Utility of Underwater Weenie Life Forms as Voluminous Organisms: A Review

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Abstract

Coral reefs are a sundry subaqueous ecological community, combined with the calcium carbonate structures secreted by converting the carbon dioxide present in the water into limestone. The biotic portion of the coral reef is marine animal known as polyps that have resemblance with jellyfish. Unlike terrestrial environment, the marine component is tightly interdependent. Taking out one component or loss of from a system can have a devastating impact or undermine the entire marine ecosystem. Reefs specifically are a vital organism among underwater life which is dependent on corals and provide key microhabitat, shelter and breeding ground for thousands of species of fish, crustaceans, mollusks, etc. Coral reef possesses vital ethnobotanical properties, which cures asthma, arthritis, and even cancer. Apart from medicinal properties, further it provides 2/3rd of oxygen on earth. However, the destructive fishing practices, pollution and ocean acidification have endangered this kingdom and have led to the threatening of the entire fabric of the underwater life. As human beings are also dependent up to much extent for centuries, there is a high probability of being severely affected if the coral reef extinct leaving the seabed barren. Corals cover almost 1 % of the oceans present on earth, but the irony is 75 % of them are on a verge of extinction. Therefore, the present review focuses on its conservation, cultivation and significance of their application in the field of biomedical science.

Keywords: *Coral reef, endangered, ethnobotany, extinction, marine ecosystem, pollution.*

Introduction

It can be appositely cited as “what can be explored is little and what remains unexplored is humongous”. The earth comprising of almost 70 % of water, in which more than 80 % of living kingdoms are found out of our planet (Malve, 2016). Over the period of years and yet to be discovered, the sea has embraced an enormous trench of corals, shaped by polyps which tentacle containing sea animals and secretes aragonite to create the reef. Tentacles comprise of nematocysts, allowing the polyps to capture small organism for growth and nutrition. As a whole, it can be stated that corals as marine structures, algal symbionts and calcifying coral animals, rightly known as rainforests of the sea. These corals belonging to the phylum Cnidaria which are branched into hard or reef, soft or flexible and gorgonian corals consisting of gorgonin (Cooper *et al.,* 2014). Deflection in the pH seriously affects growth, survivability and dissociation of the polyps (modular units of the corals) by inducing coral apoptosis. Furthermore in normal condition, the polyps started calcification and hence can rightly be termed as modular units (Kvitt *et al.,* 2015). Some corals are also holobionts in nature with endo-symbiotic dinoflagellates, bacterial and viral acquaintances (Krediet *et al.,* 2013). However, every year approximately 200 species of both hard and soft corals are evident to be used for diversified pharmaceutical purposes (Rocha *et al.,* 2011). Henceforth, the corals are essential not only to the sustainability of the reef bionetwork but also to the benefaction of humans.

These underwater weenie life forms contain various bioactive compounds which have cytotoxic, anti-inflammatory and anti-bacterial activities (Table 1). Eight different kinds of steroids are known to be produced by corals which include 5α-pregna-20-en-3-one, 5α-pregna-1,20-dien-3-one, 5α,8α-epidioxycholesta-6,22-dien-3β-ol, 25α,8α-epidioxy-24(S)- methylcholesta-6, 22-dien-3β-ol, 5α,8α-epidioxy-24(R)-methylcholesta-6, 22-dien-3β-ol, 5α,8β-epidioxycholesta-6-en-3β-ol, 5α,8β- epidioxy-24α-ethylcholesta-6,22-dien-3β-ol, 5α,8β-epidioxy-

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Table 1. Description of important species of corals and their bioactive compounds with pharmacological properties.

