

## Biodiversity and Secondary Metabolites of Marine Sponges from Turkey

Hajar Heydari<sup>1</sup>, Bülent Gözcelioğlu<sup>2</sup> and Belma Konuklugil<sup>1\*</sup>

<sup>1</sup>Pharmacognosy Department, Pharmacy Faculty, Ankara University, Ankara, Türkiye

<sup>2</sup>Science and Society Department, Scientific and Technological Research Council of Türkiye (TÜBİTAK), Ankara, Türkiye

(Received July 31, 2018; Revised December 31, 2018; Accepted January 02, 2019)

**Abstract:** Turkey is surrounded by the Black Sea, the Aegean Sea and the Mediterranean sea, comprising a rich source of marine biodiversity. Among all marine species, sponges with a wide range of secondary metabolites are an important potential for drug discovery. There are many studies on sponges and their secondary metabolites, but not enough study about Turkish sponges. The present review gives an overview of the current research trends on secondary metabolites from Turkish marine sponges and some of their biological activities. Until today alkaloids, steroids and phenolic compounds have been isolated and determined from Turkish sponges. To our knowledge, this is the first review about Turkish sponges. Furthermore, we have tried to introduce our Marine Herbarium of Ankara University Pharmacy Faculty (MAP).

**Keywords:** Bioactivity; biodiversity; secondary metabolite; sponge © 2019 ACG Publications. All rights reserved.

### 1. Introduction

Marine natural products research has increased conspicuously during the recent decades. Marine species are rich sources of biodiversity with production of structurally diverse, novel and biologically active marine secondary metabolites. Among all the investigated marine species, marine sponges (Porifera) are accepted as the richest sources of new marine natural products. About 33% of all marine natural products have been isolated from sponges, which make them currently the most important source of unique secondary metabolites [1]. More than 5300 different compounds have been isolated from sponges and their associated microorganisms, and more than 200 new secondary metabolites are reported every year [2]. The compounds isolated from sponges have diverse structures including acids, alkaloids, esters, fatty acids, glycosides, ketones, lipids, macrolides, alcohols, peptides, peroxides, quinones, polyketides, steroids, terpenes, terpenoids, sterols with a vast range of biological activities such as antioxidant, antiviral, antibacterial, antifungal, antitumor, anticancer and antifouling activities [3-11]. Because of these properties, sponges are interesting candidates for the design of new drugs for the pharmaceutical industry [12]. Concerning the geographical location, Turkey is encompassed by Black Sea at the north, the Aegean Sea at the west, and the Mediterranean Sea at the south, therefore it is a peninsula which possesses about 8400 km of coastline. Despite this feature, there

\* Corresponding author: E-Mail: [belma.konuklugil@gmail.com](mailto:belma.konuklugil@gmail.com); Phone+90312 203 30 92 Fax:+90312 213 10 81

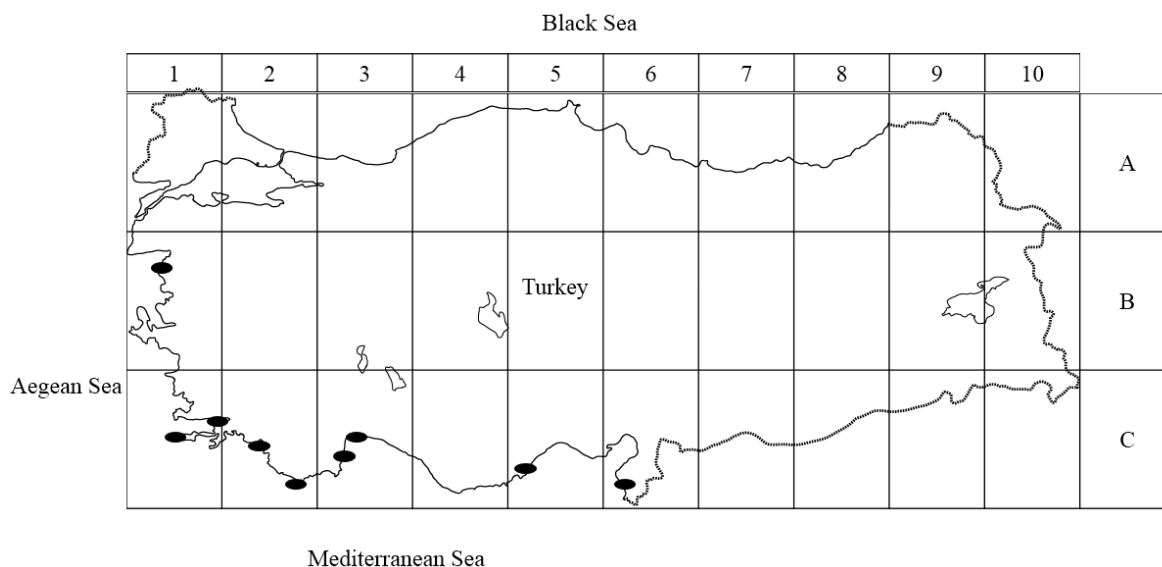
has been limited work on its marine secondary metabolites and their bioactivities. The record of marine sponges in the seas around the Turkey contains 141 species including 82 species from the Aegean Sea, 63 species from the Sea of Marmara, 51 species from the Levantine Sea, and 18 species from the Black Sea were [13-15]. It is worth notice that seven of these sponges were recorded in the previous works of our research group which are already included in sponge fauna of Turkey. These are *Haliclona sarai* (Pulitzer-Finali, 1969); *Scalarispongia scalaris* (Schmidt, 1862); *Hyrtios collectrix* (Schulze, 1880); *Dendrectilla tremitensis* (Pulitzer-Finali, 1983); *Dictyonella incisa* (Schmidt, 1880); *Axinyssa aurantiaca* (Schmidt, 1864); and *Halichondria (Halichondria) contorta* (Sarà, 1961). Moreover, a new *Hymedesmia* species, *Hymedesmia (Hymedesmia) anatoliensis* sp. nov. was also recorded by our group in west of Turkey. In 1885 the sponges from the coasts of Turkey were reported for the first time. The report contained 5 sponge species from the Strait of Çanakkale. The last report of Turkish marine sponges was released in 2016 which included 5 sponge species from the black Sea.

