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MARINE-DERIVED BIOMATERIALS FOR REGENERATIVE MEDICINE AND NANOSCAFFOLD ENGINEERING: FROM BIODIVERSITY TO BIOMEDICAL TRANSLATION

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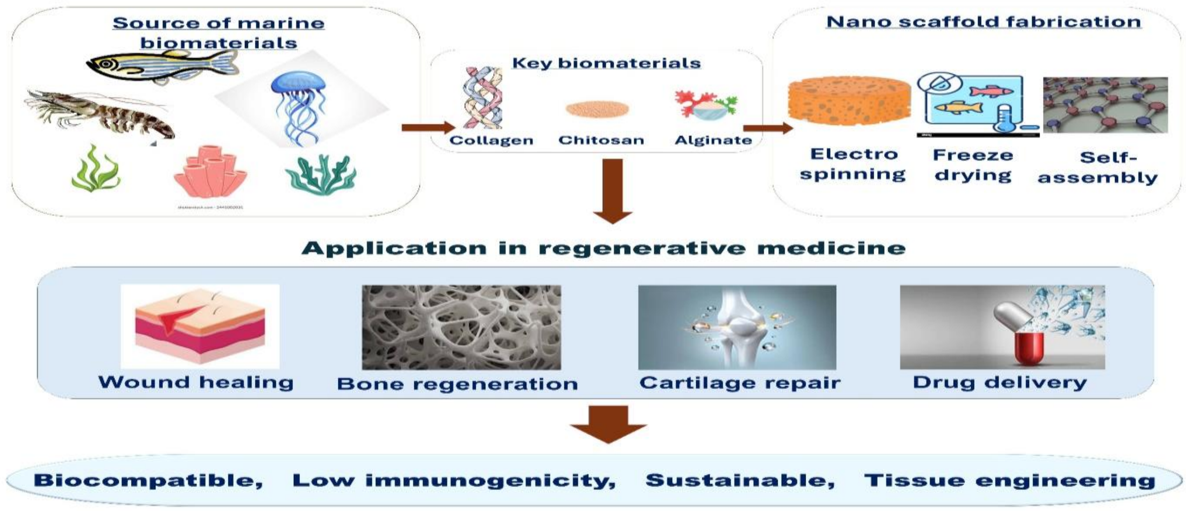
ABSTRACT
Marine ecosystems represent a vast and underexplored source of biologically active materials with unique structural, chemical and functional properties. Marine animals and macroalgae produce diverse biomolecules, including collagen, chitin, alginate, carrageenan, fucoidan and bioactive peptides, which have attracted considerable attention in zoological biotechnology. These naturally derived biomaterials exhibit excellent biocompatibility, biodegradability, low immunogenicity and intrinsic bioactivity, making them suitable candidates for advanced biomedical applications. In regenerative medicine, marine-derived biomaterials play a significant role in promoting tissue repair, cellular proliferation and extracellular matrix regeneration, particularly in skin, bone, cartilage and nerve tissue engineering. Their structural similarity to native extracellular matrices enhances cell adhesion, migration and differentiation, thereby improving healing outcomes. In addition, macroalgae- and marine animal-derived polymers have demonstrated immense potential in the fabrication of nanoscaffolds through techniques such as electrospinning, self-assembly and hydrogel formation. These nanoscaffolds provide a highly porous and interconnected architecture that supports nutrient transport, waste removal and controlled delivery of therapeutic agents. Furthermore, the incorporation of marine bioactive compounds into nanostructured systems enhances antimicrobial, anti-inflammatory and antioxidant activities, which are essential for effective tissue regeneration and wound management. Zoological biotechnology integrates these marine-derived materials with advanced nanotechnology and biomaterial engineering approaches to develop sustainable, eco-friendly and functional scaffolding systems. Despite promising advancements, challenges related to standardization, scalability and long-term safety remain critical considerations for clinical translation. This review highlights the emerging role of marine animal and macroalgae-derived biomaterials in regenerative medicine and nanoscaffold fabrication, emphasizing their biological advantages, fabrication strategies and future prospects in zoological biotechnology.

KEYWORDS: Marine biomaterials, Marine animals, Regenerative medicine, Tissue engineering, Marine polymers, Biomaterial engineering.

GRAPHICAL ABSTRACT



1. INTRODUCTION

The ocean covers more than two-thirds of the Earth's surface and harbours an extraordinary diversity of organisms that have evolved unique biochemical and structural features to survive in complex marine environments[1]. In recent decades, marine ecosystems have emerged as a valuable source of novel biomolecules and functional materials with significant applications in biotechnology and biomedical sciences[2]. Marine organisms are continuously exposed to extreme conditions such as high salinity, pressure, variable temperatures and intense competition for survival. As a result, they produce specialized metabolites and structural biomaterials that exhibit remarkable physicochemical and biological properties[3]. These characteristics make marine-derived materials particularly attractive for developing innovative biomedical technologies. The exploration of marine resources has therefore become an important area of research in biotechnology, offering promising solutions for healthcare challenges including tissue repair, wound healing and the development of advanced biomaterials[4].

Among the various marine sources, marine animals and macroalgae represent two major reservoirs of biologically active compounds and structural biomaterials. Marine animals such as sponges, molluscs, crustaceans and jellyfish produce a variety of structural polymers including collagen, chitin and other extracellular matrix components[5]. These materials possess excellent biocompatibility, biodegradability and mechanical strength, making them suitable candidates for biomedical applications. For instance, collagen extracted from marine organisms has gained attention as an alternative to mammalian collagen due to its lower risk of disease transmission and fewer ethical concerns[6]. Similarly, chitin and its derivative chitosan obtained from crustacean shells have demonstrated antimicrobial activity, haemostatic properties and the ability to support cell adhesion and proliferation. These features have encouraged their use in drug delivery systems, wound dressings and tissue engineering scaffolds[7].

Macroalgae, commonly referred to as seaweeds, also serve as an abundant source of valuable biomaterials with diverse functional properties. Brown, red and green macroalgae synthesize unique polysaccharides such as alginate, carrageenan and agar, which have attracted considerable interest in biomedical and pharmaceutical applications[8]. Alginate derived from brown algae is widely used for its gel-forming ability, high water retention capacity and mild processing conditions, making it ideal for encapsulating cells and bioactive molecules[9]. Carrageenan from red algae possesses excellent gelling and stabilizing characteristics, which have been utilized in drug delivery systems and tissue engineering matrices. In addition, agar has been extensively employed in microbiological and biomedical research due to its biocompatibility and structural stability[10]. These marine polysaccharides provide versatile platforms for designing biomaterials that can mimic the natural extracellular matrix and promote tissue regeneration[11].

The increasing demand for advanced therapeutic materials has directed significant attention toward the use of marine-derived biomaterials in regenerative medicine[12]. Regenerative medicine focuses on restoring or replacing damaged tissues and organs by combining biomaterials, cells and bioactive molecules. In this context, marine biomaterials offer several advantages, including natural origin, structural similarity to biological tissues and the capacity to support cellular functions such as adhesion, migration and proliferation[13]. Many marine-derived polymers have demonstrated the ability to modulate inflammation, stimulate angiogenesis and accelerate wound healing processes. These biological activities are crucial for successful tissue repair and regeneration[14]. Furthermore, the abundance and renewability of marine resources provide a sustainable supply of raw materials for developing next-generation biomedical products[15].

In addition to their role in regenerative medicine, marine animal and macroalgae biomaterials have shown significant potential in the fabrication of nanoscaffolds[16]. Nanoscaffolds are nanoscale structural frameworks designed to mimic the architecture of natural extracellular matrices and provide an environment conducive to cell growth and tissue formation[17]. The incorporation of marine-derived polymers into nanofibers, hydrogels, nanoparticles and composite scaffolds has enabled the development of biomimetic materials with enhanced biological performance. For example, alginate-based nanofibers and chitosan nanoparticles have been widely investigated for controlled drug delivery and tissue engineering applications[18]. These nanostructured materials offer improved surface area, mechanical strength and controlled release properties, which are essential for effective therapeutic outcomes. Advances in nanotechnology and material engineering have further expanded the possibilities of integrating marine biomaterials into sophisticated biomedical platforms[19].

Despite the growing interest in marine-derived biomaterials, a comprehensive understanding of their sources, properties and biomedical applications is still evolving[20]. Continued research is necessary to identify new marine species, optimize extraction and processing techniques and evaluate the safety and efficacy of these materials in clinical settings. Moreover, the integration of marine biomaterials with emerging technologies such as nanotechnology, bio-fabrication and tissue engineering is expected to open new avenues for developing advanced therapeutic strategies[21].

