

Marine Sponges: The untapped pharmaceutical treasures of the sea

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Introduction to marine sponges:

Sponges, classified under the phylum Porifera, represent one of the earliest metazoans, inhabiting marine, brackish, and freshwater ecosystems across the coldest Arctic seas to the warmest tropical oceans, spanning a range of depths from shallow to deep sea.¹⁻³ The term "Porifera" is derived from the Latin words "porus" (pore) and "ferre" (to bear), referring to their porous body architecture.⁵ These organisms exhibit a simple anatomical structure lacking true tissues and organs, yet they display vast morphological diversity, including growth forms, size, colors, surface structure and *etc.* Phylogenetic analyses suggest that sponges were among the earliest modern animals to evolve, with origins tracing back to the Precambrian period.⁶⁻⁷

The fascinating aquiferous systems of sponges:

Phylum Porifera comprises four classes: Demospongiae, Calcarea, Hexactinellida, and Homoscleromorpha. Within this phylum, five distinct aquiferous systems exist: asconoid, syconoid, sylleibid, leuconoid, and solenoid. Asconoid represents the simplest organization, while leuconoid and solenoid forms are remarkably sophisticated despite the animals' simplicity. Among sponge classes, only Calcarea showcases all five systems, while Hexactinellida displays leuconoid and syconoid systems, Demospongiae exhibits solely leuconoids, and Homoscleromorpha typically displays leuconoid, with a potential exception in *Oscarella filipoi*, where a sylleibid system has been observed.^{4,8} These aquiferous systems regulate water flow facilitating feeding, gas exchange, gamete release, and waste expulsion within the sponge body.⁵ However, carnivorous sponges, exclusively within the monophyletic group Poecilosclerida, lack aquiferous systems. Instead, they possess mechanisms to trap, envelop, and digest small invertebrates for feeding.⁹

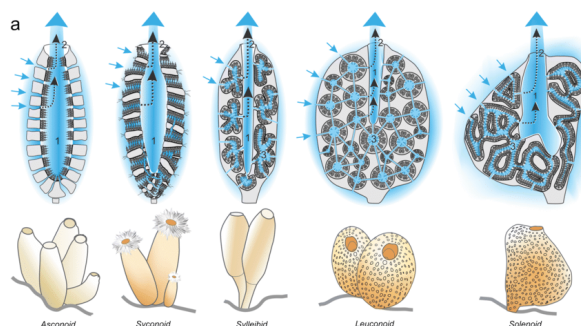


Figure 1: Graphical illustration of the five sponge body organizations. (1) Spongocoel/atrium (2) Oscule (3) Choanocyte chamber, arrows indicate the direction of the water flow.⁴

Structural diversity across sponge species:

The structural skeleton of sponges, crucial for characterization, comprises two primary components: organic and inorganic. The organic part consists mainly of collagen protein, either as fibrillar collagen or type IV collagen, forming thin fibrils within the intracellular matrix. In certain sponges, fibrillar collagen may aggregate into thin filaments or form a fibrous structure known as 'spongin'. Additionally, granular collagen aids in binding spicules together in some species. The inorganic component typically includes silicon dioxide or calcium carbonate, in the form of calcite or aragonite.^{5, 10-11} While most sponges possess a mineral skeleton composed of silica or calcium, some species of Demospongiae and Homoscleromorpha lack this mineralized structure, relying solely on fibrous collagen networks for support. In such cases, the presence of spongin fibers becomes valuable for identification. Notably, certain genera within demosponges and homoscleromorpha lack both spongin and a mineral skeleton.⁵ The sponge body has three layers: the external layer called the ectosome, which is composed of pinacocytes, the internal layer is called the choanosome, and the space between the ectosome and choanosome is called the mesohyl, which contains various cell types such as totipotent cells, archaeocytes, collencytes, sclerocytes, and myocytes.^{4-5, 12}

Responding to reproduction:

Sponges lack a neuro-signaling system but respond to environmental stimuli by closing their ostia or oscula, constricting their canals, experiencing backflow, contracting their bodies to flush the aquiferous system, and reorganizing their flagellated chambers. In addition, both positive and negative phototaxis or geotaxis of larvae have been observed.^{5,13} Sponges reproduce sexually and asexually. Sexual reproduction involves gametogenesis, with mature sperm and eggs released into the water or internally. Fertilization may occur externally or internally. Embryogenesis varies, leading to various larval types or direct juvenile formation. Asexual reproduction includes regeneration, gemmules, reduction bodies, budding, and possibly asexual larvae. Sponges also demonstrate remarkable regeneration capabilities, allowing them to recover from damage or fragmentation.^{5,14}

Understanding their vital role in marine ecosystems:

Ecologically, sponges play a crucial role through their filter-feeding mechanisms, significantly influencing pelagic ecosystems by removing particulate organic matter and various nutrients such as oxygen, silicon, and nitrogen. Additionally, they are a key source of natural products, hosting symbiotic microorganisms capable of synthesizing a wide array of bioactive compounds with potential applications in medicine and industry. Sponges engage in symbiotic relationships with a variety of marine organisms, including mollusks, fish, crustaceans, echinoderms, and opisthobranchs, contributing critically to coral reef ecosystem dynamics. Experimentally, sponges have been cultivated for over a century, initially for the production of "bath sponges" and more recently for the extraction of biologically active metabolites with pharmaceutical potential.¹⁵⁻¹⁶

Sponge identification challenges: leveraging DNA for accurate taxonomic classification

