CHAPTER 13

Marine Natural Products: Bioactive Compounds from the Ocean

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ABSTRACT: The chapter delves into Marine Natural Products (MNPs) as a unique and underexplored source of bioactive compounds, distinguishing marine compounds from terrestrial ones. It covers sources of MNPs such as bacteria, fungi, algae, sponges, tunicates, and mollusks, and their diverse bioactive compounds such as peptides, terpenes, alkaloids, polyphenols, and sterols produced under ecological pressure. The bioactivities of these compounds include anti-cancer, anti-infective, and anti-inflammatory activities. The specific examples of approved drugs include Cytarabine, Bromophenols, Trabectedin, Eribulin, Brentuximab vedotin, and Ziconotide, demonstrating therapeutic applications. Moreover, challenges in marine drug development, such as supply limitations, complex structures, regulatory hurdles, and sustainability, are also discussed. Applications of technological innovations, such as multi-omics, computational approaches, AI, and synthetic biology, promise to accelerate marine drug development. Moreover, interdisciplinary approaches and sustainable practices for future marine drug research and development underscore the contribution of MNPs to modern medicine.

From ancient times, humans looked to the sea to uncover its resources. Even today, coastal communities still rely on the sea for food and recreation. Covering about 71% of Earth's surface and containing 95% of the biosphere, oceans harbor an estimated 2.2 million species, many of which are unknown. The ocean represents a biologically and chemically diverse environment that makes it a favorable source for structurally novel and therapeutically active marine products. Natural products are essential in pharmaceuticals, accounting for 60–70% of metabolites. Marine Natural Products (MNPs) are worth 100 million tons globally (El-Regal & Satheesh, 2023).

The marine ecosystem contains about 33-34% of all animal phyla. Marine organisms have developed competitive strategies and defense mechanisms by producing a variety of bioactive natural compounds. These bioactive compounds exhibit structural and mechanistic diversity, exhibiting antimicrobial, anti-inflammatory, and antitumor effects. Moreover, the significance of marine bioactive compounds is evident by the approval of 15 marine-derived drugs in the European Union (EU) and the United States of America (USA). Furthermore, as of 2020, the clinical pipeline showed that more than 20 potential marine compounds had entered phase I, II, or III trials. Thus, the oceanic biome represents a significant but underutilized reservoir for drug discovery and development (Meng et al., 2025).

Compared to Terrestrial Natural Products (TNPs), MNPs are less soluble and contain elongated chains with bigger rings (about 8-10 members). In addition, they possess a higher proportion of halogens (especially bromine) and nitrogen atoms than TNPs, indicating diverse biosynthetic pathways. Moreover, the commonly observed Murcko frameworks in MNPs and TNPS also differ significantly. Specifically, MNP scaffolds are longer with ester-linked 10-membered rings, whereas TNPs are shorter with more stable bonds. Furthermore, the drug Naïve Bayesian (NB) model

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predicts that both groups are drug-like, with MNPs exhibiting slightly higher drug-like potential (Shang et al., 2018). This structural and chemical diversity emphasizes the potential of marine compounds as a source of novel drug discovery.

Ancient maritime civilizations used seaweed and other marine resources for healing, which led to research into marine bioactive compounds. Scientific interest in such compounds increased in the mid-20th century after the discovery that marine sponges produced antiviral nucleosides like spongothymidine, which led to the development of first drug, such as Ara-A (Bharate & Lindsley, 2024). Today, mangrove sediments, deep-sea environments, and microbial consortia are recognized as unexplored reservoirs of pharmacologically powerful compounds (Zhou et al., 2024). Additionally, high-throughput screening of marine microorganisms like actinomycetes and *Aspergillus* sp. has revealed novel bioactive compounds with antimicrobial, antitumor, and immuno-modulatory properties (Zahoor & Wani, 2025). Furthermore, marine waste from fisheries and aquaculture is being valorized as nutraceuticals and bioactive components in support of sustainable development initiatives. Integration of AI and computer screening has advanced marine drug development pipelines, enhanced sustainability, and reduced bio-prospecting costs (Igoli et al., 2025). This chapter discusses the sources and biomedical applications of MNPs.

