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REVIEW ARTICLE

Chemical diversity and biological activities of marine-derived sulphur containing alkaloids: A comprehensive update

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KEYWORDS

Sulphur-containing alkaloids;
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Chemical diversity;
Bioactivity diversity;
Cytotoxicity

Abstract *Objectives:* The ocean is a huge ecosystem with diverse marine life. Scientists have found a large number of natural products with unique structural features and excellent biological activity from these organisms. Marine-derived sulphur-containing alkaloids are a significant family of natural products with diverse structures and bioactivities. In this paper, the chemical and biological diversity of 972 sulfur-containing alkaloids derived from marine organisms reported from 1982 to 2022 were reviewed, and the structure–activity relationship was briefly analyzed, in order to provide reference for the discovery, synthesis, biological activity research and drug development of such compounds.

Key findings: A total of 972 marine-derived sulphur-containing alkaloids have been collected. Among them, 80.36% of sulphur-containing alkaloids are from marine sponges, fungi, tunicates and bacteria. Moreover, cytotoxicity is their most significant property, About 1/3 sulphur-containing organisms are reported to be cytotoxic. Aming them, discorhabdins, curacins, tanjungides, leptosins, and latrunculins exhibit better cytotoxicity. In addition, the structure–activity relationships of the cytotoxicity of these compounds have been summarized for further investigation.

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Summary: In this paper, the chemical and bioactivity diversity of marine-derived sulphur-containing alkaloids were reviewed, which are a significant family of natural products with diverse structures and bioactivities. 972 sulphur-containing alkaloids were obtained from marine algae, sponges, cnidarians, tunicates, echinoderms, molluscs, bryozoans, dinoflagellates, cyanobacteria, bacteria and fungi, which possessed a wide spectrum of pharmacology including cytotoxicity, antibacterial, antifungal, antimitotic, antiviral, and other activities.

1. Introduction

Natural medicines found from terrestrial plant and animal resources have been widely used in the clinical treatment of various diseases. However, with continuous exploitation, it has become increasingly difficult to develop drugs from terrestrial resources. Therefore, researchers have started to work on finding new sources of drugs from the ocean. (Lu et al., 2021).

The oceans are extremely rich in biological resources, including large numbers of fish, shrimps, crabs and many lower species such as molluscs, corals and seaweeds. Together, these organisms maintain the balance and stability of the marine ecosystem. (Seipp et al., 2021). It is worth noting that the marine environment has extreme living conditions such as high pressure, high salinity, hypoxia and low light. As a result, marine organisms often produce unique and active secondary metabolites, giving them an edge in the competition for limited resources. (Shang et al., 2018).

Pharmacological studies have shown that marine natural products (MNPs) have great potential in the treatment of various diseases. These results have stimulated research and development of marine organisms. After decades of in-depth studies, a large number of active ingredients have been found. (Lu et al., 2021). To date, 11 marine-derived drugs have successfully reached the market. For example, cytarabine (Cytosar-U®), ET-743 (Yondelis®), eribulin mesylate (Halaven®) and the antibody-drug conjugates (ADCs) brentuximab (Adcetris®) and polatumumab (Polivy®) have been used to treat cancer. Lovaza®, Vascepa® and Epanova® are used to treat hypertriglyceridemia. (Liang et al., 2019). In addition, 23 compounds are in various stages of clinical development. For example, the combination therapy of prambulin and docetaxel is currently in phase III clinical trials for the treatment of non-small cell lung cancer and the prevention of chemotherapy-induced neutropenia. lurbinectedin is in phase II/III clinical trials for the treatment of BRCA1/2-mutated breast cancer and small cell lung cancer. In addition, tetrodotoxin (Tectin), an alkaloid derived from the tetrodotoxin liver, is in phase III clinical trials for the treatment of severe pain. (Jiménez, 2018).

Among the many MNPs, sulphur-containing alkaloids are important natural marine products with good bioactivity. As shown in Fig. 1, about 972 sulphur-containing alkaloids have been isolated from marine organisms from 1982. (marine fungi have become an important source of sulphur-containing alkaloids in recent 10 years, Fig. 2). The sulphur-containing alkaloids displayed a variety of biological activities such as cytotoxicity, anti-proliferation, anti-virus, anti-inflammatory and antioxidant, as listed in Table 14 (Berman et al., 1999; Bu et al., 2014; Du et al., 2012; Goey et al., 2016; Guzmán et al., 2009; Harris et al., 2018; Jeong et al., 2003; Johnson et al., 1999; Jun et al., 2007; Lam et al., 2020; Lee et al., 2016; Li et al., 2021; Machihara and Namba 2020; Merrouche et al., 2020; Morgan et al., 2010; Morgan

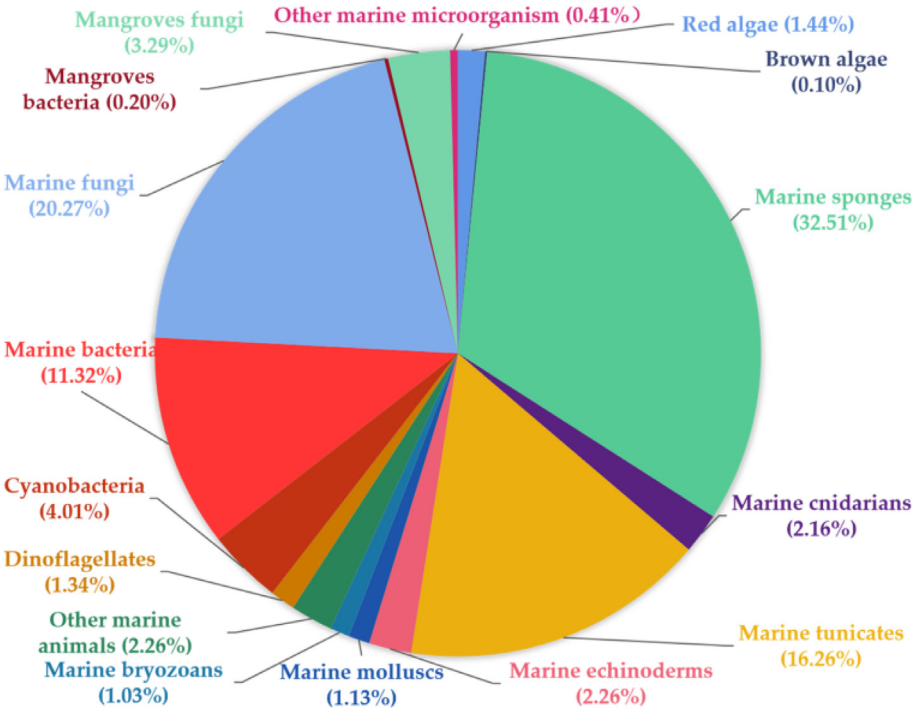

Fig. 1 The percentage of sulphur-containing alkaloids from diverse marine organisms.

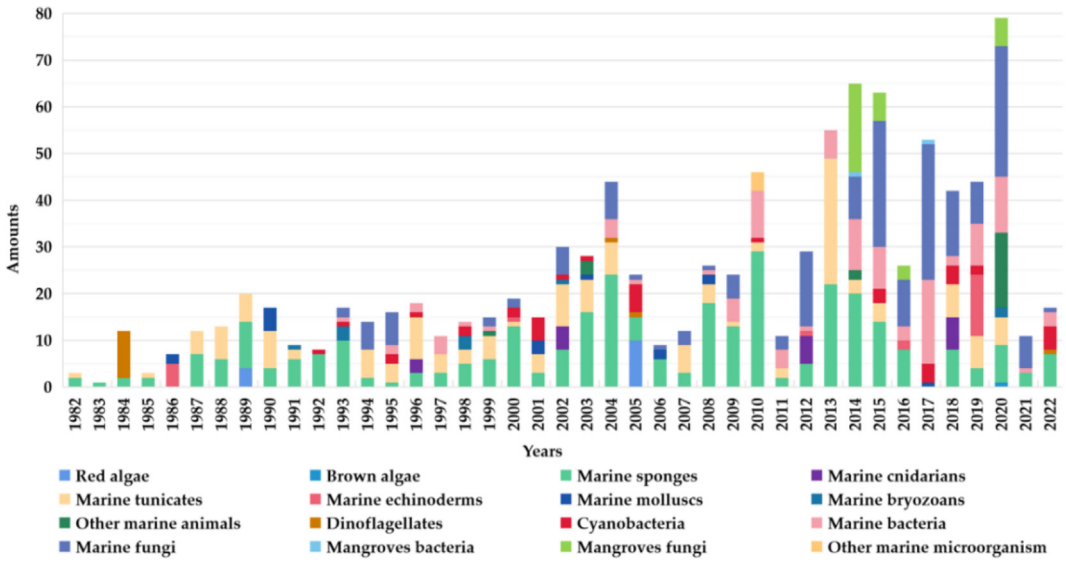

Fig. 2 All sulphur-containing alkaloids by source/year, n = 972.

et al., 2015; Oluwabusola et al., 2022; Reid et al., 1996; Sachiko Takaishi et al., 1998; Salam et al., 2013; Susana and Salvador-Reyes 2022; Wang et al., 2022; Zhao et al., 2019). Of them, ecteinascidin 743 (yondelis) has become the first modern marine drug to treat advanced soft tissue tumors (Menchaca et al., 2003). Thiomarinols have excellent antibacterial activity and can even be effective against methicillin-resistant *Staphylococcus aureus* (MRSA) (Shiozawa et al., 1995). Somocystinamide A (**601**) shows strong cytotoxicity to Jurkat and CEM cells with IC_{50} values of 3 and 14 nM, respectively (Wrasidlo et al., 2008).

In this study, we comprehensively summarized the chemistry and biological activity of sulphur-containing alkaloids in 459 publications and provided a brief analysis of the active conformational relationships between their structure and biological activity. This will help us to provide a reference for the discovery, synthesis and biological activity studies of this class of compounds and for drug discovery and development.

1.1. Search strategy

Comprehensive research and analysis of previously published literature were conducted for studies on the chemical and biological diversity of the marine-derived sulphur-containing alkaloids. The search was conducted using databases such as Sciencedirect, SciFinder, Medline PubMed, Google Scholar, Baidu Scholar, and CNKI by using the keywords such as marine alkaloids, marine-derived sulphur-containing alkaloids, sulphur-containing alkaloids. Furthermore, part of the analyzed studies was got by a manual search of articles in the reference lists of the included studies. The PRISMA template for determining the list of articles is displayed in Fig. 3. The chemical structures were drawn using ChemDraw Professional 20.0.

1.2. Chemical diversity of Marine-Derived Sulphur-containing alkaloids

1.2.1. Marine algae

The photosynthesis of algae is an extremely important source of oxygen. At the same time, the organic matter they produce and the energy they accumulate are the basis for the survival and development of the entire marine biosphere. Therefore, marine algae are considered to be an important marine biological resource. Human exploitation of marine algal resources has a long history. In the early days, some seaweeds such as roundworms, kelp and nori were used as food. Later, seaweed was used as medicine, animal feed and fertiliser. With the development of seaweed resources, one of the most important uses of seaweed is the extraction of various seaweed extracts. For example, agar is widely used as a bacterial culture medium and carrageenan is widely used in the food industry.

Although abundant compounds were isolated from the marine algae by natural product chemists, only 15 sulphur-containing alkaloids (**1**–**15**) were reported from red algae and brown algae (Fig. 4 and Table 1). Of them, sulphur-containing alkaloids reported from the red algae are all reported from *Laurencia brongniartii* (Tanaka et al., 1989). In addition, it's worth noting that these alkaloids are all indole alkaloids and compounds **4, 8**–**14** are special indole alkaloid dimers (El-Gamal et al., 2005).

1.2.2. Marine fauna

1.2.2.1. Marine sponges. Marine sponges are the most primitive multicellular animal, which have been living in the ocean since 600 million years ago. They have developed to more than 10,000 species, accounting for 1/15 of the marine animal species. Sponges have been developed very early by ancient humans. Now they are extensive used in technology, medicine and daily life and have become an important resource for marine drug development. A total of 316 (**16**–**331**) sulphur-containing alkaloids were reported from the marine sponges (Fig. 5 and Table 2). These compounds isolated from marine sponges have various bioactivities such as antitumor, antifungal, antibacterial and enzyme inhibitory activities.

Among them, discorhabdins, psammaplins and latrunculins are the three noteworthy chemical components. (1) The discorhabdin alkaloids, which have a unique structure with azacarbocyclic spirocyclohexanone and pyrroloiminoquinone units, usually have cytotoxicity against a variety of tumor cells. And when they have a sulfur-containing six-membered ring, discorhabdin alkaloids often have good cytotoxicity (Antunes et al., 2004). Notably, dimers (Lang et al., 2005) and trimers (Li et al., 2020c) of discorhabdin alkaloids, which were reported in recent years, also have good cytotoxicity. (2) Psammaplins are bromotyrosine derivatives with oxime groups and carbon–sulfur bonds. Among them, psammaplin A (**23**) is the first identified symmetrical bromotyrosine-derived disulfide dimer, which has a broad bioac-

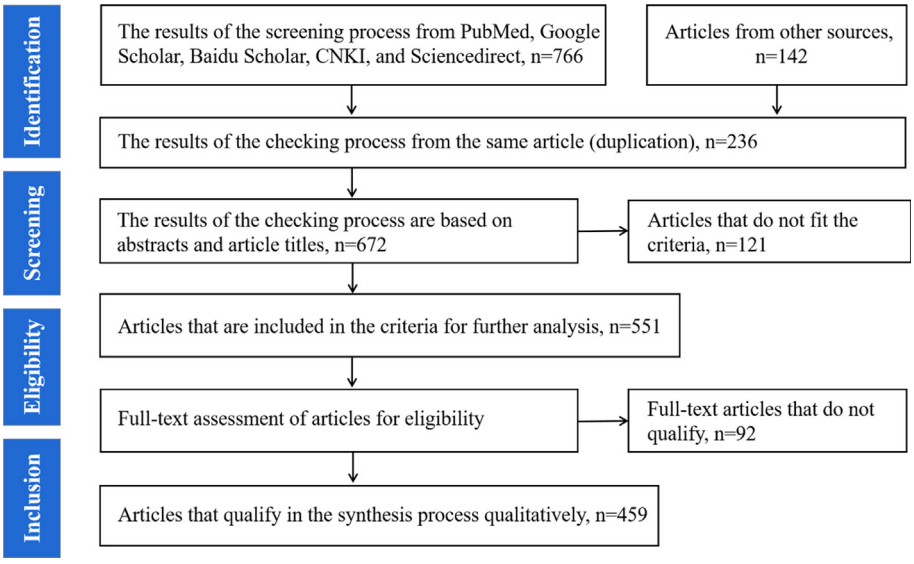

Fig. 3 Research Data Search & Selection Flow.

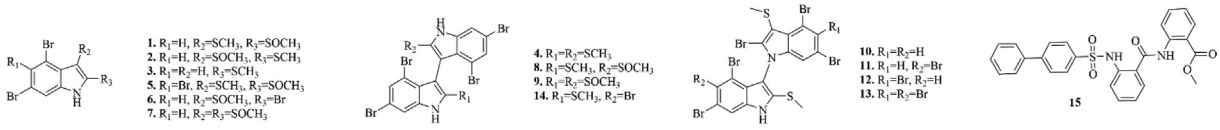

Fig. 4 Sulphur-containing alkaloids from marine algae.

Table 1 Sulphur-containing alkaloids from marine algae.

No.	Compounds	Time	From	Location	Ref.
Marine algae					
Red algae					
1.	itomanindole A	1989	*Laurencia brongniartii*	Okinawa, Japan	(Tanaka et al., 1989)
2.	itomanindole B	1989			
3.	4,6-dibromo-2-(methylthio)indole	1989			
4.	3,3-bis(4,6-dibromo-t-methyIthio)indole	1989			
5.	2-methylsulfinyl-3-methylthio-4,5,6-tribromoindole	2005		Ken-Ting National Park, South Taiwan	(El-Gamal et al., 2005)
6.	3-methylsulfinyl-2,4,6-tribromoindole	2005			
7.	4,6-dibromo-2,3-di(methylsulfinyl)indole	2005			
8.	3,3′-bis(2′-methylsulfinyl-2-methylthio-4,6,4′,6′-tetrabromo)indole	2005			
9.	3,3-bis(4,6-dibromo-2-methylsulfinyl)indole	2005			
10.	2,4,4′.6.6′-pentabromo-2′,3-bis(methylthio)-1,3′-bi-1*H*-indole	2005		Kikai Island, Japan	(Natsuki et al., 2005)
11.	2.4.4‘0.5′.6.6‘-hexabromo-2′,3-bis(methylthio)-1,3′-bi-1*H*-indole	2005			
12.	2,4,4′,5,6,6′-hexabromno-2′,3-bis(methylthio)-1,3′-bi-1*H*-indole	2005			
13.	2.4.4‘0.5.5′.6.6′-heptabromo-2′,3-bis(methylthio)-1,3′-bi-1*H*-indole	2005			
14.	2.4.4′.6.6′-pentabromo-2′-methylthio-3,3′-bi-1*H*-indole	2005			
Brown algae					
15.	sargassulfamide A	2020	*Sargassum naozhouense*	Leizhou Peninsula, Guangdong, China	(Peng et al., 2020)

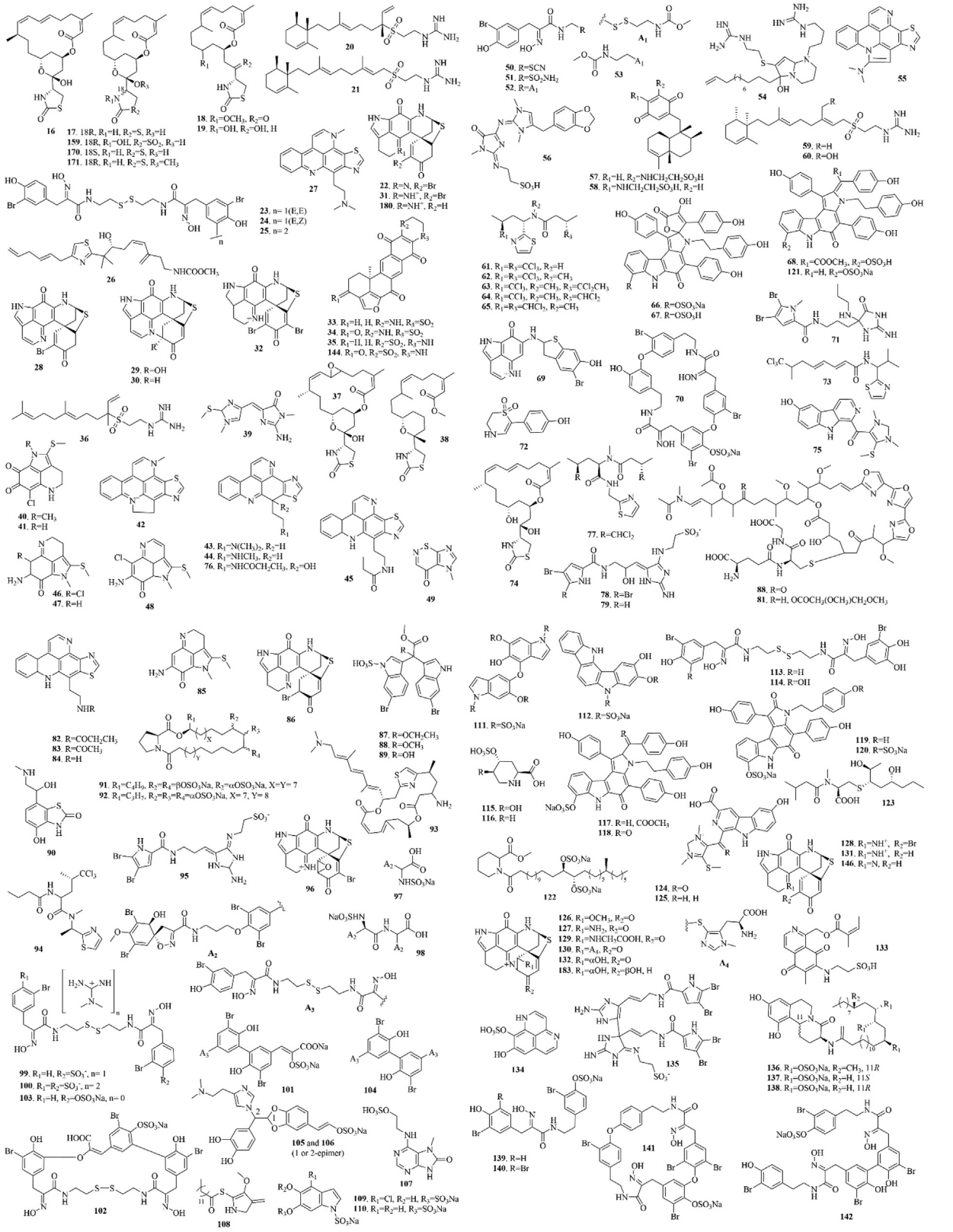

Fig. 5 Sulphur-containing alkaloids from marine sponges.

