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TOXICITY ASSESSMENT OF NITRIC ACID FUNCTIONALIZED WITH IRON OXIDE NANOPARTICLES AND SiPEG AS A NEW RADIOGRAPHIC CONTRAST MEDIA

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 other institutions."

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ABSTRACT

TOXICITY ASSESSMENT OF NITRIC ACID FUNCTIONALIZED WITH IRON OXIDE NANOPARTICLES AND SiPEG AS A NEW RADIOGRAPHIC CONTRAST MEDIA

Engineered nanoparticles have been extensively explored in various biomedical settings including nanoparticulate imaging agents due to its promising benefits to mankind. Iodine-intolerance patients have caused alarming concerns in searching new contrast media with lower toxicity effect. However, proper potential mechanism of nanoparticles has yet to be fully established despite its early acceptance and emerging usage. By using animal model system, the aim of present study is to assess acute nanotoxicity of 14 nm iron oxide nanoparticles (IONPs) coated with nitric acid and silane-polyethylene glycol (SiPEG) in comparison to iodine. Eighteen male wistar rats were used in order to explore the underlying toxicity of IONPs in liver tissues. •OH free radicals were elucidated by using reactive oxygen species (ROS) production assay and western blotting for the presence of p53 protein expression. The results revealed coated IONPs produced higher ROS level compared to iodine, however no statistical significant were observed. It can be hypothesized that higher amount of antioxidant has been produced by rats in iodine group in correlation to combat higher amount of ROS produced before assayed was conducted. Stronger expressions of p53 protein from the coated IONPs group were further observed. Expression of p53 protein suggested initiation of antioxidants production by the protein to ameliorate intracellular ROS production to further achieve normal redox balance in curtailing further damage. The outcomes highlighted that short-term administration of IONPs with different functionalization surfaces may be safe to be applied as radiographic contrast media.

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND

In molecular imaging, contrast enhancer media from different substances are widely developed in healthcare facilities nowadays. Contrast agents are used in biomedical field for identification, visualization and recognition of anatomical abnormalities of a particular tissues (Kerckhofs, Sainz, Wevers, Van de Putte, & Schrooten, 2013). Further development has proved contrast enhancer media has the ability to provide information regarding on the biological system thus lead to diseases identification based on the molecular biomarkers before the appearances of the clinical symptoms (Wathen *et al.*, 2013). Recently, development of nanoparticles in nanotechnology based of contrast agent is widely investigated such as iron oxide, gold, platinum and silver nanoparticles (Chien *et al.*, 2012). These nanoparticles-based contrast agents are useful to be used as an imaging probes and strategically targeting the tumor sites by using micro-Computed Tomograph (μCT) (Clark, Ghaghada, Moding, Kirsch, & Badea, 2013).

Nanotechnology has become a highly potential and interesting field in molecular studies. Currently, nanotechnology is widely used in research areas of science and technology because of the advantages features of small nanometer size and large surface properties. The production of nanomaterial (NM) has shown a remarkable increase by the advancement of technology nowadays (Dedeh, Ciutat, Treguer-Delapierre, & Bourdineaud, 2014). Based on the National Nanotechnology Initiative (NNI), nanoparticles defined as a structures of a solid particles or a particulate dispersions with a sizes < 100 nm in one dimension (Wilczewska, Niemirowicz, Markiewicz, & Car, 2012). In nanotechnology development, iron oxide nanoparticles (IONPs) has offer an opportunities to be used as an anti-cancer drug in circulatory systems while maintaining their imaging functions as a contrast enhancer media (Wang, Wang, Chen, & Shin, 2009).