Bioactive marine metabolites derived from The Persian Gulf compared to The Red Sea: similar environments and wide gap in drug discovery

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Abstract

Marine life has provided mankind with unique and extraordinary chemical structures and scaffolds with potent biological activities. Many organisms and secondary metabolites derived from fungi and symbionts are found to be more environment friendly to study than the marine corals *per se*. Marine symbionts such as *Aspergillus sp.*, a fungus, which can be isolated and grown in the lab would be a potential and continuous source of bioactive natural compounds without affecting the marine environment. The Red Sea is known for its biodiversity and is well-studied in terms of its marine derived bioactive metabolites. The harsh environmental conditions lead to the development of unique metabolic pathways. This in turn, results in enhanced synthesis and release of toxic and bioactive chemicals. Interestingly, the Persian Gulf and Gulf of Oman carry a variety of environmental stresses some of which are similar to the Red Sea. When compared to the Red Sea, The Persian Gulf has been shown to be rich in marine fungi as well, and is therefore, expected to contain elaborate and interesting bioactive compounds. Such compounds may or may not be similar to the ones isolated from the Red Sea environment. Astoundingly, there are a very limited number of studies on the bioactive portfolio of marine derived metabolites from the Persian Gulf and the Gulf of Oman. In this perspective, we are looking at the Red Sea as a comparator marine environment and bioactive materials repertoire to provide a futuristic perspective on the potential of the understudied and possibly overlooked bioactive metabolites derived from the marine life of the Persian Gulf and Gulf of Oman despite its proven biodiversity and harsher environmental stress.

Introduction

Over the past couple of decades, the number of totally synthetic FDA approved drugs is significantly decreasing (Patridge et al., 2016). Yet, naturally occurring compounds with unique and new scaffold characteristics constitute a virgin area of drug discovery and an inspiring space for semisynthetic and synthetic drug discovery research. In the duration 1980-2010, 26% of the newly approved drugs (1355 drugs) were natural products or natural compounds' derivatives (Newman & Cragg, 2012). Terrestrial plant-derived natural products have a long history in supplying mankind with a giant library of unique stereo-chemically complex compounds with diverse biological activities. On the other hand, marine life provided drug discovery researchers with several unique and extraordinary chemical structures and scaffolds with very potent biological activities. Marine invertebrates (animals, vascular plants, algae, cyanobacteria, fungi and actinomycetes) produce these unique and potent biologically active metabolites as a result of evolutional pressure in the form of predation, space and resources' competition. The majority of these marine bioactive metabolites are of unique chemical structure and not reported in any terrestrial origin. It can be hypothesized that the more stressful the marine environment, the more unique and diverse metabolites are expected in marine organism (Seibel & Drazen, 2007). The Red Sea is only second to the great barrier reef in Australia in terms of the biodiversity of its fauna with versatile bioactive metabolites repertoire.

63 **Rationale:**
64 In the recent couple of decades, intensive drug discovery research shed the light on the Red Sea
65 marine invertebrates and its bioactive compositions. Several bioactive metabolites with unique
66 chemical scaffolds were isolated, identified and showed promising pharmacological activities
67 from the Red Sea marine life (El-Hossary et al., 2020). Biological activity herein is referred to in
68 case of on any early experimental to late clinical evidence for potential use in the treatment of
69 any human disease. On the other hand, the Persian Gulf and Gulf of Oman which are
70 geographically close, atmospherically similar and under harsher environmental stress than the
71 Red Sea, are surprisingly understudied in terms of bioactivity and drug discovery.
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73 **Relevance to readers:**
74 Herein we are utilizing the Red Sea as a benchmark marine environment and bioactive materials
75 repertoire to provide a futuristic perspective for the high potential of the understudied and
76 overlooked bioactive metabolites derived from the marine life of the Persian Gulf and Gulf of
77 Oman despite its rich biodiversity under harsh environmental stress. This review would be of
78 special interest for researcher interested in drug discovery and in particular, those who are
79 interested in marine derived bioactive metabolites.
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83 ## Survey methodology
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85 **Search strategy:**
86 The search for all relevant studies published was conducted on PubMed and Google Scholar,
87 with the search terms being "Marine metabolites; Bioactive metabolites; Marine bioactive
88 metabolites; Drug discovery; Secondary metabolites; The Red Sea; The Persian Gulf; The
89 Arabian Gulf; Gulf of Oman; Fauna; *Aspergillus sp.*". Titles and abstracts were screened
90 superficially for potential relevance, and once articles were deemed relevant, their full-texts were
91 extracted and independently reviewed in depth to be considered for inclusion by the authors.
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94 **Inclusion criteria:**
95 Only Scopus-indexed journals were considered up to the year 2000. Eligible study designs
96 included review articles, systematic reviews and meta-analyses. English was the sole publication
97 language considered. Editorials, pre-prints that were not peer-reviewed, case reports, database
98 reports were excluded.
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Environmental stress in the Persian Gulf and Gulf of Oman compared to the Red Sea

