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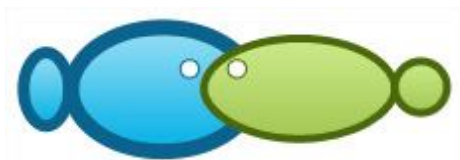
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Bioprospection of alginate lyase from bacteria associated with brown algae *Hydroclathrus* sp. as antibiofilm agent: a review

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Abstract. Infection by biofilm-producing microorganisms has been a health threat withdrawing attention around the world. The threat is increasing in developing countries due to poor sanitation conditions, suitable climates for microbial proliferation and limited economic resources. Most cases of chronic infection by pathogenic microorganisms are related to biofilm formation. Thus, biofilm degradation ability by antibiofilm agent is needed to eradicate biofilm-producing pathogenic bacteria. Alginate lyase is an antibiofilm material commonly produced by bacteria associated with alginate-rich algae. The enzyme has a potent ability to depolymerize alginate, the main component of biofilm. The search of alginate lyase enzyme-producing bacteria in the marine environment has resulted in the discovery of beneficial species of alginate-lyase producing bacteria and subsequently new types of alginate lyase enzymes. This paper assesses the bio-prospect of alginate lyase from bacteria associated with brown algae *Hydroclathrus* sp. to be used as antibiofilm of infectious bacteria. It is expected to lead to a valuable alternative treatment of infection related with pathogenic bacteria in developing countries.

Key Words: antibiofilm agent, biofilm, bioprospection, symbiont bacteria.

Introduction. Infectious disease is among the leading causes of death, yet the disease still could not be eradicated by the millennium era. Statistical data from the World Health Organization in 2016 showed that infectious diseases were the 1st cause of death in low-income countries or the 4th in the world (Jamal et al 2018). In the last 2 years, infectious disease showed the highest fatality rate worldwide due to the worldwide outbreak of Coronavirus Disease 2019 or Covid-19 (Grewelle & De Leo 2020).

Several reasons for the difficulty of eradicating infectious diseases include the following: a. new infectious diseases continue to emerge; b. old infectious diseases increase the incidence or geographical distribution; c. old, previously controlled infections began to reappear; d. increased pathogen resistance to current antimicrobial drugs; e. damage in the public health system and communication between countries (Taylor 2019; Tuite et al 2020). The National Institutes of Health (NIH) revealed that up to 80% of cases of chronic infection of pathogenic microorganisms are related to biofilm formation (Topka-Bielecka et al 2021). The threat is increased in developing countries due to poor sanitation conditions, a climate that is suitable for the proliferation of microorganisms, and low economic resources (Founou et al 2017).

It is acknowledged that around 40-80% of bacterial cells on earth could form biofilms (Flemming & Wuertz 2019). However, biofilms are more frequently associated with pathogenic bacteria causing chronic health issues in human (Jamal et al 2018). The main problem related to infection of microorganisms involving biofilm formation is due to

resistance to the human immune system, antibiotics and other treatment (Vestby et al 2020).

The main component of the biofilm is alginate. An enzyme capable of depolymerizing alginate, the main component of biofilms, is alginate lyase (enzyme code: EC 4.2.99.4). Therefore, alginate lyase is often called antibiofilm material. Biofilm degradation ability by alginate lyase is crucial in eradicating biofilm-producing pathogenic bacteria for the following reasons:

a. alginate lyase is a degrader of biofilms that can reduce the virulence of pathogenic bacteria. Biofilm itself is a form of the mechanism of self-defense of infectious bacteria (Roy et al 2018);

b. biofilm degradation by alginate lyase can increase the phagocytosis of pathogenic bacteria in the human body;

c. alginate lyase increases the efficacy of antibiotics so that it can suppress the occurrence of antibiotic resistance in pathogenic bacteria (Blanco-Cabra et al 2020).

Screening of alginate lyase-producing bacteria, both in aquatic and terrestrial environment, has produced a number of new bacterial species such as *Vibrio furnisii* H-1 (Zhu et al 2018); *Paenibacillus algicola* sp. nov. (Zhu et al 2020), *Alteromonas portus* HB161718T (Huang et al 2021), *Formosa algae* KMM 3553T (Belik et al 2020), *Defluviitalea phaphyphila* sp. nov. (Ji et al 2019), *Bacillus* sp. nov. (Zilda et al 2019), and *Vibrio hemicentroti* sp. nov. (Kim et al 2013), or the discovery of novel alginate lyases (Zhu et al 2018; Belik et al 2020; Zhu et al 2020; Huang et al 2021).

In the ocean, large quantity of alginate is produced by brown algae, and becomes the main source of organic carbon for bacteria. Alginate is found as the main polysaccharide constituent of brown algal cell wall matrix (Salmeán et al 2017). In the industrial sector, alginates are produced also from the group of marine brown algae (Peteiro 2018). Brown algae are included in the phylum Phaeophyta, which has more than 1500 species. However, industrial exploration of brown algae for their chemical and biological benefits mostly only come from the genera *Sargassum*, *Laminaria*, and *Turbinaria*. The rest, including the genus *Hydroclathrus* has not been adequately researched or utilized.

Hydroclathrus sp. is known as an edible, yellowish-brown, sponge-like macroalgae commonly found in relatively shallow sea water surrounding islands. Genus *Hydroclathrus* is represented by a number of species including *H. clathratus*, *H. minutus*, *H. rapanuii*, *H. tenuis*, *H. tilesii*, and *H. tumulis* (Santiañez et al 2018). The data related with the biochemical composition and bioactivity of genus *Hydroclathrus* have just been published in the last few decades (Wang et al 2010a; Wang et al 2010b; Vimala & Poonghuzhali 2017; Rashedul & Zafar 2018; Alzahrani et al 2020). Extract of *Hydroclathrus* sp. was reported to contain tannins, saponins, flavonoids, alkaloids, phenols, glycosides, terpenoids, coumarin, steroids, phyto steroids, anthraquinones, and phlobatanin (Vimala & Poonghuzhali 2017). A high alginate content (46.0%) of a species of *Hydroclathrus*, *H. clathratus* from Bangladesh was just reported in 2018 (Rashedul & Zafar 2018).

Considering high demand for alginate lyase to combat biofilm-involving infection and the limited study exploring *Hydroclathrus* sp., the search for alginate lyase producing bacteria associated with the brown algae is interesting to do. Such investigation offers high potential to produce new bacterial and enzyme species. The present review was carried to foresee bio-prospect alginate lyase of bacteria associated with brown algae *Hydroclathrus* sp.

Material and Method

General strategy. To reach the research goal, a descriptive qualitative method adopted from Ethica et al (2018) was initially used to obtain detailed and accurate data reckoning on relevant papers for literature review. Next, elaboration between literature study and review analysis on available data were conducted from the most relevant reports and articles related with the use of alginate lyase produced by bacteria associated with brown algae as antibiofilm agent. The following step was extracting information about the use of

genetic engineering to overexpress alginate lyase coding gene *algL* from potential brown algae to scale-up the production of antibiofilm agent.

Eligibility criteria for the studies. Literature selection was based on the following inclusion criteria: (i) studies and reports with subjects limited to bacterial isolation from brown algal samples aiming to obtain alginate lyase for use as antibiofilm agent; (ii) studies and reports with subjects limited to overexpression of alginate lyase coding gene (*algL*) or genetically modified species other than as antibiofilm agent; (iii) mention of use of alginate lyase from the mentioned bacteria to scale up production of the enzyme; (iv) published in English languages. Publication date limited to the last 10 years was determined in the search strategy (Jaroń et al 2020). Next, the extracted data were displayed in charts or tables and the bio-prospect of alginate lyase from bacteria associated with brown algae and its genetic engineering was summarized to signify its use as agent to combat infection involving biofilm formation as one of major global health issues.

