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

(MBL, MPRT 3.2, SM 1.3 & SW 4)

ABSTRACT

Colorectal cancer and infectious diseases are major problems of public health, with most of the burden falling upon developing countries. Unfortunately, current anticancer and antimicrobial chemotherapy are often compromised by side effects and drug resistance. This has led to active drug discovery from natural sources like the endophytes. Capitalising on the abundance of unexplored Malaysian endophytes that reside in marine plants, the present study aimed to assess cytotoxic and antimicrobial profiles of ethyl acetate extracts of endophytic fungi originated from *Avicennia* sp and *Sonneratia* sp. Another two extracts of marine fungi, SM 1.3 and SW 4, were also included for comparison purposes. Briefly, the fungi were grown on PDA at 28°C for 14 days before being subjected to extraction. The resultant extracts (0.01 – 100µg/mL) were screened for their cytotoxicity against HCT 116 (colorectal cancer cell line) and antimicrobial properties against *Staphylococcus aureus* and *Pseudomonas aureginosa*. For cytotoxicity, SRB assay was performed after 72 h treatment. Data generated was used to determine the IC_{50} (concentration of an inhibitor where the response is reduced by half). For antimicrobial assay, minimum inhibitory concentration (MIC) was determined. The present findings revealed the endophytic fungi derived MBL, as the most potent endophytic fungal extracts against HCT 116 with IC_{50} observed at 7.16µg/mL. Its IC_{50} falls within the NCI cut off concentration ($IC_{50} < 20$ µg/mL) for a crude extract to be considered as cytotoxic. Its potency was approximately 15.6-fold lower than that of 5- FU, the positive control. The cytotoxicity of the two marine fungal extracts appeared to be modest. In general, all fungal extracts elicited modest antimicrobial activity against both Gram-positive and negative bacteria. This study has successfully identified MBL as the

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CHAPTER 1

INTRODUCTION

Human colorectal cancers (CRC) refer to abnormal cell growths at either the colon or the rectum. It is the third most common cancer worldwide, with 1.4 million cases diagnosed in 2012. Almost 95% CRC are adenocarcinomas (World, Health Organization, 2013). In the United States of America, whilst 136,830 people were estimated to be diagnosed with CRC in 2014, 50,310 died of the same disease. In Malaysia, 13.2% Malaysians were diagnosed with CRC in 2006. In Peninsular Malaysia, the age standardised incidence of CRC is slightly higher among males (ASR 21.6 per 100,000) when compared to female (ASR 15.4 per 100,000) (Malaysian Cancer Statistics-, 2006).

Infectious diseases, on the other hand, are communicable diseases caused by bacteria, fungi, parasites and viruses. These diseases are known to be contagious as they can be transmitted directly or indirectly from one organism to the other. A bacterium may cause either a specific disease or various diseases. *Salmonella typhimurium,* for example, may cause typhoid fever whereas S*taphylococcus aureus* may cause several infectious diseases like pneumonia, toxic shock syndrome, bacteraemia and endocarditis (Minemura, Tajiri, & Shimizu, 2014). The World Health Organisation (WHO) revealed that 83% children who died under age of five were the results of infectious diseases, neonatal, or nutritional conditions (World Health Organization, 2013). The incidence of bloodstream infection caused of Gram-negative bacteria was reported as greater than 50% of all bloodstream infections (Bullard & Dunn, 2001). Besides, it was also found that incidence of nosocomial