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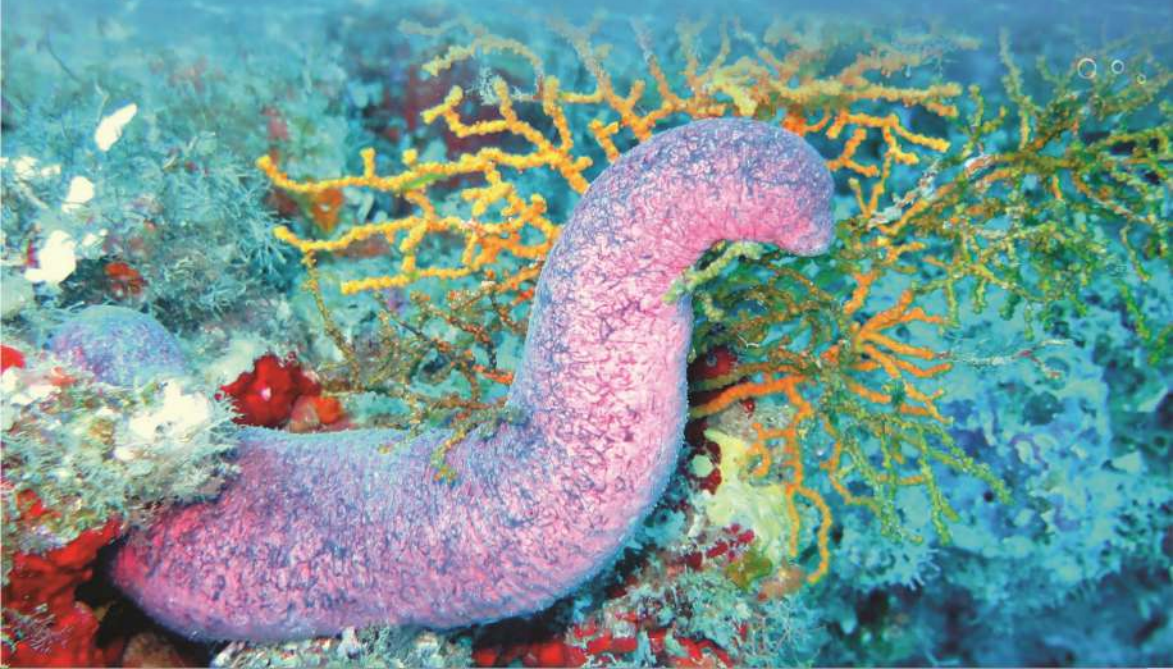
BIOACTIVE COMPOUND OF HOLOTHOROIDEA



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PREFACE

Praise be to Allah, gratitude is rightly poured forth to His presence. With the blessings, guidance, and favors from Him, the author has successfully completed the book entitled "Bioactive Compound of Holothuroidea" This book represents the author's concern for the utilization of natural resources derived from the marine biota of Indonesia.

Therefore, the existence of this book is undoubtedly a result of the contributions and assistance from all parties. Thus, on this occasion, the author extends appreciation and expresses gratitude to all those who have contributed significantly to the process of creating this book.

As imperfect beings, the contents of this book are still far from perfection. Thus, we earnestly welcome criticisms and suggestions from all parties. Finally, we hope that the presence of this book will be beneficial to all of us. Aamiin.

Bandung, August 2023

Author Team

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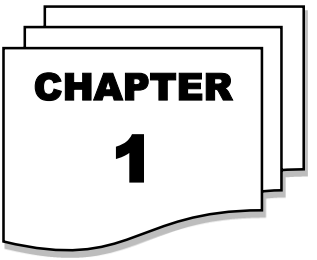


OVERVIEW BIOACTIVE HOLOTHOROIDEA

A. INTRODUCTION

Changes in lifestyle, such as diet and physical activity, increase the risk of developing diseases, which include diabetes, obesity, hypertension, cancer and others. Several prevention strategies have been tested, including the use of multiple bioactive components found in living things in the form of functional food ingredients. Sea cucumbers are a source of bioactive components that can be used in biopharmaceuticals, health foods, and industrial raw materials. Sea cucumbers have a high protein content and a variety of bioactive components. Sea cucumbers are invertebrates or thorn-skinned animals (Echinodermata) with an elongated cylindrical body and oral and aboral lines connecting the anterior and posterior parts as the axis. The potential for sea cucumbers from capture fisheries in Indonesia is quite significant, representing a 51.37% increase in average production.1

Sea cucumbers have been used and studied for a long time. The Chinese have known sea cucumbers as a food with medicinal properties since the Ming dynasty. Sea cucumber bioactive ingredients act as antioxidants (reduce cell and tissue damage), antibacterial, antifungal, antinociceptive (painkillers), and anti-inflammatory agents (fight inflammation and reduce swelling). Among the bioactive components are mucopolysaccharides, glucosamine and chondroitin sulfate, minerals and trace minerals, steroids, collagen, Omega 3 - DHA, and

EPA. Holothurians, also known as sea cucumbers, are marine invertebrates of the phylum Echinodermata.

B. GROUPING HOLOTHORUIDEA

Dendrochirotacea, Aspidochirotacea, and Apodacea are the three subclasses of Holothuroidea, and there are six orders: Aspidochirotida, Apodida, Dactylochirotida, Dendrochirotida, Elasipodida, and Molpadiida.2 Many sea cucumber species are industrially collected and dried for human consumption or pharmaceutical use, particularly in Asia. Sea cucumbers, as well as other economically valuable marine organisms, are still widely used due to their unique biological and pharmaceutical properties. Recent scientific efforts have concentrated on identifying sea cucumber bioactive constituents for nutritional use in food products or as drug candidates in the pharmaceutical sector. This review focuses on the historical benefits of sea cucumbers, in addition to their biological and medicinal characteristics.

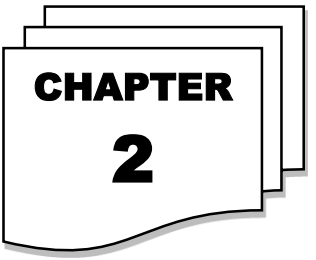
One option is to use herbal medicines derived from natural resources, particularly marine products, to reduce drug resistance through semi-synthesis or modification to increase bioactivity and minimize side effects. Indonesia is an archipelago of 17,500 islands, with 70% of its land area covered by water. The potential of Indonesia as a maritime country is vast; however, marine resources are underutilized in the pharmaceutical field, despite the fact that active compounds derived from marine ecosystems are distinct from organisms from terrestrial ecosystems.3 Chemical compounds with unusual functional groups, such as the presence of isonitrile and multi-halogenation, are frequently discovered, as is the presence of carbon skeletons. Active compounds derived from the sea can be studied further for potential drug applications. The National Cancer Institute in the United States of America tested various raw materials for cancer drugs and discovered that 4% of anti-cancer active ingredients originated from the sea, one of which is known as sea cucumber.4

Sea cucumber is a marine commodity that is widely available in Indonesian waters. So far, the families Holothuriidae and Stichopodidae,have been have significant economic value. With 457 tons exported in 2001, Indonesia was the major supplier of dried sea cucumbers. 40-80% of Indonesia's smoked or dried

sea cucumbers are exported to Hong Kong, Japan, Korea, Singapore, Taiwan, Malaysia, and Australia. Sea cucumber contains EPA and DHA, which aid in the development of brain nerves, wound healing, and antithrombotic properties. Furthermore, sea cucumber contains antihypertensive, antibacterial and antifungal, anticancer, and anticoagulant bioactive ingredients.5

Several studies have found that various compounds, such as sulfated glycans, glycosaminoglycan, triterpene glycosides, cucumariosides, deschinosides, saponins, holothurin, stichoposides, frondoside, fucoidan, and sphingoid. According to the literature, more research into the benefits of sea cucumber for human health is needed.

The purpose of this review is to provide a detailed analysis of the chemical composition, active compounds, including chemical substances and peptides, of Holothuridae sea cucumber as therapy. In addition, to determine the mechanisms of action of sea cucumbers in therapy. It is hoped that this study will lead to sea cucumbers being used as one of the candidates for new drugs in overcoming the problem disease in Indonesia.



