Overview of bioactivity studies on marine natural products

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Abstract. Marine natural products are sourced from marine biodiversity as natural raw materials for various commercial products. This study aims to review natural products of marine organisms and gap analysis for future research or challenges. A total of 109 references from 24 countries were collected. The analysis was carried out quantitatively and qualitatively. The bioactive compounds produced were antioxidants, antibacterial, anticaner, antimicrobial, anti-fouling, antifungal, and anti-tumoral substances. Some marine organisms that can store chemical compounds through secondary metabolite processes are mangroves, seagrasses, macroalgae, microalgae, soft corals, molluscs, echinoderms, gastropods, cnidarians, sponges, fungi, and bacteria. Most of the papers only discuss the identification stage of the active compound, and some focus on product development. There are very few studies on prospects of commercialization and mass production. The problem to achieve mass production is due to the lack of interdisciplinary research collaboration. Future research challenges need to develop a transdisciplinary approach to study bioprospection research from upstream to downstream, starting from the potential identification of bioactive ingredients, product development, the availability of raw materials for mass production as well as commercialization and marketing.

Keyword: biodiversity, natural product, marine organism, sustainability, antioxidants

1. Introduction

The oceans, both tropical and sub-tropical waters, and even Antarctica are a storehouse of minerals, nutrients and bioactive compounds contained in diverse marine biota [1]. In terms of biodiversity, the marine environment is among the richest and most complex ecosystems [2]. Since ancient times, humans have used natural products, such as plants, animals, microorganisms and marine organisms to extract medicinal ingredients to relieve and treat disease [3].

The marine environment is rich in a diversity of biological and chemical resources. Some plants and organisms can synthesize chemicals that can be used in various fields. The diversity of marine biota has become a source of chemical compounds that have the potential to be developed in various industrial fields such as pharmaceuticals, cosmetics, supplements, molecular probes, fine chemicals and agriculture [4]. The potential of marine biodiversity can be an opportunity to create a product derived from natural products. Products obtained from nature are likely to be very easily accepted by the public compared to chemical products. People are starting to realize or be aware that exposure to chemical products in the long term will certainly have an adverse impact on human health.
Natural product comes from the word bio which means alive and prospecting which means having potential or prospects. The definition of natural product can be defined as a process of study of living things with prospects as genetic resources and other biological materials for commercial purposes of economic value through systematic search, classification, and investigation of sources of new chemical compounds, genes, proteins, microorganisms, and other metabolic products.

Research related to marine natural product has grown quite rapidly in recent decades. The development of marine natural product research activities will further intensify the exploration of natural resources and also biotechnology to spur industrial development. Several research results have found various materials or bioactive compounds that have the potential to be developed into various commercial products. In 1995, the world's drug trade from natural product research generated revenues of $US14 billion [5].

This paper attempts to examine the extent to which natural product studies have been developed, and analyze research gaps that need to be developed in the future.

2. Methodology
The data obtained was the result of a review of various studies from various sources such as books, articles, journals and other publication media on marine natural product in Indonesia and the world. This literature search was carried out through various sites such as: Google Scholar, Scopus, Science Direct, research gates, and Elsevier. The search results on these various sites with a time range from 2005 to 2021 produced as many as 109 references on the topic "marine natural product" or "marine bioactive potential". A total of 109 papers were collected, including 55 from Indonesia, seven from India, six from China, while the four papers from Saudi Arabia, the United States, the Mediterranean, and Australia. Brazil and Italy each have three papers, Germany and Portugal have two papers each. Finally, the countries from which there are one paper include Cuba, Iran, Poland, Taiwan, South Korea, Colombia, Micronesia, Norway, Algeria, Canada, Spain, New Zealand and the Antarctic Continent (Figure 1).

The high reference search results for the territory of Indonesia was possible due to the high marine biodiversity of Indonesia. As an archipelagic country located in a tropical region, Indonesia is the richest country in terms of marine biodiversity. The Indonesian sea has 8,500 species of fish, 555 species of seaweed, and 950 species of coral reef biota. So Indonesia is a country with the largest marine biodiversity in the world (marine mega-biodiversity), has a high potential for marine natural product.

![Figure 1. Number of distribution papers.](image-url)
Furthermore, the paper information was reviewed and the data were analyzed and tabulated with components in the form of reference sources, species names, research locations, materials or sources of compounds, and potential compounds.

3. Results and Discussion

Table 1 shows the results of the review of 109 journals in terms of sources of bioactive compounds, research locations, bioactive compounds and chemical compounds. Furthermore, the results of this review are described in the form of a table to examine the source of bioactive ingredients and bioactive compounds. Table 1 also shows that publications on the potential of bioactive compounds are increasing from year to year. This shows the potential of bioactive compounds is very high needed in various areas of life especially in the health sector. Bioactive ingredients needed by the body to overcome and prevent stress. Various original natural ingredients from Indonesia contain lots of antioxidants with various active ingredients.

Table 1. Compilation of the results of reviewing journals in terms of sources of bioactive components, research sites, bioactive compounds and chemical compounds.

