Marine Biota-Derived Hydroxyapatite as a Bone Graft Material: A Scoping Review of Hydroxyapatite from Shell-Based Sources

Arief Rahadian[*], *Islamy Rahma Hutami*[**]

[*] *Department of Biochemistry, Faculty of Medicine, Universitas Dian Nuswantoro*
[**] *Department of Orthodontics, Faculty of Dentistry, Universitas Islam Sultan Agung,*

Correspondence: arief.rahadian@dsn.dinus.ac.id

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ABSTRACT

Background: *Restoring damaged or diseased bone is a major challenge in dentistry. Marine biota, such as seashells, crustacean shells, and fish bones, are rich in calcium and can be processed into safe, biodegradable materials that support bone healing. These natural sources are gaining attention for use as bone graft substitutes because they are biocompatible, widely available, and promote bone growth.*
Methods*: A scoping review was conducted using Google Scholar, PubMed, and ScienceDirect databases to identify relevant studies published between 2015 and 2025. Results: An initial total of 134.007 articles were identified across the three databases. After removing duplicates and screening based on title and abstract relevance to the inclusion criteria, 2.836 articles remained. A further selection process narrowed these down to 452 full-text articles, of which 433 were excluded due to incompatibility with the review focus. Finally, 19 studies were included in this review and analyzed for their methodology, findings, and clinical implications.*
Discussion: *Many studies have shown that marine biota can be used as effective bone graft materials. Their high calcium content, porous structure, and compatibility with body tissues help support cell attachment, growth, and new bone formation. These materials can be used in dental procedures to help regenerate bone and repair defects.*
Conclusion: *Marine-derived materials, especially from mollusks and crustaceans, are similar to human bone and show great potential as alternatives to synthetic bone grafts. Their natural properties and ability to support bone healing make them a promising, sustainable option for dental and oral bone repair.*

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INTRODUCTION

Advanced technologies and the complexity of marine ecosystems offer new opportunities for the development of innovative medical products derived from marine resources. The ocean depths represent a vast, largely untapped reservoir of biological diversity, containing a multitude of organisms that may serve as novel sources of biomaterials for future medical applications. Marine environments harbor an immense variety of plant and animal species, many of which remain unexplored. Marine and aquatic organisms are particularly rich in bioactive compounds that hold significant promise in biomedicine, including dentistry, pharmacy, cosmetology, and nutraceuticals; either as alternative raw biomaterials or biofunctional supplements. The unique structural and biochemical properties of these marine-derived materials make them highly promising candidates for tissue engineering and regenerative medicine approaches. [1, 2]

Numerous bone grafting procedures are currently available to support complete regeneration following bone trauma, to facilitate healing between two bones across a diseased joint, or to restore clinical function and aesthetics in areas affected by disease, infection, or surgical resection. To date, autografts remain the gold standard for bone grafting, offering the highest quality of bone regeneration in both trauma and dental applications due to their histocompatibility and lack of immunogenic response. However, autografts can lead to secondary complications, such as donor site morbidity, particularly when harvested from areas like the iliac crest or fibula. In dentistry, grafts are commonly obtained from intraoral sites such as the mandibular ramus, maxillary tuberosity, and jawline.[3, 4]

Marine skeletons are natural materials with unique structures that make them useful for repairing and regenerating human tissues. Examples include seashells, sea urchins, cuttlebones, and coral, which have strong and porous structures rich in bioactive elements. These materials are mainly made of calcite or aragonite, which can be easily turned into calcium phosphate that is similar to the minerals found in human bone. Because of their natural strength and compatibility with the body, marine skeletons are better than many synthetic materials and have great potential for use in tissue engineering and drug delivery.[5]

Hydroxyapatite (HA) is a bioactive, osteoconductive, and biocompatible material commonly used in dental implants. It is usually produced through chemical methods using calcium and phosphate sources; however, commercial HA is often expensive due to the high-purity chemicals required. Natural sources of HA; such as corals, seashells, eggshells, and snails, provide a more affordable and sustainable alternative, with a composition closely resembling that of human bone. These marine-derived materials have demonstrated strong bonding with hard tissues and improved biological responses.[6] The aim of this review is to explore the potential of marine biota as a natural source of hydroxyapatite for bone graft applications in dentistry. This is necessary to highlight cost-effective, biocompatible alternatives to synthetic HA and to support future innovations in regenerative dental treatments using marine-based biomaterials.