COMPOUND CONCEPTS

A. DEFINITIONS OF COMPOUNDS

Compounds are substances that can be formed in combination with elements with these subdivisions. A compound must be made by a chemical reaction between two or more elements in order to go through the reactions in formation. Compounds are substances formed by two or more elements. Through chemical reactions, compounds can be broken down into their constituent elements. In addition, the compound is also defined as a single substance that can be broken down into other simpler substances through chemical reactions. An example of a compound that we often encounter in everyday life is water. Water is a combination of the elements hydrogen (H) and oxygen (O) with the chemical formula, namely H20. Through chemical reactions, water can be decomposed back into hydrogen and oxygen. Even though at atmospheric pressure, hydrogen and oxygen are both gaseous, when they unite and bond with each other, their form can turn into a liquid. (Alex, 2023),

A compound is a single substance that can be broken down into two or more elements. Compounds have several elements that combine chemically with each other, so that the symbol for a compound consists of several element symbols. Analysis to find the constituent elements of a compound is usually called qualitative analysis, whereas if the analysis finds a comparison of each

number of elements in a compound, it is called quantitative analysis. (Detikedu, 2021)

A substance has properties that are distinct from its components. For example, in 2 hydrogen atoms which can combine with one oxygen atom to form the presence of a water molecule (H_2O). Types in one substance can be divided into 2 or more elements by means of chemical reaction processes. In general, individual substances are in the form of water compounds (H_2O), salt (NaCl), sugar ($C_{12}H_{22}O_{11}$) and others. (Alex, 2023),

B. KINDS OF COMPOUNDS

The following are various types of compounds, namely:

1. Ionic Chemical Compounds

Ionic compounds are chemical compounds made of ionic elements. The Ionic element is used as one using the elliptical style. These compound bonds are called ionic bonds. Ionic compounds are a type of compounds that are completely neutral in nature. But the ions that are formed have positive ions and negative ions. Positive ions are called cations and negative ions are called anions. Examples of ionic compounds include sodium chloride with (Na^+) and (Cl^-). Potassium chloride (K^+) and (CL) and so on.

Ionic compounds consist of cations (metallic elements) and anions (non-metallic or polyatomic elements). Ionic compounds can be basic compounds or salts. The ionic junction formula is determined by the cation and anionic charge equations.

$$\text{Formula : } Ax^+ + By+ \rightarrow AyBx$$

How to write ionic compound names:

a. The name of the cation is on the front and the name of the anion is on the back, the index number is not written.
b. Cations are named after the metallic elements. If the metals have a different oxidation state (biloxes), the oxidation states of the metals are written with Roman numerals in parentheses.
c. Monotomist or Polyatomous anions without elemental oxygen are called "-ide" endings. Polyatomic anions containing the element oxygen are given

the suffix names "-at" or "-it" according to the number of O atoms, except for the OH^- anion.

Following are a number of types of cations and anions. (Alex, 2023),

Rumus Kation	Nama Kation	Rumus Anion	Nama Anion
Na^+	Natrium	OH^-	Hidroksida
Mg^{2+}	Magnesium	Cl^-	Klorida
Fe^{2+}	Besi(II)	NO_3^-	Nitrat
Cu^+	Tembaga(I)	SO_4^{2-}	Sulfat
NH_4^+	Amonium	CrO_4^{2-}	Kromat

Example :

- NaOH = sodium hydroxide
- KNO_3 = potassium nitrate
- $FeCl_2$ = iron(II) chloride
- K_2CrO_4 = potassium chromate

2. Molecular Compounds

Molecular compounds are composed of non-metallic elements. This chapter will only discuss methods for naming molecular binary compounds (molecular compounds containing two types of elements).

There are 2 ways to write molecular compounds:

a. First

1) Elements farther to the left of the periodic table of elements are listed in front. Except for compounds containing oxygen and the halogens (except fluorine), oxygen is written on the back. If the elements are in a group, the bottom is written on the front.
2) Specifies the Bilox of the elements to write to and then the Bilox value with Roman numerals in brackets. The back element is named after the "-ida" ending.

Example :

- N_2O_5 = nitrogen(IV) oxide
- SO_3 = sulfur(VI) oxide

b. Second

1) Elements farther to the left of the periodic table of elements are listed in front. Except for compounds containing oxygen and the halogens (except fluorine), oxygen is written on the back. If the elements are in a group, the bottom is written on the front.
2) Enter the number of elements in Latin (mono, in, Tri, Tetra, etc.). But if the element in front is only 1, it doesn't have to be written "Mono-". The element behind it is called the “-Ida” suffix.

Example :

- N_2O_5 = nitrous pentaoxide
- SO_3 = sulfur trioxide

3. Oxide Chemical Compounds

Oxide compounds are a type of chemical compound whose constituent elements consist of oxygen and other elements. In general, this compound is formed because there is an oxidation element that has oxygen in the air.

Oxide compounds are compounds formed by oxygen atoms with other atoms. The presence of oxygen atoms as a characteristic of oxide compounds. Based on the elements that form oxide compounds, oxide compounds can be divided into two types, namely metal oxide compounds and non-metallic oxides. This classification is simplified in the following chart:

Figure 2.1 Oxide compounds

Broadly speaking, the reasons underlying the separation of the field of study of organic compounds and inorganic compounds are:

1. There are far more organic compounds than inorganic compounds.
2. All organic compounds contain carbon atoms, which are unique in terms of their ability to form chains with fellow carbon atoms, and have distinctive properties.

No	Organic Compounds	Inorganic Compounds
1	Most come from living things and some of the results of synthesis	Derived from mineral natural resources (not living things)
2	Organic compounds are more flammable	Non-flammable
3	The structure is more complicated	Simple structure
4	All organic compounds contain the element carbon	Not all inorganic compounds have the element carbon
5	Only soluble in organic solvents	Soluble in water or organic solvents
6	CH_4, C_2H_5OH, C_2H_6 etc.	NaF, NaCl, NaBr, NaI etc.

1. Organic Chemical Compounds

Organic compounds are a type of chemical compounds that hold as components carbon and hydrogen as the most important elements. But in these compounds there are also elements such as oxygen, halogens, sulfur and phosphorus.

2. Acid Chemical Compounds

An acidic compound is a type of chemical compound having the general formula HA. However, these compounds are dissolved in water and will be pH below 7. Acidic compounds give H+ ions in other compounds (bases). Another opinion explains that acids are compounds that contain H + ions and anions.

The way it's written is to write the word "acid" and follow the name of the anion.

Example :

- HCl = hydrochloric acid
- HF = hydrofluoric acid
- H_3PO_4 = phosphoric acid

3. Alkaline Chemical Compounds

A basic compound is a kind of chemical compound that accepts or absorbs H+ ions. This junction has a pH greater than 7 and gives OH^+ ions.

C. COMPOUND MOLECULES

1. Water (H_2O)
   Water is a compound consisting of two hydrogen atoms and an oxygen atom. Water is a compound that is widely found in nature and is an important compound of living things.
2. Carbon dioxide (CO_2)
   Carbon dioxide is a compound consisting of two oxygen atoms and a carbon atom. Carbon dioxide is a gas and is required by plants in photosynthesis and excreted by animals in respiration.
3. Vinegar Acid (CH_3COOH)
   Acetic acid or acetic acid is an organic compound consisting of the elements carbon, hydrogen and oxygen, and is widely used as a food flavoring.
4. Kitchen salt (NaCl)
   Table salt is a compound consisting of sodium (Na) and chlorine (Cl). Salt from the kitchen will dissolve on top of the water, and this salt gives a salty taste to the tongue.
5. Methane (CH_4)
   Methane is the simplest hydrocarbon compound, often found as a gas and is the main component of natural gas. Most of the methane is used for fuel, such as LPG gas cylinders for gas stove fuel.

