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Chemical diversity and therapeutic potentialities of seaweeds and marine sponges collected from the Red Sea: An update

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ABSTRACT

The marine environment is a vast and diverse ecosystem that is a valuable source of biologically active ingredients for the drug industry. For decades, natural products from marine organisms have been a major supplier of curative agents. Over 30,000 metabolites have been recorded from different marine organisms and associated microorganisms. Marine-derived compounds have diverse chemical structures, biological and pharmacological applications, making them a promising platform for drug discovery from natural sources. This review highlights a comprehensive survey of the phytochemical and biological aspects of selected seaweed and marine sponges found in the Red Sea. These organisms, such as seagrass (*Thalassia hemprichii*) and marine sponges (*Siphonochalina siphonella*, *Latrunculia magnifica*, and *Crella (Grayella) cyathophora*), have been found to contain numerous chemical ingredients with therapeutic properties. Phenolic compounds in *T. hemprichii* have antioxidant and anticancer properties while marine sponges contain structurally diverse amides, alkaloids, terpenes, and steroids with cytotoxic, antiviral, and antimicrobial activities. The habitats of these organisms affect both the chemical components and their biological properties. These findings are encouraging and may be used in the development of new pharmaceuticals.

INTRODUCTION

Natural products (NPs) have a long history in pharmacotherapy, especially in the management of cancer and infectious disturbances (Carroll *et al*., 2023; Chen *et al*., 2023). Naturally occurring bioactive chemicals have become an essential source of drugs since they have been used to treat a variety of diseases (Abdel-Aziz *et al*., 2018; Elkhouly *et al*., 2021a, 2021b; Mohammed *et al*., 2019; Yang *et al*., 2023a, 2023b; Yeung *et al*., 2018). Scientists are dealing with various illnesses in our community owing to reestablished circumference and life manner. Several researchers are working on the different emerging diseases to understand and cure them by using various chemical and natural preparations; however, still, numerous topics are untouched due to inferior knowledge and technical tools (Aditi *et al*., 2017; Bode *et al*., 2002; El-Wakil *et al*., 2022). NPs have been utilized for the remediation of several ailments and diseases since ancient times (Dias *et al*., 2012; El-Demerdash *et al*., 2012; Ghareeb *et al*., 2023; Holland and Carroll, 2023; Mohammed *et al*., 2022; Okasha *et al*., 2022; Sayed *et al*., 2022). The earliest records of NPs used were from 8000 BC. Most of the evidences for the earliest use of NPs for medication comes from archaeologists who have explored some ancient sites such as caves (Dias *et al*., 2012). The Egyptian Ebers Papyrus (2900 BC) documents up to 700 plant-based drugs to create prescriptions, ointments, potions, inhalers, and pills to cure certain conditions. Opium, cannabis, and linseed oil were used (Cragg and Newman, 2005). The Chinese materia medica (1100 BC) (Wu Shi Er Bing Fang, comprises 52 prescriptions), Shennong Herbal (~100 BC, 365 drugs), and the Tang Herbal (659 AD, 850 drugs) are documented archives of the utilization of NPs (Cragg and Newman, 2005). The Greek physician Hippocrates, (460–370 BCE), the father of modern

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medicine and possibly the most recognized name in medicine, was born in Greece (Porter, 1998). In the 8th century, the Arabs were the first to privately own pharmacies. The poet, philosopher, pharmacist, and physician "Avicenna" participated much in the disciplines of pharmacy and medicine within works like the *Canon Medicine* (Cragg and Newman, 2005). Taken together, the current review aims to explore the chemical and biological aspects of some marine algae and marine sponges collected in the Red Sea, in order to build a comprehensive and intensive vision of what has been discovered in such an environment, which is considered a strategic treasure for obtaining medicines from natural sources.

MARINE NPS (MNPS)

Recently, the marine ecosystem has attracted many attentions as it contains diverse types of marine organisms including sponges, algae, microbes, tunicates, soft corals, mollusks, seaweeds, and sea cucumbers, among others. Also, it is a rich and promising source of bioactive compounds as well as other medicinal, nutritional, and pharmacological potentials (Carroll *et al*., 2022; El-Demerdash *et al*., 2020a; Ghareeb *et al*., 2020; Holland and Carroll, 2023; Ibrahim *et al*., 2021). Moreover, the marine environment is characterized by its chemical diversity and biomedical value highlighting its massive potential as a vital source of therapeutic agents (Carroll *et al*., 2020, 2021; El-Demerdash *et al*., 2020b, 2021; Liang *et al*., 2023). In the same context, a diverse array of chemical compounds has been isolated or identified from different marine organisms such as alkaloids (Moriou *et al*., 2021; Tempone *et al*., 2021), anthraquinones (Chen *et al*., 2022), peptides (Ghareeb *et al*., 2020), polysaccharides (Ghareeb *et al*., 2020), polyketides (Ghareeb *et al*., 2020), and terpenes (Chen *et al*., 2022). Various extracts of marine organisms and/or their pure isolates exhibited a broad spectrum of bioactivities like antimicrobial (Krome *et al*., 2022; Liang *et al*., 2023), antioxidant (Catarino *et al*., 2023; Hamed *et al*., 2020), anti-Gyr-B enzyme (Agour *et al*., 2022), antiallergic (Xie *et al*., 2017), antibiofilm (Cepas *et al*., 2019), anticancer (Agena *et al*., 2023; Panggabean *et al*., 2022), anti-inflammatory (Ghareeb *et al*., 2020; Rocha *et al*., 2022), anticoagulant (Qin *et al*., 2023), antiparasitic (Mostafa *et al*., 2022), antiallergic (Chen *et al*., 2023), and antiaging (Yang *et al*., 2023a, 2023b). The marine environment is considered a strategic treasure and a huge warehouse for the production of bioactive compounds, which act as lead compounds in the pharmaceutical industry. Recently, Ghareeb *et al*. (2020) stated that numerous marine-derived molecules are still under preclinical trials (Phase III, Phase II, and Phase I) for the medication of cancer, inflammation, Alzheimer's disease, and wound healing. On the other side, several marine-derived drugs gained the Food and Drug Administration's agreement like cytarabine, trabectedin, eribulin mesylate, and brentuximab vedotin 63 for cancer treatment, while Keyhole Limpet hemocyanin, vidarabine, ziconotide were approved for viral pain and hypertriglyceridemia treatments, respectively (Ghareeb *et al*., 2020). As a part of our continued program to identify pharmacologically active MNPs, herein, we provide a concise update about the chemistry and biomedical potentialities of selected marine organisms, with emphasis on those collected from the Red Sea coastal area. A list of 74 compounds was reported and tabulated alongside their therapeutic activities wherever applicable.

MATERIALS AND METHODS

In our current study, the subsequent databases and search engines have been used to get the peer-reviewed articles: the Marin-Lit database "The Royal Society of Chemistry," Google Scholar, MDPI, Science Direct, SciFinder, and PubChem. The search keywords are "Natural products (NPs), Marine natural products (MNPs), Approved marine drugs, chemical and biological profiles of *Thalassia hemprichii*, *Siphonochalina siphonella*, *Latrunculia magnifica*, and *Crella* (*Grayella*) *cyathophora*." The search covers the period 1980–2023. The selection of topics relied on articles that give a general overview of marine organisms, including chemical and biological profiles, and then the search was focused in depth on the organisms under study from the chemical and biological aspects. Also, ChemOffice was also utilized to draw the chemical skeletons. Additionally, Excel was used to draw graphs.