In this context, the present review aims to provide a detailed overview of biomaterials derived from marine animals and macroalgae and their expanding role in modern biotechnology[22]. The review focuses on the structural characteristics, biological properties and biomedical potential of these materials, particularly in regenerative medicine and nanoscaffold fabrication. Additionally, it highlights recent research developments, emerging applications and future perspectives for utilizing marine-derived biomaterials in advanced therapeutic systems[23]. By summarizing current knowledge and identifying research gaps, this review seeks to contribute to a better understanding of the potential of marine resources in the development of innovative biomedical technologies[24].

2. Marine biodiversity as a source of biomaterials

Marine ecosystems represent one of the most biologically diverse environments on Earth, supporting an enormous variety of organisms that produce structurally unique and biologically active compounds[25]. The immense diversity found in oceans has attracted considerable interest from researchers seeking new biomaterials with applications in biotechnology, medicine and materials science[26]. Marine organisms have evolved specialized biochemical pathways that enable them to survive in harsh conditions such as fluctuating temperatures, high salinity and intense ecological competition. These adaptations have resulted in the production of distinctive polymers, proteins and polysaccharides that exhibit functional properties valuable for biomedical and industrial applications[27]. As scientific exploration of marine biodiversity continues to expand, numerous marine species are being investigated as potential sources of novel biomaterials with promising therapeutic potential[28].

2.1. Marine animals as biomaterial sources

Marine animals constitute an important reservoir of natural biomaterials with diverse structural and biological characteristics. Organisms such as sponges, crustaceans, molluscs, jellyfish and echinoderms produce a variety of structural polymers that have gained attention in biomedical research[29]. One of the most widely studied marine-derived materials is chitin, a naturally occurring polysaccharide found in the exoskeletons of crustaceans including shrimp, crabs and lobsters[30]. Through chemical modification, chitin can be converted into chitosan, a biopolymer known for its antimicrobial activity, biocompatibility and biodegradability. These properties make chitosan particularly useful in wound dressings, drug delivery systems and tissue engineering scaffolds[31].

Collagen extracted from marine organisms has also emerged as an attractive alternative to collagen obtained from terrestrial animals. Marine collagen is commonly isolated from fish skin, scales and jellyfish tissues and it possesses structural properties similar to mammalian collagen[32]. Its lower risk of transmitting zoonotic diseases and fewer cultural or ethical limitations contribute to its increasing popularity in biomedical applications. Additionally, marine sponges have been recognized for their unique skeletal frameworks composed of silica or collagen-based structures, which provide inspiration for developing biomimetic materials[33]. These natural architectures offer valuable insights for designing scaffolds that support cellular growth and tissue regeneration[34].

2.2. Macroalgae (seaweeds) as biomaterial reservoirs

Macroalgae, commonly known as seaweeds, represent another significant group of marine organisms that produce valuable biomaterials[35]. These photosynthetic organisms are broadly classified into brown, red and green algae, each characterized by the production of distinctive polysaccharides with unique physicochemical properties. Brown algae are a major source of alginate; a natural polymer widely used for its gel-forming ability and high-water absorption capacity[9]. Alginate hydrogels are frequently utilized in biomedical research for cell encapsulation, wound healing materials and controlled drug delivery systems[36].

Red algae produce carrageenan and agar; two polysaccharides extensively used in pharmaceutical and biomedical fields[37]. Carrageenan exhibits excellent thickening and stabilizing properties and has been incorporated into various biomedical formulations. Agar, on the other hand, is well known for its role in microbiological culture media and has also been explored for applications in tissue engineering and hydrogel development[38]. Green algae contribute additional polysaccharides and bioactive compounds that demonstrate antioxidant, antimicrobial and anti-inflammatory activities. The abundance and renewability of macroalgae make them particularly appealing as sustainable sources of natural biomaterials[39].

2.3. Advantages of marine-derived biomaterials over terrestrial sources

Biomaterials obtained from marine organisms offer several advantages when compared with materials derived from terrestrial sources[26]. One significant benefit is the reduced risk of disease transmission, particularly zoonotic infections that may occur with mammalian-derived biomaterials. Marine materials also present fewer ethical and cultural concerns, which broadens their acceptability in biomedical applications[40]. Furthermore, many marine polymers exhibit superior biological compatibility and unique physicochemical characteristics that enhance their functionality in biomedical systems. Marine biomaterials often possess high water retention capacity, flexible gel-forming abilities and favourable mechanical properties that support tissue regeneration and drug delivery applications[12]. In addition, marine ecosystems provide access to a vast and relatively untapped pool of organisms that synthesize uncommon biomolecules not typically found in terrestrial environments. This diversity offers researchers opportunities to discover innovative materials with novel therapeutic properties[41].

2.4. Sustainability and bioprospecting of marine organisms

The growing interest in marine-derived biomaterials has highlighted the importance of sustainable exploration and responsible utilization of marine resources[42]. Bioprospecting, the systematic search for valuable biological compounds in natural environments, plays a crucial role in identifying new marine organisms with potential biomedical applications. However, uncontrolled harvesting of marine species can threaten ecological balance and biodiversity[43]. Therefore, sustainable collection practices and cultivation strategies are essential to ensure long-term availability of these resources. Aquaculture and marine farming have emerged as practical approaches for producing large quantities of marine organisms such as algae and certain invertebrates without damaging natural ecosystems[44]. Advances in biotechnology also enable the extraction and modification of marine biomolecules using environmentally friendly processes. By combining sustainable harvesting methods with modern biotechnological techniques, it is possible to utilize marine biodiversity responsibly while continuing to discover new biomaterials that contribute to the development of advanced biomedical technologies[45].

3. Marine animal-derived biomaterials

Marine animals provide a wide range of naturally occurring biomaterials that possess structural complexity and biological compatibility suitable for biomedical applications[46]. Many marine organisms produce structural polymers and mineralized frameworks that support their bodies and protect them from environmental stresses[20]. These natural materials have attracted increasing interest because of their biodegradability, low toxicity and ability to interact favourably with biological tissues. Marine animal-derived biomaterials have been widely investigated for applications in regenerative medicine, wound healing, drug delivery and scaffold fabrication[13]. Among, the most studied materials are chitin and chitosan, marine collagen and gelatine, calcium carbonate-based coral materials and biomolecules derived from marine sponges as mentioned in the (Fig.1).

3.1. Chitin and chitosan

Chitin is one of the most abundant natural biopolymers found in marine environments. It forms the structural component of the exoskeletons of many marine organisms, particularly crustaceans such as shrimp, crabs and lobsters[47]. In addition to crustaceans, chitin is also present in squid pens and certain marine invertebrates. Structurally, chitin is a linear polysaccharide composed of repeating units of N-acetyl-D-glucosamine linked through β-(1→4) glycosidic bonds[48]. This arrangement gives chitin high mechanical strength and stability, making it an important structural material in nature. However, chitin itself has limited solubility in water and many organic solvents, which restricts its direct use in biomedical applications[49].