6. Acetylene (C_2H_2)
   Acetylene, or by the systemic name Etuna, is a chemical compound for the formula C2H2. Acetylene is the simplest hydrocarbon compound from ALCON. Acetylene is widely used as a fuel for metal welding, metal cutting, underground lighting and plastic raw materials.
7. Table sugar ($C_{12}H_{22}O_{11}$)
   Table sugar or sucrose is a naturally occurring carbohydrate found in many plants. Kitchen sugar makes a sweet taste on the tongue.
8. Ammonia (NH_3)
   Ammonia is a compound with nitrogen and hydrogen components. Ammonia is a gas that has a characteristic rotten smell, like rotten eggs.
9. Sulfuric acid (H_2SO_4)
   Sulfuric acid is a viscous, colorless liquid that dissolves in water. Sulfuric acid is widely used in batteries.
10. Silica (SiO_2)
    Silica is a compound of silicon and oxygen which is the main compound of sand.

D. CHARACTERISTICS OF COMPOUNDS

The following are the characteristics of the compound, namely:

1. Is a single substance
2. is formed from two or more elements of different types with a certain and fixed ratio
3. The properties of a compound are different from the properties of its constituent elements
4. Compounds can be broken down into their elements by chemical means

Another opinion explains that chemical compounds have 4 characteristics, including the following.

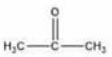
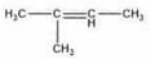
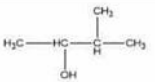
1. Formed from 2/ more elements arranged in ordinary chemical reactions.
2. Has a fixed composition ratio.
3. It loses its original substance properties when it becomes a compound.
4. Can be broken down chemically, but not physically.

E. COMPOUND STRUCTURE

1. Nomenclature of Organic Compounds

Organic compounds are chemical compounds containing carbon that have certain properties, except for carbides, carbonates and carbon oxides. In the naming system, organic compounds are relatively more complex than inorganic compounds. Not only based on molecular formulas, but also based on chemical structural formulas and cluster functions. In this table, we will only discuss the simple nomenclature of organic compounds.

Table 2.1 Nomenclature of Compounds

Gugus Fungsi*)	Rumus Senyawa	Rumus Struktur*)	Nama IUPAC
Alkana	CH_4		Metana
Keton / Alkanon	C_3H_6O		2-propanon
Alkena	C_5H_{10}		2-metil-2-pentena
Alkohol / Alkanol	C_4H_9OH		3-metil-2-butanol
Aldehida / Alkanal	CH_2O		Metanal
dll.			

2. Nomenclature of Inorganic Compounds

Inorganic compounds are chemical compounds that do not contain carbon. Inorganic compounds are grouped into ionic compounds, molecular compounds, and acids. (Alex, 2023)

3. Naming of Compound Formulas

Name a compound by writing the name of the metal element first, followed by the name of the non-metal element and ending with -ide. If the compound consists of non-metallic elements, the name of the compound uses a prefix which states the number of atoms of the constituent elements. The prefixes used are as follows:

Quantity	1	:	Mono
Quantity	2	:	Di
Quantity	3	:	Tri
Quantity	4	:	Tetra
Quantity	5	:	Penta
Quantity	6	:	Heksa
Quantity	7	:	Hepta
Quantity	8	:	Okta
Quantity	9	:	Nano
Quantity	10	:	Deka

Examples of naming compounds:

- N_2O_3 (nitrogen trioxide)
- NaCl (sodium chloride)
- PCl_5 (phosphorus penta chloride)

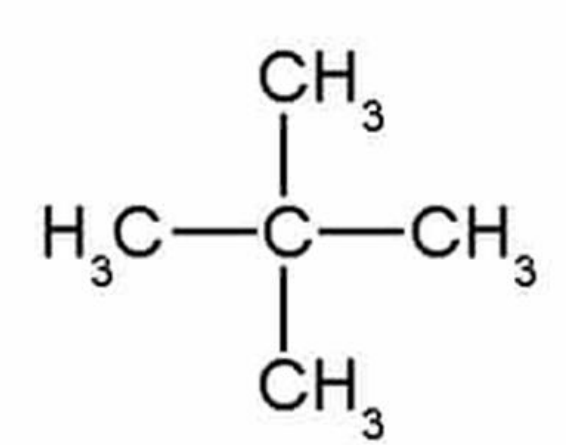
F. TYPES OF COMPOUNDS

Based on the origin of its constituents, compounds are classified into two types, namely organic compounds and inorganic compounds.

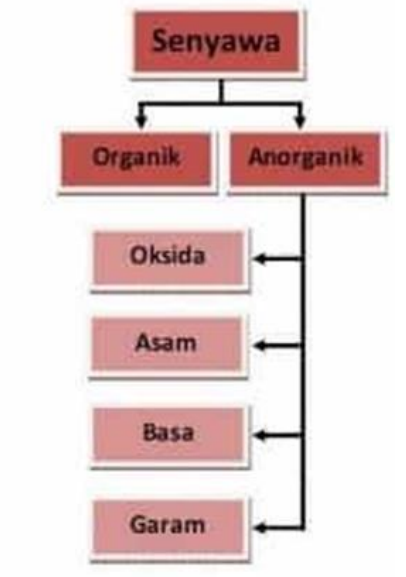
1. Organic Compounds

Organic compounds come from living things or from the process of photosynthesis. This compound consists of the element carbon (C) as its main sequence. The nature of organic compounds is not easily soluble in water, but will dissolve when mixed with organic solvents as well. In addition, due to its constituent elements in the form of carbon (C), organic compounds tend to burn easily.

Organic compounds are defined as compounds built by the element carbon as its main framework which binds other non-metallic elements (hydrogen, oxygen, nitrogen). These compounds generally come from living things or are formed by living things (organisms). These compounds are easy to find, such as urea or urea found in urine (urine). Granulated sugar or saccharose which is abundant in sugarcane and alcohol is the result of fermentation from the sea of sugar.



Compounds and salt forms, shown in the following chart:



Examples of Organic and Inorganic Compounds

a. Organic compounds: sugar ($C_{12}H_{22}0_{11}$), alcohol (C_2H_3OH), and urea ($CO(NH_2)^2$).
b. Inorganic compounds: water (H_2O), salt (NaCl), carbon dioxide (CO_2), $CaCo_3$ (Calcium Carbonate), NaOH (Sodium Hydroxide), and SiO_2 (Silicon Dioxide).

2. Bioactive Compounds

Bioactive compounds are active compounds that include secondary metabolites. Secondary metabolites are a unique and limited component of metabolic results, which are sometimes only found in certain groups, usually not needed by organism cells to live, but play a role in the interaction of organism cells with the environment, ensuring the survival of these organisms in their living ecosystem Verpoorte and Alfermann 2000 .

Alkaloids are the largest group of secondary metabolites in plants and up to now as many as 5500 types of alkaloids have been known. In general, alkaloids are alkaline compounds containing one or more nitrogen atoms as part of a cyclic system. Alkaloids are often toxic to humans, but some alkaloids have pharmacological activity and are widely used in the health sector Harborne 1987.

These compounds in plants function to protect themselves from predators because they are toxic to animals such as insects, as a growth stimulant and regulator and help plant metabolic and reproductive activities. It is derived from the acyclic C 30 hydrocarbon, namely squalene. These compounds have complex cyclic structures, most of which are alcohols, aldehydes or carboxylic acids. Triterpenoids can be classified into four groups, namely triterpenes, steroids, saponins and cardiac glycosides. Triterpenes found in plants serve as a protective barrier against insects and microbial attacks Harborne 1987.

Steroids are found in almost all types of living systems. Steroids found in animals act as hormones, besides that steroids are also widely used as drugs Verpoorte and Alfermann 2000. Saponins are triterpene and sterol glycosides which are detected in more than 90 plant families. Saponins are compounds that are like soap which can be detected based on their ability to form foam and hemolyze blood cells.

The final group of triterpenes are cardiac glycosides or cardenolides. Some cardiac glycosides are poisons, but there are also those that have pharmacological properties, especially against the heart, as reflected in their name Harborne 1987.

Flavonoids are compounds that dissolve in water and can be extracted with ethanol 70 and remain in the water layer after the extract is shaken with ether. Flavonoids are generally found in plants. Flavonoids that are abundant in

nature are flavones and flavonols, while isoflavones and biflavonols are found only in a few plant families Harborne 1987.

