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POTENTIAL FOR DEVELOPING PHYTOPHARMACY BASED ON MARINE RESOURCES: REVIEW

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ABSTRACT

Indonesia is the world's largest archipelagic country, providing abundant biodiversity potential. The rapid development of chemistry, phytochemistry, and pharmacology has increased the research and application of various plants in the health sector. Phytopharmaca is a standardized herbal medicine that has proven its efficacy through clinical trials. Various types of marine biota that are easy to find have been proven to contain bioactive compounds that can potentially develop phytopharmaceuticals based on biological resources. The development of phytopharmaceuticals made from marine plant raw materials has yet to be widely developed. Limiting factors often found are references to pharmaceutical standardization and the required research funding. However, this does not rule out the possibility of realizing phytopharmaceutical products from marine plants that meet standards and clinical trials. Therefore, the aim of the explanation regarding research, types, and potential of marine biological resources in phytopharmaceuticals is to provide information and learning media.

Keywords: Marine Biota, Pharmacology, Bioactive Compounds, Biological Resources

1. INTRODUCTION

The rapid development of chemistry, phytochemistry, and pharmacology in the 19th century meant that the application of plants as medicine was supported by science. Extensive knowledge about plants and their environment, plant metabolism, metabolic process products, and physiological influences causes the use of space to increase. Phytopharmaceuticals are medicinal preparations made from natural ingredients that have been standardized. Clinical trials have scientifically proven their safety status and efficacy[1]. The phytopharmaca group can be equated with modern medicine because the raw materials, manufacturing process, and finished products have been standardized, and their efficacy and safety have been scientifically proven through pre-clinical and clinical trials.

Indonesia is the largest archipelagic country in the world, with more than 18,000 islands, and it has the second longest coastline, 81,000 km, after Canada, among 198 countries and 55 regions (The World Factbook, 2016; Central Statistics Agency, 2016 *in*[2]). Around 75% of Indonesia's sovereign territory is sea, which provides abundant biodiversity potential. Indonesia is nicknamed "Mega Diversity in the World" because of its varied marine biota. Various types of marine biota are easy to find, such as fish, crustaceans, mollusks, echinoderms, coral (coral), and marine plants (algae, seagrass, and mangroves). The research showed that more than 10,000 bioactive compounds were isolated from marine biota. One uses sea cucumbers from the echinoderm group as nutrition and traditional medicine in Asian countries. Highly valued sea cucumber species include *Sticopus hermanii, Holothuria*

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fuccogilva, *Actinopyga mauritiana*, and *Thelenota ananas*[3]. Snakehead fish meat contains many bioactive ingredients for protein synthesis and the antioxidant glutathione in wound healing[3-4].

Data on the use of marine biota both as nutrients and medicinal raw materials still needs to be included in Indonesia. The potential of marine biota does not only come from animal groups; different types of marine plant biota also provide opportunities for its utilization. Groups of marine plants such as algae (seaweed) are often used as food ingredients, medicines, industrial chemicals, and agricultural fertilizers, and seagrass is used as nutritious food[5], and anti-cancer[6]. The potential for developing various types of marine biota as raw materials for treatment encourages research and exploration of marine biological riches, which have been widely used to treat various diseases.

In Indonesia, research on phytopharmaca has developed a lot. However, phytopharmaceuticals made from marine plants have yet to be widely known. The explanation regarding the potential of marine biota in the form of plants is expected to add information regarding the potential of phytopharmaceuticals made from natural ingredients from marine biota species from plant species.

2. RESEARCH METHOD

Method

The preparation of this article was carried out in October 2023. The writing method uses a narrative review, namely by reviewing related journals and the results of research that has been carried out. The literature sources in this literature review writing plan mainly come from online research journals that provide free journal articles in PDF format, such as Google Scholar, Science Direct, Elsevier (SCOPUS), and other relevant sources. Other literature is also from textbooks and national research results. The data and information collection results are then analyzed and presented as scientific papers containing innovative products.

3. RESULT AND DISCUSSION

Red Algae (*Rhodophyta*)

Red algae (*Rhodophyta*) is a type of seaweed with high economic potential. It can be used as a phytopharmaceutical because it has pharmacological properties and can be used for medicinal purposes[7]. The chemical compounds in red algae are predominantly from the Rhodomelaceace family, which has various anti-bacterial, antifungal, anti-inflammatory, ichthyotoxin, and insecticidal activities. Apart from that, red algae also contain several terpenoids, polyethers, acetogenin, several amino acids, and shikimate, as well as nucleic and acetic acid derivatives[8].

