

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800

Open access books available

122,000

International authors and editors

135M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



---

# Biological and Medicinal Importance of Sponge

---

Musarat Amina and Nawal M. Al Musayeib

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.73529>

---

## Abstract

Sponges are multicellular, heterotrophic parazoan organisms, characterized by the possession of unique feeding system among the animals. They are the most primitive types of animals in existence, featuring a cell-based organization where different cells have different tasks, but do not form tissues. Sponges (Porifera) are a predominantly marine phylum living from the intertidal to the abyssal (deepest ocean) zone. There are approximately 8500 described species of sponges worldwide with a prominent role in many reef coral communities. Several ecological studies reported have shown that secondary metabolites isolated from sponges often serve defensive purposes to protect them from threats such as predator attacks, biofouling, microbial infections, and overgrowth by other sessile organisms. In the recent years, interest in marine sponges has risen considerably due to presence of high number of interesting biologically active natural products. More than 5300 different natural products are known from sponges and their associated microorganisms, and every year hundreds of new substances are discovered. In addition to the unusual nucleosides, other classes of substances such as bioactive terpenes, sterols, fatty acids, alkaloids, cyclic peptides, peroxides, and amino acid derivatives (which are frequently halogenated) have been described from sponges or from their associated microorganisms. Many of these natural products from sponges have shown a wide range of pharmacological activities such as anticancer, antifungal, antiviral, anthelmintic, antiprotozoal, anti-inflammatory, immunosuppressive, neurosuppressive, and antifouling activities. This chapter covers extensive work published regarding new compounds isolated from marine sponges and biological activities associated with them.

**Keywords:** sponges, anticancer, antibacterial, chemical constituents

---

## 1. Introduction

Sponges are the ancient, efficient designed multicellular parazoan organisms and show relatively little differentiation and tissue coordination. A sponge is a sessile, sedentary, filter-feeding

---

primitive aquatic invertebrate animal which attaches itself to solid surfaces from intertidal zone to depths of 29,000 ft (85000m) or more, where they can get sufficient food to grow [1, 2]. Sponges feed on microscopic organisms (protozoa, bacteria and other small organisms in water) and organic particles [3]. There are about 10,000 known species inhabit a wide variety of marine and fresh water habitats and are found throughout deep ocean depths to rock pools, warm tropical seas to frozen arctic seas, rivers and streams [3, 4]. They are very diverse and occur in various colors, sizes and shapes such as tubular (tube-like), globular (ball-shaped), caliculate (cup-shaped), arborescent (plant-shaped), flabellate (fan-shaped) and amorphous (shapeless). The scientific term for sponges is Porifera meaning “pore-bearing” and has bodies full of pores and channels allowing water to circulate through them, consisting of jelly-like mesohyl sandwiched between two layers of cells [5]. The shapes of their bodies are adapted for maximal efficiency of water flow through the central cavity, where it deposits the nutrients, and leaves through a hole called the osculum. Several sponges have spicules of silicon dioxide or calcium carbonate and a mesh of proteins called spongin as an internal skeleton. One of the remarkable properties of sponges is their ability to suffer damage and regenerative capacity [6–8]. Marine sponges have attracted growing attention as a source of overwhelming structurally diverse secondary metabolites with potential biological activities and were placed at the top with respect to discovery of biologically active chemical constituents [9, 10]. Although thousands of chemical compounds have been reported in the literature from these sponges, only few of them are clinically described. Many studies revealed that sponge-derived metabolites are used directly in therapy or as a prototype of bioactive leads to develop more active and less toxic analogs [11, 12]. Sponges are most primitive type of aquatic animals in existence which are dominating many benthic habitats, featuring a cell-based organization where different cells conduct all forms of bodily function, but do not form tissues [13]. They consume food and excrete waste products within cells without a body cavity [14]. Several ecological studies reported that high quantity of bioactive constituents produced by sponges often serve defensive against environmental threats such as predation, microbial infection, competition for space or overgrowth by fouling organisms [15, 16]. For this reason marine sponges are the subject of attraction for chemists due to the sheer number of metabolites produced, the novelty of structure encountered, and the therapeutic potential of these compounds in the treatment of human diseases. Scientists working in the field of natural product chemistry and research suggest that these sponges have promising potential to provide future drugs which can serve various diseases. In this chapter, we describe main isolated chemical entities from sponges and their pharmacological application.

## 2. Anticancer agents

In the recent years, marine natural products bioprospecting has yielded a considerable number of drug candidates, most still being in preclinical or early clinical development, with only a limited number already in the market [17]. A typical example of marine anticancer drugs is eribulinmesylate, a derivative of halichondrin B isolated from the marine sponge. *Halichondria okadai* has achieved success in phase III clinical trials. Literature studies have shown sponge-derived discodermolides antitumor compounds can play remarkable role in future to treat cancer. Plethora of secondary metabolites is produced by marine sponges and their symbionts. The spongothymidine and spongouridine nucleosides were the first successful sponge-derived

pharmaceutical drugs isolated from *Tectitethya crypta* [18]. Ara-C (cytarabine or 1-beta-D-Arabinofuranosylcytosine) recently used for the cure of leukemia [19, 20] and its combination with Daunorubicin and other anticancer drugs, is screened in clinical trials for the treatment of acute myeloid neoplasms [21]. During the last few years several marine derived natural compounds are in the pipeline for evaluation in Phase I–III clinical trials for various cancers treatment [22]. A review in 2003 listed the most important anticancer candidate from marine natural compounds undergoing preclinical and clinical (I, II, III) trials and following compounds were from sponge origin: Isohomohalichondrin B, Halichondrin B, Laulimalide/Fijianolide, 5-methoxyamphimedine (alkaloid) Discodermolide, Hemiasterlins A and B, Fascaphysins (alkaloid), modified halichondrin B, KRN-70000, Alipkinidine (alkaloid), and Variolin (alkaloid) [23]. Moreover marine sponges are the important source for vital diverse bioactive constituents including alkaloids, terpenoids, sterols and macrolides. Renieramycins, members of tetrahydroiso-quinoline family were isolated from marine sponges from genus *Reniera* with promising anticancer potential. The preclinical results reported that Renieramycin M, a natural constituent from sponge induced lung cancer cells apoptosis through p53-dependent pathway and may inhibit progression and metastasis of lung cancer cells [24]. A novel polycyclic guanidine alkaloid monanchocidin isolated from *Monanchora pulchra* marine sponge reported to induce cell death in human cervical cancer (HeLa), human monocytic leukemia (THP-1) and mouse epidermal (JB6 Cl41) cells [25]. In the early 1987, as sesquiterpene aminoquinone, Smenospongine extracted from *Smenospongia* sp. reported to induce cytotoxic, antiproliferative, antiangiogenic, and antimicrobial activities [26]. Spongistatin a macrocyclic lactone polyether isolated from *Spongia* sp. marine sponge in 1993 was shown to inhibit microtubule assembly, mitosis, and the binding of tubulin to vinblastine thereby inducing cytotoxic cell death in numerous cancer cell lines [27, 28]. Recently a very important compound named lectin has been isolated from *Cinachyrella apion* marine sponge was evaluated for antiproliferative, hemolytic, and cytotoxic properties, besides the ability to induce cell death in tumor cells. Results showed that the lectin induces cell death by apoptosis activation by pro-apoptotic protein Bax, promoting permeabilization of mitochondrial membrane, S phase cell cycle arrest and acting as both dependent and/or independent of caspases pathway. These results indicate the potential of lectin for treating cancer [29]. Another marine sponge component, heteronemin a sesterterpene isolated from *Hyrtios* sp. has attracted the interest of researchers as an anti-tumor agent especially for its pharmacological effects on chronic myelogenous leukemia cells. Results revealed that heteronemin affected the various cellular processes such as cell cycle, nitrogen-activated protein kinases pathways, apoptosis, and nuclear factor kappa B signaling cascade. Thus the compound has shown anti-inflammatory as well as anticancer agent [30]. A collaborative program between experimental therapeutics laboratory of Henry Ford Hospital in Detroit and University of California Santa Cruz initiated in 1990 focused on the development and discovery of anticancer drugs from sponge extracts. About 2036 extracts from 683 individual sponges were examined by using novel *in vitro* assay led to the identification pure bioactive compounds from many sponges for treating solid tumors. The collaborative efforts and analogs led to the isolation of number of constituents with anticancer potential [31].

Thus the possibility of development of new anticancer drugs for curing or reducing cancer is promising. Until now, *in vitro* antitumor activity studies of sponge-derived compounds were tested. Thus, the detailed pharmaceutical studies to investigate the mechanism of action and clinical trials are needed. Moreover, the extensive ongoing research on sponges and development

of new advanced techniques have made it possible to access deep sea, new anticancer marine isolates with unprecedented carbon skeleton and inhibitory activities of human cancer cell continued to be discovered and developed, which will offer in future the new candidate for cancer therapy. The chemical constituents so far reported for anticancer activity include (Table 1).

Categories	Species	Active agents	Antitumor tested	References	
Alkaloids	<i>Papua</i>	Hyrtiocarboline	H522-T1, MDA-MB-435, U937 tumor cell lines	[31]	
	<i>Penares</i> sp.		HL-60, HeLa	[32]	
	<i>Aaptos suberitoides</i>	Aaptamine	L5178Y	[33]	
	<i>Monanchora arbuscula</i>	Norbatzelladine			
		Dinorbatzelladine		MDA-MB-231 breast cancer	[34]
		Dinordehy-drobatzelladine			
		Dinorbatzelladine			
	<i>Clathria calla</i>	Dihomodehy-drobatzelladine		MDA-MB-231 breast cancer	[34]
		Norbatzelladine			
	<i>Xestospongia</i> sp.	Clathriadic acid			
		Renieramycin T		HCT116, QC56, AsPC1 T47D tumor cell lines	[35]
	<i>Smenospongia</i> sp.	6'-Iodoaureol		MOLT-3, HepG2 cells	[36]
	<i>Hyrtios</i> sp.	Hyrtimomine A		Human epidermoid carcinoma KB, murine leukemia L1210	[37]
	<i>Pseudoceratina verrucosa</i>	Aplysamine		HeLa, NFF cells	[38]
	<i>Amphimedon</i> sp.	Pyrinodemin G		P388 murine leukemia cells	
		Pyrinodemin H			[39]
	<i>Oceanapia</i> sp.	Sagitol C		PC12, L5178Y, HeLa cells	[40]
	<i>Monanchora pulchra</i>	Monanchocidins B			
		Monanchocidins C		HL-60 human leukemia cells	[41]
Monanchocidins D					
Monanchocidins E					
<i>Agelas</i> sp.	Hexazosceptrin				
	Agelestes A-B (9S, 10R, 90S, 100R)-nakamuric acid		U937, PC9 human Cancer cell lines	[42]	
Sterols	<i>Ianthella</i> sp.	Petrosterol-3,6-dione	A549 (lung), HT-29 (colon),		
		5 $\alpha$ ,6 $\alpha$ -epoxy-petrosterol	SK-OV-3 (ovary), MCF-7 (breast) HL-60 and U937	[43]	
	<i>Lissodendryx fibrosa</i>	Manadosterol A-B	Ubc13-Uev1A complex	[44]	
Terpenoids	<i>Carteriospongia</i> sp.	Homoscalarane sesterterpenes	A2780, H522-T1, A2058	[45]	
	<i>Monanchora</i> sp.	9Sesterterpenoids	A498, ACHN (renal cancer)	[46]	
			MIA-paca, and PANC-1 (pancreatic cancer)	[47]	
	<i>Psammocinia</i> sp.	Scalarane sesterterpenes	A498, ACHN MIA-paca, PANC-1	[48]	
	<i>Pseudoaxinella flava</i>	Diterpene isonitrile	PC3 (prostate cancer cell line)	[49]	
	<i>Agelas axifera</i>	Three axistatins (pyrimidine diterpenes)	P338, BXPC-3 MCF-7, SF-268 NCI-H460, KML20L2, and DU-145 cell lines growth	[50]	