CHEMISTRY AND BIOLOGICAL IMPORTANCE OF SELECTED SEAGRASS AND MARINE SPONGES COLLECTED FROM THE RED SEA

In this manuscript, we present up-to-date insights about chemical and biological diversifications of selected marine organisms, with a focus on those collected from the Red Sea coastal areas. For the handling of this documentation, all isolated MNPs are tabulated where they have been recovered along with their recorded biological potentialities whenever possible.

Seagrass *T. hemprichii*: secondary metabolites and their bioactivities

Herein, a comprehensive outline of chemical ingredients isolated and/or identified from the seagrass *T. hemprichii* is reported. The detected compounds were categorized as sulphated flavonoids, flavonoid glycosides, sterols, sterol glycosides, phenolic acids, carotenoids, nitrogen compounds, and benzophenones. Additionally, the available pertinent bioactivities of the isolated compounds are mentioned whenever applicable. Ten compounds comprising diosmetin 7-*O*-*β*-glucosyl-2″-sulphate (Thalassiolin D) (**1**), diosmetin7-*O*-*β*-glucoside (**2**), apigenin 6,8-*C*-β-diglucoside (**3**), kaempferol 3-*O*-(6″-*O*-*p*-coumaroyl)-*β*-glucoside (**4**), β-stigmasterol (**5**), *β*-stigmasterol 3-*O*-*β*-glucoside **(6)**, *p*-hydroxy-benzoic acid (**7**), 4,4′-dihydroxybenzophenone (**8**), octopamine (**9**), and diadinoxanthin (**10**) were obtained from the methanolic extract of seagrass *T. hemprichii* obtained from the Saudi Red Sea coast. Thalassiolin D exhibited *in vitro* antiviral hepatitis C virus (HCV) protease effect with a half-maximal inhibitory concentration (IC_{50}) equal to 16 µM (Hawas and Abou El-Kassem, 2017) (Fig. 1).

Additionally, further phenolic constituents including isoscutellarein 7-*O*-β-xylopyranoside-2''-*O*-sulfate (**11**), isoscutellarein 7-*O*-β-xylopyranoside (**12**), isoscutellarein (**13**), caffeic acid (**14**), and rosmarinic acid (**15**) were recovered from the methanolic extract of the seagrass *T. hemprichii* obtained from the south Marsa Alam coast, Egypt. Isoscutellarein 7-*O*-β-xylopyranoside-2''-*O*-sulfate (**11**) showed a strong antibacterial effect with minimum inhibitory concentration (MIC) values of 2.5 and 1.5 µg/ml against *Bacillus subtilis* and *Pseudomonas aeruginosa*, respectively (Hawas, 2014) (Fig. 2).

Chemical investigations of the ethanol extract of seagrass *T. hemprichii* obtained from South China led to the isolation

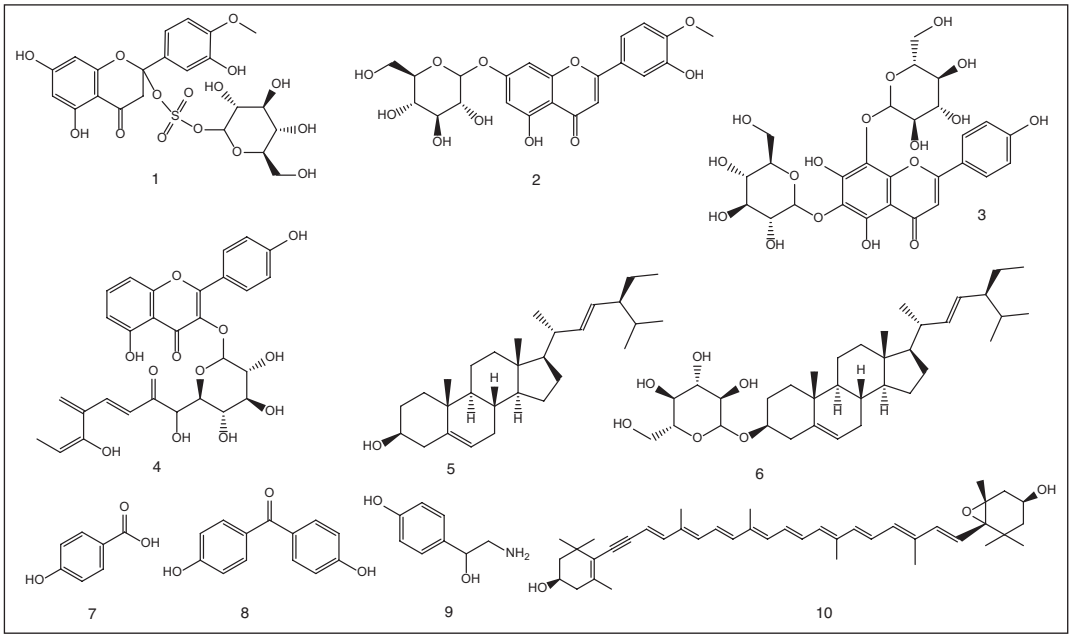

Figure 1. Chemical structures of flavonoidal, phenolic acid, sterols, amine and carotenoid compounds **(1–10**) isolated from the methanolic extract of seagrass *T. hemprichii* obtained from the Saudi Red Sea coast.

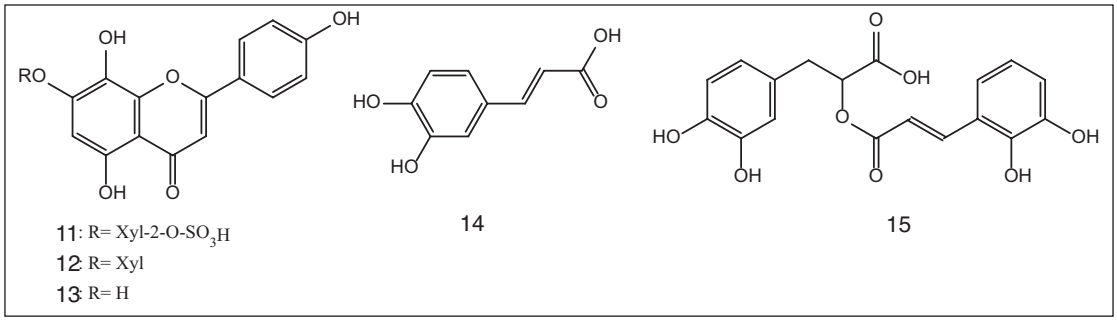

Figure 2. Chemical structures of flavonoidal and phenolic acid compounds **(11–15)** isolated from the methanolic extract of seagrass *T. hemprichii* obtained from the south Marsa Alam coast, Egypt.

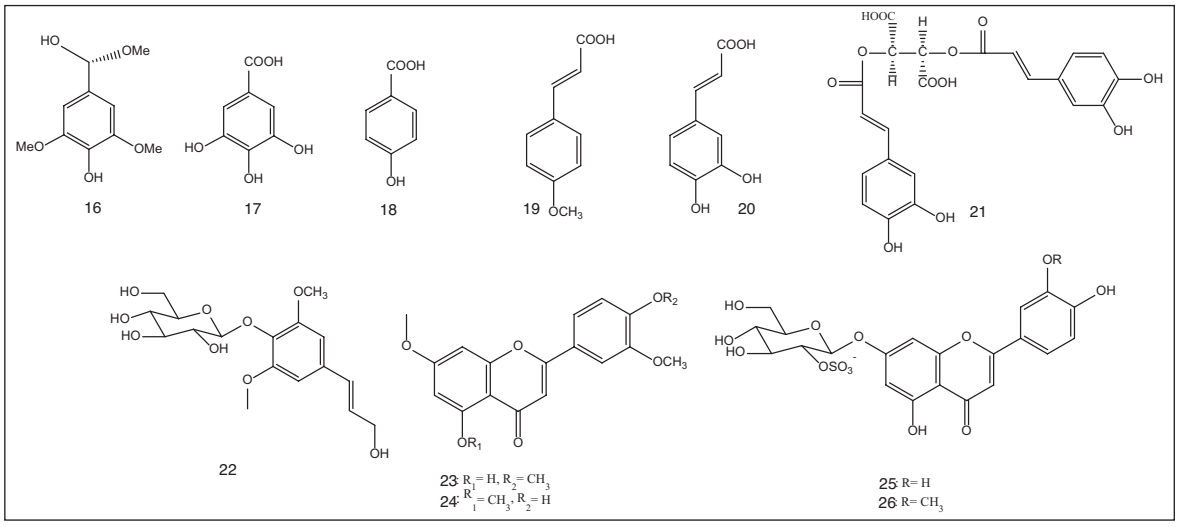

Figure 3. Chemical structures of flavonoidal, phenolic acid, and phenolic derivative compounds **(17–26**) isolated from the ethanol extract of seagrass *T. hemprichii* obtained from South China.