Sabir 2005 in his research explained that flavonoid compounds have the ability to inhibit bacterial growth with several different mechanisms, including flavonoids causing damage to the permeability of bacterial walls, microsomes and lysosomes as a result of interactions between flavonoids and bacterial DNA Bryan 1982; Wilson and Gisvold 1982 are referred to in Sabir 2005, while Mirzoeva et al. 1997 referred to in Sabir 2005 in his research argued that flavonoids are able to release energy transduction to the bacterial cytoplasmic membrane, while also inhibiting bacterial motility.

A different mechanism was suggested by Di Carlo et al. 1999 and Estrela et al. 1995 referred to in Sabir 2005 which states that the hydroxyl groups present in the structure of flavonoid compounds cause changes in organic components and nutrient transport which will eventually lead to toxic effects on bacteria. (Ika Pranata Wahyu Daluningrum, 2009)

G. PROPERTIES OF COMPOUNDS

Each compound has different properties from its constituent elements. Compounds can only be broken down into their constituent elements by a chemical reaction. Under the same conditions, a compound can have a different form from its constituent elements.

The physical and chemical properties of compounds differ from the elements that make them up. For example the reaction between two hydrogen atoms (2H) and one oxygen atom (O) can form a water molecule (H_2O).

In short, compounds have 5 properties that we can distinguish between one compound and another. Among them are as follows.

1. Compounds can be formed through chemical reaction processes
2. The constituent components present in the compound have a certain ratio that is fixed.
3. Compounds cannot be separated from their constituent components through physical reactions.
4. Compounds can be categorized as single substance compounds.
5. Compounds have certain properties that differ from their constituent elements.

H. THE ROLE OF ORGANIC CHEMISTRY IN DAILY LIFE

Organic chemistry in its role in everyday life is very much through other branches of science. Almost the same reactions in living organisms involve organic substances and the main ingredients of living organisms, namely proteins, carbohydrates, lipids, (fats), nucleic acids (DNA, RNA), cell membranes, enzymes, hormones are organic compounds.

organic compounds that we see everyday are gasoline, clothing, wooden furniture. paper for books, medicines, plastic packages, film for portraits, perfumes, carpets, etc. we also often hear various news such as polyethylene, epoxy, "styrofoam". nicotine, unsaturated fat, cholesterol and octane number.

CHAPTER
3

HOLOTHOROIDEA

A. THE DEFINITION OF HOLOTHUROIDEA

Holothuroidea in Indonesian is called sea cucumbers or sea cucumbers. Is a group of invertebrate animals that are found in many oceans around the world. They move slowly and live on the ocean floor. In the marine ecosystem, sea cucumbers are a group of animals that play a very important role in the ecosystem. They are deposit and suspension feeders.

Sea cucumbers or better known as sea cucumbers are one of the organisms from the phylum Echinodermata class Holothuroidea. Sea cucumbers (Holothuroidea) can be found or found throughout coastal waters, from shallow tidal areas to deeper waters for their life, sea cucumbers prefer polluted free waters, and the water is relatively calm. In general, each species has a specific habitat, for example, the white sea cucumber (Holothuria scabra) is found in seagrass-covered waters, while the Koro sea cucumber (Muelleria leconoro) and sand sea cucumber are found in deeper waters (Martoyo et al. al., 2007). The main habitat of sea cucumbers is on seagrasses and corals. The spread of sea cucumbers in Indonesia is very wide, including; coastal waters of Madura, East Java, Bali, Sumba, Lombok, Aceh, Bengkulu, Bangka, Riau and its surroundings, Belitung, Kalimantan (west, east and south), Sulawesi, Maluku, Papua and the Thousand Islands (Martoyo et al., 2007) . In (Handayani et al., 2017).

Sea cucumbers are a group of marine biota whose presence does not attract attention, both from those who should be concerned about biodiversity and nature conservation, let alone the general public. The species richness of sea cucumbers as a whole may yet be uncovered. Meanwhile, several types of commercial sea cucumbers have experienced exploitation pressure. Several types of sea cucumbers are fishery commodities that are traded internationally. At this time sea cucumbers were not only hunted for expensive species, but also for cheap species which were not a concern at first. Exploitation pressure on these types of sea cucumbers has caused their natural population to decline greatly. This can be a dilemma, because there is no effort to manage and conserve it. If there is an extinction of a type of sea cucumber, it means the loss of germplasm which may not have been utilized (Darsono, 2007).

Sea cucumbers are a group of marine invertebrates from the class Holothurioidea (Phylum Echinodermata), divided into six nations (orders), namely Dendrochirotida, Aspidochirotida, Dactylochirotida, Apodida, Molpadida, and Elasipoda. The species richness of sea cucumbers is estimated to be no less than 1,200 species (BAKUS, 1973) mainly spread in tropical shallow waters. Types of commercial sea cucumbers, especially from the tropics, belong to the Aspidochirotida nation of the Holothuriidae and Stichopodidae tribes, including the genera Holothuria, Actinopyga, Bohadschia, Thelenota and Stichopus. globally (Bruckner et al., 2003). Among these types, many are found in Indonesian waters as identified by Darsono (1995). In (Darsono, 2007). (Gery Purnomo, 2020)

B. HOLOTHUROIDEA CLASSIFICATION

In animal taxonomy, Holothuroidea is a class of members of the phylum Echinodermata. Currently around the world there are about 1,200 species of members of this class that have been identified. The 1,200 species are grouped into 5 Orders.

The full classification of Class Holothuroidea is as follows:

1. Kingdom : Animalia
2. Phylum : Echinodermata
3. Sub Phylum : Echinozoa
4. Class : Holothuroidea

5. Order : Apodida, Aspidochirotida, Dendrochirotida, Elasipodida and Molpadida.

C. CHARACTERISTICS OF THE HOLOTHUROIDEA

The general shape of the sea cucumber varies from nearly moon to elongated or shaped, like a worm. Body size generally ranges from 10 to 30 centimeters. The smallest species can reach a length of less than 3 centimeters and the largest can reach a length of up to 1 meter (Stichopus).

The body structure that extends from the Holothuroidea causes the body part that touches the substrate to be the side of the body, not the mouth. The ventral side consists of three ambulacral (trivium) or also called the tread, while the dorsal side consists of two ambulacral areas. Podia in this group of animals have been reduced and scattered randomly throughout the body.

The mouth is always surrounded by 10 to 30 tentacles and is a modified buccal podia. The epidermis of Holothuroidea is not ciliated and is covered by a thin cuticle. The thick dermis layer is composed of microscopic ossicles (called sclerites) which are very important for the identification of the species of this group of animals.

D. MOVEMENT

Sea cucumbers are soft animals that live on the surface of the seabed or live in sand or mud. Species that have podia will crawl/crawl along their tread, like the asteroidea. Meanwhile, species that do not have podia, including the orders Apodida and Molpadiida, are driller species. While species belonging to the order Elasipodida, have very large podia so they can be used for walking. In fact, nearly half of its species are able to swim.

E. EVISERATION AND REGENERATION

Sea cucumbers are generally able to secrete white, pink or red sticky threads from the anal area. The threads come from organs called the Tubules of Cuvier which are located in the respiratory area. In some species it even contains holothurin poison. Once removed, the Tubules of Cuvier will regenerate.

Another common phenomenon is evisceration, in which part of the intestine and its associated organs is ejected either posteriorly or anteriorly. Evisceration can occur naturally, namely in conditions of shortage of food supplies or in the process of disposing of waste stored in the network. Evisceration is also followed by regeneration of the lost parts.

F. NUTRITION

Sea cucumbers are deposit or suspension feeders. Species that settle on a substrate, for example the genus Cucumaria, are suspension feeders. Meanwhile, mobile species, such as Stichopus, are deposit feeders. The mouth is located at the base of a collection of tentacles, opens towards the pharynx and is surrounded by a calcareous ring of ossicles. The pharynx opens to the esophagus and stomach (which functions more as a gallbladder). The digestive tract ends in the cloaca and food waste exits through the anus.

