

REVIEW OF MARINE PHARMACOGNACY

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ABSTRACT

A large proportion of the current pharmacopoeia can trace its origin back to nature. Biodiversity in the Earth's largest habitat, the ocean, is greater than that on land, suggesting a huge potential for new bioactive chemistry. Compounds isolated from marine organisms have novel structures and modulate human disease targets with novel mechanisms of action. Around 15–20 marine-derived compounds have been approved for clinical use against cancer, pain, viral infection and heart disease. Some of the most potent compounds are directed towards cancer cells via linkage to an antibody. The approved marine-derived pharmaceuticals have been produced via (semi)-synthesis, while expression of the biosynthetic gene clusters in a microbial host is a future alternative for the production of those compounds. Technical improvements in the extraction, isolation and structural characterisation of marine-derived compounds, as well as the reduction in effort wasted in isolation of known compounds, have sped up the discovery process, meaning that industry is taking a renewed interest in this field as a source of pharmaceuticals with novel mechanisms of action to treat human disease with unmet need.

KEYWORDS: Marine natural products,^[1] drug discovery, aquaculture, semi-synthesis antibody-drug conjugates.^[2]

INTRODUCTION

Marine pharmacognosy is the investigation and identification of medically important plants and animals in the marine environment. It is a sub branch of terrestrial pharmacognosy. Generally the drugs are obtained from the marine species of bacteria, virus, algae, fungi and sponges. It is a relatively new field of study in western medicine, although many marine organisms were used in traditional Chinese medicine. It was not until 2004 that the first FDA approval of a drug came directly from the sea: ziconotide, which was isolated from a marine cone snail.^[3]

With 79% of the Earth's surface covered by water, research into the chemistry of marine organisms is relatively unexplored and represents a vast resource for new medicines to combat major diseases such as cancer, AIDS or malaria. Research typically focuses on sessile organisms or slow moving animals because of their inherent need for chemical defenses.

Standard research involves an extraction of the organism in a suitable solvent followed by either an assay of this crude extract for a particular disease target or a rationally guided isolation of new chemical compounds using standard chromatography techniques.

Marine natural products: Marine natural products refer to compounds or substances derived from marine organisms, such as plants, animals, and microorganisms. These compounds have potential therapeutic applications and can be used to develop new medicines.

Drug Discovery: Drug discovery is the process of identifying and developing new compounds or substances that can be used to treat diseases or conditions. Marine natural products play a significant role in drug discovery, as they provide a rich source of novel compounds with potential therapeutic applications.^[4]

Aquaculture: Aquaculture refers to the cultivation of aquatic plants and animals, such as fish, shellfish, and seaweeds, in controlled environments. Aquaculture can provide a sustainable source of marine organisms for the production of natural products.

Semi-Synthesis: Semi-synthesis refers to the process of modifying natural products or compounds to create new derivatives with improved properties or activities. Semi-synthesis can be used to optimize the therapeutic potential of marine natural products.

Antibody-Drug Conjugates (ADCs): Antibody-drug conjugates (ADCs) are a type of targeted therapy that combines the specificity of antibodies with the potency of small molecule drugs. ADCs consist of an antibody linked to a cytotoxic payload, which is delivered specifically to cancer cells or other target cells, reducing harm to healthy tissues. Marine natural products can be used as payloads in ADCs.^[5]

DESCRIPTION

These marine-derived natural products bioactive compounds from marine organisms. Biotechnological approaches exhibit diverse chemical structures and biological activities, offering promising include Bioprospecting and Metagenomics like High-throughput sequencing leads for drug discovery, biomedical research, and environmental conservation technologies and metagenomic analyses facilitate the discovery of novel efforts. Marine algae, encompassing macroalgae (seaweeds) and microalgae biosynthetic gene clusters and bioactive compounds from complex microbial are prolific sources of bioactive compounds due to their adaptation to various communities in marine environments. Synthetic biology and genetic ecological niches and environmental stressors. Macroalgae, such as brown engineering techniques enable the manipulation of biosynthetic pathways algae (Phaeophyceae), red algae (Rhodophyta), and green algae (Chlorophyta), in marine organisms to enhance the production of bioactive compounds and produce a wide array of secondary metabolites including polysaccharides, optimize their pharmacological properties.^[6]

