A Review on Marine Sponges derived Alkaloids

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ABSTRACT:

Natural products proved to be rich source of lead compounds for drug development. Ocean has numerous numbers of marine sources such as algae, fungi, sponges etc. Under competitive environments, marine sponges possess chemical richness and interesting biological activity of secondary metabolites. the current review paper highlights the marine sponges like Agelas, Aaptos, Psammaplysillapurea, Ianthella basta, Verongiaaerophoba, spongosorites, Irciniaamphimedon etc., are focussed on their bioactivity and chemical richness. Agelaspongin family reported to have more alkaloid groups such as pyrrole, imidazole, terpenoid alkaloids which exhibits Cytotoxic, Antibacterial, Broad spectrum, Antimicrobial, Immunosuppressant activities. Relevant summaries on the marine source, its compounds, and associated bioactivity belonging to various chemical classes are also provided. This article would be beneficial for future research and development of new drugs from marine sponges.

Keywords: Marine sponges, Algae, Alkaloids, Cytotoxicity, Antibacterial, Chemistry, Marine sources, Drug discovery.

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INTRODUCTION:

Natural products have been used as possible sources of lead compounds for the drug discovery and development[1]. Around 80% of all plant and animal species on the planet have their natural habitat in the open oceans and deep seas, which make up around 70% of the planet's surface[2]. The ocean is known to be host to several diverse creatures, including multicellular complex species like sharks and whales as well as prokaryotic bacteria and marine invertebrates[3]. Despite the extreme conditions of the marine environment, the accessibility of new compounds from marine organisms from the various depths of the sea is now possible due to the advancement in technologies[4,5]. It is important to study marine life since it serves as a significant source for the creation of new chemicals. The diversity of marine microorganisms exceeds that of terrestrial microorganisms, according to evolutionary history. Compared to other living microorganisms, marine sponges typically create bioactive chemicals. Sponge predators like fish, turtles, and invertebrates can easily eat them because they can't move and have no physical defences. As a result, it is not unexpected that sponges have evolved a diverse range of defence compounds to fend off predators[6]. Research on natural chemicals from marine species started in the 1950s when Bergmann and his colleagues isolated the substances spongothymidine and spongouridine from the Caribbean sponge Tectitethya crypta.

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Several marine species, including sea slugs, sponges, and soft corals, have become a significant source of novel natural bioactive chemicals in recent years. Most natural compounds that have been discovered come from marine invertebrates, particularly marine sponges, and hundreds of compounds are identified from this source every year, from the early stages of natural product marine research to the current trend of drug discovery[7].

Marine sponges have had to evolve a complex metabolic system in order to produce a variety of secondary metabolites that are physiologically active due to their physically unpredictable and competitive habitats. Between 1950 and 2019, almost 9500 novel compounds were identified from marine sponges, the majority of which displayed a diverse spectrum of biological functions[8],[9]. Sponges are spineless animals belong to phylum, "the pore bearers" (Porifera), serve as most primitive multicell animals, existing for millions of years ago. Marine sponges are soft bodied, sessile and filter feeders assembling small particles of food from sea water rising through their bodies[10]. Marine sponges have a jelly-like layer between two thin layers of cells and may have spicule skeletons made of silica, calcium carbonate, and a protein called spongin. The size and shape of the spicules are used to identify sponge species[11]. Marine sponges are filter feeders that produce neutralising bioactive substances to deal with potentially dangerous particles. Eleven genera of sponges, including the three genera Haliclona, Petrosia, and Discodemia, which are known to produce substances with potent anti-inflammatory and anti-cancer properties, have been shown to contribute to the discovery of bioactive chemicals[12],[13]. Chemically varied bioactive substances produced by sponges include nucleosides, terpenes, sterols, cyclic peptides, and alkaloids[14].

Since ancient times, alkaloids have been one of the most important classes of natural products that have provided drugs. Marine-derived alkaloids have proven to be particularly important for drug discovery in recent decades, as demonstrated by the new antitumor drug Yondelis® (ET-743). Marine alkaloids account for roughly one-quarter of the more than 25,000 marine natural products reported to date, with sponges accounting for slightly more than half of them[15]. Some marine algae alkaloids are contaminants, such as communesin, an indole derivative isolated from a Penicillium sp. found on the green algae Enteromorpha intestinalis and leptosins from Leptosphaeria on Sargassum tortillae[16].

