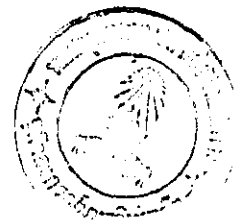


CHAPTER I

INTRODUCTION



Marine natural products, the secondary or nonprimary metabolites produced by organisms that live in the sea, have received increasing attention from chemists and pharmacologists during the last two decades. Pharmacological evaluations of marine natural products have likewise undergone an evolution over the past two decades: beginning with the early investigations of toxins, followed by studies of cytotoxic and antitumor activity, to the present day, where a myriad of activities based on whole-animal models and receptor-binding assays are being pursued (Ireland *et al.*, 1993). There are two distinct sources of marine-derived pharmaceuticals: macro-organisms such as sponges, sea squirts (ascidians or tunicates), sea anemones, corals, sea stars, sea hares and macro-algae and micro-organisms such as bacteria, fungi, actinomycetes and blue-green micro-algae (Fernández Puentes and Rinehart, 1995).

The first example, didemnin B, a cyclic depsipeptide, was isolated primarily from a Caribbean tunicate of the family Didemnidae, *Trididemnum sp.*, with high antitumor activity *in vitro* against L1201, *in vivo* against P388 and high antiviral activity against both RNA and DNA viruses (Rinehart Jr. *et al.*, 1981). It was the first marine-derived compound to be evaluated in phase I and phase II clinical trials by the National Cancer Institute (Sakai *et al.*, 1996).

The second, bryostatin 1, a polycyclic ether macrolide, was isolated primarily from the bryozoan or moss animal *Bugula neritina* with activity against P-388 lymphocytic leukemia and ovarian cancer (Schmitz, Bowden and Toth, 1993). Currently, the National Cancer Institute has entered bryostatin 1 into phase II clinical trials (Pettit *et al.*, 1996).

Marine natural products research in Thailand has been initiated only a few years ago. Thai tropical marine invertebrates have mainly remained unexplored both biologically and chemically. Some marine invertebrates from Si-chang Island were screened for their bioactivities such as anticancer, antimicrobial and immunoregulatory activities. The result showed that Thai marine organisms can be potential sources for new bioactive compounds and are urgently needed to be extensively investigated. Examples of marine natural products which have been isolated from marine invertebrates are as follows:

- Two isoquinoline quinones: N-(1''*E*-buten-3''-onyl)-1,2-dihydrorenierone and renierine B, and four isoquinoline quinones: mimosamycin, renierone, N-formyl-1,2-dihydrorenierone, and 1,6-dimethyl-7-methoxy-5,8-dihydroisoquinoline-5,8-dione have been isolated from a Thai sponge, *Reniera sp.* These compounds excluding renierine B showed antimicrobial activity against *S. aureus* and *B. subtilis* at the concentration of 0.1 mg/ml (Plubrukarn, 1993).

- Three bioactive brominated polyacetylenic acids were obtained as the methyl ester from the methanolic extract of a Thai marine sponge, *Petrosia sp.*, by utilizing brine shrimp bioassay-guided isolation (Wongsinkongman, 1993).

- Two norsesterterpene 1,2-dioxane, mycaperoxides A and B, have been isolated from a Thai sponge of the genus *Mycale*. Both compounds showed significant cytotoxicity and *in vitro* antiviral activity (Tanaka *et al.*, 1993).

- Two steroidal ketones: (24*R*)-methylcholest-4-en-6 β -ol-3-one and (24*S*)-ethylcholest-4-en-6 β -ol-3-one, were isolated from the dichloromethane extract of a Thai sponge, *Mycale* sp., and four known nucleosides: thymine, uracil, thymidine, and 2'-deoxyuridine were also isolated from the aqueous extract of the same sponge (Watthanapiromsakul, 1995).

- Three steroids and a partially elucidated bioactive polyether were isolated from a Thai sponge, *Biemna fortis* (Thitithanapluk, 1995).

- Four eunicellin diterpenoids: 3-deacetylpalmonin A, a eunicellin derivative, deacetylcladiellin (reported for the first time as natural occurring), sclerophytin A, and (1*R*, 2*R*, 3*R*, 6*S*, 9*S*, 10*R*, 14*R*)-cladiell-7(19), 11(20)-dien-3,6-diol, were isolated from the dichloromethane extract from the Thai soft coral *Cladiella tuberosa* (Pisutthanan, 1995).

- A spirocyclic sesquiterpene, axisonitrile 3, was isolated from a Thai sponge *Topsentia* sp. and four diterpenes, kalihinols I, J, X and Y, were obtained from a Thai sponge *Acanthella cavernosa* (Alvi, Tenenbaum and Crews, 1991).

The tunicate, *Didemnum* sp., was collected from Phi-Phi Island in Krabi Province. Biological screening tests showed that the dichloromethane extract of this organism exhibited antiviral (inhibit 58 % at 1.2 μ g) and cytotoxic activities, this tunicate was thus chosen for recollection and investigation. Therefore, the objectives of this project were to isolate, by means of bioassay-directed fractionation, and elucidate the chemical structures of the isolated compounds.

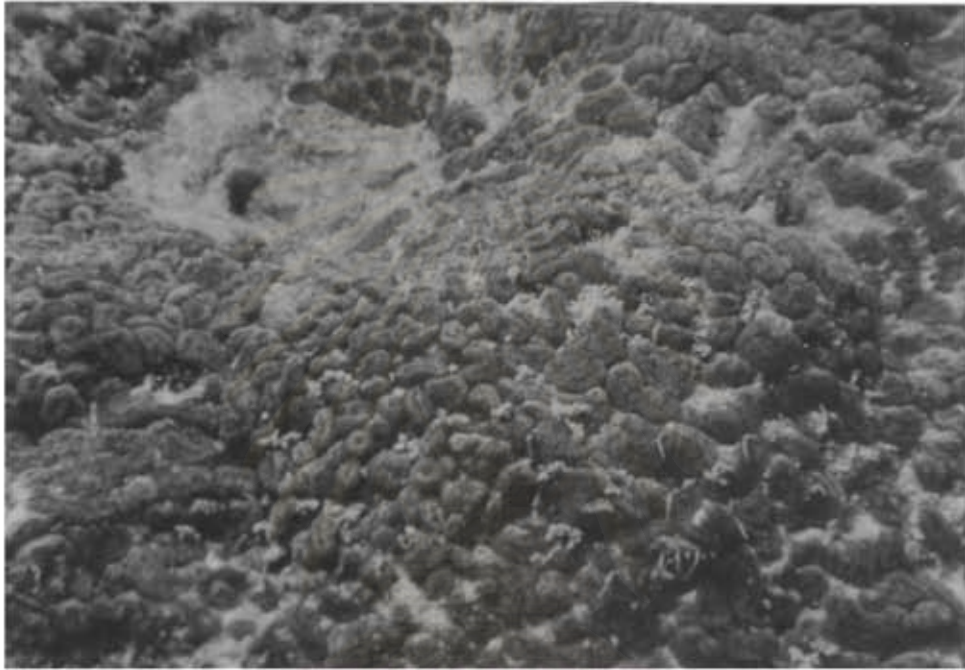


Figure 1. A Thai tunicate, *Didemnum sp.*

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย