Journal of Coastal Development
Volume 12 Number 1 : 1-12
ISSN : 1410-5217

MARINE BIODISCOVERY RESEARCH IN INDONESIA : CHALLENGES AND REWARDS

Ekowati Chasanah

Research Centre for Marine and Fisheries Product Processing and Biotechnology,
Jl. KS Tubun, Petamburan VI, Jakarta 10260, Indonesia

Received : June, 02, 2008 ; Accepted : August,27,2008

ABSTRACT

Marine biodiscovery or bioprospecting activity is a search for marine products derived from marine biodiversity that can be developed for various industrial needs. Including in this activity is the process of identifying chemical compounds made by biological organisms which is often called natural product discovery. Indonesia, well known as a mega-diversity country, is one of the world hot sport of marine biodiversity. The richness of biodiversity is claimed as mirror of the richness of the chemical compounds, therefore, Indonesian waters might be rewarded with variety of chemical compounds thought to be an endless source of novel drugs and drug leads for pharmaceutical use. Up to 2007, at least 77 new compounds from 14 sponges and 19 new compounds from non-sponge organisms with pharmacological potential have been identified from Indonesian waters. To make this richness potentials becoming real in economic value, many factors should be considered. The bioactive is produced in small quantity, and the lengthy process from discovery step of a novel compound to the preclinical and clinical trials step is usually becoming a problem. Mari culture might be one among methods that can be developed in Indonesia to overcome the degradation hazard of marine resources. Conducive environment for investments, and improvement of technology on marine bioactive production through mariculture are factors to be improved to initiate and develop a sustainable biotechnology industries in Indonesia.

Keywords : marine biodiscovery, Indonesia, pharmacological potential

Correspondence : Phone : +62-21-53650158; +62-21-53650157; email : ekowati_ch@yahoo.com

INTRODUCTION

Humans have been taking advantage of marine chemical compounds present in marine organisms for various needs such as food sources and disease remedies since ancient times. For Indonesian people, chemical compounds present in marine as well as the terrestrial organisms have popularly been used as “jamu”, a traditional medicine, through indigenous knowledge passed from one generation to generation since hundreds of years ago.

“Drug from the sea” started to boom after the 1967-symposium in Rhode Island University (Fusetani, 2000). Marine natural products, especially secondary metabolite compounds, are thought to be an endless source of novel drugs and drug leads for pharmaceutical use. Richness of the chemical compounds in marine environment generally positively correlated with the richness of biodiversity in the environment

 ISSN : 1410-5217

Indonesia is one of the ten countries with the richest biodiversity, and is often known as a mega-diversity country (Anonymous, 2003). In more than 20 years, Indonesia has become a target for bioactive marine natural product chemistry research, and numbers of novel compounds and scientific papers have been published as cited in the following section. The uniqueness and richness of biological diversity of Asia and Australia and the transitional zone of the two continents is present in Indonesia. This is supported by the geological history and topology of Indonesia which is located in the biodiversity path of the Asian continent (Sumatra, Java, Kalimantan) and Australia (Papua) and in the transitional zone of the Wallace (Sulawesi, Maluku and Nusa Tenggara Islands). More than 75% of Indonesia's area is marine with 81,000 km of shoreline, the second largest after Canada. This marine biodiversity is considered under explored and not fully studied (Anonymous, 2003; de Voogd, 2005). Therefore, Indonesian marine biodiversity has become a target of world and domestic biodiscovery, especially marine natural products chemistry research.

This review will cover natural products chemistry research using Indonesian biota, both by Indonesian as well as foreign scientists. Organisms, both micro and macro, used in these studies are from the entire Indonesian marine area, and almost all marine. Sponge, gorgonian and soft coral attracted more attention and more studied as being well known as rich sources of novel secondary metabolites.

BIODISCOVERY RESEARCH IN INDONESIA

Marine biodiscovery research, including natural products chemistry, in Indonesia has been actively conducted by several marine-related Indonesian research institutions as well as universities. Beginning in 1990, marine natural product research activities have been started by Indonesian researchers. However, due to some limitations in research resources, the progress is not significant especially in the form of international scientific papers, patent and commercial products. Mostly, biodiscovery research activities done in Indonesia is superficial (*i.e* preliminary screening towards various biological activities), and more depth activities are usually done in foreign country laboratories. Therefore, the products of invention of advance step such as structure of novel compounds, including patent of their product and process are usually under the properties of foreign-researchers.

World marine natural products chemistry research, in more than 20 years, has resulted many novel compounds, and some of them have been in the preclinical test for further commercialization, while some others are already commercialized (Faulkner, 2000). More than 2,700 research papers concerning sponges, the most secondary metabolite-rich compounds among marine organism, have been published up to year 2000 (Fusateni, 2000). There are approximately 850 species of sponge are believed to be present in Indonesia (de Voogd & van Soest, 2002), and up to 2007, at least 77 new compounds from 14 sponges and 19 new compounds from non-sponge organisms (soft coral, sea pen, octocoral and ascidians) with pharmacological potential that will be described below.