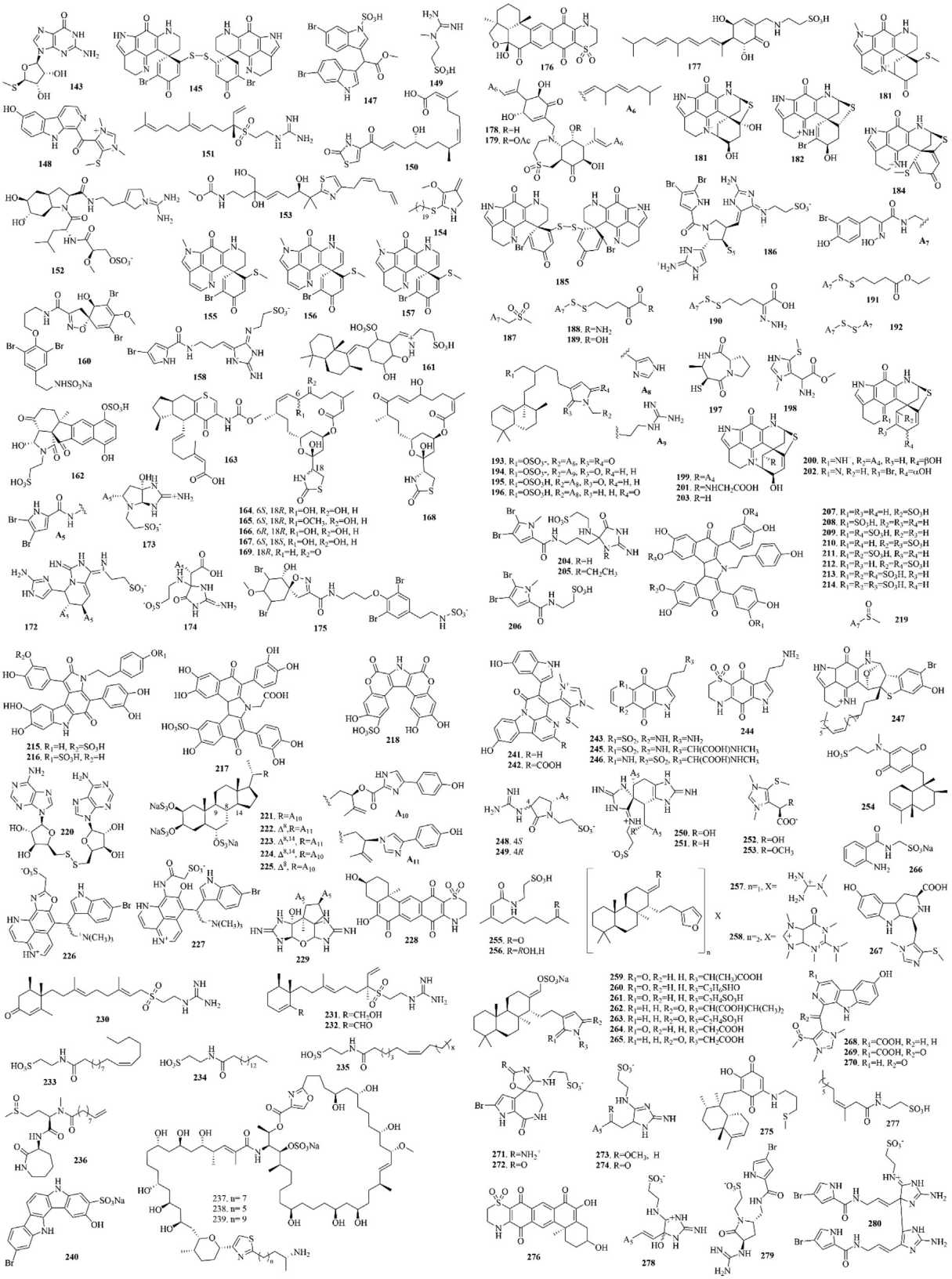

Fig. 5 (*continued*)

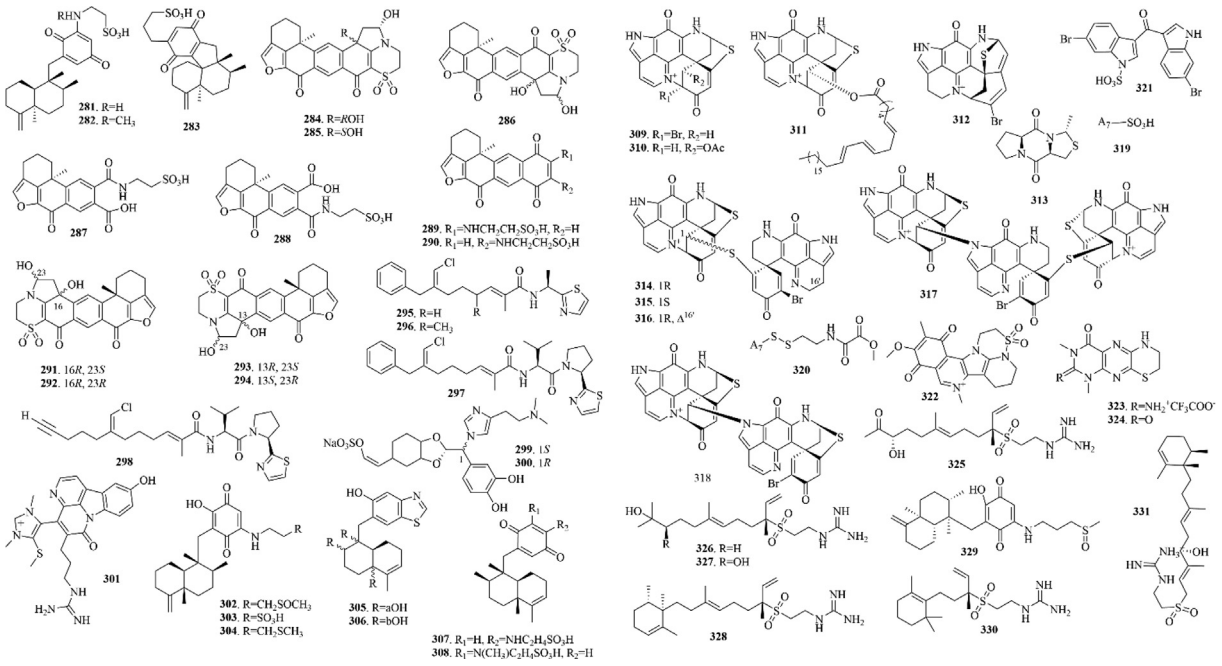

Fig. 5 (*continued*)

tive spectrum, especially in terms of antimicrobial and antiproliferative activities (Quiñoà and Crews, 1987). (3) Latrunculins, toxins from the red sea sponge *Latrunculia magnifica,* are concerned as a kind of F-actin-severing compound. Of which, latrunculin A (**16**) is the most widely used reagent to depolymerize actin filaments in experiments on live cells (Spector et al., 1983).

1.2.2.2. Marine cnidarians. Cnidarians are the most primitive metazoan, which can be divided into three classes: *Hydra*, *Aquarius* and *Corallus*. And with growing bioprospecting efforts and the screening of previously unexplored marine habitats, the phylum cnidarians have been a large, diverse and ecologically important group of marine invertebrates that includes over 11,000 extant species (Rocha et al., 2011).

A total of 21 (**332**–**352**) sulphur-containing alkaloids were reported from the marine cnidarians (Fig. 6 and Table 3). Among them, tridentatols E-H are sodium sulfate salt of tridentatols A-D. When potential predators appear, *Tridentata marginata* will rapidly convert tridentatols E-H to tridentatols A-D, which are nonprotein venom produced by cnidarian nematocysts, and repel the potential predators (Lindquist, 2002).

1.2.2.3. Marine tunicates. Tunicates, which distribute in the world's major seas, are soft-bodied solitary or colonial sessile small marine organisms belonging to the family Ascidiacea under the subphylum Urochordata, phylum Chordata. There're more than 2,800 species of tunicate species, which are divided into three classes: *Ascidiacea*, *Thaliacea* and *Appendicularia*. Tunicates will lose the notochord and post-anal tail; thus, these organisms are often referred to as the "evolutionary connecting link" between invertebrates and chordates (Ramesh et al., 2021).

158 (**353**–**510**) sulphur-containing alkaloids were reported from the marine tunicates (Fig. 7 and Table 4). Among them, eudistomins and ecteinascidins are noteworthy chemical components. (1) Eudistomins attract the attention of scientists because of their good antiviral activity. Subsequent studies have found that eudistomins have the strongest anti-tumor activity when they contain a 1,3,7-oxathiazepine ring. For example, eudistomins C and E, which contain a 1,3,7-oxathiazepine ring, are potent antiviral against RNA viruses (Coxsackie A-21 virus and equine rhinovirus) as well as DNA viruses (HSV-1, HSV-2, and Vaccinia virus). Besides the substituents on the pyridine ring of the β-carboline, the substituents (Br and/or OH) and their positions on the benzenoid ring of the β-carboline may influence the antiviral activity of eudistomins; the order of antiviral activity observed is E (5-Br, 6-OH) > C (6-OH, 7-Br) > L (6-Br). But acetylation of the phenol and primary amine functions of eudistomin C affected a 100-fold reduction in activity (Blunt et al., 1987). (2) Ecteinascidins, a kind of sulphur-containing alkaloids, are marine natural products with potent antitumor activity. These compounds have been a lot of synthetic research and structural modification. Of them, ecteinascidin 743 (yondelis) has been approved by the European Union in October 2007 for the treatment of advanced soft tissue tumors, which became the first modern marine drug (Menchaca et al., 2003).

1.2.2.4. Marine echinoderms. Echinoderms are a kind of deuterostomes, which account for up to 90% of benthic biomass in the abyssal seafloor. The common sea stars, sea urchins, sea cucumbers, and sea snake tails all are echinoderms. At present, about 6000 species of echinoderms were widely distributed from shallow sea to thousands of meters deep sea, which can be divided into five classes including *Crinoidea*, *Holothurioidea*, *Asteroidea*, *Echinoidea* and *Ophiuroidea*.

22 (**511**–**532**) sulphur-containing alkaloids were reported from the marine cnidarians (Fig. 8 and Table 5). Ovothiols are histidine-derived thiols that are receiving great interest for their biological activities in human model systems. Among them, ovothiol A (**514**) is one of the strongest natural antioxidants (Osik et al., 2021). It's worth noting that hypalocrinins are the first naturally occurring anthraquinones and anthraquinone biaryls conjugated with taurine. Hypalocrinins A-E (**520**–**524**) are five new water-soluble amido- and aminoanthraquinone pigments and hypalocrinin F-G (**525**–**526**) are two new amidoanthraquinone biaryls, which all are quite unusual among natural products (Wolkenstein et al., 2019). Likewise, microdiscusols A-F (**527**–**532**), six new polyhydroxylated steroids conjugated with taurine, are rare new polyhydroxylated steroids conjugated with taurine (Kicha et al., 2019).

Table 2 Sulphur-containing alkaloids from marine sponges.

No.	Compounds	Time	From	Location	Ref.
Marine fauna					
Marine sponges					
16	latrunculin A	1982	*Latruncularia magnifica*	Red Sea	(Spector et al., 1983)
17	latrunculin B	1982			
18	latrunculin C	1985			(Kashman et al.,
19	latrunculin D	1985			1985)
20	agelasidine B	1984	*Agefas nakamurai*	Okinawa, Japan	(Nakamura et al.,
21	agelasidine C	1984			1985)
22	prianosin A	1987	*Prianos melanos*		(Kobayashi et al., 1987)
23	psammaplin A	1987	*Psammaplysilla* sp.	Tonga	(Quiñoà and Crews, 1987)
24	(*E*,*Z*)-isomer of psammaplin A	1987	unidentified sponge	Guam, U.S.A.	(Arabshahi and Schmitz, 1987)
25	bisaprasin	1987	*Thorectopsamma xana*		(Rodriguez et al., 1987)
26	mycothiazole	1988	*Spongia mycofijiensis*	Vanuatu	(Crews et al., 1988), (Sugiyama et al., 2003)
27	dercitin	1989	*Dercitus* sp.	Bahamas	(Burres et al., 1989)
28	prianosin B	1988	*Prianos melanos*	Motobu Peninsula,	(Cheng et al., 1988)
29	prianosin C	1988		Okinawa, Japan	
30	prianosin D(discorhabdin D)	1988			
31	discorhabdin A	1988	*Latrunculia* sp.	New Zealand	(Perry et al., 1988)
32	discorhabdin B	1988			
33	adociaquinone A	1987	*Adocia* sp.	Truk Lagoon	(Schmitz and Bloor, 1988)
34	adociaquinone B	1987			
35	3-ketoadociaquinone A	1987			
36	agelasidine A	1983	*Agelas* sp.	Okinawa, Japan	(Nakamura et al., 1983)
37	6,7-epoxy-latrunculin A	1989	*Latruncularia magnifica*	Red Sea	(Blasberger et al.,
38	latrunculin M	1989			1989)
39	corallistine	1989	*Corallistes fulvodesmus*	New Caledonia	(Debitus et al., 1989)
40	batzelline A	1989	*Batzella* sp.	Bahamas	(Sakemi et al., 1989)
41	batzelline B	1989			
42	cyclodercitin	1989	*Dercitus* sp.		(Gunawardana et
43	nordercitin	1989	*Stelletta* sp.		al., 1989)
44	dercitamine	1989			
45	dercitamide	1989			
46	isobatzelline A	1990	*Batzella* sp.	Caribbean	(Sun et al., 1990)
47	isobatzelline B	1990			
48	isobatzelline D	1990			
49	neamphine	1991	*Neamphius huxleyi*	Papua New Guinea	(de Silva et al., 1991)
50	psammaplin B	1991	*Psammaplysilla purpurea*	–	(Jiménez and Crews,
51	psammaplin C	1991			1991)
52	psammaplin D	1991			
53	prepsammaplin A	1991			
54	phloeodictine B	1992	*Phloeodictyon* sp.	New Caledonian	(Kourany-Lefoll et al., 1992)
55	stellettamine	1992	*Stelletta* sp.	–	(Gunawardana et al., 1992)
56	(9*E*)-clathridine 9-*N*-(2-sulfoethyl)-imine	1992	*Leucetta microraphis*	pohnpei	(He et al., 1992)
57	melemeleone A	1992	*Dysidea avara*	Solomon Islands	(Alvi et al., 1992)
58	melemeleone B	1992			
59	(−)-agelasidine C	1992	*Agelas clathrodes*	Puerto Rico	(Morales and
60	(−)-agelasidine D	1992			Rodríguez, 1992)
61	dysideathiazole	1993	*Dysidea herbacea*	Pohnpei and Palau	(Unson et al., 1993)
62	*N*-methyldysideathiazole	1993			
63	l0-dechloro-*N*-methyldysideathiazole	1993			
64	10-dechlorodysideathiazole	1993			
65	9,l0-adechloro-*N*-methyldysideathiazo	1993			

Table 2 (*continued*)

No.	Compounds	Time	From	Location	Ref.
66	potent aldose reductase inhibitor la	1993	*Dictyodendrilla* sp.	Kagoshima, Japan	(Sato et al., 1993)
67	potent aldose reductase inhibitor lb	1993			
68	potent aldose reductase inhibitor 2a	1993			
69	makaluvamine F	1993	*Zyzzya fuliginosa*	Fijian	(Radisky et al., 1993)
70	34-*O*-sulfatobastadin-13	1993	*Zanthella* sp.	Great Barrier Reef	(Gulavita et al., 1993)
71	mauritamide A	1994	*Agelas mauritiana*	Fijian	(Jiménez and Crews, 1994)
72	6-(p-hydroxyphenyl)–2*H*-3,4-dihydro-1,1-dioxo-1,4-thiazine	1994	*Anchinoe tenacior*	Mediterranean	(Casapullo et al., 1994)
73	herbamide A	1995	*Dysidea herbacea*	Papua New Guinea	(Clark and Crews, 1995)
74	latrunculin S	1996	*Fasciospongia rimosa*	Okinawa, Japan	(Tanaka et al., 1996)
75	hyrtiomanzamine	1996	*Hyrtios erecta*	Red Sea	(Bourguet-Kondracki et al., 1996)
76	sagitol	1996	*Oceanapia sagittaria*	Palau	(Salomon and Faulkner, 1996)
77	5,5-dichloro-4-methyl-2-[methyl(4,4-dichloro-3-methyl-1-oxobutyl)amino]-*N*-(thiazol-2-ylmethyl)pentanamide	1997	*Dysidea herbacea*	southern Great Barrier Reef	(Dumdei et al., 1997)
78	tauroacidin A	1997	*Hymeniacidon* sp.	Okinawa, Japan	(Kobayashi et al., 1997)
79	tauroacidin B	1997			
80	thiomycalolide A	1998	*Mycale* sp.	Japan	(Matsunaga et al., 1998)
81	thiomycalolide B	1998			
82	kuanoniamine C	1998	*Oceanapia* sp.	Truk, Micronesia.	(Eder et al., 1998)
83	kuanoniamine D	1998			
84	*N*-deacetylkuanoniamine C	1998			
85	the methylthio derivative isobatzelline B	1990	Batzella sp.	Caribbean	(Sun et al., 1990)
86	discorhabdin Q	1999	*Latrunculia purpurea, Zyzzya massalis, Zyzzya fuliginosa, and Zyzzya* spp.	Assail Bank, between North Island and the Wallab Group, Australia,	(Dijoux et al., 1999)
87	echinosulfonic acid A	1999	*Echinodictyum* sp.	Great Australian Bight,	(Ovenden and Capon, 1999), (Neupane et al., 2020)
88	echinosulfonic acid B	1999		Southern Australian	
89	echinosulfonic acid C	1999			
90	S1319	1999	*Dysidea* sp.	Okinawa, Japan	(Suzuki et al., 1999)
91	penarolide sulfate A1	2000	*Penares* sp.	Japan	(Nakao et al., 2000)
92	penarolide sulfate A2	2000			
93	pateamine	1991	*Mycale* sp.	New Zealand	(Northcote et al., 1991)
94	(−)-neodysidenin	2000	*Dysidea herbacea*	Great Barrier Reef	(MacMillan et al., 2000)
95	taurodispacamide A	2000	*Agelas oroides*	The Bay of Naples	(Fattorusso and Taglialatela-Scafati, 2000)
96	discorhabdin R	2000	*Latrunculia* sp.	the central Prydz channel of Prydz Bay, Antarctica	(Ford and Capon, 2000)
			Negombata sp.	Victoria, Port Campbell	
97	ianthesine C	2000	*Ianthella* sp.	Australian	(Okamoto et al., 2000)
98	ianthesine D	2000			
99	psammaplin A1	2000	*Aplysinella rhax*	Pohnpei and Palau	(Shin et al., 2000)
100	psammaplin A2	2000			
101	aplysinellin A	2000			
102	aplysinellin B	2000			
103	psammaplin A 11′-sulfate	2000	*Aplysinella rhax*	Great Barrier Reef	(Pham et al., 2000)
104	bisaprasin 11′-sulfate	2000			
105	wondonin A	2001	*Poecillastra wondoensis*and	Keomun Island, Korea	(Shin et al., 2001)
106	wondonin B	2001	*Japsis* sp.		
107	microxine	2001	*Microxina* sp.	Cape Jaffa, Australian	(Killday et al., 2001)
108	irciniamine	2002	*Ircinia* sp.	Ehime Prefecture, Japan	(Kuramoto et al., 2002)

(*continued on next page*)

Table 2 (*continued*)

No.	Compounds	Time	From	Location	Ref.
109	ancorinolate A	2002	*Ancorina* sp.	Chatham Island,New Zealand	(Meragelman et al., 2002)
110	ancorinolate B	2002			
111	bis-ancorinolate B	2002			
112	ancorinazole	2002			
113	psammaplin K	2002	*Aplysinella rhax*	Fijian	(Tabudravu et al., 2002)
114	psammaplin L	2002			
115	cribronic acid	2003	*Cribrochalina olemda*	Palau	(Sakai et al., 2003)
116	(2*S*,4*S*)-4-sulfooxypiperidine-2-carboxylic acid	2003	*Stylotella aurantium,* and*Axinella carteri*	Yap State, Micronesia	
117	dictyodendrin A	2003	*Dictyodendrilla verongiformis*	Nagashima Island, Japan	(Warabi et al., 2003)
118	dictyodendrin B	2003			
119	dictyodendrin C	2003			
120	dictyodendrin D	2003			
121	dictyodendrin E	2003			
122	penasulfate A	2004	*Penares* sp.	Hachijo-jima Island,Tokyo, Japan	(Nakao et al., 2004)
123	spongiacysteine	2004	Spo*ngia* sp.	Tateyama beach,Chiba Prefecture, Japan	(Kobayashi et al., 2004)
124	dragmacidonamine A	2004	*Dragmacidon* sp.	Adaman Islands, India	(Pedpradab et al., 2004)
125	dragmacidonamine B	2004			
126	1-methoxydiscorhabdin D	2004	*Latrunculia bellae*	Thunderbolt Reef,Algoa Bay, South Africa	(Antunes et al., 2004)
127	1-aminodiscorhabdin D	2004			
128	discorhabdin G*	2004			
129	discorhabdin N	2004			
130	discorhabdin H	2004	*Strongylodesma algoaensis*		
131	discorhabdin I	2004	*Latrunculia brevis*	Tierra del Fuego, Patagonia, Argentina	(Reyes et al., 2004)
132	discorhabdin L	2004			
133	cribrostatin 7	2004	*Petrosia* sp. PC00-11–149	Kalampisauan Island, Philippines	(Sandoval et al., 2004)
134	bisdemethylaaptamine-9-O-sulfate	2004	*Aaptos* sp.	Bunaken Island, Indonesian	(Herlt et al., 2004)
135	nagelamide H	2004	*Agelas* sp.	Seragaki Beach, Okinawan	(Endo et al., 2004)
136	schulzeine A	2004	*Penares schulzei*	Hachijo-kojima Island, Japan	(Takada et al., 2004)
137	schulzeine B	2004			
138	schulzeine C	2004			
139	1-*O*-sulfatohemibastadin-1	2004	*Ianthella basta*	Mangilao, Guam, U.S.A.	(Masuno et al., 2004)
140	1-*O*-sulfatohemibastadin-2	2004			
141	34-*O*-sulfatobastadin-9	2004			
142	32-*O*-sulfatobastadin-13	2004			
143	hamiguanosinol	2004	*Mediterranean hamigera*	Elba, Mediterranean Sea	(Hassan et al., 2004),(Jamison et al., 2014)
144	3-ketoadociaquinone B	2005	*Xesto*spo*ngia* sp.	Indonesia, Sulawesi	(Cao et al., 2005)
145	discorhabdin W	2005	*Latrunculia* sp.	New Zealand	(Lang et al., 2005)
146	discorhabdin G*/I	2005			
147	echinosulfonic acid D	2005	*Psammoclemma* sp.	New Caledonia	(Rubnov et al., 2005), (Neupane et al., 2020)
148	gesashidine A	2005	An unidentified member of the Thorectidae family	Okinawan	(Iinuma et al., 2005)
149	halichondria sulfonic acid	2006	*Halichondria rugosa*	South China Sea	(Jin et al., 2006)
150	latrunculin T	2006	*Negombata magnifica*	Red Sea (near Egypt)	(El Sayed et al., 2006)
151	(−)-agelasidine A	2006	*Agelas clathrodes*	Curaçao, Caribbean sea	(Medeiros et al., 2006)
152	dysinosin A	2002	a New Genus and Species of Sponge of Dysideidae	Lizard Island, North Queensland, Australia	(Carroll et al., 2002)
153	mycothiazole-4,19-diol	2006	*Cacospongia mycofijiensis*	Vanuatu	(Sonnenschein et al., 2006)
154	ircinamine B	2006	*Dactylia* sp.	Cape Sada, Japan	(Sato et al., 2006)
155	discorhabdin S	2003	*Batzella* sp.	Bimini, Bahamas	(Gunasekera et al., 2003)
156	discorhabdin T	2003			
157	discorhabdin U	2003			
158	2-debromotaurodispacamide A	2006	*Axinella verrucosa*	Corsica, France	(Aiello et al., 2006)

