



Review Article

A review on bioactive secondary metabolites of soft corals (*Octocorallia*) and their distribution in Eritrean coast of Red Sea

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Eritrean coast of Red Sea is an epicenter of diversified marine ecosystem with high endemic biota. Environmental and ecological conditions around wide number of Islands in Eritrean coast of Red Sea are conducive for shelter and nourishment of many marine flora and fauna. Bioactive secondary metabolites have an extensive role in treatment of many diseases both in its natural forms and extensive key components in synthetic biomedicine. Soft corals belong to phylum Cnidaria are soft fleshy marine organisms which are abundantly found in Southern Red Sea. Among the 180 species of soft corals found worldwide, approximately 40 % are indigenous to Red Sea. These soft corals are rich in novel bioactive compounds with potential cytotoxic, anti-inflammatory, HIV inhibitory, antibacterial, antitumor and antifungal activity. The most abundant interesting biomedical compounds found in soft corals are steroids, alkaloids, terpenoids, prostaglandins, sterols and steroid glycosides. In the present review different bioactive compounds with novel biomedical applications and abundance of soft corals around Eritrean coast of Red Sea is discussed.

[**Keywords:** Bioactive compounds, Distribution, Eritrea, Soft Coral, Southern Red Sea]

Introduction

Soft corals are marine organisms belonging to the phylum Coelenterates (Cnidaria) class Anthozoa and sub-class Octocorallia¹. The sub-class Octocorallia comprise of more than 2000 species, with worldwide distribution in different marine habitats². They are also known as Octocorals due to the presence of 8 fold symmetry and are the colonies of small animals named polypoid Cnidarians. Their polyps rarely exceed 5 mm in diameter and are arranged in soft fleshy irregularly shaped colonies up to 1 m in size³. Soft corals are generally flexible and do not produce the rigid structural characteristics of hard corals, due to lack of calcium carbonate⁴. Octocorals are copious and widely distributed after hard corals in variety of ecological conditions⁵. They are found in all depths⁶ but mostly found on rocky or rubble low tidal areas of 200 m depths by exposing their soft tissues⁷. Depending on the depth that they are growing Octocorals can be of different colors⁸.

Most of the Octocorals have separate male and female reproductive structures, though some genera

are dominated by hermaphrodites such as species of *Hetroxenia* and *Xenia*⁹. Generally three types of reproduction are occurring in Octocorals viz. broadcasting of egg and sperm, internal brooding of larvae and external brooding of larvae. Asexual propagation is common and is the predominant mode of reproduction in soft corals. It is achieved by runner formation, colony fragmentation, fission or budding¹⁰. The environmental factors, such as temperature, primary and secondary productivity, lunar cycle and depth can affect patterns and behaviors related to gamete and larval release in both shallow-water and deep-sea soft corals¹¹.

The majority of Octocorals are suspension feeders that filter small food particles from the water including nutrients, plankton, crustaceans and mollusks¹². Some of the soft corals lives on the reef are seems to posses symbiotic relationship with zooxanthele, dinoflagellates¹³ and microorganisms¹⁴. While the zooxanthele acts as a source of nutrients for soft corals and in return the polyp of soft corals acts as a protection and supplies nutrients like N and

CO₂¹⁵. Some soft corals in the ocean feed by trapping their prey using stinging cells present in their tentacles called nematocysts. Indeed these tentacles helps the soft corals to trap, immobilize and transfer their prey to their body for digestion¹⁶. Microorganisms found in soft corals may help the host by protecting them against pathogens¹⁷. More than half of the soft corals in the great barrier reef are known to contain toxic compounds; which are aimed to be anti-predation and as an adaptation for space competition¹⁸. The ecological studies from the 1980's predicted that, shifts to the soft corals dominance could be expected due to competition with hard corals for space. Sometimes soft corals may be over tapped by hard corals but due to being hated by many predators they can colonize any space easily within a short time¹⁹.