Sponges

The distribution, ecological study as well as sponges bioactivity (based on its brine shrimp, *Artemia salina*, lethality assay) of Spermonde archipelago, Sulawesi were studied by de Voogd (2005). From the study, nine (9) sponges were considered potential to be developed. The sponge

 ISSN : 1410-5217

Acanthodendrilla sp. collected from Badi Island, Makasar, was investigated by William *et al*. (2004), identifying meroterpenoid MAPKAP (MK2) inhibitor. Mapkap kinase-2 has important role in the regulation of TNF-α production, meaning that the compound represents a potential therapeutic agent to treat inflammatory diseases. Boneratamides A-C, new sesquiterpenoids, were isolated from sponge *Axinyssa aplysinoides* from the same surrounding Makasar waters (Williams *et al*. 2004), while a new acyclic diketotriterpenoid has been isolated from *Hyrtios erectus* sponges, from the inner reef of Ujung Pandang. This new compound was biologically inactive, however, the crude extract of the sponge had significant antimitotic activity (Williams *et al*., 1999). From the sponge *Stylissa carteri,* harvested from the waters in the same area, new alkaloids latonduines A and B were isolated by Linington *et al.* (2003), while two (2) new bromopyrrole alkaloids, *i.e*. debromostevensine and debromohymenin were isolated from the same sponge species collected from Ambon and Sulawesi waters (Eder *et al*., 1999). Chemical study of the sponge *Leucetta chagosensis* from South Sulawesi waters found five (5) new imidazole alkaloids, namely naamine F, naamine G, kealiinine A, kealiinine B and kealiinine C (Hassan *et al*., 2004). Naamine G showed antifungal activity against *Cladosporium herbarum* and mild cytotoxicity against mouse lymphoma and human cervical carcinoma (*HeLa*) cell lines. Crude extract of *Phyllospongia* sp. from Makasar's surrounding waters showed cytotoxicity, and seven (7) new scalarane class sesterterpenes have been isolated. All scalaranes isolated exhibited 30-95% inhibition of KB cells at a concentration of 10 µg/mL (Roy *et al*., 2002). From sponge *Theonella swinhoei*, harvested at Baranglompo Island, barangamide A, a cyclic undecapeptide possessing three N-methylated amino acids, and three β-alanines, have been isolated (Roy *et al*., 1999). Further investigation on that sponge revealed that three (3) new cyclic peptides, barangamide B, C and D have been isolated along with four (4) new depsipeptides. Immunomodulatory test of these compounds showed that barangamide A exhibited no immunosuppressive activity up to concentration of 100 µg/mL, while all theonellapeptolides showed mild activity (Roy *et al.*, 2000).

Study on sponge *Ianthella basta* from Manado Bay resulted in two (2) more bastadins, *i.e*. bastadin 16 and bastadin 17. Bastadin compounds are well known as predominantly macrocyclic sponge metabolite compounds (Park *et al*., 1994). Bobzin *et al.* (2000) used dereplication techniques to identify aaptamine from the sponge *Aaptos* sp. which was harvested from Manado, northern Sulawesi, while Park *et al.* (1995) studied sponge *Lufariella* sp. from the same waters and isolated three (3) metabolites, *i.e*. aaptamine, germacrene alcohol and hexacyclic terpene. The metabolites showed *in vitro* activity against the KB cancer cell line. From the North Sulawesi sponge *Theonella* cf. *swinhoei*, bitungolides A-F have been isolated. The bitungolides were claimed as a new class of *Theonella* metabolites that are capable of inhibiting dual-specificity phosphatase VHR (Sirirath *et al*., 2002). A study on a sponge from Knife cape, Manado Bay, resulted in seven (7) manzamine type alkaloid compounds, *i.e*. two (2) β-carbolines and five (5) nucleosides. Among them, five (5) new compounds were identified as 32,33-dihydro-31-hydroxymanzamine A, 32,33-dihydro-6 -dihydroxymanzamine A-35-one, des-N-methylxestomanzamine A, 32,33-dihydro-6,31-dihydroxymanzamine A and 1,2,3,4-tetrahydronorharman-1-one. Most manzamines were active against *Mycobacterium tuberculosis* (H37Rv), malaria parasite *Plasmodium falciparum* and *Leishmania donovani* (Rao *et al*., 2003). In 1995, an unsymmetrical manzamine dimmer called kauluamine, was isolated from sponge *Prianos* sp. harvested from Manado Bay

 ISSN : 1410-5217

(Ohtani *et al*., 1995), while Makaluvamine G was isolated from the sponge *Histodermella* sp. The compound exhibited significant *in vitro* cytotoxicity to several tumor cell lines and moderate inhibition of topoisomerase I, DNA, RNA and protein synthesis (Carney *et a*l., 1993).