Table 2 (*continued*)

No.	Compounds	Time	From	Location	Ref.
159	oxalatrunculin B	2007	*Negombata corticata*	Red Sea (near Egypt)	(Ahmed et al., 2007)
160	araplysillin-N9-sulfamate	2007	*Aplysina fulva*	Key Largo, Florida	(Rogers and Molinski, 2007)
161	siphonodictyals B1	2007	*Aka coralliphagum*	San Salvador, Bahamas	(Grube et al., 2007)
162	exiguaquinol	2008	*Neopetrosia exigua*	Queensland, Australia	(de Almeida Leone et al., 2008)
163	CTP-431	2008	*Cacospongia mycofijiensis*	Beqa Lagoon, Fiji	(Johnson et al., 2008)
164	latrunculol A	2008			(Amagata et al., 2008)
165	latrunculol B	2008			
166	latrunculol C	2008			
167	18-epi-latrunculol A	2008			
168	latrunculone A	2008			
169	latrunculone B	2008			
170	16-epi-latrunculin B	2004	*Latruncularia magnifica*	Red Sea	
171	15-methoxylatrunculin B	2004			
172	nagelamide K	2008	*Agelas* sp.	Seragaki, Okinawa, Japan	(Araki et al., 2008)
173	nagelamide M	2008			(Kubota et al., 2008)
174	nagelamide N	2008			
175	ianthesine E	2008	*Pseudoceratina sp.*	Swain Reefs, Australia	(Kalaitzis et al., 2008)
176	alisiaquinone C	2008	An unidentified sponge	New Caledonia	(Desoubzdanne et al., 2008)
177	phorbasin D	2008	*Phorbas* sp.	Great Australian Bight,	(Zhang and Capon, 2008)
178	phorbasin E	2008		South Australia	
179	phorbasin F	2008			
180	(+)-debromodiscorhabdin A	2009	*Higginsia* sp.	South Australia	(El-Naggar and Capon, 2009)
181	(+)-discorhabdin X	2009			
182	(−)-dihydrodiscorhabdin A	2009			
183	(+)-Dihydrodiscorhabdin L	2009	Spo*ngosorites* sp.		
184	(6*R*,8*S*)-1-thiomethyldiscorhabdin G*/I	2009	*Latrunculia wellingtonesis*	Wellington, New Zealand	(Grkovic and Copp, 2009)
185	16a,17a-dehydrodiscorhabdin W	2009			
186	nagelamide Q	2009	*Agelas* sp.	Okinawan, Japan	(Araki et al., 2009)
187	psammaplin I	2003	*Pseudoceratina purpurea*	Papua New Guinea	(Piña et al., 2003)
188	psammaplin E	2003			
189	psammaplin F	2003			
190	psammaplin G	2003			
191	psammaplin H	2003			
192	psammaplin J	2003			
193	19-oxofasciospongine A	2009	*Fascio*spo*ngia* sp.	Palau	(Yao et al., 2009)
194	fasciospongine C	2009			
195	fasciospongine A	2009			
196	fasciospongine B	2009			
197	callyspongine	2010	*Cally*spo*ngia* sp.	South China Sea(Hainan island)	(Huang et al., 2010)
198	dysideanin A	2010	*Dysidea* sp.	Lingshui County, Hainan, China	(Ren et al., 2010)
199	(+)-discorhabdin H2	2010	*Latrunculia fiordensi*	New Zealand	(Grkovic et al., 2010)
200	(−)-discorhabdin K2	2010			
201	(−)-discorhabdin N	2010	*Latrunculia bellae*		
202	dihydrodiscorhabdin B	2010	*Latrunculia* sp.	Aleutian Islands, U.S.A.	(Na et al., 2010)
203	(−)-3-dihydrodiscorhabdin D	2010	*Sceptrella* sp.	Gageodo, Korea	(Jeon et al., 2010)
204	mauritamide B	2010	*Agelas linnaei*	Peniki East island, ThoU.S.	(Hertiani et al., 2010)
205	mauritamide C	2010		A. nd Islands, Indonesia	
206	mauritamide D	2010			
207	baculiferin A	2010	*Iotrochota baculifera*	Hainan island,South China	(Fan et al., 2010)
208	baculiferin B	2010		Sea	
209	baculiferin C	2010			
210	baculiferin D	2010			
211	baculiferin E	2010			
212	baculiferin F	2010			
213	baculiferin G	2010			
214	baculiferin H	2010			

(*continued on next page*)

Table 2 (*continued*)

No.	Compounds	Time	From	Location	Ref.
215	baculiferin I	2010			
216	baculiferin J	2010			
217	baculiferin M	2010			
218	baculiferin O	2010			
219	psammaplin N	2010	*Aplysinella rhax*	Inner Gneerings Reef, Queensland, Australia	(Graham et al., 2010)
220	9-(5′-deoxy-5′-thio-β-d-xylofuranosyl) adenine disulfide	2010	*Trachycladus laevispirulifer*	Great Australian Bight, South Australian	(Peng et al., 2010)
221	amaranzole B	2010	*Phorbas amaranthus*	Dry Reef Rocks, Key Largo, Florida	(Morinaka et al., 2010)
222	amaranzole C	2010			
223	amaranzole D	2010			
224	amaranzole E	2010			
225	amaranzole F	2010			
226	nakijinamine C	2011	*Suberites* sp.	Unten Port, Okinawa, Japan	(Takahashi et al., 2011)
227	nakijinamine D	2011			
228	xestosaprol N	2012	*Xestospongia* sp.	Weno island, Chuuk State, Federated States of Micronesia	(Lee et al., 2012)
229	14-*O*-sulfate massadine	2012	*Axinella* sp.	Great Australian Bight	(Zhang et al., 2012)
230	(+)-2-oxo-agelasidine C	2012	*Agelas mauritiana*	Yongxing island,South China Sea	(Yang et al., 2012)
231	(−)-agelasidine E	2012	*Agelas citrina*	Bahamas	(Stout et al., 2012)
232	(−)-agelasidine F	2012			
233	2-heptadec-11-enamidoethanesulfonic acid	2013	*Axinella* sp.	Hainan island,South China Sea	(Huang et al., 2013)
234	2-palmitamidoethanesulfonic acid	2013			
235	2-octadec-7-enamidoethanesulfonic	2013			
236	ciliatamide D	2013	*Stelletta* sp.	Oshimashinsone, Japan	(Imae et al., 2013), (Takada et al., 2017)
237	theonezolide A	2013	*Theonella* sp.	Okinawa, Japan	(Nozawa et al., 2013)
238	theonezolide B	2013			
239	theonezolide C	2013			
240	catechol sulfonate	2013	*Asteropus* sp.	Ocean Cay, Bahamas	(Russell et al., 2013)
241	hyrtimomine D	2013	*Hyrtios* sp.	Kerama island, Okinawa, Japan	(Tanaka et al., 2013c)
242	hyrtimomine E	2013			
243	thiaplakortone A	2013	*Plakortis lita*	Tydeman Reef,Queensland, Australia	(Davis et al., 2013)
244	thiaplakortone B	2013			
245	thiaplakortone C	2013			
246	thiaplakortone D	2013			
247	atkamine A	2013	*Latrunculia* sp.	Aleutian island, Alaska, U. S.A.	(Zou and Hamann, 2013)
248	nagelamide U	2013	*Agelas* sp.	Kerama islands,Okinawa, Japan	(Tanaka et al., 2013a)
249	nagelamide V	2013			
250	nagelamide Y	2013			(Tanaka et al., 2013b)
251	nagelamide Z	2013			
252	reticulatin A	2013	*Hyrtios reticulatus*	N. Sulawesi, Indonesia	(Imada et al., 2013)
253	reticulatin B	2013			
254	*N*-methylmelemeleone-A	2013	*Dysidea avara*	Fethiye, Turkey	(Hamed et al., 2013)
255	deacyl irciniasulfonic acid C	2014	Coscinoderma sp.	Weno island, Chuuk State, Micronesia	(Kim et al., 2014a)
256	sodium deacyl irciniasulfonate D	2014			
257	*N*,*N*-dimethylguanidium salt	2014			
258	*N*,*N*-dimethyl-1,3-dimethylherbipoline salt	2014			
259	coscinolactam C	2014			
260	coscinolactam D	2014			
261	coscinolactam E	2014			
262	coscinolactam F	2014			
263	coscinolactam G	2014			
264	coscinolactam A	2009	*Coscinoderma mathewsi*	Vangunu Island,Solomon Islands	(De Marino et al., 2009)
265	coscinolactam B	2009			
266	glassponsine	2014	*Anoxycalyx joubini*	Trawled, E. Weddell Sea, Antarctica	(Carbone et al., 2014)
267	hainanerectamine C	2014	*Hyrtios erecta*	Lingshui Bay, China	(He et al., 2014)
268	hyrtimomine H	2014	*Hyrtios* sp.	Kerama islands,Okinawa,	(Tanaka et al., 2014)

Table 2 (*continued*)

No.	Compounds	Time	From	Location	Ref.
269	hyrtimomine J	2014		Japan	
270	hyrtimomine K	2014			
271	callyspongisine A	2014	*Callyspongia* sp.	Great Australian Bight	(Plisson et al., 2014)
272	callyspongisine B	2014			
273	tauroacidin C	2014	*Agelas* sp.	Kerama islands,Okinawa, Japan	(Kusama et al., 2014)
274	tauroacidin D	2014			
275	5-epi-nakijiquinone U	2014	*Dactylospongia metachromia*	Ambon, Indonesia	(Daletos et al., 2014)
276	xestosaprol O	2014	*Xestospongia vansoesti*	Palawan island,Philippines	(Centko et al., 2014)
277	2-(3-methyl-dec-3-enamido)ethanesulfonic Acid	2015	*Callyspongia* sp.	Hainan island, China	(Huang et al., 2015)
278	tauroacidin E	2015	*Agelas* sp.	Kerama island, Okinawa, Japan	(Kusama et al., 2015)
279	2-debromonagelamide U	2015			(Kenta Nakamura, 2015)
280	citrinamine B	2015	*Agelas citrina*	San Salvador, Bahamas	(Cychon et al., 2015)
281	melemeleone C	2015	*Dysidea* sp.	Chuuk island, Federated States of Micronesia	(Kim et al., 2015)
282	melemeleone D	2015			
283	cycloaurenone A	2015			
284	xestoadociaminal A	2015	*Xestospongia* sp.	Manado, N. Sulawesi, Indonesia	(He et al., 2015)
285	xestoadociaminal B	2015			
286	xestoadociaminal C/D	2015			
287	xestoadociaquinone A	2015			
288	xestoadociaquinone B	2015			
289	seadociaquinone A	2015			
290	seadociaquinone B	2015			
291	petroquinone I	2016	*Petrosia alfiani*	Ti Toi, N. Sulawesi, Indonesia	(Tanokashira et al., 2016)
292	petroquinone J	2016			
293	petroquinone K	2016			
294	petroquinone L	2016			
295	conulothiazole A	2016	*Smenospongia conulosa*	Little Inagua island, Bahamas	(Esposito et al., 2016)
296	conulothiazole B	2016			
297	smenothiazole A	2016			
298	smenothiazole B	2016			
299	(–)-isowondonin A	2008	*Poecillastra wondoensis*	Keomun Island, Korea	(Chang et al., 2008)
300	(–)-isowondonin B	2008			
301	ishigadine A	2018	*Hyrtios* sp.	Ishigaki island, Okinawa, Japan	(Takahashi et al., 2018)
302	langcoquinone D	2018	Spongia sp.	Son Cha, Lang Co, Tha Thien-Hue City, Vietnam	(Ito et al., 2018)
303	langcoquinone E	2018			
304	langcoquinone B	2018			
305	dactylospongin A	2018	*Dactylospongia* sp.	Xisha island,South China Sea	(Li et al., 2018)
306	dactylospongin B	2018			
307	ent-melemeleone B	2018			
308	melemeleone E	2018			
309	(−)-2-bromo-discorhabdin D	2019	*Latrunculia biformis*	Dredge,Southern Weddell Sea, Antarctica	(Li et al., 2019)
310	(−)-1-acetyl-discorhabdin L	2019			
311	(+)-1-octacosatrienoyl-discorhabdin L	2019			
312	aleutianamine	2019	*Latrunculia austini*	Aleutian Islands, Alaska, U.S.A.	(Zou et al., 2019)
313	tedanizaine A	2020	*Tedania* sp.	Zhanjiang, Guangdong, China	(Zhang et al., 2020b)
314	(−)-(1*S*,2*R*,6*R*,8*S*,6′*S*)-discorhabdin B dimer	2020	*Latrunculia biformis*	Dredge,Southern Weddell Sea, Antarctica	(Li et al., 2020b)
315	(−)-(1*R*,2*R*,6*R*,8*S*,6′*S*)-16′,17′-dehydrodiscorhabdin B dimer	2020			
316	(−)-(1*R*,2*R*,6*R*,8*S*,6′*S*)-discorhabdin B dimer	2020			
317	(−)-tridiscorhabdin	2020		Dredge,Southern Weddell Sea, Antarctica	(Li et al., 2020c)
318	(−)-didiscorhabdin	2020			
319	psammaplin O	2020	*Aplysinella rhax*	Wainunu, Bua, Fiji island	(Oluwabusola et al., 2020)
320	psammaplin P	2020			
321	echinosulfone A	1999	*Echinodictyum* sp.	Great Australian Bight,	(Ovenden and

(*continued on next page*)

Table 2 (*continued*)

No.	Compounds	Time	From	Location	Ref.
				Southern Australian	Capon, 1999)
322	neopetrothiazide	2021	*Neopetrosia* sp.	Helen Reef, Southwest Islands, Palau	(Wang et al., 2021)
323	tedaniophorbasin A	2021	*Tedaniophorbas ceratosis*	northern New South Wales,	(Hiranrat et al.,
324	tedaniophorbasin B	2021		Australia.	2021)
325	agelasidine G	2022	*Agelas nakamurai*	Orchid Island, Taiwan	(Lin et al., 2022)
326	agelasidine H	2022			
327	agelasidine I	2022			
328	isoagelasidine B	2022			
329	24-methylsulfinyllancoquinone B	2022	*Spongia pertusa*	South China Sea	(Tang et al., 2022)
330	cyclohexylagelasidine A	2022	*Agelas nakamurai*	Orchid Island, Taiwan	(Fu et al., 2022)
331	(+)-12-hydroxyagelasidine C	2022	*Agelas citrina*	Cozumel Island, Mexico	(Pech-Puch et al., 2022)

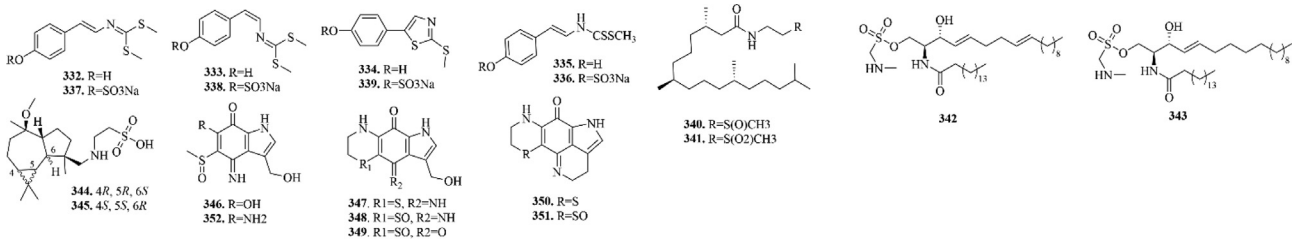

Fig. 6 Sulphur-containing alkaloids from marine cnidarians.

Table 3 Sulphur-containing alkaloids from marine cnidarians.

No.	Compounds	Time	From	Location	Ref.
Marine cnidarians					
332	tridentatol A	1996	*Tridentata marginata*	Morehead City,North	(Lindquist et
333	tridentatol B	1996		Carolina, USA.	al., 1996)
334	tridentatol C	1996			
335	tridentatol D	2002			(Lindquist,
336	tridentatol E	2002			2002)
337	tridentatol F	2002			
338	tridentatol G	2002			
339	tridentatol H	2002			
340	sinulasulfoxide	2012	*Sinularia* sp.	Manado, North Sulawesi,	(Putra et al.,
341	sinulasulfone	2012		Indonesia	2012)
342	palyosulfonoceramide A	2012	*Palythoa caribaeorum*	Paracuru beach,Fortaleza,	(Almeida et al.,
343	palyosulfonoceramide B	2012	and*Protopalythoa variabilis*	Brazil	2012)
344	(+)-4β-*N*-methenetauryl-10β-methoxy1β,5α,6β,7β-aromadendrane	2012	*Melitodes squamata*	Sanya, Hainan,South China Sea	(Huang et al., 2012)
345	(−)-4β-*N*-methenetauryl-10β-methoxy-1β,5β,6α,7α-aromadendrane	2012			
346	macrophilone B	2018	*Macrorhynchia philippina*	Northwestern Australia	(Yan et al.,
347	macrophilone C	2018			2018)
348	macrophilone D	2018			
349	macrophilone E	2018			
350	macrophilone F	2018			
351	macrophilone G	2018			
352	macrophilone A	2018			

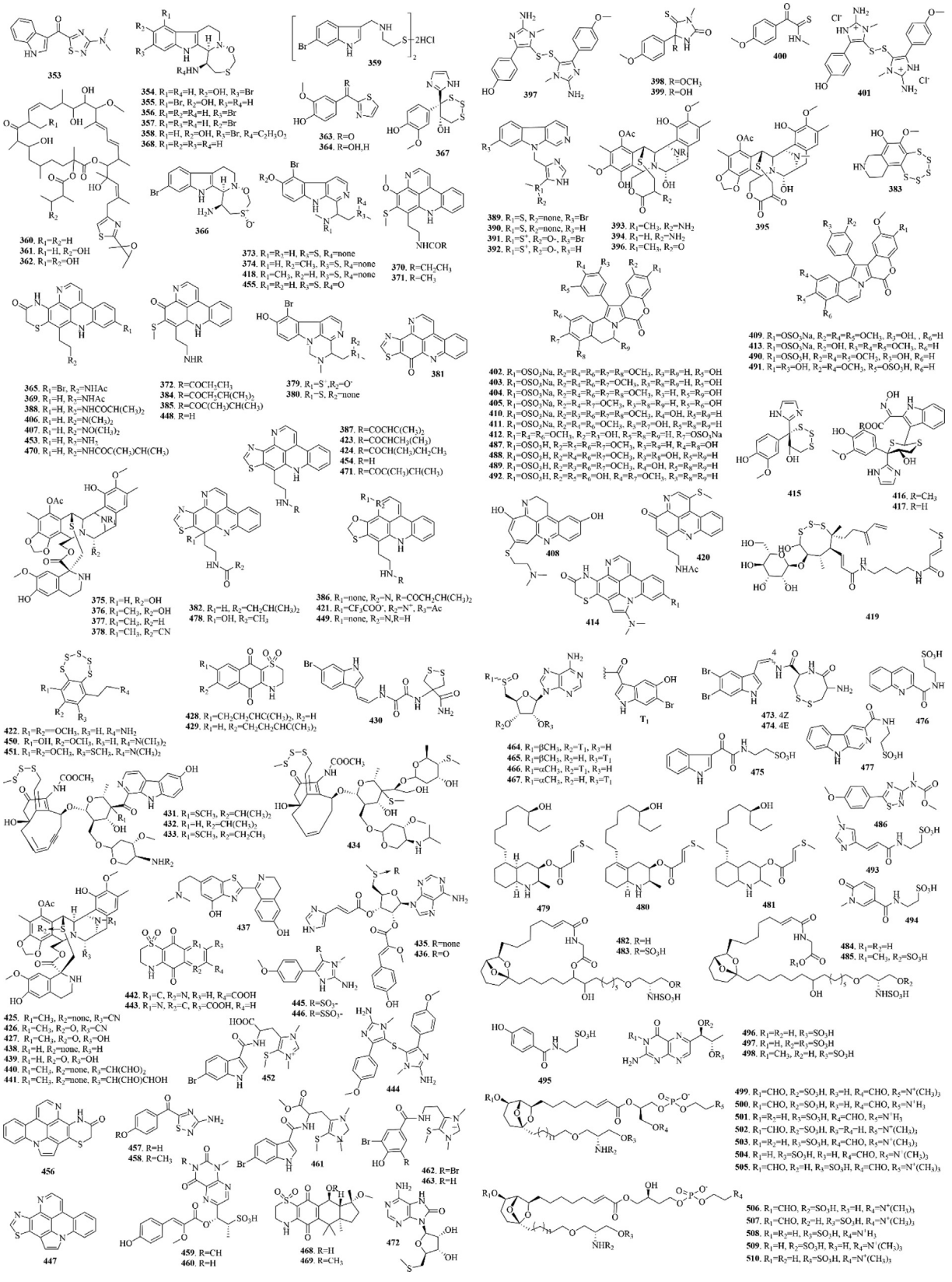

Fig. 7 Sulphur-containing alkaloids from marine tunicates.

