CHAPTER 1 INTRODUCTION

1.1 Research Background

Lead is a toxic metal which occurs in air, water, and soil that caused extensive environmental contamination and health problems in many part of the world (WHO, 2019). Prolonged lead exposure has been proved as a risk factor for neurological, cardiovascular, and reproductive disorders. It can comes from the incomplete combustion of motor vehicle fuel, industrial emissions, the use of building paints that contain lead, drinking water as lead is used in water pipes, battery making, soldering, and glass manufacturing industries (Shukla *et al.*, 2010).

Ruminant animals are animals that are sensitive to lead exposure because they can be exposed through feed contaminated by lead. Beef cattle that consume feed contaminated by lead, after being slaughtered still found lead in their meat, kidneys, liver, and intestines. Lead containing beef when consumed by human, as a result lead will enter into the human food chain and disrupt human health (Wardhayani *et al.*, 2006). Lead poisoning in children can cause serious illnesses for children's health, especially in the nervous system that can decrease the brain development and Intelligence Quotient (IQ) in children (Romli *et al.*, 2016).

The mechanism of lead toxicity is by oxidative stress, which lead can increase the productivity of free radicals or Reactive Oxygen Species (ROS) and directly suppress the body's antioxidant system (Kovacik *et al.*, 2017). Overproduction of ROS and the inability of antioxidants to prevent it leads to a state of oxidative stress and resultant damages of lipids, protein, and Deoxyribonucleic

Acid (DNA). One of the important outcome of oxidative stress is lipid peroxidation. Lipid peroxidation plays an important role in causing apoptosis (Su *et al.*, 2019).

Liver is one of the organs in the body that can be damaged due to lead exposure. Autopsy studies of lead-exposed humans indicate that liver tissue is the largest repository (33%) of lead from among the soft tissues (Sharma *et al.*, 2010). Lead is a lipophilic compound so that when the lead is transferred to the liver, it is easy to bind to the lipids of the liver cell membrane and form lipid peroxidation. Phospholipids, which are the main constituents of plasma membranes, are often the subject of lipid peroxidation. Lipid peroxidation that binds to lead increases cell membrane permeability and disrupts the distribution of ions, resulting in apoptosis or necrosis in the liver cell (Ayala *et al.*, 2014).

The presence of liver damage due to lead exposure can be detected through the liver biochemical examination. Some of liver biochemical tests are examination of the enzyme group aminotransaminase, which are the enzyme Aspartate Aminotransferase (AST), or often called the Serum Glutamic Oxaloacetic Transaminase (SGOT) and the enzyme Alanine Aminotransferase (ALT) or often called the Serum Glutamic Pyruvic Transaminase (SGPT). If the liver cells are damaged, these enzymes will be released into the circulatory system, which will cause increased levels of these enzymes in blood serum (Yuneldi *et al.*, 2018).

Substances that have hepatoprotector effect can be used to prevent the appearance of liver damage. Hepatoprotector is a compound that can provide protection to the liver from damage caused by drugs, chemical compounds, and viruses. Some natural plants have been known to have functioned as

hepatoprotector. This is related to components of plants that are rich in antioxidants that can protect the liver from damage caused by hepatotoxic induction like lead acetate. Although chelating agents are currently available for the treatment of lead poisoning, they have been shown to have many side effects and are unable to reduce some of the toxic effects of lead (Lotfi-Ghahramanloo and Baghshani, 2016)

One of the medical plants that contain natural antioxidants that can act as hepatoprotector is *Ocimum sanctum*. *Ocimum sanctum* contains antioxidants such as phenols, flavonoid, carotenoid, ascorbic acid, riboflavin, and thiamine that are needed to prevent liver cell damage caused by oxidative stress due to increased ROS in the body (Bhattacharya *et al.*, 2014). Eugenol, flavonoids, and ursolic acid components which present in *Ocimum sanctum* leaf have reported have some effects as free radical scavenging and anti-lipoperoxidative (Lahon and Das, 2011).

Based on the description above, it is known that lead can cause liver damage while *Ocimum sanctum* leaf has the potential as a liver protective material from the influence of lead. It is necessary to do research on the antioxidant activity of *Ocimum sanctum* leaf on the SGOT and SGPT levels of mice exposed by lead acetate.