METHODS

Data Search

The data used in this study are secondary, meaning they were not collected through direct observation but obtained from previous research. The sources included selected articles and journals accessed through ScienceDirect, PubMed, and Google Scholar. The search process used specific keywords (Table 1) to help identify and select relevant studies, making it easier to determine which articles or journals were suitable for review.

Table 1. Keywords Used in the Literature Search

Sources	Keywords
Science Direct	"marine shells" OR seashells OR "shell waste" OR "crustacean shells" OR "shrimp shell" OR "lobster shell" OR "crab shell" OR "fish bone" OR "marine biowaste" AND "bone graft" OR "bone tissue engineering" OR "bone regeneration" OR "orthopedic biomaterials" AND calcium OR "calcium carbonate" OR "calcium phosphate" OR hydroxyapatite OR "nano-hydroxyapatite"
Pubmed	marine shells OR seashells OR shrimp OR lobster OR crab OR fish bone AND bone graft or bone engineering AND calcium OR hydroxyapatite.
Google Scholar	"marine shells" OR seashells OR "shell waste" OR "crustacean shells" OR "shrimp shell" OR "lobster shell" OR "crab shell" OR "fish bone" OR "marine biowaste" AND "bone graft" OR "bone tissue engineering" OR "bone regeneration" OR "orthopedic biomaterials" AND calcium OR "calcium carbonate" OR "calcium phosphate" OR hydroxyapatite OR "nano-hydroxyapatite"

Inclusion Criteria and Exclusion Criteria

The inclusion criteria in searching for research data used are:

1. Research articles published in the last 10 years (2015-2025).
2. Research articles can be accessed in full text form.
3. Articles that examine the use of marine biota as bone graft material.

The exclusion criteria in searching for research data used are:

1. Journal articles with journal types other than research articles.
2. Research articles are in abstract form or cannot be accessed.
3. Research articles that use languages other than Indonesian and English.

Results

This systematic analysis identified 74.016 articles on PubMed, 4.780 on Google Scholar, and 55.211 on ScienceDirect. The literature selection process involved screening articles from 1.086 down to 19 international journals (Figure 1). All searches were conducted using indexed electronic databases. The review revealed that marine mollusk shells are the most common and versatile source of marine-derived bone graft materials. These include seashells from marine mollusks, particularly cockle shells (*Anadara granosa*), pearl oyster shells (*Pinctada maxima*), green mussel and crab shells, *Rapana venosa* (sea snail) shells, and *Corbicula moltkiana* (pensi clam).

The reviewed studies employed various experimental and fabrication methods to process marine biota—such as seashells, crab shells, oyster shells, fish bones, and coral—into bone graft materials. Common techniques included calcination, freezedrying, microwave-assisted synthesis, precipitation, and 3D printing, which were used to extract or synthesize HA or nano-hydroxyapatite (nHA).

These materials were then evaluated through in vitro tests (e.g., cell viability, SEM, FTIR, protein adsorption), in vivo animal models (e.g., rats, rabbits, guinea pigs), and mechanical or structural testing (e.g., compressive strength, porosity, degradation rate). Across the studies, the materials demonstrated strong biocompatibility, osteoconductivity, and mechanical stability, with several showing enhanced bone regeneration, anti-inflammatory effects, and antibacterial activity. The combination of marine-derived calcium sources with natural polymers like chitosan or additives like gold further improved biological performance (Table 2).

