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TOXIC PROPERTIES OF IRON OXIDE NANOPARTICLES FUNCTIONALIZED WITH CITRIC ACID AS A NEW RADIOGRAPHIC CONTRAST ENHANCER

By

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Thesis Submitted in Partial Fulfillment of the Requirements for Bachelor of Medical Laboratory Technology (Hons), Faculty of Health Science, Universiti Teknologi MARA

2015

DECLARATION

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

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ABSTRACT

Toxic Properties of Iron Oxide Nanoparticles Functionalized with Citric Acid as a New Radiographic Contrast Enhancer

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, our aim is to assess acute nanotoxicity of 14 nm iron oxide nanoparticles (IONPs) coated with citric acid in comparison to iodine. 18 male Wistar Rats were used in order to explore the underlying toxicity of IONPs in liver tissues. $^{\cdot}OH$ 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 the p53 protein from the coated IONPS groups 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 functionalization surfaces are safe to be applied as radiographic contrast enhancer.

CHAPTER 1

Introduction

1.1 Background

Mostly nanoparticles (NPs) are used in cosmetics, food, ceramics, catalysts and microelectronics. Nowadays, the functions of nanoparticle has extensive to medical field especially in microscopic imaging (Xia *et al.*, 2014). According to Thomas *et al.,* (2013) nanotechnology is mostly used in molecular imaging due to able in increasing the sensitivity of the image and specificity again to target tissue.

Superparamagnetic iron oxide nanoparticles (SPION) has appears as contrast medium for detection of tumor and chronic disease due to their capability and prevent from harm (Thomas *et al.*, 2013). Iron oxide nanoparticles (IONPs) usually need coated with biocompatible organic or inorganic material to provide stable condition and avoid agglomeration (Li *et al.*, 2013). Accordingly, Citric acid ($C_6H_8O_7$) is a biocompatible short chained tri-carboxylic acid is widely applied in development of stable IONPs for medical imaging field as contrast enhancer.

The study from (Mohamed *et al.*, 2015) have been showed IONPs is lower toxicity level and unharmful to be used as radiographic contras enhancer. Moreover, IONPs show alteration in toxicity level and enhance the sensitivity and specificity as contras media (Mandarano *et al.*, 2010). However, it very little known about the nanotoxicity of IONPs coated with citric acid induces toxicity properties as radiographic contrast media.