Name/ Group	Bioactive Compounds	Chemistry	Pharmacological activity (Drug Class)	References
Pinnigorgia sp.	Pinnisterols Secosterols	Steroid	Neutrophil superoxide and elastase inhibition (Anti-inflammatory and Cytotoxicity)	Chang *et al.,* 2016a Chang *et al.,* 2017a
Briareum asbestinum	Briarenolides	Terpenoid	Macrophage COX-2 and iNOS expression inhibition (Anti-inflammatory)	Su *et al.,* 2015
Briareum sp.	Briarenolides	Terpenoid	Macrophage COX-2 and iNOS expression inhibition (Anti-inflammatory)	Su *et al.,* 2016
Sarcophyton glaucum	Isoprenoids	Steroid	Inhibition of cancer cell proliferation (Cytotoxicity, Antimicrobial, Neuroprotective)	Chao *et al.,* 2017
Nephthea columnaris	5,6-epoxylitosterol	Steroid	Neutrophil superoxide and elastase inhibition (Anti-inflammatory)	Whuang *et al.,* 2017
Sinularia brassica	Sinubrasones	Steroid	Neutrophil superoxide and elastase inhibition, Inhibition of cancer cell proliferation (Anti-inflammatory and Cytotoxicity)	Huang *et al.,* 2017
Sinularia leptoclados	Sinuleptolide	Steroid	Inhibition of cancer cell proliferation (Anti-inflammatory and Cytotoxicity)	Chang *et al.,* 2017b
Sinularia nanolobata	Cubitanoids	Terpenoid	Nitric oxide (NO) inhibition (Cytotoxicity)	Chao *et al.,* 2016
Umbellulifera petasites	Petasitosterones	Steroid	Inhibition of cancer cell proliferation (Anti-inflammatory and Cytotoxicity)	Huang *et al.,* 2016
Sarcophyton glaucum	Glaucumolides	Terpenoid	Macrophage COX-2 and iNOS expression inhibition (Anti-inflammatory and Cytotoxicity)	Huang *et al.,* 2015
Euplexaura sp.	Euplexaurenes	Terpenoid	Cytotoxic activities against human laryngeal carcinoma (Antibacterial)	Cao *et al.,* 2017
Pinnigorgia sp.	Pinnigorgiols	Steroid	Neutrophil superoxide and elastase inhibition (Anti-inflammatory and Cytotoxicity)	Chang *et al.,* 2016b
Nephthea erecta	24-methyl-cholesta-5,24(28)-diene-3*β*,19-diol-7*β* -monoacetate (MeCDDA)	Steroid	Anti-small cell lung cancer (Anti-inflammatory, Anti-fouling, Anti-cancer)	Chung *et al.,* 2017
Nephthea columnaris	Columnariols	Terpenoid	Macrophage COX-2 and iNOS expression inhibition (Anti-inflammatory and Cytotoxicity)	Hsiao *et al.,* 2015
Sinularia gaweli	Sinulacembranolide	Terpenoid	Macrophage COX-2 and iNOS expression inhibition (Anti-inflammatory)	Lin *et al.,* 2015
Sinularia sp.	Sinulolides	Terpenoid	Inhibition of NF-κB activation	Yang *et al.,* 2014
Briareum violacea		Terpenoid	Neutrophil superoxide and elastase inhibition in response to fMLP/CB (Anti-inflammatory)	Liaw *et al.,* 2014
Cespitularia taeniata	Cespitulones	Terpenoid	Cytotoxicity activities against human medulloblastoma and colon adenocarcinoma cancer cells (Cytotoxicity)	Lin *et al.,* 2014
Cladiella sp.	Cladieunicellins	Terpenoid	Cytotoxicity activities against human leukemia (Cytotoxicity)	Chen *et al.,* 2014b
Sinularia arborea.	Sinularbols	Terpenoid	Neutrophil superoxide inhibition (Anti-inflammatory)	Chen *et al.,* 2014a
Sarcophyton sp.	Polyhydroxylated steroids	Steroid	Anti-H1N1 virus activities (Cytotoxicity, Anti-viral)	Gong *et al.,* 2013
Cladiella sp.	Cladieunicellin I	Terpenoid	Cytotoxicity activities against DLD-1 human colorectal adenocarcinoma cells (Cytotoxicity)	Chen *et al.,* 2013

