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Antiviral compounds in marine algae, soft coral and sponge: a systematic review

Senyawa antivirus pada alga, karang lunak, dan spons laut: tinjauan sistematis

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ABSTRACT

Diseases caused by viruses are always evolving due to the mutating nature of viruses and are still a threat to the health world today. One of the strategies utilized by scientists to address this challenge is the identification of bioactive compounds with antiviral properties. This article presents an overview of various marine organisms that contain antiviral compounds, including microalgae, macroalgae, soft coral, and marine sponge. This review article employs a systematic review methodology, utilizing Proquest, MDPI, and Science Direct data search bases from 2013 to 2024. The search terms employed were "Antiviral Compounds," "Marine antiviral," "Algae antiviral," "Soft Coral antiviral," and "Sponge antiviral." A total of 440 articles were identified through the use of the specified keywords. Following the screening process, 31 articles were deemed relevant for inclusion in the review. From the 31 selected articles, six articles discussed on microalgae, 11 articles for macroalgae, eight for soft corals, and six for sponges contain antiviral compounds with diverse anti-viral mechanisms. The antiviral compounds identified in the organisms discussed in this article are fatty acid group, lutein, carrageenan, fucoidan, polyphenol group, terpenoid group, sesterpenes, asteltoxin, and others.

Kata kunci: Antiviral Compounds, Marine antiviral, Algae antiviral, Soft Coral antiviral, Sponge antiviral

INTISARI

Penyakit yang disebabkan oleh virus selalu berkembang karena sifat virus yang mudah bermutasi dan masih menjadi ancaman bagi dunia kesehatan saat ini. Salah satu strategi yang digunakan oleh para ilmuwan untuk mengatasi tantangan ini adalah dengan mengidentifikasi senyawa bioaktif yang berkhasiat sebagai antivirus. Artikel ini menyajikan tinjauan umum tentang berbagai organisme laut yang mengandung senyawa antivirus, termasuk mikroalga, makroalga, karang lunak, dan spons laut. Artikel ini menggunakan metodologi tinjauan sistematis, dengan menggunakan basis pencarian data Proquest, MDPI, dan Science Direct dari tahun 2013 hingga 2024. Istilah pencarian yang digunakan adalah “Senyawa Antiviral,” “Antiviral laut,” “Antiviral ganggang,” “Antiviral karang lunak,” dan “Antiviral spons.” Sebanyak 440 artikel diidentifikasi melalui penggunaan kata kunci yang ditentukan. Setelah proses penyaringan, 31 artikel dianggap relevan untuk dimasukkan dalam tinjauan. Dari 31 artikel yang dipilih, enam artikel yang membahas tentang mikroalga, 11 artikel untuk makroalga, delapan artikel untuk karang lunak, dan enam artikel untuk spons mengandung senyawa antivirus dengan mekanisme antivirus yang beragam. Senyawa antivirus yang teridentifikasi pada organisme yang dibahas dalam artikel ini adalah kelompok asam lemak, lutein, karaginan, fucoidan, kelompok polifenol, kelompok terpenoid, sesterpen, asteltoksin, dan lain-lain.

Kata kunci: Senyawa antiviral, Antiviral laut, Antiviral algae, Antiviral karang lunak, Antiviral spons

INTRODUCTION

Diseases caused by viruses are always evolving due to the mutating nature of viruses and are still a threat to the health world today. For example, the COVID-19 virus broke out as a pandemic in 2019-2022, causing many deaths in various parts of the world. Covid-19 is still a threat in the world of health, even though its status is now endemic. The SARS-CoV-2 virus, which causes the disease known as Coronavirus Disease 2019 (Covid-19), attacks the respiratory tract, leading to the development of acute respiratory distress syndrome and pneumonia in approximately 15% of infected individuals (Prajapat et al., 2020). SARS-CoV 2 is a +ssRNA virus that acts directly as mRNA for protein synthesis templates, making it easier to evolve (V'kovski et al., 2021). This provides an insight for scientists to develop effective pharmaceuticals and vaccines for the treatment and prevention of diseases associated with the SARS-CoV-2 virus.