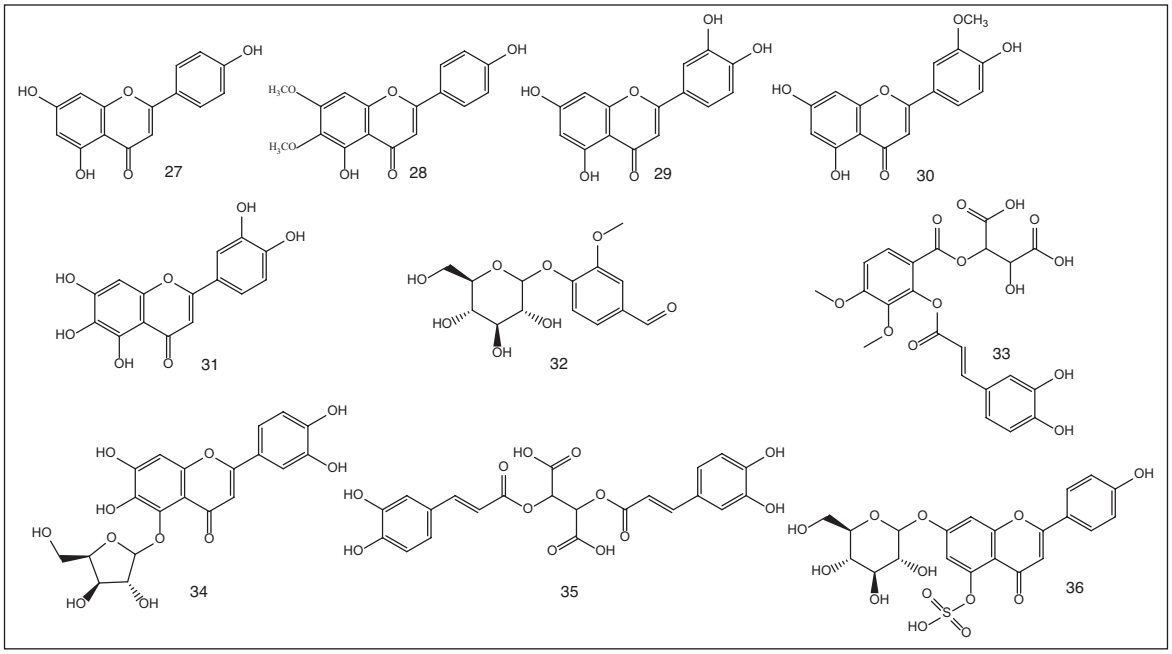

Figure 4. Chemical structures of flavonoidal and phenolic derivative compounds **(27–36)** identified in the ethanol extract of the seagrass *T. hemprichii* collected from the Red Sea, Egypt.

Table 1. Some reported bioactivities of seagrass *T. hemprichii* extracts.

Type of extract	Collection location	Biological activity	References
Ethyl acetate	Long Island, Jepara, Indonesia	Antioxidant activity against DPPH radical (IC_{50}: 25.98 µg/ml)	Tristanto *et al*., 2014;
n-hexane and ethanol	Karang Tirta Beach, Padang City, West Sumatera, Indonesia	Antibacterial activity against *Escherichia coli*, *S. aureus*, and *B. subtilis* (MIC: 62.50–500 µg/ml)	Purnama and Brahmana, 2018
Methanol	Prapat Agung Beach and Menjangan Island, Indonesia	Larvicidal activity	Yusniawati *et al*., 2018
Methanol	Barrang Lompo Island, Makassar, Indonesia	Antifouling activity against growth of biofilm-forming bacteria [Inhibition zone of bacterial growth (mm) 9–27 mm]	Fahruddin *et al*., 2019
Ethanol	Red Sea of Ras Shetan Nuweiba, Egypt	α-amylase, β-glucosidase and pancreatic lipase inhibition activities with IC_{50} values of 230.28, 332.5, and 23.7 µg/ml, respectively	Hegazi *et al*., 2021
Water and butanol	Saudi Red Sea	Antioxidant activity (DPPH, ABTS, FRAP, Fe2+ chelating, reducing power) Antitumor activity against Ehrlich ascites carcinoma	Ghandourah *et al*., 2019; Hegazi *et al*., 2019
Ethanol	Saudi Arabian Red Seacoast	Insecticidal activity against *Aedes aegypti* (L.) mosquito vector	Mahyoub *et al*., 2016
Acetone	Southern Corniche of Jeddah Governorate, Saudi Arabia	Larvicidal activity against fourth instar mosquito larvae of Anopheles d'thali (IC_{90} (ppm): 293.8).	Mahyoub, 2018
Methanol	Port Dickson coastal water, Malaysia	Antibacterial activity against six different aquaculture pathogen strains with zone of inhibition (mm) ranged from 7.25 to 11.50	Natrah *et al*., 2015
Aqueous ethanol	Mandapam, Southeast coast, India	Larvicidal activity of seagrass extracts against dengue vector *A. aegypti* (LC_{90}: 0.121)	Ali *et al*., 2013
Ethanol	Intertidal region, Mandapam coast, India	Antioxidant activity - Total antioxidant activity: 20.453 mg ascorbic acid/g - FRAP: 27.979 mg Gallic acid/g - DPPH (%): 61.64%	Rengasamy *et al*., 2012
70% ethanol	North Java Sea, Indonesia	Antibacterial activity against multidrug-resistant bacteria	Cristianawati *et al*., 2019

Continued

Type of extract	Collection location	Biological activity	References
Ethanol	Kalasey waters, Indonesia	Cytotoxic activity of using the Brine Shrimp Lethality Test (LC_{50}: 3.95 mg/l)	Karim *et al*., 2019
Methanol	Cebu, Philippines	Alpha-amylase inhibitory activity	Barrameda *et al*., 2017
n-hexane	Teluk Awur waters, Jepara, Central Java, Indonesia	Antifouling activity	Marhaeni *et al*., 2011
Ethanol	Pasauran Beach, Serang, Banten, West Java, Indonesia	Antioxidant and anticollagenase activities	Zakiah *et al*., 2018

of 11 compounds including (*S*)-methoxy-(3,5-dimethoxy-4-hydroxyphenyl)ethanediol (**16**), 3,4,5-trihydroxybenzoic acid (**17**), 4-hydroxybenzoic acid (**18**), (E)-3-(4-methoxyphenyl)-2-propenoic acid (**19**), caffeic acid (**20**), chicoric acid (**21**), syringin (**22**), 5-hydroxy-3',4',7-trimethoxyflavone (**23**), 4'-hydroxy-3',5,7-trimethoxyflavone (**24**), thalassiolin A (**25**), and thalassiolin B (**26**) (Qi *et al*., 2012) (Fig. 3).

