MARINE MICROBES: A UNIQUE GROUP FOR THE BENEFIT OF MANKIND

Roopali Roychowdhury*[1], Madhumita Roy[1], Sufia Zaman[2] and Abhijit Mitra[3]
[1]Department of Biotechnology, Techno India University, West Bengal, Salt Lake Campus, Kolkata 700091, India
[2]Department of Oceanography, Techno India University, West Bengal, Salt Lake Campus, Kolkata 700091, India
[3]Department of Marine Science, University of Calcutta, 35 B.C. Road, Kolkata 700019, India
*corresponding author

Abstract

Marine microorganisms are paramount towards the health of our environment and our welfare. They are integral components to all major biogeochemical cycles, fluxes and processes occurring in marine systems where the elements move between the two forms, oxidized and reduced. Microbes are diverse and extremely abundant and help in the production and release of carbon products that are essential in the regulation of the Earth's climate, particularly CO_2 and CH_4. Apart from these, marine microorganisms also provide essential goods and services to our society such as, production of oxygen, supporting sustainable supply of food, regulating the health of the marine environment, providing largely undeveloped source of genetic information and biomolecules for use in industrial and medical applications and products. Regardless of their importance, a dab is known about marine microbial diversity. The present paper aims to highlight the varied distribution of marine microbes in the estuaries, continental shelves and the deep sea. These habitats (except the deep-sea environment) are compatible for the growth and survival of marine microbes due to the presence of high nutrient, photon energy and optimum salinity. The application of marine microbes in the production of antibiotics, antitumour compounds, enzyme and also in the sphere of bioremediation has opened a new chapter for the benefit of mankind.

***IndexTerms- M*icrobes, applications, bioactive compounds, diverse**

INTRODUCTION

The marine environment is the abode of diverse groups of microorganisms like bacteria, filamentous fungi, yeasts, microalgae and protozoa, which inhabit various types of habitats. They are distributed at the surface of the sea as neuston (also known as pleuston) or at the photic zone of the pelagic region as plankton or at the epibiotic habitats (attached communities). Epibiotic habitats may be inanimate or animate. They are also present inside the tissues of other marine organisms (endobiotic habitats). The endobiotic usually denotes the environment within the tissues of other larger organisms. Here the relationship with the host may be beneficial (mutualism), detrimental to the host (parasitism) or may cause diseases (pathogenesis). Many marine microbes are also distributed on the seabed in the bathyal, abyssal and nodal zones. Marine microbes have an immense role in maintaining the biodiversity through nutrient cycling. In recent times, their properties are used for human benefits like production of enzyme, anti-tumour compounds, antibiotics and also for removing toxic substances from the marine and estuarine environment. Marine microbes have been reported to be resistant towards different heavy metals and metalloids. Formative life has emerged in the companionship of metals and living systems have expanded to utilizes different metals as important element of its biological systems (Diaz-Ravina et al., 1994, Gadd, 1990a and 1990b, Lehninger et al, 1993). Although, some metals, such as arsenic, cadmium, mercury, and lead have no known critical biological function (Gadd, 1992) they serves as prosthetic groups in many proteins and as redox centers transferring electrons in *vital* redox reactions. Metal transport in microorganisms is initiated across the cell membrane through energy independent or energy dependent processes (Nies, 1999; Nies and Silver, 1995; Deng and Wilson, 2001). Considering that the microbe metal interactions are inevitable in the environment, it is not unexpected that microbes (chemolithotrophs) have developed suitable means to utilize metals as electron donors or acceptors for their energy metabolism (Ehrlich, 1997). Eight different metal tolerant, *Halobacterium mediterranei*, strain from solar salterns and hypersaline soils of, Mallorca and the Canary Islands, Spain, was reported by Nieto et al. (1989). Tolerance of bacteria towards a particular metal does not correspond to its tolerance to other metals. This can be as a result of different mechanisms responsible for bacterial tolerance to heavy metals (Silver and Phung, 1996; Vieira and Volesky 2010; Xie et al 2010). Mukherjee et al. (2017) have isolated a salt-tolerant bacterial strain *Ocenobacillus species Exo1*, from the rhizosphere soil of *Avicennia marina*, a mangrove floral species of the Indian Sundarbans. The strain exhibited resistance towards many heavy metals and metalloids including arsenic. Such multiple heavy metal-resistant halo-rhizobacterial strain can be considered for bioremediation of contaminated coastal belts in and around the mangrove ecosystem.