Sinularia flexibilis	Flexibilin D	Terpenoid	Macrophage COX-2 and iNOS expression inhibition (Anti-inflammatory)	Hu *et al.,* 2013a
Sinularia flexibilis	5-dehydrosinulariolide	Terpenoid	Antitumor activities toward CAL-27 and A2058 cells	Hu *et al.,* 2013b
Sarcophyton sp.	4′-OMe-asperphenamate	Alkaloid	Antifouling and antibacterial activity.	Zheng *et al.,* 2013
Junceella fragilis	Frajunolides	Terpenoid	Neutrophil superoxide and elastase inhibition in response to fMLP/CB (Anti-inflammatory)	Liaw *et al.,* 2013
Sinularia flexibilis	Flexibilin B	Terpenoid	Neutrophil elastase inhibition (Anti-inflammatory)	Hu *et al.,* 2013
Scleronephthya gracillimum	Sclerosteroids	Steroid	Cytotoxicity activities against HepG2, A549, and MDA-MB-231 cancer cell line. Macrophage COX-2 and iNOS expression inhibition (Anti-inflammatory)	Fang *et al.,* 2013
Sinularia querciformis	11-episinulariolide acetate	Terpenoid	Improved the histopathologic features of human rheumatoid arthritis and Macrophage COX-2 and iNOS expression inhibition (Anti-inflammatory)	Lin *et al.,* 2013

24α-ethylcholesta-6-en-3β-ol (Huang *et al.,* 2016). Moreover, secondary metabolites such as diterpenes, sesquiterpenes, furanoditerpenes, terpenoids, capnellenes and steroids from *Lobophytum michaelae, Sinularia sarcophyton, Capnella sp., Dendronephthya* sp., are responsible for inhibition of HIV infection, cytotoxic, anti-inflammatory, anticancer and antimicrobial activity, as well as cardiac and vascular responses. More speciously, sesquiterpenes has anti-inflammatory activity which was isolated from *Capnella imbricate*, whereas anti-proliferative action adjacent to murine fibroblasts and cytotoxicity action against human leukemia and cervix carcinoma was shown by dihydroxycapnellene extracted from *Dendronephthya rubeola* (Rocha *et al.,* 2011).

Though having significant roles of corals (Figure 1), their survivability is at risk because of their degradation and extinction caused by marine water pollution and various natural disasters. One of the major causes of these natural disasters is climate change which leads to factors like rising in sea level, the rise in temperature, reef calcification and solar radiation etc. These changes cause bleaching effect and severely affect phenotypes, reproduction, metabolism of the organisms (Magris *et al.,* 2015). The trouncing of coral reef is also stirred due to the overfishing practices, aquaculture, and coastal development and to adjoin more in it, we comprise ocean acidification (Gurney *et al.,* 2013). The most affected reasons for coral extermination is bleaching, predation, and diseases. The evolutionarily distinct and globally endangered (EDGE) has proved that the corals reefs have been losing their reef forming species (Huang, 2012). Another main phenomenon which further accelerates the devastating degradation of reefs is eutrophication. Every year the huge amount of fertilizer added to the crops fields, are washed away by run-off water to nearby reservoirs. This leads to an increased amount of nutrition is water, hence suitable condition for algal growth but adversely affects the coral growth and causes coral mortality (Gregg *et al.,* 2013). Increasing climatic change and increase in the carbon dioxide level has caused the warming of the ocean and hence causes misbalancing in pH which points acidification, leading to coral bleaching and presently making it as endangered habitats (Anthony *et al.,* 2011; Rocha *et al.,* 2011; Kumari & Mohan, 2018). Therefore the current review is prepared for providing the basic knowledge about how these underwater weenie life forms could be conserved by culturing as well as some of their biomedical benefaction to humankind as a whole.