One of the strategies utilized by scientists to address this challenge is the identification of bioactive compounds with antiviral properties. Antiviral compounds are bioactive compounds derived from organisms that have the capacity to attack viruses by inhibiting a number of key processes, including virus attachment, virus entry, and the activity of enzymes such as polymerase, protease, nucleoside and nucleotide reverse transcriptase, and integrase (Kausar et al., 2021).

As indicated by data from the Indonesian Ministry of Tourism and Creative Economy in 2024, the Indonesia's marine area encompasses over 5.8 million square kilometers and is home to a vast array of marine biodiversity, including the largest number of coral reefs globally. The potential of Indonesia's vast ocean and abundant marine biota resources can be utilized for human needs in the field of health, especially as an antiviral while maintaining the sustainability of its ecosystem. Marine ecosystems that have different challenges from freshwater, especially in terms of salt content, tides, oxygen content, light intensity and others, make the variation of compounds in marine organisms that are certainly different and unique. The utilisation of microalgae, macroalgae, sponges and soft coral in the health field is not much yet, but there have been many studies on these marine organisms, including for antivirals. This article presents an overview of various marine organisms that contain antiviral compounds, including microalgae, macroalgae, soft coral, and marine sponge. This review article is intended to serve as a foundation for medical biology research, particularly in the area of antivirals.

METHODS

Tempat dan waktu penelitian

In this study, we conducted a comprehensive literature review from January to May 2024, encompassing all published results up to that point. In order to conduct a comprehensive literature search, three databases (Proquest, MDPI, and Science) were queried using a combination of five keywords: "Antiviral Compounds," "Marine antiviral," "Algae antiviral," "Soft Coral antiviral," and "Sponge antiviral." No contact was made with investigators, and unpublished data were not considered. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The investigators selected the manuscripts by screening the titles and abstracts, and subsequently the full texts.

RESULTS AND DISCUSSION

A total of 440 articles were obtained that had been identified through the screening process and excluded due to the presence of duplicate content and the use of inappropriate keywords. The following articles were excluded from the study: those with the dependent variable "literature review" and a publication year of more than 10 years, reports not retrieved, articles with incomplete text, and articles that use unsuitable methods, such as computational methods. The final result was 31 articles that met the inclusion and exclusion requirements, as illustrated in Figure 1.

From the 31 selected articles, six articles discussed on microalgae, 11 articles for macroalgae, eight for soft corals, and six for sponges were reported to produce antiviral compounds, as summarized on Table 1. Antiviral compounds identified in microalgae encompass a diverse range of chemical structures, including fatty acids and lutein. In contrast, macroalgae have been shown to produce carrageenan, fucoidan, and other polyphenols, which have been demonstrated to possess significant antiviral properties. Soft coral has been shown to contain primarily terpenoid-based antiviral compounds. However, marine sponges have been observed to possess a considerably more varied range of antiviral compounds, including sesterpenes, asteltoxin, and others. Each of these compounds employs a distinct mechanism to target the virus, which will be elucidated in the following sections.