Identification of relevant studies. The current literature review was carried out both electrically and manually. "Electrically" means that literature search process was conducted primarily using a set of keywords applied to search engines of literature database. "Manually" is defined as manual literature search or hand literature search with the objective to identify studies that were missed by the primary search (Sigaard 2017). It was conducted based on the protocol and guidelines previously reported by Wright & McDaid (2011). The search of relevant literature was performed for two categories: (i) alginate lyase producing bacteria associated with brown algae worldwide; (ii) global application of alginate lyase of bacteria isolated from brown algae as antibiofilm agent. For both categories, electronic as well as manual search irrespective of publication date were done using MESH (Medical Subject Heading) terms through PubMed using keywords:

- I. (((((((alginate lyase[Title]) OR Alginate digesting enzyme[Title/Abstract]) OR Alginate breaking enzyme[Title/Abstract]) OR alginate degrading enzyme[Title/Abstract]) OR "Polysaccharide-Lyases"[Mesh]) OR alginate lyase[Title/Abstract]) OR alginate lyases[Title/Abstract]) OR alginate lyase[Title/Abstract]) AND ((((((Antibiofilm[Title/Abstract]) OR antibiofilm[Title/Abstract]) OR antibiofilm agent[Title/Abstract]) OR biofilm breaker[Title/Abstract]) OR biofilm degrader[Title/Abstract]) OR "Biofilms"[Mesh]) AND (((((pathogen[Title/Abstract]) OR infectious disease[Title/Abstract]) OR pathogenic bacteria[Title/Abstract]) OR infection[Title/Abstract]) OR infectious bacteria[Title/Abstract]) OR "Infections"[Mesh]);
- II. (((((((alginate lyase[Title]) OR Alginate digesting enzyme[Title/Abstract]) OR Alginate breaking enzyme[Title/Abstract]) OR alginate degrading enzyme[Title/Abstract]) OR "Polysaccharide-Lyases"[Mesh]) OR alginate lyase[Title/Abstract]) OR alginate lyases[Title/Abstract]) OR alginate lyase[Title/Abstract])) AND ((((((Brown macroalgae[Title/Abstract]) OR brown sea grass[Title/Abstract]) OR brown seagrass[Title/Abstract]) OR brown seaweed[Title/Abstract]) OR brown algae[Title/Abstract]) OR "Phaeophyta"[Mesh])

Both keyword groups were set on January 1, 2021. In addition, search from other sources such as Google Scholar and Science Direct was also performed. Studies excluded from the present review were: [i] studies conducted before 2016 [ii]; studies of alginate lyase producing bacteria isolated from algae other than brown algae, or the use of bacterial alginate lyase from wild type or genetically modified species other than as antibiofilm agent; [iii] mention of use of alginate lyase as antibiofilm agent in non-experimental studies (reviews); [iv] enzymes used as antibiofilm agents other than alginate lyases; [v] personal opinions or reports in news, magazine, personal web (blogs).

Selection of studies. Three of the authors [DSZ, WO & OO] independently identified studies meeting inclusion criteria set in this present review. First, evaluation was conducted on both titles and abstracts of the records resulted by the search to determine unsuitable studies, which then should be excluded according to the set exclusion criteria (Ahn & Kang 2018). Although the reference lists of review articles were recovered by the electronic search, they were not included. Full text articles of the remaining studies that suit the inclusion criteria were retrieved.

Control of bias assessment. To assess the risk of bias or quality in this systematic review, the following issues were included in: (i) completeness of reporting information regarding isolation of alginate lyase producing bacteria from brown algae for consecutive years; (ii) selective data reporting; (iii) selection of studies; (iv) study design; and (v) conflict of interest in the conduct of the study. If all criteria were met, then the overall plausible risk of bias was considered as moderate to low (Gambhir et al 2016).

Data collection, extraction and analysis. This review collected the data by following the guidelines set forth by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) first reported by Liberati et al (2009). Two authors [SNE & MM] were responsible for extracting data from the obtained reports or studies. The pre-specified data was extracted from each of them, including alginolytic bacterial species, brown algae species as bacterial source, bacterial infection types (which are treated by alginate lyase), and studied brown algal origin all over the world.

Results and Discussion. The purpose of this review was to foresee bio-prospect of alginate lyase from bacteria associated with *Hydroclathrus* sp. as antibiofilm agent based on the trends in composition studies related with alginate lyase application on cases of biofilm-involved bacterial infections worldwide within the past 10 years. Alginate lyase producing bacteria associated with brown algae worldwide and the application of the bacterial alginate lyase as antibiofilm agent had become a central issue in this study. In particular, our study was focused on bio-prospect of *Hydroclathrus* sp. as a member of the brown macroalgae group known with their high alginate content as antibiofilm agent. Therefore, an insight into microbial biofilm formation, structure and component and its impact to pathogenic bacterial infection and treatment is first presented.

Biofilm formation and function. The microorganism biofilm was first observed by Van Leeuwenhoek on the surface of the tooth (Høiby 2017). Biofilm is an association of microorganisms firmly attached to a surface protected within an extracellular polymeric substance (EPS) matrix allowing character alteration of the microorganisms in terms of gene expression, protein synthesis, metabolic activities, and growth rate (Oxaran et al 2018; Abebe 2020). About 99% of the microorganisms present on earth live in communities known as biofilms, regardless they can form biofilm or not (Koo et al 2017). Biofilm-forming organisms spread in nature consist of partially known fungi and pathogenic bacteria (Jamal et al 2018). Because of biofilm formation, pathogenic bacteria are not only capable of causing the infection but are also able to survive in diverse environmental conditions (Hall & Mah 2017; Høiby 2017).

Steps of biofilm formation and development by bacterial cells are illustrated in Figure 1. As described in Figure 1, biofilm formation was initiated by the migration and adhesion of planktonic bacterial cells to an abiotic or biotic surface, which is considered as a critical step in the development of biofilms. Once attached to the surface, organisms will produce EPS, which helps biofilm formation (Lee & Yoon 2017).

A biofilm may develop into three-dimensional, multi-layered mature structures with high density of bacterial cells if conditions for sufficient growth and differentiation are suitable. The structure could be such as mushroom or tower-like structures enclosed with fluid filled channels in which nutrients, oxygen, and essential substances can be diffused and then circulate in various microenvironment. Later, the mature biofilm may detach microcolonies of cells from the main community allowing them to migrate to new

surfaces spreading the infection to different locations (Ansari et al 2017; Abu Khweek & Amer 2018; Rojo-Molinero et al 2019; Verderosa et al 2019).

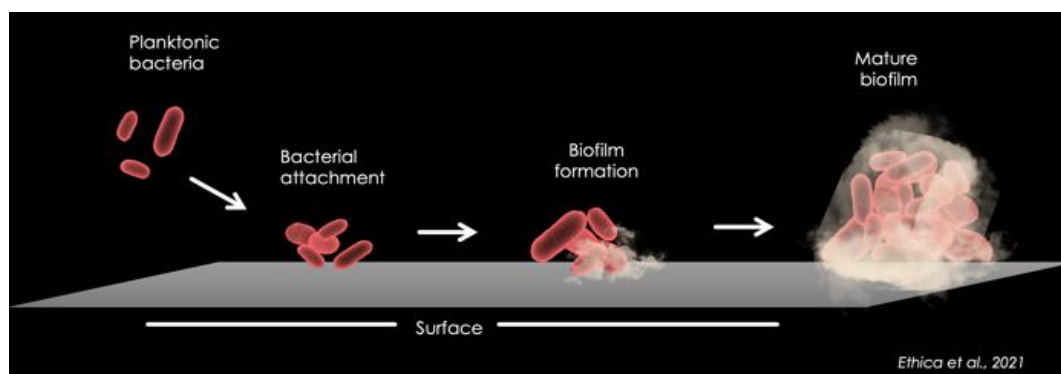


Figure 1. Simplified illustration of bacterial biofilm formation steps.

Biofilms are an example of a defense mechanism by microorganisms. Biofilms are produced by various species in their unique ways (Tasneem et al 2018). Biofilms are resistant to the mechanism of phagocytosis possessed by the human body's defense system (Jamal et al 2018). Biofilms can be found on various surfaces, such as biological tissues, medical devices, and water system pipes (Khatoon et al 2018). Biofilm formation depends on the type of microorganism and the surface it is attached to (Abu Khweek & Amer 2018). Biofilms tend to trap particles, including various minerals and host system components such as red blood cells, fibrin, and platelets. Biofilms are a cause of chronic, nosocomial, and medical-related infections (Khatoon et al 2018; Tasneem et al 2018).