In this review article, we tried to focus on the Secondary metabolite- Alkaloids found in some species of marine sponges. Even though numerous compounds have been discovered from marine life, there are few marketed products available for various infections. In the current scenario of infectious diseases and viruses, there is much need for drugs developed from marine sources. This review assists scientists and researchers in identifying and developing novel therapeutic molecules from the bioactive substances found in marine sponges.

DISCUSSION:

Approximately, 2000 alkaloids are known from marine sponges. They are frequently found in terrestrial plants, but not often in marine algae. Representation of tables which shows Species, its

Benzo naphthyridine alkaloid:

Compound	*Species*	*Bioactivity*	*Ref*
Isoaaptamine	Aaptosaaptos/Hadromeri	Not reported	[17]

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Fedoreev et al. found Isoaaptamine, which is a Benzonaphthyridine alkaloid from the species Aaptosaaptos/Hadromeri .

Bromopyrrole alkaloids:

Compound	*Species*	*Bioactivity*	*Ref*
Nagelamides D	Synthesis	cytotoxicity, immunosuppressive activities	18
Hymenidin (2-debromooroidin)	Hymeniacidon	cytotoxicity, immunosuppressive activities	19
Mukanadin D (26)	Didiscusoleata	cytotoxicity, immunosuppressive activities	20
Debromohymenialdisine	Phakellia Sp.	cytotoxicity, immunosuppressive activities	21

Compound Nagelamides D a chemically synthesized bromopyrrole alkaloid, Hymenidin (2-debromooroidin) from Hymeniacidon, Mukanadin D from Didiscusoleata, Debromohymenialdisine from Phakellia Sp. has shown cytotoxicity and immunosuppressive activities.

Bromotyrosine Alkaloid

Compound	*Species*	*Bioactivity*	*Ref*
(+)-Aeroplysinin-1	Verongiaaerophoba	antiproliferative	22
psammaplin A	Psammaplysilla purpurea, Pseudoceratina purpurea	cytotoxicity	23
Purealidin A	Psammaplysillapurea	Cytotoxic Activity, Antifungal Activity	24
aplysinones A–D	Aplysinagerardogreeni	cytotoxic activity-lung carcinoma	25
Bastadins	Ianthella basta	cytotoxicity	26
clavatadine A–E	Subereaclavata	Inhibiting Factor XIa (FXIa	27, 28

According to Koulman A et al., Aeroplysinin-1 from the species Verongiaaerophoba exhibited preferential cytotoxicity, Antiproliferative activity. Psammaplin A which is a symmetrical brominated tyrosine metabolite from the species Psammaplysilla purpurea, Pseudoceratina purpurea showed cytotoxicity.

Purealidin A from Psammaplysillapurea, aplysinones A–D from Aplysinagerardogreeni, Bastadins which are derived from oxidative coupling of two brominated tyrosine-tyramine amides, belonging to Ianthella

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basta sp. has shown cytotoxicity and antifungal activity. clavatadine A–E from Subereaclavata reported Inhibiting Factor XIa.

Dimeric pyrrole alkaloids:

Compound	*Species*	*Bioactivity*	*Ref*
sceptrin	A. sceptrum	Broad spectrum	[29, 30, 31, 32, 33]
Di-Bromo Sceptrin, De-Bromo Sceptrin, monooxygenated with aminoimidazolinone Sceptrin, Ageliferin Bromoageliferin	A. conifera	Broad spectrum	[34, 35]
nakamuric acid, Methyl Ester of nakamuric acid	A. nakamurai	Antibacterial	[36]
hexazosceptrin	Agelas sp.	Antibacterial	[37]
(9S,10R,90 S,100 R)-nakamuric acid		Antibacterial	
dioxysceptrin, dioxysceptrin	A. kosrae	Cytotoxic, antiangiogenic, inhibitor of isocitr	[38]
Benzosceptrin C	Agelas sp.	Antibacterial, quorum sensing inhibitory, inhib	[39, 40]
mauritiamine	A. mauritiana	Antifouling, antibacterial	[41]
Nagelamides A	Agelas sp.	Antibacterial, inhibitor of protein phosphatase	[42]
Nagelamides B-D		Antibacterial	
Nagelamides G-H		Antibacterial, inhibitor of protein phosphatase	
Nagelamides J-L		Antimicrobial	
Nagelamides O	Agelas sp.	Antibacterial	[43, 44]
Nagelamides Q-R		Antimicrobial	
Nagelamides X-Z	Agelas sp.	Antimicrobial	[45]
citrinamines A–D		Antimicrobial	
agelamadins A–E	Agelas sp.	Antimicrobial	[46, 47]
agelanemoechine	A. nemoechinata	Proangiogenic	[48]

The dimeric pyrrole alkaloids are a new class of alkaloids with fascinating bioactivities, novel connections, and distinctive structural features.A. sceptrum species has alkaloid sceptrin which showed

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broad spectrum activity. di- and debromo analogues, and monooxygenated analogue, aminoimidazolinone moiety, ageliferin, ,bromoageliferin and dibromoageliferin from A. conifera has shown broadspectrum action.