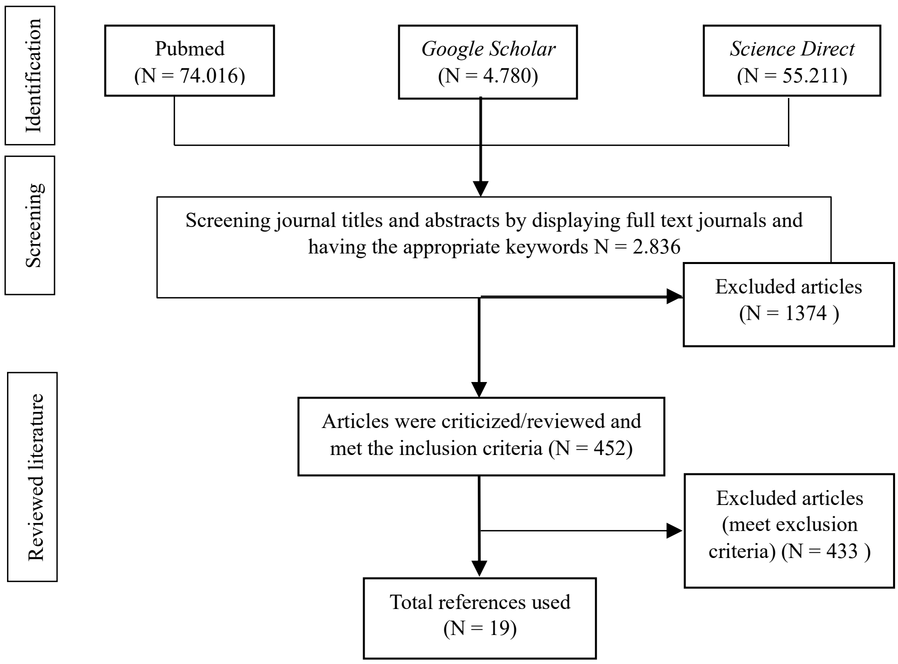

Figure 1. PRISMA Flow Diagram of the Literature Search and Study Selection Process

Table 2. Overview of Studies Investigating Marine-Derived Bone Graft Materials

Study (Year)	Key Focus	Method Summary	Main Outcome	Clinical Relevance
Chen TY, et al (2016)[15]	Alginate/HACC/OSP scaffold	Scaffold fabrication and in vitro tests	Good porosity, antibacterial, biocompatible	Promising for bone repair
Tihan GT, et al (2017)[6]	Collagen-HA sponge from seashell	MG63 cells, SEM, FTIR	Biocompatible, supports cell growth	Suitable for bone tissue engineering
Dhanaraj K and Suresh G (2018)[20]	nHA from cockle shells	Microwave method, antibacterial test	Effective against E. coli, B. cereus	Eco-friendly and safe for dental use
Desmond S, et al (2019)[9]	HA synthesis from shells	Conventional vs microwave heating	Microwave needs phosphate addition	Improvement in HA synthesis efficiency
Saharudin SH, et al (2019)[17]	Scaffold with cockle shell powder	Freeze-dry method, SBF test	Stronger scaffold, better bioactivity	Good potential for bone scaffolds
Kamadjaja MJK, et al (2019)[24]	HA from Portunus pelagicus	Fibroblast culture, MTT assay	High cell viability	Safe for oral application

