

CHAPTER 1 INTRODUCTION

1.1 Background

Cigarette smoke contains thousands chemical, including toxic and carcinogens chemicals (IARC, 2004). Cigarette smoke is known consists of two kind of smoke there are mainstream and sidestream smoke that both have similar chemicals compounds. The toxic and carcinogens chemicals of cigarette smoke can cause oxidative stress and makes imbalance between oxidant and antioxidant in the body. These chemicals are known can increase oxidant, decrease antioxidant protection, or generate of reactive oxygen species (ROS) and reactive nitrogen species (RNS). These components elicit oxidative stress in lungs by continuous generation of reactive oxygen species (ROS). Cigarette smoke impact on lungs as the main organ of respiratory. Cigarette smoke exposure causes oxidation of proteins, DNA, and lipid that cause lung injury. The existence of oxidants in cigarette smoke can increase alveolar macrophage production and recruit neutrophils and other inflammatory cells into the lungs that leading to production of ROS and membrane lipid peroxidation (Halliwell and Poulsen, 2006). Cigarette smoke causes many kind of diseases such as chronic obstructive pulmonary diseases (Yoshida and Tuder, 2007), cardiovascular disease (Barnoya and Glantz, 2005), infertility (Fitriani *et al.*, 2010), and fetal disorder (Amasha *et al.*, 2012).

One of cigarette smoke substance, nitric oxide is one of radicals that can increase oxidative stress such as ROS (Reactive Oxygen Species) and RNS (Reactive Nitrogen Species) (Halliwell and Poulsen, 2006). Other compounds of cigarette smoke like acetaldehyde and acrolein can influence alveolar and bronchial epithelial cells to elicit inflammatory responses (Aoshiba and Nakai, 2003). The inflammation causes vascular changes that lead to vasodilation and increased vascular permeability. Vasodilation can cause congestions. Inhaled oxidant gas from cigarette smoke, like nitrogen dioxide that is delivered through vasculature causes vascular damage. The oxidant gas increases ROS in vasculature and releases inflammation (Halliwell and Poulsen, 2006). This case causes vascular erosion because of inflammation and impairs vascular endothelium that can lead to rupture of vasculature then cause hemorrhage (Arimbi *et al.*, 2013). When congestions become serious, alveolar septa become thick because of the existence of inflammatory cells and dilatation of capillary on alveolar septa induce thickening of alveolar septa. Occurrence of thickening of alveolar septa offends the gas exchange in lung (Kumar *et al.*, 2013).

Imbalance situation of oxidants and antioxidants is caused by the existence of oxidants and lack of antioxidants (Halliwell and Poulsen, 2006). *Hibiscus sabdariffa* L. is usually called rosella has antioxidant properties. There are anthocyanins, phenolic compounds (Salazar-Gonzales *et al.*, 2012), and flavonoid (Anokwuru *et al.*, 2012). Antioxidant properties are known to be beneficial for acute lung injury protection caused by cigarette smoke exposure (Bao *et*

al., 2013). Some antioxidant activities of *Hibiscus sabdariffa* L. have been reported such as hepatoprotective effects (Adetutu and Owoade, 2013) and anti hypertensive (Ajay *et al.*, 2007). *Hibiscus sabdariffa* L. is also known has anti inflammatory effect (Ali *et al.*, 2011). Cigarette smoke exposure is known causes congest, hemorrhage and thickening of alveolar septa. Based on the background above, the research entitled influence of *Hibiscus sabdariffa* L. calyx extract on alveolar histopathological feature of cigarette smoke exposed mice has been conducted.

1.2 Statement of The Problem

Does *Hibiscus sabdariffa* L. calyx extract decrease congestion, hemorrhage and thickening of alveolar septa on alveolar histopathological feature of cigarette smoke exposed mice?

1.3 Theoretical Base

Cigarette smoke is the main factors that cause lung disorder. Harmful contents of cigarette smoke increase oxidative stress (Halliwell and Poulsen, 2006). Cigarette smoke cause damage of lungs tissue such as inflammations and increased alveolar macrophage (Aoshiba and Nakai, 2003). Formed of inflammation is caused by irritants or odd things enter the tissue. Inflammation begins from irritation of cells in the tissue then cells are activated to release chemical mediators. Vasodilatation occurred then increase blood flow and increase tissue permeability. Vasodilatation can causes

congestion (Arimbi *et al.*, 2013). Oxidant of cigarette smoke through vasculature cause vascular damage (Halliwell and Poulsen, 2006) that leads to hemorrhage (Arimbi *et al.*, 2013). Inflammation case causes inflammatory cells come out from circulation into the tissue (Arimbi *et al.*, 2013). The existence of inflammatory cells and congestion induce thickening of alveolar septa (Kumar *et al.*, 2013).

Hibiscus sabdariffa L. is contain antioxidant properties such as anthocyanin, flavonoid, and phenolic compound (Direktorat Obat Asli Indonesia, 2010). Flavonoid is known has anti inflammation activity and antioxidant activity. Anthocyanins is different compound of flavonoid that has same activity. Flavonoid and phenolic compound is known that has similar antioxidant activity as free radical scavenge and metal chelators. Flavonoid also acts as chain breaking (Ebadi, 2007). Polyphenolic content (flavonoid and phenolic compound) of *Hibiscus sabdariffa* L. could prevent formed of free radical and lipid peroxidation (Anokwuru *et al.*, 2011). Antioxidants mechanisms to neutralize free radicals by accepting or donating electrons to eliminate the unpaired condition of the radical. The antioxidant molecules may directly react with the reactive radicals and destroy them, while they may become new free radicals which are less active. Others mechanisms of antioxidant by scavenging initiating free radicals or stabilizing transition metal radicals (Lu *et al.*, 2010). Thereby, antioxidant properties of *Hibiscus sabdariffa* L. is expected to prevent and decrease alveolar

histopathological feature such as congestion, hemorrhage and thickening of alveolar septa.

1.4 The aim of The Research

1. To prove influence of *Hibiscus sabdariffa* L. calyx extract on congestion of alveolar histopathological feature of cigarette smoke exposed mice through microscopic observation using *hematoxylin-eosin* staining.
2. To prove influence of *Hibiscus sabdariffa* L. calyx extract on hemorrhage of alveolar histopathological feature of cigarette smoke exposed mice through microscopic observation using *hematoxylin-eosin* staining.
3. To prove influence of *Hibiscus sabdariffa* L. calyx extract on thickening of alveolar septa of alveolar histopathological feature of cigarette smoke exposed mice through microscopic observation using *hematoxylin-eosin* staining.

1.5 The Outcome of The Research

The outcome of this research on veterinary to introduces the exploitation of rosella (*Hibiscus sabdariffa* L.) calyx as the complementary treatment or alternative treatment on lung disease, especially caused by cigarette smoke.

1.6 Hypothesis

1. The rosella (*Hibiscus sabdariffa* L.) calyx extract decreases congestion at alveolar septa on alveolar histopathological feature of cigarette smoke exposed mice.
2. The rosella (*Hibiscus sabdariffa* L.) calyx extract decreases hemorrhage at alveolar septa on alveolar histopathological feature of cigarette smoke exposed mice.
3. The rosella (*Hibiscus sabdariffa* L.) calyx extract decreases thickening of alveolar septa on alveolar histopathological feature of cigarette smoke exposed mice.