Habitat of marine organisms

About 71% of the surface of the planet Earth is covered by saline water. The water depth averages 3.8 km, a volume of 1370 × 10^6 km^3. This is the marine ecosystem and is the reservoir of food, oil, natural gas, minerals and several bioactive substances that have immense importance in the pharmaceutical industries. The ecosystem sustains the livelihood of millions of people. The oceans serve as the main highway for international trade as well as the main stabilizer of the world's climate. The oceanic waters and sediments are also the dwelling place of a large variety of flora and fauna. According to the Global Biodiversity Assessment, produced by the United Nations Environment Programme (UNEP), there are 178,000 marine species in 34 phyla (UNEP, G. M. A. (2002). Rich in seagrass, salt marsh grass, seaweeds, mangroves *etc*., the intertidal zone of the marine environment offers unique dwelling sites for marine microbes. Evidences suggest that grasses possess a narrower range of microorganisms than seaweeds. It has earlier been observed by marine microbiologists that cord grass (*Spartina alterniflora*) is colonized initially by fungi (*Sphaerulina pedicellata)*, where as eel grass (*Zostera marina*) mostly possess the pinnate diatom (*Cocconeis scutellum*). On seaweeds, microorganisms like diatom, yeast and bacteria thrive luxuriantly. The mangrove swamps also sustain a wide range of microbes.

The deep-sea environment is also an important habitat of marine microorganisms. Bacteria on the surface of fecal pellets was observed by Turner (1979), and it was concluded that different deep-sea microorganisms have their origin at the surface layer of the ocean. This prospect has been supported by the results of some experiments, which demonstrated an enhanced rate in metabolic activity of marine microorganisms along with a reduction of pressure (Jannach and Wirsen, 1982). This helps to conclude towards an inference that the activity of marine microorganisms increases in shallow water and decreases with the increase of depth and pressure. With respect to the distribution of microbes in the deep-sea environment, some interesting facts have been documented particularly around the vent region. The deep-sea vents occur in the ocean floor where the ocean crustal plates spread apart and cause plumes of hot lava to erupt into the ocean. Higher concentrations of electron rich elemental compounds are very congenial for the growth and survival of eubacteria such as the chemoautotrophs (Campbell, 1993). Different types of bacteria have special adaptations that enable the organisms to obtain metabolic energy and to withstand the extreme environmental conditions of high pressure and temperature (over 100°C). The concentration of microbial population drops dramatically as one move away from the deep-sea vent region (Atlas, 1998). There are heterotrophic bacteria in the sea floor sediments, which feed on photoautotrophic cyanobacteria that drift down attached to sediment particles

Distribution of microorganisms is also found in the deep-sea sediments. Epifluorescence microscopy was used by Deming and Colwell (1985), to determine the vertical distribution of bacteria in deep-sea sediments. Thus, using cores collected at depths exceeding 4000 m, it was recorded that bacterial populations at the surface layer of sediment amounted to 4.65×10^8 bacteria/gm dry weight. However, there was a doubling in numbers to 8.29×10^8 bacteria/gm dry weight at a sediment depth of 3 cm followed by a progressive decline to 1.7×10^7 bacteria/gm dry weight of a core sample at 15 cm from the surface of the sediment. Parallel results were obtained in a second core collected from a similar depth. Higher counts of approximately 3.07×10^{10} bacteria/gm dry weight were recorded from fecal pellets. These counts were 9-72 folds higher than in the underlying surface sediment (Deming, 1985). Constantly changing environmental parameters in the estuaries can create a wide diversity of ecological niches in this brackish water ecosystem (Atlas, 1998) which is the main reason behind microbial diversity. Estuaries have high nutrients and high photon energy and are the most productive ecosystem for photosynthetic aerobes. The range of saline concentrations creates three types of niches: fresh water, brackish water and saline water. Each niche is occupied by organisms that are adapted to those conditions. This form of ecological partitioning reduces exploitative competition and enhances growth of different types of microbial communities (Campbell, 1993). Similarly, the continental shelf and the coral reefs are areas of high productivity due to high nutrient and photon energy, but without the extreme salinity gradient (Atlas, 1998).

Application of marine microbes

Marine microorganisms comprise a comparative prime reservoir of commercially valuable compounds. Marine microorganisms have eccentric properties that they can adapt themselves to the extreme marine environment conditions of alkaline or acidic water, high pressure and limited substrate, variation in temperature *i,e* high or low temperature, in the deep-sea waters. These peculiar characteristics have inspired many researchers to initiate a probe in depth as these microbes have the potential to be used in industry (Baharum, et al. , 2010). Many bacteria are able to produce and secrete polymers and enzymes. Some marine bacteria are potent producers of DNase, lipase, alginases and proteases. Hence, the economic backbone of any country may be strengthened if special thrust is given to a certain applied sector of microbiology like production of biochemical compounds, enzymes, single cell protein and pharmaceutical compounds. The various advantages that can be derived from marine microbes are discussed here in brief.

