1. Introduction

1.1. Background

Inflammation can be defined as an immune response to harmful stimuli, for instance damaged cells, pathogens, irradiation and toxic compounds (Medzhitov, 2010), then it will remove harmful stimuli and start the recovery process (Ferrero-Miliani, Nielsen, Andersen, & Girardin, 2007). In other words, inflammation is humans' body defense mechanism which is important to health (Nathan & Ding, 2010). Generally, cellular and molecular interactions will reduce the infection or injury during acute inflammatory responses. This mitigation process will help restore the tissue homeostasis and resolve the acute inflammation. However, there is very possibile that uncontrolled acute inflammation may be the cause of chronic inflammatory diseases, e.g. cardiovascular diseases, neurological diseases, endothelial dysfunctions, and infection (Carrero, Yilmaz, Lindholm, & Stenvinkel, 2008; Machowska, Carrero, Lindholm, & Stenvinkel, 2016; Zhou, Hong, & Huang, 2016).

Bacterial lipopolysaccharides (LPS) is a powerful immunostimulant that may cause inflammation, fever and septic shock, which may lead to death of the patient. A strong inflammatory response will be trigerred when bacteria multipy in the bloodstream because the bloodstream is the ideal transportion method for bacteria to spread in the body. Immune cells in the blood are very sensitive to LPS and may cause excessive inflammation, which can lead to organ failure and patient death. This phenomenon is also called septic shock (Opal, 2010; Salomao et al., 2012).

The mechanism of inflammation is as follows : stimuli will trigger the activation of inflammatory cells, for examples macrophages and adipocytes; afterwards, cytokines, proteins and enzymes related to inflamation are produced (Chen et al., 2018). Therefore, inflammation-related cytokines, proteins and enzymes are commonly used as biomarkers for diseases diagnosis, prognosis, and therapeutic decision making (Bhowmik, Seemungal, Sapsford, & Wedzicha, 2000; Lindahl, Toss, Siegbahn, Venge, & Wallentin, 2000; Cesari et al., 2003; Pecoits-Filho et al., 2003; Shlipak et al., 2003; Pai et al., 2004; Bautista, Vera, Arenas, & Gamarra, 2005; Goldstein, Kemp, Soczynska, & McIntyre, 2009; Miller, Maletic, & Raison, 2009; Ross et al., 2009 Gupta et al., 2012).

Nowadays, people are paying more and more attention to edible dark-colored fruits, which are abundant with anthocyanins, because of their health benefit. One of the example is Jaboticaba (*Myrciaria cauliflora (Mart.) O. Berg*) fruit, a native Brazilian fruit. Jaboticaba fruit contains many bioactive compounds exhibited several properties such as anti-inflammatory, antioxidant, anti-diabetes, and anti-cancer, as well as preventing from COPD (Chronic Obstructive Pulmonary Disease), cardiovascular diseases, and stroke (Wu, Long, & Kennelly, 2013). According to reports, the biologically active compounds in Jaboticaba are carotenoids, anthocyanins, tannins, phenolic acids and lesser-known polyphenols, such as depsides (Einbond, Reynertson, Luo, Basile, & Kennelly, 2004; Reynertson et al., 2006; Plagemanna, Kringsa, Bergera, & Marostica, 2012; Wu, Dastmalchi, Long, & Kennelly, 2012).

Zebrafish, also called *Danio rerio*, is a small vertebrate fish which habitates in tropical freshwater. It has gathered attention as beneficial vertebrate model organism due to the tiny size, sizeable clutches of eggs, transparency, low-up keep, and morphological & physiological similarity to mammals (Eisen, 1996; Fishman, 1999). Lately, the merit of the zebrafish as modal animal for *in vivo* drug toxicity and efficacy studies has been acknowledged due to the advantages mentioned above (Ali, Champagne, Spaink, & Richardson, 2011; Den Hertog, 2005; He et al., 2013).On the other side, the optical translucency of zebrafish embryos helps in noninvasive and dynamic imaging of inflammation *in vivo*. Thus, zebrafish model is widely adopted and it is considered as one of the best methods for anti-inflammation determination (Lee et al., 2013; Liao et al., 2011; K. H. Park & Cho, 2011).

The use of Jaboticaba to treat inflammatory diseases has been previously studied. Reynertson et al., (2006) investigated the effect of 2-O-(3,4-dihydroxybenzoyl)-2,4,6trihydroxyphenylacetic acid and jaboticabin, potential bio-compounds in jaboticaba fruit, on COPD (Chronic Obstuctive Pulmonary Disease) characterized by irreversible airflow obstruction, using SAE (Small Airway Epithelial) cells treated with cigarette smoke extract (CSE). It was reported that bio-compound of (2-O-(3,4-dihydroxybenzoyl)-2,4,6trihydroxyphenylacetic acid) reduced IL-8 production up to 81.3% in SAE cells without CSE treatment. While SAE cells treated with CSE had decreased 47.3% of IL-8 level. Jaboticabin may also attenuate IL-8 production up to 74.9% and 70.3% in untreated and CSE-treated SAE, respectively.

Zhao et al. (2019) updated research to explore more information about different parts of Jaboticabin (including peel, seeds, pulp and veneer) and applied it to SAE cells treated with CSE to confirm the role of Jabaticabin on COPD. From the report, Jaboticabin significantly decrease IL-8 levels up to 523.28 pg/mL in CSE-induced and 190.50 pg/mL in non-induced SAE cells. *In vivo* studies conducted by da Silva-Maia et al. (2019) and Lamas et al. (2020) also observed the anti-inflammatory effect of jaboticaba using murine model. Even many reports have shown positive effects of jaboticaba on many health-related disorders, scientific study regarding the effect of jaboticaba on neuroinflammation is limited. Therefore, the purpose of this study is to explore the anti-inflammatory mechanism of jaboticaba fruit in LPS-induced zebrafish.