Diadinoxanthin (**10**) (a carotenoids pigment) was detected by high-performance liquid chromatography technique in the seagrass *T. hemprichii* sample collected from Menjangan Kecil Waters, Karimunjawa Islands, Indonesia (Nugraheni *et al*., 2010). Moreover, chemical profiling of the ethanol extract of the seagrass *T. hemprichii* collected from the Red Sea of Ras Shetan, Nuweiba, Egypt, led to isolation of flavonoid aglycones namely apigenin (**27**), isoscutellarein (**13**), cirsimaritin (**28**), luteolin (**29**), chrysoeriol (**30**), and 6-hydroxyl luteolin (**31**). In the same context, UPLC-HRMS/MS analysis of the desired extract led to tentative identification of about 144 secondary metabolites among them are vanillin-*O*-glucoside (**32**), *O*-caffeoyl-*O*-hydroxyl dimethoxy benzoyl tartaric acid (**33**), luteolin 7-*O*-glucoside sulphate (Thalassioline A) (**25**), 6-hydroxyl luteolin-*O*-xyloside (**34**), di-*O*-caffeoyl tartaric acid (**35**), chrysoeriol 7-*O*-glycoside sulphate (Thalassioline B) (**26**), and apigenine7-*O*-glucoside sulphate (Thalassioline C) (**36**) (Hegazi *et al*., 2021) (Fig. 4).

Biological activities of seagrass T. hemprichii extracts

Previous reports revealed that different extracts and fractions obtained from the seagrass *T. hemprichii* showed numerous biological activities like antimicrobial (Supaphon *et al*., 2013), antioxidant (Tristanto *et al*., 2014; Ulfa *et al*., 2014), cytotoxicity (Dewi *et al*., 2012), antidiabetic (Jayaprakash *et al*., 2017), and larvicidal (Yusniawati *et al*., 2018). Herein, we listed some reported biological activities of some extracts obtained from seagrass *T. hemprichii* (Table 1).

Marine sponge *S. siphonella* (*Callyspongia siphonella*)

Marine sponge S. siphonella: secondary metabolites and their bioactivities

Phytochemically, different extracts from the marine sponge *S. siphonella* were investigated for their phytoconstituents using chromatographic and spectroscopic tools. Numerous classes of secondary metabolites were detected in such extracts including polyacetylene amides (Ki *et al*., 2021), steroids (Alam *et al*., 2020), triterpenes (Carmely and Kashman, 1983), polyacetylene alcohols (Ki *et al*., 2019), and brominated oxindole alkaloids (El-Hawary *et al*., 2019). Three diacetylenic amides (Siphonellamide A–C) (**37–39**), one monoacetylenic amide (Siphonellamide D) (**40**), one fatty amide (Siphonellamide E) (**41**), alkamide, *N*-[2-(1H-indol-3-yl)ethyl] hexadecanamide (**42**), and callyspongamide A (**43**) were isolated from the chloroform-soluble fraction of *S. siphonella* collected from the reefs southwest of Magawish Island, Hurghada, Egypt. Siphonellamide A and B showed cytotoxic actions with IC_{50} values varying from 9.4 to 34.1 µM, while Siphonellamide E (**41**) showed cytotoxic effect against HeLa cells with an IC_{50} value of 78.4 µM. Callyspongamide A exhibited a medium cytotoxic effect versus HeLa, MCF-7, and A549 cell lines (Ki *et al*., 2020) (Fig. 5).

A steroid (Siphonocholin) (**44**) was isolated from an aqueous ethanol extract of *S. siphonella* obtained from Sharm Obhur (Jeddah, Saudi Arabian red seacoast). The compound exhibited anti-QS and antibiofilm activity against some bacterial pathogens including *Chromobacterium violaceum*, *P. aeruginosa*, Methicillin-resistant *Staphylococcus aureus* and *Acinetobacter baumannii* with MIC values varying from 64 to 256 µg/ml (Alam *et al*., 2020). Eight squalene-derived triterpenes were isolated from petroleum ether extract of marine sponge *S. siphonella* collected from Naima in the Gulf of Eilat, Red Sea. The isolated compounds have been identified as Sipholenol-A (**45**), Sipholenone-A (**46**), Sipholenone-B (**47**), Sipholenone-C (**48**), Sipholenol-B (**49**), Sipholenol-C (**50**), Sipholenol-D (**51**), and Sipholenol-E (**52**) (Carmely and Kashman, 1983) (Fig. 6).

Additionally, five triterpenes were isolated from CH_2Cl_2-MeOH extract (1:1) of the marine sponge *S. siphonella* obtained from Sharm Obhur, Jeddah, Saudi Arabia. These compounds were characterized as Neviotine-A (**53**), Neviotine-C (**54**), sipholenol-A (**55**), sipholenone-A (**56**), and sipholenol-L (**57**). Compounds **53–54** and **56** were evaluated against MCF-7, PC-3, and A549 cell lines and showed antiproliferative activities with IC_{50} in the range of 7.9–87 µM (Angawi *et al*., 2014) (Fig. 7).

Ki *et al*. (2019) reported the isolation of five polyacetylenic alcohols from the chloroform-soluble fraction of the marine sponge *S. siphonella*, obtained from southwest of Magawish Island, Hurghada, Egypt. The isolated compounds were identified as siphonellanol A (**58**), siphonellanol B (**59**), siphonellanol C (**60**), dehydroisophonochalynol (**61**), and siphonchalynol (**62**). Siphonellanols A-C exhibited mild cytotoxic effects against HeLa, MCF-7, and A549 with IC_{50} values ranging from 25.9 to 69.2 µM (Ki *et al*., 2019). Additionally, two brominated oxindole alkaloids namely 5-bromo trisindoline (**63**) and 6-bromo trisindoline (**64**) were isolated from the marine sponge *Callyspongia siphonella* collected from Hurghada, Red

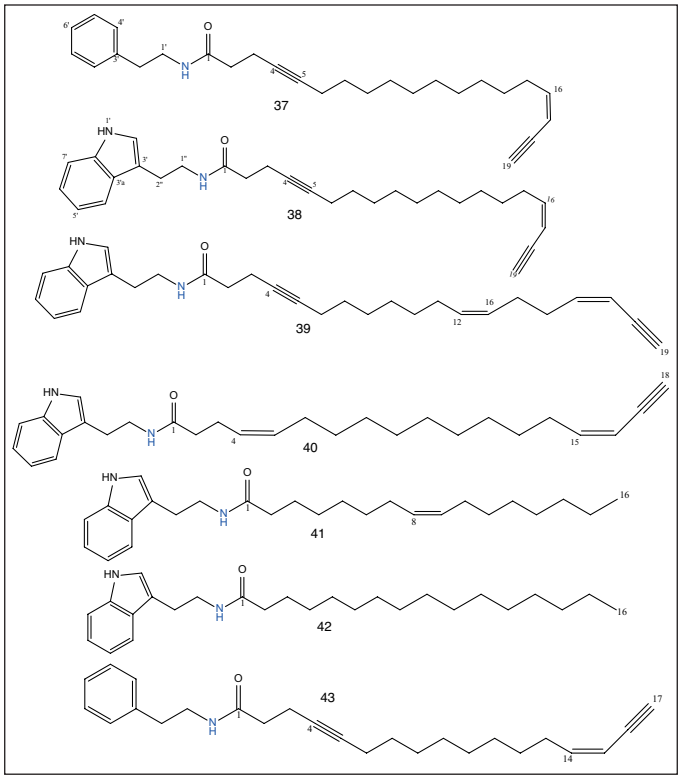

Figure 5. Chemical structures of mono and diacetylenic amide compounds **(37–43)** isolated from the chloroform-soluble fraction of *S. siphonella* collected from the reefs southwest of Magawish Island, Hurghada, Egypt.

