UNIVERSITI TEKNOLOGI MARA

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

MOHD KHAIRUL AMRAN BIN MOHAMMAD

Thesis submitted in fulfilment
of the requirements for the degree of
Master of Sciences

Faculty of Health Sciences

November 2015

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.

Name of Student	:	Mohd Khairul Amran Bin Mohammad
Student I.D. No.	:	2013225964
Programme	:	Master of Health Sciences (Medical Laboratory Technology)
Faculty	:	Health Sciences
Thesis Title	:	Radioprotective Role of 50 % Watermelon Juice Against Low Dose Radiation-Induced Oxidative DNA Damage and Apoptosis in ICR Mice.
Signature of Student	:	
Date	:	November 2015

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.

ACKNOWLEDGEMENT

In the Name of Allah, the Beneficent, the Merciful.

First and foremost, I would like to express my thankful towards Allah S.W.T for all His Mercy and Protection that He has bestowed until I am able to complete my master research project.

At the very onset, I would like to express my deep sense of gratitude and respect to my supervisor Dr Wan Mazlina Md Saad and co-supervisor, Dr Hairil Rashmizal Abdul Razak, for their opinions and guidance during the entire course of my research work. They imbibed in me the virtues of professionalism and hard work during my maiden attempt at doing meaningful scientific research. Their hard working nature, unconventional approach, openness and flexibility at accepting new ideas and creativity provided me with a perfect environment in which I was able to mould myself both at the personal and academic levels to achieve the very best and to explore new frontiers with a single-minded devotion and confidence.

I will always be indebted to my lab mate/ best friend, Mr. Muhamad Idham Mohamed, for being a constant source of inspiration and help during the entire master's degree program. His enthusiasm, hard work and interest in providing the best in knowledge and facilities, in spite of debilitating constraints, cannot be simply expressed in mere words.

I take this opportunity to thank Department of Postgraduate Studies, Department of Medical Laboratory Technology, Department of Medical Imaging Faculty of Health Sciences and Imaging Center (IMACE) Faculty of Pharmacy and Integrative Pharmacogenomic Institute (iPROMISE) for their generous help, continued support and well wishing during the course of project work.

No words of thanks are enough for wife (Safura Ramli) and my friends; Ebby, Ain, Iqa and others for making the entire period of work a truly enjoyable and a memorable one.

The acknowledgement will be incomplete if I do not mention the role of my Parents in making me what I am today. My family has been a constant source of energy for me and I thank them for their unconditional support, love and faith in me.

Apart from the above-mentioned names, I would also like to thank all the people who have somehow or the other helped in the successful completion of my master's degree program.

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 ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2) and hydroxyl radical ($^{\bullet}OH$) in the presence of water and oxygen with $^{\bullet}OH$ 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.