Marine pharmacognosy represents a burgeoning field at the intersection of marine biology, chemistry, pharmacology, and biotechnology. It explores the vast biodiversity of oceanic life forms from microscopic algae to majestic corals and deep-sea organisms-to uncover novel bioactive compounds with potential pharmaceutical applications. These marine-derived natural products exhibit diverse chemical structures and biological activities, offering promising leads for drug discovery, biomedical research, and environmental conservation efforts.^[7] Marine algae, encompassing macroalgae (seaweeds) and microalgae are prolific sources of bioactive compounds due to their adaptation to various ecological niches and environmental stressors. Macroalgae, such as brown algae (Phaeophyceae), red algae (Rhodophyta), and green algae (Chlorophyta), produce a wide array of secondary

metabolites including polysaccharides, polyphenols, terpenes, and halogenated compounds. These compounds exhibit a broad spectrum of biological activities such as antioxidant, anti-inflammatory, antimicrobial, antiviral, and anticancer properties. For instance, fucoidan extracted from brown algae has shown promise as an anticoagulant, antioxidant, and immunomodulator. Carrageenans derived from red algae are widely used in pharmaceuticals and food industries for their gelling and thickening properties.^[8]

Classification

Classification of marine drugs:

1. Cytotoxic/Antineoplastic Agents
2. Cardiovascular Active Drugs Marine Toxins
3. Antimicrobial Drugs
4. Antibiotic Substances.
5. Anti-inflammatory
6. Antiparasitic Agents
7. Antispasmodic Agents
8. Miscellaneous Pharmacologically Active Agents

Antineoplastic agents

- Crassin acetate
- It is a member of Cembranoids which are cyclic diaterpenes.
- Biological source: It is obtained from caribbean gorgonian pseudoplexaura pe
- Chemical constituents: The main active constituent is Crassin acetate,
- Uses: Crassin acetate was observed to be extremely cytotoxic to human leukaemia cells in vitro.

Cardiovascular Agents

- Eldoisin
- Eldoisin is a powerful hypotensive compound. It also shows strong vasodilator effect.
- Biological source: Eldoisin is obtained from the posterior salivary glands of [small octopus] eldono moschata.

Uses

1. It is found to stimulate extra vascular smooth muscle.
2. Eldoisin is acts as a potent vasodilator and hypotensive activity.
3. It also stimulate lacrimal secretion.
4. It causes salivation and enhance capillary permeability in certain specific species.^[9]

Antibiotics

1.Cephalosporin-c

Biological source: It is obtained from Cephalosporium acrimonium fun

Uses: It is antibiotic agent.

2.Instamycin-A

Biological source: It is obtained from Streptomyces tenjimariensis.

Uses: In vitro activity against Gram(-) and Gram(+) bacteria.

3. Istamycin-B

Biological source: It is obtained from *Streptomyces tenjimariensis*.

Uses: In vitro activity against Gram(-) and Gram(+) bacteria.^[14]

Anti-inflammatory drugs:

Plethora of chemical substance have been isolated from the broad spectrum marine organisms which attribute either anti-inflammatory or anti-spasm activities.

TETRADO TOXIN

Biological source: Tetradoxin is obtained from liver and ovaries of puffer fish.

Uses:

1. It is used as anti-inflammatory.
2. It has analgesic effect.
3. It acts as muscle relaxant.^[10]

Anti-parasitic agents

DIGENIA SIMPLEX (Red Algae)

Biological source: *Degenia simplex* is a marine red algae native to pacific (Philippines, Japan)

Chemical constituents: Alpha-kianic acid.

Uses: It is a broad spectrum anthelmintic effective against round worm, tapeworm and whipworm.

Anti-microbial agents

1.ZONAROL:

Biological source: Zonarol and Iso-zonarol are both obtained *Dictyopteris zonaroides* (Brown algae).

Uses: It is used as antifungal drug

2.TETRABROMO-2-HEPTANONE

Biological source: tetrabromo-2-heptanone is obtained from the another species of Red algae *Bonnemaisonia hemifera*.