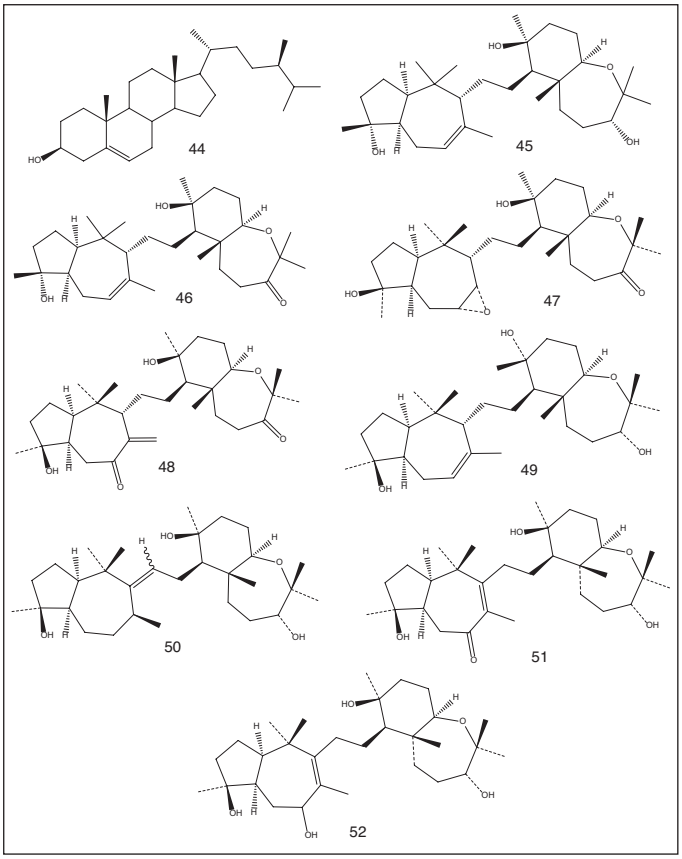

Figure 6. Chemical structures of steroidal compound **(44)** isolated from aqueous ethanol extract of *S. siphonella* obtained from Sharm Obhur (Jeddah, Saudi Arabian red seacoast) and squalene-derived triterpene compounds **(44–52)** isolated from petroleum ether extract of marine sponge *S. siphonella* collected from Naima in the Gulf of Eilat, Red Sea.

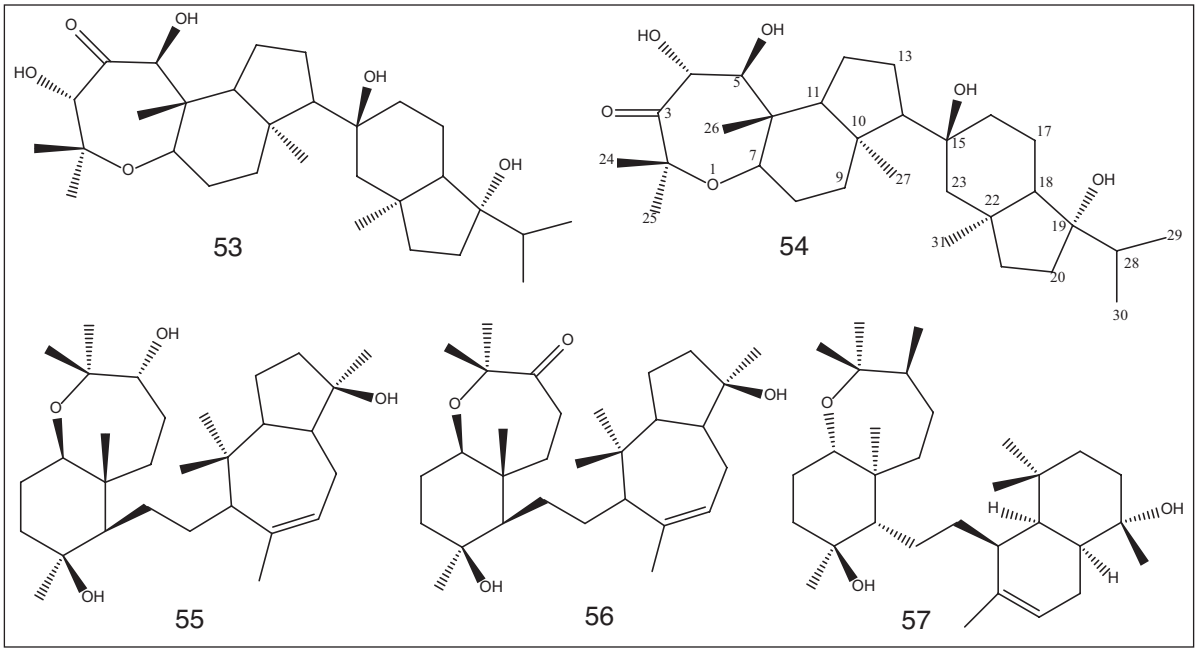

Figure 7. Chemical structures of triterpene compounds **(53–57)** isolated from CH_2Cl_2-MeOH extract (1:1) of the marine sponge *S. siphonella* obtained from Sharm Obhur, Jeddah, Saudi Arabia.