From West Sumatra waters, four (4) new polybrominated diphenyl ether congeners along with 3 known derivatives have been isolated from sponge of *Dysidea herbacea* Keller (Handayani *et al*, 1997). The new polybrominated compounds were active against a brine shrimp, and all the compounds isolated were positive against gram positive bacteria *Bacillus subtilis* and the phytopathogenic fungus *C. cucumerinum*.

A sponge *Acanthodendrilla* sp. from Kundingarengke Island was investigated by Elkhayat *et al*. (2004), and 5 new luffariellolide-related sesterterpenes namely acantholides A-E, in addition to known luffrariellolide and its 25-O-methyl and 25-O-ethyl derivatives, have been isolated. The luffariellolide, its 25-O-methyl derivative and acantholide E exhibited cytotoxic activity against the mouse lymphoma L5187Y cell line. Acantholide B, luffariellolide and its 25-O-methyl derivative were active against *Escherichia coli*, *Candida albicans* and the pathogenic fungus *Cladosporium herbarum*. Twelve new sesterterpenes, honulactones A-L have been isolated from a lipophilic extract of the sponge *Stresichordaia aliena*, family Thorectidae, and further investigation led to the isolation of 6 new compounds of 20, 24-bishomoscalaran sesterterpenes, namely honu'enone, phyllofolactones H-K and phyllofenone C. The sponge was harvested from Turtle Bay, Sangkali, Eastern Indonesia waters (Jimenez *et al*., 2000). Additionally, from the dichloromethane/2-propanol extract of the same organism, 12 new 20,24-bishomoscalaranes, namely honulactones A-L were isolated (Jiminez *et al*., 2000). Honulactones A, B, C and D showed cytotoxicity against P-388, A-549, HT-29 and MEL-28 cancer cell lines with IC_{50} values of 1µg/mL.

Marine sponges harvested from waters surrounding Jakarta showed antimicrobial activity as well as cytotoxicity. The compounds isolated from the sponge *Xestospongia* were 4 novel alkaloids of the aaptamine class as well as known aaptamine, isoaaptamine, demethyl (oxy) aaptamine and its dymethylketal (Calcul *et al*., 2003). Their antimicrobial activity towards *S. aureus* (gram +), *E. coli* and *V. angillarum* (gram -), and the fungus *C. tropicalis* as well as cytotoxicity against human buccal carcinoma KB was investigated. The results showed aaptamine 1 and isoaaptamine 2 exhibited antifungal activity, while significant cytotoxicity against KB cells was detected in aaptamine 1, isoaaptamine2 and demethyl (oxy) aaptamine 3. Bisdemethylaaptamine, a proposed biosynthetic precursor of aaptamine and bisdemethylaaptamine-9-O-sulfate, has been isolated from the sponge *Aaptos* sp. from near Bunaken Island, Manado. This was the first report of a sulfated aaptamine of bisdemethylaaptamine -9-O-sulfate (Herlt *et al*., 2004). Meanwhile, the reddish brown, branching sponge *Echinochalina* sp. collected from Derawan Island, contained upenamide. This compound was a new class of macrocyclic marine alkaloid having both spirooxaquinolizidinone and hemiaminal ring systems (Jimenez *et al*., 2000). Two compounds of of 3,6-epidioxy fatty acid, monadic acids A and B have been isolated from an undescribed species of sponge *Plakortis* sp. These new structural types of fatty acids possess both 4-alkyl and 6-methoxy substituent (Ichiba *et al*., 1995).

Non Sponge (Soft corals, Seapen, Octacorals, Marine algae)

From West Sumatera, two new oxygenated sesquiterpenes, i.e. hydroxycolorenone and methoxycolorenone have been isolated from

 ISSN : 1410-5217

soft coral *Nephthea chabrolii* (Handayani *et al*, 1997). Hydroxycolorenone showed insecticidal activity against neonate larvae of the polyphagus pest insect *Spodoptera littoralis.*

The gorgonian *Briareum* sp. from Togian Island, near South Sulawesi, was studied by Rodriguez *et al.* (1998). They isolated 2 new briarane stecholide diterpenes, namely 2,9 - diacetyl – 2 - debutyrylstecholide H and 13-dehydroxystecholide J, with the first reported cytotoxic activity of the stecholide. New briarane diterpenes have been reported to be isolated from Indonesian sea pen *Veretillum malayense*, designated as malayenolides A-D. Instead of containing acetate and alkanoat groups, this four new diterpenes contains benzoate and senecioate substituent. This compounds showed toxicity to brine shrimp with LC_{50}s of <2-100 ug/mL (Fu *et al.*, 1999). Soft coral *Xenia* sp. from Togian Island waters produced 2 new xeniolides, *i.e.* xeniolide –F and 9-hydroxyxeniolide-F (Anta *et al*., 2002). All the compounds isolated showed an IC_{50} > 1 µg/mL against mouse (P-388) and human (A-549, HT-29, MEL-28) tumor cell lines. The soft coral *Lobophytum* sp. collected from a reef wall of Mayu Island, Molluca sea, was studied by Morris *et al*. (1998), and a secosterol with a gorgosterol side chain and unusual oxygenation pattern on the A and B rings has been isolated. The compound, having A and B rings with hydroxyl group at C-3 and C-7 and an epoxide ring at C-5 – C-6, was found active against human ovarian tumor and human leukemia cell lines.