Alginate as biofilm component and substrate of alginate lyase enzyme. Alginate, which is also known as algal polysaccharide, is reported as the major extracellular polymeric substances (EPS) in biofilms (Boutin et al 2019; Heriot et al 2019). Degradation of biofilm structural component allows the increased penetration of antibiotics which enhances the antibiotics efficiency (Sharma et al 2019). Thus, targeting alginate as major biofilm component has become an intriguing therapeutic strategy for handling biofilm-involved bacterial infections and involved antibiotic resistance. Alginate is a linear polysaccharide between β -D-manuronate (M) and its epimer, α -L-guluronate (G) which binds covalently (Jamal et al 2018; Taylor 2019; Grewelle & De Leo 2020; Tuite et al 2020), and is connected in a different order. Alginate is mainly used as a food additive to modify food texture due to its high viscosity and gelling properties (Xu et al 2018; Kothale et al 2020).

Alginate lyase, on the other hand, is a group of enzymes that catalyze the depolymerization of alginate into oligosaccharides. The enzyme degrades alginate as substrate by breaking the glycosidic bonds through an β elimination reaction, producing oligomers with 4-deoxy-L-erythro-hex-4-enepyransyluronate at the non-reduction chain end (Vuoristo et al 2019).

Alginate lyase enzyme is a product of the expression of the alginate lyase gene (*algL*). The *algL* is a component of the alginate-producing operon which with glycosidase activity produces a primer to synthesize other enzymes in this cluster. Alginate lyase can lyse biofilms by reducing their adhesion to the surface, and increasing phagocytosis and antibiotic susceptibility (Ji et al 2019; Huang et al 2021). Alginate lyase is a pharmaceutical ingredient that is important because it increases the performance of antibiotics in killing biofilm forming bacteria (Jamal et al 2018; Del Pozo 2021).

Alginate lyase has been isolated from a variety of organisms with different substrate specificities, including algae, marine mollusks, marine and terrestrial bacteria, and some viruses and fungi (Zhu et al 2018; Ji et al 2019; Zilda et al 2019; Belik et al 2020; Zhu et al 2020; Huang et al 2021). With the advancement of structural biology, many types of alginate lyases and other families of lyase polysaccharides have been identified as crystalline structures, and with known catalytic mechanisms (Xu et al 2018). The product of the enzymatic reaction between alginate lyase and the alginate substrate

is alginate oligosaccharide (AOS) which because of its various biological activities can act as prebiotic, immune modulation, anticoagulant, antioxidant, and anticancer. In addition, AOS is also able to stimulate endothelial cell growth and stimulate the secretion of cytotoxic cytokines from human macrophages (Liu et al 2019; Xing et al 2020).

Trend of data in Table 1 shows that worldwide, the most studied infection cases caused by biofilm-producing bacteria treated using bacterial alginate lyases in the last 5 years are cystic fibrosis caused by *Pseudomonas aeruginosa*. Though rare, gastric and urinary tract bacterial infections caused by *Helicobacter* sp. and *Enterococcus* sp. have also been reported to be treated using alginate lyase isolated from various beneficial bacteria.

Table 1

Studies reporting application of bacterial alginate lyase as antibiofilm agent in bacterial infection in the last 5 years worldwide

<i>Infectious bacteria</i>	<i>Infection case</i>	<i>Alginate lyase producing bacteria</i>	<i>Country</i>	<i>Authors</i>
<i>Helicobacter pylori</i>	Gastric	<i>Flavobacterium</i> sp.	Italy	Bugli et al (2016)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	<i>Azotobacter vinelandii</i>	Korea	Jang et al (2016)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	unspecified	Portugal	Alves et al (2016)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	unspecified	Korea	Cho et al (2016)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	unspecified	NZ	Germoni et al (2016)
<i>Enterococcus faecalis</i> & <i>Enterococcus faecium</i>	Urinary tract	unspecified	Italy	Torelli et al (2017)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	<i>Pseudomonas aeruginosa</i>	Iran	Tavafi et al (2018)
<i>Pseudomonas aeruginosa</i>	Gastric	<i>Flavobacterium</i> sp.	Italy	Bugli et al (2016)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	<i>Azotobacter vinelandii</i>	Korea	Jang et al (2016)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	unspecified	India	Patel et al (2019)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	unspecified	China	Li et al (2019)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	<i>Pseudoalteromonas</i> sp.	Canada	Daboor et al (2019)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	<i>Flavobacterium multivorum</i> , <i>Zobellia galactanivorans</i> , <i>Sphingomonas</i> sp.	Spain	Blanco-Cabra et al (2020)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	unspecified	China	Wan et al (2020)
<i>Pseudomonas aeruginosa</i>	Cystic fibrosis	<i>Cellulophaga algicola</i>	India	Mahajan et al (2021)

Application of alginate lyases as antibiofilm agents to treat bacterial infection cases have been continuously conducted worldwide. Table 1 shows last reports investigating the use of bacterial alginate lyase as antibiofilm agents against biofilms produced by pathogenic bacteria causing infections (Bugli et al 2016; Daboor et al 2019; Mahajan et al 2021).

Aside of *P. aeruginosa*, *Helicobacter* sp. and *Enterococcus* sp., there are still many other infectious bacteria associated with the formation of biofilms including *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Enterococcus faecalis*, and *Escherichia coli* (Macià et al 2018). Considering that recent studies (see Table 1) were successful in demonstrating the role of

alginate lyase as antibiofilm agent of *P. aeruginosa*, studies about the same application against other bacteria in different cases should be enhanced

Brown algae as main sources of alginolytic bacteria. Alginate lyase-producing organisms are very diverse. They have reported to be found in decomposed seaweed, seawater, etc. However, the group of bacteria associated with brown algae is the most widely reported to produce this enzyme. Table 2 shows studies worldwide reporting brown algae associated bacteria as source of alginate lyase in the last 5 years.

Table 2

Studies reporting brown algae (Phaeophyta) associated bacteria as source of alginate lyase in the last 5 years

Association of brown algae and alginate lyase producing bacteria		Country	Authors
Bacterium	Brown algae		
<i>Helicobacter pylori</i>	Gastric	Italy	Bugli et al (2016)
<i>Bacillus litoralis</i>	<i>Sargassum horneri</i>	Australia	Wang et al (2016)
<i>Pseudomonas stutzeri</i> MSEA04	unspecified	Egypt	Beltagy et al (2016)
<i>Cobetia</i> sp. Nap1	unspecified	Japan	Yagi et al (2016)
<i>Algibacter alginolytica</i> sp. nov.	<i>Laminaria japonica</i>	China	Sun et al (2016)
<i>Microbulbifer</i> sp. ALW1	unspecified	China	Zhu et al (2016a)
<i>Bacillus weihaiensis</i>	unspecified	China	Zhu et al (2016b)
<i>Exiguobacterium</i> sp. Alg-S5	<i>Sargassum</i> sp.	Barbados	Mohapatra (2017)
<i>Bacillus halosaccharovorans</i>	unspecified	China	Wang et al (2017)
<i>Vibrio furnissii</i> H1	unspecified	China	Zhu et al (2018)
<i>Formosa algae</i>	<i>Fucus evanescens</i>	Russia	Belik et al (2019)
<i>Defluviitalea phaphyphila</i>	unspecified	China	Ji et al (2019)
<i>Marinimicrobium</i> sp. H1	unspecified	China	Yan et al (2019)
<i>Martellella</i> sp. MAK4	unspecified	Egypt	Ali et al (2020)
<i>Staphylococcus arlettae</i> , <i>S. pasteurii</i> , <i>Bacillus megaterium</i> , <i>Alteromonas macleodii</i>	<i>Sargassum mcclurei</i>	Vietnam	Dieu et al (2020)
<i>Psychromonas</i> sp. C-3	<i>Laminaria</i> sp.	China	Xu et al (2020)
<i>Paenibacillus algicola</i> sp. nov.	unspecified	China	Zhu et al (2020)
<i>Cobetia</i> sp. nov.	<i>Sargassum fusiforme</i>	China	Cheng et al (2020)
<i>Pseudoalteromonas</i> sp. Alg6B	<i>Laminaria japonica</i>	China	Sun et al (2020)
<i>Thalassomonas</i> sp. LD5	unspecified	China	Zhang et al (2020)
<i>Tamlana</i> sp. s12	unspecified	China	Yin et al (2021)
<i>Alteromonas portus</i> HB161718 ^T	unspecified	China	Huang et al (2021)

Trend of data in Table 2 shows that most of the studies reported the alginate producing bacteria from unspecified species of brown algae. In terms of the specified species of brown algae as source of alginate lyase producing bacteria studied are limited from genera *Laminaria* and *Sargassum*. It also appears that in the last 5 years, most publications related to the discovery of bacterial alginate lyases associated with brown algae were from China.