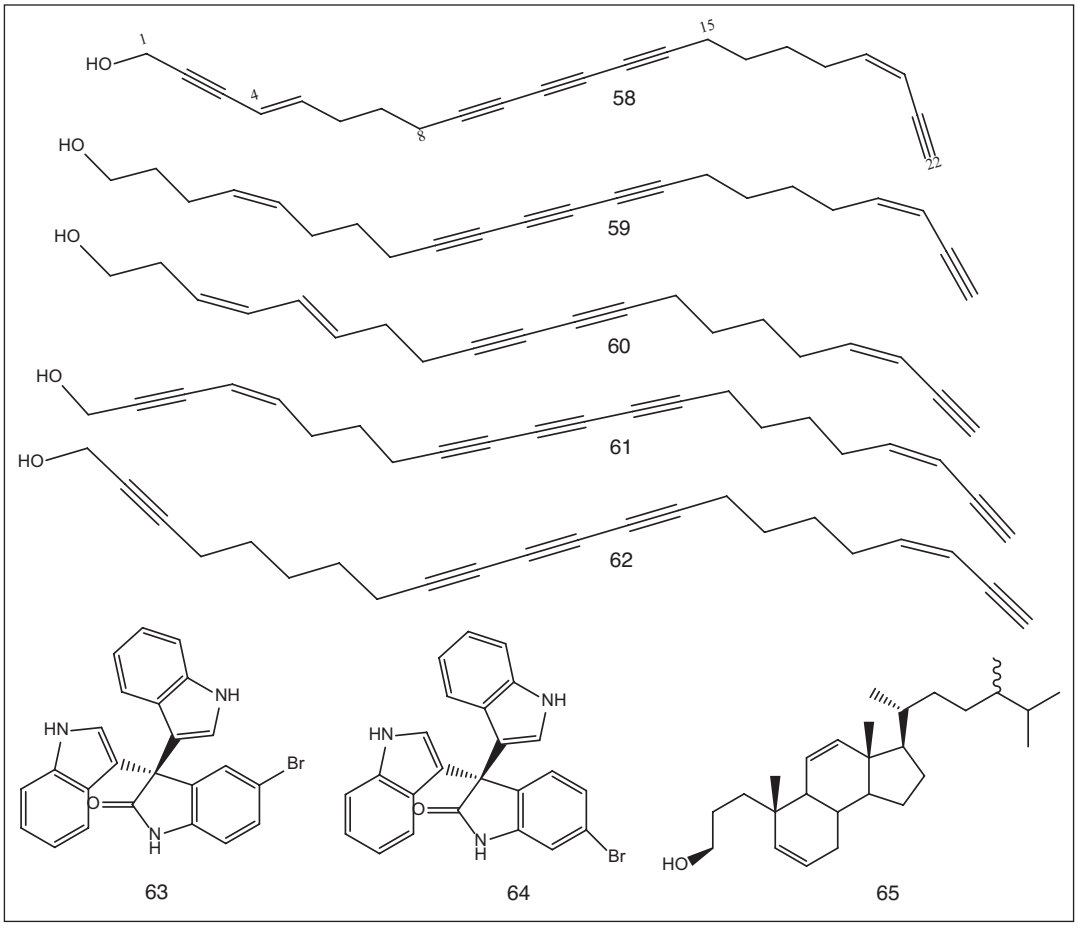

Figure 8. Chemical structures of polyacetylenic alcohols compounds **(58–62)** isolated from the chloroform-soluble fraction of the marine sponge *S. siphonella*, obtained from southwest of Magawish Island, Hurghada, Egypt; brominated oxindole alkaloids compounds **(63, 64)** isolated from the marine sponge *C. siphonella* collected from Hurghada, Red Sea Coast, Egypt; and a sterol compound **(65)** separated from the marine sponge *C. siphonella* obtained from the Red Sea, Egypt.

Table 2. Summarized list of the reported compounds (Source, location of organism, and available bioactivity).

No.	Compound name	Source/Location	Bioactivity	Reference
1	Diosmetin 7-*O*-β-glucosyl-2″-sulphate (Thalassiolin D)	Seagrass *T. hemprichii*/ KSA	*In vitro* antiviral HCV protease effect with IC_{50} equal to 16 µM	Hawas and Abou El-Kassem, 2017
2	Diosmetin7-*O*-β-glucoside	Seagrass *T. hemprichii*/ KSA	-	Hawas and Abou El-Kassem, 2017
3	Apigenin 6,8-*C*-β-diglucoside (Vicenin-2)	Seagrass *T. hemprichii*/ KSA	-	Hawas and Abou El-Kassem, 2017
4	Kaempferol 3-*O*-(6″-*O*-*p*-coumaroyl)-β-glucoside	Seagrass *T. hemprichii*/ KSA	-	Hawas and Abou El-Kassem, 2017
5	β-Stigmasterol	Seagrass *T. hemprichii*/ KSA	-	Hawas and Abou El-Kassem, 2017
6	β-Stigmasterol 3-*O*-β-glucoside	Seagrass *T. hemprichii*/ KSA	-	Hawas and Abou El-Kassem, 2017
7	*p*-Hydroxybenzoic acid	Seagrass *T. hemprichii*/ KSA	-	Hawas and Abou El-Kassem, 2017
8	4,4′-Dihydroxybenzophenone	Seagrass *T. hemprichii*/ KSA	-	Hawas and Abou El-Kassem, 2017
9	Octopamine	Seagrass *T. hemprichii*/ KSA	-	Hawas and Abou El-Kassem, 2017
10	Diadinoxanthin	Seagrass *T. hemprichii*/ KSA, Indonesia	-	Hawas and Abou El-Kassem, 2017

Continued

No.	Compound name	Source/Location	Bioactivity	Reference
11	Isoscutellarein 7-*O*-β-xylopyranoside-2''-*O*-sulfate	Seagrass *T. hemprichii*/ Egypt	Antibacterial effect with MIC values of 2.5 and 1.5 µg/ml against *B. subtilis* and *P. aeruginosa,* respectively	Hawas, 2014
12	Isoscutellarein 7-*O*-β-xylopyranoside	Seagrass *T. hemprichii*/ Egypt	-	Hawas, 2014
13	Isoscutellarein	Seagrass *T. hemprichii*/ Egypt	-	Hawas, 2014; Hegazi *et al*., 2021
14	Caffeic acid	Seagrass *T. hemprichii*/ Egypt	-	Hawas, 2014
15	Rosmarinic acid	Seagrass *T. hemprichii*/ Egypt	-	Hawas, 2014
16	(*S*)-methoxy-(3,5-dimethoxy-4-hydroxyphenyl)ethanediol	Seagrass *T. hemprichii*/ China	-	Qi *et al*., 2012
17	3,4,5-trihydroxybenzoic acid	Seagrass *T. hemprichii*/ China	-	Qi *et al*., 2012
18	4-hydroxybenzoic acid	Seagrass *T. hemprichii*/ China	-	Qi *et al*., 2012
19	(E)-3-(4-methoxyphenyl)-2-propenoic acid	Seagrass *T. hemprichii*/ China	-	Qi *et al*., 2012
20	Caffeic acid	Seagrass *T. hemprichii*/ China	-	Qi *et al*., 2012
21	Chicoric acid	Seagrass *T. hemprichii*/ China	-	Qi *et al*., 2012
22	Syringin	Seagrass *T. hemprichii*/ China	-	Qi *et al*., 2012
23	5-Hydroxy-3',4',7-trimethoxyflavone	Seagrass *T. hemprichii*/ China	-	Qi *et al*., 2012
24	4'-Hydroxy-3',5,7-trimethoxyflavone	Seagrass *T. hemprichii*/ China	-	Qi *et al*., 2012
25	Thalassiolin A	Seagrass *T. hemprichii*/ China, Egypt	-	Hegazi *et al*., 2021; Qi *et al*., 2012
26	Thalassiolin B	Seagrass *T. hemprichii*/ China, Egypt	-	Hegazi *et al*., 2021; Qi *et al*., 2012
27	Apigenin	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
28	Cirsimaritin	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
29	Luteolin	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
30	Chrysoeriol	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
31	6-Hydroxyl luteolin	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
32	Vanillin-*O*-glucoside	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
33	*O*-Caffeoyl-*O*-hydroxyl dimethoxy benzoyl tartaric acid	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
34	6-Hydroxyl luteolin-*O*-xyloside	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
35	Di-*O*-caffeoyl tartaric acid	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
36	Apigenine7-*O*-glucoside sulphate	Seagrass *T. hemprichii*/ Egypt	-	Hegazi *et al*., 2021
37	Siphonellamide A	Marine sponge *S. siphonella*/Egypt	Cytotoxic action with IC_{50} values varying from 9.4 to 34.1 µM	Ki *et al*., 2020
38	Siphonellamide B	Marine sponge *S. siphonella*/Egypt	Cytotoxic action with IC_{50} values varying from 9.4 to 34.1 µM	Ki *et al*., 2020