Nakamuric acid and its corresponding methyl ester which were obtained from A. nakamurai has reported Antibacterial activity. Hexazosceptrin from Agelas species reported to show Antibacterial action. dioxysceptrin and ageleste C from A.kosrae exhibited Cytotoxic, antiangiogenic, inhibitor of isocitrase lyase. benzosceptrin C, mauritiamine, nagelamides A from Agelas species has shown activities like Antibacterial, quorum sensing inhibitory, antifouling. Other compounds from Agelas species exhibited antimicrobial activity.

Fused cyclic pyrrole alkaloids:

Compound	*Species*	*Bioactivity*	*Ref*
Dibromoagelaspongin hydrochloride	Agelas sp.	Stimulator of wheat roots growth	[49]
Phakellin alkaloids	A. mauritiana	Inhibitor of bacterial biofilm, antipredatory	[50, 51]
Bromoisophakellin, bromophakellin, dibromoisophakellin	Agelas sp.	Inhibitor of bacterial biofilm, antipredatory	[52]
(-)-7-N-methyldibromophakellin	Agelas sp.	Inhibitor of lipoxygenase isozymes	[53]
5-bromophakelline, cylindradine A	Agelas sp.	Cytotoxic	[54, 55]
Dibromocantharillin	A. kosrae	Antifungal, inhibitor of glycogen synthase kina	[56, 57]
Agelastatins A	A. dendromorpha	Cytotoxic, inhibitor of glycogen synthase kinas	[58, 59, 60]
Longamide	A. longissima	Antibacterial	[61]
Longamide B	A. dispar	Antibacterial, trypanocidal, antileishmanial	[62, 63]
(±)-longamides D–F	Agelas sp.	antifungal	[64]
+longamide B methyl ester		Antibacterial, antifungal	

Dibromoagelaspongin hydrochloride from Agelas species has shown stimulation of wheat roots growth. Dibromophakellin, monobromoisophakellin, monobromophakellin and dibromoisophakellin from A. mauritiana has shown inhibition of bacterial biofilm, antipredatory activity. The enantiomer of (-)-7-N-methyldibromophakellin, (±)-longamides D–F shows inhibitory activity on lipoxygenase isozymes and antifungal, antibacterial activity repectively.Thelongamides A AND B from genus A.longissima and A.dispar proved to have antibacterial activity. 5-bromophakelline, cylindradine A from Agelas species proved to be cytotoxic.

Imidazole alkaloid:

Compound	*Species*	*Bioactivity*	*Ref*
Naamine D	Leucetta cf. chagosensis	C.neoformans	[65]

Naamine D from Leucetta cf. chagosensis showed activity against C.neoformans.Four imidazo-azolo-imidazole alkaloids, axinellamines A-D, have been isolated from an Australian marine sponge, Axinella sp. (order: Halichondrida: family: Axinellidae). These compounds contain a unique perhydrocyclopenta-imidazo-azolo-imidazole carbon skeleton. Three of these compounds had bactericidal activity against Helicobacter pylori.

Indole alkaloid:

Compound	*Species*	*Bioactivity*	*Ref*
Hamacanthin A	Spongosorities sp.	C.albicans	[66]
Macanthins A–B	Spongosoritiessp	C.albicans, C.neoformans	

HamacanthinA ,Macanthins A–B from Spongosoritiessp exhibited activity against c.albicans, C.neoformans.

