

UNIVERSITI TEKNOLOGI MARA

**DIFFERENTIAL CYTOTOXICITY OF ETHYL
ACETATE EXTRACT OF MALAYSIAN MARINE
ENDOPHYTIC FUNGUS (MKS3) AGAINST
HUMAN BREAST CANCER CELL LINES**

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**Dissertation submitted in partial fulfilments of the requirements for
the Bachelor of Pharmacy (Hons.)**

Faculty of Pharmacy

July 2016

ACKNOWLEDGMENTS

First of all, I would like to express my fullest gratitude to the Almighty Allah for giving me strength and patience to complete my final year project 2016 as partial fulfilment for Research II (PHC567)

I wish to express my fullest appreciation to my supervisor, A/ Prof. Dr. Kalavathy A/P Ramasamy, and co-supervisor, Dr. Lim Siong Meng, for their continuous support, guidance and assistance throughout the course of my project. For without their supervision, I would not have been able to complete this project on time.

I would also like to dedicate my gratitude to all members of Collaborative Drug Discovery Research (CDDR) Laboratory, Faculty of Pharmacy, especially Ms. Nur Syakila Rohawi and Mr. Mohamad Zaki Zakaria, who had been generous in sharing their knowledge throughout this project. I would like also to thank Mr. Mohd Shahrul Izan Ibrahim for assisting me in ESEM.

Many thanks also to all my group members, Ms. Elinaz Jamine Hj Jamaludin, Ms. Nursyafira Hendarto, Ms. Nur Hidayah Ahmad Bahir, Ms. Nur Syafiqah Mohd Lotpi and Ms. Wan Nadrah Wan Zakri. I truly cherish the wonderful experience of supporting each other towards completion of this project.

Last but not least, I wish to thank my family especially my father, Mr. Abdul Nuri Judnarun and my mother, for all their love and support along this project.

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ABSTRACT

Bioactive compounds produced by endophytes are progressively becoming significant in the process of drug discovery. Endophytes are microorganisms that inhabit plants and are known to produce valuable metabolites that could be potential drug leads against cancer. This study was undertaken to assess the cytotoxic profiles of ethyl acetate extract of marine endophytic fungus MKS3 originated from *Terminalia* sp. (locally known as “Ketapang” tree) against breast cancer cells. The fungal cultures were first examined using gross observation and environmental scanning electron microscope (ESEM). The cultures were extracted using ethyl acetate and concentrated using rotary evaporator. MCF7 and MDA468 were treated with the MKS3 (0.01-100 $\mu\text{g/mL}$) for 72 h. SRB assay was performed and data generated was used to plot the dose-response curve from which IC_{50} (concentration required to inhibit 50% cell population) was determined. In general, MKS3 was more selective towards MCF7 when compared to MDA468. MKS3, however, exhibited weak cytotoxicity, with mean IC_{50} of 39.5 ± 21.7 $\mu\text{g/mL}$ and 36.0 ± 5.7 $\mu\text{g/mL}$ against MDA468 and MCF7, respectively. When compared to paclitaxel (positive control) MKS3 was at least 1,200 times less potent against breast cancer cells. When compared to tamoxifen (positive control), MKS3 was at least 5 times less potent against MCF7. Future study could be performed against other cancer cell types.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Breast cancer is an uncontrolled growth of breast tissues (American Cancer Society, 2015). In the United Kingdom, there were around 49,900 women who were diagnosed with breast cancer in 2011 (Cancer Research UK, 2011). In Malaysia, breast cancer is also the most common form of cancer affecting women (Malaysia Oncology Society, 2012).

Breast cancer treatments include surgery, radiotherapy, hormonal therapy and chemotherapy (National Cancer Institute, 2015). Chemotherapy, in particular, involves the combinational use of cancer-killing drugs such as doxorubicin and epirubicin. These drugs kill cancer cells that multiply rapidly in the body. Unfortunately, they also kill normal cells that are actively dividing (Cancer Research UK, 2014). This in turn results in unwanted side effects. The use of doxorubicin, for example, often causes side effects like hair loss, fatigue, nausea and vomiting. Besides, multidrug resistance whereby cancer cells no longer respond to chemotherapy can also occur. This happens because chemotherapy kills drug-sensitive cells, but leaves behind a proportion of drug-resistant cells (Nature Biotechnology, 1999). Given the limitations of