Some of the physical environmental factors that affect the growth, distribution and diversity of soft corals are tidal range, degree of wave exposure, depth, light, nutrients, sedimentation, salinity, temperature variation, and natural and human induced disturbance²⁰. The key factors for the decline in abundance and species richness of soft corals are sedimentation and temperature²¹. Generally soft corals prefer a temperature range of 24.2 – 35.5 °C³ and pH of 8.35 – 8.45^(ref. 22). Several biosynthetic studies have been carried out on the metabolites of soft corals and some of those compounds have been proved to possess great potential for the development of new pharmaceuticals compounds²³.

Bioactive compounds from soft corals

The marine environment is a big reservoir of bioactive natural compounds, which produce several novel structures with unique biological properties which may not be found in terrestrial natural products²⁴. Marine organisms account for more than half of the world's total biodiversity and marine natural products represent a potentially diverse, rich and largely unexploited source of novel chemical structures and biological activities²⁵. Soft corals are common marine organisms; which dwell in tropical and subtropical oceans²⁶ and are potential sources of marine biomedical compounds with promising medical properties²⁷.

Despite the lack of efficient physical defense system in the hostile and competitive environment, soft corals rely on the chemical protection mechanism by accumulating secondary metabolites in their bodies or releasing them to the surroundings for survival²². These secondary metabolites from soft

corals show not only great significance in chemical ecology, but also display interesting various biological activities, such as larvicidal, insecticidal, anti-neoplastic¹, insect growth regulator²⁴, anti-predatory²⁸, antimicrobial²⁹, allopathic³⁰, anti-fouling³¹, antioxidant, antiviral (HIV inhibitor), antifungal³², antitumor, cytotoxic and anti-inflammatory³³ activities. Among all the biomedical compounds extracted from Cnidarians 94 % were identified from soft corals³⁴.

The bioactive compounds from soft corals have interesting medical properties. The sterols and lipids are the major (90-95 %) bioactive compounds present in organo-solvent extract of different genera of soft corals, while 10 % are biologically active alkaloids, diterpenes and sesquiterpenes²⁶, prostaglandins, cembrene derivatives³³, terpenoid compounds, steroid and steroid glycoside³⁵. The macrocyclic derivatives of cembrane compounds are the major diterpenoidal metabolites in soft corals³⁶. Diterpenes make up to 65 % of bioactive natural products published from soft corals and gorgonians³⁷.

Soft corals of the genus *Xenia* (family Xeniidae) have proved to be rich sources of terpenoids especially several diterpenes with promising bioactivity. These compounds have shown potential antitumor, anti-bacterial and antifungal activity³⁸. Diterpenes extracted from *Xenia elongate* have shown Apoptosis inducing activity³⁹ and diterpenoids from *X. umbellata* have shown cytotoxicity against cancer cells⁴⁰. The steroids isolated from *Umbellulifera petasites*, namely Petasitosterones A, Petasitosterones B and a spirosteroid Petasitosterone C have inhibited the proliferation of a limited panel of cancer cell lines and anti-inflammatory activity to inhibit nitric oxide (NO) production²⁹.

Heteroxenia species also possess a variety of bioactive compounds. Various spectral data of *H. fuscescens* have confirmed the presence of 6-Hydroxy - α - Muurolene which has a potential antibacterial and antifungal activity; 1-Nonadecyloxy-2,3-propanediol and N-Hexadecanoyl-2-amino 4,8-octadecadiene-1,3-diol have shown cytotoxic activity against different human tumor cell lines⁴¹. Along with these compounds the ethanolic extracts of *Heteroxenia* species have reported the presence of Gorgosten-5(E)-3 β -ol, (+)- α -Muurolene and Sarcoaldosterol-A which have shown antioxidant, antipyretic, antiglycemic and anti-inflammatory activity⁴². Ceramide compounds isolated from *H. ghardaqensis* have shown anti Cadmium toxicity, can be used to treat disorders caused by Cadmium uptake⁴³.