Categories	Species	Active agents	Antitumor tested	References
	<i>Thorectare ticutate</i>	Metachromins U Metachromins V	SF-268, H460, MCF-7, HT-29, and CHOK1 (mammalian cell line)	[51]
	<i>Dactylospongia elegans</i>	Nakijinol B and CHO-K1	SF-268, H460, MCF-7, HT-29	[51]
	<i>Coscinoderma</i> sp.	Sesterterpenes coscinolactams C Coscinolactams D, Coscinolactams E Coscinolactams F Coscinolactams G	K562 and A549 (human cancer cells)	[52]
<b>Macrolide</b>	<i>Cinachyrella enigmatica</i>	Enigmazole A	NCI 60 human tumor cells	[54]
	<i>Jaspis splendans</i>	Jaspamide M Jaspamide N Jaspamide O Jaspamide P	MCF-7 and HT-29 (antimicrofilament)	[55]
	<i>Mycale hentscheli</i>	Peloruside A Peloruside B	P388 HL-60 cells	[56]
	<i>Pipestela candelabra</i>	Pipestelide A Pipestelide B	KB cell lines	[57]
<b>Polyketone</b>	<i>Plakortis simplex</i>	Simplextone C Plakortoxide A	HeLa, K562, A-549 cell lines	[58]
	<i>Plakortis halichondrioides</i>	Epiplakinidioic acid Plakortoxide A	DU-145, A2058 tumor cell lines	[59]
	<i>Lithoplocamialithistoides</i>	Polyketides PM050489 Polyketides PM060184	HT-29, A549, MDA-MB-231 Human tumor cell lines	[60]
<b>Peptides</b>	<i>Homophymia</i> sp.	Homophymines B Homophymines E Homophymines A1-E1	KB, MCF7, MCF7R, HCT116 HCT15, HT29, OVCAR 8, OV3, PC3, Vero, MRC5, HL60, HL60R, K562, PaCa, SF268, A549, MDA231, MDA435, HepG2, and EPC human tumor cells	[61]
	<i>Neamphius huxleyi</i>	Neamphamide B Neamphamide C Neamphamide D	A549, HeLa, LNCaP, PC3, NFF human tumor cell lines	[62]
	<i>Eurypon laughlini</i>	Rolloamide A	LNCaP, PC3MM2, PC3, DU145 (Prostrate), MDA361, MCF7, MDA231 (breast), OVCAR3, SKOV3, U87MG (Glioma), (ovarian), A498 (renal)	[63]
	<i>Stylissa caribica</i>	Stylissamide H	HCT-116.	[64]
	<i>Homophymia lamellose</i>	Pipecolidepsin A Pipecolidepsin B	A549, HT-29 MDA-MB-231 Human tumor cells	[65]
<b>Glycosides</b>	<i>Pandaros acanthifolium</i>	Acanthifoliosides A-E	L6 cell lines	[66]
	<i>Rhabdastrella globostellata</i>	Rhabdastin E-G	HL-60	[67]
<b>Quinones</b>	<i>Dysidea avara</i>	Dysidavarone A Dysidavarone D	HeLa, A549, MDA231, QGY7703 HeLa tumor cells	[68]
	<i>Dactylospongia metachromia</i>	5 Sesquiterpene aminoquinones	L5178Y mouse cancer cell lines	[69]

Categories	Species	Active agents	Antitumor tested	References
	<i>Dactylospongia avara</i>	3 Dysideanones A–C	HeLa HepG2 cancer cell lines	[70]
Miscellaneous	<i>Petrosia</i> sp.	3(-) Petrosynoic acids A–D	A2058, H522-T1, H460 human tumor cell line IMR-90 human fibroblast cells	[71]
	<i>Subereamollis</i>	Subereaphenol D	HeLa cell lines	[72]
	Mixture of <i>Smenospongia aurea</i>	(E)-10-benzyl-5,7-dimethylun-1 deca,5,10-trien-4-ol	HL-60 human leukemia	
	<i>Smenospongia cerebriformis</i>			
	<i>Verongula rigida</i>			[73]
	<i>Myrmekioderma dendyi</i>	Myrmekioside E-2	NSCLC-N6 and A549 tumor cell lines	[74]
	Genus <i>Suberea</i> .	Four novel Psammaplysin analogs	Cytotoxicity	[75]

**Table 1.** Marine sponge-derived anticancer compounds and their effects.

### 3. Antibacterial active agents

Marine sponges are among the richest sources of interesting chemicals produced by marine organisms. Exploitation of bioactive metabolites by natural product chemist from marine sources by using antimicrobial or cytotoxic assays started back in 1970s. Later, various reputed pharmaceutical companies joined hands for this effort using more advance assay systems, including enzyme inhibition assays. As a result several new promising bioactive candidates have been discovered from marine sponges [76]. Bioactive constituents are claimed for potent *in vivo* or *in vitro* activity against infectious and parasitic diseases, such as bacterial, fungal, viral and protozoan infections. Studies revealed that the crude extracts of marine sponge have shown high incidences of antibacterial activity against terrestrial pathogenic bacteria, but very low incidences of antibacterial activity against marine bacteria [77, 78]. Very few cases of sponge infection by exogenous microorganisms are known, presumably due to the accumulation/or product by the marine sponges of substances which have antimicrobial activity [1]. A number of new metabolites with antibiotic applications are discovered every year, but in marine sponges their ubiquity is remarkable. Antibacterial screening of marine sponges led to identification and characterization of wide range of active chemical constituents, including some with promising therapeutic leads [79, 80]. Around 850 antibiotic constituents are reported from marine sponges [81]. Various antibacterial substances were identified from marine sponges by continuous efforts of marine natural product community. Despite of discovery of huge number of natural product from marine sponges, none of them has yet led to antibacterial product, but currently several are under investigation. Examples of some isolated substances from marine sponges with antibacterial activity are shown in **Table 2**. The first discovered antibiotic from a marine sponge was manoalide, a sesterterpenoid isolated from *Luffariella variabilis* [82]. The most promising constituents with antibacterial properties reported from marine sponges include: agelasine D, cribrostatin 3 and 6, petrosamine B, psammaplin A and alkylpyridines (haliclonacyclamine E, arenosclerins) and among these constituents, manzamine A and psammaplin A are in preclinical trials. Many of these have excellent potential for drug development, but no commercial medication has been originated from them so far.

Categories	Species	Active agents	Antibacterial tested	References
Alkaloids	<i>Axinella</i> sp.	Axinellamines B-D	<i>H. pylori</i> Gram(-ve)	[83]
	<i>Acanthostrongylophora</i> sp.	12,34-Oxamanzamine E,	<i>M. tuberculosis</i>	[84]
		8-Hydroxymanzamine J		
		6-Hydroxymanzamine E		
	<i>Arenosclera brasiliensis</i>	Haliclonacyclamine E,	<i>S. aureus</i> , <i>P. aeruginosa</i>	
		Arenosclerins A-C		[85]
	<i>Spongosorites</i> sp.	Deoxytopsentin, bromotopsentin	<i>S. aureus</i> (MRSA strain)	
		4,5-Dihydro-6''-deoxybromotopsentin, bis(indole)		[86]
	<i>Cribrochalina</i> sp.	Cribrostatin 3	<i>N. gonorrhoeae</i>	[87]
	<i>Cribrochalina</i> sp.	Cribrostatin 6	<i>S. pneumonia</i>	[88]
	<i>Spongosorites</i> sp.	Hamacanthin A	<i>S. aureus</i> (MRSA strain)	[86]
	<i>Oceanapia</i> sp.	Petrosamine B	<i>H. pylori</i>	[89]
<i>Latrunculia</i> sp.	Discorhabdin R	<i>S. aureus</i> , <i>M. luteus</i>	[90]	
		<i>S. marcescens</i> , <i>E. coli</i>		
<i>Hamacantha</i> sp.	Hamacanthin A 1	<i>C. albicans</i>		
	Hamacanthin B 2	<i>C. neoformans</i>	[91]	
Nitrogenous	<i>Pachychalina</i> sp.	Cyclostelletamines A-I,	<i>S. aureus</i> (MRSA strain),	[92]
		Cyclostel K-L	<i>P. aeruginosa</i> (antibiotic-resistant strain), <i>M. tuberculosis</i>	[93]
	<i>Pachychalina</i> sp.	Ingenamine G	<i>S. aureus</i> (MRSA strain)	
			<i>E. coli</i> , <i>M. tuberculosis</i>	[92]
<i>M. sarassinorum</i>	Melophlin C	<i>B. subtilis</i> , <i>S. aureus</i>	[47]	
<i>Agelas</i> sp.	Agelasine D	<i>M. tuberculosis</i> Gram (+ve, -ve)	[94]	
Terpenoids	<i>Cacospongia</i> sp.	Isojaspic acid, cacospongins D, jaspinquinol	<i>S. epidermidis</i>	[95]
	<i>Myrmekiodermastyx</i>	(S)-(+)-curcuphenol	<i>M. tuberculosis</i>	[96]
Miscellaneous	<i>Oceanapia</i> sp.	C14 acetylenic acid	<i>E. coli</i> , <i>P. aeruginosa</i> , <i>B. subtilis</i> , <i>S. aureus</i>	[97]
	<i>C. sphaeroconia</i>	Caminsides A-D	<i>E. coli</i>	[98]
	<i>A. coralliphaga</i>	Corallidictyals A-D	<i>S. aureus</i>	[99]
	<i>C. varians</i>	CvL	<i>B. subtilis</i> , <i>S. aureus</i>	[100]
	<i>N. magnifica</i>	Latrunculins	<i>S. aureus</i> and <i>B. cereus</i>	[101]
	<i>Discodermia</i> sp.	Polydiscamide A	<i>B. subtilis</i>	[93]
<i>Psammaphysilla</i>	Psammaphin A	<i>S. aureus</i> (MRSA strain)	[102]	

**Table 2.** Marine sponge-derived antibacterial compounds and their effects.

#### 4. Antiviral compounds and their efficacy

The search for new antiviral substances from marine sources led to the isolation of several promising therapeutic leads which are presented in **Table 3**. The literature presents a good number of reports about different biological activities of marine sponges. Several papers



Categories	Species	Active agents	Antiviral tests	References
Alkaloid	<i>Aaptosa aptos</i>	4-Methylaaptamine	HSV-1	[110]
	<i>Halicortex</i> sp.	Dragmacidin F	HSV-1	[111]
	Indo-Pacific	Manzamine A, 8-hydroxymanzamine A, 6-deoxymanzamine X neokauluamine	HIV-1	[112]
Nucleosides	<i>Mycale</i> sp.	Mycalamide A-B	A59 coronavirus, HSV-1	[113]
	<i>Hamacantha</i> sp.	Coscinamides 60-62, Chondriamides 63-65	Anti-HIV	[91]
Cyclic depsipeptides	<i>Theonella</i> sp.	Papuamides A-D	HIV-1	[114]
	<i>S. microspinoso</i>	Microspinosamide	HIV-1	[115]
Sterols	Haplosclerid sponges	Haplosamates A	HV-1	
		Haplosamates B		[116]
Terpenoids	<i>D. avara</i>	Avarol 6'-hydroxy avarol, 3'-hydroxy avarone	HV-1	[117]
Nucleoside	<i>Cryptotethya crypta</i>	Ara-A	HSV-1, HSV-2, VZV	[105]
	<i>Mycale</i> sp.	Mycalamide A-B	A59 coronavirus, HSV-1	[118]
Miscellaneous	<i>Dysidea avara</i>	Callyspongymic acid	HIV, hepatitis B virus	[119]
		2'-5' Oligoadenylylates	Viral replication	[120]
	<i>H. tarangaensis</i>	Hamigeran B	Herpes, polio viruses	[121]
	<i>Petrosia weinbergi</i>	Weinbersterols A-B	Leukemia virus, mouse influenza virus, mouse corona virus	[122]

**Table 3.** Antiviral compounds from marine sponges and their effects.

reports the screening results of marine organisms for antiviral activity, and a diverse range of active constituents have been isolated and characterized from them [80, 103, 104]. For some of these isolated substances important antiviral activities were reported. Perhaps the most important antiviral lead of marine origin reported thus far is the nucleoside ara-A (vidarabine) isolated from the sponge *Cryptotethya crypta*. Ara-A is a semisynthetic compound, based on the arabinosyl nucleosides, that inhibits viral DNA synthesis [105]. Once it was realized that biological systems would recognize the nucleoside base after modifications of the sugar moiety, chemists began to substitute the typical pentoses with acyclic entities or with substituted sugars, leading to the drug azidothymidine (zidovudine). Ara-A, ara-C (1- $\beta$ -Darabinosyl cytosine, cytarabine), acyclovir, and azidothymidine are in clinical use and are all examples of products of semisynthetic modifications of the arabinosyl nucleosides [106]. Several of these substances have a great potential for drug development. Ara-A has been used for the treatment of herpes virus infections, but it is less efficient and more toxic than acyclovir [107, 108]. However, ara-A is capable of inhibiting a cyclovir-resistant HSV and VZV (varicella-zoster virus) [109]. The most promising antiviral substances from sponges appear to be 4-methylaaptamine, avarol, manzamines, mycalamide A and B. Among these substances, preclinical assessments were started for avarol and manzamine A. In general, antiviral molecules from sponges do not give protection against viruses, but they may result in drugs to treat already infected individuals. In addition, broad-based antiviral agents such as 2-5A and  $\alpha$ -glucosidase inhibitors may be useful in cases of sudden outbreaks of (less familiar) viruses such as SARS and Ebola [80].