The Persian Gulf/Gulf of Oman is a semi-enclosed sea, located in a subtropical region of the
Middle East between latitudes of 24° and 30° North and longitudes 48° and 57° East. It is part of
the Indo-Pacific Ocean ecoregion and consists of a shallow sedimentary basin with a relative
depth of 35 meters and covering a total area of 240,000 km². The maximum depth of the Persian
Gulf/Gulf of Oman is approximately 110 meters and its photic zone extends between 6 to 15
meters. The Iranian shores have steep sloping sections while the Persian shores are sedimentary
with a gradual slope. Considering the combination of high latitudinal position, high evaporation
rates, relative shallowness, coastline alterations, heavy traffic volume, frequent oil spills,
excessive industrial effluents and restricted freshwater flow into the Gulf; the Persian Gulf/Gulf
of Oman is subject to extreme environmental conditions. Therefore, marine organisms residing
in the Persian Gulf/Gulf of Oman are surviving close to their environmental tolerance limits
(Naser, 2014).
With respect to the Red Sea, it is also a semi-enclosed sea, between latitudes of 22° North and
longitudes 38° East. It covers an area of approximately 438,000 km2 and is connected from its
south end via the strait of Bab el Mandeb and Gulf of Aden to the Indian Ocean. The Red sea is
known for its coastal fringing coral reefs and its clear and warm water. The central trough
reaches over 2,000 meters in the northern and central regions of the Red Sea. The sea bed rises
from this trough to reach a depth of less than 300 to 400 meters (Ellis et al., 2019).
The water temperature of the Persian Gulf fluctuates between 15°C to 36°C and the maximum
recorded sea-surface temperatures was 38°C in the summer of 1998 (Paparella et al., 2019).
Whereas, the Red sea surface temperatures ranges from 18°C to 31.5°C. The temperature is
lowest within the Gulf of Suez and increases gradually towards the southern half of the Red Sea
(Gladstone, Facey & Hariri, 2006; Hariri, Gladstone & Facey, 2014).
The ecosystem in the Persian Gulf/Gulf of Oman is highly adapted to extreme environmental
conditions but recent works have shown that it is not the maximum temperatures but rather the
length of exposure that harms the marine life (Paparella et al., 2019). The reports demonstrated
that mild bleaching occurs after a week of exposure to a sea-surface temperature of >35°C and
severe bleaching would occur after three weeks of exposure to temperatures ≥35°C or even
≥34°C exposure for eight weeks. Therefore, it is observed that the average temperature-related
stress in the Persian Gulf/Gulf of Oman is higher than in the Red Sea.
The Persian Gulf receives its freshwaters from Shatt al Arab waterway through three different
rivers: Euphrates, Tigris and Karun. Although, recent damn constructions have resulted in
significant reduction of freshwater entering the Persian Gulf through these rivers, together with
waters from Hilleh, Mand and Hendijan rivers in Iran, the annual input of freshwater into the