Table 4 Sulphur-containing alkaloids from marine tunicates.

No.	Compounds	Time	From	Location	Ref.
Marine tunicates					
353	dendrodoine	1982	*Dendrodoa grossularia*	–	(Heitz et al., 1980)
354	eudistomin C	1987	*Eudistoma olivaceum*	Caribbean	(Rinehart et al., 1987),(Blunt et al., 1987)
355	eudistomin E	1987			
356	eudistomin K	1987			
357	eudistomin L	1987			
358	eudistomin F	1987			
359	citorellamine	1985	*Polycitorella mariae*	Suva, Fiji	(Roll and Ireland, 1985),(Moriarty et al., 1987)
360	patellazole A	1988	*Lissoclinum patella*	Palau	(Zabriskie et al., 1988)
361	patellazole B	1988			
362	patellazole C	1988			
363	(4-hydroxy-3-methoxyphenyl)(thiazol-2-yl)methanone	1988	*Aplydium pliciferum*	Australian	(Arabshahi and Schmitz, 1988)
364	4-(hydroxy(thiazol-2-yl)methyl)-2-methoxyphenol	1988			
365	shermilamine A	1988	*Tridemnum* sp.	Pago Bay, Guam	(Cooray et al., 1988)
366	eudistomin K sulfoxide	1988	*Ritterella sigillinoides*	New Zealand	(Lake et al., 1988)
367	*cis*-5-hydroxy-4-(4′-hydroxy-3′-methoxyphenyl)-4-(2″-imidazolyl)-1,2,3-trithiane	1989	*Aplidium* sp.		(Copp et al., 1989)
368	debromoeudistomin K	1989	*Ritterella sigillinoides*		(Lake et al., 1989)
369	shermilamine B	1989	*Tridemnum* sp.	Pago Bay, Guam	(Carroll et al., 1989)
370	varamine A	1989	*Lissoclinum vareau*	Yasawa island chain, Fiji	(Molinski and Ireland, 1989)
371	varamine B	1989			
372	diplamine	1989	*Diplosomra* sp.	Fiji	(Charyulu et al., 1989)
373	eudistomidin C	1990	*Eudistoma glaucus*	Ie Island, Okinawan, Japan	(Kobayashi et al., 1990)
374	6-*O*-methyleudistomidin C	1990			
375	ecteinascidin 729	1990	*Ecteinascidia turbinata*	Caribbean	(Menchaca et al., 2003)
376	ecteinascidin 743	1990			
377	ecteinascidin 745	1990			
378	ecteinascidin 770	1990			
379	eudistomidin E	1991	*Eudistoma glaucus*	Ie Island, Okinawan, Japan	(Murata et al., 1991)
380	eudistomidin F	1991			
381	kuanoniamine A	1990	an unidentified Micronesian tunicate	Mante Channel, Pohnpei, Micronesia	(Carroll and Scheuer, 1990)
382	kuanoniamine B	1990			
383	lissoclinotoxin B	1994	*Lissoclinum perforatum*	Northern Brittany, France	(Litaudon et al., 1994)
384	lissoclin A	1994	*Lissoclinum* sp.	Great Barrier Reef	(Searle and Molinski, 1994)
385	lissoclin B	1994			
386	benzo-1,3-oxathiazoline	1994			
387	dehydrokuanoniamine B	1994	*Cystodytes* sp.	Fiji	(McDonald et al., 1994)
388	shermilamine C	1994			
389	didemnoline A	1995	*Didemnum* sp.	Rota, Northern Mariana Islands	(Schumacher and Davidson, 1995)
390	didemnoline B	1995			
391	didemnoline C	1995			
392	didemnoline D	1995			
393	ecteinascidin 597	1996	*Ecteinascidia turbinata*	Caribbean	(Sakai et al., 1996)
394	ecteinascidin 583	1996			
395	ecteinascidin 594	1996			
396	ecteinascidin 596	1996			
397	polycarpine	1996	*Polycarpa clavataPolycarpa aurata*	Western AustraliaChuuk, Federated States of Micronesia	(Kang and Fenical, 1996),(Abas et al., 1996)
398	4-methoxy-4-(4-methoxyphenyl)-1-methyl-5-thioxoimidazolidin-2-one	1996			
399	4-hydroxy-4-(4-methoxyphenyl)-1-methyl-5-thioxoimidazolidin-2-one	1996	*Polycarpa clavata*	Western Australia	(Kang and Fenical, 1996)
400	*N*-methyl-(4-methoxyphenyl)-2-oxothioacetamide	1996	*Polycarpa aurata*	Chuuk, Federated States of Micronesia	(Abas et al., 1996)
401	polycarpine dihydrochloride	1996			

Table 4 (*continued*)

No.	Compounds	Time	From	Location	Ref.
402	the 20-sulfate of lamellarins T	1997	An unidentified ascidian	Arabian Sea (near India)	(Reddy et al., 1997)
403	the 20-sulfate of lamellarins U	1997			
404	the 20-sulfate of lamellarins V	1997			
405	the 20-sulfate of lamellarins Y	1997			
406	shermilamine D	1998	*Cystodytes violatinctus*	Mayotte lagoon, ComorosIslands, Madagascar	(Koren-Goldshlager et al., 1998)
407	shermilamine E	1998			
408	tintamine	1998			
409	the 20-sulfates of lamellarin B	1999	Didemnum chartaceum	Great Barrier Reef	(Davis et al., 1999)
410	the 20-sulfates of lamellarin C	1999			
411	the 20-sulfates of lamellarin L	1999			
412	the 20-sulfates of lamellarin G	1999			
413	lamellarin α 20-sulfate	1999	an unidentified ascidian	Arabian Sea(near Trivandrum, India)	(Reddy et al., 1999)
414	cycloshermilamine D	2000	*Cystodytes violatinctus*	Mayotte lagoon, ComorosIslands, Madagascar	(Koren-Goldshlager et al., 2000)
415	(−)-enantiomer	2001	*Hypsistozoa fasmeriana*	New Zealand	(Pearce et al., 2001)
416	fasmerianamine A	2001			
417	fasmerianamine B	2001			
418	14-methyleudistomidin C	2001	*Eudistoma gilboverde*	Sias Tunnel, Palau	(Rashid et al., 2001)
419	(2*E*,4′*R*,5′*S*,6′*R*,7′*R*,8′*S*,2′′′*E*)-3-{8′-hydroxy-4′,6′-dimethyl-4′-(3′′-methylenepent-4′′-enyl)-7′-(-L-mannopyranosyloxy)-[1′,2′,3′]-trithiocan-5′-yl}-*N*-[4′′′-(3′′′-methylsulfanylacryloylamino)-butyl]aerylamide	2002	*Perophora viridis*	Atlantic coast (near North Carolina)	(Řezanka and Dembitsky, 2002)
420	isodiplamine	2002	*Lissoclinum notti*	Leigh Harbour, Northland, New Zealand	(Appleton et al., 2002)
421	lissoclinidine	2002			
422	varacin	2002			
423	kuanoniamine E	2002	an unidentified Singaporean ascidian	Pulau Subar Laut, Singapore	(Nilar et al., 2002)
424	kuanoniamine F	2002			
425	ecteinascidin 770	2002	*Ecteinascidia thurstoni*	Phuket Island, Thai	(Suwanborirux et al., 2002)
426	ecteinascidin 786	2002			
427	ecteinascidin 759B	2002			
428	conicaquinone A	2003	*Aplidium conicum*	Capo Caccia, Alghero, Italy	(Aiello et al., 2003)
429	conicaquinone B	2003			
430	kottamide E	2003	*Pycnoclavella kottae*	New Zealand	(Appleton and Copp, 2003)
431	shishijimicin A	2003	*Didemnum proliferum*	South Japan	(Oku et al., 2003)
432	shishijimicin B	2003			
433	shishijimicin C	2003			
434	namenamicin	2003			
435	methylthioadenosine	2004	*Atriolum robustum*	Heron Islands, Wistari Reef, Great Barrier Reef	(Kehraus et al., 2004)
436	methylsulfinyladenosine	2004			
437	violatinctamine	2004	*Cystodytes* cf. *violatinctus*	Kenya	(Chill et al., 2004)
438	ecteinascidin 731	2004	*Ecteinascidia turbinata*	Caribbean	(Blunt et al., 2006)
439	ecteinascidin 745b	2004			
440	ecteinascidin 808	2004			
441	ecteinascidin 815	2004			
442	ascidiathiazone A	2007	*Aplidium* sp.	Tom Bowling Bay, Northland, New Zealand	(Pearce et al., 2007)
443	ascidiathiazone B	2007			
444	polycarpaurine A	2007	*Polycarpa aurata*	Lembeh Strait, Indonesia	(Wang et al., 2007)
445	polycarpaurine B	2007			
446	polycarpaurine C	2007			
447	nordehydrocyclodercitin	2007	*Aplidium* sp.	Arab Reef, Australia	(Agrawal and Bowden, 2007)
448	diplamine B	2008	*Lissoclinum* cf. *badium*	Port Moresby,Papua New Guinea	(Clement et al., 2008)
449	lissoclinidine B	2008			
450	isolissoclinotoxin B	2008			
451	*N*,*N*-dimethyl-5-methylvaracin	2008			
452	leptoclinidamine C	2009	*Leptoclinides durus*	Heron island, Queensland, Australia	(Carroll and Avery, 2009)

(*continued on next page*)

Table 4 (*continued*)

No.	Compounds	Time	From	Location	Ref.
453	*N*-deacetylshermilamine B	2010	*Cystodytes dellechiajei*	Catalonia, Spain	(Bontemps et al., 2010)
454	*N*-deacetylkuanoniamine D	2010			
455	eudistomidin J	2011	*Eudistoma glaucus*	Ie island, Okinawa, Japan	(Suzuki et al., 2011)
456	13-didemethylaminoshermilamine D	2011	*Cystodytes dellechiajei*	Catalonia, Spain	(Bry et al., 2011)
457	polycarpathiamine A	2013	*Polycarpa aurata*	Ambon, Indonesia	(Pham et al., 2013)
458	polycarpathiamine B	2013			
459	duramidine A	2013	*Leptoclinides durus*	Swains Reef, Great Barrier Reef	(Rudolph et al., 2013)
460	duramidine C	2013			
461	leptoclinidamine D	2013			
462	leptoclinidamine E	2013			
463	leptoclinidamine F	2013			
464	momusine A	2013	*Herdmania momus*	Jeju island, Korea	(Li et al., 2013)
465	momusine B	2013			
466	momusine C	2013			
467	momusine D	2013			
468	conthiaquinone A	2013	*Aplidium conicum*	Porto Cesareo, Lecce, Italy	(Menna et al., 2013)
469	conthiaquinone B	2013			
470	shermilamine F	2013	*Cystodytes violatinctus*	Solomon islands	(Bontemps et al., 2013)
471	dehydrokuanoniamine F	2013			
472	salvadenosine	2014	*Didemnum* sp.	Little San Salvador island, Bahamas	(Jamison et al., 2014)
473	tanjungide A	2014	*Diazona cf formosa*	East Timor	(Murcia et al., 2014)
474	tanjungide B	2014			
475	stolonine A	2015	*Cnemidocarpa stolonifera*	Peel island, Australia	(Tran et al., 2015)
476	stolonine B	2015			
477	stolonine C	2015			
478	sagitol D	2015	an unidentified Vietnamese ascidian	PhuQuok, Vietnam	(Utkina, 2015)
479	lepadin I	2018	*Didemnum* sp.	Stirrup Cay, Bahamas	(Ómarsdóttir et al., 2018)
480	lepadin J	2018			
481	lepadin K	2018			
482	siladenoserinol M	2018	*Didemnum* sp.	Siladen, North Sulawesi, Indonesia	(Torii et al., 2018)
483	siladenoserinol N	2018			
484	siladenoserinol O	2018			
485	siladenoserinol P	2018			
486	polyaurine B	2019	*Polycarpa aurata*		(Casertano et al., 2019)
487	lamellarin K-20-sulfate	2019	*Didemnum ternerratum*	Eua, Kingdom of Tonga	(Bracegirdle et al., 2019)
488	lamellarin E-20-sulfate	2019			
489	lamellarin A3-20-sulfate	2019			
490	lamellarin B1-20-sulfate	2019			
491	lamellarin D-8-sulfate	2019			
492	lamellarin B2-20-sulfate	2019			
493	ireneamide A	2020	*Cnemidocarpa irene*	Oshima-Kojima Islet off the Oshima Peninsula, Hokkaido, Japan	(Miyako et al., 2020)
494	ireneamide B	2020			
495	ireneamide C	2020			
496	6-biopterin-2′-sulfate	2020			
497	6-biopterin-1′-2′-disulfate	2020			
498	3-methyl-6-biopterin-2′-sulfate	2020			
499	siladenoserinol A	2013	a tunicate of the family Didemnidae	NorthSulawesi, Indonesia	(Nakamura et al., 2013)
500	siladenoserinol B	2013			
501	siladenoserinol C	2013			
502	siladenoserinol D	2013			
503	siladenoserinol E	2013			
504	siladenoserinol F	2013			
505	siladenoserinol G	2013			
506	siladenoserinol H	2013			
507	siladenoserinol I	2013			
508	siladenoserinol J	2013			
509	siladenoserinol K	2013			
510	siladenoserinol L	2013			

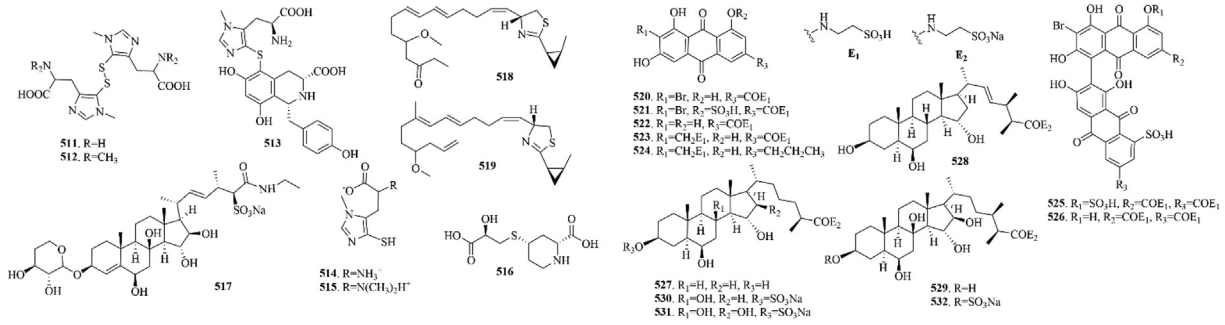

Fig. 8 Sulphur-containing alkaloids from marine echinoderms.

Table 5 Sulphur-containing alkaloids from marine echinoderms.

No.	Compounds	Time	From	Location	Ref.
Marine echinoderms					
511	bis(l-methyl-L-histidin-5-yl) disulphide	1986	unfertilized echinoderm eggs	–	(Faulkner, 1986)
512	bis(N^{α}.N^{α},l-trimethyI-L-histidin-5-yl)disulphide	1986	unfertilized echinoderm eggs		
513	imbricatine	1986	*Dermasterias imbricata*	–	(Pathirana and Andersen, 1986)
514	ovothiol A	1986	*Evasterias troschelii*	–	(Turner et al., 1987)
515	ovothiol C	1986	*Strongylocentrotus purpuratus*	–	
516	pucherrimine	2000	*Hemicentrotus pulcherrimus*	Japanese sea	(Murata and Sata, 2000)
517	fisherioside A	2012	*Leptasterias fisheri*	Sakhalin island, Sea of Okhotsk	(Kicha et al., 2012)
518	curacin E	2016	*Ophiocoma scolopendrina*	Kabira Reef, Ishigaki island, Okinawa, Japan	(Ueoka et al., 2016)
519	curacin A	2016			
520	hypalocrinin A	2019	*Hypalocrinus naresianus*	Shima Spur, Kumano-nada Sea, Japan	(Wolkenstein et al., 2019)
521	hypalocrinin B	2019			
522	hypalocrinin C	2019			
523	hypalocrinin D	2019			
524	hypalocrinin E	2019			
525	hypalocrinin F	2019			
526	hypalocrinin G	2019			
527	microdiscusol A	2019	*Asterias microdiscus*	Eastern part of the Chukchi Sea, Arctic Ocean	(Kicha et al., 2019)
528	microdiscusol B	2019			
529	microdiscusol C	2019			
530	microdiscusol D	2019			
531	microdiscusol E	2019			
532	microdiscusol F	2019			

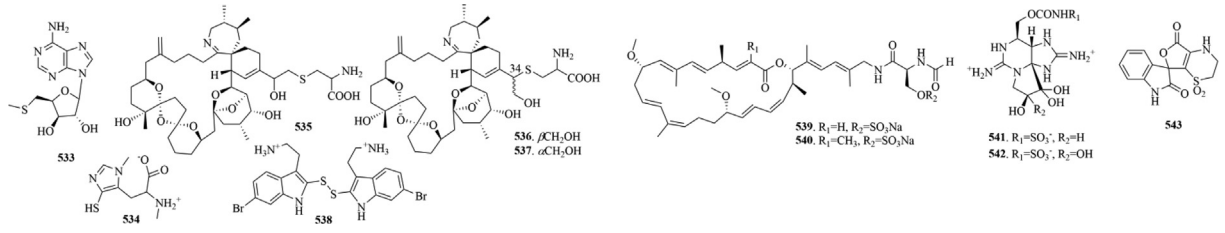

Fig. 9 Sulphur-containing alkaloids from marine molluscs.

Table 6 Sulphur-containing alkaloids from marine molluscs.

No.	Compounds	Time	From	Location	Ref.
Marine Molluscs					
533	9-(5-deoxy-5-methylthio-β-D-xylofuranosyl)adenine	1986	Extracts of the digestive gland of the dorid nudibranch*Doris verrucosa*	–	(Faulkner, 1988)
534	ovothiol B	1986	*Chlamys hastata*	–	(Turner et al., 1987)
369	shermilamine B	1990	*Chelynotus semperi*	Mante Channel, Pohnpei, Federated States of Micronesia	(Carroll and Scheuer, 1990)
381	kuanoniamine A	1990			
382	kuanoniamine B	1990			
82	kuanoniamine C	1990			
83	kuanoniamine D	1990			
535	pteriatoxin A	2001	*Pteria penguin*	Okinawa, Japan	(Takada et al., 2001)
536	pteriatoxin B	2001			
537	pteriatoxin C	2001			
538	the disulfide-linked dimer of 6-bromo-2-mercaptotryptamine	2003	*Calliostoma canaliculatum*	Monterey Bay, California	(Kelley et al., 2003)
539	iejimalide C	2006	*Eudistoma* cf. *rigida*	Okinawa, Japan	(Kikuchi et al., 1991)
540	Iejimalide D	2006			
541	11β-hydroxy-N-sulfocarbamoylsaxitoxin	2008	*Wild mussels (Mytilus edulis* and*Mytilus trossulus)*	Eastern Canada coasts	(Dell'Aversano et al., 2008)
542	11,11-dihydroxy-N-sulfocarbamoylsaxitoxin	2008			
543	orbicularisine	2017	*Codakia orbicularis*	Guadeloupe	(Goudou et al., 2017)

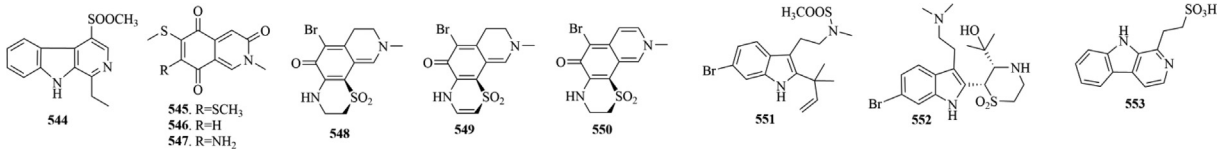

Fig. 10 Sulphur-containing alkaloids from marine bryozoans.

Table 7 Sulphur-containing alkaloids from marine bryozoans.