Based on our literature review, we underline that brown algae are definitely a rich source of alginate lyase-producing bacteria, regardless of the limited information about the algal species. This is actually not surprising because brown algae usually have a high alginate content. However, the data suggests that brown algae species other than *Sargassum* and *Laminaria* were limitedly reported.

Brown algae as main sources of alginolytic bacteria. *Hydroclathrus* sp. (Figure 2) belongs to a family of photosynthetic multicellular brown algae having yellowish-brown in color, with an average length of 6-10 cm, forming a sponge-like lump, which is very porous and chain-like with irregularly rounded thallus. The outer zone consists of palisade cells that extend radially, cylindrical, and are less compact (Vimala & Poonghuzhali 2017).



Figure 2. Morphology of brown algae *Hydroclathrus* sp. found in South Eastern Sulawesi sea of Indonesian (Documented by Ethica et al in 2021).

Brown macroalgae are included in the Stramenopiles Kingdom, which is not closely related to land plants and green algae. The cell wall consists mainly of polyanionic alginate polysaccharides and fructose-containing sulfate polysaccharides (Salmeán et al 2017). Brown algae or seaweed is included in Phaeophyta Phylum which has the largest number of algae species and is complex compared to other algae groups. Phaeophyta has a fucoxanthin pigment that is not owned by red and green algae, so it is included in the kingdom Chromista (Al Ashwal & Abdelbary 2021). Brown algae are a large phylum consisting of a variety of marine and photoautotrophic organisms, consisting of more than 250 genera and more than 2000 species (Mekinić et al 2019; El Rashed et al 2020). Interestingly, since it has been discovered in 1920, the taxonomic status *Hydroclathrus* sp. is currently in the verification process and categorized as distinct (Santiañez et al 2018).

The distribution of *Hydroclathrus* sp. includes the tropics to subtropics; from the Atlantic Ocean to the Indian and Pacific Oceans; and across various islands including Cape Verde, Maldives, Hawaii, Samoa, and Polynesia. These macroalgae are found in various countries including the United States of America, South Africa, Mexico, Japan, Bangladesh, China, Australia, New Zealand, the Philippines, and also Indonesia (Jamal et al 2018; Rashedul & Zafar 2018; Santiañez et al 2018; Kepel et al 2019; Santiañez et al 2020).

Hydroclathrus sp. has been used for centuries in traditional cooking and medicine in the Hawaiian Islands. But it is only in the last few decades that the macroalgae has been known to have anticancer and antitumor, antiviral, antiherpes, anti-inflammatory, anticoagulant, and antimicrobial abilities (Vimala & Poonghuzhali 2017; Alharbi 2020; Santiañez et al 2020). Compared with other groups of brown algae species such as *Sargassum* spp., *Laminaria* spp., and *Turbinaria*, *Hydroclathrus* spp. is still not much researched and utilized. For example, the content of mixed-linked MLG glucan related to alginate in many species of brown algae has been reported, but in *H. clathrathus* it is unknown. In the world, the alginate content of the algae group was just recently reported in 2018 by 45.7%, from samples obtained at rocky shore of the St. Martin's Island, Bangladesh (Rashedul & Zafar 2018). In fact, bacteria associated with *Hydroclathrus* sp. are also limitedly studied. In Indonesia *Hydroclathrus* spp. are quite abundant however they are considered to be of less economic value because they don't belong to the main group of agar and carrageenan producers. *Sargassum* should be explored for more opportunities to obtain novel alginolytic bacteria.

Based on data from literature review, high levels of alginate in *Hydroclathrus* sp. offer high chance of finding alginolytic enzyme-producing bacteria associated with the brown algae. The reason is because alginate is a specific substrate of alginate lyase. Hence, the abundance of *Hydroclathrus* sp. in nature gives the added value of bacteria as an easily grown enzyme producer, and potential for novelty and invention related to the isolation of alginolytic bacteria from brown algae are among strength and opportunity to bring good prospects of *Hydroclathrus* sp.

Strategy to develop alginate lyase from bacteria associated with *Hydroclathrus* sp. *Hydroclathrus* sp. is an attractive substrate for alginate degrading bacteria due to its high alginate content. Bacteria are among beneficial enzyme producers because they could be grown in large quantities only in short span of time, could be targeted for genetic manipulations to enhance the enzyme production source (Anbu et al 2017). On the other hand, to date, many feasible facilities are available to isolate, purify and characterize extracellular alginolytic enzymes produced by bacteria. They include techniques to immobilize the enzymes (Alves et al 2016; Li et al 2019; Patel et al 2019) or to test their ability to degrade biofilms of pathogenic bacteria (Bugli et al 2016; Germoni et al 2016; Tavafi et al 2018; Vuoristo et al 2019). Alginate lyase could even be purified only in the one-step stage using the affinity chromatography method, while its characterization could be done by the SDS PAGE Method (Ghadam et al 2017; Zilda et al 2019). The specificity of the alginate lyase enzyme could then be determined later using molecular methods including genomic and proteomic analysis (Pilgaard et al 2019). Thus, it is much possible to obtain biofilm agent from groups of alginolytic bacteria isolated from brown algae *Hydroclathrus* sp. by following those previously reported techniques.

A detailed scheme as a strategy to obtain alginate lyase from bacteria associated with *Hydroclathrus* sp. according to those reported successful methods is displayed in Figure 3.

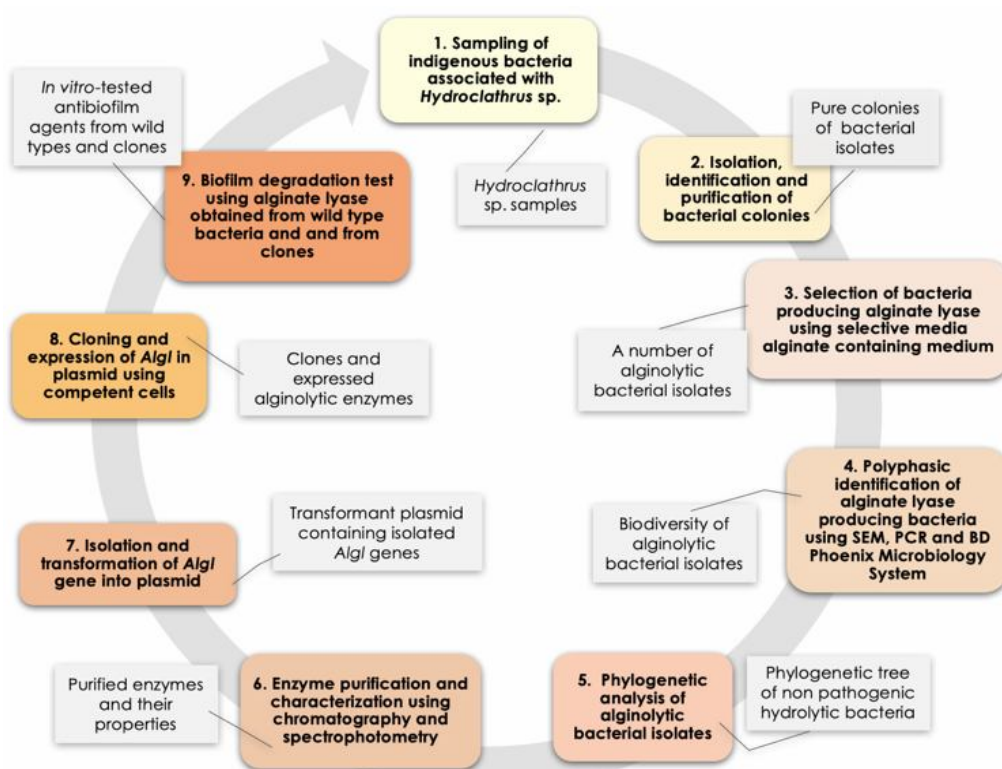


Figure 3. Scheme of steps required to obtain biofilm agent from groups of alginolytic bacteria isolated from brown algae *Hydroclathrus* sp. and the targeted outcomes of each step.