Alhussary BN, et al (2020)[16]	nHA from egg/seashells	Calcination, rabbit bone model	Accelerates bone healing	Cost-effective nano-HA source
Dadhich P, et al (2021)[12]	3D-printed CaP scaffold from seashell	Extrusion printing, rabbit model	Biocompatible, good tissue growth	Novel 3D scaffold for bone graft
Otero-Pérez R, et al (2021)[18]	Graft from shark teeth	Rabbit defect model, CT, histology	High bone density and integration	Effective sustainable bone graft
Baek JW, et al (2022)[10]	HAp from plankton exoskeleton	Cell culture, in vivo test	Good osteogenic activity	Viable bone graft alternative
Hadi AN, et al (2022)[8]	Bioepoxy with shell/HA nanoparticles	Mechanical tests, FTIR	Enhanced strength and compatibility	Suitable for bone replacement
Gani A, et al (2022)[13]	Chitosan + HA from crab	Wistar rats, IL-1/BMP-2 markers	Reduced inflammation, increased BMP-2	Enhances periodontal regeneration
Chandha MH, et al (2022)[23]	HAp from Pinctada maxima	Guinea pig model, BMP-2/OPG	High osteogenic markers	Promising in dental bone grafts
Kim SC, et al (2022)[21]	CHA/PCL scaffold with marine collagen	3D printing, in vitro/in vivo	Improved osteogenic activity	Marine byproducts for bone tissue
Ismail R, et al (2022)[19]	$CaCO_3$ from green mussel/crab	Calcination, XRD, SEM	Similar to commercial $CaCO_3$	Potential biomaterial use
Pascawinata A, et al (2023)[11]	nHA from Corbicula moltkiana	Rat tooth extraction model	↑ Osteoblasts, ↑ bone formation	Effective alveolar graft material
Taqa AA, et al (2023)[14]	Nano-HA + gold from seashell	FTIR, rabbit model	↑ Bone density, good remodeling	Enhanced bone repair material
Djamaluddin N, et at (2023)[7]	HA from catfish bone	FTIR, ELISA, histology	Biocompatible, improves healing	Fish-bone HA feasible for graft
Chandha MH, et al (2023)[22]	Pearl shell for periodontal graft	RT-PCR, SEM, guinea pigs	↑ Osteoblasts & OCN	Potential periodontal graft option

DISCUSSION

Bone grafting plays a pivotal role in modern regenerative medicine and dentistry, aiming to repair or replace lost bone structure due to trauma, disease, or congenital defects. Autologous bone grafts remain the gold standard due to their osteogenic properties and biocompatibility.[2] However, limitations such as donor site morbidity, limited availability, and increased surgical complexity have driven the search for alternative biomaterials. In this context, marine biota—comprising seashells, corals, crustacean exoskeletons, fish bones, and mollusk shells—emerge as sustainable and promising candidates due to their high calcium carbonate and calcium phosphate content, primarily in the form of aragonite and calcite, which can be transformed into hydroxyapatite (HA).[5]

Biological Composition and Osteogenic Properties

Hydroxyapatite (HA) $Ca_{10}(PO_4)_6(OH)_2$) is the main inorganic component of natural bone and teeth. Marine-derived biota offers mineral compositions strikingly similar to human bone, facilitating cell attachment, proliferation, and differentiation. Marine biota, especially seashells and coral, have a highly porous microstructure and inherent bioceramic properties that mimic cancellous bone. This intrinsic osteoconductivity, combined with high bioavailability and low immunogenicity, makes marine-derived HA ideal for bone graft applications.[3]

The transformation of marine calcium carbonate to calcium phosphate (hydroxyapatite) can be achieved via thermal treatment or wet precipitation, enhancing its bioactivity. Nano-hydroxyapatite (nHA) derived from marine sources shows superior mechanical strength, increased surface area, and more efficient osteointegration compared to conventional HA.[6]

HA has been widely developed as a bone substitute due to its structural similarity to the mineral component of human bone. As a bioactive bioceramic, hydroxyapatite is biocompatible, biodegradable, non-toxic, osteoconductive, and osteoinductive. These properties make it a highly promising material for bone replacement and regeneration in cases of bone damage and defects.[7]

Phases of Bone Healing and the Role of Bone Graft Materials

Bone healing after tooth extraction or implantation occurs in several distinct yet overlapping phases, each influenced by the presence of bone graft materials.

1. Hemostasis and Coagulation Phase: This initial phase begins immediately after microvascular damage and bleeding. Blood fills the socket, and clot formation begins. Platelets within the clot release a variety of signaling molecules, including cytokines, chemokines, interleukins, and growth factors. During this stage, the bone graft becomes embedded in the fibrin mesh, which stabilizes the graft material and initiates healing.[8]

2. Inflammatory Phase: This phase starts at the onset of injury and typically lasts up to the fifth day. Leukocytes infiltrate the site to debride necrotic tissue and eliminate pathogens. The presence of a bone graft further stimulates the migration of inflammatory cells and osteoclasts to the graft surface, often triggering mild resorption as part of the body's response to the foreign material.[9]

