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A comprehensive review on various marine drugs possesing wound healing activity

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Abstract
Wound healing is a dynamic biological process involving haemostasis, inflammation, proliferation, and remodelling. Conventional wound treatments often show limitations such as infection, delayed healing, poor biocompatibility, and inadequate tissue regeneration. Marine-derived bioactive compounds and biomaterials have emerged as promising alternatives due to their biodegradability, biocompatibility, antimicrobial activity, anti-inflammatory effects, and ability to promote tissue regeneration. This review summarizes the wound healing potential of various marine-derived agents including fucoidan, chitosan, alginate, carrageenan, marine collagen, marine gelatine, bioactive peptides, sea cucumber extracts, and marine sponge-derived compounds. Their sources, mechanisms of action, pharmacological activities, advantages, limitations, and applications in advanced wound dressings are discussed. A comparative analysis of these marine drugs highlights their potential in the development of innovative wound healing formulations. The review also addresses challenges such as extraction, stability, standardization, and clinical translation, while emphasizing prospects in nanotechnology, hydrogel systems, tissue engineering, and combination therapies. Overall, marine-derived compounds represent a valuable resource for the development of safe, effective, and advanced wound healing therapies.

Keywords: Marine drugs, wound healing, fucoidan chitosan, alginate, carrageenan, marine biomaterials, wound dressing

Introduction

Wound: A wound is defined as a disruption in the normal anatomical and functional continuity of the skin or underlying tissues caused by physical, chemical, thermal, or biological injury [1]. Wounds may be acute or chronic depending on their healing duration and underlying pathology. Acute wounds usually heal through a predictable sequence of biological events, whereas chronic wounds fail to progress through the normal healing stages due to factors such as infection, diabetes, poor circulation, or persistent inflammation [2].

Wound healing: Wound healing is a complex and highly coordinated process involving cellular, molecular, and biochemical events. It occurs through four overlapping phases [3] Successful healing requires adequate blood supply, oxygenation, nutrient availability, infection control, and proper extracellular matrix formation.

Stages of Wound Healing

- **Haemostasis:** Platelet aggregation and clot formation immediately after injury.
- **Inflammation:** Recruitment of neutrophils and macrophages to remove debris and pathogens.
- **Proliferation:** Fibroblast proliferation, collagen synthesis, angiogenesis, and granulation tissue formation.
- **Remodelling:** Collagen maturation, tissue strengthening, and scar formation.

Factors Affecting Wound Healing

- Age and nutritional status
- Diabetes mellitus
- Infection
- Oxygen supply and blood circulation
- Stress and medications
- Smoking and lifestyle factors

Wound Treatment Methods

- Conventional dressings.
- Antimicrobial dressings
- Hydrogel dressings.
- Foam dressings.
- Bioactive wound dressings,
- Tissue-engineered skin substitutes.

Need for Improved Wound Healing Formulations:

Conventional wound therapies may not provide optimal moisture balance, antimicrobial protection, or tissue regeneration. Therefore, advanced wound healing formulations with biocompatibility, biodegradability, antimicrobial activity, and regenerative potential are required [4].

Marine-Derived Biomaterials in Wound Healing

Marine organisms such as algae, crustaceans, fish, sea cucumbers, and sponges are rich sources of bioactive compounds and biomaterials with therapeutic potential. These marine-derived agents exhibit antimicrobial, anti-inflammatory, antioxidant, haemostatic, and tissue regenerative properties, making them attractive candidates for wound healing applications [5]

Marine Drugs Possessing Wound Healing Activity

Focoidan

Fucoidan is a sulphated polysaccharide mainly obtained from brown seaweeds such as Fucus vesiculosus and Laminaria japonica [6]. It exhibits anti-inflammatory, antioxidant, anticoagulant, and angiogenic properties. Fucoidan promotes fibroblast proliferation, collagen synthesis, and angiogenesis, thereby accelerating wound closure and tissue regeneration.

Chitosan
Chitosan is a deacetylated derivative of chitin obtained from crustacean shells [7]. It possesses excellent biocompatibility, biodegradability, antimicrobial activity, and haemostatic properties. Chitosan enhances fibroblast proliferation, collagen deposition, and granulation tissue formation, making it a widely used biomaterial in wound dressings.