A) Biodiscovery and bioactive compounds

The marine environment is unfolding as a 'gold mine' for novel bioactive compounds with various researches reported in this field (Blunt et al., 2009) (Bhatnagar et al., 2010). Marine organisms including sponges, fishes, soft corals, molluscs, echinoderms, prawns, and marine microorganisms are sources of bioactive compounds used as oils and cosmetics (Donia and Hamann, 2003). In the late 1950's Bergmann reported the first biologically active marine natural product marine-derived natural products, present a vast range of novel chemical structures and provide an interesting and challenging pattern for creating a new establishment *via* synthetic chemistry. In particular, marine invertebrates and certain plants represent an enriched environment containing microorganisms that produce compounds having bioactive properties which includes certain antibacterial, anticancer, antifouling, antifungal, antiviral, and antibiofilm activities. However, isolation of only 1% of these microorganisms is possible using conventional culturing techniques, which has been a major impediment while unearthing the marine environment for innovative bioactive molecules. A great interest of researchers have risen towards exploration of marine organisms as new sources of antibacterial compounds, due to the expanding resistance of pathogenic microbes towards presently found antibiotics. A new antibacterial protein marinocine, obtained from *Marinomonas mediterrane*, is an example of anti bacterial protein isolated from the *melanogenic* marine bacterium commonly found in the MedittaraneanSea (Lucas-Elio et al., 2005).

Rosenfeld and Zobell (1947) described the production of antibiotics by marine bacteria. Interestingly, in their study the majority of the antibiotic-producers were equated with *Bacillus* and *Micrococcus*, which are usually regarded as terrestrial organisms rather than representative of the true marine micro -fauna. Further work by Krassil'nikova (1961) and Buck et al. (1962) confirmed antibiosis among marine bacteria, with the latter study pointing to inhibitory effects against yeasts. Then a proliferation of research resulted in numerous publications, starting in 1966. Of these, the work of Burkholder et al (1966) is relevant insofar as characterization of the inhibitory compound revealed a novel chemical structure. This was confirmed by Lovell (1966) as 2, 3, 4-tribromo-5 (1'-hydroxy-2', 4'- dibromophenyl) - pyrrole. The compound was recovered from bacteria, which had been isolated from *Thalassia* sp. (turtle grass) collected in the vicinity of Puerto Rico.

Within a decade of this work, another inhibitory bromopyrrole was recovered from marine bacteria. Using non-selective isolation techniques, Anderson et al., (1974) recovered an antibiotic producing purple-pigmented *Chromobacterium*, designated strain 1-L-133, from seawater in the North Pacific. The organism was described as motile, gram-negative rods, which produce oxidase but not catalase or indole, hydrolysed starch and gave negative responses to the methyl red test and Voges Proskauer reaction. From these traits, the organism was equated with *Chromobacterium* and in particular, considered to resemble *C. marinum.* Interest in the production of antibiotics by marine Gram-negative bacteria did not stop and the researches continued. Lemos et al., (1985) examined the micro flora from seaweeds (*Enteromorpha intestinalis, E. compressa, Fucus ceranoides, Pelvetia canalicula and Ulva lactuca)*, which were collected in Spain from the intertidal zone at low tide. Antibacterial activity was maximum in the micro-flora originating from *an E. intestinalis.* Many marine heterotrophic bacteria are known producers of antibacterial substances capable of inhibiting other bacteria. Researches have shown that these antibacterial compounds are not limited to inhibition of terrestrial bacteria but also towards indigenous bacterial strains, which is of significant ecological importance (Nair and Simidu, 1987). Many studies have also focussed on the screening of marine bacteria for antibacterial activity against human pathogenic bacteria (Blunt and Prinsep, 2006).

