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Antibacterial Compounds from Microorganisms Isolated from Deep Sea Sediment: A Mini Review

Rega Permana[1,2*] and Aulia Andhikawati[1,2]

[1]Department of Fisheries, Faculty of Fisheries and Marine Science, Universitas Padjadjaran, Indonesia.
[2]Tropical Marine and Fisheries Laboratory, Faculty of Fisheries and Marine Science, PSDKU Universitas Padjadjaran, Indonesia.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors contribute equally in designing, performing observation, data analysis as well as manuscript writing. Both authors read and approved the final manuscript.

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ABSTRACT

The search for new antibacterial compounds using sources derived from marine biota is interesting to develop, considering that Indonesia has diversity of a very large microorganisms and has the potential to produce antibacterial substances. One of the microbial resources that has not been widely exploited is the microorganisms present in deep sea sediments. The deep sea has variations in the availability of nutrients, light, oxygen, concentration, pressure, salinity, and temperature. This condition also triggers marine microorganisms to develop unique physiological abilities. The physiological ability of deep sea microorganisms not only to survive, but also has an impact on their ability to produce unique metabolites that are not owned by terrestrial microorganisms. Here we will review some reported study on the search of antibacterial compounds from microorganisms isolated from the deep sea sediment. The fundamental basic of antibacterial will be discussed followed by several reported antibacterial compounds from the sediment bacteria. This opens door for the search of new microorganisms that produced new chemical compounds with beneficial application in human health as well as in other field.

**Corresponding author: E-mail: rega.permana@unpad.ac.id;*

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1. INTRODUCTION

In the last 50 years, the marine environment has become the source of more than 20,000 natural products although this is still rarely done [1]. However, with the development of the times and the emergence of new techniques such as scuba diving, marine organisms began to be collected and studied for their secondary metabolites. From these efforts, more than 22,000 secondary metabolites were isolated from marine microorganisms and a significant percentage was found that these metabolites have biological activity [1].

One of the microbial resources that has not been widely exploited is the microorganisms present in deep sea sediments. Deep sea habitats are aquatic environments with a depth of 3000 m or more and part of the environment is in the form of biogenic sediments [2]. The deep sea has variations in the availability of nutrients, light, oxygen, concentration, pressure, salinity, and temperature [3]. This condition also triggers marine microorganisms to develop unique physiological abilities. The physiological ability of deep-sea microorganisms not only to survive, but also has an impact on their ability to produce unique metabolites that are not owned by terrestrial microorganisms [3,4].

Through molecular studies of the ecology of marine microorganisms, especially those from deep sea sediments, various active compounds have been isolated and identified including antibacterial [5,6]. The types of microbes originating from deep sea sediments are grouped as microorganisms that thrive in an environment with low temperature (*psychrophiles*) and high pressure (*bartolerance*) [7]. The high pressure experienced by deep-sea microorganisms causes cell membranes and fluids to become waxy, and relatively impermeable to nutrients. In this condition. microorganisms are triggered to produce secondary metabolites that can protect them from external conditions [8].

Based on several studies that have been carried out, samples of sedimentary microorganisms from Mariana Trench have been investigated to produce 7 dermacozines AG produced by *Dermacoccus abyssi* sp. at a depth of 1089m [9]. Developed countries such as South China have also conducted research on deep-sea sedimentary microorganisms which have been shown to produce AC pseudonocardians, grincamycins BF and abyssomicins JL which have the potential as bioactive components, namely antitumor, antibacterial, and anti-fibrotic activity [10,11]. In addition, several other antibacterial substances have been found, such as lynamicins isolated from *Marinispora* sp. and has the potential to fight gram-positive and negative bacteria [12], caboxamicin which acts as an inhibitor of the growth of gram-positive bacteria and tumor cell-lines [13], and tirandamicin C which is produced by *Streptomyces* sp. and plays a role in inhibiting *Enterococcus faecalis* activity [14].