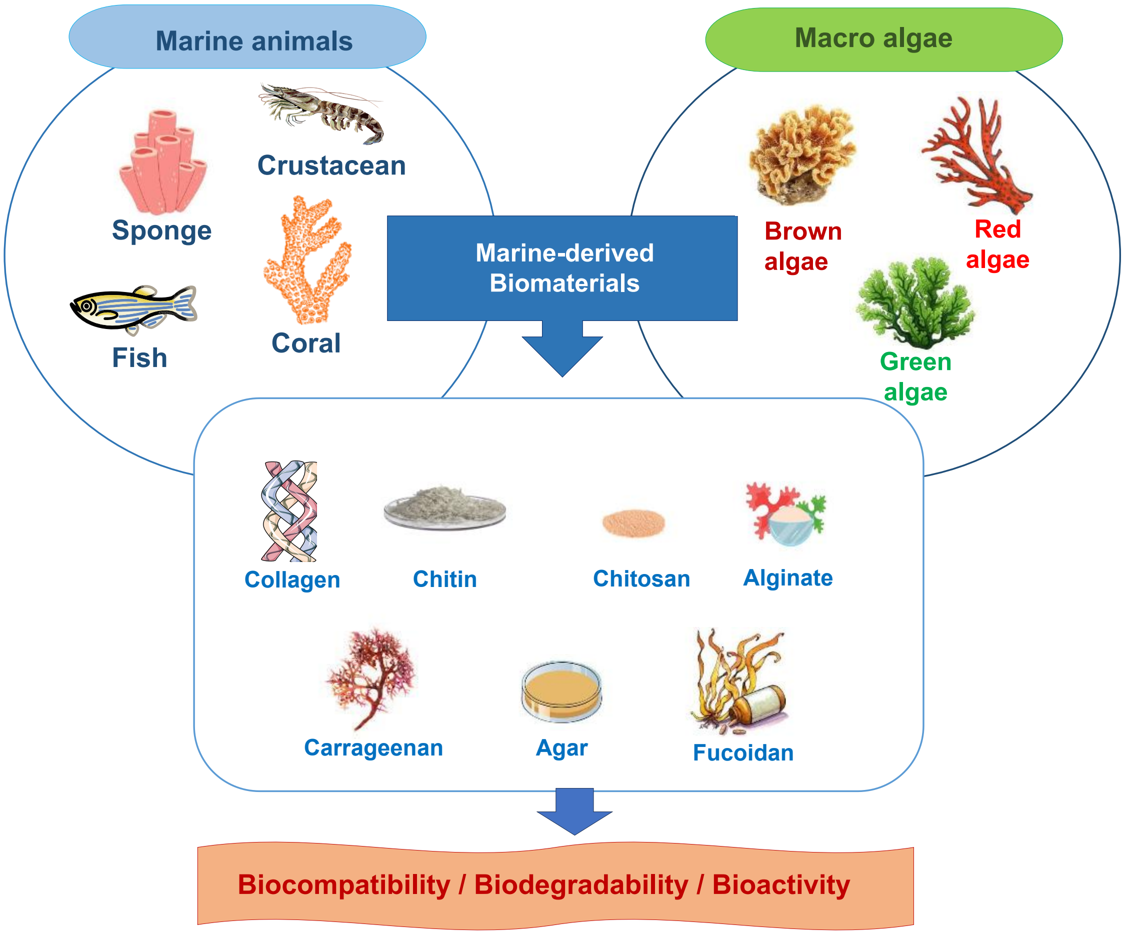


Fig. 1: Marine biomaterials and their sources in biotechnology

To enhance its usability, chitin is often converted into chitosan through a chemical process known as deacetylation[50]. Chitosan differs from chitin in that it contains free amino groups, which improve its solubility and biological activity. This modification significantly expands its potential applications in biotechnology and medicine[51]. Chitosan exhibits several properties that are highly desirable for biomedical materials, including biocompatibility, biodegradability, antimicrobial activity and the ability to form films, fibres and hydrogels[52]. Because of these properties, chitosan has been extensively explored in various biomedical fields. In wound healing, chitosan-based materials can accelerate tissue repair by promoting cell adhesion and supporting the formation of new tissue[31]. Its antimicrobial characteristics also help reduce the risk of infection in damaged tissues. Additionally, chitosan has been widely used as a carrier for drug delivery systems due to its ability to encapsulate therapeutic molecules and release them in a controlled manner[53]. Researchers have also investigated chitosan in the development of tissue engineering scaffolds, where it provides structural support for cell growth and differentiation[54].

3.2. Marine collagen and gelatine

Collagen is a fundamental structural protein that forms a major component of the extracellular matrix in many tissues[55]. While collagen has traditionally been obtained from terrestrial animals such as cattle and pigs, marine organisms have emerged as valuable alternative sources[6]. Marine collagen is commonly extracted from fish skin, fish scales and jellyfish tissues. These sources are particularly attractive because they utilize by-products from the seafood industry, thereby reducing waste and supporting sustainable resource utilization[56]. Marine collagen possesses several advantages compared with mammalian collagen. One important benefit is the reduced risk of transmitting animal-borne diseases, which has raised concerns regarding mammalian sources[57]. In addition, marine collagen is generally considered more acceptable across different cultural and religious communities. Structurally, marine collagen retains the characteristic triple-helix configuration typical of collagen molecules, enabling it to provide mechanical strength and biological support within tissues[58].

Gelatine, a derivative of collagen produced through partial hydrolysis, is also obtained from marine organisms. Marine gelatine maintains many of the functional characteristics of collagen while offering improved solubility and processing flexibility[59]. Both marine collagen and gelatine demonstrate excellent biocompatibility and low immunogenicity, making them suitable for biomedical applications[40]. In tissue engineering, marine collagen-based scaffolds are widely investigated for their ability to mimic the natural extracellular matrix. These materials provide a favourable environment for cell attachment, proliferation and differentiation[60]. Marine collagen has been incorporated into hydrogels, nanofibers and composite biomaterials designed for skin regeneration, cartilage repair and bone tissue engineering. Furthermore, collagen-based biomaterials have been explored in cosmetic and pharmaceutical industries due to their moisture-retaining properties and biological compatibility[61].

3.3. Calcium carbonate and coral-based materials

Marine organisms such as corals produce mineralized skeletal structures primarily composed of calcium carbonate[62]. These natural structures exhibit porous architectures that resemble the mineral composition and structural organization of human bone. Because of this similarity, coral-derived materials have been extensively investigated as bone graft substitutes in orthopaedic and dental applications[63]. Coral skeletons can be processed into biocompatible scaffolds that support bone regeneration. One of the most important features of coral-based biomaterials is their osteoconductive property, meaning they can facilitate the growth of new bone along their surfaces. The interconnected porous structure of coral allows for the infiltration of cells and the formation of blood vessels, both of which are essential for successful bone healing[64]. In many biomedical applications, coral materials are converted into calcium phosphate compounds such as hydroxyapatite while maintaining their natural porous architecture. This transformation enhances their similarity to human bone mineral and improves their integration with surrounding tissues[65]. As a result, coral-derived scaffolds have been used in bone defect repair, dental implants and other regenerative therapies aimed at restoring skeletal function[66].

3.4. Sponge-derived biomaterials

Marine sponges are among the oldest multicellular organisms and are known for their complex skeletal structures composed of silica-based elements and structural proteins[67]. These skeletal frameworks exhibit intricate three-dimensional architectures that have inspired the development of biomimetic materials for tissue engineering[68]. One of the key components found in many marine sponges is basilica, a naturally occurring form of silica that contributes to the formation of rigid skeletal elements known as spicules. Basilica structures possess unique mechanical and structural properties that make them attractive for biomedical research[69]. Studies have shown that bio-silica can influence cellular activities such as proliferation and differentiation, particularly in bone-forming cells. In addition to silica-based components, marine sponges produce specialized proteins that help organize and stabilize their skeletal structures. These proteins play important roles in the formation of complex biological architectures[70].

The natural porous framework of sponge skeletons provides an ideal template for scaffold development[71]. Their interconnected channels allow for efficient nutrient diffusion and cell infiltration, which are essential for tissue growth. Researchers have explored the use of sponge-derived biomaterials in the design of scaffolds for bone regeneration and other tissue engineering applications[72]. By studying the structural features of sponge skeletons, scientists aim to replicate their architecture in synthetic or hybrid biomaterials that support tissue repair[71]. Overall, marine animal-derived biomaterials represent a diverse and promising group of natural materials with significant potential in biomedical science. Their unique structural characteristics and biological compatibility provide valuable opportunities for developing innovative biomaterials for regenerative medicine and advanced scaffold fabrication[73]. Continued exploration of marine organisms and their biomaterials is expected to further expand their applications in modern biotechnology[74]. (Table 1) provides a concise summary of key marine-derived biomaterials and highlights their source organisms, chemical composition, functional properties, and translational relevance in biomedical applications.

Table 1. Marine-derived biomaterials and their sources with key properties

Biomaterial	Source Organism	Chemical Nature	Key Properties	Biomedical Significance	Reference

Chitin	Crustaceans (shrimp, crab)	Polysaccharide (N-acetyl-D-glucosamine)	Biodegradable, mechanical strength	Scaffold fabrication, wound healing	[75]
Chitosan	Derived from chitin	Deacetylated polysaccharide	Antimicrobial, biocompatible, film-forming	Drug delivery, tissue engineering	[76]
Collagen	Fish skin, jellyfish	Structural protein	Low immunogenicity, ECM mimicry	Skin, bone, cartilage regeneration	[40]
Alginate	Brown algae	Anionic polysaccharide	Gel-forming, high-water retention	Hydrogels, cell encapsulation	[77]
Carrageenan	Red algae	Sulphated polysaccharide	Stabilizing, gel-forming	Drug delivery, tissue scaffolds	[78]
Agar / Agarose	Red algae	Neutral polysaccharide	Thermal reversibility, stability	Cell culture, hydrogels	[79]
Fucoidan	Brown algae	Sulphated polysaccharide	Anti-inflammatory, antioxidant	Wound healing, immune modulation	[80]

4. Macroalgae-derived biomaterials

Macroalgae, commonly known as seaweeds, are large photosynthetic organisms that grow abundantly in marine environments and represent a significant source of naturally occurring biomaterials[35]. These marine plants are broadly classified into brown, red and green algae based on their pigmentation and biochemical composition. Unlike terrestrial plants, macroalgae contain unique polysaccharides and bioactive molecules that provide structural support and protection in dynamic marine habitats[81]. Over the past few decades, researchers have increasingly focused on macroalgae because of their ability to produce biodegradable, biocompatible and functionally versatile polymers. These marine-derived biomaterials have gained attention in biotechnology, pharmaceuticals and biomedical engineering due to their potential in developing hydrogels, scaffolds and drug delivery systems[82]. Among the most important macroalgae-derived biomaterials are alginate, carrageenan, agar, agarose and sulphated polysaccharides such as fucoidan[83].

