NATURAL BACTERIA AND ANTIBIOTIC RESISTANCE FROM THE SEA

Christi Diana Mambo[*1](Christi.mambo@unsrat.ac.id)
Kristin IF Kondoy[1](kristin.kondoy@unsrat.ac.id)
Yanti Meilen Mewo[1](yanti.mewo@unsrat.ac.id)
Finny Waro xb uw[1](finnywarouw@unsrat.ac.id)
Felly Ferol Warouw[2](ferolwarouw@unima.ac.id)
Angle Maria Hasthee Sorisi[1](hestisorisi@unsrat.ac.id)
Brianne EJ Komedien[2](brianne.komedien@unima.ac.id)
Viktory Nicodemus Joufree Rotty[2] (viktoryrotty@unima.ac.id)
[*1]Faculty of Medicine Sam Ratulangi University, Manado, Indonesia
[2]Faculty of Education Management, Manado State University

Abstract

Antibiotics are not only used for the treatment of infections in humans but are also used in livestock, aquaculture and food. Antibiotics are used to control disease attacks or protect against bacterial contamination that causes disease. The use of antibiotics or antimicrobials in food is often combined with processing. Research on disease control in aquaculture is still limited to the use of chemicals such as formalin, malachite green and several types of antibiotics such as chloramfenicol. The use of antibiotics often does not follow the recommended rules, for example too low or repeatedly, as a result bacteria become resistant to antibiotics. Bacterial resistance to antibiotics is influenced by the environment. Good environmental management or health management is needed in the management of aquaculture and other livestock. The role of the government and related agencies is also needed in dealing with this problem.

Keywords: *resistance, antibiotics, infection, marine potential, drugs, bacteria*

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INTRODUCTION

Initially antibiotics were used for the treatment of infectious diseases in humans. Then developed its use for livestock and now other fields such as fisheries and food. In the field of fisheries, antibiotics are needed in handling disease attacks in aquaculture. The problem of disease in aquaculture is an obstacle both in the nursery and in aquaculture in ponds or ponds. From inventory research, it has been reported that the types of diseases that often attack tiger shrimp such as protozoan parasites (Zoothamnium, Epystilis, Vorticella), fungi (Lagenidium, Fusarium), bacteria (Vibrio harvey, V. alginoliticus) and viruses (Monodon bacula virus) (Suryati et al. al., 1999). al., 1999). Luminous vibriosis has been reported to cause death in shrimp in the Philippines and this disease is a major problem in the shrimp industry not only in the Philippines but also in other countries. Various technologies have been introduced to treat this disease in shrimp (Tendencia et al., 2004). Research on disease control in aquaculture is still limited to the use of chemicals such as formalin, malachite green and several types of antibiotics such as chloramphenicol, oxytetracyclin, prefuran (Brown, 1989). However, the use of antibiotics in the

fisheries sector is also still experiencing very serious obstacles. Research on disease control in aquaculture is still limited to the use of chemicals such as formalin, malachite green and several types of antibiotics such as chloramphenicol, oxytetracyclin, prefuran (Brown, 1989). However, the use of antibiotics in the fisheries sector is also still experiencing very serious obstacles. Research on disease control in aquaculture is still limited to the use of chemicals such as formalin, malachite green and several types of antibiotics such as chloramphenicol, oxytetracyclin, prefuran (Brown, 1989). However, the use of antibiotics in the fisheries sector is also still experiencing very serious obstacles.

Some time ago, the issue of chloramphenicol residue became global after the European Union Commission Decision was issued on September 27, 2001 which stated that 0.075 ppb of chloramphenicol contamination had been detected in Indonesian export shrimp products that entered the EU and had to be rejected, destroyed and not given the opportunity to re-use. export. The presence of antibiotics in shrimp or other foodstuffs can occur due to the error of cultivators or business people. Of course, this problem is very detrimental to us as an exporting country.