New tetracyclic pyridoacridine alkaloids have been claimed to be isolated from Ujung Pandang waters of ascidian *Eusynstyela latericius* (Cropp *et al*., 1998). Four compounds, namely styelsamines A-D, exhibited mild cytotoxicity against the human colon tumor cell line HCT-116 with IC_{50} values of 33, 89, 2.6 and 1.6 µM, respectively. Three new compounds, lissoclibadins, together with 4 known compounds have been isolated from the Indonesian ascidian *Lissoclinum* cf. *badium.* The new compounds have polysulfur aromatic amine, and were able to inhibit the human promyelocytic leukemia cell line HL-60. The effect of 7 compounds on IL-8 production in PMA-stimulated HL-60 cells revealed the relation of their structures to the IL-8 production activity, the inhibition of cell proliferation and the survival of HL-60 cells (Oda *et al.*, 2000).

A new secosterol compound, along with pachyclavulariaenone B, was isolated from octacoral *Pachyclavularia violacea* (Anta *et al*., 2002), from Togian Island.

Marine red alga (*Rhodophyta*) *Ceratodictyon spongiosum* and its symbiotic sponge *Sigmadocia symbiotica* harvested from Biaro Island, have been investigated for their chemical substances. Two isomers of a new and bioactive thiazole-containing cyclic heptapeptide, namely cis,cis-ceratospongamide and trans, trans-ceratospongamide have been isolated (Tan *et al*., 2000). The last compound was capable of inhibiting the expression of a human-sPLA2 promoter-based reporter by 90%, while the first one did not show activity.

Activity of Indonesian Research Institution on Marine Biodiscovery

A group of scientists from Diponegoro University, Indonesia, have studied 10 marine organisms (sponges, gorgonians and soft corals) from Flores waters, and 5 organisms from Jepara, Central Java waters. The research found that all crude extracts were active on the L-1210 mouse lymphocytic leukemia cell line, giving the activity value of $\leq$ 10 mg/L. The most active compound from gorgonian *Isis hippuris* was identified as gorgosterol derivative (Trianto *et al*., 2006).

The research group of Sam Ratulangi University, Manado have investigated sponges, soft corals and algae for

 ISSN : 1410-5217

antibacteria, bio-insecticides, antifeedant and other bioactive compounds. Results showed that extracts of sponges *Hymanicidon* sp., *Placortis nigra, Theonella* sp., and *Placortis nigra, Ianthella* sp., and soft corals of *Sinularia gravis and Sarcophyton cinereu* had antibacterial activity, while those from *Petrosia nigricans, Placospongia melobesioides, Rhabdastrella cf globostellata, Stylissa cf carteri, Placospongia melobesiodes, Theonella* sp., *Placospongia melobesioides* were active against *Aedes aegypti* larvae. Extracts of *Placospongia melobesioides, Acervochalina confusa, Petrosia nigricans* and *Petrosia contignata* possesed analgesic activity. Extracts of sponges of *Cinachyra* sp., *Theonella* sp., *Xestospongia* sp., *Halichondria, Hoplochalina* and *Perissinella* and soft corals *Sinularia ramosa, S. capillosa, S. procera, S. compressa, S. gravis, Sarcopyton crassocaule, S. Cinereum* and *Nephtea* sp. had the capability of preventing cell development of sea urchin embryos. Antifeedant activity has been detected in extracts of soft corals of *Sinularia ovispiculata, S. granosa, S.inexplicita, Sarcophyton cinereum* and extracts of alga *Dunaliella sp., Halymenia durvillaei, Laurencia papillosa, Padina australis, Liagora* sp., *Kappaphycus alvarezii, Kappaphycus striatum* and *Turbinaria decurrens* (Mantiri, 2005).

Gadjahmada University scientists screened seaweed, sponge and soft coral extracts harvested from surrounding Yogyakarta waters and Bali against pathogenic bacteria and fungal, *i.e.* methicillin resistant *S. aureus* (MRSA) and vancomycin-resistant *S. aureus* (VRSA). A compound identified as Jaspamide has been isolated from *Stylissa flabelliformis* (Setyowati *et al.*, 2003; 2004; 2005). The compound exhibited cytotoxicity against myeloma cells with an LC_{50} of 0.08 µg/mL, and active inhibiting C*andida albicans.*

Bogor Agricultural Institute (IPB) scientists did marine biodiscovery research based on traditional knowledge with various target screens, *i.e.* antimicrobial, bioinsecticide, anticancer, antioxidant, biopigment, enzymes and their inhibitors, UV protection etc. Antimicrobial compounds were extracted from *Caulerpa racemosa, Sesuvium postulacastrum, Xylocarpus granatum, Ulva lactuca.* and sea cucumber *Stichopus* sp. Antioxidants were do tained from sea stars *Astropecten* sp., *Pemphis* sp., and *Discodoris* sp., while steroid compounds was detected from *Discodoris* sp., and *Eunice* sp.

