CHAPTER V

CONCLUSION

As part of our continuing investigation on bioactive substances from mangrove actinomycetes, the strain TRA 9875-2 was collected and identified as *Streptomyces* based on morphological, cultural, physiological, biochemical, and cell wall component studies. The antimicrobial activity screening of the EtOAC extracts of fermentation broth of this strain showed the activity against *Candida albicans* ATCC 10231 and *Staphylococcus aureus* ATCC 25923. Large-scale fermentation of *Streptomyces* sp. TRA 9875-2 was performed using two fermentation media (GPM and YM). The bioassay guided fractionation of the EtOAc extract by using antimicrobial activity yielded geldanamycin and 17-*O*-demethylgeldanamycin from both GPM and YM fermentation broths and a new derivative, 17-*O*-demethyl-dihydrogeldanamycin was obtained from GPM fermentation broth.

Geldanamycin exhibited antimicrobial activity against *C. albicans* ATCC 10231 with 16.20 mm zone of inhibition at the concentration of 100 μg/disc and showed significant cytotoxicity against human epidermoid carcinoma cell line of the nasopharynx (KB) and breast cancer cell line (BC) with ED_{50} = 1.1 and 0.33 μg/ml, respectively. It also possessed potent antimalarial activity against *Plasmodium falciparum* (K1, multidrug resistant strain) at EC_{50} = 0.063 μg/ml. Acetylation product, 11-*O*-acetylgeldanamycin showed no antimicrobial activity, but established antimalarial activity against *P. falciparum* at EC_{50} = 11.7 μg/ml and cytotoxic activity against BC cell line at ED_{50} = 2.1 μg/ml. The methylation product, 11-*O*-methylgeldanamycin showed antibacterial activity against *Staphylococcus aureus* with 8.7 mm zone of inhibition, and also exhibited antimalarial activity at EC_{50} = 7.1 μg/ml and cytotoxic activity against BC cell line at ED_{50} = 6.8 μg/ml. Compound 17-*O*-demethylgeldanamycin (KTR75008k) showed weak cytoxicity toward KB and BC cell lines at ED_{50} = 10.4 μg/ml and 3.1 μg/ml, respectively but exhibited no antimicrobial activity at concentration 100 μg/disc. The new compound, 17-*O*-demethyldihydrogeldanamycin, exhibited no antimicrobial activity at the same

concentration. Because of limited amount of sample, other biological activities of 17-*O*-demethyldihydrogeldanamycin have not been determined.