Linear-Pyrrole-imidazole alkaloids:

Compound	*Species*	*Bioactivity*	*Ref*
oroidin	A. oroides	Broad spectrum	[67, 68, 69, 70, 71, 72]
clathrodin	A. clathrodes	Broad spectrum	[73, 74]
hymenidin	A. sventres	Inhibitor of potassium channel	[75, 76]
sventrin		Antipredatory	[77]
Keramadine	Agelas sp.	Serotonergic receptors antagonist, antibacteria	[78, 79, 80]
9,10-dihydrokeramadine, debromokeramadine		NRb	[81]
dispacamides A	A. clathrodes, A. dispar, A. longissima, A. c	Antihistaminic, antipredatory	[82, 83]
dispacamides B		Antihistaminic, antimalarial	[84]
dispacamides C-D		Antihistaminic	[85]
nemoechine H	A. nemoechinata	Cytotoxic	46
taurodispacamide A	A. oroides	Antihistaminic, antimicrobial	16 and 49

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tauroacidins A	Agelas sp.	Inhibitor of tyrosine kinase, antibacterial	[86]
nagelamides M-N	Agelas sp.	Antimicrobial	[87]
nagelamides U	Agelas sp.	Antimicrobial	[88]
nagelamides W		Antimicrobial	
mukanadin G	Agelas sp.	Antimicrobial	[89]
clathramides A, B	A. clathrodes	Antifungal	[90]
clathramides C-D	A. dispar	Antifungal	[91]
Slagenins A-B		Cytotoxic	
Ageladine A	A. nakamurai	Antiangiogenic, fluorescent pH sensor	[92,93]

Many linear pyrrole alkaloids are pyrrole-imidazole alkaloids (PIAs), which are made of an aliphatic tract connecting a bromo- or debromopyrrole-2-carboxamide core to an aminoimidazole group.s oroidin from A.oroides, clathrodin from A.clathrodes has broad spectrum activity.

D-Hymenidinand N-methylated derivative Sventrinfrom A. Sventresreported to have Antipredatory, inhibitor of potassium channel. Keramadine, 9,10-dihydrokeramadine, 2-bromokeramadine and 2-bromo-9,10-dihydrokeramadine from Agelas sp. Reported to have Serotonergic receptors antagonist, antibacterial activity. DispacamidesA,B from A. clathrodes, A. dispar, A. longissima, A. Has shown Antihistaminic, antipredatory, antimalarial activity.

Manzamine Alkaloid:

Compound	*Species*	*Bioactivity*	*Ref*
manzamine A (1)	Haliclona	cytotoxicity against P388 murine leukemia cells	[94]
ircinals A (2)	IrciniaAmphimedon	Anti-Malarial	[95]
ircinals B (3)	IrciniaAmphimedon	Anti-Bacterial	[96]
2-N-methylmanzamine A (6)	Synthetic	antiplasmodial activity	[97]
nakadomarin A	Acanthostrongylophora	inhibition of Mycobacterium tuberculosis	[98]
ma'eganedin A	Acanthostrongylophora	inhibition of Mycobacterium tuberculosis	[99]
manadomanzamines A B	Amphimedon	inhibition of Mycobacterium tuberculosis	[100]
zamamidines A B C	Amphimedon	Against Plasmodium falciparum	[101]
neo-kauluamine	Acanthostrongylophora	Against Infectious Parasitic Diseases	[102]

The manzamines are polycyclic b-carboline-derived alkaloids. ircinalsA ,ircinals B from IrciniaAmphimedon species has shown antibacterial and anti-malarial activity. It is reported that 2-N-methylmanzamine A has antiplasmodial activity. nakadomarin A, ma'eganedin A from species Acanthostrongylophora exhibited inhibition of mycobacterium tuberculosis.

Pyrrole alkaloids without Imidazole moeity:

Compound	*Species*	*Bioactivity*	*Ref*
4,5-dibromopyrrole-2-carboxylic acid	A. oroides	Immunosuppressive, antipredatory	[103], [104]
4,5- dibromopyrrole-2-methylcarboxylate,		Inhibitor of protein tyrosine phosphatase	[105]
4,5-dibromopyrrole-2-carboxamide,		Promotor of ascidian larval metamorphosis, inhi	[106]
5-bromopyrrole-2-carboamide, 5-bromopyrrole-2-(-N-methoxymethyl)carboxamide	A. nakamurai	Antimicrobial	[107], [108]
agelongine	A. longissima	Antiserotonergic	[109]
dispyrin	A. dispar	Ligand and antagonist of several receptors	[110], [111], [112]
agelanesins A–D	A. linnaei	Cytotoxic	[113]

The pyrrole alkaloids without an imidazole moiety were found in the initial analysis of the components of A. oroides found in the Bay of Naples**.** 4,5-dibromopyrrole-2-carboxylic acid displayed immunosuppessive and Antipredatory effect. 4,5- dibromopyrrole-2-methylcarboxylate could be the Inhibitor of protein tyrosine phosphatase. 4,5-dibromopyrrole-2-carboxamide showed promotor activity against larval metamorphosis. 5-bromopyrrole-2- carboamide (63) and 5-bromopyrrole-2-(-N-methoxymethyl)carboxamide from species A.nakamurai reported to have Antimicrobial activity. 7—agelongine from A.longissima showed Antiseraonergic activity. Dispyrin from A.dispar reported to have the ability of Ligand and antagonist of several receptors(G-protein coupled receptors.)agelanesins A–D from species of A.linnaei has cytotoxic activity.