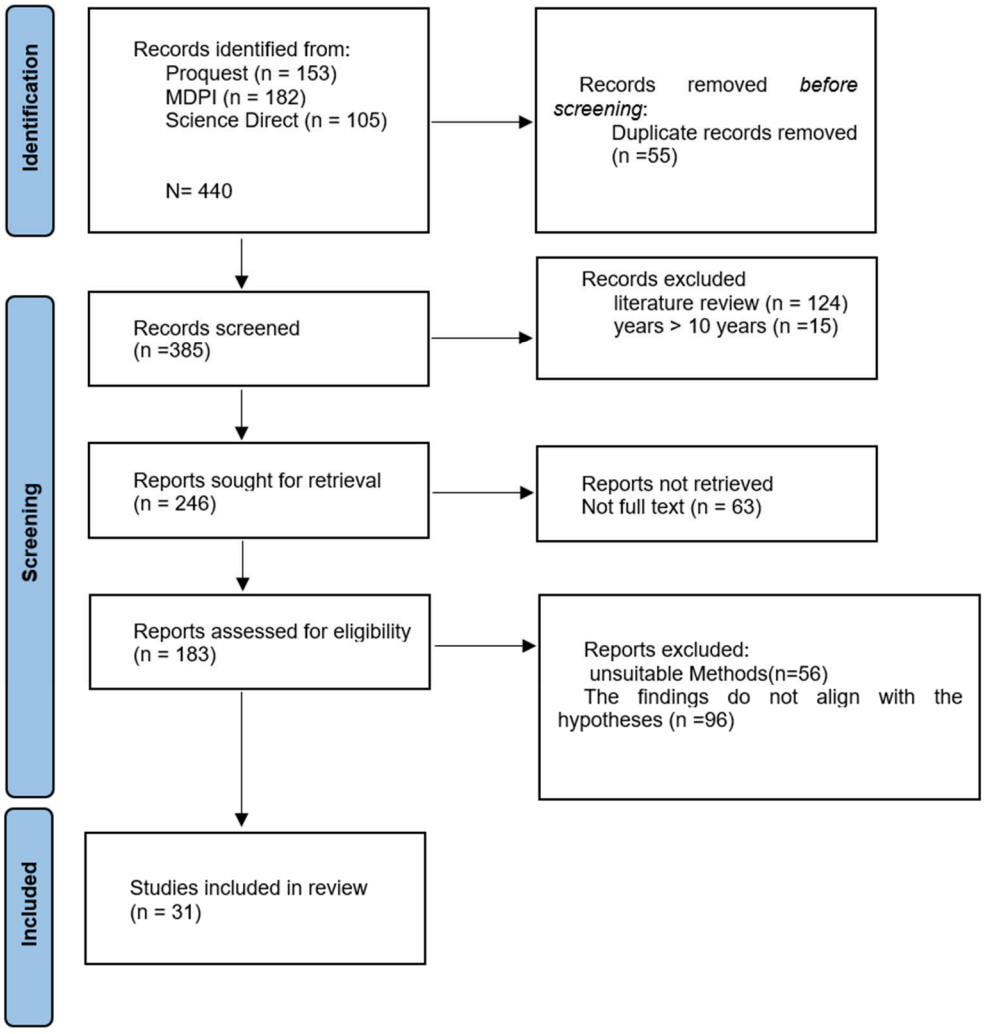

Figure 1. PRISMA Flow Chart of the systematic review on antiviral compounds in marine algae, soft coral and sponge

