



Marine organisms, especially those inhabiting extreme marine ecosystems, produce a huge variety of natural products exhibiting diverse structures and biological activities. To date, more than 40,000 compounds, including terpenoids, polypeptides, alkaloids, and fatty acids have been discovered in marine organisms such as marine microorganisms, sponges, cnidarians and algae^{[1][2]}.

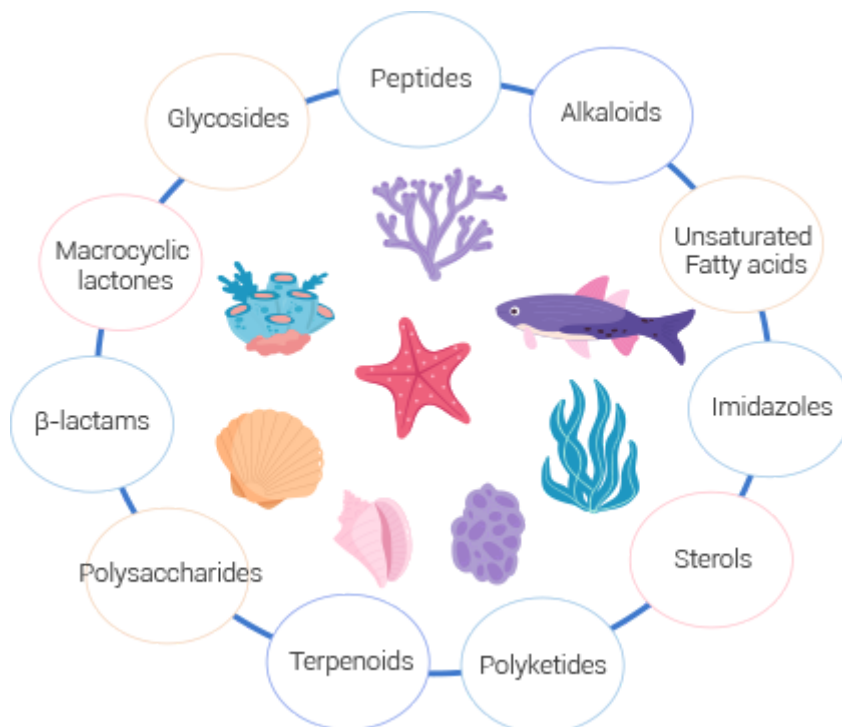


Figure 1. Main structure and origin of marine natural products^{[1][2]}

Unlike Terrestrial Natural Products (TNPs), Marine Natural Products (MNPs) contain unique distinctive structures with diversity^[3]:

Different element composition

Nitrogen, sulfur, and non-fluorine halogens (Br, Cl) are more common in MNPs, such as Clionastatin A (C₁₆H₂₅Cl₂N), (-)-Majusculoic acid (C₁₅H₂₃BrO₂), and Squalamine (C₃₄H₆₅N₃O₅S). Especially, the introduction of halogen atoms results in valuable physiochemical properties and they are widely used in drug design^[4].

Unique chemical structure

MNPs usually have larger scaffolds and more flexible structures due to the presence of many chiral centers, like Halichondrin B (Eribulin deriving from it). By comparing 3,802 MNPs molecules with nearly 30,000 TNPs, about 70% of the skeleton is unique to MNPs. In addition, the percentage of drug-likeness of MNPs and TNPs are 78.06% and 76.61% respectively.

Considering to these, MNPs can be a desirable source of new drug discovery and development.

Application of MNPs

About 20 MNPs derived drugs have been approved by FDA to treat cancer (four of them are ADCs), chronic neuropathic pain, cardiovascular diseases, and other disorders^[5]. Over 30 MNPs derived compounds are in different phases of clinical trials (above 70% are ADCs)^[6]. From 2016 to 2020, about 7,547 MNPs have been reported to be active. The most commonly investigated bioactivities were cytotoxic (3,972, 53%), antibacterial (28%), and anti-inflammatory (11%)^[1]. The targets of some MNPs are listed in the Figure 2^[7]. For example, Trabectedin, approved for cancer treatment, can interfere with transcription process by binding to the minor groove of DNA. Manzamine A targets vacuolar ATPases and inhibit autophagy in pancreatic cancer cells. It also acts as an RSK1 Inhibitor as reported in a recent study^[8].