| No. | Reference | Species | Name | Location | Compounds | Bioactive Compounds |
|-----|-----------|---------|------|----------|-----------|-------------------|
| 1   | Pratitis et al., 2010 [6] | Aspergillus ustus MFW 26-28 | Fungi | Collection from BBRP2B-KP, Indonesia | - | Antioxidant and anticancer |
| 2   | Marhaeni et al., 2011 [7] | Bacterial symbionts T. hemprichii and E. acoroides | Marine bacteria | Jepara, Central Java | - | AntiFouling |
| 3   | Ali et al., 2012 [8] | S. isostefilium, C. serrulata and H. beccarii | Seagrass | India | - | Insecticide |
| 4   | Fajarningsih et al., 2012 [9] | Mold association | Fungi | Seribu Islands, Indonesia | - | Anticancer |
| 5   | Karthikeyan et al., 2012 [10] | Donax incarnates | Shell | India | Glycosaminoglycans | Anticoagulant |
| 6   | Prumo et al., 2012 [11] | Holothuria scabra | Sea cucumber | Semarang, Indonesia | alkaloids, saponins and triterpenes | Antifungal |
| 7   | Siregar et al., 2012 [12] | Caulerpa sp, Eucheuma sp., Gracilaria sp. and Sargassum sp. | Seaweed | Jepara, Indonesia | Steroids, Alkaloids, Flavonoids, Triterpenoids, Tannins | Antibacterial |
| 8   | Wusqy et al., 2012 [13] | Sea anemone association bacteria | Marine bacteria | Jepara, Indonesia | - | Antibacterial |
| 9   | Karina et al., 2013 [14] | Curvularia sp., Penicillum sp., Aspergillus sp. and Cladosporium sp. | Fungi | Panggang Island, Seribu Islands, Indonesia | - | Antibacterial |
| 10  | Sukmarianti et al., 2013 [15] | Iantheilla basta | Sponge | Flores, Indonesia | - | Anticancer |
| 11  | Al-Saif et al., 2014 [16] | U. reticulate, C. occidentalis, C. socialis, D. ciliolate, and G. Dendroides | Seaweed | Red Sea, Saudi Arabia | Chloroform and ethanol | Antibacterial |
| 12  | Sari et al., 2014 [17] | Callyspongia sp | Sponge | Makassar, Indonesia | Triterpenoids | Antioxidant |
| 13  | Sari et al., 2014 [18] | Holothuria edulis | Sea cucumber | Karimun Jawa, Indonesia | - | Antibacterial |
| 14  | Hardoko et al., 2015 [19] | Gracilaria gigas | Agar-agar/lubu kawang | Serang, Indonesia | Agar-Agar, Agarose, and Agaropetein | Antidiabetic |
| No. | Reference | Species | Name | Location | Compounds | Bioactive Compounds |
|-----|-----------|---------|------|----------|-----------|---------------------|
| 15  | González et al., 2016 [20] | Thalassia testudinum and Syringodium filiforme | Seagrass | Havana, Kuba | Phenolic | Antioxidant         |
| 16  | Faoziah and Kurniawan, 2017 [21] | Rhizophora mucronata sp. | Mangrove | Cilacap, Indonesia | Nanoemulsion | Anticancer         |
| 17  | Paupasari, 2017 [22] | Cymodocea rotundata | Seagrass | Panjang Beach, Yogyakarta | Flavonoids and Phenolics | Antioxidant         |
| 18  | Ridlo et al., 2017 [23] | Rhizophora mucronata | Mangrove | Tugurejo, Semarang, Indonesia | Phenolates | Antioxidant         |
| 19  | Cahyati et al., 2018 [24] | Golden stichoupus variegatus | Gold sea cucumber | Surabaya, Indonesia | Glutathione | Antioxidant, Anticancer |
| 20  | Hakim et al., 2018 [25] | Sargassum sp. | Seaweed | Yogyakarta, Indonesia | Alkaldoids, quinones, steroids, triterpenoids, and flavonoids | Antifouling |
| 21  | Szmurt et al., 2018 [26] | Spirulina subsalsa | Brown seaweed | Puck Bay, Polandia | - | Anticancer         |
| 22  | Alhaddad et al., 2019 [27] | Avicenia sp. | Mangrove | Donggala, Indonesia | - | Antibacterial      |
| 23  | Liu et al., 2019 [28] | Enteromorpha prolifera and Ulva lactuca | Seaweed | Yellow sea, China | Sulfate oligosaccharides | Antising and Antioxidant |
| 24  | Syahputra, 2019 [29] | Ekstrak mangrove | Mangrove | Aceh, Indonesia | Tannins | Antifouling |
| 25  | Al-Malki et al., 2020 [30] | Ulva lactuca | Sea lettuce | Red Sea, Saudi Arabia | Phycocyanin | Antioxidant, Antiproliferative, Antibacterial |
| 26  | Bhattacharyya et al., 2020 [31] | Thalassiosira, Skeletonema and Chaetoceros Bacillus subtilis | Diatom | South Sea, India | Phenols, flavonoids, methanol | Antioxidant and Antibacterial |
| 27  | Cao et al., 2020 [32] | Suaeda nudiflora, Laminites racemosa, Ipomoea tuba and Avicennia alba | Mangrove | Beihai, China | - | Anticoagulant |
| 28  | Eswaraiah et al., 2020 [33] | L.laevigata, A. typicus, P. nodosus | Starfish | Manado's Tongkaina seas | Phenol, Steroids, Emodin | Antioxidant         |
| 29  | Gangadharan et al., 2020 [34] | Serratia marcescens | Marine bacteria | Arab Sea | - | Antioxidant and Antibacterial |
| 30  | Alshuniaber et al., 2021 [35] | Spirulina | Spirulina | University of Texas Laboratory Collection at Austin, USA | Polyphenol | Antibacterial |
| 31  | Nowrui et al., 2017 [36] | Nostoc cyanobacteria | Seaweed | Iran | Cyclic depsipeptides, cyclic peptides, lipopeptides, fatty acids, polyketides, alkaloids, amides, terpenes, carbohydrates and other organic compounds | Antivirus, Antitumor, Antibacterial, anti HIV |
| 32  | Al-Amoudi et al., 2016 [37] | Bacillus spp., Pseudomonads fluorescens, and Paederus fascipes | Marine bacteria | Red Sea, Saudi Arabia | Bescitracin, Mupirocin and Pederin | Antibacterial and Antitumor |
| 33  | Piter et al., 2019 [38] | L.sieviigata, A. typicus, P. nodosus | Starfish | Manado's Tongkaina seas | - | Antioxidant, Antibacterial, antiinflammatory, antifungal and immunostimulator |
| No. | Reference | Species | Name | Location | Compounds | Bioactive Compounds |
|-----|-----------|---------|------|----------|-----------|---------------------|
| 34  | Rocha et al., 2011 [39] | Cnidaria sp. | Jellyfish | Italy | Terpenoids (terpenoids, diterpenoids, sesquiterpenoids, sesterterpenoids, embranoids) | HIV inhibition, cytotoxic, anti-inflammatory, anticancer and antimicrobial |
| 35  | Setyoningrum et al., 2020 [40] | Enhalus acoroides | Seagrass | Paciran Sea, Lamongan | alkaloids, flavonoids, tannins, steroids, and saponins | Antibacterial |
| 36  | Kim et al., 2021 [41] | T. ciliatum | Seagrass | Catechin | Antioxidant, Antiviral and Cytotoxicity against cancer cell lines |
| 37  | Gazali et al., 2017 [42] | Sargassum sp. | Brown seaweed | South west coast (barsselra), Aceh | phenols and tannins | - |
| 38  | Gazali et al., 2017 [43] | Sargassum sp. | Brown seaweed | West Aceh Coast | Polyphenol | Antioxidant |
| 39  | Winowoda et al., 2020 [44] | Chlorophyta, Ochrophyta, and Rhodophyta | Green algae | Atep Oki Coast, Minahasa, North Sulawesi | - | - |
| 40  | Zhi et al., 2020 [45] | Rhizophora mucronata | Mangrove | Dong Zhai Gang-Mangrove Garden on Hainan Island, China | fumiquinazoline, fumigaclavine C, sulochrin, monomethylsulochrin, questin | Antimicrobial, ergot alkaloids, antibacterial and antifungal |
| 41  | Mangamuri, et al., 2016 [46] | Mangrove ecosystem | Mangrove | Nizampatnam mangrove ecosystem, south east coast of Andhra Pradesh | (3S,8aS)-3-isobutylhexahydropyrrolo[1,2-a]pyrazine-1,4 dione | Antimicrobial, cytotoxic compounds |
| 42  | Rajasabapathy et al. 2019 [47] | Marine sponges and coral | Sponge and coral | Gulf of Mannar and Palk Bay regions of Tamilnadu | - | Antimicrobial compounds |
| 43  | Rimper, 2014 [48] | Brachionus rotundiformis | Rotifer | Manado | - | Antibacterial |
| 44  | Lubis, 2017 [49] | H. micronesica and H. macroloba | Green algae | Maspari Island | Hmi- EA | inhibits free radicals and antioxidants |
| 45  | Dolorosa et al., 2017 [50] | S. plagophyllum and E. cottonii | Seaweed | Banten | alkaloids, steroids, flavonoids, saponins and tannins | Antioxidants and tyrosinase inhibitors |
| 46  | Zulfadhli and Rinawati, 2018 [51] | Ulva lactuca | Sea lettuce | Banda Aceh | alkaloids, steroids, and phenolics/tannins | Antifungal |
| 47  | Febrianto et al., 2019 [52] | Gracilaria verrucosa | Seaweed | Gumung Kidul Beach, Yogyakarta | - | Antioxidant |
| 48  | Santi et al., 2014 [53] | Sargassum duplicatum | Brown seaweed | Teluk Awur, Jepara | alkaloids, saponins, quinones, phenolics, steroids, and flavonoids | Antifouling |
| 49  | Nurjanah et al., 2018 [54] | Sargassum sp. and E. cottonii | Seaweed | Lhok Bubon beach, Aceh and Banten | alkaloids, flavonoids, phenols, saponins, tannins, and steroids | Antibacterial |
| No. | Reference | Species | Name | Location | Compounds | Bioactive Compounds |
|-----|-----------|---------|------|----------|-----------|---------------------|
| 50  | Stabili et al., 2019 [55] | Chaetomorpha linum | Green algae | Mar Piccolo of Taranto (Mediterrania, Ionia Sea) | fatty acid, linoleic acid, eicosapentaenoic acid, arachidonic acid | Antioxidant |
| 51  | Zerrifi et al., 2018 [56] | Cyanobacteria | Bakteri laut | Xisha Islands, China | Copper sulfate (CuSO 4 5H 2 O) | Antibacterial, antifungal, antimicroalgae, and Antioxidant |
| 52  | Fajaminsih et al., 2013 [57] | Aaptos sp. | Sponge | TNL Sea, Wakatobi Islands | - | - |
| 53  | Lister and Duckworth, 2010 [58] | Coscinoderma mastig matthewsi, Hyrtios erecta, and Ianthella basta | Sponge | Masig Island, central Torres Strait, Australia | - | Antioxidant |
| 54  | Fristiohady et al., 2020 [59] | Monanchora viridis, Hyrtios erectus, and Xestospongia | Sponge | - | 5-hydroxy-3-(2hydroxyethyl), Crambescidin 800 (C800), and Araguspongine C | Antiproliferative, proapoptotic and proinflammatory |
| 55  | Mayefis et al., 2021 [60] | Demospongiae | Sponge | Natuna, Riau Islands | alkaloids, flavonoids, steroids and tannins | Anticancer |
| 56  | Jin et al., 2016 [61] | - | - | Portugal | polyketides, alkaloids, peptides, lactones, terpenoids and steroids | Anticancer, antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, antibiotic and cytotoxic properties |
| 57  | Suparno, 2005 [62] | Halichondria sp, Callyspongia pseudoreticulata, Callyspongia sp. and Asulettia sp. | Sponge | Padang, Indonesia | Lokisterolamine A and B, Cortic acid A,B,C | Antibacterial, Antifungal, Antibiofoiling |
| 58  | Norhayati, 2006 [63] | Eucheuma alvarezii | Seaweed | Surabaya Sea, Indonesia | flavonoids, alkaloids, terpenoids and steroids | Anticancer |
| 59  | Ismet M.S, 2007 [64] | Aaptos aaptos and Petrosia sp. | Sponge | South and North of Pari Island | norharman (β-carboline, 9H-Pyrido [3,4-b] Indole) | Antimicrobial |
| 60  | Tamat, 2007 [65] | Ulva reticulata | Seaweed | Banten and Jakarta | Triterpenoids and nonyl phenol | Antioxidant |
| 61  | Rahmadi, et al., 2011 [66] | Laminaria japonica, Coralina pilulifera, Sargassum macrorcarpum | Seaweed | Borneo | polysaccharides, carotenes, phenolic compounds, MAAs, sargafuran | Antioxidant, Antiradiation, antiacne |
| 62  | Putri, 2012 [67] | Telescopium telescopium | Conch | Tapak Sea, Semarang | alkaloids, steroids, flavonoids | Antitumor |
| 63  | Tarman, 2012 [68] | Culcina schmideliana | Starfish | Lampung Sea | alkaloids, steroids, flavonoids, saponins, ninhydrin, steroids and saponins | Antimicrobial |
| 64  | Rumengan A.P, 2013 [69] | Nepthea sp. | Soft coral | Malalayang Sea, Southeast Sulawesi Indonesia | - | Antibacterial |
| 65  | Faisal M.R, 2014 [70] | Calcarea, Demospongiae, and Hexactinellida | Sponge | - | triterpenoids and flavonoids | Antibiotics |