4.1. Alginate

Alginate is one of the most widely studied polysaccharides obtained from brown macroalgae such as *Laminaria*, *Macrocystis* and *Ascophyllum* species. It is a naturally occurring linear polymer composed primarily of two uronic acid residues: β-D-mannuronic acid and α-L-guluronic acid[84]. These monomeric units are arranged in varying sequences along the polymer chain, which influences the physical properties of the resulting material. The extraction of alginate typically involves alkaline treatment of dried brown algae followed by purification and precipitation processes that yield sodium alginate as the final product[85].

One of the most notable features of alginate is its ability to form hydrogels in the presence of divalent cations such as calcium ions. This ionic cross-linking process leads to the formation of a three-dimensional network structure that can retain large amounts of water while maintaining mechanical stability[86]. The gel-forming capacity of alginate makes it particularly useful for biomedical applications. Alginate hydrogels provide a hydrated and protective environment that supports cellular growth and biological activity[87]. Because of these characteristics, alginate has been widely used in tissue engineering and regenerative medicine. It has been employed to encapsulate living cells, protect therapeutic agents and create scaffolds that mimic the extracellular matrix[88]. In wound healing applications, alginate-based dressings help maintain a moist environment that promotes tissue regeneration while also absorbing excess wound exudate. Additionally, alginate has been incorporated into microcapsules and nanoparticles for controlled drug delivery, enabling gradual release of therapeutic compounds at targeted sites within the body[89].

4.2. Carrageenan

Carrageenan is another important marine polysaccharide derived primarily from red algae such as *Kappaphycus*, *Eucheuma* and *Chondrus* species[90]. This sulphated polysaccharide consists of repeating galactose units linked through alternating glycosidic bonds. Depending on the number and position of sulphate groups within its structure, carrageenan is classified into several structural variants, the most common being kappa (κ), iota (ι) and lambda (λ) carrageenan. Each type exhibits distinct physicochemical characteristics that influence its functional properties[91].

Kappa-carrageenan forms strong and rigid gels when combined with potassium ions, while iota-carrageenan produces softer and more elastic gels in the presence of calcium ions[92]. Lambda-carrageenan, in contrast, does not form gels but functions effectively as a thickening and stabilizing agent. These differences in structural composition allow carrageenan to be utilized in a wide range of biomedical and pharmaceutical applications[93]. In pharmaceutical formulations, carrageenan has been used as a stabilizer, emulsifier and controlled-release agent in various drug delivery systems. Its ability to form hydrogels also supports its use in tissue engineering and wound healing materials[94]. Carrageenan-based hydrogels can provide structural support for cells and serve as matrices for delivering therapeutic compounds. In addition, certain carrageenan derivatives have demonstrated biological activities such as antiviral, antioxidant and anti-inflammatory effects, which further enhance their potential for biomedical applications[95].

4.3. Agar and agarose

Agar is a gel-forming polysaccharide extracted from several species of red algae, particularly those belonging to the genera *Gelidium* and *Gracilaria[96]*. Chemically, agar is composed of two main components: agarose and agaropectin. Among these, agarose is responsible for the strong gel-forming properties that make agar widely useful in scientific and biomedical research[97]. Agarose is a neutral polysaccharide consisting of repeating units of agarobiose, which form stable gel networks when dissolved in hot water and subsequently cooled. One of the distinctive characteristics of agarose gels is their thermal reversibility[98]. This means that the gel can melt when heated and solidify again upon cooling without losing its structural integrity. Such behaviour provides flexibility for various laboratory and biomedical procedures[99].

In tissue engineering, agarose-based hydrogels have been investigated as scaffolding materials due to their high-water content and ability to create a supportive environment for cell growth. These hydrogels can mimic aspects of natural extracellular matrices and provide a three-dimensional framework that facilitates cellular interactions[100]. Agarose is also frequently used in drug delivery research, where it functions as a carrier for controlled release systems[101]. The porous structure of agarose gels enables the gradual diffusion of therapeutic molecules, allowing for sustained delivery over time[102]. Beyond biomedical uses, agarose has long been utilized in molecular biology for techniques such as electrophoresis, where it forms a stable matrix for separating nucleic acids. The versatility and biocompatibility of agar and agarose continue to support their expanding role in biomedical and biotechnological applications[103].

4.4. Fucoidan and other sulphated polysaccharides

In addition to structural polysaccharides such as alginate and agar, macroalgae also produce a variety of sulphated polysaccharides with significant biological activity[104]. Fucoidan is one of the most well-known compounds in this group and is primarily extracted from brown algae including *Fucus*, *Undaria* and *Sargassum*. Structurally, fucoidan consists mainly of sulphated fucose residues along with smaller amounts of other monosaccharides[105]. Fucoidan has attracted considerable attention because of its diverse biological activities. Numerous studies have reported that fucoidan exhibits anti-inflammatory, antioxidant, anticoagulant and immunomodulatory effects[106]. These biological properties make it particularly valuable in the development of therapeutic materials aimed at promoting tissue repair and controlling inflammatory responses[107]. One area where fucoidan shows significant promise is wound healing. [108].

Other sulphated polysaccharides derived from macroalgae also demonstrate similar therapeutic potential. These compounds have been investigated for applications in cancer therapy, immune regulation and antiviral treatments[109]. Their natural origin, combined with their broad biological activity, makes them attractive candidates for the development of novel biomedical formulations. Overall, biomaterials derived from macroalgae represent an important class of marine resources with wide-ranging biomedical potential[40]. Their unique chemical structures, gel-forming abilities and biological activities provide valuable opportunities for developing advanced biomaterials for regenerative medicine, drug delivery and tissue engineering[110]. Continued research into macroalgal polysaccharides is expected to reveal new applications and improve the design of innovative biomaterial systems for future therapeutic use[111].

5. Extraction and processing of marine biomaterials

The development of marine-derived biomaterials for biomedical applications requires efficient methods for extracting, purifying and characterizing bioactive compounds from marine organisms[112]. Marine animals and macroalgae contain complex biological structures in which valuable polymers, proteins and minerals are embedded within cellular matrices. Therefore, specialized extraction and processing techniques are necessary to isolate these materials while maintaining their functional and structural integrity[113]. Advances in biotechnology and analytical methods have significantly improved the efficiency of recovering marine biomaterials and have also supported the development of environmentally friendly extraction processes[114]. Proper extraction and processing are essential to ensure the quality, safety and reproducibility of marine biomaterials used in biomedical and pharmaceutical applications[26].

5.1. Conventional extraction techniques

Traditional extraction techniques have long been used to isolate biomaterials from marine organisms[115]. These methods typically involve mechanical processing followed by chemical treatments to separate the desired compounds from biological tissues. For example, in the extraction of chitin from crustacean shells, the raw material is first cleaned, dried and ground into smaller particles[116]. This is followed by demineralization using dilute acids to remove calcium carbonate and other mineral components[117]. Subsequently, deproteinization is carried out using alkaline solutions to eliminate proteins and other organic impurities. The resulting purified chitin can then be further processed into chitosan through deacetylation[118].

Similarly, the extraction of polysaccharides from macroalgae generally involves hot water or alkaline extraction procedures[119]. In the case of alginate extraction from brown algae, the biomass is treated with alkaline solutions to dissolve alginic acid, which is then converted into sodium alginate through neutralization and precipitation steps. Agar and carrageenan extraction from red algae also rely on heat-assisted extraction followed by filtration and gel formation processes to isolate the polysaccharides[120]. Although conventional extraction techniques are effective, they often require high temperatures, strong chemicals and multiple processing steps[121]. These conditions can sometimes lead to partial degradation of sensitive biomolecules or generate chemical waste that may pose environmental concerns. Nevertheless, conventional methods continue to be widely used due to their simplicity and ability to produce large quantities of biomaterials[122].

5.2. Enzymatic and green extraction approaches

In response to the limitations associated with traditional extraction methods, researchers have increasingly explored enzymatic and environmentally friendly extraction approaches[123]. Enzymatic extraction involves the use of specific enzymes to selectively break down cellular structures and release target biomolecules. For instance, proteases and cellulases can be applied to degrade proteins and cell wall components in marine tissues, allowing easier recovery of structural polymers such as chitin or algal polysaccharides[124].