## 5. Antifungal compounds

Marine sponges have been considered a gold mine for the discovery of marine natural products during the past 50 years. The need of new antifungals in clinical medicine due to various kinds of mycoses, in particular invasive mycoses have become serious health problems as their incidences has increased dramatically during last few years in relation to AIDS, transplant recipients, hematological malignancies, transplant recipients and other immunosuppressed individuals. One of the major causes of death in patients suffering from malignant disease is fungal infections and emerging resistance is also an important problem. Immunocompromised patients are mainly infected by *Aspergillus*, *Cryptococcus*, *Candida*, and other opportunistic fungi. *Candida albicans* is most often associated with serious invasive fungal infections, but other *Candida* species and yeast-like organisms (*Blastoschizomyces*, *Trichosporon* and *Malassezia*) have emerged as etiological agents of severe mycoses problem [123–126]. Fungicides which are presently being used are less diverse than antimicrobials, and the usage of many of them is restricted because of their toxic effects to animals, plants and humans. Moreover the progress in this area is slow as comparison to antibacterial agents [126]. Antifungal compounds isolated from marine sponges are listed in **Table 4**.

Categories	species	Active agents	Antifungal tests	References
Alkaloids	<i>A. brasiliensis</i>	Arenosclerins A-C	<i>C. albicans</i>	[127]
		Haliclonacyclamine E		
	<i>Acanthostrongylophora</i> sp.	Manzamine A	<i>C. neoformans</i>	[112]
	<i>Leucetta</i> cf.	Naamine D	<i>Chagosensis C. neoformans</i>	[128]
	<i>Pseudoceratina</i> sp.	Ceratinadins A-C	<i>C. albicans</i>	[129]
	<i>A. citrina</i>	(-)-Agelasidine F,	<i>C. albicans</i>	[130]
(-)-Agelasidine C				
Terpenoids	<i>M. arbuscular</i>	Batzelladine L	<i>A. flavus</i>	[131]
		Secmanoalide	<i>C. glabrata</i> , <i>C. krusei</i>	
	<i>L. variabilis</i>		<i>C. albicans</i>	[132]
Sterols	<i>M. herdmanni</i>	Microsclerodermins A-B	<i>A. fumigatus</i>	[133]
	<i>Hyrtilos</i> sp.	Puuphenonol	<i>C. neoformans</i> , <i>C. krusei</i>	[134]
	<i>Eurysongia</i> sp.	Eurysterols A-B	<i>C. albicans</i>	[135]
	<i>Topsentia</i> sp.	Geodisterol-3-O-sulfite, 29-demethylgeodisterol-3-OCI-sulfite	<i>S. cerevisiae</i> , <i>C. albicans</i>	
Peptides	<i>Discodermia</i> sp.	Discobahamin A-B	<i>C. albicans</i>	[137]
		Jasplakinolide or jaspamide		
	<i>Latrunculia</i> sp.	Callipeltins F-I	<i>C. albicans</i>	[139]
	<i>Latrunculia</i> sp.	Callipeltin J-K	<i>C. albicans</i>	[42]
	<i>T. swinhoei</i>	Theonellamide G	<i>C. albicans</i>	[140]
	<i>Theonella</i> sp.	Theonellamide TNM-F	<i>Candida</i> spp, <i>Trichophyton</i> spp, <i>Aspergillus</i> sp.	[141]
Purine derivatives	<i>Agelas</i> sp.	Agelasines, agelasimines	<i>C. krusei</i>	[142]

Categories	species	Active agents	Antifungal tests	References
Miscellaneous	<i>P. reticulate</i>	Crambescin A2 392	<i>C. albicans</i>	
		Crambescin A2 406	<i>C. neoformans</i> var. <i>gattii</i> ,	
		Crambescin A2 420	<i>C. glabrata</i> , <i>C. krusei</i>	
		Sch 575948		[143]
	Sponge	Theonellamides	Antifungal	[144]
	<i>Melophlus</i> sp.	Aurantoside K	<i>C. albicans</i> (wild-type)	[145]
	<i>P. halichondrioides</i>	Plakortide F	<i>C. albicans</i> , <i>C. neoformans</i> , <i>A. fumigatus</i>	[146]
	<i>H. viscosa</i>	Haliscosamine	<i>C. neoformans</i> , <i>C. albicans</i>	[147]
	<i>D. herbacea</i>	3,5-Dibromo-2-(3,5-dibromo-2-methoxyphenoxy) phenol	<i>Aspergillus</i>	[148]
	<i>P. onkodes</i>	Two $\alpha$ and $\beta$ 1,2-dioxolane peroxide acids	<i>C. albicans</i>	[149]
	<i>T. laevispirulifer</i>	Nematocide, onnamide F	<i>S. cerevisiae</i>	[150]
	<i>T. swinhoei</i>	Swinhoeiamide A	<i>C. albicans</i> , <i>A. fumigatus</i>	[151]
	Family <i>Neopeltidae</i>	Neopeltolide	<i>C. albicans</i>	[152]
	Plakinastrella	Epiplakinic acid F	<i>C. albicans</i>	[153]
<i>H. communis</i>	(-)-Untenosponggin B	<i>C. albicans</i> , <i>C. tropicalis</i> , <i>F. oxysporum</i>	[154]	
<i>H. lachne</i>	Hippolachnin A	<i>C. neoformans</i> , <i>T. rubrum</i> , <i>M. gypseum</i>	[155]	

**Table 4.** Antifungal compounds from marine sponges and their effects.

## 6. Anti-inflammatory compounds

Marine organisms and microorganisms have provided a large proportion of the anti-inflammatory and natural antioxidants products over the last years. Reports suggest that marine invertebrates represent new marine resources for the isolation of novel agents which are active on inflammatory conditions have also been found in the literature. Herencia and coworkers [156] studied the effects of dichloromethane and methanol extracts from some Mediterranean marine invertebrates on carrageenan-induced paw edema in mice. Extracts partially decreased elastase activity and PGE2 levels measured in homogenates from inflamed paws, without affecting the levels of this prostanoid present in stomach homogenates. Within the framework of the European MAST III Project, extracts of different polarity from sponges, ascidians and cnidarians have been screened for immunomodulating activities [157]. It was demonstrated that endotoxin-free samples of marine origin possess effects on certain components of the immune system. As a result of all these investigations, bioassay-directed separation of active extracts identified many structurally diverse compounds as future leads. Anti-inflammatory compounds found in the marine environment include terpenes and steroids, alkaloids, peptides and proteins, polysaccharides and others. Examples of anti-inflammatory compounds marine sponge origin are presented in **Table 5**. Also includes diterpenes of (8*E*, 13*Z*, 20*Z*)-strobilin and (7*E*, 13*Z*, 20*Z*)-felinin from a marine sponge *Psammocinia* sp. [158], and novel anti-inflammatory spongian diterpenes from the New Zealand marine sponge *Chelonaplysilla aviolacea* [159].

Categories	species	Active agents	Anti-inflammatory tests	References
Terpenoids	<i>F. cavernosa</i>	Cavernolide	TNF- $\alpha$ , NO and PGE2 production	[160]
	<i>Axinella</i> spp.	6-Cycloamphilectenes	NO, PGE2 and TNF- $\alpha$ production	[161]
		2-Cycloamphilectenes	Inhibit NF-KB pathway	[161]
	<i>Psammocinia</i> spp.	Chromarols A-E	Inhibition of 15-LOX	[162]
	<i>Psammocinia</i> spp.	(8E, 13Z, 20Z)-strobilinin	Anti-inflammatory	
		(7E, 13Z, 20Z)-felixinin	Anti-inflammatory	[158]
	<i>C. violacea</i>	Spongian	Anti-inflammatory	[163]
	<i>D. avara</i>	Avarol, avarone,	Inhibition of eicosanoid release	[164]
		Spongiaquinone, ilimaquinone	and depression of superoxide generation	[165]
	<i>Dysidea</i> spp.	Dysidotronic acid	Inhibited production of TNF- $\alpha$ , IL-1 PGE2, and LTB4	[166]
	<i>Plakortis</i> spp.	Plakolide A	Inhibit iNOS	[167]
	<i>D. elegans</i>	Cymopol	DNA binding of NF-KB	[168]
	<i>L. variabilis</i>	Manoalide, scalaradial	Inhibited IL-1 and TNF- $\alpha$	[169]
	<i>F. cavernosa</i>	Cacospongiolide B	Inhibited PLA2	[170]
	<i>Dysidea</i> spp	Dysidenones A-B	Inhibited human synovial PLA2	[171]
	<i>L. variabilis</i>	Cladocorans A-B	Inhibition of secretory PLA2	[172]
	<i>P. nigra</i>	Petrosa spongiolides	Inhibitor of PLA2	[173]
	<i>P. nigra</i>	Petrosa spongiolide M	Inhibited LTB4 levels	[174]
	<i>Cacospongia</i> spp.	Scalaradial	Inactivate the enzyme PLA2	[175]
	<i>G. sedna</i>	Homoscalarane	Moderate activity to inhibit mammalian PLA2	[176]
<i>Hyrtilos</i> sp.	Puupehenone, hyrtenone	A high potency against 12-human, 15-human and 15-soybean LOX	[177]	
<i>C. linteiformis</i>	Cyclolinteinone	iNOS and COX-2 protein expression in LPS-stimulated J774 macrophages	[178]	
<i>Callyspongia</i> spp.	Akaterpin	Inhibitor of phosphatidylinositol-specific Phospholipase C	[179]	
Steroids	<i>C. lissosdera</i>	Clathriol	<i>In vitro</i> anti-inflammatory activity against human neutrophil and rat mast cells	[180]
	<i>Euryspongia</i> spp.	Petrosteroil, 3 $\beta$ -hydroxy-26-nor-campest-5-en-25 oic acid	Against 6-keto-PGF1 $\alpha$ release in a human keratinocyte cell line HaCaT	[181]
Alkaloids	<i>X. testudinaria</i>	Hymenialdisine	Inhibitor of NF-KB and ILs production	[182]
	<i>Agelas</i> spp.	Nagelamides A-H	NF-KB in inflammatory diseases	[183]
	<i>S. flabellate</i>	Stylissadines A-B	Antiinflammatory activity	[184]

**Table 5.** Anti-inflammatory compounds from marine sponges and their effects.

## 7. Marine sponge-derived compounds with enzyme inhibitory activity

Derivatives of halenaquinone and xestoquinone showed various enzyme inhibitory activities besides the phosphatidylinositol 3-kinase and topoisomerase I and II inhibitory activities mentioned above. Compound xestoquinone inhibited both Ca<sup>2+</sup> and K<sup>+</sup>-ATPase of skeletal muscle myosin [185]. SAR Investigations showed that halenaquinone and three synthetic analogs with a quinone structure significantly inhibited Ca<sup>2+</sup> ATPase activity. In contrast, four xestoquinone