The characterization of the antimicrobial activity of marine microorganisms collected from the Indian coastline has been reported, and it has been identified that the most widely studied microbial species, from the Indian coastal waters as a source of antibiotics is *Streptomyces* sp. (Anand et al., 2006). In a study, 75 bacterial strains from 4 species of marine sponges were reported, among which 21% of the isolates had shown outstanding antibacterial activity, with some showing species specificity. Thus, the study indicated the variance of antibiotic producing marine bacteria and validated, that sponges are rich in bacteria capable of producing novel bioactive molecules. (Anand et al., 2006)

B) Production of antitumor compounds

More than 20,000 natural products have been discovered in the marine environment over the past 50 years (Blunt et al., 2016). Drug discovery based on marine natural products is evident from the increase in number of isolated MNPs (from an annual number of approximately 20 in 1984 to an annual number of more than 1000 in 2010) (Choudhary et al., 2017) (Mayer et al., 2016) (Mayer et al., 2017) From the continuing progress in the area of MNPs seven approved drugs and 12 agents currently in clinical trials have been discovered (Blunt et al., 2017).

Flavobacterium uliginosum is a marine strain from which a water-soluble compound named marinactum was produced. Okami (1986) discussed the isolation of a polysaccharide from marine *Flavobacterium* with marked activity in mice against Sarcoma -180 solid tumor virus (s-180). From the seaweed disturbed along the Sagami Bay, Japan, bacterial isolations were carried out on a non-selective nutrient medium with incubation at 27˚C for 1-3 days. Isolated colonies were examined for the ability to produce polysaccharide on a medium containing sugar after incubation at 27˚C for 2 days.

The total number of approved drugs from the marine environment steadily increased from four in 2010 to seven in 2014 (Mayer et al. 2013) (Mayer et al. 2017) The first U.S. Food and Drug Administration (FDA) The first approved marine-derived drug cytarabine was isolated from the Caribbean sponge *Cryptotheca crypta*, which was marketed in 1969 as an anticancer drug. Thereafter, six of the marine natural products that have passed clinical trials and approved as drugs, include the snail-derived peptide ziconotide (Prialt®), and macrolide, eribulin mesylate (Halaven®), derived from sponge as anti cancer element as well as four other products with anticancer, antiviral and antihypertriglyceridemia activities (Mayer et al. 2011). Twenty one out of the 23 most recently identified marine-derived compounds, are in several different stages of the clinical testing chains for their potential use as anticancer agents, while two of them are being assessed for treatment of chronic pain and neurological disorders like schizophrenia and Alzheimer's disease (Mayer et al., 2010). Novel bioactive compound has also been isolated from a very important group of microalgae, the diatoms. This algal class has traditionally been regarded as providing the bulk of the food that sustains the marine food chains to top consumers, which includes variety of fishes of commercial importance. However, this beneficial role has been extended based on recent laboratory findings showing that diatoms produce antibiotic compounds that block embryogenesis in copepod and sea urchin eggs, and arrest proliferation of human carcinonoma cells (Miralto et al., 1999).

C) Production of enzyme

Marine microorganisms are a genesis of novel enzymes as they are substantial compared to the relevant plants and animals derived enzymes. Salinity, pressure, temperature, and lighting conditions are the differentiating factors related to marine and terrestrial enzymes. Marine microbial enzymes also have the potential towards diverse industrial applications (Nguyen and Nguyen, 2017). It has been established earlier that some marine bacteria produce copious quantities of alginate, lyases and chitinases, which may warrant commercial exploitation. There are many examples of marine bacterium that produce lipase enzymes. Yumoto et al (2003) had successfully isolated a facultatively psychrophilic bacterium, strain MD17T, capable of hydrolyzing lipids at 5ºC. The deep-sea thermophilic bacteria that dwell in the hydrothermal region may provide useful sources of heat stable enzymes (Deming, 1986). Okami (1986) recovered a useful isolate of *Bacillus circulans* (No MT-GT2) from marine mud in Tokyo Bay, which produced an enzyme capable of hydrolyzing glucan. The production of industrial enzymes from marine microbes have proven that marine microorganisms have many beneficial bioactivities (Chatellier et al., 2011; Manasi, 2011), antifungal activity (Jayaprakashvel et al., 2010), biocontrol activity in terms of plant disease control (Gobalakrishnan et al., 2010;

Bhagat et al., 2010a), some antibacterial and probiotic activity (Kaarthikeyan et al., 2010) along with some plant growth promotion characteristics including production of phytohormones and phosphate solubilisation (Jayaprakashvel et al., 2011). The high G+C rich gram positive bacteria, filamentous, Actinomycetes, are the most economically and biotechnologically valuable prokaryotic microorganisms known till now.

