

Review Article

Acyl Homoserine Lactone-Based Quorum Sensing and its Role in Regulation of Extracellular Hydrolytic Enzymes in Marine Snow Associated Bacteria

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ABSTRACT

The discovery of quorum sensing (QS) amongst bacterial cells substantiates the coordinated activities in these microscopic organisms. QS is a system of cell-to-cell communication through which bacteria express certain genes to achieve various physiological and biological functions. Presently, several kinds of autoinducers have been reported in microbial cells, however *N*-acyl homoserine lactones (AHLs) are known as the most significant QS autoinducers, frequently produced by large numbers of Gram-negative bacteria. QS system in marine snow associated bacteria has a great concern with respect to regulate extracellular enzymatic activities. Substantially, marine aggregates are large sinking particles composed of both organic and inorganic detritus and living organisms including phytoplankton, zooplankton and bacteria, and perform a critical role in moving materials from upper levels to deep Ocean. Intriguingly, findings of AHL signaling molecules in marine snow aggregates and associated microbial cells have been attributed to play a crucial role in dissociation of these large carbon rich particles with a profound impact on marine food webs along with biogeochemical cycles in marine environment. This mini review highlights the role of AHL based QS system in marine snow with respect to enhanced enzymatic activities (EEA) of marine snow associated bacterial populations and hydrolysis of these carbon rich aggregates.

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Key words

Quorum-sensing, AHLs, Extracellular enzymes, Marine snow

INTRODUCTION

Quorum sensing (QS) is a mechanism of detection and responding cell density population by regulation of specific genes (Lim *et al.*, 2014). Bacteria assess cell density by sensing threshold concentration of QS signaling molecules produced by the same or neighboring bacterial cells (Platt and Fuqua, 2010). Principally, bacteria produce different types of signaling molecules also called as autoinducers; for instance, *N*-acyl homoserine lactones (AHLs) are the major autoinducers frequently produced

by Gram-negative bacterial species, whereas small oligopeptides have been found as the QS autoinducers in several Gram-positive bacterial species (Jatt *et al.*, 2015). Moreover, several enzymes have been reported in some bacterial species that disrupt particularly AHL based QS system and this whole mechanism is generally called as quorum-quenching (QQ) (Tang and Zhang, 2014). Predominantly, three major QQ enzymes have been shown to degrade AHL molecules such as AHL-oxidase-reductase, AHL-lactonase and AHL-acylase (Chu *et al.*, 2014). Significantly, AiiA (AHL lactonase) enzyme produced by *Bacillus* species has been reported to degrade several types of AHL molecules (Dong *et al.*, 2000). Heretofore AiiA protein has been widely used to degrade AHL signaling molecules without affecting microbial numbers and composition (Park *et al.*, 2008; Bai *et al.*, 2008).

QS bacteria associated with natural snow particles are of great importance in marine environments characterized with higher levels of extracellular enzymatic activity (Hmelo *et al.*, 2011; Jatt *et al.*, 2015). Marine snow

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represents the sinking aggregates, composed of organic and inorganic detritus, fecal pellets and living organisms including phytoplankton, bacteria, and zooplankton, resulting in transporting organic matter from the surface to deep levels of ocean (Piontek *et al.*, 2009). Natural marine snow aggregates are highly fragile and usually degraded quickly during sampling and handling processes. Marine snow degradation may be attributable to two physical and biological processes. Physical degradation is due to a shear stress that breaks down the marine aggregates, whereas biological degradation is due to a very high flora and fauna attached to marine aggregates being responsible for elevated heterotrophic activity (Kiorboe, 2001; Arnosti, 2004).

Extracellular hydrolytic enzymes produced by marine snow associated bacteria are considered as beneficial tools for breaking down these large aggregates full of nutrients and resulting as transmission of these nutrient rich compounds to free-living communities in marine environment (Ziervogel *et al.*, 2010; Jatt, 2021). Bacterial populations take the components of the dissolved organic matter (DOM) directly and use extracellular hydrolytic enzymes to cleave high molecular weight compounds prior to uptake (Arnosti, 2004). The QS system has been indicated mainly to regulate the production of large numbers of extracellular hydrolytic enzymes in marine aggregates and plays a beneficial role in degradation of these large particles with a pronounced impact on carbon dioxide moving from atmosphere to deep Ocean (Hmelo *et al.*, 2011; Jatt *et al.*, 2015).

