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ETHICAL PERSPECTIVES OF SUSTAINABLE USE OF REEF'S INVERTEBRATES AS A SOURCE OF MARINE NATURAL PRODUCTS

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ABSTRACT

Among marine animals, reef's invertebrates are the most prolific producers of secondary metabolites and have become sources of great interest to natural product chemistry, since they provide a large proportion of bioactive compounds with different biological activities. Supply's problem has hampered the investigation of secondary metabolites from marine invertebrates, and many highly active compounds produced contribute to<10^{-6} % of the body-wet weight. Providing sufficient amounts of these biologically active substances, hence, may be a difficult task. In addition, it has often proven extremely difficult, and some cases impossible, to provide from invertebrates sufficient amounts of many of these substances due to limited amounts found in the producing organism, or to limited quantity of the organism itself, or to geographic, seasonal or sexual variations in the amounts and in the nature of produced secondary metabolites. There has an increasing concerns regarding the collecting reef's organisms for the discovery and development of pharmaceuticals since it has been perceived variously as sustaining and threatening conservation. There is an urgent need to take into account the bioethical considerations in anticipating the potential consequences of these activities and proposing management options for sustainable use of reef's invertebrates as the sources of bioactive compounds.

Key Words: *Bioethics, bioactive compounds, coral reef, invertebrates*

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INTRODUCTION

At the World Summit on Sustainable Development held at Rio de Janeiro, Brazil in 1992, five major areas were outlined for progress in achieving a sustainable future for humanity, namely water and sanitation, energy, health, agricultural productivity, and biodiversity and ecosystem management. Hence, it has become clear that biodiversity has become one of the cornerstones of sustainable development and has been defined as the sum of genetic and phenotypic differences existing in living organisms at the molecular, individual, population, and ecosystem levels. The increased emphasis on

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biodiversity is the result of, on the one hand, an increased demand, driven by factors as diverse as plant breeding, drug development, and ecosystem services, and, on the other hand, by decreasing supplies, caused by overpopulation and globalization and the ensuing habitat destruction and cultural homogenization (Gepts, 2004).

Coral reefs are some of the most productive ecosystems on earth, and are certainly the most productive and species-rich environments in the oceans. Coral reefs provide critical protection to coastlines from storm damage, erosion and flooding by reducing wave action. Coral reefs are crucial sources of income and resources through their role in tourism, fisheries, and building materials. Despite the apparent value of coral reefs to humans, most of the reefs around the world are threatened or already been destroyed by human activities. The 1998 Reefs at Risk report (Bryant *et al.* 1998) reported that 58% of the world's reefs are potentially threatened by human activities.

The oceans are the source of a large group of structurally unique natural products that are mainly accumulated in invertebrates that are common to coral reef ecosystems, such as sponges, tunicates, bryozoans, soft corals and molluscs. Several of these secondary metabolites showed pronounced pharmacological activities and are interesting candidates for new drugs and coral reef ecosystem has been one of the main sources for the search of bioactive compounds (Radjasa, 2003).

Serious obstacle to the ultimate development of most marine natural products that are currently undergoing evaluation and trials is the problem of supply due their low concentrations (Munro *et al.* 1999). The concentrations of many highly active compounds in marine invertebrates are often minute, sometimes accounting for less than 10^{-6} % of the wet weight (Procksch *et al.* 2002).

In addition, it has often proven extremely difficult, and some cases impossible, to provide from invertebrates sufficient amounts of many of these substances due to limited amounts found in the producing organism, or to limited quantity of the organism itself, or to geographic, seasonal or sexual variations in the amounts and in the nature of produced secondary metabolites (Kelecom, 2002).

The urgent need to protect and study tropical biodiversity is widely known. Scientists from all over the world have identified the need to intensify field studies in tropical biodiversity and to make its protection a high priority for this century (Raven, 2000).