D) Bioremediation of petroleum hydrocarbon

Bioremediation is the utilization of microorganism to remove pollutants from the environment. It is infact an acceleration of the natural fate of biodegradable pollutants and hence can be regarded as green solution to oil pollution. Bioremediation is a necessary and cost effective method of removing certain environmental pollutants that adversely affects human health or environmental quality. The enormous natural quality of diverse microorganisms to degrade numerous organic compounds (ranging from petroleum hydrocarbon to chlorinated solvents) and to transform various inorganic substances to metals, form the basis of bioremediation. The metabolic activities of microorganisms are used to change an undesirable chemical into one that has less objectionable properties for example changing a toxic pesticide or a carcinogenic petroleum hydrocarbon into non-toxic carbon dioxide and water. To date, most bioremediation projects have relied on the use of naturally occurring microorganisms (often the indigenous micro-organisms) at contaminated sites (Leahy and Colwell, 1990) (Swannell et al., 1996). Presently some new projects are attempting to use genetically engineered species to degrade the pollutants at a much faster rate or to grow under more adverse conditions. This research is very important in present *era*, as many pollutants are non-aqueous and often occurs in environment that do not favour microbial growth and biodegradative properties. Petroleum hydrocarbon is a widespread environmental pollutant, that are amendable to removal by bioremediation.

Bioremediation of oil pollution usually relies on modifying the environment so that the growth of indigenous hydrocarbon degrading micro-organism is stimulated. Diverse groups of bacteria are known to feed exclusively on hydrocarbons (Yakimov et al. 2007). Hydrocarbon degrading bacteria and Hydrocarbon degrading fungi isolated from marine environment, have been listed by Floodgate in 1984. Microorganism require nitrogen, phosphorus and other mineral nutrient for incorporation into biomass, thus the availability of these nutrients within the area of hydrocarbon degradation is critical. In this situation, the addition of nitrogen and phosphorus containing fertilizer overcomes the nutritional limitation for microbial growth, because petroleum contains concentration of these substances well below those needed for microbial growth. The typical ratio carbon to nitrogen in a microbial cell is 10:1 and has carbon to phosphorus 30:1. Besides nitrogen and phosphate, rapid hydrocarbon degradation requires molecular oxygen because the initial steps in biodegradation of hydrocarbon by most microorganismssuch as *Pseudomonas sp.* involve the incorporation of hydrocarbon of oxygen by oxygenase (Guo et al., 2014).

E) Marine microbes in probiotics and their uses in aquaculture

Nowadays, certain emerging disease outbreaks in the aquaculture industry, greatly affects the aquaculture production. Other than causing loss of a stable production of larva culture and limitations on trade due to economic losses, over usage of antimicrobials in aquaculture for controlling diseases, a natural bacterial resistance through genes emerges, which can further be transferred to other strains by certain alterations in the existing genome or transfer of genetic material through plasmids or bacteriophages. Hence, an increase in aquatic disease management through alternative strategies and techniques for antibiotic usage is required. Further, the use of probiotics in the aquaculture field for the eradication of antimicrobial drug usage is fast originating. The use of probiotics in aquaculture, is widely acclaimed with an increasing demand of environment-friendly aquaculture. Therefore, scientists in the aquaculture field have paid an extensive attention towards probiotics. Bacteria *Vibrio sp*., *Pseudomonas sp*., and *Bacillus sp.* and many other *Lactobacilli sp.* have been in use as probiotics in molluscs, crustacean, and finfish aquaculture which were mostly identified from the cultural environment of aquatic animals or from the intestine of different aquatic species. Isolation of *Pseudomonas* sp. PM11 from the gut of sub-adult shrimp *Penaeus monodon* and their effect on the immunity indicators of black tiger shrimp was done by Alavandi et al. (2004). Irianto and Austin (2002) reported the inhibitory roles of P*seudomonas* I-2 against *V. harveyi and V. fluvialis* in shrimp culture was reported by Irianto and Austin (2002). Moreover, Gram *et al*. (1999) reported that a *Pseudomonas fluorescens* AH2, which was capable of efficiently reducing the mortality of rainbow trout (*Oncorhynchus mykiss*) infected with a pathogenic *V. anguillarum* strain. The use of probiotic bacteria as microbial control agents can serve to be an alternative towards antimicrobial disease control.

As the probiotic research in aquaculture is still budding and gaining acceptance in the industry, extensive research is needed to understand and rectify the debatable concepts of probiotics, due to lack of evidence of real environmental presentations on successful usage of probiotics including their mode of action, and mechanism thoroughly. As probiotics, the usage of terrestrial bacteria in aquaculture has a limited success and the characteristics of these bacteria depend upon their habitual living environment. Thus, a better option is the identification of potential probiotics from marine environment where their growth is optimal (Nikapitiya, 2013).