Pyrrole Imidazole alkaloid:

Compound	*Species*	*Bioactivity*	*Ref*
sceptrin, oxysceptrin, and ageliferin	Synthesis	cytotoxicity, immunosuppressive activities	[114]

Sceptrin, oxysceptrin, and ageliferin from A.oroides has shown cytoxicity and Immunosuppressive activity.

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Terpenoid alkaloids:

Compound	*Species*	*Bioactivity*	*Ref*
agelasines A–D	A. nakamurai	Inhibitor of Na+,K+-ATPase	[115, 116]
Agelasines C		Inhibitor of Na+,K+-ATPase, antituberculosis	[117, 118]
Agelasines D		Broad spectrum	[119, 120]
Agelasines G	Agelas sp.	Cytotoxic, inhibitor of protein tyrosine phosph	[121, 122]
agelasines J–L	A. cf. mauritiana	Antimalarial, cytotoxic	[123]
epi-agelasine C	A. mauritiana	Antifouling	[124]
agelasimines A, B	A. mauritiana	Broad spectrum	[125, 126]
(-)-agelasine D	A. nakamurai	Cytotoxic, antifouling	[127]
(-)-agelasine D analogue		Cytotoxic, antifouling, radiosensitizer	[128, 129]
agelasine M	Agelas sp.	Trypanocidal, cytotoxic	[130]
agelasines O–R	Agelas sp.	Antimicrobial	[131]
agelasines T-U		Antimicrobial	
2-oxoagelasine A, 2-oxoagelasine F, 10-hydro-9-hydroxyagelasine F	A. nakamurai	Antibacterial	[132]
(+)-agelasine B		Cytotoxic, antibacterial	
ageloxime B		Antibacterial, antileishmanial	
241	A. nakamurai	Cytotoxic, antimicrobial	[133]
nemoechines D ((-)-80 -oxo-agelasine G,		Cytotoxic	
axistatins 1–3	A. axifera	Cytotoxic, antimicrobial	[134]
agelasidine A	Agelas sp.	Antispasmodic, antimicrobial	[135, 136]
agelasidines B-C	A. nakamurai	Smooth muscle relaxant, inhibitor of Na+,K+-ATP	[137]
agelasidines C, (-)-agelasidine D		Cytotoxic	
isoagelasidine B	A. nakamurai	Cytotoxic, antifungal	[138]

From the species Agelasnakamurai, Agelasines A–F possessed inhibitory effects against Na+ ,K+ -ATPase, Anti tuberculosis and broad spectrum activity respectively. agelasine G exhibited cytotoxic activity and inhibition on protein tyrosine.From the species A.mauritiana, agelasines J–L showed Anti malarial,

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cytotoxicity. D-epi-agelasine C, agelasimines A and B reported to have Antifouling and broad spectrum activity. A.nakamurai has -agelasine D and its analogue as key compound which showed Antifouling, cytotoxicity and radiosensitizer.

Agelasine M, agelasines O–R from Okinawan Agelas sp. Showed Antimicrobial activity. Labdane, and clerodane compounds also shown Anti microbial activity respectively. From the species A.nakamurai, compounds like 2-oxoagelasine A , 2-oxoagelasine F and 10-hydro-9- hydroxyagelasine F has shown Anti bacterial activity. agelasine B, ageloxime B, isoagelasine C, D (--)-80 -oxo-agelasine G, axistatins 1–3 from A.nakamurai and A.axifera has shown cytotoxic, anti microbial activities respectively.

