

CHAPTER 1 INTRODUCTION

1.1. Background

Cigarette, despite containing many dangerous substances is still widely consumed by people among ages. Cigarette exposure happens by both active smoking and passive smoking. Active smoking defined as directly consuming cigarette, while passive smoking defined as inhaling the smoke produced by active smoker. Everyone can be exposed to those harmful ingredients without exception. One of the harmful substances inside cigarette is nicotine.

Nicotine is an addictive substance that compose the majority of cigarette (Rezonzew *et al.*, 2012). The unfavorable characteristic of nicotine is that it acts as free radical (Ozbek, 2012). Nicotine triggers production of reactive oxygen species (Diraman *et al.*, 2018) and drops antioxidant like glutathione, glutathione peroxidase and superoxide dismutase activity (Akkoyun, 2015). By continuously consuming nicotine, the level of ROS inside the body will also increase.

Excess amount of ROS can cause imbalance between the amount of free radical and antioxidant. In normal circumstances body counters free radical compound with enzymatic and non-enzymatic antioxidant system (Mironczuk-Chodakowska *et al.*, 2018). However, if the amount of oxidant is too abundant for antioxidant system inside the body, then the organs will experience oxidative stress.

Kidney is especially vulnerable to oxidative stress because it is rich of poly-unsaturated fatty acid (PUFA). PUFA is the main target of lipid peroxidation process of oxidative stress (Ayala *et al.*, 2014). However, kidney is usually the last organ that shows significant signs when it's damaged.

Damages done by nicotine may include the increase excretion of albumin and increase artery stenosis in kidney, while decreasing glomerular filtration rate (Mishra *et al.*, 2015). These changes are not obvious to be detected. It is often too late to detect the damage in the kidney. In this case, preventive protection for the organ is preferable. The best way to protect kidney is by adding additional antioxidant from outside the body.

Some plants like *Nigella sativa* have tremendous amount of antioxidant. This plant has been used as a medicinal plant through centuries in Middle East, North Africa and Asia for treatment for various disease (Yildiz and Balikci, 2015). *Nigella sativa* contains an active compound named thymoquinone which showed strong antioxidant activity (Kazemi, 2014). Thymoquinone and its derivate, dithymoquinone, showed similar effect with SOD enzyme. In some studies, the giving of *Nigella sativa* can maintain amount of glutathione and antioxidant enzyme like superoxide dismutase-1, catalase and glutathione peroxidase-2 (Leong *et al.*, 2013). The findings gained from the studies before, indicating that *Nigella sativa* is an antioxidant-rich plants and more likely to protect organ from oxidative stress induced by nicotine.

1.2. Problem Formulation

Is *Nigella sativa* extract able to protect kidney damage induced by nicotine?

1.3. Theoretical Base

Nigella sativa for a long time is used as a medicinal plant in Middle East, North Africa and Asia. This plant is famous for its high antioxidative activity. Four major active components of *Nigella sativa* contribute to its antioxidative characteristic are: thymoquinone (TQ), dithymoquinone, thymohydroquinone and thymol. Thymoquinone is considered as a powerful antioxidant (Alenzi *et al.*, 2010). Thymoquinone also cuts down pro-inflammatory mediator, increases antioxidative enzyme activity like superoxide dismutase, glutathione, catalase, and decrease hepatic lipid peroxidase (Ahmad *et al.*, 2013). By this mechanism, *Nigella sativa* will be able to fuel antioxidant system inside that provides protection.

A simple example of inevitable oxidative agent is cigarette. Cigarette contains high amount nicotine which is known to be an oxidative agent (Diraman *et al.*, 2018). Nicotine induces COX-2 isoform that causes inflammation (Mishra *et al.*, 2015). COX-2 enhances ROS generation by polymorphonuclear neutrophils at inflammation site, causing endothelial dysfunction and tissue injury (Mittal *et al.*, 2014).

Nicotine also decrease the amount of enzymatic antioxidant system such as superoxide dismutase and glutathione peroxidase (Oyeyipo *et al.*, 2014). Oxidative stress will happen under the imbalance condition between the amount of free radical and antioxidant. It leads to tissue damage and cell death (Ayala *et al.*, 2014). To prevent damage in the kidney the best choice is to give additional antioxidant as protective agent which will help to prevent tissue damage.

1.4. Purpose of Research

To find out the ability of *Nigella sativa* extract to protect kidney damage induced by nicotine.

1.5. Benefit of Research**1.5.1. Theoretical benefit**

To know the renal protective effect of *Nigella sativa* extract to kidney of mice induced by nicotine.

1.5.2. Practical benefit

1. To give public information about the effect of nicotine to kidney.
2. To find a probable alternative renal-protector.
3. To give information to the next researcher.

1.6. Hypothesis

Nigella sativa extract is able to protect kidney damage induced by nicotine.