

**CYTOTOXIC AND ANTIMICROBIAL EFFECTS INDUCED BY ETHYL
ACETATE EXTRACTS OF MALAYSIAN ENDOPHYTIC FUNGI**

(MKS 3.1 AND MBFT TIP 2.1)

ABSTRACT

Drug resistance has always been the major obstacle of current treatment against infectious diseases and cancers. This has led to constant need for new drugs. Capitalizing on the abundance of unexplored Malaysian endophytes that reside in marine plants without causing significant harm, the present study was undertaken to assess the cytotoxic and antimicrobial profiles of ethyl acetate extracts of endophytic fungi originated from *Terminalia* and *Avicennia* plants. Another two marine fungal extracts, SM 2.2 and SW 2.3 Plate 2 originated from sea mud and sea water, were also included for comparison purposes. Basically, the extracts were prepared by soaking the fungi in ethyl acetate overnight before being extracted using a rotary evaporator. For cytotoxic assay, HCT 116 (human colorectal carcinoma cells) were seeded at 2,500 cells/ 200 μ L and incubated overnight to allow attachment. The cells were then treated with the extracts (0.01 – 100 μ g/mL) for 72h. SRB assay was performed to generate data from which the IC₅₀ (inhibitory concentration of HCT 116 cells at 50%) was determined. The antimicrobial assay involved addition of pathogenic bacteria (Gram-positive and negative) into extracts (0.01 – 100 μ g/mL) prior to determination of the minimal inhibitory concentration (MIC). The present study found MKS 3.1 to be the most potent ethyl acetate extracts against HCT 116 (IC₅₀ = 1.18 \pm 0.63). Its IC₅₀, however, was approximately 2.6 fold higher than that of 5-FU, the positive control. In general, the endophytic fungal extracts elicited weak antimicrobial activity against both Gram-positive and negative bacteria (MIC = 1mg/mL). The present study has uncovered the potential anticancer and antimicrobial effects of local endophytic fungi isolated from marine plants. The use of other organic solvents for extractions could perhaps harness other bioactive compounds produced by these endophytes.

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CHAPTER 1: INTRODUCTION

Infectious diseases which can spread directly or indirectly from one person to another are caused by pathogenic microorganisms like bacteria, virus, parasites and fungi (WHO, 2014). The continuous emergence of infectious disease has become a major concern among health care providers worldwide (van Doorn, 2014). Factors such as changes in human demographics and behavior, international travel and commerce as well as breakdown in public health measures have all contributed to the rise of infectious disease. The recent spread of cholera in South Sudan, for example, is a *Vibrio cholera*-induced severe watery diarrhoea under poor prevailing sanitary condition (WHO, 2014). Conventionally, antibiotics and vaccines are used to treat infectious diseases. Continuous and excessive usage of antibiotics over time, however, have led to drug resistance (Zolaly & Hanafi, 2011).

Colorectal cancer (CRC), on the other hand, remains a public health issue worldwide. It is estimated that more than 1 million new CRC cases are diagnosed each year (Lee & Chu, 2014). In fact, it is the third most common cancer after lung and breast cancer. Currently, combination therapies like FOLFOX (folinic acid, 5-FU, and oxaliplatin), XELOX (capecitabine and oxaliplatin) or FOLFIRI (folinic acid, 5-FU, and irinotecan) serve as standard regimen for first- and second-line treatment of CRC patients (Lee & Chu, 2014). The emergence of resistant cancer cells, however, has significantly reduced the efficacy of cancer chemotherapy, leading to treatment failure. Besides, there are also several recognised causes of drug resistance such as the