G. RESPIRATION, CIRCULATION AND EXCRETION

Gas exchange (Respiration) in most of the Holothuroidea is carried out by a system called the respiratory tree. The system is located in the body cavity, on the right and left of the digestive tract. Members of the orders Elasipodia and Apodia do not have a respiratory tree, they obtain oxygen from the entire surface of their bodies.

Most of the ammonia which is the rest of the metabolism is excreted by diffusion in the respiratory tree. Particulate wastes, as well as nitrogenous material in the form of crystals, are carried by coelomocytes from various parts of the body to the gonadal tubules, respiratory tree and intestines. then ejected through these parts. The hemal system in this class plays a role in the transport of gases and nutrients. Peritoneal cilia provide a flow of body fluids that serve as a medium for general circulation in the body.

H. NERVOUS SYSTEM

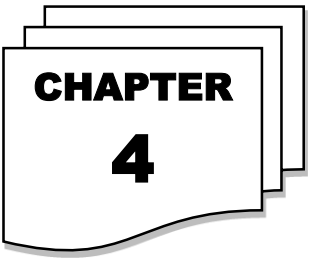
The circummoral nerve environment is located on the buccal membrane, i.e. on the tentacles. Five radian nerves descend leaving a loop of nerves along the ambulacral.

I. REPRODUCTION

The Holothuroidea are dietic and have a single situated gonad, with the gonophores located between the bases of the two tentacles. During spawning, the eggs are caught by the tentacles and transferred to the underside or back of the body for incubation. Fertilization and development take place in the body cavity and the young leave the mother's body through an opening in the anal area.

J. BENEFITS OF HOLOTHURIDEA FOR HUMANS

Holothuridea has many benefits for humans, it can be consumed by humans especially in China. Sea cucumbers are written in traditional Chinese medical books



STUDY ANALYSIS BIOACTIVE HOLOTHOROIDEA

A. LINKAGE AND CLUSTERING OF THEMES IN POTENTIAL BIOACTIVE COMPOUND HOLOTHOROIDEA

This category describes the ideas contained in 132 visualization techniques discovered in 148 articles that are related to the study's theme. A VOSviewer review also revealed 12 concept clusters (see table 1). Figure 4.1 depicts the concept identities deduced from the cluster density view. Furthermore, the color code for each cluster is used to identify the key concepts of each cluster. The goal is to identify as many themes as possible that have been frequently discussed in previous research and to make them available for future use. Figure 4.1 depicts the density of clusters as indicated by the different colors of each cluster.

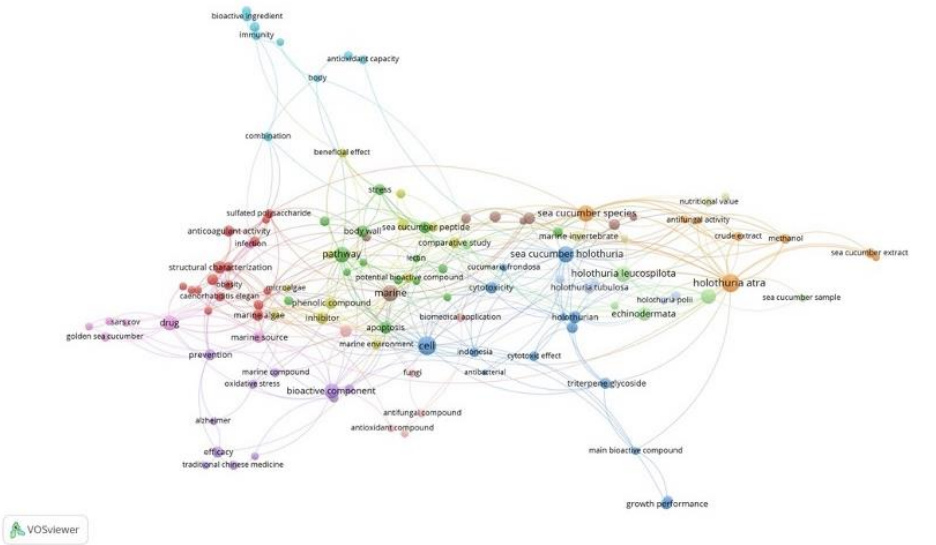


Figure 4.1 depicts the density of clusters while using multiple colors for each cluster.

The identifying in the pattern of mapping in Figure 4.1 can assist scientists, terribly new ones, get a head start on their research. While people discover a subject of interest in a certain area about which they are curious, they can use this study to read articles on that topic. Cluster 1 consists of, antibacterial; anticancer; apoptosis induction; bioactive metabolite; cytotoxic effect; holothurian; inhibition while Cluster 2 purification; Bioactive compound; bioactive polysaccharidea; anticoagulant activity; glycosaminoglycan; hydrolysate; lectin; sea cucumber peptide; sulfated polysaccharidae; immunity In the case of Cluster 3, Pathway; apoptosis; macrophage; antiinflammatory effect; molecular mechanism; active substance; and as for Cluster 4, Holothuria Scabra; cancer; inhibitor; phytochemical; molecular docking; antifungal compound; antioxidant compound; medicine; bioactive molecule; novel bioactive compound.

Furthermore, Cluster 5 SEA; echinoderm; marine invertebrata; crustacean; brown algea; urchin;, while Cluster 6, DISEASE; oxidative stress; antiiflamatory activity; oxidative stress; alzheimere; fucoidan; marine compound. This clustering will assist researchers who would like to explain the topic of H.scabra in defining that what concepts are associated. For example, if a researcher prefers cluster 3, the concept of H.scabra bioactive compound should be the

basic foundation for the body literature. Furthermore, researchers can use the reference manager to search for similar literature utilizing keywords from Cluster 2, that are cancer; inhibitor; phytochemical; molecular docking; antifungal compound; antioxidant compound; medicine; bioactive molecule; novel bioactive compound, and more.

Cluster	Concept Name	Total
Cluster 1	Holothurian, antibacterial; anti-cancer; apoptosis induction; bioactive metabolite; cytotoxic effect; inhibition	18
Cluster 2	purification; Bioactive compound; bioactive polysaccharidea; anticoagulant activity; glycosaminoglycan; hydrolysate; lectin; sea cucumber peptide; sulfated polysaccharidae; immunity	18
Cluster 3	Pathway; apoptosis; macrophage; antiinflammatory effect; molecular mechanism; active substance;	16
Cluster 4	Holothuria Scabra; cancer; inhibitor; phytochemical; molecular docking; antifungal compound; antioxidant compound; medicine; bioactive molecule; novel bioactive compound	14
Cluster 5	Sea; echinoderm; marine invertebrata; crustacean; brown algea; urchin;	14
Cluster 6	Disease; oxidative stress; antiiflamatory activity; oxidative stress; alzheimere; fucoidan; marine compound	10
Cluster 7	Crude Extract; methanol; holothuria atra; sea cucumber species; hepatoprotective activity;	10
Cluster 8	Cell; main bioactive compound; protective; triterpene glycoside; ethanol	9
Cluster 9	Antibacterial Activity; therapeutic application; immunostimulary activity; antioxidant capacity	8
Cluster 10	Drug; marine bioactive compound; sars cov; infection; response	7
Cluster 11	Bioactive; iimunity; nutraceutical	5
Cluster 12	Holothoroidea; h.leucospilota; echinodermata; anti inflmmatory effect	5

In the case of cluster 1 (Holotoruidea (sea cucumber) effect), the related article as a reference would be one written by Wulandari et al.6, which explained The bioactive compound present in sea cucumber could constrain cancer cell growth through a number of mechanisms. The results show that sea cucumber contains 44-82% protein, amino acids, fatty acids, collagen, peptides, and micro essentials. Each sea cucumber species produced unique secondary metabolites that can be used as anticancer agents. Furthermore, sea cucumber also contains bioactive ingredients as antihypertensive, antibacterial and anti-fungal, anti-cancer, and anticoagulant.7,8 The same discussion is also found in clusters 6, 7, 9, 10, and 11.