No.	Compounds	Time	From	Location	Ref.
Marine Bryozoans					
544	1-ethyl-4-methylsulfone-β-carboline	1991	*Cribricellina cribraria*	New Zealand	(Prinsep et al., 1991)
545	perfragilin B	1993	*Membranipora perfragilis*	Rapid Bay, South Australia	(Choi et al., 1993)
546	2-methyl-6-methylthioisoquinoline-3,5,8(2*H*)trione	1993	*Blflustra perfragilis*	Bass Strait	(Blackman et al., 1993)
547	perfragilin A	1993	*Membranipora perfragilis*	Rapid Bay, South Australia	(Choi et al., 1993)
548	euthyroideone A	1998	*Euthyroides episcopalis*	Fiordland, New Zealand	(Morris and Prinsep, 1998)
549	euthyroideone B	1998			
550	euthyroideone C	1998			
551	*N*-(2-[6-bromo-2-(1,1-dimethyl-2-propenyl)-1H-indol-3-yl] ethyl)-N-methy-lmethanesulfonamide	2002	*Flustra foliacea*	"Steingrund", North Sea, Helgoland, Germany	(Peters et al., 2002)
552	flustramine R	2020	*Flustra foliacea*	Iceland	(Di et al., 2020)
553	orthoscuticelline E	2020	*Orthoscuticella ventricosa*	Korora beach, Coffs Harbour, NSW, Australia	(Kleks et al., 2020)

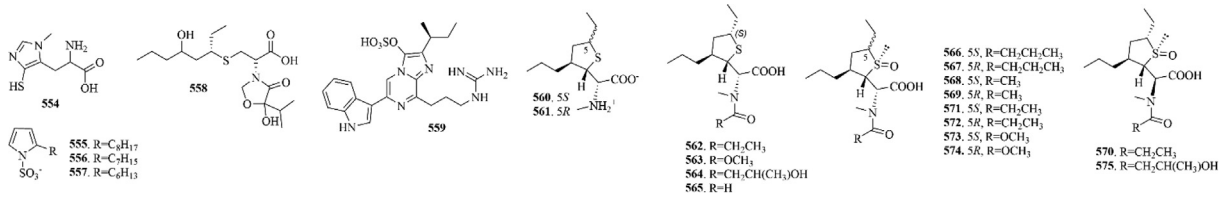

Fig. 11 Sulphur-containing alkaloids from other marine animals.

Table 8 Sulphur-containing alkaloids from other marine animals.

No.	Compounds	Time	From	Location	Ref.
Other marine animals					
554	L-ovithiol A	1999	*Platynereis dumerilii*	–	(Röhl et al., 1999)
555	2-*n*-octylpyrrole sulfamate	2003	*Cirriformia tentaculata*	Florida	(Barsby et al., 2003)
556	2-*n*-heptylpyrrole sulfamate	2003			
557	2-*n*-hexylpyrrole sulfamate	2003			
558	thelepamide	2014	*Thelepus crispus*	Friday Harbor, WA, U.S.A.	(Rodríguez et al., 2014)
559	cypridina luciferyl sulfate	2014	*Vargula hilgendorfii*	Chita, Aichi, Japan	(Nakamura et al., 2014)
560	nebulosin A	2020	*Eupolymnia nebulosa*	Intertidal area of Corranroo, West coast of Ireland	(Calabro et al., 2020)
561	nebulosin B	2020			
562	nebulosin C	2020			
563	nebulosin D	2020			
564	nebulosin E	2020			
565	nebulosin F	2020			
566	nebulosin G	2020			
567	nebulosin H	2020			
568	nebulosin I	2020			
569	nebulosin J	2020			
570	nebulosin K	2020			
571	nebulosin L	2020			
572	nebulosin M	2020			
573	nebulosin N	2020			
574	nebulosin O	2020			
575	nebulosin P	2020			

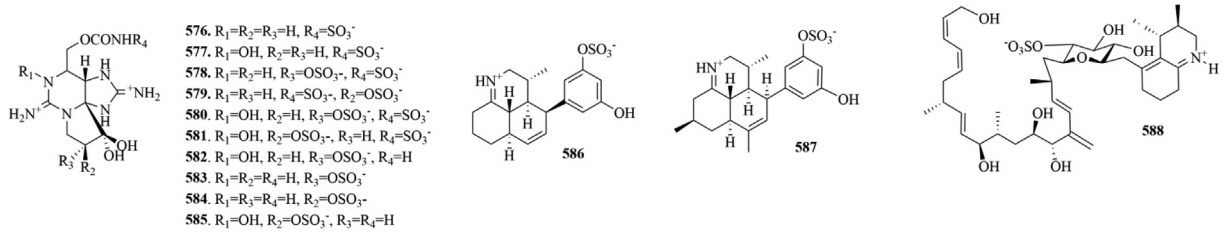

Fig. 12 Sulphur-containing alkaloids from dinoflagellates.

1.2.2.5. Marine molluscs. Molluscs, a kind of soft marine animal usually with a calcareous shell, are the largest group of animals in the ocean, with more than 100,000 species, more than half of which live in the ocean. Mollusks have 7 classes, including *Aplacophora*, *Bivalvia*, *Monoplacophora*, *Polyplacophora*, *Scaphopoda*, *Gastropoda* and *Cephalopoda*. These mollusks are widely distributed, from the cold, temperate to tropical, from the highest point of the intertidal zone to 10,000 m deep at the bottom of the ocean.

16 (**533–543, 82–83, 369, 381–382**) sulphur-containing alkaloids were reported from the marine molluscs (Fig. 9 and Table 6). Notably, pteriatoxins A-C (**535–537**) are a group of cyclic imine toxins only isolated from Japanese shellfish, which can cause rapid death in mouse (Selwood et al., 2010). Now pteriatoxins have been considered emerging toxins in the European Union and a scientific opinion has been published by the European Food Safety Authority in which an assessment of the risks to human health related to their consumption has been carried out (Moreiras et al., 2020).

Table 9 Sulphur-containing alkaloids from dinoflagellates.

No.	Compounds	Time	From	Location	Ref.
Dinoflagellates					
576	toxin B1	1984	*Protugonyaulax catenella*	Northeast Pacific	(Hall et al., 1984)
577	toxin B2	1984			
578	toxin C1	1984			
579	toxin C2	1984			
580	toxin C3	1984			
581	toxin C4	1984			
582	GTX-1	1984			
583	GTX-2	1984			
584	GTX-3	1984			
585	GTX-4	1984			
586	symbioimine	2004	*Symbiodinium* sp.	Sesoko Island, Okinawa, Japan.	(Kita et al., 2004)
587	neosymbioimine	2005			(Kita et al., 2005)
588	ovataline	2022	*Ostreopsis* cf. *ovata*	Kimyong, Jeju island	(Lee et al., 2022)

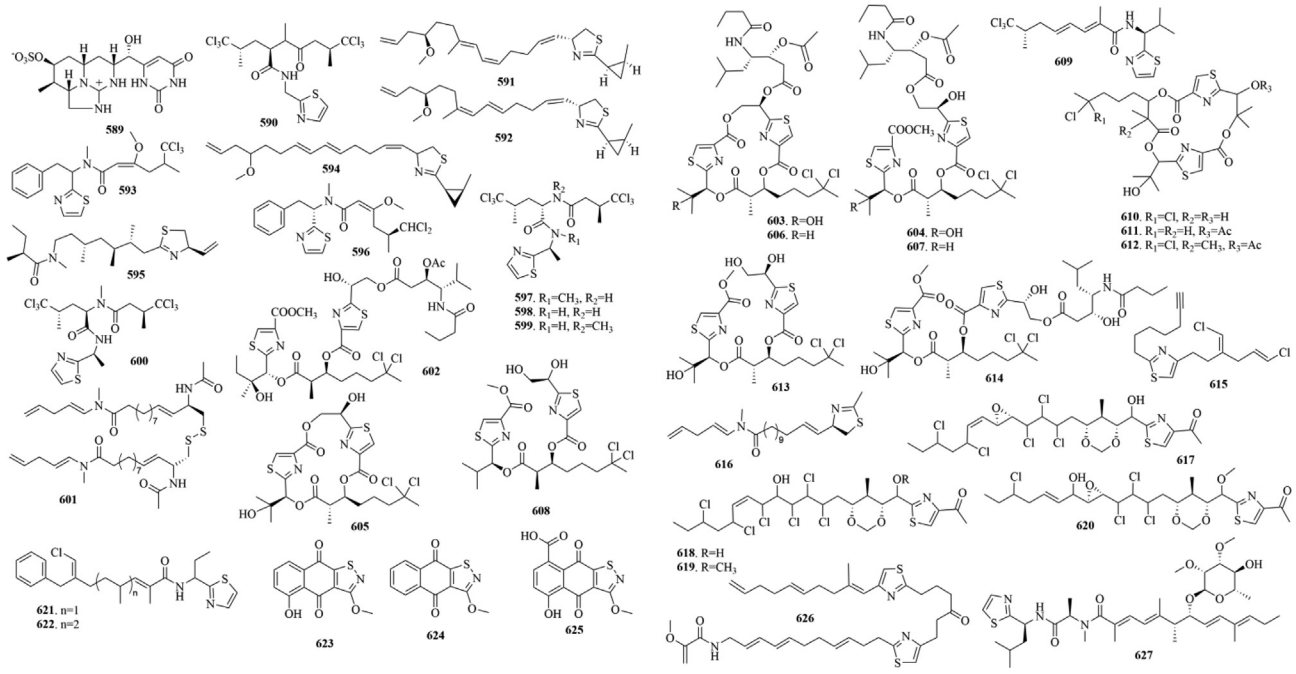

Fig. 13 Sulphur-containing alkaloids from cyanobacteria.

1.2.2.6. Marine bryozoans. Bryozoans are bryophyte-like animals, which had complete digestive apparatus, including the mouth, esophagus, stomach, intestines and anus. The individual bryozoans are small and undivided, with a body cavity. Their bones are formed by a layer of colloid which was secreted in vitro. They can devour microorganisms and organic impurities in water and have a positive effect on water purification.

10 (**544**–**553**) sulphur-containing alkaloids were reported from the marine bryozoans (Fig. 10 and Table 7). Perfragilin A (**547**) and B (**545**) were isolated from *Membranipora perfragilis*. As cytotoxic isoquinolines quinone, they contain a relatively uncommon thiomethyl ether functionality. And Both perfragilin A and B were toxic to murine leukemia cells (P388), with perfragilin B being considerably more potent: ED_{50} = 0.8 and 0.07 μg/ml, respectively (Choi et al., 1993).

1.2.2.7. Other marine animals. 22 (**554**–**575**) sulphur-containing alkaloids were reported from other marine animals (Fig. 11 and Table 8). Of them, nebulosins A-P (**560**–**575**) were reported from the northeastern Atlantic marine terebellid *Eupolymnia nebulosa*. It's worth noting that nebulosins feature an unprecedented highly substituted thiolane ring leading to up to four contiguous chiral centers (Calabro et al., 2020).

Table 10 Sulphur-containing alkaloids from cyanobacteria.

No.	Compounds	Time	From	Location	Ref.
Cyanobacteria					
589	cylindrospermopsin	1992	*Cylindrospermopsis raciborskii*	Palm Island, Queensland, Australia	(Ohtani et al., 1992)
590	13-demethylisodysidenin	1993	*Oscillatoria spongeliae*	–	(Faulkner, 1995)
591	curacin B	1995	*Lyngbya majuscula*	Curaçao, Caribbean sea	(Yoo and Gerwick, 1995)
592	curacin C	1995			
593	barbamide	1996			(Orjala and Gerwick, 1996)
519.	curacin A 519	1998		Virgin Islands, British	(Márquez et al., 1998)
594	curacin D	1998			
595	kalkitoxin	2000		Curaçao, Caribbean sea	(Yokokawa et al., 2004)
596	dechlorobarbamide	2000			(Sitachitta et al., 2000)
597	pseudodysidenin	2001	*Lyngbya majuscula*	Boca del Drago Beach, Bocas del Toro, Panama	(Jiménez and Scheuer, 2001)
598	nordysidenin	2001			
599	dysidenin	2001			
600	isodysidenin	2001			
61.	dysideathiazole 61	2001			
601	somocystinamide A	2002	*Lyngbya majuscula* and*Schizothrix* sp.	Fijian	(Nogle and Gerwick, 2002)
602	lyngbyabellin D	2003	*Lyngbya* sp.	Guam, U.S.A.	(Williams et al., 2003)
603	lyngbyabellin E	2005	*Lyngbya majuscula*	Alotau Bay, Papua New Guinea	(Han et al., 2005)
604	lyngbyabellin F	2005			
605	lyngbyabellin G	2005			
606	lyngbyabellin H	2005			
607	lyngbyabellin I	2005			
608	dolabellin	2005			
609	herbamide B	2010		Bocas del Toro, Panama	(Balunas et al., 2010)
610	hectochlorin B	2015	*Moorea producens*	–	(Paul and Boudreau, 2015)
611	hectochlorin C	2015			
612	hectochlorin D	2015			
613	lyngbyabellin O	2017	*Okeania* sp.	Algetah Alkabira reef, Jeddah, Saudi Arabia	(Petitbois et al., 2017)
614	lyngbyabellin P	2017			
615	trichothiazole A	2017	*Trichodesmium* sp.	Gulf of Mexico	(Belisle et al., 2017)
616	laucysteinamide A	2017	*Caldora penicillata*	Lau Lau Bay, Saipan	(Zhang et al., 2017a)
617	aranazole A	2018	*Fischerella* sp. PCC 9339	–	(Moosmann et al., 2018)
618	aranazole B	2018			
619	aranazole C	2018			
620	aranazole D	2018			
621	isoconulothiazole B	2019	*Trichodesmium* sp.	Mayaguana Island, Bahamas	(Teta et al., 2019)
622	conulothiazole C	2019			
623	aulosirazole A	2022	*Nostoc* sp. UIC 10771	Reykjavık, Iceland	(Davis et al., 2022)
624	aulosirazole B	2022			
625	aulosirazole C	2022			
626	caldorazole	2022	*Caldora* sp.	Ishigaki Island, Okinawa, Japan	(Ohno et al., 2022)
627	iezoside	2022	*Leptochromothrix valpauliae*	Ie Island, Okinawa, Japan,	(Kurisawa et al., 2022)

1.3. Marine microorganism

1.3.1. Dinoflagellates

Dinoflagellates are a group of single cells with double flagella, whose shape is variable. They have both plant and animal characteristics, which could perform photosynthesis and move by the rotation of two flagella. Dinoflagellates are widely distributed, especially in tropical oceans. When the light and water temperature are appropriate, dinoflagellates can multiply in a short period of time to become the main feed of marine animals.

13 (**576**–**588**) sulphur-containing alkaloids were reported from dinoflagellates (Fig. 12 and Table 9). Among them, compounds **576**–**585** are thought as the carbamoyl-N-sulfo derivatives of saxitoxin and neosaxitoxin (Hall et al., 1984). In addition, it's worth noting that symbioimine (**586**) and neosymbioimine (**587**) both have a characteristic 6,6,6-tricyclic iminium ring structure and an aryl sulfate moiety. And the plausible biogenetic pathway of them can be explained by an intramolecular Diels-Alder reaction followed by imine cyclization (Kita et al., 2005).

1.3.2. Cyanobacteria

Cyanobacteria, also known as blue-green algae, are large, single-celled prokaryotes with a long evolutionary history. They have chlorophyll which enabled them to perform oxygen-producing photosynthesis. The photosynthesis of cyanobacteria is also thought as the reason why the earth's atmosphere develops from an anaerobic state to an aerobic state. At present, there are about 2000 species of cyanobacteria, which are mainly divided into two classes: *Chroococcus* and *Phytoplankton*. As highly adaptable organisms, they are widely distributed in all kinds of natural water bodies, soil and some organisms, even in the rock surface and other harsh environments.

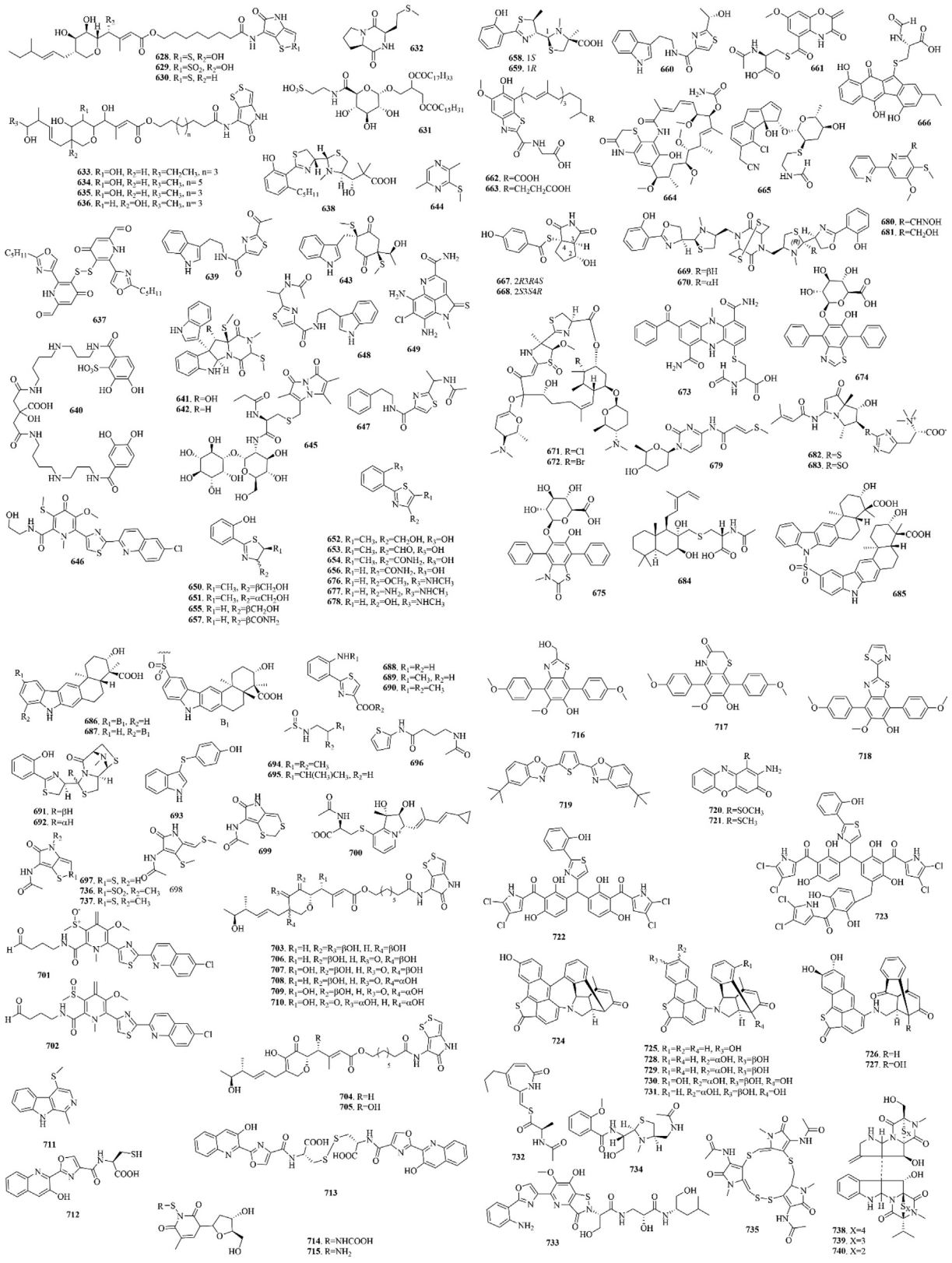

Fig. 14 Sulphur-containing alkaloids from marine bacteria.

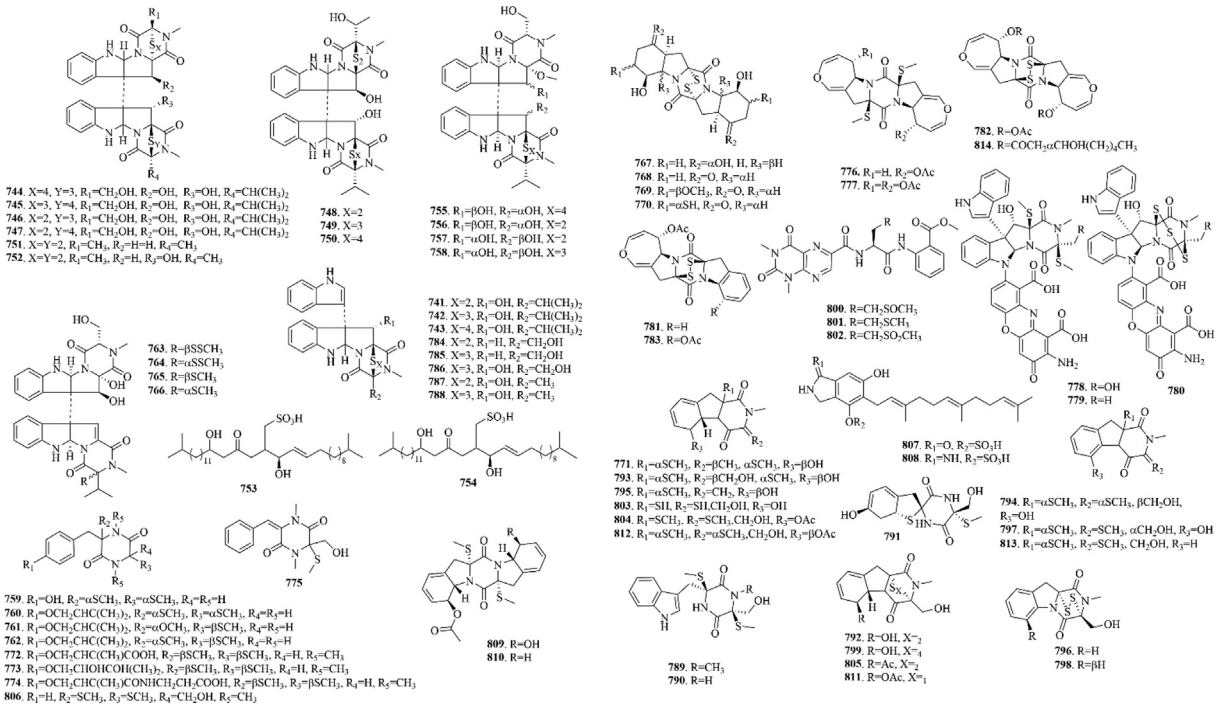

Fig. 14 (*continued*)

41 (**589–627, 61, 519**) sulphur-containing alkaloids were reported from cyanobacteria (Fig. 13 and Table 10). Curacins A-D (**519, 591–592** and **594**) are toxic metabolites isolated from the cyanobacteria, which are thought of as antimitotic agents. In addition, lyngbyabellins are a kind of depsipeptide derivatives, whose typical structural features are two thiazole rings and a chlorinated 2-methyloctanoate residue (Choi et al., 2012). They generally display various activities such as cytotoxicity, antimalarial, and antifouling activities (Fathoni et al., 2020). Lyngbyabellins O (**613**) and P (**614**) both exhibit strong antifouling activity, which may be related to the fact that compounds don't have a side chain (Petitbois et al., 2017). Notably, aulosirazoles A-C (**623–625**) are the structurally unique isothiazolonaphthoquinone aulosirazole, which possess selective antitumor cytotoxicity. Although its mechanism of action is unknown, biological evaluation of them identified one potential target as the immunoregulatory enzyme indoleamine-2,3-dioxygenase (IDO) (Blunt et al., 2015).

