CHAPTER 1 INTRODUCTION

1.1 Research Background

Heavy metal are subtances with high electrical conductivity which volluntarily lose their electrons to form cations (Jaishankar *et al.*, 2014). Arsenic, cadmium, chromium, copper, lead, nickel and zinc are the most commonly found heavy metal in the surroundings. Lead pollution in the world has continued to increase in the last 10 years (Zhai *et al*., 2018) and many developing countries like Indonesia are facing serious lead pollution problem. Lead toxicity had resulted in significant public health problem in many part of the world as one of ten major public health concern (WHO, 2018). High amount of lead exposure has resulted in poor performance, poisoning, and death in animal because of it affect on producing serious disorders on central nervous, hematopoietic, hepatic and renal system (Assi *et al*., 2016).

Kidney are highly sensitive to the toxic effects of metals pollution, this was confirmed by the high rate of renal diseases among the population of the urban and industrial areas. The mechanism of lead nephrotoxicity is caused by oxidative stress and the imbalance between detoxify capacity of antioxidants and the high generation of Reactive oxygen species (ROS) in the kidney (Sudjarwo and Koerniasari, 2015). ROS caused stressed situation at cellular level and made structral damage to cells, protein, nucleic acid, membranes and lipids (Mathew *et al.*, 2011). Research by Mohammed (2010) proved kidney of mice exposed to lead acetate resulted in serious changes in the histology and function of the organ.

The common treatment used for lead poisoning was using chelating agents which bind and remove lead from lead-burdened tissue, but the usage of conventional chelating agen have lack of safety and efficacy (Gurer and Ercal, 2000). Medicinal plants are commonly used for various treatment than conventional drugs that are more expensive and have harmful effects. Research by Flora *et al*., (2012) showed that uptake of certain nutrients like mineral elements, flavonoids and vitamins can provide protection from the environmental lead and some lead that already present in the body by chelating the heavy metals. Based on Mervat *et al.*, (2012) antioxidant activity have an important role in protection against heavy metal. Natural products and medicinal plants that have antioxidant properties for reducing free radical-induced tissue damage has also been reported by Jackie *et al.*, (2011).

Ocimum sanctum is well-known plant that are easily found and grows throughout Indonesia. Various parts from *Ocimum sanctum* provide serveral advantages as anti-inflamatory, antiallergic, radioprotective, anticarcinogenic, and antioxidant (Kusindarta *et al*., 2016). Pattanayak *et al.*, (2010) stated that *Ocimum sanctum* contains some nutrional value such as vitamin A and C, mineral (calcium, zinc and iron), chlorophyl, and many other phytonutrient. The stem and leaves of *Ocimum sanctum* contains saponins, flavonoids, triterpenoids, and tannins that acts as antioxidants which is capable to banish free radicals that are responsible for initiation of the chain reaction through chain breaking mechanism (Flora *et al*., 2012).

Based on the background due to the adverse effect of lead acetate exposion that may cause kidney damage, and the potential of *Ocimum sanctum* due its antioxidant effect against the free radicals might be considered as natural medicine resource to protect the effects of lead acetate exposures.

1.2 Problem Statement

Does *Ocimum sanctum* leaves ethanol extract have protective effect on the histopathological changes in mice (*Mus musculus*) kidney exposed by lead acetate?

1.3 Research Aim

To know about the protective effect of *Ocimum sanctum* leaves ethanol extract on the histopathological changes in mice (*Mus musculus*) kidney exposed by lead acetate.

1.4 Research Outcome

This research can provide information about the benefits of *Ocimum sanctum* leaves ethanol extract as an alternative medicine to protect kidney from lead acetate exposure.

1.5 Theoretical Base

Ocimum sanctum has antioxidant properties such as eugenol, ascorbic acid, mineral, saponins, flavonoids, triterpenoids, and tannins (Pattanayak *et al*., 2010). The essential oil from *Ocimum sanctum* is a natural source of eugenol which is one of the main chemosystematic features of *Ocimum santum* (Singh and Chaudhuri, 2018). Antioxidants properties from *Ocimum sanctum* bind with free radical by giving up their electrons and results in the termination of oxidative chain reactions,

and prevent free radical from attacking the cell (Ahmad, 2018). Antioxidant also acts as radical scavenging agent by scavenge the active radicals to suppress chain initiation and break the chain propagation reactions (Lobo *et al.*, 2010).

Lead can induce Reactive Oxygen Spesies (ROS) like hydroxyl radicals, lipid peroxide, superoxide radicals and hydrogen peroxide that can cause oxidative stess in the living cell (Hsu and Guo, 2002). Oxidative stess is caused by the imbalance between the production of free radicals and the generation of antioxidant to repair the resulting damage. ROS can react with cellular macromolecules such as lipids, nucleic acids, and proteins (Lobo *et al*., 2010).

Cell membrane are rich of poly-unsaturated fatty acid that can be easily damaged by free radical (Ahmad, 2018). Lipid peroxides are the form of peroxy radicals which result from peroxidation of polyunsaturated fatty acids with two or more double bond that have the capability to generate malondialdehydes (MDA) (Shahreza, 2017). Oxidative damage to protein products may affect the activity of enzymes, receptors, and membrane transport in the living cell (Lobo *et al*., 2010). The alteration of DNA structure and gene expression are produced from interaction of MDA and nucleic acids which form cancerous cell (Shahreza, 2017). Histopathological result of lead-induced nephrotoxicity showed structural changes in the renal tissue such as necrosis and degeneration in tubules, and glomerular necrosis that may demonstrate extensively atrophied glomerulus (Sudjarwo *et al.*, 2017).

Pretreatment with ethanolic *Ocimum sanctum* leaves extract significantly inhibits oxidative stress by reducing the extent of lipid and protein oxidation and

up-regulating antioxidant defence (Manikandan *et al*., 2007). Protective ability of *Ocimum sanctum* against various heavy metal such as lead, arsenic, cadmium, chromium and mercury are stated by Cohen (2014) and proved by Banu *et al.*, (2009) that showed significant role in protecting animals from arsenic-induced oxidative stress and depleting the arsenic concentration. The eugenol and flavonoid properties in *Ocimum sanctum* leaves extract scavenge important reactive oxygen species like superoxide radical and hydrogen peroxide, prevent oxidative damage to liposomal lipids and plasmid DNA induced by various oxidant, and reduced the level of lipid peroxidation (Baliga *et al*., 2016).

1.6 Hypothesis

Ocimum sanctum leaves ethanol extract have protective effect on the histopathological changes in mice (*Mus musculus*) kidney exposed by lead acetate.