| No. | Reference                  | Species                        | Name                        | Location                                      | Compounds                                | Bioactive Compounds                  |
|-----|---------------------------|--------------------------------|------------------------------|-----------------------------------------------|-------------------------------------------|--------------------------------------|
| 66  | Rahakbauw, et al., 2016   | Enhalus acoroides              | Seagrass                     | Coastal Waters of Waai Village, Central Maluku | flavonoids                               | Antioxidant                          |
| 67  | Mushofatul et al., 2017   | Enhalus acoroides              | Seagrass                     | Lancang Island, Seribu Islands                | alkaloids, flavonoids, tannins, steroids, hydroquinone and saponins | Antifouling and Antibacterial         |
| 68  | Idiawati et al., 2017     | Thalassia hemprichii           | Seagrass                     | Lemukutan Sea, West Borneo                    | -                                         | Antibacterial                        |
| 69  | Nurafi, 2018 [74]         | Halodule pinifolia, Cymodocea rotundata and Enhalus acoroides | Seagrass                     | Juanga Village Sea, Pandanga and Posi, Posi, Morotai Island | -                                         | -                                    |
| 70  | Hutabarat et al., 2018    | Enhalus acoroides              | Seagrass                     | Malang Rapat Village, Riau Islands            | Flavonoids, Phenols, Steroids, Tannins and Saponins | Antioxidant, Antimicrobial           |
| 71  | Nurachmi et al., 2018     | Eucheuma cottonii              | Seaweed                      | Jaga Island Beach, Riau Islands               | flavonoids, alkaloids, terpenoids and steroids | Anticancer                           |
| 72  | Helena and Sanjaya, 2018  | Sargassum sp.                 | Seaweed                      | Sea of Jepara                               | flavonoids and saponins                   | Antioxidant                          |
| 73  | Soamode et al., 2018      | Turbinaria sp., Gracilaria sp., and Halimeda macroloba | Seaweed                      | Nain Island, North Minahasa                  | alkaloids, flavonoids, terpenoids/steroids, saponins and tannins flavonoids, phenolics, saponins and tannins | Antioxidant, Anticancer |
| 74  | Malo, A et al., 2018      | Padina sp., Hormophysa sp., Gracillaria sp., Acantophora sp., Catinella sp., Amphiroa sp., Botleca sp., Enteromorpha sp. and Halimeda sp. | Seaweed                      | Arubara Beach, Ende, Indonesia               | flavonoids, phenolics, saponins and tannins | Antioxidant, Antibacterial           |
| 75  | Sibero, 2019 [80]         | Trichoderma asperellum         | Mold                         | Panjang Island Sea, Jepara                   | alkaloids, flavonoids, phenol hydroquinone and saponins | Antibacterial                        |
| 76  | Julyasih et al., 2020     | Caulerpa spp., Gracilaria spp., Eucheuma spinosum, Eucheuma cottonii | Seaweed                      | Sanur beach, Bali                           | flavonoids, alkaloids                      | Antioxidant, anticancer              |
| 77  | Julyasih et al., 2020     | Ulva lactuca, Gracilaria sp., Padina sp. | Seaweed                      | Sanur beach, Bali                           | Phenolics, flavonoids, alkaloids           | Antioxidant                          |
| 78  | Batubara et al 2020       | Xylocarpus granatum           | Mangrove                     | Togeun, Sulawesi teggara                    | Alkaloids, flavonoids, phenol hydroquinone and saponins | Tyrosinase inhibition, Antiglycation activity |
| 79  | Gazali et al 2015         | Xylocarpus granatum           | Mangrove                     | Togeun, Sulawesi teggara                    | Alkaloids, flavonoids, phenol hydroquinone and saponins | Tyrosinase inhibition               |
| 80  | Mao et al., 2009          | Monostroma latissimum         | Green alga                   | Zhejiang Province, China                     | flavonoids, alkaloids, Polysaccharide     | Anticoagulant                        |
| No. | Reference                     | Species                                      | Name                          | Location       | Compounds                        | Bioactive Compounds               |
|-----|-------------------------------|----------------------------------------------|-------------------------------|----------------|----------------------------------|-----------------------------------|
| 81  | Wei et al., 2013 [86]         | Capnella imbricata, Lobophytum sarcophytoideos, Lobophytum durum, Lobophytum crassum, Sinularia discrepa, Sinularia giberroosa, Sinularia grandilobata, Sinularia querciformis, Sinularia triangular, Sinularia flexibilis, Sinularia crassa, Sarcophyton crassocaule, Pocelliastra compressa | Soft coral                    | Taiwan         | Sesquiterpenoid, Diterpenoid and Steroid | Anti-inflammatory, Antioxidant   |
| 82  | Calabro et al., 2017 [87]     | Poecillastra compressa                      | Spons                         | Mediterania    | Steroidal Saponins               | Antifungal                       |
| 83  | Pimentel-Elardo et al., 2010 [88] | Streptomyces sp.                             | Spons                         | Mediterania    | Cyclic depsipeptide, Indolocarbazole, Alkaloid staurosporine and Butenolide | Antiparasitic, Antimicrobial     |
| 84  | Mhadhebi et al., 2012 [89]    | Cystoseira compressa                        | Brown seaweed                 | Mediterania    | Chloroform and Ethyl acetate fractions | Anti-inflammatory               |
| 85  | Jeon et al., 2010 [90]        | Sceptrella sp.                               | Spons                         | South korea    | Alkaloid                         | Antibacterial                    |
| 86  | Tello et al., 2009 [91]       | Eunicea knighti                             | Coral                         | Colombia       | Terpene                          | Antibacterial                    |
| 87  | Tagliatala-Scafati et al., 2010 [92] | Plakortis simplex                           | Spons                         | Italy          | Polyketide                       | Antimalarial                     |
| 88  | Dos Santos et al., 2011 [93]  | Canistrocarpus cervicornis                   | Brown algae                   | Brazilia       | Terpene                          | Antiprotozoal                    |
| 89  | Vicente et al., 2009 [94]     | Prosuberites lauglini                       | Spons                         | USA            | Alkaloid                         | Antituberculosis                 |
| 90  | Muddala et al., 2017 [95]     | Enhygromyxa saliva                          | Myxobacterium (bacteria)      | USA            | Enhydroide A                     | Antibiotic                       |
| 91  | Teta et al., 2017 [96]        | Thermactinomyces vulgaris                   | Thermophilic bacterium         | Italy          | Thermoactinoamide A              | Antibiotic                       |
| 92  | Cai et al., 2016 [97]         | Bacillus amyloliquefaciens P3               | Strain p3c3                   | Antarctic       | Isothyrophan                     | Antifungal                       |
| 93  | Medeiros et al., 2007 [98]    | Heterosiphonia gibbesi, Bryothammnon seafortii, Jania rubens, and Dictyopteris delicatula | Seaweed                       | Brazil          |                                 | Antifouling                      |
| 94  | Lim et al., 2014 [99]         | Hyrtios sp.                                  | Marine sponge                 | Chuk, Micronesia |                                 | Anticancer                       |
| 95  | Palomo et al., 2013 [100]     | Kocuria and Micrococcus spp.                | Actinomycetes                 | USA            | Thiazoyl Peptide                 | Antibiotic                       |
| 96  | Myhren et al., 2013 [101]     | Streptosporangium sp                        | Marine actinomycetes          | Norway          | Iodinin                         | Anti-leukemic                    |
| 97  | Djinni et al., 2013 [102]     | Streptomyces sundarbanensis                 | Marine bacteria               | Algerian        | Polyketide                       | Antibacterial, Antimicrobial     |
| 98  | McCulloch et al., 2021 [103]  | Pseudopterogorgia elisabethae              | Soft coral                    | Canada          | Pseudopterosazole and Pseudopterosin | Antitubercular                  |
| 99  | Schubert et al., 2010 [104]   | Enhygromyxa salina                         | Marine mycobacteria           | Germany         |                                 | Antibiotics                      |
| 100 | Wright et al., 2012 [105]     | Sinularia sp.                                | Soft coral                    | Australia       | Cytotoxic Diterpenes             | Anticancer                       |
| No.  | Reference                          | Species                  | Location       | Compounds                     | Bioactive Compounds                  |
|------|-----------------------------------|--------------------------|----------------|-------------------------------|--------------------------------------|
| 101  | González P et al., 2021 [106]     | Algae                    | Spain          | Xanthophylls                  | Anti-tumor and anti-inflammatory     |
| 102  | Soliga et al., 2021 [107]         | Sponge                   | Germany        | Diglycosyl Tetramic Acid      | Microbial biofilm inhibitor          |
| 103  | Harper et al., 2015 [108]         | Aplidium sp.             | Sea squirts    | Thiaplidiquinones A and B     | Antimarial                           |
| 104  | Bahrami and Franco, 2015 [109]    | Holothuria lessonii      | Sea cucumber   | Saponin                       | Anticancer                           |
| 105  | Hou et al., 2021 [110]            | Hypoxylon sp.            | Mangrove-derived fungus | Diterpenoids and Isocoumarin | Antibacteri                          |
| 106  | Benkendorff K, 2013 [111]         | Dicathais orbita         | Australian dogwhelk or carrot shell | Tyrain purple | Dye                                 |
| 107  | Conde et al., 2021 [112]          | Chlorella vulgaris, Chlorococcum amblystomatidis, Scenedesmus obliquus, Tetraselmis chui, Phaeodactylum tricornutum, Spirulina sp., and Nannochloropsis oceanica | Portugal | Fatty acid | Antioxidant                          |
| 108  | Monks et al., 2002 [113]          | Marine sponges           | Brazil         |                               | Anticancer, antichemotactic and antimicrobial |
| 109  | Harikrishnan et al., 2021 [114]   | Fungi                    | India          |                               | Antibacterial, antioxidant and cytotoxic |