SOURCES OF MARINE BIOACTIVE COMPOUNDS

Marine microorganisms

Bioactive compounds with potential medical uses can be found in marine microorganisms. Bacterial genera like *Bacillus, Streptomyces,* and *Virgibacillus* demonstrate notable antioxidant and anticancer activities (Galaviz-Silva et al., 2018; Siddharth & Vittal, 2018). Marine fungi primarily from phylum *Ascomycota,* with *Aspergillus* and *Penicillium*, produce 150–200 novel metabolites. These compounds possess bactericidal, antiviral, cytotoxic, and neuro-protective potential (Jones et al., 2015).

Unicellular marine algae consist phytoplankton, which is the foundation of the marine food web and produces about half of the oxygen in atmosphere. Microalgae are an excellent source of bioactive compounds, including proteins, carotenoids, lipids, and secondary metabolites with medicinal potential (Coêlho et al., 2019).

Marine Invertebrates

Bioactive secondary metabolites are abundant in marine sponges. From 2010 to 2019, more than 2,600 compounds with cytotoxic and antibacterial activity were identified. Many of these compounds belong to structural classes of terpenes, alkaloids, and lipids. Analysis from 2010 to 2019 has shown that cnidarians are the second most common producers of MNPs, with 5761 compounds belonging to structural classes terpenoids, steroids, and alkaloids (Carroll et al., 2020).

There are over 7000 species in the phylum *Echinodermata*. It is one of the biggest groups of deuterostomes and the largest phylum that does not include any members living in freshwater or on land. Echinoderms are major producers of glycosylated compounds, particularly steroids, sulphated compounds, saponins, and glycolipids (Ivanchina et al., 2011). Sea cucumbers have many medicinal properties, including anticancer, anti-hypertensive, anti-angiogenic, anti-inflammatory, anticoagulant, antibacterial, antioxidant, and anti-osteoclastogenic (Hossain et al., 2020). Tunicates produce diverse compounds including macrolides, terpenes, and alkaloids, with approximately 40 novel structures reported annually. Although there were initial failures with compounds like didemnin B, but significant progress has been made. For example, marine anticancer drugs trabectedin and aplidine were derived from tunicate *Tridemnum solidum* (Rogulska et al., 2013).

Marine Fishes

Marine fish provide many health benefits, namely, fish oils containing omega-3 fatty acids are approved for cardiac health under the name Lovaza/Omacor. In addition, shark liver oil contains squalene, which has antibacterial and vaccine-adjuvant effects. Furthermore, tetrodotoxin, derived from pufferfish, helps in treating neuropathic pain and is currently in Phase III trials (Nieto et al., 2012). Tilapia piscidin 4 obtained from Nile tilapia exhibited bactericidal activity against

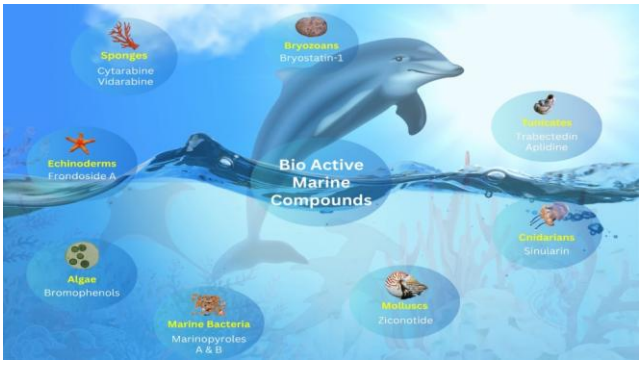

Fig 1. Source of marine bioactive compounds and representative compound from each source

Helicobacter pylori and arrested the progress of gastric ulcer (Narayana et al., 2015). The sources of marine bioactive compounds and a representative compound from each source is presented in Fig. 1.