141   Gulf averages 110 km^3 per year. On the other hand, the annual evaporation rates in the Persian
142   Gulf ranges between 1.37 to 4.8 meters. As a result, the marine system of Persian Gulf possesses
143   high salinity > 40 ppt, increasing to >50 ppt in the southern bays of open ocean conditions and
144   exceeding 70 ppt in evaporative lagoons (Ben-Hasan & Christensen, 2019). Similarly, the
145   evaporation rate in the Red sea reaches 1 to 2 meters per year during both summer and winter.
146   The Gulf of Aqaba experiences evaporation rate of 2 meters per year and 2.35 meters per year in
147   the southern Red sea. As a result, the water salinity increases during summers reaching 37 ppt at
148   Bab el Mandeb and 41ppt towards the entrance of Gulf of Suez and Aqaba (Gladstone, Facey &
149   Hariri, 2006; Hariri, Gladstone & Facey, 2014). The combined limited freshwater input with
150   high evaporation rate makes the Red sea and similarly the Persian Gulf/Gulf of Oman to be the
151   most saline water in direct contact with the world oceans (Naser, 2014; Ben-Hasan &
152   Christensen, 2019).
153   The Persian Gulf and Gulf of Oman are known for their high shipping traffic either oil and gas
154   import or foods and materials export. The high volume of shipping traffic and the sediments
155   curbed within these ships ballast tank has resulted in the introduction of various exotic biotas to
156   the marine system of the Persian Gulf/Gulf of Oman. The oil transportation alone accounts for
157   53,000 ships passing through the Hormuz corridor into the Persian Gulf annually. To a lesser
158   extent, the Red sea is navigated by some of the most prominent shipping lanes in the world. It is
159   estimated that over 20,000 ships (oil and non-oil products) crosses through Bab el Mandeb strait
160   annually (Sheppard, 2018). It was reported that several exotic zooplankton and phytoplankton
161   organisms were collected from a ships ballast tank passing through the Persian Gulf (Al Muftah
162   et al., 2016). It can be concluded that shipping traffic and its consequent marine life stress in the
163   Persian Gulf significantly overweighs the Red sea.
164   The Persian Gulf is reported to have the largest oil reserves in the world and subsequently, oil
165   spills and pollution in water constitutes a permanent stress and survival challenge to its marine
166   life. The exploration, production and transportation of oil adds to the pollution in the Persian
167   Gulf. Various sources of oil spills were reported in the Persian Gulf such as oil tanker incidents,
168   offshore oil wells, weathered oil and tar balls, underwater pipelines, oil terminals, illegal ballast
169   water dumping and military activities (Naser, 2014). The Persian Gulf/Gulf of Oman has
170   witnessed several oil spill incidents in the near history, particularly in years 1980, 1990, 1991
171   and 2019. (Sale et al., 2011; Issa & Vempatti, 2018; Eidnes, Batalden & Sydnes, 2019). On the
172   other hand, the Regional Organization for the Conservation of the Environment of the Red Sea
173   and Gulf of Aden (PERSGA) prepared a partial report on Maritime incidents and accidents but
174   did not provide any accurate record of spills. So far, there has been no report of a major oil spill
175   or chemical pollution due to shipping incidents in the Red sea (Gladstone, Facey & Hariri, 2006).
176   Yet, the number and the impact of oil spill incidents in the Persian Gulf/Gulf of Oman are way
177   higher compared to the Red sea.
178   In addition to oil spills, the Persian Gulf is considered a hotspot for receiving intensive industrial
179   effluents with high concentrations of hydrocarbons and heavy metals (Naser, 2014). The
180   pollutants reside in the Persian Gulf for a considerable amount of time due to its relatively slow

181   flushing time (between 3 to 5 years) and semi-enclosed nature. The organic pollutants from the
182   agricultural runoffs enter the Persian Gulf through the rivers causing lower oxygen levels in
183   coastal waters (Sale et al., 2011). Similarly, and due to the semi-enclosed nature of the Red sea,
184   its water content renewal is limited. It is estimated that it would take 200 years for the renewal of
185   the entire water in the Red sea. (Gladstone, Facey & Hariri, 2006; Hariri, Gladstone & Facey,
186   2014). Dumping toxic waste products in any semi-enclosed oceanic space such as the Persian
187   Gulf or the Red Sea constitutes a considerable stress condition towards its marine life (Table 1).

188   **Common microorganism isolates in the Persian Gulf and Gulf of Oman in relation to the**
189   **Red Sea**

