scaffolds.

### **Why Bovine Bone Extracted HAp Is Biologically Attractive**

The apatite that is mined in the bone of bovines is not only valuable in terms of economics but also biologically. Synthetic apatite is sometimes monophasic and reproducible but tends to be stoichiometric and biologically less complex than bone mineral. By contrast, naturally obtained apatite is a closer match to the chemistry of living bone and may have a multi-scale porous structure, which is conducive to cell penetration, diffusion of nutrients and vascularization. Even in current literature, this biomimicry is still viewed as a significant rationale behind the use of apatites derived out of animal bone in regenerative biomaterials (Adhikara et al., 2024; Okpe et al., 2024; Liu et al., 2025).

Another important factor is sustainability. The idea of converting the waste of slaughterhouses into a medical grade biomaterial is a perfect fit with the existing trend towards the circular bio economy and valorization of waste. Both Okpe et al. (2024) and Liu et al. (2025) propose that hydroxyapatite (HAp) obtained using biowaste needs to be considered not only as a physicochemically similar substance to bone, but also as a more sustainable process, its impact on the environment, and its integration into the innovative manufacturing methods. This view is especially applicable to those scientific journals whose focus is biological in nature since such journals provide a connection between the processing of animal waste and the health of the people, as well as biotechnology and translational biomaterials.

However, “natural” does not automatically mean “better.” Biological origin introduces variability from batch to batch, the potential presence of organic residues, and the requirement for rigorous deproteinization and pathogen inactivation. Subsequently, the question is no longer whether bovine bone can produce HAp, but rather which processing method achieves the best compromise between purity, structural integrity, ionic retention, and biological performance.

### **Conversion Approaches and Process–Property Relationships**

Current literature classifies bovine bone conversion methods into five practical categories: direct calcination; hydrothermal or subcritical water treatment; chemical deproteinization/degreasing followed by heat treatment; post-extraction ion substitution; and integration into scaffolds/composites. These processes differ not only in their ease of implementation; they induce distinct profiles of crystallinity, surface chemistry, porosity, and

degradation—all biologically important parameters.

Direct calcination is the least complicated since it is simple to apply, comparatively cheap, and useful in eliminating the organic fraction. The classic work of Londoño-Restrepo et al. (2016) has indicated that the slow furnace heating rates and controlled cooling maintain a well-defined structure of apatite and the more recent article by Irfa'i et al. (2024) has shown that the use of 900 °C in the form of 5 to 6 h calcining bovine bone waste produces a high-quality nanoc. The same processing principle is observed in the works by the author, which created a correlation between the calcination temperature and the changes in the crystallinity, the size of the crystallites, functional groups, and the ratio of Ca/P in HAP recovered out of the bovine bones (Bano et al., 2017; Bano et al., 2019a; Bano et al., 2019b). All these studies indicate that the end product is extremely sensitive to temperature, holding time, heating rate, and size of the sample. These variables also have a strong effect on crystallinity, growth of grain, loss of carbonate, and formation of secondary calcium phosphate phases during high temperatures. This is the main limitation. Large-scale conversion is however best done by calcination, but the process must be carefully optimized in cases where the biologically relevant structural properties are required, as opposed to simply achieving a highly crystalline powder of ceramics.

Hydrothermal and subcritical water treatment is of interest, as it positively affects the reduction of using aggressive organic solvents and maintains carbonate substitution and generates finer microstructures. Recent synthesis Studies indicate that aqueous methods are more likely to enhance the formation of carbonate apatite, which is more like bone apatite, compared to intensive heat treatments only (Adhikara et al., 2024; Okpe et al., 2024). This method is verified by the works of the author on the bovine bone, where after the hydrothermal treatment, the bone was calcinated, which produced biologically relevant bovine apatite without any heavy treatment (Bano et al., 2017; Bano et al., 2019a; Bano et al., 2019d). Overall, these reactions prefer smaller crystals, increased surface activity, and ionic chemistry more compatible with biological conditions, but usually necessitate pressure vessels and extensive post-reaction drying/ calcinating. In the case of the desired application scaffold mineralization or ion-release osteogenesis, such low-temperature procedures can be more favorable than bare-knuckle sintering.