Bioprospection of alginate lyase as antibiofilm agent in infection treatment.

Treatment of infections all over the world in the last decade using antibiotics has faced ineffective problems due to the resistance mechanism of bacteria by biofilm formation (Jamal et al 2018; Vestby et al 2020; Topka-Bielecka et al 2021). Hence, the development of an antibiofilm agent targeting most infectious species of bacteria is a necessity. Based on all data obtained from our literature study, a diagram describing factors supporting the importance of bioprospection of antibiofilm agent development from alginate lyase producing bacteria associated with *Hydroclathrus* sp. could be generated (Figure 4).

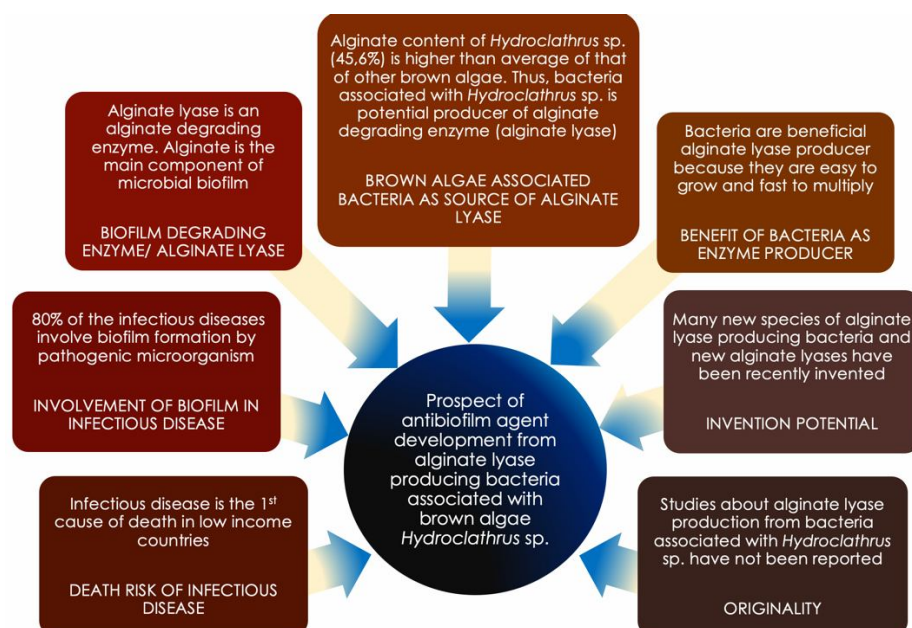


Figure 4. Factors contributing to the good prospect of antibiofilm agent development from alginate lyase producing bacteria associated with *Hydroclathrus* sp.

As mentioned in Figure 4, death risk of infectious disease and involvement of biofilm in infectious disease are among reasons why studies related with antibiofilm agent should be intensified. Alginate lyase potential as antibiofilm agent, brown algae as a rich source of alginate lyase producing bacteria, and bacteria as beneficial enzyme producer offer potentially new enzymatic treatment to biofilm involved infection.

As a summary, diagram in Figure 5 highlights our opinion and strategy about the bio-prospect of *Hydroclathrus* sp. as a potential source of important bacteria producing alginate enzyme lyase. Biofilms are known to be resistant to antibiotics, even to disinfectants such as chlorine. Because of such nature, the use of antibiotics alone is not effective in treating biofilm-related infections (Sun et al 2019; Yan et al 2020).

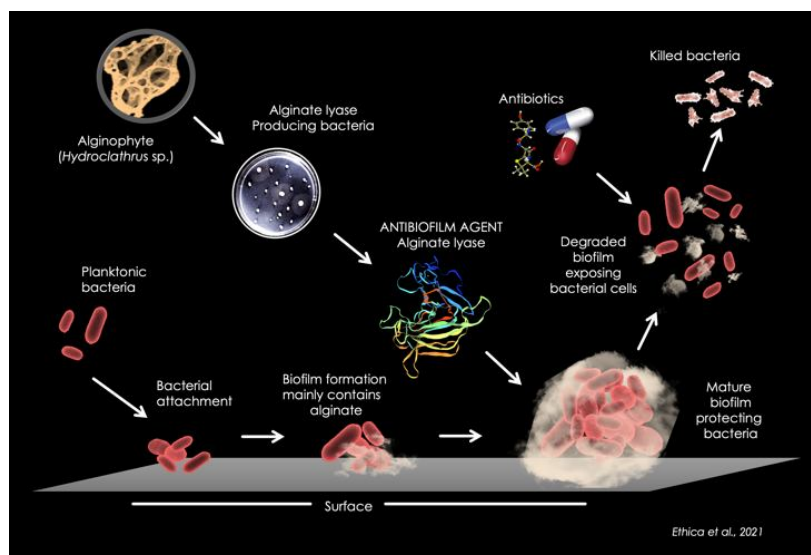


Figure 5. Bioprospection of alginate lyase isolated from bacteria associated with alginophyte *Hydroclathrus* sp. as antibiofilm agent of pathogenic bacterial biofilms.

The conceptual strategy mapped in Figure 5 is intended to help overcome the problem of biofilm-related infections that are troubling the world, particularly the developing countries today. Eradication of biofilms is not easy to do when counting only on antibiotics. Thus, we suggest the use of various species of brown algae, specifically those

with high content of alginate as breakthrough to obtain novel bacterial alginate lyases as new antibiofilm agent.

Conclusions. It could be concluded from our literature review that most studies on the application of alginate lyase as antibiofilm agent in the world were to cystic fibrosis case of infection caused by *Pseudomonas aeruginosa*. Along with this, it is also clear that unspecified brown algae, followed by *Sargassum* sp. and *Laminaria* sp. have been mostly targeted as source of bacterial alginate lyase without regards to their alginate contents. *Hydroclathrus* sp., a species of brown algae with high content of alginate, appears to be a prospective as a source of bacterial alginate lyase as antibiofilm agent in the treatments of bacterial infection cases. It is expected that in general, the use of alginate lyase as antibiofilm agent could be expanded to broader cases of troubling biofilm-related infections in developing countries, not only limited to cystic fibrosis cases.