Research Center for Marine and Fisheries Product Processing and Biotechnology, Research of Marine Fisheries Agency has been doing marine bioprospecting research focusing in both primary and secondary metabolites from marine sources for food and non food use. Enzymes and secondary metabolite compounds from seaweed, invertebrates, fishery-industrial waste, marine derived microbes have become subjects of the natural product discovery research. Extracts of sponges and soft corals from Binuangen (West Java), Seribu Island, Yogyakarta, Karimunjawa, Mataram, South Bali, South Sulawesi (Bonarote and Wakatobi) were investigated for the active compounds against brine shrimp, human cancer cell line, antimicrobes and antiangiogenesis. Active compounds have been identified as hymeniasidine, stevensine, and dibromocantharelline, aaptamine and its isomer isoaaptamine, trigonelline and homarine, stelliferin riboside, sarcophytoxide, stelletamine, etc, and confirmation of other chemical structure is in progress. Work in progress is on marine enzyme and secondary metabolites discovery using metagenomic approach as well as cultivable approach from bacteria and fungi derived from the sponges.

 ISSN : 1410-5217

CHALLENGES AND PRECAUTIONARY EFFORT

From the papers reviewed, marine biodiscovery research is strongly needed to gain revenue from the marine resources. Marine biodiscovery, the first gate of marine biotechnology, offers not only potential benefit in economics through the development of biotechnology industries but also by generating employment. Marine bioactive compounds can be developed as drugs, industrial enzymes, herbicides, cosmetics etc. as their terrestrial counterparts do. It was reported that global pharmaceutical sales were reported to be worth US$550 billion in 2004, and about half of these are made or inspired from natural products isolated from nature (Anonymous, 2005). Biodiscovery research is the frontier activity before developing biotechnology industries, and numbers of benefits can be obtained from this activity, such as gaining understanding of marine biota and other marine natural environmental systems. However, as with other countries' experience, there is a long way and an expensive cost required to jump from bioprospecting/biodiscovery research into the commercial step of the target compounds found. It was reported that only 1 compound could be obtained out of 4000-10,000 compounds examined, costing about $ US 1 billion per new drug (Battershill *et al*, 2005).

To bring the active compounds to pharmacies, it needs lengthy process from discovery step of a novel compounds to the preclinical and clinical trials. Supply of raw material is a big problem, because direct extraction of the compound from marine organisms is almost certainly unsustainable. Concentration of the bioactive is often extremely low, chemical synthesis of the compound may be difficult and costly due to its structural complexity, and biosynthesis is frequently induced by a combination of so called marine factor. Mariculture is considered one among methods that can be developed in such Indonesia country. An assessment of mariculture for 6 potential sponges, *i.e. Aaptos suberitoides*, *Amphimedon paraviridis*, *Callyspongia* (*Euplacella*) biru, *Hyrtios reticulates*, *Ircina ramosa* and *Pseudoceratina purpurea* has been conducted in Spermonde archipelago, South Sulawesi (de Voogd, 2005). The study resulted *Callyspongia* (E.) blue sponge as promising candidate due to the high survival rate and significant growth of this species. Further trial development of mariculture of *Callyspongia* (E.) blue showed that survival, growth rates and yield of amphitoxin, the active metabolites from this organism, were relatively high (de Voogd, 2005).

Since marine biodiscovery research and its development to biotechnology industry is very high risk and expensive, collaboration between research institutions and industries is obviously needed along with government support for this activity. Local cosmetics and traditional medicine industries have used some marine organisms and plants extracts along with terrestrial plants. Participation of local industries in a biodiscovery-terrestrial plant has initiated, however, their role in marine biodiscovery is very limited.

A marine-biotechnological industry in Indonesia has not been developed yet. The government and business companies along with researchers have to side by side to develop marine-based biotechnology industries using local materials. Minimizing imported products such as nutraceuticals, enzymes etc. by producing the products in Indonesia will save Indonesian currency. Favorable environment and government support for investment should encourage the industry to grow. Intellectual property right and law enforcement system in Indonesia is another hindrance of foreign investment involving high technology such as marine biotechnology industries, and the system should be improved.

 ISSN : 1410-5217

To strengthen sustainable marine biodiscovery research activities, the Department of Marine Affairs and Fisheries of "Indonesia through Research Agency for Marine and Fisheries Research and Directorate of Marine, Coastal and Small Islands has initiated founding a scientific forum called "Indonesian Marine Bio-pharmaceutical" in July 2005. The networking among research institutions, universities, government and industries is expected to speed up marine biodiscovery activities by sharing the research resources among the member and encouraging industries to use the technology developed by the researcher. Through this networking, bargaining position in international research collaborations or other activities could be improved, obtaining better benefit sharing without sacrificing the marine resource. This Forum will have a significant role in helping the government in setting up the sampling protocols and other technical matters regarding sustainable marine biodiscovery activities.