The *Sarcophyton* species contain Sarcotol and 13-membered carbocyclic cembranoid compounds with strong ichthyotoxic activity against Japanese killifish *Oryzia latipes*. Ethyl acetate extract of the Red Sea soft coral *S. glaucum* have shown inhibition of cytochrome P450 1A activity, inducers of glutathione S-transferases (GST), quinone reductase (QR), epoxide hydrolase (mEH), and tumor anti-initiating activity⁴⁴. The Cembranoid diterpene present in *S. glaucum* had found to be potential antitumor agents against melanoma cells¹⁸ and also exhibited potential antifungal activity⁴⁵. Sarcomililatin A and (+)-isosarcophytoxide extracted from the ethanol soluble fraction of acetone extract of *Sarcophyton mililatensis* have shown strong cytotoxic activity and inhibitory activities against the tumor necrosis factor which is a key target for the treatment of inflammatory diseases and cancer⁴⁶. The ethanol, chloroform and distilled water extracts have shown the bioactive metabolites including terpene, alkaloids and tannins having insecticidal activity²⁴. The Cembranoids isolated from *S. crassocaula* have shown a significant anti-inflammatory activity and cytotoxic activity against cancer cell lines⁴⁷. While in other cases n-hexane and ethyl acetate extracts of the Red Sea soft coral *S. trocheliophorum* were reported to contain unsaturated fatty acids that are active against brine shrimp and promote paclitaxel cytotoxicity in the human colon cancer cell line²⁵. However the concentration of bioactive diterpenes and Cembranoid compounds varies with change in ecological condition like reef flat to deep water⁴⁸.

The soft corals of the genus *Sinularia* are one of the most widespread octocorals having good number of secondary metabolites with potential bioactivities such as anti-inflammatory, cytotoxic activities, antitumor and anti-allergic activities⁴⁹. Chinese soft coral *Sinularia polydactyla* contains 7-hydroxy-8-methoxy-4(1H)-quinolone, which has increased the blood flow rate in the brain and heart of mice, protected against hypoxia and pituitrin-induced acute ischemia in myocardium, and mitigated aconitine-induced arrhythmia²². *S. brassica* is a good source of bioactive steroids with methyl ester groups and shown a significant cytotoxic activity, inhibition of elastase release and also inhibit the formation of super oxide anion⁵⁰. The extract of *Sinularia flexibilis* contains terpenoid derivatives Flexibilide and Sinulariolide which have shown antimicrobial activity against fungal pathogens *Candida albicans* and *Aspergillus flavus*⁵¹.

Red Sea soft coral *Lobophytum pauciflorum* contains different bioactive compounds including

Nephthenol and Gorgost-5-ene-3 β -ol with momentous in-vitro anti-inflammatory activity. Other alcohol compounds like Heptadecan-1-ol and batilol, fatty acids, palmitic acid and stearic acid have shown antimicrobial activity against pathogenic bacteria and fungi²⁸. Different Cembranoid compounds have been isolated from *L. crassum* including Lobophyolide A which has an ability to reduce IL – 12 and also shown anti-inflammatory activity⁷. Various solvent extracts of *Lobophytum* spp., from Indonesian coast have shown heme polymerization inhibitory activity which is related to antimalarial potential⁵².

The genus *Dendronephthya* is copious and widely distributed throughout the Indo-Pacific Ocean to Red Sea. The secondary metabolites are rich in unique steroids and sesquiterpenes. The Ylangene-type sesquiterpenoids named Dendronephthol A (7,13-dihydroxy-3,4-dihydroylangen-5-one) and Dendronephthol C (6,7,13-trihydroxy-a-ylang-5-one) isolated from chloroform fraction of methanol and acetone extracts of *Dendronephthya* collected from Red Sea have shown cytotoxicity against murine lymphoma cancer cell line⁵³. The *Dendronephthya* species from South China Sea has reported to control macrofouling on its surface by producing secondary metabolites. The different organic extracts have inhibited the growth and attachment of bacteria from natural biofilm on rocks⁵⁴. The extracts of unidentified *Nephthea* species contains wax esters, 1-O-alkylglycerols, cholesterol, fatty acids and D(-)-2S,3R-2-aminooctadeca-4E,8E-diene-1,3-diol-N-palmitate. These compounds have shown potential antiviral activity against Ranikhet disease virus *in vitro* condition and Vaccina virus in both *in vitro* and *in vivo* conditions⁵⁵.