Compared with harsh chemical treatments, enzymatic processes operate under milder conditions, including moderate temperatures and neutral pH levels[125]. This helps preserve the structural integrity and biological activity of the extracted biomaterials. Additionally, enzymatic extraction often reduces the need for strong acids or alkalis, thereby minimizing environmental impact[126]. Green extraction techniques have also gained attention as sustainable alternatives for recovering marine biomaterials[114]. These approaches may include microwave-assisted extraction, ultrasound-assisted extraction and supercritical fluid extraction. Such methods enhance extraction efficiency by improving mass transfer and reducing processing time. They also decrease solvent consumption and energy usage, which contributes to more sustainable production of marine biomaterials[127]. As environmental considerations become increasingly important in biotechnology, green extraction technologies are expected to play a larger role in marine biomaterial processing[128].

5.3. Purification and characterization methods

Once biomaterials have been extracted from marine organisms, purification steps are required to remove impurities and obtain materials suitable for biomedical use[46]. Common purification techniques include filtration, centrifugation, dialysis and precipitation methods. These processes help eliminate unwanted substances such as salts, pigments, proteins and other organic contaminants[129]. Chromatographic methods are frequently used for further purification of marine biomolecules, particularly when high levels of purity are required for pharmaceutical or research applications[130]. Techniques such as gel filtration chromatography and ion exchange chromatography allow separation of molecules based on size, charge or chemical interactions. Through these methods, researchers can isolate specific fractions of biomaterials with well-defined properties[131]. Characterization of the purified materials is also a crucial step in ensuring their suitability for biomedical applications. Basic characterization involves determining molecular weight, chemical composition and purity levels. These parameters help researchers evaluate the consistency and quality of the extracted biomaterials[132].

5.4. Structural and physicochemical analysis

Understanding the structural and physicochemical properties of marine biomaterials is essential for predicting their behaviour in biological systems. Various analytical techniques are employed to examine molecular structure, functional groups and material morphology[3]. Spectroscopic methods such as Fourier transform infrared spectroscopy are commonly used to identify characteristic chemical bonds and confirm the presence of specific functional groups within biomaterials[133]. Microscopic techniques, including scanning electron microscopy and transmission electron microscopy, allow detailed observation of surface morphology and internal structures. These methods provide valuable information about pore size, surface texture and overall architecture, which are important factors in scaffold design and tissue engineering applications[134].

Thermal analysis techniques, such as differential scanning calorimetry and thermogravimetric analysis, are used to evaluate the thermal stability and degradation patterns of marine biomaterials[135]. Mechanical testing may also be performed to assess properties such as tensile strength, elasticity and compressibility. Together, these structural and physicochemical analyses provide a comprehensive understanding of marine-derived biomaterials and their functional characteristics[112]. Such information is essential for optimizing processing techniques and designing biomaterials that meet the requirements of specific biomedical applications[136].

6. Marine biomaterials in regenerative medicine

Regenerative medicine focuses on restoring damaged tissues and organs by integrating biomaterials, cells and bioactive molecules to support the body's natural healing processes[137]. In recent years, marine-derived biomaterials have gained considerable attention in this field because of their unique biological properties and structural versatility. Materials obtained from marine organisms such as crustaceans, fish, corals and macroalgae possess characteristics including biodegradability, biocompatibility and low toxicity, which make them suitable for therapeutic applications[29]. Additionally, many marine polymers resemble components of the natural extracellular matrix, allowing them to interact effectively with biological tissues. These properties have encouraged the exploration of marine biomaterials in several areas of regenerative medicine, including wound healing, bone and cartilage repair, skin tissue engineering and advanced drug delivery systems, as represented in (Fig.2)[138].

Wound healing is a complex biological process that involves multiple stages, including inflammation, tissue formation and remodelling[139]. The development of effective wound dressings plays an important role in supporting these processes and preventing infection. Marine biomaterials have demonstrated considerable potential in designing advanced wound healing materials due to their bioactive and protective properties[46].

Polymers such as chitosan, alginate and collagen are commonly incorporated into wound dressings because they can maintain a moist environment that facilitates tissue regeneration[140]. Chitosan, derived from marine crustaceans, exhibits natural antimicrobial properties that help inhibit the growth of pathogenic microorganisms at the wound site. This reduces the risk of infection and promotes faster healing[141]. Alginate-based dressings obtained from brown algae are widely used for highly exuding wounds because of their excellent fluid absorption capacity[142]. When these materials come into contact with wound exudate, they form a soft gel that protects the injured tissue while allowing oxygen exchange. Marine collagen also contributes significantly to wound healing applications[143]. Its structural similarity to human collagen enables it to support cell attachment and migration, which are essential for tissue repair. As a result, marine collagen has been incorporated into wound healing matrices, hydrogels and bioactive dressings designed to accelerate the healing process[40].

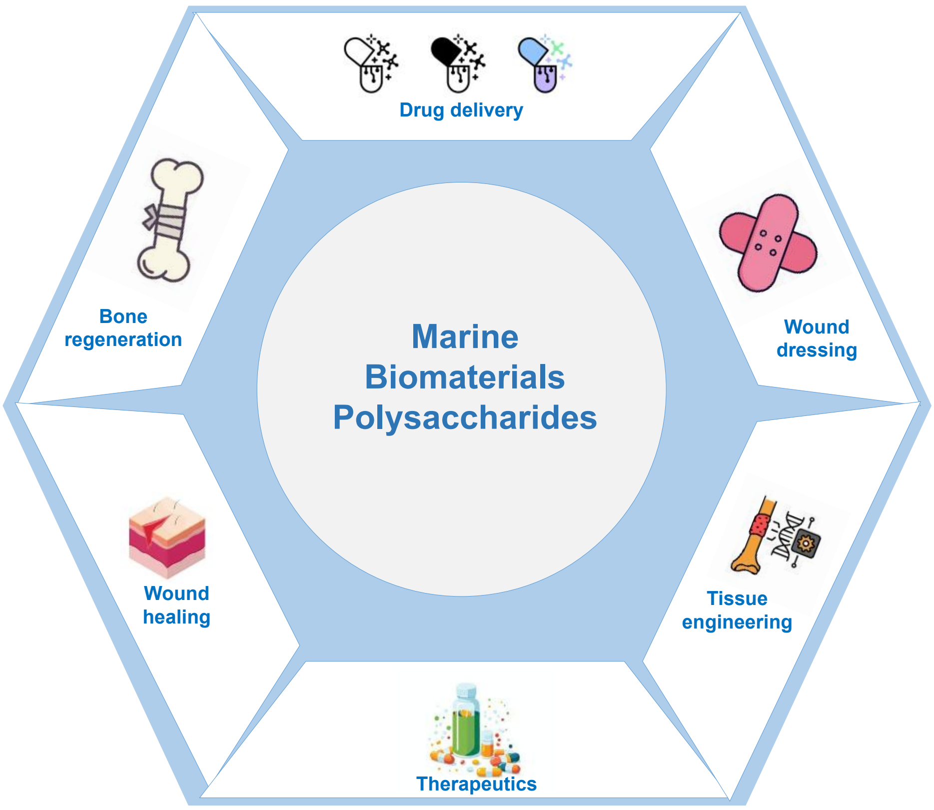


Fig. 2: Marine biomaterials in regenerative medicine

6.1. Wound healing applications

6.2. Bone and cartilage regeneration

Repairing damaged bone and cartilage tissues remains a major challenge in regenerative medicine[144]. Marine-derived biomaterials have shown promise in this area because many of them possess structural and chemical properties similar to natural skeletal tissues. Materials derived from marine organisms such as corals and fish bones contain mineral components that resemble the composition of human bone[67].

Coral-based biomaterials, for example, have been widely investigated as bone graft substitutes. Their naturally porous structure allows the infiltration of cells and blood vessels, which are essential for new bone formation[145]. These materials also demonstrate osteoconductive properties, meaning they support the growth of bone cells along their surface. Through chemical processing, coral skeletons can be converted into calcium phosphate materials that closely resemble the mineral phase of bone[66]. In addition to mineral-based biomaterials, marine collagen and alginate have been explored for cartilage regeneration. These polymers can be fabricated into hydrogels or scaffolds that provide a supportive environment for chondrocytes, the cells responsible for cartilage formation. Such scaffolds help maintain cell viability and encourage the production of extracellular matrix components necessary for cartilage repair[146].

6.3. Skin tissue engineering

Skin tissue engineering aims to develop biological substitutes that can restore the structure and function of damaged skin[147]. Marine biomaterials have been extensively studied in this field due to their compatibility with human tissues and their ability to form hydrogels and scaffold structures. Materials such as marine collagen, gelatine, alginate and chitosan have been used to design biomimetic matrices that resemble the natural extracellular matrix of skin[6].