Regarding the use of reef's invertebrates as sources of bioactive compounds, it has been primarily concerned with protection of the environment and sustainability. The ecological ethics need to be taken into account, especially in the light of the importance of coral reefs for human population in tropical coastal communities. Thus, considering bioethical persperctives and finding alternative solutions to the problem supply for bioactive compounds mainly produced by reef's invertebrates should be given high priority.

THE SEARCH FOR BIOACTIVE COMPOUNDS FROM REEF'S INVERTEBRATES

Marine organisms including those from coral reef ecosystems have become sources of great interest to natural product chemistry, since they provide a large proportion of bioactive metabolites with different biological activities (Faulkner 2000). In particular, marine invertebrates with high species diversity in the tropical coral reefs are often rich in secondary

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metabolites and are preferential targets in the search for bioactive natural products (Sammarco and Coll 1992).

Many marine species have been collected in the search for novel bioactive compounds and for developing pharmaceutical drugs (Hooper *et al.* 1998; Quinn *et al.* 2002). The collections tend, however, to focus on organisms containing chemicals, known as secondary metabolites that primarily serve ecological functions in competition for space and in protection from predation, fouling, and ultraviolet light (Harper *et al.* 2001), as well from bacterial infections (Correa, 1997; Rohwer *et al.* 2002) To date, the majority of novel compounds have been secondary metabolites from soft-bodied, sessile invertebrates, such as Porifera (sponges); Cnidaria (jellyfish, corals, sea anemones); and Urochordata (ascidians).

Marine species have become of increasing interest to bioprospectors for Western medicinals. Over 14 000 new chemical entities have been identified from marine sources, and at least 300 patents have been issued on marine natural products (Hunt and Vincent, 2006).

A set of new generation of marine-derived pharmaceuticals are expected to enter the market, including a chronic pain treatment, Prialt (ziconitide)—which is based on a peptide isolated from the cone shell, *Conus magnus* (Olivera, 2000)—and the anticancer drug Yondelis (ecteinascidin 743), from the ascidian *Ecteinascidia turbinata* (Rinehart *et al.* 1990).

BIOETHICAL CONSIDERATIONS

In the context of marine biodiversity, bioethics may be concerned with the ethical questions and evaluations of animal, plants and microorganisms that being used for human needs.

Temperate marine ecosystems are some of the most productive and diverse of all ecosystems. Over the past century the resources contained within these communities have been subjected to gross mismanagement (Suchanek, 1994).

The most significant threat regarding the development of pharmaceutical from reef's invertebrates is the problem of supply. Providing sufficient amounts of these biologically active substances, hence, may be a difficult task. Limited amounts and low yields of bioactive compounds produced **(Table 1),** further complicate the study of secondary metabolites of aquatic organisms (Radjasa *et al.* 2007a). In addition, as a result of the enormous marine natural product development of recent decades and their applications, many unforeseen problems of an ethical nature have also arisen.

Table 1. Low yields of bioactive compounds from reef's invertebrates

No	Compound	Invertebrate	Yield/wet weight (gr/metric ton)
1	Anticancer ET 743	Tunicate *Ecteinascidia turbinata*	1
2	Anticancer Halicondrin	Sponge *Lissodendroryx* sp.	0.3
3	Anti-inflamatory Pseudopterosins	Soft coral *Pseudopterogorgia elisabethae*	1

Sources: (Mendola, 2000; Hart *et al.* 2000 ; Mayer *et al*. 1998)

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There is a pressing need, now more than ever, to call worldwide attentions to the widening gap between the exploitation of marine organisms and its ethical implications. The rapid development of marine natural products, in particular those related to the use of reef's invertebrates as the source of bioactive compounds needs the ethical implications that must develop alongside.