Table 1. Antiviral compound in marine algae, soft coral and sponge

No	Organism	Region	Antiviral compounds	References
Microalgae				
1	Red microalgae *Galdieria sulphuraria*	University of Naples, Italy. University Federico II (ACUF)	fatty acid amides (PFAM) : hydroxylinoleamide, oleamide, palmitamide, stearamide, linoleamide, and palmitamide pheophorbid a(PPBa)	(Ambrosino et al., 2023)
2	Green microalga *Neochloris oleoabundans*		primary fatty acids (PFAAs): palmitam, pheophorbide A. and oleamide; lectin and glucose, mannose, galactose, xylose, ribose, arabinose and rhamnose	(Baldisserotto et al., 2023)
3	Green microalgae *Tetraselmis* sp.	Marine Bioenergy R&D Consortium (MBE) of Inha University, Incheon, Korea.	2,2-diphenyl-1-picryl-hydrazyl-hydrate and lutein	(Kim et al., 2023)
4	Green microalga *Neochloris oleoabundans*		lipids, exo-polysaccharides, total phenolics, proteins dan pigmen	(Baldisserotto et al., 2023)
5	Microalga and Cyanobacteria		C-Phycocyanin (CPC)	(Prasetiya et al., 2023)
6	Cyanobacterium *Trichodesmium erythraeum*		aplysiatoxin, debromoaplysiatoxin dan anhydrodebromoaplysiatoxin, as well as two new analogues, 3-methoxyaplysiatoxin dan 3-methoxydebromoaplysiatoxin	(Gupta et al., 2014)
Macroalgae				
7	Rhodophyta *Halymenia floresii*	Sisal beach in Yucatan, Mexico and Saint Gildas de Rhuys coastal zone in Brittany, France	carrageenans	(Jousselin et al., 2023)
8	Rhodophyta *Chondrus armatus*		κ- and Σ-carrageenans (CRGs)	(Krylova et al., 2022)
			iota-carrageenan	(Setz et al., 2023)
9	*Laminaria japonica*		crude Polysaccharide dari Seaweed (CSP)	(Ren et al., 2022)
10	*Solieria chordalis*	Sisal beach in Yucatan, Mexico and Saint Gildas de Rhuys coastal zone in Brittany, France	carrageenans	(Jousselin et al., 2023)
11	Macroalgae (*Hizikia fusiforme* and *Sargassum horneri*), *Haliotis discus hannai* (abalone) viscera		crude polysaccharide	(Kang et al., 2022)
12	Rhodophyta *Amphiroa anceps*		polyphenols, including caffeic acid, ellagic acid, catechins, chlorogenic acid, gallic acid, quercetin, ferulic acid dan myricetin	(El-Bilawy et al., 2022)
13	*Macrocystis pyrifera, Ecklonia arborea (*formerly *Eisenia arborea), Silvetia*	Baja California, Yucatan	polyphenol-rich extracts (PPs)	(Morán-Santibañez et al., 2018)

No	Organism	Region	Antiviral compounds	References
	*compressa (*formerly *Pelvetia compressa)*			
14	Green seaweed *Ulva intestinalis*	Baja California, Yucatan	polyphenol-rich extracts (PPs)	(Morán-Santibañez et al., 2018)
15	Red seaweed *Solieria filiformis*	Baja California, Yucatan	polyphenol-rich extracts (PPs)	(Morán-Santibañez et al., 2018)
16	Brown Algae *Ascophyllum nodosum, Macrocystis pyrifera, Undaria pinnatifida* and *Fucus vesiculosus*	Sigma-Aldrich (St. Louis, MO, USA)	fucoidan, sulfated polysaccharide	(Zhang et al., 2015)
17	*Ulva lactuca*	Keelung Coast, Taiwan	sulfated polysaccharide extract	(Chiu et al., 2012)
Soft Coral				
18	*Sinularia polydactya*, *Cespitularia simplex*, *Lobophytum patulum*, and *Lobophytum crissum*	Pereybere Coast	terpenoids (abundant), alkaloids, esters, flavonoids, steroids and coumarins	(Jahajeeah et al., 2023)
19	*Antillogorgia americana* and *Antillogorgia elisabethae*		pseudopterosin A, seco-pseudopterosin A, sandresolide B, elisabatin A, and elisapterosin A	(Pokharkar et al., 2023)
20	*Heteroxenia fuscescens*	The Red Sea in front of the National Institute of Oceanography and Fisheries, Hurghada, Egypt	sesquiterpene fusceterpene A dan sterol fuscesterol A	(Abdelkarem et al., 2022)
21	*Sarcophyton* sp.		cembranoid diterpenes	(Ibrahim et al., 2021)
22	*Sinularia* sp	Yongxing Island Xisha Islands in the South China Sea	sesquiterpenoids (sinuketal, sinulins A and B; cembranoids (sinulins C and D)	(Qin et al., 2018)
23	*Sarcophyton ehrenbergi*	San-Hsian-Tai, Taitong, Taiwan,	*polyoxygenated cembranoids*, named (+)-1,15-epoxy-2-methoxy-12-methoxycarbonyl-11E-sarcophytoxide, (+)-2-epi-12-methoxycarbonyl-11E-sarcophine, 3,4-epoxyehrenberoxide A (3), ehrenbergol D dan ehrenbergol E.	(Cheng et al., 2015)
24	*Lobophytum crissum*	Dongsha Atoll off the coast of Taiwan	seco-cembranoid, secocrassumol.	(Cheng et al., 2014)
25	Soft Coral *Paralemnalia thyrsoides*	Di Sansiantai, Taitong, Taiwan,	parathyrsoidins A–D, sesquiterpenoid	(Tseng et al., 2013)
Marine Sponge				
26	Marine sponge		(+)-curcuphenol, naamine, Naamidines A, B, and C, Latrunculin A, B, and S, Xestodecalactones A, B, C, D, E, and F (+)-Curcudiol Tetillapyrone and nortetillapyrone	(Pokharkar et al., 2022)