The Government of Indonesia through the Indonesian Ministry of Science and Technology, gave attention to this bioprospecting/biodiscovery activity by developing and building the Bio-island project. The aims of the project include creating a special economic zone for biotechnology activity, both research and its commercialization, in Rempang Island by 2007 (Anonymous, 2003), with focused activity on biotechnology of agriculture and food, pharmacology, marine and fisheries, and industries & environment. Along with Bio-island, a center of bio prospecting activities will be built and called Bio park in Serpong, West Java. The center, complete with microbe and other biodiversity collections as well as a gene bank, will be posted as a place for interaction between industries and bio-prospecting researchers. However, with unknown reason, the project is stuck without progress.

Regulation related with marine organism access and its law enforcement is essential in biodiscovery activities. The government has updated regulation on how Indonesian organisms can be accessed by foreign researcher, *i.e.* Government Regulation (PP) no. 41, 2006 by Ministry of Science and Technology. Collection protocols of the genetic resources as well as protocols on benefit sharing by using the resources should be made to follow up the regulation. In the past, lack of the regulation led to unmanageability of sample access especially from the marine environment, including allowable quantity and sample depository. Numbers of Indonesian marine organisms have been deposited at foreign institutes, such as the Netherlands and Hawaii museums or foreign universities. Lack of the protocols led to excessive sampling of marine organisms, sometimes in excessive size, to be taken from their inhabitances. Furthermore, due to limited equipments for biodiscovery activity in Indonesia, the research is mostly done in foreign countries without proper benefit sharing guided by government.

CONCLUDING REMARKS

Global commercial interest in marine biodiscovery is increasing. Being mega-biodiversity blessed, Indonesia has an opportunity to develop marine biodiscovery program, and biotechnology industry for their people's prosperity. However, a lot of homework is needed to be done to make biodiscovery activity in Indonesia is in Convention on Biological Diversity (CBD) corridor. The government support and encouragement to research institutions and biotechnological industries to induce biodiscovery activities in a sustainable manner are needed. This include developing regulation on the access including establishing an efficient and sustainable collection of biodiversity, introducing benefit sharing, providing support to the research center and stimulating biodiscovery

 ISSN : 1410-5217

research by improving research resources. These actions are definitely in urgent need otherwise the blessing of marine mega-biodiversity is lost to foreign prosperity.

ACKNOWLEDGMENT

This study is supported by AUSAID through PSLP-Indonesia project ROU 37118. Thank you to Dr. Anthony D. Wright and Prof. Ris. Dr. Endang Sri Heruwati for reviewing the manuscript.

REFERENCES

Anonymous, 2006. National Report on the implementation of the Convention on Biological Diversity. The first national report: Implementation of art. 6. General measures for conservation and sustainable use.

Anonymous. 2003. Indonesia Biodiversity Strategy and Action Plan 2003-2020. IBSAP. National Document the Republic of Indonesia.National Development Planning Agency (Bappenas)

Anta C., Gonzalez N., Santafe G., Rodriguez J., and Jimenez C. 2002. New Xenia diterpenoids from the Indonesian soft coral *Xenia* sp. *J. Nat. Prod*. 65 : 766-768

Baker DD. 2004 Industrially-held microbial diversity : Are culture collections really necessary? In Microbial Genetic Resources and Biodiscovery. Ed. By Ipek Kurtboke and Jean Swings. Queensland Complete Printing Service.269 pp

Battershill C., Jaspar M. and Long P. 2005. Marine biodiscovery : new drugs from the ocean depths.*Biologist* 52 (2) :107-114

Bobzin, SC., Yang S. and Kasten TP. 2000. LC-NMR: a new tool to expedite the dereplication and identification of natural products. *J. Industrial Microb Biotechnol* (25): 342-345

Calcul L., Longeon A., Mourabit AA., Guyot M. and Bourguet-Kondracki ML. 2003. Novel alkaloids of the aaptamine class from an Indonesian marine sponge of the genus *Xestospongia*. *Tetrahedron* 59 : 6539-6544

Carney, JR., Scheuer PJ. Kelly-Borges M. 1993. Makaluvamine G, a cytotoxic pigment from an Indonesian sponge *Histodermella* sp. *Tetrahedron* 49 (38) : 8483-8486

Chasanah E., Fawzya YN., Wikanta T. and Suryani E. 2005. Present status of marine and fisheries research on bio-pharmaceutical at Research Agency for Marine and Fisheries. Proceeding of Marine and Fisheries Bio-pharmaceutical. Research Agency for Marine and Fisheries, Jakarta. (Indonesian): 203pp

Copp BR., Jompa J., Tahir A., and Ireland CM. 1998. Stylsamines A-D : new tetracyclic pyridoacridine alkaloids from the Indonesian ascidian *Eusynstyela latericius*. *J. Org. Chem.* 63 : 8024-8026

De Voogd NJ. 2005. Indonesian sponges : Biodiversity and mariculture potential. PhD thesis, University of Amsterdam, the Netherlands.