Alginate
Alginate is a polysaccharide extracted from brown algae [8]. It forms hydrogels capable of maintaining a moist wound environment, absorbing exudates, and promoting haemostasis. Alginate dressings are particularly useful for highly exuding wounds.

Carrageenan
Carrageenan is a sulphated polysaccharide derived from red seaweeds [9]. It exhibits anti-inflammatory and gel-forming properties, making it suitable for hydrogel wound dressing formulations.

Marine Collagen
Marine collagen, mainly obtained from fish skin and scales, provides a natural extracellular matrix for cell adhesion, proliferation, and tissue regeneration [10]. It supports collagen deposition and wound remodelling.

Marine Gelatin
Marine Gelatine is derived from collagen hydrolysis and possesses excellent film-forming and biocompatible properties [11]. It is used in wound dressing films, sponges, and hydrogels.

Marine Bioactive Peptides
Marine peptides obtained from fish, molluscs, and other marine organisms exhibit antimicrobial, antioxidant, and anti-inflammatory activities [12]. They promote cell migration and tissue repair.

Sea Cucumber Derived Compounds
Sea cucumber extracts contain triterpene glycosides, sulphated polysaccharides, and collagen-like compounds that promote wound healing through anti-inflammatory and regenerative mechanisms [13].

Marine Derived Sponge Compound
Marine sponges produce secondary metabolites with antimicrobial, anti-inflammatory, and tissue regenerative properties [14]. These compounds are being explored for advanced wound healing formulations.

Comparative Summary of Marine Drugs

Marine Drug	Source	Mechanism	Advantages	Applications
Fucoidan	Brown algae	Angiogenesis, collagen synthesis	Anti-inflammatory, antioxidant	Hydrogels, films
Chitosan	Crustacean shells	Hemostasis, antimicrobial	Biocompatible, biodegradable	Dressings, scaffolds
Alginate	Brown algae	Moisture retention	Hemostatic, absorbent	Exudative wound dressings
Carrageenan	Red algae	Gel formation	Anti-inflammatory	Hydrogels
Marine collagen	Fish skin/scales	Tissue regeneration	ECM support	Scaffolds, dressings
Marine gelatin	Fish collagen	Film formation	Biocompatible	Films, sponges
Marine peptides	Fish/mollusks	Antimicrobial	Antioxidant	Bioactive dressings

Marine-Based Wound Dressing Systems
Marine-derived biomaterials have emerged as promising materials for the development of advanced wound dressing systems due to their excellent biocompatibility, biodegradability, low toxicity, and inherent biological activities. Unlike conventional wound dressings, marine-based wound dressings not only protect the wound from external contamination but also maintain a moist environment, facilitate gas exchange, absorb excess wound exudate, and promote tissue regeneration [1].

- **Hydrogels**

Hydrogels are three-dimensional polymeric networks capable of retaining large amounts of water, thereby maintaining an optimal moist environment for wound healing. Marine-derived polymers such as alginate, chitosan, fucoidan, and carrageenan are commonly used in hydrogel formulations. These hydrogels enhance cell proliferation, angiogenesis, collagen deposition. Their cooling and soothing effects also help relieve wound-associated pain [14,16].

- **Films and Membranes**

Marine-based films and membranes are thin, flexible wound dressings prepared using marine collagen, chitosan, alginate. These dressings serve as protective barriers against microbial contamination while allowing adequate oxygen exchange and maintaining appropriate wound moisture [14, 17].

- **Sponges**

Marine-derived sponges are porous biomaterial dressings prepared mainly from chitosan, marine collagen. Their highly porous structure enables efficient absorption of wound exudate while maintaining a moist environment favourable for tissue repair [14, 17].

- **Scaffolds**

Scaffolds are three-dimensional biomaterial matrices designed to mimic the natural extracellular matrix and provide structural support for tissue regeneration. Marine collagen, chitosan, and alginate-based scaffolds facilitate cell adhesion, fibroblast proliferation, angiogenesis, collagen synthesis. These scaffolds are extensively investigated in tissue engineering and regenerative medicine for the treatment of chronic and non-healing wounds [17,18].

- **Nanoparticles**

Nanoparticles prepared from marine biomaterials have attracted considerable interest as advanced drug delivery systems for wound management. Chitosan and fucoidan nanoparticles exhibit antimicrobial, antioxidant, and anti-inflammatory activities while enabling sustained and targeted drug release. These nanoparticles improve drug penetration, reduce microbial infection, stimulate angiogenesis, and enhance tissue regeneration, resulting in faster wound closure [6, 16].