CONCLUSION

The marine environment is home to an immense number of macro and microorganisms with unexploited biosynthetic activities which are used immensely, to shield their survival in this diverse and unsympathetic, habitat. This unique environment facilitates the biosynthesis of an array of secondary metabolites which act as chemical resistance and display a broad range of antimicrobial bioactivities. Only seven marine-derived metabolites are approved as drugs, while 12 other marine natural products are presently under different phases of clinical trials. Regardless of multiple challenges, the preclinical chain continues to supply studies with several hundred novel bioactive marine compounds with the potential for use as therapeutics and other multidisciplinary fields. There is no doubt that the potency of different marine compounds against pathogens is promising their exploitation and application will continue to develop. Marine microorganisms offer an indispensable appreciation into the biosynthetic, and opposing mechanisms these organisms employ to survive in the marine environment. Collaborative approach involving different fields marine natural products chemistry with organic chemistry, medicinal chemistry, pharmacology, biology, bioinformatics and associated disciplines will help to verify and promote an increase in the availability of bioactive products in the market to be used as antimicrobial therapeutics.

The existing study depicts that the marine organisms have more than one capability for diverse packages. The promising consequences received from the existing study can be regarded as a preliminary screening of the isolated traces for several purposes and those strains can be appeared as capable candidates for future prospects. Similarly investigations towards large-scale manufacturing of metabolites and to maximize its use is to be considered for future prospects.

REFERENCES

1. Alavandi, S. V., Vijayan, K. K., Santiago, T. C., Poornima, M., Jithendran, K. P., Ali, S. A., & Rajan, J. J. S. 2004. Evaluation of Pseudomonas sp. PM 11 and Vibrio fluvialis PM 17 on immune indices of tiger shrimp, Penaeus monodon. *Fish & Shellfish Immunology*, *17*(2), 115-120.
2. Anand, T. P., Bhat, A. W., Shouche, Y. S., Roy, U., Siddharth, J., & Sarma, S. P. 2006. Antimicrobial activity of marine bacteria associated with sponges from the waters off the coast of South East India. *Microbiological research*, *161*(3), 252-262.
3. Anderson, R.J., Wolfe, M.S. and Faulkner, D.J. 1974. Autotoxic antibiotic production by a marine *Chromobacterium.* Marine Biology, 27: 281-285.
4. Atlas, R. 1998. In: Microbial Ecology: Fundamentals and Applications. Benjamin Cummings. Menlo Park, Ca. p.694.
5. Baharum, S.N., Beng, E.K. and Mokhtar, M.A.A. 2010. Marine microorganisms: potential application and challenges. J. Biol. Sci.10: 555-564.
6. BERGMANN, W., & STEMPIEN Jr, M. F. 1957. Contributions to the Study of Marine Products. XLIII. The Nucleosides of Sponges. V. The Synthesis of Spongosine1. *The Journal of Organic Chemistry*, *22*(12), 1575-1577.