Clusters 2 and 3 examine the bioactive molecular components of the Holothoroidea as well as the underlying molecular mechanisms. A study conducted by Suryaningrum et al. can explain the above.9 According to Suryaningrum, sea cucumbers contain mucopolysaccharides such as glucosamine sulfate and chondroitin sulfate. Glucosamine is a component of glycoproteins, proteoglycans, and glycosaminoglycans, all of which play a role in proteoglycan synthesis. By inhibiting fibrin monomers and increasing plasmin activity, glycosaminoglycans can prevent blood clotting. The fatty acids found in sea cucumbers, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are fatty acids that our bodies require. EPA, in particular, can reduce fibrinogen levels, while DHA plays an important role. The development of the nervous system can help to improve memory and learning abilities. Sea cucumbers contain terpenoid compounds, saponins, and polysaccharides, triterpene glycosides and lectins that can inhibit tumor growth.10

Cluster 4 focuses on H. scabra research on novel bioactive compounds with anticancer, antioxidant, antibacterial, and antifungal properties. Pranweerapaiboon et al. discovered that the methanol extract of H. scabra inhibited the growth of cancer cells in vitro.11 Meanwhile, Shi et al. reported in a review article that the bioactive components of H. scabra have anti-cancer, anti-bacterial, antioxidant, and even hepatoprotective potential.12 The author chose this cluster because H. scabra is widely distributed in Indonesia, implying that this extract is widely used. Furthermore, few experimental and clinical studies have been conducted specifically on the bioactive potential of H. scabra

and its potentiation effect. Further research is required to demonstrate the extract's effect both experimentally and clinically.

Cluster 5 discusses marine biota species that are commonly used as research centers, one of which is the Holotoroidea. This is consistent with the findings of Karthikeyan et al. research's.13 Cluster 8 focuses on bioactive components that are commonly used in cell-based in vitro studies, as summarized in a review by Kalinin et al.14

B. THE DOMINANT THEME IN BIOACTIVE COMPOUND ON HOLTHOROIDEA

Word Frequency Queries investigates the most frequently occurring words in study results. As a result, words that have a similar significance could be categorized within the same group to use this analytical model. Based on the data analysis findings from the 148 articles, the dominant themes analyzed by past study were bioactive, holothuria, sea cucumber, and scabra. As a consequence, this might be defined as the whole focus of this subject's research. This is explained further in, with a concentrate on words in bold.

Cancer, apoptosis, antioxidant, antibacterial, anti-inflammatory, antifungal, and hepatoprotective are all important terms to remember, given that the potentiation of the effects of H. scabra extract is quite extensive and involves complex molecular mechanisms. Aside from that, the docking mechanism is an issue that must be investigated as part of the preliminary reference before proceeding to the experimental phase in the laboratory or clinical trial.

Figure 4.2 The dominant theme in watershed governance studies

C. THE CATEGORIZATION OF HOLOTHOROIDEA BIOACTIVE COMPOUND STUDY THEMES

There seem to be 9 main clusters with in Holothoroidea Bioactive Compound study (see Figure 3), based on the cluster analysis with NVivo 12 plus derived from 148 Google Scholar publications, notably Holothoruidea scabra, Purification, Crude extract, Sea, Holothurian, Antibacterial activity, cell, disease, and Aposthicopus japonicus. Furthermore, the categorization of the study themes results indicate that studies upon the Holothoroidea bioactive compound describes a lot about nine themes.

Figure 4.3 The categorization of watershed governance study themes

Various species have adapted to survive in cruel and difficult conditions in the marine environment. Because of their ability to produce compounds valuable for therapeutics, marine organisms are getting interest. The role of marine organisms in developing new therapeutic effects is becoming a promising area, owing to the breadth and richness of the marine environment. Right now, there is a lot of interest in biologically active compounds derived from natural resources, especially compounds that can act efficiently on molecular targets associated with various diseases.

Many studies have been conducted on marine invertebrates, primarily sponges, mollusks, tunicates, coelenterata and crustaceans. Marine bacteria and fungi, in addition to marine macro-organisms such as sponges, algae, and corals, have been discovered to produce unique bioactive substances with unique and intricate chemical compositions that could hold the key to the development of new drugs. The use of marine bioactive compounds is important to therapeutic applications in a wide variety of diseases.

Marine natural products (MNP) exhibit a wide range of pharmaceutically significant bioactivities, such as antibiotic, antiviral, neurodegenerative, anticancer, and anti-inflammatory properties. The MNP discussed in this review is from the holothuria class, with the species specification being H.scabra, which has potential antioxidant, antifungal, and anti-cancer effects. As a consequence, the review concentrates on the importance of strong relevance bioactive compounds, their contribution to various diseases, and their possible contribution to humanity.

D. THE RELATIONSHIP BETWEEN THE TOPICS OF BIOACTIVE COMPOUNDS OF H.SCABRA

Based on the clustering findings with NVivo 12 plus, there's a significant link between H.scabra, MNP, antioxidant activity, antibacterial activity, antifungal activity, and cancer (Table 2). Despite the reality that such a correlation has different Pearson's coefficient values, the fact that H.scabra, as well as the five selected topics, affirms that this research needs to be balanced with the issues of MNP, antioxidant activity, antibacterial activity, antifungal activity and cancer.[15,16,17.]

The marine environment is a rich source of chemical structures with many beneficial effects. Marine macro-organisms have been proven to produce new secondary metabolites with specific chemical structures that can be key to discovering new drugs and significant compounds that act on molecular targets in various diseases.

One of the many marine biotas explored to study the potential effects of the bioactive compounds it contains is H.scabra, which causes a close correlation between Marine Natural Products and the possible impact on the bioactive content contained in H.scabra. H.scabra has significant effects on a

variety of molecular diseases ranging from antifungal to cancer. This relationship has been shown to be very beneficial in terms of its antifungal and anti-cancer properties.18 These correlations offer opportunities to develop new approaches, as well as enhance exploration with existing studies.

Table 4.1 Relation of H.Scabra Bioactive Compound Study topics

Code A	Code B	Correlation's coefficient
Holothuria	Sea	0,996194
Holothuria	Antifungal	0,975643
Holothuria	Antioxidant	0,973002
Holothuria	Antibacterial	0,964955
Holothuria	Purification	0,964635
Holothuria	Cancer	0,900057

E. MAPPING OF THE THEME OF HOLOTHURUIDEA BIOACTIVE COMPOUND STUDIES

The review of 148 articles using the matrix framework feature and the NVivo 12 plus project map feature revealed that studies on the theme of H. scabra bioactive compounds are generally related to 5 main topics, namely marine natural products, antifungal, antioxidant, antibacterial, and anticancer. In addition, each of these themes is derived from a number of explanatory indicators. Sea cucumbers are high in nutrition and are beneficial to the body. Wet matter contains 44-55% protein, 3-5% carbohydrate, and 1.5% fat. Dry matter contains 82% protein, 1.7 grams of fat, 4.8% carbohydrates, and 455 g of vitamin A and B (0.04% thiamine, 0.07% riboflavin, and 0.4% niacin).

The total number of calories in 100 grams of dried sea cucumbers is 385. Unsaturated fatty acids found in sea cucumbers include EPA, oleic, DHA, linoleic, and arachidonic acid, all of which are necessary for heart and brain health. Omega-3 fatty acids include linoleic fatty acid, EPA, and DHA, while omega-6 fatty acids include linolenic and arachidonic fatty acids. Palmitic acid (1.18%) has the highest fatty acid content in dried sea cucumbers, followed by arachidonic acid (1.11%) and docosadienoic acid. Another study discovered that the fatty acid content of stewed sea cucumbers contains palmitic acid (1.27%), arachidonic acid (3.20%), and docosahexaenoic acid (1.31%).

