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Biosynthetic Potential of Marine Microbial Symbionts

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ABSTRACT

Marine plants and animals are well known to harbor diverse microorganisms. These marine microbial symbionts are a prolific source of a large variety of bioactive natural products with diverse pharmacological potential. Genome mining of marine microbial symbionts is widely developing techniques to discover novel natural products biosynthetic genes and metabolites. The ever rapidly increasing available whole-genomes of microbes has revealed plethora of secondary metabolites encoding genes than discovered metabolites. The development in genome sequencing technology has triggered the natural products biosynthesis genetics and biochemistry. This review, highlights biosynthetic potential of marine symbiotic microorganisms and their metabolites.

KEYWORDS: Marine organisms, Microbial symbionts, Secondary metabolites, Biosynthesis

1. INTRODUCTION

Symbiosis is the ecological process where two or more diverse species interact with each other close and often long-term interaction. They can either have a positive or negative effect on the symbionts or in hosts. Marine microbial symbionts are microorganisms those living in the surface or in the internal parts of plants (endo- or epi-phytes) and animals (epi- or endo- zoic). The discovery of penicillin in 1929 by Alexander Fleming is the first chemotherapeutic agent isolated from a microbe and it was opening of the golden age of antibiotics[1]. The remarkable success in combat against disease with penicillin initiated and developed the antibiotic research. Apart from the base for discovery of numerous antibiotics, penicillin still remains one of the most active compounds.The discovery of novel drugs begin to slowed down in 1990, with the rapid rediscovery of known compounds[2]. Development of structurally complex natural products into drugs using synthetic methods were also challenging and too expensive. Ever increasing new diseases and emergence of drug resistant pathogens is the pressing issue on discovery of novel drugs[3]. The traditional process of isolation, screening and dereplication in natural products drug discovery has undergone a major transformation in the modern genomic era in which in silico-based bioprospecting leads to access the biosynthetic potentials from the genomic information[4,5]. The hidden natural product biosynthetic potential of the microorganisms have revealed from the available genome sequences. Secondary metabolites of cryptic biosynthetic genes such as polyketides, non-ribosomal peptides, terpenes etc., can also be deduced from the known sequence information for enzymes involved in natural products biosynthesis[6,7]. The chances to discover novel drug leads is high in extreme and unique environment when comparing to the normal habitats.

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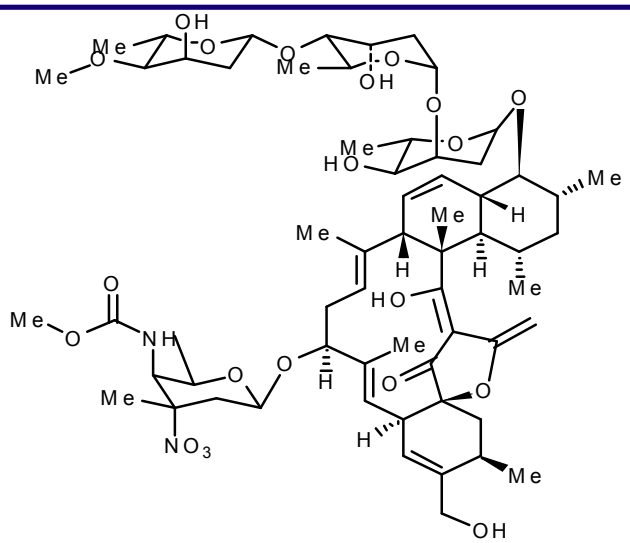
2. MICROBIAL SYMBIONTS FROM MARINE ECOSYSTEMS

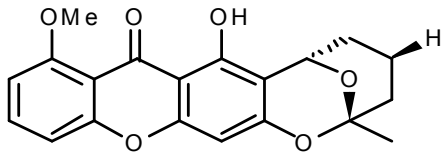
The marine ecosystems represent the heart of the earth's biodiversity and which represent 34 out of 37 phyla of life (in land only 17).Thus it represent virtually unexploited resource for diverse microbial symbionts discovery and only fraction in fraction have been disclosed till date. The extreme environmental parameters in the marine environments exert great stress on hosts and their symbionts. In the marine ecosystem functionally critical symbioses is between various animals and plants[8]. Marine microbial symbionts exists in diverse shape and colors. In order to survive in such condition, symbiotic microbes have the powerful capability to produces remarkable metabolites. The marine natural products search have turned to microorganisms, as the symbiotic microbes have begun recognized as an interesting source of valuable bioactive natural products. Natural products isolated from marine symbiotic microorganisms are a highly prolific source for diverse novel therapeutics agents. Marine microbial symbionts derived natural products have yielded various structures with antimicrobial, antiviral and antiprotozoal potentials[9]. The role of symbiotic microorganisms in the host is only a little information available[10].