This review aims to summarize the biodiversity of the marine sponges of Turkey. Considering that more than 200 sponge species have been reported in Greek Aegean Sea, it is expected that the number of known sponge species of Turkey increases substantially with further fieldwork.

## 2. Results and Discussion

### 2.1. Marine Herbarium of Ankara University Pharmacy Faculty

Sponge samples were collected by scuba diving with a maximum diving depth of 40 meters. All samples were fixed in 70% ethyl alcohol. Sponge species were identified at the Zoological Museum of Amsterdam, the Netherlands. During our research on marine species, an herbarium of the collected samples was made and all the species were identified by Dr. Gözcelioğlu and Dr. Soest. This herbarium is located in Ankara University, Faculty of Pharmacy, Department of Pharmacognosy (MAP). The list of sponges and collected locations are shown in Table 1 and Figure 1. The most common species in Turkey as shown in Table 1, is *Agelas oroides*. Furthermore, in this herbarium there are other marine species like tunicate, coral, anemone, etc. that were not included in this study.



**Figure 1.** Geographic locations of collected samples

**Table 1.** Distribution of the species among Turkish seas and the location of collected samples (MAP)

Species in MAP	Localities								
	Ayvalik	Guvercinlik	Turgutreis	Fethiye	Kas	Kemer	Antalya	Taşucu	Samandağ
<i>Acanthella acuta</i>			+		+				
<i>Agelas oroides</i>	+		+	+	+	+	+	+	+
<i>Aplysina aerophoba</i>	+	+							
<i>Axinella cannabina</i>			+					+	+
<i>Axinella damicornis</i>	+								
<i>Axinella polypoides</i>				+					
<i>Axinella verrucosa</i>					+		+		
<i>Chondrilla nucula</i>		+							
<i>Chondrosia reniformis</i>		+		+		+	+	+	
<i>Ciocalyptra carballoi</i>					+				
<i>Dendrectilla tremitensis</i>	+								
<i>Dictyonella incisa</i>	+								
<i>Dysidea avara</i>					+		+	+	
<i>Haliclona (Reniera) flavescens</i>					+				
<i>Haliclona (Reniera) mediterranea</i>					+				
<i>Haliclona (Rhizoniera) sarai</i>					+				
<i>Haliclona (Reniera) cratera</i>					+				
<i>Hemimycale columella</i>					+				
<i>Hyrtilis collectrix</i>		+		+					
<i>Ircinia fasciculata</i>				+				+	+
<i>Ircinia oros</i>				+			+		
<i>Ircinia variabilis</i>		+			+				
<i>Petrosia ficiformis</i>				+					
<i>Pleraplysilla spinifera</i>			+						
<i>Sarcotragus spinosulus</i>	+					+	+		
<i>Scarispongia scalaris</i>					+				
<i>Spongia officinalis</i>				+					

## 2.2. Secondary Metabolites Sponges from Turkey

Secondary metabolites which have been isolated from different species of sponges, collected from the coasts of Turkey, are classified by species. The list of isolated compounds is shown in Table 2.

**Table 2.** The secondary metabolites from Turkish sponges

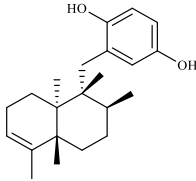
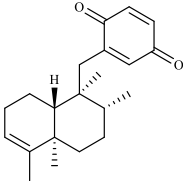
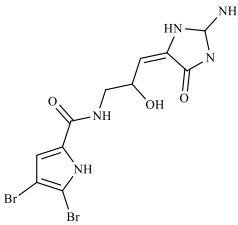
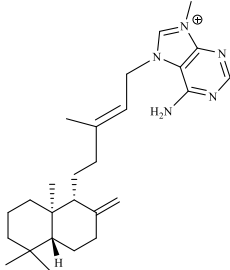
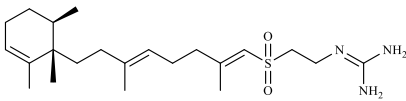
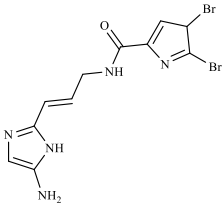
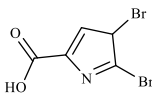
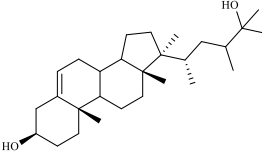
Sponges	Compound	Structure	References
<i>Dysidea avara</i>	Avarol		[17]
<i>Dysidea avara</i>	Avarone		[17]
<i>Agelas oroides (Hatay)</i>	Dispacamide C*		[20]
<i>Agelas oroides (Hatay)</i>	Agelasine D*		[20]
<i>Agelas oroides (Ayvalık)</i>	(+)-Agelasidine C*		[20]
<i>Agelas oroides</i>	Oroidin		[22]
<i>Agelas oroides</i>	4,5-Dibromo pyrrol-2-carboxylic acid		[22]
<i>Agelas oroides</i>	25-Hydroxy-24-methyl cholesterol		[22]

Table 2. Continued..