The emergence of diseases in aquaculture and other livestock, rejection of fishery products by importing countries, inappropriate use of antibiotics and the emergence of antibiotic resistance become interesting topics for discussion. These problems can have an impact on other related fields such as the economy and trade or industry. For that, it is necessary to find a solution

Infection is still one of the health problems faced by people in developing countries such as Indonesia. Antibiotics are a class of drugs that are most often used in cases of infection. Unfortunately, inappropriate and irrational use of antibiotics often occurs, resulting in a very high increase in antibiotic resistance in all parts of the world. Antibiotics are likely to become increasingly ineffective as drug resistance spreads globally leading to amore difficult to treat the infection.

Without immediate action, we are heading into a post-antibiotic era, where common infections and minor injuries can once again kill.IncreasedresistanceAntibiotics seem to be accompanied by the discovery of new antibiotics, but the discovery of new antibiotics seems to be decreasing. In 2019 WHO identified 32 antibiotics in developmentclinical trials but only six were classified as giving results (WHO, 2021).

For this reason, in an effort to overcome resistance, new sources of antibiotics are needed and one source of antibiotics comes from the ocean. The ocean is the largest ecosystem on earth.physicalappearancecovers 70% of the earth's surface and has a variety of habitat conditions ranging from tropical, shallow seas with coral reefs to deep seas, ocean trenches. This habitat is inhabited by various plantsandinvertebratesthe majority of which are unique to the sea.

Marine bacteria is onea source of marine natural products that are invaluable resources, have secondary metabolite bioactive compounds and play an important role in biomedical research and the pharmaceutical industry. Secondary metabolites are produced as a self-defense mechanism from extreme conditions of the marine environment such as high pressure, light and limited oxygen and as a self-protection against various predators. Secondary metabolites produced by microorganisms, such as marine bacteria have effective bioactivity against other

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microorganisms or the specific physiological conditions of the diseased body. Since the discovery of the first antibiotic penicillin in 1920However, it has been assumed that the secondary metabolites of microorganisms are the main source of new secondary metabolites with antimicrobial activity. Microorganisms, particularly bacteria, are considered to be attractive sources of structurally diverse and effective bioactive compounds.

Bacteria from seawater, can produce a variety of new therapeutic compounds with various applications. The associated marine bacteria use the nutrients produced by their hosts to defend themselves against harmful entities in the environment by secreting biologically active chemicals. Many bioactive compounds were identified from marine bacteria, such as antibacterial, antiviral, antifungal, anticancer substances. The production of these secondary metabolites by marine bacteria opens new avenues for developing new natural compounds. Moreover, marine bacteria are proving to be an attractive source for the development of new therapeutic agents. For example, if adequately screened and researched, marine bacteria might provide us with the antimicrobials we need to fight drug-resistant pathogens for the next 100 years.

Marine bacteria are estimated to produce about 23,000 bioactive secondary metabolites. Secondary metabolites produced by marine bacteria have many biological activities, including antimicrobial potential. Six phyla of marine bacteria (Actinobacteria, Bacteroidetes, Cyanobacteria, Firmicutes, Planctomycetes, and Proteobacteria) appear to be the main sources of antimicrobial compounds from several studies conducted.One of the results of the dissertation research for the 2021 Unsra Marine Science Study Program revealed the findings of various marine bacteria from tailings sediments on the sea floor of Buyat Bay. Some of them are bacteria with potential therapeutic compounds, such as Streptomyces camponoti, Rhodococcus sp., and Pseudoruegeria sp. Furthermore, compoundthose isolated form the basis of the active ingredients in the preparation of drugs for use in clinical practice, while others are in the preclinical or clinical study stage. Much attention has been paid in recent years to producers of marine-derived antibiotics isolated from deep-sea habitats.

Nature will continue to be an important resource in the supply of new bioactive compounds that are important in treating various human ailments. Although a large number of bioactive compounds have been isolated from marine bacteria, there is a great unexplored hidden marine diversity of these organisms. Rapid advances in genomic information with simultaneous advances in marine science and biotechnology will surely stimulate the search for secondary metabolite producers and secondary metabolite biosynthesis.