1.2 Problem Statement

Based on the background the problem statement are:

1. Does the *Ocimum sanctum* leaf extract has an effect to decrease SGOT level in mice (*Mus musculus*) exposed by lead acetate?
2. Does the *Ocimum sanctum* leaf extract has an effect to decrease SGPT level in mice (*Mus musculus*) exposed by lead acetate?

1.3 Research Purpose

The purpose of this research are:

1. To prove the effect of *Ocimum sanctum* leaf extract as hepatoprotector in decreasing Serum Glutamic Oxaloacetic Transaminase (SGOT) level of mice (*Mus musculus*) exposed by lead acetate.
2. To prove the effect of *Ocimum sanctum* leaf extract as hepatoprotector in decreasing Serum Glutamic Pyruvic Transaminase (SGPT) level of mice (*Mus musculus*) exposed by lead acetate.

1.4. Research Benefit

1.4.1 Theoretical benefit

The theoretical aim is to give explanation about the effect of *Ocimum sanctum* leaf extract as hepatoprotector in decreasing Serum Glutamic Oxaloacetic Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT) levels of mice (*Mus musculus*) exposed by lead acetate.

1.4.2 Practical benefit

The results of this study can be applied to mice exposed by lead by giving *Ocimum sanctum* leaf extracts towards SGOT and SGPT levels in mice (*Mus musculus*) exposed by lead acetate.

1.5 Theoretical Base

Lead (Plumbum / Pb) is a heavy metal with a high level of toxicity. Excessive lead exposure can cause poor performance, poisoning, and death in animals (Assi *et al.*, 2016). The mechanism of lead toxicity is oxidative stress.

Oxidative stress produced when there is an increased production of free radicals or *Reactive Oxygen Species* (ROS) like singlet oxygen, superoxide, hydroxyl radical, hydrogen peroxide, and hydroperoxyl radical while the antioxidant enzymes in body are decreased (Manisha *et al.*, 2017). If the ROS formed exceeds the ability of endogenous antioxidants like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), the effects of ROS cannot be inhibited, causing damage to the liver cells. According to Ayala *et al.*, (2014), the consequences of uncontrolled oxidative stress is cells, tissues, and organs injury.

Polyunsaturated Fatty Acid (PUFA), which present in the phospholipid membrane, is sensitive to attacked by ROS. Lipid peroxidation mostly associated with cellular damage as a result of oxidative stress (Halder and Bhattacharyya, 2014). Research from Barrera (2012) showed lipid peroxidation can lead to changes in the permeability and fluidity of membrane lipid bilayer and can dramatically alter cell integrity. The process of lipid peroxidation consists of three steps: initiation, propagation, and termination. Research from Koerniasari *et al.*, (2015) proved that oral administration of lead acetate at 20 mg/kg BW could cause increased SGOT and SGPT levels due to the degeneration of hepatocytes by necrosis which causes leakage of these enzymes into blood circulation. Enzymatic activities of SGOT and SGPT are considered as sensitive serological indicators of liver toxicity (Kumar and Kar, 2013).

Cell damage caused by oxidative stress can be prevented by using antioxidants. *Ocimum sanctum* consists of antioxidants such as vitamin C, A, carotenoid, saponins, flavonoids, triterpenoids, eugenol, ursolic acid, and tannins

which are potential sources of natural antioxidant. Eugenol, which the main phenolic component in *Ocimum sanctum* leaf has an antioxidant effect as free radical scavenging and can inhibit lipid peroxidation at the level of initiation, which caused by lead acetate (Pramod *et al.*, 2010; Bezerra *et al.*, 2017).

Manikandan *et al.*, (2007) proved that ethanolic *Ocimum sanctum* leaf extract with doses of 100, 200, and 400 mg/kg of body weight could inhibit DMBA-induced oxidative stress and the incidence of bone marrow micronuclei by modulating xenobiotic-metabolizing enzymes, reducing the extent of lipid and protein oxidation, and enhancing antioxidant defense systems.

1.6 Hypothesis

According to problem statement and purpose of this research, concluded hypothesis of this research are:

1. *Ocimum sanctum* leaf extract has an effect to decrease SGOT level in mice (*Mus musculus*) exposed by lead acetate.
2. *Ocimum sanctum* leaf extract has an effect to decrease SGPT level in mice (*Mus musculus*) exposed by lead acetate.