1.3.3. Marine bacteria

Marine bacteria are the most important members of marine microorganisms, which are widely distributed and abundant in the ocean. The common bacteria include *Pseudomonas*, *Vibrio*, *Achromobacter*, *Nocardia* and *Streptomyces*. Almost all known bacteria can be found in the marine environment. Meanwhile, most marine bacteria are decomposers, which play an important role in the whole process of marine material decomposition and transformation. Moreover, because the deep-sea environment has the characteristics of high salt, high pressure, low temperature and low nutrition, the physiological and ecological characteristics of deep-sea bacteria are very different from those of terrestrial bacteria. This is also the reason why scientists are paying more attention to deep-sea bacteria.

110 (**628–737**) sulphur-containing alkaloids were reported from marine bacteria (Fig. 14 and Table 11). Notably, thiomarinols are a kind of naturally occurring double-headed antibiotic, whose structure comprises two antimicrobial subcomponents, pseudomonic acid analogue and holothin, linked by an amide bond (Dunn et al., 2015). Such ingredients usually have excellent antibacterial activity and can even be effective against MRSA (Shiozawa et al., 1995). And sulfadiximycins A-C (**685–687**), sulfonyl-bridged alkaloid dimers, are isolated from recombinant *Streptomyces* species. They have both aromatic sulfonamide and diarylsulfone substructures. In addition, sungeidines A-H (**724–731**), a class of microbial secondary metabolites with unique structural features, are likely to be assembled from two octaketide chains following processing by oxygenases/oxidases and cyclases.

1.3.4. Marine fungi

The distribution of fungi in the ocean mainly depended on the distribution of hosts. According to their habitat habits, marine fungi could be divided into four basic ecological types: (1) woody fungi. The largest number and most widely distributed higher fungi in marine waters is saprophytic life. (2) Parasitic algae fungi. It accounted for about 1/3 of the number of marine fungal species, most of which were ascomycetes. (3) Seaweed fungi. The number of seaweed fungi was small and mostly inhabited the leaves. (4) Parasitic animal fungi. Only parasitic in the exoskeleton and shell. Marine fungi participate in the decomposition of marine organic matter and the regeneration of inorganic nutrients and continuously provide effective nutrition for marine plants.

197 (**738–934**) sulphur-containing alkaloids were reported from marine fungi (Fig. 15 and Table 12). It's worth noting that leptosins, amphiepicoccins (**912–921**), penicisulfuranols (**869–874**), gliotoxins and chetracins E, F, C (**875, 876, 877**) all are epipolythiodioxopiperazines (ETPs) which are a class of biologically active fungi secondary metabolites characterized by a unique bridged disulfide or polysulfide dioxopiperazine six-membered ring (Gardiner et al., 2005). These compounds occur in many fungi. And due to their broad spectra of bioactivities, ETPs have drawn wide attention in recent years (Jiang and Guo, 2011). Moreover, graphiumins A-J (**814–823**), rostratins A-D (767–770), aranotins (**777, 781–783, 904**) and eutypellazines A-S (**849–866**) all are thiodiketopiperazine alkaloids. Among them, eutypellazines N-P (**861–863**) are characteristic of unique spirocyclic skeletons. Meanwhile, eutypellazines N-O bearing a spirocyclic tetrahydrobenzothiophene motif is found in wide-type fungus for the first time (Niu et al., 2017b). In summary, thiodioxopiperazines are the main type of sulphur-containing alkaloids in fungi.

Table 11 Sulphur-containing alkaloids from marine bacteria.

No.	Compounds	Time	From	Location	Ref.
Marine bacteria					
628	thiomarinol A(Thiomarinol)	1993	*Alteromonas raw* sp. *nov*. SANK 73390	–	(Shiozawa et al., 1993)
629	thiomarinol B	1995			(Shiozawa et al., 1995)
630	thiomarinol C	1995			
631	1,2-diacyl-3-α-d-glucuronopyranosyl-sn-glycerol taurineamide	1996	*Hyphomonas jannaschiana*	–	(Batrakov et al., 1996)
632	cyclo(L-Pro-L-Met)	1996	*Pseudomonas aeruginosa*	Ross Island, Antarctica	(Jayatilake et al., 1996)
633	thiomarinol D	1997	*Alteromonas raw* sp.	–	(Shiozawa et al., 1997)
634	thiomarinol E	1997	*nov*. SANK 73390		
635	thiomarinol F	1997			
636	thiomarinol G	1997			
637	B-90063	1998	*Blastobacter* sp. SANK 71894	Japan	(SACHIKO TAKAISHI, 1998)
638	agrochelin	1999	*Agrobacterium* sp.	–	(Cañedo et al., 1999)
639	bacillamide A	2011	*Bacillus* sp.	Masan Bay, Korea.	(Zou et al., 2011)
640	petrobactin sulfonate	2004	*Marinobacter hydrocarbonoclasticus*	–	(Hickford et al., 2004)
641	gliocladin A	2004	*Gliocladium* sp.	Coast of Kata, Wakayama Prefecture, Japan	(Yoshihide Usami, 2004)
642	gliocladin B	2004			
643	glioperazine	2004			
644	2,5-dimethyl-3-(methylsulfanyl) pyrazine	2005	*Alphaproteobacteria Loktanella* sp.	North Sea	(Dickschat et al., 2005)
645	*N*-propionyl-desacetyl-mycothiol	2008	MAR2 strain CNQ703	Guam	(Newton et al., 2008)
646	lodopyridone	2009	*Saccharomonospora* sp.	La Jolla, California	(Maloney et al., 2009)
647	neobacillamide A	2009	*Bacillus vallismortis*	Sanya island, South China Sea	(Yu et al., 2009)
648	bacillamide C	2009			
649	ammosamide A	2009	*Streptomyces* sp.	Bahamas	(Hughes et al., 2009)
650	pulicatin A	2010	*Streptomyces* sp.	Mactan island, Cebu, Philippines	(Lin et al., 2010)
651	pulicatin B	2010			
652	pulicatin C	2010			
653	pulicatin D	2010			
654	pulicatin E	2010			
655	aerugine	2010			
656	pulicatin F	2010			
657	pulicatin G	2010			
658	watasemycin A	2010			
659	watasemycin B	2010			
660	bacillamide B	2009	*Bacillus endophyticus*	Sanya island, South China Sea	(Yu et al., 2009), (Sun et al., 2015)
661	benzoxacystol	2011	*Streptomyces griseus*	deep sea sediment, Canary Basin	(Nachtigall et al., 2011)
662	erythrazole A	2011	*Erythrobacter* sp.	Trinity Bay, Galveston, Texas, U. S.A.	(Hu and MacMillan, 2011)
663	erythrazole B	2011			
664	heronamycin A	2012	*Streptomyces* sp.	Heron island, Queensland, Australia	(Raju et al., 2012)
665	cyanosporaside F	2013	*Streptomyces* sp.	Bahamas	(Lane et al., 2013)
666	(−)-homoseongomycin	2013	*Salinispora pacifica* DPJ-0019	–	(Woo et al., 2013)
667	nitrosporeusine A	2013	*Streptomyces nitrosporeus*	Arctic Chukchi Sea	(Yang et al., 2013)
668	nitrosporeusine B	2013			
669	tetroazolemycin A	2013	Streptomyces olivaceus	southwest Indian Ocean	(Liu et al., 2013)
670	tetroazolemycin B	2013			
671	forazoline A	2014	*Actinomadura* sp.	Florida, U.S.A.	(Wyche et al., 2014)
672	forazoline B	2014	WMMB-499		
673	dermacozine J	2014	*Dermacoccus abyssi*	Challenger Deep,	(Wagner et al.,

Table 11 (*continued*)

No.	Compounds	Time	From	Location	Ref.
				Mariana Trench	2014)
674	echoside D	2014	*Streptomyces* sp.	Jimei, China	(Deng et al., 2014)
675	echoside E	2014			
676	anithiactin A	2014	*Streptomyces* sp.	Jaebu island, South	(Kim et al., 2014b)
677	anithiactin B	2014		Korea	
678	anithiactin C	2014			
679	streptcytosine B	2014	*Streptomyces* sp.	Iriomote island,	(Bu et al., 2014)
680	collismycin B	2014		Japan	
681	SF2738 C	2014			
682	spithioneine A	2015	*Streptomyces*	Bahamas	(Fu and
683	spithioneine B	2015	*spinoverrucosus*		MacMillan, 2015a)
684	*N*-acetyl-S-(((1*R*,2*S*,3*S*,4a*S*,8a*S*)-2,3-dihydroxy-5,5,8a-trimethyl-1-((*E*)-3-methylpenta-2,4-dien-1-yl) decahydronaphthalen-2-yl)methyl)-L-cysteine	2015	*Streptomyces* sp.	Parangipettai, India	(Shanthi et al., 2015)
685	sulfadixiamycin A	2015	*Streptomyces* sp.	–	(Baunach et al.,
686	sulfadixiamycin B	2015			2015)
687	sulfadixiamycin C	2015			
688	thiasporine A	2015	*Actinomycetospora*	Vava'u, Tonga	(Fu and
689	thiasporine B	2015	*chlora*		MacMillan,
690	thiasporine C	2015			2015b),(Seitz et al., 2016)
691	ulbactin F	2016	*Brevibacillus* sp.	Ohtsuchi, Iwate,	(Igarashi et al.,
692	ulbactin G	2016		Japan	2016)
693	4-(1*H*-indol-3-yl-sulfanyl)phenol	2016	*Vibrio splendidus*	S. Orkney island	(Nair et al., 2016)
694	*N*-isobutylmethanesulfinamide	2017	*Salinispora pacifica*	Fiji	(Harig et al., 2017)
695	*N*-isopentylmethanesulfinamide	2017			
696	3-acetylamino-*N*-2-thienyl-propanamide	2017	*Streptomyces* sp. Q24	Zhuhai, Guangdong, China	(Ye et al., 2017)
697	holomycin	2017	*Streptomyces* sp. DT-A37	Dongtou, Wenzhou, Zhejiang Province, P. R. China	(Ding et al., 2017)
698	(1*Z*)-S,S'-dimethyldihydroholomycin	2017			
699	holomycin A	2017			
700	streptopertusacin A	2017	*Streptomyces* sp. HZP-2216E	Turtle Islet located, South China Sea	(Zhang et al., 2017b)
701	lodopyridone B	2017	*Saccharomonospora* sp.	La Jolla Submarine Canyon, California	(Le et al., 2017)
702	lodopyridone C	2017			
703	8-hydroxythiomarinol C	2017	*Pseudoalteromonas* sp.	–	(Gao et al., 2017)
704	6,7-diketothiomarinol C	2017			
705	6,7-diketothiomarinol A	2017			
706	7-ketothiomarinol C	2017			
707	7-ketothiomarinol A	2017			
708	8-*epi*-7-ketothiomarinol C	2017			
709	8-*epi*-7-ketothiomarinol A	2017			
710	8-*epi*-7-epi-6-ketothiomarinol A	2017			
711	1-methyl-4-methylthio-β-carboline	2017	*Pseudomonas benzenivorans*	California State Beaches	(Lorig-Roach et al., 2017)
712	(2-(3-hydroxyquinolin-2-yl)oxazole-4-carbonyl)-L-cysteine	2018	*Streptomyces*	Avilés Canyon,	(Ortiz-López et al.,
713	(2*R*,2′*R*)-3,3′-disulfanediylbis(2-(2-(3-hydroxyquinolin-2-yl)oxazole-4-carboxamido)propanoic acid)	2018	*cyaneofuscatus* M−157	Cantabrian Sea	2018)
714	thymidine-3-mercaptocarbamic acid	2019	*Streptomyces* sp.	Red Sea	(Shaala et al.,
715	thymidine-3-thioamine	2019			2019)
716	nocarterphenyl A	2019	*Nocardiopsis* sp.	Dongzhaigang	(Wang et al., 2019)
717	nocarterphenyl B	2019	OUCMDZ-4936	Mangrove Reserve, China	
718	nocarterphenyl D	2021	*Nocardiopsis* sp. HDN154086	South China Sea	(Chang et al., 2021)
719	2,5-bis(5-*tert*-butyl-2-benzoxazolyl)thiophene	2019	*Streptomyces* sp. G278	Cu Lao Cham - Quang Nam, Vietnam	(Cao et al., 2019a)
720	questiomycin C	2019	*Alteromonas* sp. D	Hiroshima-bay,	(Umetsu et al.,
721	questiomycin D	2019		Hiroshima, Japan	2019)
722	mindapyrrole B	2019	*Pseudomonas*	Sultan Kudarat,	(Lacerna et al.,
723	mindapyrrole C	2019	*aeruginosa*	Mindanao, Philippines	2019)

(*continued on next page*)

Table 11 (*continued*)

No.	Compounds	Time	From	Location	Ref.
671	forazoline A	2020	*Actinomadura* sp. WMMB-499	–	(Zhang et al., 2020a)
724	sungeidine A	2020	*Micromonospora* sp.	Sungei Buloh Wetland Reserve, Singapore	(Low et al., 2020)
725	sungeidine B	2020			
726	sungeidine C	2020			
727	sungeidine D	2020			
728	sungeidine E	2020			
729	sungeidine F	2020			
730	sungeidine G	2020			
731	sungeidine H	2020			
732	monathioamide A	2020	*Pseudomonas* sp. ZZ820R	Zhoushan Archipelago, Zhejiang, China	(Yi et al., 2020a)
733	levesquamide	2020	*Streptomyces sp.* RKND-216	Burnt Point, PE, Canada	(Liang et al., 2020)
734	streptothiazomycin A	2020	*Streptomyces sp.* SY1965	Mariana Trench	(Yi et al., 2020b)
735	thiolopyrrolone A	2022	*Streptomyces* sp. BTBU20198885	Xiamen, China	(Song et al., 2022)
736	2,2-dioxidothiolutin	2022			
737	thiolutin	2022			

1.3.5. Mangroves bacteria, fungi and other marine microorganism

Mangrove is a special ecosystem for the transition from land to sea. In recent years, mangrove bacteria and fungi have gradually become the focus of research. 2 (**935**–**936**) and 34 (**937**–**968, 767, 909**) sulphur-containing alkaloids were reported from mangroves bacteria and fungi, respectively. Brocazines A-F (**937**–**942**), phomazines A-C (**943**–**945**), epicorazines A-C (**946**–**948**), penicibrocazines A-E (**955**–**959**) and penispirozines A-D (**964**–**967**) all are thiodiketopiperazines alkaloids. Moreover, epicoccins A-E (**949**–**953**) are epipolythiodioxopiperazines. This shows that thiodioxopiperazines are the main type of sulphur-containing alkaloids in fungi again. Notably, spirobrocazines A-B (**961**–**962**) are characteristic of a unique spirocyclic skeleton (Meng et al., 2016) and penispirozine B (**965**) possesses a 6/5/6/5/6 pentacyclic ring system with two rare spirocyclic centers (Zhu et al., 2020). In addition, penispirozine A (**964**) has an unusual pyrazino[1,2]oxazadecaline coupled with a thiophane ring system and trichodermamide G (**968**) has a similar cyclic system. In addition, 4 (**969**–**972**) sulphur-containing alkaloids, new pigments with an unprecedented skeleton, were reported from marine ciliates *Pseudokeronopsis riccii* (Fig. 16 and Table 13).

1.4. Bioactivities of Marine-Derived Sulphur-containing alkaloids

The biological activities of marine-derived sulphur-containing alkaloids have been studied extensively. As listed in Table 14, marine-derived sulphur-containing alkaloids had a broad range of bioactive properties including cytotoxicity, antibacteria, antifungi, antimitotic, antiviral, and other activities.

In summary, while research on the biological activity of marine sulphur-containing alkaloids has explored a wide range of directions, the primary focus remains on their cytotoxicity against tumour cells. Over the past four decades, numerous compounds with potent cytotoxic properties have been discovered, displaying strong efficacy against various types of tumour cells. Here, we have summarized the compounds with superior activity according to the type of tumour they target.

1.5. Cytotoxicity

1.5.1. Leukemia

Leukemia is a collection of malignant tumours that affect the blood system. Clonal leukemia cells undergo uncontrolled proliferation and accumulate in the bone marrow and other haematopoietic tissues due to impaired differentiation, apoptosis, and other mechanisms, ultimately inhibiting normal haematopoietic function. (Whiteley et al., 2021). Several marine sulphur-containing alkaloids have demonstrated cytotoxicity against different types of leukemia cells. For instance, prianosin A (**22**), C (**29**), D (**30**), varamine A (**370**), B (**371**), diplamine (**372**), and eudistomidin J (**455**) exhibited IC_{50} values of 0.037, 0.15, 0.18, 0.03, 0.05, 0.02, and 0.047 μg/ml, respectively, against L1210 cells. (Kobayashi et al., 1987; Cheng et al., 1988; Molinski and Ireland, 1989; Charyulu et al., 1989; Suzuki et al., 2011). Similarly, compounds such as discorhabdin B (**32**), discorhabdin W (**145**), (6*R*,8*S*)-1-thiomethyldiscorhabdin G*/I (**184**), 16a,17a-dehydrodiscorhabdin W (**185**), discorhabdin G*/I (**146**), discorhabdin A (**31**), dercitin (**27**), curacin E (**518**), agrochelin (**638**), eudistomidin J (**455**), pateamine (**93**) have been reported to inhibit P388 cells with IC_{50} values of 0.084, 0.087, 0.28, 0.45, 0.6, 0.13, 0.11, 0.081, 0.02, 0.053 μM and 43, 0.15 ng/ml, respectively. (Lang et al., 2005; Grkovic and Copp, 2009; Burres et al., 1989; Suzuki et al., 2011; Northcote et al., 1991; Ueoka et al., 2016; Cañedo et al., 1999). Meanwhile, compounds such as perfragilins B (**545**), leptosin A (**738**), B (**739**), C (**740**), D (**741**), E (**742**), F (**743**), G (**744**), G1 (**745**), G2 (**746**), H (**747**), K (**748**), K1 (**749**) and K2 (**750**), N (**757**), N1 (**758**) and P (**764**) exhibited EC_{50} values of 70, 1.85, 2.40, 1.75, 86, 46, 56, 4.6, 4.3, 4.4, 3.0, 3.8, 2.2, 2.1 180, 190 and 100 ng/ml, respectively, against P388 cells. (Choi et al., 1993; Takahashi et al., 1994; Takahashi et al., 1995b; Takahashi et al., 1995a; Yamada et al., 2002; Takeshi Yamada, 2004). Among them, shishijimicin A (**431**), B (**432**), C (**433**) and namenamicin (**434**) have shown excellent cytotoxicity against P388 cells with IC_{50} values of 0.47, 2.0, 1.7 and 3.3 pg/ml, respectively. (Oku et al., 2003).