Conservation of coral reef

Coral reefs are the chief constituents of several eco-chains, natural barriers, and more importantly, they are the pharmacy underwater and key to an enormous count of medicines and hence, it needs attention for their preservation. The damage due to environmental stresses may be mild, halfway or detrimental. According to the levels of stress impact, the management of coral reefs takes certain measure in favour of the coral reef protection. These management ensure that the conservation needs to be done first at a local scale level where people are more inclined on the coral reef for their usage and then finally, ecosystem’s toughness could be improved (Anthony *et al.,* 2015). For this several strategies should be followed by a common man such as to avoid striking or touching a coral reef, don't fish or boat near a coral reef populations, don't litter on the beach or in the ocean, don't purchase coral souvenirs, snorkel and scuba dive with care,

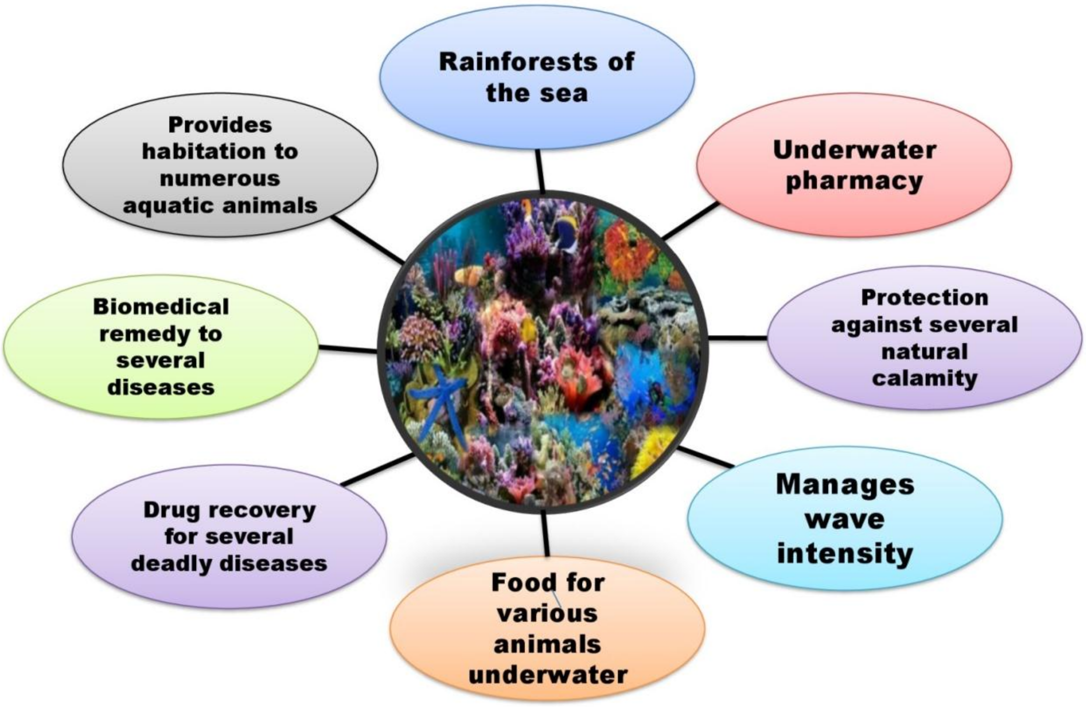

Fig. 1. Diversified importance of Coral reefs.

choose a hotel that embraces environmentalism and after all it needs to educate the local communities by different government and nongovernment organizations (Rinkevich, 2005; Saxena, 2015).

As natural restoration takes away too long, therefore, conservation by artificial methods is highly essential. A limited number of literature are found however according to Biggs (2013), the coral reef restoration completely depends on substratum stability and reestablishment of corals. In order to achieve the proper erected growth of corals, two reefs of *Curacao* were treated with coral rubble alone, rubble seeded with sponge fragments, rubble bound by concrete, and concrete ''rubble'' bound by concrete. This setup concluded that the use of rubble piles is very much supportive and appropriate for growth and reinstallation of sponges (Biggs, 2013).