- **Composite Wound Dressings**

Composite wound dressings combine two or more marine-derived biomaterials to obtain synergistic therapeutic effects. Examples include chitosan–alginate, fucoidan–chitosan, and collagen–gelatin composites. These multifunctional dressings exhibit enhanced mechanical strength, superior moisture retention, improved antimicrobial activity, and greater regenerative potential compared with single-component dressings, making them promising candidates for advanced wound care [15,15,17].

- **Bioactive Wound Dressings**

Bioactive wound dressings incorporate marine-derived bioactive compounds that actively participate in the healing process rather than merely covering the wound. Consequently, these dressings have shown significant potential in the management of chronic wounds, diabetic ulcers, burn injuries, pressure ulcers

Methodology

This review summarizes the formulation methods employed in the development of marine-derived wound healing systems. Relevant scientific literature was collected from peer-reviewed research articles, review papers, and standard reference books. The selected studies focused on marine biomaterials such as fucoidan, chitosan, alginate, carrageenan, marine collagen, and marine gelatine, along with their formulation techniques and wound healing applications. The commonly reported formulation methods are summarized in Table 2 and discussed in the following sections.

Formulation Method	Marine-Derived Compounds	Major Application
Hydrogel	Fucoidan, Chitosan, Alginate, Carrageenan	Moist wound healing
Film Casting	Chitosan, Marine Collagen, Marine Gelatin	Protective wound films
Freeze-Drying	Chitosan, Alginate, Marine Collagen	Porous sponges
Scaffold Fabrication	Marine Collagen, Chitosan	Tissue regeneration
Electrospinning	Chitosan, Gelatin, Collagen	Nanofiber dressings
Nanoparticle Preparation	Chitosan, Fucoidan	Controlled drug delivery
Composite Dressing	Chitosan + Alginate	Multifunctional wound dressing

- **Hydrogel Preparation**

Hydrogels prepared from marine polysaccharides maintain a moist wound environment, absorb wound exudate, and promote cell proliferation and tissue regeneration. They are widely used in chronic and burn wound management [2, 6].

- **Film Casting**

Film casting is commonly used to prepare thin and flexible wound dressings from chitosan, marine collagen, and marine gelatine. These films protect the wound from microbial contamination while allowing oxygen exchange [14, 17].

- **Freeze-Drying (Lyophilization)**

Freeze-drying produces highly porous marine biomaterial sponges with excellent fluid absorption and haemostatic properties. These dressings are particularly suitable for highly exuding wounds [14, 16].

- **Scaffold Fabrication**

Marine collagen- and chitosan-based scaffolds mimic the extracellular matrix and provide structural support for cell attachment, proliferation, and tissue regeneration [16, 17].

- **Electrospinning**

Electrospinning is employed to fabricate nanofibrous dressings with high surface area and porosity, promoting cell adhesion and sustained drug release for improved wound healing [14, 18].

- **Nanoparticle Preparation**

Marine-derived nanoparticles, especially those based on chitosan and fucoidan, improve antimicrobial activity and enable controlled release of therapeutic agents at the wound site [6, 18].

- **Composite Dressing Preparation**

Composite dressings combine two or more marine biomaterials to improve mechanical strength, moisture retention, antimicrobial activity, and overall wound healing performance [14, 16].

Challenges and Limitations

1. Variability in marine source composition.
2. Extraction and purification difficulties.
3. Stability issues during formulation.
4. Limited clinical studies.
5. Regulatory and standardization concerns

Future prospectives

- **Future research should focus on:**

1. Nanotechnology-based marine wound dressings
2. Smart hydrogel systems
3. Combination therapies using multiple marine biomaterials
4. 3D bioprinting and tissue engineering applications
5. Clinical trials for safety and efficacy evaluation

Conclusion

Marine-derived bioactive compounds and biomaterials possess significant wound healing potential due to their antimicrobial, anti-inflammatory, antioxidant, haemostatic, and tissue regenerative properties. Fucoidan, chitosan, alginate, carrageenan, marine collagen and other marine compounds offer promising opportunities for the development of advanced wound healing formulations. Although challenges related to extraction, standardization, and clinical translation remain, continued research and technological advancements may enable these marine drugs to become valuable therapeutic agents in modern wound management.

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