Enhancement of Cytotoxic Metabolite production from HAB10R12 an Endophyte

ACKNOWLEDGEMENTS

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ABSTRACT

Natural products have played an important role in treating cancer by serving as compounds in their natural form or as templates for synthetic compounds. In the recent years, endophytes hold a new source of novel cytotoxic drug discovery. The endophyte HAB10R12 used throughout this study was isolated from a local medicinal plant. Preliminary screening found this endophyte to possess cytotoxic activity against P388, a murine leukaemic cell line. The aim of this study was to determine the effect of different culture conditions on the cytotoxic metabolite production of HAB10R12 against human colon (HCT116) and breast (MCF7) cancer cell lines. The various fermentation parameters include type of media (agar vs. broth), water source (tap water vs. deionized water), incubation time (1, 2 and 4 weeks) as well as strength of media (full media strength vs. one fifth media strength). The sensitivity of HAB10R12 extracts encoded PDA1, PDA2, PDA4, PDB2(B), PDB2(M), TPDA, TPDB(B), TPDB(M), 1/5PDA, 1/5PDB(B) and 1/5PDB(M) were determined against HCT116 and MCF7 cell lines. All the extracts were evaluated for *in vitro* cytotoxic activity against HCT116 and MCF7 cell lines using the MTT assay. The sensitivity of each cell line was characterized by the IC_{50} value. The result of this study indicated that endophytic fungus HAB10R12 incubated for 4 weeks and that prepared by using full strength medium with deionized water to possess stronger cytotoxic activity when compared to other fermentation parameters. The endophytic fungus HAB10R12 with its promising cytotoxic activity has the potential to be developed as cytotoxic drug.

CHAPTER 1

INTRODUCTION

Cancer is one of the leading causes of death in the world. In 2005 and 2007, cancer amounted for 7.6 – 7.9 million deaths which are about 13% of all death worldwide (WHO, 2006; 2007). In Malaysia, the incidence of cancer is on the rise as it is now the second leading cause of death after heart diseases. Lung cancer is the main cause of cancer deaths and breast cancer is the number one cause of cancer deaths among women in Malaysia (National Cancer Council Malaysia, 2006). Based on projections, cancer deaths will continue to rise with an estimated 9 million people dying from cancer in 2015, and 11.4 million dying in 2030 (WHO, 2007).

The major problem in achieving successful cancer treatment is the acquired or inherent resistant of tumor cells to chemotherapeutic drugs (Mary-Ellen et al., 2002). This is due to the presence of excess P-glycoprotein, a drug efflux pump which pumps out various kinds of drugs from the cells, resulting in the decrease of intracellular drug concentration. Furthermore, in most cases tumor cells are dose-dependant where high doses of chemotherapeutic is required to compress huge cancer population. This on the