Chapter 1

Introduction

1.1 Background

The aging process is the buildup of various adverse changes within cells or tissues that progressively leads to their dysfunction (Harman, 2001). This is most apparent on the skin, as it is the largest and the outermost organ of the body, and as such would be exposed to adverse external factors such as xenobiotics, aerial pollutants, and UV (ultraviolet) radiation (Rinnerthaler et al., 2015). All of these external stressors would trigger Reactive Oxygen Species/ROS-induced cell damage; primary actors of the aging process (Devasagayam et al., 2004; Sosa Torres et al., 2015). ROS species would induce DNA damage, trigger proteins unfolding, and enhance mitochondrial dysfunction (López-Otín et al., 2013). Excessive amounts of ROS within the cell would also trigger some of the cell's stress related signaling cascades, culminating in the changes in expression levels of several genes that contribute to the aging phenotype. Two of which are *MMP1* and *COX2*, coding for the proteins MMP-1 (Matrix metalloproteinase-1) and COX-2 (Cyclooxygenase-2) respectively. Expressions of both genes have been shown to increase when the cell undergoes ROS-induced aging process (Singh et al., 2008; Kay et al., 2019). MMP-1 degrades type 1 collagen; the most abundant protein type in the human skin and a large component of the cell's extracellular matrix. Collagen degradation is a typical characteristic of an aged human skin (Kim et al., 2012; Di Lullo et al., 2002). Meanwhile, COX-2 would play a direct role in the inflammation pathway; resulting in a premature aging phenotype on the skin and the creation of more ROS, as well as inducing cellular senescence.

Antioxidants are a proven method to inhibit skin aging as they scavenge ROS and directly counteract the effects of oxidative damage. There has been a trend over the last decade to replace synthetic anti-aging (antioxidant) agents with natural ones due to unforeseen health and environmental risks they might pose (Tajkarimi et al., 2010; Kobus-Cisowska et al., 2014; Lourenço et al., 2019). The

Marchantia genus of liverworts have been used as traditional medicine throughout the world due to its various medicinal effects (Asakawa et al., 2009). In Indonesia, the plant exists as the species *Marchantia paleacea*; a proven antioxidant agent (Siregar et al., 2021). So far however, there have been no studies that test how the *M. paleacea* extracts affect the expression of aging-related genes. Thus the focus of the research would be to investigate how the *M. paleacea* extracts affect the HaCaT cells under ROS-induced damage via a gene expression analysis of *MMP1* and *COX2*.

1.2 Objective

The objective of the study is to investigate the anti-aging properties *M. paleacea* extracts on HaCaT cell lines. The sub-objectives of this study are to determine *M. paleacea* extracts' ability to minimize the effects of ROS-induced oxidative stress on HaCaT cells and to specify the means by which the *M. paleacea* extracts would elicit its anti-aging properties via a gene expression analysis on *MMP1* and *COX2*.

1.3 Hypothesis

The hypothesis for this study are that the oxidative stress elicited by H_2O_2 would upregulate the gene expression of both *MMP1* and *COX2* in HaCaT cells, and that this upregulation would be attenuated by treating the cells with the *M. paleacea* extract due to its radical scavenging capabilities.