These findings did not differ significantly from the fatty acid content of dried sea cucumbers. Furthermore, sea cucumbers contain amino acids, which include both essential and non-essential amino acids. Other essential amino acids found in sea cucumber include glycine (8.09%), glutamate acid (7.18%), alanine (4.18%), leucine (1.34%), and aspartic acid (4.27%).[19]

Sea cucumbers (Holothuria) contain high-value-added compounds that have health benefits. Peptides, vitamins, minerals, fatty acids, saponins, carotenoids, collagen, gelatin, chondroitin sulfate, amino acids, fatty acids, and some other bioactive compounds all are obtained from sea cucumbers.[20] In this sense, the presence of saponins is linked to the antimicrobial properties of sea cucumber extract. These secondary metabolites have been shown to have a variety of pharmacological benefits, including antifungal, antibacterial, and antiviral properties.[21]

Several triterpene glycosides isolated from sea cucumbers have already demonstrated significant antifungal activity. Three triterpene glycosides isolated from Holothuria scabra showed antifungal activity, according to Han et al. They also discovered that Actinopyga lecanora triterpene glycoside isolates could be an useful source of antifungals.[12] Triterpene glycoside isolates from B.marmorata and Holothuria have been found to have antimicrobial activities against six different fungal strains.[22]

Triterpene glycosides and their desulfurated analogs were discovered to have antifungal activity against phytopathogens at high concentrations. In a double-blind, randomized controlled study, Yano et al. looked into the impact of consuming jelly-containing sea cucumber extract just on oral Candida albicans burden in the elderly. The agar contains Stichopus japonicus hydrolyzate, which includes holotoxins, which are triterpene glycosides. The results showed that sea cucumber jelly inhibited oral Candida, implying that consuming S. japonicus jelly on such a daily has the potential to reduce the oral Candida burden in nursing home patients.[23] Furthermore, the secondary metabolites produced by sea cucumbers, namely saponins, have antifungal properties.

Sterol is required for maintaining membrane establishment and regulating eukaryotic signal transduction.[24] Ergosterol is a key sterol in fungal membranes that regulates membrane fluidity, plasma membrane biogenesis, and function. As a result, ergosterol homeostasis is essential for fungal cells.Azole drugs such

as fluconazole, are widely utilized in treating fungal infections by inhibiting ergosterol biosynthesis. Saponins have cytotoxic and other biological activities, such as antimicrobial activity. Saponin's antifungal activity is due to its capacity to complex sterols in fungal membranes and induce membrane integrity damage via the structure of transmembrane pores. The antifungal activity of sea cucumbers could be due to bioactive compounds such as saponins.[25]

In a study conducted by Nugroho et al., a GC-MS analysis revealed the presence of long-chain fatty acids (LCFA) but no additional bioactive compounds with potential antimicrobial activities, such as phenolic or terpene compounds.[26] LCFAs are the primary components of a number of antibacterial herbs and antimicrobial food additives, and they have intriguing biological properties such as antibacterial activity. Bacterial growth is actively inhibited by C16-C20 LCFAs.[27]

In other words, the compounds discovered have a strong relationship with bacterial growth inhibition. A thorough examination reveals that each compound restricts bacterial growth in a unique way. The main mechanisms are increased cell wall permeability and cell lysis, disruption of the electron transport chain and the initiation of oxidative phosphorylation, and inhibition of bacterial enzyme activity.[28] Other studies have found LCFA in S. horrens, H. atra, S. hermanni, T.anax, H. fuscogilva, H. leucospilota, and H. scabra.[29,30]

Sea cucumbers are high in bioactive compounds such as phenolic content, polysaccharides, proteins (collagen and peptides), carotenoids, and saponins, all of which have antioxidant and other properties. These marine invertebrates are rich in phenolic compounds, particularly phenolic acids and flavonoids, which have antioxidant properties. The antioxidant capacity of sea cucumber peptides and protein hydrolysates differed depending on composition, amino acid sequence, and molecular weight. The antioxidant capacity of sea cucumber protein and peptide hydrolysates varied depending on their composition, amino acid sequence, and molecular weight.

Furthermore, the antioxidant activity of sea cucumber polysaccharides like fucosylated chondroitin sulfate and fucan is influenced by a variety of factors, the majority of which are related to molecular weight, sulfation degree, and primary sugar type.31 Antioxidants are substances that scavenge free radicals and thus protect the body from oxidation. The primary mechanisms at work are hydrogen atom transfer (HAT), single electron transfer (SET), metal

chelation, and power reduction. Sea Cucumber's Phenolic Antioxidant Potency Phenolic compounds are secondary metabolites that contain one or more aromatic rings and hydroxyl groups. The majority of phenolic acids and flavonoids found in sea cucumbers.[32] This could be due to phenolic uptake from phytoplankton, sea cucumbers' primary food source. Antioxidants scavenge free radicals and thus protect the body from oxidation. Darkori et al. investigated the antioxidant efficacy of phenolic-rich H. atra extract against 7,12-dimethylbenzanthracene (DMBA)-induced hepatorenal dysfunction.

DMBA increased hepatic malondialdehyde (MDA) levels while decreasing glutathione-S-transferase (GST), glutathione (GSH), catalase (CAT), and SOD levels in a rat model.33 Hydrolyzed proteins and peptides have antioxidant properties. Protein hydrolysates, collagen, and peptides are abundant in marine products. The functionality of protein hydrolysates and peptides is primarily determined by the amino acid composition and sequence, molecular weight, and hydrophobicity and hydrophilicity. In general, bioactive peptides with 3-20 amino acid units have antioxidant activity. In the presence of amino acids such as tyrosine, phenylalanine, proline, glutamic acid, histidine, and arginine, the antioxidant activity of bioactive peptides can be increased.

According to Alcalase et al., C. frondosa has the highest radical scavenging activity against ABTS and DPPH radicals, as well as metal chelation activity. When compared to other enzymes, amino trypsin had the highest in vitro antioxidant activity.[34] Polysaccharide antioxidant activity is determined by the conformation of the polysaccharide chains. The antioxidant activity of sulfated polysaccharides is specifically related to their molecular weight, degree of sulfation, major sugar type, and glycosidic bond.

As a result, rather than being the result of a single factor, the antioxidant activity of sea cucumber polysaccharides is the result of several. According to Dang et al., the polysaccharides of Apostichopus japonicus are primarily composed of glucosamine, glucuronic acid, galactosamine, mannose, galactose, glucose, and fructose, all of which have high hydroxyl radical, DPPH, and superoxide scavenging and reducing power.[35] This could be due to the ability of free radicals to extract anomeric hydrogens from polysaccharides..[36]

Each type of sea cucumber produces different secondary metabolites that can be used as anticancer. Several studies of active compounds from sea cucumber as anticancer showed that holothurin A3 and A4 produced from

Holothuria scabra exhibit cytotoxicity through blocking of growth of cancer cells with toxic effect in carcinoma, epidermoid (KB) dan hepatocellular (Hep-G2).[37]

Similarly, philinopside E sulfated triterpene glycoside derived from Pentacta quadrangularis, exhibit strong cytotoxicity with IC50 of 0.75-3.50 µg/mL that can inhibit the growth of fibroblast, leukimia cells, lymphocytic leukemia cells, hepatoma cells, lung cancer cells, gastric cancer cells, lung adenocarcinoma cells, human epithelial carcinoma cells and human ovarian carcinoma.[2]

Additionally, the complex compound of cucumariosides monosulfated isolated from Cucumaria japonica also showed immunomodulatory effect in low doses of C57Bl6 mice. Study on displayed frondoside A 0.2 µg increases the innate immune response where the host immune response was inhibited by cytotoxic agents against antigens or tumor growth.

Moreover, triterpene glycoside isolated from Mensamaria intercedens showed anti-tumorigenic properties in sarcoma cells-S180 and rat lung cancer cells.38 Stichopus japonicas extract also reported to inhibit proliferation of human colon cancer cells (Caco-2 cells). Sea cucumber is marine organism candidates as anticancer agents.

Peptides from sea cucumbers have activity to inhibit Hela cells, AGS and DLD-1 from gelatin hydrolyzed with flavourzyme or called low-molecular-weight gelatin hydrolysate (LMW-GH) with molecular weight of 700-1700 Da as an inhibitor of melanin fusion and tyrosinase activity in B16 cells. Some peptide compounds from protein hydrolysate of sea cucumbers also have potential as anticancer with enzymatic hydrolysis namely collagen can be a cancer inhibitor agent in the gastrointestinal, moreover according to amino acids of alcalase, trypsin, pepsin, chymotrypsin, pancreatin and thermolysin can also inhibit cancer cells growth.