Categories	Species	Active agents	Enzyme-inhibitory	References
Quinones	<i>X. exigua</i>	Halenaquinone	Ca <sup>2+</sup> ATPase activity	[191]
	<i>X. exigua</i>	Xestoquinone	Ca <sup>2+</sup> and K <sup>+</sup> -ATPase activity	[192]
	<i>X. sapra</i>	Halenaquinol	Protein tyrosine kinase activity	[193]
	<i>X. cf. carbonaria</i>	14-Methoxyhalenaquinone	Protein tyrosine kinase activity	[187]
	<i>Xestospongia</i> sp.	Adociaquinone B	Protein tyrosine kinase activity	[194]
	<i>Xestospongia</i> sp.	3-Ketoadociaquinone B	Cdc25B phosphatase activity	[195]
	<i>Xestospongia</i> sp.	Adociaquinone A	Cdc25B phosphatase	[194]
	<i>Xestospongia</i> sp.	3-Ketoadociaquinone	Cdc25B phosphatase	[195]
Cyclostellatamines	<i>Xestospongia</i> sp.	Cyclostellatamine	A histone deacetylase derived inhibition	[189]
		Cyclostellatamine G		
		Dehydrocyclostellatamine D		
		Dehydrocyclostellatamine E		
Fatty acids	<i>X. testudinaria</i>	Xestospongiic acid ethyl ester	inhibit the Na <sup>+</sup> /K <sup>+</sup> ATPase	[190]

**Table 6.** Marine sponge-derived compounds showing enzyme-inhibitory activities.

analogs in which the quinone structure was converted to quinol dimethyl ether did not inhibit the Ca<sup>2+</sup> ATPase activity [186]. The protein tyrosine kinase (PTK) inhibitory activities of halenaquinone, halenaquinol, and 14-methoxyhalenaquinone were the most remarkable with IC<sub>50</sub> values <10 μM. The other analogs were either less potent or inactive, and a rationalization for this SAR pattern was also reported [187]. Xestoquinone also showed significant protein kinase inhibitory activity toward Pfnek-1, a serine/threonine malarial kinase, with an IC<sub>50</sub> value of ca. 1 μM, and moderate activity toward PfPK5, a member of the cyclin-dependent kinase (CDK) family [188]. Adociaquinone B and 3-ketoadociaquinone B were the most potent inhibitors of the Cdc25 B phosphatase inhibitory activities, and the dihydro-benzothiazine dioxide in compounds Adociaquinone A, Adociaquinone B, 3-Ketoadociaquinone A, and 3-Ketoadociaquinone B appeared to be an important structural feature for this enhanced activity. Four cyclostellatamines, cyclostellatamine A, cyclostellatamine G, dehydrocyclostellatamine D and dehydrocyclostellatamine E inhibited histone deacetylase derived from K562 human leukemia cells with IC<sub>50</sub> values ranging from 17 to 80 μM [189]. Xestospongiic acid ethyl ester (207) was found to inhibit the Na<sup>+</sup>/K<sup>+</sup> ATPase [190]. Compounds are listed in **Table 6**.

## 8. Sponge-derived immunosuppressive compounds and their efficacy

Recently natural constituents isolated from marine sponges were tested for immunosuppressive activities and in the end of 1980s, deep water marine sponges resulted in isolation of pure compounds with immunosuppressive properties. Two important compounds: 4α-methyl-5α-cholest-8-en-3-ol and 4,5-dibromo-2-pyrrolic acid discovered by American scientist from deep water sponge *Agelasia belliformis* showed significant immunosuppressive activity. Both compounds were found significantly active in suppression of the response of murine splenocytes in the two-way mixed lymphocyte reaction (MLR) with little to no demonstrable cytotoxicity at low doses [196]. Constituents isolated from the *Aurora globostellata* marine sponge showed

immunomodulatory potential. The immunomodulatory potential was evaluated by oral administration of ethyl acetate extract of marine sponge (200 mg/kg) to Wistar rats and the results obtained showed that extracts exhibited immunosuppressant activity and can further be studied [197]. A recent investigation on an Indian marine sponge aimed to isolate and characterize bacteria with immunomodulatory and antimicrobial activity. *Callyspongia difusa* (Gulf of Mannar province) a marine sponge resulted in isolation of 10 marine bacterial strains which exhibited remarkable antagonistic activity against clinical bacterial pathogens. These findings suggested that the sponge associated bacterial strain *Virgibacillus* sp. can contribute the search for novel antibiotics to overcome infections and also for the production of potential immunomodulators [109].

## 9. Hypocholesterolemic compounds

In the last decade studies reported that marine sponges could have been a source of hypocholesterolemic compounds. For example, lysophosphatidylcholines and lyso-PAF analogs derived from *Spirastrella abata* are reported as successful inhibitors of cholesterol biosynthesis in vitro study [198, 199]. Zhao et al. [200] extracted novel lysophosphatidylcholines from marine sponges with hypocholesterolemic properties and thereby aroused an interest of compounds from marine sponge due to short lifespan of conventional lysophosphatidylcholines *in vivo*.

## 10. Sponge-derived antibiotics

Also, over the years marine sponges are considered as a rich source of natural products and metabolites for antibiotics possessing strong inhibitory against bacteria, fungi and microbes. Several studies revealed that many natural bioactive components isolated from various marine sponges can be useful for the production of new antibiotics and antimicrobial drugs. In the recent years many scientific studies provided evidences for marine sponge metabolites with efficient antibiotic, antibacterials and antimicrobial properties. Purpuroines A-J, halogenated alkaloids isolated from *Lotrochota purpurea* marine sponge showed promising inhibitory activities against bacteria and fungi related diseases [201]. *Haliclona* sp. sponge from Korea resulted in isolation of novel cyclic bis-1,3-dialkylpyridiniums and cyclostelletamines, which showed moderate cytotoxic and antibacterial activities against A549 cell-line and Gram-positive strains, respectively [202]. A number of new alkaloids were isolated from the marine sponge *Agelas mauritiana*: (+)-2-oxo-agela-sidine C, (-)-8'-oxo-agelasine D, 4-bromo-N-(butoxymethyl)-1H-pyrrole-2-carboxamide, ageloxime B, and (-)-ageloxime D and some of these isolated components exhibited antifungal activity against *Cryptococcus neoformans*, antileishmanial activity in vitro and antibacterial activity against *S. aureus* and methicillin-resistant *S. aureus* in vitro [203]. Extracts prepared from the sponge's species *Petromica citrina*, *Haliclona* sp. and *Cinachyrella* sp. exhibited antibacterial activity against 61% of the coagulase-negative staphylococci (CNS) strains, including strains resistant to conventional antibiotics. *P. citrina* extracts showed the largest spectrum of inhibitory activity. This current study according scientist shows potential of marine sponges to become new sources of antibiotics and disinfectants for the control of CNS involved in bovine mastitis in future [204]. Isolation of isonitriles ditenene from *Cymbastela hooperi*, tropical marine sponge and the axisonitrile-3 sesquiterpene isolated *Acanthella kletra*, from

the tropical marine sponge were tested for series of bioassays antibacterial, antiphotosynthetic, antifouling, antialgal, antifouling, antialgal, antiphotosynthetic, antifungal, and antitubercular. The results showed majority of the tested compounds were active against at least two of the applied test systems [152]. Recently, sponge-derived actinomycetes and sediments isolated from marine sponge were tested for bioactive constituents with antifungal and antimicrobial activity. Out of 15 prepared active extract nine were found active against *Enterococcus fascism* (vancomycin-resistant) and *Candida albicans* multidrug-resistant [132], including strains resistant to conventional antibiotics. Thus the bacterial actinomycetes from marine sponges and other marine organisms have been proved prolific producers of pharmacologically active compounds. Literature studies revealed that 70% of naturally derived antibiotics which are currently in clinical use have been derived from actinomycetes. In the recent study, *Streptomyces* sp. strains from Mediterranean sponges and secondary metabolite namely, cyclic depsipeptide valinomycin, indolocarbazole alkaloid staurosporine and butenolide, were screened for anti-infective activities. All the isolated compounds along with *Streptomyces* sp. exhibited antiparasitic activities. Researchers also claim the anti-infective potential of marine actinomycetes is very promising.

## 11. Marine sponges-derived antifouling and antibiofilm compounds

Bacterial biofilms are surface-attached microorganism's communities that are protected by an extracellular matrix of biomolecules. Continuous use of chemical antifoulants resulted in increased tributyltin concentration and created extensive pollution problems in marine organisms. Natural antifouling molecules from marine have been recently reviewed and researches hope that will provide more specific and less toxic antifouling activity in future. Antifouling compounds derived from sponges were found to be very effective, environmentally friendly biocides and less toxic [205]. In the last few years several studies were directed to find the most promising alternative technologies to antifouling in marine organisms, especially from sponges. In a recent study structurally different compounds containing 3-alkylpyridine moiety were evaluated for antifouling potential. The compounds, namely haminols, saraine and 3-alkylpyridinium salts extracted from *Reniera sarai*, *Haliclona* sp. and the mollusk *Haminoea fusar* is obtained by synthesis, showed very good antifouling potential larvae of the barnacle *Amphibalanus amphitrite*. Bromopyrrole or diterpene alkaloids derivatives isolated from *Agelas linnaei* and *Ageles nakamurai* Indonesian marine sponges exhibited cytotoxic activity. Moreover, agelasine derivatives inhibited settling of larvae of *Balanus improvisus* in an antifouling bioassay as well as the growth of planktonic forms of biofilm forming bacteria *S. epidermidis* [206].

## 12. Conclusion

Marine invertebrates (Porifera, Cnidaria, Mollusca, Arthropoda, Echinodermata, etc.) are considered as one of the major groups of biological organisms which gave huge number of natural products and secondary metabolites with interesting pharmacological properties and led in the formation of novel drugs. Among marine invertebrates, marine sponges (phylum: Porifera) is the most dominant responsible group for discovering significant number of natural compounds, which has been used as template to develop therapeutic drugs. These natural products

possesses vast range of therapeutic application, including antimicrobial, antihypertensive, antioxidant, anticancer, anticoagulant, anti-inflammatory, immune modulator, and wound healing and other medicinal effects. Therefore, marine sponges are considered a rich source of chemical diversity and health benefits for developing drug candidates, nutritional supplements, cosmetics, and molecular probes that can be supported to increase the healthy life span of humans. In this chapter we included the most important and biologically active marine sponge-derived compounds and presented selected studies of most important bioactive and promising natural products and secondary metabolites from marine sponges.

## Conflict of interest

The authors declare that they have no conflict of interest.

## Author details

Musarat Amina\* and Nawal M. Al Musayeib

\*Address all correspondence to: musarat.org@gmail.com

Department of Pharmacognosy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

## References

- [1] Hentschel U, Schmid M, Wagner M, Fieseler L, Gernert C, Hacker J. Isolation and phylogenetic analysis of bacteria with antimicrobial activities from the Mediterranean sponges *Aplysina aerophoba* and *Aplysina cavernicola*. *FEMS Microbiology Ecology*. 2001;**35**:305-312
- [2] Radjasa OK, Sabdono A, Junaidi, Zocchi E. Richness of secondary metabolite-producing marine bacteria associated with sponge *Haliclona* sp. *International Journal of Pharmaceutics*. 2007;**3**:275-279
- [3] Thomas TR, Kavlekar DP, LokaBharathi PA. Marine drugs from sponge-microbe association—A review. *Marine Drugs*. 2010;**8**:1417-1468
- [4] Perdicas S, Vlachogianni T, Valavanidis A. Bioactive natural substances from marine sponges: New developments and prospects for future pharmaceuticals. *Natural Products Chemistry and Research*. 2013;**1**:1-8
- [5] Mehbub MF, Lei J, Franco C, Zhang W. Marine sponge derived natural products between 2001 and 2010: Trends and opportunities for discovery of bioactive. *Marine Drugs*. 2014;**12**:4539-4577
- [6] Taylor MW, Radax R, Steger D, Wagner M. Sponge-associated microorganisms: Evolution, ecology, and biotechnological potential. *Microbiology and Molecular Biology Reviews*. 2007;**71**:295-347