QUORUM-SENSING (QS) SYSTEM

The term QS refers to a conversation mechanism in microorganisms based on production, secretion, and detection of signals. QS system regulates expression of specific genes in contradiction of cell density in several types of microorganisms (Myszka and Czaczyk, 2012; Lim *et al.*, 2014). Initially, QS was observed in marine bacterium *Vibrio fischeri* that produces signaling molecules during its colonization and growth in light organs of cephalopods and marine fish, coordinating the expression of bioluminescence encoded genes in response to cell density (Nealson *et al.*, 1970). Bacterial cells assess the cell density when threshold concentration of QS signaling molecules induced by same type of cells or neighboring bacterial cells (Platt and Fuqua, 2010). Several kinds of QS signal molecules have been detected in bacterial species. i.e., AHLs, oligopeptides, quinolones and furanosyl-borate diesters (Chen *et al.*, 2002; Jatt, 2021). These all signaling molecules are secondary metabolites, which are not involved in primary metabolism.

Biosynthesis of AHL- signal molecule

In AHL biosynthesis, *S*-adenosyl methionine (SAM) binds to an active site of enzyme; an acyl carried protein (ACP) transfer proper acyl-group to this composite, which creates bond (amide) with amino-group of SAM. This action of complex acyl-ACP and SAM is conserved in QS systems of bacterial populations belonging to different species (Myszka and Czaczyk, 2012). A general structure of AHL molecule produced by bacteria has been shown in Figure 1. Bacterial species characterized with AHL based QS system usually recognize AHL signal molecules through a protein (LuxR) that works as receptor of AHL molecules (Zheng *et al.*, 2006). While, enzyme AHL synthase (LuxI type protein) is involved to synthesize AHL signal molecules. AHL synthases in various bacterial species share an analogues sequence homology with *luxI* gene of luminescence bacterium *V. fischeri*. AHL signal molecules produced by *luxI* homologues consist of ring of homoserine lactone, which is bound with acyl-chain by an amide bond that differentiated into carbon atoms of 4 to 18 carbons and with variable fatty acyl groups such as carbonyl or hydroxyl group.

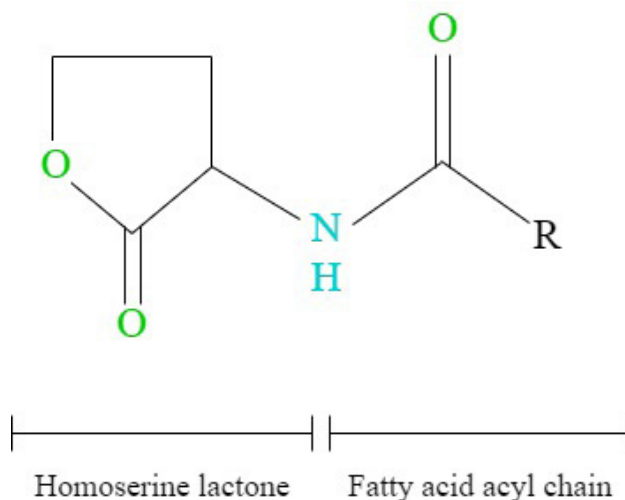


Fig. 1. A general structure of *N*-acyl homoserine lactone (AHL) signal molecule.

Quorum sensing in gram-negative bacterial species

Gram-negative bacterial species frequently use AHLs as QS signaling molecules to regulate various biological and physiological activities (Christopher and Bassler, 2005; Jatt, 2021). Essentially, LuxR/I type regulators are involved to produce AHL based QS signals in Gram negative bacterial cells (Fig. 2). AHLs are very crucial QS signaling molecules, usually used in communication between bacterial populations of same and even in

different bacterial species, genera, and families (Myszka and Czaczky, 2012). AHL signal molecule in Gram-negative bacterial species have been classified as short and long chain AHLs based on length of acyl groups with carbon 4 to carbon 18 acyl side chains particularly with groups of either oxo or hydroxyl or even no substitution at carbon 3. Substantially, proteobacterial Gram-negative bacterial species belonging with alpha, beta and gamma sub-groups have been confirmed with AHL based QS mechanism (Chhabra *et al.*, 2005).