Terpenoid alkaloid agelasidine A from species Agelas shown Antispasmodic, Antimicrobial activity. From A.nakamurai species, compounds like agelasidine B and C, has shown smooth muscle relaxant activity. Agelasidine (-)C and agelasidine (-)D possess cytotoxic activity. agelasidine A were found to produce Cytotoxicity, potent antifungal activity against C.albicans

Tricyclic guanidine alkaloids:

Compound	*Species*	*Bioactivity*	*Ref*
Mirabilin B	Monanchoraunguifera	C.neoformans	[139]

Guanidine alkaloid namely Mirabilin B was isolated from species Monanchoraunguifera.

Other alkaloids:

Compound	*Species*	*Bioactivity*	*Ref*
Dragmacidin F	Halicortex sp.	HIV-1	[140]
Oroidin	Stylissacarteri	Antiviral (HIV-1)	[141]
Manzamine A	Haliclona sp./ Haplosclerida	T. gondii, P. berghei, P. falciparum	[142]
(E)-Oroidin	Agelas oroides	P. falciparum	[143]

Dragmacidin F, a bromoindole alkaloid, was isolated from a marine sponge of the genus *Halicortex. w*hich has shown Antiviral activity against HIV-1. Compound Oroidin from the species *Stylissacarteri*has shown Antiviral activity (HIV-1). Manzamine A from Halicone species found to have Anti-malarial activity against T. gondii, P. berghei, P. falciparum. Marine sponge Agelas oroides have active compound (E)-oroidin which shows anti malarial activity against P.falciparum.

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CONCLUSION:

The huge variety of marine natural products and the increased global interest in discovering novel therapeutic agents for the treatment of various diseases serve as the impetus for the evaluation of marine natural products in clinical trials. Finding effective marine drugs is difficult due to a lack of supply and low concentrations of some compounds[144].

Researchers from academia and pharmaceutical companies alike are now focusing on the sea in search of new lead structures from nature because the continuous and exhaustive harvesting of terrestrial drug lead resources proved to be unreliable and led to the frequent re-isolation of known compounds. Although it is a real challenge to produce marine natural products on a large scale for clinical use, there is a need for alternatives that are both ethically sound and practical from an economic standpoint[145].

Aquaculture of the source organisms, such as sponges, tunicates, and bryozoans, has advanced significantly in cancer applications, with the goal of ensuring a sustainable supply of the active constituent(s). However, in most cases, the biomass currently generated falls far short of what is required if a marine-based drug ever makes it to the pharmaceutical market[146].

If it turns out that bacteria or other related microorganisms can produce the desired compounds, careful planning of special culture media would be essential for large-scale fermentation. Only 5% or less of the symbiotic bacteria found in marine specimens can currently be grown under normal conditions[147]

The effectiveness of sponge-derived medicines is due to the fact that each of these thousands of metabolites and their derivatives has its own unique dose-related efficacy, inhibitory effect, and potential side effects that determine its suitability for medicinal use. Unfortunately, these secondary metabolites are typically present in trace amounts, and natural stocks are insufficient, which is one of the major impediments to the development of widely available medicines[148].

Secondary metabolites isolated from marine sponges of the genus Agelas present an intriguing case that has stimulated research advancements in the field of marine natural products. This review focuses on the chemical diversity and biological activities of compounds isolated from Agelassponges, Aaptos, Irciniaamphimedon, and other organisms. Pyrrole alkaloids are abundant in Agelas sponges, accounting for 56% of Agelas-derived secondary metabolites. These pyrrole alkaloids are classified into three structural types: linear pyrrole alkaloids, fused cyclic pyrrole alkaloids, and dimeric pyrrole alkaloids, which account for approximately 52, 20, and 28% of total pyrrole alkaloids, respectively. Terpenoid alkaloids are another structural class represented, accounting for 17% of Agelas-derived secondary metabolites. Only 61 terpenoid alkaloids from the species A. nakamurai (28%), A. mauritiana (25%), A. axifera (5%), A. citrina (5%), A. clathrodes (5%), and A. nemoechinata have been reported thus far (3 %). The remaining 29% came from unclassified species of Agelas. The antimicrobial activity of pyrrole alkaloids was the most common activity, and about 24 % of the compounds displayed this property. With the above-mentioned secondary metabolites particularly alkaloids, from different species of marine sponges, it is clearly known that molecular level approaches can lead to the development of new drug entities that are effective against novel viruses, and different strains of bacteria as well as possess a variety of pharmacological properties. With the combination of synthetic chemistry and biology, these findings revealed the opportunity to find and discover valuable molecules for ongoing growth in medicinal applications. Despite of significant development of new entities from marine sources, more efforts need to be done for chemical groups to reach to the stage therapeutic trials.

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