Chemical treatment followed by heat treatment remains widely used to effectively remove fats, collagen residues, and marrow deposits prior to calcination. However, recent publications increasingly question the sustainability of protocols heavily reliant on sodium hydroxide, hypochlorite, acetone, or other solvents. The issue extends beyond environmental safety; aggressive chemical treatment can also alter surface chemistry and potentially reduce the biological benefits associated with naturally extracted apatite. Therefore, recent studies by Okpe et al., 2024; Liu et al., 2025 recommend more environmentally friendly processes or hybrid protocols that minimize the use of hazardous reagents while maintaining biosecurity

A more recent approach involves post-extraction ion substitution. Ratnayake et al. (2024) used a modified sol-gel process to generate a porous, fluoride-substituted bovine apatite scaffold. This modified scaffold retained the porous architecture of bovine HAP while exhibiting improved yield strength, Young's modulus, and osteogenic markers, such as alkaline phosphatase activity. In 2025, the same research team extended this concept to silicate substitution, demonstrating how ion engineering can modulate biological signaling and regenerative potential without sacrificing the advantages of bovine bone as a basic mineral source (Ratnayake et al., 2025). These studies are important because they are shifting bovine HAP from the status of a "natural substitute" to that of a "designed bioactive platform."

Lastly, insertion into composites and structured scaffolds is also one of the most promising

directions of translational studies. Pinteala et al. (2024) also used cellulose-collagen matrices with the addition of hydroxyapatite and bovine bone mineral and found better performance of osteogenesis. Certainly, more general literature on scaffolds also indicates that the combination of HAp and natural or synthetic polymers enhances handling, toughness, printability, and biological functionality (Amiryaghoubi and Esfahlan, 2024; Liu et al., 2025). The given direction also aligns with the research by an author on a biogenic PLA/nano-HAp nanobiocomposite, which showed that bovine-derived nano-HAp may be incorporated in a polymer matrix with quantifiable physico-mechanical properties (Bano et al., 2019c). Thereby, the present research interest does not lie in self-isolated HAP powder, but in hierarchical structures in which the bovine-derived mineral is a single phase of a biologically targeted scaffold. To draw comparisons among the key conversion pathways of bovine bone-derived HAP enumerated above, key literature, processing procedures, findings made, and implications on the same have been encapsulated in Table 1.

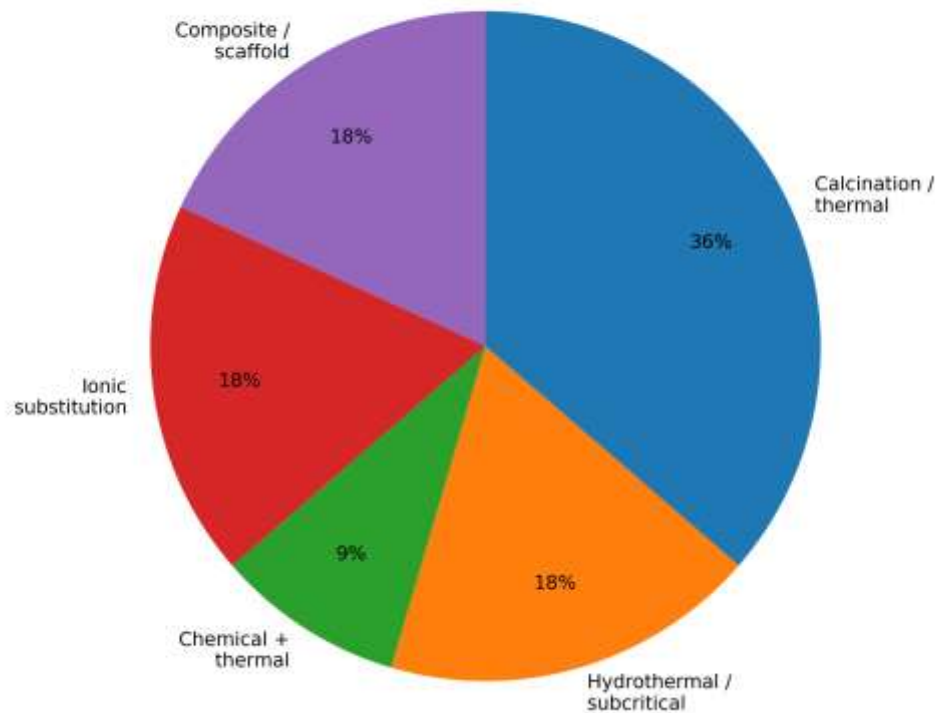
**Table 1. Selected studies from the last decade (2016-2025) on the processing of HAP extracted from bovine bones and the relationships between the process and the properties.**