STRUCTURAL DIVERSITY AND FUNCTIONAL ROLES OF MARINE BIOACTIVE COMPOUNDS

Marine organisms provide many biologically active chemicals. Some of the significant classes of compounds are given below:

Proteins and peptides: derived from marine animals have potential applications in medicine and nutrition. For example, proteins from algae, notably phycobiliproteins from cyanobacteria and red algae, demonstrate antioxidant and anti-inflammatory effects. Furthermore, marine peptides from squid, fish, and algae have shown specific health benefits, such as reducing blood pressure, inhibiting cancer cell growth, fighting bacterial infections, and protecting body from oxidative damage (Hamed et al., 2015).

Terpenes: are synthesized from isoprene (C_5H_8) and are classified according to molecular size. Antimicrobial terpenoids have been found in bacteria, fungi, algae, sea cucumbers, and poriferans in the last five years (Liu et al., 2024).

Alkaloids: extracted from marine sources, such as b-Carboline, indole, imidazole, and pyrrole, exhibit significant antimalarial activity (Negm et al., 2023).

Plants, microbes, and other marine species synthesize polyketides, a broad class of bioactive chemicals. These polyketides exhibit immune-suppressive, antitumor, antibacterial, anti-parasitic, and cholesterol-lowering properties (Barbosa et al., 2020).

Polyphenols and sterols: are significant classes of marine bioactive compounds. Polyphenols are potent antioxidants, antibacterial agents, UV protectors, and chemo-preventives. Moreover, sterols are abundantly found in brown and red algae and exhibit anti-inflammatory properties and, help in lowering the cholesterol levels. In addition to above structures, marine organisms also produce structurally diverse lipids and polysaccharides. According to Hamed et al. (2015), polyunsaturated fatty acids (PUFAs) (e.g., EPA, $C_{20:5}$ and DHA, $C_{22:6}$) have promising role in cardiovascular and immune health, while sulphated polysaccharides are abundantly present in algae and act as antitumor, antiviral, antioxidant, and anticoagulant substances. Table 1 demonstrates the classes of different bioactive compounds obtained

Table 1. Source, class, biomedical applications and representative drugs from marine organisms

Source	Class of Bioactive Compounds	Biomedical Applications	Representative Compound / Drug
Sponges	Terpenes, Peptides Alkaloids, Macrolides, Nucleosides	Antitumor, Antiviral, Antimicrobial,	Cytarabine (Ara-C), Vidarabine (Ara-A)
Tunicates	Alkaloids	Anticancer	Trabectedin / Yondelis®
Bryozoans	Alkaloids, Macrolides	Anticancer, Neuroprotective Immunomodulatory,	Bryostatin-1 (clinical trials)
Echinoderms	Triterpene, Glycosides, Steroids	Antitumor, anticoagulant, anti-inflammatory,	Frondoside A (preclinical)
Cnidarians	Steroids, Peptides, Diterpenoid	Anticancer, antioxidant, anti-inflammatory, antimicrobial	Sinularin (Preclinical)
Mollusks	Peptides, Polyketides, Terpenes, Polyphenols, Sterols	Analgesic, Neuroprotective	Ziconotide (Prialt®)

from marine sources and their biomedical applications (Romano et al., 2022).

BIOMEDICAL APPLICATIONS OF MARINE BIOACTIVE COMPOUNDS

Marine organisms are adapted to complex and harsh environments; hence they produce an array of bioactive substances as defense tools for survival. These compounds possess biocompatibility and biodegradability, and have shown anti-proliferative, antioxidant, antimicrobial, cardio-protective, and anti-inflammatory applications (Wan et al., 2021). Moreover, they are also applied for the treatment of diabetes (Yuan et al., 2019), diabetic foot ulcers (Ghonam et al., 2021), and liver regeneration (Kang et al., 2018).

