CHAPTER 1

INTRODUCTION

1.1. Background

Since ancient times, pathogenic microorganisms have continued to become some of the greatest threats to humanity. Infectious diseases caused by these pathogens are one of the leading causes of death worldwide, which is responsible for 15 millions of deaths annually or more than 25% of annual deaths worldwide (Morens, Folkers & Fauci, 2004). Pathogenic microorganisms pose a significant challenge to the global health system in terms of their treatment and prevention. Even though antimicrobial agents have been put into clinical use, the appearance and widespread of antimicrobial resistance strains towards multiple drugs have led to the crisis of effective therapeutic drugs and even higher morbidity and mortality. The problem with infectious diseases does not stop there; humans are continuously at risk of encountering novel pathogens that humans have little or no immunity towards. With the increased global travel and urbanization, these novel pathogens are easily carried to many parts of the world. Eventually, the widespread outbreaks can result in a pandemic which causes significant economic, social, and political turmoil.

One of the greatest and worst pandemics known to human history was the influenza A(H1N1) pandemic in 1918, known as the Spanish flu. This pandemic affected over 500 million people and caused mortality in 1–3% of the global population or at least 50 million deaths (WHO, n.d.). Influenza A virus (IAV) is an enveloped single-stranded RNA virus that has long been viewed as pandemic threats. Due to their segmented genome and lack of proofreading, IAVs are very prone to mutations that give rise to novel IAV strains with unique genes. While vaccination is available for IAV and reformulated twice a year, vaccine development in general takes a very long and complex process. Especially in the case of an ongoing pandemic, vaccination may not be available for an unknown period and hence antiviral or antimicrobial treatments are our only

option. Given the widespread resistance of antimicrobial drugs, there is a need to strengthen the treatment sector by looking for potential antimicrobial agents that are effective, non-toxic, and less likely to induce resistance.

Natural products in drug discovery are now very common as they have also been used for centuries by our ancestors in treating and preventing diseases. Today, bioactive compounds from natural products have been extensively used to treat many diseases, both in their natural form and synthetic form (Chin et al., 2006). Marine organisms render a great source of potentially bioactive compounds or secondary metabolites due to taxonomic diversity, differences in their physiology and habitat conditions (El Gamal, 2010). Among the marine organisms, algae exhibit a potential source of drug compounds, with approximately 9% of biomedical compounds from marine resources are all isolated from algae (Ahmadi, Moghadamtousi, Abubakar, & Zandi, 2015).

Macroalgae or seaweed is a diverse group of multicellular, plant-like protists that are classified based on their pigmentation into brown (Phaeophyceae), green (Chlorophyceae), and red algae (Rhodophyceae) (Andersen, 2004; Dittami et al., 2009). Among the three, the most consumed type of seaweed is brown algae (66.5%), followed by red (33%) and green (5%) algae (Lorenzo et al., 2017). Up to 70% of the dry algal weight is composed of polysaccharides (Charoensiddhi et al., 2016). One of the significant constituents of brown algae polysaccharides is fucoidan, a class of sulfated polysaccharides mainly composed of sulfated L-fucose and a lesser amount of monosaccharides (Ahmadi et al., 2015; Fitton, Stringer, & Karpiniec, 2015; Yang et al., 2008). Fucoidan has a highly diverse structure and composition in its branching, linkage, and monosaccharide composition (January, Naidoo, Kirby-McCullough, & Bauer, 2019; Venkatesan, Anil, & Kim, 2017). Not only that fucoidan differs between species, but also within the same species depending on the harvesting season, the geographic location of the algae, and the extraction method used (Sinurat, Peranginangin, & Saepudin, 2015). Because of its complex and diverse structure, the structural analysis of fucoidan has been difficult (Prokofjeva et al., 2013). Regardless, most fucoidans are classified into three types of backbone: a repeating α(1→3)-linked,

alternating α(1→3)- and α(1→4)-linked, or branching α(1→2)-linked L-fucopyranose residues (Ale & Meyer, 2013; Wang & Chen, 2016).

In recent years, fucoidan has been actively studied for its therapeutic effects. While fucoidan is well known for its antioxidant and anticancer properties, previous studies have reported other notable biological activities such as anticoagulant, anti-inflammatory, immunoregulatory, and antimicrobial activities (Song et al. 2015; Wang et al. 2019). Fucoidan has a varying degree of bioactivities, which are linked to its high structural and compositional diversity. It has been reported that the structure of fucoidan, sulfate content, and the molecular weight influence the effectiveness of its bioactivities (Yang et al. 2008; Sinurat et al. 2015). While this information mostly comes from anticancer and anticoagulant studies, there is limited information on different fucoidan effects against microorganisms.

1.2. Objectives

In this thesis project, the author aimed to elucidate the antimicrobial activities of fucoidan from brown algae. In completing the main objective, the project was divided into two parts: experimental lab and dry lab. For the experimental lab, the author aimed to analyze the antiviral activity of crude fucoidan from brown algae *Undaria* sp. towards IAV *in vitro*. The wet lab was divided into three major procedures: isolation and characterization of seasonal IAV from clinical samples, extraction and characterization of fucoidan from *Undaria* sp., and analysis of antiviral activities of fucoidan towards the seasonal IAV. Aside from IAV, the antimicrobial potentials of fucoidan were also assessed against other viruses, bacteria, parasites and fungi through a systematic review as a dry lab.