The Octacorals of *Clavulariidae* family is reported to be a good source of Prostanoids, aromadendrane-type Sesquiterpenoid, Punaglandins and Pregnane-based steroids. The Pregnane-based steroids have shown antileishmanial activity, Punaglandins exhibited antiproliferative properties and the other compounds have elicited to mild toxicity to murine leukemia cells⁵⁶.

Soft corals in Eritrean coast of Red Sea

Eritrea is located in horn of Africa (12°45' - 18°03' N; 37°35' - 43°07' E) stretching from Sudan to Djibouti, which retains 3300 km of shoreline along the south-western coast of the Red Sea⁵⁷. In addition to the mainland coastline is of 1950 kilometers; more than 350 islands in Dahlak Archipelagos contributes a shoreline of more than 1350 km to the total seashore of Eritrea⁵⁸. The Red Sea is an epicenter habitat

for unprecedented bio-diversified marine biota. Approximately 40 % of the soft coral species identified so far in world's marine ecosystem are native to the Red Sea⁵⁹.

Biogeographically Red Sea can be divided into northern, central, and southern regions. Highly diversified biota of soft corals has been documented from Northern Red Sea, especially Israel coast Red Sea²². Central region of Red Sea reefs are concentrated with diversified stony corals. The most plentiful soft coral genera included all over the Red Sea are *Sinularia*, *Xenia*, *Ovabunda*, *Sarcophyton* and *Tubipora*. Species richness of soft corals are limited in southern Red Sea compared to northern Red Sea, it might be due to high temperature; for example average SST in northern Red Sea varies between 21-27 °C⁵⁸ where as in southern Red Sea it ranges between 26-32 °C⁶⁰. The global climate change, overexploitation and pollution are also determinant

factors for decreased distribution of Octacorallia biota²⁰.

Early exploration on soft corals in the southern Red Sea around Eritrean coast was done for the first time by Verseveldt in 1962^(ref. 61). These soft corals are mainly found in different depths around Dhalak Archipelago in Southern Red Sea. The members of the Alcyoniidae are fast growing organisms, able to grow effectively in moderately turbid and well-lit coastal areas²⁰. Hence the species of *Lobophytum*, *Rhytisma*, *Sarcophyton* and *Sinularia* are mostly found in shallow reef habitats of 1–3 m depth. While the species of *Ovabunda* and *Xenia* commonly grows in dense patches down to 12 m^(ref. 5). Though diversified soft coral biota is found in Eritrean reefs, not even single soft coral species has been catalogued till date⁶². The most abundantly found soft corals around islands of Eritrean Red Sea are given in Plate 1^(ref. 63).