3. BIOSYNTHETIC POTENTIAL AND SECONDARY METABOLITES OF MARINE MICROBIAL SYMBIONTS

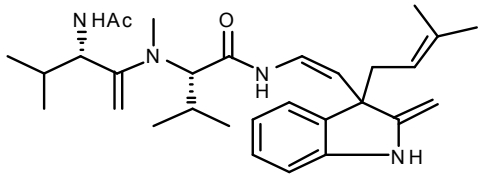
The distinguished feature of the marine symbiotic microbes in their metabolic versatility and the production of biologically active as well as chemically unique natural products[11]. Genomic analyses have elucidated the range of their secondary metabolic ability[12].The secondary metabolites biosynthetic pathways are numerous and diverse, the recent advances in the molecular basis of natural product assembly have made possible for prediction of chemistry and structures. Genome sequencing and bioinformatics investigations of marine microbial symbionts exposed a great number of "cryptic" gene cluster encoding for secondary metabolites. These gene cluster have the ability to proliferation of the diverse natural products.The several well characterized microorganisms have also identified as a hidden treasures to discover a larger variety of chemical structures. The increasing info of metabolic diversity has encouraged new strategies to explore novel bioactive metabolites synthesized by marine symbiotic microbes. Microorganisms derived small-molecule secondary metabolites have afford the chemical scaffolds of a large fraction of today's pharmaceuticals[13]. The marine discovery is recent activity when compare to the terrestrial counter parts. The major target of marine bioprospecting is in the highly diverse ecosystems such as coral reefs, mangroves, and seagrass because of their rich biodiversity and unique intense competition chemical warfare in the different organisms. The sponges (phylum Porifera), most primitive multicelled animals have existed for 700–800 million years. Most of the sponges inhabits in the marine and only about 1% species living in freshwater environment among the estimated 15,000 sponge species[14]. Marine sponges are well known to harbor diverse range of microbes and represent a significant source of bioactive natural molecules isolated from the oceans[15]. It has also estimated that sponge can hosts up to 40 % of their total biomass. The sponge associated microbes have been uncovered recently, and numerous previously undescribed species with wide array of novel metabolites. Microbial symbionts in marine sponges provide a potential sources of novel natural products with diverse bioactive molecules in a sustainable amount[16]. Some of the recent findings has explored that the many of the bioactive natural products have remarkable similarities to the symbionts of the hosts[17]. The harvesting of enough quantity from some marine macroorganisms is extremely difficult and it might also leads to the biodiversity loss in some instances. In some investigations, marine microbial symbionts have also been recorded as host specific[18]. Other invertebrates such as cnidarians, bryozoans, molluscs, tunicates and echinoderms also have diverse microbial symbionts and they also poses great metabolic diversity[3]. As a unique ecosystem, mangroves endowed with diverse microorganisms including endophytic fungi as an auspicious source of structurally diverse and unique bioactive metabolites which attract considerable attention. Mangrove symbiotic microbes derived compounds exhibited different biological activities, such as cytotoxic, anti-infective, enzyme inhibitory activities, antiangiogenic and neovascularisation effects, radical scavenging, DNA-binding affinity, and calcium and potassium channel blocking activity[19]. The extreme environmental conditions in the mangroves, including extensive salinity, high temperature and moisture, anaerobic soil, tidal variations and great faunal and microbial competition provide unique niche to the symbiotic microorganisms[20,21]. The mangroves hosts a diverse endophytes and which includes soil, marine and fresh water fungi[22]. In the marine ecosystem, the second largest ecological group is marine derived fungi and more than 200 species have been recorded[23,24]. Apart from mangroves, other marine plants such as algae, seagrass and phytoplankton also associated with diverse microbial symbiont and thus by becoming a significant hosts[3].



Lobophorin C , from sponge-*Streptomyces carnosus* IC_{50} 0.6 µg/ml^{-1} (Human liver cancer 7402)



Chaetoxanthone B,from alga-*Chaetomium* sp. IC_{50} 0.6 µg/ml^{-1} (*Plasmodium falciparum*)



Terpeptin A, from mangrove-*Aspergillus* ssp. IC_{50} 23.3 µg/ml^{-1} (A549 cells)

Figure 1. Selected biologically active natural products from the marine microbial symbionts

4. CONCLUSION

It is apparent that metabolic potentials of marine microbial symbionts are an untapped reservoir and the proper utilization of these source will definitely leads to the discovery of novel drugs. Among the different marine organisms, sponges and mangroves microbial symbionts yielded considerable number diverse bioactive natural products. The great metabolic diversity among marine microbial symbionts is the results of complex and unique habitats. As many of the macroorganisms derived metabolites are similar with the metabolites of microbial symbionts, it also possible to overcome ecosystem degradation issues and loss of biodiversity with ecofriendly bioprospecting and drug discovery. In order to overcome various drug resistance cancer and microbial pathogenesis, the discovery of new drugs must be augmented. In this context, the poorly explored unique habitats always becoming a gold mine for discovery of novel biologically active lead molecules. Marine microbial symbionts living in such environment bring hope in the novel natural products discovery. There are many challenges in harvesting the natural products from these microbes and it start from laboratory cultivation to exploring their factual metabolic potentials. This become now possible with the rapid developments in the sequencing technology and novel cultivation techniques such as mixed fermentation, alteration in the culture physicochemical parameters and using chemical cues in finding and expressing different cryptic metabolite genes.

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