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ASSESSMENT OF MOLECULAR DNA DAMAGE AND OXIDATIVE STRESS IN MICE INTESTINAL TISSUES FOLLOWING 50% WATERMELON JUICE SUPPLEMENTATION

By

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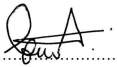
DECLARATION

I hereby declare that this thesis is my original work and has not been submitted previously or currently for any other degree at UiTM or any others institutions.



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ABSTRACT

ASSESSMENT OF MOLECULAR DNA DAMAGE AND OXIDATIVE STRESS IN MICE INTESTINAL TISSUES FOLLOWING 50% WATERMELON JUICE SUPPLEMENTATION

Ionizing radiation (IR) has been extensively used as therapy and diagnostic modality to detect abnormalities inside human body, but elicit both beneficial and deleterious role. Interaction between and IR and cells can leads to production of free radicals thus causing oxidative stress. By using animal model system, our aim is to assess molecular DNA damage and oxidative stress in mice intestinal tissue following 50% watermelon juice supplementation for 14 days. Twenty four (24) of 6 weeks old male ICR mice were randomly selected into four groups, which are negative control group (-ve), antioxidant group (Aox), radiation group (Rx) and treatment group (Tx). Cx were treated with normal diet and filtered tap water; Aox were treated with normal diet and 50% watermelon juice; Rx were treated with normal diet, filtered tap water and irradiated with 100 μGy x-ray; Tx were treated with normal diet, 50% watermelon juice and irradiated with 100 μGy x-ray. After 14 days, the levels of superoxide dismutase (SOD), reduced glutathione (GSH) and malondialdehyde (MDA) in intestinal tissues were elucidated by using biochemical analysis and comet assay for demonstration of oxidative stress and DNA damage. Comet assay revealed significant reduction of DNA damage in 50% watermelon juice supplemented group compared to radiation group (p=0.00) and pair-wise relationship between Aox and Cx showed significant difference with p=0.003. Between Rx and Cx, the DNA damage were statistically significant at p=0.00. GSH levels for Rx and Tx yield significant reduction compared to Cx with p=0.00 and p=0.00 respectively. Significant reduction of DNA damage confirmed ameliorative effect of 50% watermelon juice while reduction of GSH level suggested a high consumption of natural antioxidant to combat oxidative stress prior to IR exposure. The outcomes highlighted that supplementation of 50% watermelon juice for 14 days have a radioprotective properties against DNA damage induced by IR.

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND

Ionizing radiation (IR) is a radiation energy that is capable of removing tightly bound electrons from the atomic orbital during an interaction, thus will ionize the atom. According to World Health Organization (WHO), IR exhibits wide beneficial applications in medicine involving the management of a wide range of tumours, along with chemotherapy and surgery. Despite its efficacy in killing tumour cells, radiation suffers from several major drawbacks like damage to surrounding healthy tissue and deoxyribonucleic acid (DNA) to the patients and radiotherapy workers (Mansour, 2013). Devasagayam *et al.*, (2004) and Waer & Shalaby, (2012) reported that ionizing radiation contributes to water radiolysis, as an important source for generation of a highly reactive chemical entities known as reactive oxygen species (ROS) which leads to several pathological conditions like cancer, diabetes, osteoporosis and others.

ROS including superoxide anion (O_2-), hydroxyl radical ($OH-$) and hydrogen peroxide (H_2O_2) are produced by aerobic organisms, and they possess a higher reactivity than molecular water (Meydan *et al.*, 2011). Overproduction of ROS may cause oxidative damage to cellular macromolecules like DNA, lipids, and proteins. Some important consequences are lipid peroxidation, which involves oxidative conversion of polyunsaturated fatty acids (PUFA) to malondialdehyde (MDA) as an important indicator for oxidative stress, protein damage, DNA damage, and cell death (Saada *et al.*, 2010; Meydan *et al.*, 2011; Eltahawy *et al.*, 2012; Mansour, 2013; Shastry *et al.*, 2014). However, ROS also can be beneficial in regulating homeostasis at cellular level in normal healthy tissue. There is a check and balance mechanism in normal healthy human body by the antioxidant to combat