3. Proliferative Phase: During this phase, the socket is filled with granulation tissue composed of macrophages, fibroblasts, new blood vessels, and osteoblasts. Around day 14 post-extraction, provisional matrix and newly formed woven bone become evident alongside areas of mineralized tissue. In the current study, nanocrystalline hydroxyapatite (nHA) enhanced osteogenesis by promoting the formation of osteoblasts and neovascularization, leading to early bone formation.[10]

4. Modeling and Remodeling Phase: This final phase involves both the shaping and the long-term integration of new bone. Initially, a strong pro-inflammatory response may cause macrophages to accumulate and fuse into multinucleated giant cells. These cells can stimulate fibroblasts to deposit dense, avascular collagen around the implant, isolating it from host tissue. Over time, a shift to an anti-inflammatory state occurs, in which macrophages release growth factors that support angiogenesis and promote tissue remodeling and integration.[11,12]

Marine-Derived Bioceramics and Scaffolds for Bone Regeneration

Gani A, et al (2022) explained that bone grafts made from a combination of chitosan gel and hydroxyapatite (HA) derived from blue swimmer crab shells have the potential to replace lost or damaged bone structures due to trauma or periodontal disease. In this application, chitosan and HA gels serve as scaffolds—critical structures that support stem cell attachment and function at bone defect sites. These scaffolds also contribute to the formation of the initial extracellular matrix necessary for facilitating bone healing.[13]

In recent decades, several alternative bone graft materials have emerged, including demineralized bone matrix, bone morphogenetic proteins, calcium phosphate, calcium sulfate, and hydroxyapatite. More recently, nanomaterials such as nanoporous hydroxyapatite (nHA) have gained interest due to their enhanced regenerative potential. For instance, the addition of gold to HA derived from seashells has shown improved bone healing, supporting findings that gold-containing injectable hydrogels can stimulate bone regeneration and serve as biodegradable grafting materials for bone defects.[13,14]

Chen TY, et al (2016) found that scaffolds made with oyster shell powder (OSP) had a porous, interconnected structure that supported cell attachment and new tissue growth. The even distribution of OSP improved the scaffold’s strength and surface area. As more OSP was added, the scaffold became more stable, with better biomineralization and protein adsorption. It also showed good biocompatibility and antibacterial activity, making it a strong candidate for bone regeneration.[15]

Other studies on HA from seashells showed better bone healing and integration at defect sites, likely due to its ideal pore size and structure that support bone cell growth. Because of its natural origin and low cost, seashell-derived HA is promising for clinical use.[16,17]

Additionally, calcium carbonate from marine sources like green mussel and crab shells is seen as a useful raw material for making bioceramics. These materials are cost-effective, easy to obtain, and environmentally friendly. Bioceramics from seashells are already being used in bone grafts, dental applications, and drug delivery. In particular, calcium phosphate materials like HA and tricalcium phosphate (TCP) are valued for their strong biocompatibility and ability to support new bone growth.[18, 19]

Several researchers have tested different processing methods for oyster shells to ensure the final product retains a high calcium content. One commonly used technique is precipitation. Studies have shown that the mineral composition of oyster shells from three different sources is nearly identical, with calcium carbonate and carbon making up more than 98.7% of the total mineral content. In particular, bone grafts made from pearl oyster shells (*Pinctada maxima*) contain a significant amount of hydroxyapatite, indicating strong potential for use as bone graft material.[20,21,22]

Crab shells also contain a high level of calcium carbonate (between 40% and 70%) making them another valuable source for HA synthesis. HA is the most stable form of apatite and is widely used in bone grafts due to its bioactivity, biocompatibility, and chemical similarity to human bone. While crab shell-derived HA shows promise, further research, especially on biocompatibility, is still needed to support its use in broader clinical applications.[23, 24]

Likewise, nano-hydroxyapatite (nHA) obtained from seashells has demonstrated an ability to promote bone formation, thanks to its ideal pore size and structure that support cell growth and tissue regeneration. Its natural origin and low production cost make it a strong candidate for future use in bone repair and regeneration.[16]

