CHAPTER I

INTRODUCTION

Viruses are one of the infectious agents that are known to mankind, it is, among other agents, the smallest in size. It is a non-cellular individual infectious unit comprising a nucleic acid genome, a protein coat, a lipid-containing envelope membrane (only present in certain types of viruses), and is commonly known as a viral particle or virion (Jung et al., 2008). Since viruses are acellular, in order to continue procreation, viruses must infect a host and take over its internal cellular machinery for the production of new virions due to this aspect, viruses are considered to be a parasite to its host. (Lodish et al., 2016). Viruses have several types of the genome which include double-stranded DNA, single-stranded DNA, double-stranded RNA, and single-stranded RNA (Saunders & Carter, 2007)

As an infectious agent, viruses often cause pandemics and or epidemics throughout the course of time. From the first global pandemic caused by the influenza virus to the most recent one caused by SARS-CoV-2, almost all of them are caused by viruses as its etiological factor. Viruses also dominated most of the listed pandemic, epidemic diseases listed by the WHO; 17 out of 20 diseases. In order to remediate this problem, antivirals and vaccines are used as a mode of treatment and prevention. Antivirals are designed with a certain target protein that is an integral part of the viral infection cycle while vaccines are used for the purpose of establishing the host's immunological memory (Saunders & Carter, 2007). However, viruses have the ability to adapt to the administration of these remedies where it often leads to resistance.

With the current difficulty at hand, in regards to the insufficient use of antivirals due to the emerging resistance and the use of vaccination as a mode of prevention, the need for an alternative approach is required. Presently, the use of natural products is one of the suggested methods for the development of future remedies for pathogen infections. Since the products are natural, it is believed to have fewer side effects when processed by the human body. One of the promising

natural compounds with potential antiviral activity is a polysaccharide known as Fucoidan, obtained from brown algae species which one of them is *Sargassum* spp..

Brown algae are macroalgae that can be found throughout tropical and subtropical areas of the world, in coastal regions, between high tide to low tide and also in subtidal regions up to a depth where 0.01% photosynthetic light is still available (Yende, Harle & Chaugule, 2014). The algae are found predominantly brown due to the presence of carotenoid fucoxanthin and also the primary polysaccharides present in the organism which include alginates, laminarins, fucans, and cellulose (Yende, Harle & Chaugule, 2014). *Sargassum* spp. is one of a genus under the class of brown algae (Phaeophyceae), subclass Cyclosporeae, order Fucales, and family Sargassaceae with approximately 400 species (Mattio & Payri, 2010). It is also known to produce metabolites such as polysaccharides, terpenoids, and polyphenols which retain several known therapeutic activities which one of them is antiviral activity (Yende, Harle & Chaugule, 2014). With this knowledge, further investigation needs to be done in order to confirm the possible use of *Sargassum* spp. as an antiviral agent.

1.1 Scope of Work

The scope of this project revolves around the use of acid extraction method for the isolation of fucoidan in *Sargassum spp.* that will be further tested for its antiviral activity against seasonal influenza strain. Viral samples will be obtained from screened volunteers and identified by using the qRT-PCR method. Identified samples will then be propagated into eggs in order to produce more viruses that will be further determined by the use of rapid hemagglutination assay. *In vitro* investigation method will be used to further elucidate viral titer and antiviral activity of fucoidan by using the Madin Darby Canine Kidney (MDCK) cell line with the use of $TCID_{50}$ assay.

Systematic review is also conducted to investigate further on the possible use of *Sargassum* spp. as an antiviral agent. The review is conducted according to the PRISMA guideline on the topic of antiviral activity of *Sargassum* spp. Published studies will be screened based on its title and abstract and then followed by a thorough review of the literature itself. A set of inclusion and exclusion criteria will be used in order to determine which study will be further reviewed systematically. The

target question itself revolves around the possibility of antiviral activity in *Sargassum* spp., what certain properties contained in *Sargassum* spp. that is responsible for its antiviral activity and what are the possible mechanisms to the antiviral activity.

1.2 Objectives

The objective of this thesis project will be divided into 3 different aspects which include optimization and determination of the methods used for the extraction of crude fucoidan, examine the presence of antiviral activity from extracted crude fucoidan against seasonal influenza strain and last but not least to investigate the possible mechanistic pathway of fucoidan in inhibiting seasonal influenza strain. Observing the results of the study, it is seen that further investigation can be done in this topic. Thus, the study was continued by using systematic review to compensate possible future data and other aspects to the study. The objective of this systematic review is to outline recent studies with the focus of *Sargassum* spp. usage as a potential antiviral agent against various possible pathogenic viruses. This systematic review intends to provide an organized and structured reference for future researchers by a detailed analysis of the possible substances contained in the algae and the suggested mechanism of action in the role of *Sargassum* spp. as a possible antiviral agent and thus contribute towards a more forward research aim in the scope of *Sargassum* spp. as a natural source of antiviral. Several other possible factors such as toxicity and possible drug resistance reversal properties in the use of *Sargassum* spp. will also be evaluated and reviewed.

1.3 Hypothesis

The hypothesis for this project is that the administration of fucoidan isolated from *Sargassum spp.* will be able to inhibit seasonal IAV either through inhibiting its entry, replication or its release. Systematic review is hypothesized to compensate and add further findings to the main study and thus add more insight into the topic itself.