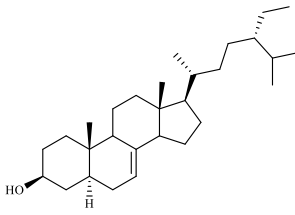
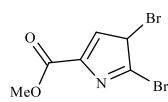
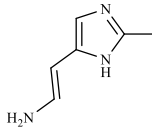
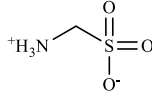
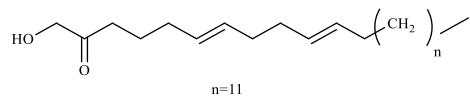
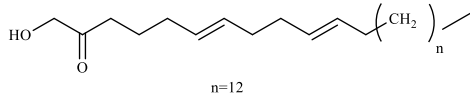
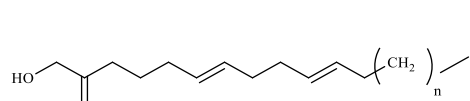
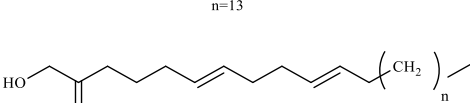
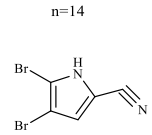
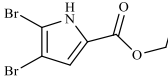
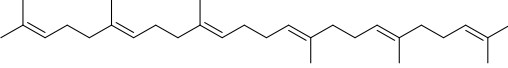
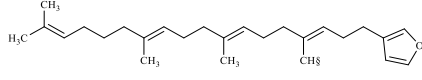
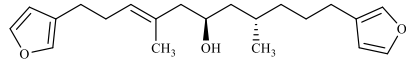
<i>Agelas oroides</i>	24-Ethyl-cholest-5a-7-en-3- $\beta$ -ol		[18]
<i>Agelas oroides</i>	4,5-Dibromopyrrole-2-carboxylic acid methyl ester		[18]
<i>Agelas oroides</i>	( <i>E</i> )-Oroidin, 3-amino-1-(2-aminoimidazolyl)-prop-1-ene		[18]
<i>Agelas oroides</i>	Taurine		[18]
<i>Agelas oroides</i>	(5 <i>Z</i> ,9 <i>Z</i> )-5,9-Tricosadienoic acid		[18]
<i>Agelas oroides</i>	(5 <i>Z</i> ,9 <i>Z</i> )-5,9-Tetracosadienoic acid		[18]
<i>Agelas oroides</i>	(5 <i>Z</i> ,9 <i>Z</i> )-5,9-Pentacosadienoic acid		[18]
<i>Agelas oroides</i>	(5 <i>Z</i> ,9 <i>Z</i> )-5,9-Hexacosadienoic acid		[18]
<i>Agelas oroides</i>	4,5-Dibromo-1 <i>H</i> -pyrrol-2-carbonitrile		[19]
<i>Agelas oroides</i>	4,5-Dibromo-1 <i>H</i> -pyrrol-2-carboxylic acid ethyl ester		[19]
<i>Spongia officinalis</i>	Squalene		[24]
<i>Spongia officinalis</i>	Furospinulosin-1		[24]
<i>Spongia officinalis</i>	Furosponginsin-1		[24]

Table 2. Continued..

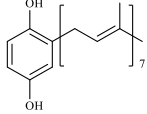
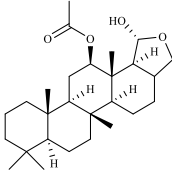
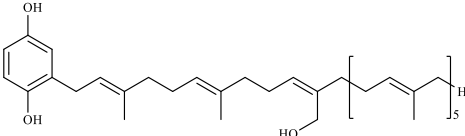
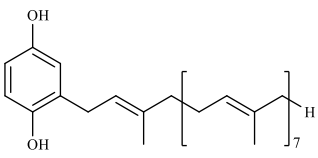
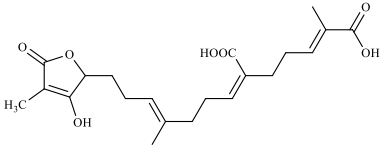
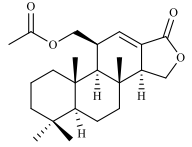
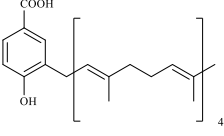
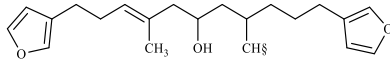
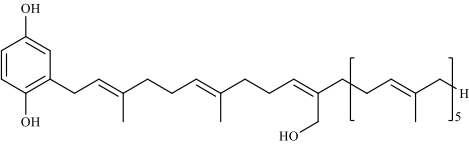
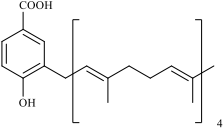
<i>Spongia officinalis</i>	Heptaprenyated <i>p</i> -quinol		[24]
<i>Spongia officinalis</i>	12 <i>epi</i> -Deoxoscalarin		[24]
<i>Spongia officinalis</i>	1,4,44-Trihydroxy-2-octaprenylbenzene		[24]
<i>Ircinia spiculosa</i>	4-Hydroxy-3-tetra-prenylphenyl acetic acid		[24]
<i>Ircinia spiculosa</i>	Dimethyl-furospongini-4		[24]
<i>Ircinia spiculosa</i>	11 $\beta$ -Acetoxyspongi-12-en-16-one		[24]
<i>Ircinia spiculosa</i>	4-Hydroxy-3-octaprenylbenzoic acid		[24]
<i>Spongia officinalis</i>	Furospongini		[26]
<i>Spongia</i> sp.	1,4,44-Trihydroxy-2-octaprenylbenzene		[23]
<i>Ircinia</i> sp	4-Hydroxy-3-octaprenylbenzoic acid		[23]

Table 2. Continued..