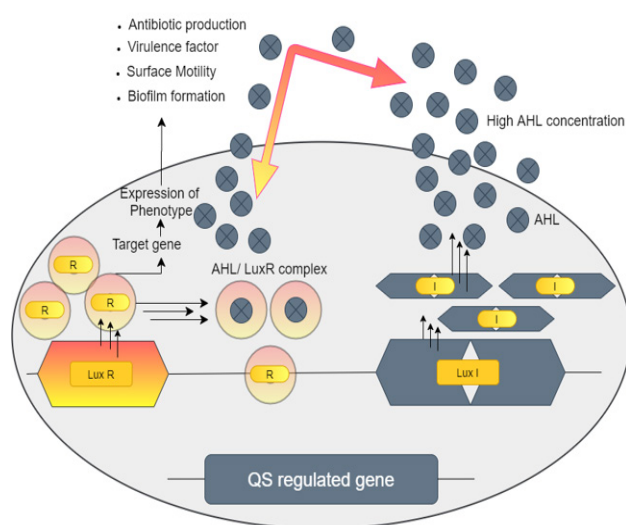


Fig. 2. LuxR/I Quorum-sensing (QS) system in Gram-negative bacteria. In threshold cell density, AHL based QS signaling molecules attach to LuxR. AHL/LuxR complex initiates transcription of target gene to carry out phenotype expression.

Quorum sensing in Gram-positive bacterial species

QS mechanism found in Gram-positive bacterial species is dissimilar with the QS mechanism found in Gram-negative bacterial species. In Gram-positive bacteria, species-specific QS is mostly mediated through small oligopeptides and are called as autoinducing peptides (AIPs) characterized with 5 to 34 amino acids in length (Chan *et al.*, 2004). Principally, histidine kinases (two-component type membrane bound) are used as sensors and conversation is achieved by phosphorylation cascade (Christopher and Bassler, 2005). Three families of AIPs have been identified based on their structural uniqueness, i.e., oligopeptide lantibiotics, 16-membered thiolactone peptides and tryptophan peptides, respectively (Okada *et al.*, 2005). Generally, peptides cannot diffuse through membrane, hence oligopeptide exporters are responsible to release signaling molecules. Mostly, QS-peptide molecules are usually cleaved into small peptide

units from large precursors and further characterized with different rings of lanthionine, thiolactone, isoprenyl and lactone rings (Christopher and Bassler, 2005). AIPs based QS mechanism is found in large numbers of Gram-positive bacteria, i.e., *Staphylococcus aureus*, *Bacillus ceruss*, *Bacillus subtilis* and *Enterococcus faecalis*, *Lactobacillus plantarum* and *Listeria monocytogenes* (Autret *et al.*, 2003; Sturme *et al.*, 2005).

AI-2 (Autoinducer-II) based quorum-sensing mechanism

AI-2 based QS mechanism consists of diffusible and interconvertible signaling molecules such as furanosyl borate diester (Williams *et al.*, 2007). Interestingly, both Gram-negative and Gram-positive bacterial species exhibit AI-2 QS mechanism (Hermann, 2007). AI-2 QS signaling molecules are induced by LuxS-type enzyme that breaks down S-ribosyl-L-homocysteine and results in production of AI-2 precursor (e.g., 4,5-dihydroxy-2,3-pentanedione), and homocysteine with the ability to cyclize spontaneously with the production of furanone derivatives (Miller *et al.*, 2004). Generally, *LuxS* gene responsible for AI-2 has been detected in large numbers of bacterial species (i.e., more than sixty bacterial species) belong to different classes such as beta (β), gamma (γ), sigma (δ) and epsilon (ϵ) proteobacteria, spirochetes, firmicutes, actinobacteria and also genera belong to the groups of green-sulphur, Cytophaga and Deinococcus bacteria (Vendeville *et al.*, 2005; Williams *et al.*, 2007).

AI-2 based QS mechanism has been reported widely in several *Vibrio* species specially in *V. cholerae* and *V. harveyi*, and the role of this QS system in these bacterial species has been shown to be involved in regulation the traits of bioluminescence and pathogenicity (Lenz *et al.*, 2004).