Antitumor Activities

Cancer is a major global health concern; scientists have been trying to find less toxic and effective treatments. Marine-derived compounds exhibit immense anti-tumor potential by triggering apoptosis through mechanisms such as DNA cleavage via inhibition of topoisomerase I or II, permeabilization of mitochondrial membrane, inhibition of tumor angiogenesis, and suppression of signal transduction enzymes (i.e., proteases) (Gomathi & Gothandam, 2016).

The main mechanism of most anticancer drugs is activation of apoptotic pathways. These pathways can be triggered via the intrinsic pathway (mitochondrial) and the extrinsic pathways (receptor-mediated). The Intrinsic pathway starts with intracellular stress signals such as oxidative stress, DNA impairment, and cytokine removal. However, the extrinsic pathway is initiated when cell-surface death receptors, including tumor necrosis factor and Fas (CD95/TNFRSF6/Apo-1) are activated by external signals (Burke, 2017; Yi et al., 2018).

P53 is essential in regulating the cell cycle to prevent uncontrolled cell division. It activates p21 and Bax (pro-apoptotic proteins) that initiate the release of cytochrome c by mitochondrial membrane permeabilization. This activates caspase cascade, leading to cell death. However, overexpression of anti-apoptotic protein i.e., Bcl-2, and deregulation of pro-apoptotic protein i.e., Bax suppress apoptosis and cause cellular immortality. P53 antagonizes Bcl-2 through a transcription-dependent process and direct activation of Bax, thereby inducing apoptosis. The apoptotic pathways are crucial because they specifically target cancer cells while sparing normal cells, thereby minimizing potential side effects. In various cancers, P53 loses its ability to trigger apoptosis, thus contribute to tumor progression (Jan, 2019).

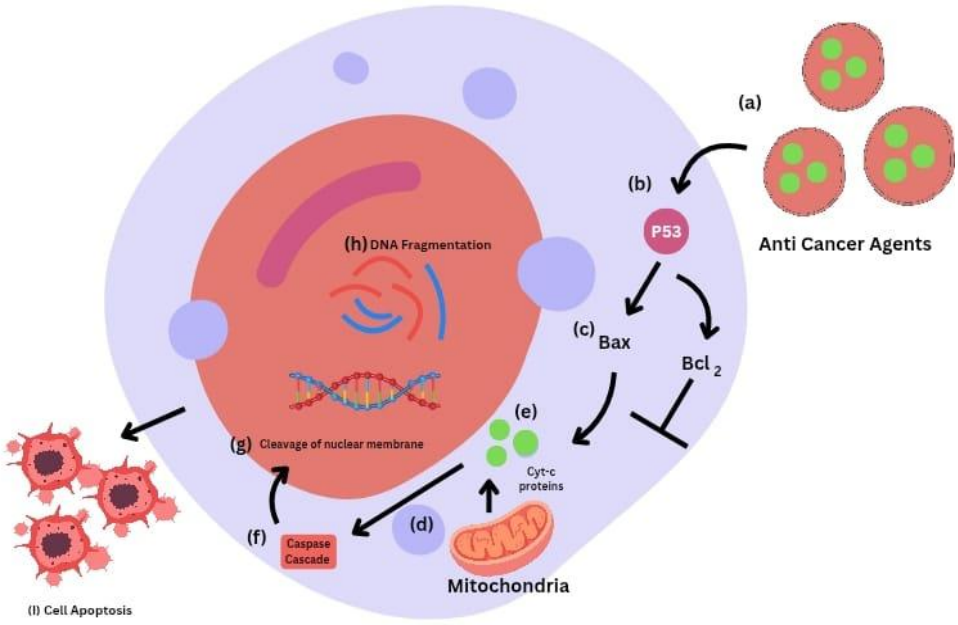

Fig 2. Mechanism of apoptotic cell death induced by anti-cancer drugs

Apoptotic mechanism of action by anticancer drugs has been illustrated in Fig. 2.