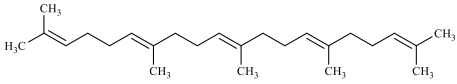
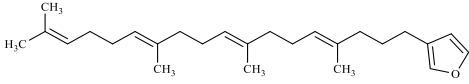
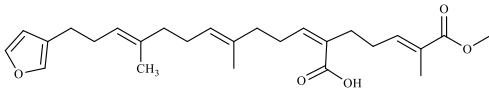
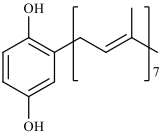
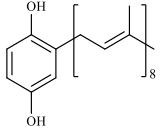
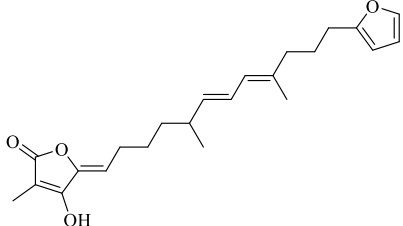
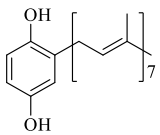
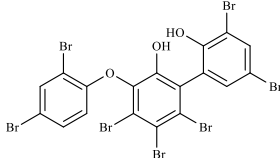
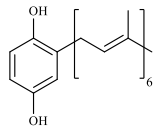
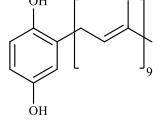
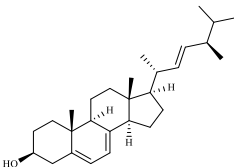
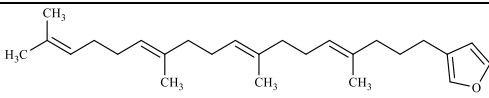
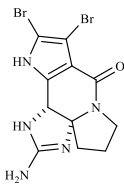
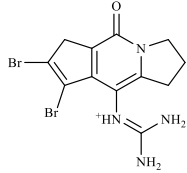
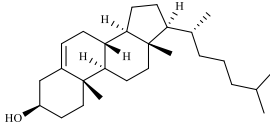
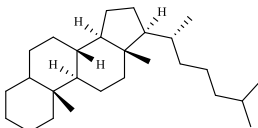
<i>Spongia</i> sp.	Squalene		[23]
<i>Spongia</i> sp.	Furanospinulosin-1		[23]
<i>Spongia</i> sp.	Furospingon-4		[23]
<i>Sarcotragus spinulosus</i>	Heptapregnyl hydroquinone		[27]
<i>Sarcotragus spinulosus</i>	Octapregnyl hydroquinone		[27]
<i>Ircinia variabilis</i>	Fasciculatin		[19]
<i>Ircinia fasciculata</i>	Heptaprenylhydroquinone		[19]
<i>Sarcotragus muscarum</i>	Ambigol A derivatives		[19]
<i>Sarcotragus muscarum</i>	Hexaprenylhydroquinone		[19]
<i>Sarcotragus muscarum</i>	Nonaprenylhydroquinone		[19]
<i>Spongia officinalis</i>	Ergosterol		[25]

Table 2. Continued..

<i>Spongia officinalis</i>	Furospinulosin-II		[25]
<i>Axinella cannabina</i> (Hatay)	Cylindradine A*		[20]
<i>Axinella damicornis</i>	Ugibohlin*		[20]
<i>Dictyonella incisa</i>	Cholesterol		[31]
<i>Dictyonella incisa</i>	Cholestane		[31]

### 2.2.1. *Dysidea* Species

According to the literature survey avarol and avarone are the major compounds of *Dysidea avara*. These compounds were also isolated from *D. avara*, which was collected from İbrice, on the Aegean coast [17].

### 2.2.2. *Agelas* Species

24-Ethyl-cholest-5a-7-en-3- $\beta$ -ol and 4,5-dibromopyrrole-2-carboxylic acid methyl ester were isolated from the hexane fraction of *A. oroides* as major components. 4,5-dibromopyrrole-2-carboxylic acid, (*E*)-oroidin, 3-amino-1-(2-aminoimidazolyl)-prop-1-ene, taurine, and some minor, complex fatty acid mixtures consisting of a 1:2 mixture of (5*Z*,9*Z*)-5,9-tricosadienoic and (5*Z*,9*Z*)-5,9-tetracosadienoic acids, also another mixture of (5*Z*,9*Z*)-5,9-pentacosadienoic and (5*Z*,9*Z*)-5,9-hexacosadienoic acids were detected in this sponge [18]. 4,5-dibromo-1*H*-pyrrol-2-carbonitrile, 4,5-dibromo-1*H*-pyrrol-2-carboxylic acid ethyl ester, 4,5-dibromo-1*H*-pyrrol-2-carboxylic acid and oroidin were isolated from *A. oroides* which was collected from Fethiye [19]. Agelasine D, diterpene derivative of hypotaurocyamine, agelasidine C were isolated from *Agelas oroides* which was collected from different regions of Hatay and Ayvalik [20]. Bromotyrosine alkaloid, indole alkaloid, pyrrole imidazole alkaloid, bromopyrrole alkaloid and terpenes were detected by DAAD- HPLC from *A. oroides* which was collected from Kemer [21]. Oroidin, 4,5-dibromopyrrol-2-carboxylic acid, and 25-hydroxy-24-methylcholesterol were also isolated from *Agelas oroides* [22].