QS based regulation of bacterial phenotypic characteristics

Generally, bacterial species release several kinds of QS signaling molecules and once a threshold concentration of these signalings (correlating to specific cell density) is achieved then initiate transcription of QS regulated genes. Large numbers of bacterial communities inhabiting natural environment use QS mechanisms to regulate a variety of phenotypes such as extracellular hydrolytic enzyme production, toxin secretion, biofilm formation and motility (Whitehead *et al.*, 2001; Gonzalez and Keshavan, 2006). These QS regulated phenotypes are crucial for establishment of a pathogenic, symbiotic or beneficial relationship with a host (Myszka and Czaczky, 2012).

In natural environments, the coordinated mechanism for microbial cells is highly essential to regulate the most important phenotypes for the adaptation of new trends of growth, which may help in protection from

hazardous environments. The regulation of a wide variety of phenotypes in several Gram-negative bacterial species based on LuxI/R QS mechanism has been reported such as bioluminescence in *V. fischeri*, biofilm and exo-protease in *Aeromonas hydrophila*, swarming, exoenzyme and biofilm in *Burkholderia cenocepacia*, exopolysaccharides in *Pantoea stewartii*, plasmid conjugation in *Agrobacterium tumefaciens* and pigment production in *Chromobacterium violaceum* (Jatt *et al.*, 2015).

QUORUM QUENCHING (QQ)

Quorum sensing is a conversation mechanism reported in several bacterial species in order to regulate various biological functions including pathogenicity. Unlike QS mechanism, quorum quenching is a mechanism of preventing QS system by disrupting QS signaling molecules (Dessaux *et al.*, 2011). QQ bacteria have been isolated from various environments. Several abundant and strong QQ agents have been recognized from various synthetic and natural chemical products. Many types of bacterial species particularly isolated from natural marine environments have been shown to release inhibitors and use these small QS inhibitors to gain benefits in competitive environment (Tang and Zhang, 2014). Several QS inhibitor molecules have been identified to disrupt the signaling generation and leading to the process QS inhibition. AHL based QS mechanism can be inhibited simply by exploiting the unique specificity of LuxR-type proteins and can also be inhibited by interrupting the biosynthetic pathways that leads to AHL synthesis. Mainly, analogues to precursors of AHL molecule can be employed to control the autoinducer synthesis. Dong *et al.* (2000) reported an enzyme (AiiA) from *Bacillus*, capable of degrading AHL molecules. It has been recorded that AiiA enzyme in *Erwinia carotovora* has drastically inhibited production of AHL QS signaling molecules and significantly reduced pectolytic enzyme synthesis (Dong *et al.*, 2000).

MARINE SNOW

Marine snow term indicates large marine aggregates in ocean environment that play a critical role in transporting components from upper to deeper layers. These marine aggregates are the sites of elevated levels of biological activities and involved in energy flow through marine ecosystems (Jatt *et al.*, 2015). Bacterial communities associated with marine snow particles play a vital role in breaking down of these particles and remineralization of carbonic materials. Marine snow aggregates range from few μm to several centimeters in size. Marine aggregates are enriched in nutrients that enhance the colonization by

microbial communities (Artolozaga *et al.*, 1997; Hmelo *et al.*, 2011). These large particles are characterized with bacterial numbers and biomass in greater concentration than those present in the surrounding sea water (Simmon *et al.*, 1990; Alldredge, 2000; Kiorboe, 2000).

Marine snow aggregates are found ubiquitous from the surface to the deep oceans and the highest levels have been reported in euphotic zone with maximum production (Lampitt, 2001). Predominantly, the major characteristics of these marine snow particles which render this aggregated material very crucial are high sinking rates, microenvironment, enhanced biogeochemical rates and sites of food source for living organisms surrounding these aggregates. Marine snow aggregates have been found in all over the world's oceans in every part of the water column. These are not uniformly dispersed either in space or time; however, elevated rates of these marine particles have been reported in upper water column (Jatt *et al.*, 2015). These aggregates are comprised of 60% of particulate organic carbon (POC), which decreases with increasing depth (Martin *et al.*, 2011). Some potential mechanisms are described as the responsible for reduction with depth of particulate organic carbon flux such as solubilization to dissolved organic matter, consumption by zooplankton, abiotic stress-induced fragmentation and the most important one is microbial decomposition (Goldthwait *et al.*, 2004).