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References

- Abebe G. M., 2020 The role of bacterial biofilm in antibiotic resistance and food contamination. *International Journal of Microbiology* 2020:1705814.
- Abu Khweek A., Amer A. O., 2018 Factors mediating environmental biofilm formation by *Legionella pneumophila*. *Frontiers in Cellular and Infection Microbiology* 8:38.
- Ahn E., Kang H., 2018 Introduction to systematic review and meta-analysis. *Korean Journal of Anesthesiology* 71(2):103-112.
- Al Ashwal A. A., Abdelbary E. M., 2021 Marine macroalgae in Qatar marine zone. In: *The Arabian seas: biodiversity, environmental challenges and conservation measures*, Jawad L. A. (ed), Springer pp. 363-410.
- Alharbi R. M., 2020 *Hydroclathrus clathratus* as anti-damaging agent against lung injury in male albino rats. *Beni-Suef University Journal of Basic and Applied Sciences* 9:21.
- Ali A. A. A., Ebraheem A. M., Mohammed A. B. A., 2020 Purification, characterization and sequencing of alginate lyase from *Martellella* sp. strain MAK4. *Journal of Biochemistry, Microbiology and Biotechnology* 8(1):29-36.
- Alves D., Sileika T., Messersmith P. B., Pereira M. O., 2016 Polydopamine-mediated immobilization of alginate lyase to prevent *P. aeruginosa* adhesion. *Macromolecular Bioscience* 16(9):1301-1310.
- Alzahrani R. R., Alkhulaifi M. M., Al-Enazi N. M., 2020 *In vitro* biological activity of *Hydroclathrus clathratus* and its use as an extracellular bioreductant for silver nanoparticle formation. *Green Processing and Synthesis* 9(1):416-428.
- Anbu P., Gopinath S. C., Chaulagain B. P., Lakshmipriya T., 2017 Microbial enzymes and their applications in industries and medicine 2016. *BioMed Research International* 2017:2195808.
- Ansari F. A., Jafri H., Ahmad I., Abulreesh H. H., 2017 Factors affecting biofilm formation in *in vitro* and in the rhizosphere. In: *Biofilms in plant and soil health*. Ahmad I., Husain F. M. (eds), Wiley & Sons Ltd., pp. 275-290.
- Belik A. A., Tabakmakher K. M., Silchenko A. S., Makarieva T. N., Minh C. V., Ermakova S. P., Zvyagintseva T. N., 2019 Sulfated steroids of Halichondriidae family sponges—natural inhibitors of polysaccharide-degrading enzymes of bacterium *Formosa algae*, inhabiting brown alga *Fucus evanescens*. *Carbohydrate Research* 484:107776.
- Belik A., Silchenko A., Malyarenko O., Rasin A., Kiseleva M., Kusaykin M., Ermakova S., 2020 Two new alginate lyases of PL7 and PL6 families from polysaccharide-

- degrading bacterium *Formosa algae* KMM 3553^T: structure, properties, and products analysis. *Marine Drugs* 18(2): 130.
- Beltagy E. A., El-Borai A., Lewiz M., ElAssar S. A., 2016 Purification and characterization of alginate lyase from locally isolated marine *Pseudomonas stutzeri* MSEA04. *Acta Biologica Hungarica* 67(3): 305-317.
- Blanco-Cabra N., Paetzold B., Ferrar T., Mazzolini R., Torrents E., Serrano L., LLuch-Senar M., 2020 Characterization of different alginate lyases for dissolving *Pseudomonas aeruginosa* biofilms. *Scientific Reports* 10(1): 9390.
- Boutin R., Munnier E., Renaudeau N., Girardot M., Pinault M., Chevalier S., Chourpa I., Clément-Larosi re B., Imbert C., Boudesocque-Delaye L., 2019 *Spirulina platensis* sustainable lipid extracts in alginate-based nanocarriers: an algal approach against biofilms. *Algal Research* 37: 160-168.
- Bugli F., Palmieri V., Torelli R., Papi M., De Spirito M., Cacaci M., Galgano S., Masucci L., Paroni Sterbini F., Vella A., Graffeo R., Posteraro B., Sanguinetti M., 2016 *In vitro* effect of clarithromycin and alginate lyase against *Helicobacter pylori* biofilm. *Biotechnology Progress* 32(6): 1584-1591.
- Cheng W., Yan X., Xiao J., Chen Y., Chen M., Jin J., Bai Y., Wang Q., Liao Z., Chen Q., 2020 Isolation, identification, and whole genome sequence analysis of the alginate-degrading bacterium *Cobetia* sp. cqz5-12. *Scientific Reports* 10(1): 10920.
- Cho H., Huang X., Piao Y. L., Kim D. E., Lee S. Y., Yoon E. J., Park S. H., Lee K., Jang C. H., Zhan C. G., 2016 Molecular modeling and redesign of alginate lyase from *Pseudomonas aeruginosa* for accelerating CRPA biofilm degradation. *Proteins: Structure, Function, and Bioinformatics* 84(12): 1875-1887.
- Daboor S. M., Raudonis R., Cohen A., Rohde J. R., Cheng Z., 2019 Marine bacteria, a source for alginolytic enzyme to disrupt *Pseudomonas aeruginosa* biofilms. *Marine Drugs* 17(5): 307.
- Del Pozo J. L., 2021 Novel treatment dynamics for biofilm-related infections. *Expert Review of Anti-Infective Therapy* (just-accepted). DOI: <https://doi.org/10.1080/14787210.2021.1917993>
- Dieu T. V. T., Hang H. C. T. T., Hoai T. P. T., Duy N. N. T., Nhu K. H. H., Thanh V. T. T., 2020 Isolation of marine bacteria from sponges in the South-Central coastal region of Vietnam with brown seaweed polysaccharide-degrading activities. *Vietnam Journal of Science and Technology* 58(6A): 41-51.
- El Rashed Z., Grasselli E., Khalifeh H., Canesi L., Demori I., 2020 Brown-algae polysaccharides as active constituents against nonalcoholic fatty liver disease. *Planta Medica*. doi:10.1055/a-1273-3159.
- Ethica S. N., Saptaningtyas R., Muchlissin S. I., Sabdono A., 2018 The development method of bioremediation of hospital biomedical waste using hydrolytic bacteria. *Health and Technology* 8(4): 239-254.
- Flemming H. C., Wuertz S., 2019 Bacteria and archaea on Earth and their abundance in biofilms. *Nature Reviews Microbiology* 17(4): 247-260.
- Founou R. C., Founou L. L., Essack S. Y., 2017 Clinical and economic impact of antibiotic resistance in developing countries: a systematic review and meta-analysis. *PLoS ONE* 12(12): e0189621.
- Gambhir R. S., Pannu P. R., Nanda T., Arora G., Kaur A., 2016 Knowledge and awareness regarding swine-influenza A (H1N1) virus infection among dental professionals in India- a systematic review. *Journal of Clinical and Diagnostic Research* 10(9): 10-13.
- Germoni L. A. P., Bremer P. J., Lamont I. L., 2016 The effect of alginate lyase on the gentamicin resistance of *Pseudomonas aeruginosa* in mucoid biofilms. *Journal of Applied Microbiology* 121(1): 126-135.
- Ghadam P., Akhlaghi F., Ali A. A., 2017 One-step purification and characterization of alginate lyase from a clinical *Pseudomonas aeruginosa* with destructive activity on bacterial biofilm. *Iranian Journal of Basic Medical Sciences* 20(5): 467-473.
- Grewelle R., De Leo G., 2020 Estimating the global infection fatality rate of COVID-19. medRxiv, 45 pp.
- Hall C. W., Mah T. F., 2017 Molecular mechanisms of biofilm-based antibiotic resistance and tolerance in pathogenic bacteria. *FEMS Microbiology Reviews* 41(3): 276-301.