No	Organism	Region	Antiviral compounds	References
			Aurantosides I and K	
27	*Red Sea marine* sponge *Hyrtios erectus*	Red Sea, Sharm el-Sheikh.	15 scalaranes sesterterpenes	(Elhady et al., 2021)
28	Red Sea sponge *Amphimedon chloros*	Red Sea, Saudi Arabia	3-alkylpyridinium	(O'Rourke et al., 2018)
29	Sponge *Stylissa carteri*	Al Fahal, East	debromohymenialdisine (DBH), hymenialdisine (HD), dan oroidin.	(O'Rourke et al., 2016)
30	Marine sponge (*Callyspongia* sp.), - symbiosis with *Aspergillus* sp.	Xuwen County, Guangdong Province, China	Two new asteltoxins named asteltoxin E and F and a new chromone	(Tian et al., 2016)
31	Marine Sponge *Dysidea granulosa*	Sulawesi, Muna, dan Buton Islands, Indonesia.	3,5-dibromo-2-(2,4-dibromophenoxy)-phenol (compound 1) and 3,4,5-tribromo-2-(2,4-dibromophenoxy)-phenol (compound 2), which are classified as polybrominated diphenyl ethers (PBDEs)	(Yamashita et al., 2015)

A. Microalgae

Microalgae are microscopic algae that are cultivated for their biomass, which is utilized to fulfill human necessities. These include the production of biofuels, pharmaceuticals (such as antiviral, anti-inflammatory, and anticancer drugs) and food supplements (Setyaningrum et al., 2023). It has been established that a number of bioactive compounds present in microalgae have the potential to act as antivirals. These include a mixture of fatty acid amides, namely linoleamide, oleamide, palmitamide, stearamide, and hydroxylinoleamide, which have been isolated from the red microalgae *Galdieria sulphuraria* (Ambrosino et al., 2023). These amid fatty acids have been demonstrated to exhibit robust antiviral activity against members of the Coronaviridae (SARS-CoV-2 and HCoV-229E) and Herpesviridae (HSV-1 and HSV-2) families. They have the capacity to interact with viral envelope glycoproteins, thereby preventing cell entry (Ambrosino et al., 2023). The microalgae *Neochloris oleoabundans* contains primary fatty acids (PFAAs), including oleamide, palmitic acid, and pheophorbide A, which have been demonstrated to possess antiviral properties against the Coronaviridae family. These compounds have been observed to penetrate the membrane enveloping HCoV-229E and destabilize its envelope arrangement (Baldisserotto et al., 2023). This type of microalgae also contains lectins that act as preventive agents, which inhibit the interaction of viruses (or microbes in general) with cell membranes because they occupy the place where viruses attach to cell membranes (Baldisserotto et al., 2023). Compounds known as antioxidants such as 2,2-diphenyl-1-picryl-hydrazyl-hydrate were found in the green microalga *Neochloris oleoabundans* that served as hydrogen peroxide scavenging activity and reduced plaque formation in infected Vero E6 cells infected with vaccinia virus (Kim et al., 2023).

Various microalgal pigments have been demonstrated to possess antiviral properties. One such pigment is C-phycocyanin (CPC), which has been demonstrated to possess a high affinity for ACE2 and the potential to inhibit the binding of ACE2 (angiotensin-converting enzyme II) and SARS-CoV-2 receptors (Prasetiya et al., 2023). The angiotensin-converting enzyme 2 (ACE2)

receptor is a viral receptor that functions to convert the octapeptide angiotensin II (Ang II) into angiotensin (1-7), which is a peptide hormone that plays a role in regulating the body's fluid balance and cardiovascular function. ACE2 is used by the SARS-CoV-2 virus for entry into host cells (Arthur et al., 2021). The combination of pigments with lipids, exo-polysaccharides, proteins, and phenolics for extracts derived from autotrophic cultures and acidic proteins/exo-polysaccharides/lipids in the green microalga *Neochloris oleoabundans* also has antiviral potential (Baldisserotto et al., 2023).