Types of Marine Biota Used for Bone Grafting

Numerous marine organisms have been explored as HA sources: Seashells (e.g., oyster, mussel, cockle, clam): Rich in calcium carbonate, seashells have been widely studied for HA synthesis. Studies demonstrated that mussel and crab shells processed into HA scaffolds showed enhanced biocompatibility, mineralization, and cell proliferation.[22]

a) Corals: Due to their naturally porous structure, corals are highly suitable for use in 3D-printed scaffold designs. Coral-derived HA mimics trabecular bone and has been used in maxillofacial and orthopedic applications.[21]
b) Crustacean shells (shrimp, crab, lobster): Besides calcium carbonate, crustacean shells also contain chitin and proteins, contributing to biocompatibility. Shrimp shell-derived HA using microwave calcination showed excellent cytocompatibility.[22]
c) Fish bones: Fish bones, particularly from tilapia or sea bream, are abundant in HA and are processed through hydrothermal methods. Fish bone HA was shown to enhance osteoblast differentiation and matrix mineralization.[23]
d) Pearl oyster (*Pinctada maxima*): Known for its nacre, the shell provides a dual-layer structure of calcium carbonate and organic matrix. Studies have shown pearl shells to express high levels of osteoinductive markers such as BMP-2 and OCN in vivo.[24]

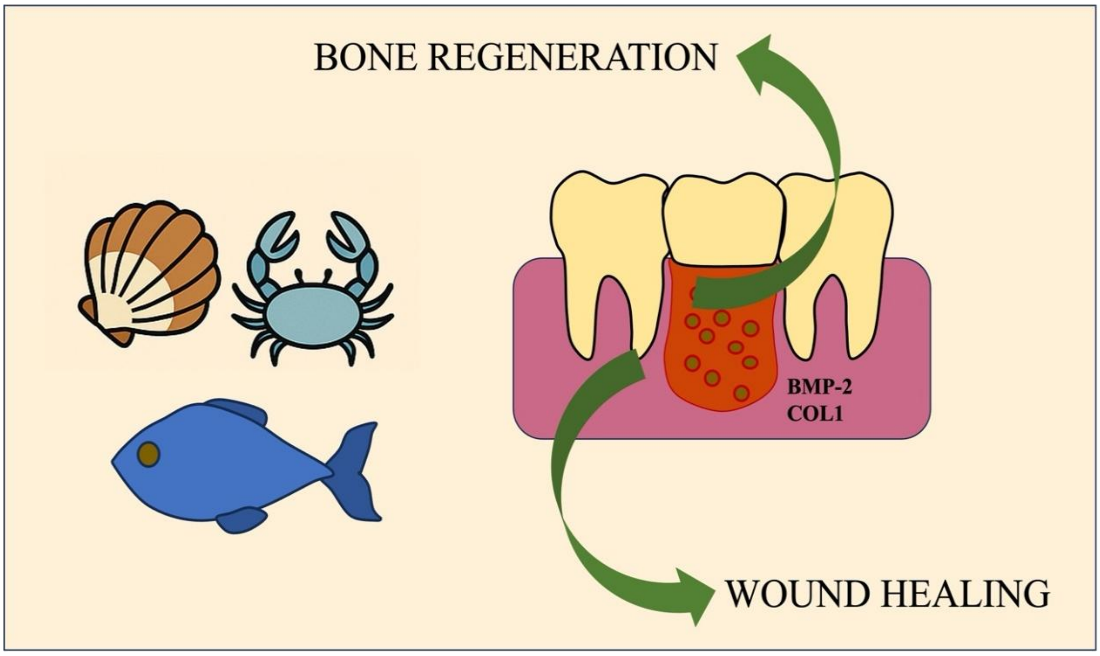

Figure 2. Clinical Applications of Marine-Derived Bone Graft Materials in Dentistry

Marine collagen (MC), an abundant resource free from religious restrictions and disease transmission risks, plays an increasingly important role in bone tissue engineering (BTE) due to its osteoconductivity, biocompatibility, and ability to support cell adhesion. Its characteristic triple-helix structure provides mechanical integrity and structural support, making it suitable for biomedical applications. In cases of bone injury, collagen-based scaffolds can effectively replace damaged tissue by promoting cellular activity and facilitating the integration of new bone with host tissue.[24]