190   Due to the environmental stress conditions in marine life, many organisms pull through by
191   releasing secondary metabolites which might be toxic and bioactive at the same time (Vaseghi et
192   al., 2018). These bioactive compounds may be considered as an important source for drug
193   discovery. Soft corals, seaweed and algae, sponges, bacteria, and fungi are some of the marine
194   organisms that have been researched for potential bioactivity (Dobretsov et al., 2016). They have
195   been reported to elaborate alkaloids, anthraquinones, ethers and many other chemical families
196   that possess antioxidant, antimicrobial, anti-inflammatory, antitumor and cytotoxic activities
197   (Lee et al., 2013a).
198   Fungi are more environment friendly to study than other marine corals and organisms. They are
199   easily isolated and grown in the lab which makes it safer for the marine environment. The
200   extreme conditions of marine life have caused fungi to become stress-resistant by forming many
201   useful secondary metabolites (Alwakeel, 2017). These metabolites are said to have important
202   biological activities including antimicrobial, anticancer, antioxidants and even antidiabetic,
203   which is one of the reasons fungi are becoming more popular in marine drug discovery research
204   (Hasan et al., 2015).
205   The Red Sea and Persian Gulf and Gulf of Oman are rich in marine fungi, and therefore, rich in
206   bioactive compounds due to their high stress environments enhancing the synthesis and release
207   of toxic and bioactive chemicals. Several common organisms have been found in both the Red
208   Sea and Persian Gulf such as, *Aspergillus sp.*, *Penicillium sp.*, *Talaromyces sp.* and *Trichoderma*
209   *sp.* (Nosratabadi et al., 2017).
210   Nonetheless, *Aspergillus* species have been found and extensively researched in the Red Sea
211   marine environment. However, *Aspergillus* species isolated from the Persian Gulf such as, *A.*
212   *flavus*, *A. niger*, *A. fumigatus* and *A. terreus* are significantly under-researched compared to the
213   same species isolated from the Red Sea. In addition, many other *Aspergillus* species were found
214   in the Red Sea (*A. sydowii*, *A. ochraceus*, *A. unguis*, *A. clavatus*, *A. versicolor*, *A. utus* and *A.*
215   *caespitosus*) but yet to be isolated and reported from the Persian Gulf (Alwakeel, 2017). This
216   leads us to the following questions: 1) Are these fungi unable to survive the marine stress of the
217   Persian Gulf rather than surviving the environmental stress of the Red Sea or simply not isolated
218   yet? 2) Are the same *Aspergillus* species isolated from the Persian Gulf likely to synthesize the
219   same portfolio of bioactive compounds like those isolated from the Red Sea?

220 *Aspergillus* is considered a terrestrial fungus which can survive in the marine environment in
221 specific conditions. It has numerous species that produce multiple bioactive metabolites.
222 Bioactive metabolites from *A. fumigatus* show potent broad spectrum antimicrobial (Shaaban et
223 al., 2013). *A. versicolor* has plenty of bioactive compounds which were found to be antioxidant,
224 antibacterial, fungicidal, and lipid lowering agents (Ahmed et al., 2017). *A. unguis* possesses a
225 bioactive metabolite with α-glucosidose inhibitory, antimicrobial and antioxidant effects (Abd
226 El-Hady et al., 2015). Indole alkaloids isolated from *A. ochraceus* shows antitumor effects
227 against several tumor types. *A. utus* also possesses cytotoxic metabolites against several cancer
228 types (Lee et al., 2013b).

229 **Biological activities and chemical structures of some secondary metabolites isolated from**
230 ***Aspergillus Spp.***

231 The fungal flora, *Aspergillus* in specific, is understudied in the Persian Gulf. However, according
232 to the available literature, *A. flavus*, *A. fumigatus*, *A. niger* and *A. terreus* were found in the soil
233 sediment of the Persian Gulf. It is worth mentioning that *A. fumigatus, A. flavus,* and *A. niger*
234 account for more than 95% of the *Aspergillus* species pathogens (Nosratabadi et al., 2017).
235 *Aspergillus flavus* is a saprophytic soil type fungus which contaminates and infects seed crops. It
236 is best known for aflatoxin secondary metabolite, which acts as a potent carcinogenic compound
237 (Cary et al., 2018) and aspergillosis disease which affects immunocompromised patients
238 (Amaike & Keller, 2011; Cary et al., 2018). The aflatoxins are highly substituted
239 difuranocoumarins fused with dihydrofurofuran moiety (Marchese et al., 2018). Different toxins
240 belong to aflatoxins family such as Aflatoxin B1 (AFB1(1)) which is known to be the most
241 harmful and Aflatoxin M1 (AFM1(2)) (Table 2), the hydroxylated metabolite of AFB1 (1), both
242 are classified as human carcinogens through the activation of CYP450 (Marchese et al., 2018).
243 *Aspergillus fumigatus* belongs to the filamentous fungi family that is present in the environment
244 and can cause many diseases and life-threatening conditions in immunocompromised patients
245 (Van De Veerdonk et al., 2017). Due to the stressful environmental conditions, *A. fumigatus*
246 adapts via the production of several secondary metabolites and different mycotoxins such as,
247 gliotoxin (4), fumagillin (5) and pseurotin A (6) (Table 3). Interestingly, *A. fumigatus* is reported
248 to produce up to 226 secondary metabolites. Since the time of its discovery; studies focused on
249 the biological activities of fumagillin such as its antitumor, antibacterial and antiparasitic effects.
250 (Guruceaga et al., 2020).
251 *Aspergillus niger* is a human pathogenic filamentous ascomycete fungi which is known to have a
252 vital economic role in the industrial scale fermentation for the production of citric acid (Baker,
253 2006). In addition, A. niger is known to produce ochratoxin A (7) and fumonisins (8-13) (Table
254 4). Fumonisins are toxic and carcinogenic metabolites, amongst Fumonisins B1 (FB1) (8), B2
255 (FB2) (9) and B3 (FB3) (10) are the most abundant in the fungal cultures (Baker, 2006; Tamura
256 et al., 2014).
257 *Aspergillus terreus* is an important bio-processor fungus as it is useful in the production of many
258 bioactive metabolites such as, itaconic acid (14) and metatartaric acid (15) lovastatin (16),