### 2.2.3. *Spongia* Species

*Spongia* sp. which was collected from Bodrum, was investigated and according to obtained results 1,4,44-trihydroxy-2-octaprenylbenzene, 4-hydroxy-3-octaprenylbenzoic acid, squalene, furanospinulosin-1, furospingin, 2-(hexaprenylmethyl)-2-methylchromenol and 112-epi-deoxoscalarin were isolated [23].



Seven known terpenoids, squalene, furospinulosin-1, furospingonin-1, 2-(hexaprenylmethyl)-2-methylchromenol, heptaprenyated *p*-quinol, 12 *epi*-deoxoscalarin, 1,4,44-trihydroxy-2-octaprenylbenzene and a mixture of furospingonin-3- and 4 were isolated from *Spongia officinalis* [24]. Ergosterol and furospinulosin-II were isolated from *S. officinalis*. This sponge species was collected from Bodrum, Turkey [25]. Furanoterpenoids (polyprenyl-hydroquinones), furospingonins and furospinulosins (polyprenyl-furans) were also isolated from this sponge [26].

#### 2.2.4. *Ircinia* Species

Dimethyl-furospingonin-4, 4-hydroxy-3-tetraprenyl phenylacetic acid, 4-hydroxy-3-octaprenylbenzoic acid and 7  $\beta$ ,11  $\beta$ -diacetoxyspongi-12-en-16-one were isolated from *Ircinia* sp., which was collected from Bodrum, Turkey [23]. Four known terpenoids, 4-hydroxy-3-tetraprenylphenyl acetic acid, dimethyl-furospingonin-4 dorisenone D, 11 $\beta$ -acetoxyspongi-12-en-16-one and 4-hydroxy-3-octaprenylbenzoic acid were isolated from *I. spinulosa* [24]. Furanoterpenoids (polyprenyl-hydroquinones), furospingonins and furospinulosins (polyprenyl-furans) were isolated from three sponges *I. spinulosa*, *I. muscarum* which were collected from the Mediterranean Sea [26]. Fasciculatin and heptaprenylhydroquinone were isolated from *I. variabilis* (Mersin) and *I. fasciculata* (Fethiye) respectively [19]. Bromopyrrole, indol alkaloids which were also determined by HPLC-DAD were isolated from *I. oros* and *I. variabilis* [21].

#### 2.2.5. *Sarcotragus* Species

Heptaprenyl hydroquinone, octaprenyl hydroquinone and prenylated hydroquinone were isolated from *S. spinulosus* which was collected from Antalya, Turkey [27]. Ambigol A derivatives, hexaprenyl hydroquinone and nonaprenyl hydroquinone were isolated from *Sarcotragus muscarum* which was collected from Fethiye [19]. Bromopyrrole type alkaloids (Purealidin R, Oroidin, Spongiacidin D, Hymenialdisin, Hymenidin, Stevensin, Aeroplysinin-1), indoline alkaloid (Communesin B), furanosester terpenes (Fasciculatin), and terpenes (Agelanesin A), were detected by DAAD- HPLC from *S. spinulosa*, sponge species which was collected from Kemer [21].

#### 2.2.6. *Axinella* Species

Cylindradine A and Ugibohlin were isolated from *A. cannabina* and *A. damicornis* respectively [20]. Bromopyrrole type alkaloids (Purealidin R, Oroidin, Spongiacidin D, Hymenialdisin, Hymenidin, Stevensin, Aeroplysinin-1), indoline alkaloid (Communesin B), furanosester terpenes (Fasciculatin), and terpenes (Agelanesin A), were detected by DAAD- HPLC from *A. polypoides*, sponge species collected from Kemer [21].

### 2.3. Bioactivity of Sponge Samples from Turkey

#### 2.3.1. Antimicrobial Activities

The methanol extracts of sponges *Agelas oroides* (Kemer, Hatay, Ayvalik), *Axinella damicornis* (Kemer, Hatay, Antalya, Ayvalik), *Axinella cannabina* (Hatay and Ayvalik), *Ircinia spinulosa*, *Ircinia fasciculata* (Kemer and Hatay), *Ircinia variabilis*, *Dysidea avara* and *Sarcotragus spinulosus* (Antalya), which were collected from the Mediterranean sea, were screened for antimicrobial activities against standard and isolated microorganism. Selected sponge extracts showed high activity against *Staphylococcus aureus* (ATCC 25923) with MIC values between 0.5 – 1 mg /mL, where ofloxacin and ampicillin had MIC at 0.25 and 0.12 mg/mL, respectively [22].