Composition of natural marine snow particles

Natural marine snow particles are composed of both organic and inorganic detritus and living organisms including phytoplankton, zooplankton, and bacteria. Formation of marine snow in marine environment occurs by aggregating small marine particles with the help of several processes. The major processes that play a role in marine snow aggregation are physical coagulation and zooplankton mediated aggregation (Kiorboe, 2001). Moreover, formation of particulate organic matter (POM) takes place by aggregation of colloidal organic material from dissolved organic matter (DOM) (Kepkay, 1994). Presence of transparent exopolymer particles (TEP) in increased levels has been reported within POM pool in coastal as well as open oceanic environment (Alldredge *et al.*, 1993). TEP influences aggregation process in different ways and may involve in rapidly development of marine snow aggregates (Alldredge *et al.*, 1993). Zooplanktons aggregated with marine snow are considered as food source for various types of planktonic organism including fish, copepods and euphausiids (Lampitt, 2001).

Marine snow particles provide a substrate for microbial attachment, while the production and release of refractory organic material by bacterial communities

associated with these marine snow aggregates results in formation of the fibrillar matrix, aggregating together of particles, ultimately leading to the formation of large particles (Alldridge and Silver, 1988; Jatt *et al.*, 2015).

Degradation of marine snow aggregates

Several processes are involved in high rates of dissolved organic carbon of marine snow aggregates; however, there are two major processes believed to be involved in degradation of marine snow aggregates such as physical process and biological process. Physical degradation of marine snow particles is due to shear stress that breaks down the large marine aggregates into small particles, while, biological degradation of marine snow aggregates is due to a very high flora and fauna associated with these aggregates and responsible for enhanced heterotrophic activities (Kiorboe, 2001). Moreover, the hydrolytic activities by bacterial extracellular enzymes are known as the vital source that degrade and solubilize the components of particulate organic matter aggregates. It has been reported that the hydrolytic activities of bacterial populations associated with marine snow aggregates are substantially higher (up to 10^5 times) as compared to free living microbial communities (Ivancic *et al.*, 2018; Jatt, 2021).

EXTRACELLULAR HYDROLYTIC ENZYMES

Bacterial cells use specific QS systems that perform coordination to express certain genes encoding behaviors that support the cells in extracellular hydrolytic enzymes production, luminescence and formation of biofilms specifically at high cellular density and communicate within and between species. Extracellular or exoenzymes are the enzymes that are secreted by cells and work outside of these cells. Extracellular enzymes are mainly hydrolases, which breakdown bonds of C-O and C-N used in connection of monomers, i.e., glycosidases, peptidases or esterases (Cunha *et al.*, 2010). Extracellular hydrolytic enzymes are the essential components of biological processes and may play a crucial role in degradation of large organic matter. Extracellular enzymatic activity (EEA) in bacteria is regulated by various factors including QS signaling molecules. Since, particulate organic matter and dissolved organic matter components are dominated by high molecular-weight substances and thus complex substrates are first degraded externally into small molecules. This type of degradation of complex substrates is achieved by extracellular hydrolytic enzymes (i.e., protease, lipase, amylase, phosphatase, cellulase etc.), produced by several types of bacterial species inhabiting

various ecological niches. Extracellular enzymes secreted by marine bacteria are of great importance in degradation of particulate organic matter in ocean environments (Baltar *et al.*, 2010).

Extracellular hydrolytic enzymes have also been potentially used in biomedical sciences, food industries and different chemical industries. Mainly, proteases, glucosidases, chitinases, lipases and phosphatases are the hydrolytic extracellular enzymes widely studied in marine water (Cunha *et al.*, 2010). Bacteria associated with marine snow are of highly important in hydrolysis of marine snow particles by producing wide range of extracellular enzymes (Su *et al.*, 2019). In general, marine snow associated bacteria exhibit higher levels of exoenzymes, hence it is speculated that free-living organisms may benefit from their overproduction of hydrolytic enzymes (Hmelo *et al.*, 2011; Jatt, 2021).