Study	Processing approach	Characteristic material outcomes	Significance
Londoño-Restrepo et al. (2016)	Low-heating calcination with furnace cooling	Controlled heating preserved apatite structure and highlighted the sensitivity of bovine HAp to thermal history.	Foundational evidence that phase quality in natural HAp depends strongly on processing, not only source material.
Bano et al. (2017)	Hydrothermal pretreatment followed by calcination at different temperatures	Natural bovine HAp was obtained with temperature-dependent changes in morphology, functional groups, and Ca/P ratio.	Important early evidence from the author that bovine bone waste can yield biologically relevant HAp through a relatively simple conversion route.
de Carvalho et al. (2019)	Chemical deproteinization followed by sintering	Sintering changed microstructure and altered in vivo biological behavior.	Directly links thermal processing to regenerative performance rather than to physicochemical characterization alone.
Bano et al. (2019a)	Hydrothermal processing plus comparative calcination-temperature study	Thermally stable, highly crystalline biological apatite with calcination-dependent crystallite size was obtained from cow bone.	Adds the author's comparative evidence that thermal window selection directly affects phase quality and microstructural outcomes.

Study	Processing approach	Characteristic material outcomes	Significance
Bano et al. (2019b)	Green calcination-based extraction without chemical solvents	Nanocrystalline bovine HAp with hexagonal rod-like morphology was produced, and crystallinity increased as calcination temperature rose.	Strengthens the case for low-chemical, waste-to-biomaterial processing that fits sustainability-oriented journal framing.
Irfa'i et al. (2024)	Direct calcination of bovine bone waste at 900 °C	Five to six hours produced high-purity nanocrystalline HAp precursor with grain-size evolution over time.	Supports a simple and potentially scalable waste-to-HAp route for biomedical feedstock production.
Ratnayake et al. (2024)	Sol-gel fluoride substitution of porous bovine HAp	Porous scaffold architecture (~200-600 µm pores) was retained while mechanical and cell-response metrics improved.	Demonstrates that post-extraction ionic tuning can strengthen both structure and biological performance.
Diansari et al. (2025)	Calcination-temperature optimization for dental use	Bovine HAp showed application-relevant crystallinity and composition across a controlled thermal window.	Useful for dentistry-focused translation and for aligning bovine HAp characterization with application needs.
Ratnayake et al. (2025)	Silicate substitution of bovine-extracted HAp	Interconnected porosity and a Ca/P ratio in the biologically relevant range were maintained after silicon incorporation.	Shows how defect-specific chemical tailoring can push bovine HAp toward regenerative dentistry applications.

The relative distribution of selected studies according to the main conversion pathways of HAp extracted from bovine bone discussed in this review is summarized in Figure 1.

Representative process distribution in the review (n = 11)



**Figure 1.** Distribution of particular studies according to the main method of conversion of hydroxyapatite extracted from bovine bones debated in this review, including calcination/heat treatment, hydrothermal/subcritical treatment, chemical treatment followed by heat treatment, ion substitution and integration into composites/scaffolds

As presented in Figure 1, calcination treatment remains the most frequently reported approach among the selected studies, due to its ease of implementation and large-scale adaptability. In contrast, ion substitution and the integration of composites/scaffolds represent more recent but increasingly important avenues, as they allow us to move from simple extraction of bovine HAP to the design of biomaterials tailored to biological and application-specific needs.

### **Critical Characterization Parameters for Naturally Evocative Bovine HAp**

A frequent weakness in the literature is the hypothesis that effective extraction is confirmed as soon as HAp peaks are detected by X-ray diffraction. As a matter of fact, a bone regeneration material must be characterized as a biological interface, not simply as a ceramic powder. For HAp extracted from cattle, the minimum relevant characterization should include phase composition (XRD), functional groups and carbonate substitution (FTIR or Raman), elemental composition and trace ions (ICP-OES, XRF, or EDX), morphology and porous architecture (SEM/TEM and porosimetry), specific surface area, and degradation/ion release behavior in physiological solutions. These parameters together govern protein adsorption, wettability, cell adhesion, and mineral transformation potential as reported by Okpe et al., 2024; Adhikara et al., 2024.