259 territrem B (17) and terreulactone (18) (Table 5). In addition, there are many other mycotoxins
260 secondary metabolites of A. terreus such as, patulin (19) (Table 5), ochratoxins A (7) (Table 4),
261 citrinin (20), emodin (21) and sulochrin (22) (Table 5) (Varga et al., 2005). Amongst the above,
262 lovastatin (16) is the first to be discovered (HMG)-CoA reductase inhibitor with potent
263 antihyperlipidemic effects. Another notable metabolite of *A. terreus* is Terrein (23) (Table 5) that
264 was isolated for the first time in 1935 and attracted a lot of attention due to its versatile
265 bioactivities including inhibition of plant growth, anti-microbial, anti-proliferative, and anti-
266 oxidative activities (Zhang et al., 2018). Yet, the chemical structures and accordingly the
267 biological activities of *A. terreus* isolated secondary metabolites are non-surprisingly very
268 versatile (Boruta & Bizukojc, 2017).
269 *Asperigllus versicolour* is a marine endophytic fungus that is isolated from the inner tissue of the
270 green alga called Halimeda opuntia found in the Red Sea (Finefield et al., 2011). A. versicolour
271 contain diverse set of secondary metabolites such as Diketopiperazine (DKP) (24), Fellutamides
272 F (25), sterigmatocystin (26), Dihydrosterigmatocystin (27), Cottelosines A and B (33 and 34)
273 several anthraquinones (28-32), isorhodoptilometrin-1- methyl ether (35), siderin (37), emodin
274 (22) evariquinone (36), arugosin-C (38), and variculanol (39) (Table 6), sesquiterpenoid
275 nitrobenzoyl esters, chormone derivatives, meroterprnoid and quinazolinone alkaloids which are
276 reported to possess anti-cancer, antibacterial, insecticidal, fungicidal, antioxidant, lipid lowering
277 properties and HCV protease inhibitory action (Lee et al., 2010, 2011; Zhuang et al., 2011;
278 Hawas, El-Beih & El-Halawany, 2012; Ahmed et al., 2017)
279 *Aspergillus ochraceus* is a marine mitosporic fungus from the trichocomaceae family which was
280 isolated from brown mold/clay of the Red Sea sediments. It can also be found in dried food, such
281 as; dried beans, nuts dried fish and oilseeds (de W Blackburn, 2006). Several secondary
282 metabolites were isolated from *A. ochraceus* such as the phenylated indole alkaloids
283 Stephacidines (40,41) (Table 7) which showed potent antitumor activity against several tumor
284 types (Artman, Grubbs & Williams, 2007; Finefield et al., 2011; Lee et al., 2013b). Yet,
285 Stephacidine B (41) is the most complex isolated alkaloids found until the beginning of the
286 twenty first century (Qian-Cutrone et al., 2002).
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296 **Conclusion**
297 The marine environmental stress conditions indue many faunae and symbiont microorganisms to
298 synthesize and release secondary metabolites of unique structure and interesting biological