7. Bhagat, J., Muthezhilan, R., Jaffar Hussain, A. and Jayaprakashvel. M. 2010a. Siderophore producing antagonistic rhizobacteria from coastal sand dune vegetation. In: National seminar on biotechnological applications in human welfare held on 26 th March 2010. Department of Biotechnology, University of Madras, Chennai, India.
8. Bhatnagar, I., & Kim, S. K. 2010. Immense essence of excellence: marine microbial bioactive compounds. *Marine drugs*, *8*(10), 2673-2701.
9. Blunt, J. W., Copp, B. R., Keyzers, R. A., Munroa, M. H., & Prinsepd, M. R. 2016. Natural product reports. *Nat Prod Rep*, *33*, 382-431.
10. Blunt, J. W., Copp, B. R., Hu, W. P., Munro, M. H., Northcote, P. T., & Prinsep, M. R. 2009. Marine natural products. *Natural product reports*, *26*(2), 170.)
11. Blunt, J. W., Copp, B. R., Keyzers, R. A., Munro, M. H., & Prinsep, M. R. 2017. Marine natural products. *Natural product reports*, *34*(3), 235-294.
12. Blunt, J.W. and Prinsep, M.R. 2006. Marine natural products. Nat. Prod. Rep.23: 26-78
13. Buck. J.D., Meyers, S.P. and Kamp, K.M. 1962. Marine bacteria with antiyeast activity. Science (New York), 138: 1339-1340.
14. Buckholder, P.R., Pfister, R.M. and Leitz, F.H. 1966. Production of a pyrrole antibiotic by a marine bacterium. Applied Microbiology, 14: 649-653.
15. Campbell, N. 1993. In: Biology. Third Edition. Benjamin Cummings. Redwood City, Ca. p.1190.
16. Chatellier, M.A., Jacky Bhagat, Karthik, K., Jaffar Hussain, A. and Jayaprakashvel. M. 2011. Deproteination of shrimp shell wastes using immobilized proteolytic marine bacteria.
17. Choudhary, A., Naughton, L. M., Montánchez, I., Dobson, A. D., & Rai, D. K. 2017. Current status and future prospects of marine natural products (MNPs) as antimicrobials. *Marine drugs*, *15*(9), 272.
18. Deming, J.W. 1985. Bacterial growth in deep-sea sediment trap and box core samples. Marine Ecology-Progress Series, 25: 305-312.
19. Deming, J.W. 1986. The biotechnological future for newly described, extremely thermophilic bacteria. Microbial Ecology, 12: 111-119.A.
20. Deming, J.W. and Colwell, R.R. 1985. Observations of barophilic microbial activity in samples of sediment and intercepted particulates from the Demerara Abyssal Plain. Applied and Environmental Microbiology, 50: 1002-1006.
21. Donia, M., & Hamann, M. T. 2003. Marine natural products and their potential applications as anti-infective agents. *The Lancet infectious diseases*, *3*(6), 338-348.
22. Floodgate. G. 1984 The fate of petroleum in marine ecosystems, in: Petroleum Microbiology, edited by R. M. Atlas, Ed., pp. 355–398, Macmillion, New York, NY, USA.
23. Gobalakrishnan, S., Muthezhilan, R., Jaffar Hussain, A. and Jayaprakashvel. M. 2010. Antagonistic activity of cyanogenic marine bacteria from coastal vegetation.
24. Gram, L., J. Melchiorsen, B. Spanggaard, I. Huber and T.F. Nielsen, 1999. Inhibition of *Vibrio anguillarum* by *Pseudomonas fluorescens* AH2, a possible probiotic treatment of fish. Applied Environ. Microbiol., 65: 969-973.
25. Guo, P., Lin, J., Cao, B., & Ta, N. (2014). Isolation of Petroleum Hydrocarbon Degrading Bacteria from the Liaohe estuary at cold climate. *Advanced Materials Research*.
26. Irianto, A. and B. Austin, 2002. Probiotics in aquaculture. J. Fish Dis., 25: 633-642.

