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RADIOPROTECTIVE ROLE OF 50 % WATERMELON JUICE AGAINST LOW DOSE RADIATION-INDUCED OXIDATIVE DNA DAMAGE AND APOPTOSIS IN ICR MICE

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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iii
ABSTRACT

Watermelon is a natural product that contains high level of antioxidants and may prevent oxidative damage and apoptosis following an exposure to ionising radiation. The present study aimed to investigate the radioprotective role of 50 % watermelon juice against low dose radiation (LDR)-induced oxidative DNA damage and apoptosis in ICR mice. Eighteen male ICR mice were equally divided into three groups: control (Cx), radiation (Rx) and supplementation (Tx) groups (n=6). Cx and Rx received filtered tap water while Tx was supplemented with 50 % watermelon juice ad libitum for 28 consecutive days. A total body irradiation of 100 μGy X-ray was given to Rx and Tx on day 29. Liver and lung tissues were assessed for the levels of reactive oxygen species (ROS) and DNA damage. The alteration of p53, Bax, and Bcl-2 protein expressions were determined followed by ultrastructural changes confirmation. Present study showed exposure to LDR was able to enhance oxidative DNA damage and alter the expression of p53, Bax and Bcl-2. The onset of apoptosis following LDR exposure was confirmed by ultrastructure evaluation of nucleus via transmission electron microscope (TEM). Interestingly, supplementation with 50 % watermelon juice prior to LDR exposure was able to diminish the levels of oxidative DNA damage compared to Cx. Additionally, mice in Tx showed significant restoration of altered apoptotic related protein expressions and reverted the abnormal structural changes to near normal morphology (Cx). These findings propose that 50 % watermelon juice may serve as an effective natural radioprotective agent against LDR-induced oxidative DNA damage and alteration of apoptotic-related protein expressions in ICR mice.
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CHAPTER ONE
INTRODUCTION

1.1 BACKGROUND OF THE STUDY

Medical radiation professions, including radiologists, dentists, nurses and radiographers are among individuals who have been mainly exposed to low dose radiation (LDR) during radiological examinations, including diagnostic X-ray, computed tomography (CT), and nuclear medicine scans. These individuals are the largest occupations cohort exposed to ionising radiation (IR) (Zielinski et al., 2009). IR has some unique characteristics as carcinogenic and mutagenic agents which cause several impacts on human health depending on the exposed and absorbed doses, duration of exposure and time interval after exposure, and susceptibility of tissues to IR (Mohamed et al., 2014, Klaunig, Kamendulis, and Hocevar, 2010).

IR can directly disrupt atomic structures as being absorbed by living cells, produce chemical and biological changes (Azzam, Jay-Gerin, and Pain, 2012) and cause damage to important macromolecules indirectly through radiolysis of water and activation of oxygen molecules that generate reactive oxygen species (ROS) (Suzuki and Yamashita, 2012; Pollycove and Feinendegen, 2003). IR can result in free radicals production including superoxide anion (O$_2^-$), hydrogen peroxide (H$_2$O$_2$) and hydroxyl radical (·OH) in the presence of water and oxygen with ·OH being the major deleterious ROS (Klaunig et al., 2010; Fang, Yang, and Wu, 2002). Total body irradiation may contribute to multiple organ dysfunctions caused by oxidative stress resulted from overproduction of ROS (Gultekin et al., 2013). The ROS may result in oxidative damage as they act with biomolecules including DNA, lipids and proteins (Cardozo-Pelaez, Brooks, Stedeford, Song, and Sanchez-Ramos, 2000). Recent studies by Mohamed et al. (2014) and Zakaria et al. (2014) reveal that total body irradiation of 100 μGy of X-ray (LDR) has induced oxidative stress and inflammatory response in male ICR mice in radiation group.