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Review

MICROBIAL SYMBIONTS IN MARINE SPONGES: Marine natural product factory

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ABSTRACT

Marine sponges (phylum Porifera) are among the oldest multicellular animals (metazoans), the sea's most prolific producers of bioactive metabolites, and of considerable ecological importance due to their abundance and ability to filter enormous volumes of seawater. In addition to these important attributes, sponge microbiology is now a rapidly expanding field. Marine sponges produce numerous bioactive compounds with promising pharmaceutical properties. Sponges are well known to harbor diverse microbes and represent a significant source of bioactive natural compounds derived from the marine environment. Recent studies of the microbial communities of marine sponges have uncovered previously undescribed species and an array of new chemical compounds. Microbial symbionts in marine sponges offer potential sources of marine natural products and serve as marine natural product factory that supplies bioactive compounds in a sustainable way.

Key words*: microbial symbionts, sponge, natural product, factory*

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INTRODUCTION

The ocean is a rich source of biological and chemical diversity. It covers more than 70% of the earth's surface and hosts more than 300,000 described species of plants and animals to date with much higher numbers of microorganisms to be expected. This diversity has been the source of unique chemical compounds with the potential for industrial development as pharmaceuticals, cosmetics, nutritional supplements, molecular probes, enzymes, and agrichemicals. A relatively small number of marine plants, animals, and microbes have already yielded more than 12,000 novel chemicals[i]. The ocean represents a virtually unexploited resource for discovery of even more novel compounds with useful applications.

Although the ocean represents the centre of biological diversity with 34 of 37 phyla of life represented (compared to only 17 on land), prospecting marine resources for biotechnological use, particularly in drug discovery, is a relatively recent activity. Unlike bioprospecting on land, marine bioprospecting is a relatively new phenomenon. Some estimates, however, suggest that the probability of discovering a drug from marine sources is approximately a

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thousand times more than that from terrestrial ones.

To date, the primary target for marine bioprospecting has been tropical seas. Coral reefs and other highly diverse ecosystems such as mangroves, and seagrass have been targeted for bioprospecting because they host a high level of biodiversity and are often characterised by intense competition for space, leading to a chemical warfare among sessile organisms. Coral reefs are some of the most productive ecosystems on earth, and are certainly the most productive and species-rich environments in the oceans.

Marine organisms, in particular marine invertebrates from coral reefs have become sources of great interest to natural product chemistry, since they produce metabolites with different biological activities. Marine invertebrates, which are plentiful in the Indo-Pacific regions including Indonesia, are rich in secondary metabolites and are becoming targets of continuing search for bioactive compounds.

MARINE SPONGES AND MARINE NATURAL PRODUCTS

Sponges *(phylum Porifera)* are most primitive of the multicelled animals that have existed for 700–800 million years. Of the approximately 15,000 sponge species, most occur in marine environments. Only about 1% of the species inhabits freshwater (Belarbi et al, 2003).

It has been known that sponges produce secondary metabolites to repel and deter predators (Pawlik et al., 2002), compete for space with other sessile species (Davis et al., 1991; Becerro et al., 1997), and for communication and protection against infection. In addition, potentially therapeutic compounds identified in sponges include anticancer agents and immunomodulators. Some sponges seem to produce potentially useful antifouling agents (Hellio et al., 2005).

Recent research progresses reported that many bioactive natural products from marine invertebrates have striking similarities to metabolites of their associated microorganisms including bacteria (Proksch et al, 2002; Thiel and Imhoff, 2003; Radjasa et al, 2007a). Thus, it is important to highlight the possible role of marine bacteria associated with sponges in providing solution to the problem of infection by pathogenic bacteria. Bacteria-sponge association that occurs on the sponges then could be of great interest to search for potential use as new source of bioactive compounds, in particular as a solution of the problem of supply of most bioactive compounds produced by reef's invertebrates. In addition, the search for bioactive compounds from invertebrates of the coral reefs represents another threat for sustainable use of coral reef.

In addition, it has often proven extremely difficult, and some cases impossible, to provide from invertebrates sufficient amounts of these substances due to limited amounts found in the producing organism, or to limited quantity of the organism itself, or to geographic, seasonal or sexual variations in the amounts and in the nature of produced secondary metabolites.

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The bacteria are found associated with all organisms. Outstanding examples from the sea are the 50% bacterial biomass in sponges of the order Verongida, abundant cyanobacteria in many sponges, and oxychlorobacteria in colonial ascidians of the family Didemnidae. In the latter, *Acaryochloris marina* is an unusual photoautotroph based on mostly chlorophyll d, with only minor amounts of chlorophyll a. Many eukaryotic microorganisms are also known as symbionts of marine species, *e.g.* dinoflagellates in sponges and fungi in a

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variety of invertebrates, algae and seagrass (Taylor et al, 2007).