Continued

No.	Compound name	Source/Location	Bioactivity	Reference
39	Siphonellamide C	Marine sponge *S. siphonella*/Egypt	-	Ki *et al*., 2020
40	Siphonellamide D	Marine sponge *S. siphonella*/Egypt	-	Ki *et al*., 2020
41	Siphonellamide E	Marine sponge *S. siphonella*/Egypt	Cytotoxic effect against HeLa cells with an IC_{50} value of 78.4 µM	Ki *et al*., 2020
42	Alkamide, N-[2-(1H-indol-3-yl) ethyl]hexadecanamide	Marine sponge *S. siphonella*/Egypt	-	Ki *et al*., 2020
43	Callyspongamide A	Marine sponge *S. siphonella*/Egypt	Medium cytotoxic effect versus HeLa, MCF-7 and A549 cell lines	Ki *et al*., 2020
44	Siphonocholin	Marine sponge *S. siphonella*/KSA	Anti-QS and anti-biofilm activity against some bacterial pathogens including *C. violaceum*, *P. aeruginosa*, methicillin-resistant *S. aureus* and *A. baumannii* with MIC values varying from 64 to 256 µg/ml	Alam *et al*., 2020
45	Sipholenol-A	Marine sponge *S. siphonella*/Eilat	-	Carmely and Kashman, 1983
46	Sipholenone-A	Marine sponge *S. siphonella*/Eilat	-	Carmely and Kashman, 1983
47	Sipholenone-B	Marine sponge *S. siphonella*/Eilat	-	Carmely and Kashman, 1983
48	Sipholenone-C	Marine sponge *S. siphonella*/Eilat	-	Carmely and Kashman, 1983
49	Sipholenol-B	Marine sponge *S. siphonella*/Eilat	-	Carmely and Kashman, 1983
50	Sipholenol-C	Marine sponge *S. siphonella*/Eilat	-	Carmely and Kashman, 1983
51	Sipholenol-D	Marine sponge *S. siphonella*/Eilat	-	Carmely and Kashman, 1983
52	Sipholenol-E	Marine sponge *S. siphonella*/Eilat	-	Carmely and Kashman, 1983
53	Neviotine-A	Marine sponge *S. siphonella*/KSA	Anti-proliferative activity	Angawi *et al*., 2014
54	Neviotine-C	Marine sponge *S. siphonella*/KSA	Anti-proliferative activity	Angawi *et al*., 2014
55	Sipholenol-A	Marine sponge *S. siphonella*/KSA	Anti-proliferative activity	Angawi *et al*., 2014
56	Sipholenone-A	Marine sponge *S. siphonella*/KSA	Anti-proliferative activity	Angawi *et al*., 2014
57	Sipholenol-L	Marine sponge *S. siphonella*/KSA	-	Angawi *et al*., 2014
58	Siphonellanol A	Marine sponge *S. siphonella*/Egypt	Cytotoxic effect against HeLa, MCF-7, and A549	Ki *et al*., 2019
59	Siphonellanol B	Marine sponge *S. siphonella*/Egypt	Cytotoxic effect against HeLa, MCF-7, and A549	Ki *et al*., 2019
60	Siphonellanol C	Marine sponge *S. siphonella*/Egypt	Cytotoxic effect against HeLa, MCF-7, and A549	Ki *et al*., 2019
61	Dehydroisophonochalynol	Marine sponge *S. siphonella*/Egypt	-	Ki *et al*., 2019
62	Siphonchalynol	Marine sponge *S. siphonella*/Egypt	-	Ki *et al*., 2019
63	5-Bromo trisindoline	Marine sponge *C. siphonella*/Egypt	- Antibacterial effect versus *S. aureus* with MIC values of 8 and *B. subtilis* with MIC values of 16 µg/ml - Biofilm inhibitory effect in *P. aeruginosa* (49.32% inhibition) - *In vitro* antitrypanosomal effect (13.47 µM) - Cytotoxic activity was recorded against various human cancer cell lines	El-Hawary *et al*., 2019

Continued

No.	Compound name	Source/Location	Bioactivity	Reference
64	6-Bromo trisindoline	Marine sponge *C. siphonella*/Egypt	- Antibacterial effect versus *S. aureus* with MIC values of 4 µg/ml and *B. subtilis* with MIC values of 4 µg/ml - Biofilm inhibitory effect in *P. aeruginosa* (41.76% inhibition) - *In vitro* antitrypanosomal effect (10.27 µM) - Cytotoxic activity was recorded against various human cancer cell lines	El-Hawary *et al*., 2019
65	Callysterol (ergosta-5,11-dien-3β-ol)	Marine sponge *C. siphonella*/Egypt	Anti-inflammatory activity using the rat-hind paw edema assay	Youssef *et al*., 2010
66	Latrunculin A	Marine sponge *L. magnifica*/Red Sea	-	Kashman *et al*., 1980
67	Latrunculin B	Marine sponge *L. magnifica*/Red Sea	-	Kashman *et al*., 1980
68	Latrunculin C	Marine sponge *L. magnifica*/Red Sea	-	Kashman *et al*., 1980
69	Latrunculin A	Marine sponge *L. magnifica*/Eilat	-	Groweiss *et al*., 1983
70	Latrunculin B	Marine sponge *L. magnifica*/Eilat	-	Groweiss *et al*., 1983
71	Latrunculins A	Marine sponge *L. magnifica*/Red Sea	-	Kashman *et al*., 1985
72	Latrunculins B	Marine sponge *L. magnifica*/Red Sea	-	Kashman *et al*., 1985
73	Latrunculins C	Marine sponge *L. magnifica*/Red Sea	-	Kashman *et al*., 1985
74	Latrunculins D	Marine sponge *L. magnifica*/Red Sea	-	Kashman *et al*., 1985

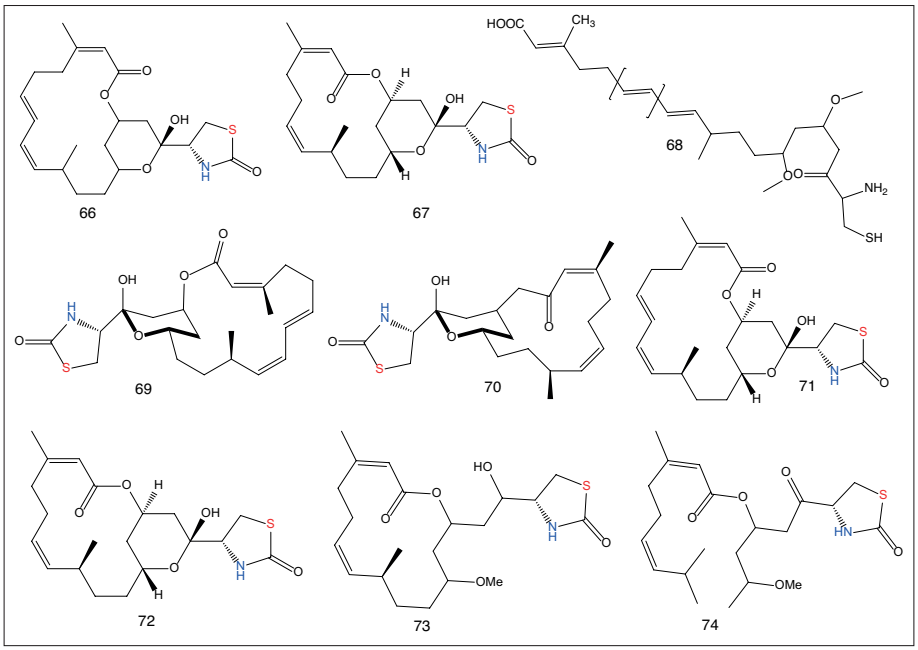

Figure 9. Chemical structures of macrolide compounds **(66–68)** separated from the Red Sea sponge *L. magnifica*; compounds **(69, 70)** isolated from petroleum ether extract of *L. magnifica* collected from Gulf of Eilat; and compounds (**71–74**) separated from the Red Sea sponge *L. magnifica.*