The purpose of this paper is to discuss the use of antibiotics and their effects if they are used incorrectly, as well as to provide an overview of natural antibiotics as a relatively safe alternative.

ANTIBIOTIC ?

Now almost everyone is familiar with antibiotics, not only sick people. In the past, the use of antibiotics was only limited to the treatment of an infectious disease in humans, so only the medical community was familiar with antibiotics. Now starting to penetrate the industry such as animal husbandry, fisheries, and food. They use antibiotics to stimulate the growth of livestock, control disease attacks or protect their products from attack by pathogenic microbes so that products are free from disease-causing

microbes. Disease is one of the problems in the production of livestock, including fish or shrimp. The safety and health of production animals is of utmost priority. Countries such as the USA, Canada and Norway apply very strict rules in controlling the use of antibiotics,

Antibiotics or antimicrobials are chemical compounds that can kill or inhibit the growth of microorganisms. When referring to a specific group of organisms, terms such as antibacterial, antifungal, and so on are often used (Frazier and Westhoff, 1988). Metting and Pyne (1986) stated that antibiotics are antimicrobial components produced naturally by organisms and are toxic to microalgae, bacteria, fungi, viruses or protozoa.The term antibiotic comes from the word antibios which means a substance produced by a microorganism which in small amounts can inhibit the growth or kill other microorganisms. The discovery of antibiotics was initiated by Alexander Fleming in 1928.

Antimicrobials can be synthetic chemical compounds or natural products. Synthetic antimicrobials can be produced by making a compound whose properties are similar to the original which is made on a large scale, while the natural one is obtained directly from the organism that produces the compound by carrying out the extraction process. Chemicals that can kill organisms are called cidal, such as bactericidal, fungicidal, algicidal. Meanwhile, chemicals that inhibit organisms are called static, such as bacteristatic, fungstatic and algastatic materials

Antibacterial compounds as an antimicrobial agent have 3 types of action, namely bacteriostatic, bactericidal and bactericidal. Bacteriostatic mechanism of action is to inhibit protein synthesis by binding to ribosomes, while bactericidal prevents growth and causes death, but does not cause bacterial cells to lyse. In contrast to bactericidal, bactericidal works by making the lysis of bacterial cells. The lysis process of bacterial cells can be seen from the decrease in the number of cells or turbidity after the material is added (Brock and Madigan, 1994). The work of antibacterial compounds is influenced by several factors, including the concentration of antibacterial compounds used, the number and species of bacteria, temperature, the presence of other organic materials, and pH (Pelczar and Chan, 1988).

Some examples of compounds that have antibacterial activity are penicillin, cephalosporin, glycopeptide, tetracycline, chloramphenicol, aminoglycoside, sulfonamide, while compounds that have antifungal activity are amphotericin, flucytocin, griseofulin, imidazole and nystatin (Greenwood et al., 1992).

Antibiotics can be classified based on the antimicrobial spectrum, mechanism of activity, strain formation, biosynthetic properties and chemical structure. Classification of antibiotics based on chemical structure (Crueger, 1984) is as follows:

1. Antibiotics with carbohydrate groups
2. Antibiotics with a macrocyclic lactone group
3. Antibiotics with a quinone group
4. Antibiotics with amino acid and peptide groups
5. Heterocyclic antibiotics with nitrogen content
6. Heterocyclic antibiotics containing oxygen
7. Derivative A cyclic
8. Aromatic antibiotics
9. aliphatic antibiotics

Mechanism of Action and Uses of Antibiotics

Based on the mechanism of action, antibiotics are divided into several groups (Effionora,

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1990), namely:

1. Inhibits microbial cell metabolism.

With this mechanism of action, a bacteriostatic effect is obtained

2. Inhibits microbial cell wall synthesis

Antibiotics will inhibit the process of cell wall synthesis. The osmotic pressure inside the microbial cell is higher than outside the cell, so damage to the microbial cell wall will cause lysis, which is the basis of its bactericidal effect on sensitive microbes.