Culturing of coral reef

Generally, marine resources are termed as 'blue gold' due to its abundant availability of diverse origin of heterogeneous bioactive clinically important compounds. But presently due to intense human interference with the marine life, the sustenance of these organisms is under critical condition. So in order to conserve this marine life and for its sustenance, it is necessary to neutralize or balance disrupted or destructed invertebrates by their cultivation. Though the significance of these invertebrate sea creatures is previously known still, its conservation through cultivation is not widely adopted. Hence, a necessary and fruitful step should be considered by the mankind. For culturing, initially needs to culture these weenie forms of life by understanding and neutralizing the factors responsible for its degradation. Some of the common degrading factors include physical disturbance, internal tides, erosion, sedimentation, predation, partial bleaching, and parasitism (Saxena, 2015). For growing strategies, it is essential to get access the available resources, required spaces, retaining reproductive capability and maturity (Riegl, 2009). Micro-colony fusion is an excellent coral aquaculture technique. Generally, rare coral species should be first considered for culture and restoration of the reefs. In this process, mini coral fragments are spaced equidistantly in cyanoacrylate gel with required nutrient and vitamins which results in their growth and development. Generally, growth of algae inhibits the coral reefs, therefore *Trochus inextus* and *Tripneustes gratilla* are used to control algal growth (Forsman *et al.,* 2015).

Presently aquaculture leads as a technique through which desired marine invertebrates are cultured either *in situ* or *ex situ*. The *in situ* or mariculture is a culturing process of desired invertebrates including reefs in natural conditions. The factors affecting this process are flow of water, hydrodynamics, light, nutrients, etc. whereas *ex situ* is done under controlled climatic condition, which is quite expensive where manpower also plays a significant role in the collection of the cultured products (Pomeroy *et al.,* 2006; Lirman & Schopmeyer, 2016). However, *ex situ* cultivation has major advantages over *in situ* cultivation, in many different ways like single species can grow under a controlled condition which estimates the amount of required nutrients, vitamins, optimum pH, ion concentration. Moreover, the presence of diversified bioactive, pharmaceutically beneficiary compound as well as their quantity could be accurately evaluated. Again, the limitations associated with the natural growth and development of these sea creatures could also be assessed and eliminated. Specifically, some of the commonly associated limitations such as required time duration, viral infection, and inability to reproduce by the cell to cell interactions under harsh marine environmental condition could be better studied and understood (Rinkevich & Shafir, 2000; Rocha *et al.,* 2015; Leal *et al.,* 2016).

Applications in biomedical field

Corals have widespread application in the biomedical sphere. From extraction of steroids to the production of several potent medications for diseases like several organ oriented cancers, neurodegenerative diseases like Parkinson's and Alzheimer's disorder, arthritis, acquired immune deficiency syndrome (AIDS), malaria etc. (Cooper *et al.,* 2014; Ganguly, 2016). The calcifying nature of the polyps also helps in the calcinations of bones and teeth. Coral reefs have an ethnobotany to play in the production of potential medicines which cures strokes, head injury, artery bypass surgery, chronic pain of cancer, and peripheral neuropathies (Alves & Rosa, 2007). The never ending list runs along with other diseases like hypertension, cardiovascular, injuries related to head, etc. This is all made possible by the venom of cone snails, of which approximately 500 species dwelling in the coral reef of the tropics (Peters, 2013). With this many applications, the "tropical rainforests of the sea" have definitely a great deal to do in the biomedical field however, various properties of major diseases are described below.