These materials can be processed into porous scaffolds, films or hydrogels that provide structural support for skin cells[148]. The interconnected pore networks within these scaffolds allow nutrients and oxygen to diffuse easily, promoting cell survival and tissue development. Marine collagen-based scaffolds are particularly valuable because they enhance the attachment and proliferation of skin cells, including fibroblasts and keratinocytes[149]. Furthermore, marine biomaterials can be combined with growth factors, antimicrobial agents or stem cells to improve their therapeutic performance. Such advanced biomaterial systems are being investigated as skin substitutes for treating burns, chronic wounds and other severe skin injuries[150].

6.4. Drug delivery and controlled release systems

Another important application of marine biomaterials in regenerative medicine is the development of drug delivery and controlled release systems[151]. Effective delivery of therapeutic molecules is essential for improving treatment outcomes and minimizing side effects. Marine polymers provide versatile platforms for designing carriers capable of encapsulating drugs, proteins and other bioactive compounds[2]. Alginate, chitosan and agar-based materials can be formulated into nanoparticles, microcapsules or hydrogels that protect therapeutic agents from degradation while allowing gradual release at targeted sites[102]. The porous structure and gel-forming properties of these materials enable precise control over drug diffusion rates. This controlled release behaviour is particularly beneficial in regenerative medicine, where sustained delivery of growth factors or anti-inflammatory agents can significantly enhance tissue repair[152].

Additionally, marine-derived biomaterials can be engineered to respond to environmental stimuli such as pH or temperature, enabling the development of smart drug delivery systems[153]. These advanced carriers improve the efficiency of therapeutic treatments while reducing the need for repeated drug administration. Overall, marine biomaterials have become valuable tools in regenerative medicine because of their unique structural features and biological compatibility[112]. Continued research in this field is expected to expand their applications and contribute to the development of innovative therapeutic strategies for tissue repair and regeneration[154]. (Table 2) highlights the diverse roles of marine-derived biomaterials in regenerative medicine, emphasizing their functional mechanisms and therapeutic benefits across different tissue engineering applications.

Table 2. Applications of Marine Biomaterials in Regenerative Medicine

Application Area	Biomaterials Used	Mechanism of Action	Outcome/Benefit	Reference
Wound Healing	Chitosan, Alginate, Collagen	Antimicrobial action, moisture retention, cell adhesion	Faster healing, reduced infection	[155]
Bone Regeneration	Coral-derived $CaCO_3$, Collagen	Osteoconduction, mineral similarity to bone	Enhanced bone growth	[156]
Cartilage Repair	Alginate, Collagen	ECM mimicry, chondrocyte support	Improved cartilage formation	[157]
Skin Tissue Engineering	Collagen, Gelatine, Chitosan	Scaffold formation, cell proliferation	Skin regeneration	[158]

Drug Delivery Systems	Alginate, Chitosan, Agarose	Controlled release, encapsulation	Targeted therapy, reduced side effects	[89]

7. Nanoscaffold fabrication using marine biomaterials

The field of tissue engineering has increasingly focused on the development of nanoscale scaffolds that can replicate the complex architecture of natural tissues. Nanoscaffolds are three-dimensional structures engineered at the nanometre scale to support cellular attachment, proliferation and differentiation[159]. Their structural similarity to the extracellular matrix allows them to provide a favourable microenvironment for tissue regeneration. Marine-derived biomaterials have gained significant attention in nanoscaffold fabrication due to their biocompatibility, biodegradability and versatile physicochemical characteristics[4]. Polymers such as chitosan, alginate, collagen, gelatine and other polysaccharides obtained from marine organisms can be processed into nanoscale structures with controlled porosity and mechanical properties[160]. These materials offer promising opportunities for developing biomimetic scaffolds that enhance cellular responses and improve regenerative outcomes. The Nanoscaffold fabrication can be done by different methods such as Nanofibrous scaffolds, Hydrogels and nanogels, Electrospinning and fabrication techniques and Biomimetic scaffold design, as given below in (Fig.3)[161].

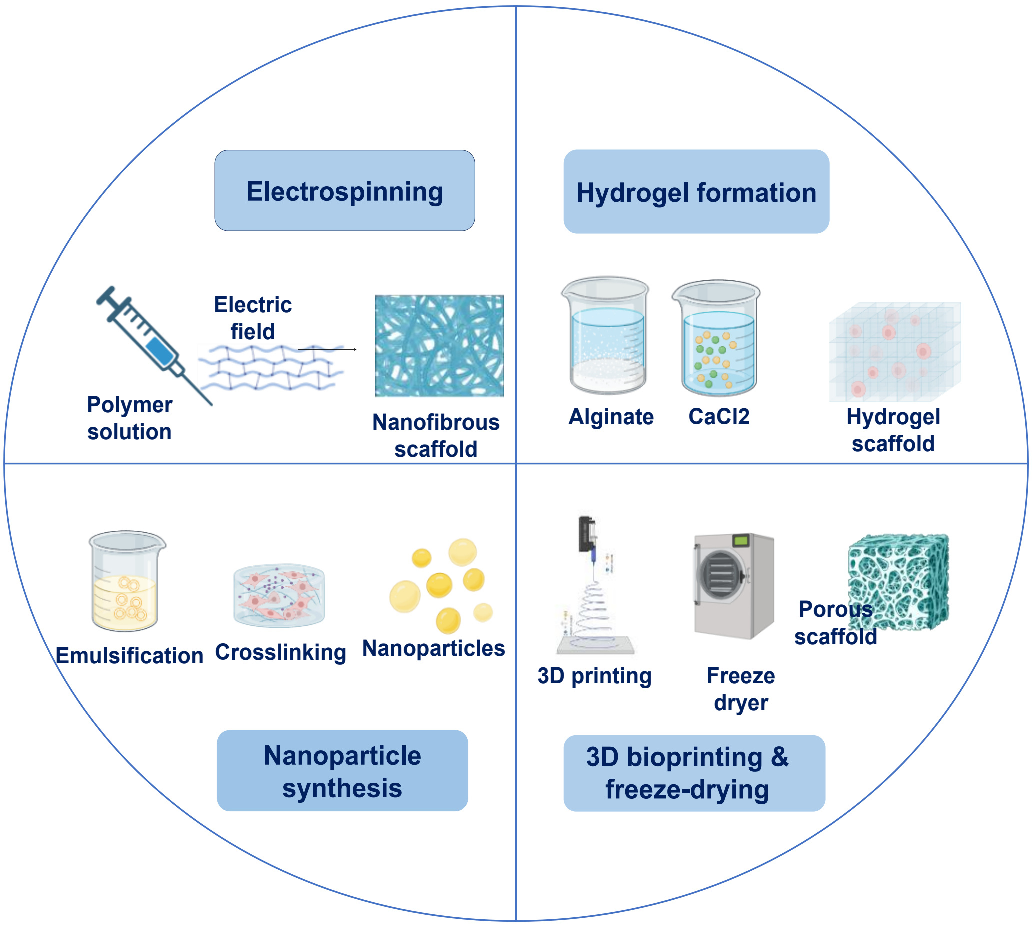


Fig. 3: Nanoscaffolds fabrication using marine biomaterials

7.1. Nanofibrous scaffolds

Nanofibrous scaffolds represent one of the most widely explored nanostructures in tissue engineering[162]. These scaffolds consist of fibres with diameters typically ranging from a few nanometres to several hundred nanometres, closely resembling the fibrous network of the natural extracellular matrix. This structural similarity enables nanofibrous scaffolds to provide physical support while facilitating communication between cells and their surrounding environment[163].

Marine-derived polymers have been extensively utilized in the fabrication of nanofibrous scaffolds[12]. Chitosan, derived from marine crustaceans, is commonly incorporated into nanofibrous structures because of its antimicrobial activity and ability to promote cell adhesion[164]. When processed into nanofibers, chitosan can form porous networks that allow efficient nutrient transport and waste removal, both of which are essential for maintaining cellular viability. Similarly, collagen extracted from marine organisms can be fabricated into nanofibrous scaffolds that closely mimic the structural characteristics of human connective tissues[165]. Alginate and other marine polysaccharides can also be integrated into composite nanofibrous scaffolds. Combining different marine biomaterials allows researchers to tailor the mechanical strength, degradation rate and biological functionality of the scaffold[26]. These hybrid systems are particularly useful in applications such as wound healing, nerve regeneration and bone tissue engineering, where specific structural and biological properties are required to support tissue formation[166].

7.2. Hydrogels and nanogels

Hydrogels are another important class of scaffolding materials used in regenerative medicine. They are three-dimensional polymer networks capable of absorbing and retaining large amounts of water while maintaining structural stability[167]. Marine-derived polymers such as alginate, agarose and carrageenan are particularly suitable for hydrogel formation due to their natural gel-forming capabilities[77].