3. Antimicrobials that interfere with the integrity of the microbial cell membrane

Damage to the cell membrane causes the release of various components from the microbial cell

4. Antimicrobials inhibit microbial cell protein synthesis

5. Antimicrobials that inhibit nucleic acid synthesis of microbial cells

Antimicrobials that have this mechanism of action generally lack selective toxicity because they are cytotoxic to human cells.

In the field of animal husbandry and fish farming, antimicrobial agents are sometimes used to control disease attacks. Disease is one of the problems in livestock production. The safety and health of production animals is of utmost priority. In the UK, there are four antimicrobials permitted for fish, namely: oxytetracycline, oxolinic acid, amoxylin and co-trimazine (Alderman and Hasting, 1998). The recommended doses are presented in Table 1.

Table 1. Recommended dosage in UK

Generic name	Trade name	Fish species	Dosage (mgkg-1day-1)
Oxytetracycline	Aquatest	Atlantic salmon	75
		Rainbow trout	75
	Tetraplex	Atlantic salmon	75
Oxolinic acid	Aqualinic	Atlantic salmon, Rainbow trout	10-30
	Aquinox	Atlantic salmon	10-30
Amoxylin trihydrate	Aquacil	Atlantic salmon	40-80
	Clamoxyl	Atlantic salmon	80
	Micromox	Atlantic salmon	80
	Vetremox	Atlantic salmon	80
Co-trimazine	Sulfatrim	Atlantic salmon	15-30
	Tribissen	Atlantic salmon, Rainbow trout	15-30

Source: Alderman and Hasting (1998)

The use of this antibiotic invites many pros and cons, because of the impact it causes. Use of antibiotics in food must be careful. Because improper use can be fatal. The use of antibiotics in foodstuffs needs to pay attention to the following things:

1. Antibiotics can kill or inhibit microbial growth, but must not react with the ingredients contained in the product
2. Antibiotics no can disabled oleh component product
3. Antibiotics should not stimulate the formation of resistant microbial strains
4. Antibiotics should not be used as preservatives (food additives) in food for medicinal purposes

One of the properties of antibiotics why they are used as food preservatives is that they have high activity compared to preservatives,

but are expensive. Besides, the use of antibiotics can also cause dangers such as sensibility, supra-infection and resistance. The use of antibiotics in foodstuffs is often combined with processing processes such as the application of low pH in the canning process.

The requirements for an antibiotic that can be used as a preservative (Harry, 1975 in Effionora, 1990) are as follows:

1. Can kill or inhibit the growth of bacteria effectively
2. Non-toxic
3. Can be destroyed by digestive enzymes
4. Does not change the taste or smell of food
5. Not dangerous
6. Easy to use and detectable

Antibiotic Resistance in Bacteria

Synthetic antibiotics are widely used in various circles because they are easy to obtain and easy to apply. However, this antibiotic has weaknesses, including being able to cause resistance and be carcinogenic. In fact, the use of antibiotics has rules, both in the type, dosage, and method of use

Improperly and repeatedly can have an indirect impact, namely microbial resistance. The impact of using antibiotics can occur on the product itself or on the environment, which is very dangerous and can bring huge losses.

Drug residues for fish can affect sedimentary microorganism communities and stimulate the proliferation of antibiotic-resistant strains of pathogenic bacteria. In their report, Weston (1996 and Capons et al., 1996) stated that antibacterial residues have been found in marine sediments and invertebrates used in fish farming.This proves that the effect of antibacterial use does not only occur in ponds or farms that use antibacterial agents, but also in fish farming. it can also affect the surrounding environment that is close to the pond or farm, for example rivers, lakes, seas, etc. In other words, uncontrolled use of antibiotics can have a negative impact on the environment.

The increase in bacteria that are resistant to antibiotics in some areas of livestock or production animals over the years can have implications for human health. Transmission of antibiotic-resistant bacteria to humans can occur when we consume food containing antibiotic-resistant bacteria that is cooked imperfectly or cross contamination occurs from the raw food to ready-to-eat food. This needs special attention. The use of growth promoters in animal husbandry can also promote antibiotic resistance in pathogenic bacteria and provide opportunities for reproduction. Therefore its use must be really selective.