The development of marine natural products not only depends on biodiversity, abundance and the types of compounds it contains, but also the continuity stock for mass production. Natural resources function as producers of food, shelter, energy, and other human needs. The most dominant food sources are proteins, carbohydrates, fat, and vitamins. Living organism in the waters are very important because in addition they play a role in maintaining climate balance, they can also store chemical compounds that are needed by humans for medicine or other products. The marine exploration process requires special skills ranging from satellite surveillance to in situ observation using scuba or ROV (remote observation vehicle). A deeper search also requires in-depth knowledge of the area to be observed. One example of the exploration process regarding natural product is Seaweed. The problems faced in exploration activities are the limitations of the slow growth of species, and the abundance of these species. Exploring to find potential compounds from species also goes hand in hand with technological developments. The more technology development, the higher the percentage of potential obtained in only one species.

The management of potential compounds from biodiversity exploration in the sea is still scarce due to the limited number or stock. All methods and analyzes carried out in each research were almost the same and there were only slight differences. All methods used to see the activity of bioactive compounds using agar media. The significant difference between the methods applied is the amount of extraction used in each sample and also the temperature during the incubation process.
Based on research studies and literature collected, many researchers conducted activity tests of bioactive compounds from the exploration of compounds in the marine environments. The identified compounds included antioxidants, anticancer, antifouling, antifungal, antimicrobial, antibacterial, insecticidal, and other functions (Figure 2). Table 2 shows the meaning of the analyzed bioactive compounds.

**Table 2. Potential of bioactive compounds.**

| No | Function     | Definition                                                                 | Compound Sources                                      |
|----|--------------|---------------------------------------------------------------------------|-------------------------------------------------------|
| 1  | Antibacterial| Substances that can interfere with the growth or even kill bacteria by interfering with the metabolism of harmful microbes. | Macroalgae, Bacteria, Starfish, Seagrass, Mangroves, Plankton and Seaweed |
| 2  | Antifouling  | Techniques to prevent contamination or reduce the growth of organisms     | Seaweed                                               |
| 3  | Anti HIV     | Compounds that can be used to treat HIV                                   | Invertebrates                                         |
| 4  | Antiinflammatory | Properties that reduce inflammation                                    | Invertebrates                                         |
| 5  | Antifungal   | A substance that is fungicidal or fungistatic that can be used to treat fungal infections | Seaweed, Mangroves                                     |
| 6  | Antimicrobial| Substances that can kill gram-positive and gram-negative bacteria         | Mangroves                                             |
| 7  | Anticancer   | Substances that can inhibit and kill cancer cells                        | Invertebrates, Seaweed                                 |
| 18 | Antidiabetic | An activity given by certain compounds that can treat diabetes            | Seaweed                                               |
| 19 | Anticoagulants| Drugs used to prevent blood clotting                                     | Bacteria, Seaweed                                     |
| 8  | Antioxidant  | Molecules capable of slowing or preventing the oxidation of other molecules. Oxidation is a chemical reaction that can produce free radicals, thus triggering a chain reaction that can damage cells | Seaweed, Seagrass, Macroalgae, Mangrove, Sponge         |
| 9  | Antiproliferative| To maintain cell order and tissue homeostasis                           | Sponge                                               |
| 10 | Antitumor    | Substances that can inhibit and kill tumor cells                          | Sponge                                               |
| 11 | Antivirus    | Substances used to treat diseases caused by viral infections              | Algae                                                |
| 16 | Cytotoxic    | The degree of damage to a substance in cells                              | Invertebrates, Seagrasses, Mangroves                   |
| 17 | Insecticide  | Toxic chemicals used to kill insects                                      | Seaweed                                               |
| 12 | Imunostimulator| Substances that stimulate the immune system by inducing activation or increasing the activity of its components. | Starfish                                              |
| 14 | Proapoptotic | Enzymes used to carry out the process of apoptosis. The process of apoptosis aims to get rid of cells that are no longer needed by the body. | Sponge                                               |
| 15 | Proinflammatory| For defense and immune system against potential infection or harm       | Sponge                                               |
| 13 | Tyrosinase inhibitor| Molecules that can inhibit the enzyme tyrosinase                     | Seaweed                                               |
There are 28 types of tests for bioactive substances from marine organisms, both plants and animals. The five most potentially bioactive compound functions that have been studied based on Figure 2 respectively, were antioxidant, antibacterial, anticancer, antimicrobial and antifungal. Antioxidants are closely related to the world of health in general. The main benefit of antioxidants for the body is to protect cells from free radical damage. To be able to get these benefits, you need to consume a variety of food sources that contain antioxidants. Free radicals are substances that are formed naturally during metabolic processes in the body. In addition, these substances can also come from outside the body, for example from pollution, cigarette smoke, pesticides, or drugs. Free radicals can damage the DNA structure of cells, increase levels of bad cholesterol in the body, cause inflammation, and weaken the immune system.