- [7] Stowe SD, Richards JJ, Tucker AT, Thompson R, Melander C, et al. Anti-biofilm compounds derived from marine sponges. *Marine Drugs*. 2011;**9**:2010-2035
- [8] Thompson JE, Walker RP, Faulkner DJ. Exudation of biologically-active metabolites in the sponge *Aplysina fistularis*. I. Biological evidence. *Marine Biology*. 1985;**88**:11-21
- [9] Becker S, Terlau H. Toxins from cone snails: Properties, applications and biotechnological production. *Applied Microbiology and Biotechnology*. 2008;**79**:1-9
- [10] Fenical W, Jensen P, Palladino M, Lam K, Lloyd G, Potts B. Discovery and development of the anticancer agent salinosporamide A (NPI-0052). *Bioorganic & Medicinal Chemistry*. 2009;**17**:2175-2180
- [11] Gerwick WH, Moore BS. Lessons from the past and charting the future of marine natural products drug discovery and chemical biology. *Chemistry & Biology*. 2012;**19**:85-98
- [12] Huyck TK, Gradishar W, Manuguid F, Kirkpatrick P. Fresh from pipeline: Eribulin mesylate. *Nature Reviews. Drug Discovery*. 2011;**10**:173-174
- [13] Johns WE, Schott F. Meandering and transport variations of the Florida current. *Journal of Physical Oceanography*. 1987;**17**:1128-1147
- [14] Hooper JN, editor. *Sponguide. Guide to Sponge Collection and Identification*. Queensland, Australia: Queensland Museum; 2000
- [15] Paul VJ, Puglisi MP. Chemical mediation of interactions among marine organisms. *Natural Product Reports*. 2004;**21**:189-209
- [16] Paul VJ, Puglisi MP, Ritson-Williams R. Marine chemical ecology. *Natural Product Reports*. 2006;**23**:153-180
- [17] Beedesse G, Ramanjooloo A, Aubert G, Eloy L, et al. Cytotoxic activities of hexane, ethyl acetate and butanol extracts of marine sponges from Mauritian Waters on human cancer cell lines. *Environmental Toxicology and Pharmacology*. 2012;**34**:397-408
- [18] Bergmann W, Feeney RJ. The isolation of a new thymine pentoside from sponges. *The Journal of the American Chemical Society*. 1950;**72**:2809-2810
- [19] Proksch P, Edrada RA, Ebel R. Drugs from the seas—Current status and microbiological implications. *Applied Microbiology and Biotechnology*. 2002;**59**:125-134
- [20] Schwartzmann G. Marine organisms as a source of new anticancer agents. *Annals of Oncology*. 2000;**11**(3):235-243
- [21] Feldman EJ, Lancet JE, Kolitz JE, Ritchie EK, et al. First-in-man study of CPX-351: A liposomal carrier containing cytarabine and daunorubicin in a fixed 5:1 molar ratio for the treatment of relapsed and refractory acute myeloid leukemia. *Journal of Clinical Oncology*. 2011;**29**:979-985
- [22] Mayer AM, Glaser KB, Cuevas C, Jacobs RS, et al. The odyssey of marine pharmaceuticals: A current pipeline perspective. *Trends in Pharmacological Sciences*. 2010;**31**:255-265

- [23] Crews P, Gewick WH, Schmitz FJ, France D, Bair KW, et al. Molecular approaches to discover marine natural product anticancer leads—An update from a drug discovery group collaboration. *Pharmaceutical Biology*. 2003;**141**:39-52
- [24] Halim R, Gladman B, Danquah MK, Webley PA. Oil extraction from microalgae for bio-diesel production. *Bioresource Technology*. 2011;**102**(1):178-185
- [25] Guzii AG, Makarieva TN, Denisenko VA, Dmitrenok PS, et al. Monanchocidin: A new apoptosis-inducing polycyclic guanidine alkaloid from the marine sponge *Monanchora pulchra*. *Organic Letters*. 2010;**12**(19):4292-4295
- [26] Kondracki ML, Guyot M. Smenospongine: A cytotoxic and antimicrobial aminoquinone isolated from *Smenospongia* sp. *Tetrahedron Letters*. 1987;**27**:5815-5818
- [27] Kong D, Yamori T, Kobayashi M, Duan H. Antiproliferative and antiangiogenic activities of smenospongine, a marine sponge sesquiterpene aminoquinone. *Marine Drugs*. 2011;**9**:154-161
- [28] Valeriote FA, Tenney K, Media J, Pietraszkiewicz H, et al. Discovery and development of anticancer agents from marine sponges: perspectives based on a chemistry-experimental therapeutics collaborative program. *Journal of Experimental Therapeutics & Oncology*. 2012;**10**:119-134
- [29] Rabelo L, Monteiro N, Serquiz R, Santos P, et al. A lactose-binding lectin from the marine sponge *Cinachyrella apion* (Cal) induces cell death in human cervical adenocarcinoma cells. *Marine Drugs*. 2012;**10**:727-743
- [30] Rothmeier E, Pfaffinger G, Hoffmann C, Harrison CF, et al. Activation of Ran GTPase by a *Legionella* effector promotes microtubule polymerization, pathogen vacuole motility and infection. *PLoS Pathogens*. 2013;**9**:e1003598. DOI: 10.1371/journal.ppat.1003598
- [31] Inman WD, Bray WM, Gassner NC, Lokey RS, et al.  $\beta$ -Carboline alkaloid from the Papua New Guinea marine sponge *Hyrtios reticulatus*. *Journal of Natural Products*. 2010;**73**:255-257
- [32] Lyakhova EG, Kolesnikova SA, Kalinovskiy AI, Afiyatulloev SS, et al. Bromine-containing alkaloids from the marine sponge *Penares* sp. *Tetrahedron Letters*. 2012;**53**:6119-6122
- [33] Pham CD, Hartmann R, Muller WE, de Voogd N, Lai D, Proksch P. Aaptamine derivatives from the Indonesian sponge *Aaptos suberitoides*. *Journal of Natural Products*. 2013;**76**:103-106
- [34] Laville R, Thomas OP, Berru e F, Marquez D, Vacelet J, Amade P. Bioactive guanidine alkaloids from two Caribbean marine sponges. *Journal of Natural Products*. 2009;**72**:1589-1594
- [35] Daikuhara N, Tada Y, Yamaki S, Charupant K, et al. Renieramycins T and U, novel renieramycin–ecteinascidin hybrid marine natural products from Thai sponge *Xestospongia* sp. *Tetrahedron Letters*. 2009;**50**:4276

- [36] Prawat H, Mahidol C, Kaweetripob W, Wittayalai S, Ruchirawat S. Iodo-sesquiterpene hydroquinone and brominated indole alkaloids from the Thai sponge *Smenospongia* sp. *Tetrahedron*. 2012;**68**:6881-6886
- [37] Momose R, Tanaka N, Fromont J, Kobayashi J. Hyrtimomines A-C, new heteroaromatic alkaloids from a sponge *Hyrtios* sp. *Organic Letters*. 2013;**15**:2010-2013
- [38] Tran TD, Pham NB, Fechner G, Hooper JN, Quinn RJ. Bromotyrosine alkaloids from the Australian marine sponge *Pseudoceratina verrucosa*. *Journal of Natural Products*. 2013;**76**:516-523
- [39] Kubota T, Kura KI, Fromont J, Kobayashi JI. *Tetrahedron*. 2013;**69**:96
- [40] Ibrahim SRM, Mohamed GA, Elkhayat ES, Fouad MA, Proksch P. Marine pyridoacridine alkaloids: Biosynthesis and biological activities. *Bulletin of Faculty of Pharmacy, Cairo University*. 2013;**51**:229
- [41] Makarieva TN, Tabakmaher KM, Guzii AG, Denisenko VA, et al. Monanchocidins B-E: Polycyclic guanidine alkaloids with potent antileukemic activities from the sponge *Monanchora pulchra*. *Journal of Natural Products*. 2011;**74**:1952
- [42] Sun YT, Lin B, Li SG, Liu M, et al. New bromopyrrole alkaloids from the marine sponge *Agelas* sp. *Tetrahedron*. 2017;**73**:2786-2792
- [43] Nguyen HT, Chau VM, Tran TH, Phan VK, et al. C29 sterols with a cyclopropane ring at C-25 and 26 from the Vietnamese marine sponge *Ianthella* sp. and their anticancer properties. *Bioorganic & Medicinal Chemistry Letters*. 2009;**19**:4584-4585
- [44] Ushiyama S, Umaoka H, Kato H, Suwa Y, et al. Manadosterols A and B, sulfonated sterol dimers inhibiting the Ubc13-Uev1A interaction, isolated from the marine sponge *Lissodendryx fibrosa*. *Journal of Natural Products*. 2012;**75**:1495
- [45] Harinantenaina L, Brodie PJ, Maharavo J, Bakary G, et al. Antiproliferative homoscalarane sesterterpenes from two Madagascan sponges. *Bioorganic & Medicinal Chemistry*. 2013;**21**:2912-2917
- [46] Rateb ME, Houssen WE, Schumacher M, Harrison WTA, et al. Bioactive diterpene derivatives from the marine sponge *Spongionella* sp. *Journal of Natural Products*. 2009;**72**:1471-1476
- [47] Wang CY, Wang BG, Wiryowidagdo S, Wray V, et al. Melophlins C-O, thirteen novel tetraric acids from the marine sponge *Melophlus sarassinorum*. *Journal of Natural Products*. 2003;**66**(1):51-56
- [48] Hahn D, Won DH, Mun B, Kim H, et al. Cytotoxic scalarane sesterterpenes from a Korean marine sponge *Psammocinia* sp. *Bioorganic & Medicinal Chemistry Letters*. 2013;**23**(8):2336-2339
- [49] Lamoral-Theys D, Fattorusso E, Mangoni A, Perinu C, et al. Evaluation of the antiproliferative activity of diterpene Isonitriles from the Sponge *Pseudoaxinella flava* in apoptosis-sensitive and apoptosis-resistant cancer cell lines. *Journal of Natural Products*. 2011;**74**(10):2299-2303

- [50] Pettit GR, Tang Y, Zhang Q, Bourne GT, et al. Isolation and structures of axistatins 1-3 from the Republic of Palau marine sponge *Agelas axifera* Hentschel(1). *Journal of Natural Products*. 2013;**76**(3):420-422
- [51] Ovenden SPB, Nielson JL, Liptrot CH, Willis RH, et al. Metachromins U–W: Cytotoxic merosesquiterpenoids from an Australian specimen of the sponge *Thorecta reticulata*. *Journal of Natural Products*. 2011;**73**(3):467-471
- [52] Bokesch HR, Pannell LK, McKee TC, Boyd MR. Coscinamides A, B and C, three new bis indole alkaloids from the marine sponge *Coscinoderma* sp. *Tetrahedron Letters*. 2000;**41**:6305-6308
- [53] Kim CK, Song IH, Park HY, Lee YJ, et al. Suvanine sesterterpenes and deacyl irciniasulfonic acids from a tropical *Coscinoderma* sp. sponge. *Journal of Natural Products*. 2014;**77**(6):1396-1403
- [54] Oku N, Takada K, Fuller RW, Wilson JA, et al. Isolation, structural elucidation, and absolute stereochemistry of enigmazole A, a cytotoxic phosphomacrolide from the Papua New Guinea marine sponge *Cinachyrella enigmatica*. *Journal of the American Chemical Society*. 2010;**132**(30):10278-10285
- [55] Gala F, D'Auria MV, De Marino S, Sepe V, et al. Jaspamides M–P: New tryptophan modified jaspamide derivatives from the sponge *Jaspis splendens*. *Tetrahedron*. 2009;**65**:51-56
- [56] Singh AJ, Razzak M, Teesdale-Spittle P, Gaitanos TN, et al. Structure-activity studies of the pelorusides: New congeners and semi-synthetic analogues. *Organic & Biomolecular Chemistry*. 2011;**9**(12):4456-4466
- [57] Sorres J, Martin MT, Petek S, Levaique H, et al. Pipestelides A-C: Cyclodepsipeptides from the Pacific marine sponge *Pipestela candelabra*. *Journal of Natural Products*. 2012;**75**(4):759-763
- [58] Zhang J, Tang X, Li J, Li P, et al. Cytotoxic polyketide derivatives from the South China sea sponge *Plakortis simplex*. *Journal of Natural Products*. 2013;**76**(4):600-606
- [59] Jiménez-Romero C, Ortiz I, Vicente J, Vera B, Rodríguez AD, et al. Bioactive cycloperoxides isolated from the Puerto Rican sponge *Plakortis halichondrioides*. *Journal of Natural Products*. 2010;**73**(10):1694-1700
- [60] Pelay-Gimeno M, García-Ramos Y, Martin MJ, Jan S, et al. The first total synthesis of the cyclodepsipeptide pipecolidepsin A. *Nature Communications*. 2013;**4**:2352
- [61] Zampella A, Sepe V, Luciano P, Bellotta F, et al. Homophymine A, an anti-HIV cyclodepsipeptide from the sponge *Homophymia* sp. *The Journal of Organic Chemistry*. 2008;**73**(14):5319-5327
- [62] Tran TD, Pham NB, Fechner G, Zencak D, et al. Cytotoxic cyclic depsipeptides from the Australian marine sponge *Neamphius huxleyi*. *Journal of Natural Products*. 2012;**75**(12):2200-2208