Uses: It is used as Antimicrobial agents.

Anti-spasmodic agents

Agelasidine

A sesquiterpene derivative isolated from Okinawa sea sponge *Agelas* spp. has demonstrate very good antispasmodic activity in animals model.

Product containing guanine and sulfone units.

MISCELLANEOUSPHARMACOLOGICALLY ACTIVI DRUGS

1. Insectisides

Nereis toxin an insecticidal compound has been isolau from the marine annelid *Lumbriconereis heteropoda*. Many semisynthetic and synthetic analogs have been produce the structural model of nereis toxin. One of the derivative named as cartap is used as an insecticide in Japan.

2. Anticoagulants

Anticoagulants reported from the marine sources are mostly polysaccharide derivatives obtained from marine algae.

Carrageenans from *Chondrus crispus* and galactan sulphuric acid from *Iridaea laminarioides* have shown anticoagulant activity.^[11]

Techniques

1. Bioassay-guided fractionation

This technique involves testing extracts for biological activity and then isolating the active compounds. It's like a step-by-step process to find the "needle in the haystack."^[12]

Process

1. Extract marine organism
2. Test extract for biological activity
3. Fractionate extract into smaller parts
4. Test each fraction for activity
5. Repeat process until pure compound is isolated.^[13]

2. Metabolomics

Metabolomics is like taking a snapshot of all the metabolic processes in an organism. It helps researchers identify bioactive compounds.

Techniques

1. Mass spectrometry (MS)
2. Nuclear magnetic resonance (NMR) spectroscopy
3. Data analysis software

3. Genomics

Genomics helps researchers identify gene clusters responsible for compound production.^[14]

Applications

1. Identifying biosynthetic pathways
2. Predicting compound structures
3. Optimizing compound production

4. Chemical profiling

Chemical profiling involves identifying and characterizing compounds using techniques like:

1. NMR spectroscopy
2. Mass spectrometry (MS)
3. High-performance liquid chromatography (HPLC).^[15]

5. In vitro and in vivo testing

These tests evaluate compound efficacy and safety.

In vitro

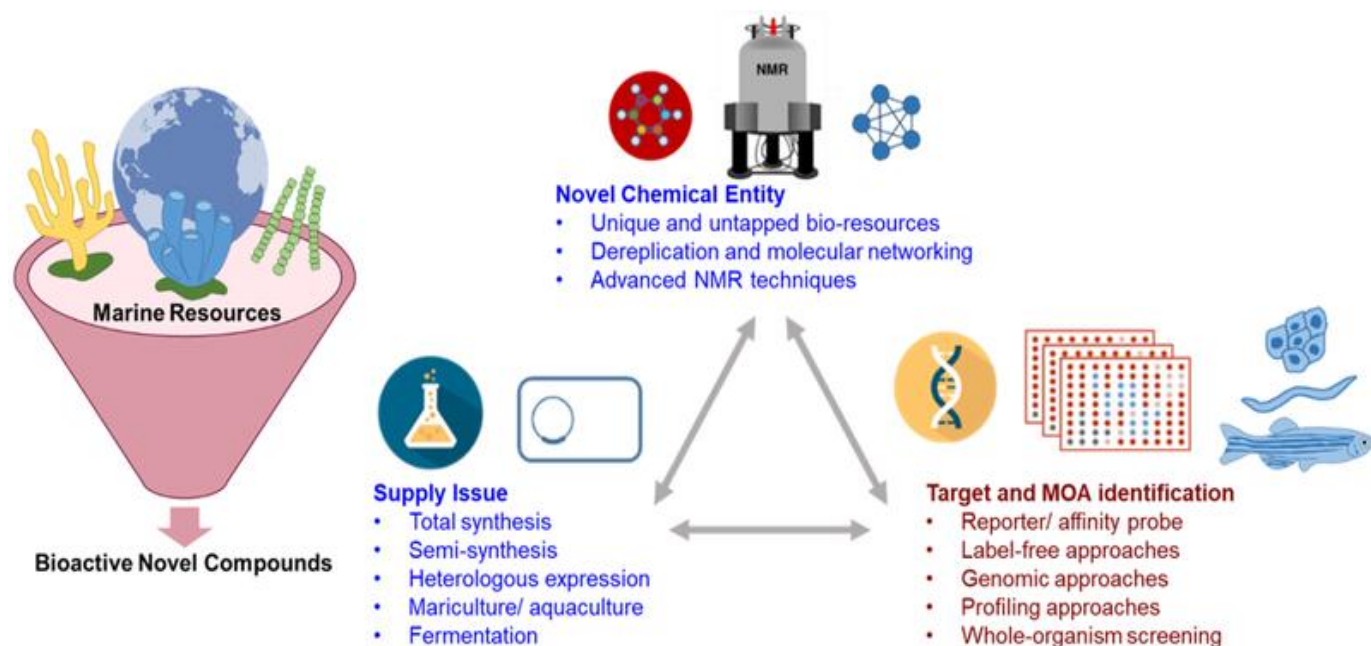
1. Cell-based assays
2. Enzyme inhibition assays