Excessive and continuous exposure to free radicals can increase the risk of premature aging and several diseases, such as heart disease, cancer, and dementia. Frequent exposure to free radicals can also make the body susceptible to illnesses and increase the risk of developing cataracts.

Therefore, the body needs antioxidants to eliminate the effects of exposure to these free radicals. Some substances that have antioxidant properties are flavonoids, polyphenols, beta carotene, lutein, lycopene, selenium, zinc, anthocyanins (colorants in fruits and vegetables), as well as vitamin A, vitamin C and vitamin E. Figure 2 shows that there are still many study opportunities related to natural product such as studies on substances against anti-aging, antiviral, antibiotic, anticancer and others that have great economic value and benefits.

Most of the research from the publications reviewed was recently on the order of exploration of bioactive compounds and their chemical contents. Very few have investigated product and commercialization. This happens because of the lack of coordination between researchers from various fields to build cooperation. Generally, each researcher works alone and studies starting from downstream and never reaches upstream.

Figure 2. Potential number of bioactive compounds based on literature studies.
Figure 3 shows 15 sources of marine bioactive ingredients that have been analyzed, ranging from bacteria, plants to animals. From 15 types of the marine organisms that have been analyzed, 13 types contain anti-bacterial. The highest number of antibacterial studies was found in sponge [6], and seagrass [8], seaweeds and bacteria [115], respectively. Phenolic compounds that function as antioxidants were found in different seagrass species *Thalassia testudineum*, *Syringodium filiforma* and *Cymodocea rotundata* as well as mangrove species *Rhizopora mueronata* and *Avicenia alba* [20, 22-23, 33]. Phenolic compounds were also found in marine animals, namely the golden sea cucumber (*Golden Stichopus variegatus*) [24].

Macroalgae types *Ulva lactuca* and *Enteromorpha prolifera* contain antioxidant compounds from phycocyanins and oligosaccharides [30, 116]. Antioxidant phenolic bioactive compounds, flavonoids, methanol were also found from extracts of microalgae species *Thalassiosira*, *Skeletonema*, and *Chaetocerus* [31]. Extracts from the sponge type *Callyspongia* produce alkaloids [17]. In addition to plants and animals, bacteria can also potentially produce antioxidant bioactive compounds, such as *Serratia marcescens* bacteria and *Aspergillus usit* bacteria associated with sponges [34, 6].

The five main sources of marine material that have become the object of research are: seaweeds (26 papers), sponges (23 papers), bacterial (20 papers), macroalgae (17 papers) and seagrasses (15 papers). The least researched information is plankton, mollusks and chordates, each with only 1 reference. Seaweeds are the most studied because they are easy to cultivate, so they can be mass produced. The most studied types of seaweeds are *Caulerpa* sp., *Eucheuma* sp, *Gracilaria* sp and *Sargassum* sp.

Figure 3. Sources and potential results of bioactive compounds.
The graph (Figure 3) shows the potential for bioactive compounds from various groups of animals and plants being explored in the marine environment. One of the most abundant potential bioactive are Antioxidant and Antibacterial. These antioxidants and antibacterial substances were found in almost every species or group of animals and plants including mangroves, seagrasses, sponges, bacteria, macroalgae, seaweeds, fungi, echinoderms and microalgae. Antibacterial activity was also detected in soft corals and plankton.

Antibacterial potential can be found in mangroves, seagrass, macroalgae, microalgae, fungi and bacteria. Extracts from mangrove leaves of *Avicenia* sp. can have the potential as antibacterial agents because it contains steroid compounds, triterpenoids, flavonoids, alkaloids and polyphenols [20]. The type of seagrass *Holothuria edulis* which contains triterpenoids has potential as antibacterial [21]. Seaweed species *Caulerpa* sp., *Euchema* sp., *Gracilaria* sp. and *Sargassum* sp. contains steroid compounds, alkaloids, triterpenoid flavonoids and tannins which have potential as antibacterial [22]. Spirulina microalgae contain polyphenol compounds which have potential as antibacterial compounds [23]. Bacteria and fungi are also potential organisms as sources of antibacterial compounds. Bacterial extract that has the potential as an antibacterial is the type of *Serratia mercesnes* [18]. Several types of marine fungi can inhibit the growth of *Mycobacterium tuberculosis* bacteria, this is certainly very useful if developed in the medical world because it can help overcome Tuberculosis (TBC) disease [24].

Almost all papers that have been analyzed in the present study generally only reached the testing stage and the discovery of new compounds. Even though it has been proven, for example, as anti-cancer, anti-aging, anti-microbial, etc., many of the results of studies on natural marine products do not reach the downstream level for mass production. Some marine products that are widely available on the market are gamat water, fish oil, Spirulina, and several sea weed products. However, when viewed in the e-commerce market, in general, relatively more natural medicinal ingredients come from land plants such as Sambiloto, turmeric, garlic extract, java noni. What are the real problems faced by researchers in bringing natural ingredients from the ocean to pharmaceuticals? There are many studies that have been carried out related to chemical compounds of natural products. One of them is Carroll et al. [113] which has reviewed 740 papers. Their study recorded as many as 1490 bioactive compounds extracted from marine natural products in 477 papers from 740 papers reviewed [113]. However, of the many findings of bioactive compounds from this natural marine resource, very few end up being commercial products. The results of the review of 109 papers in this study also only examined the bioactivity and bioactive compounds they contain. No one has integrative studied that evaluate or assess the process of natural ingredients of products from the sea to pharmaceuticals or consumers.

The discontinuation of these research is due to the study approach which is still mono-disciplined. Generally, the background of many researchers in this field comes from natural sciences such as biochemists, natural product science experts, biologists and ecologists. Very few involve medical personnel, economists and entrepreneurs. As a result, many of the findings of bioactive compounds from the sea only end up as papers.

Another problem with the commercialization of marine natural products is the limited availability of natural stocks. Tropical marine ecosystems that are rich in biodiversity have very low natural species abundances that do not allow them to be exploited on a large scale. Massive exploitation of tropical marine biological resources will disrupt the balance of the existing system, therefore in the utilization of marine natural products it is necessary to study stock availability, environmentally friendly product propagation techniques and integrated management of marine biological resources. This cross-disciplinary study is still very weak in studies of the use of marine biological resources. Very few journals involve chemists, ecologists, marine aquaculture experts, pharmacists, economists and entrepreneurs. The downstream process of these natural products requires the continuity of cross-disciplinary research with a transdisciplinary approach as a unified research team. The findings of these bioactive compounds must be followed up in an integrated manner in a unified research package. The readiness to provide stock on a mass scale is one of the challenges in the commercialization of marine natural products.
4. Conclusion

The search results of literature studies show that there are many variations of potential bioactive compounds produced by marine organism for the use of their antioxidants, antibacterial, anticancer, anticoagulants, antidiabetics, antifungals, antiaging, antifouling and insecticides functions due to the abundant marine biodiversity.

The findings of the study of bioactive compounds from natural marine materials are numerous. Various chemical compounds from marine natural products have been identified. Many of these findings are not processed until the commercialization of natural medicinal products. Some end up as synthetic drugs. The limited stock of marine natural resources is one of the challenges, so it does not continue to the stage of testing the scale of mass production. The lack of integrated reset across disciplines is one of the future challenges that need to be done to reach the commercialization.