Sponges play vital roles in pharmaceuticals and ecology but present identification challenges due to diverse morphology. DNA barcoding, utilizing PCR and sequencing, assists in their classification, complementing traditional methods. It offers insights into evolution and reduces the workload and time

required for identification, benefiting from its accessibility to non-specialists. However, it is crucial to integrate DNA barcoding with morphological and biochemical data for accurate taxonomic identification, ensuring a comprehensive understanding of sponge diversity and evolutionary relationships.¹⁷⁻¹⁸

Holobionts and eDNA:

Sponges function as holobionts, hosting diverse microbial symbionts acquired through their filter-feeding behavior. Recent studies reveal a vast array of symbiotic bacteria and archaea in sponge microbiomes. These microbes produce specialized metabolites with potential pharmaceutical applications, exemplified by nucleosides like spongouridine and spongothymidine, which led to the development of anticancer and antiviral drugs.¹⁹ Metagenomics offers insights into these symbiont-driven biosynthetic pathways, identifying novel compounds like cytotoxic polyketides from sponge symbionts, enhancing drug discovery. However, challenges remain in culturing symbionts and elucidating biosynthetic mechanisms, underscoring the importance of metagenomic approaches in natural product discovery. Sponges, aside from harboring various microbial symbionts, also hold potential for environmental DNA (eDNA) studies. Through their filter-feeding behavior, sponges accumulate eDNA from the surrounding environment, including genetic material shed by vertebrates. Extracting eDNA from sponge samples enables the identification of vertebrate species in aquatic environments, offering a non-invasive and effective means to monitor vertebrate species and evaluate biodiversity.²⁰ This method is particularly valuable given the widespread distribution of sponges across diverse aquatic habitats.

Bioactive compounds and drug development:

Since the 1970s, numerous specialized metabolites have been discovered in sponges, many with potential pharmacological applications, including antibacterial, antiviral, anti-inflammatory, antitumor, and cytotoxic compounds, as well as channel blockers and antifouling agents. These findings have renewed scientific interest in sponges due to their symbiotic relationships with diverse microorganisms and the richness of biologically

active metabolites they produce.

The primary bioactive compounds isolated from marine sponges include:

1. Terpenes: sesquiterpenes, diterpenes, sesterterpenes, triterpenes
2. Alkaloids: pyrroles, bromopyrroles, pyrroloquinoline, and pyrroloiminoquinone alkaloids
3. Heterocycles
4. Steroids
5. Polyacetynes, peptides, polyethers, polyketides, and macrolides
6. Glycosides and nucleosides²¹

Terpenes, synthesized from five-carbon isoprene units, are the most abundant secondary metabolites in sponges. These units can be modified to produce various derivatives with diverse chemical structures and biological activities. Marine sponges are prolific sources of terpenes, including sesquiterpenes, diterpenes, sesterterpenes, and triterpenes.²² Sesterterpenes, for example, display a range of bioactivities, such as antibiotic, anti-inflammatory, cytotoxic, and antileishmanial properties. Manoalide, a sesterterpene from *Luffariella variabilis*, shows potent antibacterial and anti-inflammatory effects, as well as phospholipase A2 inhibition. Other sesterterpenes like secmanoalide and neomanoalides also exhibit antibacterial activity against Gram-positive bacteria. Sesterstamides from *Hyrtilos* sponges possess antileishmanial properties.²³⁻²⁵

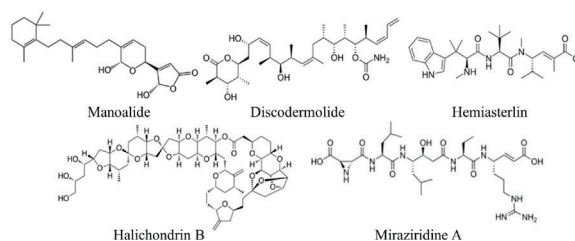
Sesquiterpenes, such as (+)-5-epi-Nakijinol E and (+)-5-epi-20-O-Ethylsmenoquinone from *Smenospongia* species, exhibit cytotoxic activities, while Smenoaimien A-E show anti-inflammatory effects. Isomalabaricane triterpenes from *Rhabdastrella globostellata* include stelletins, stelliferins, and globostellatic acids, many of which have significant cytotoxic activity.²⁶

Polyketides such as discodermolide from *Discodermia dissoluta* demonstrate potent cytotoxicity to human and murine cell lines.²⁷ Hemiasterlin, a cytotoxic tripeptide from *Hemiasterella minor*, shows sub-nanomolar potency against several cancer cell lines.²⁸ Halichondrin B, from *Halichondria okadai*, has

been modified to create eribulin, an FDA-approved drug for metastatic breast cancer treatment.²⁹

Theonella swinhoei is known for antiprotease and anti-HIV metabolites, while *Theonella aff. mirabilis* produces protease inhibitors and anti-HIV compounds like miraziridine A and papuamides A and B. Additionally, *T. swinhoei* contains antifungals such as cyclolithistide A and theopalauamide, along with cytotoxic polytheonamides.³⁰

Several drugs on the market today were originally sourced from marine sponges. For instance, Cytarabine, employed in treating leukemia and lymphoma, and Vidarabine, utilized against herpes and RNA tumor viruses, have been pivotal in antiviral and anticancer treatments. Additionally, Eribulin Mesylate (Halaven), derived from sponges, shows promise in combating metastatic breast cancer.³¹ Though not directly extracted from sponges, these drugs were discovered *via* sponge research, synthesized artificially, and subsequently developed into pharmaceuticals.



Given Sri Lanka's prominence as a marine sponge hotspot, studies concentrating on the taxonomic classification and bioactive compounds derived from these organisms are crucial. New researches on marine sponges help identify species with promising medicinal properties and warrant for drug discovery and development.



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