- [63] Williams DE, Yu K, Behrisch HW, Van Soest R, Andersen RJ. Rolloamides A and B, cytotoxic cyclic heptapeptides isolated from the Caribbean marine sponge *Eurypon laughlini*. *Journal of Natural Products*. 2009;**72**(7):1253-1257
- [64] Wang X, Morinaka BI, Molinski TF. Structures and solution conformational dynamics of stylissamides G and H from the Bahamian sponge *Stylissa caribica*. *Journal of Natural Products*. 2014;**77**(3):625-630
- [65] Coello L, Reyes F, Martín MJ, Cuevas C, Fernández R. Isolation and structures of pipercolidepsins A and B, cytotoxic cyclic depsipeptides from the Madagascan sponge *Homophymia lamellosa*. *Journal of Natural Products*. 2014;**77**(2):298-303
- [66] Regalado EL, Jimenez-Romero C, Genta-Jouve G, Tasdemir D, et al. Acanthifoliosides, minor steroidal saponins from the Caribbean sponge *Pandaros acanthifolium*. *Tetrahedron*. 2011;**67**:1011-1018
- [67] Ye J, Zhou F, Al-Kareef AMQ, Wang H. Anticancer agents from marine sponges. *Journal of Asian Natural Products Research*. 2015;**17**:64-88
- [68] Jiao W-H, Huang X-J, Yang J-S, Yang F, et al. Dysidavarones A–D, new sesquiterpene quinones from the marine sponge *Dysidea avara*. *Organic Letters*. 2012;**14**(1):202-205
- [69] Daletos G, de Voogd NJ, Müller WE, Wray V, et al. Cytotoxic and protein kinase inhibiting nakijiquinones and nakijiquinolins from the sponge *Dactylospongia metachromia*. *Journal of Natural Products*. 2014;**77**(2):218-226
- [70] Jiao WH, Xu TT, Yu HB, Chen GD, et al. Dysideanones A-C, unusual sesquiterpene quinones from the South China Sea sponge *Dysidea avara*. *Journal of Natural Products*. 2014;**77**(2):346-350
- [71] Shaala LA, Bamane FH, Badr JM, Youssef DT. Brominated arginine-derived alkaloids from the red sea sponge *Suberea mollis*. *Journal of Natural Products*. 2011;**74**(6):1517-1520
- [72] Williams A, Bax NJ, Kloser RJ, Althaus F, et al. Australia's deep-water reserve network: implications of false homogeneity for classifying abiotic surrogates of biodiversity. *ICES Journal of Marine Science*. 2009;**66**:214-224
- [73] Hwang IH, Oh J, Kochanowska-Karamyan A, et al. A novel natural phenyl alkene with cytotoxic activity. *Tetrahedron Letters*. 2013;**54**(29):3872-3876
- [74] Farokhi F, Wielgosz-Collin G, Robic A, Debitus C, et al. Antiproliferative activity against human non-small cell lung cancer of two O-alkyl-diglycosylglycerols from the marine sponges *Myrmekioderma dendyi* and *Trikentrion laeve*. *European Journal of Medicinal Chemistry*. 2012;**49**:406-410
- [75] Lee Y-J, Han S, Lee H-S, Kang JS, et al. Cytotoxic psammaphysin analogues from a *Suberea* sp. marine sponge and the role of the spirooxepinisoaxoline in their activity. *Journal of Natural Products*. 2013;**76**(9):1731-1736
- [76] Kobayashi M. In search for biologically active substances from marine sponges. In: Fusetani N, editor. *Drugs from the Sea*. Basel, Switzerland: Karger; 2000. pp. 46-58

- [77] Amade PG, Chariou G, Baby C, Vacelet J. Antimicrobial activity of marine sponges of Mediterranean. *Sea. Marine Biology*. 1987;**94**:271-275
- [78] McCaffrey EJ, Endeau R. Antimicrobial activity of tropical and subtropical sponges. *Marine Biology*. 1985;**89**:1-8
- [79] Mayer AM, Hamann MT. *Marine pharmacology in 2000: Marine compounds with antibacterial, anticoagulant, antifungal, anti-inflammatory, antimalarial, antiplatelet, antituberculosis, and antiviral activities; affecting the cardiovascular, immune, and nervous systems and other miscellaneous mechanisms of action*. *Marine Biotechnology* New York. 2004;**6**(1):37-52
- [80] Sipkema D, Franssen MC, Osinga R, Tramper J, Wijffels RH. Marine sponges as pharmacy. *Marine Biotechnology* New York. 2005;**7**(3):142-162
- [81] Torres YR, Berlink RGS, Nascimento GGF, Fortier SC, et al. Antibacterial activity against resistant bacteria and cytotoxicity of four alkaloid toxins isolated from the marine sponge. *Arenosclera brasiliensis*. *Toxicon*. 2002;**40**(7):885-891
- [82] De Silva ED, Scheuer PJ. Manoalide, an antibiotic sesterpenoid from the marine sponge *Luffariella variabilis*. *Tetrahedron Letters*. 1980;**21**:1611-1614
- [83] Urban S, Leone Pde A, Carroll AR, Fechner GA, et al. Axinellamines A–D, novel imidazo–azolo–imidazole alkaloids from the Australian marine sponge *Axinella* sp. *The Journal of Organic Chemistry*. 1999;**64**(3):731-735
- [84] Rao KV, Kasanah N, Wahyuono S, Tekwani BL, et al. Three new manzamine alkaloids from a common Indonesian sponge and their activity against infectious and tropical parasitic diseases. *Journal of Natural Products*. 2004;**67**(8):1314-1318
- [85] Torres YR, Berlinck RG, Magalhães A, Schefer AB, Ferreira AG, et al. Arenosclerins A–C and haliclonyclamine E, new tetracyclic alkaloids from a Brazilian endemic Haplosclerid sponge *Arenosclera brasiliensis*. *Journal of Natural Products*. 2000;**63**(8):1098-1105
- [86] Oh KB, Mar W, Kim S, Kim JY, et al. Antimicrobial activity and cytotoxicity of bis(indole) alkaloids from the sponge *Spongosorites* sp. *Biological & Pharmaceutical Bulletin*. 2006;**29**(3):570-573
- [87] Pettit GR, Knight JC, Collins JC, Herald DL, et al. Antineoplastic agents 430. Isolation and structure of cribrostatis 3, 4, and 5 from the Republic of Maldives *Cribrochalina* species. *The Journal of Natural Products*. 2000;**63**:793-798
- [88] Pettit GR, Collins JC, Knight JC, Herald DL, et al. Antineoplastic agents 485. Isolation and structure of cribrostatin 6, a dark blue cancer cell growth inhibitor from the marine sponge *Cribrochalina* sp. *Journal of Natural Products*. 2003;**66**:544-547
- [89] Carroll AR, Ngo A, Quinn RJ, Redburn J, Hooper JN. Petrosamine B, an inhibitor of the *Helicobacter pylori* enzyme aspartyl semialdehyde dehydrogenase from the Australian sponge *Oceanapia* sp. *Journal of Natural Products*. 2005;**68**(5):804-806

- [90] Ford J, Capon RJ. Discorhabdin R: A new antibacterial pyrroloiminoquinone from two latrunculiid marine sponges, *Latrunculia* sp. and *Negombata* sp. *Journal of Natural Products*. 2000;**63**(11):1527-1528
- [91] Gupta L, Talwar A, Chauhan PMS. Bis and tris indole alkaloids from marine organisms: New leads for drug discovery. *Current Medicinal Chemistry*. 2007;**14**:1789-1803
- [92] Oliveira JHHL, Grube A, Köck M, Berlinck RGS, et al. Ingenamine G and cyclostelletamines G–K from the new Brazilian species of marine sponge *Pachychalina* sp. *Journal of Natural Products*. 2004;**67**:1685-1689
- [93] Oliveira JHHL, Selegim MHR, Timm C, Grube A, et al. Antimicrobial and antimycobacterial activity of cyclostelletamine alkaloids from sponge *Pachychalina* sp. *Marine Drugs*. 2006;**4**:1-8
- [94] Vik A, Hedner E, Charnock C, Samuelsen O, et al. (+)-Agelasine D: Improved synthesis and evaluation of antibacterial and cytotoxic activities. *Journal of Natural Products*. 2006;**69**(3):381-386
- [95] Rubio BK, Soest RW, Crews P. Extending the record of meroditerpenes from *Cacospongia* marine sponges. *Journal of Natural Products*. 2007;**70**(4):628-631
- [96] Gul FA, Jaggi BL, Krishnan GV. Auditor independence: Evidence on the joint effects of auditor tenure and nonaudit fees. *Auditing: A Journal of Practice & Theory*. 2007;**26**(2):117-142
- [97] Matsunaga S, Okada Y, Fusetani N, van Soest RWM. An antimicrobial C<sub>14</sub> acetylenic acid from a marine sponge *Oceanapia* species. *Journal of Natural Products*. 2000;**63**(5):690-691
- [98] Linington RG, Robertson M, Gauthier A, Finlay B, et al. Caminosides B–D, antimicrobial glycolipids isolated from the marine sponge *Caminus sphaeroconia*. *Journal of Natural Products*. 2006;**69**(2):173-177
- [99] Grube A, Assmann M, Lichte E, Sasse F, et al. Bioactive metabolites from the Caribbean Sponge *Aka coralliphagum*. *Journal of Natural Products*. 2007;**70**(4):504-509
- [100] Moura RM, Queiroz AF, Fook JM, Dias AS, et al. CvL, a lectin from the marine sponge *Cliona varians*: Isolation, characterization and its effects on pathogenic bacteria and *Leishmania* promastigotes. *Comparative Biochemistry and Physiology. Part A, Molecular & Integrative Physiology*. 2006;**145**(4):517-523
- [101] El Sayed KA, Youssef DT, Marchetti D. Bioactive natural and semisynthetic latrunculins. *Journal of Natural Products*. 2006;**69**(2):219-223
- [102] Nicolaou KC, Hughes R, Pfefferkorn JA, Barluenga S, Roecker AJ. Combinatorial synthesis through disulfide exchange: Discovery of potent Psammaphin A type antibacterial agents active against methicillin-resistant *Staphylococcus aureus* (MRSA). *Chemistry – A European Journal*. 2001;**7**(19):4280-4295
- [103] Donia M, Hamann M. Marine natural products and their potential applications as anti-infective agents. *The Lancet Infectious Diseases*. 2003;**3**:338-348