References

[1] Rimper J R T S L 2014 Deteksi senyawa bioaktif rotifera Brachionus rotundiformis dari perairan Laut Sulawesi Utara Jurnal Ilmu Hewani Tropika 3(1) 17-21
[2] Rocha J, Peixe L, Gomes N and Calado R 2011 Cnidarians as a source of new marine bioactive compounds an overview of the last decade and future steps for bioprospecting Mar. Drugs 9(10) 1860-6
[3] Yuan H, Ma Q, Ye L and Piao G 2016 The traditional medicine and modern medicine from natural products Molecules 21 559
[4] Kijjoa A and Sawangwong P 2004 Drugs and cosmetics from the sea Mar. Drugs 2 (2) 73-82
[5] Riyadi I 2008 Potensi pengelolaan bioprospeksi terhadap pertumbuhan ekonomi Indonesia Jurnal Litbang Pertanian 27(2) 69-73
[6] Pratitit A, Patantis G, Mangunwardoyo W and Chasanah E 2010 Produksi Senyawa bioaktif dari Aspergillus Ustus MFW 26-08 yang berasosiasi dengan spons laut dalam berbagai media J. Pascapanen Dan Bioteknol. Kelaut. Dan Perikan 5(2) 93-101
[7] Marhaeni B, Radjasa O K, Khoeri M M, Sabdono A, Bengen D G and Sudoyo H 2011 antifouling activity of bacterial symbionts of seagrasses against marine biofilm-forming bacteria J. Environ. Prot. 2(09) 1245-9
[8] Ali M S, Ravikumar S and Beula J M 2012 Bioactivity of seagrass against the dengue fever mosquito aedes aegypti larvae Asian Pac. J. Trop. Biomed. 2(7) 570-3
[9] Fajarningsih N D, Pratitit A, Wikanta T and Chasanah E 2012 Bioprospeksi kapang yang berasosiasi dengan biota laut asal kepulauan seribu sebagai antitumor T47D dan Hepg2 J. Pascapanen Dan Bioteknol. Kelaut. Dan Perikan. 7 21-30
[10] Karthikeyan V, Gopalakrishnan A, Vijayakumar R and Bharathirajan P 2012 anticoagulant activity of marine bivalve Donax incarnates Lin, 1758 collected from Thazhanguda, Southeast Coast of India. Asian Pac. J. Trop. Biomed. 2 S1798-801
[11] Pranoto E N, Ma’ruf W F and Pringgenies D 2012 Kajian aktivitas bioaktif ekstrak teripang pasir (Holothuria scabra) terhadap jamur Candida albicans J. Pengolah. Dan Bioteknol. Has. Perikan. 1(1) 1-8
[12] Siregar A F, Sabdono A and Pringgenies 2012 Potensi antibakteri ekstrak teripang pasir (Holothuria scabra) terhadap jamur Candida albicans J. Pengolah. Dan Bioteknol. Has. Perikan. 1(2) 152-60
[13] Wusqy N K, Prayitmo D I, Radjasa O K, Limantara L and Karwur F F 2012 Penelusuran senyawa bioaktif bakteri yang berasosiasi dengan anemon laut serta identifikasi molekulernya berbasis 16S RDNA J. Perikan. Univ. Gadjah Mada 14 1-10
[14] Karina T, Primastia N, Rahmatika N, Rizki M and Purwati N 2013 anti tuberkulosis dari laut: potensi jamur sebagai anti Mycobacterium tuberculosis dari alga coklat dan karang E-Proc. PKM-P 1-5
[15] Sukmarianti N W S, Suaniti N M and Swantara I M D 2013 Identifikasi dan uji aktivitas antikanker ekstrak spons Ianthella basta terhadap larva Artemia salina L. CAKRA KIMIA (Indonesian E-Journal of Applied Chemistry) 1(1) 14-9

[16] Al-Saif S S A, Abdel-Raouf N, El-Wazanani H A and Aref I A 2014 Antibacterial substances from marine algae isolated from Jeddah Coast of Red Sea, Saudi Arabia Saudi J. Biol. Sci 21 57-64

[17] Sari N I, Ahmad A and Dali S 2014 Isolasi dan Karakterisasi Protein Bioaktif dari Spons Callyspongia Sp. Sebagai Zat Antioksidan Hasanuddin University Repository p 8 (repository.unhas.ac.id: 123456789/8695)

[18] Sari E M, Ma’ruf W F and Sumardianto 2014 Kajian senyawa bioaktif ekstrak teripang hitam (Holothuria edulis) basah dan kering sebagai antibakteri alami J. Pengolah. dan Bioteknol. Has. Perikanan 3(4) 16-24

[19] Hardoko H, Febriani A and Sirantri T 2015 Invitro antidiabetic activities of agar, agarosa, and agarpectin from Gracilaria gigas seaweed J. Pengolah. Has. Perikan. Indones. 18 128-39

[20] González K L, Gutiérrez R, Hernández Y, Valdés-Iglesias O and Rodriguez M 2016 Determination of the antioxidant capacity of two seagrass species according to the extraction method J. Pharm. Pharmacogn Res. 4(5) 199-205

[21] Puspasari A, Dewi E and Rianingsih L 2017 Aplikasi antioksidan dari ekstrak lamun (Cymodocea rotundata) pada minyak ikan tongkol (Euthynnus affinis) AGRITECH 37 115

[22] Szubert K, Wiglusz M and Mazur-Marzec H 2018 Bioactive metabolites produced by Spirulina subsalsa from The Baltic Sea Oceanologia 60 245-55

[23] Alhaddad Z A, Tanod W A and Wahyudi D 2019 Bioaktivitas antibakteri dari ekstrak daun mangrove Avicennia sp. J. Kelaut. Indones. J. Mar. Sci. Technol 12(1) 12-22

[24] Liu X, Liu D, Guopeng L, Wu Y, Gao L, Ai C, Huang Y, Wang M, El-Seedi H, Chen X and Zhao C 2019 Anti-ageing and antioxidant effects of sulfate oligosaccharides from green algae Ulva lactuca and Enteromorpha Prolifera in SAMP8 mice Int. J. Biol. Macromol 139 342-51

[25] Syahputra F S 2019 Penambahan ekstrak larutan kulit mangrove pada cat minyak sebagai antifouling Acta Aquat. Aquat. Sci. J. 6 (1) 37-40

[26] Al-Malki A L 2020 In vitro cytotoxicity and pro-apoptotic activity of phycocyanin nanoparticles from Ulva lactuca (Chlorophyta) algae Saudi J. Biol. Sci. 27 894-8

[27] Bhattacharjya R, Marella T K, Tiwari A, Saxena A, Singh P K and Mishra B 2020 Bioprospecting of marine diatoms thalassiosira, skeletonema and chaetoceros for lipids and other value-added products Bioresour. Tech. 318 124073

[28] Cao X, Che Z, Zhou B, Guan B, Chen G, Zeng W and Liang Z 2020 Investigations in ultrasound-assisted anticoagulant production by marine Bacillus subtilis ZHX Ultrason. Sonochem 64 104994

[29] Esswariah G, Phee K K, Krupanidhi S, Kumar R B and Venkateswarulu T C 2020 Studies on phytochemical, antioxidant, antimicrobial analysis and separation of bioactive leads of leaf extract from the selected mangroves J. King Saud Univ. Sci. 32 842-7

[30] Gangadharan A, Jolly J and John N 2020 Bioprospecting of novel therapeutic agents from marine bacterium; Serratia marcescens Materials Today Proc. 25 298-301