299 activities. These bioactive compounds can serve as an important source for drug discovery. The
300 Persian Gulf/Gulf of Oman have a significantly harsher environment when compared to The Red
301 Sea due to fluctuating temperatures between summer and winter which leads to high evaporation
302 rates. Moreover, high salinity also contributes to the harsh environment leading microorganisms
303 to live close to their limits of environmental tolerance. The Red Sea marine symbionts derived
304 bioactive metabolites are very well studied while very much untapped in the Persian Gulf/Gulf of
305 Oman. In the current perspective, and due to similar fungal species isolated from both
306 environments, we are expecting interesting and unique secondary metabolites to be found and
307 isolated from the marine life of the Persian Gulf/Gulf of Oman. The authors believe that using
308 the Red Sea as a reference to target similar microorganisms that have elaborated bioactive
309 metabolites is worthwhile. With the extreme environmental conditions in the Persian Gulf and
310 Gulf of Oman, it is likely that marine research will lead to the isolation and identification of
311 novel metabolites of medicinal value.
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422

Table 1

Comparative summary on general aspects of the Red Sea and Persian Gulf and Gulf of Oman

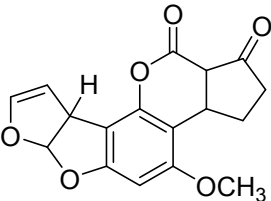
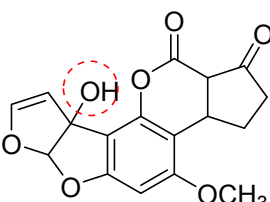
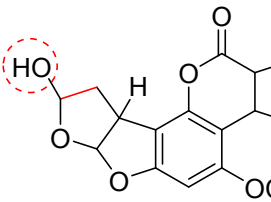
1   **Table 1.** Comparative summary on general aspects of the Red Sea and Persian Gulf and Gulf of Oman

Aspect	The Red Sea	The Persian Gulf & Gulf of Oman
Temperature	• Minimum sea-surface temperature: 18°C • Maximum sea-surface temperature: 26.6°C	• Sea temperature: 15°C to 36°C during the winter and summer seasons • Average sea-surface temperature: 37.7°C
Salinity	• The evaporation rate in the Red sea reaches 1 to 2 meters per year	• The annual input of freshwater into the Gulf averages 110 km3 per year • The annual evaporation rates ranges between 360 to 1250 km3 per year
	• There is no significant difference in the salinity of the Persian Gulf and the Red sea except for some areas in the Persian Gulf where the salinity exceeds 40ppt.	
Shipping Traffic	• Over 20,000 ships (oil and non-oil products) crosses through Bab el Mandeb strait annually	• The oil transportation accounts for 53,000 ships passing through the Hormuz into the Gulf annually
	• Shipping traffic in the Persian Gulf is much higher compared to the Red sea. • There is no official data available on the overall shipping traffic of the Persian Gulf as just the oil shipment in the Persian Gulf is two times more than the overall shipping traffic in the Red sea.	
Oil Spill	• The Persian Gulf has witnessed significant oil spill incidents in the world • The number of oil spills in the Red sea has not been recorded • It is evident that the number of oil spills in the Persian Gulf is way higher when comparing it to the Red sea	
Industrial Effluents	• An estimate of 200 years for the renewal of the entire water	• The flushing time of the seawater is between 3 to 5 years

Table 2

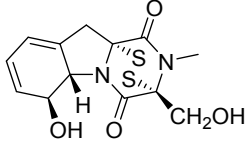
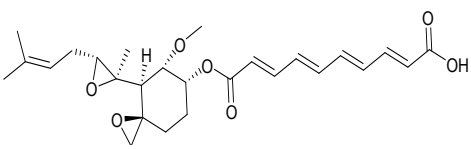
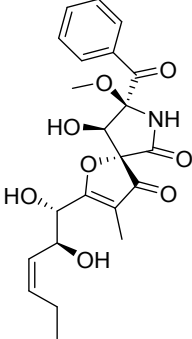
Example of some bioactive metabolites derived from the marine fungi *Aspergillus flavus*

1 **Table 2.** Example of some bioactive metabolites derived from the marine fungi *Aspergillus*
2 *flavus*

4

Table 3

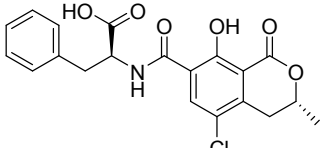
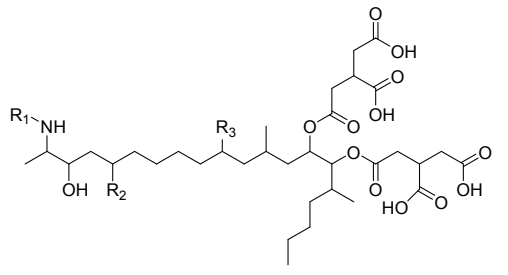
Example of some bioactive metabolites derived from the marine fungi *Aspergillus fumigatus*