Antimicrobial activities of methanolic extracts of *Spongia officinalis*, *Spongia agaricina*, *Aplysina aerophoba* (Saros) were tested against *Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Aspergillus niger*, *Aspergillus fumigatus* var. *elipticus*, *Aspergillus flavus*, *Penicillium granulatum*, *Penicillium rugulosum*, *Penicillium jenseii*, *Aspergillus candidus*, *Geotrichum candidum* and *Candida albicans* strains. Sponges were collected from three different regions of Saros: six sponges from Saros-Gallipoli (3-4m), seven sponges from Saros-Gallipoli (10-30m), seven sponges from Saros-Gallipoli

(10m). Antimicrobial activity of these samples showed that *Aplysina aerophoba* and *Spongia agaricina* significantly inhibited both bacterial and fungal growth [28,32].

### 2.3.2. Antioxidant Activity

Antioxidant activities of selected samples were determined by DPPH assay. According to the results *Ircinia variabilis* (Antalya) exerted the highest scavenging activity rather than the other samples (65.92% inhibition at 2000 mg/ mL). *Ircinia fasciculata* -Hatay (68.64%), *Ircinia spinulosa* -Kemer (68.19%), and *Dysidea avara* (66.90%) exhibited acetylcholinesterase inhibitory effect at 200 mg/ mL concentration [22].

Antioxidant activities of methanolic extracts of eleven species from six different regions of Turkey were demonstrated by 2,2-diphenyl-1-picrylhydrazil (DPPH), nitric oxide (NO) and superoxide (SO) assays. These sponge samples were collected from Kemer, Güvercinlik, Ayvalık, Hatay, Turgutreis and Kaş. According to the results localities of the sponges were found to be effective for the potency of their activities. DPPH radical scavenging activity of methanolic extracts of *Dysidea avara* (IC<sub>50</sub>:92.8 µg/mL) from Kemer, *Axinella cannabina* (IC<sub>50</sub>: 788 µg/mL) from Ayvalık, *Agelas oroides* (IC<sub>50</sub>: 553.7; 545.1 µg/mL) from Kemer and Ayvalık, *Axinella damicornis* (IC<sub>50</sub>: 519.5; 738.5 µg/mL) from Kemer and Ayvalık, *Axinella verrucosa* (IC<sub>50</sub>: 432.32 µg/mL) from Turgutreis were more active than the other sponge samples. SO radical scavenging activity of methanolic extracts of *Dysidea avara* (IC<sub>50</sub>:34.1 µg/mL) from Kemer, *Axinella cannabina* (IC<sub>50</sub>:1286.9 µg/mL) from Ayvalık, *Ircinia fasciculata* (IC<sub>50</sub>:1675.9 µg/mL) and *Axinella damicornis* (IC<sub>50</sub>:1579.6 µg/mL) from Kemer and *Agelas oroides* (IC<sub>50</sub>:1617.2 µg/mL) from Hatay were most active. NO radical scavenging activity of methanolic extracts of *Agelas oroides* (IC<sub>50</sub>: 1977.7 µg/mL), *Dysidea avara* (IC<sub>50</sub>:1759.1 µg/mL), *Ircinia spinulosa* (IC<sub>50</sub>:1937.9 µg/mL), *Axinella damicornis* (IC<sub>50</sub>:1150 µg/mL) from Kemer, *Axinella cannabina* (IC<sub>50</sub>: 1668.9 µg/mL) from Hatay and *Ciocalypta carbolloi* (IC<sub>50</sub>:700.7 µg/mL) from Kaş showed high antioxidant activity [29].

### 2.3.3. Cytotoxic Activity

The hexane, chloroform and methanol extracts prepared from *Axinella* sp., were screened for their cytotoxic activity by MTT assay against B16 melanoma cells. The chloroform extract of the sponge showed significant cytotoxic activity [30].

### 2.3.4. Other Activities

The crude extracts and pure compounds and fatty acids mixture which were isolated from *Agelas oroides* exhibited inhibitory activity against the recombinant PjFabI enzyme. Among the tested components the mixture of fatty acids exerted the highest inhibitory potential (IC<sub>50</sub>: 0.35 lg/mL). Fatty acids mixtures also inhibited FabI of *Mycobacterium tuberculosis* (MtFabI, IC<sub>50</sub>s 9.4 and 8.2 lg/ml, respectively) and *Escherichia coli* (EcFabI, IC<sub>50</sub>s 0.5 and 0.07 lg/ml, respectively). The secondary metabolite isolated from *Agelas oroides* exhibited in vitro anti plasmodial, trypanocidal and leishmanicidal activities without cytotoxicity towards mammalian cells [18].

Furanoterpenoids, furospingins and furospinosulins which were isolated from *Spongia officinalis*, *Ircinia spinulosa*, *Ircinia muscarum* sponges showed CDC25 (Cell division cycle 25) phosphatase inhibitor activity. These compounds were screened for their activity against Ser/Thr phosphatase Protein phosphatase 2C (PP2C-α) and three kinases cyclin-dependent kinase 1 (CDK1 and CDK5), glycogen synthase kinase 3 (GSK-3), but they did not show any activity against these enzymes [26].

Agelasine D which was isolated from *Agelas oroides* and its butanol fraction significantly inhibited the growth of *Trypanosoma brucei* to the extent of 98.9% and 99.2% respectively at 20µg/ml of test solutions, which were 1.9% and 2.2% more active than that of reference drug (suramin; p<0.01). Both agelasine D and *A. oroides* butanol fraction exhibited 98.3% and 93% of prominent growth inhibitory activity against *S. aureus* (p<0.01), but were less active against *E. coli*. Isolation of agelasine D from Mediterranean sponge *Agelas oroides* was unprecedented [20].