The role of AHL based QS system in regulation of extracellular hydrolytic enzymes in marine snow

Bacterial species characterized with QS system have been reported in wide range of marine environments such as marine snow, dinoflagellates, sponges, and corals (Gram *et al.*, 2002; Mohamed *et al.*, 2008; Tait *et al.*, 2010). The marine environments generate unique challenges to bacterial communities characterized with QS system, i.e., signaling molecules can be lost very rapidly by the diffusion in aqueous environment, pH of sea water that is slightly basic and thus degradation of signal molecules by base-catalyzed hydrolysis occurs (Yates *et al.*, 2002). The activation of gene expression in bacterial communities by AHL based QS system is dependent on the threshold concentration of AHL producing bacterial species and also depends on the ability of extracellular environment to retard diffusion of signaling molecules away from related bacterial cells. Intriguingly, this can be retained within the micro-environments such as marine snow aggregates that will slow down the hydrolysis of signaling molecules by diffusion and abiotic base-catalyzed hydrolysis. Moreover, marine snow isolates can be able to evolve tactics to compete with challenges generated by chemical environment, i.e., these bacterial species use long chain AHL molecules or with oxo-substitution on 3-carbon at acyl chain of AHL signals. Essentially, long acyl chain AHL signals have been found more stable in the sea water and are hydrolyzed more slowly by base-catalyzed hydrolysis as compared to AHL molecules with short acyl chains (Hmelo *et al.*, 2011).

Generally, detection of a broad range of AHL based QS signals in marine snow directly and in associated bacteria is vigorous and may influence on coordination of expression of certain genes encoding behaviors that

support the cells to promote the extracellular hydrolytic enzymes production involved in marine snow degradation process. Several extracellular hydrolytic enzymes such as elastase, chitinase, cellulase, lipase, phosphatase and gelatinase are believed to be regulated by AHL based QS system (Jatt *et al.*, 2015). Extracellular hydrolytic enzymes are regulated based on environmental factors, ecosystem, and enzyme-substrate interactions. Enzymatic activities are mainly controlled by enzyme-substrate interactions, i.e., adsorption, inhibition, stabilization and humification (Jatt *et al.*, 2018). Moreover, growth phase is considered as a major interesting factor for regulation of extracellular enzymes. Related to this, there is a QS system that deals with the coordinated functions at high cell density. The maximum enzyme production has been reported at late logarithmic to early stationary phase for proteases and lipases (Jatt *et al.*, 2015). This suggests extracellular enzymes production at high cell density and thus QS might be involved in regulation of these enzymes. The regulation of extracellular enzymes by QS system has been reported in several bacterial species such as cell wall hydrolyzing enzymes in *Erwinia carotovora*, metalloprotease gene expression in *Vibrio vulnificus*, metalloprotease synthesis in *Vibrio anguillarum*, pectate lyases in *Erwinia chrysanthemi*, and protease synthesis in *Burkholderia cetaceans*, extracellular protease synthesis in *Serratia liquefaciens* and exoprotease in *Aeromonas salmonicida* (Reverchon *et al.*, 1998; Shao and Hor, 2001). Some studies have directly shown addition of exogenous QS autoinducers such as AHLs and AI-2 signal molecules to marine snow aggregates and resulted a profound effect on EEA in these natural marine particles (Hmelo *et al.*, 2011; Krupke *et al.*, 2016). Moreover, Su *et al.* (2019), reported AHL based QS in marine snow bacterium *Ruegeria mobilis* Rm01 and identified two AHL synthase genes such as *psal* and *psbl* by genomic analysis. Similarly, addition of exogenous AHL QS signaling molecules was shown to influence enzymatic activities particularly increased production of extracellular lipase activity in bacterium Rm01 associated with marine snow particles (Su *et al.*, 2019). Mainly, lipids, glycerols and fatty acids are highly

important components in oceanic environment and the cytoplasmic membranes of dead organisms are a major source of these lipo-particles along with other biological materials found in marine environmental area.

