CHAPTER I

INTRODUCTION

Marine sponges have been proven to be the excellent sources of diverse secondary metabolites including alkaloids, polycyclic quinones and hydroquinones polyacetylenic derivatives, aminoalcohols, aminoacids, heterocyclic compounds, original steroids, etc. (Calcul, *et al.*, 2003). Some of these bioactive compounds exhibited significant cytotoxicity, and anticancer activity which are valuable in the discovery and development of novel sponge-derived anticancer drugs. For instance, the pharmacologically active compounds spongothymidine and spongouridine were reported from the Caribbean sponge *Tethya crypta*. The compounds were the first marine source-derived drugs which were further developed as the potent anticancer agents for acute myelocytic leukemia and non-Hodgkin's lymphoma (Minigo *et al.*, 1990; Andrea *et al.*, 1990; Newman and Cragg, 2004). Recently, the tetrahydroisoquinoline alkaloid ecteinascidin-743 (ET-743; Yondelis^{TM}) was isolated from the marine tunicate *Ecteinascidin turbinata* and showed promising potent antitumor activity. This compound has been currently in phase II/III clinical trials and has been predicted to be approved to the market soon (Haefner, 2003; Liu *et al.*, 2006; Mayer and Gustafson, 2006).

Renieramycins are the bistetrahydroisoquinoline alkaloids that were demonstrated to possess significant cytotoxicity toward several cell lines. The compounds were mainly isolated from marine sponges belonging to genera *Reniera* (Frincke and Faulkner, 1982; He and Faulkner, 1989), *Xestospongia* (Davidson, 1992), *Haliclona* (Parameswaran *et al.*, 1998), *Cribrochalina* (Pettit *et al.*, 2000) and *Neopetrosia* (Oku *et al.*, 2003). Currently, Suwanborirux and coworkers have succeeded in gram-scale preparation of renieramycins from the Thai blue sponge *Xestospongia* sp. by pretreatment with potassium cyanide (Suwanborirux *et al.*, 2003; Amnuoypol *et al.*, 2004; Saito *et al.*, 2004). Therefore, the sponge *Xestospongia* is a promising natural source to provide renieramycins for further investigation to develop the compounds as new anticancer agents.

The chemical variation of secondary metabolites is related to several influencing factors including habitat differences, local adaptation, and physical stresses (Wulff, 2005). However, the production of bioactive chemicals by marine sponges is also believed to enhance their competitiveness on coral reefs. The processes of secondary metabolism that lead to the natural products are not yet well understood in marine systems, and there has been much speculation about whether symbionts are involved in the production of chemicals, thereby enhancing the ecological competitiveness of the sponge-symbiont assemblage (Garson, *et al.*, 1998). The ecological roles of renieramycins are important to establish whether the sponge or its symbionts produces the renieramycins. In this thesis, we have focused on qualitative and quantitative determination of renieramycins contents in annual variation by correlating with environmental factors such as water temperature, salinity, pH, chlorophyll-a, and total dissolved and suspended solids. Subsequently, localization of renieramycins in the Thai blue sponge *Xestospongia* sp. is also studied.