Red algae have biological activities such as anti-viral, antioxidant, antifungal, anti-bacterial, and anti-inflammatory[9-10]. Secondary metabolite compounds synthesized by red algae are flavonoids, carotenoids, polyphenols, terpenoids, xanthophylls, β-carotene, β-apo-8'-carotenal and α-tocopherol and alkaloids, which act as antioxidants[11-12]. Red algae can be used to heal wounds such as gunshot wounds, post-operative wounds, exposure to sunlight, electric shock, exposure to corrosive chemical liquids, and heat sources[5]. In general, seaweed boiled water is usually used for internal treatment as an antiseptic and externally as skin care. Another way to use seaweed is to grind it first and then use it as an external medicine in porridge[10].

Spirulina platensis

Spirulina platensis is a blue-green microalga that grows in fresh water and seawater. This alga is known for its abundant nutritional content, especially in the form of protein (60-70%), carbohydrates (15-25%), fat (6-8%), minerals (7-13%), fibre (8-10%), and water (3%). Microalga also has the potential to be effective anti-cancer agents. The pigment and nutritional content of *S.platensis* acts as

an antioxidant in cancer healing therapy, namely the pigment phycocyanin, chlorophyll a, carotenoids, the fatty acid Gamma Linoleic Acid (GLA), the enzyme superoxide dismutase, and oligosaccharides[13-16].

One of the main ingredients in *spirulina* sp extract is phycocyanin. It has antioxidant, anti-inflammatory, anti-viral, immunostimulant, and anti-cancer properties, so it is effective in inhibiting and killing cancer cells without producing toxic effects for the human body depending on time and dose[17-19]. According to research conducted by Coolla et al.[20] in vivo, administration of *Spirulina* at a dose of 0.5 g/day was able to reduce total blood cholesterol to 516±163 mg/dL compared to the group without *Spirulina* administration of 1054±101 mg/dL. Accumulating evidence shows that phycocyanin has anti-cancer solid effects on various types of cancer, such as breast cancer[21-22], liver cancer[23], lung cancer[24,25], colon cancer[26], leukemia[27], and bone marrow cancer[28] in vitro and in vivo.

In addition, it is known that the mechanism for treating tumors is the induction of cell apoptosis. Various pathways have been described that Phycocyanin compounds can disrupt tumor cells and induce apoptosis. Mechanistically, phycocyanin exerts its anti-cancer activity by reducing cell proliferation and migration, inducing apoptosis, and cell cycle arrest[29].

Avicennia marina

Avicennia marina is a mangrove species most widely distributed in Indonesia, known as grey or white mangrove[30]. *A.Marina* is highly resistant to environmental stress and can thrive under hostile conditions such as extreme tides, high salinity, strong winds, and anaerobic soil[31-32].

The *A. Marina* plant has been used traditionally in traditional medicine. The plant leaves are a medical treatment for boils, abscesses, rheumatism, and burns[33]. Traditionally, it has been used to reduce rheumatic pain[34] and treat smallpox and snake bites. The bark, leaves, and fruit are used for skin diseases such as fish stings, ringworm, boils, skin ulcers, and scabies. The seeds' aqueous extract has also been used to treat sore throats[35-36], the decomposition of aerial parts and leaf decomposition of *A.Marina* has been proven to have anti-malarial activity and an antidote to food poisoning. *A. marina* fruit has been used to treat digestive disorders, including constipation, and the leaves and root paste are used to treat wounds[37].

The *A.Marina* plant has demonstrated important pharmacological activities[38]. It is a rich source of various classes of phytochemicals[39], including carbohydrates, alkaloids, carotenoids, hydrocarbons, free fatty acids, esters, phenolic, steroids, triterpenes, glycosides, aliphatic alcohols, acids, and amino acids[21].

The main phytochemical classes identified in *A.marina* include flavonoids in leaves, roots, stem bark, and fruit as antioxidants[40]. The bark of this plant is rich in tannins and acts as a chemopreventive scavenger agent against free radicals[41]. Methanol extract from the whole plant is an anti-cancer, antioxidant, and anti-inflammatory[42]. It has antidiabetic properties of *A. Marina* is influenced by flavonoids, tannins, and phenols in plant extracts[43]. *A.marina* leaf extract shows anti-bacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*[44]. The anti-viral activity of *A. marina* is due to the presence of flavonoids, phenols, and tannins[45]. Crude aqueous, ethanol, and butanol extracts from the aerial parts of *A.marina* were screened for anti-viral activity.

The methanol extract of *A.marina* shows significant anthelmintic activity by causing paralysis and death of worms[46]. Then, the phytochemical content of *A.marina* is flavonoids such as quercetin, a plant pigment used as a food supplement to

increase immunity and support heart health conditions[47].