- Heriot M., Nottelet B., Garric X., D'Este M., Richards G. R., Moriarty F. T., Eglin D., Guillaume O., 2019 Interaction of gentamicin sulfate with alginate and consequences on the physico-chemical properties of alginate-containing biofilms. *International Journal of Biological Macromolecules* 121:390-397.
- Høiby N., 2017 A short history of microbial biofilms and biofilm infections. *APMIS* 125(4): 272-275.
- Huang H., Li S., Bao S., Mo K., Sun D., Hu Y., 2021 Expression and characterization of a cold-adapted alginate lyase with exo/endo-type activity from a novel marine bacterium *Alteromonas portus* HB161718T. *Marine Drugs* 19(3):155.
- Jamal M., Ahmad W., Andleeb S., Jalil F., Imran M., Nawaz M. A., Hussain T., Ali M., Rafiq M., Kamil M. A., 2018 Bacterial biofilm and associated infections. *Journal of the Chinese Medical Association* 81(1):7-11.
- Jang C. H., Piao Y. L., Huang X., Yoon E. J., Park S. H., Lee K., Zhan C. G., Cho H., 2016 Modeling and re-engineering of *Azotobacter vinelandii* alginate lyase to enhance its catalytic efficiency for accelerating biofilm degradation. *PLoS ONE* 11(6):e0156197.
- Jaroń A., Jedliński M., Grzywacz E., Mazur M., Trybek G., 2020 Kinesiology taping as an innovative measure against post-operative complications after third molar extraction - systematic review. *Journal of Clinical Medicine* 9(12):3988.
- Ji S., Dix S. R., Aziz A. A., Sedelnikova S. E., Baker P. J., Rafferty J. B., Bullough P. A., Tzokov S. B., Agirre J., Li F. L., Rice D. W., 2019 The molecular basis of endolytic activity of a multidomain alginate lyase from *Defluviitalea phaphyphila*, a representative of a new lyase family, PL39. *Journal of Biological Chemistry* 294(48):18077-18091.
- Kepel R. C., Lumingas L. J., Tombakan J. L., Mantiri D. M., 2019 Biodiversity and community structure of seaweeds in Minahasa Peninsula, North Sulawesi, Indonesia. *AACL Bioflux* 12(3):880-892.
- Khatoun Z., McTiernan C. D., Suuronen E. J., Mah T. F., Alarcon E. I., 2018 Bacterial biofilm formation on implantable devices and approaches to its treatment and prevention. *Heliyon* 4(12):e01067.
- Kim D., Baik K. S., Hwang Y. S., Choi J. S., Kwon J., Seong C. N., 2013 *Vibrio hemicentroti* sp. nov., an alginate lyase-producing bacterium, isolated from the gut microflora of sea urchin (*Hemicentrotus pulcherrimus*). *International Journal of Systematic and Evolutionary Microbiology* 63(10):3697-3703.
- Koo H., Allan R. N., Howlin R. P., Stoodley P., Hall-Stoodley L., 2017 Targeting microbial biofilms: current and prospective therapeutic strategies. *Nature Reviews Microbiology* 15(12):740-755.
- Kothale D., Verma U., Dewangan N., Jana P., Jain A., Jain D., 2020 Alginate as promising natural polymer for pharmaceutical, food, and biomedical applications. *Current Drug Delivery* 17(9):755-775.
- Lee K., Yoon S. S., 2017 *Pseudomonas aeruginosa* biofilm, a programmed bacterial life for fitness. *Journal of Microbiology and Biotechnology* 27(6):1053-1064.
- Li S., Wang Y., Li X., Lee B. S., Jung S., Lee M. S., 2019 Enhancing the thermo-stability and anti-biofilm activity of alginate lyase by immobilization on low molecular weight chitosan nanoparticles. *International Journal of Molecular Sciences* 20(18):4565.
- Liberati A., Altman D. G., Tetzlaff J., Mulrow C., Gøtzsche P. C., Ioannidis J. P., Clarke M., Devereaux P. J., Kleijnen J., Moher D., 2009 The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *Journal of Clinical Epidemiology* 62(10): 1-34.
- Liu J., Yang S., Li X., Yan Q., Reaney M. J., Jiang Z., 2019 Alginate oligosaccharides: production, biological activities, and potential applications. *Comprehensive Reviews in Food Science and Food Safety* 18(6):1859-1881.
- Macià M. D., Del Pozo J. L., Díez-Aguilar M., Guinea J., 2018 Microbiological diagnosis of biofilm-related infections. *Enfermedades infecciosas y microbiología clínica (English ed.)*. 36(6):375-381.

- Mahajan S., Ramya T. N. C., 2021 *Cellulophaga algicola* alginate lyase inhibits biofilm formation of a clinical *Pseudomonas aeruginosa* strain MCC 2081. IUBMB Life 73(2): 444-462.
- Mekinić G. I., Skroza D., Šimat V., Hamed I., Čagalj M., Popović Perković Z., 2019 Phenolic content of brown algae (Pheophyceae) species: extraction, identification, and quantification. Biomolecules 9(6):244.
- Mohapatra B. R., 2017 Kinetic and thermodynamic properties of alginate lyase and cellulase co-produced by *Exiguobacterium species* Alg-S5. International Journal of Biological Macromolecules 98: 103-110.
- Oxaran V., Dittmann K. K., Lee S. H., Chaul L. T., de Oliveira C. A. F., Corassin C. H., Alves V. F., De Martinis E. C. P., Gram L., 2018 Behavior of foodborne pathogens *Listeria monocytogenes* and *Staphylococcus aureus* in mixed-species biofilms exposed to biocides. Applied and Environmental Microbiology 84(24):e02038-18.
- Patel K. K., Tripathi M., Pandey N., Agrawal A. K., Gade S., Anjum M. M., Tilak R., Singh S., 2019 Alginate lyase immobilized chitosan nanoparticles of ciprofloxacin for the improved antimicrobial activity against the biofilm associated mucoid *P. aeruginosa* infection in cystic fibrosis. International Journal of Pharmaceutics 563: 30-42.
- Peteiro C., 2018 Alginate production from marine macroalgae, with emphasis on kelp farming. In: Alginates and their biomedical applications. Rehm B. H. A., Moradali M. F. (eds), Springer, Singapore, pp. 27-66.
- Pilgaard B., Wilkens C., Herbst F. A., Vuillemin M., Rhein-Knudsen N., Meyer A. S., Lange L., 2019 Proteomic enzyme analysis of the marine fungus *Paradendryphiella salina* reveals alginate lyase as a minimal adaptation strategy for brown algae degradation. Scientific Reports 9(1):12338.
- Rashedul A. C. S. M., Zafar M., 2018 Oil and alginate content in *Hydroclathrus clathratus* of the St. Martin's Island, Bangladesh. MOJ Ecology & Environmental Sciences 3(5): 322-324.
- Rojo-Molinero E., Macià M. D., Oliver A., 2019 Social behavior of antibiotic resistant mutants within *Pseudomonas aeruginosa* biofilm communities. Frontiers in Microbiology 10:570.
- Roy R., Tiwari M., Donelli G., Tiwari V., 2018 Strategies for combating bacterial biofilms: a focus on anti-biofilm agents and their mechanisms of action. Virulence 9(1):522-554.
- Salmeán A. A., Duffieux D., Harholt J., Qin F., Michel G., Czjzek M., Willats W. G., Hervé C., 2017 Insoluble (1→3),(1→4)-β-D-glucan is a component of cell walls in brown algae (Phaeophyceae) and is masked by alginates in tissues. Scientific Reports 7(1): 1-11.
- Santiañez W. J. E., Lee K. M., Uwai S., Kurihara A., Geraldino P. J. L., Ganzon-Fortes E. T., Boo S. M., Kogame K., 2018 Untangling nets: elucidating the diversity and phylogeny of the clathrate brown algal genus *Hydroclathrus*, with the description of a new genus *Tronoella* (Scytosiphonaceae, Phaeophyceae). Phycologia 57(1):61-78.
- Santiañez W. J. E., Al-Bader D., West J. A., Bolton J. J., Kogame K., 2020 Status, morphology, and phylogenetic relationships of *Iyengaria* (Scytosiphonaceae, Phaeophyceae), a brown algal genus with a disjunct distribution in the Indian Ocean. Phycological Research 68(4):323-331.
- Sharma D., Misba L., Khan A. U., 2019 Antibiotics versus biofilm: an emerging battleground in microbial communities. Antimicrobial Resistance and Infection Control 8(1):76.
- Sigaard K. T., 2017 Advanced literature search. In: A practical guide to biomedical research. Agger P., Stephenson R. S., Hasenkam M. (eds), Springer, Cham, pp. 47-53.
- Sun C., Fu G. Y., Zhang C. Y., Hu J., Xu L., Wang R. J., Su Y., Han S. B., Yu X. Y., Cheng H., Zhang X. Q., Huo Y. Y., Xu X. W., Wu M., 2016 Isolation and complete genome sequence of *Algibacter alginolytica* sp. nov., a novel seaweed-degrading Bacteroidetes Bacterium with diverse putative polysaccharide utilization loci. Applied and Environmental Microbiology 82(10):2975-2987.