27. Jannasch, H.W. and Wirsen, C.O. 1982. Microbial activities in undercompressed and decompressed deep-sea water samples. Applied and Environmental Microbiology, 43: 1116-1124.
28. Jayaprakashvel, M., Muthezhilan, R., Srinivasan, R., Jaffar Hussain, A., Gopalakrishnan, S Jacky Bhagat, Kaarthikeyan, C. and Muthulakshmi, R. 2010. Hydrogen cyanide mediated biocontrol potential of Pseudomonas sp. AMET1055 isolated from the rhizosphere of coastal sand dune vegetation. Adv. Biotech. 9(10): 39 - 42.
29. Kaarthikeyan, C., Jayaprakashvel, M., Jaffar Hussain, A. and Muthezhilan, R. 2010. Lactobacillus An lternative for sea food preservation.
30. Krassil'nikova, E.N. 1961. Antibiotic properties of microorganismsisolated from various depth of world oceans. Microbiologiya, 30: 545-550.
31. Leahy, J. G., & Colwell, R. R. 1990. Microbial degradation of hydrocarbons in the environment. *Microbiological reviews*, *54*(3), 305-315.
32. Lemos, M.L., Teranzo, A.E. and Barja, J.L. 1985. Antibiotic activity of epiphytic bacteria isolated from intertidal seaweeds. Microbial Ecology, 11: 149-163.
33. Lovell, F.M. 1966. The structure of a bromine rich antibiotic. Journal of the American Chemical Society, 88: 4510-4511.
34. Lucas - Elio, P., Hernandez, P., Sanchez-Amat, A. and Solano, F. 2005.Purification and partial characterization of marinocine, a new broad - spectrum antibacterial protein produced by Marinomonas mediterranea Biochimica Biophysica Acta (BBA).1721: 193-203
35. Manasi, N., Kaarthikeyan, C., Karthik, K., Jaffar Hussain, A. and Jayaprakashvel, M. 2011. Screening of bacteria isolated from marine environment for industrially important enzymes.
36. Mayer, A. M., Glaser, K. B., Cuevas, C., Jacobs, R. S., Kem, W., Little, R. D., ... & Shuster, D. E. 2010. The odyssey of marine pharmaceuticals: a current pipeline perspective. *Trends in pharmacological sciences*, *31*(6), 255-265.
37. Mayer, A. M., Nguyen, M., Newman, D. J., & Glaser, K. B. 2016. The marine pharmacology and pharmaceuticals pipeline in 2015. *The FASEB Journal*, *30*(1_supplement), 932-7.
38. Mayer, A. M., Rodríguez, A. D., Berlinck, R. G., & Fusetani, N. 2011. Marine pharmacology in 2007–8: Marine compounds with antibacterial, anticoagulant, antifungal, anti-inflammatory, antimalarial, antiprotozoal, antituberculosis, and antiviral activities; affecting the immune and nervous system, and other miscellaneous mechanisms of action. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *153*(2), 191-222.
39. Mayer, A., Rodríguez, A. D., Taglialatela-Scafati, O., & Fusetani, N. 2013. Marine pharmacology in 2009–2011: Marine compounds with antibacterial, antidiabetic, antifungal, anti-inflammatory, antiprotozoal, antituberculosis, and antiviral activities; affecting the immune and nervous systems, and other miscellaneous mechanisms of action. *Marine drugs*, *11*(7), 2510-2573.
40. Mayer, A., Rodríguez, A. D., Taglialatela-Scafati, O., & Fusetani, N. 2017. Marine pharmacology in 2012–2013: Marine compounds with antibacterial, antidiabetic, antifungal, anti-inflammatory, antiprotozoal, antituberculosis, and antiviral activities; affecting the immune and nervous systems, and other miscellaneous mechanisms of action. *Marine drugs*, *15*(9), 273.
41. Miralto, A., Barone, G Romano., Poulet, S.A., Lanora, A., Russo, G.L., Buttino, I., Mazzarella, G., Laabir, M Cabrini and Giacobbe, M.G. 1999. The insidious effect of diatoms on copepod reproduction. Nature, 402: 173-176.
42. Nair, S. and Simidu, U. 1987. Distribution and significance of heterotrophic marine bacteria with antibacterial activity. Appl. Environ. Microbiol. 53(12): 2957-2962.
43. Nguyen, T. H., & Nguyen, V. D. 2017. Characterization and Applications of Marine Microbial Enzymes in Biotechnology and Probiotics for Animal Health. In *Advances in food and nutrition research* (Vol. 80, pp. 37-74). Academic Press.
44. Nguyen, T. H., & Nguyen, V. D. 2017. Characterization and Applications of Marine Microbial Enzymes in Biotechnology and Probiotics for Animal Health. In *Advances in food and nutrition research* (Vol. 80, pp. 37-74). Academic Press.
45. Nikapitiya, C. 2013. Marine bacteria as probiotics and their applications in aquaculture. *Marine Microbiology: Bioactive Compounds and Biotechnological Applications*, 97-126.
46. Okami. Y. 1986. Marine microorganismsas a source of bioactive agents. Microbial Ecology, 12: 65-78.
47. R.P.J.Swannell, K.Lee, M.McDonagh 1996. Field evaluations of marine oil spill bioremediation. Microbiological Reviews 60, pp. 342–365]
48. Rosenfeld, W.D. and Zobell, C.E. 1947. Antibiotic production by marine microorganisms. Journal of bacteriology, 54: 393-398.
49. Turner, J.T. 1979. Microbial attachment to copepod feacal pellets and its possible ecological significance. Transactions of the American Microscopic Society, 98: 131-135.
50. UNEP, G. M. A. 2002. United Nations Environment Programme. *Chemicals, Geneva, Switzerland*.
51. Vijayan, N., Sagadevan, E., Arumugam, P., Jaffar Hussain, A., & Jayaprakashvel, M. (2012). Screening of Marine bacteria for multiple Biotechnological applications. *Journal of Academia and Industrial Research*, *1*(6), 348-353.
52. Yakimov, M. M., Timmis, K. N., & Golyshin, P. N. 2007. Obligate oil-degrading marine bacteria. *Current opinion in biotechnology*, *18*(3), 257-266.
53. Yumoto, I., Hirota, K., Sogabe, Y., Nodasaka, Y., Yokota, Y. and Hoshino, T., 2003. Psychrobacter okhotskensis sp. nov., a lipase-producing facultative psychrophile isolated from the coast of the Okhotsk Sea. *International journal of systematic and evolutionary microbiology*, *53*(6), pp.1985-1989.