The advantage of obtaining secondary metabolites from microorganisms, especially bacteria, is that these compounds can be produced easily, quickly, and can be developed on a large scale with the help of biotechnology. However, there are still many compounds produced by deep sea microorganisms that have not been identified [1].

2. ANTIBACTERIAL

Antibiotics are chemical compounds produced by microorganisms, and in very low levels have the ability to inhibit or kill the growth of other microorganisms [15]. If The inhibition in question is the inhibition of bacterial growth the term used is antibacterial [16]. Antibacterial varies depending on the nature, structure and level of affinity for the target certain substances in different bacterial cells and are substances that can interfere with the growth or even kill bacteria by interfere with the metabolism of harmful microbes. The antibacterial activity is divided bacteriostatic activity which inhibits cell growth target or multiplication of target cells and slowly eliminate target cells sel and bactericidal activity that induces target cell death with or without competent immune system of the host so that it kills the target bacterial cells [17].

Some of the inhibition mechanisms possessed by antibacterials include: cell wall inhibitors, membrane function inhibitors, protein synthesis inhibitors, inhibitors nucleic acid synthesis, and inhibitors of metabolic processes [18]. Some of these mechanisms can be explained as follows:

A. Inhibition of nucleic acid synthesis (DNA and RNA)

1. Some antibacterials work by binding involved in the process of DNA or RNA synthesis, which causes disruption of normal cell processes that will eventually harm bacterial survival. Examples of this type of antibacterial are quinolones, metronidazole, and rifampicin [18].
2. Quinolones will trap the DNA gyrase enzyme (topoisomerase II) at the DNA cleavage and prevent DNA strands from rejoining. Although topoisomerase II and IV have functional similarities, Several studies have shown that Topoisomerase IV is the main target of Quinolones in Gram-positive bacteria (*Streptococcus pneumoniae*), while Topoisomerase II is the main target and topo IV secondary targets of this drug in Gram-negative bacteria (eg, *Escherichia coli* and *Neisseria gonorrhoea*) [19,20].
3. Rifampycin will inhibit RNA synthesis before it occurs addition of two ribonucleotides, which was associated with drug molecule to block the newly formed RNA strand. Rifamycin will strongly bind the subunit of the DNA binding and actively transcribing RNA polymerase [21].

B. Inhibition of cell wall synthesis

1. Cell wall structure is very important for life and survival live bacterial species. If the target of a compound is the cell wall, then these compounds can selectively kill or inhibit bacteria. Examples of this type of antibacterial are penicillins, cephalosporins, bacitracin, and vancomycin [18].
2. B-lactams (including penicillins, carbapenems and cephalosporins) will block the PG unit by inhibiting the -bond formation reaction peptides catalyzed by penicillin-binding protein (PBP) [22,23]. The active site of bound PBP penicilloylation is analogue of the dipeptide PG and acts as a substrate for the enzyme during the acylation phase of cross-link formation, which inactivates enzymes due to the inability to hydrolyze the bonds [24,25].
3. Several studies have shown that non-lytic pathways are regulated by 2 components of the bacterial system that help in expressing LytA autolysin and regulate tolerance to vancomycin and penicillin [26].

C. Inhibition of protein synthesis

1. Several types of antibacterial agents target bacterial protein synthesis by binding to the intracellular ribosomal subunit. This activity This then results in disruption of normal bacterial cell metabolism and consequently lead to death or growth inhibition and bacterial multiplication. Examples of this type of antibacterial are: aminoglycosides, macrolides, lincosamides, chloramphenicol, tetracyclines [18].
2. The 50S inhibitor lincosamide (clindamycin) works by block the initiation or translation of the protein, which would Inhibits the reaction of peptidyltransferase which elongates the chain peptides. This will then trigger the dissociation of the peptidyl-tRNA [27].
3. 30S inhibitors, namely tetracycline, work by blocking access aminoacyl-tRNA to the ribosome [28], whereas Aminocyclitol works by binding to the 16S rRNA component of the subunit 30S ribosomal, which will cause mistranslation by tRNA [29].