[31] Alshuniaber M A, Krishnamoorthy R and Alqhtani W H 2021 Antimicrobial activity of polyphenolic compounds from spirulina against food-borne bacterial pathogens Saudi J. Biol. Sci. 28 459-64
[36] Nowruzia B, Haghighat S, Fahimic H and Mohammadi E 2017 Nostoc cyanobacteria species: a new and rich source of novel bioactive compounds with pharmaceutical potential JPHS 2018 9 5-12
[37] Al-Amoudi S, Essack M, Simões M F, Bougouffia S, Soloviev I, Archer J A C, Lafi F F and Bajic V B 2016 Bioprospecting Red Sea coastal ecosystems for culturable microorganisms and their antimicrobial potential Mar. Drugs 2016 14(9) 165
[38] Piter D, Ester D A and Fitje L 2019 The antibacterial potential of starfish from the coastal waters of The Kelurahan Tongkaina Jurnal Pesisir dan Laut Tropis 7 167-73
[39] Setyoningrum D, Yamindago A, Sari S H J and Maftuch M 2020 Phytochemical analysis and in vitro antibacterial activities of seagrass Enhalus acoroides against Staphylococcus aureus Res. J. Life Sci. 7 85-91
[40] Kim D H, Mahomoodally M F, Sadeer N B, Seok P G, Zengin G, Palaniveloo K, Khalile A A, Rauf A, and Rengasamy K R 2021 Nutritional and bioactive potential of seagrasses: a review S. Afr. J. Bot. 137(2021) 216-27
[41] Gazette M, Eri S, Zulfadhli, Neviaty P Z and Nurjanah 2017 Eksplorasi potensi senyawa bioaktif makroalga Sargassum sp sebagai antibakteri asal PesisirBarat Selatan (Barsela) Aceh Pros. Semdi Unaya (Seminar Nasional Multi Disiplin Ilmu Unaya) 1(1) 289-300
[42] Gazali M, Neviaty P Z, Nurjanah, Zulfadhli and Eri S 2017 Eksplorasi potensi senyawa bioaktif makroalga laut Sargassum sp asal Pesisir Aceh Barat sebagai agen antioksidan J. Aceh Aquatic Sci. 1 43-52
[43] Winowoda S D, Marina F O S and Ratna S 2020 Kekayaan dan potensi senyawa bioaktif makroalga di Pesisir Atep Oki, Kabupaten Minahasa, Sulawesi Utara Jurnal Pesisir dan Laut Tropis 8 7-16
[44] Zhi Y X, Zhang X X, Ma J K, Yang Y, Zhou J and Xu J 2020 Secondary metabolites produced by mangrove endophytic fungus Aspergillus fumigatus HQD24 with immunosuppressive activity Biochem. Syst. Ecol. 93 104166
[45] Lubis D O 2017 Potensi Senyawa Bioaktif Rumput Laut Halimeda micronesica dan Halimeda macroloba sebagai Antioksidan dan Skrining Fitokimia Ekstrak Aktif Rumput Laut dari Pulau Maspari Bachelor Thesis Universitas Sriwijaya, Sriwijaya
[46] Rajasabapathy R, Ghadb S C, Manikandan B, Mohandass C, Surendrane A, Dastagere S G, Meena R M and James R A 2020 Antimicrobial profiling of coral reef and sponge associated bacteria from Southeast Coast of India Microb. I Pathog. 141 103972
[47] Dolorosa M T, Nurjanah, Sri P, Effionora A and Taufik H 2017 Kandungan senyawa bioaktif bubur rumput laut Sargassum plagyophyllum dan Eucheuma cottonii sebagai bahan baku krim pencerah kulit Jurnal Pengolahan Hasil Perikanan Indonesia 20 633-44
[48] Zulfadhli and Rinawati 2018 Potensi selada laut ulva lactuca sebagai antifungi dalam pengendalian infeksi Saprolegnia dan Achlya pada budidaya ikan kerling (Tor sp) Jurnal Perikanan Tropis 5 183-8
[49] Santi I W, Ocky K R and Ita W 2014 Potensi rumput laut Gratacila verrucosa dari Pantai Gunung Kidul, Yogyakarta Jurnal Kelautan Tropis 22 81-6
[50] Febrianto W, Ali D, Suryono, Gunawan W S and Sunaryo 2019 Potensi antioksidan rumput laut Gracilaria verrucosa dari Pantai Gunung Kidul, Yogyakarta Jurnal Kelautan Tropis 22 81-6
[51] Stabili L, Acquaviva M I, Angilè F, Cavallo M A, Cecere E, Coco L D, Fanizzi F P, Gerardi C, Narracci M and Petrocelli A 2019 Screening of Chaetomorpha linum lipidic extract as a new potential source of bioactive compounds Mar. Drugs 17 313
[52] Zerrifi S E A, Khalloufi F E, Oudra B and Vasconcelos V 2018 Seaweed bioactive compounds against pathogens and microalgae: potential uses on pharmacology and harmful algae bloom control Mar. Drugs 16 55
[55] Fajarningsih N D, Nursid M, Januar H I and Wikanta T 2013 Bioprospeksi spons, karang lunak dan ascidian asal Taman Nasional Laut Kepulauan Wakatobi: antitumor dan antioksidan JPB Perikanan 8 (2) 161
[56] Luter H M and Duckworth A R 2010 Influence of size and spatial competition on the bioactivity of coral reef sponges Biochem. Syst. Ecol. 38 146-53
[57] Fristiohady A and Haruna L A 2020 Review jurnal: potensi spons laut sebagai anti kanker payudara Jurnal Mandala Pharmacon Indonesia 8 (2) 161
[58] Mayefis D, Hainil S and Sari N 2021 Aktivitas sitotoksik ekstrak spons laut natuna dengan metode brine shrimp lethality test (BSLT) Scientia J. Far. Kes. 11 56-61
[59] Jin L, Quan C, Hou X and Fan S 2016 Potential pharmacological resources: natural bioactive compounds from marine-derived fungi Mar. Drugs 14(4) 76
[60] Suparno 2005 Kajian Bioaktif Spons Laut (Forifera: Demospongiae) Suatu Peluang Alternatif Pemanfaatan Ekosistem Karang Indonesia dalam Dibidang Farmasi Makalah Pribadi Falsafah Sains (PPs 7002) IPB University, Bogor
[61] Nurhayati A P D, Abdulgani N and Febrianto A 2006 Uji toksisitas ekstrak eucheuma alvarezii terhadap Artemia salina sebagai studi pendahuluan potensi antikanker Akta Kimindo. 2(1) 41-6
[62] Ismet M S 2007 Penapisan Senyawa Bioaktif Spons Aaptos aaptos dan Petrosia sp. dari Lokasi yang Berbeda Master Thesis IPB University, Bogor
[63] Tamat S R 2007 Aktivitas antioksidan dan toksisitas senyawa bioaktif dari ekstrak rumput laut hijau Ulva reticulata Forsskål Jurnal Ilmu Kefarmasian Indonesia 5(1) 31-6
[64] Rahmadi P, Pangestuti R and Salim G 2011 Potensi rumput laut sebagai bahan dasar kosmeseutikal Jurnal Harpodon Borneo 4(1) 77-88
[65] Rumengan A P 2013 Antibakteri dari ekstrak karang lunak Nephtea sp. Jurnal Pesisir dan Laut Tropis 3(1) 31-5
[66] Faisal M R, Kawaroe M and Satria F 2014 Potensi senyawa bioaktif ekstrak kasar bakteri simbion spons sebagai antibakteri Jurnal Omni-Akuatika 10(2) 77-84
[67] Rahakbauw I D and Watuguly T 2016 Analisis senyawa flavonoid daun lamun Enhalus acoroides di perairan Pantai Desa Waai Kabupaten Maluku Tengah Biopendix 3(1) 53-62
[68] Mushofatul A 2017 Potensi Antifouling Dari Senyawa Bioaktif Lamun Enhalus Acoroides Dari Pulau Lancang, Kepulauan Seribu JPHPI 15(3) 207-15
[69] Hutabarat L S, Syakti A D and Ilhamdy A F 2017 Aktivitas Antioksidan dan Bioaktif dari Ekstrak Lamun E. Acoroides Repository UMRAH
[70] Nurrachmi I, Amin B and Yoswaty D 2018 Analisis senyawa flavonoid daun lamun Eucheuma cottonii di perairan Pantai Pulau Jaga, Karimun Provinsi Kepulauan Riau Asian J. Energy Environ. 2(1) 105-12
[78] Sibero M T, Sabdaningsih A, Radjasa K, Sabdono A, Trianto A and Subagyo 2019 Karakterisasi senyawa bioaktif kaping laut Trichoderma asperellum MT02 dengan aktivitas anti-Extended Spectrum B-Lactamase (ESBL). *E. coli Jurnal Kelautan Tropis* 22(1) 9-18

[79] Julyash K S M and Widiyanti N L P M 2020 Komponen fitokimia makro alga yang diseleksi dari Pantai Sanur Bali *SENARI* 7 28-31

[80] Julyash K S M, Wirawan I G P, Wiwik S H and Wiludjeng W 2009 Aktivitas Antioksidan Beberapa Jenis Rumput Laut (Seaweeds) Komersial di Bali *Seminar Nasional Fakultas pertanian dan Lppm Veteran Jawa Timur*

[78] Batubara I, Maily , Wulan T W, Kilala T, Waras N, Fransiska D J, Yogo S P, Erna M S, Saat E and Nevianty P Z 2020 Tyrosinase inhibition, antiglycation, and antioxidant activity of *Xylocarpus granatum Journal of Biology & Biology Education Biosaintifika* 12(1) 70-5

[82] Gazali M, Neviaty P Z and Irmanida B 2014 Potensi limbah kulit buah nyirih *Xylocarpus granatum* sebagai inhibitor tyrosinase *Jurnal Ilmu periran, pesisir dan perikanan (DEPIK)* 3 (3) 187-94

[83] Mao W, Hongyan L, Yi L, Huijuan Z, Xiaohui Q, Haihong S, Yin C and Shoudong G 2009 Chemical characteristic and anticoagulant activity of the sulfated polysaccharide isolated from *Monostroma latissimum* (Chlorophyta) *Int. J. Biol. Macromol.* 44(1) 70-4