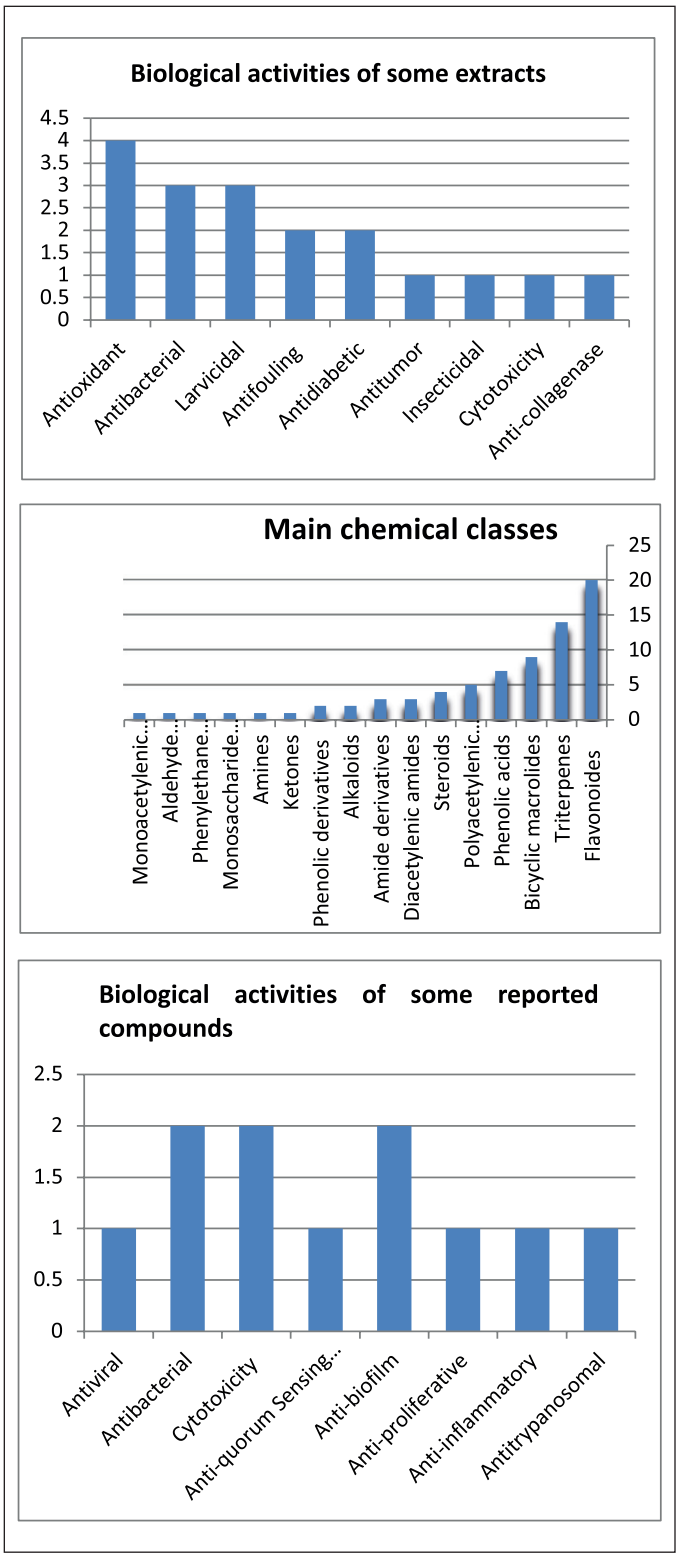

Figure 10. Reported biological activities for compounds isolated seaweed and marine sponge collected from Red Sea marine organisms.

Sea Coast, Egypt. These compounds exhibited antibacterial effects versus *S. aureus* with MIC values of 8 and 4 µg/ml and *B. subtilis* with MIC values of 16 and 4 µg/ml, respectively. Also, they showed mild biofilm inhibitory effects in *P. aeruginosa* (49.32% and 41.76% inhibition), respectively. Moreover, they showed a mild *in vitro* antitrypanosomal effect (13.47 and 10.27 µM), respectively, and a strong cytotoxic activity was recorded against various human cancer cell lines (El-Hawary *et al*., 2019). Callysterol (ergosta-5,11-dien-3β-ol) (**65**), a sterol, was separated from the marine sponge *C. siphonella* obtained from the Red Sea, Egypt. It showed anti-inflammatory activity using the rat-hind paw edema assay (Youssef *et al*., 2010) (Fig. 8).

Marine sponge *L. magnifica* (*Negombata magnifica*)

Marine sponge L. magnifica: secondary metabolites and their bioactivities

Three toxins, namely latrunculin A–C (**66–68**), were separated from the Red Sea sponge *L. magnifica* (Kashman *et al*., 1980). Two latrunculins A (**69**) and B (**70**) were isolated from petroleum ether extract of *L. magnifica* collected from the Gulf of Eilat (Groweiss *et al*., 1983). Latrunculins A–D (**71–74**) were separated from the Red Sea sponge *L. magnifica* (Kashman *et al*., 1985) (Fig. 9). All the reported compounds are listed in Table 2.

Marine sponge *C.* (*Grayella*) *cyathophora*

Marine sponge C. (Grayella) cyathophora: secondary metabolites and their bioactivities

Reviewing the literature indicates that there are inadequate previous studies related to the chemical characterization of various extracts of *C.* (*Grayella*) *cyathophora*.

Biological and pharmacological activities of marine sponge C. (Grayella) cyathophora extracts

The aqueous ethanol extract of marine sponge *C.* (*Grayella*) *cyathophora* collected from the Gulf of Aqaba, Red Sea, Egypt, showed cytotoxic activity to Vero cells with hepatitis A virus with a MIC value of 2.929 µg/ml. The extract showed antibacterial activity against *P. aeruginosa*. Also, it showed antioxidant activity with IC_{50} value of 748 µg/ml. Moreover, the anti-inflammatory activity was 89.91% (El-Damhougy *et al*., 2017).

To sum up, the biological activities of some extracts and the main chemical classes as well as the biological activities of some reported compounds are summarized in Figure 10.

CONCLUSION

One of the distinguishing characteristics of marine-derived compounds is the diversity of their chemical structural, biological and pharmacological applications, which makes it a promising dais for drug discovery from natural sources. This review highlights an up-to-date comprehensive survey regarding the phytochemical and biological aspects of seaweed and marine sponges. Additionally, this review delivers a sign that numerous chemical ingredients have been isolated or identified from seagrass (*T. hemprichii*) and marine sponges (*S. siphonella*, *L. magnifica*, and *C.* (*Grayella*) *cyathophora*). The dominant compounds in *T. hemprichii* are phenolic compounds, while the dominant compounds in marine sponges are amides, alkaloids, terpenes, and steroids. Some of the reported compounds showed a broad spectrum of biological activities including antiviral, antibacterial, cytotoxicity, anti-quorum sensing (anti-QS), antibiofilm, anti-proliferative, anti-inflammatory, and antitrypanosomal activities.

Moreover, it was noted that both types of chemical components and their biological properties are affected by the habitats of these organisms. These marine organisms are considered the most attractive biological targets and deserve more biological exploration due to the biological activities demonstrated by their chemical components as well as their various extracts. Moreover, this review sheds light on the enormous correlation between the chemical entities and the biological activities of marine-derived fungi. To sum up, these findings are likely to be used in the development of the pharmaceutical industry.

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LIST OF ABBREVIATIONS

NPs: Natural products; MNPs: Marine natural products; IC_{50}: The half-maximal inhibitory concentration; MIC: Minimum inhibitory concentration; HeLa: Immortal cell line; MCF-7: Breast cancer cell line; A549: Adenocarcinomic human alveolar basal epithelial cells; DPPH: 2,2-diphenyl-1-picrylhydrazyl; ABTS: 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid; FRAP: Ferric reducing antioxidant power; LC_{50}: Lethal concentration 50; Anti-QS: Anti-quorum sensing; PC-3: Human prostate cancer cell Line; HCV: Hepatitis C virus.

AUTHOR CONTRIBUTION

S.E.A.A., M.A.G., and A.A.H. wrote the main manuscript text. M.A.G. and E.M. prepared Figures 1–10 and Tables 1 and 2. M.A.G. and A.A.H. revised the manuscript. S.E. supervised the work. All authors reviewed the manuscript.

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The authors declare that they have no known competing commercial interests or personal relationships that could have appeared to influence the work reported in this paper.

ETHICAL APPROVALS

This study does not include conducting any experiments on humans or animals.

DATA AVAILABILITY

All data generated or analyzed during this study are included in this published article.

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