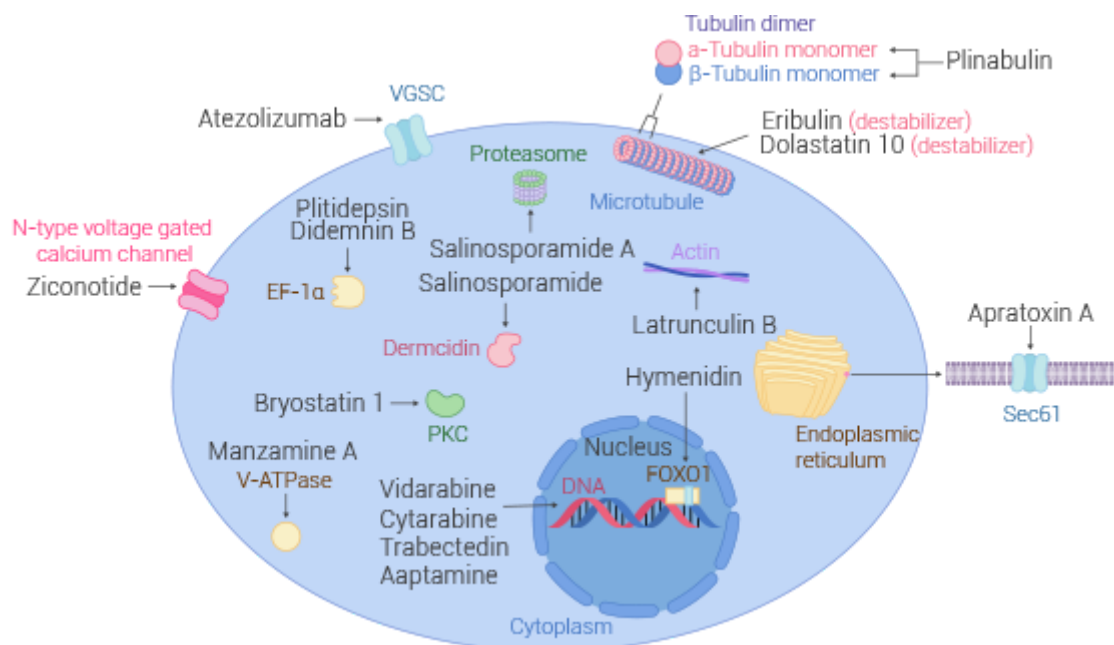


Figure 2. Representative MNPs and their cellular (and extracellular) targets^[7]

At present, more studies focus on TNPs than MNPs. But given the diversity and unique characteristics of their structures, MNPs provide a resourceful avenue for new drug discovery and development in the near future.

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Origin	Product Name
Marine Algae	<p>Dieckol Possesses antibacterial, anticancer, antioxidant, anti-aging, anti-diabetic, and neuroprotective effects.</p>
	<p>Fucoxanthin Has activities such as antioxidant stress, anti-inflammatory, anticancer, antibacterial, antiviral, anti-obesity and neuroprotective effects.</p>
Sponge	<p>Latrunculin B A competitive antagonist of α-adrenergic receptors. It can bind to DNA.</p>
	<p>Aaptamine An actin polymerization inhibitor with cardiovascular-protective antifungal and antiprotozoal activity.</p>
Mollusk	<p>Okadaic acid Inhibiting protein phosphatase and increasing phosphorylation of multiple proteins (such as tau protein), exhibiting tumor promoter effects.</p>
Many Organisms	<p>Pristane Non-antigenic adjuvant and induces MHC II-restricted arthritis T cells in rats.</p>