1 Introduction

Healthcare-associated infections (HCAIs) are infections that patients acquire during their stay at a healthcare facility and were absent at the time of admission (World Health Organization [WHO], 2011). They are a significant concern for public health as they contribute to the spread of antimicrobial resistant strains of pathogens, cause higher morbidity and mortality in patients, extend the patients' length of stay at medical facilities and increase the economic burden for both patients and medical providers (Teerawattanapong, et al., 2018). They lead to fatal results in vulnerable patient groups such as those who are immunocompromised, suffering from burn wounds, receiving organ transplants and those who with in-dwelling medical devices. They are also dangerous for neonates and patients in intensive care units (ICUs).

In 2002, HCAIs caused an estimated 99,000 deaths in the US (Klevens, et al., 2007). In Europe, approximately 8,650 people have died as a result of HCAIs from 2008 to 2012 (ECDC, 2018). Ling's team (2015) also reported that mortality rates attributed to HCAIs in Southeast Asia reached up to 46% in some cases.

Pseudomonas aeruginosa is one of the most frequently isolated pathogens in the four major categories of HCAI: Catheter-associated urinary tract infections (CAUTI), central line-associated bloodstream infections (CLABSI), ventilator-associated pneumonia (VAP) and surgical site infections (SSI) (Percival, Suleman, Vuotto, & Donelli, 2015). But it is predominant in CAUTI and VAP cases. In a study conducted by Weiner, et al. (2016) on 4,515 US hospitals, *P. aeruginosa* was responsible for 10.3% and 16.5% of all CAUTI and VAP cases respectively. As a result, it was ranked the third most isolated pathogen for CAUTIs and second most isolated pathogen for VAP cases.

P. aeruginosa can be treated using several classes of drugs. However, with the emergence of multidrug-resistant (MDR), extensively drug-resistant (XDR) and pandrug-resistant (PDR) strains of *Pseudomonas aeruginosa* (PA), conventional antibiotics may no longer be effective in combating

infections related to this bacteria. Bacteria that are resistant towards more than one antibiotic in three or more antibiotic categories are considered as MDR while those that are resistant to more than one antibiotic in all classes of antibiotics (except for one or two classes) are classified as XDR. Pandrug-resistant bacteria are the most dangerous as they are resistant to all antibiotic classes.

MDR-PA and XDR-PA have already been reported in one Indian hospital where they respectively accounted for 50% and 2.3% of 88 isolates (Gill, Arora, Khanna, & Kumar, 2016). Meanwhile, in one hospital in Nepal, out of 66 clinical isolates, 89.4% was found to be MDR-PA and 6.1% was found to be PDR-PA (Bhandari, Banjara, Lekhak, Bhatta, & Regmi, 2012). As the rate of antibiotic resistance in *P. aeruginosa* continues to increase, it is clear that there is a need for new alternatives to conventional antibiotics. Natural products, such as brown seaweed, may serve as a good source for finding these candidate drugs.

Marine algae are ocean-dwelling, photosynthetic eukaryotes that can be unicellular (microalgae) or multicellular (macroalgae or seaweed). The latter is further classified into three types – red, brown or green seaweeds - based on pigmentation and the ocean depth at which the organism resides (Sulaiman, et al., 2015). Indonesia is a key player in the global production of seaweeds. In 2014 alone, Indonesia cultivated 10 million tonnes of seaweed, which makes up 36.9% of the world's total output of seaweed for that year (Food and Agricultural Organization of the United Nations [FAO], 2016). Both red and brown seaweeds can be found in Indonesia, but only red seaweeds are farmed for carrageenan and agar while brown seaweeds are neglected by local farmers despite their abundance and them being excellent sources for alginates (Mulyati, 2016). The lack of public awareness towards the potential uses of brown seaweeds may be one reason why research on this seaweed remains limited in Indonesia.

Brown seaweeds (class Phaeophyceae) such as *Sargassum* spp. are essential raw materials for pharmaceutical, energy, agriculture and food industries. They are used to create dietary supplements, biofuels, animal feed, and thickening agents. However, they are extensively studied as they have

demonstrated antibacterial**,** antiviral, antifungal, antioxidant and anticancer activities. These properties are attributed to their diverse range of bioactive constituents such as polysaccharides, fatty acids, polyphenols, terpenes, vitamins, minerals, and essential amino acids. Due to the multitude of bioactive compounds that exhibit antimicrobial activity, brown seaweed is a potentially good candidate to use in the search for novel antibiotics.

Current literature is dominated by studies on the antimicrobial activity of non-Indonesian *Sargassum* spp. against Gram-positive and Gram-negative bacteria. As there is only limited information on the activity of Indonesian species of *Sargassum*, in this preliminary study, the antibacterial effects of Indonesian *Sargassum* extracts against *P. aeruginosa* were investigated.