Eder C., Proksch P., Wray V., Steube K., Bringmann G., van Soest RWM., Sudarsono, Ferdinandus E., Pattisina LA., Wiryowidagdo S. and Moka W.

 ISSN : 1410-5217

1999. New alkaloids from the Indopacific sponge *Stylissa carteri*. *J. Nat. Prod* , 62 : 184-187

Elkhayat E., Edrada RA., Ebel R., Wray V., van Soest R ., Wiryowidagdo S., Mohamed MH, Muller WEG., and Proksch. 2004. New Luffariellolide derivatives from the Indonesian sponge *Acanthodendrilla* sp. *J. Nat. Prod*. 67 : 1809-1817

Faulkner DJ,. 2002. Marine Natural Products. *Nat. Prod. Rep*. 19: 1-48

Fusetani N. 2000. Drugs from the sea. Karger. 158 pp.

Fu X., Schmitz FJ., and Williams GC. 1999. Malayenoldes A-D, novel diterpenes from the Indonesian sea pen *Veretillum malayense*. *J. Nat. Prod*. 62 : 584-586

Handayani D., Edrada RA., Proksch P., Wray V., Witte L., Van Soest RWM., Kunzmann A., and Soedarsono. 1997. Four new bioactive polybrominated diphenyl ethers of the sponge *Dysidea herbacea* from west Sumatra, Indonesia. *J. Nat. Prod*. 60 : 1313-1316

Handayani D., Edrada RA., Proksch P., Wray V., Witte L., Van Soest RWM., Van Ofwegen L., and Kunzmann A.. 1997. New oxygenated sesquiterpenes from the Indonesian soft coral *Nephthea chabrolii* . *J. Nat. Prod*. 60 : 1313-1316

Hassan W., Edrada RA., Ebel R., Wray V., Berg A., van Soest R, Wiryowidagdo S. And Proksch P. 2004. New Imidazole alkaloids from the Indonesian sponge *Leucetta chagosensis*. *J. Nat. Prod*. 67 : 817-22.

Herlt A., Mander L., Rombang W., Rumampuk R., Soemitro S., Steglich W., Tarigan P. And von Nussbaum F. 2004. Alkaloids from marine organisms. Part 8 : isolation of bisdemethylaaptine and bisdemethylaaptine-9-O-sulfate from an Indonesian *Aaptos* sp. marine sponge. *Tetrahedron* 60 : 6101-6104

Ichiba T. and Scheuer PJ. 1995. Two cytotoxic 3,6-epidioxy fatty acids from an Indonesian sponge, *Plakortis* sp. *Tetrahedron* 51 (45) : 12195-12202

Jimenez JI., Goetz G., Mau CMS, Yoshida WY., Scheuer PJ., Williamson RT., and Kelly M. 2000. Upenamide : an unprecedented macrocyclic alkaloid from the Indonesian sponge *Echinochalina* sp. *J. Org. Chem*. 65 : 8465-8469

Jimenez JI., Yoshida WY., Scheuer PJ., and Kelly M. 2000. Scalarane-based sesterterpenes from an Indonesian sponge *Strepsichordaia aliena*. *J. Nat. Prod*. 63 :1388-1392

Jimenez JI., Yoshida WY., Scheuer PJ., Lobkovsky E., Clardy J. and Kelly M. 2000. Honulactones : New bishomoscalarane sesterterpenes from the Indonesian sponge *Stresichordaia aliena*. *J. Org. Chem*. 65 : 6837-6840

Kobayashi M. 2000. Search for biologically active substance from marine sponges In Drugs from the Sea. Edited by N. Fusatani. Karger. 158 pp

Kurtboke DI. Uniqueness of the “Smart State’s” microbial diversity. In Microbial genetics resources and biodiscovery. Ed. by Ipek Kurtboke and Jean Swings.2004. Queensland Complete Printing Service. 269pp

 ISSN : 1410-5217

Linington RG., Williams DE., Tahir A., van Soest R., and Andersen RJ. 2003. Latonduines A and B, new alkaloids isolated from the marine sponge *Stylissa carteri* : Structure elucidation, sysnthesis, and biogenic implications. *Organic Letters* 5 (15) : 2735-2738

Mantiri D. 2005. Present status of Marine and fisheries research on bio-pharmaceutical at Sam Ratulangi University. Proceeding of Marine and Fisheries Bio-pharmaceutical. Research Agency for Marine and Fisheries, Jakarta. (Indonesian): 203pp

Morris LA., Christie EM., Jaspars M., and van Ofwegen L. 1998. A bioactive secosterol with unusual A- and B-ring oxygenation pattern isolated from an Indonesian soft coral *Lobophytum* sp. *J. Nat. Prod*. 61 : 538-541