Alginate-based hydrogels are widely used in tissue engineering because they can be easily cross-linked with calcium ions to form stable networks[168]. These hydrogels provide a highly hydrated environment that resembles the extracellular matrix of many tissues. The porous structure of alginate hydrogels allows cells to be encapsulated within the material, creating a supportive environment for cell growth and tissue development[169]. Additionally, the mechanical properties of alginate hydrogels can be modified by adjusting polymer concentration and cross-linking conditions. Nanogels represent a nanoscale version of hydrogels and have gained increasing interest for biomedical applications[170]. These tiny hydrogel particles typically measure less than 200 nanometres in diameter and can serve as carriers for drugs, proteins or growth factors. Marine polymers such as chitosan and alginate have been used to produce nanogels capable of delivering therapeutic molecules directly to targeted tissues. The high surface area and tuneable properties of nanogels enable controlled release of bioactive compounds, which is particularly beneficial in regenerative therapies where sustained delivery of growth factors is required[171].

7.3. Electrospinning and advanced fabrication techniques

The fabrication of nanoscaffolds requires precise techniques that allow control over fibre diameter, pore structure and material composition[172]. One of the most widely used methods for producing nanofibrous scaffolds is electrospinning. This technique involves applying a high-voltage electric field to a polymer solution, causing it to form fine fibres that are collected on a grounded surface[173]. The resulting fibres create interconnected networks with high surface area and porosity, which are favourable for cell attachment and nutrient exchange[174].

Marine-derived polymers can be electro spun either individually or in combination with synthetic polymers to improve their mechanical strength and stability[175]. For example, chitosan is often blended with biodegradable polymers such as polycaprolactone or polylactic acid to enhance the electrospinning process and produce uniform nanofibers. These composite materials combine the biological advantages of marine polymers with the structural stability of synthetic materials[176]. In addition to electrospinning, several advanced fabrication techniques are being explored to develop nanostructured scaffolds from marine biomaterials. Methods such as freeze-drying, 3D bioprinting and self-assembly allow precise control over scaffold architecture[177]. Freeze-drying, for instance, can produce highly porous scaffolds by removing frozen solvent from polymer solutions, leaving behind interconnected pore networks. Three-dimensional bioprinting enables the creation of customized scaffold designs that match the shape and structure of specific tissues. These advanced technologies have significantly expanded the possibilities for utilizing marine biomaterials in scaffold engineering[178].

7.4. Biomimetic scaffold design

A key objective in nanoscaffold fabrication is the development of biomimetic materials that closely replicate the structural and functional characteristics of natural tissues[179]. Biomimetic scaffold design focuses on reproducing essential features of the extracellular matrix, including fibre arrangement, porosity, mechanical strength and biochemical signalling[179]. Marine biomaterials are particularly suitable for biomimetic design because their chemical structures and biological properties resemble those of natural tissue components. For example, marine collagen provides structural proteins similar to those found in human connective tissues, while polysaccharides such as alginate and chitosan contribute to hydrated matrix environments that support cellular activity[40].

By combining marine biomaterials with nanotechnology and advanced fabrication methods, researchers can create scaffolds that promote cell adhesion, proliferation and differentiation[13]. These biomimetic scaffolds may also be functionalized with bioactive molecules such as growth factors or peptides to further enhance tissue regeneration. The integration of biological signals within scaffold structures allows cells to receive cues that guide tissue development and repair. Overall, nanoscaffold fabrication using marine-derived biomaterials represents a rapidly evolving area in regenerative medicine and biomaterials science[180]. The unique structural features and biological compatibility of marine polymers provide valuable opportunities for designing advanced scaffolds that closely mimic natural tissues. Continued progress in fabrication technologies and biomaterial engineering is expected to further improve the performance of marine-based nanoscaffolds and expand their applications in tissue regeneration and therapeutic delivery systems[4]. (Table 3) presents a comparative overview of the principal fabrication approaches for marine biomaterial-based nanoscaffolds, highlighting their architectural features and regenerative medicine applications."

Table 3. Nanoscaffold Fabrication Strategies Using Marine Biomaterials

Fabrication Method	Biomaterials Used	Structural Features	Advantages	Applications	Reference
Electrospinning	Chitosan, Collagen blends	Nanofibrous network	High surface area, ECM mimicry	Skin, nerve regeneration	[181]
Hydrogels	Alginate, Agarose, Carrageenan	3D hydrated network	Cell encapsulation, biocompatibility	Tissue engineering	[182]
Nanogels	Chitosan, Alginate	Nanoscale particles (<200 nm)	Controlled drug release	Targeted delivery	[183]
Freeze-drying	Collagen, Alginate	Porous scaffolds	High porosity, nutrient diffusion	Bone regeneration	[184]
3D Bioprinting	Composite marine polymers	Custom structure	Precision design, tissue matching	Advanced tissue engineering	[185]

8. Biological Properties Supporting Regeneration

Marine-derived biomaterials have gained considerable attention in regenerative medicine because of their favourable biological characteristics[40]. Materials obtained from marine animals and macroalgae often exhibit properties that support tissue repair and regeneration while minimizing adverse biological responses. Their natural origin, structural similarity to biological macromolecules and ability to interact with living cells make them highly suitable for biomedical applications[138]. Several key biological features contribute to their effectiveness in regenerative therapies, including biocompatibility, biodegradability, antimicrobial activity, anti-inflammatory effects and the ability to stimulate cellular growth and differentiation[186]. These properties enable marine biomaterials to function as supportive platforms for tissue engineering and therapeutic delivery systems.

8.1. Biocompatibility and biodegradability

One of the most important requirements for any biomaterial used in medical applications is biocompatibility[187]. A biocompatible material should be able to interact with biological tissues without causing toxic effects or triggering harmful immune responses[188]. Many marine-derived biomaterials naturally possess this quality because their molecular structures are similar to those found in biological tissues. For example, marine collagen resembles human collagen, which allows it to integrate effectively with cells and surrounding tissues[26]. This compatibility helps promote cellular attachment and tissue development when these materials are used in scaffolds or wound dressings. Biodegradability is another essential characteristic that supports the use of marine biomaterials in regenerative medicine[138]. Biodegradable materials gradually break down into non-toxic components within the body over time. This property eliminates the need for surgical removal after implantation and allows the material to be replaced naturally by newly formed tissue[189]. Polymers such as chitosan and alginate are well known for their controlled degradation rates, which can be adjusted depending on the intended biomedical application. This balance between structural stability and gradual degradation plays a critical role in successful tissue regeneration[190].

8.2. Antimicrobial activity

Infections represent a major challenge during the healing of injured tissues. Therefore, biomaterials with antimicrobial properties are particularly valuable in regenerative medicine[191]. Several marine-derived polymers demonstrate natural antimicrobial activity that helps inhibit the growth of harmful microorganisms. Chitosan, for instance, has been widely studied for its ability to disrupt bacterial cell membranes and interfere with microbial metabolism[192]. This antimicrobial effect is especially beneficial in wound healing applications where the risk of infection is high. By reducing microbial colonization at the injury site, marine biomaterials can help create a safer environment for tissue repair[193]. Additionally, the antimicrobial nature of these materials can reduce the dependence on conventional antibiotics, which is an important consideration in addressing the growing problem of antibiotic resistance[194].

8.3. Anti-inflammatory effects

Inflammation is a natural part of the body's response to injury, but excessive or prolonged inflammation can delay healing and damage surrounding tissues[195]. Certain marine biomaterials contain bioactive compounds that help regulate inflammatory responses and promote a balanced healing process. Sulphated polysaccharides derived from macroalgae, such as fucoidan, have been reported to exhibit anti-inflammatory properties by modulating immune signalling pathways[40]. These compounds can help reduce the production of inflammatory mediators while supporting tissue recovery. By controlling inflammation, marine-derived biomaterials create a more favourable environment for tissue regeneration. This property is particularly important in chronic wounds and degenerative conditions where persistent inflammation often interferes with normal healing mechanisms[196].

8.4. Promotion of cell proliferation and differentiation

Successful tissue regeneration depends largely on the ability of cells to grow, multiply and develop into specialized cell types[197]. Marine biomaterials often provide structural and biochemical cues that encourage these cellular activities. Their three-dimensional structures can mimic aspects of the natural extracellular matrix, allowing cells to attach and interact within a supportive environment[198]. Marine collagen, chitosan and alginate-based scaffolds have been shown to promote cell proliferation by providing surfaces that support cellular adhesion and nutrient exchange. In addition, certain marine biomolecules can stimulate signalling pathways involved in cell differentiation. This means that stem cells or progenitor cells can be guided to develop into specific tissue types such as bone, cartilage or skin[199].