Anti-Angiogenesis

Inhibiting angiogenesis, development of new blood vessels in cancer cells that nourish tumors, is another significant pathway. Many marine-derived peptides suppress the angiogenic factors i.e., vascular endothelial growth factor (VEGF), which prevents tumors from receiving nutrition and oxygen needed for tumor growth. Moreover, marine peptides disrupt signaling mechanisms (PI3K/Akt & MAPK), which are over-reactive in cancer cells and lead to their proliferation and survival. By disrupting these pathways, marine compounds suppress cancer proliferation and improve the effectiveness of current cancer treatments (De La Fuente et al., 2022).

Antimicrobial Activities

Antibiotics are the most effective substances to combat infectious diseases, improving the health of humans and animals. However, emergence of antibiotic-resistant microorganisms, primarily due to excessive and improper use of antibiotics has complicated infection treatment. The urgent need for novel antibiotics has led to exploration of the marine ecosystem, which previously received little attention (Velmurugan et al., 2020). Marine microorganisms and invertebrates produce antimicrobial agents against multidrug-resistant pathogens.

Antimicrobial peptides (AMPs) are small, amphipathic molecules (12–45 amino acids). These peptides target bacterial cell membranes due to their cationic nature at physiological pH. Halocidin stands as an AMP which scientists discovered from the tunicate species *Halocynthia aurantium*. The research conducted by Han et al., (2016) demonstrated that halocidin exhibits strong bactericidal effects against both vancomycin-resistant *Enterococcus* (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA). The marine Streptomyces species produce two bisanthraquinone metabolites named BE-43472B and BE-43472A which belong to the class of polyketides. The studied metabolites demonstrate activity against *E. faecium*, *S. aureus*, MRSA and VRE (Yamashita et al., 2018). The marine Streptomyces bacterium produces marinopyrroles A and B which demonstrate antibacterial effects against MRSA (Clive & Cheng, 2013). Table 2 demonstrates the antimicrobial compounds obtained from marine organisms.

Antiviral Activity

Viral diseases including avian influenza and SARS have become a major health problem which has affected people during the last few years. The search for marine-based compounds became necessary because conventional antiviral drugs brought about adverse reactions and drug resistance. The examples include carrageenan and ulvan, which are sulfated polysaccharides isolated from marine algae. The bioactive substances show particular

Table 2. Marine-based Antimicrobial Bioactive Compounds

Active compounds	Source	Against infections	References
Arenicin-1	Lugworm *Arenicola marina*	*E. coli*, *P. mirabilis*, *Staphylococcus aureus*	Panteleev et al., 2015
Clavanin A	*Styela clava*	*S. aureus*, *E. coli*, *E. faecium*, *P. aeruginosa*	De Miranda et al., 2017
Hedistin	*Nereis diversicolor*	*Micrococcus luteus*, *M. nishinomiyaensis S. aureus*	Cuvillier-Hot et al., 2014
Pestalone	Fungus	MRSA, VRE	Liu et al., 2016
Isoaaptamine	*Aaptos aaptos*	*S. aureus*	Thawabteh et al., 2019
Bromopyrrole	*Agelas* sp	*M. luteus*, *B. subtilis*	Das et al., 2016
Guanidine	*Monanchora unguifera*	*P. aeruginosa*	Pessoa et al., 2013
Xeniolide I diterpenes	*Xenia novaebrittanniae*	*B. subtilis*, *E. coli*	Thawabteh et al., 2021
Ieodoglucomide C, ieodoglycolipid	*Bacillus licheniformis*	*C. albicans*, *Rhizoctonia solani*, *Aspergillus niger*	Tareq et al., 2015
Bromophenols	*Symphyocladia latiuscula*	*Candida albicans*	Xu et al., 2014

antiviral activity against human papillomavirus (HPV) and herpes simplex virus (HSV) (Laurie et al., 2021). SU1F1, a modified carbohydrate obtained from ulvan and carrageenan, exhibits activity against HSV-1 (Lopes et al., 2017). Additionally, sulfated polysaccharides have demonstrated potent activity against COVID-19 (Pereira & Critchley, 2020). The results show potential but scientists need to conduct more studies to understand how drugs interact with each other and with diseases and to uncover their underlying pharmacological mechanisms.

