CHAPTER 6

CONCLUSION

Biotransformation of artemisinin was conducted by five fungal strains of *Aspergillus* sp. which were *A. oryzae* (Ozykat-1), *A. niger* TISTR 3254, *A. usamii* TISTR 3258, *A. terricola* TISTR 3109 and *A. melleus* TISTR 3128. Among these strains, *A.oryzae* (Ozykat-1) and *A. terricola* TISTR 3109 had abilities to transform artemisinin into a transformed product. The transformed product was isolated from the culture broth and identified as deoxyartemisinin. The suitable conditions for the transformation of artemisinin to deoxyartemisinin were observed when *A. oryzae* (Ozykat-1) and *A. terricola* TISTR 3109 were pre-cultured to log phase before the addition of artemisinin with a concentration of 0.5 mg/ml to the transformed medium II (SDB) for 6 days at 37^{o}C on the rotary at a speed of 160 rpm. The yielded deoxyartemisinin was 12% and 11% for *A. oryzae* (Ozykat-1) and *A. terricola* TISTR 3109, respectively. This research demonstrated that the biotransformation of artemisinin into deoxyartemisinin by the whole cells of *A. oryzae* (Ozykat-1) and *A. terricola* TISTR 3109 was not dependent on the growth of the fungi.

The *in vitro* biological activity of deoxyartemisinin was examined for antimalarial, antimicrobial and cytotoxicity activities. Deoxyartemisinin showed less antimalarial activity than artemisinin, dihydroartemisinin and mefloquine. Based on the antimicrobial results, it was clear that the transformed product derived from

A. oryzae (Ozykat-1) and *A. terricola* TISTR 3109 did not provide more desirable antimicrobial activities against *S. aureus* TISTR 1466, S. *typhimurium* TISTR 292, *E. coli* TISTR 780, *C. albicans* BCC 5390 and *A. niger* TISTR 3254. According to the *in vitro* cytotoxicity study, deoxyartemisinin was able to inhibit growth of all tested cells but the obtained IC_{50} values were not in the range to define as anticancer agents based on the U. S. National Cancer Institute (NCI) definition (IC_{50} < 4µg/ml). This non-endoperoxide compound showed the inhibition of cells growth at the LD_{50} value of 1.621 ± 0.095 mg/ml for normal mouse fibroblast L929 cell line and the IC_{50} value of 0.585 ± 0.058, 0.394 ± 0.049, 1.292 ± 0.213 and 0.940 ± 0.087 mg/ml for mouse melanoma B10F16, human lung carcinoma A549, human colorectal adenocarcinoma HT-29 and human colorectal adenocarcinoma Caco-2 cell lines, respectively. Deoxyartemisinin was significantly more effective than artemisinin in the inhibition of B16F10 cell growth but not significantly more effective in the inhibition of A549 growth when compared to that of artemisinin at 95% significance level. In addition, the ratio of the lethal dose (LD_{50}) to the inhibition concentration (IC_{50}) of the tested cancer cell lines suggested that deoxyartemisinin showed the most effective in the inhibitory of A549 followed by B16F10, Caco-2 and HT-29 at the values of 4.120 ± 0.523, 2.763 ± 0.302, 1.718 ± 0.161 and 1.271 ± 0.134, respectively. It is hoped that this study will provide useful information for the preparation of deoxyartemisinin and others bioactive derivatives. Further studies could investigate mechanisms and essential factors contributing to biotransformation of artemisinin by fungi.