Carbonate content justifies particular attention as biological apatite is carbonated. The author's study on type A and B carbonated bovine apatite (HAp) confirms this point by showing that the calcination temperature modifies the carbonate-related FTIR/XRD signature and,

consequently, the degree of biomimeticity, not just the apparent crystallinity (Bano et al., 2019d). Excessive calcination can produce a highly crystalline, low-carbonate HAp that is stable but less bone-like. In another studies by Adhikara et al., 2024; Okpe et al., 2024; Liu et al., 2025 conversely told that insufficient removal of organic matter can compromise purity and biosafety. The goal, therefore, is not to obtain the most crystalline powder possible, but a reproducible material of acceptable purity with a biologically favorable balance between crystallinity and resorbability. This question is central to apatites extracted from waste and is now highlighted in several recent reviews on naturally occurring and bio-waste-extracted Hap.

Porosity is vigorous also. Interlinked macropores allow tissue invasion and vascularization and micropores augment definite surface region and fluid trade. Nonetheless, porosity is too large to the detriment of mechanical integrity. Bovine bone is one of the most interesting since the original structure may be used as a first step towards hierarchical porosity. Recently, bovine scaffolds that were replaced with fluoride still had a natural microporous structure but were stronger and more osteogenic, which suggests that careful post-processing may be used to maintain a biologically favorable structure without negative effects on functionality (Ratnayake et al., 2024). To be able to translate, future research will have to characterize the porous morphology as well as the actual distribution of pore sizes, open or closed porosity, and alterations after sterilization or composite fabrications.

Another understudied aspect concerns the host response. While the classical conception of HAp emphasizes osteoconduction, recent publications on biomaterials increasingly recognize that scaffold chemistry and topography can regulate macrophage behavior, early inflammation, and the coupling between angiogenesis and osteogenesis. The finding by Gani et al. (2023) that bovine HAp accelerates the inflammatory phase and bone growth is therefore significant. It suggests that bovine HAp should be investigated within the framework of osteoimmunology, particularly by analyzing macrophage polarization, cytokine release, and vascular markers, especially for periodontal or craniofacial regeneration, where interactions with soft tissues are critical. This shift from static characterization of ceramics to dynamic biological profiling will make future studies on bovine HAp more relevant to journals specializing in biological sciences.

Another underreported area is the host-response dimension. The classical view of HAp emphasizes osteoconduction, but the newer biomaterials literature increasingly recognizes that scaffold chemistry and topography can regulate macrophage behavior, early inflammatory tone, and coupling between angiogenesis and osteogenesis. The finding by Gani et al. (2023) that bovine HAp accelerated the inflammatory phase and bone growth is therefore important. It suggests that bovine-extracted HAp should be studied through osteoimmunology frameworks, including macrophage polarization, cytokine release, and vascular markers, especially when the intended use is periodontal or craniofacial regeneration where soft-tissue interactions are decisive. This shift from static ceramic characterization to dynamic biological profiling will make future bovine-HAp studies more relevant to journals focused on biological sciences.

### **Biological Performance in Bone Regeneration**

Biological performance depends on more than chemical identification of HAp by XRD or FTIR. For bone regeneration, the most important outcomes include cytocompatibility, protein adsorption, osteoblast adhesion, osteogenic differentiation, immune response, vascular support, degradation behavior, and actual new-bone formation in vivo. Recent bovine-HAp research has become more convincing precisely because it evaluates these endpoints rather than stopping at phase confirmation.

Earlier biological evidence already indicated that bovine HAp can do more than provide

passive mineral support. Pizzicannella et al. (2018) reported miR-210-mediated VEGF upregulation in periodontal ligament stem cells cultured on a bovine-extracted hydroxyapatite ceramic scaffold, suggesting pro-angiogenic and pro-osteogenic signaling. A clear *in vivo* example is the work of de Carvalho et al. (2019), who showed that sintering temperature can significantly alter the behavior of chemically deproteinized bovine hydroxyapatite. This structure-function principle was reinforced in the later preclinical study by de Carvalho et al. (2024), where a novel bovine HAp showed guided bone regeneration performance comparable to a widely used reference bovine graft in a canine mandibular defect model.