- [104] Blunt JW, Copp BR, Munro MH, Northcote PT, Prinsep MR. Marine natural products. *Natural Product Reports*. 2004;**21**:1-49
- [105] Bergmann W, Feeney RJ. Contribution to the study of marine products of sponges. *The Journal of Organic Chemistry*. 1951;**16**:981-987
- [106] De Clercq E. New anti-HIV agents and targets. *Medicinal Research Reviews*. 2002;**22**:531-565
- [107] Collum LM, O'Connor M, Logan P. Comparison of the efficacy and toxicity of acyclovir and of adenine arabinoside when combined with dilute betamethasone in herpetic disciform keratitis: Preliminary results of a double-blind trial. *Transactions of the Ophthalmological Societies of the United Kingdom*. 1983;**103**:597-599
- [108] Whitley RJ, Gnann JW Jr, Hinthorn D, Liu C, et al. The NIAID Collaborative Antiviral Study Group. Disseminated herpes zoster in the immunocompromised host: A comparative trial of acyclovir and vidarabine. *The Journal of Infectious Diseases*. 1992;**165**:450-455
- [109] Kamiyama T, Kurokawa M, Shiraki K. Characterization of the DNA polymerase gene of varicellazoster viruses resistant to acyclovir. *The Journal of General Virology*. 2001;**82**:2761-2765
- [110] Souza TM, Abrantes JL, Epifanio R, Leite-Fontes CF, Frugulhetti IC. The alkaloid 4-methylaaptamine isolated from the sponge *Aaptos aaptos* impairs Herpes simplex virus type 1 penetration and immediate-early protein synthesis. *Planta Medica*. 2007;**73**(3):200-205
- [111] Cutignano A, Bifulco G, Bruno I, Casapullo A, et al. Dragmacidin F: A new antiviral bromoindole alkaloid from the Mediterranean sponge *Halicortex* spp. *Tetrahedron*. 2000;**56**:3743-3748
- [112] Yousaf M, Hammond NL, Peng J, Wahyuono S, et al. New manzamine alkaloids from an Indo-Pacific sponge. Pharmacokinetics, oral availability, and the significant activity of several manzamines against HIV-I, AIDS opportunistic infections, and inflammatory diseases. *Journal of Medicinal Chemistry*. 2004;**47**(14):3512-3517
- [113] Perry WL, Hustad CM, Swing DA, O'Sullivan TN, et al. The itchy locus encodes a novel ubiquitin protein ligase that is disrupted in a18H mice. *Nature Genetics*. 1998;**18**(2):143-146
- [114] Ford PW, Gustafson KR, McKee TC, Shigematsu N, et al. Papuamides A-D, HIV-inhibitory and cytotoxic depsipeptides from the Sponges *Theonella mirabilis* and *Theonella swinhoei* collected in Papua New Guinea. *Journal of the American Chemical Society*. 1999;**121**(25):5899-5909
- [115] Rashid MA, Gustafson KR, Cartner LK, Shigematsu N, et al. Microspinosamide, a new HIV-inhibitory cyclic depsipeptide from the marine sponge *Sidonops microspinosa*. *Journal of Natural Products*. 2001;**64**(1):117-121
- [116] Qureshi A, Faulkner DJ. Haplosamates A and B: New steroidal sulfamate esters from two haplosclerid sponges. *Tetrahedron*. 1999;**55**(28):8323-8330



- [117] Muller WEG, Sobel C, Diehl-Seifert B, Maidhof A, Schroder HC. Influence of the anti-leukemic and anti-human immunodeficiency virus agent avarol on selected immune responses *in vitro* and *in vivo*. *Biochemical Pharmacology*. 1987;**36**:1489-1494
- [118] Perry NB, Blunt JW, Munro MHG, Thompson AM. Antiviral and antitumor agents from a New Zealand sponge, *Mycale* sp. *The Journal of Organic Chemistry*. 1990;**55**:223-227
- [119] Mehta A, Zitzmann N, Rudd PM, et al. Alpha-glucosidase inhibitors as potential broad based anti-viral agents. *FEBS Letters*. 1998;**430**:17-22
- [120] Kelve M, Kuuskalu A, Lopp A, Reintamm T. Sponge (2',5')oligoadenylate synthetase activity in the whole sponge organism and in a primary cell culture. *Journal of Biotechnology*. 2003;**100**:177-180
- [121] Wellington KD, Cambie RC, Rutledge PS, Bergquist PR. Chemistry of sponges. 19. Novel bioactive metabolites from *Hamigera tarangaensis*. *Journal of Natural Products*. 2000;**63**:79-85
- [122] Sun HH, Cross SS, Gunasekera M, Koehn FE. Weinbersterol disulfates A and B, antiviral steroid sulfates from the sponge *Petrosia weinbergi*. *Tetrahedron*. 1991;**47**:1185-1190
- [123] García-Ruiz JC, Amutio E, Pontón J. Invasive fungal infection in immunocompromised patients. *Revista Iberoamericana de Micología*. 2004;**21**:55-62
- [124] Walsh TJ, Groll A, Hiemenz J, Fleming R, et al. Infections due to emerging and uncommon medically important fungal pathogens. *Clinical Microbiology and Infection*. 2004;**10(S1)**:48-66
- [125] Giusiano G, Mangiaterra M, Rojas F, Gámez V. Yeasts species distribution in Neonatal Intensive Care Units in northeast Argentina. *Mycoses*. 2004;**47**:300-303
- [126] Giusiano G, Mangiaterra M, Rojas F, Gámez V. Azole resistance in neonatal intensive care units in Argentina. *Journal of Chemotherapy*. 2005;**17**:347-350
- [127] Rashid MA, Gustafson KR, Boswell JL, Boyd MR. Haligramides A and B, two new cytotoxic hexapeptides from the marine sponge *Haliclona nigra*. *Journal of Natural Products*. 2000;**63**:956-959
- [128] Dunbar DC, Rimoldi JM, Clark AM, Kelly M, Hamann MT. Anti-cryptococcal and nitric oxide synthase inhibitory imidazole alkaloids from the Calcareous sponge *Leucettacif chagosensis*. *Tetrahedron*. 2000;**56**:8795-8798
- [129] Kon Y, Kubota T, Shibasaki A, Gono T, Kobayashi J. Ceratinadins A–C, new bromotyrosine alkaloids from an Okinawan marine sponge *Pseudoceratina* sp. *Bioorganic & Medicinal Chemistry Letters*. 2010;**20**:4569-4572
- [130] Stout EP, Yu LC, Molinski TF. Antifungal diterpene alkaloids from the Caribbean sponge *Agelas citrina*: Unified configurational assignments of agelasidines and agelasines. *European Journal of Organic Chemistry*. 2012;**2012**:5131-5135
- [131] Arevabini C, Crivelenti YD, de Abreu MH, Bitencourt TA, Santos MF, et al. Antifungal activity of metabolites from the marine sponges *Amphimedon* sp. and *Monanchora*

- arbuscula* against *Aspergillus flavus* strains isolated from peanuts (*Arachis hypogaea*). Natural Product Communications. 2014;**9**:33-36
- [132] Ettinger-Epstein P, Tapiolas DM, Motti CA, Wright AD, Battershill CN, de Nys R. Production of manoalide and its analogues by the sponge *Luffariella variabilis* is hard-wired. Marine Biotechnology. 2008;**10**(1):64-74
- [133] Zhang X, Jacob MR, Rao RR, Wang YH, et al. Antifungal cyclic peptides from the marine sponge. Research and Reports in Medicinal Chemistry. 2012;**2**:7-14
- [134] Xu WH, Ding Y, Jacob MR, Agarwal AK, Clark AM, Ferreira D, et al. Puupehanol, a sesquiterpene-dihydroquinone derivative from the marine sponge *Hyrtios* sp. Bioorganic & Medicinal Chemistry Letters. 2009;**19**:6140-6143
- [135] Boonlarppradab C, Faulkner DJ. Eurysterols A and B, cytotoxic and antifungal steroidal sulfates from a marine sponge of the Genus *Euryspongia*. Journal of Natural Products. 2007;**77**(4):818-823
- [136] Digirolamo JA, Li XC, Jacob MR, Clark AM, Ferreira D. Reversal of fluconazole resistance by sulfated sterols from the marine sponge *Topsentia* sp. Journal of Natural Products. 2009;**72**:1524-1528
- [137] Gunasekera SP, Pomponi SA, McCarthy PJ. Discobahamins A and B, new peptides from the Bahamian deep water marine sponge *Discodermia* sp. Journal of Natural Products. 1994;**57**(1):79-83
- [138] Scott VR, Boehme R, Matthews TR. New class of antifungal agents: Jasplakinolide, a cyclodepsipeptide from the marine sponge, *Jaspis* species. Antimicrobial Agents and Chemotherapy. 1988;**32**(8):1154-1157
- [139] Sepe V, D'Osri R, Borbone N, D'Auria MV, et al. Towards new ligands of nuclear receptors. Discovery of malaitasterol A, and unique bis-secosterol from marine sponge *Theonella swinhoei*. Tetrahedron. 2006;**62**:833-840
- [140] Youssef DT, Shaala LA, Mohamed GA, Badr JM, et al. Theonellamide G, a potent antifungal and cytotoxic bicyclic glycopeptide from the Red Sea marine sponge *Theonella swinhoei*. Marine Drugs. 2014;**12**:1911-1923
- [141] Matsunaga S, Fusetani N, Hashimoto K, Walchli M. Theonellamide F. A novel antifungal bicyclic peptide from a marine sponge *Theonella* sp. Journal of the American Chemical Society. 1989;**111**:2582-2588
- [142] Vik A, Hedner E, Charnock C, Tangen LW, et al. Antimicrobial and cytotoxic activity of agelasine and agelasimine analogs. Bioorganic & Medicinal Chemistry. 2007;**15**(12):4016-4037
- [143] Jamison MT, Molinski TF. Antipodal crambescin A2 homologues from the marine sponge *Pseudaxinella reticulata* antifungal structure-activity relationships. Journal of Natural Products. 2015;**78**:557-561
- [144] Nishimura S, Arita Y, Honda M, Iwamoto K, et al. Marine antifungal theonellamides target 3beta-hydroxysterol to activate Rho1 signaling. Nature Chemical Biology. 2010;**6**:519-526

- [145] Kumar R, Subramani R, Feussner KD, Aalbersberg W. Aurantoside K, a new antifungal tetramic acid glycoside from a Fijian marine sponge of the genus *Melophlus*. *Marine Drugs*. 2012;**10**:200-208
- [146] Rudi A, Kashman Y. Three new cytotoxic metabolites from the marine sponge *Plakortis halichondrioides*. *Journal of Natural Products*. 1993;**56**:1827-1830
- [147] El-Amraoui B, Biard JF, Fassouane A. Haliscosamine: A new antifungal sphingosine derivative from the Moroccan marine sponge *Haliclona viscosa*. *Springer Plus*. 2013;**2**:252
- [148] Sionov E, Roth D, Sandovsky-Losica H, Kashman Y, et al. Antifungal effect and possible mode of activity of a compound from the marine sponge *Dysidea herbacea*. *The Journal of Infection*. 2005;**50**:453-460
- [149] Chen Y, McCarthy PJ, Harmody DK, Schimoler-O'Rourke R, et al. New bioactive peroxides from marine sponges of the family plakiniidae. *Journal of Natural Products*. 2002;**65**:1509-1512
- [150] Vuong D, Capon RJ, Lacey E, Gill JH, et al. Onnamide F: A new nematocide from a southern Australian marine sponge, *Trachycladus laevispirulifer*. *Journal of Natural Products*. 2001;**64**:640-642
- [151] Edrada RA, Ebel R, Supriyono A, Wray V, et al. Swinhoeiamide A, a new highly active calyculin derivative from the marine sponge, *Theonella swinhoei*. *Journal of Natural Products*. 2002;**65**:1168-1172
- [152] Wright AD, McCluskey A, Robertson MJ, MacGregor KA, et al. Anti-malarial, anti-algal, anti-tubercular, anti-bacterial, anti-photosynthetic, and anti-fouling activity of diterpene and diterpene isonitriles from the tropical marine sponge *Cymbastela Hooperi*. *Organic & Biomolecular Chemistry*. 2011;**9**:400-407
- [153] Chen Y, Killday KB, McCarthy PJ, Schimoler R, et al. Three new peroxides from the sponge *Plakinastrella* species. *Journal of Natural Products*. 2001;**64**:262-264
- [154] Rifai S, Fassouane A, Kijjoo A, VanSoest R. Antimicrobial activity of Untenospongins B, a metabolite from the marine sponge *Hippospongia communis* collected from the Atlantic Coast of Morocco. *Marine Drugs*. 2004;**2**:147-153
- [155] Piao SJ, Song YL, Jiao WH, Yang F, et al. Hippolachnin A, a new antifungal polyketide from the South China sea sponge *Hippospongia lachne*. *Organic Letters*. 2013;**15**:3526-3529
- [156] Herecia F, Ubeda A, Ferrandiz ML, Terencio MC, et al. Anti-inflammatory activity in mice of extracts from Mediterranean marine invertebrates. *Life Sciences*. 1998;**62**:PL115
- [157] Sturm C, Paper DH, Franz G. Screening for immune response modifiers from marine origin. *Pharmaceutical and Pharmacological Letters*. 1999;**9**:76
- [158] Jiang YH, Ryu S-H, Ahn E-Y, You S, et al. Antioxidant activity of (8E,13Z,20Z)-strobilinin/(7E,13Z,20Z)-felixinin from a marine sponge *Psammocinia* sp. *Natural Product Sciences*. 2004;**10**(6):272-276