B. Macroalgae

Macroalgae are multicellular algae that are widely utilized for the needs of the food, pharmaceutical and health industries. Many types of macroalgae also contain antiviral compounds. Iota-carrageenan is one of the antiviral compounds found in macroalgae (Setz et al., 2023). Iota-carrageenan represents an important family of naturally-occurring sulfated polysaccharides that possess gelling properties. Its use as a food additive is well documented (Czechtizky et al., 2022). As an antiviral compound, iota-carrageenan inhibits replication of SARS-CoV-2 Wuhan Type and VoC Alpha, Beta, Gamma and Delta, as well as various SARS-CoV-2 VoC Omicron subvariants (Setz et al., 2023).

One of the macroalgae phyla that contain carrageenan is Rhodophyta. Algae belonging to the Rhodophyta phylum, namely *Halymenia floresii* and *Solieria chordalis*, contain carrageenan, which has been demonstrated to be effective in the treatment of respiratory infections (Jousselin et al., 2023). In particular, carrageenan has been shown to inhibit the attachment of SARS-CoV-2 to the mucous membranes of the respiratory tract and thus to prevent the transmission of the virus. The mechanism appears to be related to inhibiting viral attachment to the cell surface (Jousselin et al., 2023). Another member of the Rhodophyta phylum that contains carrageenan is *Chondrus armatus*. *Chondrus armatus* contains κ- and Σ-carrageenans (CRGs) that have been demonstrated to exhibit significant anti-HSV-1 activity, primarily due to their virucidal and prophylactic properties, as well as their capacity to inhibit virus-cell interactions. The liposomal form of the Σ-CRG complex was observed to effectively reduce HSV-1 plaque formation following adsorption and penetration of the virus into cells, indicating that this form may be a promising anti-HSV-1 treatment (Krylova et al., 2022).

Crude Polysaccharide from Seaweed (CSP) from the Phaeophyceae Laminaria japonica significantly inhibited IHNV (infectious hematopoietic necrosis virus) infection by preventing virus attachment and release in host cells (Ren et al., 2022). Furthermore, CSPs have been demonstrated to exhibit anti-IPNV (infectious pancreatic necrosis virus) activity through the inhibition of virus attachment, entry, and release. Furthermore, CSP demonstrated efficacy in preventing co-infection by IHNV and IPNV (Ren et al., 2022). The crude polysaccharide derived from the *Hezikia fusiforme* and *Sargassum horneri* species has been demonstrated to impede the replication of the SARS-CoV-2 virus. This inhibitory effect is achieved through the interference of virus entry, effectively hindering the spread of SARS-CoV-2 both prior to and subsequent to infection. Furthermore, in vitro studies have corroborated the complete inhibition of replication through the prevention of virus entry (Kang et al., 2022).

One of the antiviral compounds isolated from macroalgae is polyphenols. A variety of polyphenols have been identified in the red algae *Amphiroa anceps*, including myricetin, gallic acid, chlorogenic acid, ellagic acid, ferulic acid, caffeic acid, catechins, chlorogenic acid and quercetin (El-Bilawy et al., 2022).

Erulic acid has been demonstrated to stiffen the viral protein envelope (El-Bilawy et al., 2022). Polyphenol-rich extracts (PPs) are also present in various types of macroalgae, including *Solieria filiformis*, *Macrocystis pyrifera, Ulva intestinalis*, *Peltia compressa* and *Ecklonia arborea* (Morán-Santibañez et al., 2018). It has been demonstrated that PPs possess significant virucidal activity against the measles virus in vitro. The antiviral activity of the extracts represents a prophylactic strategy that can be employed prior to viral infection, as well as a potential treatment following infection, thereby preventing the further dissemination of the virus (Morán-Santibañez et al., 2018).