MC is a critical component of the extracellular matrix (ECM), known to inhibit inflammation, induce chondrocyte differentiation, enhance bone mineral density, and stimulate both osteogenesis and collagen synthesis.[25] However, pure type I collagen degrades rapidly and lacks sufficient mechanical strength, limiting its long-term effectiveness in bone grafting and clinical applications. To overcome these limitations, cross-linking modifications have been explored to improve its structural stability, mechanical properties, and resistance to enzymatic degradation. Such modifications are essential to broaden the clinical utility of MC in BTE.[25] Considering the unique biological properties of MC and recent advancements in collagen cross-linking technologies, this paper discusses the role of MC in bone repair and highlights modified marine collagen forms used in various bone regeneration applications.

Clinical Implication in Dentistry

Marine biota-derived bone graft materials is highly promising. These materials; particularly HA and calcium carbonate derived from marine mollusk shells (e.g., cockle, oyster, mussel), crustaceans (e.g., crabs), and fish bones demonstrate excellent biocompatibility (Table 2), bioactivity, and osteoconductive properties. They have shown significant potential in promoting bone regeneration, enhancing osteoblast proliferation, and accelerating healing in periodontal defects, extraction sockets, and maxillofacial reconstructions. Additionally, the incorporation of chitosan and marine collagen enhances wound healing, antimicrobial activity, and scaffold stability.[25]

The natural origin, abundance, and low cost make them sustainable and accessible alternatives to synthetic or bovine-derived grafts. These findings support the translation of marine-derived grafts into clinical dental practice, particularly for periodontal therapy, alveolar ridge preservation, implant site preparation, and bone augmentation procedures. [15,17]

To enhance the clinical utility of marine-derived bone graft materials in dentistry, several areas of improvement are needed. First, standardized processing protocols must be developed to ensure consistency in composition, mechanical strength, and bioactivity, as the natural variability of marine sources can lead to unpredictable outcomes. To overcome the limited osteoinductive potential of pure HA, combining these materials with bioactive agents such as chitosan, growth factors (BMP-2), or stem cells could significantly enhance bone regeneration. [12,23,25]

Additionally, rigorous purification techniques should be applied to eliminate potential contaminants, including heavy metals and microbial residues, ensuring the safety and biocompatibility of the grafts. Strengthening the mechanical properties through composite formulations with polymers or synthetic ceramics may also expand their application to load-bearing areas. Finally, more robust in vivo and clinical studies are essential to validate long-term efficacy, biocompatibility, and integration within oral tissues. By addressing these challenges, marine-derived graft materials can evolve into reliable, safe, and effective alternatives for bone regeneration in dentistry. [13,22,23]

Sustainability and Future Perspectives

One of the key advantages of marine biota over synthetic or bovine-derived HA is its environmental and economic sustainability. Marine biowaste is abundant, renewable, and often underutilized. Transforming this waste into high-value medical materials aligns with circular economy principles. showed that using marine waste can reduce production costs by 45% and decrease the carbon footprint.[15]
Future directions include:

a) Standardizing extraction and fabrication protocols to ensure reproducibility and quality.
b) Enhancing osteoinductivity through functionalization with growth factors or nanoparticles (e.g., gold, silver).
c) Conducting long-term clinical trials to validate marine HA's safety and efficacy.
d) Scaling production through partnerships with fisheries and aquaculture industries.[17]

CONCLUSION

Marine biota shells are materials that share several structural and compositional similarities with human bone. The combination of inorganic minerals and an organic matrix in nacre provides both good mechanical strength and biological compatibility, allowing for effective integration with bone tissue. These shells offer multiple advantages, including low cost, natural hierarchical structure, biocompatibility, low immunogenicity, minimal cytotoxicity, and ease of storage. Additionally, their structure can be adapted or modified to meet various clinical needs, making them promising candidates for use as bone graft materials.

CONFLICT OF INTEREST

We declare that there are no conflicts of interest related to the publication of this review.

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