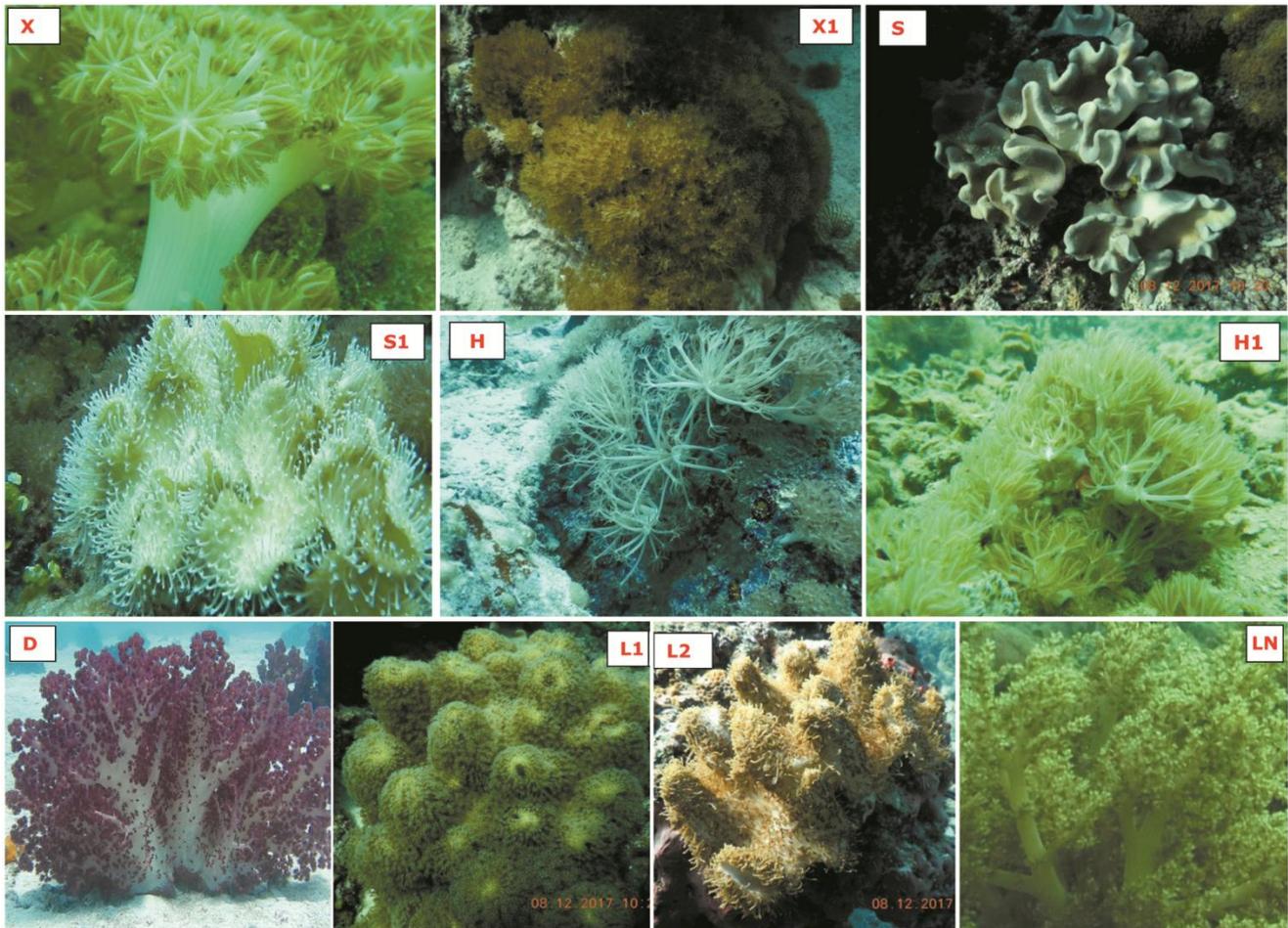


Plate 1 — Abundant soft corals distributed in Eritrean coast of Red Sea, X = *Xenia* species; X1 = *Xenia* species 1; S = *Sarcophyton* species; S1 = *Sarcophyton* species 1; H = *Heteroxenia* species; H1 = *Heteroxenia* species 1; D = *Dendronephthya* species; L1 = *Lobophytum* species 1; L2 = *Lobophytum* species 2; LN = *Lemnalicia* species (Source: Ministry of Marine Resources⁶³, Eritrea)

Table 1 — Soft coral species distributed in Eritrean coast of Red Sea (Source: Verseveldt⁶¹, Benayahu *et al.*⁶² and Ministry of Marine Resources⁶³)