Anti-Inflammatory Activity

Inflammation is body's defense response that maintains homeostasis and supports tissue repair. It may be triggered by infection, injury, or stress. However, chronic inflammation can pose a serious threat to health (Hotamisligil, 2017). Marine organisms, mainly seaweeds, are rich sources of anti-inflammatory compounds such as terpenoids, phenolics, alkaloids, peptides, polysaccharides, and glycoproteins. These substances inhibit cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, and reduce levels of ROS and NOS. Furthermore, they suppress pro-inflammatory cytokines (IL-6, TNF-α) through inhibition of nuclear factor-κB (NF-κB). In addition to seaweeds, other marine sources such as bryozoans (e.g., *bryostatin-1*), jellyfish, and shellfish produce a variety of anti-inflammatory compounds, including bile acids, lipids, and monoterpenes (Khursheed et al., 2023).

APPROVED ANTICANCER BIOACTIVE COMPOUNDS

Cytarabine

Cytarabine was the first commercially available marine based chemotherapeutic drug. It is a pyrimidine nucleoside analog that acts as a powerful cytotoxic medication by interfering with DNA synthesis during the S phase of cell cycle. The US Food and Drug Administration (FDA) approved Cytarabine under the brand name Cytosar-U®. It is widely used to treat lymphoma and leukemia (Krauss et al., 2019).

Bromophenols

Bromophenols are secondary metabolites produced by marine red, green, and brown algae. They exhibit strong anticancer potential. In human adenocarcinomic (A549) cells, they cause cell cycle arrest in G0/G1 phase and ROS-mediated apoptosis (Choi et al., 2018).

Trabectedin

Trabectedin (Yondelis®) is a tetrahydro isoquinoline alkaloid isolated from the tunicate *Ecteinascidia turbinate*. It was approved for treatment of advanced soft tissue sarcomas (Ratan & Patel, 2017). Trabectedin is a DNA-alkylating agent that selectively inhibits RNA polymerase II transcription and initiates apoptosis in tumor-associated macrophages (TAMs). This action modulates tumor microenvironment, reduces inflammation and metastasis of tumors. Its selective inhibition of oncogenic genes does not impact basal transcription in the body, thereby exhibiting cytotoxic effects against resistant tumors.

Eribulin

Eribulin (Halaven®) is a synthetic version of halichondrin B, which is a natural substance extracted from marine sponge. It has been approved to treat gastric cancer (Kurata et al., 2018), and breast cancer (Perez-Garcia & Cortes, 2019). Eribulin binds to soluble α and β tubulin and disrupts microtubule polymerization. As a result, it causes cell cycle arrest at G2/M phase, which triggers mitotic catastrophe and apoptosis.

Brentuximab vedotin

Brentuximab vedotin (Adcetris®) is the first CD30-targeting antibody-drug conjugate (ADC) approved by the US FDA in 2011 to treat Hodgkin's lymphoma (HL). It is derived from a sea hare, *Dolabella auricularia and* combines a monoclonal antibody (cAC10) with a cytotoxic agent (Nguyen et al., 2023). CD30 receptor, a member of tumor necrosis factor receptor family, is minimally expressed on normal cells but overexpressed on tumor cells. That makes this receptor a potential target of ADC-related therapy. Upon binding to the CD30 receptor, ADC is internalized, releasing cytotoxic materials that disrupt microtubules,

leading to cell cycle arrest and apoptosis (Connors et al., 2018).