It has often been surmised that certain products isolated from marine macroorganisms may have microbial origin. Much work has also been devised to find a biotechnological route to therapeutically promising compounds isolated from rare marine macroorganisms, and too complex for a practical chemical synthesis; however, in only a few cases has a microbial origin been proven if 'dietary' metabolites are omitted. One of the best proven, and over-reviewed cases concerns a brominated diphenyl ether isolated from both the tropical sponge *Dysidea* sp. and its symbiontic bacterium *Vibrio* sp. in culture.

MICROBIAL SYMBIONTS AS SOURCES OF NATURAL PRODUCTS

The term "symbiosis" is currently used to describe two different biological concepts, which has caused a substantial amount of confusion. According to the original definition, symbiosis is a close physical association between two organisms belonging to different species. However, in many later sources the term is exclusively applied to an association that is beneficial to both partners. A beneficial symbiosis is therefore called "mutualism" (Piel, 2004).

Perhaps the most significant problem that has hampered the investigation of secondary metabolites produced by reef's invertebrates is their low concentration. In marine invertebrates many highly active compounds contribute to$<10^{-6}$ % of the body-wet weight. Providing sufficient amounts of these biologically active substances, hence, may be a difficult task (Radjasa et al 2007a)

Sponges are currently the most important marine source of biologically active natural products (Proksch et al, 2002). Many sponge derived metabolites are suspected to be truly produced by bacteria, since they resemble bacterial natural products or belong to substance classes typical for these microorganisms, such as complex polyketides or nonribosomal peptides.

In almost all cases development and production of sponge-derived drugs is seriously hampered by the environmental and technical problems associated with collecting or cultivating large amounts of animals. The possible existence of producing bacterial symbionts is therefore especially intriguing, because a sustainable source of sponge-derived drug candidates could be generated by establishing a symbiont culture or by transferring symbiont biosynthetic genes into culturable bacteria. **Table.1** and **Fig.1**, list some of structurally related sponge metabolites that resemble bacterial metabolites.

Table 1. Structurally related microbial metabolites with sponge metabolites*)

No	Sponge metabolite	Source	Bacterial metabolite	Source
1	Arenastatin A	*Dysidea arenaria*	Cryptophycin 1	*Nostoc* sp.
2	Jaspamide	*Jaspis* spp.	Chondramide	*Chondromyces crocatus*
3	Mimosamycin	*Petrosia* sp.	Mimosamycin	*Streptomyces lavendulae*
4	Salicylihalamide	*Haliclona* sp.	Apicularen A	*Chondromyces* sp.
5	Swinholide A	*T. swinhoei*	Tolytoxin	*Tolypothrix* sp.

***)** Adapted from Piel (2004)

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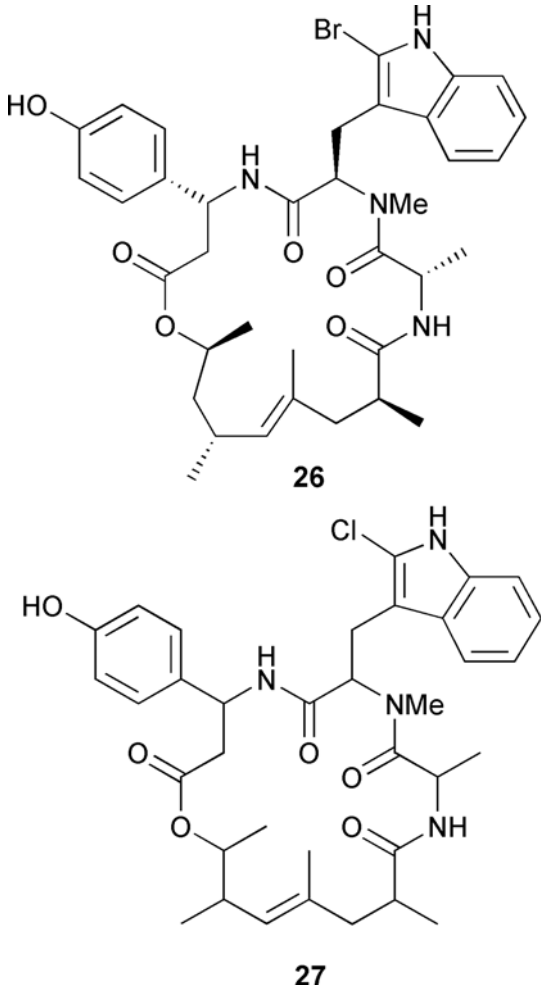

Fig. 1 Structurally related sponge metabolite of Jaspamide (26) and microbial metabolite Chondramide(27) adapted from Piel (2004).

CONCLUDING REMARKS

In conclusion, the possible existence of producing bacterial symbionts is therefore especially intriguing, because a sustainable source of sponge-derived drug candidates could be generated by establishing a symbiont culture or by transferring symbiont biosynthetic genes into culturable bacteria. Marine sponges exhibited diverse secondary metabolite producing-marine microorganism with various potential against different diseases.

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