In addition to the various compounds above, another antiviral compound found in macroalgae is sulfated polysaccharide. Sulfated polysaccharide is contained in brown macroalgae species such as *Fucus vesiculosus*, *Macrocystis pyrifera, Ascophyllum nodosum*, and *Undaria pinnatifida* and green algae *Ulva Lactuca* (Zhang et al., 2015), (Chiu et al., 2012). The sulfated polysaccharide derived from *Ulva* has been demonstrated to impede the adsorption of the Japanese encephalitis virus (JEV), rendering it incapable of entering the cell (Chiu et al., 2012). A particular type of sulfated polysaccharide, isolated from marine macroalgae, is known as fucoidan (Zhang et al., 2015). The isolation of fucoidan from *M. pyrifera* has the potential to yield a valuable therapeutic agent for the treatment of infectious diseases and cancer; it may also prove effective as an adjuvant for vaccines (Zhang et al., 2015). It has been established that *M. pyrifera* is a powerful immunological modulator that can increase Th1 immune response, DC maturation, CTL activity, NK cell activation, antigen-specific antibody generation, and memory T cell development (Zhang et al., 2015).

C. Soft Coral

Soft coral is a marine organism that forms part of the structure of coral reefs. It belongs to the Cnidaria family, which comprises a variety of marine animals that possess a sting. It is classified within the Alcyonaria class and the Alcyoniidae family (Candri et al., 2023). One of the compounds isolated from soft coral is terpenoids. Soft coral species that contain terpenoids include *Lobophytum crissum, Sinularia polydactya, Lobophytum patulum* and *Cespitularia simplex* (Jahajeeah et al., 2023). The antiviral effectiveness of the *L. patulum* extract against HPV and SARS-CoV-2 pseudovirus infections has been proven, indicating its potential as a therapeutic agent for the prevention of infectious illnesses (Jahajeeah et al., 2023).

The soft coral species *Sinularia* sp. was also found to have novel chemicals known as sesquiterpenoids and cembranoids. One kind of substance is sinuketal, which exhibits modest target inhibitory action against acetylcholinesterase and inhibitory effects against the influenza A H1N1 and PR8 viruses (Qin et al., 2018). The soft coral *Paralemnalia thyrsoides* has been found to contain four different types of sesquiterpenoids, namely parathyrsoidins A-D, which have been demonstrated to exhibit antiviral activity against the Human Cytomegalovirus (HCMV), as evaluated through in vitro analysis (Tseng et al., 2013). The class of natural products known as sesquiterpenoids is notable for its diversity and is derived from a common precursor, farnesyl pyrophosphate (FPP), which consists of 15 carbon atoms (Nguyen et al., 2012). Another Sof coral that also contains sesquiterpene is *Heteroxenia fuscescens* which inhibits the SARS-CoV-2 Mpro by binding to the amino acids (active side) of the pockets of the SARS-CoV-2 Mpro (Abdelkarem et al., 2022).

Other compounds that have been demonstrated to possess antiviral functions are cembranoids, which are found in soft coral. Cembranoids are

macrocyclic diterpenoids, comprising four isoprene units bonded end-to-end. These molecules feature a fourteen-membered ring with three methyl groups arranged in a symmetrical fashion and a fourth, isopropyl group (Al-Harrasi et al., 2021). Cembranoid diterpenes represent one of the most expansive and structurally diverse classes of diterpenoids. The genus Sarcophyton of soft coral contains five cembranoid diterpenes that demonstrate sufficient binding affinity as Mpro inhibitors with a ΔGbinding value of less than -33.0 kcal/mol (Ibrahim et al., 2021).