The crude extract of *Axinella damicornis* (Ayvalık) was found to have greatest inhibitory effect against trypanosome. Its cytotoxic effect is specific against trypanosome as it inhibits only 8% of *S. aureus* population and 25.8% of the population of *E.coli*. Ethyl acetate extract of *A. damicornis* (Hatay)

is also a potent anti-trypanosome agent as its inhibition towards trypanosome is only slightly lesser than the crude extract of *A. damicornis* (Ayvalik). However, its cytotoxic effect is not as specific as the crude extract of *A. damicornis* (Ayvalik) as it inhibits 19.5% of *S. aureus* population and 28.1% of *E. coli* population. So, it can be concluded that the crude extract of *A. damicornis* (Ayvalik) is a more potent anti-trypanosome agent. Butanol extract of *A. cannabina* (Hatay) was found to be the least potent anti-trypanosome agent as it only inhibits 17.4% of the population of trypanosome. Besides, its cytotoxic activity against the normal flora (*S. aureus* and *E. coli*), was found to be greater than the crude extract of *A. damicornis* (Ayvalik), which is a most potent agent. This means that the butanol extract has greater inhibitory effect against normal flora compared to trypanosome. So, it can be concluded that the butanol extract of *A. cannabina* (Hatay) is not suitable to be used as anti-trypanosome agent. All eight samples were found to have greater inhibitory effect towards *E. coli* than against *S. aureus* [20].

In conclusion marine sponges produce a vast array of anticancer, anti-inflammatory, antibiotic, antiviral, immunosuppressive, bioactive compounds that can affect the pathogenesis of many diseases. These different compounds are produced by sponges as means of survival. Sponges with different bioactive compounds can be new and unique sources for drug discovery and industrial uses. Turkey has a long border of sea and a wide diversity of marine species. Despite this, our literature survey demonstrated that there are not enough studies on Turkish marine species, especially on sponges. In this review we have tried to assemble studies about sponge species which were collected from Turkey. Furthermore, there are no studies on Black sea species. The pH, temperature, pressure and salt rate of the Black sea make it a different habitat for sponges and also other marine species. These conditions result in the production of new secondary metabolites with different activities.

Moreover, a new *Hymedesmia* species, *Hymedesmia (Hymedesmia) anatoliensis* sp. nov. was also recorded by our group in west of Turkey, also *Axinyssa aurantiaca* (Schmidt, 1864), *Halichondria (Halichondria) contorta* (Sarà, 1961), and *Dictyonella incisa* (Schmidt, 1880), were added to the fauna of Turkey [16].

## Acknowledgment

These studies presented in this review were partially supported by a TÜBİTAK-Julich Project (SBAG104S109)

## ORCID

Hajar Heydari: [0000-0001-6297-4618](https://orcid.org/0000-0001-6297-4618)

Bülent Gözcelioğlu: [0000-0003-1835-2701](https://orcid.org/0000-0003-1835-2701)

Belma Konuklugil: [0000-0002-4753-0450](https://orcid.org/0000-0002-4753-0450)

## References

- [1] M.F. Mehbub, J. Lei, C. Franco and W. Zhang (2014). Marine sponge derived natural products between 2001 and 2010: trends and opportunities for discovery of bioactives, *Mar. Drugs*. **12**, 4539-4577.
- [2] M. Laport, O. Santos and G. Muricy (2009). Marine sponges: potential sources of new antimicrobial drugs. *Curr. Pharma. Biotechnol.* **10**, 86-105.
- [3] J.W. Blunt, B.R. Copp, W.P. Hu, M.H. Munro, P.T. Northcote and M.R. Prinsep (2003). Marine natural products, *Nat. Prod. Rep.* **20**, 1-48.
- [4] J.W. Blunt, B.R. Copp, W.P. Hu, M.H. Munro, P.T. Northcote and M.R. Prinsep (2004). Marine natural products, *Nat. Prod. Rep.* **21**, 1-49
- [5] J.W. Blunt, B.R. Copp, W.P. Hu, M.H. Munro, P.T. Northcote and M.R. Prinsep (2006). Marine natural products, *Nat. Prod. Rep.* **23**, 26-78.
- [6] J.W. Blunt, B.R. Copp, W.P. Hu, M.H. Munro, P.T. Northcote and M.R. Prinsep (2007). Marine natural products, *Nat. Prod. Rep.* **24**, 31-86.
- [7] J.W. Blunt, B.R. Copp, W.P. Hu, M.H. Munro, P.T. Northcote and M.R. Prinsep (2008). Marine natural products, *Nat. Prod. Rep.* **25**, 35-94.
- [8] J.W. Blunt, B.R. Copp, W.P. Hu, M.H. Munro, P.T. Northcote and M.R. Prinsep (2009). Marine natural products, *Nat. Prod. Rep.* **26**, 170-244.
- [9] J.W. Blunt, B.R. Copp, W.P. Hu, M.H. Munro, P.T. Northcote and M.R. Prinsep (2010). Marine natural products, *Nat. Prod. Rep.* **27**, 165-237.

