CHAPTER I

INTRODUCTION

1.1 Background

Oxidative stress is a state in which pro-oxidative processes overwhelm cellular antioxidant defense due to the disruption of redox signaling and adaptation. It caused by an imbalanced between oxidant and antioxidants, leading to the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) that can modify macromolecules in living organisms resulting in a wide range of measurable damage (Ji & Yeo, 2021). Oxidative stress is implicated in the development of various chronic disease such as neurodegenerative disease, cardiovascular disease, cancer, diabetes and inflammatory disorders. Factors contributing to oxidative stress include genetic causes, abnormal regulation of redox-sensitive transcriptional factors, mitochondrial dysfunction, metabolic abnormalities and immune dysfunction (Ermakov *et al*., 2021). According to statistical data from the World Health Organization (WHO), specifically the Global Status Report on Non-Communicable Diseases, by the end of 2008, deaths caused by degenerative diseases such as cancer, heart disease, stroke, and diabetes had already claimed nearly 6 million lives. It is estimated that by 2030, there will be 36 million deaths per year due to these diseases (World Health Organization, 2010).

Oxidative stress treatment has been developed through various strategies and treatments including lifestyle changes, dietary adjustments, the use of dietary supplements and specific ROS-targeting strategies to reduce or prevent oxidative stress. Lifestyle approaches such as consuming antioxidant rich foods, avoiding

calorie dense refined sugars and saturated fats, and minimizing exposure to environmental pollutants can help reduce oxidative stress. Antioxidant rich foods such as fruits, vegetables, nuts and seeds can help counteract oxidative stress (Sharifi-Rad *et al*., 2020). Dietary supplements, such as nuclear factor erythroid 2-related factor 2 (NRF2) activators and antioxidant supplements have been developed to help protect against oxidative stress-related damage and diseases. Strategies have been developed to target specific ROS such as O_2^-, H_2O_2 and lipid hydroperoxides to prevent cellular damage (Yang *et al*., 2020).

Furthermore, there are drawbacks or adverse effects of an antioxidants used in oxidative stress treatment. High doses of synthetic antioxidative vitamins, such as vitamins A, E, C, and β-carotene, are often used on a long-term basis in numerous preventive and therapeutic medical applications. Also, the use of ROS-scavenging antioxidant supplementation, such as high-dose (pharmacological) ascorbate, has been investigated in the treatment of oxidative stress-related diseases. However, the use of those vitamins may lead to cases of hypervitaminosis and even to intoxication (Rutkowski & Grzegorczyk, 2012). Currently, there is no clinal trial evidence support for the use of antioxidant supplements in oxidative stress-related diseases. (Meulmeester *et al*., 2022). These adverse effects highlight the need for further research and development in the field of oxidative stress treatment to address the limitations and challenges associated with the findings, methods, and strategies currently available.

Natural products have garnered significant attention as potential sources of candidates for oxidative stress treatment. These products, rich in bioactive molecules, are being explored for their antioxidant properties and their ability to

protect against ROS and oxidative stress-related diseases (Chen *et al*., 2016). Plant-based natural medicines with antioxidant properties are being identified as reliable sources of treatment against oxidative stress and neurodegenerative disorders. (Chandran & Abrahamse, 2020). Furthermore, natural products have been the focus of research aimed at ameliorating oxidative stress, inflammation, cell death in metabolic and cardiovascular diseases. Naturally occurring compounds found in these products act as antioxidants, helping to reduce the risk of oxidative stress-related diseases such as diabetes and obesity (Kosuru *et al*., 2023)(Park *et al*., 2022). The potential of natural products in reducing or preventing the generation of oxidative stress is being increasingly recognized and their application in lifestyle approaches and as sources of antioxidants is being explored as a promising strategy.

Curcuma sumatrana is a Zingiberaceae species endemic to West Sumatra, Indonesia. It has been rediscovered and studied for its potential medicinal properties and antioxidant properties (Ardiyani *et al*., 2011). In a study screening the antioxidant activity of several plants in the Zingiberaceae family, *C. sumatrana* has been studied for its phenolic profile, antioxidant, and anticancer properties, indicating its potential as a a source of natural antioxidants and other bioactive compounds for oxidative stress treatment. (Alamsjah *et al*, 2021)(Rahman *et al*., 2022). These studies collectively indicate that *C. sumatrana* holds potential as a natural source of antioxidants, which could be valuable in the context of oxidative stress treatment. However, research on the phytochemical effects of the *C. sumatrana* rhizome on antioxidant activity has not been extensively conducted. Therefore, in-depth studies are needed to determine the antioxidant activity of the *C. sumatrana* rhizome.

1.2 Problem Formulation

Problem formulations of this study are as follows:

1. Does *C. sumatrana* ethanolic extract could exert antioxidant activity by scavenging DPPH, ABTS and reducing Fe^{3+} *in vitro*?
2. What are the compounds in *C. sumatrana* ethanolic extract that have the potential as antioxidant base on *in silico* study?

1.3 Research Purposes

The purposes of this study are:

1. To reveal that *C. sumatrana* ethanolic extract could exert antioxidant activity by scavenging DPPH, ABTS and reducing Fe^{3+} *in vitro*.
2. To identifiy the compounds in the *C. sumatrana* ethanolic extract that have the potential as antioxidant base on *in silico* study.

1.4 Research Benefit

This study is expected to provide scientific information on the health beneficial of ethanolic extract of *C. sumatrana* as an alternative source of antioxidants.