UNIVERSITI TEKNOLOGI MARA

ALOE EMODIN REGULATES THE SUPPRESSION OF BREAST CANCER CELL PROLIFERATION VIA CALCIUM SIGNALLING

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ABSTRACT

Deregulation of Ca^{2+} signaling is one of the characteristics of breast cancer cells. Our preliminary findings have demonstrated antiproliferative effects of aloe emodin (AE), anthraquinone extract of *Aloe barbadensis Miller* on breast cancer cells, MCF-7. However, the influence of Ca^{2+} regulation in AE-treated breast cancer cells is not well known. Therefore, this study was done to discover the intracellular calcium dynamics of AE-suppressed proliferation in breast cancer cells, MCF-7. Cell viability after AE treatment for 1, 6 and 12 hours on MCF-7 cells were studied using trypan blue exclusion method. Intracellular calcium study was done by loading the MCF-7 cells with calcium specific fluorescent dye Fluo4-AM for 45 minutes and the fluo4 intensity changes over time were recorded using confocal laser scanning microscope. Fluorescence intensity was measured for untreated cells, Thapsigargin (TG) and AE treated cells. TG was used as positive control in this study as it is known to result in high cytosolic Ca^{2+} dynamics. Throughout cell viability determination, there is no significant cell death for all time points. However, AE treatment leads to a significant increase in cytoplasmic Ca^{2+} (mean ± SD: 10.38±1.02; $p<0.05$) in comparison to untreated cells (5.55±0.35). As expected TG treatment shows an expected increase in cytoplasmic Ca^{2+} intensity (25.39±0.59; $p<0.05$). These remarkable findings are crucial due to the facts that calcium is an important regulator of cell survival and apoptosis. An alteration in intracellular Ca^{2+} homeostasis ultimately leading to cell apoptosis and possibly is one of the pathways in AE-induced apoptosis in MCF-7 cells. Thus, our finding suggests that cytoplasmic Ca^{2+} regulation is involved in AE-suppressed proliferation of human breast cancer cells, MCF-7 . Furthermore, this study provides valuable preliminary findings to further explore on the involvement of calcium signaling in the AE-breast cancer study.

CHAPTER 1

INTRODUCTION

1.1 Cancer

Cancer is define by uncontrolled growth with the ability of the cells to spread to any other part of the body (Gabriel & Ebrary, 2007). Furthermore, characteristics of cancer cells include growth signals self-sufficiency, signal insensitivity for growth limitation, apoptotic evasion, unlimited replication, sustainability of angiogenesis and also ability to invade and metastasize (Hanahan & Weinberg, 2000). Cancer continue to be major health issue of our time and contributes to the 10% of mortality worldwide and 25% in some countries (Pelengaris & Khan, 2006). According to Kreeger & Lauffenburger (2010), cancer is a disease that occur as consequences of the deregulation of various pathways governing basic cellular processes such as cell death, cell proliferation, differentiation, and also migration which altering the activities of molecular networks in complex manner.

In addition, cancer can be classified as heterogeneous disease which results from the cumulative defects of multiple genetic and also epigenetic and this later leads to deregulation in the cellular physiology such as cells signaling and as an ultimate outcomes resulting in the impaired control of the cell division, motility, adhesion and also apoptosis (Hanahan & Weinberg, 2011).

In Malaysia, cancer is one of the most common causes of death. According to National Cancer Registry 2007 done by Ministry of Health of Malaysia, cancer is the third common cause of death in Ministry of Health Malaysia Hospitals after Heart Diseases of Pulmonary Circulation and Septicaemia (Zainal & Nor Saleha, 2011).