Ziconotide

In 2004, the FDA and the European Medicines Agency approved Ziconotide, a synthetic derivative of the ω-conotoxin MVIIA. It was initially discovered in 1982 from the sea snail *Conus magus'* venom (Lin et al., 2024). Ziconotide produces significant analgesic effects by inhibiting neurotransmitter release; however, its clinical use is limited by the need for intrathecal injection and a narrow therapeutic window, as high dosages may induce severe central nervous system toxicity. Current research aims to optimize the pharmacokinetics and N-type-selective calcium channel blockers to improve safety and efficacy (Lambe et al., 2023).

PROMISING MARINE-DERIVED BIOACTIVE COMPOUNDS AND CLINICAL TRIALS

As of 2022, fifteen marine-derived pharmaceuticals received FDA approval. New compounds, including E7130 and antibody-drug conjugates such as BT5528 (EPhA2-MMAE) and BT8009 (Nectin-4-MMAE), entered Phase-I trials for cancer treatment. Other ADCs such as MORAb-202, A-166, ARX-788, and Upifitamab rilsodotin advanced to later Phases. Overall, 34 marine-derived pharmaceuticals were in active clinical trials: 19 in Phase I, 15 in Phase II, and 6 in Phase III (Haque et al., 2022; Mayer et al., 2023).

TECHNIQUES AND TECHNOLOGIES IN THE DEVELOPMENT OF MARINE-DERIVED BIOACTIVE COMPOUNDS

Methanol and acetone are used as solvents for extracting marine bioactive compounds. The Kupchan partitioning method, which separates chemicals based on polarity, is often utilized (Kupchan, 1973). Following extraction, extracts are purified using medium-pressure liquid chromatography (MPLC), size exclusion, and liquid-liquid chromatography. High-performance liquid chromatography (HPLC) is used to purify substances for final bioactivity testing (Kiuru et al., 2014).

Modern analytical techniques, such as Nuclear Magnetic Resonance (NMR) spectroscopy for non-destructive analysis and Mass Spectrometry (MS) in conjunction with liquid or gas chromatograph, are used to analyze the structures of marine compounds. Circular dichroism (CD), infrared (IR) spectroscopy, and J-based configuration analysis are used to evaluate 3D structure and stereochemistry of these compounds (Breton & Reynolds, 2013).

HTS is commonly used to evaluate thousands of samples quickly using imaging technologies and whole-cell models. The effectiveness of this process depends on quality natural product libraries. Early implementation of dereplication and metabolic profiling helps scientists to focus on novel compounds rather than known ones (Fishburn, 2013).

Due to structural complexity, a few of these compounds are in approved drugs. These complicated structures are modified by medicinal chemists into drug-like analogs. Some of these chemicals are difficult to synthesize, thus researchers focus on discovering their pharmacophores. Diversity-oriented synthesis (DOS), which balances natural complexity with lab capabilities, making these molecules better for medication development (Lee & Berg, 2013).

CHALLENGES IN MARINE-BASED DRUG DEVELOPMENT

Supply and Sustainability

Marine organisms often produce bioactive compounds in low quantities, making large-scale supply impossible, and causing the danger of overexploitation of vulnerable species. Overharvesting sponges, tunicates, and corals can harm local fisheries and ecosystems, reduce biodiversity, which can impede drug development. Thereby, natural harvests are impractical from an ecological and economic standpoint. Thus, regulatory agencies now require sustainable sourcing plans and environmental impact assessments prior to large-scale development. Decisions about conservation and supply may become difficult if the host is removed since some

species are symbiont-dependent. However, Aquaculture, microbial fermentation, and heterologous expression have emerged as alternatives to natural harvest. Each of these methods has benefits, but it also has drawbacks, including scalability, sustainability, and challenges related to cost, space use, environmental impact, contamination, and yield optimization (Martínez et al., 2025).