We recognize the dependence of marine biotas on intact, functioning ecosystems, and the essential services that ecosystems provide. There is an urgent action to reduce environmental damage by humans that reduces reef's biodiversity. Whereas these invertebrates provide medicinal metabolites, this group of soft-bodied organism is in grave danger from over exploitation by humans. Reef's often cannot protect themselves from humans, so without our help they cannot survive. Therefore, it is important to make the protection of reef's invertebrates and their habitat a top priority.

Bioethical wisdom that combines ecological knowledge with a sense of moral responsibility for a livable world is what is needed at the moment. What we must do for the health and survival of the next several generations in a recovering biosphere is what we ought to do for the generations in the far future.

Impacts from stresses on coastal marine communities are manifested at the individual species level, but magnify in effect throughout the entire ecosystem because of complex inter-connected relationships between species at different trophic levels, including interactions such as predation, competition and mutualism. In addition, we should be conservative about protecting systems even before we understand the processes fully (Suchanek, 1994)

REEF'S INVERTEBRATE ASSOCIATED MICROORGANISMS AS ALTERNATIVE SOURCE OF BIOACTIVE COMPOUNDS

Globally, since 1995, there are signals of decreased interest in the search of new metabolites from traditional sources such as macroalgae, molluscs, tunicates and octocorals, and the number of annual reports on marine sponges stabilized. On the contrary, the metabolites from microorganisms is a rapidly growing field, due, at least in part, to the suspicion that a number of metabolites obtained from algae and invertebrates may be produced by associated microorganisms (Kelecom, 2002).

It is a widely observed phenomenon that microbial cells attach firmly to almost any surface submerged in marine environments, grow, reproduce, and produce extracellular polymers that provide structure to the assemblage termed as biofilm (Kioerboe *et al.* 2003). In addition, surfaces of many marine invertebrates providing a nutrient rich habitat for heterotrophic bacteria that leading to the formation of biofilm-forming microbial communities.

It has been estimated that less than 2% of microbial flora have been successfully isolated from marine environment as pure cultures. It is expected that still quite a few parts of unexplored culturable invertebrate-associated microorganisms exists in the reef environments. Thus, such information might be desirable, as some of these bacteria may serve beneficial purposes as the source of secondary metabolites including marine natural products (Radjasa and Sabdono, 2003; Radjasa *et al*. 2007a, 2007b).

Understanding of marine invertebrate-microbial associations is a fundamental step in

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studying biologically potential active, possible medicinal compound from associated microorganisms. In particular, from sustainability point of view, isolating bioactive-producing bacteria is obviously offers a much better approach than cultivating and harvest invertebrates, which are in most cases extremely difficult.

It has been suggested that natural products from marine invertebrates have stricking similarities to metabolites of their associated microorganisms (Proksch et al, 2002; Thiel and Imhoff, 2003). Thus, it is important to highlight the possible role of bacteria associated with marine invertebrates as an alternative of biologically active substances.

Studies regarding screening on secondary metabolites-producing invertebrate-associated bacteria are important for understanding principal processes inhibitory interaction among invertebrate-associated bacteria as well as their biotechnological potentials. In this context, it is of importance to assess the application of sustainable approach on the screening of invertebrate-associated microbial populations with specific consideration of the secondary metabolites-producing part which has been up to now strongly neglected in comparison to the invertebrate parts (Radjasa and Sabdono, 2003; Radjasa *et al.* 2007a). The results will further influence isolation approaches and will show alternative choice in order to obtain representative reef's active metabolites coral reef ecosystems without endangering this precious environment.

CONCLUDING REMARKS

One of the main conservation concerns about the exploitation of reef's invertebrates in bioprospecting for the search of bioactive compounds is possible overcollection of target organisms. Due to the low yields of particular active metabolites from reef's invertebrates, it is very urgent to consider the bioethical considerations that will guide in the sustainable use of these important groups within coral reefs.

Studies regarding the possible roles of marine microorganisms associated reef's invertebrates should be highlighted as alternative sources of bioactive compounds that will protect the invertebrates from unsustainable exploitation.

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