1 **Table 3.** Example of some bioactive metabolites derived from the marine fungi *Aspergillus*

2 *fumigatus.*

Aspergillus fumigatus		
Gliotoxin (4)	Fumagillin (5)	pseurotin A (6)

Table 4

Example of some bioactive metabolites derived from the marine fungi *Aspergillus niger*

1   **Table 4.** Example of some bioactive metabolites derived from the marine fungi *Aspergillus niger.*

Aspergillus niger	
Ochratoxins A (7)	FB₁ R₁= H, R₂= OH, R₃= OH FB₂ R₁= H, R₂= OH, R₃= H FB₃ R₁= H, R₂= H, R₃= OH FA₁ R₁= CH₃CO, R₂= OH, R₃= OH FA₂ R₁= CH₃CO, R₂= OH, R₃= H FA₃ R₁= CH₃CO, R₂= H, R₃= OH Fumonisins (8-13)

Ochratoxins A (7)

FB_1 R_1= H, R_2= OH, R_3= OH
FB_2 R_1= H, R_2= OH, R_3= H
FB_3 R_1= H, R_2= H, R_3= OH
FA_1 R_1= CH$_3$CO, R_2= OH, R_3= OH
FA_2 R_1= CH$_3$CO, R_2= OH, R_3= H
FA_3 R_1= CH$_3$CO, R_2= H, R_3= OH

Fumonisins (8-13)

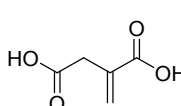
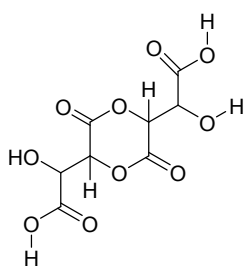
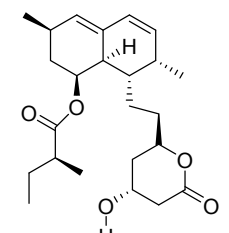
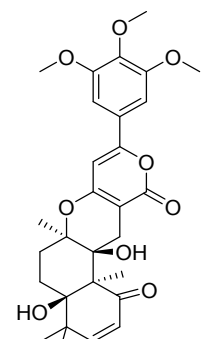
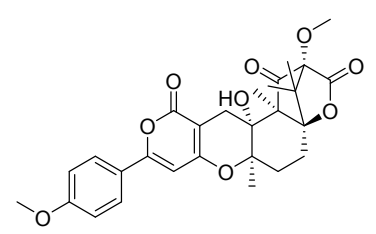
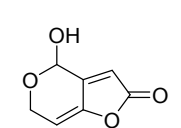
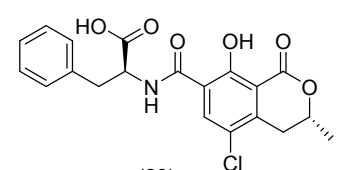
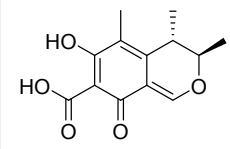
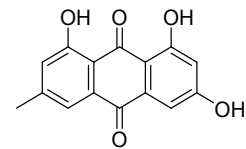
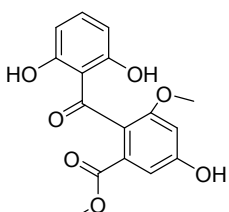
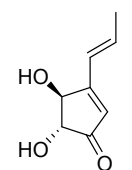



Table 5

Example of some bioactive metabolites derived from the marine fungi *Aspergillus terreus*

2 **Table 5.** Example of some bioactive metabolites derived from the marine fungi *Aspergillus terreus*

Aspergillus terreus		
Itaconic acid (14)	Metatartaric acid (15)	Lovastatin (16)
Territrem B (17)	Terreulactone (18)	Patulin (19)
		Ochratoxins A (7)
Citrinin (20)	Emodin (21)	Sulochrin (22)
		Terrein (23)

