CHAPTER 1

INTRODUCTION

Free radicals, atoms or molecules that are reactive due to possessing unpaired electrons, exist in the human body as the by-products of the ATP (adenosine triphosphate) production in the form of reactive oxygen species (ROS) and reactive nitrogen species (RNS) (Liguori *et al*., 2018; Pham-Huy *et al*., 2008). The existence of the highly unstable reactive oxygen and nitrogen species (RONS) not only comes as a result of the ATP production, but also comes from external sources such as water pollution, air pollution, alcohol, tobacco, food, and radiation (Liguori *et al*., 2018). It was well-known that moderate or amount of RONS is useful for a cellular response such as reduction-oxidation regulation for protein activation (Dröge, 2002; Kim *et al*., 2002), however, a high amount of RONS is known to cause oxidative stress. This oxidative stress could result in cellular damage by oxidizing lipid in the membrane, thus disrupting the cellular structure (Pham-Huy *et al*., 2008), as well as inducing abstraction and addition reaction to the DNA structure, which alter the gene expression (Dizdaroglu *et al*., 2002; Kumar *et al*., 2012).

Oxidative stress could cause oxidative modification which results in the damage of cellular macromolecules, such as DNA, protein, lipid, and carbohydrate (Liguori *et al*., 2018). Prolongation of the damage could increase the risk of several chronic diseases such as cancer, autoimmune disease, cardiovascular diseases, neurodegenerative diseases, mental disorders, and skin aging (Pham-Huy *et al.*, 2008). In order to minimize the damage, antioxidants are needed. Antioxidants are compounds that able to stabilize free radicals by a mechanism of hydrogen atoms donation, inhibition of low-density lipoprotein (LDL) oxidation, and chelation of metal ions which could prevent and repair the damage (Santos-Sanchez *et al*., 2019; Pham-Huy *et al*., 2008). In a state of oxidative stress, the body is incapable of producing an adequate amount of antioxidant to neutralize free radicals, therefore, the exogenous antioxidant is needed to overcome the oxidative stress. One of the sources for antioxidants is from the consumption of plants containing antioxidant compounds. Phenolic and flavonoids

compounds that are easily found in vegetables, fruits, and legumes are some of the phytochemicals that are known for their antioxidant activity (Santos-Sanchez *et al*., 2019).

Mangosteen (*Garcinia mangostana*) is a tropical fruit whose biological activities such as antimicrobial activity (Chomnawang *et al*., 2005), antidiabetic activity (Taher *et al*., 2016), antitumor activity (Nakagawa *et al*., 2007), anti-inflammatory activity (Chen *et al*., 2008), and antioxidant activity (Weecharangsan *et al*., 2006) have been extensively studied. Among these studies, its antioxidant activity is the one receiving prominent interest. Several studies have confirmed that administration of mangosteen extract could help in improving the condition of oxidant related diseases such as diabetes, hyperlipidemia, neurological disorders, skin aging, acne, and others (Huang *et al*., 2014; Im *et al*., 2017; Leontowicz *et al*., 2006; Nelli *et al.*, 2013). Due to these findings, patents and commercialization of several mangosteen-based products such as Verve®, Vemma®, and Mastin® have recently risen. However, despite the commercialization, conflicting results of the study about their antioxidant effect in various disease models are still discovered. Also, an extensive review that summarizes the antioxidant effect of mangosteen products towards oxidant-related diseases is not available. Due to these facts, a systematic review is needed to properly assess the effectiveness of mangosteen antioxidant activity in alleviating oxidant-related diseases in various clinical and *in vivo* study models. Hence, this study was aimed to perform a systematic review to evaluate scientific evidence regarding the antioxidant activity of mangosteen on animal models and clinical trials about its role in improving the pathology of the related diseases.