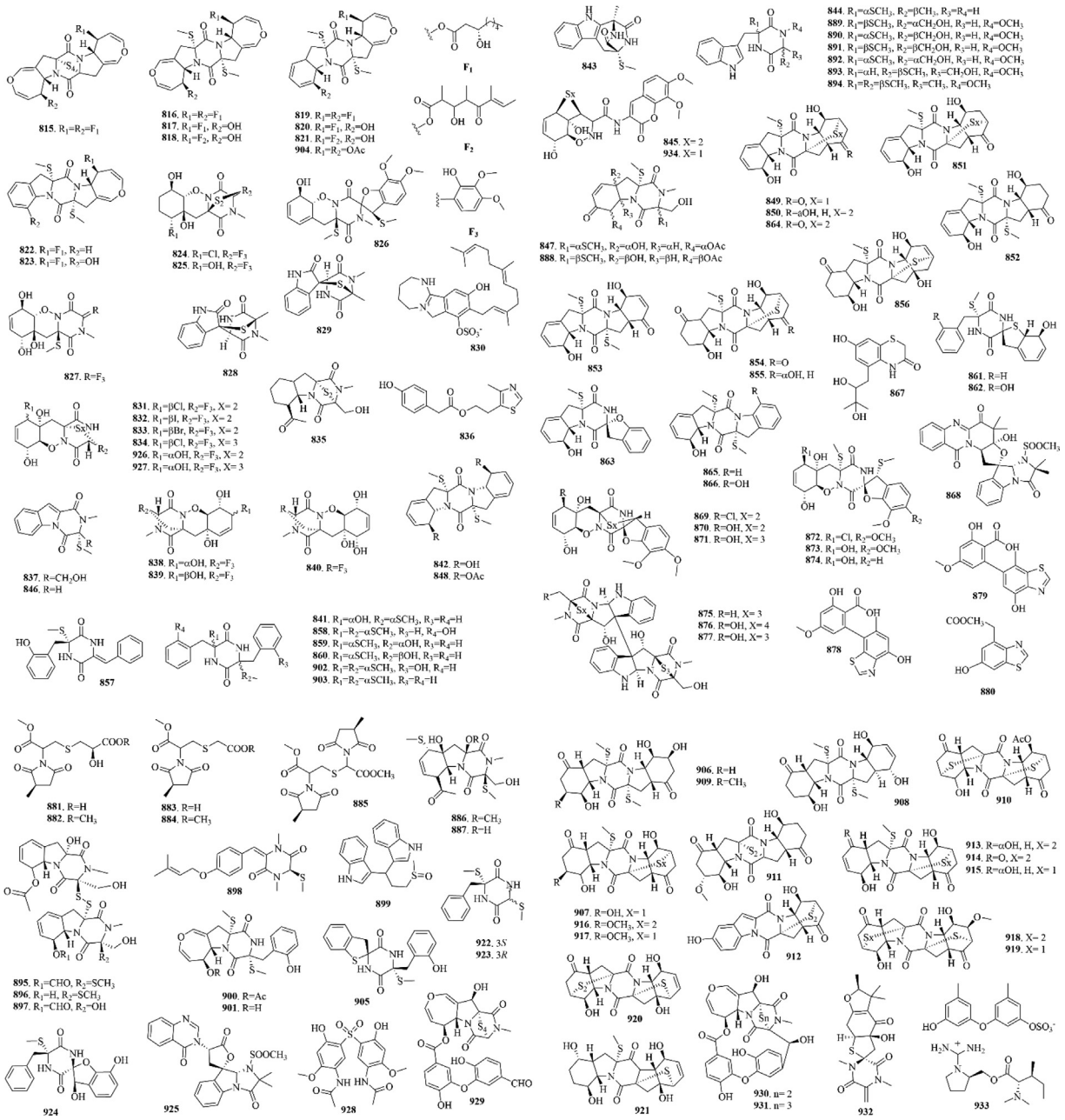

Fig. 15 Sulphur-containing alkaloids from marine fungi.

Moreover, chetracin E (**875**) exhibited IC_{50} values of 0.4 μM against K562 cells. (Yu et al., 2018). Moreover, somocystinamide A (**601**) and 14-methyleudistomidin C (**418**) exhibited IC_{50} values of 60 nM and 0.57 μg/ml against Molt4 cells, and compound **601** also inhibited CEM cells with an IC_{50} of 14 nM. (Wrasidlo et al., 2008; Rashid et al., 2001). It is worth noting that dercitin (**27**) demonstrated cytotoxicity against HL-60 and HL-60/AR cells by reducing DNA replication, with IC_{50} values of 0.15 and 0.24 μM, respectively. (Burres et al., 1989). Meanwhile, somocystinamide A (601) exhibited cytotoxicity against Jurkat cells with an IC_{50} value of only 3 nM. (Wrasidlo et al., 2008).

1.5.2. Lymphomas

Lymphomas are a heterogeneous group of malignant tumors that originate from the lymphatic hematopoietic system. Although these tumors typically arise in the lymph nodes, the distribution of the lymphatic system allows them to spread throughout the body and invade nearly any tissue or organ. (Jiang et al., 2017). Prianosin A (**22**), C (**29**), and D (**30**) exhibited strong cytotoxicity against L5178Y cells with IC_{50} values of 0.014, 0.024, and 0.048 μg/mL, respectively. (Kobayashi et al., 1987; Cheng et al., 1988).

Table 12 Sulphur-containing alkaloids from marine fungi.

No.	Compounds	Time	From	Location	Ref.
Marine fungi					
738	leptosin A	1994	*Lepto*sph*ueriu* sp.	Tanabe Bay, Japan	(Takahashi et al., 1994)
739	leptosin B	1994			
740	leptosin C	1994			
741	leptosin D	1994			
742	leptosin E	1994			
743	leptosin F	1994			
744	leptosin G	1995			(Takahashi et al., 1995b)
745	leptosin G1	1995			
746	leptosin G2	1995			
747	leptosin H	1995			
748	leptosin K	1995			(Takahashi et al., 1995a)
749	leptosin K1	1995			
750	leptosin K2	1995			
751	11,11′-dideoxyverticillin A	1999	*Penicillium* sp. CNC-350	–	(John, 1999)
752	11′-deoxyverticillin A	1999			
753	flavochristamide A	2000	*Flavobacterium* sp.	lshikari Bay, Hokkaido	(Kohayashi et al., 1995)
754	flavochristamide B	2000			
755	leptosin M	2002	*Lepto*sph*aeria* sp.	Tanabe Bay, Japan	(Yamada et al., 2002)
756	leptosin M1	2002			
757	leptosin N	2002			
758	leptosin N1	2002			
759	fusaperazine A	2002	*Fusarium chlamydosporum*	–	(Blunt et al., 2004)
760	fusaperazine B	2002			
761	Sch 54,794	1993			(Chu et al., 1993)
762	Sch 54,796	1993			
763	leptosin O	2004	*Lepto*sph*aeria* sp.	Tanabe Bay, Japan	(Takeshi Yamada, 2004)
764	leptosin P	2004			
765	leptosin Q	2004			
766	leptosin R	2004			
767	rostratin A	2004	*Exserohilum rostratum*	Lanai Island, Hawaii	(Tan et al., 2004)
768	rostratin B	2004			
769	rostratin C	2004			
770	rostratin D	2004			
771	dehydroxybisdethiobis(methylthio)gliotoxin	2006	*Pseudallescheria* sp.	Uljin, Gyeongbuk, Korea	(Li et al., 2006)
772	bilain A	2007	*Penicillium bilaii*	Huon estuary, Tasmania	(Capon et al., 2007)
773	bilain B	2007			
774	bilain C	2007			
775	(*Z*)-6-benzylidene-3-hydroxymethyl-1,4-dimethyl-3-methylsulfanylpiperazine-2,5-dione	2008	*Order Pleosporales* CRIF2	Surin Island	(Prachyawarakorn et al., 2008)
776	alternarosin A	2009	Alternaria raphani	Qingdao, China	(Wang et al., 2009)
777	bisdethiobis(methylthio)acetylaranotin	2009			
778	plectosphaeroic acid A	2009	*Plectosphaerella cucumerina*	Barkley Sound, British Columbia	(Carr et al., 2009)
779	plectosphaeroic acid B	2009			
780	plectosphaeroic acid C	2009			
781	deoxyapoaranotin	2011	*Arthrinium versicolor*	East Sea, Korea	(Choi et al., 2011)
782	acetylaranotin	2011			
783	acetylapoaranotin	2011			
784	luteoalbusin A	2012	*Acrostalagmus luteoalbus*	South China Sea	(Wang et al., 2012a)
785	luteoalbusin B	2012			
786	T988A	2012			
787	gliocladines C	2012			
788	gliocladines D	2012			
789	chetoseminudin B	2012			
790	chetoseminudin C	2012			
791	spirogliotoxin	2012	*Aspergillus fumigatus* YK-7	Yingkou, China	(Wang et al., 2012b)
792	gliotoxin				
793	bisdethiobis(methylthio)gliotoxin				
794	didehydrobisdethiobis(methylthio)gliotoxin				
795	bis(dethio)-10a-methylthio-3a-deoxy-3,3a-didehydrogliotoxin	2012	*Penicillium* sp.	Suruga Bay, Japan	(Sun et al., 2012)
796	6-deoxy-5a,6-didehydrogliotoxin	2012			
797	bis(dethio)bis(methylthio)-5a,6-	2012			

Table 12 (*continued*)

No.	Compounds	Time	From	Location	Ref.
	didehydrogliotoxin				
798	5a,6-didehydrogliotoxin	2012			
799	gliotoxin G	2012			
800	penilumamide	2014	*Aspergillus* sp.	Xisha islands,South China Sea	(Reddy et al., 2017)
801	penilumamide B	2014			
802	penilumamide C	2014			
803	reduced gliotoxin	2014	*Neosartorya pseudofischeri*	Hainan Sanya National Coral Reef Reserve, China	(Liang et al., 2014)
804	acetylgliotoxin				
805	bis-*N*-norgliovictin				
806	6-acetylbis(methylthio)gliotoxin				
807	chartarutine C	2014	*Stachybotrys chartarum*	Beibuwan Bay, China	(Li et al., 2014)
808	chartarutine D	2014			
809	cladosporin A	2015	*Cladosporium* sp.	Yangshashan Bay, Ningbo, Zhejiang, China	(Gu et al., 2015)
810	cladosporin B	2015			
811	6-acetylmonodethiogliotoxin	2015	*Dichotomomyces cejpii*	Bare island, Sydney, Australia	(Harms et al., 2015)
812	6-acetylbisdethiobis(methylthio)gliotoxin	2015			
813	5a,6-anhydrobisdethiobis(methylthio)-gliotoxin	2015			
814	graphiumin A	2015	*Graphium* sp.	Ishigaki island, Okinawa, Japan	(Fukuda et al., 2015)
815	graphiumin B	2015			
816	graphiumin C	2015			
817	graphiumin D	2015			
818	graphiumin E	2015			
819	graphiumin F	2015			
820	graphiumin G	2015			
821	graphiumin H	2015			
822	graphiumin I	2015			
823	graphiumin J	2015			
824	adametizine A	2015	*Penicillium adametzioides*	Hainan island, China	(Liu et al., 2015b)
825	adametizine B	2015			
826	peniciadametizine A	2015	*Penicillium adametzioides*	Wenchang, Hainan, China	(Liu et al., 2015c)
827	peniciadametizine B	2015			
828	pseudellone A	2015	*Pseudallescheria ellipsoidea* F42 – 3	National Coral Reef Reserve, Hainan, China	(Liu et al., 2015a)
829	pseudellone B	2015			
830	stachybotrin G	2015	*Stachybotrys chartarum* MXH-X73	Xisha island, China	(Ma et al., 2015)
831	DC1149B	2015	*Trichoderma* cf. *brevicompactum*	Palau	(Yamazaki et al., 2015a)
832	iododithiobrevamide	2015			
833	DC1149R	2015			
834	chlorotrithiobrevamide	2015			(Yamazaki et al., 2015b)
835	acetylgliotoxin G	2015	*Dichotomomyces cejpi*i	Pecém's offshore port, Ceará, Brazil	(Rodrigues et al., 2015)
836	acaromyester A	2016	*Acaromyces ingoldii*	South China Sea	(Gao et al., 2016)
837	dichotocejpin A	2016	*Dichotomomyces cejpii* FS110	South China Sea	(Fan et al., 2016)
838	pretrichodermamide D	2016	*Penicillium* sp. KMM 4672	Vietnam, South China Sea	(Yurchenko et al., 2016)
839	pretrichodermamide E	2016			
840	pretrichodermamide F	2016			
841	pseuboydone C	2016	*Pseudallescheria boydii*	Hainan Sanya National Coral Reef Reserve, China	(Lan et al., 2016)
842	pseuboydone D	2016			
843	lasiodipline F	2016	*Pseudallescheria ellipsoidea* F42-3		(Wang et al., 2016)
844	pseudellone D	2016			
845	dithioaspergillazine A	2016	*Trichoderma* cf. *brevicompactum*	Palau	(Yamazaki et al., 2016)
846	dichocerazine A	2017	*Dichotomomyces cejpii* F31-1	Hainan Sanya National Coral Reef Reserve, China	(Chen et al., 2017b)
847	dichocerazine B	2017			
848	haematocin	2017			
849	eutypellazine A	2017	*Eutypella* sp. MCCC 3A00281	South Atlantic Ocean	(Niu et al., 2017a)
850	eutypellazine B	2017			
851	eutypellazine C	2017			
852	eutypellazine D	2017			
853	eutypellazine E	2017			
854	eutypellazine F	2017			

(*continued on next page*)

Table 12 (*continued*)

No.	Compounds	Time	From	Location	Ref.
855	eutypellazine G	2017			
856	eutypellazine H	2017			
857	eutypellazine I	2017			
858	eutypellazine J	2017			
859	eutypellazine K	2017			
860	eutypellazine L	2017			
861	eutypellazine N	2017			(Niu et al., 2017b)
862	eutypellazine O	2017			
863	eutypellazine P	2017			
864	eutypellazine Q	2017			
865	eutypellazine R	2017			
866	eutypellazine S	2017			
867	gliomastin B	2017	*Gliomastix* sp.	Ain El-Sokhna, Eygpt	(Elnaggar et al., 2017)
868	scedapin C	2017	*Scedosporium apiospermum*	Hainan Sanya National Coral Reef Reserve, China	(Huang et al., 2017)
869	penicisulfuranol A	2017	*Penicillium janthinellum* HDN13-309	Hainan, China	(Zhu et al., 2017)
870	penicisulfuranol B	2017			
871	penicisulfuranol C	2017			
872	penicisulfuranol D	2017			
873	penicisulfuranol E	2017			
874	penicisulfuranol F	2017			
875	chetracin E	2018	*Acrostalagmus luteoalbus* HDN13-530	Liaodong Bay, China	(Yu et al., 2018)
876	chetracin F	2018			
877	chetracin C	2018			
878	altenusinoide A	2018	*Alternaria* sp. SCSIOS02F49	Xuwen County, Guangdong, China	
879	altenusinoide B	2018			
880	methyl 2-(6-hydroxybenzothiazol-4-yl) acetate	2018			
881	violaceimide A	2018	*Aspergillus violaceus*	South China Sea	(Yin et al., 2018)
882	violaceimide B	2018			
883	violaceimide C	2018			
884	violaceimide D	2018			
885	violaceimide E	2018			
886	geospallin A	2018	*Geosmithia pallida* FS140		(Sun et al., 2018)
887	geospallin B	2018			
888	geospallin C	2018			
889	(+)-acrozine A	2019	*Acrostalagmus luteoalbus* TK-43	Sinop, Turkey	(Cao et al., 2019b)
890	(–)-acrozine A	2019			
891	(+)-acrozine B	2019			
892	(–)-acrozine B	2019			
893	acrozine F	2021			(Cao et al., 2021)
894	acrozine G	2021			
895	dechdigliotoxin A	2019	*Dichotomomyces cejpii*	South China Sea	(Liu et al., 2019b)
896	dechdigliotoxin B	2019			
897	dechdigliotoxin C	2019			
898	fusaperazine F	2019	Penicillium crustosum HDN153086	Prydz Bay, Antarctica	(Liu et al., 2019a)
899	pseudboindole B	2019	*Pseudallescheria boydii* F44-1	Hainan Sanya National Coral Reef Reserve, China	(Yuan et al., 2019)
900	emestrin L	2020	*Aspergillus terreus*	Weizhou coral reefs, South China Sea	(Wu et al., 2020)
901	emestrin M	2020			
902	emethacin C	2020			
903	emethacin B	2020			
904	bisdethiobis(methylsulfanyl)acetylapoaranotin	2020			
905	spiroepicoccin A	2020	*Epicoccum nigrum*	–	(Li et al., 2020d)
906	7-dehydroxyepicoccin H	2020	*Epicoccum nigrum* SD-388	Western Pacific	(Chi et al., 2020b)
907	7-hydroxyeutypellazine F	2020			
908	5′-hydroxy-6′-ene-epicoccin G	2020			(Chi et al., 2020a)
909	7-methoxy-7′-hydroxyepicoccin G	2020			
910	8′-acetoxyepicoccin D	2020			
911	7′-demethoxyrostratin C	2020			
912	amphiepicoccin A	2020	*Epicoccum nigrum* HDN17-88	Western Pacific	(Wang et al., 2020)
913	amphiepicoccin B	2020			

Table 12 (*continued*)

No.	Compounds	Time	From	Location	Ref.
914	amphiepicoccin C	2020			
915	amphiepicoccin D	2020			
916	amphiepicoccin E	2020			
917	amphiepicoccin F	2020			
918	amphiepicoccin G	2020			
919	amphiepicoccin H	2020			
920	amphiepicoccin I	2020			
921	amphiepicoccin J	2020			
922	citriperazine A	2020	*Penicillium* sp. KMM 4672	South China Sea	(Yurchenko et al., 2020)
923	citriperazine B	2020			
924	citriperazine C	2020			
925	scetryptoquivaline A	2020	*Scedosporium apiospermum* F41-1	Hainan Sanya National Coral Reef Reserve, China	(Li et al., 2020a)
926	5-*epi*-pretrichodermamide A	2020	*Trichoderma* cf. *brevicompactum*	Palau	(Yamazaki et al., 2020)
927	5-*epi*-trithiopretrichodermamide A	2020			
928	pensulfonamide	2021	*Penicillium aculeatum*	Red Sea (Egypt)	(Hawas et al., 2022)
929	secoemestrin C	2021	*Aspergillus quadrilineatus* FJJ093	Jeju Island, Republic of Korea	(Hwang et al., 2021)
930	emestrin	2021			
931	emestrin B	2021			
932	talaromanloid A	2022	*Talaromyces mangshanicus* BTBU20191089	–	(Zhang et al., 2022)
933	ochraceopetalin	2021	*Aspergillus ochraceopetaliformis*	–	(Park et al., 2021b)
934	aspergillazine A	2005	*Spicaria elegans*	Jiaozhou Bay, China	(Liu et al., 2005)

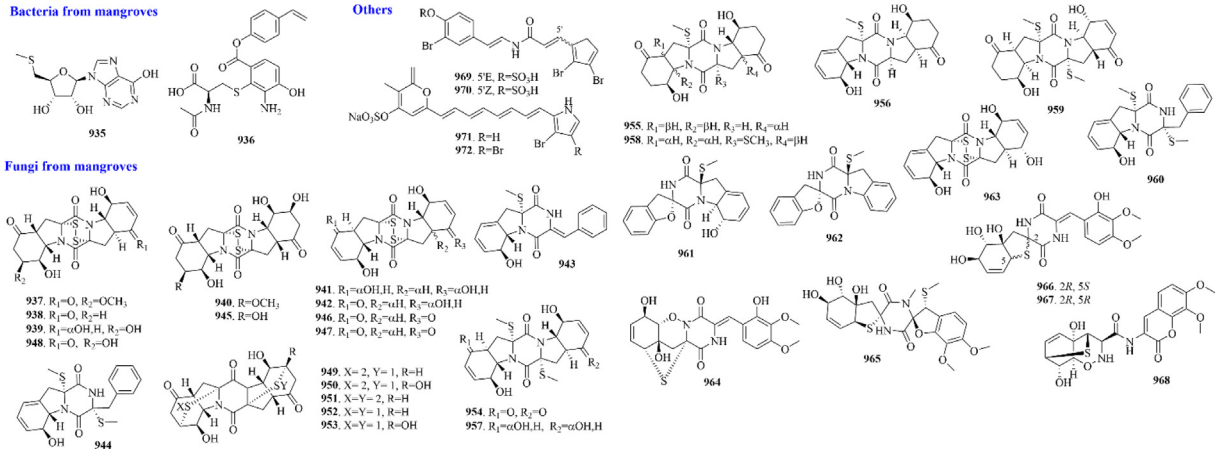

Fig. 16 Sulphur-containing alkaloids from mangroves bacteria, fungi, other marine microorganism.

1.5.3. Colorectal cancer

Colorectal cancer is a prevalent malignant tumor that includes colon and rectal cancers. Tumor cells can metastasize to lymph nodes through lymphatic vessels or to the liver, lungs, and bones through the bloodstream. The primary treatment regimen is currently a combination of chemotherapy, with chemotherapeutic agents such as 5-fluorouracil, oxaliplatin, irinotecan, and other drugs. (Biller et al., 2021). HCT116 cells are a commonly used in vitro model of colorectal cancer. Discorhabdin A (**31**), (-)-(1*R*,2*R*,6*R*,8*S*,6′*S*)-discorhabdin B dimer (**316**), latrunculone A (**168**), patellazole A (**360**), B (**361**), C (**362**), acetylgliotoxin (**804**), reduced gliotoxin (**803**), chetracin E (**875**), C (**877**), epicorazine A (**946**) and rostratin C (**769**) have been reported to inhibit HCT116 cells with IC_{50} values of 7, 160, 480, 0.62, 0.39, 4.7, 0.66, 0.62, 5.6, 890, 430, 400, 300, 330 nM and 0.76 μg/ml, respectively. (Antunes et al., 2004; Li et al., 2020b; Amagata et al., 2008; Richardson et al., 2005; Liang et al., 2014; Liang et al., 2014; Yu et al., 2018; Tan et al., 2004). In addition, compound **360**, **361** and **362** also exhibited IC_{50} values of 0.66, 0.62 and 5.6 nM against HCT 116 cells $p53^{-/-}$. Meanwhile, discorhabdin I (**131**), L (**132**), tanjungide A (**473**), agrochelin (**638**), dercitin (**27**), latrunculin A (**16**), ecteinascidin 743 (**376**), 729 (**375**), 597 (**393**), 583 (**394**) and 594 (**395**) exhibited cytotoxicity against HT-29 cells with GI_{50} values of 0.35,

Table 13 Sulphur-containing alkaloids from mangroves bacteria, fungi and other marine microorganism.