QS regulation of EEA has also been reported in marine snow isolates of *Trichodesmium consortia* and *Ruegeria* bacterial species (Van-Mooy *et al.*, 2012; Su *et al.*, 2019). In addition to EEA, QS system has also been involved in regulation of several other phenotypic traits particularly in particle attached ecological niche such as biofilm formation and flagella mediated motility in *Ruegeria* species, biosynthesis of indigoidine antimicrobial agent in *Phaeobacter* species and production of TDA (tropodithietic acid) in bacterium *Phaeobacter inhibens* DSM17395 (Zan *et al.*, 2012; Cude *et al.*, 2015). Several types of bacterial species, e.g., *Pseudomonas aeruginosa*, *Vibrio cholerae* and *Burkholderia pseudomallei* use QS system to compete and resist QQ producing bacterial communities with a pronounced effect on microbial ecology (Garcia-Conteras *et al.*, 2015). Intriguingly, bacterium *Deinococcus radiodurans* has been reported to regulate a specific gene involved in regulation of oxidative stress resistance by coordinated effect of both QS and QQ mechanism (Lin *et al.*, 2016). QS signal molecules found directly in natural marine snow particles are due to microbial species characterized with different QS systems associated with these large particles. Generally, QS has a great concern with biofilm formation in carbon rich marine aggregates and accelerates the production of extracellular enzymes (Table I). Likewise, QS has been considered as a major constituent involved in regulation of biofilms and enhanced EEA in marine snow aggregates. One of the studies has shown that AHL based QS signaling molecules significantly influenced extracellular aminopeptidase, phosphatase, and lipase enzymatic activities in marine snow aggregates collected from the region of Atlantic and Pacific Ocean (Krupke *et al.*, 2016). Moreover, further incubation of marine snow aggregates with exogenous AHLs increased and decreased the rate of hydrolysis of marine particles and thus indicated a link between QS system and hydrolysis of marine particles (Krupke *et al.*, 2016).

Table I. AHL based QS signal molecules produced by marine snow associated bacteria and their influence on extracellular enzymatic activities (EEA).

Marine snow associated bacteria	Major AHLs	Phenotypes	References
<i>Citrobacter freundii</i> B1	C6-HSL, C8-HSL, C10-HSL, C12-HSL, C14-HSL	Cellulase	Jatt, 2021
<i>Ruegeria mobilis</i> RMO1	3OC10-HSL, C10-HSL, C12-HSL	Lipase	Su <i>et al.</i> , 2019
<i>Pantoea ananatis</i> B9	C4-HSL, 3OC6-HSL, C6-HSL, C10-HSL, C12-HSL, C14-HSL	Phosphatase	Jatt <i>et al.</i> , 2015
<i>Roseobacter</i> strain HP12	C6-HSL, C8-HSL	ND	Gram <i>et al.</i> , 2002

ND*, Not detected.

Several numbers of bacterial species associated with marine aggregates are reported to produce AHL signaling molecules with elevated rates of EEA (Jatt *et al.*, 2015). Previously, 43 marine associated bacterial strains were reported and four of them showed production of AHL based QS signals (Gram *et al.*, 2002). Moreover, in our previous study, 53 bacterial strains associated with marine snow were isolated and ten of these isolates affiliated with different bacterial groups indicated as positive for AHL based QS signals (Jatt *et al.*, 2015). Amongst the marine snow isolates, *Pantoea ananatis* B9 was shown to produce five different extracellular enzymes, i.e., alkaline phosphatase, lipase, amylase, protease and gelatinase. Interestingly, phosphatase was reported as a dominant extracellular enzyme and the biosynthesis of this enzyme was shown possibly regulated by AHL based QS system in marine snow bacterium *P. ananatis* B9 and cellulase activity in *C. freundii* B1 (Jatt *et al.*, 2015; Jatt, 2021). Moreover, another study has also reported substantially higher levels of EEA in marine snow aggregates as compared to sea water and the extracellular alkaline phosphatase was shown to be critically increased followed by extracellular peptidase (Ivancic *et al.*, 2018). Intriguingly, the extracellular hydrolytic enzymes are critically influenced by QS systems and are the major components to carry out nutrient transport in marine environments by hydrolysis of large marine aggregates.

CONCLUSION

This mini review focuses on AHL based QS system in marine snow and associated bacterial communities and its role in regulation of extracellular hydrolytic enzymes. AHL based QS signaling molecules influence and accelerate extracellular enzymatic activities (EEA) *in situ* natural marine snow particles. QS regulation of EEA plays a critical role in hydrolysis of large marine aggregates. Heterotrophic bacteria associated with marine aggregates secrete several kinds of extracellular hydrolytic enzymes to degrade these large marine particles into small molecules consumed by free-living microbial cells. Carbon flux associated with marine snow aggregates in ocean plays an imperative role in regulation of earth's climate. The regulation of extracellular hydrolytic enzymes by QS system particularly produced by microbes associated with natural marine snow particles might have a great influence on a wide range of biological activities by degradation of large marine aggregates with a pronounced impact particularly on carbon cycle.

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Statement of conflict of interest

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