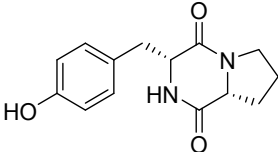
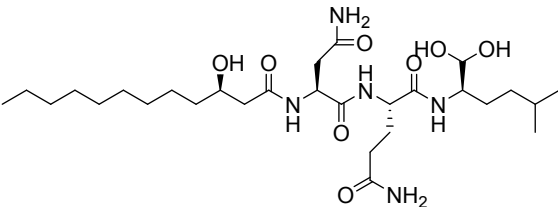
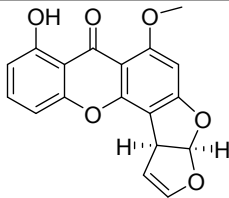
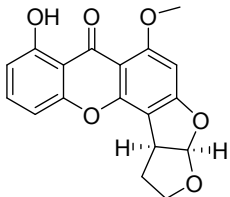
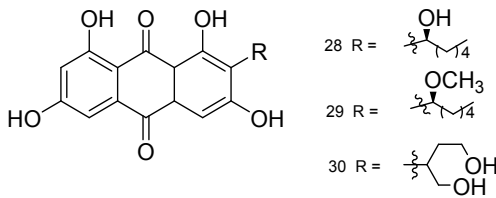
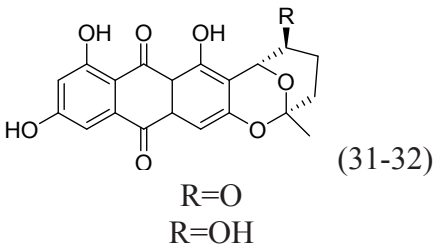
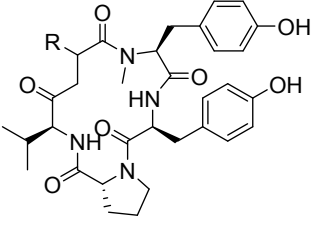
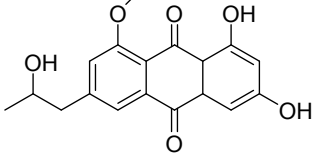
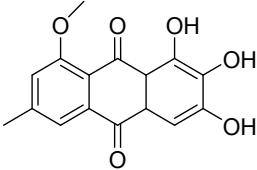



Table 6

Example of some bioactive metabolites derived from the marine fungi *Aspergillus versicolor*

1 **Table 6.** Example of some bioactive metabolites derived from the marine fungi *Aspergillus*
2 *versicolor*

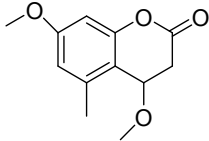
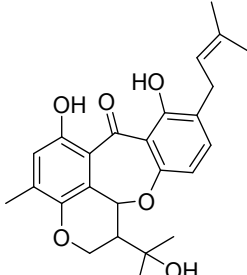
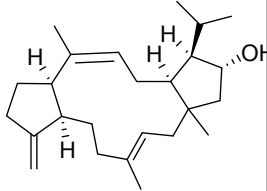
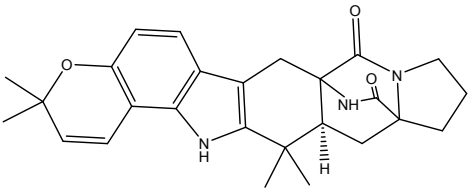
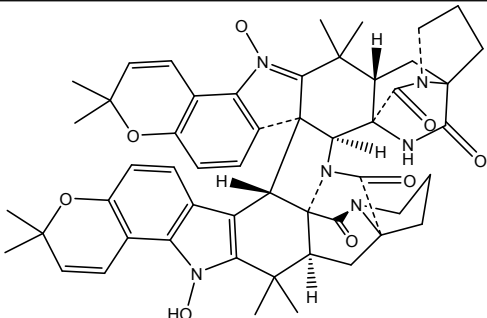
Aspergillus versicolor		
Diketopiperazine (DKP) (24)	Fellutamides F (25)	Sterigmatocystin (26)
Dihydrosterigmatocystin (27)	Anthraquinones (28-30) (31-32) R=O R=OH	
Cottelosines A and B (33 and 34)	Isorhodoptilometrin-1- methyl ether (35)	Evariquinone (36)

| Siderin (37) | Arugosin C (38) | Variculanol (39) |

Table 7

Example of some bioactive metabolites derived from the marine fungi *Aspergillus ochraceus*

2 **Table 7.** Example of some bioactive metabolites derived from the marine fungi *Aspergillus*
3 *ochraceus*

Aspergillus ochraceus	
Stephacidines A (40)	Stephacidines B (41)