Arthritis

The main reason for rheumatoid arthritis, sclerosis, or asthma is basically inflammation. So, before proceeding towards arthritis, its initiation in form of inflammation should be acknowledged. This inflammatory response is generally shown by macrophages, mast cells, and dendritic cells, when tissues are injured by bacteria, trauma, toxins, heat, or any other cause. There are two forms of inflammation namely; acute inflammation and chronic inflammation, which later on cause the pathological diseases including cancer, sclerosis, asthma or arthritis (Ashley *et al.,* 2012). In last few years, soft corals like *Cladiella* and *Klyxum* have been a great source of eunicellin-based diterpenes (Liang *et al.,* 2008). These diterpenes include krempfielins, hirsutalins, klymollins, klysimplexin, klysimplexin sulfoxide, simplexin, and cladieunicellin hold a major anti-inflammatory property. Further, corals like *Briareum* and *Pachyclavularia* also produce diterpenoid and mostly inhibit superoxide generation (Gonzalez *et al.,* 2015). Sinulariolide acetate produced by *Sinularia ouerciformis,* when injected into the rat, as a therapy for arthritis showed promising results. It is believed to do wonders in humans as well, and prevent this chronic inflammatory disease of rheumatoid arthritis (Cooper *et al.,* 2014). The gorgonian species *Euplexaura flava* secrete anti-inflammatory butanolide lipid and anti-inflammatory briarane-type diterpene whereas, excavatolide B is extracted from Taiwanese gorgonian coral *Briareum excavatum* (Rocha *et al.,* 2011; Lin *et al.,* 2017).

Cancer

While the hunt for cancer remedies was going on, meanwhile in the 1950's sponges were experimented and found that an anti-cancer agent known as ara-C (Cytarabine) was the first to be derived by the marine sponge called *Cryptotethya crypta.* With the successful implementation as a drug, it cured lymphoma, leukemia, as well as lung, pancreatic, bladder and breast cancer (Anjum *et al.,* 2016). Extracts of soft corals such as *Cladiella australis*, *Clavularia viridis* and *Klyxum simplex* were also able to inhibit the growth of human oral squamous and carcinoma cells (Liang *et al.,* 2008). Bioassay-guided fractionations of *Sarcophyton* sp. and *Lobophytum* sp., provide the information about some of the known antitumor promoters. These antitumor promoters include cembrane diterpenoid, (+)-sarcophytol-A as well as lobane diterpenoid, carbomethoxyfuscol from *Sarcophyton* sp. and cembranoid, crassumolide E from *Lobophytum* sp. (Bonnard *et al.,* 2010). Some of the species like *Sinularia ouerciformis* and *Nephthea chabrolii* yield important cytotoxic exhibiting steroids such as nebrosteroids Q, R, and S which are fruitful therapy for different cancer (Cooper *et al.,* 2014). Some compounds are obtained from soft corals which are rich in anti-cancer activity namely malformin A, kuanoniamine D, hymenialdisine, and gallic acid (Dobretsov *et al.,* 2016). Oncologists also used compound like capnell-9(12)-ene-8β,10α-diol, which prevents the transcription factor Myc with the help of its partner protein Max that causes good cytotoxicity against the cancer cell. Cytotoxicity of human hepato-cellular carcinoma, human breast carcinoma, human lung carcinoma, and human gingival carcinoma is terminated by Klysimplexin B and Klysimplexin H, which is extracted from *Klyxum simplex* (Rocha *et al.,* 2011).

AIDS

Despite a large number of applications, the research related to extracting or isolation of therapeutics against AIDS is limited. However, corals like *Sinularia heterospiculata*, *Sinularia maxima* and *Litophyton arboreum* have been reported having inhibitory activity against human immunodeficiency virus (Ellithey *et al.,* 2014). Another report says about the discovery of a new protein, called cnidarins which supports blocking of HIV infection (Anonymous, 2017).