Secocrassumol (seco-Cembranoid) is another cembranoids compound found in soft coral that has been demonstrated to possess antiviral properties. The soft coral *Lobophytum crissum* has been demonstrated to contain secocrassumol, which has been shown to exhibit antiviral activity against HCMV (human cytomegalovirus) (Tseng et al., 2013). *Sarcophyton ehrenbergi* contains 5 new polyoxygenated cembranoids, one of which is (+)-2-epi-12-methoxycarbonyl-11E-sarcophine which showed little antiviral activity against HCMV (human cytomegalovirus) (Cheng et al., 2015). Another diterpens compound owned by soft coral is pseudopterosin A. This compound is found in *Antillogorgia americana* and *Antillogorgia elisabethae* which is proven to fight NSP (non-structural protein) SARS COV 2 (Pokharkar et al., 2023).

D. Sponge

Sponges represent one of the most primitive multicellular aquatic animals, belonging to the phylum Porifera. It is estimated that there are approximately 5,000 described species of sponges, which are found in all oceans and can be seen attaching themselves to the water's surface, from the intertidal zone to depths of up to 8,500 metres (29,000 feet) or beyond (Ruocco et al., 2024). Some of the chemical compounds that potentially inhibit SARS CoV 2 are (+)-curcuphenol, naamine, naamidines A, B, and C, latrunculin A, B, and S, xestodecalactones A, B, C, D, E, and F, (+)-curcudiol tetillapyrone, and nortetillapyrone aurantosides I and K (Pokharkar et al., 2022). The marine sponge *Hyrtios erectus*, which is found in the Red Sea, contains compounds that bind the main protease of the SARS-CoV-2 virus and the endoribonuclease cavity Nsp15 of the virus, namely scalaranes and sesterterpenes (Elhady et al., 2021).

Another bioactive compound found in sponges is a 3-alkylpyridinium (3-AP) compound isolated from the Red Sea sponge *Amphimedon chloros* (O'Rourke et al., 2018). It has been demonstrated that this compound is capable of inhibiting the NS3 protease associated with West Nile virus (O'Rourke et al., 2018). West Nile virus (WNV) is a rapidly spreading virus that has infected humans and mammals across five continents over the past decade, resulting in disease and mortality. The NS3 protein is a viral trypsin-like serine protease, encoded by the N-terminal 184 amino acids of NS3. It is only active when bound to its cofactor, NS2B. The protease, NS2B/NS3pro, facilitates the cleavage of viral polyproteins, thereby releasing both structural and non-structural viral proteins that are indispensable for the replication of the virus and the assembly of new viral particles (Chappell et al., 2008).

Alkaloid compounds that function as antivirals are debromohymenialdisine (DBH), hymenialdisine (HD), and oroidin isolated from *Stylissa carteri* (O'Rourke et al., 2016). DBH and HD demonstrated inhibition of HIV-1 replication by 30%–40% at concentrations of 3.1 μM and 13 μM, respectively. In comparison, oroidin exhibited a 50% reduction in viral replication at 50 μM without associated cytotoxicity. Additionally, oroidin inhibited the activity of

HIV-1 reverse transcriptase by up to 90% at a concentration of 25 μM (O'Rourke et al., 2016).

Some marine sponges also associate with fungi. One of them is *Callyspongia* sp. which is associated with *Aspergillus* sp. Two new asteltoxins, designated as asteltoxin E and F, along with a newly identified chromone, were subjected to investigation. These compounds showed remarkable efficacy against the H3N2 strain, exhibiting notable IC50 values of 6.2 ± 0.08 and 8.9 ± 0.3 μM, respectively. Moreover, compound 2 also displayed potential inhibitory activity against the H1N1 strain, with an IC50 value of 3.5 ± 1.3 μM (Tian et al., 2016)

CONCLUSION

Antiviral compounds with different antiviral mechanisms were found in six articles on microalgae, 11 on macroalgae, eight on soft corals and six on sponges. The antiviral compounds identified in microalgae encompass a range of fatty acids and lutein. In macroalgae, carrageenan, fucoidan, and other polyphenols are the most prevalent antiviral compounds. The antiviral compounds found in soft coral are primarily of the terpenoid group, while those in marine sponges vary considerably, including sesterpenes, asteltoxin, and others.

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