In vivo

1. Animal models
2. Clinical trials

These techniques work together to help researchers discover new marine-derived compounds with potential medicinal applications.^[16]

Three bottlenecks and corresponding research highlights in marine natural product drug discovery



Process of marine pharmacognosy

Here's the process of marine pharmacognosy:

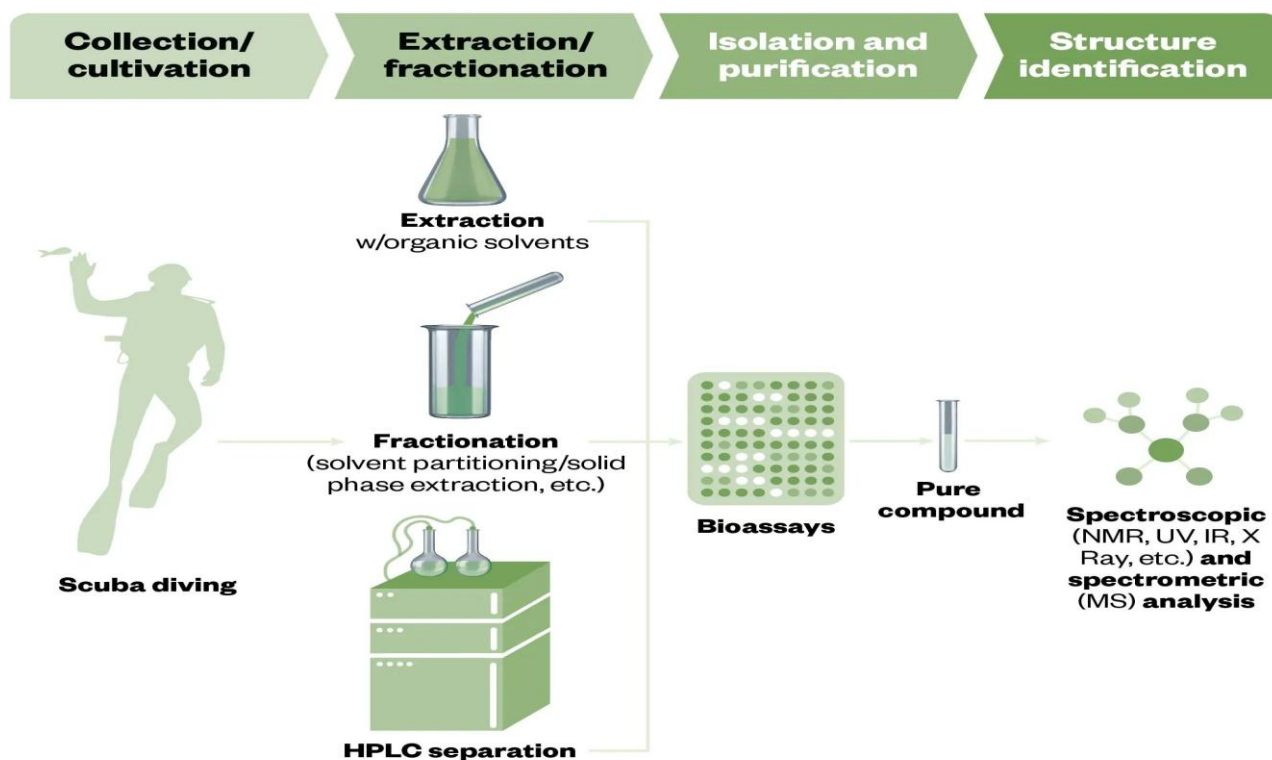
- 1. Collection and Identification:** Collecting marine organisms and identifying them taxonomically.
- 2. Extraction:** Extracting bioactive compounds from the organisms using solvents.
- 3. Bioassay-Guided Fractionation:** Testing extracts for biological activity and isolating active compounds.