3. MARINE SEDIMENT BACTERIA

The sea has many mineral sources consisting of various variations include polymetallic nodules, abundant sulfate, and cobalt (Co) [30]. Although the mechanism of metallic mineral formation is not fully understood, marine microorganisms are thought to play an important role in the biomineralization process [31]. marine microorganisms, especially bacteria have an important role in various processes that takes place in the sea. One of these processes is the microbial loop or microbial circle which includes the process of mineralization of dissolved organic compounds, respiration, nutrient cycles, growth and grazing of bacteria [32]. The marine environment has been studied which consists of many microorganisms that produce new components and 20% of them are reported to be components active compound. The study reported by Schinke, *et al.* [33] shows interesting thing where it turns out that marine sediment is one point that has a the largest percentage of bacteria producing new secondary metabolites that are active compared to other sources such as sponges, algae, coral, and others. In addition, in the sediment also found various types of microorganism families such as actinobacteria and bacilli.

Deep sea bacteria are more heat sensitive than pressure sensitive. Many of them cannot survive at a temperature of 30^{o}C and less than 20% of deep sea bacteria can survive at 40^{o}C [34]. The unique life necessities of deep sea bacteria, seen of pressure, temperature, and nutrients make these bacteria uncharacterized with standard culture procedures. Morphologically, deep sea bacteria resemble soil and water, but physiologically these bacteria show significant differences makes deep-sea bacterial species unique and not easy to describe [35]. Although deep-sea bacteria are dominated by aerobic bacteria, some There are deep sea bacteria that grow anaerobically. Besides that, also found types of marine bacteria that are active in converting organic components and reducing sulfate [36]. Deep sea bacteria estimated has 0.2-2 mg/liter of organic carbon and these bacteria can optimize energy needs and carbon is needed by taking it from the components organic matter carried by the movement of water masses [34]. Around 95% of organic components are produced by marine microorganisms on the surface water around a depth of 100-300 m, while 1% of these components produced in the deepest part of the ocean by photosynthesis. This is wrong one piece of evidence that the community of these deep-sea microorganisms varies and has resistance to high pressure [37,38].

Several studies have shown that the deep sea has considerable microbial diversity, influenced by minerals rich in the interior of the sea. Several bacterial families have been identified using phylogenetic analysis of 16S rRNA was Gammaproteobacteria and Alphaproteobacteria [39]. In addition, other research from from the Fracture Zone in the Pacific Deep Sea also shows the presence of Deltaproteobacteria and 14 other microbial groups found in the environment metal-rich sea [40]. Apart from microorganisms proteobacteria, in the deep sea are also found actinobacteria which are one of the one of the largest types of bacteria that produce antibiotic substances [41].

Actinobacteria, also known as Actinomycetes, are gram-positive bacteria positive originating from the order Actinomycetales and includes several unicellular microorganisms [42]. Actinobacteria is a type of bacteria that can live in places such as soil, compost, and marine habitats. Actinobacteria that live in the soil is a component that plays an important role in plant decomposition and other materials especially in the degradation of complex polymers [43]. Actinobacteria themselves have been observed to be denser in the ocean shallower than the deep sea. In addition to being in marine sediments, actinobacteria also associated with other organisms such as sponges, corals, molluscs, seaweed, seagrass and mangroves. Several genera of actinobacteria include: Streptomyces, Actinomyces, Arthrobacter, Corynebacterium, Frankia, Micrococcus, Micromonospora, etc. [44]. Among the whole the actinobacteria, Streptomyces and Micromonospora genera are produce large amounts of bioactive molecules and biosynthetic pathways that do not can be rivaled by other microbial groups and produce antibiotics that have been used in large quantities such as erythromycin, streptomycin, rifamycin, and gentamicin [45].

4. ANTIBACTERIAL COMPOUNDS FROM MARINE SEDIMENT BACTERIA

Basically, many antibacterial compounds have been isolated from microorganisms land that has been considered potential and does produce compounds that role in the pharmaceutical sector. However, not a few studies have reported that marine microorganisms, especially those from the deep sea. Research that conducted in previously reported several components of new antibacterial compounds originating from the sea and inhibiting a number of pathogenic bacteria, such as those contained in Table 1.

