UNIVERSITI TEKNOLOGI MARA

INDUCTION OF APOPTOSIS BY FUNGAL EXTRACTS HAB10R12 AND HAB14R3 AGAINST COLON (HCT116) CANCER CELL LINES.

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ABSTRACT

Natural products play an extremely important role as the major source of drugs used for cancer treatment. Endophytes, a new source of natural products, are microorganisms that reside in the living tissues of the host plant and may produce substances that have potential to be used in modern medicine. This study aims to determine the cytotoxic activity of endophytic extracts (HAB10R12 and HAB14R3) against colon (HCT116) cancer cells. The mode of cell death elicited by HAB10R12 and HAB14R3 and apoptotic related genes involved in the cell death were also investigated. The endophytic fungi were subcultured on half strength PDA agar and extracted with ethyl acetate. The cytotoxic activities of the extracts against HCT116 were evaluated using the MTT assay. Cell death detection was carried out using Cell Death Detection ELISAPLUS. The results from present study showed that the cytotoxic activity (IC_{50}) of the extracts were 0.055μg/ml for HAB10R12 and 0.056μg/ml for HAB14R3.The results also indicated that the mechanism of cell death elicited by extracts against HCT116 were mainly due to apoptosis. The HAB14R3 exhibited better apoptotic activity when compared to HAB10R12. The study of apoptotic related genes however, was inconclusive. PCR methods needs to be optimised to confirm the expression of gene related to the apoptotic pathway. In future, more studies also should be conducted with pure compounds of HAB10R12 and HAB14R3 in the future to discover the other potentials possess by these endophytic fungi.

CHAPTER 1

INTRODUCTION

Cancer is characterized by cells which have lost their control over proliferation, thus multiplying in a continuous and uncoordinated manner. The uncontrolled growth of cancer will eventually lead to systemic spread of cancerous cells, a process known as metastasis. Unfortunately cancer is the world's leading cause of death and the incidence of cancer has been forecasted to continue to be the centre of worldwide attention in years to come. According to the World Health Organization (WHO, 2007), from the total of 58 million deaths in the world in 2005, 7.6 million people died of cancer. In the United States, cancer is the second most common cause of death and it accounts for 1 in every 4 death in the country (American Cancer Society, 2007), and about 1.4 million of American people are diagnosed with cancer in 2007. In fact, it is suggested that the mortality due to cancer will be increasing from 9 to 11.4 million people in 2015 and 2030 (WHO, 2007). In Malaysia, cancer being the second leading cause of death after the cardiovascular disease (National Cancer Council Malaysia, 2007), is indeed a serious national health crisis. There are more than 40,000 new cases of cancer are reported each year and it is estimated that the cancer incidence in Malaysia would be 150 per 100,000 population (National Cancer Registry, 2005).