By promoting both cell proliferation and differentiation, marine-derived biomaterials play a crucial role in the regeneration of damaged tissues. Their ability to create a biologically supportive environment makes them valuable components in modern tissue engineering strategies[11]. Overall, the biological properties of marine biomaterials contribute significantly to their effectiveness in regenerative medicine. Their compatibility with living tissues, combined with antimicrobial, anti-inflammatory and cell-stimulating activities, supports the development of advanced biomaterial systems designed to enhance tissue repair and healing[200].

9. Challenges and limitations

Although marine-derived biomaterials have demonstrated significant promise in regenerative medicine and biomedical engineering, several challenges still limit their widespread application[82]. Marine organisms represent a complex and diverse source of biological materials and the translation of these resources into clinically approved products requires overcoming technical, environmental and regulatory barriers[28]. Factors such as variability in raw materials, difficulties in extraction and purification, limitations in large-scale production and strict safety regulations all influence the development of marine biomaterial-based technologies. Addressing these challenges is essential for ensuring the consistent quality, safety and availability of marine-derived biomaterials for biomedical use[26].

9.1. Variability of marine biomaterials

One of the primary challenges associated with marine biomaterials is the natural variability in their composition and structure[46]. Marine organisms grow under different environmental conditions, including variations in temperature, salinity, nutrient availability and ecological interactions. These environmental factors can influence the biochemical composition of biomolecules produced by marine animals and macroalgae. As a result, biomaterials extracted from the same species may exhibit differences in molecular weight, structural arrangement and biological activity depending on their geographic origin or seasonal conditions[201]. This variability can affect the reproducibility and performance of biomaterials used in biomedical applications. For example, changes in the composition of alginate or chitosan may alter their mechanical properties, degradation behaviour or interaction with cells[202]. Maintaining consistent material quality is therefore an important consideration in the development of reliable biomedical products. Standardization of harvesting practices and improved quality control methods are necessary to minimize variations in marine-derived biomaterials[203].

9.2. Extraction and purification challenges

Another significant limitation involves the complexity of extracting and purifying biomaterials from marine organisms. Marine tissues often contain mixtures of proteins, polysaccharides, minerals and pigments that must be separated through multiple processing steps[46]. Traditional extraction methods frequently rely on strong acids, alkalis or high temperatures, which may partially degrade sensitive biomolecules or alter their functional properties. In addition, purification procedures can be time-consuming and may require specialized equipment and chemical reagents[204]. These processes increase production costs and can generate chemical waste that raises environmental concerns. Achieving high purity levels is particularly important for biomedical applications, as impurities may cause adverse biological reactions or compromise the safety of the final product. Consequently, improving extraction efficiency while preserving the structural integrity of marine biomolecules remains a major focus of ongoing research[205].

9.3. Scalability and manufacturing constraints

While laboratory-scale studies have demonstrated the effectiveness of many marine-derived biomaterials, scaling up production for industrial or clinical use presents additional challenges[206]. Large-scale manufacturing requires reliable sources of raw materials, consistent processing techniques and cost-effective production methods. However, harvesting marine organisms in large quantities may lead to ecological disruption or depletion of natural populations if not carefully managed[207]. Furthermore, the complex structures of certain marine biomaterials may make them difficult to process using conventional industrial techniques. Producing biomaterials with uniform quality and reproducible properties at a commercial scale requires advanced processing technologies and strict manufacturing standards[208]. Developing sustainable aquaculture systems and optimized processing strategies may help overcome some of these limitations while ensuring a steady supply of marine resources[209].

9.4. Regulatory and safety concerns

The introduction of new biomaterials into medical practice requires thorough evaluation to ensure their safety and effectiveness[210]. Marine-derived biomaterials must undergo extensive testing before they can be approved for clinical use. These evaluations include studies on biocompatibility, toxicity, immunogenicity and long-term stability within biological systems[211]. Regulatory agencies require detailed documentation of manufacturing processes, quality control measures and clinical performance before granting approval for biomedical products[212].

Another concern involves the potential presence of contaminants such as heavy metals, marine toxins or microbial residues that may originate from the marine environment. Proper purification and quality assessment procedures are therefore essential to ensure that these materials meet strict safety standards[213]. Compliance with regulatory guidelines can be time-consuming and costly, which may slow the translation of marine biomaterial research into practical medical applications. Overall, despite their considerable potential, marine-derived biomaterials face several challenges that must be addressed to enable their broader use in regenerative medicine and biotechnology[203]. Continued research focusing on standardization, sustainable production, improved extraction methods and rigorous safety evaluation will be crucial for overcoming these limitations and advancing the development of marine biomaterial-based therapies[23].

10. Future perspectives

The rapid progress in marine biotechnology has opened new opportunities for the development of innovative biomaterials with applications in regenerative medicine, tissue engineering and advanced therapeutic systems[13]. Marine organisms provide a vast and largely unexplored source of biologically active materials that possess unique chemical structures and functional properties. As scientific understanding of marine biomaterials continues to expand, future research is expected to focus on improving material performance, integrating advanced technologies and ensuring sustainable utilization of marine resources[203]. Several emerging trends are shaping the future direction of this field, including advanced biomaterial engineering, integration with nanotechnology and bio-fabrication, sustainable harvesting practices and the translation of research findings into clinical and commercial products[214].

Advances in biomaterial engineering are enabling the design of marine-derived materials with improved functionality and tailored properties. Through chemical modification and material blending, researchers can enhance the mechanical strength, stability and biological activity of marine polymers such as chitosan, alginate and collagen. These modifications allow the development of hybrid biomaterials that combine the advantages of natural marine compounds with the structural benefits of synthetic polymers[215]. Such engineered materials can be designed to respond to biological signals, regulate degradation rates or deliver therapeutic molecules in a controlled manner. Continued progress in biomaterial engineering is expected to generate next-generation scaffolds and therapeutic platforms with improved regenerative capabilities[216].

The combination of marine biomaterials with nanotechnology and bio fabrication techniques is another important trend shaping future biomedical applications. Nanotechnology enables the creation of nanoscale structures that closely mimic the architecture of natural tissues, improving the interaction between biomaterials and living cells[217]. Marine polymers can be incorporated into nanofibers, nanoparticles and nanogels to develop advanced delivery systems and tissue engineering scaffolds. In addition, bio fabrication technologies such as three-dimensional bioprinting offer new possibilities for constructing complex tissue structures using marine-derived materials[218]. These techniques allow precise control over scaffold architecture, cell placement and material composition. By integrating marine biomaterials with these emerging technologies, researchers can create highly sophisticated tissue models and regenerative therapies[134].

As interest in marine biomaterials grows, it is essential to ensure that their extraction does not harm marine ecosystems. Sustainable harvesting strategies and responsible resource management will play a key role in the long-term development of marine biotechnology. Cultivation methods such as aquaculture and seaweed farming provide practical alternatives to wild harvesting, enabling the large-scale production of marine organisms without damaging natural habitats[219]. In addition, advancements in biotechnology may allow certain marine biomolecules to be produced through microbial or cell-based systems, reducing dependence on natural marine populations. Promoting sustainable practices will help protect marine biodiversity while supporting the continued discovery of valuable biomaterials[220].

The successful application of marine biomaterials in healthcare ultimately depends on their translation from laboratory research to clinical practice. Future efforts will focus on improving manufacturing processes, ensuring product safety and meeting regulatory requirements for biomedical materials[221]. Collaborative research involving scientists, clinicians and industry partners will be essential for advancing marine biomaterial technologies toward commercialization. As regulatory approval processes become more streamlined and production methods improve, marine-derived biomaterials are expected to play a growing role in the development of medical devices, wound care products and regenerative therapies. These advancements will contribute to the creation of innovative treatment strategies that harness the unique potential of marine biological resources[23].

11. CONCLUSION

Marine-derived biomaterials have emerged as valuable resources for advancing regenerative medicine and nanoscaffold fabrication. The vast biodiversity of marine organisms, including marine animals and macroalgae, provides a rich source of structurally diverse polymers and bioactive compounds such as chitin, collagen, alginate, carrageenan and fucoidan. These materials exhibit beneficial properties including biocompatibility, biodegradability, antimicrobial activity and the ability to support cellular growth and tissue regeneration. Their versatility allows them to be incorporated into various biomedical systems, including wound healing materials, bone substitutes, drug delivery platforms and nanoscale scaffolds. Despite their promising potential, challenges such as variability in raw materials, complex extraction procedures, scalability issues and regulatory considerations must be addressed to facilitate their broader clinical use. Continued research focusing on advanced biomaterial engineering, sustainable resource utilization and integration with emerging technologies will further enhance their biomedical applications. Overall, marine biomaterials represent a promising frontier for developing innovative therapeutic solutions and next-generation regenerative technologies.

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