This trend is consistent with the scaffold series reported by Budiatin and co-workers. In a bone-defect model, a gentamicin-loaded bovine hydroxyapatite scaffold accelerated vascularization and remodeling (Budiatin et al., 2021), and later work showed faster fracture healing when bovine hydroxyapatite-gelatin implants were paired with oral bovine hydroxyapatite supplementation (Budiatin et al., 2022). Likewise, Gani et al. (2023) reported that a bovine hydroxyapatite-based scaffold accelerated the inflammatory phase and promoted bone growth in a rat defect model. Together, these studies indicate that bovine HAp can actively shape early healing events rather than merely occupying space.

The newer substitution studies further strengthen this interpretation. Ratnayake et al. (2024) found that fluoride-substituted bovine apatite supported Saos-2 cell proliferation and showed higher alkaline phosphatase expression than unsubstituted bovine HAp, suggesting enhanced osteogenic differentiation. Their later silicate-substituted system was developed specifically for regenerative dentistry, again highlighting that ionic tuning is a practical strategy for improving biological function in a tissue-specific context (Ratnayake et al., 2025). These results are consistent with the broader HAp literature, where fluoride, silicon, magnesium, zinc, and strontium are frequently explored as bioactive substitutions that modify dissolution, protein interactions, and osteoblastic signaling (Ielo et al., 2022; Liu et al., 2025).

The composite strategies are also relevant, as pure HAp is brittle and cannot be easily formed into clinically reliable structures. The study by Pinteala et al. (2024) demonstrated that the incorporation of cellulose collagen matrices with HAp or bovine bone mineral enhanced the osteogenesis-related characteristics, which demonstrated the advantage of combining the mineral bioactivity with the flexibility and matrix mimicry of polymers. Equally, scaffold-centric reviews of 2024 and 2025 also find that HAp polymer systems are superior to HAp alone in terms of supporting cell adhesion, proliferation, vascularization, and defect-specific mechanical needs (Amiryaghoubi and Esfahlan, 2024; Liu et al., 2025). This is one of the main considerations to AFJBS readers; most successful bovine-HAp constructs are typically hybrid systems and not single phase ceramics.

Bovine-HAp research has especially been prolific in the dentistry field in recent years. Diansari et al. (2025) placed the calcined bovine HAp to serve dental purposes, whereas Ratnayake and colleagues developed fluoride- and silicate-modified bovine scaffolds to serve regenerative purposes. Such a trend is rational since the process of alveolar bone regeneration requires its materials to be osteoconductive, slowly resorbing, moldable, and able to keep the space during healing. Apatite extracted by bovine meets most of these requirements especially when it retains the connected porous structure and biologically significant mineral chemistry. In order to underscore the biological applicability and translatability of bovine bone-derived HAp, summaries of representative *in vitro*, *in vivo* and scaffold-based studies are provided in Table 2.

***Table 2. Selected biological and translational studies from the past decade (2018-2025).***

Study	Model/system	Key biological finding	Why it matters
Pizzicannella et al. (2018)	hPDLSCs on bovine-extracted ceramic scaffold	miR-210-mediated VEGF upregulation supported angiogenic and osteogenic signaling.	Shows that bovine HAp can influence cell signaling, not just provide mineral support.
Budiatin et al. (2021)	Gentamicin-loaded BHA scaffold in bone defect	Accelerated vascularization and remodeling around the defect site.	Adds an infection-aware dimension to regenerative scaffold design.
Budiatin et al. (2022)	Rabbit femur defect with BHA-gel implant ± oral BHA	Implant plus oral bovine HAp improved fracture-healing indicators versus calcium lactate control.	Suggests multifunctional regenerative strategies beyond scaffold placement alone.
Gani et al. (2023)	Bovine HAp scaffold in rat bone defect	Accelerated inflammatory phase and bone growth during early repair.	Supports the view that bovine HAp can modulate host-response biology.
de Carvalho et al. (2024)	Canine mandibular guided-bone-regeneration model	Novel bovine HAp showed favorable osteoconductive behavior in a clinically relevant preclinical defect.	Provides stronger translational evidence than material-only studies.
Pinteala et al. (2024)	Cellulose-collagen matrices reinforced with HAp/bovine bone mineral	Hybrid matrices showed enhanced osteogenesis-related performance.	Highlights the value of composite design for balancing bioactivity and handling.
Ratnayake et al. (2025)	Silicate-substituted bovine HAp for regenerative dentistry	Silicon incorporation improved the scaffold profile for dental bone-regeneration use.	Shows application-specific tuning of bovine HAp for craniofacial regeneration.