No.	Compounds	Time	From	Location	Ref.
Mangroves bacteria					
935	9-((2*R*,3*R*,4*S*,5*S*)-3,4-dihydroxy-5-((methylthio)methyl) tetrahydrofuran-2-yl)-6-hydroxy-9*H*-purin-3-ium	2014	*Micromonospora* sp. K310	Butre river, Ghana	(Kyeremeh et al., 2014)
936	bagremycin C	2017	*Streptomyces* sp. Q22	Qiao Mangrove Forest, Zhuhai City, Guangdong, China	(Chen et al., 2017a)
Mangroves fungi					
937	brocazine A	2014	*Penicillium brocae* MA-231	Hainan island, China	(Meng et al., 2014)
938	brocazine B	2014			
939	brocazine C	2014			
940	brocazine D	2014			
941	brocazine E	2014			
942	brocazine F	2014			
943	phomazine A	2014	*Phoma* sp. OUCMDZ-1847	Wenchang, China	(Kong et al., 2014)
944	phomazine B	2014			
945	phomazine C	2014			
946	epicorazine A	2014			
947	epicorazine B	2014			
948	epicorazine C	2014			
949	epicoccin A	2014			
950	epicoccin B	2014			
951	epicoccin C	2014			
952	epicoccin D	2014			
953	epicoccin E	2014			
954	exserohilone A	2014			
767.	rostratin A	2014			
955	penicibrocazine A	2015	*Penicillium brocae*	Hainan island, China	(Meng et al., 2015)
956	penicibrocazine B	2015			
957	penicibrocazine C	2015			
958	penicibrocazine D	2015			
959	penicibrocazine E	2015			
960	analog	2015			
961	spirobrocazine A	2016	*Penicillium brocae* MA-231		(Meng et al., 2016)
962	spirobrocazine B	2016			
963	brocazine G	2016			
964	penispirozine A	2020	*Penicillium janthinellum* HDN13-309		(Zhu et al., 2020)
965	penispirozine B	2020			
966	penispirozine C	2020			
967	penispirozine D	2020			
968	trichodermamide G	2020	*Trichoderma harzianum* D13		(Zhao et al., 2020)
909.	aspergillazine A	2020			
Other marine microorganism					
969	keronopsamide B	2010	*Pseudokeronopsis riccii*	Tyrrhenian Coast, Sardinia, Italy	(Guella et al., 2010)
970	keronopsamide C	2010			
971	keronopsin A1	2010			
972	keronopsin A2	2010			

0.12 and 0.19 μM and IC_{50} values of 0.268, 0.063 μM, 60, 0.5, 0.5, 2.0, 10 and 25 ng/ml, respectively. (Reyes et al., 2004; Murcia et al., 2014; Cañedo et al., 1999; Burres et al., 1989; Longley et al., 1993; Sakai et al., 1996).

RKO cells and COLO-205 cells are two other in vitro cellular models of colon cancer. A study showed that gliotoxin (**792**) and reduced gliotoxin (**803**) were cytotoxic to RKO cells (IC_{50} values of 0.8 and 0.41 μM, respectively), while 14-methyleudistomidin C (**418**) was cytotoxic to COLO-205 cells (IC_{50} = 0.42μg/ml). (Liang et al., 2014; Rashid et al., 2001).

1.5.4. Pancreatic cancer

Pancreatic cancer is a highly prevalent malignant disease of the gastrointestinal tract with a very low survival rate. Patients with untreated pancreatic cancer typically have a survival time of approximately four months. (Park et al., 2021a). In vitro studies have shown that discorhabdin T (**156**), U (**157**), and DC1149B (**831**) are effective inhibitors of PANC-1 cells, with IC_{50} values of 0.7, 0.069 and 0.02 μM, respectively. (Gunasekera et al., 2003; Tang et al., 2020).

1.5.5. Breast cancer

Breast cancer is a common malignant tumor that affects women. It occurs due to the uncontrolled proliferation of epithelial cells in the breast, influenced by various carcinogenic factors. Common early symptoms include breast lumps, nipple discharge, and swollen lymph nodes in the armpits, while in advanced stages, cancer cells can metastasize to distant organs, leading to life-threatening multi-organ lesions. (Harbeck et al., 2019). Kuanoniamine C (**82**) and A (**381**) have demonstrated cytotoxicity against MCF-7 cells with GI_{50} values of 0.81 and 0.12 nM, respectively, as well as against MDA-MB-231 cells with

GI_{50} values of 10.23 and 0.73 nM, respectively. (Kijjoa et al., 2007). Curacin A (**519**), B (**591**), D (**594**), Luteoalbusin A (**784**), B (**785**), T988A (**786**), Gliocladine C (**787**) and D (**788**) were reported to inhibit MCF-7 cells with IC_{50} values of 0.038, 0.32, 0.34, 0.23, 0.25, 0.91, 0.23, and 0.65 μM, respectively. (Verdier-Pinard et al., 1998; Márquez et al., 1998; Wang et al., 2012a).

1.5.6. Lung cancer

Lung cancer is a malignant tumor that originates in the lining or glands of the bronchi in the lungs. It is one of the fastest-growing malignancies in terms of morbidity and mortality and poses a serious threat to public health. Currently, there are two main classifications of lung cancer: small cell lung cancer and non-small cell lung cancer, which can be further divided into adenocarcinoma, squamous cell carcinoma, large cell carcinoma, bronchoalveolar carcinoma, and others depending on the pathology. (Hirsch et al., 2017). Several compounds have been reported to inhibit lung cancer cell growth. Dercitin (**27**), somocystinamide A (**601**), ecteinascidin 743 (**376**), latrunculin A (**16**), ecteinascidin 729 (**375**), 597 (**393**), 583 (**394**), 594 (**395**), agrochelin (**638**), chetracin E (**875**), and C (**877**) have been reported to inhibit A549 cells with IC_{50} of 7, 160, 480, 0.62, 0.39, 4.7, 0.66, 0.62, 5.6, 890, 430, 400, 300, 330 nM and 0.76 μg/ml, respectively. (Burres et al., 1989; Wrasidlo et al., 2008; Simoens et al., 2003; Longley et al., 1993; Sakai et al., 1996; Cañedo et al., 1999; Yu et al., 2018). Lyngbyabellin E-I (**603**–**607**) have also been shown to inhibit NCI-H460 cells, with IC_{50} values ranging from 0.2 to 2.2 μM. (Williams et al., 2003). Meanwhile, kuanoniamine C (**82**) and A (**381**) demonstrated cytotoxicity against MCF-7 cells, with GI_{50} values of 0.81 and 0.12 nM, respectively. (Kijjoa et al., 2007). Additionally, Chetracin E (**875**) and C (**877**) exhibited IC_{50} values of 0.2 and 0.8 μM, respectively, against NCI-H1975 cells. (Yu et al., 2018). Notably, compound **376** showed significant inhibition of NCI-H292 cells with an IC_{50} value of 1.1 nM. (Simoens et al., 2003).

1.5.7. Cervical cancer

Cervical cancer is a prevalent malignancy in women, and persistent high-risk HPV infection is a well-established major risk factor for the disease. More than 90% of cervical cancers are associated with high-risk HPV infection. (Cohen et al., 2019). In vitro, Hela cells are widely used as a model for cervical cancer. Among tested compounds, iejimalide C (**539**), caldorazole (**626**), and iezoside (**627**) exhibited IC_{50} values of 2.7, 23, and 6.8 nM, respectively, against HeLa cells. Compound **626** also inhibited HeLa S3 and HeLa S3Mer$^-$ cells, with IC_{50} values of 44 and 48 nM, respectively. (Kazami et al., 2014; Ohno et al., 2022; Kurisawa et al., 2022). Notably, shishijimicin A (431), B (432), C (433), and namenamicin (434) showed excellent cytotoxicity against HeLa cells, with IC_{50} values of 1.8, 3.3, 6.3, and 43 pg/ml, respectively. (Oku et al., 2003).

1.5.8. Melanoma

Melanoma is a highly malignant tumor that develops from melanocytes commonly found in the skin. Due to its aggressive nature, melanoma is prone to infiltrative growth and metastasis, making it one of the deadliest types of skin cancer. (Schadendorf et al., 2018). Agrochelin (**638**), ecteinascidin 743 (**376**), 729 (**375**), 597 (**393**), 583 (**394**), and 594 (**395**) have been reported to inhibit MEL-28 cells with IC_{50} values of 0.268 μM, 5.0, 5.0, 2.0, 5.0, and 25 ng/ml, respectively (Cañedo et al., 1999; Sakai et al., 1996).

1.5.9. Ovarian cancer

Ovarian cancer is a malignant tumor that grows on the ovary, with 90% to 95% of cases being primary ovarian cancers. Despite having a lower incidence rate than cervical and endometrial cancers, ovarian cancer has the highest mortality rate among gynecological cancers, ranking first. (Matulonis et al., 2016). 14-methyleudistomidin C (**418**) and aulosirazole A-B (**623**–**624**) demonstrated IC_{50} values of 0.98 μg/ml, 0.301, and 0.6 μM, respectively, against OVCAR-3 cells (Davis et al., 2022; Rashid et al., 2001). Additionally, brocazine G (**963**) exhibited inhibition of A2780 and A2780 CisR cells with IC_{50} values of 664 and 661 nM, respectively (Meng et al., 2016).

1.5.10. Others

In addition to their activity against the aforementioned tumour cells, sulphur-containing marine alkaloids have demonstrated promising cytotoxic properties against other types of cancer cells. For instance, luteoalbusin A (**784**), B (**785**), T988A (**786**), gliocladine C (**787**) and D (**788**) were reported to inhibit the growth of SF-268 and HepG-2 cells, with IC_{50} values ranging from 0.46 to 2.49 μM. Moreover, kuanoniamine C (**82**) and A (**381**) exhibited excellent cytotoxicity against SF-268 cells, with IC_{50} values of 33.16 and 4.67 nM, respectively. (Kijjoa et al., 2007). Of particular note, shishijimicin A (**431**), B (**432**), C (**433**) and namenamicin (**434**) displayed potent cytotoxicity against 3Y1 cells, with IC_{50} values of 2.0, 3.1, 4.8 and 13 pg/ml. (Oku et al., 2003).

1.5.11. Structure-activity relationships of the cytotoxicity

It is noteworthy that discorhabdins, curacins, tanjungides, leptosins, and latrunculins exhibit better cytotoxicity than any other reported compounds. Thus, the structure–activity relationships of the cytotoxicity of these compounds have been summarized for further investigation.

As depicted in Fig. 17**a**, the cytotoxicity of discorhabdins is decreased when there is a double bond between C-4 and C-5 of discorhabdins, which is also confirmed in Fig. 17**b**. When there is a hydroxyl substitution at C-3′, the cytotoxicity of the compound is increased. Fig. 17**c** reveals that the presence of substituents at C-2′ affects the cytotoxicity of the compound, and the degree of influence is related to the nature of the substituents, as confirmed in Fig. 17**d**. Simultaneously, Fig. 17**c** also shows that replacing the carbonyl group at C4′ with more hydroxyl groups does not affect the cytotoxicity, indicating that the presence of a carbonyl group does not affect cytotoxicity. Fig. 17**d** shows that the cytotoxicity of the compound is reduced when there is a double bond between C-5′ and C-6′, and converting the *N* atom at the C-6 position to NH^+ also reduces the cytotoxicity. The cytotoxicity of latrunculins is strongly related to the configuration at C-18. When C-18 has an *R*-configuration, the cytotoxicity of the compounds increases, and when it has an *S*-configuration, the cytotoxicity decreases (Fig. 17**e**). When the hydroxyl group at C-17 is replaced by methoxy, the toxicity of the compound is also weakened. In addition, we found that as the lactone ring of these compounds becomes larger, their cytotoxicity increases, which may be related to the increase in the number of hydroxyl groups on the lactone ring.

The cytotoxicity of curacins and tanjungides is related to the configuration of the double bond in their structures. When the double bond is of the *E*-type, the cytotoxicity of the compounds increases, and when it is of the *Z*-type, it decreases. If there is a methyl group at C-9 of curacins, the cytotoxicity of the compound also increases (Fig. 17**f**). The cytotoxicity of leptosins is related to the number of sulfur atoms in the sulfur bridge. As the number of sulfur atoms increases, the cytotoxicity is attenuated, but if the sulfur bridge is missing, the cytotoxicity of leptosins is greatly reduced. It can be seen that the sulfur bridge is an important cytotoxic basis of leptosins. Cytotoxicity is reduced in the presence of methyl group at C-7, and increased in the presence of hydroxymethyl groups. Cytotoxicity is similarly reduced in the presence of hydroxyl groups in C-3. (Fig. 17**g**). In addition, the configuration of the hydroxyl groups at the C-3 and C-3′ positions will affect the cytotoxicity. The cytotoxicity will decrease when both are *S*-configurations, and it will increase when both are *R*-configurations. (Fig. 17**h**).

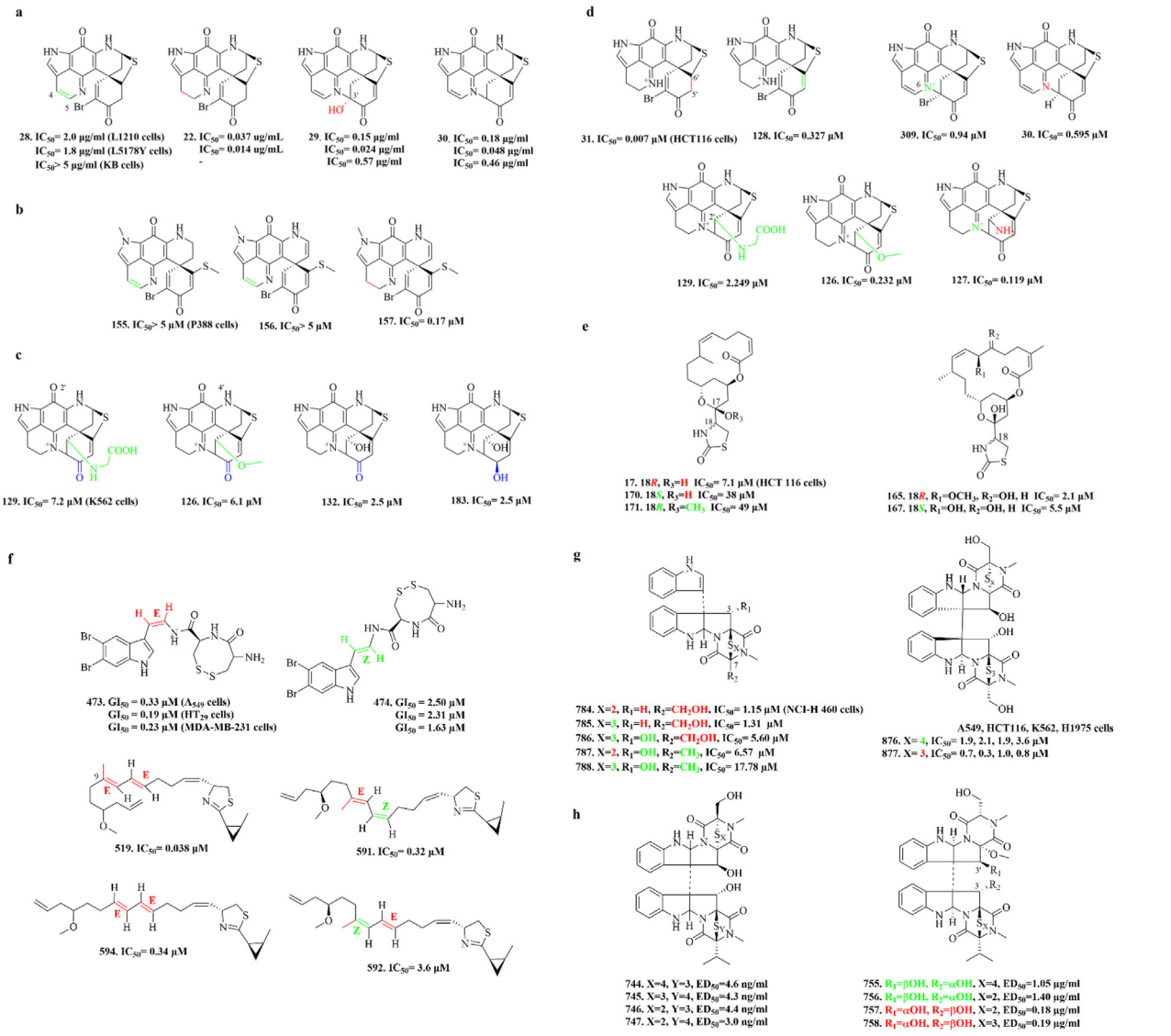

Fig. 17 Structure-activity relationships of the cytotoxicity.

2. Conclusions and outlook

This review summarized current research regarding the chemical and bioactivity diversity of marine-derived sulphur-containing alkaloids from 1992 to 2022. More than 972 sulphur-containing alkaloids have been isolated and identified from the marine. Meanwhile, modern pharmacological research revealed that the sulphur-containing alkaloids have significant pharmacological properties including cytotoxicity, anti-proliferation, anti-virus, anti-inflammatory, antioxidant, antibacteria, antifungal, anti-malarial, antiparasitic and enzyme inhibitory activity. Regardless, there are still several aspects that need to be concerned in the further development of marine-derived sulphur-containing alkaloids.

Firstly, as shown in Fig. 1, sponges are the dominant producer of marine-derived sulphur-containing alkaloids, yielding 316 of these 972 compounds (32.51%). Marine animal tunicates also produce massive sulphur-containing alkaloids with a combined percentage of 16.26%. In addition, marine fungi and bacteria are also important sources, producing 20.27% and 11.32%, respectively, of the alkaloids reviewed. It can be seen that almost 80.36% of marine-derived sulphur-containing alkaloids are from marine sponges, fungi, tunicates and bacteria. This suggests that we can focus more on marine sponges, fungi, tunicates and bacteria in the search for more marine-derived sulphur-containing alkaloids.

Secondly, sulphur-containing alkaloids obtained from sponges have fallen since 2010, while microbes, especially fungi, have grown to be important producers (Fig. 2). There may be two reasons for this. (1) with the increasing demand for new bioactive substances, the attraction of terrestrial fungi in drug screening has gradually decreased. Scientists began to pay attention to marine fungi living in complex environments such as high pressure, high salt and low temperature. Meanwhile, the complex environment makes the secondary metabolites of marine fungi have diverse structures and unique

biological activities, which attracts scientists to increase the research and development of marine fungi. (2) Biochemists have begun to generally acknowledge that sampling slow-growing sessile organisms to identify natural products is not an economical and environmentally friendly approach. Fungi can reproduce indefinitely under suitable conditions, and their genomes can be easily mined for targeted metabolites. This also makes fungi get more attention.

Thirdly, sulphur-containing alkaloids have been shown to have a variety of biological activities such as cytotoxicity, anti-proliferation, anti-virus, anti-inflammatory, antioxidant, antibacteria, antifungal, anti-malarial, antiparasitic and enzyme inhibitory activity. Of them, ecteinascidin 743 (yondelis) has been approved by the European Union in October 2007 for the treatment of advanced soft tissue tumors, which became the first modern marine drug (Menchaca et al., 2003). Thiomarinols, a kind of naturally occurring double-headed antibiotic, usually have excellent antibacterial activity and can even be effective against MRSA (Shiozawa et al., 1995). But more sulphur-containing alkaloids with various activities also need to be found in the marine. Of course, it can not be ignored that monomeric compounds with outstanding pharmacological activities can be considered the source of new drugs with excellent therapeutic effects. For example, shishijimicin A (**431**), B (**432**), C (**433**) and namenamicin (**434**) exhibited extremely cytotoxic to 3Y1, HeLa and P388 cells with IC_{50} values from 0.47 to 43 pg/ml. Gliotoxin (**792**), acetylgliotoxin (**804**) and reduced gliotoxin (**803**) have been reported to inhibit HCT-116 and RKO cells with IC_{50} values from 0.41 to 4.49 μM. Chetracin E (**875**), F (**876**) and C (**877**) also have cytotoxicity against A549, HCT116, K562, H1975 cells with GI_{50} from 0.2 to 3.6 μM.

Fourth, although many compounds with excellent activity have been found in sulphur-containing alkaloids, only a few components have been fully and deeply studied, and a large number of active components have only been tested for simple biological activity. This may be related to active compounds being too few to support a more in-depth study of the mechanism. Such problems usually need to be solved by chemical synthesis, but it is not realistic to synthesize each compound without purpose. At present, it is proposed to simulate the combination of active components and target receptors by molecular docking technology to achieve preliminary screening of active compounds, which may be a method to reduce the workload (Chen et al., 2020). All in all, it is still necessary to further study the mechanism of active sulphur-containing alkaloids to provide a scientific basis for the development of new drugs.

Fifth, the remarkable chemical diversity and biological activities of marine-derived sulphur-containing alkaloids make them attractive candidates for drug discovery and development. With the continued development of advanced techniques for marine natural product isolation, structure elucidation, and biosynthesis studies, we can expect to discover even more diverse and potent sulphur-containing alkaloids.The future impact of marine-derived sulphur-containing alkaloids in the drug discovery avenue will be more significant too.

Finally, the ocean is a huge treasure house of medicine awaiting human exploration. Among the natural marine products, sulphur-containing alkaloids are important potential drugs that deserve further research and development. This review could be a useful tool in assisting researchers in the selection of interesting species or isolated compounds for further studies, as well as expand the research of marine-derived sulphur-containing alkaloids.

Author contributions

Z.L. Zhang, Y.Z. Li, W. Wang and Y. Sun searched and collected literature; Z.L. Zhang and Y.Z. Li carried out the writing work; X.M. Song and D.D. Zhang designed this review. All authors have read and agreed to the published version of the manuscript.

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Appendix A. Supplementary material

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