CHAPTER 1 INTRODUCTION

1.1 Research Background

One of the most hazards and cumulative environmental pollutants that can affect all biological systems is lead, it can be exposure through to air, water, food sources, and others (Patra et al., 2011). Lead is one of the global environment health consider, mainly found in industrial region. Animal can be easily exposed to lead from numerous sources in the general environment, such as agricultural practice, contaminated feed and soil from industrial pollution (Assi et al., 2016).

Lead exposure is considered to be injurious and associated with hearing deficits, neuromuscular weakness, behavioral abnormalities, and impaired cognitive functions in human as well as in animals (Flora et al., 2012). Lead has effects on interfere thiol content of erythrocytes, sulfhydryl-containing enzymes, antioxidant defenses, and tissue rich in mitochondria, which can cause clinical syndrome. In addition to the cerebellar hemorrhage and edema associated with capillary damage, lead is also nephrotoxic, irritating, teratogenic, gametotoxic, immunosuppressive, and toxic to the hematopoietic system (Blakley, 2019). This exposure attribute to the induction of oxidative stress caused by the elevation of reaction oxygen species such as hydroxyl radicals, lipid peroxides, superoxide radicals and hydrogen peroxide (Flora, 2011).

Oxidative stress is the state of imbalance of the reactive oxygen species (ROS) and the ability of biological system to detoxify readily the reactive intermediates, which can cause lipid peroxidation. Lipid peroxidation is a chain reaction occurring during oxidative stress leading to formation of various active

compounds and resulting to cellular damage. Lipid peroxide is derived from polyunsaturated fatty acids, generally present in cell membrane. They readily elaborate to form a complex series of compounds, including malondialdehyde (Singh et al., 2014).

Malondialdehyde (MDA) is produced during polyunsaturated fatty acid peroxidation and arachidonic acid metabolism. It has characters as tumorigenic, mutagenic, and highly reactive three-carbondialdehyde (Singh et al., 2014). The measurement of MDA levels in biological systems can be used as an important biomarker of lipid peroxidation for various health disorders. Determination of MDA level in blood plasma or tissue is one of the practical methods to predict the oxidative stress levels.

Liver is an essential organ because of its responsible for the metabolism of xenobiotics and endogenous molecules to maintain homeostasis in the organism. The liver is composed of highly active metabolic tissue containing a huge complement of detoxification machinery that ideally serve to guard other physiological systems from the toxic effect of xenobiotics compounds (Mudipalli, 2007). According to Mudipalli (2007) and Moneim (2016), the accumulation of significant amounts of lead in liver tissue was implicated in the induction of an oxidative stress response in the liver. Lead is reported to cause lipid peroxidation in the liver. Malondialdehyde is a secondary products of lipid peroxidation. Increasing of MDA levels suggest enhanced lipid peroxidation in liver leading to tissue damage and failure of antioxidant mechanism to prevent formation of excessive free radicals (Koerniasari et al., 2015).

Interest has recently grown in the role of natural antioxidants, like fruits and vegetables as a strategy to prevent oxidative damage caused by oxidative stress. Many researchers recommend that administration of various natural antioxidants could prevent and cure the toxic effects of lead that causes the generation of free radicals. Natural antioxidant has the ability to reduce the toxic effects of lead by banishing reactive oxygen species at molecular level and chelating lead ions (Garcia and Gonzalez, 2008).

The examples of enzymatic antioxidants, such as catalase, superoxide dismutase and glutathione peroxidase are endogenously produced in cells, and non-enzymatic antioxidants like polyphenols, flavonoids, carotenoids, vitamins (vitamin B, vitamin C, vitamin E) are provide in our daily food as fruits, vegetables, nuts, grains, meat and milk (Flora, 2009). Several studies (in-vivo and in-vitro) have already demonstrated the antioxidative properties present in different kind of plants.