- Sun C., Zhou J., Duan G., Yu X., 2020 Hydrolyzing *Laminaria japonica* with a combination of microbial alginate lyase and cellulase. *Bioresource Technology* 311:123548.
- Sun Y., Hu X., Guo D., Shi C., Zhang C., Peng X., Yang H., Xia X., 2019 Disinfectant resistance profiles and biofilm formation capacity of *Escherichia coli* isolated from retail chicken. *Microbial Drug Resistance* 25(5):703-711.
- Tasneem U., Yasin N., Nisa I., Shah F., Rasheed U., Momin F., Zaman S., Qasim M., 2018 Biofilm producing bacteria: a serious threat to public health in developing countries. *Journal of Food Science and Nutrition* 1(2):25-31.
- Tavafi H., Ali A. A., Ghadam P., Gharavi S., 2018 Screening, cloning and expression of a novel alginate lyase gene from *P. aeruginosa* TAG 48 and its antibiofilm effects on *P. aeruginosa* biofilm. *Microbial Pathogenesis* 124:356-364.
- Taylor S., 2019 The psychology of pandemics: preparing for the next global outbreak of infectious disease. Cambridge Scholars Publishing, 178 pp.
- Topka-Bielecka G., Dydecka A., Necel A., Bloch S., Nejman-Faleńczyk B., Węgrzyn G., Węgrzyn A., 2021 Bacteriophage-derived depolymerases against bacterial biofilm. *Antibiotics* 10(2):175.
- Torelli R., Cacaci M., Papi M., Sterbini F. P., Martini C., Posteraro B., Palmieri V., De Spirito M., Sanguinetti M., Bugli F., 2017 Different effects of matrix degrading enzymes towards biofilms formed by *E. faecalis* and *E. faecium* clinical isolates. *Colloids and Surfaces B: Biointerfaces* 158:349-355.
- Tuite A. R., Bhatia D., Moineddin R., Bogoch I. I., Watts A. G., Khan K., 2020 Global trends in air travel: implications for connectivity and resilience to infectious disease threats. *Journal of Travel Medicine* 27(4):taaa070.
- Verderosa A. D., Totsika M., Fairfull-Smith K. E., 2019 Bacterial biofilm eradication agents: a current review. *Frontiers in Chemistry* 7:824.
- Vestby L. K., Grønseth T., Simm R., Nesse L. L., 2020 Bacterial biofilm and its role in the pathogenesis of disease. *Antibiotics* 9(2):59.
- Vimala T., Poonghuzhali T. V., 2017 *In vitro* antimicrobial activity of solvent extracts of marine brown alga, *Hydroclathrus clathratus* (C. Agardh) M. Howe from Gulf of Mannar. *Journal of Applied Pharmaceutical Science* 7(04):157-162.
- Vuoristo K. S., Fredriksen L., Oftebro M., Arntzen M. Ø., Aarstad O. A., Stokke R., Steen I. H., Hansen L. D., Schüller R. B., Aachmann F. L., Horn S. J., Eijsink V. G. H., 2019 Production, characterization, and application of an alginate lyase, AMOR_PL7A, from hot vents in the Arctic Mid-Ocean ridge. *Journal of Agricultural and Food Chemistry* 67(10):2936-2945.
- Wan B., Zhu Y., Tao J., Zhu F., Chen J., Li L., Zhao J., Wang L., Sun S., Yang Y., Zhang X., Zhang Y., 2020 Alginate lyase guided silver nanocomposites for eradicating *Pseudomonas aeruginosa* from lungs. *ACS Applied Materials and Interfaces* 12(8):9050-9061.
- Wang H., Chiu L. C. M., Ooi V. E. C., Ang P. O., 2010a A potent antitumor polysaccharide from the edible brown seaweed *Hydroclathrus clathratus*. *Botanica Marina* 53(3):265-274.
- Wang H., Ooi V. E., Ang Jr. P. O., 2010b Anti-herpesviral property and mode of action of a polysaccharide from brown seaweed (*Hydroclathrus clathratus*). *World Journal of Microbiology and Biotechnology* 26(9):1703-1713.
- Wang M., Chen L., Liu Z., Zhang Z., Qin S., Yan P., 2016 Isolation of a novel alginate lyase-producing *Bacillus litoralis* strain and its potential to ferment *Sargassum horneri* for biofertilizer. *MicrobiologyOpen* 5(6):1038-1049.
- Wang M., Chen L., Zhang Z., Wang X., Qin S., Yan P., 2017 Screening of alginate lyase-excreting microorganisms from the surface of brown algae. *AMB Express* 7(1):74.
- Wright K., McDaid C., 2011 Reporting of article retractions in bibliographic databases and online journals. *JMLA Journal of the Medical Library Association* 99(2):164-167.
- Xing M., Cao Q., Wang Y., Xiao H., Zhao J., Zhang Q., Ji A., Song S., 2020 Advances in research on the bioactivity of alginate oligosaccharides. *Marine Drugs* 18(3):144.
- Xu F., Wang P., Zhang Y. Z., Chen X. L., 2018 Diversity of three-dimensional structures and catalytic mechanisms of alginate lyases. *Applied and Environmental Microbiology* 84(3):e02040-17.

- Xu F., Chen X. L., Sun X. H., Dong F., Li C. Y., Li P. Y., Ding H., Chen Y., Zhang Y. Z., Wang P., 2020 Structural and molecular basis for the substrate positioning mechanism of a new PL7 subfamily alginate lyase from the arctic. *Journal of Biological Chemistry* 295(48):16380-16392.
- Yagi H., Fujise A., Itabashi N., Ohshiro T., 2016 Purification and characterization of a novel alginate lyase from the marine bacterium *Cobetia* sp. NAP1 isolated from brown algae. *Bioscience, Biotechnology, and Biochemistry* 80(12):2338-2346.
- Yan J., Chen P., Zeng Y., Men Y., Mu S., Zhu Y., Chen Y., Sun Y., 2019 The characterization and modification of a novel bifunctional and robust alginate lyase derived from *Marinimicrobium* sp. H1. *Marine Drugs* 17(10):545.
- Yan Z., Huang M., Melander C., Kjellerup B. V., 2020 Dispersal and inhibition of biofilms associated with infections. *Journal of Applied Microbiology* 128(5):1279-1288.
- Yin R., Yi Y. J., Chen Z., Wang B. X., Li X. H., Zhou Y. X., 2021 Characterization of a new biofunctional, exolytic alginate lyase from *Tamlana* sp. s12 with high catalytic activity and cold-adapted features. *Marine Drugs* 19(4):191.
- Zhang Z., Tang L., Bao M., Liu Z., Yu W., Han F., 2020 Functional characterization of carbohydrate-binding modules in a new alginate lyase, TsAly7B, from *Thalassomonas* sp. LD5. *Marine Drugs* 18(1):25.
- Zhu J., Mo K., Zheng Z., Wang Z., Hu Y., Zou X., Gu H., Wang H., Bao S., Huang H., 2020 *Paenibacillus algicola* sp. nov., a novel alginate lyase-producing marine bacterium. *International Journal of Systematic and Evolutionary Microbiology* 70(9):5087-5092.
- Zhu X., Li X., Shi H., Zhou J., Tan Z., Yuan M., Yao P., Liu X., 2018 Characterization of a novel alginate lyase from marine bacterium *Vibrio furnissii* H1. *Marine Drugs* 16(1):30.
- Zhu Y., Wu L., Chen Y., Ni H., Xiao A., Cai H., 2016a Characterization of an extracellular biofunctional alginate lyase from marine *Microbulbifer* sp. ALW1 and antioxidant activity of enzymatic hydrolysates. *Microbiological Research* 182:49-58.
- Zhu Y., Chen P., Bao Y., Men Y., Zeng Y., Yang J., Sun J., Sun Y., 2016b Complete genome sequence and transcriptomic analysis of a novel marine strain *Bacillus weihaiensis* reveals the mechanism of brown algae degradation. *Scientific Reports* 6(1):38248.
- Zilda D. S., Yulianti Y., Sholihah R. F., Subaryono S., Fawzya Y. N., Irianto H. E., 2019 A novel *Bacillus* sp. isolated from rotten seaweed: identification and characterization alginate lyase its produced. *Biodiversitas Journal of Biological Diversity* 20(4):1166-1172.

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