4. Chemical Profiling: Identifying and characterizing compounds using techniques like NMR, MS, and HPLC.

5. Structure Elucidation: Determining the chemical structure of isolated compounds.

6. Pharmacological Evaluation: Assessing the efficacy and safety of compounds through in vitro and in vivo testing.

7. Preclinical and Clinical Trials: Conducting trials to evaluate the therapeutic potential of promising compounds.^[17]



Applications of Marine Pharmacognosy

- **Cancer Treatment:** Marine compounds have shown potential in treating various types of cancer, with several drugs already approved or in clinical trials, such as Eribulin Mesylate (E7389) and Trabectedin (ET-743).
- **Infectious Disease Treatment:** Marine compounds have demonstrated potential in treating bacterial, viral, and fungal infections, with examples including antiviral agents like Vidarabine (Ara-A) and antimicrobial agents like Zonanol and Iso-zonanol.
- **Pain Management:** Marine compounds, such as Ziconotide, have been used to develop pain relief medications.^[18]
- **Cardiovascular Disease Treatment:** Marine compounds have shown potential in reducing blood pressure and cholesterol levels, with examples including Omega-3 Fatty Acid Ethyl Esters (Lovaza).

Benefits of Marine Pharmacognosy

- **Novel Drug Discovery:** Marine pharmacognosy can lead to the discovery of new and innovative medicines, with many marine-derived compounds exhibiting unique chemical structures and biological activities.^[19]
- **Diverse Chemical Structures:** Marine organisms produce a wide range of bioactive compounds with diverse chemical structures, offering potential for developing new treatments.
- **Potential for Sustainable Development:** Marine pharmacognosy can promote sustainable development of marine resources, ensuring long-term benefits for human health and the environment.^[20]

Challenges in Marine Pharmacognosy

- **Sustainable Supply:** Ensuring a sustainable supply of marine organisms and compounds is crucial for the development of marine pharmacognosy.
- **Scalability:** Scaling up the production of marine-derived compounds can be challenging due to complexities in culturing and harvesting marine organisms.
- **Regulatory Framework:** Establishing a regulatory framework for marine pharmacognosy is essential for ensuring the safety and efficacy of marine-derived medicines.^[21]

Future Directions

- **Further Research:** Continued research is needed to fully explore the potential of marine pharmacognosy and discover new bioactive compounds.
- **Collaboration:** Collaboration between researchers, industry, and regulatory agencies is essential for advancing marine pharmacognosy and developing new treatments.
- **Sustainable Development:** Sustainable development of marine resources is crucial for the long-term success of marine pharmacognosy, ensuring benefits for both human health and the environment.^[22]

CONCLUSION

The achievements to date in the discovery of novel chemicals from Marine species that have shown promise as

new therapies for Cancer, infectious diseases and inflammation suggest that the production of drugs from marine sources needs to be more Focused. Two underexplored prospects for the discovery of novel chemicals with therapeutic potential are provided by the exploration Of unusual ecosystems, such as deep sea environments, and the Isolation and culture of marine microorganisms. Based on the usual Physiological unction of their secondary metabolites, marine Organisms also offer the ability o understand and establish therapies for diseases. The mechanisms of action of the metabolites are well known in certain processes, e.g., conus toxins, and can be extended to the creation of new groups of drugs.

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