- [159] Keyzers RA, Northcote PT, Zubkov OA. Novel anti-inflammatory spongian diterpenes from the New Zealand marine sponge *Chelonaplysilla violacea*. *European Journal of Organic Chemistry*. 2004;(2):419-425
- [160] Posadas I, Terencio MC, De Rosa S, Paya M. Cavernolide: A new inhibitor of human sPLA2 sharing unusual chemical features. *Life Sciences*. 2000;**67**:3007
- [161] Lucas R, Casapullo A, Ciasullo L, Gomez-Paloma L, Payá M. Cycloamphilectenes, a new type of potent marine diterpenes: Inhibition of nitric oxide production in murine macrophages. *Life Sciences*. 2003;**72**(22):2543-2552
- [162] Cichewicz RH, Kenyon VA, Whitman S, Morales NM, et al. Redox inactivation of human 15-lipoxygenase by marine-derived meroditerpenes and synthetic chromanes: Archetypes for a unique class of selective and recyclable inhibitors. *Journal of the American Chemical Society*. 2004;**126**:14910-14920
- [163] Keyzers C, Wicker B, Gazzola V, Anton JL, et al. A touching sight: SII/PV activation during the observation and experience of touch. *Neuron*. 2004;**42**(2):335-346
- [164] Ferrandiz ML, Sanz MJ, Bustos G, Paya M, et al. Avarol and avarone, two new anti-inflammatory agents of marine origin. *European Journal of Pharmacology*. 1994;**253**:75-82
- [165] Muller WEG, Bohm M, Batel R, De Rosa S, et al. Application of cell culture for the production of bioactive compounds from sponges: Synthesis of avarol by primmorphs from *Dysidea avara*. *Journal of Natural Products*. 2000;**63**:1077-1081
- [166] Posadas I, Terencio MC, Giannini C, D'Auria MV, Paya M. Dysidotronic acid, a new sesquiterpenoid, inhibits cytokine production and the expression of nitric oxide synthase. *European Journal of Pharmacology*. 2001;**415**:285-292
- [167] Gunasekera SP, Isbrucker RA, Longley RF, Wright AE, et al. Plakolide A, a new gamma-lactone from the marine sponge *Plakortis* sp. *Journal of Natural Products*. 2004;**67**:110
- [168] Lu PH, Chueh SC, Kung FL, Pan SL, et al. Ilimaquinone, a marine sponge metabolite, displays anticancer activity via GADD153-mediated pathway. *European Journal of Pharmacology*. 2007;**556**:45-54
- [169] Glase KB, Lock YW. Regulation of prostaglandin H synthase 2 expression in human monocytes by the marine natural products manoalide and scalaradial. Novel effects independent of inhibition of lipid mediator production. *Biochemical Pharmacology*. 1995;**50**:913-922
- [170] Pastor PG, De Rosa S, De Giulio A, Paya M, Alcaraz MJ. Modulation of acute and chronic inflammatory processes by cacospongionolide B, a novel inhibitor of human synovial phospholipase A2. *British Journal of Pharmacology*. 1999;**126**:301-311
- [171] Giannini C, Debitus C, Lucas R, Ubeda A, et al. New sesquiterpene derivatives from the sponge *Dysidea* species with a selective inhibitor profile against human phospholipase A<sub>2</sub> and other leukocyte functions. *Journal of Natural Products*. 2001;**64**:612-615

- [172] Miyaoka H, Yamanishi M, Mitome H. PLA2 inhibitory activity of marine sesterterpenoids cladocorans, their diastereomers and analogues. *Chemical & Pharmaceutical Bulletin*. 2006;**54**:268-270
- [173] Dal-Piaz F, Casapullo A, Randazzo A, Riccio R, Pucci P, et al. Molecular basis of phospholipase A2 inhibition by petrosaspongiolide M. *Chembiochem*. 2002;**3**:664-671
- [174] Garcia P, Randazzo A, Gomez-Paloma L, Alcaraz MJ, Paya M. Effects of petrosaspongiolide M, a novel phospholipase A2 inhibitor, on acute and chronic inflammation. *The Journal of Pharmacology and Experimental Therapeutics*. 1999;**289**:166-172
- [175] Barnette MS, Rush J, Marshall LA, Foley JJ, et al. Effects of scalaradial, a novel inhibitor of 14 kDa phospholipase A2, on human neutrophil function. *Biochemical Pharmacology*. 1994;**47**:1661-1667
- [176] Fontana A, Mollo E, Ortea J, Cavagnin M, Cimino G. Scalarane and homoscalarane compounds from the nudibranchs *Glossodoris sedna* and *Glossodoris dalli*: Chemical and biological properties. *Journal of Natural Products*. 2000;**63**:527-530
- [177] Amagata T, Whitman S, Jonson TA, Stessman CC, et al. Exploring sponge-derived terpenoids for their potency and selectivity against 12-human, 15-human, and 15-soybean lipoxygenases. *Journal of Natural Products*. 2003;**66**:230-235
- [178] D'acquisto F, Lanzotti V, Carnuccio R. Cyclolinteinone, a sesterterpene from sponge *Cacospongia linteiformis*, prevents inducible nitric oxide synthase and inducible cyclooxygenase protein expression by blocking nuclear factor-kappa B activation in J774 macrophages. *The Biochemical Journal*. 2000;**346**(3):793-798
- [179] Fukami A, Ikeda Y, Kondo S, Naganawa H, et al. Akaterpin, a novel bioactive triterpene from the marine sponge *Callyspongia* sp. *Tetrahedron Letters*. 1997;**38**:1201-1202
- [180] Keyzers RA, Norticote PT, Webb V. Clathriol, a novel polyoxygenated 14 $\beta$  steroid isolated from the New Zealand marine sponge *Clathria lissosclera*. *Journal of Natural Products*. 2002;**65**:598-600
- [181] Mandeau A, Debitus C, Ariès M-F, David B. Isolation and absolute configuration of new bioactive marine steroids from *Euryspongia* n. sp. *Steroids*. 2005;**70**:873-878
- [182] Sharma V, Lansdell TA, Jin G, Tepe JJ. Inhibition of cytokine production by hymenialdisine derivatives. *Journal of Medicinal Chemistry*. 2004;**47**(14):3700-3703
- [183] Tasdemir D, Mallon R, Greenstein M, Feldberg LR, et al. Aldisine alkaloids from the Philippine sponge *Stylissa massa* are potent inhibitors of mitogen-activated protein kinase kinase-1 (MEK-1). *Journal of Medicinal Chemistry*. 2002;**45**:529-532
- [184] Buchanan MS, Carroll AR, Addepalli R, Avery VM, Hooper JN, Quinn RJ. Natural products, stylissadines A and B, specific antagonists of the P2X7 receptor, an important inflammatory target. *The Journal of Organic Chemistry*. 2007;**72**:2309-2317

- [185] Sakamoto H, Furukawa K-I, Matsunaga K, Nakamura H, Ohizumi Y. Xestoquinone activates skeletal muscle actomyosin ATPase by modification of the specific sulfhydryl group in the myosin head probably distinct from sulfhydryl groups SH1 and SH2. *Biochemistry*. 1995;**34**:12570-12575
- [186] Nakamura M, Kakuda T, Oba Y, Ojika M, Nakamura H. Synthesis of biotinylated xestoquinone that retains inhibitory activity against  $\text{Ca}^{2+}$  ATPase of skeletal muscle myosin. *Bioorganic & Medicinal Chemistry*. 2003;**11**:3077-3082
- [187] Alvi KA, Rodriguez J, Diaz MC, Moretti R, et al. Protein tyrosine kinase inhibitory properties of planar polycyclics obtained from the marine sponge *Xestospongia cf. caribonaria* and from total synthesis. *The Journal of Organic Chemistry*. 1993;**58**:4871-4880
- [188] Laurent D, Jullian V, Parenty A, Knibiehler M, et al. Antiplasmodial marine natural products in the perspective of current chemotherapy and prevention of malaria. A review. *Marine Biotechnology*. 2006;**14**:433-477
- [189] Oku N, Nagai K, Shindoh N, Terada Y, et al. Three new cyclostelletamines, which inhibit histone deacetylase, from a marine sponge of the genus *Xestospongia*. *Bioorganic & Medicinal Chemistry Letters*. 2004;**14**:2617-2620
- [190] Bourguet-Kondracki ML, Rakotoarisoa MT, Martin MT, Guyot M. Bioactive bromoacetylenes from marine sponge *Xestospongia testudinaria*. *Tetrahedron Letters*. 1992;**33**:225-226
- [191] Roll DM, Scheuer PJ, Matsumoto GK, Clardy J. Halenaquinone, a pentacyclic polyketide from a marine sponge. *Journal of the American Chemical Society*. 1983;**105**:6177-6178
- [192] Nakamura H, Kobayashi J, Kobayashi M, et al. Xestoquinone, a novel cardiogenic marine natural product isolated from the Okinawan sea sponge *Xestospongia sapra*. *Chemistry Letters*. 1985;**(6)**:713-716
- [193] Kobayashi M, Shimizu N, Kitagawa I, Kyogoku Y, et al. Absolute stereostructures of halenaquinol and halenaquinol sulfate, pentacyclic hydroquinones from the okinawan marine sponge *xestospongia sapra*, as determined by theoretical calculation of CD spectra. *Tetrahedron Letters*. 1985;**26**:3833-3836
- [194] Concepcion GP, Foderaro TA, Eldredge GS, Lobkovsky E, et al. Topoisomerase II-mediated DNA cleavage by adocia- and xestoquinones from the Philippine sponge *Xestospongia* sp. *Journal of Medicinal Chemistry*. 1995;**38**:4503-4507
- [195] Cao S, Foster C, Brisson M, Lazo JS, KDG. Halenaquinone and xestoquinone derivatives, inhibitors of Cdc25B phosphatase from a *Xestospongia* sp. *Bioorganic & Medicinal Chemistry*. 2005;**13**:999-1003
- [196] Gunasekera SP, Cranick S, Longley RE. Immunosuppressive compounds from a deep water marine sponge, *Agelas flabelli*. *Journal of Natural Products*. 1989;**52**:757-761
- [197] Chairman K, Jeyamala M, Sankar S, Murugan A, Singh R. Immunomodulating properties of bioactive compounds present in *Aurora globostellata*. *International Journal of Marine Science*. 2013;**3**:151-157

- [198] Schumacher M, Cerella C, Eifes S, Chateauvieux S, et al. Heteronemin, a spongean ses-  
terterpene, inhibits TNF alpha-induced NF-kappa B activation through proteasome  
inhibition and induces apoptotic cell death. *Biochemical Pharmacology*. 2010;**79**:610-622
- [199] Shin BA, Kim YR, Lee IS, Sung CK, et al. Lyso-PAF analogues. and lysophosphatidyl-  
cholines from the marine sponge *Spirastrella abata* as inhibitors of cholesterol biosynthe-  
sis. *Journal of Natural Products*. 1999;**62**:1554-1557
- [200] Zhao Q, Mansoor TA, Hong J, Lee CO, et al. New lysophosphatidylcholines and mono-  
glycerides from the marine sponge *Stelletta* sp. *Journal of Natural Products*. 2003;  
**66**:725-728
- [201] Shen S, Liu D, Wei C, Proksch P, Lin W. Purpuroines A–J, halogenated alkaloids from  
the sponge *Iotrochota purpurea* with antibiotic activity and regulation of tyrosine  
kinases. *Bioorganic & Medicinal Chemistry*. 2012;**20**:6924-6928
- [202] Lee Y, Jang KH, Jeon JE, Yang WY, et al. Cyclic bis-1,3-dialkylpyridiniums from the  
Sponge *Haliclona* sp. *Marine Drugs*. 2012;**10**:2126-2137
- [203] Yang F, Hamann MT, Zou Y, Zhang MY, et al. Antimicrobial metabolites from the  
Paracel Islands sponge *Agelas mauritiana*. *Journal of Natural Products*. 2012;**75**:774-778
- [204] Laport MS, Marinho PR, Santos OC, de Almeida P, et al. Antimicrobial activity of  
marine sponges against coagulase-negative staphylococci isolated from bovine mastitis.  
*Veterinary Microbiology*. 2012;**155**:362-368
- [205] Fusetani N. Biofouling and antifouling. *Natural Product Reports*. 2004;**21**:94-104
- [206] Blihoghe D, Manzo E, Villela A, Cutignano A, et al. Evaluation of the antifouling prop-  
erties of 3-alkylpyridine compounds. *Biofouling: Journal of Bioadhesion and Biofilm  
Research*. 2010;**27**:90-109

IntechOpen