[84] Wei W, Ping-Jyun S, Chang-Yih D, Bo-Wei C, Jyh-Horng S and Ning-Sun Y 2013 Anti-inflammatory activities of natural products isolated from soft corals of taiwan between 2008 and 2012 *Mar. Drugs* 11 4083-126

[85] Calabro K, Elaheh L K, Daniel R, Caridad D, Mercedes D L C, Bastien C, Rémi L, Fernando R, Thierry P, Bassam S and Olivier P T 2017 Poecillastrosides, steroidal saponins from the Mediterranean Deep-Sea sponge *Poecillastra compressa* (Bowerbank, 1866) *Mar. Drugs* 15(7) 199

[86] Pimentel-Elardo S M, Svtlana K, Tim S B, Chris M I, Heidrun M and Ute H 2010 Anti-parasitic compounds from *Streptomyces* sp. strains isolated from Mediterranean sponges *Mar. Drugs* 8 373-80

[87] Mhadhebi L, Afef D, Audrey C, Rafik B S, Jacques R and Abderrahman B 2012 Anti-inflammatory and antiproliferative activities of organic fractions from the Mediterranean brown seaweed, *Cystoseira Compressa Drug Dev. Res.* 73 82-9

[88] Jeon J E, Na Z, Jung M, Lee H S, Sim C J, Nahm K, Oh K B and Shin J 2010 Discorhabdins from the Korean marine sponge *Sceptrella sp* *J. Nat. Prod.* 73 258-62

[89] Tello E, Castellanos L, Arevalo-Ferro C, Duque C 2009 Cembranoid diterpenes from the Caribbean Sea whip *Eunicea knighti* *J. Nat. Prod.* 72 1595-602

[92] Vicente, J, Vera B, Rodríguez A D, Rodríguez-Escudero I, Raptis R G 2009 Euryjanicin A: A new cycloheptapeptide from the Caribbean marine sponge *Prosuberites laughlini* *Tetrahedron Lett.* 50 4571-74

[93] Muddala R, Acosta J A M, Barbosa L C A and Boukouvalas J 2017 Synthesis of the marine myxobacterial antibiotic enhygrolide A *J. Nat. Prod.* 80 2166-9

[94] Teta R, Marteinsson V T, Longeon A, Klonowski A M, Groben R, Bourguet-Kondracki M L and Mangoni A 2017 Thermoactinoamide A, an antibiotic lipophilic cyclopeptide from the icelandic thermophilic bacterium *Thermoactinomyces vulgaris* *J. Nat. Prod.* 80(9) 2530–5

[95] Cui P, Guo W, and Chen X 2017 Isotryptophan from Antarctic *Bacillus amyloliquefaciens* Pc3: purification, identification, characterization, and antifungal activity *Nat. Product Research* 31 2153–7

[96] Medeiros H E, Gama B A P and Gallerani G 2007 Antifouling activity of seaweed extracts from Guaruja, Sao Paulo, Brazil *Braz. J. Oceanogr.* 55 257–64
[97] Lim H K, Bae W, Lee H S and Jung J 2014 Anticancer activity of marine sponge Hyrtios sp. Extract in human colorectal carcinoma RKO cells with different p53 status BioMed. Res. Int. 2014 413575

[98] Palomo S, González I de la Cruz M, Martín J, Tormo J, Anderson M and Genilloud O 2013 Sponge-derived Kocuria and Micrococcus spp. as sources of the new thiazoyl peptide antibiotic kocurin Mar. Drugs 11(12) 1071–86

[99] Myhren L, Nygaard G, Gausdal G, Sletta H, Teigen K, Degnes K and Herfindal L 2013 Iodinin (1,6-Dihydroxyphenazine 5,10-Dioxide) from Streptosporangium sp. induces apoptosis selectively in myeloid leukemia cell lines and patient Cells Mar. Drugs 11(12) 332–49

[100] Djinni I, Defant A, Kecha M and Mancini I 2013 Antibacterial polyketides from the marine alga-derived endophytic streptomyces sundarbansensis: a study on hydroxypryne tautomerism Mar. Drugs 11 124–35

[101] McCulloch M W B, Halti B, Marchbank D H and Kerr R G 2012 Evaluation of pseudopteroxazole and pseudopterosin derivatives against mycobacterium tuberculosis and other pathogens Mar. Drugs 10 1711–28

[102] Schäberle T F, Goralski E, Neu E, Erol Ö, Hölzl G, Dörmann P and König G M 2010 Marine myxobacteria as a source of antibiotics—comparison of physiology, polyketide-type genes and antibiotic production of three new isolates of Enhygromyx salina Mar. Drugs 8(9) 2466–79

[103] Wright A D, Nielson J L, Tapiolas D M, Liprot C H and Motti C A 2012 A Great Barrier Reef Simulalia sp. yields two new cytoxigenic diterpenes Mar. Drugs 10 1619–30

[104] González P A, Otero P, Escamez Álvarez J, Carreira-Casais A, Rivo F N, Collazo N, Jarboui A, Lourenço-Lopes C, Simal-Gandara J and Prieto Lage M 2021 Xanthophylls from the sea: algae as source of bioactive carotenoids Mar. Drugs 19(4) 188

[105] Soliga K J, Bär S I, Oberhuber N, Zeng H, Schrey H and Schobert R 2021 Synthesis and bioactivity of ancorinoside b, a marine diglycosyl tetracyclic acid Mar. Drugs 19 583

[106] Harper J L, Khalil I M, Shaw L, Bourguet-Kondracki M L, Dubois J, Valentin A, Barker D and Copp B R 2015 Structure-activity relationships of the bioactive thiazinoquinone marine natural products thiaplidiaquinones A and B Mar. Drugs 13 5102–10

[107] Bahrami Y and Franco C 2015 Structure elucidation of new Acetylated Saponins, Lessoniosides A, B, C, D, and E, and Non-Acetylated Saponins, Lessoniosides F and G, from the viscerum of a sea Cucumber Holothuria lesson Mar. Drugs 13 (1) 597–617

[108] Hou B, Liu S, Huo R, Li Y, Ren J, Wang W, Wei T, Jiang X, Yin W and Liu H 2021 New Diterpenoids and isocoumarin derivatives from the mangrove-derived fungus Hypoxylon sp. Mar. Drugs 19 362

[109] Benkendorff K 2013 Natural product research in the australian marine invertebrate Dicathais orbita Mar. Drugs 11 (4) 1370–98

[110] Conde T A, Neves B F, Couto D, Melo T, Neves B, Costa M, Silva J, Domingues P and Domingues M R 2021 Microalgae as sustainable bio-factories of healthy lipids: evaluating fatty acid content and antioxidant activity Mar. Drugs 19 357

[111] Monks N R, Lerner C, Henriques A T, Farias F M, Schapoval E E S, Suyenaga E S, da Rocha A B, Schwartzman G and Mothes B 2002 Anticancer, antichemotactic and antimicrobial activities of marine sponges collected off The Coast of Santa Catarina, Southern Brazil J. of Exp. Mar. Biol. and Ecol. 281 1–12

[112] Harikrishnan M, Saipriya P P, Prakash P, Jayabaskaran C and Bhat S G 2021 Multi-functional bioactive secondary metabolites derived from endophytic fungi of marine algal origin CRMICR 2 100037

[113] Carrol R A, Copp B R, Davis R A, Keyzers R A and Prinsep M R 2019 Marine natural product Nat. Prod. Rep. 36 122

[114] Radjasoa O K, Salasia S I O, Sabdono A and Jutta W 2007 Antibacterial activity of marine bacterium Pseudomonas sp. associated with soft coral Simulalia Polyactyla against Streptococcus Equi Subsp. Zooepidemicus Int. J. Pharmacol 3(2) 170–4

[115] Vallinayagam K, Arumugam R, Kannan R, Thrirumar G and Anantharaman P 2009 Antibacterial activity of some selected seaweeds from Pudumadom Coastal Regions Glob. J. Pharmacol. 3(1) 50-2
[116] Liu X, Liu D, Guopeng L, Wu Y, Gao L, Ai C, Huang Y, Wang M, El-Seedi H, Chen X and Zhao C 2019 Anti-ageing and antioxidant effects of sulfate oligosaccharides from green algae Ulva lactuca and Enteromorpha prolifera in SAMP8 mice Int. J. Biol. Macromol. 139(15) 342-51