The main role of Actinobacteria in biotechnology applications is the production of secondary metabolites that can be used as antimicrobial substances, inhibitors enzymes, immunomodifiers, and growth-promoting substances for plants, as well as as an antibiotic [46]. Actinobacteria are well known because it is rich in antibiotics and is one of the largest producers of antibiotics because the antibiotics derived from these bacteria help in the field of science, pharmaceuticals, industry and agriculture [47]. From several studies that carried out in recent years, it is shown that it has produced more than 10,000 antibiotics, 70% of which are produced by actinobacteria, while 30% of them are produced by fungi and other bacteria [48].

Table 1. Antibacterial produced from microorganisms isolated from deep sea sediment [33]

Source of Isolates	Bacteria	Antibacterial Compounds	Activity
Red Sea, Jeddah Beach, Saudi Arabia	*Streptomyces caelestis*	Citreamicin, citreaglycon	Inhibits growth of *Staphylococcus haemolyticus, B. subtilis, and S. aureus*
Marine sediments	*Streptomyces fradiae*	Fradimycins A and B	Inhibits growth of *S. aureus*
Marine sediments from the China Sea Southern	*Streptomyces scopuliridis*	Desotamida BD, Destoamide A	Inhibits the growth of S. aureus, S. pneumoniae, and S. epidermidis (MRSE)
Marine Sediments from the South China Sea	*Pseudonocardia* sp.	Diazaanthraquinone (Pseudonocardians A, B)	Inhibits the growth of *S. aureus, E. faecalis*, and *B. thuringiensis*.
Marine sediments Gageocho, Korea	*Bacillus* sp.	Lipotetrapeptidasubtilis,namely gageotetrins A, B, and C.	Inhibit the growth of *Salmonella typhi* and *P.aeruginosa*
South China Sea	*Bacillus amyloliquefaciens*	Macrolactin V and S	Inhibits Growth of *S. aureus* and *E. coli*
Red Sea Aqaba, Jordan	*Vibrio* sp.	Aqabamycin E and F.	Inhibit the growth of *E. coli, B. subtilis*, and *Micrococcus luteus*.

The production of actinobacterial secondary metabolites is influenced by several fermentation parameters such as available nutrients, temperature, oxygen pressure, agitation, metal ions, inducers, and inhibitors. Molecular basis in producing These actinobacterial secondary metabolites have successfully discovered thousands of antibiotics derived from actinobacteria. Many actinobacteria come from the sea in possessing non-ribosomal polyketide synthetase (NRPS) and polyketide. pathways synthetase (PKS) which is a hallmark of the production of metabolites secondary [49,45]. Most of the bioactive substances of actinobacteria are divided into four types: The main structures are amino glycosides (streptomicin and kanamicin), ansamycins (rifamin), anthracyclines (doxorubicin), and macrolides (erythromicin) [48]. In addition to the previously mentioned antibiotics, many substances other antibiotics produced by actinobacteria, some of which are also produced anthracyclines, aminoglycosides, b-lactams, chloramphenicol, tetracyclines, nucleosides, quinolones, rifampicin, kanamycin, myomycin [50]. Besides actinobacteria, not a few bacteria from other groups are isolated from the deep sea produces many new secondary metabolites with various activities [51-55].

5. CONCLUSION

The deep sea exploration allowed us to investigate the diverse form of life in its sediment, particularly microorganisms. It has been discussed several discoveries of many new chemical compound with multiple application from the deep sea sediment including as antimicrobial substances, inhibitors enzymes, immunomodifiers, and growth-promoting substances for plants, as well as as an antibiotic. The search of new microorganisms that produced new chemical compounds with beneficial application in human health is generally desirable and still an exploratory research. An advance sampling methods and characterization technique is critically essentials to better understand the nature of the natural products which biosynthetically produced by the deep sea microorganisms.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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