Antibacterial-resistant bacteria isolated from livestock have been widely reported abroad. The mechanism of resistance can be genetic or non-genetic. Genetically, resistance can occur by conjugation and transudation between the same strains, while non-genetic resistance can occur through excessive antibacterial administration, continuous or irregular low-dose administration (Soeripto, 1996). Resistant bacteria can threaten human or animal life because it can increase disease morbidity and mortality

due to treatment failure. In addition, treatment costs also increase because they have to use high doses of antibacterial or more than one type of antibacterial, or use new antibacterials that are expensive (Tollefson et al., 1999; Williams, 2000 cited by Soeripto, 2002).Bacterial resistance to antibiotics is also influenced by the environment. Good environmental management or health management is needed in the management of aquaculture

and other livestock. The role of the government and related agencies is also needed in dealing with this problem. Good cooperation between pond/pond managers, environmental experts and policy makers is needed. All information related to cultivation must be immediately conveyed to interested parties.

Natural Antibiotics From the Sea

Now many researchers are paying attention to the sea, because apart from being a source of food, the sea is also a source of medicine. Research into pharmaceuticals is aimed at anticipating the widespread issue of antibiotic resistance in bacteria. Natural antibiotics are antibiotic ingredients that come from natural products, such as plants, tubers, animals and microorganisms, both from land and sea.

The active ingredients are mostly distributed in marine organisms. Ocean metazoans that have the potential for antimicrobial active ingredients include sponges, soft corals, red algae and others. Even recently, sponges have attracted the attention of natural product researchers because they have been shown to contain active compounds (Murniasih and Satari, 1999). Antimicrobial compounds found in sponges include aeroplicinin-1 which is found in the Pseudocerasina and Verongia aeroppbha species (Martin, 1992 cited by Murniasih and Satari, 1999) and Minale (1994) cited Murniasih and Satari, 1999) succeeded in isolating the antimicrobial compound acanthellin. -1 of the type Acanthella acuta.

Suryati et al. (1997) in Suryati et al. (1999) have pioneered the use of bioactive content from the sea to overcome disease problems in aquaculture, including the bioactive content of sponges to treat bacterial, fungal and anti-biofouling diseases which provide quite exciting prospects for the future. Besides sponges, other marine biota are also reported to have bioactive content that is effective as a bactericide, including hydrozoans which are often given the nickname as pesticide in paradise because they are able to clean the environment from various diseases (Nybakken, 1982 as quoted by Suryati et al. 1999). One of its outstanding properties is that it can clean the environment from organisms that are around it, thus earning the nickname disinfectant from the sea. Suryati et al.

Ireland et al. (1989) quoted by Suryati et al. (1999) also reported that several species from the Coelenterata group from the Anthozoa, Hydrozoa and Schypozoa classes have bioactive compounds that have activity against several types of bacteria, fungi and viruses so that they are often dubbed bactericides from the sea.

Microalgae is one type of marine biota that has the potential as an antibiotic. Personal (1998) has investigated Chaetoceros gracilis to produce antimicrobial compounds. Crude extract of C. gracilis could inhibit the growth of Pseudomonas sp, Escherichia coli, and Bacillus subtilis bacteria with inhibition areas of 7-8 mm, 6-7 mm and 7-30 mm, respectively. Santioso (1998) also reported that Nitzschia sp, which is a type of marine diatom, also had an inhibitory effect on the growth of Bacillus subtilis, Escherichia coli and Pseudomonas sp bacteria.

Conclusion

To anticipate bacterial resistance to antibiotics, research has been developed on the exploration of natural antibiotics from the sea, such as sponges, sea corals, algae (microalgae and macroalgae), molluscs, coelenterates and so on. Research on marine products towards pharmaceuticals is very helpful in efforts to solve the problem of bacterial resistance. Indonesia's waters, which are rich in biodiversity, need to be

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utilized more and more. Many of our aquatic biota contain active and undeveloped substances. The development and application of aquatic biotechnology is very much needed.

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