CHAPTER 4

CONCLUSION

The bioassay-guided fractionation of the Thai sponge *Brachiaster* sp., collected from Koh-Tao, Surat Thani, led to the isolation of three new naturally-occurring sesterterpenes, 12-deacetoxy-scalarin acetate (**40**), (*E*)-neomanoalide diacetate (**44**) and (*Z*)-neomanoalide diacetate (**45**), along with five known sesterterpenes, heteronemin (**18**), heteronemin acetate (**41**), 12-epi-19-deoxy-scalarin (**42**), 12-deacetyl-12-epi-19-deoxyscalarin (**43**) and manoalide-25-acetate (**46**).

The results from bioactivity evaluation showed that, among the eight isolated sesterterpenes, the most active antituberculosis agents are compounds **40**, **18**, **41** and **46** with MICs ranging from 3-7 μM, whereas the significant cytotoxicity was observed in compounds **18** and **46**. Furthermore, the correlation between the antituberculosis and cytotoxic activities is prominently evident. Most of the isolated compounds that show the potent antituberculosis activity are also strongly cytotoxic and vice versa. Thus, their antituberculosis activity could possibly, and simply, stem from the cytotoxicity. However, among these, 12-deacetoxy-scalarin acetate (**40**) shows the otherwise result. Its MIC of antituberculosis activity is at 4 μM whereas the IC_{50} of cytotoxicity is higher than 12 μM. The potent and selective activity of the compound indicates that the

scalarane-type sesterterpenes, in fact, can be well regarded as a group of potential lead compounds for the development of antituberculosis agents, at a time when the efficacy of certain currently available drugs is declining. In addition, the preliminary structure-activity relationship of the scalaranes suggested that the 19-acetal moiety influences the potency of antituberculosis activity to certain extent.

Overall, this work has demonstrated that Thai marine organisms are among the potential sources of antituberculosis agents, as well as several agents of chemotherapeutic uses that may be useful in drug development. The further exploring will, therefore, yield compounds with greater efficacy and specificity for the treatment of many human diseases.