Bone and tooth regeneration

Marine products are nowadays frequently utilized in regenerating oral tissues, augmenting craniofacial tissues, replacing dysfunctional dentine and bone. The bioactive metabolites which are to be achieved for the regeneration purpose are cloned. For teeth regeneration generally two ways are followed, which includes either directly filling of the sample into the affected part where it will further grow into the desired part or culturing the tissues and then transplanting on spot. The marine products not only help in the regeneration but also protect the newly formed product from bacterial attack (Green *et al.,* 2014). The aragonite and calcite present in the hard and soft corals respectively, containing the calcium part are now used in the repairing and regeneration of both bones and teeth (Cooper *et al.,* 2014). A hydrocoral (*Millepora dichotama*) constructs a skeleton out of aragonite, and this species has a remarkable growth rate which helps in the increase in cloning speed and hence can be used in bone grafting. For the purpose of generation of skeleton, *M. dichotama* acts as a biolattice in neural tissue engineering. The coral *Porites lutea* was potential enough to form hippocampus neurons in its exoskeleton (Razak & Hoeksema, 2003; Vago, 2008). Hydroxyapatite being a major component of bone mineral and coral is truly beneficial in bone grafting, auto grafting, osteoconductivity and bone tissue integration (Vago, 2008). Several coral genus are used as bone substitutes because of their calcium carbonate secretion, namely *Pocillopora, Acropora, Montipora, Porites, Goniopora, Fungia, Polyphyllia, Favites, Acanthastrea, Lobophyllia,* and *Turbinaria* (Parizi et *al.,* 2013).

Neurodegenerative disease

Neurodegenerative disease like Parkinson's disease can be cured by a compound, 11-dehydrosinularolide which is extracted from corals (Chen *et al.,* 2012). A soft coral, *Sinularia flexibilis* releases a terpenoid (11-dehydrosinulariolide), which also cures this neurodegenerative disorder (Grosso *et al.,* 2014). This disease is dangerous as leads to memory loss and lack of sensory input. Steroids like (3β,4α,5α,8β,11β)-4-methylergost-24(28)-ene-3,8,11-triol and ergost-4,24(28)-diene-3-one from soft coral *Sinularia depressa* is effective against this disease (Grosso *et al.,* 2014). Bioactive compounds from *Clavularia* sp. also acts as a neurotrophic factor on the nervous system and can prevent Alzheimer's disease by synthesizing acetylcholine (Rocha *et al.,* 2011). Chitin being the major component of corals, the derived chitosan has effects on neurodegenerative diseases as well as anti-tumour properties. B-amyloid and acetylcholinesterase has anti-neuroinflammatory effect which was reported by Hao *et al.* (2017).

Antiprotozoal activity

From the Vietnamese sea, 34 cembranes extracted from different species like *Lobophytum crassum*, *Lobophytum laevigatum*, and *Sinularia maxima* which were found to possess antiprotozoal activity. Compounds of 7S,8S-epoxy-1,3,11-cembratriene-16-oic methyl ester, (1R,4R,2E,7E,11E)-cembra-2,7,11-trien-4-ol, crassumol D, crassumol E, (1S,2E,4S,6E,8S,11S)-2,6,12(20)-cembrantriene-4,8,11-triol and their different derivatives from these soft corals have effective antiprotozoal activity against *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, *Leishmania donovani* and *Plasmodium falciparum* under *in vitro* experimental condition (Thao et al. 2015). *Pseudopterogorgia bipinnata* was as considered as anti-malarial agent due to the presence of potent compound caucanolides A–F (Ospina *et al.,* 2005).

Conclusion

It is righteously quoted that, "the part that is discovered is minimal, and the gigantic part is yet to be discovered". This statement corresponds to the present day situation of the marine environment. The present researchers are settling down and getting content with the lesser land but the humongous marine flora and fauna that are yet to be discovered. The marine biotas are completely neglected though they provide an enormous source of medicinal derivatives, secondary metabolites and cure to several diseases, which are evidenced from above described points that to be in favour of corals only. Due to enormous medicinal benefits, sometimes they are named as blue gold/ pharmaceuticals supplies/ medicinal storehouse/ and many more. Therefore such immense treasure should be preserved and cultured in maximum in order to fight the devastating impacts of ocean acidification, high tidal waves, etc. This mishap should be avoided and action should be taken against its devastation so that such beneficial gift of nature should be protected. Meanwhile, strategies should be taken to familiarize these natural products among common people by enhancing its entry to the drug market.

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