In Indonesia, among the medical plants for healing properties, the genus *Ocimum* (commonly known as ‘Basil’ or ‘Tulsi’) is very useful for its curative potential. Basil contains a wide range of essential oil rich of phenolic compounds and other natural products with a great pharmacological importance for antioxidant such as flavonoids and anthocyanins (Joshi et al., 2011). *Ocimum sanctum L.*, is an erect, herb or sub-shrub with strongly scented and hairy stems, found as a cultivated garden plant. It is used for traditional medicine as cardioprotective, antioxidant, antifungal, antidiabetic and immunostimulant (Bhattacharya et al., 2014). By the research that Bhattacharya et al., (2014) had

done, *Ocimum sanctum* contains phenols, flavonoid, carotenoid, ascorbic acid, riboflavin, and thiamine. It also contains vitamin E and vitamin A (Kusuma, 2010).

Phenols and flavonoids are the important groups of secondary metabolites synthesized by plants and have been profusely linked with antioxidative activities. Carotenoid is a low molecular weight antioxidant, acts as photoprotective agent and may reduce photo-allergy, risk of sunburns and even skin cancer. Ascorbic acid or vitamin C is considered as the most important water-soluble antioxidant and capable of neutralizing reactive oxygen species before lipid peroxidation is initiated (Afolabi, 2009).

According to the analysis that have been done before, it is required to do a research regarding the antioxidant activity of basil leaf (*Ocimum sanctum*) extract to decrease malondialdehyde level of mice (*Mus musculus*) exposed by lead.

1.2 Problem Statement

Does the extract of *Ocimum sanctum* leaf has potential in decreasing liver malondialdehyde level of mice (*Mus musculus*) exposed by lead?

1.3 Research Purpose

Purpose of this research is to prove: the potential of *Ocimum sanctum* leaf extract in decreasing liver malondialdehyde level of mice (*Mus musculus*) exposed by lead.

1.4 Aim of Research

1.4.1 Theoretical aim

The theoretical aim is to give explanation about the potential of *Ocimum sanctum* leaf extract to decrease malondialdehyde level of mice (*Mus musculus*) exposed by lead.

1.4.2 Practical aim

Result of this research is expected to give information and knowledge about prevention to oxidative stress on lead exposure by natural antioxidant *Ocimum sanctum.*

1.5 Theoretical Base

Ocimum sanctum has antioxidant properties such as carotenoid, phenolic, flavonoid, ascorbic acid, riboflavin, and thiamine (Bhattacharya et al., 2014). Eugenol and rosmarinic acid were found to be predominant phenolic compound in *Ocimum sanctum* extract (Hakkim et al., 2007). Antioxidants are compounds that can delay or inhibit the oxidation of lipids or other molecules by inhibiting the initiation or propagation of oxidative chain reactions, they counteract the harmful reactive oxygen species and free radicals generated in living organism during regular metabolism (Bhattacharya et al., 2014). Antioxidant is needed to prevent or as a therapy for decreasing reactive oxygen species. They can banish free radicals by retarding the process of lipid peroxidation (Rindhe, 2018).

In animal systems, lead is considered one of the persistent ubiquitous heavy metals and it has been accused in a wide view of toxic effects (Assi et al.,

2016). It is caused by induction of oxidative stress and enhancement of reactive oxygen species (ROS) like hydroxyl radicals, lipid peroxide, superoxide radicals and hydrogen peroxide. Lipid peroxidation is a chain reaction occurring during oxidative stress leading to the formation of various active compounds that result in cellular damage, they decompose to form a complex series of compounds, which include malondialdehyde (MDA). Malondialdehyde is used as a biomarker for measuring oxidative stress level in biomedical fields (Singh et al., 2014).

Based on Siva et al., (2016), oral feeding of *Ocimum sanctum* provides significant liver and aortic tissue protection from hypercholesterolemia induced peroxidative damage by the works of those antioxidant properties. By radical scavenging activity, iron reducing power, Fe^{2+} chelating activity, superoxide anion scavenging activity, hydroxyl radical scavenging activity, and hydrogen peroxide scavenging activity, those antioxidant properties of *Ocimum sanctum* will delay or inhibit the lipid peroxidation process initiated by the lead-induced oxidative stress with the result of decreasing or defending the malondialdehyde level.

1.6 Hypothesis

According to the problem statement and purpose of research aforementioned, it is concluded hypothesis: *Ocimum sanctum* leaf extract has potential in decreasing liver malondialdehyde (MDA) level of mice (*Mus musculus*) exposed by lead.