Oda T., Fujiwara T., Liu H., Ukai K., Mangindaan REP., Mochizuki M., and Namikoshi M. 2006. Effects of lissoclibadines and lissoclinotoxins, isolated from a tropical ascidian *Lissoclinum* cf. *badium*, on IL-8 production in a PMA-stimulated promyelocytic leukemia cell line. *Marine Drugs* 4 : 15-21

Ohtani I I., Ichiba T., Isobe M., Kelly-Borges M., and Scheuer PJ. 1995. Kauluamine : an unprecedebted manzamine dimmer from an Indonesian marine sponge *Prianos* sp. *J. Am. Soc*. 117 : 10743-10744

Park SK., Jurek J., Carney JR., and Scheuer PJ. 1994. Two more bastadin, 16 and 17, from an Indonesian sponge *Ianthella basta. J. Nat. Prod*. 57 (3) 407-410

Park, SK., Kim SS., Hong JS and Kim IK. 1995. A study on the chemical constituents from marine sponge *Luffariella* sp. *Korean Chemical Society* 39 (7) : 559-563

Pramono E. 2002. The commercial use of traditional knowledge and medicine plants in Indonesia. Presented at Multi-stakehoder dialogue on trade, intellectual property right and biological resources in Asia. Bangladesh, April 19-21

Rao KV., Santarsiero BD., Mesecar AD., Schinazi RF., Tekwani BL., and Hamann MT. 2003. New manzamine alkaloids with activity against infectious and tropical parasitic diseases from an Indonesian sponge. *J. Nat. Prod*. 66 : 823-828

Rodriguez J., Nieto RM and Jimenez. 1998. New briarane stecholide diterpenes from the Indonesian gorgonian *Briareum* sp. *J. Nat. Prod*. 61 (3)

Roy, MC., Tanaka J., de Voogd N., and Higa T. 2002. New scalarane class sesterterpenes from an Indonesia sponge, *Phyllospongia* sp. *J. Nat. Prod*. 65 : 1838-1842

Roy MC., Ohtani I I., Tanaka J., Higa T. And Satari R. 1999. Barangamide A, a new cyclicpeptide from the Indonesian sponge *Theonella swinhoei*. *Tetrahedron Letters* 40 : 5373-5376

Roy MC., Ohtani I I., Ichiba T., Tanaka J., Satari R. And Higa T. 2000. New cyclic pepteides from the Indoensian sponge *Theonella swinhoei*. *Tetrahedron Letters* 56 : 9079-9092

Sirirath S., Tanaka J., Ohtani I I., Ichiba T., Rachmat R., Ueda K., Usui T., Osada H., and Higa T. 2002. Bitungolides A-F, new polyketides from the Indonesian sponge *Theonella swinhoei*. *J. Nat. Prod*. 65 : 1820-1823

 ISSN : 1410-5217

Setyowati, E.P., Sudarsono, S. Wahyuono. 2003. Active fraction from sponge *Stylissa flabelliformis* collected from Menjangan National Park West Bali, *Technoscience*. 16(3): 499-513.

Setyowati, E.P., Sudarsono, S. Wahyuono. 2004. Cytotoxic and antimicrobial test of the bioactive compound isolated from *Stylissa flabelliformis* sponge. *Indonesian Journal Pharmacy*. 15(2): 50-56.

Setyowati, E.P., Sudarsono, S. Wahyuono. 2005**.** Jaspamide: structure identification of citotoxic and fungicide compound from *Stylissa flabelliformis* Sponges**.** *Indonesian Journal Pharmacy*. 16(1): 67-73.

Tan LT., Williamson T. and Gerwick WH. 2000. Cis, cis- and trans, trans-ceratospongamide, new bioactive cyclic heptapeptides from the Indonesia red alga *Ceratodictyon spongiosum* and symbiotic sponge *Sigmadocia symbiotica*. *J. Org. Chem*. 65 : 419-425.

Triatno. 2006. Present status of marine and fisheries research on bio-pharmaceutical at Diponegoro University. Proceeding of Marine and fisheries bio-pharmaceutical. Research Agency for Marine and Fisheries, Jakarta. (Indonesian): 203pp

Williams DE., Tahir A., and Andersen RJ. 1999. A new acyclic diketotriterpenoid isolated from the Indonesian marine sponge *Hyrtios erectus*. *J. Nat. Prod*., 62: 653-654

Williams, DE., Patrick BO., Tahir A., van Soest R., Roberge M.. and Andersen RJ. 2004. Boneratamides A-C, new sesquiterpenoids isolated from the marine sponge *Axinyssa aplysinoides*. J. Nat. Prod, 67 : 2127-2129. *J. Nat. Prod*., 67 : 1752-1754

Williams, DE., Telliez JB, Liu J., Tahir A., van Soest R. and Andersen RJ. 2004. Meroterpenoid MAPKAP (MK2) inhibitors isolated from the Indonesian marine sponge *Acanthodendrilla* sp. *J. Nat. Prod*, 67 : 2127-2129

ISSN : 1410-5217