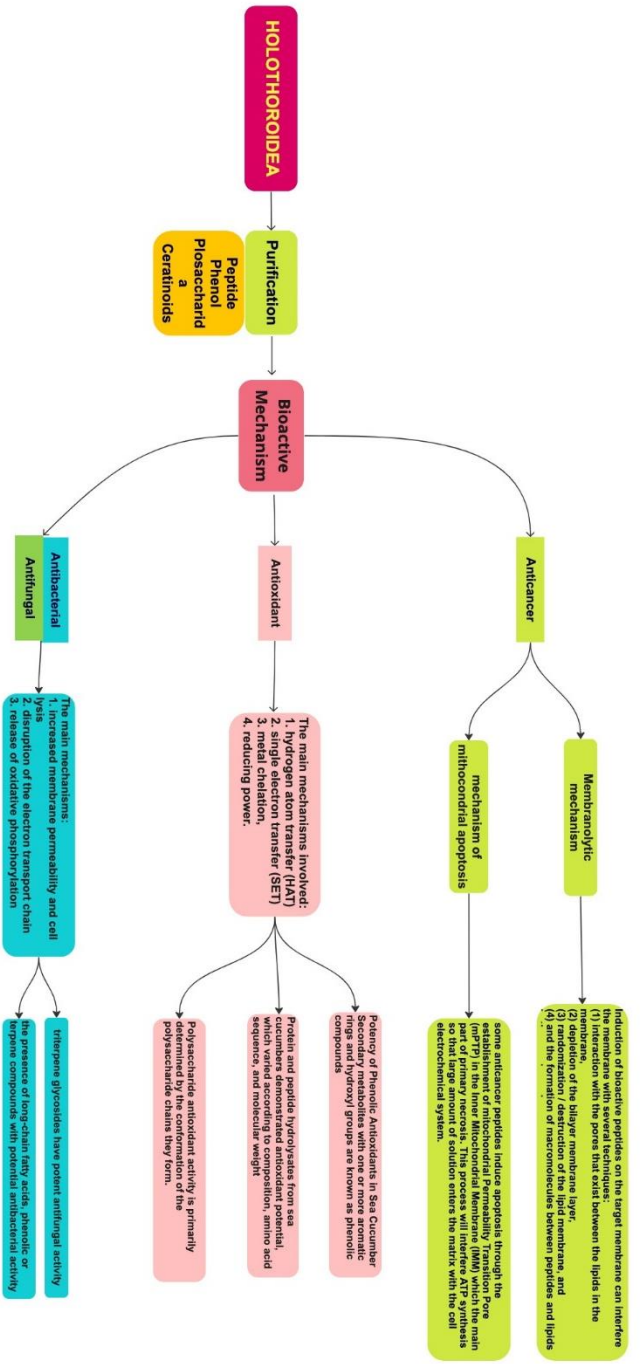
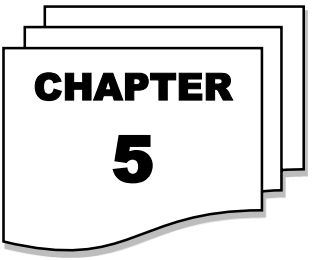


Figure 4.4 Diagram of potential of bioactive compound in Holothoruidea



CONCLUDING CONCLUSION

A. CONCLUSION

Sea cucumbers, particularly H.atra, H.scabra, C.frondosa, and A.japonicus, contain antioxidants such as phenolic acids, flavonoids, peptides, fucosylated chondroitin sulfate (FCS), fucoidan, and triterpene glycosides. These compounds may also have anticancer, anti-inflammatory, anti-glycation, anti-tyrosinase, anti-hypertension, antithrombotic, anti-diabetic, and antimicrobial properties. As a result, sea cucumber antioxidants have the potential to be used in nutraceuticals, pharmaceuticals, cosmetics, and functional foods. More research is needed to understand the detailed chemical structures, mechanisms of action, and bioaccessibility and bioavailability of sea cucumber-derived value-added products through in vivo analysis and clinical trials in order to support the health claims and commercialize sea cucumber-derived value-added products.

Sea cucumbers are marine invertebrates that have potential as anticancer. Sea cucumber contains a significant amount of protein, vitamins, fatty acid, collagen, essential and non-essential amino acids, and minerals that are beneficial to the body. Active compound as anticancer such as philinopside A and B, patagonicosides, holothurin A and echinosides, colohiroside A, Intercedenside A, Okhotosides and Frondoside A sticoposide originating from Thelenota anax, sticoposide, bivittoside A, Holocosinos A and Holotox, cucumariosides produced from different types of sea cucumbers. Each active

compound has a different mechanism of action to inhibit cancer cells. In general, inhibition of cancer cell growth from sea cucumber active compound through the mechanism of apoptosis in cells and mitochondria.

Sterol is essential for the maintenance of membrane organization and the regulation of signal transduction in eukaryotic membranes.[24] Ergosterol is a key sterol in fungal membranes that regulates membrane fluidity, plasma membrane biogenesis, and function. As a result, ergosterol homeostasis is essential for fungal cells. Fluconazole and other azole drugs are commonly used to treat fungal infections by inhibiting ergosterol biosynthesis. [39] Saponins have antimicrobial, cytotoxic, and other biological activities. Saponin's antifungal activity is due to its ability to complex sterols in fungal membranes and induce membrane integrity loss via transmembrane formation.

The study's limitation is that the publications it analyzed were only sourced from Google Scholar, so it lacks comparable data. As a consequence, the next study will need to use an analysing the data collected strategy that incorporates all databases.

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Irena Ujianti is a highly accomplished and respected lecturer in medical physiology at the Faculty of Medicine, University of Muhammadiyah Prof. Dr. Hamka. With a Doctorate degree in physiology from the prestigious Faculty of Medicine, University of Indonesia, Irena's research interests primarily revolve around nutrition and metabolic diseases. She has published several articles in top-tier academic journals related to her research interests and her work has been instrumental in advancing the understanding of diabetes mellitus and other metabolic diseases.

Irena's expertise lies in the application of physiological and biomolecular methods to investigate complex medical conditions. In addition to her academic responsibilities, Irena is an active member of several professional organizations, including the Indonesian Doctors Association (IDI), the Indonesian Association of Clinical Physiologists (PDFKI), and the Jakarta Association of Indonesian Physiological Sciences (IAIFI).

Irena's dedication to her field is further demonstrated through her involvement in several ongoing research projects related to nutrition and metabolic diseases. Her contributions to the field have been widely recognized, making her a highly sought-after speaker and consultant in the medical community.

BIOACTIVE COMPOUND OF HOLOTHOROIDEA

Holothoroidea (sea cucumbers) are a commercially significant variety of marine invertebrates that are widely consumed in Asian countries. Sea cucumbers contain various bioactive substances such as lipids, phenols, peptides, triterpene glycosides, and polysaccharides, which have a wide range of beneficial biological effects. Our research aims to provide a thorough understanding of these bioactive compounds. We discuss natural stock fishery and aquaculture as management strategies for ensuring sustainable sea cucumber populations. We also describe the extraction and purification of bioactive compounds, providing insights into the preparation of functional ingredients derived from sea cucumbers. This review aims to give academics and industry a better understanding of sea cucumbers and their potential for the development of high-value nutraceutical products.

The goal of our study is to categorize themes related to the study of Holothoroidea bioactive components and mechanisms. We analyzed 200 research articles using descriptive analysis and the Nvivo-12 software. Our findings revealed 151 relationships between the bioactive components of Holothoroidea, which could be classified into 11 groups. The discovery of the mechanism of action of the bioactive components of Holothoroidea is significant as it can aid in the development of a conceptual framework for the study of these organisms. However, a limitation of this study is the lack of references to the articles reviewed. Future research should employ a comparative analysis approach to address this limitation.

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