Complexity and Yield Issues

Marine bioactive chemicals are produced at levels of micrograms per kilogram of biomass and exhibit complex chemical structures with various chiral centers, unique rings, and rare functional groups. These properties make isolation, purification, and chemical characterization difficult and time-consuming (El-Seedi et al., 2025). To counter this, scientists use total and semi-synthetic approaches but these are time-intensive, costly and low yielding. However, synthetic biology and metabolic engineering are promising solutions but these techniques are still in development.

Regulatory and Technical Hurdles

MNPs possess unique functional groups or complex structures that result in unpredictable toxicity profiles and pharmacokinetics, complicating preclinical research and delaying clinical entry (Domingo-Fernández et al., 2024). Moreover, unclear frameworks and laws related to marine genetic resources, including the provenance, permitting, and benefit-sharing requirements imposed under the Nagoya Protocol, new regulations on digital sequence information (DSI) and the Biodiversity Beyond National Jurisdiction (BBNJ) agenda, can complicate research, collaborations, transactional risk, and increase in contractual and legal expenses for developers (Haque et al., 2022).

TECHNOLOGICAL INNOVATIONS AND FUTURE DIRECTIONS

Recent years have witnessed major technological advances in the exploration, development, and production of MNPs. A key innovation is the application of multi-omics (genomics, transcriptomics, proteomics, and metabolomics) to marine organisms and their micro biomes. For instance, genomic and metagenomic sequencing of marine microbial groups has revealed a massive reservoir of “cryptic” biosynthetic gene clusters encoding novel secondary metabolites, which previously were not observed (Rosic, 2021). Metabolomics and molecular networking tools now permit rapid dereplication (i.e., distinguishing known compounds from novel ones) and the prioritization of exotic chemical scaffolds with minimal sample quantities (Liang et al., 2019).

At the same time, computational approaches such as bioinformatics platforms and machine-learning models are employed to extract large chemical and genetic datasets, predict biosynthetic pathways, and assess drug-likeness (Chang, 2013). For example, distortions in scaffold space enabled by marine compounds are being algorithmically mapped and added into predictive models to analyze synthetic feasibility. Moreover, the combination of AI-driven molecular generation with marine-based scaffolds is emerging as a promising route to discover “next-generation” leads.

On the production side, advances in synthetic biology are gradually enabling heterologous expression of marine biosynthetic genes in simpler microbial hosts (*E. coli*, *Streptomyces*) (Francesch et al., 2024). Further, micro-fermentation, marine microbial culture optimization, and bio-reactor engineering are being refined to enable scalable production of marine-derived metabolites. To ensure sustainability, instead of harvesting large volumes of macro-organisms, researchers are turning to marine microbes, micro-algae and deep-sea strains. Eventually, reducing ecological impact and biodiversity risk (Cabral et al., 2024). Importantly, technological advances are also shifting drug-development such as high-throughput screening (HTS) combined with high-content phenotypic assays, plus improved target-identification technologies (like chemical proteomics) (Liang et al., 2019).

CONCLUSION

The ocean is home to a vast biodiversity of animal phyla, microbes, and unexplored habitats. This diversity presents marine natural products (MNPs), developed over millions of years in complex marine environments. MNPs represent

immense structurally unique and pharmaceutically bioactive compounds, which make them a valuable scaffold for novel drug discovery. Over the past decades, noteworthy progress has been made in identifying marine-derived bioactive compounds with prominent anticancer, anti-inflammatory, antiviral, and antimicrobial activities. Several of these, such as cytarabine, trabectedin, eribulin, and ziconotide, have already progressed to clinical application. However, despite these advancements, large-scale development is constrained by issues such as low yield, structural complexity, difficulties in sustainable harvesting, and regulatory barriers. Moreover, the integrating synthetic biology, fermentation technology, and advanced analytical tools offers promising solutions to overcome these limitations. Furthermore, future marine drug discovery will increasingly depend on multidisciplinary collaboration accelerating the identification and optimization of new compounds while ensuring environmental sustainability. Conclusively, ocean's biodiversity holds the promise of delivering the next generation of therapeutics.

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