- [10] J.W. Blunt, B.R. Copp, W.P. Hu, M.H. Munro, P.T. Northcote and M.R. Prinsep (2011). Marine natural products, *Nat. Prod. Rep.* **28**,196–268.
- [11] J.W. Blunt, B.R. Copp, W.P. Hu, M.H. Munro, P.T. Northcote and M.R. Prinsep (2012). Marine natural products, *Nat. Prod. Rep.* **29**, 144–222
- [12] S. Perdicaris, T. Vlachogianni, A and Valavanidis (2013). Bioactive natural substances from marine sponges: new developments and prospects for future pharmaceuticals, *Nat. Prod. Chem. Res.* **1**, 1000114-1000128.
- [13] B. Topaloğlu and A. Evcen (2014). Updated checklist of sponges (Porifera) along the coasts of Turkey, *Turk. J. Zool.* **38**,665–676.
- [14] A. Evcen, M.E. Çınar, M. Zengin, S. Süer and M. Rüzgar (2016). New records of five sponge species (Porifera) for the Black Sea, *Zootaxa* **4103**, 267–275
- [15] B. Topaloğlu, A. Evcen and M.E. Çınar (2016). Sponge fauna in the sea of Marmara, *Turk. J. Fish. Aquat. Sci.* **16**, 51-59.
- [16] B. GözcelioğluB. , R.V. Soest, B. Alvarez and Konuklugil (2015). New species of sponges (Porifera, Demospongiae) from the Turkish coast, *Turk. J. Zool.* **39**, 555-559.
- [17] N. Aktas, B. Gözcelioğlu, Y. Zang, W. Lin and B. Konuklugil (2010). Avarone and Avarol from the marine sponge *Dysidea avara* Schmidt from Aegean coast of Turkey, *FABAD J. Pharm. Sci.* **35**, 119-123.
- [18] D. Tasdemir, B. Topaloglu, R. Perozzo, R. Brun, R. O'Neill, N.M. Carballeira, X. Zhang, P.J. Tonge, A. Lindeng and P. Rüedi (2007). Marine natural products from the Turkish sponge *Agelas oroides* that inhibit the enoyl reductases from *Plasmodium falciparum*, *Mycobacterium tuberculosis* and *Escherichia coli*, *Bioorg. Med. Chem.* **15**, 6834–6845.
- [19] A. Putz (2009). Secondary metabolites from marine sponges, with focus on the chemical ecology and biochemical characterisation of the stress-induced biotransformation of Aplysina alkaloids Ph.D, Düsseldorf University, Düsseldorf, Germany.
- [20] T.M. Ming (2010). Metabolomic profiling of anti-trypanosomal active sponge extracts. Final year research project, University of Strathclyde, England.
- [21] N. Aktas, B. Gözcelioğlu and B. Konuklugil (2011). Qualitative detection of some secondary metabolites from Turkish marine sponges collected in Kemer, *FABAD J. Pharm. Sci.* **36**, 129-136.
- [22] I.E. Orhan, B. Ozcelik, B. Konuklugil, A. Putz, U.G. Kaban and P. Proksch (2012). Bioactivity screening of the selected Turkish marine sponges and three compounds from *Agelas oroides*, *Rec. Nat. Prod.* **6**, 356-367,
- [23] I. Erdoğan, J. Tanaka, T. Higa and B. Sener (1999). Terpenoids from two sponge species of Aegean sea, *Nat. Prod. Sci.* **5**, 177-180.
- [24] I. Erdoğan, J. Tanaka, T. Higa and B. Sener (2000). Two new hydroquinone derivatives from two new sponge species of Aegean sea, *J. Chem. Soc. Pak.* **22**,200-204.
- [25] I. Erdoğan and B. Şener (2001) Two metabolite from the marine sponge *Spongia officinalis* L, *Acta Pharma. Sc.* **43**,17-19.
- [26] I. Erdoğan-Orhan, B. Sener, S. de Rosa, J. Perez-Baz, O. Lozach, M. Leost, S. Rakhilin and L. Meijer (2004). Polyprenyl-hydroquinones and -furans from three marine sponges inhibit the cell cycle regulating phosphatase CDC25A, *Nat. Prod. Res.* **18**,1-9.
- [27] B. Ergene (2009). Deniz süngerinden sarcotragus spinulosus'un biyoaktif etken maddelerinin izolasyonu ve yapı tayini, Master of science, Ankara university, Ankara, Turkey.
- [28] H.M. Canakay and B.M. Yapici (2016). Antifungal and antibacterial activities of three marine sponges obtained from the gulf of saros in Turkey, *Ann. Bio. Res.* **7**, 1-6.
- [29] N. Aktas, Y. Genc, B. Gözcelioğlu, B. Konuklugil and U.S. Harput (2013). Radical scavenging effect of different marine sponges from mediterranean coasts, *Rec. Nat. Prod.* **7**, 96-104.
- [30] F.N. Yalçın (2007). Biological activities of the marine sponge *Axinella*, *Hacettepe Univ. J. Facul. Pharm.* **27**, 47-60.
- [31] H. Heydari, B. Gozcelioglu and B. Konuklugil (2018). In vitro evaluation of bioactivity of *Dictyonella incisa* from Turkey, *Kafkas Univ. Vet. Fak. Derg.* **24**, 479-482.
- [32] P. Ferriol, F.J. T. Marante, I. B. Martin, J.J. S. Rodriguez, R.G. Alonso, A. G. Benkovics and R. Mioso (2018). Identification and quantification, by NMR and LC-MS, of sterols isolated from the marine sponge *Aplysina aerophoba*, *Rec. Nat. Prod.* **12(5)**, 470-479.