Nevertheless, even with promising advances, the literature is hard to compare directly due to the variety of extraction conditions, pretreatments of raw bones and characterization protocols across studies. Such a lack of standardization undermines cross-study interpretation and complicates determining whether the observed differences are due to the extraction route per se or experimental design. Subsequent work must thus present processing parameters more rigorously and compare methodologies by similar benchmarks of crystallinity, phase purity, Ca/P ratio, carbonate retention, particle morphology and biological response.

Second, biosafety and sustainability should not be considered separately, but they should be viewed as one. Valorization of waste is appealing, yet, a biomaterial derived by bovines should also show it can be traced, has a consistent source, capable of destroying pathogens, and have a manufacturing process that can be accepted by regulators. According to Okpe et al.

(2024) and Liu et al. (2025), future biogenic HAp studies need, among others, greener chemistry, life-cycle considerations, and scale-up viability. A sustainable conversion approach to bovine bone-extracted HAp therefore ought to involve reduction of potentially dangerous reagents, minimization of energy requirements where feasible, and generation of a substance whose biological safety is proven and not presumptive.

Third, the discipline must get rid of the HAp that fits-all. Variations in clinical cues necessitate varying degradation rates, pore structures and mechanical behavior. Craniofacial augmentation, periodontal regeneration, and load-sharing orthopedic defects cannot be equated with the applications. Ionic substitution, hybrid matrices or additive manufacturing of bovine-extracted HAp is thus a rational step to take. New developments in the fluoride substitutions, silicate substitutions, and composite scaffold fabrication are hinting at the possibility that bovine HAp is capable of being used as a flexible mineral base instead of a single commodity biomaterial (Ratnayake et al., 2024; Ratnayake et al., 2025; Pinteala et al., 2024).

### **Advanced Manufacturing and Application-Specific Design**

Application-oriented manufacturing is expected to be the next step in the bovine-HAp research instead of mere extraction. Recent publications on HAp composites and scaffold translation also highlight extrusion printing, stereolithography, foaming, freeze-drying, and fiber-reinforced composites as the pathways that are most likely to transform powders into clinically relevant constructs (Ielo et al., 2022; Liu et al., 2025). In the case of bovine-extracted mineral, this is especially true since the biological potential will not be fulfilled until the pore geometry, handling properties and defect matching can be reproduced in a reproducible manner. That is, the competitiveness in the future will not only be based on the chemistry of bovine HAp, but on the capability to produce patient- and site-specific architectures.

Specific design is also important. Dense granules can be suitable in the ridge preservation, however, periodontal defects, sinu lifts, load-sharing segmental defects, and osteochondral interfaces demand various combinations of stiffness, degradation rate, particle mobility, and biologic activity. Designing of composites should be hence indication-based. HAp extracted in bovines can be potentially the most effective as a mineral phase in collagenous, cell-instructive scaffolds to repair craniofacial defects, whereas more mechanically reinforced or printed systems may be required to repair larger orthopedic defects. This approach fits into the general HAp scaffold literature, as more and more of these scaffolds are being viewed as a multifunctional regenerative microenvironment, including hydroxyapatite as one of its components, rather than an independent filler (Amiryaghoubi and Esfahlan, 2024; Liu et al., 2025).

### **Conclusion**

The waste of the bovine bones is an attractive natural source of hydroxyapatite which could be transformed into value-added biomaterials using many extraction paths with various benefits and drawbacks. The most practical and scalable production Calcination is the easiest, and the hydrothermal and other similar methods could have enhanced chemical fidelity to the biological apatite under controlled conditions. However the science needs to be more standardized, have stricter comparisons of procedures and have clearer evidence on the relationship between extraction parameters and biological performance. The next step to take will involve the combination of optimized conversion plans with strict characterization and application-directed design in such a way that bovine-bone-extracted HAp will be able to transition out of the laboratory preparation and into the assured biomedical usage.

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