Sea Grapes (*Caulerpa racemose*)

Sea grapes (Caulerpa racemose) are a valuable plant for treatment. Sea grapes contain chemical compounds that function as anti-bacterial and antioxidants, such as alkaloids, flavonoids, tannins, saponins, and protein steroids, polysaccharides, polyphenols, xanthoproteins, sesqui-terpenoids, diterpenoids, sitosterol, caulerpicin, gallochincatechin, epicatechin, and catechin gallate[48-49]. Sea grapes also contain typical compounds such as caulerpin and caulerpenin, which are bioactive antioxidant compounds[50]. Seagrape 70% ethanol extract can inhibit the growth of Staphylococcus aureus bacteria at concentrations of 80% and 60%. It effectively inhibits bacterial growth up to 33 mm and 29 mm inhibition zone diameter. Meanwhile, 40% and 20% concentrations fall into the intermediate category or are less effective in inhibiting bacterial growth, with inhibitory zone diameters of 26 mm and 24 mm[51].

Sea grapes can also be used to treat high blood pressure and rheumatism. Bioactive substances in sea grapes have been observed to have anti-neoplastic, anti-bacterial, anti-viral, and antiproliferative activities[52]. Several studies have revealed that consuming sea grapes regularly can potentially prevent and treat neurodegenerative, chronic, and aging-related diseases[53, 50]. Research by Ngadiarti et al.[54] showed that feeding test mice made from sea grapes on a diet rich in cholesterol and fat could significantly reduce blood sugar levels. The results of this study follow other studies that provide evidence that sea grapes have antidiabetic and anti-hyperglycemic activities, which are beneficial for health, significantly minimizing aging and chronic diseases[55].

Research by Permatasari et al.[49] using sea grapes as a primary ingredient for giving kombucha tea from sea grapes has the activity of lowering blood glucose levels in mice fed a diet high in cholesterol and fat. In line with this, antioxidants contained in food can contribute to reducing oxidative stress cell and protein damage caused by chronic hyperglycemia[56]. Providing sea grape extract and fermented sea grapes can significantly reduce total cholesterol[57-58].

Challenges on Phytopharmaceuticals

Based on the Decree of the Head of BPOM Number HK.00.05.4.2411 of 2004 concerning Basic Provisions for Grouping and Labeling Indonesian Natural Medicines, Indonesian traditional medicines can be grouped into Jamu, Traditional Herbal Medicine (OHT) and Phytopharmaceuticals. Jamu is part of traditional medicine that has been used for generations and only has claims of use following traditional types of evidence (from generation to generation). OHT is a traditional medicine scientifically proven for its quality, safety, and benefits. It uses raw materials that meet standards. Meanwhile, phytopharmaceuticals are standardized herbal medicines that have undergone higher levels of scientific evidence because clinical trials have been carried out.

Various diseases are being discovered, including infectious, non-infectious, and degenerative diseases, as well as new diseases in the future (new emerging diseases/NED) that require standardized bioactive ingredients from medicinal plants. Each plant type has unique bioactive ingredients so that they become raw materials for treating certain diseases. The Ministry of Health has made regulations so that the development of traditional medicine can be scientifically accountable. The development of traditional medicines and phytopharmaceuticals must consist of six stages, namely selection, screening of biological substances, pharmaco-dynamic testing, toxicity testing, development of drug formulations, and clinical testing on humans[59].

Referring to data from the National Research and Innovation Agency (BRIN,

Indonesia), of the 30 thousand plant species that have the potential to be used as medicinal plants, there are at least 7,500 types of plants that are known to have medicinal properties of which 800 are used as herbal medicine. From the marine ecosystem, Indonesia also has species that can be developed as medicinal plants, such as coral reefs, seaweed, and seagrass. So far, it is acknowledged that marine biota has yet to be focused much on research aimed at acting as an immune booster (immunomodulator). Production from marine biota is still limited to herbal medicine.

One of the obstacles to developing research to the phytopharmaceutical level or having its safety and efficacy scientifically tested is that chemicals for research still need to be imported. Apart from that, the most fundamental factor is that phytopharmaceuticals must meet the criteria: being safe according to the specified requirements, claiming efficacy is proven through clinical trials, standardizing the raw materials used in finished products, and meeting quality requirements using high-tech machines.

Interest in conducting research and developing traditional medicines into phytopharmaceuticals is quite good. However, it is often hampered by pharmaceutical standardization standards and the problem of research funds, which are difficult to obtain. The development of potential phytopharmaceutical drugs involves multidisciplinary fields of pharmacognosy, ethnobotany, ethnopharmacology, agroindustry, agronomics, phytochemistry, pharmacology and toxicology, pharmaceutical technology, and medicine, including dentistry.

4. CONCLUSION

Eighteen types of fish were found; the most types of fish from the Cyprinidae family were 14 types, the fish species diversity index (H') was classified as medium, the species evenness index (E) was classified as high, the community was stable, the dominance index (C') was medium, and the richness index (R) was classified as low. The number of fish caught from year to year has decreased, and some species are no longer found, so it is necessary to collaborate between the community, fishermen, and government in managing sustainable capture fisheries in the waters of the Batang Bungo River.

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