Family name	Genus name	Species	Location
Tubiporidae	<i>Tubipora</i>	<i>Tubipora musica</i>	Dejen shipwrecks
	<i>Lobophytum</i>	<i>Lobophytum pauciflorum</i>	DurGaam Island
	<i>Rhytisma</i>	<i>Rhytisma fulvumfulvum</i>	Harat and shumua Islands
	<i>Sarcophyton</i>	<i>Sarcophyton ehrenbergi</i>	Harat and shumua Islands
		<i>Sarcophyton glaucum</i>	DurGaam, Durguham and Dehil Islands
Alcyoniidae	<i>Sinularia</i>	<i>Sinularia compressa</i>	Cundabilu Island
		<i>Sinularia erecta</i>	Cundabilu Island
		<i>Sinularia gardineri</i>	Cundabilu Island
		<i>Sinularia gravis</i>	Cundabilu Island
		<i>Sinularia leptoclados</i>	Cundabilu Island
		<i>Sinularia macrodactyla</i>	Cundabilu Island
		<i>Sinularia polydactyla</i>	Cundabilu Island
	<i>Dendronephthya</i>	<i>Dendronephthya formosa</i>	Cundabilu, Madote and Dahret Islands
		<i>Dendronephthya klunzingeri</i>	Harat and Dehil Islands
		<i>Dendronephthya pharonis</i>	Cundabilu and Durguham Islands
Nephtheidae	<i>Paralemnalia</i>	<i>Paralemnalia sinaiensis</i>	Cundabilu Island
		<i>Paralemnalia hamprichii</i>	Cundabilu and Durguham Islands
	<i>Scleronephthya</i>	<i>Scleronephthya thyrsoides</i>	Cundabilu, Madote and Harat Islands
	<i>Stereonephthya</i>	<i>Scleronephthya corymbosa</i>	Cundabilu, Madote and Harat Islands
	<i>Umbellulifera</i>	<i>Stereonephthya cundabiluensis</i>	Duliacus Island
	<i>Siphonogorgia</i>	<i>Umbellulifera oreni</i>	Durguham Island
		<i>Siphonogorgia mirabilis</i>	Durguham Island
<i>Heteroxenia</i>		Harat Island	
Nidallidae	<i>Ovabunda</i>	<i>Heteroxenia fuscescens</i>	Harat Island
		<i>Ovabunda farauensis</i>	Madote and Dahret Islands
	<i>Xenia</i>	<i>Ovabunda obscuronata</i>	Madote and Dahret Islands
		<i>Ovabunda verseveldti</i>	Madote and Dahret Islands
Xeniidae	<i>Xenia</i>	<i>Xenia blumi</i>	Madote and Dahret Islands
		<i>Xenia hicksoni</i>	Cundabilu and Madote Islands
		<i>Xenia umbellata</i>	Dahret, Cundabilu and Dehil Islands
		<i>Xenia elongata</i>	Shaek Sied island, Madote, Dahret and Cundabilu Islands

Dendronephthya is a colourful soft coral familiar as carnation coral in the aquarium trade. These corals are green, yellow, pale orange, pink, purple, maroon and mix of these colours as well⁶⁴. *Dendronephthya* colonies were occasionally found on the reef flat to reef slope, edge and sometimes on sandy bottoms⁵ and on the shipwrecks at depths of 1–8 m and even deeper. Usually *Nephthea* colonies were frequently observed at various sites growing together with the colonies of *Xeniidae*. *Xenia* is the most dominant genera of soft corals in all the reef sites of Dhalak archipelago⁶⁵. Combined data given by Verseveldt⁶¹, Benayahu *et al.*⁶² and Ministry of Marine Resources⁶³ resulted to the compilation of 30 species of soft corals in Eritrean coast of Red Sea, details of which are given in Table 1.

Conclusion

The important secondary metabolites with biological activity from unexploited marine resources, soft corals and their distribution in Eritrean coast of Red Sea have been reviewed. Numerous genera of soft corals and several species of *Sinularia* are distributed around the Cundabilu Island. Soft coral species, *Xenia elongate* is distributed from the coast to deep waters and islands of Dahlak archipelago; while the other species are distributed only in deep Sea Islands with less anthropogenic stressors reduced eutrophic conditions and minimum sedimentation rate. A thorough submarine study has to be taken to investigate the effect of pollutants and anthropogenic effects on the distribution of soft corals. Though soft corals are the best candidates for potential bioactive

compounds, the biological activity of soft corals from the Eritrean coast has to be investigated.

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Conflict of Interest

The Authors declare no conflict of interest.

Author Contributions

MK: Conceived, designed and wrote the paper, prepared photographs and tables; BH: Wrote, reviewed and edited the paper; BAA and GGH: Collected the data, and helped in writing the paper; AHH and OMH: Collected the photographs and distribution information.

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